

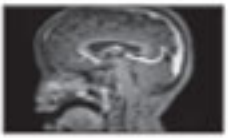

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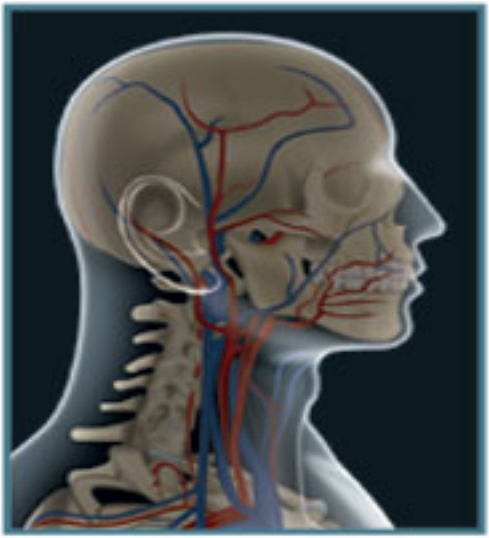

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# PEDIATRIC OTOLARYNGOLOGY

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# PEDIATRIC OTOLARYNGOLOGY

## Vol. 6


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***Dedicated to***

*Dr Robert T Sataloff*
*without whose tireless enthusiasm and*
*endless determination this textbook*
*would never have materialized…*

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# Foreword

*Sataloff's Comprehensive Textbook of Otolaryngology: Head and Neck Surgery* is a component of the most extensive compilation of information in otolaryngology—head and neck surgery to date. The six volumes of the comprehensive textbook are part of a 12-volume, encyclopedic compendium that also includes a six-volume set of detailed, extensively illustrated atlases of otolaryngologic surgical techniques. The vision for the *Comprehensive Textbook* was realized with the invaluable, expert collaboration of eight world-class volume editors. Chapter authors include many of the most prominent otolaryngologists in the world, and coverage of each subspecialty is extensive, detailed and scholarly.

Anil K Lalwani, MD edited the volume on otology/neurotology/skull base surgery. Like all six of the volumes in the *Comprehensive Textbook*, the otology/neurotology/skull base surgery volume is designed not only as part of the multivolume book, but also to stand alone or in combination with the atlas of otological surgery. Dr Lalwani's volume covers anatomy and physiology of hearing and balance, temporal bone radiology, medical and surgical treatment of common and rare disorders of the ear and related structures, occupational hearing loss, aural rehabilitation, cochlear and brainstem implantation, disorders of the facial nerve, and other topics. Each chapter is not only replete with the latest scientific information, but also accessible and practical for clinicians.

The rhinology/allergy and immunology volume by Marvin P Fried and Abtin Tabaee is the most elegant and inclusive book on the topic to date. Drs Fried and Tabaee start with a history of rhinology beginning in ancient times. The chapters on evolution of the nose and sinuses, embryology, sinonasal anatomy and physiology, and rhinological assessment are exceptional. The volume includes discussions of virtually all sinonasal disorders and allergy, including not only traditional medical and surgical therapy but also complementary and integrative medicine. The information is state-of-the-art.

Anthony P Sclafani's volume on facial plastic and reconstructive surgery is unique in its thoroughness and practicality. The volume covers skin anatomy and physiology, principles of wound healing, physiology of grafts and flaps, lasers in facial plastic surgery, aesthetic analysis of the face and other basic topics. There are extensive discussions on essentially all problems and procedures in facial plastic and reconstructive surgery contributed by many of the most respected experts in the field. The volume includes not only cosmetic and reconstructive surgery, but also information on diagnosis and treatment of facial trauma.

The volume on laryngology edited by Dr Michael S Benninger incorporates the most current information on virtually every aspect of laryngology. The authors constitute a who's who of world experts in voice and swallowing. After extensive and practical discussions of science and genetics, the volume reviews diagnosis and treatment (traditional and complementary) of laryngological disorders. Chapters on laser physics and use, voice therapy, laryngeal dystonia, cough, vocal aging and many other topics provide invaluable "pearls" for clinicians. The volume also includes extensive discussion of surgery for airway disorders, office-based laryngeal surgery, laryngeal transplantation and other topics.

For the volume on head and neck surgery, Drs Patrick J Gullane and David P Goldstein have recruited an extraordinary group of contributors who have compiled the latest information on molecular biology of head and neck cancer, principles of radiation, immunobiology, medical oncology, common and rare head and neck malignancies, endocrine neoplasms, lymphoma, deep neck space infections and other maladies. The surgical discussions are thorough and richly illustrated, and they include definitive discussions of free flap surgery, facial transplantation and other subjects.

Dr Christopher J Hartnick's vision for the volume on pediatric otolaryngology was expansive, elegantly scholarly and invaluable clinically. The volume begins with information on embryology, anatomy, genetics, syndromes and other complex topics. Dr Hartnick's contributors include basic discussions of otolaryngologic examination in a pediatric patient, imaging, hearing screening and aural rehabilitation, and diagnosis and treatment of diseases of the ear, nose, larynx, oral cavity, neck and airway. Congenital, syndromic and acquired disorders are covered in detail, as are special, particularly vexing problems such as chronic cough in pediatric patients, breathing and obstructive sleep apnea in children, pediatric voice disorders, and many other subjects. This volume will be invaluable to any otolaryngologist who treats children.

All of us who have been involved with the creation of the six-volume *Sataloff's Comprehensive Textbook of Otolaryngology: Head and Neck Surgery* and its companion six-volume set of surgical atlases hope and believe that our colleagues will find this new offering to be not only the most extensive and convenient compilation of information in our field, but also the most clinically practical and up-to-date resource in otolaryngology. We are indebted to Mr Jitendar P Vij (Group Chairman) and Mr Ankit Vij (Group President) of M/s Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, India, for their commitment to this project, and for their promise to keep this work available not only online but also in print. We are indebted also to the many otolaryngologists who have contributed to this work not only by editing volumes and writing chapters, but also by asking questions that inspired many of us to seek the answers found on these pages. We also thank especially the great academic otolaryngologists who trained us and inspired us to spend our nights, weekends and vacations writing chapters and books. We hope that our colleagues and their patients find this book useful.

**Robert T Sataloff** MD DMA FACS
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# Preface

This book represents an enormous amount of hard work and the collective wisdom of a large swath of our Pediatric Otolaryngology community. I challenged the authors to be current, to be clinical, and to provide not only the background required to understand the chapter's topic, but also some sense of best practice and, when possible, evidence-based treatment algorithms. All "written" textbooks are of necessity beginning to become dated the moment they are published, as more recent articles and literature come out. Yet this textbook, I hope, should give the reader some sense of the framework underlying today's as well as tomorrow's knowledge of the underpinnings that are used to understand the clinical problems, particular issues in management that arise, and how they are handled.

I hope you enjoy and learn!

**Christopher J Hartnick** MD

# Acknowledgments

The editor would like to thank Joseph Rusko, Marco Ulloa, Carol Rogers Field, Bridget Meyer, Thomas Gibbons and the rest of the Jaypee Brothers team. Without their perseverance and hard work, this volume would not have been possible. Special thanks are offered to the authors, who have shared their expertise and experience in order to improve the care of the Pediatric Otolaryngology patients.

I would also like to thank Mr Jitendar P Vij (Group Chairman), Mr Ankit Vij (Group President), Ms Chetna Malhotra Vohra (Associate Director), Mr Umar Rashid (Development Editor) and Production team of Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, India.

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## Section 1: Pediatric Otology

# SECTION 1

# Pediatric Otology

CHAPTER

# Embryology of the Facial Nerve and Related Structures

1

***Robert Thayer Sataloff***

## INTRODUCTION

Facial nerve embryology is discussed in detail by Sataloff and Sataloff.[1] This chapter is a brief overview of material presented in that book. This chapter is also modified in part from an article on this topic, with permission.[2] In studying the embryology of the facial nerve, it is helpful to keep in mind the final structure toward which development progresses. In the adult, the motor nucleus of the facial nerve (VIIIth cranial nerve) is located deep in the reticular formation of the caudal portion of the pons. The axons leave the motor nucleus and extend dorsally and medially, cranially, and superficially. They bend around the abducens nucleus to form the first genu of the facial nerve. The fibers then course deep through the pons and exit from the central nervous system between the olive and the inferior cerebellar peduncle. At this point, the axons join to form the motor root. The sensory root (nervus intermedius) consists of central processes of neurons located in the geniculate ganglion and axons of parasympathetic neurons from the superior salivatory nucleus. The nervus intermedius enters the central nervous system at the pontocerebellar groove lateral to the motor root and synapses with neurons in the upper part of the solitary tract of the medulla oblongata. The facial nerve and nervus intermedius course with the vestibuloacoustic nerve from the brainstem and enter the internal auditory canal (Fig. 1.1). For approximately 20% of its course, the nervus intermedius is fused with the VIIIth cranial nerve.[3]

At the point where the facial nerve enters the middle ear, it bends a second time at the geniculate ganglion (the second genu) and courses horizontally through the middle ear. It then curves (the pyramidal bend) to course vertically through the mastoid bone and exits at the stylomastoid foramen (Fig. 1.2). The nerve is ordinarily surrounded by a bony sheath called the fallopian canal. Several branches are given off during the intrapetrosal course. The facial nerve spreads extratemporally to innervate the facial musculature (Figs. 1.3A and B).

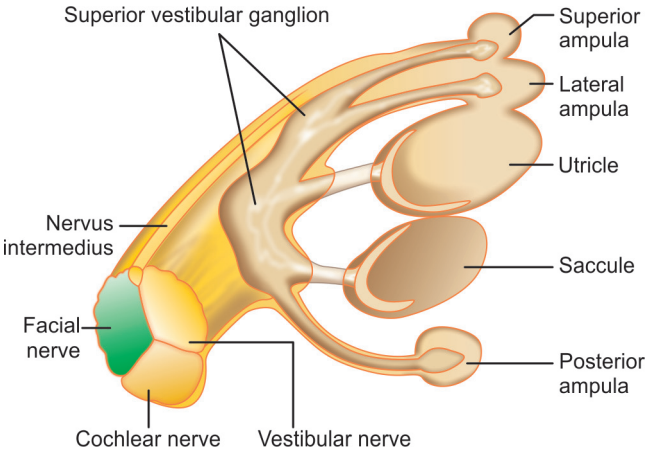



**Fig. 1.1:** The usual relationships of the 7th and 8th cranial nerves as they enter the internal auditory canal and temporal bone.

Medially to laterally, the facial nerve branches include 11 structures of note (Fig. 1.4):

1. Communications in the internal auditory canal with the VIIIth cranial nerve
2. The greater superficial petrosal nerve, which supplies taste fibers to the palatal mucosa, preganglionic parasympathetic axons to the pterygopalatine ganglion,

The figures in this chapter originally appeared as part of Chapters 3 and 4: Embryology and Anomalies of the Facial Nerve by Sataloff RT and Sataloff JB. Philadelphia, Jaypee Medical Inc., 2014.

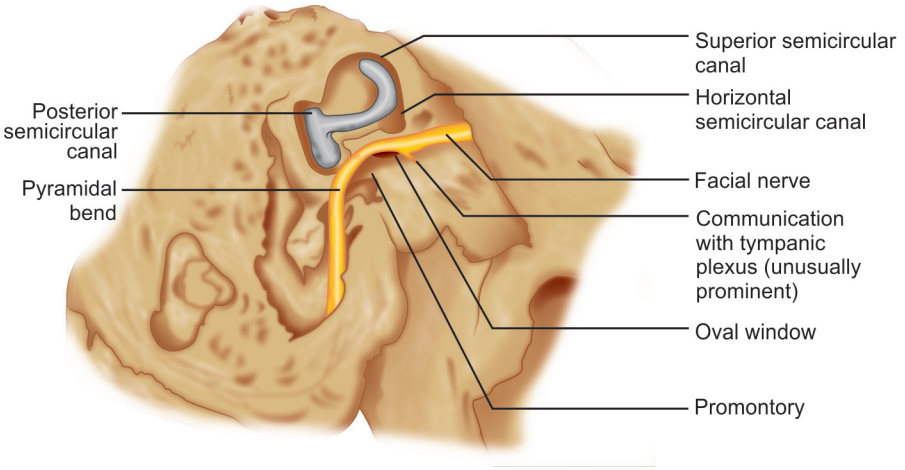
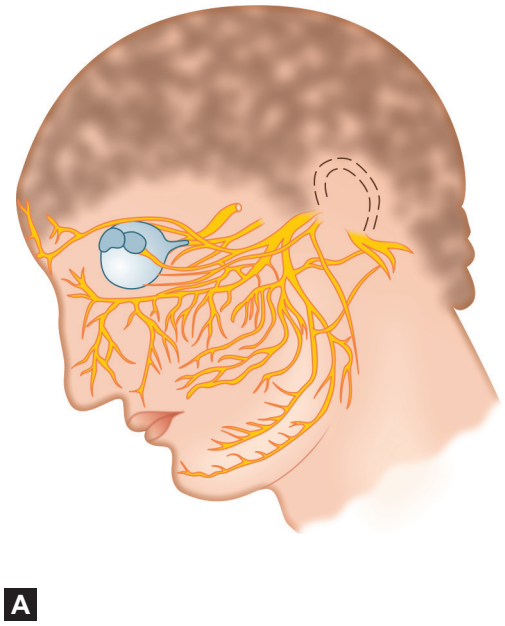
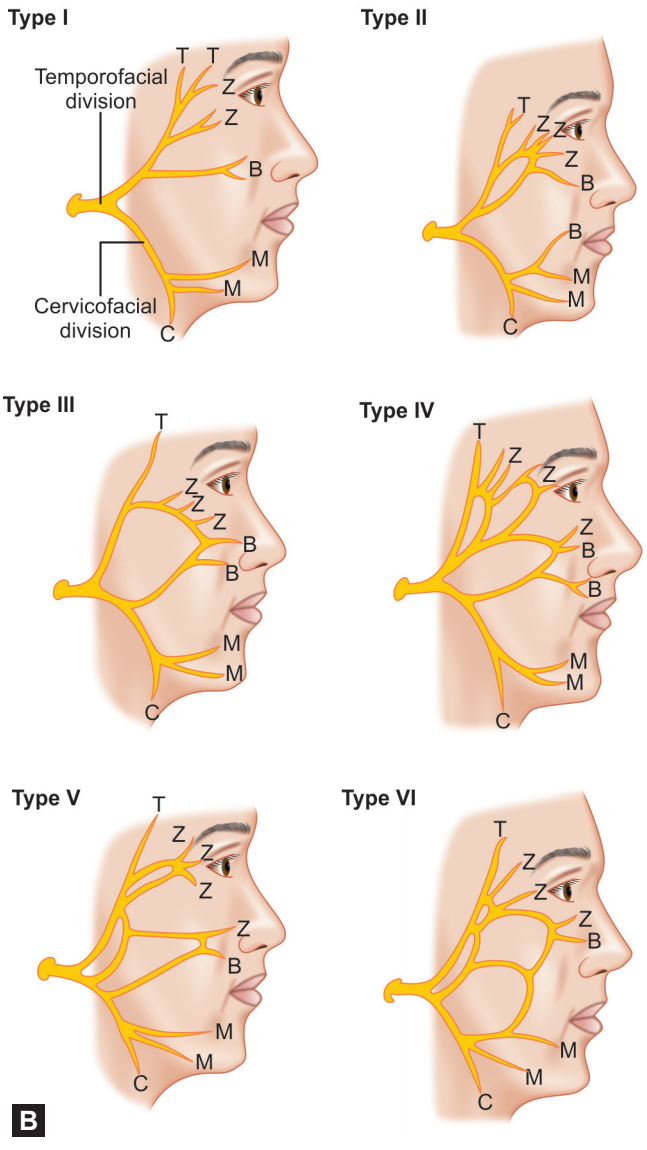



**Fig. 1.2:** The relationship of the facial nerve in its horizontal and vertical portions to other temporal bone landmarks.




**Figs. 1.3A and B:** (A) The distribution of the facial nerve to muscles of the face after the nerve has exited from the stylomastoid foramen. The extratemporal anatomy of the facial nerve is variable. (B) Common patterns of branching of the extracranial portion of the facial nerve. Type I is seen in 20% of cases; Type II, in 37.5%; Type III in 20%; Type IV, in 15%; Type V, in 15%; and Type VI, in 2.5%, according to Coker and Fisch. (T: Temporal branch; Z: Zygomatic branch; B: Buccal branch; M: Marginal mandibular branch; C: Cervical branch).

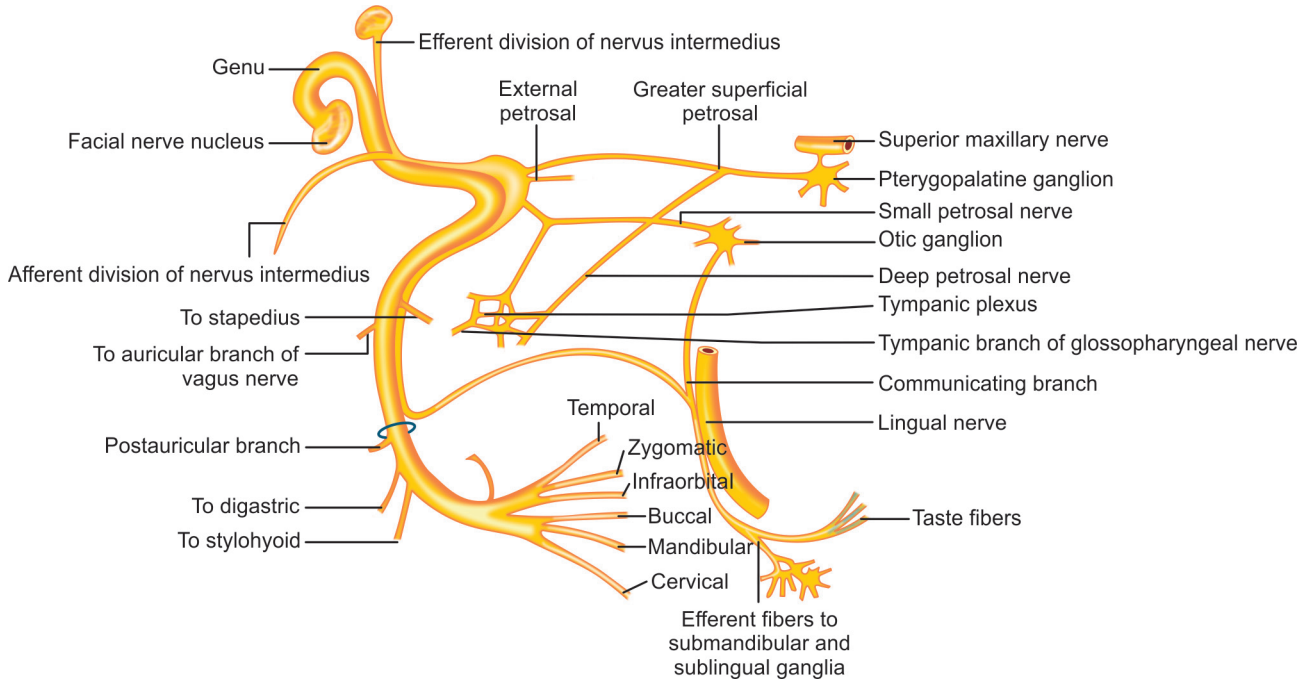



**Fig. 1.4:** Branches of the facial nerve.

and postganglionic axons to the lacrimal glands, nasal glands, and palatine mucosal glands; it also communicates with the lesser petrosal nerve[3]

3. The nerve to the stapedius muscle
4. The chorda tympani nerve, which supplies taste fibers to the anterior two-thirds of the tongue, preganglionic parasympathetic fibers to the submandibular gland, and postganglionic fibers to the submandibular and sublingual glands
5. The posterior auricular branch, which innervates the auricularis posterior, the cranially oriented muscles of the auricle, and the occipital muscles-communicates with the greater auricular nerve, the auricular branch of the vagus nerve, and the lesser occipital nerve[3]
6. The branch to the posterior belly of the digastrics muscle
7. The branch to the stylohyoid muscle
8. The temporal branch that supplies the lateral intrinsic muscle of the auricle, the anterior and superior auricular muscles, the frontalis, the orbicularis oculi, and the corrugator
9. The buccal branch, which innervates the procerus, the zygomaticus major and minor, the levator labii superioris, the levator anguli oris, nasal muscles, the buccinator, and the orbicularis oris
10. The marginal mandibular branch to the risorius muscle and the muscles of the lower lip and chin
11. The cervical branch to the platysma; there are interconnections between the facial nerve and primarily the sensory nerves, including the trigeminal, glossopharyngeal, vagus, and cervical nerves.[4]

The intracranial portion of the facial nerve is supplied by the anterior inferior cerebellar artery. The intrapetrosal portion is supplied by the superficial petrosal branch of the middle meningeal artery and the stylomastoid branch of the posterior auricular artery. The extracranial portion is supplied by the stylomastoid, posterior auricular, superficial temporal, and transverse facial arteries. The anastomosis between the intratemporal branches usually occurs in the upper one-third of the vertical portion.

## EMBRYOLOGY OF THE INTRACRANIAL PORTION OF THE FACIAL NERVE

This discussion includes information on the development of only the extracranial portions of the facial nerve. We encourage the reader to consult other literature for a brief review of the embryology of the intracranial portions,[1] and for new information on differentiation and migration of the facial nerve.[1] This information is very helpful for the purpose of orientation.

*Fertilization through week 4*: The facioacoustic primordium appears during the third week of life. It is attached

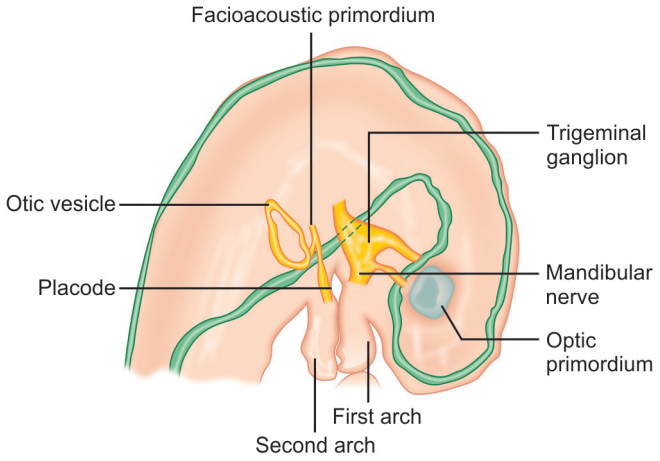



**Fig. 1.5:** A 4.2-mm embryo approximately 3-and-a-half weeks old. The region of the epibranchial placode of the second arch is labeled.

to the metencephalon just rostral to the otic vesicle. It becomes more superficial and rostral as it proceeds ventrally, and it ends adjacent to the deep surface of the epibranchial placode on the dorsal and caudal aspect of the first branchial groove. There are no branches, and the geniculate ganglion is not yet present (Fig. 1.5). During the fourth week, by the time the embryo reaches 4.8 mm in length, the facial nerve splits into two parts. The chorda tympani nerve comes off rostrally, courses ventrally to the first pharyngeal pouch, and enters the mandibular arch. The caudal main trunk terminates in mesenchyme. By the time the embryo reaches 6 mm in length, the nerve approaches the epibranchial placode, and large, dark nuclei mark the development of the geniculate ganglion.[5]

*Weeks 5 and 6*: By the time the embryo has reached 7 mm in length, near the beginning of the fifth week, the mesenchymal concentrations that form the cephalic muscles can be seen in association with their nerves (Fig. 1.6).[6] The geniculate ganglion and the nervus intermedius also appear, although the latter is not always visible as a separate nerve until approximately the seventh week.[5] The geniculate ganglion is lateral and rostral to the VIIIth nerve ganglion. The greater superficial petrosal nerve is present. The chorda tympani is large and enters the mandibular arch; it terminates near a branch of the mandibular nerve, which will become the lingual nerve. By the middle of the fifth week (embryo length: 10 mm), the facial nerve gives off small branches to the posterior digastric premuscle mass. The nerve terminates in mesenchyme.

In the 8-mm embryo, all the cranial nerves except the olfactory and optic nerves are recognizable. All the cranial nerves that carry sensory fibers have prominent ganglia near their points of connection with the brain. These include cranial nerves V, VII, VIII, IX, and X. The primarily efferent cranial nerves (III, IV, VI, and XII) have no external ganglia. In the 8- to 14-mm period, the posterior auricular nerve appears near the chorda tympani. Complete separation of the facial and acoustic nerves is apparent, and a discrete nervus intermedius develops.

By the time the embryo reaches 14 mm in length, the geniculate ganglion and the greater superficial petrosal nerve are well defined, and the epibranchial placode has disappeared. The greater superficial petrosal nerve courses ventrally and rostrally to the lateral aspect of the developing internal carotid artery. Here it joins the deep petrosal nerve and continues as the nerve of the pterygoid canal. It terminates in a group of cells that will become the pterygopalatine ganglion. At 16–17 mm (middle of the sixth week), a branch arises from the ventral aspect of the geniculate ganglion and courses caudally and dorsally to the glossopharyngeal ganglion. The chorda tympani and lingual nerves end near the developing submandibular ganglion. Some facial nerve fibers terminate in the mandibular arch superficially and caudally.

During this period, the superficial layer of the mesenchymal lamina of the second arch spreads to establish four laminae (Fig. 1.7):

1. The occipital lamina (the occipitalis, auricularis posterior, and transverse nuchae muscles)
2. The cervical lamina (the cervical part of the platysma)
3. The mandibular lamina (the depressor labii inferioris, the mentalis, the risorius, the depressor anguli oris, the inferior part of the orbicularis oris, and perhaps the buccinator and the levator anguli oris)
4. The temporal lamina, which spreads during the latter part of this stage (the auricularis superior).

When the embryo is between 10 and 18 mm in length, the deep layer of the second mesenchymal lamina differentiates into the posterior digastrics complex (the stapedius muscle, the posterior belly of the digastric muscle, the digastric tendon, and the stylohyoid muscle).

*Weeks 7 through 9*: By the beginning of the seventh week, the embryo has reached approximately 18 mm in length (Fig. 1.8). The nervus intermedius, which is smaller than the motor root of the facial nerve, passes into the brainstem between the acoustic nerve and the facial nerve motor root. The chorda tympani and lingual nerves unite proximal to the submandibular tympani nerves, and it divides into cranial and caudal branches.

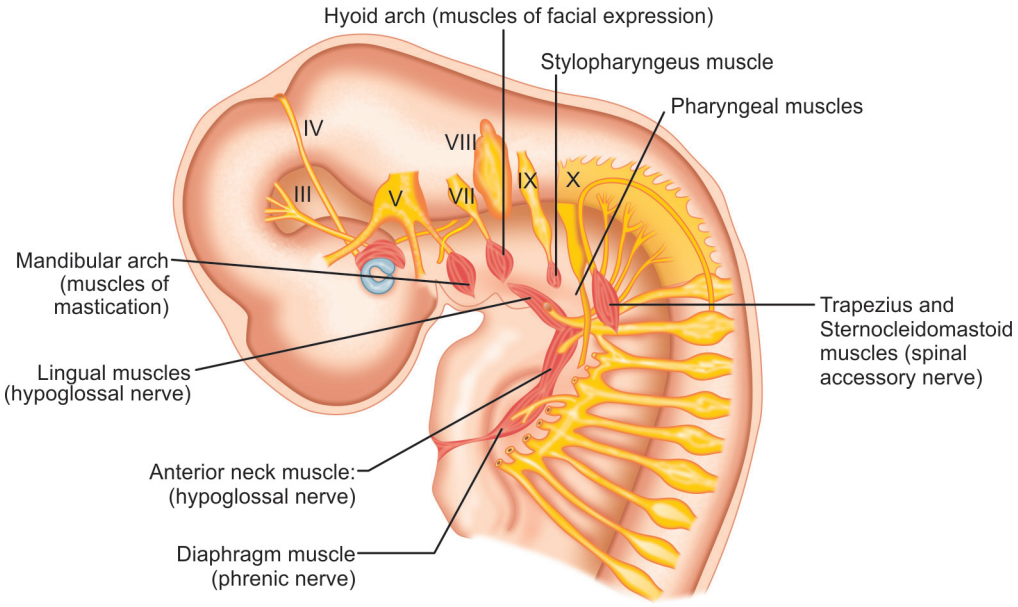



**Fig. 1.6:** Diagram of a 4-and-a-half-week-old embryo illustrating the mesenchymal concentrations that will give rise to the cephalic muscles, as well as the cranial nerves associated with them.

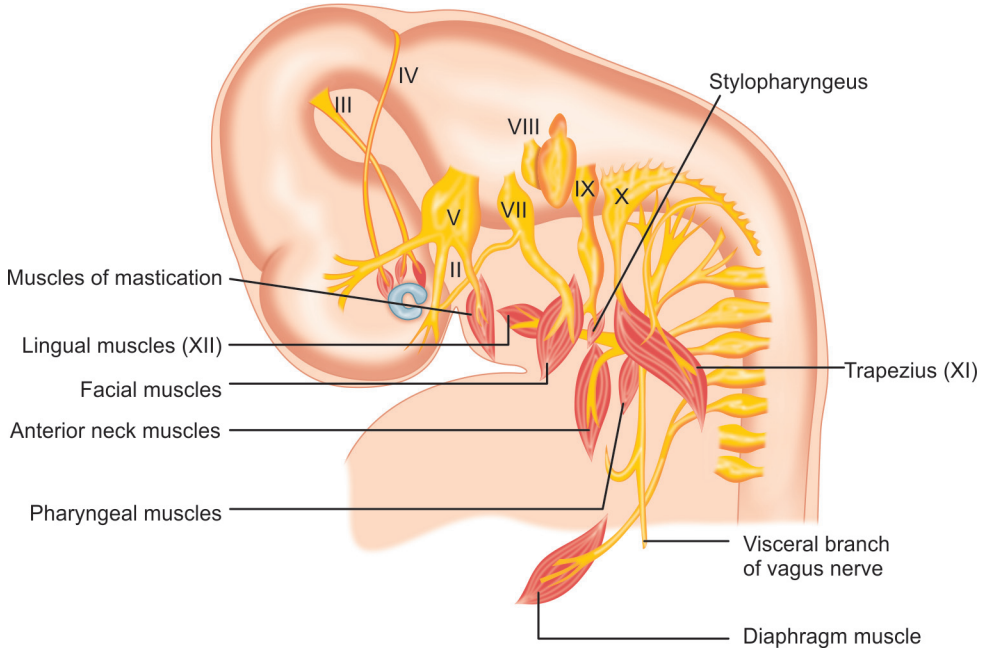



**Fig. 1.7:** A 6-week-old embryo (11 mm) showing further development of the premuscle masses of the cephalic muscles.

The caudal branches communicate with branches of cervical nerves C2 and C3. Several branches are visible in the peripheral portion of the VIIth nerve. The most caudal branches communicate with nerves from the second and third cervical ganglia in a plexus in the second arch. Another portion courses ventrally, terminating deep to the platysma myoblastic lamina. The rest of the branches course to the angle of the mouth, or caudally and superiorly into the mandibular arch. By the time the embryo is 19 mm long, some caudal branches have reached the infraorbital

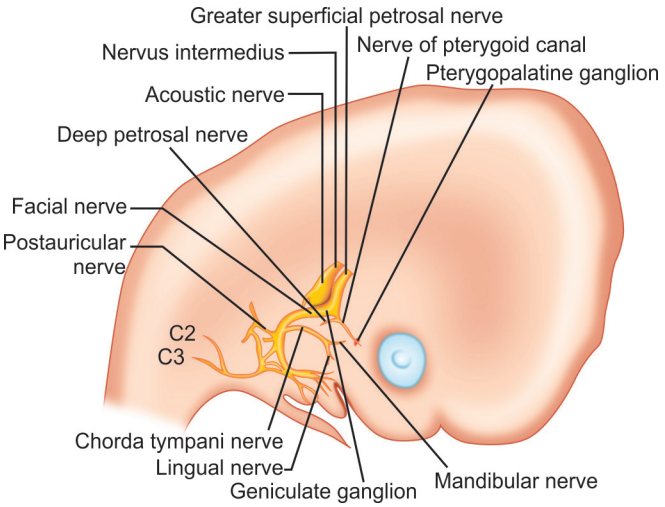



**Fig. 1.8:** The relationship between the facial nerve and parotid primordium at approximately 7 weeks (18 mm).

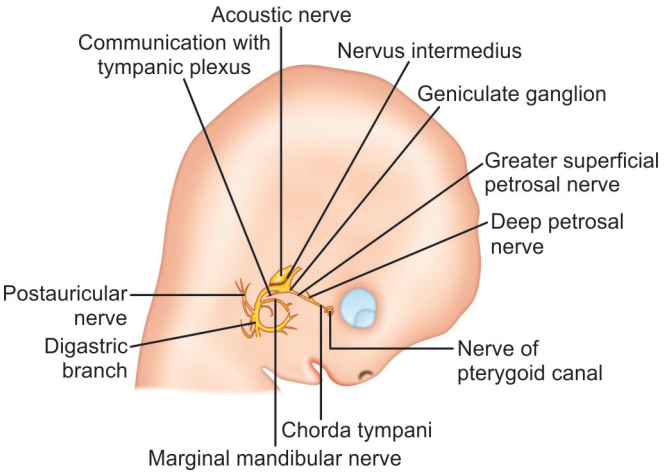



**Fig. 1.9:** By the middle of the 7th week (22 mm), additional branching has occurred. However, the structures of the facial nerve are still anterior with respect to the external auditory meatus, which is in the process of migration from its original location low on the developing embryo.

rim. All of the peripheral branches lie close to the deep surfaces of the myoblastic laminae that will form the facial muscles. Very few fibers course dorsally. The zygomatic and temporal nerves will arise higher in the facial nerve. At 18 mm, the parotid bud is rostral and unbranched, appearing as an evagination from the lateral oral cavity area.

In the 22-mm embryo (middle of the seventh week), the posterior belly of the digastric muscle and the stapedius and stylohyoid muscles are developing (Fig. 1.9). A branch from the geniculate ganglion near the greater superficial petrosal nerve, which developed earlier, is reduced to a communication as the tympanic plexus and the lesser petrosal nerve develop from the IXth cranial nerve. The interanastomoses of the peripheral branches of the facial nerve are visible as separations of the main trunk. A small nerve branch approaches the buccal region superficial to the parotid bud.

Separations between nerve branches increase considerably in number and size by the end of the seventh week (26 mm). By then, the branch to the stapedius muscle is visible. This branch was probably present earlier, but it can be seen only after the branch separates from the main trunk.[5] Peripheral branches course cranially to become the zygomatic and temporal divisions. The buccal, mandibular, and cervical divisions constitute approximately one-half of the peripheral branches. All the peripheral divisions can be identified, but the temporal branches have not yet reached the frontal region. Anastomoses are well established with the infraorbital, buccal, auriculotemporal, and mental branches of the trigeminal nerve. Previously established communications with branches of C2 and C3 have become communications with the greater auricular and transverse cervical nerves. A combined marginal mandibular-cervical branch appears between the time the embryo grows from 20 to 45 mm (seventh through the middle of the eighth week).

The superficial layer of the second-arch mesenchyme differentiates into two more laminae:[4]

1. Infraorbital (zygomaticus major and minor, the levator labii superioris alaeque nasi, the superior part of the orbicularis oris, and possibly the compressor naris, the depressor septi nasi, the orbicularis oculi, the frontalis, the corrugator supercilii, and the procerus)
2. Occipital platysma.

Between 24 and 26 mm, the zygomaticus major, the depressor anguli oris, and the buccinators appear. Between 27 and 45 mm, the frontalis and zygomaticus minor appear. The branch that connects the VIIth cranial nerve with the lesser petrosal nerve (from cranial nerve IX) apparently carries small myelinated fibers that contain interspersed autonomic fibers from the auricular branch of cranial nerve X. In addition, by 26 mm the embryo develops first-order ductules of the parotid primordium, which lies next to the masseter muscle, and several branches of the facial nerve course superficial to it.[7] By 27 mm, second-order ductules appear. At this time, the buccal, marginal mandibular, and cervical nerve branches approach the parotid primordium. By 32 mm (eighth week), third-order

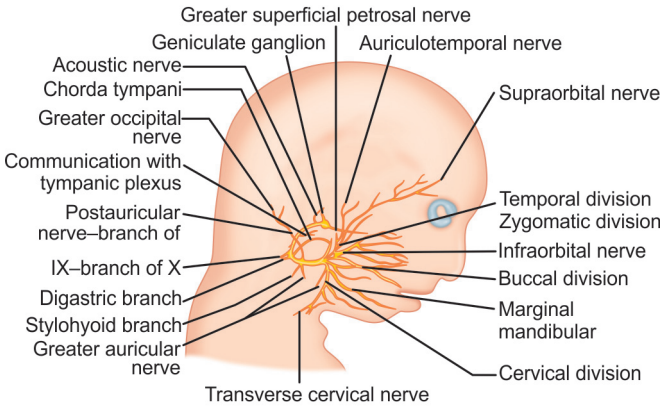



**Fig. 1.10:** During the 11th week (80 mm), extensive branching including communications with other cranial nerves can be seen. The vertical portion of the facial nerve is still anterior with respect to the external auditory meatus (not shown). The vertical portion and main trunk could be injured easily during surgery if the relationship of the auricle to the facial nerve were assumed to be that of an adult.

ductules are present, and the primordium has entered the parotid space. In the 37-mm embryo (8.5 weeks), fourth-order parotid ductules are present, and buccal nerve branches are superficial to the main duct. The temporal, zygomatic, and upper buccal branches are superficial on the parotid primordium. The lower buccal, mandibular, and cervical branches are deeper. The postauricular nerve goes to the occipital region, and a branch to the dorsal aspect of the auricle is present. Although there are no branches to the fused eyelids, yet a branch from the temporal division approaches the frontal region.

During the eighth week, a sulcus develops around the facial nerve, blood vessels, and stapedius muscle on the posterior aspect of the cartilaginous otic capsule. The sulcus is the beginning of the fallopian canal. The orbicularis oris, the levator anguli oris, and the orbicularis oculi also appear at approximately 37 mm.[4] During the ninth week (50–60 mm), the auricularis anterior, the corrugator supercilii, the occipital and mandibular platysma, and the levator labii superioris appear. Also about the ninth week, the laterohyale fuses to the otic capsule to form part of the anterior wall of the fallopian canal and the pyramidal eminence. The segment of the anterior wall of the fallopian canal distal to the laterohyale is formed by Reichert's cartilage. The cranial nerves move closer to their adult relationships.

*Weeks 10 through 15*: During the 58- to 80-mm period, extensive branching of the peripheral portions of the facial nerve occurs (Fig. 1.10). Some divisions reach the midline. Extensive communication with branches of the trigeminal nerve occurs in the perioral and infra-orbital regions. Communications exist between the nervus intermedius and both the VIIIth nerve and the motor root of the VIIth nerve. Despite extensive branching, the facial nerve begins its vertical course while still in the middle ear, and its relationship to the external and middle ear structures is far more anterior than it is in the adult.

During the 11th week (80 mm), the external petrosal nerve arises from the facial nerve distal to the geniculate ganglion and courses with a branch of the middle meningeal artery. Branches also arise from the facial nerve between the stapedius and the chorda tympani nerves. Together, these branches and branches of cranial nerves IX and X provide sensory innervation to the external auditory canal. Branches to the lateral aspects of the eyelids are present, and communication with the zygomaticotemporal nerve has begun to develop. Previous communications with branches of cervical nerves have now become communications with the lesser occipital and transverse cervical nerves. The horizontal portion of the facial nerve can be distinctly seen adjacent to the developing otic capsule. The nasal muscles arc also differentiated at approximately 80 mm.

The relationship between the facial nerve and the parotid gland is about the same at 12 weeks as it was at 7 weeks. However, by the time the embryo reaches 80 mm in length, complicated connections between the superficial and deep portions of the parotid primordium can be seen.[7] At 14 or 15 weeks, the geniculate ganglion is fully developed, and facial nerve relationships to middle ear structures have developed more fully. During this growth period, the facial nerve has remained in association with the mesenchyme, which differentiates into the labyrinth and the mastoid.

*Week 16 through birth*: Between 16 and 20 weeks, the facial nerve, arterioles, venules, and the stapedius muscle lie in a sulcus on the canalicular wall. The mesenchyme in which they are surrounded is differentiating into connective tissue. Although the middle ear continues to enlarge, the facial nerve remains more superficial and anterior in relation to the auricle than it is in the adult. All definitive communications of the facial nerve are established by the 16th week (146 mm).

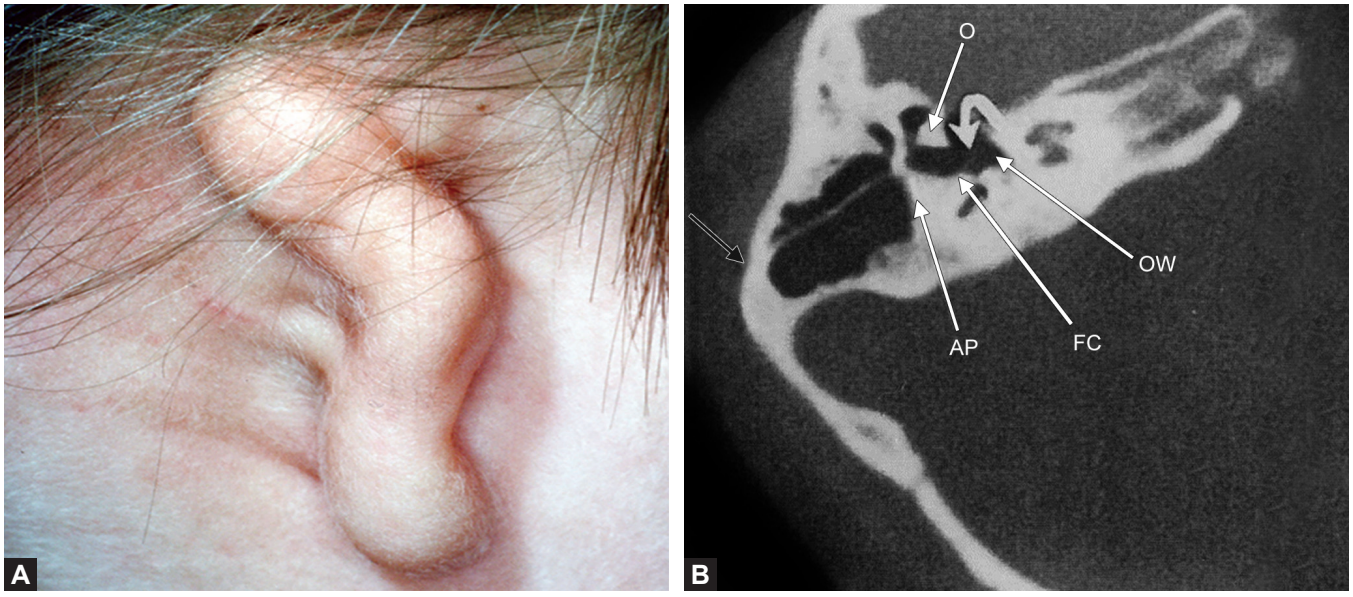
By 26 weeks, ossification has progressed, and growth of the outer layer of periosteal bone has resulted in a partial closure of the sulcus, forming the fallopian

canal. The deep surface is completed first. By 35 weeks, a bony ridge has formed that separates the geniculate ganglion from the epitympanic rim. Late in fetal life, the facial canal in most cases is closed by bone except in the anterior cranial portion, where it remains open to form the facial hiatus along the floor of the middle cranial fossa. However, at least 25% of fallopian canals have this dehiscence; the most common site is adjacent to the oval window.[8] The length of the dehiscence ranges from 0.5 mm to the length of the entire horizontal portion, but they are usually no larger than about 2 × 3 mm. This most common area of dehiscence is probably secondary to the failure of ossification after the stapedial artery (which passes through this area) resorbs prior to birth. The incidence of dehiscence has been reported to be as high as 55%.[9]

By the time of birth, the facial nerve has developed into a complex but generally consistent structure. In an interesting study of the mandibular ramus in stillborns by Sammarco et al.,[10] the authors found that in 17 of 24 facial halves, some or all of the mandibular branches of the cervical facial ramus were below the angle of the mandible. Moreover, 19 of the 24 specimens had 2 or 3 mandibular branches. All mandibular branches were above the mandibular margin as they crossed the facial artery. In 16 specimens, all branches passed over the facial artery; in the other 8, they straddled the facial artery. At birth, the anatomy of the facial nerve approximates that of the adult with the exception of the nerve's exit through the superficially Iocated stylomastoid foramen. Adult anatomy occurs in this region as the mastoid tip develops postnatally.

## CLINICAL APPLICATIONS

In patients with congenital malformations, it is usually possible to determine the fetal age at which developmental arrest occurred. This information allows the surgeon to predict the anatomy of the deformed ear and facial nerve on the basis of their usual embryologic development at the time when the arrest occurred. Moreover, if anomalies are also present in other organ systems (e.g., the kidney), they often reflect interference with development at the same time in fetal life. Hence, when a congenital anomaly of any portion of the ear can be observed visually, radiologically, or surgically, and if the clinician recognizes the fetal age at which normal development ceased in that portion, the physician should be able to predict the position of the facial nerve. If the facial nerve is anomalous, its development is most likely to have been interrupted at the same time that the development of the ear was interrupted, particularly in the case of a middle ear malformation.




**Figs. 1.11A and B:** (A) Appearance of the auricle prior to otoplasty. (B) CT scan revealing absence of the external auditory canal (open arrow), an atresia plate (AP) at the level where the tympanic membrane should be, and the ossicular mass (O). The dehiscent horizontal portion of the facial nerve (curved white arrow) is seen coursing above the oval window (OW) and entering the fallopian canal (FC) at the pyramidal bend.

To test the validity of such predictions, surgical observations were made of 13 ears in 11 patients with congenital malformations.[1,11] We describe one of these cases to illustrate the clinical application of information about facial nerve embryology. The patient was a 6-year-old boy who had been followed by the author since the age of 3 months. His auricle was malformed, and only portions of the helix, lobule, and tragus were recognizable. Computed tomography (CT) revealed the absence of the external auditory canal and the presence of a small middle ear space with an ossicular mass (Figs. 1.11A and B).

The appearance of the auricle placed the time that the defect occurred at approximately the eighth week, and the relationship of the nerve to middle ear structures had been fairly well established. However, because the middle ear was small and not fully formed, it and the vertical portion of the facial nerve appeared to the surgeon to be anteriorly and inferiorly displaced. Moreover, the vertical portion of the nerve coursed more superficially than it does in the normal adult. The nerve coursed through the region where the surgeon planned to construct the new ear canal.

After creating an ear canal and removing the atresia plate, the surgeon identified the moderately malformed ossicles. The malleus and incus were fused, but an incudomallear joint was seen. The stapes was fully developed but immobile, although it was easily manipulated. The horizontal portion of the facial nerve was in a normal position relative to the stapes, but dehiscent. As predicted, the facial nerve and middle ear were more anterior than is the case in a fully developed ear, and the facial nerve coursed anteriorly and laterally more abruptly distal to the pyramidal bend.

If adult relationships are used to gauge the position of the middle ear with respect to the position of the external meatus, the surgeon would enter the middle ear and mastoid region posterior to the vertical portion of the facial nerve and hypoplastic middle ear. Exploration from the point of entry forward would put the facial nerve at risk of injury, especially in light of its abruptly superficial course from the pyramidal bend to the stylomastoid foramen. However, with an understanding of the embryology of the facial nerve, its location can be predicted easily and accurately.

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CHAPTER

# Update on Inner Ear Regeneration/Basic Science Update

2

*Judith S Kempfle, Albert SB Edge*

## INTRODUCTION

About 12–17% of the American population has some degree of hearing loss[1] (http://www.nidcd.nih.gov/health/statistics/Pages/quick.aspx), including sensorineural hearing loss (SNHL) in 2–3 out of 1,000 newborns and conductive hearing loss or malformations that affect the outer and middle ear in a large number of children.

To date, no cure is available for SNHL. Sensory cells that are lost do not regenerate. Hearing aids only provide limited effectiveness to children with severe SNHL, and even for children who qualify for a hearing aid, only one fifth of them are compliant.[2] Cochlear implants are effective in children with severe SNHL. Despite all technical advances, however, hearing quality remains far below natural hearing, which complicates speech and language development in these children.

The most common causes of SNHL are the loss of sensory cells and loss or degeneration of spiral ganglion neurons (SGN). Genetic causes are prevalent in children, but a variety of environmental causes also cause loss of sensory cells and neurons. These include noise, trauma, ototoxic drugs, and toxins. Once the cells are lost, the inner ear undergoes rapid degenerative changes and does not recover.[3,4] In order to restore hearing for children before or during speech development, regenerative approaches for hearing loss, in particular medical treatments, would be highly attractive.

## THE FLIPSIDE OF EVOLUTION

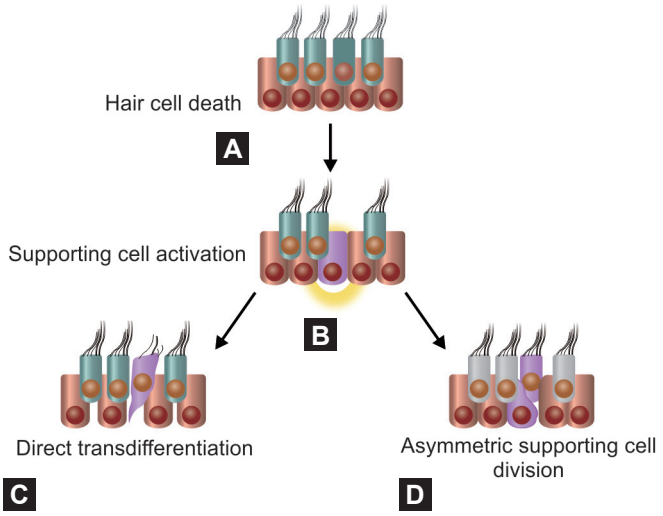
Lower vertebrates replace hair cells after damage. In the vestibular organs of fish and amphibians, vestibular hair cells are produced throughout life, and the overall number of hair cells increases with the growth of the animal.[5,6] In birds, the number of hair cells does not increase while the animal is growing; rather, new cells replace old, dying cells.[7,8] This suggests that the sensory epithelia of lower vertebrates contain mitotic cells that act like stem cells. Mammals, however, do not retain a capacity to replace hair cells after damage. The inability to replace hair cells has been hypothesized to be due to the complex anatomy of the inner ear, as well as a more rigid cytoskeletal structure in the mammal compared to other animals, which prevents proliferation and cell cycle re-entry.[9–11]

Destruction of hair cells with a laser in the lateral line of zebra fish led to massive regeneration of hair cells.[12,13] Similar regeneration was shown in the auditory and vestibular organs of birds after ototoxic or noise damage.[11,14] In all cases, supporting cells are the source of hair cells.

Replacement and regeneration of hair cells occurs by asymmetric division or by direct transdifferentiation. In asymmetric division, a pre-existing supporting cell divides and forms a new hair cell and supporting cell. In direct transdifferentiation, a supporting cell dedifferentiates to redifferentiate into a hair cell, and the replacement takes place without proliferation, thereby depleting the supporting cell pool (Figs. 2.1A to D).[15,16]

## INNER EAR DEVELOPMENT

The developmental processes that lead from the very early stages of inner ear development to the final mature cochlear and vestibular structures could provide clues for designing strategies to regenerate cells of the inner ear.




**Figs. 2.1A to D:** *Hair cell replacement in birds and fish*. After death and disappearance of hair cells in birds or amphibians, supporting cells become activated (A) and turn into hair cells (B) through direct transdifferentiation of one supporting cell into one hair cell (C) or asymmetric division of one supporting cell to become both a hair cell and a supporting cell (D).

In regeneration strategies, the developmental mechanisms can be employed to (re)activate genes and pathways that specify cell fates and cause differentiation into inner ear cell types from stem cells.

Thickening of ectoderm on each side of the neural tube forms the otic placodes and constitutes the first stage in inner ear development. The surrounding tissues help to induce this process with secreted fibroblast growth factors (FGFs). The otic placode invaginates and ultimately closes and forms the otocyst. With continuing development, inner ear morphogenesis separates the otocyst into vestibular and cochlear regions.

The Wnt pathway directs the ectoderm toward an otic fate and specifies the size of the otic placode.[16a] The FGF family is comprised of a number of different secreted growth factors and their receptors (FGFRs). Fibroblast growth factors influence proliferation and differentiation in many tissues. In the inner ear, FGFs are present during otocyst formation and are active in prosensory domain induction to specify neural progenitors and a subset of supporting cells (pillar cells).[17–19] The Notch pathway is active during the earliest induction stages of otic development, and Notch and the members of its canonical pathway are differentially expressed in the otocyst. Recent research suggests that Notch can induce the prosensory stages of development,[20] and pharmacological inhibition of Notch before induction of the prosensory domain leads to a loss of the prosensory area.[21] BMP4 belongs to the TGFb family and is a secreted molecule that plays a key role in signaling for prosensory domain specification, acting along a concentration gradient after release from the surrounding tissues.[22,23] BMP4 is also secreted later in development within the cochlea at different concentration levels, with high concentrations leading to neural cell formation and low concentrations leading to sensory cell formation[24] (J. Kempfle et al., in preparation).

## SENSORY CELL FATE

Precursor cells undergo divisions to give rise to the vestibular and cochlear organs, and this is followed by specification of hair cell, supporting cell, and neuronal fate. Mechanisms that are active during this stage are important for regeneration strategies, since they can be employed to differentiate stem cells into the mature cell types of the inner ear.

Notch, as noted above, is not only important for establishing the prosensory domain but also active during cell fate specification, acting to prevent supporting cells from differentiating into hair cells by a process of lateral inhibition.[25] Notch signaling also cooperates with the Wnt pathway to determine cell fates in the inner ear.[26] The Wnt/β-catenin pathway, which as mentioned above plays a role in development of the prosensory region, also participates in specification of cell fate like the Notch pathway.[27] Other pathways, such as BMP and sonic hedgehog (Shh) also continue to be active during cell fate specification (Fig. 2.2). It is assumed that a gradient of BMP4 exists in the inner ear along a neural-abneural axis, with high concentrations of BMP4 supporting neuron formation and low levels favoring hair cell development.[24] Similarly, high concentrations of Shh also seem to lead to neural differentiation in the ear.[27a]

A key gene for hair cell formation is Atoh1 (Math1). Atoh1 is part of the family of basic helix-loop-helix (bHLH) transcription factors, and it is necessary for hair cell fate but not required for sensory epithelium formation.[28–30]

Overexpression of Atoh1 leads to additional hair cells in nonsensory areas of the inner ear,[28] whereas lack of Atoh1 leads to dying cochlear progenitors and missing hair cells with deafness.[31,32,32a] Stimulating the expression of Atoh1 would be one way to effectively regenerate hair cells but the signaling that leads to its expression remains poorly understood. Interaction of Pax2 and Sox2, and Sox2 with Six1/Eya1, has been implicated in Atoh1 stimulation and the promotion of hair cell fate[33] (J. Kempfle et al., in preparation).

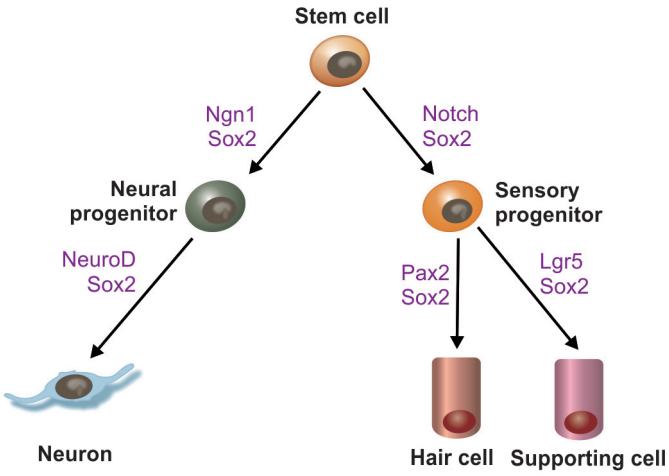



**Fig. 2.2:** *Inner ear cell fate specification*. Development and differentiation of inner ear stem cells follow a stepwise differentiation process from one common stem cell (yellow) into neural (green) or sensory progenitors (orange). Neural progenitors develop into neurons (blue). Sensory progenitors give rise to hair cells (brown) and supporting cells (fuchsia). Crucial factors needed for cell fate and differentiation at the various steps are written in purple.

The fate of cochlear progenitors is directed toward neurons by neurogenin1 (Ngn1). In neural progenitors, Sox2 and Ngn1 interact and activate each other, which leads to subsequent activation of NeuroD and development of SGN.[34] Sox2 is a key gene in conferring stem cell characteristics[35] and plays a critical role in specifying hair cell and supporting cell fate in neural and sensory progenitors. Loss of Sox2 early in development leads to complete loss of the sensory epithelium without development of hair cells and supporting cells.[36] Sox2 is important in continued maintenance of supporting cell fate and while it is ultimately turned off in hair cells and neurons, it continues to be expressed in supporting cells throughout life. Continuous high Sox2 expression may be responsible for the regenerative capacity of supporting cells. Lgr5, which is active in the Wnt pathway, marks a subset of Sox2-positive supporting cells, which have been shown to proliferate and transdifferentiate into hair cells in vivo.[37]

## THE PHANTOM "INNER EAR STEM CELL"

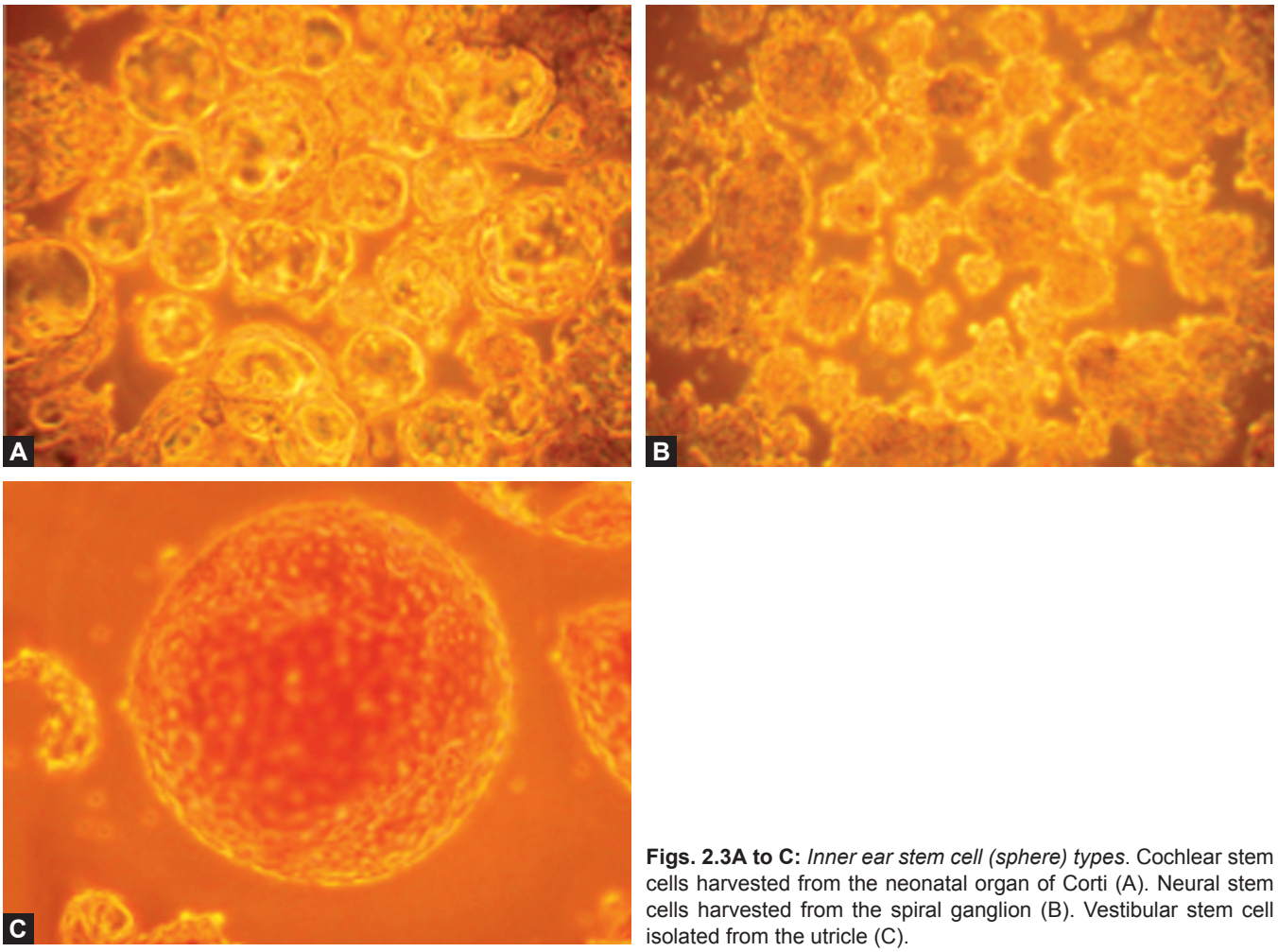
Totipotent embryonic stem cells can renew indefinitely and differentiate into cell types representative of all three germ layers (ectoderm, mesoderm, and endoderm). In postnatal tissue, stem cells with a more limited potential retain the ability to renew their cells and regenerate after damage. These stem cells are pluripotent or multipotent; they remain active throughout life in several organ systems such as blood, skin, and intestine where they replace damaged or old cells. Some organs contain dormant or facultative stem cells with the ability to differentiate after damage to the tissue, whereas other organs such as the brain and heart, which do not repair themselves, may show some turnover, albeit at a very slow rate. Stem cell niches have been discovered in the subventricular zone as well as in the hippocampus in the brain, where neurons are turned over even in the adult.[38] Dormant stem cells may be present in the inner ear.

Tissue isolation from the organ of Corti of neonatal mice has demonstrated cells in the sensory epithelium that undergo cell division, similar to neurospheres harvested from neural tissue, with the addition of growth factors.[39,39a] These spheres can proliferate and increase in number and purity with passage, similar to neural stem cells.[40–42] Expanded spheres contain cells that can give rise to all the cell types of the inner ear similar to the differentiation from the otic placode (Figs. 2.2 and 2.3).

When inner ear stem cells proliferate, they express the stem cell marker, Sox2, similar to the otic placode. Once plated and differentiating, early inner ear progenitors express progenitor markers, Sox2, Musashi, nestin, islet1, and Pax2, similar to those in the brain at early developmental stages. After several days in vitro, the cells downregulate early progenitor markers and begin to express mature neural or sensory cell genes.[41,42]

In the neonatal mouse, such stem cells can be harvested from the organ of Corti (cochlear stem cells), the spiral ganglion (neural stem cells), and the utricle (vestibular stem cells). All of these stem cell types, when put into culture, can proliferate and differentiate into the cell types found in the inner ear. However, only the utricle retains its proliferative qualities until adulthood, whereas the cochlear and neural stem cells lose that ability shortly after birth. Postmortem studies on inner ear tissue of the adult human show limited sphere formation from vestibular cells in vitro, and no sphere formation from cochlear tissue.[43]

In vitro studies have shown that the inner ear harbors cells that may be induced to regenerate hair cells. However, until very recently, it was not known which cells in the ear had stem cell-like capacities. Even though they are not mitotically active in the living animal, supporting cells harvested from neonatal tissue and placed in culture divide and differentiate into hair cells.[16] A subset of supporting cells with stem cell-like properties was




**Figs. 2.3A to C:** *Inner ear stem cell (sphere) types*. Cochlear stem cells harvested from the neonatal organ of Corti (A). Neural stem cells harvested from the spiral ganglion (B). Vestibular stem cell isolated from the utricle (C).

identified: third row of Deiters' cells, inner pillar, and inner border cells, as well as the greater epithelial ridge. All those cells expressed Lgr5, which labels stem cells in the intestine and enhances Wnt pathway activity.[37,44] Wnt signaling plays a role in proliferation and cell fate specification in embryonic development and in stem cells and is highly conserved throughout species. Studies in mice have shown that postnatal supporting cells that express Lgr5 are Wnt dependent.[37] These cells behave as hair cell precursors[37] and are induced to proliferate by Wnt signaling. Future regeneration strategies could thus target supporting cells that express Lgr5.

## REGENERATION AND ITS PITFALLS

Hearing loss or vestibular dysfunctions can be caused by a variety of different factors, such as noise damage, ototoxic substances, trauma, hereditary defects, infectious disease, or aging. Hair cells or neurons that are destroyed cannot be regenerated and treatment options for damage of the inner ear are limited to hearing aids and cochlear implants. Vestibular implants have been tested in monkeys with promising results.[45] Electronic aids could be combined with biologic agents to improve regeneration. A number of recent advances have been made in applying biological methods to repair the inner ear: drug treatment to activate endogenous stem cell-like cells (supporting cells) to proliferate and replace damaged cells,[46] gene transfer with viruses to express genes in remaining cells of the inner ear that lead to regeneration or transdifferentiation into the needed target cell type,[47] and transplantation of stem cells that can replace damaged cells[48,49] (Fig. 2.4).

One obstacle to regenerating the inner ear is the anatomically complex structure of the cochlea and the vestibule. The cells lack planar alignment and are difficult to reach in different compartments of the inner ear.[50] Application of

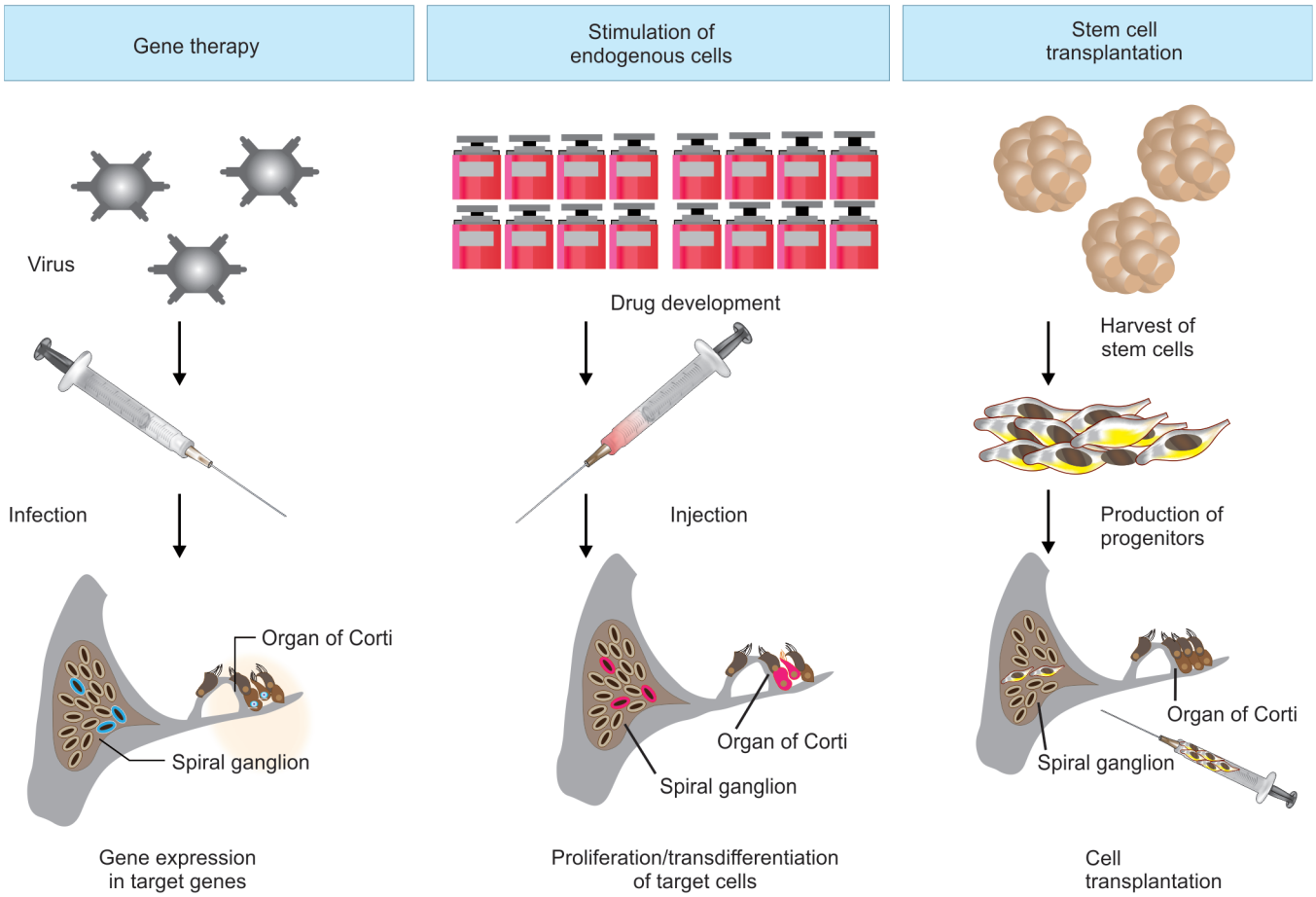



**Fig. 2.4:** *Inner ear regeneration strategies*. Gene therapy: Infection of inner ear target cells with a virus carrying an effector gene. Overexpression of the gene in target cells leads to proliferation or to a switch in cell fate. Stimulation of endogenous cells: Drugs with regenerative potential are injected into the middle ear or directly into the inner ear and activate endogenous cells with regenerative potential (e.g. supporting cells) to transdifferentiate or proliferate. Stem cell transplantation: Embryonic stem cells are differentiated into inner ear cell types and directly injected into the inner ear to replace lost cells.

agents via the middle ear only allows direct access to the basal turn of the cochlea; the spiral ganglion or vestibular organs will require more difficult surgical routes.[51,52]

## TREATMENT WITH GROWTH FACTORS AND DRUGS

Different approaches to the treatment of inner ear dysfunction have involved delivery of protein and small molecule drugs. Neurotrophin-3 (NT3) and brain-derived neurotrophic factor (BDNF) are secreted in the inner ear from early embryonic development to adulthood and are important for survival of neurons. NT3 and BDNF are broadly expressed in the otocyst and are later restricted to the sensory epithelium and then the organ of Corti.[53,54] The receptors for NT3 and BDNF, tyrosine receptor kinases C and B (TrkC, TrkB), respectively, are expressed in the spiral ganglion.[55] Mouse mutants lacking BNDF or NT3 show >80% reduction of SGN.[56,57] Exogenous application of NT3 or BDNF or their agonists in animal models in vitro and in vivo lead to increased neurite outgrowth and survival of SGN.[58–61] The performance of cochlear implants can be compromised by neuronal damage.[62] New techniques including gene therapy with continuous expression of BDNF or NT3 slow release of neurotrophins from polymers, or delivery via coated or filled cochlear implants are under development as a way to treat loss of neurons that result from implantation of the device.[62,63]

In addition to factors used in combination with implants, drug treatment of the inner ear could activate regeneration from cochlear cells after hair cell or neuronal damage. Inhibition of Notch in inner ear stem cells increased hair

cell numbers in vitro.[64] γ-Secretase inhibitors interfere with lateral inhibition and upregulate Atoh1 by inhibiting the Notch pathway. After noise induced hearing loss, application of γ-secretase inhibitors, drugs developed for treatment of Alzheimer's, led to regeneration of hair cells with partial recovery of hearing.[46] Lineage tracing identified supporting cells as the origin of the newly formed hair cells. These supporting cells turned into hair cells by direct transdifferentiation.[46]

## GENE THERAPY

Gene therapy relies on transfer of genes into the cochlea. Different vehicles target different cell types.[50] Viruses, plasmids, and lipid packages have been used as shuttle systems for genes into inner ear cells.[65] Various viral vectors were tried: adenovirus (AV) has a fast onset of gene expression after infection but may only be expressed transiently, as it does not integrate into the host DNA and may cause severe immune reaction or toxicity.[66] Genes delivered with an adeno-associated virus (AAV) are expressed over years in the genome, and AAV has demonstrated very little toxicity, but packaging capacity in AAV is limited. AAV carrying the RPE65 gene was recently applied to the retina in patients with Leber's congenital amaurosis, resulting in partial restoration of vision.[67,68] Lentivirus is less commonly used due to the immune response and toxicity in the inner ear, although it permits long-term expression with high packaging capacity.[50,69] Only 3.4% of clinical trials for gene therapy have used lentivirus (http://www.abedia.com/wiley/vectors.php).

Injection of adenoviruses carrying the Atoh1 gene into the inner ear of rats and mature guinea pigs in vitro and in vivo resulted in additional immature hair cells in nonsensory areas in the ear.[28,69a] Furthermore, adult deafened guinea pigs recovered some hearing after gene therapy with Atoh1-AV, which entered nonsensory cells.[47]

Downregulation of gene expression might be a therapeutic option in the treatment of hereditary diseases. Small interfering RNAs (siRNA), which interfere with transcription by binding to complementary sequences, and microRNAs, which inhibit messenger RNAs at the post-transcriptional level, can be used to inhibit gene expression.[70–72] siRNA to NOX3, which is responsible for production of superoxides in the ear, has been successfully delivered to the inner ear via the transtympanic approach, and inhibition of NOX3 effectively protected hair cells and neurons after ototoxic insult.[73]

## TRANSPLANTATION OF CELLS

Another option for future therapies that would provide alternatives to cochlear implants as well as auditory brainstem implants[74] would be cell replacement in an attempt to rebuild the ear. For such a therapy to be successful requires derivation of fully functional sensory neurons from stem cells, transplantation of neurons into the inner ear, and migration or neurite outgrowth to reinnervate both the cochlea and cochlear nucleus. With a cocktail of secreted neurotrophic molecules, including BMP4, embryonic stem cells were pushed toward a sensory neuron cell fate in vitro.[51] Identification of sensory neuron progenitors indicated that the differentiation programs that define this fate had been at least partially reproduced. After damage of the original neurons in an animal model, transplantation of the neural progenitors was then tested in the animal models by injection into the nerve trunk.[48,51,74a] Progenitors survived in vivo and grew processes that contacted hair cells. They also grew processes into the cochlear nucleus. The formation of functional synapses between hair cell and neurons and in the cochlear nucleus remains to be established, but partial recovery of hearing in the transplanted animal model of auditory neuropathy has been observed.[74a,74b]

## DELIVERY ROUTES TO THE INNER EAR

The major concerns for delivering biological agents into the inner ear are the efficiency and side effects. Several possible means of access for a surgical opening include the round window, accessed from the middle ear though the tympanic membrane, a direct cochleostomy through the lateral wall of the cochlea, and a canalostomy into a semicircular canal. However, the risks of damage to the inner ear including a perilymphatic fistula are high. The least invasive delivery method would be systemic application, as no surgical intervention would be needed, but the efficiency of this approach may be limited by the blood–cochlear barrier[75] and the concentrations of reagents needed to achieve sufficient levels in the perilymph and endolymph may cause systemic side effects such as systemic inflammatory response syndrome (SIRS).[76]

The transtympanic approach provides a safe route for delivery of substances into the middle ear and is commonly used by otologists. To permeate the inner ear in sufficient quantity requires contact with the round window membrane. Large molecules are likely to require an extended time due to lower permeability of the membrane. Several trials have used gelfoam sponges or hyaluronic

acid to increase the time of contact with the round window membrane.[77,78,78a] Alternatively, partial digestion of the membrane with collagenase led to increased entrance of AAV viruses across the membrane into the inner ear. No severe systemic side effects have been reported with either method. Direct application into the inner ear would offer the highest treatment efficiency. Viruses injected into the perilymph can reach the endolymph and target cells.[79,80] Osmotic pumps have achieved long-term delivery.[78,81,82]

## CONCLUSION

Until the introduction of cochlear implant technology some 30 years ago, treatments that would address inner ear dysfunction seemed a remote possibility. Auditory research was a fairly neglected area, but improved understanding of the pathophysiology of SNHL and the discovery of hair cell regeneration in nonmammalian vertebrates provided hope that biological treatments for cellular repair might be possible. Emerging techniques in auditory research and microsurgery allowed for better understanding, but the technologies remain at an early stage of development. The vast improvements and new findings in inner ear research bring regeneration strategies closer, but have yet to enter clinical practice. Gene therapy, small molecules or growth factors, and cell therapy have great promise for both neural and hair cell replacement, but numerous challenges remain. The system is highly resistant to regeneration and the complex anatomy complicates surgical approaches.

Nonetheless, progress in basic inner ear research has been immense and the field is poised for translation of new knowledge into therapies. A mix of bioengineered devices, nanotechnology, and cell therapies is already a reality (e.g. in the cochlear implant), and there is reason for cautious optimism about new treatments for deafness.

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CHAPTER

# Impact of Evolution on Eustachian Tube Function and Otitis Media

3

***Charles D Bluestone, J Douglas Swarts, Jeffrey T Laitman***

Otitis media (OM) is a major health-care problem since it is the most frequent diagnosis made by health-care professionals who provide care for infants and children, and is not uncommonly encountered in adults. There is general agreement that the etiology and pathogenesis of middle-ear (ME) disease is multifactorial, but the consequences of human evolutionary history[1] for the presence and prevalence of OM have not been addressed until relatively recently. We have hypothesized that otitis media is most likely a disease that occurs only in humans and is unlikely to be present in other species in the wild.[2] Since hearing loss is associated with ME disease, if animals in the wild developed it they most likely would have been selected out by predation. Normal hearing is essential for survival in the wild.

We also posit that OM in humans is probably a consequence of human evolutionary history, i.e. a side effect of adaptations for bipedalism, the development of a large brain, and speech, producing changes in craniofacial skeleton that underlie the pathogenesis of this unique human disease. In this chapter, we describe these evolutionary events and how their consequences may impact management. Similarly, this evolutionary pathway may also contribute to the occurrence of rhinosinusitis in humans, which is also posited to be present only in humans, and is described in Chapter 27.

## BIPEDALISM, BIG BRAIN, AND BORN TOO SOON

Habitual bipedalism is one of the distinguishing features of hominids when compared with our predecessors, including our nonhuman primate ancestors (Fig. 3.1). Adaptations for bipedality are evident in one of our earliest ancestors, *Ardipithecus ramidus*, who lived > 4 million years ago.[3] There is no consensus on the evolutionary advantages of either walking and running on two legs or knuckle walking as in the great apes over quadrupedal locomotor patterns. But among the hypothesized advantages of bipedality are improved thermoregulation due

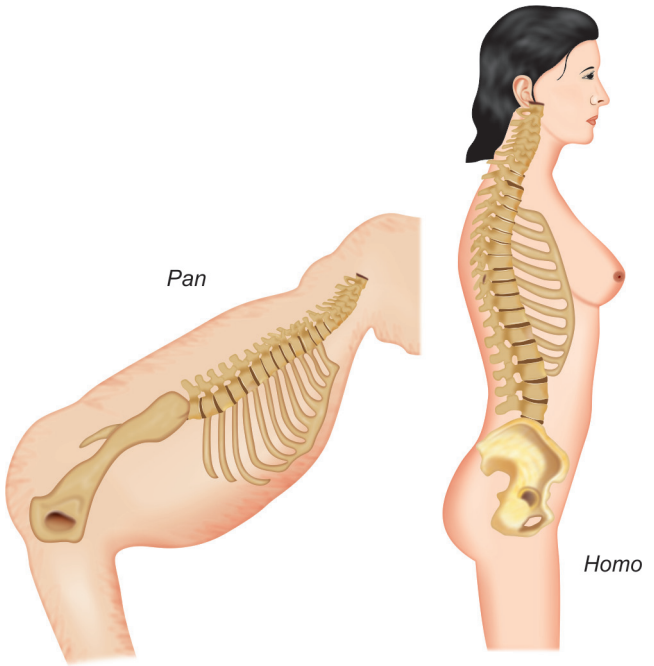



**Fig. 3.1:** Cartoon depicting the locomotive posture of the chimpanzee (*Pan troglodytes*) with that of the human (*Homo sapiens*). With permission from Bluestone and Swarts.[2]

to decreased exposure of the body to sun, ability to carry (including food and infants), the ability to see over the savannah for food and predators, and freeing of the hands, allowing tool- and weapon-making.

On the other hand, there are disadvantages to walking on two legs, such as disorders of the back and lower limb joints, both which are relatively common, but develop after reproductive age. But an even more significant disadvantage arising from bipedality is the constriction of the female pelvic outlet. The narrowing of the outlet is thought to arise as a consequence of the need for osseous support of the abdominal contents and changes that increase biomechanical efficiency in locomotion. For early hominids, these anatomical changes did not impair the delivery of newborns since their brains and bodies were small relative to their mother's size. However, during the subsequent 2 million years the hominid brain doubled in size, such a large increase that humans are born 12 months too early because of the constraints imposed by our big brain on passing through the narrowed pelvic outlet. This sequence of events is well known to anthropologists, as Martin[4] concluded, based on brain development, humans should have a 21 months' gestation period: 9 months in the uterus and 12 months outside the womb. This is illustrated in Figure 3.2 which depicts the relative sizes of the female bony pelvic birth canal to the size of the brain in the chimpanzee and human.[5] Delivery of human newborns through the birth canal is so tight that almost all pregnancies require birth attendants, a situation unique to humans. Anthropologists describe humans as being "secondarily altricial"; some higher mammals, including primates, are mature ("precocious") at birth, whereas others, such as dogs and cats, are "altricial", i.e. relatively helpless at birth. Humans should be precocious at birth but are not.

We previously described, in detail, the comparative anatomic and birthing differences between humans and our primate relatives, and the consequences of being "born too soon" for the ears, nose, and throat.[6] Among these consequences is that the Eustachian tube (ET) is too short and floppy during the first year of life. This structural and functional immaturity, in the context of an immature immune system, helps to explain the high incidence of acute OM in the first year of life, especially now that child day-care attendance exposes these highly susceptible babies to respiratory pathogens. A report from Norway finds recurrent ME infection more prevalent during the first 18 months of life in premature infants when compared with normal term babies. This difference was attributed to gestational age differences, not weight at birth[6]; thus, premature infants are "born way too soon". However, being born too soon does not explain why OM remains common throughout childhood and in some individuals into adulthood.

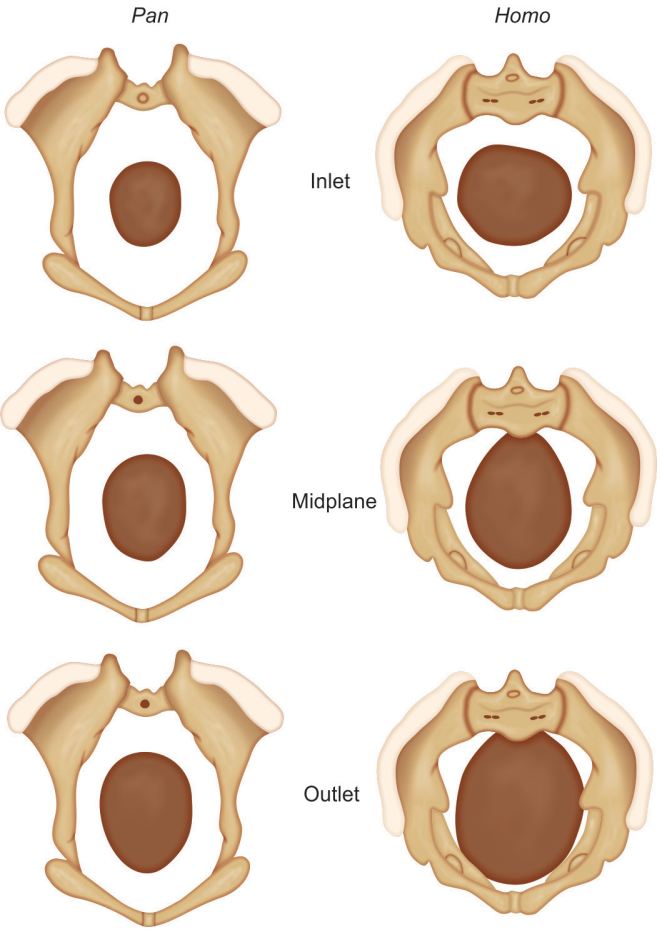
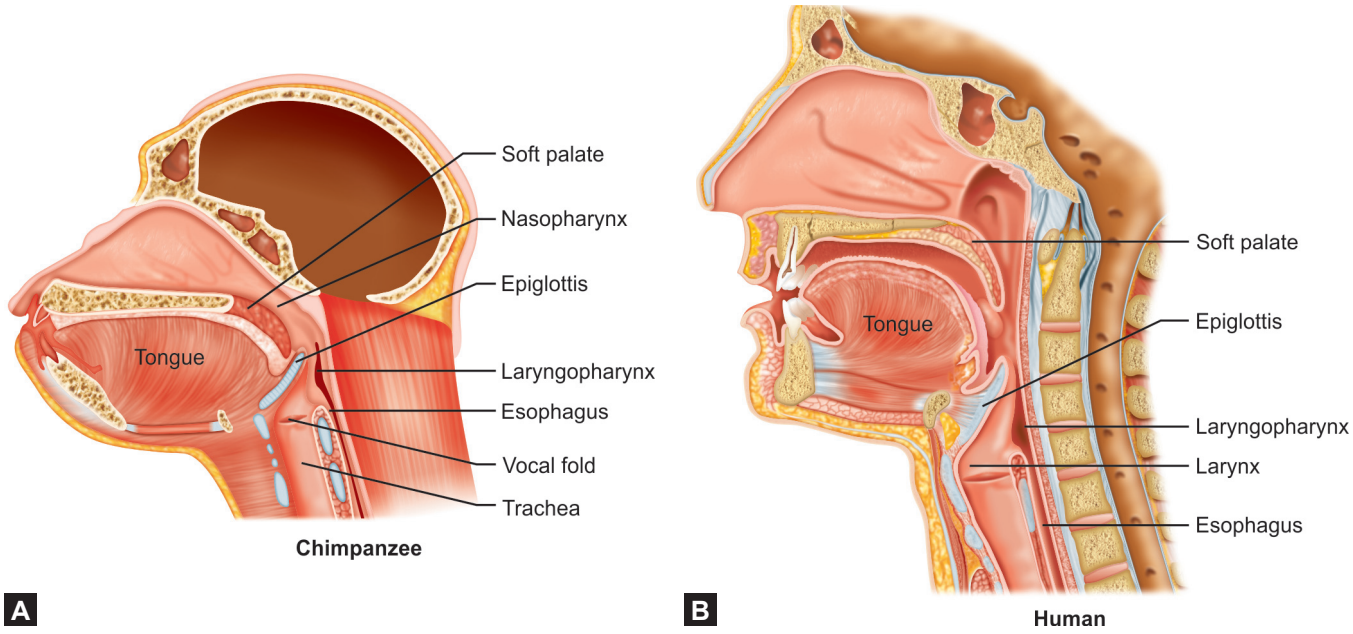



**Fig. 3.2:** Line drawing comparing the pelvic outlet with the brain size (shaded) of *Pan* (chimpanzee) to that of *Homo* (human) at birth. The brain of the chimpanzee easily fits in the relatively large pelvic outlet, but the human brain even at 9 months' gestation has an extremely tight fit. With permission from Bluestone and Swarts.[2]

## LOSS OF HUMAN PROGNATHISM

Another important difference of modern humans, when compared with our hominid ancestors and extant nonhuman primates, is facial flattening, or the loss of facial prognathism.[7] This is depicted in Figures 3.3A and B, a human-chimpanzee skull comparison that shows the reduction and repositioning of the maxillofacial complex in the human. Facial flattening, along with descent of the hyoid, contributed to shortening of the palate.[8] We have described these evolutionary adaptations in detail elsewhere.[9] So why have we lost our facial prognathism?


**Figs. 3.3A and B:** Comparison of the facial prognathism in skulls of the chimpanzee (A) and the facial flattening of the human (B).




**Figs. 3.4A and B:** Line drawing in the midsagittal plane comparing the chimpanzee and human showing the shorter palate, an oropharyngeal tongue, a narrower pharynx and a descended larynx (loss of "epiglottic—soft palate lock-up") in the human when compared with the chimpanzee.

## Adaptation for Speech

Another unique adaptation of *Homo sapiens* is that we are the only species that developed speech. During our evolution, in a short 40,000 years, our larynx descended, elongating the supralaryngeal vocal tract that enhanced speech[8] (Figs. 3.4A and B). This adaptation narrowed the pharyngeal airway and shortened the palate, which probably aids in the production of vowels and consonants, but also has consequences for the palatal muscles (described later).

## Cooking

Another possible explanation for our facial flattening is the cooking of food. As described by Wrangham,[10] the earliest evidence of cooking by hominids dates back about 1.8 million years to *Homo erectus*. He hypothesizes that cooking provided the necessary caloric density to meet the energy requirements of our rapidly growing brain. Cooking reduces the need for large masticatory forces releasing the selective pressures on the teeth and musculature, thus allowing a decrease in dental and craniofacial size, i.e.

a smaller maxilla and mandible, in comparison to other hominids. We consider this to be an attractive hypothesis to explain both the increase in human neonatal body and brain size and the loss of facial prognathism.[11]

## EUSTACHIAN TUBE FUNCTION RELATED TO ALTERED MORPHOLOGY OF THE PALATE

We have proposed that the loss of prognathism altered palatal morphology including the muscles of the palate involved in ET function, the tensor veli palatini, and levator veli palatini muscles. These muscles became less effective physiologically than in the nonhuman primate (*Macaca mulatta*).[2] When we compared the tubal function of monkeys and humans, monkey dilatory tubal function was consistently superior.[12] Humans have relatively poor active tubal function. The consequences of poorer tubal function becomes evident during activities that impose nonphysiologic stresses on the ET, such as flying in airplanes and scuba diving, activities in which equalizing ME negative pressure becomes problematic. In contrast, even the application of sudden large negative ME pressures in the monkey were easily equilibrated with a single swallow.

The relatively poor function of the human ET compared with that of the monkey is most likely due to differences in the anatomy of the paratubal muscles. Figure 3.5 is a cross section of the ET from a human temporal bone specimen showing a relatively slim tensor veli palatini muscle attached to the lateral lamina of the tubal cartilage and the relatively large belly of the levator veli palatini muscle as a rounded mass that abuts the inferior portion of the tubal lumen. Despite their genomic similarity and their use as a model for studies of ET physiology and pathophysiology and the pathogenesis of OM, rhesus monkey paratubal muscles are not identical to those of humans.[13] Comparison of the anatomy of these two muscles between the monkey and the human reveals two major differences: first, the monkey tensor veli palatini muscle is bulkier and attaches along the entire length of the cartilaginous ET, whereas in the human this muscle is less robust and only attaches to the midportion of the ET; and second, the belly of the levator palatini muscle is not as prominent and does not impinge on the inferior portion of the tubal lumen in the monkey in contrast to the human condition (Figs. 3.6A and B).

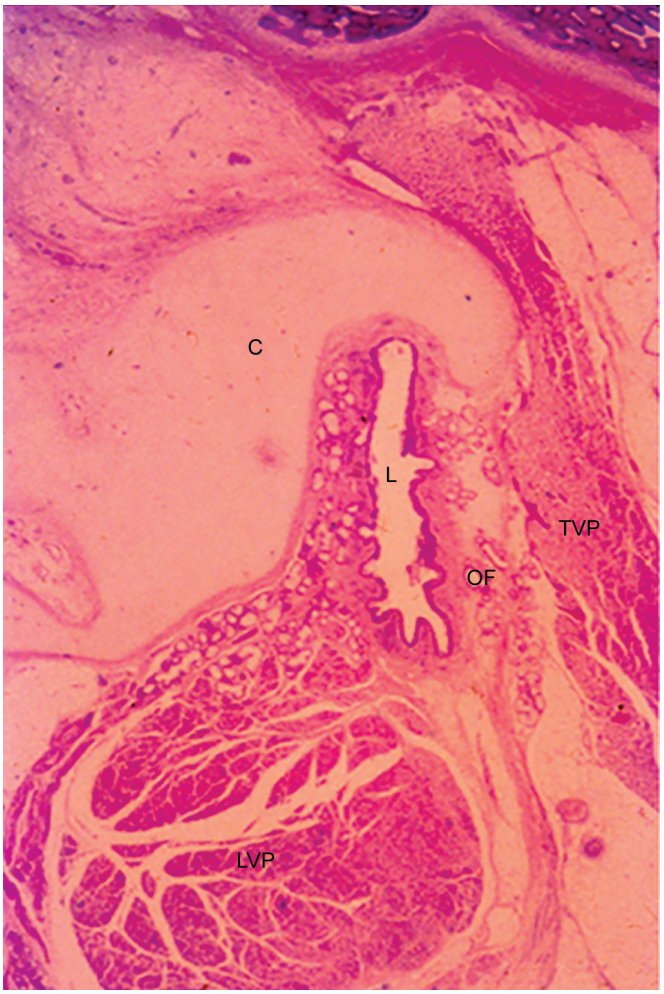
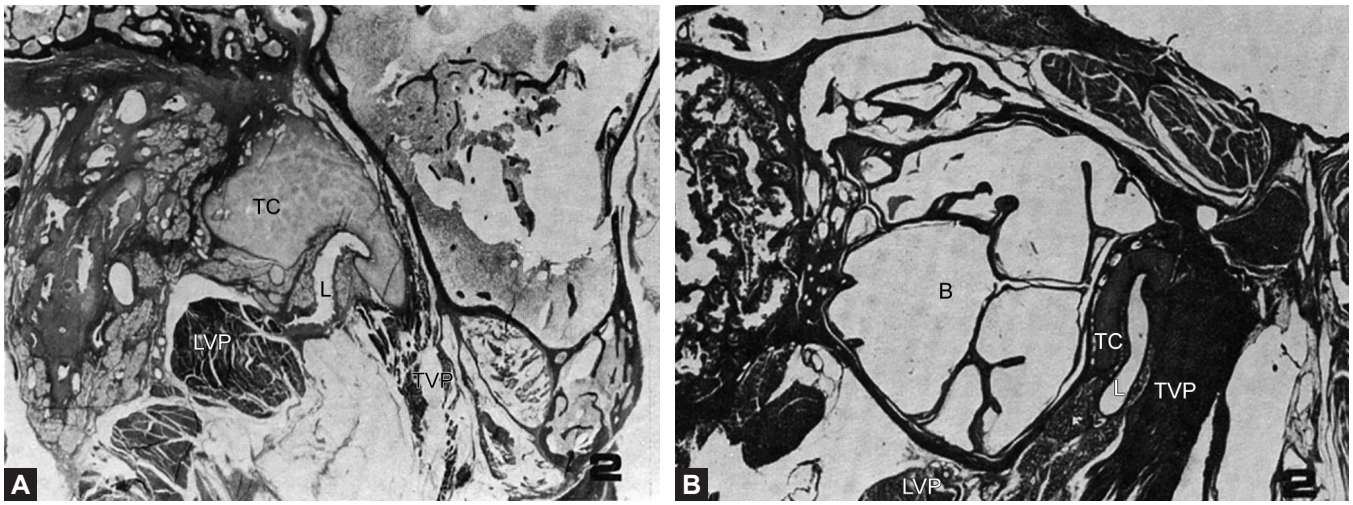



**Fig. 3.5:** Cross section through the midcartilaginous portion of the left human Eustachian tube, showing the robust rounded belly of the levator veli palatini muscle abutting the inferior portion of the tubal lumen, and the rather thin slip of the attachment of the tensor veli palatini to the lateral lamina of the tube. (C: Tubal cartilage; L: Tubal lumen; LVP: Levator veli palatini muscle; OF: Ostmann's fat pad; TVP: Tensor veli palatini muscle).
*Courtesy*: Late I Sando, MD (1928-2014).

## PATHOGENESIS OF HUMAN OTITIS MEDIA RELATED TO MUSCLES OF THE EUSTACHIAN TUBE

In contrast to the prevalence of OM in humans, especially in infants and young children, we have never observed spontaneous ME disease in the outbred animals (e.g. ferrets and monkeys) used in our laboratory over the past 30 years. Is this remarkable difference in the rate of OM related to the comparatively poor human ET function, a consequence of differences in paratubal muscular anatomy




**Figs. 3.6A and B:** Coronal view of the left Eustachian tube and related structures in the temporal bone specimen from a 13-year-old human female (A) compared with a coronal view of the left Eustachian tube in a temporal bone specimen from a rhesus monkey (B). Note that the levator veli palatini muscle in the human has a rounded belly and closely approximates the inferior portion of the tubal lumen. In the monkey, this muscle is more sparse and there is a distinct separation between the muscle and tubal lumen. Also note, the robust belly of the tensor veli palatini muscle in the monkey compared with the human. (TC: Tubal cartilage; L: Tubal lumen; TVP: Tensor veli palatini muscle; LVP: Levator veli palatini; B: Bulla of monkey). With permission from Doyle and Rood.[13]

in *H. sapiens* as compared with the monkey? Experiments with the monkey in our laboratory undergirded our understanding of the pathogenesis of ME disease in the human.[14] We have successfully created OM in this animal model by inactivating the tensor veli palatini muscle either by severing the tendon at the hamulus of the pterygoid bone or by injecting botulinum toxin into its belly. The consequence of these manipulations is an inability to dilate the ET lumen during swallowing, resulting in a ME effusion. Our conclusion was that a healthy tensor veli palatini muscle is critically important in the prevention of ME disease. We postulated that the monkey's larger tensor veli palatini muscle with a longer insertion on the cartilaginous portion of the ET could explain their excellent tubal function. Furthermore, if tubal inflammation did occur in the monkey its efficient ET function would prevent the development of ME disease. By contrast, since humans have comparatively poor tubal function and are susceptible to upper respiratory tract infections, OM is a common disease. Buchman and colleagues[15] reported that some adult volunteers who had nasal challenge with virus developed ME disease. Why viral infection affected some subjects and not others may be explained by the results of a later study in which adult volunteers who had signs of tubal dysfunction prior to a viral challenge developed more severe dysfunction and ME negative pressure. Subjects with good tubal function before the challenge did not develop OM.[16] We concluded from these observations and experiments that the relative inefficiency of the human tensor veli palatini muscle is a viable explanation for the pathogenesis of ME disease in some individuals, especially under nonphysiologic and inflammator conditions.

Obviously, due to their transient nature, these conditions cannot be invoked to explain why ME disease persists in a subgroup of patients. We have reported that older children and adults with chronic OM with effusion had ET dysfunction characterized by constriction of the lumen as opposed to dilation during swallowing during the forced response test.[17] This observation in the context of experimental electrical stimulation of the monkey paratubal muscles during the forced response test[18] suggests that the observed constriction is most likely due to contraction of the levator veli palatini muscle, which collapses the dilated tubal lumen. This hypothesis has yet to be confirmed, but is currently under investigation in our laboratory.

Eustachian tube constriction has been identified in children with cleft palate. The infant with an unrepaired cleft palate is a natural model of chronic OM with effusion, due to a functional, as opposed to an anatomic, obstruction of the ET. Similarly, surgical clefting of the monkey soft

palate induced OM with effusion that persisted until the cleft had healed.[19] During the interval when the soft palate was clefted, ET function tests revealed constriction of the tubal lumen during swallowing that we now attribute to a dysfunction of the levator veli palatini muscle. We posit that in an effort to prevent OM in these babies, surgical repair of the palate should focus on anchoring the tensor veli palatini muscle at the hamulus and repositioning the levator veli palatini muscle to preclude tubal constriction, as well as correcting their velopharyngeal insufficiency and hypernasal speech.

## OTHER FACTORS INVOLVED IN PATHOGENESIS

The above describes the consequences of our evolutionary history for the pathogenesis of OM in humans; however, the extremely high incidence of OM today cannot be explained solely as a consequence of evolutionary adaptations in humans. Other factors, such as heredity and immunity,[20,21] as well as those derived from living in novel environments (those we are not adapted to) such as a decrease in breast-feeding, smoking in the household, use of pacifiers and very importantly, child day-care attendance, are well known to increase the risk of ME disease. [22]

## SUMMARY AND CONCLUSION

It is well known that the pathogenesis of OM is multifactorial, but the role of evolutionary adaptation on its development has not been addressed until recently. Our hypothesis is that OM is most likely restricted to humans, in contrast to other species in the wild, because the associated hearing loss would have reduced the fitness of affected individuals. The byproducts of two human adaptations may have resulted in an increased prevalence of OM: the interaction of bipedalism with increased brain size, and the loss of facial prognathism, which may have been the result of adaptation for speech or the advent of cooking almost 2 million years. As a consequence of our adaptation for bipedalism, the female pelvic outlet is constricted, which in the context of a rapidly enlarging brain results in humans being born 12 months too soon. Significantly, immature ET structure and function in conjunction with an immature immune system helps to explain the high incidence of OM in the first year of life. But the persistence of ME disease beyond that stage is not explained by "immaturity". The morphology of the palate changed with the adaptations that produced facial flattening, with concomitant effects on the paratubal muscles that affected ET function. These changes resulted in relatively poor human physiologic tubal function in comparison to a nonhuman primate.

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CHAPTER

# 4

# Genetics of Hearing Loss

***Anne BS Giersch***

## INTRODUCTION

The human genome is the complete set of genetic information contained in almost every cell in our bodies. The 3 billion base pairs of DNA that make up our genome are located on the 23 pairs of chromosomes in each cell nucleus and the small mitochondrial chromosome found in the cytoplasmic mitochondria. The genome includes both protein coding and noncoding sequences. The protein coding sequences, which have been most extensively studied, comprise 1–2% of the genome and encode ~22,000 genes. A total of 99.9% of the genome sequence is identical between individuals. That still leaves 0.1% of the genome, or 3 million base pairs, of sequence variation between any two people. The vast majority of this variation is benign and referred to as single-nucleotide polymorphisms (SNPs). However, the concern of this chapter is our understanding of the relatively rare mutations in protein coding genes that cause clinically important traits, in particular, hearing loss.

The genetics of deafness and hearing loss is more complex than perhaps any other medical condition. Hearing impairment is a prime example of how a relatively common medical condition can be caused by a defect at any one of numerous genetic loci. About 60% of hearing loss is thought to have a genetic etiology in developed countries (Fig. 4.1). As modern medicine makes inroads in reducing the environmental causes of hearing loss, such as vaccination programs to combat infectious diseases that can damage the inner ear, the percentage of hearing loss attributed to genetic factors will continue to rise. It should be noted, however, that even the "environmental" causes of hearing loss listed in Figure 4.1 can have a genetic component.

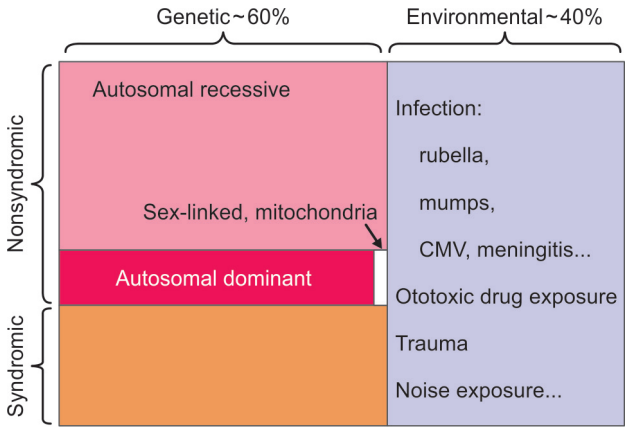



**Fig. 4.1:** Representation of proportion of hearing impairment that has a genetic or environmental cause. Some of the more common environmental causes are listed. Genetic hearing loss is further divided into syndromic, nonsyndromic hearing loss, mitochondrial and sex linked.

For example, genetic background can make an individual more or less sensitive to ototoxic drugs or noise exposure.

Determining the cause of hearing loss can be difficult, in part due to its variability of presentation. It can have a prelingual or postlingual onset. It can be stable or progressive. It can be unilateral or bilateral, conductive or neurosensory, mild or profound. If there is a clear family history of hearing loss, or a known etiologic agent of acquired hearing loss, such as a maternal rubella infection during pregnancy, establishing the cause of hearing loss in a child as genetic or acquired can be quite straightforward. However, often determining the cause of a recently diagnosed hearing loss may require a comprehensive evaluation, especially if there are no obvious culprits. At a minimum, an initial evaluation should include a targeted

patient history including family history and a physical exam, concentrating on key genetic and clinical features of the many forms of syndromic and nonsyndromic hearing loss, discussed in more detail below and in additional chapters.

## SYNDROMIC HEARING LOSS

The genetic causes of hearing impairment are generally divided into two conceptual categories: syndromic and nonsyndromic. Syndromic hearing loss is the association of hearing impairment with other clinical findings, such as retinitis pigmentosa in Usher syndrome, pigmentary anomalies in Waardenburg syndrome, cardiac arrhythmia in Jervell and Lange-Nielsen syndrome, and renal anomalies in Alport syndrome. Over 400 syndromes list hearing loss as a clinical symptom.[1] Sometimes the hearing loss is the most serious component of the syndrome, and sometimes it is of lesser concern in the face of potentially life threatening clinical manifestations. Occasionally, hearing loss is recognized early, but the syndromic nature of the disorder is not appreciated until much later in life. For example, in the Usher syndromes, hearing loss can be present at birth, but the visual deterioration may not begin until the teen years. In Perrault syndrome, which manifests with early onset deafness and ovarian dysgenesis in females, the infertility is frequently unrecognized until delayed puberty is noted. Otologic syndromes will be addressed more fully in a later chapter, but in thinking about inheritance and genetic diagnosis, it is important to keep in mind that without genetic testing it can be difficult to determine clinically if a child has syndromic or nonsyndromic hearing loss. Newborn screening, which will also be addressed in a later chapter, can recognize congenital hearing loss but does not identify the additional clinical symptoms of syndromic disorders.

## NONSYNDROMIC HEARING LOSS

Approximately 70% of hearing loss is nonsyndromic, and can be inherited in an autosomal recessive, autosomal dominant, sex-linked, mitochondrial, or multigenic fashion (Fig. 4.2). It is frequently congenital (present at birth) in which case it should be detected by newborn hearing screening. However, the onset may not be until months or years later. To date, 54 autosomal dominant (DFNA#) loci have been mapped with the affected gene identified at 27 of those loci. Seventy-five autosomal recessive loci (DFNB#) have been mapped, with the causative gene found in 44 loci. Six sex-linked loci (DFN#) have been mapped with the affected gene found in 3 loci.[2]

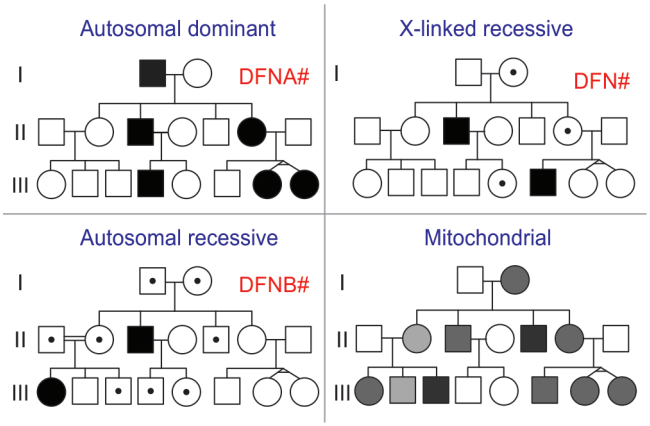



**Fig. 4.2:** A primer on modes of inheritance. In each Figure, generations are listed from oldest (I) to youngest (III) from top to bottom, connected by vertical lines. Males are squares; females are circles. Filled circle/square is an affected individual; open circle/square is unaffected. Shades of gray (mitochondrial) reflect variable degrees of symptom severity. A dot reflects a carrier of a recessive mutation. Matings are connected by horizontal lines. A double horizontal line reflects a consanguineous mating, where the partners are related and thus have an increased risk of both being carriers of the same recessive mutation. Hearing loss disorders with an autosomal dominant mode of inheritance are named DFNA# where the # reflects the order of discovery or report. DFNB# reflects recessive hearing loss. DFN# refers to X-linked hearing loss. In autosomal dominant disorders, a mutation is passed from parent to child and one expects approximately half the offspring to be affected. In autosomal recessive disorders, each parent is a carrier of one mutation and only offspring who receive a mutated gene from both parents manifest the disorder. Approximately 25% of offspring are expected to be affected. In X-linked recessive disorders, generally only males are affected, receiving the mutation from a carrier mother. In mitochondrial disorders, the mitochondrial genome is only passed from mother; thus, while both males and females can be affected, only females pass along the mutation. The variability of phenotype is related to the percentage of mutated mitochondria per cell (heteroplasmy).

Eighty percent of genetic nonsyndromic hearing loss is inherited in an autosomal recessive fashion, making it by far the most common category. About 20% of nonsyndromic hearing loss is inherited in an autosomal dominant manner, and a small percentage has an X chromosome-linked or mitochondrial mode of inheritance. Taking a detailed family history going back three generations as shown in Figure 4.2 may reveal a dominant, X-linked or mitochondrial inheritance pattern, since the hearing impairment will "run in the family". However, in autosomal recessive hearing impairment, which is the most common, both parents can be unaffected carriers and thus have no family history of hearing impairment. In fact, 90% of congenitally deaf babies are born to hearing parents.

The gene most frequently involved in nonsyndromic hearing loss is *GJB2*, which encodes the protein gap junction beta 2, more commonly referred to as connexin 26. This protein functions as a membrane channel, regulating the passage of ions in and out of the cell. The presentation of hearing impairment caused by *GJB2* mutations is somewhat variable, but most frequently profound and prelingual.

Over a hundred different mutations have been identified in this small gene (only one coding exon). Most of the mutations are inherited in a recessive fashion (both alleles are mutated); however, a few dominant mutations have also been noted. Different ethnic populations tend to have different mutations in the gene. Deletion of a G at nucleotide position 35 (c.35delG) is most common among Caucasians, whereas deletion of a C at nucleotide position 235 (c.235delC) is more common in Asians. Because of different carrier rates in different populations, *GJB2* mutations can account for anywhere from 10% to 50% of autosomal recessive nonsyndromic deafness in a given geographical region.

The second most commonly mutated gene in autosomal recessive nonsyndromic hearing loss is *SLC26A4*, accounting for 3–4% of cases. *SLC26A4* encodes the protein pendrin, which is an anion transporter. *SLC26A4* mutations also cause Pendred syndrome, which is associated with developmental abnormalities of the cochlea, sensorineural hearing loss, and diffuse thyroid enlargement (goiter). Because the goiter often does not manifest until later in life, Pendred syndrome is often misdiagnosed as nonsyndromic hearing loss.

Other genes relatively commonly mutated in nonsyndromic hearing impairment are *TMPRSS3*, *CDH23*, *TMC1*, *OTOF*, and *MYO15A*. The frequency of finding one of these genes depends on the population being evaluated, but multiple independent mutations have been identified in each, thus ruling out any common founder effect.

## MITOCHONDRIAL CAUSES OF HEARING LOSS

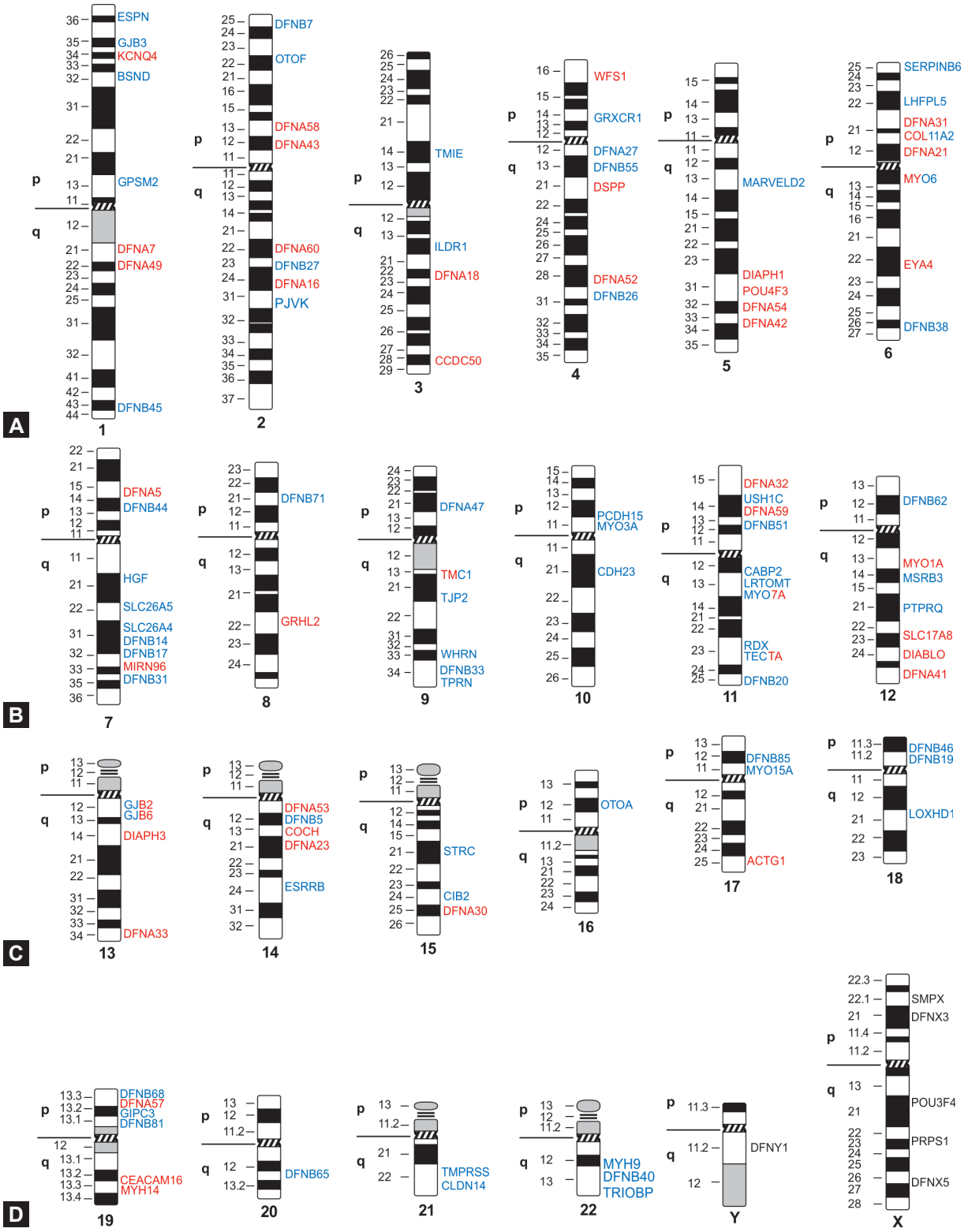
Mitochondrial mutations account for only a small percentage of genetic hearing loss, and have a unique inheritance pattern (Fig. 4.2). The mitochondrion has its own genome and is only inherited from the mother, through the egg. Thus, both males and females can be affected, but only females can pass the mutations along to subsequent generations. In addition, there can be hundreds to thousands of copies of the mitochondrial genome in a cell; usually only some of which carry a mutation (a condition known as heteroplasmy). Depending on the percentage of mutated mitochondria per cell and the cell type(s), which have the most or fewest mutant mitochondria, the presentation of symptoms can vary considerably between individuals, even among members of the same family who presumably have the same mutation.

Mitochondrial mutations can cause either syndromic or nonsyndromic hearing impairment. Among the mitochondrial syndromes in which hearing loss is a component are MERRF (myoclonus, epilepsy and ragged red fibers on muscle biopsy) and MELAS (mitochondrial encephalopathy, lactic acidosis and stroke-like episodes). In both syndromes, hearing loss is variable in presentation and not always present. Nonsyndromic mitochondrial hearing loss can be due to mutations in the mitochondrial *MTTS1* or *MTRNR1* genes. The latter is most commonly associated with aminoglycoside-induced hearing loss, i.e. the patient develops hearing loss only after exposure to aminoglycoside antibiotics.

## IDENTIFICATION OF DEAFNESS GENES

Many genetic disorders are associated with mutations in only one gene. For example, cystic fibrosis is caused by mutations in the *CFTR* gene on chromosome 7, Huntington's disease is caused by expansion of a short repetitive sequence in the *HTT* gene on chromosome 4, and mutations in the *NF1* gene on chromosome 17 cause neurofibromatosis type 1. These are all examples of monogenic disorders—one gene, one disease. Even though Huntington's disease or any of the other monogenic diseases is relatively rare compared to hearing loss, the fact that every case of Huntington disease is caused by a mutation in the same gene aided in the early identification of the disease-causing gene in 1983.[3]

Hearing impairment and deafness, by contrast, shows extreme genetic heterogeneity. Over 125 nonsyndromic deafness loci have been mapped by various means, with the causative gene identified in ~70 of these loci to date. Figures 4.3A to D show the known nonsyndromic hearing loss loci displayed by their map position on the human chromosomes. If the gene has been identified, it is listed. Otherwise, the deafness locus is referred to as DFN#. It would be impossible to also display the more than 400 syndromic loci! Figure 4.3 demonstrates the extreme heterogeneity that is observed in genetic hearing impairment.




**Figs. 4.3A to D:** Nonsyndromic hearing loss loci. The name of the genes that cause nonsyndromic deafness/hearing impairment and their chromosomal loci are indicated. DFNA or DFNB refers to a genetic locus where a hearing disorder has been mapped but the gene has yet to be identified. Red refers to dominant inheritance; blue refers to recessive inheritance; black refers to sex-linked inheritance. A gene that is both blue and red has been shown to cause both dominant and recessive hearing loss, depending on the mutation. For an up-to-date list of genes and loci, *see* the Hereditary Hearing Loss homepage.

## LINKAGE ANALYSIS IN HUMAN PEDIGREES

There are a number of techniques for identifying hearing loss genes. One tactic that has been productive over the past 15 years or so is linkage mapping. Linkage is defined as a tendency for genes close together on the same chromosome to be inherited together through multiple generations; thus, they are physically linked. The further apart two loci are on a chromosome, the higher the likelihood a recombination event will separate them. Linkage analysis begins with a large family, or pedigree, in which hearing loss is clearly inherited, in either a dominant, recessive, or X-linked manner.

Inheritance of the hearing impairment is tracked through the pedigree in conjunction with the inheritance of hundreds of genetic markers mapped to the human genome. Some combination of genetic markers will be inherited more often in the deaf family members than in the hearing family members, i.e. these markers are believed to be linked to the hearing loss. Narrowing in on the linked region can identify a chromosomal locus in which the deafness gene lies. The difficulty lies in the fact that depending on the size of the linked chromosomal region, dozens or even hundreds of genes may reside there. Each of these genes becomes a potential candidate. Sometimes an educated guess can be made as to which gene in the interval might be the culprit, but often a lab will need to sequence many genes before identifying the deafness causing mutation. The first nonsyndromic deafness gene, *GJB2*, was identified in 1997[4] by this method. Many of the other genes displayed in Figure 4.3 were identified by linkage mapping as well.

Using linkage mapping, a large family in which hearing loss segregates will usually yield the smallest genetic interval in which to hunt for the causative gene. However, due to the extreme genetic heterogeneity of hearing impairment, identifying a "deaf family" can be difficult. Deaf people have a tendency to marry deaf people and may have deaf or hearing children. If the individuals in a family are deaf for different genetic reasons, analysis of the segregation of a hearing impairment gene through a pedigree can be confounding and lead to inconclusive results. Figure 4.4 illustrates just such a situation. It is difficult to say if the hearing impairment (filled in figures) segregating through the families shown is recessive or dominant. Sometimes when deaf individuals marry, they have all deaf children or no deaf children. The only firm conclusion a geneticist can make is that there are at least two independent causes of the hereditary hearing loss segregating in the families in Figure 4.4.

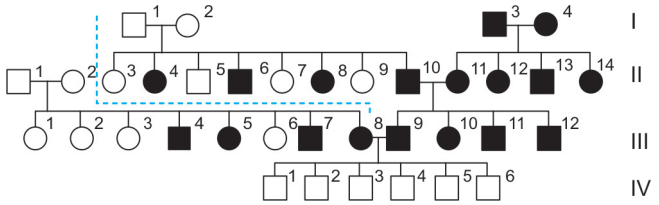



**Fig. 4.4:** Deafness segregating through several families. When deaf individuals (filled in circles/squares) mate with other deaf individuals, their offspring may or may not be deaf, depending on the gene(s) affected in the different families and the mode(s) of inheritance of mutations involved. This example illustrates how difficult it is to do linkage studies in unrelated families.

Because of assortative mating (individuals mating based on a shared phenotype, such as deaf people), many successful linkage studies have begun with isolated populations, where deaf family members are at least partially either physically (e.g. an island or isolated village) or culturally (e.g. religion or language) separated from the general population. This is particularly important for investigations of recessive hearing loss. In recessive disorders, *two* mutated alleles of the same gene must be inherited together to cause the phenotype, so a setting in which some degree of inbreeding occurs (i.e. first cousin marriages) helps to keep the deafness genes "in the family". Figure 4.5 is an example of a family pedigree from the Punjab province in Pakistan in which autosomal recessive deafness segregates. Note that deafness is observed only after genetically related individuals (double horizontal lines, in this example, first cousins) have offspring together.[5] Linkage analysis mapped the gene to chromosome 3 and the responsible gene was eventually identified by sequencing candidate genes in the region as *ILDR1*, immunoglobulin-like domain containing receptor 1, a putative transmembrane receptor.[6]

## MOUSE MODELS

The laboratory mouse has been an invaluable resource for studying mammalian hearing impairment. Unlike humans, the mouse has a short life span, is amenable to experimental manipulation, and, with controlled breeding, can have limited genetic heterogeneity. The physiology of the mouse auditory system is remarkably similar to humans, allowing insights into the morphogenesis and molecular mechanisms of human hearing and hearing

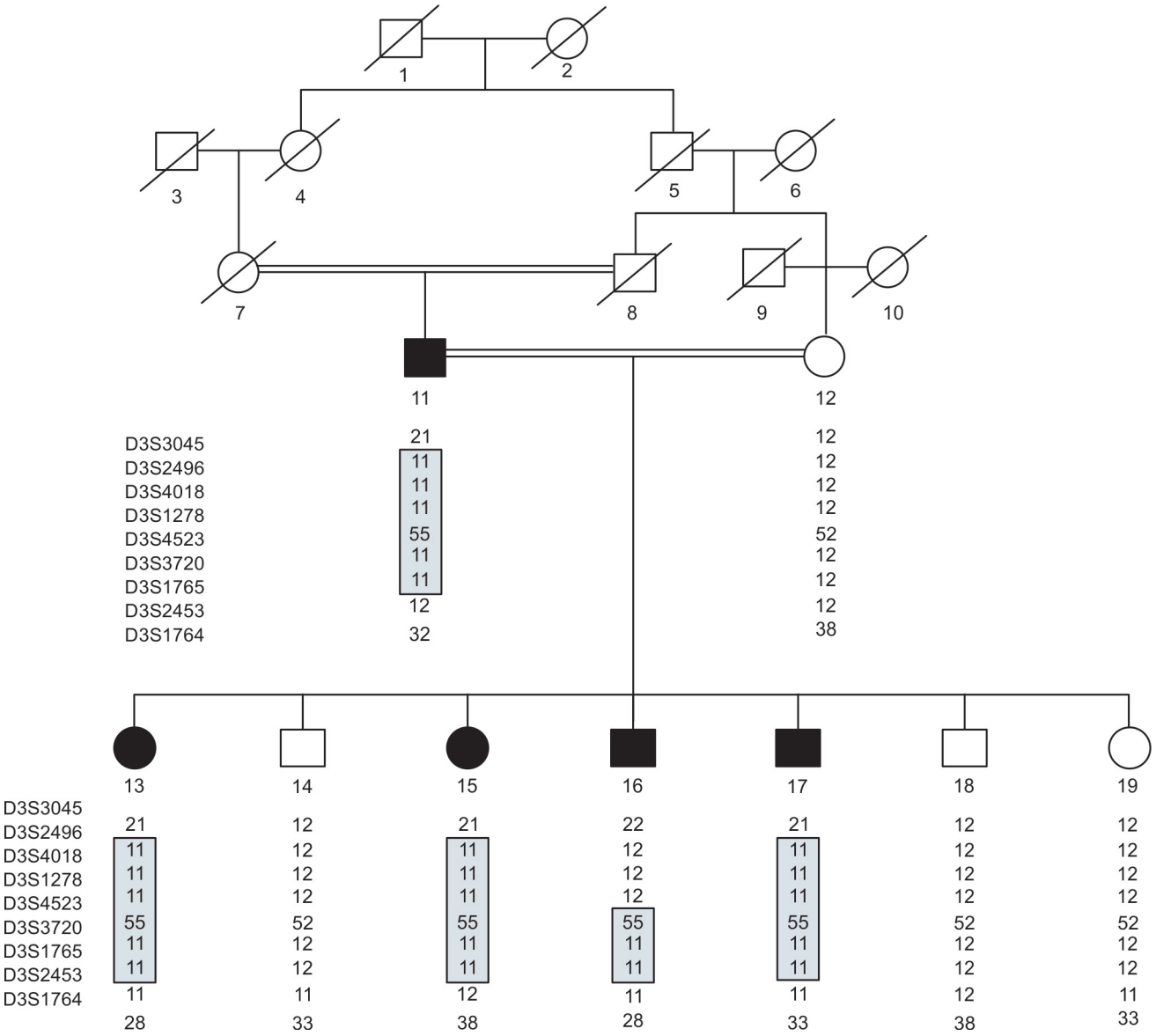



**Fig. 4.5:** Recessive deafness segregating through a Pakistani family from the Punjab region. The deafness locus (DFNB42) was mapped by linkage analysis to chromosome 3q13.31-q22.3 in this large family from an isolated village. Molecular markers linked to chromosome 3 are listed to the left. Marker alleles are listed below each individual. Homozygous regions are boxed. Reproduced from Aslam et al.[5] with permission from John Wiley and Sons.

loss. Combined with the fact that ~99% of human genes have orthologs in mice, these common laboratory animals have played an integral part in our understanding of genetic causes of deafness.

Mouse strains with hearing impairment were first recognized by their vestibular defect. Strains with names like waltzer, whirler, circler, and shaker had an obvious behavioral phenotype that made them a curiosity to mouse breeders. Because of considerable redundancy of function between the cells of the vestibular system and the cochlea, these strains also have hearing loss. Genetic manipulation available in the mouse enabled cloning of the mutant gene in these strains. Study of human pedigrees with hearing impairment demonstrated the same genes also cause human syndromic or nonsyndromic deafness. Table 4.1 lists some examples of such strains, the corresponding mutated gene and human hearing disorder.

Because genetic, histopathological, and molecular studies can be performed on mouse inner ear, much of what we now understand in terms of cochlear pathophysiology

**Table 4.1:** Mouse hearing loss mutants first recognized based on the behavioral phenotype caused by concomitant vestibular defects. Mutations in the human ortholog of each gene ultimately was shown to cause either syndromic or nonsyndromic hearing loss

| *Mouse strain* | *Affected mouse gene* | *Orthologous human hearing disorder* |
|---|---|---|
| Ames waltzer | *Pcdh15* | Usher syndrome type 1D |
| Deaf circler | *Ush1c* | Usher syndrome type 1C |
| Dreidel | *Pou4f3* | DFNA15 |
| Jackson circler | *Ush1g* | Usher syndrome type 1G |
| Jerker | *Espn* | DFNB36 |
| Shaker 1 | *Myo7a* | Usher syndrome type 1B, DFNB2 |
| Shaker 2 | *Myo15a* | DFNB3 |
| Snell's waltzer | *Myo6* | DFNA22 |
| Twister | *Otog* | DFNB18 |
| Waltzer | *Cdh23* | Usher syndrome type ID, DFNB12 |
| Whirler | *Whrn* | Usher syndrome type IID |

comes from mouse studies. For example, the Usher syndrome proteins, some of which are listed in Table 4.1, are now understood to be structural components of the hair cell stereocilia. Mutations in genes responsible for ion transport through the cochlear supporting cells, such as *Gjb2* encoding connexin 26, *Kcnq1* encoding potassium voltage-gated channel Q1, and *Slc26a4*, encoding solute carrier 26a4, have informed our knowledge of cochlear ionic homeostasis. Some mouse models are even teaching us about the middle ear conditions, such as otitis media. The induced mouse mutants Jeff and Junbo both develop otitis media with effusion. The Jeff strain has a mutation in the *Fbxo11* gene; Junbo has a mutation in *Evi1*.[7,8] The mechanism of action of these two genes is still being investigated, but it is clear that a disorder that was previously believed to have a purely infectious etiology can also have an underlying genetic predisposition.

## GENETIC TESTING

Genetic testing is recommended for all newborns identified by newborn hearing screening, once follow-up testing confirms a positive result. Likewise for an older child whose hearing loss may be identified through routine pediatric care or even school-based hearing screening, unless a known nongenetic cause has been identified (e.g. cytomegalovirus infection). Taking a family history of hearing loss may reveal a pattern of inheritance, as described above, but, since the majority of hearing loss is recessive, a negative family history does not rule out genetic hearing loss (absence of evidence is not evidence of absence!). Additional diagnostic testing to assess for a syndrome could proceed in a stepwise fashion—temporal bone imaging to evaluate for enlarged vestibular aqueduct associated with Pendred syndrome, electrocardiogram to assess for long QT interval associated with Jervell and Lange-Nielsen syndrome..., but comprehensive genetic testing can confirm or rule out these syndromes and many others, as well as nonsyndromic hearing loss. Thus, genetic testing can ultimately save time, money, and yield more prognostic information than ordering one test at a time.

The field of clinical genetic testing is evolving at an incredible pace as of this writing, thus the definition of a "comprehensive" genetic test is a moving target. Whole genome or exome sequencing is on the horizon, but not yet routine for hearing impairment. Currently, the most comprehensive genetic tests are conducted by laboratories using massively parallel sequencing to screen gene panels. The panels all include the genes most frequently mutated in the most common syndromic, nonsyndromic, and mitochondrial forms of hearing impairment. Up-to-date clinical genetic testing information can be obtained at the GeneTest website: http://www.genetests.org/. This site lists more than a dozen clinical laboratories around the world that offer testing for panels of hearing loss genes. Other useful web-based resources are listed in Table 4.2.

In the United States, the nationally certified laboratories that offer the largest deafness gene panels are as follows:

- The *OtoGenome* panel—71 genes—Partners Center for Personalized Genomic Medicine affiliated with Harvard Medical School—http://pcpgm.partners.org/lmm/
- The *OtoScope* panel—66 genes—Molecular Otolaryngology and Renal Research Laboratories at the University of Iowa—http://www.healthcare.uiowa.edu/labs/morl/
- The *Hearing Loss Expanded* Panel—56 genes—ARUP Laboratories affiliated with the University of Utah—http://www.aruplab.com/

"Comprehensive" genetic testing sounds ideal, but the reality is that even laboratories that test more than 50 deafness genes are able to report a positive result in fewer than half the cases. There are multiple reasons for a negative result:

1. The patient may not have genetic deafness. Perhaps the hearing loss should in fact be attributed to an infectious, environmental, or toxic exposure

**Table 4.2:** Internet resources to find additional, up-to-date information about genetic hearing loss

| *Website and URL* | *Brief description* |
|---|---|
| Hereditary Hearing Loss Home Page<br>http://hereditaryhearingloss.org/ | Maintained by the University of Iowa and the University of Antwerp, the Hereditary Hearing loss Homepage gives an up-to-date overview of the genetics of hereditary hearing impairment for researchers and clinicians working in the field |
| OMIM – Online Mendelian Inheritance in Man<br>http://www.omim.org/ | An online catalog of human genes and genetic disorders maintained by Johns Hopkins School of Medicine. OMIM is intended for use primarily by physicians and other professionals concerned with genetic disorders, by genetics researchers, and by advanced students in science and medicine |
| Gene Tests<br>http://www.genetests.org/ | Maintained by the University of Washington, GeneTests is a medical genetics information resource developed for physicians, genetic counselors, other healthcare providers, and researchers. Gene Tests includes a Laboratory Directory of over 600 international laboratories offering molecular genetic testing, biochemical genetic testing, and specialized cytogenetic testing for >3000 inherited disorders |
| National Center for Biotechnology Information Genetic Test Registry<br>http://www.ncbi.nlm.nih.gov/gtr/ | Maintained by the NIH, the Genetic Testing Registry (GTR) provides a central location for voluntary submission of genetic test information by providers. The overarching goal of the GTR is to advance the public health and research into the genetic basis of health and disease |
| Deafness Variation Database<br>http://deafnessvariationdatabase.com/ | Maintained by the University of Iowa, the Deafness Variation Database provides a guide to genetic variation in genes known to be associated with deafness. It includes all known genetic variants present in any gene that is included on University of Iowa's OtoSCOPE genetic deafness screening platform to facilitate variant analysis |

2. The patient has a very rare form of genetic deafness. Over 130 genetic deafness loci have been mapped and there may be an equal number yet to be unidentified. The causative mutation may lie in one of these many genes that are not on the current test panels
3. The mutation lies in an intron or other extragenic region. Most of the available testing sequences coding exons only, so mutations in an intron or regulatory regions upstream or downstream of a gene may not be sampled
4. A mutation is found but is a VUS—Variant of Unknown clinical Significance.

Once a sequence variant is found in one of the gene panels, it must be assessed as to the likelihood that it is pathogenic or benign. Not all sequence alterations are pathogenic; many are benign variants. There are thousands of polymorphisms throughout the genome that can be found in electronic databases of variants or SNPs. Most laboratories have a list of criteria that must be met before calling a sequence alteration pathogenic. Has it been observed previously, either by the testing laboratory or in the literature, to be associated with hearing loss? Does it alter a highly conserved amino acid or splice site? If there are multiple affected family members, do all the affected family members carry the same mutation(s), while none of the unaffected have it? If these criteria cannot be met, then a novel sequence variant is usually considered a VUS.

When genetic testing results are positive for a pathogenic mutation, it can help inform the prognosis (i.e. whether the hearing loss will worsen), the best intervention (e.g. hearing aids, cochlear implant, and sign language) and recurrence risks to future children and other family members. Furthermore, it can either eliminate the possibility that a syndrome is present, with likely clinical symptoms that have not yet manifested (e.g. adolescent-onset retinitis pigmentosa in Usher syndrome, long QT in JLNS, renal abnormalities in BOR or thyroid abnormalities

in Pendred syndrome), or predict the onset of such features if a test for a syndromic cause is positive. Of individuals with sensorineural hearing loss detected in the newborn period, up to 5% have hearing loss associated with Pendred syndrome and up to 10% have Usher syndrome. Knowing that a child will eventually develop vision problems suggests a course of action in managing the hearing loss. ASL only would be ill advised for a child with Usher syndrome; cochlear implant(s) would be a better choice.

If a child is found to have two recessive mutations, the parents will be tested to confirm they are both carriers. If so, then they have a 25% risk with each subsequent pregnancy of having another child with the same type of hearing loss. This risk may seem too high to some couples. They may opt to not have more children, to have prenatal diagnosis to detect an affected fetus, or to have preimplantation genetic diagnosis of fertilized embryos, to implant only unaffected embryos. Many otolaryngologists may not feel equipped to counsel patients about the implications of their genetic test results, beyond the immediate management of the hearing loss. Genetic counselors are an invaluable resource for interpreting the implications of a genetic diagnosis and conveying that information to a family.

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CHAPTER

5

# Otologic Syndromes

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## INTRODUCTION

The otologic system is composed of the external, middle, and inner ear including the cochlea and associated vestibular organs. Hence, defects in this system encompass a wide range of anomalies. Patients may present with a wide range of hearing loss, sensory, conductive, or mixed in origin. External ear anomalies are also at times associated with syndromes affecting the otologic system. Vestibular symptoms are less common, but several syndromes are associated with these anomalies. Isolated vestibular syndromes are rare.

The otologic system is involved in many syndromes with over 200 named syndromes associated with hearing impairment. The classification of otologic syndromes into specific categories is difficult as there is a wide range of heterogeneity and overlap in the systems involved. In general, syndromes may be classified as hereditary or nonhereditary. Many syndromes are discovered with initial diagnosis of hearing impairment in a child. Physical appearance, laboratory tests, imaging of the temporal bone, or consultation with other specialists often leads to a specific diagnosis. The following is a review of otologic syndromes most commonly encountered.

## DOMINANT SYNDROMES

### Branchio-Oto-Renal Syndrome

Branchio-oto-renal (BOR) syndrome is characterized by the triad of branchial anomalies, otologic anomalies usually coupled with hearing loss, and renal anomalies. The branchial anomalies often present in the form of cervical fistulas, sinuses, and cysts and renal anomalies range from agenesis to dysplasia. Renal anomalies are found in 25% of individuals.[1] Less common phenotypic findings include lacrimal duct aplasia, short palate, and retrognathia.[1]

#### *Genetics*

There are several implicated genes that are known to cause BOR syndrome. One causative gene is EYA1, the human homologue of the Drosophila eyes absent gene, which is found in approximately 25% of patients with a BOR phenotype.[2] This phenotype is hypothesized to reflect a reduction in the amount of the EYA1 protein.[2] Recently, mutations in two additional genes, SIX1 and SIX5, have also been shown to cause BOR syndrome.[3,4] Both of these newly implicated genes act within the same genetic network as the EYA and PAX genes for regulation of organogenesis during fetal development. Inheritance of BOR syndrome is autosomal dominant, penetrance is nearly 100%, and prevalence is estimated at 1 in 40,000 newborns.[1] BOR affects 2% of profoundly deaf children.[1]

#### *Presentation*

Hearing impairment is the most common feature of BOR syndrome and is reported in almost 90% of affected individuals.[1] Hearing loss in BOR syndrome is most often mixed (50%) but can be selectively conductive (30%) or sensorineural (20%). Hearing loss is severe in one-third of affected individuals and is progressive in one quarter.[1]

Otologic anomalies can involve the external, middle, or inner ear. External ear anomalies include preauricular pits (82%), preauricular tags, auricular malformations (32%), microtia, and external auditory canal narrowing (Fig. 5.1).[5] Middle ear anomalies include various ossicular malformations, facial nerve dehiscence, absence of the oval window, and reduction in size of the middle ear cleft.[5] Inner ear anomalies include cochlear hypoplasia and dysplasia occasionally with enlargement of the cochlear or vestibular aqueducts, or merely hypoplasia of the lateral semicircular canal.[6]

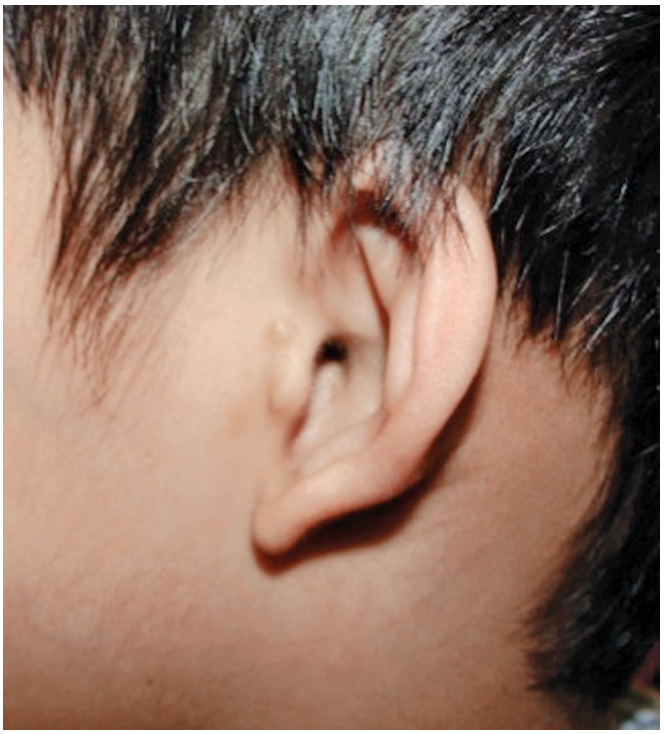
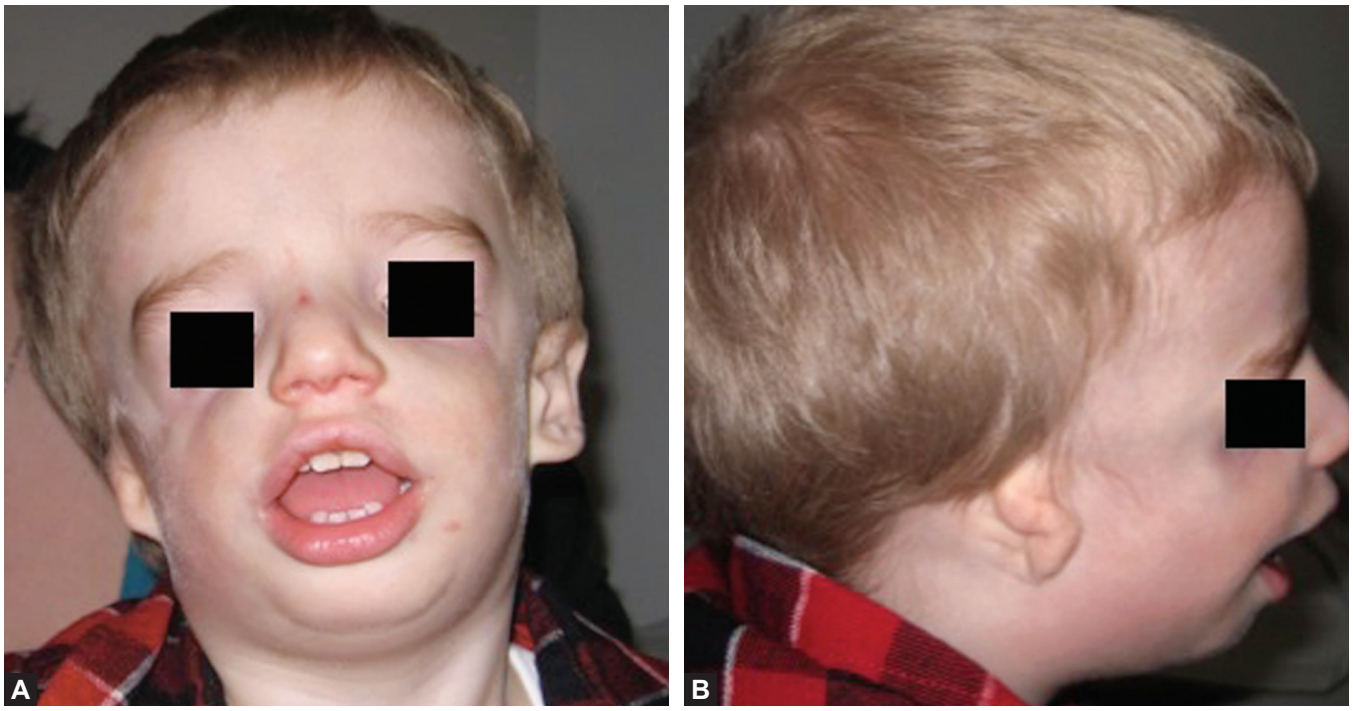


**Fig. 5.1:** Ear findings of a patient with branchio-oto-renal syndrome. Note the presence of a preauricular tag.
*Courtesy*: Lan Krantz, MD, Department of Genetics, Children's Hospital of Philadelphia.

## Treacher Collins Syndrome

Treacher Collins syndrome (TCS), alternatively called mandibulofacial dysostosis (MFD), is characterized by abnormalities of craniofacial development. The obligatory features of the phenotype include antimongoloid palpebral fissures, colobomas, eyelash malformations, molar defects, preauricular hair displacement, micrognathia, and "fishlike" facial features (Figs. 5.2A and B). Patients often also have auricular defects, nasal deformities including choanal atresia, macrostomia, and high arching palate. Patients often have a conductive hearing loss secondary to ossicular fixation.[7]




**Figs. 5.2A and B:** Patient with Treacher Collins syndrome.
*Courtesy*: Craniofacial Clinic, Division of Pediatric Surgery, Children's Hospital of Philadelphia.

### Genetics

Treacher Collins syndrom is inherited in an autosomal dominant fashion with an incidence of 1 in 50,000 live births, and while it has nearly complete penetrance, it has variable phenotypic expression.[8] However, up to 60% of cases do not have a family history and are therefore thought to result from de novo mutations. The causative gene is *TCOF* located on chromosome 5q, which encodes for the protein treacle.[7] During embryologic development, treacle is expressed at peak levels in the first and second branchial arches,[9] and it has been shown that the disease results from interference in the development of these arches.[8, 10] Greater than fifty mutations in the *TCOF* gene have been detected thus far and most appear to result in a truncated protein.

### Presentation

Patients with TCS are often identified at birth. Of note, although developmental anomalies arise bilaterally, they are often not truly symmetric. Mandibulofacial dyso stosis is associated with Pierre Robin sequence and palatal clefting in 35% of cases. Severe obstructive apnea secondary to the micrognathia and glossoptosis often requires surgical intervention.

The external ear is notably deformed in TCS patients. Patients usually present with bilateral microtia or anotia of varying severity with auricular remnants malpositioned.[11] This may be accompanied by stenosis or atresia of the external auditory meatus and, at times, aberrant tympanic membranes. The middle ear may be deformed or absent entirely. The inner ear is usually morphologically normal; however, from a functional standpoint, the pathologic ossicular chain results in a conductive hearing loss. This can be a maximum conductive hearing loss of up to 60 dB; however, the degree of deficit can vary.[11]

## Stickler Syndrome

Stickler syndrome (SS), also known as arthro-ophthalmopathy, is classically defined by the features of myopia, hearing loss, and cleft palate.[12]

### Genetics

Stickler syndrome is a rare autosomal dominant disorder with a preva-lence of 1:10,000,[13] and is caused by mutations in genes encoding proteins that make up type II and XI collagen: COL2A1, COL11A2, and CO11A1.[14,15] Based on the genetic mutation and phenotypically characterized by the particular ocular findings, SS can be broken down into three types. SS type 1 is caused by mutations in COL2A1[14] and the phenotype is characterized by the classic ocular findings with a "membranous" vitreous. SS type 2 is due to mutations in COL11A2 that is not expressed in vitreous,[15] thus making it distinct in that it displays no ocular abnormalities. SS type 3 is caused by mutations in COL11A1,[16] and phenotypically, the vitreous in these patients shows irregularly thickened fiber bundles.[16,17]

### Presentation

Snead and Yates,[17] set forth criteria for the diagnosis of SS that requires (1) congenital vitreous anomaly and (2) any three of myopia with onset before age 6 years, rhegmatogenous retinal detachment or paravascular pigmented lattice degeneration, joint hypermobility, sensorineural hearing loss, or midline clefting. Other manifestations that can be seen, but are not criteria, include midfacial flattening, mandibular hypoplasia, short upturned nose, or a long philtrum. Micrognathia is common, and, if severe, leads to Robin sequence with complete cleft palate (28–65%); however, clefting in SS is more commonly limited to submucous cleft.[18] The ocular findings in SS are the most prevalent feature with most having mypoia[17,18] and many also having vitreoretinal degeneration, retinal detachment, cataract, and blindness.[12] Retinal detachment in adolescence or early adulthood leading to blindness is the most severe ocular complication and affects approximately 50% of individuals with SS.[18]

The hearing loss associated with SS can be conductive, sensorineural, or mixed. If conductive, the loss typically reflects the eustachian tube dysfunction that commonly occurs with palatal clefts. SNHL is more common in older patients and possible mechanisms of pathogenesis include primary neurosensory deficits due to alterations in the pigmented epithelium of the inner ear or abnormalities of inner ear collagen.[18] Computed tomography has not shown gross structural abnormalities. Patients with type 1 SS tend to have either normal hearing or mild loss, whereas at the other end of the spectrum, type 3 patients tend to have moderate-to-severe hearing loss, and patients with SS type 2 fall in between.[13]

## Waardenburg Syndrome

Waardenburg syndrome (WS) is classified under four types with considerable heterogeneity and distinctive

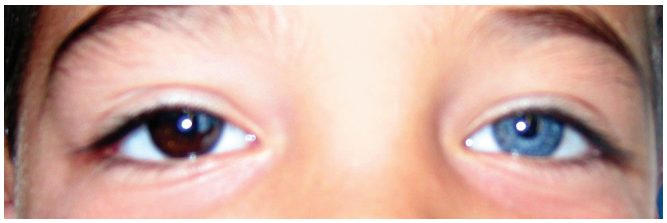


**Fig. 5.3:** Heterochromia in a patient with Waardenburg syndrome. *Courtesy*: John Germiller, Department of Pediatric Otolaryngology, Children's Hospital of Philadelphia.

phenotypic characteristics. WS type 1 is recognized by SNHL, white forelock, pigmentary disturbances of the iris, and dystopia canthorum, a specific displacement of the inner canthi and lacrimal puncti.[19] WS type 2 is distinguished from WS type 1 by the absence of dystopia canthorum. WS type 3, also called Klein-Waardenburg syndrome, is characterized by type 1 features with the addition of hypoplasia or contracture of the upper limbs.[20] WS type 4, also known as Waardenburg–Shah syndrome, involves the association of WS with Hirschsprung disease. Other features often seen include synophrys, broad nasal root, hypoplasia of the alae nasi, patent metopic suture, and a square jaw (Fig. 5.3).[19,20]

### *Genetics*

WS has an aggregate prevalence of 1:10,000–1:20,000.[20] WS type 1, which is the most common type, is caused by mutations in PAX3, a DNA-binding transcription factor expressed in neural crest cells early in development, and mutation results in the absence of strial melanocytes in affected individuals.[21] WS type 2, which is the second most common type, has been associated with mutations in MITF, a transcription factor involved in melanocyte development, in approximately 15% of cases.[21] In addition, mutations in SNAI2, a zinc-finger transcription factor expressed in migratory neural crest cells, have also been shown to cause WS type 2.[22] Similar to WS type 1, PAX3 is the causative gene in WS type 3.[23] Three genes have been implicated in WS type 4: endothelin 3 (EDN3), endothelin receptor B gene (EDNRB), and SOX10.[24,25] It is important to note that although WS types 1 to 3 are inherited as dominant diseases, WS type 4 is autosomal recessive.

### *Presentation*

Classically, the hearing impairment seen in WS is profound, bilateral, and stable over time and is responsible for approximately 2% of profound congenital SNHL.[26] However, it shows considerable variability between and within families. Congenital SNHL is present in 36–66% of cases of WS type 1 versus 57–85% of cases of WS type 2 and is most associated with individuals having pigmentary disturbances of the eyes and skin.[19,20] Audiogram configuration varies, with low-frequency loss being more common. Temporal bone imaging is typically normal, although malformation of the semicircular canals and cochlear hypoplasia can be found.[27]

## Apert Syndrome

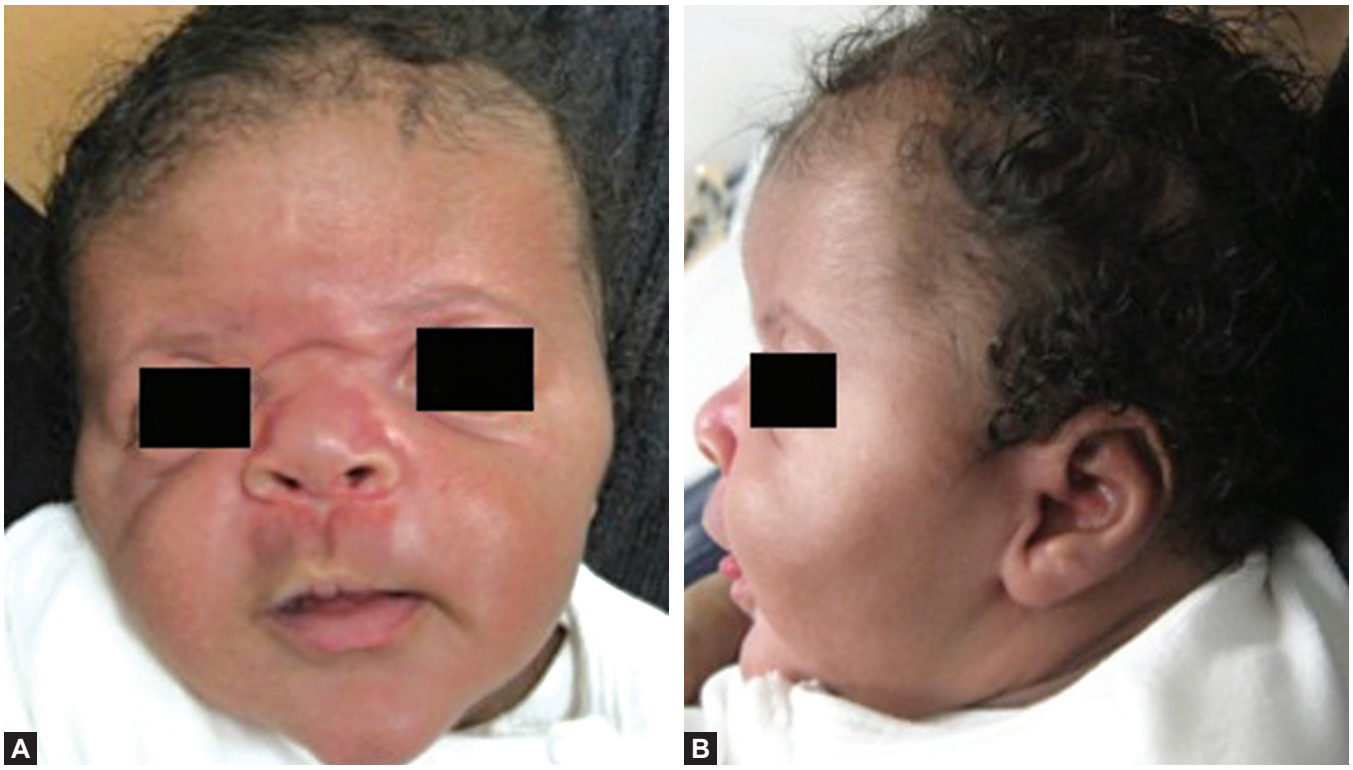
Apert syndrome is a rare form of acrocephalosyndactyly involving the cranium, midface, hands, and feet. Manifestations include brachycephaly or acrocephaly, midface hypoplasia and retrusion, and symmetric syndactyly.[28] Also associated is hypertelorism, proptosis, deep fore head, downward sloping palpebral fissures, shallow nasal bridge with a broad nasal root, and bulbous tip (Figs. 5.4A and B).[28] The palate frequently has a high arch and may be cleft.

### *Genetics*

Apert syndrome is inherited in an autosomal dominant pattern with an incidence of 1:200,000 live births.[29] Apert syndrome is caused by a mutation within fibroblast growth factor receptor 2 (FGFR2) located on 10q26 and results in premature closure of calvarial suture lines.[30] Most cases of Apert syndrome arise sporadically through new mutations, although some familial cases with autosomal dominant transmission have been reported.[31]

### *Presentation*

The defects in Apert syndrome are present at birth. While other aspects of Apert syndrome often take priority in terms of treatment, many patients with Apert syndrome have a variety of middle and inner ear anomalies. Middle ear anomalies most often sited are stapes or ossicular chain fixation and middle ear effusions causing conductive hearing loss.[28,32] Inner ear anomalies include dilation of the vestibule, structural anomalies of the cochlea, and semicircular canals.[32] In a 2005 report; Rajenderkumar et al. reviewed 70 cases of Apert syndrome from 1970 to 2003 and found the incidence of congenital hearing loss to be between 3% and 6%, but 56% of patients went on to develop permanent conductive hearing loss by 20 years of life.[32]




**Figs. 5.4A and B :** Patient with Apert syndrome.
*Courtesy*: Craniofacial Clinic, Division of Pediatric Surgery, Children's Hospital of Philadelphia.

## AUTOSOMAL RECESSIVE DISORDERS

### Pendred Syndrome

Pendred syndrome (PS) is an autosomal recessive disorder characterized by bilateral SNHL, often with enlarged vestibular aqueducts, and an iodine organification defect that can lead to thyroid goiter later in life.[33] PS is the most common syndromic form of hereditary sensori neural hearing loss, accounting for approximately 10% of hereditary deafness.[33,34]

#### *Genetics*

Pendred syndrome is autosomal recessive with a prevalence estimated at 7.5–10 per 100,000 individuals.[33] Most cases of PS result from mutations in the SLC26A4 gene that encodes a chloride and iodide transporter known as pendrin that is expressed in the inner ear, thyroid, and kidney.[35] Expression of SLC26A4 has been shown throughout the endolymphatic duct and sac, in distinct areas of the utricle and saccule, and in the external sulcus region within the developing cochlea.[36] Of note, mutations in SLC26A4 also cause a type of nonsyndromic autosomal recessive deafness called DFNB4 in which it is postulated that there may be a degree of residual function in the abnormal pendrin protein. More recently, mutations in the transcription factor FOXI1 have also been shown to cause PS in patients heterozygous for a mutation in SLC26A4.[37]

#### *Presentation*

The hearing loss in PS is usually congenital and severe to profound, although progressive mild-to-moderate SNHL is sometimes seen.[33] Bilateral dilation or enlargement of the vestibular aqueduct (EVA) is common, and may be accompanied by cochlear hypoplasia. A thyroid goiter develops usually in the second decade, although patients often remain euthyroid.[35] Thyroid dysfunction can be shown with a perchlorate discharge test, in which radioactive iodide and perchlorate are administered with a release of >10% radioactivity considered diagnostic for PS; however, the sensitivity of this test is low, making genetic testing the preferred diagnostic method.[34] The hearing impairment is usually prelingual, bilateral, and profound, although it can be progressive.[34] Radiologic studies always show a temporal bone anomaly, either dilated vestibular aqueducts or Mondini dysplasia.[34]

## Jervell and Lange-Nielsen Syndrome

Long QT syndrome can be dominantly or recessively inherited. The dominant disease, called Romano–Ward syndrome, is more common and does not include deafness.[38] The less common and recessive disease is known as Jervell and Lange-Nielsen syndrome (JLNS) and it is characterized by congenital deafness, prolonged QT interval, and syncopal attacks.[38]

### *Genetics*

Jervell and Lange-Nielsen syndrome is genetically heterogeneous with mutations in the KVLQT1 and KCNE1 genes causing defects in subunits of a potassium channel expressed in the heart and inner ear that account for the phenotype.[39] Although the prevalence of JLNS among children with congenital deafness is only 0.21%,[40] it is an important diagnosis to consider because of its cardiac manifestations.

### *Presentation*

Hearing impairment in JLNS is congenital, bilateral, and severe to profound.[39] It is due to changes in endolymph homeostasis caused by malfunction of the ion channel.[39] The prolonged QT interval can lead to ventricular arrhythmias, syncopal episodes, and death in childhood.[40] Importantly, treatment of the long QT interval with β-adrenergic blockers can reduce mortality from 71% to 6%.[40]

## Usher Syndromes

The Usher syndromes (US) are a genetically and clinically heterogeneous group of diseases characterized by sensorineural hearing loss, retinitis pigmentosa with night blindness and gradual vision loss, and often vestibular dysfunction.[41] Three clinical subtypes of US are recognized and are defined according to the severity and onset of the hearing loss, the presence/absence of vestibular dysfunction, and the age at onset of retinitis pigmentosa. The collective prevalence of the US is estimated at 4.4: 100,000 in the United States.[41,42]

### *Genetics*

The Usher syndrome is inherited in an autosomal recessive manner. Numerous genes have been implicated in causing the US and even within each subtype of US there is genetic heterogeneity. The two most common forms are US type 1B and type 2A, which, together, account for 75–s80% of all US.[43] US type 1B accounts for three fourths of US type 1 and is caused by mutations in a myosin gene called MYO7A.[44] US type 2A is the most common of the US overall, and is caused by mutations in a gene, USH2A, which encodes a 1551-amino acid protein named usherin, a putative extracellular matrix molecule.[45] Despite the numerous genes involved, at a basic phenotypic level, the hearing loss in the US is largely attributed to abnormal shape of the auditory hair bundles in the inner ear.

### *Presentation*

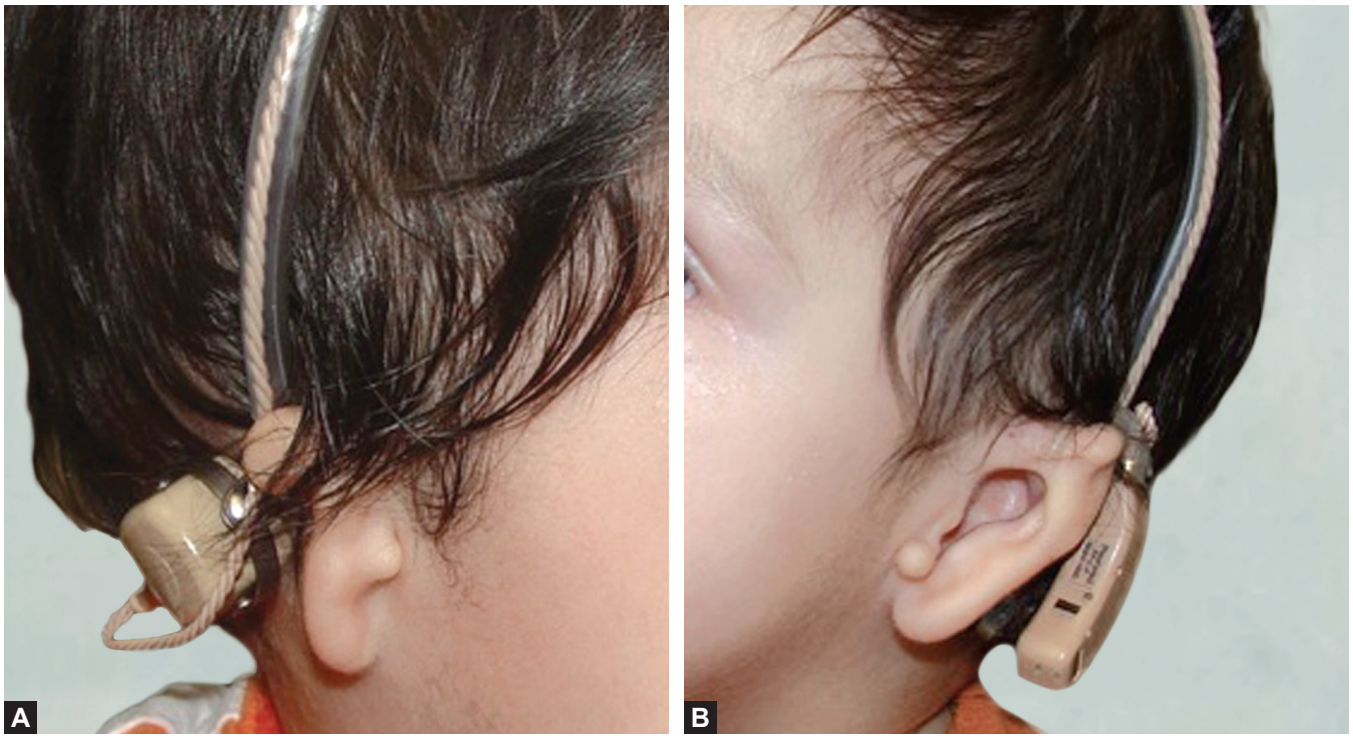
In the United States, US account for between 3% and 6% of congenitally deaf patients and is the cause of approximately 50% of deaf-blindness.[42] Type 1 (USH1) is phenotypically distinguished by the presence of severe-to-profound congenital hearing loss, vestibular dysfunction (bilateral caloric areflexia of the vestibular system), and retinitis pigmentosa that develops in childhood.[42] Type 2 (USH2) is distinguished by moderate-to-severe congenital hearing loss, which can often be treated with hearing aids, no vestibular dysfunction, and retinal degeneration that begins in the third-to-fourth decade;[42] and type 3 (USH3) is characterized by progressive hearing loss, variable vestibular dysfunction, and variable onset of retinitis pigmentosa.[42] Vision loss for each type is progressive and begins with loss of peripheral vision and night blindness.

## Goldenhar Syndrome/ Oculoauriculovertebral Spectrum

Goldenhar syndrome, also known as hemifacial microsomia or oculoauriculovertebral spectrum (OAVS), is composed of a spectrum of malformations involving the first and second branchial arches.[46] The typical presentation includes epibulbar dermoids or lipodermoids, microtia, mandibular hypoplasia, and vertebral anomalies.

### *Genetics*

Goldenhar syndrome appears to be a heterogeneous disease with an incidence of 1 in 5,600 to 26,550 live births.[47] Most cases are sporadic, although there are reports of both autosomal dominant and recessive forms. It exhibits a 3:2 predilection for males and most commonly affects the right ear.[48]




**Figs. 5.5A and B:** Ear findings in patient with Goldenhar syndrome.
*Courtesy*: Craniofacial Clinic, Division of Pediatric Surgery, Children's Hospital of Philadelphia.

### *Presentation*

External ear malformations present in almost all cases of OAVS that range from slightly dysmorphic to absent ears and are usually associated with the involved side of the face (Figs. 5.5A and B).[49] While commonly unilateral, occasionally both ears may be involved.[49] Common minor ear anomalies in these patients include preauricular appendages and pits both of which may be unilateral or bilateral, and have been described in 53–90% of OAVS patients.[49] Reported rates of middle ear anomalies ranges from 67% to 75%[50,51] and include displaced or malformed ossicles that are known to develop from the dorsolateral terminations of the cartilage in the first and second branchial arches. Inner ear alterations are less common and range from agenesis of the inner ear canal to altered cochlear and semicircular canal morphology.[50] Because the most common ear anomalies in the OAVS are external and middle ear abnormalities, secondary conductive hearing loss predominates in these patients,[48] and the degree of hearing loss correlates directly with the level of involvement of structures.[52,53] Although less common, mixed hearing loss with a sensorineural component has been observed, as evidenced by inner ear malformations.[50,52,53] Bilateral profound hearing loss is rare in these patients.

## X-LINKED SYNDROMES

### Alport Syndrome

Alport syndrome is characterized by glomerulonephritis often resulting in progressive renal failure, and a variable degree of sensorineural hearing loss. Patients may also display ophthalmic complications including lenticonus and retinopathy.

### *Genetics*

The underlying defect in Alport syndrome is damaged collagen IV, a key component of basement membranes. Clinical variability among those affected exists secondary to the variety of defects that exist in genes that code for collagen as well as the inconsistency in collagen formation. Several genetic mutations have been attributed to the disease. The most common is found in 85% of patients and consists of a mutation in the COL4A5 gene that results in

an X-linked recessive inheritance pattern of the disease. Autosomal recessive and dominant patterns have also been described, the latter being rare. Males have a more severe form of the disease and often progress to renal failure. Women have variable penetrance depending on the degree of mosaicism.[54]

### *Presentation*

The presenting sign of Alport syndrome is most often hematuria and can be seen as early as infancy, although the renal disease may remain asymptomatic for years. As mentioned, differing mutations in collagen genes have an impact on the severity of disease in patients. In the juvenile form of Alport syndrome, patients may develop renal failure and profound SNHL before the age of 30. In the adult onset form, disease progression does not begin till the age of 30 and hearing loss may be limited to a mild form or late-onset deafness.[54]

Generally, sensorineural hearing loss in Alport syndrome presents in the second decade of life, affects both ears equally, and is progressive in nature. Configurations vary and may be flat across frequencies, downsloping, or "U" shaped and does not usually exceed 70 dB. Speech discrimination scores are generally maintained.[55] Cochlear micromechanics have been faulted for the hearing impairment secondary to histopathologic abnormalities found in the basement membrane of cells in the organ of Corti.[56]

## OTHER SYNDROMES

### Osteogenesis Imperfecta

Osteogenesis imperfecta (OI) is a congenital disorder in which patients have fragile, brittle bones. Four original forms of OI are described; however, more recently, attempts have been made to expand the classification and include four more forms. Most patients share the common defect in a gene that codes for collagen type I.[57]

### *Genetics*

Mutations of COL1A1 or COL1A2 have been identified as the cause of most forms of OI. Several types have not been associated with a mutation to date. A mutation affecting a glycine residue in either of these genes produces a combination of normal and abnormal collagen resulting in variable expression of the disease. A mutation leading to a premature stop codon in COL1AI results in a milder form of OI in which collagen is formed but at a lesser rate.[57] Most types of OI are inherited in an autosomal dominant manner, although autosomal recessive forms have been described. A high de novo rate is characteristic of the more severe forms of the disease.

### *Presentation*

The main presenting sign of OI is fragile bone. The range of severity is wide and varies from fetal fractures and demise to a mild form without fractures. Other abnormalities with variable expression include blue sclerae, hyperlaxity of ligaments and skin, dentinogenesis imperfecta leading to discoloration of teeth, and hearing impairment.[57]

The hearing impairment associated with OI often does not present until the second to fourth decade of life. At onset, the loss is conductive in nature often progressing to a mixed hearing loss. Rarely, an isolated sensorineural hearing loss exists.[58] The conductive hearing loss in patients with OI is caused by otosclerotic lesions leading to a fixed stapes footplate. The mixed loss results from more extensive otosclerosis involving the cochlea. Ossicular discontinuity may play a part as well. The severity of hearing loss has not been correlated to the severity of bone fragility and a wide variability exists in its presentation among patients.[59]

### Crouzon Syndrome

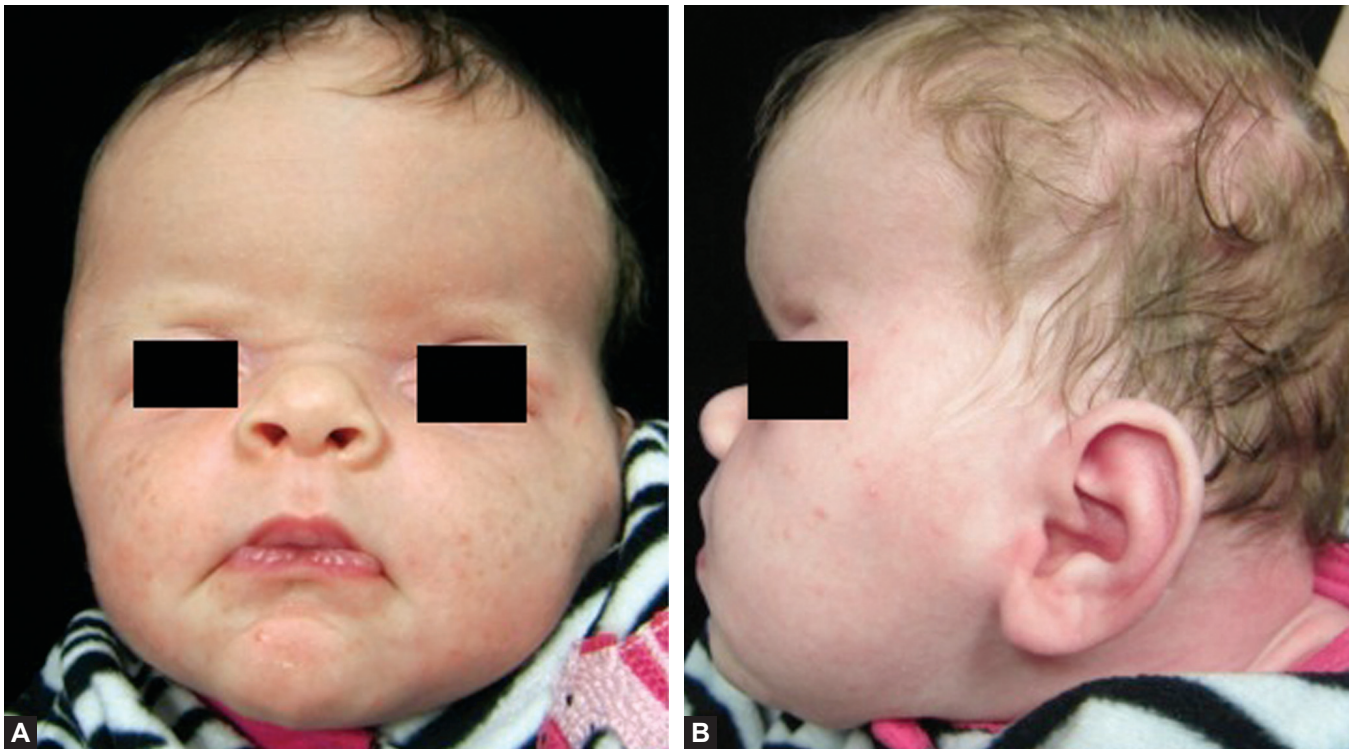
Crouzon syndrome is part of a family of syndromes referred to as craniofacial dysostosis. Premature craniosynostosis, or fusing of the fibrous sutures of the skull, leads to abnormal cranial and facial features. Crouzon syndrome is estimated to occur in 1 per 65,000 births (Figs. 5.6A and B).[60]

### *Genetics*

Crouzon syndrome is inherited as an autosomal dominant trait. Penetrance is complete, while expression is variable. Sporadic cases are common have been associated with advanced paternal age. A mutation in the gene that codes for FGFR2 has been shown to be the cause of the syndrome.[61] A different variant associated with acanthosis nigricans is linked to a mutation in FGFR3. [62]

### *Presentation*

Patients may show varying cranial deformities secondary to inconsistent craniosynostosis. Patients most often present with brachycephaly resulting from craniosynostosis




**Figs. 5.6A and B:** Patient with Crouzon syndrome.
*Courtesy*: Craniofacial Clinic, Division of Pediatric Surgery, Children's Hospital of Philadelphia.

of the coronal, sagittal, and lambdoid sutures. In addition to cranial deformities, most display hypoplasia of the midface, exorbitism (secondary to decreased bony orbital volume). A high incidence of obstructive sleep apnea and increased intracranial pressure exists in this population. Mental development is generally normal.

External appearance of the ears is usually normal in these patients, but some may show mild abnormalities including low-set ears or abnormal rotation.[63] The prevalence of hearing loss in patients with Crouzon syndrome has been estimated to be around 35%.[64] The hearing loss can be conductive, sensorineural, or mixed in origin Conductive hearing loss often is associated with Eustachian tube dysfunction and associated findings including perforation, chronic otitis media, and retraction. Ossicular chain fixation and external auditory canal atresia have also been described. The sensorineural component of hearing loss is not as well defined and occurs infrequently.

## Down Syndrome

Down syndrome occurs in approximately 1 in 650 births. It is the most common malformation syndrome. A variety of physical signs are associated with this syndrome and patients have a characteristic physical appearance.

### *Pathogenesis*

Down syndrome is the result of an extra copy of the genetic material of chromosome 21. This can be in the form of an extra chromosome from a nondisjunction event or a translocation. Advanced maternal age has been strongly correlated with the risk of manifestation of the syndrome.

### *Presentation*

Physical signs often associated with Down syndrome include brachycephaly, upward slanting palpebral fissures, epicanthic folds, and macroglossia. Patients often display growth retardation as well as mental delay. Hypotonia and joint laxity are also common.

Patients with Down syndrome have distinctive small, low-set auricles and small ear canals. The Eustachian tube is often dysfunctional due to its shape and easy collapsibility. These patients are more prone to problems with chronic otitis media and suffer from other complications resulting from chronic Eustachian tube dysfunction. Historically, a high rate of hearing loss was reported in this population. More recently, aggressive management of chronic ear disease, the most common cause of hearing loss in this population, has shown a great improvement in rates of permanent loss.[65]

## CHARGE Syndrome

CHARGE syndrome was initially described as an association of malformations often identified concurrently. Characteristics include coloboma, heart defects, choanal atresia, growth retardation, genital defects, and ear anomalies. In the past decade, a genetic mutation confirmed the association as a syndrome.[66] The incidence of the syndrome is about 1 in 10,000 births.

### *Pathogenesis*

De novo mutations in CH7 gene are thought to lead to the development of CHARGE syndrome. The gene encodes a protein that deals with chromatin remodeling and likely has an effect on cell-cycle regulation. Rare familial instances have been documented with autosomal dominant inheritance of the syndrome.

### *Presentation*

The characteristics of patients with CHARGE syndrome are often variable and not all patients possess all abnormalities encompassed in the mnemonic attributed to the syndrome. Features seen in the syndrome include unilateral or bilateral colobomas at times associated with microphthalmos, unilateral or bilateral choanal atresia or stenosis, cranial nerve dysfunction, swallowing problems, external and internal ear anomalies, genital anomalies, developmental delay, cardiovascular malformations, growth deficiency, orofacial clefts, and tracheoesophageal fistula.

Patients with CHARGE syndrome display a wide variety of ear anomalies and a high rate of hearing loss. External, middle, and inner ear anomalies have all been described. The external ear, while characteristically hypoplastic and low-set, may present as microtia. Accessory auricles may be present.[67] Moderate-to-profound hearing loss is common among these patients secondary to ossicular anomalies, Eustachian tube dysfunction, and varying inner ear anomalies. Common inner ear anomalies include cochlear dysplasia, semicircular canal aplasia, atresia of the oval window, and cochlear nerve deficiency. Atypical routing of the facial nerve and facial nerve palsies is also common.[68]

## Kabuki Syndrome

Patients with Kabuki syndrome are distinguished by typical facial features, most significant of which include elongated palpebral fissures with lower eyelid eversion, a broad and depressed nasal tip, and large prominent ears. These patients also display a wide variety of musculoskeletal and cardiac anomalies.

### *Pathogenesis*

Two gene mutations have been shown to be associated with Kabuki syndrome: MLL2 (myeloid/lymphoid or mixed-lineage leukemia and KDM6A [lysine (K)-specific demethylase 6A]. The majority of cases are sporadic, although the genes are inherited in an autosomal dominant fashion. The incidence of this rare syndrome is approximately 1 in 32,000 births.[69]

### *Presentation*

Apart from the typical facial features, patients with Kabuki syndrome display postnatal growth retardation and a spectrum of developmental delay. A large percentage of patients also have cleft lip and palate. Cardiac anomalies, skeletal abnormalities, and immunodeficiency are also seen and their presentation varies greatly among patients.[70]

The external ear anomalies displayed in Kabuki syndrome vary. The majority of patients have large, prominent ears or cup ear deformities. Aural atresia and preauricular pits have also been described. It has been estimated that approximately half the patients with Kabuki syndrome will have a hearing impairment. This loss is usually conductive in nature and due to recurrent or chronic otitis media. Sensorineural hearing loss has been reported in rare cases with associated inner ear anomalies ranging from enlarged vestibular aqueduct to complete cochlear aplasia.[71]

## Turner Syndrome

Turner syndrome is marked by the absence of all or part of one X chromosome. Patients are phenotypically female, but have characteristic physical appearances.

### *Pathogenesis*

Turner syndrome, also referred to as gonadal dysgenesis, is caused by complete or partial absence of one X chromosome. The most common karyotype is 45, XO that signifies a complete absence of one X chromosome. Loss of material from the short arm of the X chromosome is thought to result in the common physical signs and symptoms of the syndrome. Turner syndrome occurs in up to 1 in 2000 phenotypically female patients.

### *Presentation*

Patients with Turner syndrome have characteristic physical appearances consisting of short stature with webbed neck, gonadal dysgenesis, and lack of secondary sex characteristics. Patients also have cardiac, renal, and ophthalmologic abnormalities. Cleft palate or other palatal abnormalities are also common.[72]

Externally the ears are most often normal; however, cup ear deformity and low-set ears are described. Eustachian tube dysfunction causing chronic ear disease is common and conductive hearing loss occurs in as many as 70% of patients.[73] Sensorineural hearing loss is less common and is thought to occur in the second or third decade of life and progress slowly. Mid frequency losses as well as a form of early presbycusis with prominence in the higher frequencies have been described. Sensorineural hearing loss has been postulated to be related to the patient's karyotype.[74]

## Nager Syndrome

Nager syndrome is a congenital anomaly syndrome also known as Nager acrofacial dysostosis. Preaxial limb and mandibulofacial anomalies are the predominant features of the syndrome.

### *Pathogenesis*

Recently, Nager syndrome was found to be caused by haploinsufficiency, or inactivation of one of two copies, of the gene SF3B4, a spliceosomal factor.[75] It is a rare condition and is believed to be autosomally inherited. The majority of cases to date have been sporadic.

### *Presentation*

Patients with Nager syndrome have similar facial characteristics as those with TCS. These features include downslanting palpebral fissures, malar hypoplasia, micrognathia, external ear anomalies, and cleft palate. Limb anomalies, including hypoplasia of the radial aspect of the hand especially the thumb, foreshortened forearms, and duplications of the thumbs, are the other common findings in these patients.[76]

Otologic anomalies, including external and middle ear malformations, are noted in the majority of patients with Nager syndrome. Auricular anomalies can range from preauricular pits to anotia with external auditory canal atresia or stenosis. The most commonly encountered form of hearing loss is conductive secondary to chronic otitis media (middle ear disease is ubiquitous in this population), canal atresia or stenosis, and ossicular anomalies. Moderate-to-severe conductive loss is most common. Sensorineural hearing loss is not considered a factor in this syndrome, although some reports show patients with mixed hearing loss. Several reports have shown most patients present with normal inner ear anatomy.[77]

## Velocardiofacial Syndrome

Velocardiofacial syndrome (VCFS), also known as 22q11.2 deletion syndrome, encompasses multiple presentations. All share a common genetic basis: a deletion on the short arm of chromosome 22. The genes affected are involved in pharyngeal arch development, and the phenotypic presentation of this VCFS is secondary to this fact.

### *Pathogenesis*

Several genes have been found to contribute to the phenotypic variability encountered in patients with VCFS. These include TBX1, TBX2, TBX3, and VEGF, all of which are involved in pharyngeal arch development. VCFS affects an estimated 1 of every 4000 newborns. In < 10% of patients, the syndrome is inherited in an autosomal dominant fashion.

### *Presentation*

The presentation of patients with VCFS is diverse. The face in these patients often appears long and hypotonic with narrow palpebral fissures. A squared nasal root with a narrow alar base is seen. Congenital cardiac anomalies are common and can include tetralogy of Fallot, pulmonary artery alterations, and septal defects. Immune deficiency is common secondary to the thymic aplasia (a third arch derivative) and manifests as problems with T-cell-mediated response. Hypocalcemia secondary to decreased parathyroid function is a frequent manifestation. Clefting of the secondary palate can be obvious or can manifest overtly as a submucous cleft. Velopharyngeal insufficiency is common in this population.[78]

Small auricles that at times are morphologically abnormal are often seen in patients with VCFS (Fig. 5.7). Eustachian tube dysfunction leading to chronic otitis media is the main cause of conductive hearing loss in this population. Middle ear anomalies have been reported. Inner ear anomalies with resulting SNHL have also been described in approximately 10% of patients.[79] TBX1 is reported to be important in the development of the inner ear.[80]

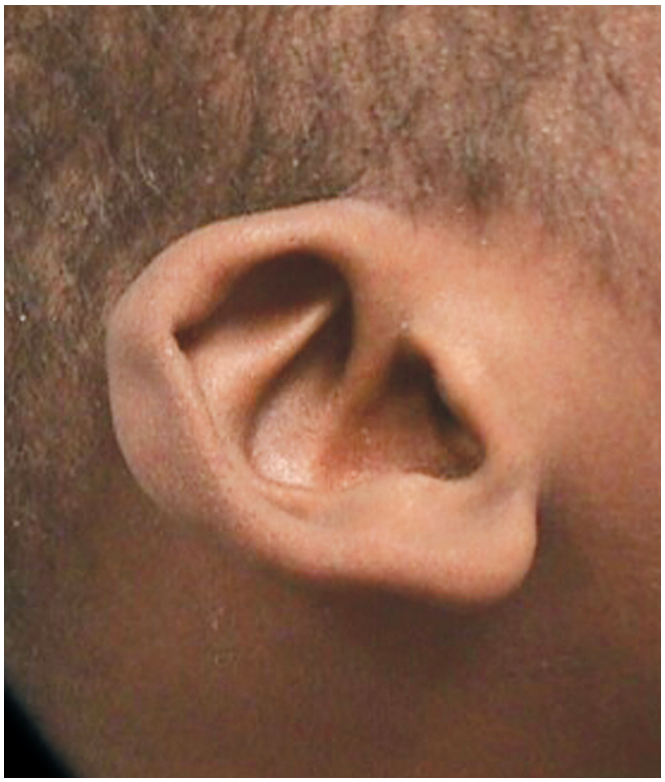


**Fig. 5.7:** Ear findings in patient with velocardiofacial syndrome. *Courtesy*: Lan Krantz, Department of Genetics, Children's Hospital of Philadelphia.

## CONCLUSION

An abundance of syndromes associated with otologic findings exists. These syndromes may affect one or several parts of the otologic system. Management of patients with otologic syndromes is best approached by a multidisciplinary team as many have concomitant anomalies.

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CHAPTER

6

# Congenital Hearing Loss

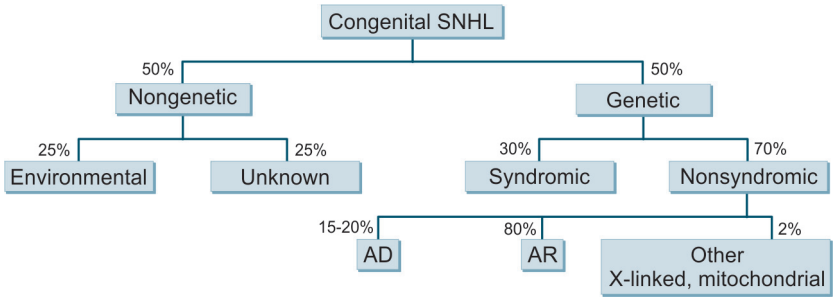
***Gillian R Diercks, Leila A Mankarious***

## INTRODUCTION

Sensorineural hearing loss (SNHL) in the pediatric population is the most common congenital abnormality and the most common sensory disorder, with an estimated incidence of 1.1 per 1000 births.[1] Roughly 20–30% of congenital hearing loss cases are profound (hearing level > 90 dB)[2] and an estimated 30% of children with hearing loss have additional disabilities, such as cognitive impairment.[3] Hearing loss in children can be classified according to the age of onset and etiology. The term "congenital" refers to the age at which hearing loss develops; however, it does not point toward the particular etiology of the sensory deficit.

There are multiple causes for congenital hearing loss, which include genetic, metabolic, infectious, and environmental etiologies (Flowchart 6.1). A total of 50% of SNHL cases have a genetic basis, where 30% are syndromic and associated with other organ system abnormalities, and 70% are nonsyndromic. With the advent of genetic testing, the etiologic distribution likely has not changed; however, the ability to identify a specific diagnosis has improved. Of the nonsyndromic cases, approximately 80% are autosomal recessive, 20% are autosomal dominant, 1% are X-linked, and < 1% demonstrate a mitochondrial pattern of inheritance.[4] Infectious causes including toxoplasmosis, rubella, cytomegalovirus (CMV), herpes simplex, syphilis, and H. influenza type B meningitis once represented the majority of acquired hearing loss cases. With advancements in immunization programs, prenatal and neonatal care, the incidence of infection-associated hearing loss has decreased significantly.[5] However, neonatal intensive care unit (NICU) admissions are becoming increasingly prevalent, and premature infant survival is increasing. As a result, hearing loss associated with hypoxia, hyperbilirubinemia, extracorporeal membrane oxygenation (ECMO), sepsis, and exposure to ototoxic medications, such as aminoglycosides and

**Flowchart 6.1:** Etiologies of congenital hearing loss.



diuretics, is increasing.[6] Other causes of congenital hearing loss include otitis media with effusion, congenital malformation of the external or middle ear, noise exposure, and trauma.[7] The prevalence of childhood hearing loss increases until roughly 6 years of age due to delayed diagnosis and progressive hearing loss associated with genetic or infectious conditions, such as CMV and meningitis.[2]

Hearing loss that occurs early in life is present during the most critical periods for language and social development and may have long-lasting consequences for affected children and their families.[2] Though prelingual hearing loss has an obvious and direct effect on spoken language development, it may also affect indices of academic achievement, impart psychosocial and parental stress, and decrease future employment opportunities.[8,9] Lack of auditory input changes the function of the auditory system, affecting interactions between cortical areas, and may impair cortical development.[10] If hearing is established later in life, after this critical period, complex auditory functions cannot be restored fully, and auditory input may become uncoupled from other sensory modalities.[2]

Prior to initiation of widespread newborn hearing screening, children born with hearing impairment were identified at an average of 1.5–3 years of age, typically due to impaired language development.[11] Because of diminished auditory input during critical developmental periods, most children with hearing loss lagged in their language and other academic skills even after educational support and devices to augment hearing were initiated. In the 1990s, studies demonstrated that early intervention before 6 months of age—a critical period for language development—could substantially improve language acquisition. There was a movement toward early identification of SNHL, resulting in the implementation of universal newborn hearing screening in the United States in 1999, which has been instrumental in the early recognition and interdisciplinary treatment of congenital hearing loss. Fortunately, these interventions, which include speech therapy, amplification, and cochlear implantation, have allowed for improved language outcomes, including reading ability and communication, which improve life opportunities for children with congenital deafness.[2,12]

## EARLY HEARING DETECTION AND INTERVENTION

All infants under the age of 3 months should be screened in accordance with recommendations from the NIH consensus statement in 1993 on early identification of hearing impairment in infants and young children in order to minimize the lasting effects of prolonged auditory deprivation. These recommendations have now been mandated by federal law. In addition, the Joint Committee on Infant Hearing (JCIH), a group of specialists composed of representatives from audiology, otolaryngology, pediatrics, and nursing, has made additional recommendations that infants should be hearing-screened by 1 month of age and intervention should be initiated for those infants who have significant hearing loss by 6 months of age. In addition, neonates who have been in the intensive care unit for more than 5 days should also have auditory brain stem response (ABR) testing as part of their screening so that neural loss is not missed.[13]

## NEWBORN HEARING SCREENING

Newborn testing protocols primarily utilize either automated auditory brain stem response (aABR) to a transient stimulus or an otoacoustic emission (OAE), again after a brief stimulus. Transient-evoked OAEs test over a broad frequency range and distortion-product OAEs evaluate distortion product in response to two pure tones. Both aABR and OAEs have advantages and limitations that are important to be aware of and are reviewed in further detail in a separate chapter (Chapter 14). aABR requires attachment of surface electrodes to the skin to produce a well-defined waveform; thus, recording time is increased in comparison to OAE testing which does not require scalp recording. However, unlike OAE, which only test the function of cochlear outer hair cell function, ABR evaluates proper functioning of both inner and outer hair cells, as well as acoustic neural tracts within the brain. OAEs may miss patients with hearing loss due to isolated inner hair cell dysfunction (auditory neuropathy/auditory dyssynchrony) or central nervous system pathology. Lastly, OAEs are more susceptible to middle ear pathology, external canal collapse, and vernix as well as ambient noise. Audiologic screening of the newborn infant is a rapidly changing and growing field requiring frequent equipment updates. The choice of which screening test to use will be influenced by institutional resources as well as regional differences in audiologic education and training.

Of all neonates screened using aABR, 2–3% "refer" for further evaluation, and of those, repeat testing shows that less than 1% fail. Initial "refer" rates for OAE screening are higher with an initial rate of 5–10% and subsequent

2% on rescreening. Hence, aABR appears to be a more accurate test for screening but has some disadvantages as mentioned above. Once an infant has failed two newborn screens, a diagnostic ABR is obtained that tests both ears even if only one has failed. Audiologic testing in children older than the newborn period is beyond the scope of this chapter and will be reviewed elsewhere.

## ETIOLOGY OF CONGENITAL HEARING LOSS

### Genetic

Up to 50% of congenital hearing loss cases are hereditary, and over 400 forms of genetic deafness have been described.[14] A total of 30% of these cases are syndromic and associated with other organ system abnormalities. The most common syndromes associated with hearing loss include Pendred, Usher, Waardenburg, and Branchio-oto-renal. The remaining 70% of genetic cases are nonsyndromic in which hearing loss is most often sensorineural.[4] The majority of nonsyndromic cases, up to 80%,[4] demonstrate an autosomal recessive pattern of inheritance. While autosomal dominant forms of nonsyndromic hearing loss are often associated with progressive, postlingual deafness, autosomal recessive hearing loss is typically prelingual.[4] Up to 50% of autosomal recessive cases are due to mutations in *GJB2* and/or *GJB6* at the DFNB1 locus, which encode connexin 26 and 30.

While a complete description of all the genetic causes of congenital hearing loss is beyond the scope of this chapter and is described elsewhere in this text, we summarize the most common causes of syndromic and nonsyndromic congenital loss.

### Syndromic

#### *Autosomal Dominant*

*Waardenburg:* This syndrome, characterized by variable degrees of prelingual SNHL and pigmentary changes involving the skin, eyes (heterochromia iridis), and hair (white forelock), is the most common form of autosomal dominant syndromic hearing loss. There are four types of Waardenburg syndrome: WSI, WSII, WSIII, and WSIV. These four disorders are linked by the common feature of melanocyte dysfunction but each has distinguishing features. In WSI, dystopia canthorum, which is lateral displacement of the medial canthus, is present. Patients with WSIII also demonstrate upper limb abnormalities, and patients with WSIV have Hirschsprung disease. WSI and WSIII are associated with mutations in *PAX3*, WSII is associated with mutations in *MITF* and *SNA12*, and WSIV is associated with mutations in *EDNRB*, *EDN3*, and *SOX10*.[14]

*Branchio-Oto-Renal*: This is the second most common form of autosomal dominant syndromic hereditary hearing loss. It is associated with conductive, sensorineural, or mixed hearing loss as well as malformations of the external ear, preauricular pits, branchial cleft fistulas or cysts, and renal abnormalities. It has been associated with mutations in *EYA1* and *SIX1*; there are also a number of hereditary cases in which the genetic mutation has not yet been identified.[14]

*Stickler Syndrome*: This is an autosomal dominant disorder involving mutations in *COL2A1*, *COL11A1*, or *COL11A2*, which are involved in type 2 collagen synthesis. Patients with this syndrome demonstrate SNHL, spondyloepiphyseal dysplasia, cleft palate, and congenital myopia. Because of their myopia, as well as increased risk for retinal detachment, patients with Stickler syndrome require routine ophthalmologic evaluations.[14]

#### *Autosomal Recessive*

*Pendred:* This is the most common form of autosomal recessive syndromic hearing loss. It is associated with congenital severe to profound SNHL as well as temporal bone defects, including Mondini malformation and enlarged vestibular aqueduct. Pendred syndrome is also associated with euthyroid goiter, which develops due to delayed iodine organification. Goiter is not sensitive or specific for the disorder, however. Due to incomplete penetrance, some patients will never develop goiter, and others will not present with goiter until adolescence or adulthood.[4] Most patients with Pendred syndrome are euthyroid with normal thyroid function tests.[15] The perchlorate discharge test is diagnostic. A total of 50% of families with Pendred syndrome demonstrate mutations in *SLC26A4*, a chloride/iodide transporter.[4] This gene is also associated with autosomal nonsyndromic hearing loss at the DFNB4 locus.[14]

*Usher:* This is a common form of autosomal recessive syndromic hearing loss and affects over 50% of deaf and blind

individuals in the United States.[14] It is characterized by SNHL and retinitis pigmentosa, a form of retinal degeneration. There are three forms of Usher syndrome, which are distinguished by the degree of hearing and vestibular impairment. In type 1 (USH1), vestibular dysfunction and severe to profound SNHL are present at birth. Patients with type 2 (USH2) have normal vestibular function, and congenital SNHL may range from mild to severe. In type 3 (USH3), the rarest form of the disease, patients develop progressive hearing loss and vestibular dysfunction. Patients with impaired vestibular function may not meet their motor developmental milestones. Retinal degeneration in patients with Usher syndrome is usually not symptomatic until adolescence; however, electroretinography can identify photoreceptor abnormalities in patients as young as 2 years of age.[14] Therefore, if Usher syndrome is suspected, ongoing ophthalmologic evaluation is critical. It is also important to identify patients with Usher syndrome early, as it may help guide decisions about the most appropriate communication strategies—for example, choosing cochlear implantation over sign language. Multiple genetic mutations have been identified, including *MYO7A*, *USH1C*, *CDH23*, *PCDH15*, *USH1G* for USH1, *USH2A*, *GPR98*, and DFNB31 for USH2, and *USH3A* for USH3.[16]

*Jervell and Lange-Nielsen:* This is the third most common form of syndromic autosomal recessive hearing loss. Affected individuals demonstrate SNHL and the cardiac conduction abnormality of QT interval prolongation, which may result in syncopal episodes and sudden death. In cases with a positive family history of sudden death, sudden infant death syndrome, syncope or QT prolongation, ECG is warranted.[14,15] This syndrome is associated with mutations in *KCNQ1* and *KCNE1*, which together encode a potassium channel important for maintenance of the electrochemical gradient of the inner ear and cardiac myocardium.

### X-linked

*Alport Syndrome:* This syndrome is characterized by progressive bilateral SNHL, typically postlingual, glomerulonephritis that leads to renal failure, and ophthalmologic abnormalities, including anterior lenticonus that results in myopia. Hearing loss usually is not apparent until after the first decade of life; however, Alport syndrome may be diagnosed earlier secondary to its associated ophthalmologic findings. Up to 85% of cases demonstrate an X-linked pattern of inheritance associated with mutations in*COL4A5*, which is associated with type 4 collagen production; autosomal recessive forms of the disease and, rarely, autosomal dominant inheritance have also been described.[14]

### Mitochondrial

*MTRNR1:* A total of 50% of patients with aminoglycoside-related ototoxicity harbor the 12S ribosomal RNA mutation 1555A>G. This gene is also associated with maternally inherited, nonsyndromic hearing loss that is not related to antibiotic exposure.[17] Another significant mutation that puts individuals at risk for SNHL is the *MT-TS1* within mitochondrial tRNA.

## Nonsyndromic

### Autosomal Recessive

*DFNB1:* This locus on chromosome 13q11 has been implicated in autosomal recessive nonprogressive mild to profound SNHL. Mutations in two genes, *GJB2* and/or *GJB6*, have been identified that encode connexin 26 and connexin 30, respectively. Connexin 26 and connexin 30 are gap junction proteins expressed in the cochlea and felt to be important for potassium recirculation and maintenance of an electrochemical gradient.[4] Mutations in *GJB2* have been identified in up to 50% of autosomal recessive, nonsyndromic hearing loss cases. Over 220 mutations in this gene have been identified, which occur in different frequencies across populations.[17] Approximately 1 in 33 US residents of Northern European descent carry a mutation in this gene.[18] The most common mutation, seen in up to 2/3 of cases, is the deletion of guanine at position 35 (35delG). This deletion results in a frame shift mutation and premature termination of protein synthesis.[4] A total of 10–15% of patients with hearing loss have a mutation in only 1 copy of *GJB2*. In these patients, a neighboring gene, *GJB6*, also harbors a mutation. The most common abnormalities in *GJB6* are large deletions that truncate *GJB6* or abolish *GJB2* expression.[17] Patients who are homozygous for a mutation in *GJB6* demonstrate autosomal recessive SNHL, or may develop SNHL if there is also mutation in *GJB2* on the opposite allele.[4]

*OTOF (otoferlin):* This mutation, located at the DFNB9 locus, is associated with nonsyndromic autosomal recessive hearing loss. Up to 50% of cases with mutations in

both *OTOF* alleles demonstrate auditory neuropathy in which OAEs are present in the absence of ABR responses. Testing for this mutation should be considered in cases of suspected auditory neuropathy auditory dyssynchrony.[17]

### X-linked

*DFN3:* In this genetic form of hearing loss, patients exhibit a mixed conductive-SNHL, characteristic inner ear dysplasia, and stapes fixation.[17] Imaging demonstrates dilation of the internal auditory canal with abnormal communication between the subarachnoid space and endolymph. This abnormality is associated with the development of perilymph gusher with disruption of the oval window and is a contraindication to stapedectomy.[4,17] It has been mapped to mutations in the gene *POU3F4*.

## Nongenetic

Approximately 25% of congenital hearing loss cases are acquired secondary to environmental causes such as infection, prematurity, ototoxic exposures, and trauma. In the remaining 25% of cases, the cause of hearing loss is unknown; however, some authors suggest these cases are due to unknown genetic factors.[4] This is not surprising given the complexity of the auditory system and genetic heterogeneity, which make gene identification a challenge.[4] It is likely that whole exome sequencing will become more available over time due to a decrease in cost and a progressive increase in understanding of the identified mutations. In the future, it is likely that a number of the cases with no known cause will be rediagnosed with a specific genetic mutation.

### Perinatal Causes

Low birth weight, asphyxia, hypoxia, and NICU admission are all associated with hearing loss. Additional perinatal risk factors for hearing loss include persistent pulmonary hypertension, respiratory distress syndrome, hyperbilirubinemia, and ECMO. These peri- and neonatal risk factors account for 12.6–18.9% of bilateral profound SNHL cases and prevalence may reflect trends in improved NICU survival.[19] Low birth weight, <1500 g, is the most common risk factor in the NICU population.[19] Neonatal infections, such as sepsis and meningitis, and exposure to ototoxic medications are also associated with increased hearing thresholds.[6]

### Infectious Causes

Prenatal infections secondary to maternal exposure to the TORCH organisms (toxoplasmosis, rubella, CMV, herpes simplex, and syphilis) and viruses, as well as postnatal meningitis from *Neisseria meningitides, Haemophilus influenzae, Streptococcus pneumoniae, Escherichia coli, Listeria monocytogenes, Streptococcus agalactiae,* and *Enterobacter cloacae*, are associated with hearing loss.[14] However, with improved prenatal care and immunization programs, these are becoming increasingly less common.[7,19] Congenital CMV infection, however, may be asymptomatic and remains an important cause of congenital hearing loss.

### Cytomegalovirus

CMV is the most prevalent congenital infection in the United States and the most common cause of acquired (nongenetic) congenital hearing loss, accounting for 10–60% of cases.[20,21] Infection occurs by vertical transmission, which can be intrauterine, intrapartum, or postnatal. Maternal infection may be primary, result from reactivation of a latent infection, or due to reinfection with a different viral strain,[20] and occurs in 2–6% of pregnancies.[22] Postpartum infection is most commonly caused from the breast milk of an infected mother.[20] The worldwide prevalence of congenital CMV infection is 7 per 1000 births. Only 12.7% of infections are symptomatic at birth[23]; infection cannot be identified by clinical examination in the majorty of neonates affected by congenital CMV.[24] Neonates with symptomatic infection exhibit a "blueberry muffin rash", petechiae, intrauterine growth restriction, microcephaly, hepatosplenomegaly and jaundice with associated hyperbilirubinemia, thrombocytopenia, and elevated hepatic transaminases. Over 50% of symptomatic infants develop neurologic sequelae, including SNHL, learning disability, and visual impairment.[25]

A total of 15–65% of affected patients develop hearing loss,[21] including 4.4–10% of patients who are asymptomatic at birth.[20,26] The pattern of hearing loss associated with CMV infection is variable—it may be unilateral or bilateral, delayed in onset, or progressive.[14] Hearing may be normal at birth; therefore, only approximately 50% of congenital CMV-related SNHL is identified by newborn hearing screening.[24,27] The median age at first progression of loss and detection of hearing loss in children affected by congenital CMV is 18 months and 27 months, respectively.[28]

After 3 weeks of age, it is difficult to diagnose if CMV infection is congenital or acquired. While universal screening for congenital CMV is not recommended currently, the development of dried blood spot, urine, and saliva polymerase chain reaction (PCR) amplification assays makes congenital CMV easier to detect and newborn screening a growing possibility.[24,29] PCR is replacing urine viral culture, the previous gold standard, as the most efficient and sensitive method of CMV detection.[20] In particular, PCR of both liquid and dried salivary samples is gaining popularity due to its high rates of sensitivity and specificity, as well as ease of collection, storage, and transport.[20,24] Some authors argue that salivary PCR is now the diagnostic test of choice to detect congenital CMV.[20,24]

Evidence-based recommendations for the management of congenital CMV are limited.[20] Complete blood count (CBC) and liver function tests (LFTs) should be obtained. If hepatic disease is present, coagulation studies should also be ordered.[20] Cranial ultrasounds (CrUSS) should be used to assess for intracerebral calcifications and other abnormalities in all children with confirmed congenital CMV. MRI imaging is reserved for children with symptomatic disease, or as follow-up imaging in patients found to have abnormal CrUSS.[20] All infants with congenital CMV should also undergo an ophthalmologic assessment as well as a baseline audiologic evaluation, which should be repeated every 3–6 months until age three, then annually until age six.

Several trials have demonstrated that early treatment of children with symptomatic congenital CMV with 6 weeks of intravenous ganciclovir at 6 mg/kg dosing twice daily results in hearing improvement or stabilization as well as decreased developmental delay independent of hearing level.[30-32] Currently, antiviral treatment is only recommended for symptomatic newborns (< 30 days) with central nervous system or severe focal organ system involvement.[20] Due to lack of data proving its efficacy, antiviral therapy is not indicated for older patients, patients with asymptomatic disease, or those without CNS involvement. Neonates on ganciclovir treatment are at risk for central venous catheter infections and pancytopenia, requiring weekly monitoring. Additionally, because ganciclovir is renally excreted, patients receiving therapy require weekly testing of creatinine clearance and therapeutic drug levels. Whole blood CMV viral load levels should also be obtained weekly to assess drug efficacy. Valganciclovir, the oral prodrug of ganciclovir, is also being studied; however, there is not yet published data from prospective randomized trials on its efficacy or comparing outcomes to those obtained using ganciclovir therapy, which is the current standard of care.[20,33,34]

### *Metabolic Disorders*

Multiple metabolic disorders are associated with the development of SNHL, and should be considered in children with affected siblings, from consanguineous unions, developmental delay, or dysmorphic features.[6] Metabolic conditions include disorders of amino acid production (phenylketonuria), polysaccharide metabolism and storage (Hurler, Hunter), neurotransmitter metabolism (Canavan disease), mitochondrial metabolism (MELAS, MERRF), and peroxisomes (Refsum, Zellweger syndromes).[6]

### *Other Causes*

Noise exposure, even in utero, is associated with high-frequency hearing loss. Infants born to mothers with occupational noise exposure are at increased risk for SNHL by as much as threefold. After birth, noise-induced hearing loss can result from recreational activities and exposure to fireworks.[6] Head trauma may result in hearing loss due to temporal bone fracture, posttraumatic perilymphatic fistula, or in children with temporal bone abnormalities, such as enlarged vestibular aqueduct. Exposure to ototoxic medications, including aminoglycosides and platinum-based chemotherapeutic agents, as well as radiation, can also lead to hearing deficits.[6]

## MEDICAL EVALUATION

A careful history and physical examination, including objective audiometric data, are the first steps in determining the cause of a child's hearing loss. This information may be sufficient to diagnose the cause of hearing loss or may help direct further diagnostic studies, such as genetic testing or imaging.

### History

A careful history should be obtained to determine maternal and prenatal risk factors, perinatal events and risk factors, and history of environmental exposures (such as to drugs or trauma). A directed history of speech and language development milestones may help determine when hearing loss occurred. The point at which

**Table 6.1:** History taking: Risk factors for congenital and childhood hearing loss

| *Prenatal* | *Examples* |
|---|---|
| Maternal infections | TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex, syphilis) |
| Maternal exposure to toxic agents | Aminoglycosides, furosemide, quinine, chloroquine, thalidomide, alcohol, tobacco |
| Maternal metabolic disorders | Diabetes, hypothyroidism |
| *Perinatal* | *Examples* |
| Prematurity | |
| Low birth weight | < 1500 g |
| Hypoxia, low APGAR scores | 0–3 at 5 min; 3–6 at 10 min |
| Hyperbilirubinemia | |
| Sepsis | |
| NICU admission | |
| Extracorporeal membrane oxygenation (ECMO) | |
| Exposure to ototoxic medications | |
| *Postnatal* | *Examples* |
| Viral illness | Varicella, measles, mumps |
| Bacterial meningitis | |
| Otitis media with effusion | |
| Trauma | Head trauma, noise exposure |
| Metabolic disorders | Hypothyroidism, glycogen storage disease |
| Neurodegenerative disorders | |
| Genetic syndrome, other organ system abnormalities | Visual impairment, kidney disease, history of syncope |
| *Family history* | *Examples* |
| First and second degree relatives with hearing loss | |
| Common origin from ethnically distinct areas of the world | Ashkenazi Jews, Japanese |
| Consanguinity | |

Adapted from Lin and Oghalai[7] and Mafong et al.[15]

hearing loss developed, whether it was identified during prenatal screening or occurred in a delayed fashion, may help to determine the etiology; however, it should be noted that some genetic forms of hearing loss, as well as infectious disease-related loss, may be progressive or occur after the postnatal period. Over 400 syndromes associated with congenital hearing loss have been identified involving abnormalities of many other organ systems.[35] Therefore, other system abnormalities should be noted in the history, bearing in mind that collaboration with other specialists may be needed to identify the syndromic causes of hearing loss when present.[7] Identification of syndromic cases is crucial, as it may help guide discussions of prognosis, anticipated complications or involvement of other organ systems, such as in Usher's syndrome, and further management.[15]

Obtaining a detailed family history that includes three generations may help in determining if there is a hereditary basis for the hearing loss and guide confirmatory genetics testing.[14] Table 6.1 summarizes important elements of the history.[6,7]

## Physical Examination

A focused otolaryngologic physical examination of the head and neck should be performed to assess craniofacial

structures and the external and middle ear. Head size and symmetry, maxillary development, jaw size, and facial movement, and other cranial nerve function should be noted. The size, position, and shape of the pinna and external ear, as well as middle ear morphology, should be examined. These may help to identify syndromic features or causes of a conductive hearing loss, such as middle ear effusion, microtia or external canal atresia, branchial cleft pits or fistulae, pigmentary and ocular abnormalities.[6,7]

An important adjunct to the physical examination is the objective data from audiologic evaluations. ABR and auditory-steady state evoked potentials (ASSR) can be measured in neonates to help identify auditory thresholds. In older children, behavioral audiometry, obtained with visual reinforcement, or play audiometry may also be used. OAEs, the absence of which may suggest a cochlear abnormality, may also be useful, though not specific. Nonsyndromic, genetic hearing loss is most commonly sensorineural, while acquired and syndromic hearing loss may be conductive, sensorineural, or mixed.[7]

## DIAGNOSTIC TESTING

### Laboratory Testing

History, physical examination, and audiologic testing are essential components in the workup of congenital hearing loss. The use of further diagnostic studies in the workup of pediatric hearing loss is less clear. When the history and physical examination point toward a specific diagnosis, the decision about which ancillary tests to order can be straightforward. However, when the cause of hearing loss is unknown, the number of studies available is exhaustive. These include ECG and various laboratory tests, such as a CBC, platelets studies, autoimmune tests, such as ANA, ESR, and rheumatoid factor, thyroid function studies, blood urea nitrogen, creatinine, and urinalysis.[15] Routine laboratory testing has a low diagnostic yield, leading some authors to reconsider their use of a comprehensive battery of testing to evaluate children with unexplained SNHL.[15,36] Instead, laboratory testing should be individualized and directed toward a suspected diagnosis.[4]

Most authors, however, agree that all children with profound bilateral hearing loss of unknown etiology should undergo an ECG to evaluate for QT interval prolongation, which is suggestive of Jervell and Lange-Nielsen syndrome, or other conductive abnormalities. Albeit rare, the detection of these cardiac abnormalities could be lifesaving.[15,37] Similarly, if the results for maternal syphilis screens are unknown, venereal disease research laboratory and fluorescent treponemal antibody should be performed to identify cases of asymptomatic neurosyphilis, as initiation of treatment could prevent progression or the development of symptomatic disease.[37] Because congenital CMV infection is another important cause of idiopathic congenital SNHL, and treatments are available, we argue that CMV testing using urine or saliva PCR should be performed in children with nonsyndromic SNHL of unknown etiology within the first 6 months of life.

A summary of ancillary tests and their utility is provided in Table 6.2.

### Radiographic Imaging

Of all the tests used to determine an etiologic diagnosis for congenital hearing loss, high-resolution CT imaging has the highest yield, identifying a cause in up to 26–37% of cases.[15,19] CT imaging is used to evaluate bony anatomy, while MRI allows for visualization of the membranous labyrinth, internal auditory canal, and cortical structures which are essential components of the auditory system.[15] Radiographic imaging may not only identify the specific cause of hearing loss, but also guide appropriate treatment options.[15] For example, in children found to have enlarged vestibular aqueduct and Mondini malformation, Pendred syndrome should be considered and patients should be counseled regarding activity restrictions, as even minor head trauma may result in progressive hearing loss.[15] If internal auditory canal dysplasia is noted, calling the presence of an auditory nerve into question, cochlear implantation should be reconsidered.

### Genetic Testing

In patients who demonstrate no clear etiology for hearing loss based on physical examination and imaging studies, genetic testing can increase the likelihood of identifying a diagnosis.[38] Genetic testing may allow for accurate and early diagnosis, which can help to maximize early intervention strategies to facilitate cognitive development and provide information about prognosis. Identification of syndromic cases before a particular phenotype is exhibited may guide additional testing or interventions.[38] Identification of the genes involved also allows for genetics counseling and risk stratification.[4,38] It may also reduce parental guilt and anxiety.[17]

Over the past several decades, significant advances have been made in the field of genetics, with identification of new genetic targets in SNHL, as well as the development of more cost-effective, efficient methods of genetic

**Table 6.2:** Ancillary studies and associated hearing loss etiologies

| *Diagnostic yield* | *Study* | *Associated etiology of sensorineural hearing loss* | *Cases in which testing may be helpful* |
|---|---|---|---|
| Low | ANA, ESR, RF, anticardiolipin, immunoglobulins, complement studies | Autoimmune hearing loss (juvenile rheumatoid arthritis, lupus) | Other symptoms of autoimmune disease |
| | CBC | Thalassemia, sickle cell trait, leukemia, lymphoma | Clinical suspicion for leukemia or lymphoma based on other findings (prolonged illness, gingival bleeding, bone or joint pain) |
| | Platelet studies | Hereditary macrothrombocytopenia (Fechner syndrome, a variant of Alport syndrome) | Family history of Fechner syndrome (autosomal dominant inheritance pattern) |
| | Glucose | Wolfram syndrome, Alstrom syndrome, diabetes | Maternal inheritance or autosomal recessive pattern of type 2 diabetes or diabetes insipidus, ocular abnormalities, obesity |
| | Urinalysis looking for proteinuria, hematuria | Alport syndrome, metabolic disorders | Personal or family history of Alport syndrome or hematuria |
| | BUN, creatinine | Alport syndrome | History of abnormal urinalysis |
| | Antibody titers | Toxoplasmosis, Rubella, CMV, herpes simplex | Within 3 weeks of birth with maternal history of disease or exposure |
| | Thyroid studies (FT4, T3, TSH, perchlorate test) | Pendred syndrome, cretinism | Goiter, history of hypothyroidism, evidence of Mondini malformation or EVA on imaging |
| Low but intervention may be lifesaving, preserve vision | RPR, FT-ABS | Syphilis | Maternal history is unknown |
| | ECG | Jervell and Lange-Nielsen syndrome | History of syncope, arrhythmias, family history of sudden death. |
| | Ophthalmology consultation | Usher syndrome, Alport syndrome, Cogan's syndrome, Norrie disease, Stickler syndrome, congenital CMV | History of vestibular abnormalities or myopia; family history |
| High | CT Temporal bone | Temporal bone abnormality (EVA, Mondini malformation) | Consider in cases where etiology is unknown |
| | MRI of IAC, brain | Cochlear nerve hypoplasia/aplasia, CPA mass, brain lesion | |
| | Genetic testing | Connexin 26/30 Mutation | |
| | Viral culture or PCR | Cytomegalovirus (CMV) | |

Adapted from Lin and Oghalai.[7] and Mafong et al.[15]

testing. Because *GJB2* is the most common cause of nonsyndromic genetic SNHL, most authors agree that *GJB2* analysis should be the first step in mutation analysis.[4] If genetics testing reveals no or only one copy of a mutation in *GJB2*, analysis of *GJB6* should also be considered.[4,17,38] *SLC26A4* testing should be performed if imaging demonstrates evidence of Mondini dysplasia or enlarged vestibular aqueduct, if hearing loss is progressive, or if a goiter is present.[17] If auditory neuropathy is suspected, *OTOF* should be evaluated.[17] *COCH*, the mutation of which is associated with an autosomal dominant form of hearing loss, should be tested for mutations in cases with progressive hearing loss and vestibular dysfunction.[17] Many genes have also been identified for Usher's syndrome and should be considered for analysis in the presence of an Usher's phenotype.

The methods used for genetic testing are evolving. DNA sequencing, such as with the Sanger method, is the most comprehensive and definitive method of analysis, because it allows for the detection of small deletions and

insertions, as well as point mutations. This method is limited, however, because it may not detect deletions of entire exons or genes, analysis and interpretation are labor intensive, and sequencing is expensive.[4,17,38] Therefore, only the small number of genes responsible for a large proportion of hearing loss, such as *GJB2*, are sequenced to screen for mutations in the routine clinical setting.[38] This limits the number of patients in whom a genetic cause can be identified.

Many genetic forms of hearing loss result in phenotypically similar severe-to-profound hearing loss. Therefore, it is difficult to predict the genetic cause to guide genetic testing. As an increasing number of genes are identified for testing, Sanger sequencing is becoming a less practical option. New DNA sequencing technologies that allow for cost-effective, complete screening of all known deafness genes are being developed.[17,38] Most laboratories currently use solution-based capture, in which DNA probes customized to genomic regions of interest are hybridized to fragmented DNA samples. Fragments that hybridize with the selected probes associated with hearing loss are then sequenced. Gene chip technology, such as the Affymetrix DNA resequencing microarray platform, was previously used; however, sequencing was inaccurate, making interpretation difficult.[17] Next generation sequencing technologies offer improved sequencing accuracy[17] and are being introduced into the market as a diagnostic tool. The clinical utility and interpretation of these assays are more reliable than gene chip testing but are still being investigated. Currently, there are a limited number of laboratories (University of Iowa, OtoSCOPE and Harvard Medical School Laboratory for Molecular Medicine, OtoGenome) in the United States that offer solution-based capture and next generation sequencing for diagnosing SNHL as a diagnostic tool for patient care. They do not offer whole exome sequencing but rather assess patients' DNA for mutations in a limited number of known genes that cause hearing loss. There are many more laboratories that offer testing on a research basis only. This field is rapidly expanding and when a complete genetic screening system is available and affordable, it will allow for genetic testing of patients who fail their universal newborn hearing screen and dramatically increase the number of hearing loss cases with an etiologic diagnosis.[38–40]

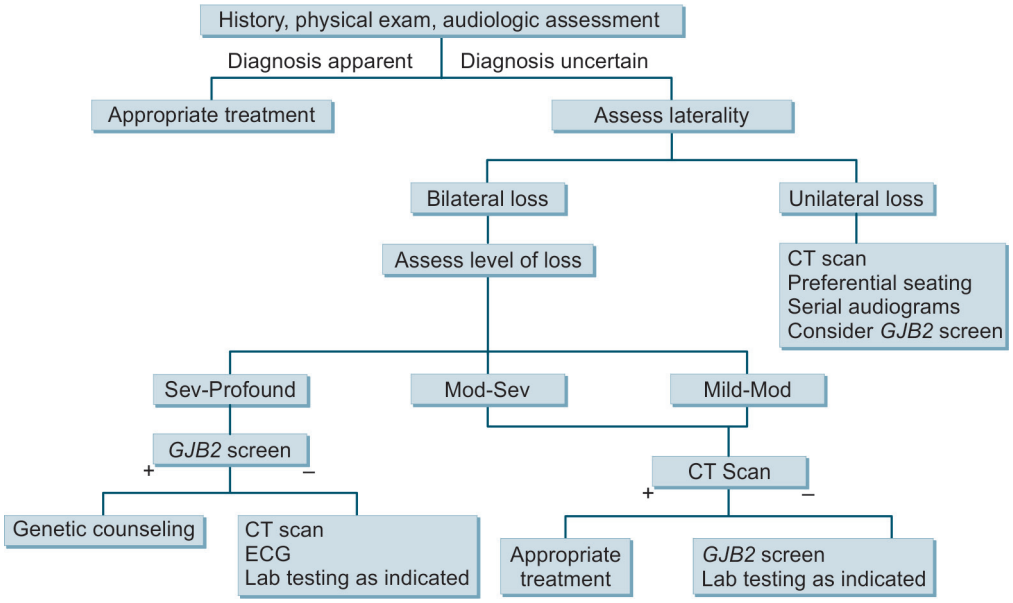
The results of genetics testing should be interpreted with caution—not all mutations are pathogenic and a negative test does not exclude genetic deafness, as discovery of genes associated with congenital hearing loss is ongoing. Results need to be interpreted correctly and communicated clearly to patients and their families. This burden often falls on pediatricians or clinical geneticists with a genetic counseling background.[17] Genetic testing also raises ethical concerns and should not be performed without consent and full disclosure to a child's parent or guardian. Importantly, genetic testing is not necessarily perceived as advantageous, particularly in the deaf community. However, recent surveys indicate that genetic testing for hearing loss is becoming increasingly accepted, in both the hearing and nonhearing communities.[41]

## Testing Algorithms

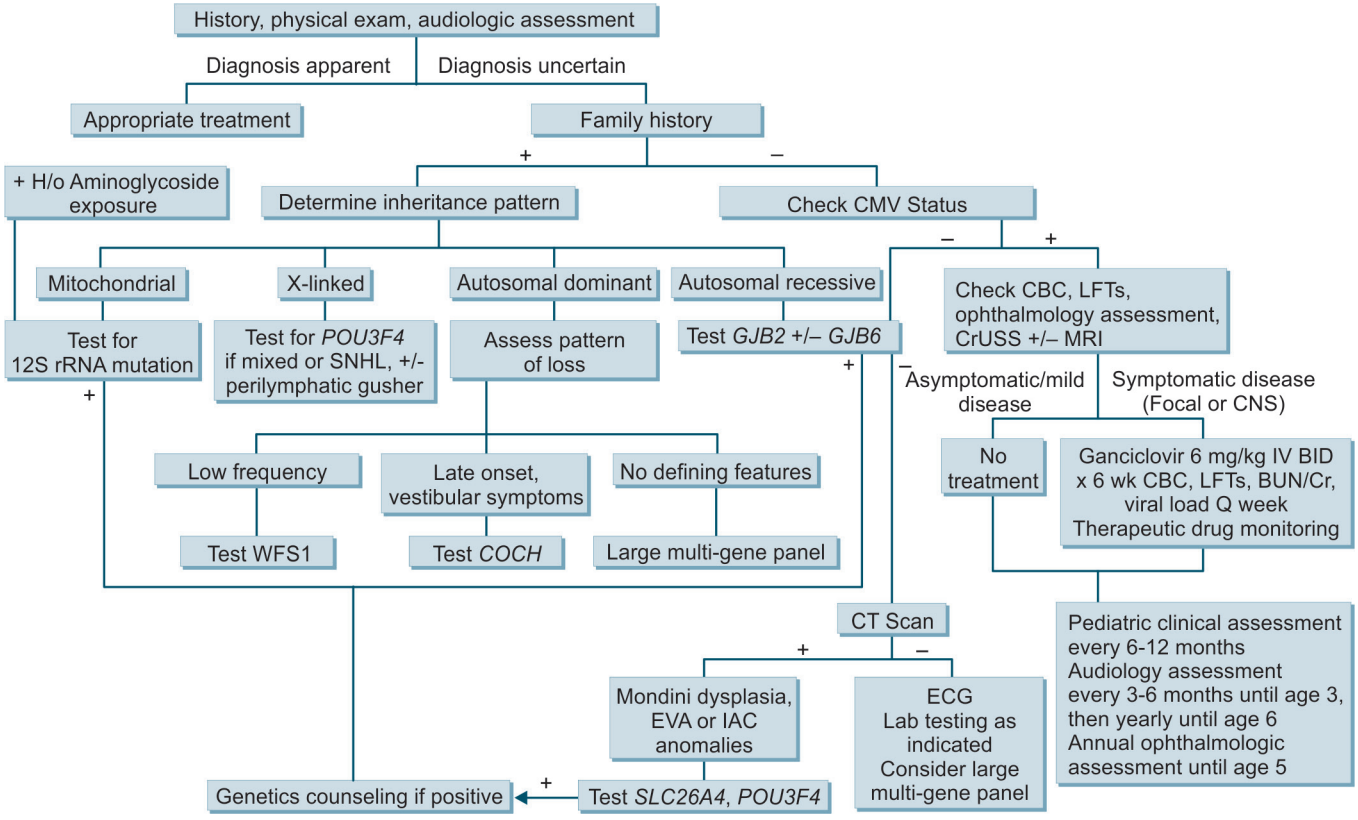
Currently, there is no consensus regarding the battery of tests that should be performed in cases where the cause of hearing loss in unknown. However, evidence-based, cost-effective models have been proposed.[15,37,42] In 2005, Preciado et al. published a sequential diagnostic algorithm tailored to the level of hearing loss in children with bilateral SNHL of unknown etiology; this method was found to be more diagnostically and cost-effective than a simultaneous testing approach.[37] Flowchart 6.2 outlines Preciado's algorithm. In this model, children with unilateral hearing loss should first undergo diagnostic imaging, as this testing provides the highest diagnostic yield. Children with bilateral hearing loss are stratified based on level of impairment—mild-moderate, moderate-severe, severe-profound. Those with mild-moderate and moderate-severe loss first undergo CT imaging, then go on to genetics testing for *GJB2* if imaging workup demonstrates no abnormalities, with additional laboratory testing if indicated. Children with severe-profound loss first undergo *GJB2* testing. If genetics evaluation is negative, they then undergo imaging studies, followed by ECG and additional laboratory testing if indicated.

While Preciado's model is evidence based, it does not take the prevalence of CMV-related nonsyndromic hearing loss into account. Additionally, since 2005 significant progress has been made in the field of hearing loss genetics. New algorithms have also been proposed to guide further genetics testing in cases where *GJB2* testing is negative.[38] In Flowchart 6.3, we provide a sequential diagnostic algorithm which incorporates additional genetic testing and the role of congenital CMV. The cost-effectiveness of this algorithm has not been tested; however, it may increase diagnostic yield over Preciado's algorithm. All patients should undergo a thorough history, physical examination, and audiologic evaluation. If the diagnosis is apparent by history, appropriate treatment should be offered. If not, family history should be considered. If the family history demonstrates

**Flowchart 6.2:** Preciado's sequential diagnostic paradigm, 2005. Adapted from Preciado et al.[37]




**Flowchart 6.3:** Diagnostic algorithm for determining the etiology of congenital hearing loss. Adapted from Preciado et al.[37]; Brown and Rehm[38]; and Kadambari et al.[20] Genetic testing would be indicated if testing for WRS1, COCH and large multi-gene panel were positive.



a particular inheritance pattern this should guide genetics testing. For patients who have no family history, testing for CMV should be initiated within the first 6 months of life. If CMV testing is negative, or if the family history suggests an autosomal recessive inheritance, *GJB2* with or without *GJB6* testing should be performed. For patients who test negative, imaging should be pursued. Further genetics testing should be performed if imaging suggests internal auditory canal dysplasia (*POU3F4*), Mondini malformation, or EVA (*SLC26A4*). In cases where imaging yields no apparent abnormality and the etiology of hearing loss remains unknown, ECG and further laboratory testing (such as urine analysis and syphilis testing) should be considered. Further multigene panel testing may also be performed to identify the presence of less common genetic mutations associated with congenital hearing loss. In children who test positive for CMV, additional studies including CBC, LFTs, an ophthalmologic evaluation and cranial ultrasound should be performed. Children who are symptomatic should receive ganciclovir therapy if they are less than 30 days of age. All children with evidence of CMV, whether symptomatic or asymptomatic, required close follow-up with serial audiograms and ophthalmology evaluations.

## HEARING INTERVENTION

The overriding goal of hearing rehabilitation is to maintain both social and academic integration within society. It is well known that children who are inadequately rehabilitated often lag in both these indices. For patients who have a hearing loss that cannot be corrected with early medical management, hearing intervention is indicated. Infants who have failed a newborn hearing screen and have hearing loss confirmed by follow-up ABR can be fit with hearing aids as early as 3 months of age. There is some difficulty in fitting infants due to the small ear canal size and the inherent masking of near-normal sounds due to the fit of the ear mold. Hence, not all hearing professionals agree that hearing aids are indicated in children with mild hearing loss and very small ear canals. For children with a mild hearing loss of 25 dB or greater in both ears, hearing aids and/or frequency modulation (FM) systems are generally indicated. There is growing evidence that patients with a unilateral loss may also benefit from amplification in the diminished ear[43,44]; however, considerable uncertainty and variability in practice exists among care providers. Research in this area began after multiple studies highlighted academic and language difficulties experienced by children with unilateral hearing impairment. However, not all children with unilateral loss benefit from amplification. Current practice trends appear to be leaning toward a trial of amplification.

The use of hearing aids with or without an FM system for patients with bilateral moderate-to-severe hearing loss is fairly well accepted and little variability exists in recommendations as to the use of auditory rehabilitation. Currently, cochlear implantation is indicated for children who have > 80 dB hearing loss in both ears and can be performed as early as 1 year of age. Cochlear implants can partially restore hearing by directly stimulating surviving hair cells, supporting cells and acoustic nerve fibers. Optimally, cochlear implant candidates should demonstrate favorable anatomy, including a normal cochlea and robust acoustic nerves, and minimal to no cognitive impairment. However, hearing professionals have found a wide array of patient variants that have benefitted from cochlear implants.[45] A full discussion of hearing restoration in the pediatric patient can be found in Chapters 16, 21, 22, and 23.

Many factors are taken into account to determine the optimal hearing restoration plan for each patient. These include but are not limited to performance using a hearing aid, anatomic factors within the cochlea and acoustic nerve, confounding developmental diagnoses that may affect cognitive and/or motor abilities (such as the cognitive delays precluding the ability to develop language, inability to use sign language or expected decline in vision inherent in Usher's syndrome) and the family's belief about the correct form of communication for their child. Infants and children with hearing loss are best served by a multidisciplinary team that includes otolaryngology, speech pathology, audiology, neurology, ophthalmology, genetics, neuropsychology, and social work. Often children need to be followed over time since their developmental status may not be apparent early-on. Families need to be supported, not only to help guide making good clinical decisions for their children, but also because of the added emotional and financial burden of caring for a child with hearing loss. Lastly, members of the deaf community may have expectations about what constitutes the best form of communication for their child, which should be respected by the health-care professional.[46]

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CHAPTER

# 7 Embryology and Congenital Abnormalities of the External Ear

*Douglas R Sidell, Daniel I Choo*

## INTRODUCTION

The external ear plays an important role in the overall appearance of the face. Although slight variation in the position, shape, and size of the auricle are seen across populations, auricular abnormalities often distract a viewer's gaze away normal facial anatomy. Several congenital auricular abnormalities have been described, and each is derived from disturbances in the normal development of the external ear. Embryogenesis of the auricle occurs in harmony with the development of other branchial arch derivatives, including the external auditory canal and middle-ear cleft. As a result, auricular abnormalities frequently occur in the setting of abnormalities of the external auditory canal and middle ear. While this is an important consideration for the clinician and surgeon, this chapter deals primarily with the etiology, classification, presentation, and management of auricular abnormalities.

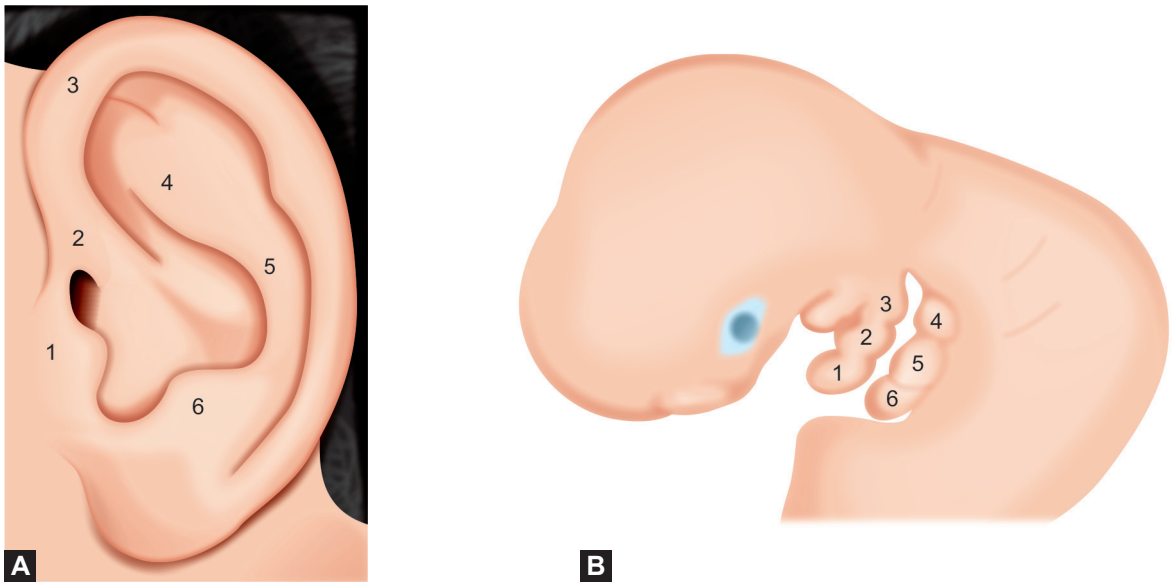
## A BRIEF REVIEW OF EMBRYOLOGY

Otologic development lies on a continuum that begins during the third week of embryogenesis, at which time the auditory placode is recognized as a thickening lateral to the acousticofacial ganglion. During the fifth gestational week, mesenchymal proliferation of the first and second branchial arches produces hillocks that surround a primitive external auditory meatus. The auricle itself is arguably derived from three hillocks that arise from the first arch (hillocks 1–3) and three hillocks that arise from the second arch (hillocks 4–6) (Figs. 7.1A and B). Some authors suggest that the first arch contributes only to the tragus (hillock 1), while the remaining structural components of the auricle (hillocks 2–6) are derived from second-arch mesenchyme.[1,2] Regardless of derivation, most authors would agree that by the end of the sixth gestational week, all hillocks are visible. The six hillocks then merge, achieving a near normal appearance by 17–18 weeks. Over the following 14 weeks, the auricle continues to migrate from its origin adjacent to the primitive pharynx, to its final destination at the lateral aspect of the head.[1] By 8 years of age, the auricle has reached > 95% adult size, yet it continues to enlarge throughout life.[1,2]

Any developmental arrest occurring along the prenatal embryologic continuum will result in varying degrees of auricular abnormalities, each detectable on physical examination. Additionally, some changes to the appearance of the auricle may occur after the majority of embryologic development has been completed. Pliability of the auricle is enhanced by elevated levels of hyaluronic acid under the direct influence of maternal estrogen. As a result, the auricle may be influenced by extrinsic compression prior to delivery but after the greater part of embryologic development.[3–5] This phenomenon is thought to be one mechanism leading to congenital anomalies in which the auricle is completely formed, but has an abnormal shape and appearance. The same principle of increased pliability can also be advantageous in the treatment of such patients.

## HEREDITY OF AURICULAR ABNORMALITIES

A tight association exists between our genetic makeup and embryologic tissue abnormalities. Several genes have been implicated in the normal development of the




**Figs. 7.1A and B:** The auricle itself is arguably derived from three hillocks that arise from the first arch (hillocks 1–3) and three hillocks that arise from the second arch (hillocks 4–6).

pinna, and as such, mutations in these genes may contribute to frank auricular abnormalities. Although some specific mutations have been described in their association with abnormal development of the external ear, the majority of events occur in patients in the absence of an associated syndrome or known genetic abnormality. In contrast, several genes have been implicated in syndrome-associated auricular abnormalities, and may be inherited in an autosomal recessive, dominant, or X-linked pattern. Treacher-Collins syndrome (autosomal dominant), branchio-oto-renal syndrome (autosomal dominant), and oto-palatal-digital syndrome (X-linked) are but a few examples.

## AURICULAR ANATOMY

Auricular abnormalities include subtle variations among the anatomic proportions of an auricle that is otherwise normal; they may also present more obviously, with a complete or partial absence of the external ear. The former category includes abnormalities such as the prominent ear or protruding ear, and represents those variations that are considered to deviate from established esthetic norms. In contrast, more obvious auricular abnormalities, such as those seen in patients with microtia, have a strong genetic influence and are more frequently associated with other otologic abnormalities or genetic syndromes. The specific embryologic influence of the genetic code on various components of auricular development is becoming a topic of increasing interest. A complete understanding of normal anatomic proportions and growth patterns of the auricle are therefore an important element of the pediatric otolaryngologist's practice. Several attempts have been made to classify the esthetic properties of the auricle, and a series of accepted normal values for auricular dimensions has been established and are discussed below. Despite this, the esthetic norms attributed to the auricle have seen changes over time, and differ between races and cultures. As a result, it is important to remember that a single definition of "correct" esthetic proportions does not exist, and each evaluation should be taken in the context of the whole patient.

### Normal Dimensions

The adult auricle ranges in length from approximately 5–6.5 cm, and the width is typically 50–60% of auricular length. Although the ear continues to grow slowly throughout life, the vast majority of both vertical and horizontal growth occurs in the first decade. However, the pediatric auricle grows disproportionately, such that the length of the ear reaches adult measurements prior to the width, and the rapidity of growth is thought to be faster in females.[6] The pediatric auricle reaches 85–90% of adult width within the first year of life, and >95% of predicted width within 10 years. In contrast, the length of the ear is approximately 70–75% of adult length within the first year, reaching >90% of expected adult length within 10 years. [6,7]

### Normal Orientation

The auricle resides on a line approximately one ear-length posterior to the lateral canthus, extending from the level of the brow posterosuperiorly at a 15°–30° angle. The vertical and horizontal position of the ear must be evaluated when considering the individual patient's facial structure and adjacent anatomy. It should be noted that some degree of variability when considering ear position within the individual is also acceptable. The majority of patients have some amount of positional asymmetry between each ear. However, the ability for one to recognize this difference is probably the only factor that brings an acceptable difference into the realm of being abnormal; the definition is thus very subjective.

The normal auriculocephalic angle is crudely defined as the angle between the pinna and the cranium. Although this angle can be acceptably more obtuse when the ear is wide, a normal measurement is described as being < 35°, and may range from 15° to 20° at birth to > 30° during adulthood.[8] As described by Farkas[7] the mean measurement of this angle is 25° in adult men and 21° in adult women.[6,7]

## THE PROMINENT OR ABNORMALLY SHAPED EAR

The true incidence of abnormally shaped ears is likely underestimated, as many abnormalities fall on the less-severe spectrum of auricular deformities and are thus frequently excluded from the literature.[6] The prominent ear is loosely defined as falling outside of the boundaries of the previously described measurements for protrusion. In reality, the presence of a protruding ear reflects abnormalities in the normal folds of the auricle itself, thus manifesting as the composite result of such abnormalities. For example, the antihelical crease is created by the folding of auricle between the helix and scapha, thus placing the helical rim adjacent to the scalp. Loss of the antihelical crease results in an obtuse conchoscaphal angle (> 90°), thereby creating an obtuse auriculocephalic angle and wide or deep conchal bowl. As a result, prominence of the ear can be explained by abnormalities in the development of the antihelix and concha. Other variations in the development of the auricular subunits may occur in conjunction with the prominent ear, or represent unique manifestations that vary from the esthetically accepted normal. Some of these abnormalities may overlap with the definition of microtia, and a list of such auricular abnormalities is presented in Table 7.1.

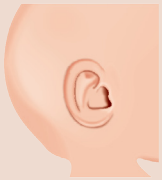
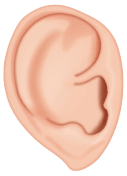
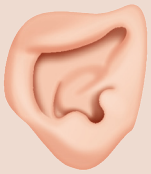
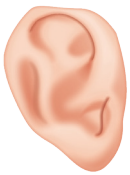
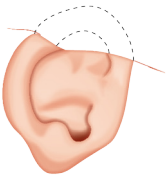
## PATIENT EVALUATION

Otoplasty for the correction of the protruding or abnormally shaped auricle is the most frequently performed esthetic surgery in the pediatric population. Evaluation of the patient suspected to have auricular prominence must be performed in the context of the individual, using standard measurements only as guidelines during the examination. More importantly, facial structure, auricular symmetry, head shape, and hairline must all be considered during analysis. Because definitions vary greatly among the literature, true prominence is often a matter of opinion.[9] As a result, the decision to intervene is unlikely to be made based on physical findings alone, but instead relies on a discussion between the patient, the family, and the physician. Additionally, nonsurgical interventions have gained increasing popularity over the past two decades. These methods, using external splints, provide a low-risk intervention that may be implemented in the neonatal period.[3]

### Nonsurgical Intervention

Multiple studies exist that demonstrate the ability to nonsurgically mold congenital auricular abnormalities shortly after birth. The first publications formally discussing these techniques originated in the Japanese literature in the 1980s. Several variations in nonsurgical molding have subsequently been described,[10–13] but all techniques rely on external splinting to maintain the normal shape and position of the auricular cartilage during early development. Of the previously mentioned congenital deformities of auricle, the cup ear, prominent ear, and Stahl ear are all amendable to nonsurgical molding.[10] The fundamental efficacy of this process is thought to occur secondary to estrogen-driven increases in the concentration of hyaluronic acid in the extracellular matrix of the auricle in the early days of life.[4,5,14,15] After birth, hyaluronic acid concentrations decline in concert with estrogen concentrations, thereby reducing auricular pliability. Despite the common belief that the ideal window for nonsurgical intervention is during the neonatal period only, some suggest that nonsurgical intervention may take place several weeks after birth. In one of the few prospective studies evaluating nonsurgical correction of the protruding ear, van Wijk and colleagues suggest that the time required for splinting increases proportionally with the age at the time of initiating treatment. The authors conclude that the best chance of success occurs in patients

**Table 7.1:** Auricular abnormalities

| *Auricular abnormality* | *Description* | *Figures* |
|---|---|---|
| Cup ear | Flat antihelix, helical overhang, wide concha, and a deceptively small auricle |  Cup ear |
| Shell ear | Underdeveloped helical rim; often accompanied by poorly defined antihelix |  Shell ear |
| Lop ear | Helical overhang; loss of support of helical rim |  Lop ear |
| Stahl ear | Flat antihelix; inconspicuous superior crus with a horizontal orientation; malformed scaphoid fossa |  Stahl ear |
| Macrotia | Ear size that exceeds normal anatomic proportions; enlargement often limited to superior 1/2 to 1/3 of ear. May have associated effacement of the helical fold | |
| Cryptotia | The superior auricle is buried beneath the skin of the scalp. May be accompanied by an underdeveloped scapha. Also referred to as "pocket ear" or "hidden ear" deformity |  Cryptotia |

who are treated prior to 6 weeks of age. In their study, 132 children (209 ears) were nonsurgically treated, with an average age of 8.8 weeks at the initiation of treatment. Efficacy was shown to deteriorate with age and older children were noted to require longer periods of splinting.[3] Although opinions vary among practitioners, many would agree that noninvasive auricular molding techniques have little applicability after 3 months of age. Additional arguments in favor of early intervention include the lack of manual dexterity, decreased head mobility, and decreased production of sweat during the neonatal period, all contributing to a greater degree of success with regard to maintaining splint placement. Regardless, the decision to attempt nonsurgical molding carries little risk to the patient, and does not preclude later surgical intervention. Skin irritation and difficulty maintaining splint placement are the most frequently encountered risk factors, and permanent sequelae are nearly nonexistent. Recently, commercially available devices for nonsurgical ear molding have become available, and reduce many of the difficulties

associated with splint placement and irritation. In 2010, the United States Food and Drug Association (US FDA) approved the EarWell (Becon Medical Ltd, Naperville, IL), a manufactured external splint with a touted 90% rate of success.[16]

## Surgical Intervention

After the neonatal period, or in patients experiencing unsuccessful nonsurgical intervention, surgical correction of auricular abnormalities is an available option. Timing of surgical intervention is based on our knowledge of auricular development during childhood, the patient's social environment, and parental concern. Waiting to intervene until age 3 allows the ear to reach 85–90% of adult dimensions, whereas operating prior to age 6 obviates exposure to ridicule in the school environment.

The goals of surgery for the protruding ear include the creation of the antihelical fold and reduction of the auriculocephalic angle. Correction of antihelical fold should occur in multiple locations along the length of the ear, and the postauricular crease should not be distorted. Several hundred otoplasty techniques exist; however, satisfaction among patients is relatively high regardless of the technique used. Techniques are often chosen based on the specific characteristics of the defect, the pliability of the cartilage (often more malleable in patients under 5 years of age) and surgeon preference and experience. Because protrusion of the auricle (unlike microtia) is frequently bilateral, the procedure should begin with correction of the most involved ear first. The second ear can then be corrected while maintaining symmetry with the first. If unilateral surgery is performed, discrete abnormalities in the less-involved auricle may become more noticeable, and patients often return for correction of the second ear. As a result, in the setting of a protruding ear that is predominantly unilateral, patient satisfaction is often enhanced when bilateral surgery is performed. The surgical technique most commonly employed for the correction of the protruding ear is the placement of horizontal mattress sutures on the posterior auricle as described by Mustarde.[18–19] This allows for the precise recreation of the antihelical fold. Reduction of the auriculomastoid angle and correction of the antihelix can also be performed if necessary by means of a conchal setback technique as described by Furnas.[20] This method draws the ear posteriorly by suturing the conchal cartilage to mastoid periosteum and fascia, and may improve esthetic results in select patients. Finally, elements of cartilage sculpting, suturing, and conchal setback are combined in the Farrior technique. This method involves using a "graduated approach" to achieve a customized outcome for the unique abnormalities of each ear. The simplest interventions are used first, and the ear is repetitively evaluated intraoperatively until the desired outcome is achieved.[21]

Similar to the protruding ear, cup ear deformity and Stahl ear deformity are both amendable to surgical correction. Stahl ear deformity is the result of a normal quantity of abnormally shaped cartilage that results in an inconspicuous superior crus with a horizontal orientation and a flat antihelix. Cup ear deformity is also frequently described interchangeably with lop-ear deformity. The cup ear deformity is notable for a flat antihelix, helical overhang, wide concha, and a deceptively small appearance of the auricle. Several surgical techniques exist for the correction of each abnormality, and involve cartilage scoring and suturing techniques as well as excision and grafting methods.[17,21,22]

Major complications following otoplasty are relatively rare, and include hematoma, wound infection, tissue necrosis, and keloid formation. Minor complications include persistent or recurrent protrusion, small ulcerations and the development of Herpes zoster infection.[21]

# MICROTIA

Significant variability exists among the definition of microtia within the literature. For the purposes of this chapter, microtia will be used to describe abnormalities of the external ear in which a component of the auricle is absent or small; the most extreme end of this spectrum being anotia, or complete absence of the auricle.

## Epidemiology

Luquetti and colleagues reviewed the epidemiology of microtia and determined that the reported prevalence varies from approximately 0.8–4 individuals per 10,000 births.[23] The heterogeneity in prevalence estimates is speculated to occur due to differences in inclusion criteria between studies, and due also to variations in the definition of microtia among researchers. Mild cases of microtia may be misclassified or not brought to clinical attention, thus impacting incidence and prevalence figures. It is agreed upon that males are more frequently diagnosed, and nonsyndromic microtia is thought to be unilateral in 70–90% of patients.[24] The right ear is more frequently affected for unknown reasons.[25]

## Genetics

The genetic complexities that are associated with the development of the external ear have become an area of expanding research over the past decade. Scientific advances in genetics research have allowed for the development of novel animal models, controlled human genetics studies, and subsequent investigations into single-gene disorders that are associated with microtia. Research has thus amassed in strong support of the genetic influence on microtia development.

Microtia may occur in isolation or in the setting of a syndrome or disorder. Inheritance patterns in familial microtia or syndromic patients with microtia are thought to be primarily Mendelian, and several genes have been identified in this setting. In support of this genetic basis for microtia, several syndromes with single-gene abnormalities are known to exist in conjunction with microtia, such as *EYA1* mutations in patients with branchio-otic syndrome. Additional syndromes having strong associations with microtia include Treacher-Collins syndrome, Miller syndrome, and the oculo-auriculo-vertebral spectrum.[23,26,27] To date, >20 syndromes associated with microtia have been reported, with varying incidences of auricular abnormalities among them. Although a detailed discussion of the genetic influences of microtia is beyond the scope of this chapter, to the interested reader we recommend "Microtia: Embryology and Genetics" by Daniella Luquetti and colleagues, for a more comprehensive discussion on the subject.[23]

In contrast to syndrome-associated microtia, sporadic cases are more likely to be due to multiple genetic abnormalities and/or environmental influences. Although the exact etiology of microtia is unknown, several environmental risk factors have been identified. Some of the more established risks include maternal acute illness, congenital rubella, low birth weight, higher parity, and maternal diabetes mellitus. In addition, medications such as thalidomide and retinoids have also been linked to the development of microtia.[23,28,29] Evidence has also been established in support of other risk factors leading to the development of microtia. Of these, living at high altitude, neural crest disruptions and vascular compromise to developing tissue have been cited as potential contributing events.[26,29–31]

**Table 7.2:** Weerda classification system for microtia

| | |
|---|---|
| First-degree dysplasia:<br>Most structures present | A. Macrotia<br>B. Protruding ear<br>C. Cryptotia<br>D. Upper helix absent<br>E. Small deformity<br>F. Colobomata<br>G. Lobule deformities<br>H. Cup ear deformity |
| Second-degree dysplasia:<br>Some structures present | A. Cup Ear deformity type III<br>B. Mini ear |
| Third-degree dysplasia:<br>No recognizable structures present | A. Unilateral<br>B. Bilateral<br>C. Anotia |

## Classification

With the broad spectrum of auricular abnormalities that accompany the diagnosis of microtia comes a multitude of classification systems developed to better categorize this phenomenon. Although several systems exist, the most commonly cited classification systems include the Weerda classification system (Table 7.2) and the Marx classification system (Table 7.3).[32,33] The Weerda classification system provides several terms that are frequently used in the diagnosis of microtia, yet the complexity of this system has been seen as a limitation to use in the clinical setting. In contrast, the Marx system is more simplified, and is possibly the most frequently employed classification system to date. Other systems have been described, and base their classification on physical characteristics, management approaches, or for specific research purposes.[23,34] Ultimately, when considering the complexities of embryologic development, all systems may be criticized as oversimplified.

## Clinical Presentation and Management

The clinical presentation of microtia can exist anywhere along the continuum between a small pinna with all structures present, to complete absence of the auricle. When considering treatment options, several important

**Table 7.3:** Marx classification system for microtia

| | |
|---|---|
| Grade I | Abnormal (small) auricle. All landmarks present and identifiable |
| Grade II | Abnormal auricle. Some landmarks absent |
| Grade III | Small auricular tag or anotia |

elements of the history and physical examination must be considered. The clinical setting and patient presentation will often be dictated by the severity of microtia and the presence or absence of an associated syndrome. Patients with severe microtia or syndrome-associated microtia are frequently brought to clinical attention during the neonatal period. When microtia is first diagnosed, a thorough history and physical examination with possible genetic analysis is warranted to evaluate for the presence of an associated syndrome. Syndromic patients may have other, more life-threatening organ system abnormalities that warrant early treatment. Notably, the treatment of other congenital systemic abnormalities almost always takes precedence over microtia repair. Other important considerations include the presence or absence of canal atresia, the hearing status of the patient, and the specific desires of the patient and parent. Canal atresia may influence hearing status, hearing rehabilitation options, and surgical planning strategies. If hearing loss is present, hearing rehabilitation or alternative communication modalities should be instituted prior to 6 months of age to maintain age-appropriate developmental milestones and to prevent speech and language delay. Lastly, patient and parent wishes are important to elucidate during the initial consultation and during ongoing patient visits. Microtia alone is not a life-threatening process, and although auricular abnormalities are associated with a known social stigma, the decision to treat and the timing of treatment are ultimately up to the parent and/or patient to decide. Regardless of an often-early presentation, the timing of microtia repair is commonly delayed until early childhood. This is frequently performed prior to the beginning of grade school but after the contralateral auricle (if unilateral microtia) has had an opportunity to grow to a near-adult size. Patients are often 5–6 years of age at the time of repair.

Although the origins of auricular reconstruction date back to 600 BC, modern microtia repair using cartilage grafting did not arise until the 1920s. Today, auricular reconstruction is frequently performed in 2–4 stages using autologous cartilage or semisynthetic biomaterials. Alternatively, anchored prostheses are occasionally used in a smaller subset of patients. Advances in prosthetics have resulted in the ability to create several prosthetic options that are realistic and difficult to recognize by the casual observer. Unfortunately, the use of prosthetic devices requires the removal of all remaining soft tissue remnants of the auricle, and frequently precludes future staged auricular reconstruction if the patient comes to desire this approach. In addition, due to the activity of school-age children, prosthetic anchoring methods are often inadequate. The risk of peer-based ridicule in the event that the prosthesis becomes dislodged or torn-free during sports or activities is often an overwhelming consideration that leads young patients away from this treatment option.

## Staged Surgical Reconstruction

Staged microtia repair requires the implantation of cartilage autograft or a synthetic allograft framework that is subsequently elevated from the lateral aspect of the head in subsequent stages. Two of the most frequently employed methods of surgical reconstruction include the Brent Technique[35,36] and the Nagata Technique.[37] Both methods use costal cartilaginous grafts in a staged approach to recreate the natural appearance of the auricle. Results vary among physicians; however, results likely coincide with the frequency by which the surgeon performs the technique. Regardless, a life-like auricle is a highly complex anatomic structure, and therefore difficult to recreate with precision. If one were to consider the results of all surgeons the majority of outcomes would likely be considered adequate rather than excellent, and primarily serve the purpose of redirecting the casual observer from the once-absent auricle to other features of the face. For this reason, a realistic understanding should be established between the parent/patient and surgeon preoperatively with regard to the specific outcomes expected and desired. Fortunately, the vast majority of patients are satisfied with their outcome, and microtia surgery can be a very rewarding experience.

Preoperative measurements are essential in ensuring an acceptable cosmetic outcome. Measurements taken from the contralateral ear can serve as a template for microtia repair. The use of X-ray film or transparent plastic is often used to create this template. In addition, the use of facial landmarks is important when establishing normal auricular position. This is exceedingly important in the patient with bilateral microtia. Patients and families should be counseled preoperatively that due to the frequently low hairline ipsilateral to microtia repair, a hair-bearing auricle may require further cosmetic hair-removal treatment following auricular reconstruction.

Both the Brent and Nagata techniques use contralateral cartilage, often from the synchondroses of the 6th, 7th,

and 8th ribs. Dissection is performed in the subcutaneous plane, with judicious use of cautery in young patients and patients with atresia so as to reduce the risk of cautery-induced injury to the facial nerve. One final consideration is the timing of atresia repair in the patient with external auditory canal atresia. This is frequently performed either prior to or immediately after the creation of the postauricular sulcus. These patients present a unique challenge in that the position of the auricle may not align appropriately with the position of the external auditory canal after atresia repair. For this reason, slight refinement in position of the pinna may be required after reconstruction of the external canal.

## The Brent Technique

The Brent technique has been modified and perfected over the past three decades, and is one of the most commonly employed techniques used for auricular reconstruction to date. This technique involves the use of costal cartilage auricular reconstruction using a four-stage procedure:

Stage 1: The appropriate position for the ear to be reconstructed is marked using the previously described template. Rib is harvested from the contralateral 6th–8th ribs. An auricle is created by carving the synchondrosis of the 6th and 7th ribs to resemble an antihelix and triangular fossa. The 8th rib is then sutured to this structure to replicate the helix. A judicious skin pocket is then dissected to receive the carved structure and provide vascular supply to the auricular graft. Excess subcutaneous fat is removed during this stage, and hair follicles associated with the skin flap may be transected at this stage. Some prefer to bank a small piece of cartilage for use during tragal reconstruction (stage 4), and a piece of cartilage for to serve as a wedge to improve auricular projection (stage 3).

Stage 2: The second stage involves creation of a lobule, and is performed between 4 and 6 months following stage 1. A malformed lobule is commonly present in grade 3 microtia patients, and this tissue is used if available. Transposition of the lobule requires exposure of the inferior aspect of the previously buried cartilage framework; suturing the lobule to the base of the framework contributes to a more natural appearance.

Stage 3: The third stage involves the elevation of the previously buried auricle to create a postauricular sulcus. This is generally performed 4–6 months following lobule transposition. A marginal incision is created extending from the attachment site of the lobule to the helical root. Dissection is then performed between the cartilage graft and the underlying periosteum. A thinned full-thickness skin graft is then placed over the postauricular sulcus. At this stage, the previously banked wedge of cartilage (stage 1) may be placed deep to the skin graft and sutured in place to increase auricular projection. The skin graft harvest site is often from the low-midline abdomen and sutured in place using a chromic suture. A bolster is placed over the graft site and removed after 7–10 days.

Stage 4: Tragal reconstruction is performed following elevation of the auricle. This stage is occasionally skipped by the patient who is happy with their reconstruction, and does not want to undergo further surgery. Otherwise, tragal reconstruction requires the use of cartilage placed in a pocket anterior to the external auditory meatus. This cartilage graft may be harvested from the contralateral ear as a composite graft, or previously banked cartilage (stage 1) may be used if adequate and available.

## The Nagata Technique

In 1996, Nagata presented a modified technique for microtia repair. Although similarities exist between the Nagata and Brent techniques, there are several important differences. The Nagata technique is classically described as a two-stage procedure and is recommended for patients 9 years of age and older to allow for adequate cartilage size:

Stage 1: The first stage requires rib harvest in a similar fashion as that described by Brent. The rib cartilage framework incorporates a tragal component and is buried in a subcutaneous pocket. The lobule is also transposed during this stage.

Stage 2: After approximately 6 months, the buried cartilaginous construct is elevated using a small, elliptical, or crescent-shaped piece of costal cartilage as a posterior wedge. This is harvested via the patient's previous incision site. To obviate the necessity for a second rib harvest, some prefer to harvest and bank cartilage during stage 1 if adequate skin coverage is possible. Posterior coverage is accomplished using a temporoparietal facial flap rather than skin grafting.

## Microtia Repair Complications

The majority of patients have acceptable outcomes following microtia repair and are satisfied with their

result. However, follow-up and communication with the patient are essential to maintain acceptable outcomes. Complications, when they occur, can often be managed conservatively if identified early. One of the more common major complications includes skin necrosis, either with or without a coinciding infection. This may be due to intraoperative damage to the subdermal plexus, or secondary to fluid collection (hematoma, abscess, or seroma) at the operative site. In addition, secondary or primary infection occurring at the operative site may lead to skin loss or cartilage breakdown. Management of soft tissue complications includes treating infection when present and conservative debridement of skin and cartilage when necessary. Many wounds will heal by secondary intention. Rarely, revision surgery with skin grafting is required. Additional complications include the formation of keloids or hypertrophic scars at the incision site, cartilage migration, or improper sizing or orientation of the auricle itself. Lastly, one must also consider the risks of donor-site complications and donor-site morbidity when performing costal cartilage grafting. The risk of pneumothorax when harvesting rib cartilage is a potential complication leading to intraoperative ventilator difficulty and the requirement for a chest tube. Postoperatively, atelectasis or immobility associated with chest wall pain at the donor site is not uncommon.

## FUTURE DIRECTIONS

The management of auricular abnormalities is a demanding but rewarding discipline with a high level of patient and provider satisfaction. As the diagnosis and treatment of this patient population is continuously enhanced by modern techniques and technology, this high level of satisfaction is expected to persist. Promising improvements in our understanding of congenital auricular abnormalities and their genetic origins is expected to result in exciting changes to our current classification systems and management strategies. Likewise, advances in material science and tissue engineering are also likely to prove promising in their application to auricular reconstruction.

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CHAPTER

8

# Congenital Aural Atresia

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## INTRODUCTION

Congenital aural atresia (CAA) is a rare condition resulting from malformation of the first and second branchial arch derivatives. The severity of this condition ranges from ear canal stenosis to complete atresia of the external auditory canal and middle ear structures. The more severe form of atresia, osseous atresia, is more frequently found than the milder membranous atresia. The reported incidence of aural atresia is one in every 10,000–20,000 live births. Males are affected more commonly than females, with the right ear more commonly affected than the left. Unilateral atresia has a higher incidence than bilateral atresia with studies reporting a three- to sevenfold difference.[1-3]

CAA may be found in isolation, in association with other external and middle ear deformities, or as part of a spectrum of congenital disorders such as Treacher Collins syndrome or Goldenhar/hemifacial microsomia. Microtia is the most common external deformity associated with aural atresia. The severity of the microtia tends to correlate with the severity of the middle ear deformity.[4] Of the middle ear deformities, fusion of the malleus and incus bones is the most frequently occurring malformation. The stapes footplate, which has dual origin from the second branchial arch and the otic capsule, is typically normal.[5,6] Cochlear function is also usually normal, though there is a higher incidence of inner ear abnormalities in the atresia population compared to the general population, as high as 22% in one study.[7] The facial nerve can also be affected by abnormal temporal bone embryogenesis, and while it can be found in a normal position, the nerve often lies more lateral and anterior than normal, and can take a more acute angle at the second genu.

As noted, CAA can be an associated malformation in certain syndromes. Approximately 10% of patients with CAA have an associated named syndrome including Treacher Collins, Goldenhar, hemifacial microsomia, branchio-oto-renal syndrome, de Grouchy syndrome, and Crouzon syndrome. Of the sporadic cases, 5% are due to genetic transmission but are nonsyndromic. Abnormalities of chromosome 18 have been identified in one group (de Grouchy syndrome) of atresia patients.[8] CAA may also be associated with kidney and spine problems, and facial weakness.

Evaluation and management of aural atresia poses a significant set of challenges to the otolaryngologist, and several factors must be taken into consideration. Of paramount importance is the provision of adequate hearing habilitation to support normal speech and language development. This issue is especially critical in children with bilateral atresia, although children with unilateral atresia, perhaps a more subtle disability, may also need services and habilitation.[9] These factors include not only decisions regarding the need for amplification, but also decisions regarding how to ensure the best possible scholastic environment for children to succeed in the school setting.

Surgery to open the ear canal and restore the natural sound conducting mechanism of the ear canal, eardrum, and middle ear may be an option for some families, in carefully selected candidates. If a surgical approach is chosen, the timing of surgical repair in coordination with repair of microtia must also be taken into account. This chapter reviews the concepts needed to meet the unique challenges faced in managing the patient with aural atresia.

## EMBRYOLOGY

Development of the ear is a complex process of cellular migration and differentiation into mature structures beginning in utero and continuing after birth. Development of both the ear canal and middle ear may arrest at any point resulting in a spectrum of malformations. Knowledge of the normal embryologic development of the temporal bone, specifically the external auditory canal and middle ear, is vital to understanding the pathogenesis of aural atresia, allowing the surgeon to anticipate the abnormal position of anatomic structures and avoid unnecessary injury during surgery. The inner ear has a completely separate embryologic anlagen (otic placode) than the outer and middle ear (branchial apparatus). The implication is that most (but certainly not all) children with CAA have normal cochlear function and normal bone conduction thresholds. For a detailed discussion of the embryology of the ear, the reader is referred to Chapter 1 of this section.

## EVALUATION

Aural atresia is frequently recognized at birth due to its association with microtia and other craniofacial malformations. Newborn hearing screening should identify the associated hearing loss and refer the infant for further testing. However, some children with only minor or no other congenital anomalies may escape detection until school age. Auditory evaluation including auditory brainstem response (ABR) testing with air and bone conduction thresholds should be performed as soon as feasible. Toddlers and older children can be tested behaviorally with visual reinforced audiometry (VRA; ages 1–3) and conditioned play audiometry (CPA; ages 3–6). Many states in the United States have a 1–3–6 goal for their newborn hearing screening program—identify by 1 month, confirm by 3 months, intervene by 6 months.

After a complete hearing evaluation, decisions can be made among the patient, the family, and hearing healthcare professionals regarding hearing habilitation and amplification. For children with more complex abnormalities, a cohesive multidisciplinary treatment plan should be instituted and may include referrals to plastic surgery, genetics, developmental pediatrics, and speech and language pathology to maximize the possibility for a good outcome for each patient.

### History and Physical Examination

A full history and physical examination should be the focus of the initial evaluation. There are multiple scenarios in which the patient will present to the otologist. The patient may be sent to the otologist shortly after birth when the CAA is recognized in conjunction with microtia or after identification by newborn hearing screening; as an older child as a referral from a plastic surgeon intending to perform microtia repair; as a child referred from the pediatrician or school after failing a hearing screening examination; or as a referral from another clinician who has noted canal stenosis. Patients may even occasionally present as an adult if they did not have the problem addressed in childhood. Regardless of presentation, the patient should be assessed for syndromic conditions as well as additional nonsyndromic anomalies. This assessment should entail a thorough prenatal, birth, postnataly and family history. History taking should also include an evaluation of possible psychosocial issues. Assessment of cognitive abilities, speech and language delays, developmental milestones, and behavioral problems will aid in the formation of a comprehensive therapeutic plan.

A careful physical examination of the head and neck should be performed with an emphasis on craniofacial development. All derivative structures of the first and second branchial arches should be carefully examined. Close inspection of the mandible and hemiface with palpation should be performed to assess for the presence of hemifacial microsomia, maxillary or mandibular hypoplasia. A thorough oral cavity examination is necessary to evaluate the palate and other intraoral structures.

Following examination of the other head and neck systems, attention may then turn to the otologic portion. Beginning with the external ear, the auricle is evaluated to determine the degree of microtia present. The integrity and function of each division of the facial nerve should be carefully assessed as facial nerve dysfunction has been associated with microtia and aural atresia.[7,10] The mastoid tip, condyle, and zygomatic arch should be palpated to estimate the size of the mastoid and temporal bone, which can aid in surgical planning. Under binocular microscopy, the size and caliber of the ear canal, if present, presence of a tympanic membrane, and appearance of the ossicles should be assessed. In patients with unilateral atresia, the unaffected side also warrants thorough evaluation.

The patient may also present with a draining or moist ear. Aural drainage in the setting of ear canal stenosis should alert the clinician to the possibility of an ear canal cholesteatoma—skin trapped in a stenotic canal. Such drainage demands more careful evaluation—possible examination and cleaning under anesthesia and/or computed tomography (CT) imaging. Congenital middle ear cholesteatoma in patients with CAA is extremely rare.[11]

Finally, the focus of the examination should be shifted to nonotolaryngologic systems. Due to frequent association of neurologic, cardiac, renal, skeletal, and urologic anomalies, these systems should be reviewed and assessed. Unrelated conditions such as hemangioma, umbilical and inguinal hernia, and anemia can also be found on rare occasions.[12]

### *Audiometric Data*

Assessment of cochlear function in patients with CAA should be obtained as early as possible. Ideally, ABR testing should be performed within the first few weeks to months of life in children with both unilateral and bilateral atresia. If early assessment is not possible, behavioral audiometry using VRA or CPA, or even standard audiometry depending on age may be performed. In bilateral atresia, the masking dilemma may confound standard audiometric results; bone conduction thresholds for individual ears may be assessed through sensorineural acuity level (SAL) testing. Using bone conduction ABR testing, detection of a wave I response in either ear corresponds with a functional auditory nerve confirming cochlear function.[13]

Accurate assessment of cochlear function in patients with bilateral atresia prevents future errors such as operating on an only hearing ear or in an ear with little possibility of a good hearing outcome. In either case, amplification in children with bilateral atresia should occur in the first 3–4 weeks of life, at least within the first 3–4 months. Early amplification is paramount to maximizing speech and language development in patients with bilateral CAA.

A more lenient approach may be taken with patients with unilateral atresia if the contralateral ear has normal hearing. It is critical to determine that the contralateral ear is functioning well and to monitor the hearing in the normal ear with routine follow-up testing. By traditional standards, these patients do not necessarily require amplification. The data are unclear how helpful amplification is for children with unilateral CAA, although certainly amplification is strongly recommended in children with unilateral sensorineural hearing loss (SNHL).[14,15] Whether or not the patient has unilateral or bilateral atresia, it is important to detect any additional hearing loss not otherwise explained by atresia, and provide the patient with the option of at least a short-term amplification solution while a long-term treatment plan is formulated.

### *Radiologic Data*

Radiographic assessment of CAA can provide valuable anatomic information that is not only beneficial for diagnostic purposes, but also important for determination of surgical candidacy, surgical planning, and prediction of outcomes. High-resolution computed tomography of the temporal bone with thin sections (minimum 1 mm sections) is the study of choice. Projections in the axial and coronal planes are necessary for complete evaluation of the inner ear and middle ear structures. The incus, malleus, incudostapedial joint, stapes, and round window are typically best seen on axial sections. The oval window, height of the tegmen, vestibule, distance between atretic plate and malleus–incus complex, and connection of the malleus to the atretic plate are better seen on coronal sections. For a full evaluation of the facial nerve, from internal auditory canal to stylomastoid foramen, both projections are important.

If audiometric data have confirmed normal cochlear function and no other indication for radiographic evaluation exists (acute facial palsy, otorrhea with concern for cholesteatoma), imaging of the temporal bone can typically be deferred until the patient is 5–6 years of age, the time when atresia surgery is considered. The rationale for this delay is to avoid unnecessary radiation exposure until the child is near the age in which surgical intervention is considered. Older children receive overall less total body radiation exposure. In addition, patient cooperation is unlikely in younger children necessitating sedation for an adequate study. Finally, a majority of patients with CAA who go on to develop cholesteatoma do not do so until after the age of 3.[16] Therefore, in the vast majority of cases, it is prudent to delay radiographic imaging until the patient is older, more cooperative, and will receive less total body radiation.

Once the imaging study has been performed, it is important to systematically assess the auditory pathway. The status of the inner ear should be evaluated to ensure there are no associated inner ear malformations. Next, the middle ear and mastoid should be evaluated. Extent of temporal bone pneumatization, size and status of the middle ear cavity, position/height of the tegmen, thickness of the bony atretic plate as well as the soft tissue component are well delineated by CT and are important components for surgical planning (Fig. 8.1). Patients with dysplastic inner ear structures, poor pneumatization and/or hypoplastic middle ear cleft, or low-lying tegmen (Fig. 8.2) are typically poor surgical candidates (*see* classification below).

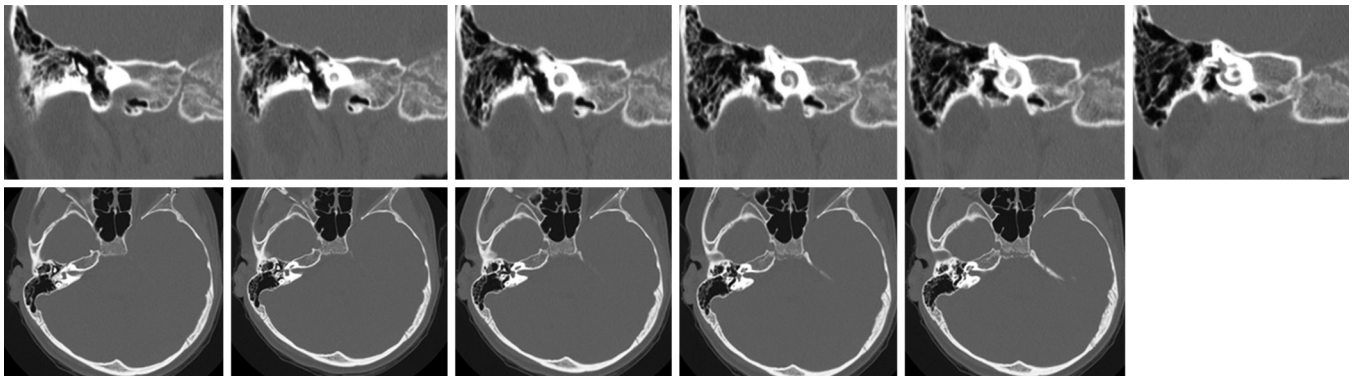


**Fig. 8.1:** Series of coronal and axial high-resolution CT scans of the temporal bone. Good candidate for atresiaplasty. On coronal imaging, note good height of tegmen, well-aerated middle ear and mastoid, fused malleus–incus, incudostapedial joint intact, stapes better seen on axial sections, oval window open, good distance between malleus–incus complex and atretic plate. On axial imaging, incudostapedial joint nicely imaged, stapes present, oval window open, fused malleus–incus, well-aerated mastoid and middle ear.

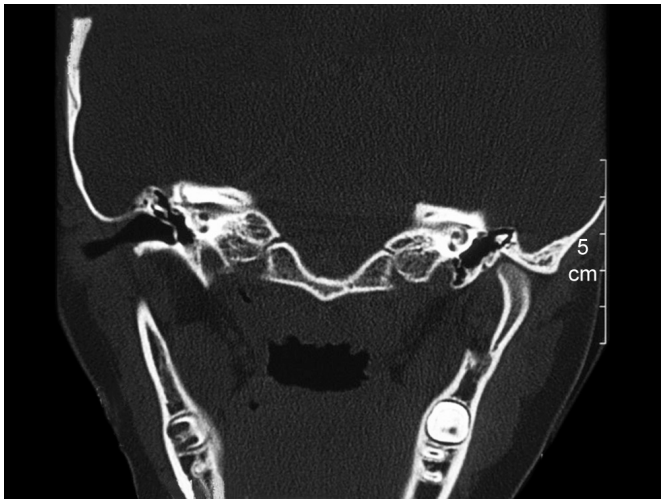


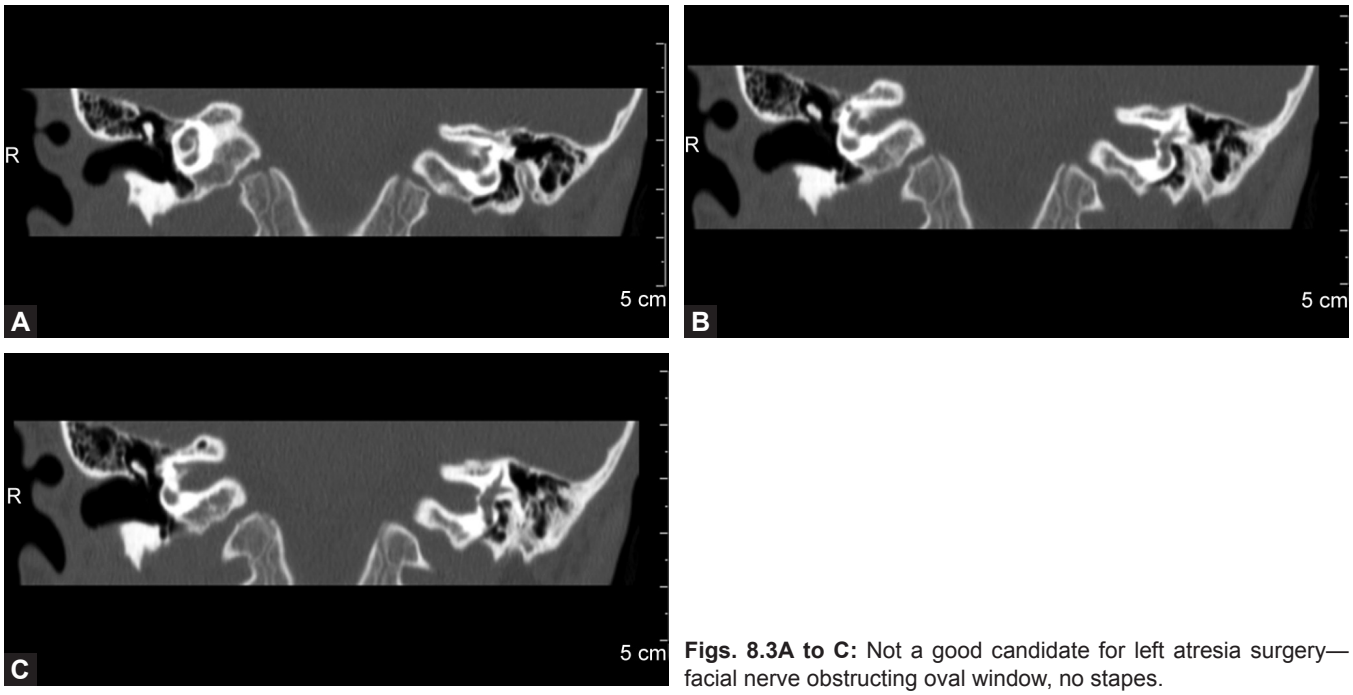

**Fig. 8.2:** Not a good candidate for left atresia surgery—tegmen too low.

The status of the ossicles, particularly the stapes, is also very important. The presence of a normal stapes, stapes footplate, and oval window must be ensured if atresiaplasty is being considered. Although stapes fixation can only be determined intraoperatively, if immobile, stapes surgery with or without ossicular reconstruction should be performed at a later date. Finally, the course of the facial nerve should be analyzed with particular attention to the relationship of the horizontal portion to the stapes footplate and location in the mastoid segment. CT may help anticipate any potential obstruction of the stapes footplate due to an aberrant facial nerve (Figs. 8.3A to C).

If a patient with an atretic ear complains of pain and/or drainage, this may be indicative of a developing or progressing cholesteatoma and should prompt immediate imaging. Patients with congenital aural stenosis are at significant risk of harboring a cholesteatoma (up to 14% according to Ishimoto et al.[17]). Among patients with aural stenosis who have canal diameters of 3 mm or less, 50% will develop cholesteatoma.[16] As such, patients with severe canal stenosis precluding adequate in-office cleaning should be imaged around 4–5 years regardless of symptomatology to ensure that there is no cholesteatoma. If cholesteatoma is discovered, congenital or otherwise, surgical management to eradicate disease and create a safe ear is mandatory.

## Classification Systems

As innovation and advancement in atresia surgery have progressed, the development of classification systems has been important in guiding therapeutic decision making. These systems help characterize the severity of the malformation as well as stratify patients who would do well with surgical repair versus those who would be better served with conservative management or other options for amplification. More recently, there has been emphasis on honing classification schemes so they not only determine surgical candidacy but also predict surgical outcomes.[18] Many systems have developed over the years, which utilize a variety of different parameters including examination findings, radiographic results, and intraoperative observations. The two predominant grading systems, the De la Cruz classification system and the Jahrsdoerfer classification system, rely primarily on CT scan findings. These will be reviewed briefly as well as the predominant classification system for microtia.




**Figs. 8.3A to C:** Not a good candidate for left atresia surgery—facial nerve obstructing oval window, no stapes.

The De la Cruz system is a modification of an earlier system initially proposed by Altmann in 1955.[1] Altmann divided patients into three groups based on their anatomical variations. De la Cruz altered this system dividing abnormalities of the external and middle ear into major and minor categories based on CT scan findings. Patients who have normal mastoid pneumatization, a normal oval window, footplate and inner ear, as well as a good facial nerve–footplate relationship are determined to have minor malformations. These patients are deemed to have a good possibility of obtaining serviceable hearing after atresiaplasty. Patients with abnormalities in any of the above structures are deemed to have major malformations and would be better served with conservative management.

The Jahrsdoerfer grading system assigns a point to each normal appearing anatomic structure in the middle ear seen on the high-resolution temporal bone CT scan, with a point for the degree of microtia and two points awarded for a normal stapes bone (Table 8.1).[19] Each affected ear is thus given a score of 1–10. Using this scale, Shonka et al. showed that a score of 7 or higher corresponded with an 89% chance of achieving good hearing results (speech reception threshold [SRT] ≤30 dB HL), while ears scoring 6 or less had a 45% chance of achieving good hearing results.[20] Shonka also found that, when evaluating individual anatomical features alone, poor middle ear aeration was the only feature predictive of poor audiometric outcome.[20] In cases of bilateral atresia, the surgeon may be less rigid in selection of surgical candidates.

**Table 8.1:** Jahrsdoerfer grading scale

| *Parameters* | *Points* |
|---|---|
| Stapes present | 2 |
| Oval window open | 1 |
| Middle ear space | 1 |
| Facial nerve | 1 |
| Malleus–incus complex | 1 |
| Mastoid pneumatized | 1 |
| Incus-stapes connection | 1 |
| Round window | 1 |
| Appearance external ear | 1 |
| Total available points | 10 |

Jahrsdoerfer et al.[19]

Classification of microtia is considered separately from CAA. Grade I microtia corresponds to a smaller than normal auricle that is otherwise normal with all anatomic subunits. Patients with deficient or absent anatomic subunits are categorized as Grade II. In Grade III, the auricle has a classic "peanut" appearance with only remnant soft tissue, or there is complete anotia. Interestingly, Ishimoto et al. compared the relationship of hearing levels in microtic ears with temporal bone anomalies using the

Jahrsdoerfer scale. He found that hearing level in microtic ears correlated with oval window and round window formation, as well as ossicular development; hearing levels, however, did not correlate with severity of microtia, middle ear aeration, or facial nerve aberration.[17]

## MANAGEMENT

Initial management of children with aural atresia is focused on parental reassurance, establishing a multidisciplinary team, and addressing the possible need for hearing amplification. In establishing a long-term treatment plan, the primary options include (1) observation with behavioral strategies (e.g. preferential seating in class); (2) assistive listening device, e.g. Frequency modulated (FM) system; (3) amplification (bone conducting or bone-anchored hearing devices); and (4) atresia repair (canaloplasty). These options are not mutually exclusive, and it is important for the parents and/or patient to understand the risks and benefits associated with each. Additionally, the need for speech and language therapy and other resources should be discussed with the family. Traditionally, management considerations for children with unilateral atresia have been somewhat different from children with bilateral atresia. Where present, these differences will be highlighted in the following sections.

### Observation

Observation implies that no intervention is made toward hearing rehabilitation. This option, along with its consequences of possible speech and language delays and psychosocial problems should be discussed. Nonetheless, observation without amplification is only practical in children with unilateral atresia with a normal hearing contralateral ear. In general, these patients will most likely develop normally from a speech, language, and intellectual standpoint. Preferential seating in school for these children is a must. The use of hearing aids in children with unilateral atresia is gaining more support in the literature; however, until recently, it has not been recommended. This is primarily due to poor patient compliance in young children. Nevertheless, close monitoring of academic progress in children with unilateral CAA is essential, as unilateral hearing loss in children can be a barrier to scholastic success.[21-23] Serial audiometric evaluation is also important to ensure normal functioning of the contralateral ear. Observation in children with bilateral atresia is not recommended.

### Amplification

Early hearing amplification for children with bilateral aural atresia is essential for optimizing speech and language development. In patients with complete atresia of the canal, a bone conducting hearing aid should be used within 3–4 weeks of age. Bone conduction hearing aids deliver auditory stimuli transcutaneously through the scalp using a headband apparatus with a bone conduction oscillator situated behind the ear. These systems are relatively inexpensive and can be utilized within the first several weeks of life. The major drawbacks for conventional bone conduction hearing aids include discomfort from constant pressure of the steel spring, the ability for the transducer to easily shift over the head, poor esthetics, and relatively poor sound quality due to attenuation of high frequency sounds by the skin. Softer headbands have been developed in attempts to minimize patient discomfort and maximize usage. Children with canal stenosis without atresia and relatively normal pinna development can typically be fitted with air conduction aids that are more comfortable and discreet.

Adults with unilateral CAA can be offered a trial of a hearing aid if it can be fitted or a bone conducting device. Adults are more likely to accept hearing aids than younger children with unilateral atresia as the perceived benefits gained from binaural hearing generally outweigh the nuisance of wearing a device.

#### *Bone-Anchored Hearing Aids*

The development of bone-anchored hearing aids (BAHAs) has been a significant advance in the management of conductive hearing loss, and is a viable alternative to atresiaplasty. BAHA systems have a vibrational transducer coupled directly to the skull via a titanium implant. The primary indications for BAHA include patients with a pure tone average (PTA) bone conduction threshold of 45 dB HL or less, and a speech discrimination score of 60% or better using a phonetically balanced word list.[24] The US Food and Drug Administration has approved these devices for children 5 years and older when cortical bone reaches the appropriate thickness to accept an implant. Under local or general anesthesia, the titanium implant/abutment is implanted behind the ear in the hair-bearing scalp. Following surgery, 3–6 months are typically allowed for healing and osseointegration before the sound processor is connected.

This osseointegrated coupling is much more effective than conventional, transcutaneous bone conducting

hearing aids. BAHA provides enhanced sound quality and is more efficient in sound energy transmission offering a 10–15 dB improvement over bone conducting aids.[18,25] In fact, review articles have shown that speech recognition and discrimination scores for BAHAs are significantly better compared to conventional bone conducting aids.[26,27]

There are several disadvantages to the BAHA. It is more expensive than bone conducting aids and requires a minor operation, often under general anesthesia. Compared with atresiaplasty, BAHA commits the patient to an appliance that is vulnerable to mechanical failure. Local wound infections can occur at the site of the abutment, which must be frequently cleaned. There is also the possibility of repeat surgery if the abutment does not osseointegrate. Finally, placement of the abutment may preclude the child from future microtia repair, but careful coordination between plastic microtia surgeon and otologic BAHA surgeon should allow a BAHA to be placed along with conventional microtia repair.

There is a paucity of data comparing BAHA directly to atresiaplasty. BAHA remains a reasonable alternative to atresiaplasty, especially in patients who are poor surgical candidates. In patients who are good surgical candidates, they are as likely to have good results regardless of which intervention is selected. Therefore, it is important to thoroughly discuss the risks and benefits of both atresia surgery and BAHA surgery, highlighting quality of life issues surrounding dependence on a device and difference in degree of risk between both procedures.[18] Hearing outcomes with the BAHA tend to be more reliable.[28,29]

## Surgery

Surgical repair of the atretic ear is a viable option in appropriately selected patients. The primary goals of surgery include correction of the air–bone gap (ABG), creation of a "safe" well-epithelialized canal, and maintenance of canal patency. The operation must not only be successful, but remain so over a long period of time. Even with meticulous technique, late onset hearing loss and even the need for revision surgery may occur.[30]

### *Patient Selection*

The key components in considering elective atresiaplasty include audiometric data demonstrating normal cochlear function in the atretic ear and a high-resolution CT scan of the temporal bone demonstrating favorable anatomy. Children with dysplastic or hypoplastic inner ear structures are poor surgical candidates and should be directed toward amplification. Secondary to inner ear development, assessment of the development of the middle ear cleft, ossicles, oval and round windows, as well as assessment of the facial nerve course and mastoid pneumatization have a profound impact on surgical management. A well-pneumatized mastoid and middle ear cleft increases the likelihood of surgical success. Identifiable ossicles as well as good oval window/footplate/facial nerve relationship are ideal. On the other hand, poor pneumatization of the mastoid is one of the most common causes of inoperability in a patient with CAA. An anteriorly displaced facial nerve can restrict the field of dissection and increases the possibility of facial nerve injury. The facial nerve may also overlie the oval window preventing ossicular reconstruction thus preventing hearing improvement.

In patients with the most favourable anatomy, the decision to operate becomes more difficult. Historically, otologists only operated in cases of surgical need, such as bilateral CAA, acute facial nerve paralysis, cholesteatoma, or otorrhea. The surgical option would be deferred until adulthood so that the patient could make an informed decision based on the risks and benefits of atresia surgery.

Given the well-documented academic difficulties of a subset of children with unilateral SNHL,[22] surgeons have offered atresia surgery to patients with unilateral CAA to overcome the problems of sound localization and difficulty hearing in background noise. Preliminary data indicate that after surgery, patients are able to hear better in background noise.[31] More research is needed to clarify the ability of patients to "use their new ear" in tests of sound localization and binaural hearing after atresia surgery. Of course, only those patients with favorable anatomy should be selected for unilateral atresia repair.

### *Timing of Surgery*

As the majority of CAA patients also present with microtia, the timing of surgery must take into account both reconstructive procedures. Auricular reconstruction typically relies on autologous rib cartilage as the substrate for microtia repair. Rib cartilage does not reach adequate size for auricular reconstruction until the child is 5-8 years old.[32] Once of appropriate age, rib graft auricular reconstruction precedes atresia repair to avoid disruption of surgical planes as well as the blood supply needed to maintain viability of the cartilage graft and local flaps. Atresiaplasty is generally delayed at least 3 months following the final stage of microtia repair.

### Alternative Techniques

In recent years, more plastic surgeons have been opting to use the Medpor® implant (Stryker, Kalamazoo, MI) covered with a vascularized temporoparietal fascia flap in lieu of autologous cartilage for auricular reconstruction.[33] Medpor is a porous high-density polyethylene, which is a well tolerated implant compared to earlier alloplastic materials. Use of Medpor avoids the risk of pneumothorax and provides more flexibility in the timing and traditional sequence of surgery. Current recommendations are for atresia surgery to precede Medpor microtia repair because exposure of the implant during an atresia operation would greatly jeopardize the viability of the implant. The operation can also be done at an earlier age. Roberson et al. performed atresiaplasty prior to microtia repair with an average age of 4.2 years, with comparable results to traditional atresia repair with autologous rib cartilage.[34] Other novel techniques have been attempted, including atresiaplasty at the time of elevation of the cartilage framework.[35]

### Surgical Approach

Each surgical step must be done meticulously to gain acceptable hearing results. Accurate identification and use of anatomic landmarks is vital to ensuring a safe dissection and avoidance of the facial nerve and inner ear structures.

There are two general approaches in atresia surgery, the anterior approach and the mastoid approach. The transmastoid approach involves drilling through mastoid air cells to reach the atretic plate,[36] while in the anterior approach, the bone directly posterior to the temporomandibular joint (TMJ) is drilled to reach the atretic plate.[3,37] The anterior approach creates a more natural ear canal with care taken to minimize opening of mastoid air cells, and carries less risk of a draining ear. The basics of this approach will be reviewed briefly.

### Patient Preparation

General anesthesia is induced, and the patient is placed supine with the head turned away (standard otologic positioning). The arm ipsilateral to the operated ear is tucked loosely on an arm board in preparation for future skin graft harvest. The postauricular area is shaved and a local anesthetic is instilled into the postauricular skin. Electrodes for continuous facial nerve monitoring are placed, reducing the risk for intraoperative facial nerve injury. Muscle relaxants other than short-acting paralytics for induction should not be used; this must be communicated to the anesthesiologist.

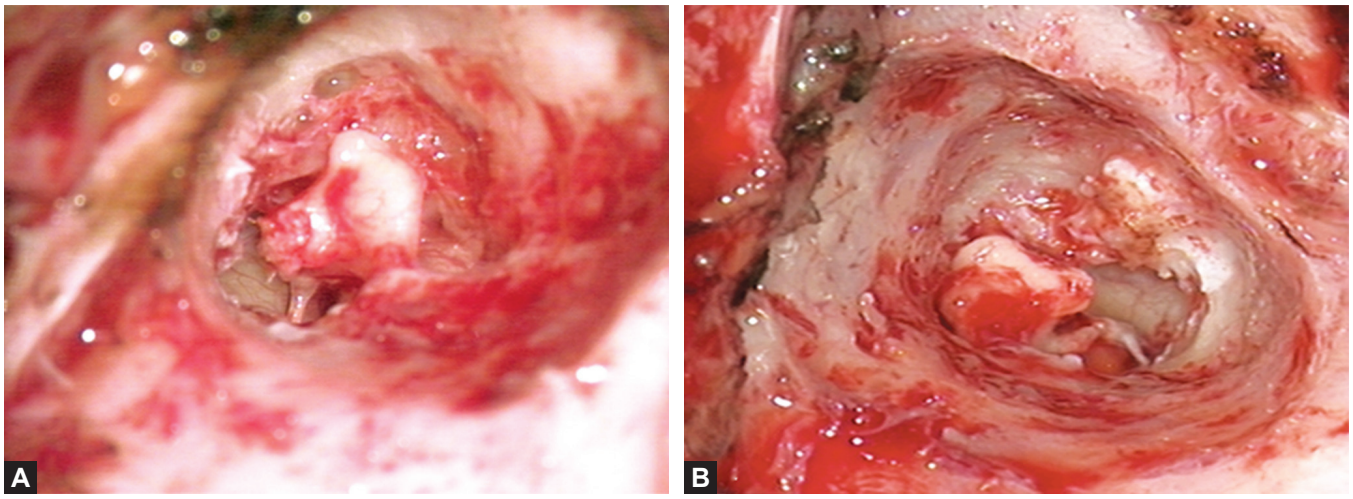
### Exposure and Dissection

A postauricular incision is made to the level of the temporalis fascia and a quarter-sized piece of fascia is harvested and set aside. A T-shaped incision is made in the periosteum with the superior–inferior limb made anteriorly along the posterior rim of the glenoid fossa. The periosteal flap is elevated until the linea temporalis, cribriform area, and posterior edge of the glenoid fossa are exposed. If there is remnant tympanic bone, drilling begins at the cribriform area. If no remnant tympanic bone is present, the junction of the linea temporalis and posterior rim of the glenoid fossa is used as the site of initial drilling. Drilling proceeds anterior and superior to identify the tegmen. The tegmen is followed medially to the epitympanum. Exposure of the temporomandibular joint and mastoid air cells is avoided. This approach minimizes the risk of injury to an aberrantly oriented anterior and lateral facial nerve.

Upon entry into the epitympanum, the ossicular mass is identified. Atretic bone is carefully removed with diamond micro drills and microsurgical instruments. Drilling of the ossicular mass should be avoided to reduce the risk of a high frequency SNHL. Once the ossicular mass is freed from atretic bone, ossicular chain and stapes footplate mobility are assessed (Figs. 8.4A and B). Reconstruction may be done with the patient's own ossicular chain, or a partial or total prosthesis if needed depending on anatomy. In general, reconstruction with an ossicular prosthesis results in about a 10 dB loss in the PTA and SRT.[38] If the stapes footplate is not mobile, stapes surgery should be deferred to a later date. The canal is widened to a diameter of 12 mm, which is purposely larger than the average canal size of 9 mm. This compensates for the natural contraction that occurs during the healing process.

### Grafting

The ipsilateral arm is exposed and a split thickness skin graft is taken from the nonhair bearing upper arm. The graft is harvested with a dermatome set for a thickness of 0.005–0.006 in. The skin graft is washed of blood and cut to 4 × 5 cm. If the ossicular chain is intact and mobile, the dehydrated fascia graft is trimmed to the appropriate size and draped over the ossicular mass with 1–2 mm of graft extending up onto the canal wall in all dimensions (Fig. 8.5).




**Figs. 8.4A and B:** Intraoperative view of canal with fused malleus–incus complex in the middle ear: (A) left ear and (B) right ear.

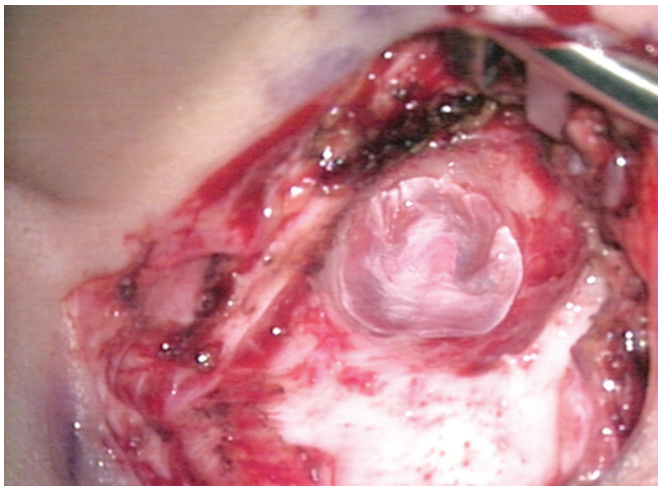


**Fig. 8.5:** Intraoperative view of the fascia graft draped over the fused malleus–incus (left ear).

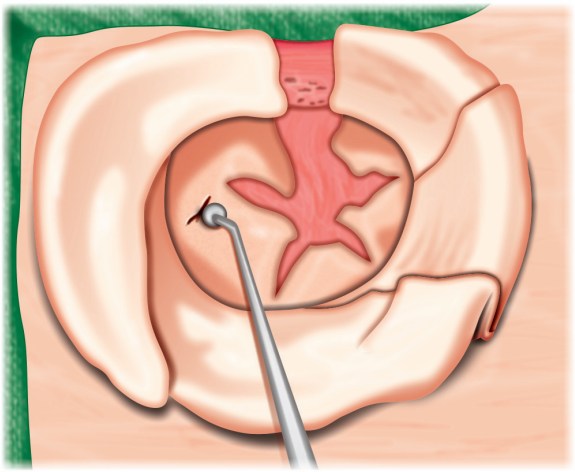


**Fig. 8.6:** Schematic drawing of the placement of notched ends of the split thickness skin graft.

The skin graft is notched at the medial end so that each notch comes together to cover completely the temporalis fascia. The graft is also circumferentially positioned so that it covers the bone of the canal; the edges should meet anteriorly (Fig. 8.6). The purpose of this is to prevent epithelial growth into the mastoid air cells. A 0.04 in. silastic disk is fashioned and placed over the skin graft and fascia to hold the fascia and skin grafts in place. Four to five wicks are delivered down into the ear canal standing on end and hydrated with ototopical antibiotic drops that when hydrated, expand and hold the skin graft against the bony canal (Fig. 8.7). Excess lateral skin is draped over the hydrated wicks.

### *Meatoplasty*

An anteriorly based conchal skin flap is created, and the underlying soft tissue and cartilage are excised creating the meatus (Fig. 8.8). The skin flap is delivered through the meatus and sutured to periosteum at the glenoid fossa, creating the anterior–lateral canal wall. The mastoid periosteal flap and postauricular incision are closed with absorbable suture. The skin graft is then delivered laterally through the meatus and sutured to the native conchal bowl skin. The remaining lateral canal is packed with additional wicks soaked with ototopical antibiotic drops. A mastoid dressing is applied and the skin graft donor site is dressed.[2]

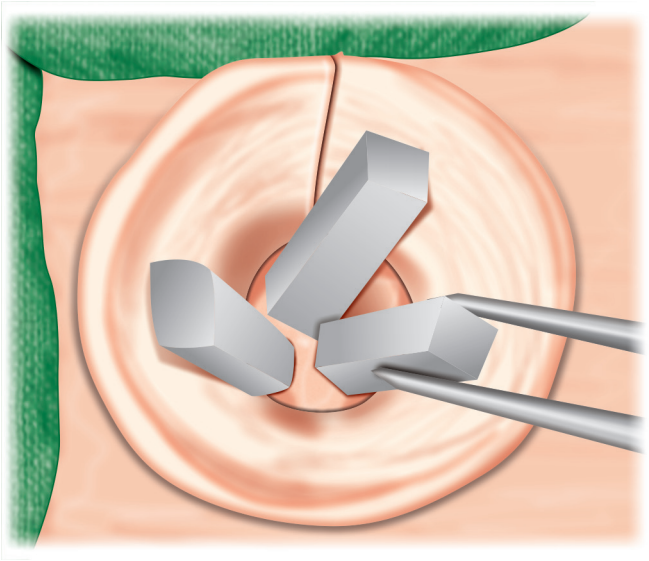


**Fig. 8.7:** Schematic drawing of the placement of the wicks in the bony canal.

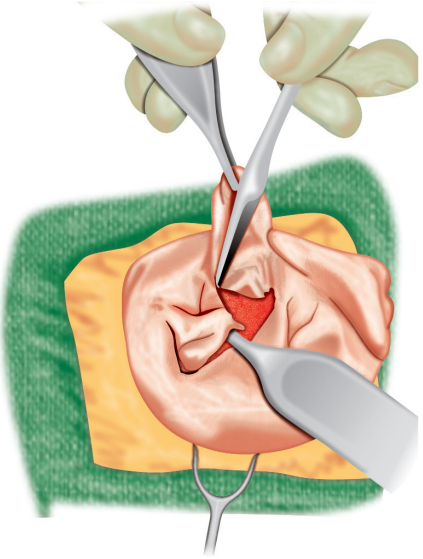


**Fig. 8.8:** Schematic drawing of the anteriorly based conchal skin flap that will serve as the anterior-lateral canal wall.

### *Postoperative Care*

The mastoid and arm dressings are removed on the first postoperative day. The patient is discharged home with instructions to apply antibiotic ointment to the postauricular incision and on a cotton ball that is placed over the meatus and changed daily. The packing and remaining absorbable skin sutures are removed at the 1-week postoperative visit. At the first postoperative visit, corticosteroid antibiotic drops are given to use twice daily for 1 week and strict dry ear precautions should be followed. The ear canal is otherwise exposed. At the 1-month postoperative visit, the ear canal is debrided of sloughed epithelium and an audiogram is obtained to evaluate postoperative results. Assuming no postoperative complications, dry ear precautions are relaxed, and follow-up is scheduled for annual or biannual canal debridement.

### *Complications*

Complications can be minimized with proper patient selection, good surgical technique, close follow-up, and patient adherence to postoperative instructions. The most commonly seen complications are graft lateralization, mucosalization with a moist ear, meatal stenosis, and high-frequency SNHL. The incidence of these complications ranges anywhere from 3% to 26% depending on the report.[6,30] Facial nerve palsy is much less frequent, with an incidence of <0.1%.[39] Salivary fistula and canal cholesteatoma are two very rare complications, but should be suspected in a draining postoperative ear.[40]

### *Outcomes*

The two most important factors in achieving consistently good hearing outcomes in atresia surgery are careful preoperative selection of patients and meticulous surgical technique at each step of the operation. With favorable anatomy and careful technique, postoperative hearing results can reach in the normal or near-normal range (SRT ≤ 30 dB HL) in 80–90% at 1 month.[20]

There is a paucity of data on long-term hearing results after this operation, but Lambert examined the stability of hearing results after atresia surgery and found that almost two-thirds of patients maintained an SRT < 30 dB HL for the longer follow-up (> 1 year; mean, 2.8 years); about one-third required a revision procedure.[41] Similarly, De la Cruz reported a long-term (> 6 months) ABG of 30 dB or less in 51% of primary cases and 39% of revisions.[6]

Even if the hearing deteriorates, a conventional hearing aid can be worn in the new canal many times to bring the air conduction thresholds into the normal range.

## CONCLUSION

Bilateral CAA requires relatively prompt evaluation to determine bone conduction thresholds, with intervention

aimed at bypassing the atretic ear canals through bone conduction hearing devices. In most patients with bilateral atresia, normal speech and language development an progress with the appropriate use of resources including amplification and speech therapy.

Unilateral CAA requires close monitoring of the nonatretic ear to ensure normal hearing with close attention to speech and language progress and performance in the school setting. Resources to help children with unilateral CAA include preferential seating in class, individualized education programs, FM systems, amplification, and surgery.[9] The decision to amplify is made among the family and hearing health-care professionals. Surgery can be undertaken in both unilateral and bilateral CAA after careful evaluation of the audiologic and radiologic data.

Meticulous surgical technique can bring air conduction thresholds in patients with CAA to the normal or near-normal ranges. Further research is needed to determine the long-term stability of these audiometric results and whether children with unilateral CAA can "use" their new ear in tests of binaural hearing.

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CHAPTER

# 9 Management of Children with Inner Ear Malformations

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## INTRODUCTION

Inner ear malformations may account for up to 20% of congenital hearing loss cases based on temporal bone computed tomography (CT). The majority of these children who have an associated bilateral severe to profound hearing loss are cochlear implant (CI) candidates. However, those cases with severe malformations may require special surgical approaches to facilitate implant placement, making clinical decisions challenging.

Although inner ear malformations have been traditionally separated into five groups,[1–3] recent findings suggest that inner ear malformations can also be classified into eight distinct groups.

## COMPLETE LABYRINTHINE APLASIA (MICHEL DEFORMITY)

### Definition and Radiology

Labyrinthine aplasia is the absence of the cochlea, vestibule, semicircular canals (SCCs), and vestibular and cochlear aqueducts (Fig. 9.1). The petrous bone is reported to be hypoplastic, whereas the otic capsule may be hypoplastic or aplastic.[4] In the majority of patients, the internal auditory canal (IAC) is abnormal, consisting only of the facial canal, although the labyrinthine, tympanic, and mastoid segments of the facial nerve can be seen in the temporal bone. However, in a portion of patients, it may not be possible to observe the facial canal in the temporal bone even though there is no facial paralysis. The middle ear ossicles are usually present.

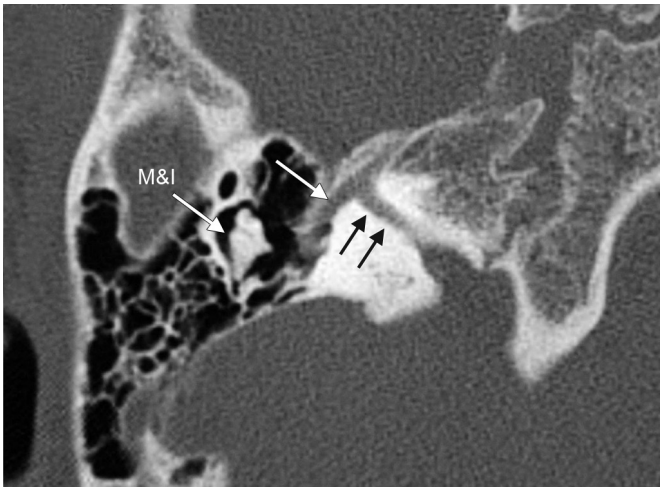



**Fig. 9.1:** Axial CT image of a patient with labyrinthine aplasia demonstrates a hypoplastic otic capsule with complete absence of the inner ear structures. The facial canal with the labyrinthine (black arrows) and tympanic (white arrow) segments is well visualized.

### Audiological Findings

Audiological examination reveals either no response at all or profound sensorineural hearing loss (SNHL) at 125, 250, and 500 Hz at the upper limits of the audiometer. The latter finding demonstrates that this is not true hearing, but rather vibrotactile sensations. This can also be appreciated in cases of children with a rudimentary otocyst and cochlear aplasia.

### Management

As there is no inner ear development, it is not possible to perform CI surgery in these children. Auditory brainstem

implantation (ABI), in which the electrode is placed into the lateral recess to directly stimulate the cochlear nuclei, is thus the only surgical option for hearing habilitation. Although translabyrinthine, retrosigmoid and retrolabyrinthine approaches can be used for ABI surgery, the retrosigmoid approach is preferred in children.[5] The temporal bone is much smaller in children of 2–3 years of age when compared to that of an adult. As a result, the translabyrinthine approach provides a much more limited surgical exposure than the retrosigmoid approach. In addition, drilling the temporal bone with a translabyrinthine approach to expose the brainstem requires longer surgical times compared to retrosigmoid craniotomy. Therefore, we favor the latter approach for ABI surgery in children.

Based on the findings in 48 children who have undergone ABI surgery in Hacettepe University, there is no real correlation between the type of inner ear malformation and the development of the cochlear nuclei. Even in the absence of an inner ear, the cochlear nuclei may be developed and it may be possible to obtain electrically evoked far-field responses of the upstream auditory pathways (electrical auditory brainstem response) during ABI surgery. Unfortunately, there is no way of preoperatively determining whether the cochlear nuclei are present and functional in children with labyrinthine aplasia based on current magnetic resonance imaging (MRI) techniques and evoked response testing methods. Indeed, children with labyrinthine aplasia have demonstrated hearing benefits that mimic those of children with other inner ear pathologies who underwent ABI surgery.

## RUDIMENTARY OTOCYST

### Definition and Radiology

A rudimentary otocyst consists of incomplete millimeter-sized representations of the otic capsule (round or ovoid in shape) without an IAC (Fig. 9.2). Sometimes parts of the SCCs may be present. This pathology falls somewhere between a Michel deformity and common cavity (CC) in the spectrum of inner ear anomalies. In Michel deformity, there is no inner ear development, while in CC, there is an ovoid or round cystic space instead of a separate cochlea and vestibule. The CC is usually similar in size to cochlea/vestibule and it communicates with the cerebellopontine cistern via the IAC. The rudimentary otocyst is a few millimeters in size and does not communicate with the subarachnoid space via an intact IAC.

Audiological findings are similar to those found in complete labyrinthine aplasia.

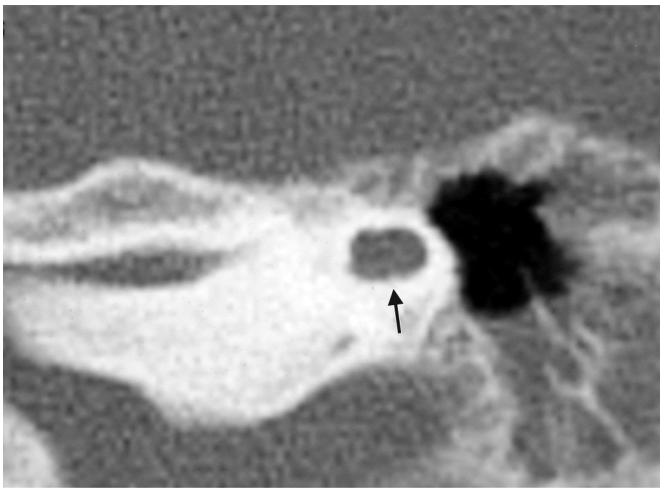


**Fig. 9.2:** A rudimentary otocyst is seen with a small ovoid structure (black arrow) that has no communication with the cerebellopontine angle.

### Management

The fact that there is no connection between the otocyst and the brainstem is a contraindication to CI surgery. As a result, these patients are candidates for ABI.

## COCHLEAR APLASIA

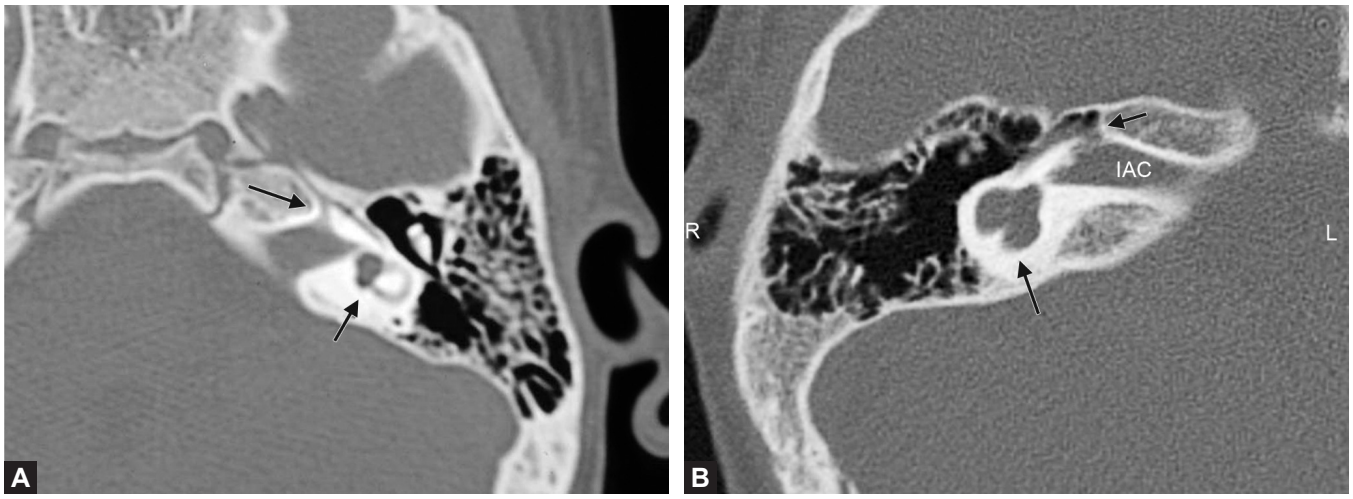
### Definition and Radiology

Cochlear aplasia is simply described as the absence of the cochlea. The accompanying vestibular system may be normal (Fig. 9.3A) or it may have an enlarged vestibule (Fig. 9.3B).[1] The labyrinthine segment of the facial nerve is anteriorly displaced and usually occupies the normal location of the cochlea. It is essential to distinguish cochlear aplasia with a dilated vestibule (CADV) from CC. If the cochleovestibular nerve (CVN) is present, cochlear implantation can be done in CC. However, CI surgery should not be done in CADV. The challenge is that in some patients, it is very difficult to distinguish between these entities. Detailed differences between the two pathologies are described in more detail in the section on CC.

It has been observed that cochlear aplasia with normal labyrinth is symmetric, with similar features found in different patients. The etiology is most likely genetic. Given the asymmetric development of CADV, this pathology may be genetic or environmental.

### Audiological Findings

In a typical audiologic evaluation, these patients will have no response at all or profound hearing loss at low




**Figs. 9.3A and B:** Cochlear aplasia with normal (A) and dilated (B) vestibule (thick arrow). Note the facial canal (thin arrow) in each case.

frequencies. Collectively, these findings in complete labyrinthine aplasia, otocyst deformity and cochlear aplasia demonstrates that profound hearing loss at low frequencies is purely a vibrotactile response and should not be interpreted as hearing in CI candidates with other pathologies.

### Management

As there is no inner ear development, ABI is the only feasible surgical option to provide hearing sensations in children with cochlear aplasia.

## COMMON CAVITY

### Definition and Radiology

A CC is defined as a single chamber (ovoid or round in shape) representing the cochlea and vestibule (Fig. 9.4). Theoretically, this structure has cochlear and vestibular neural structures. The IAC usually enters the cavity at its center, with the SCCs or their rudimentary parts accompanying the CC. Cases with vestibular dilatation are occasionally termed as "vestibular common cavity"; however, this is not a correct term.

As noted above, it is very important to differentiate between cochlear aplasia with vestibular dilatation (CAVD) and CC. In contrast to a CC (Fig. 9.4), which is described above, CAVD (Fig. 9.3B) usually has a vestibule and SCCs whose external outline resembles the normal labyrinth. The vestibule is at its expected location at the posterolateral

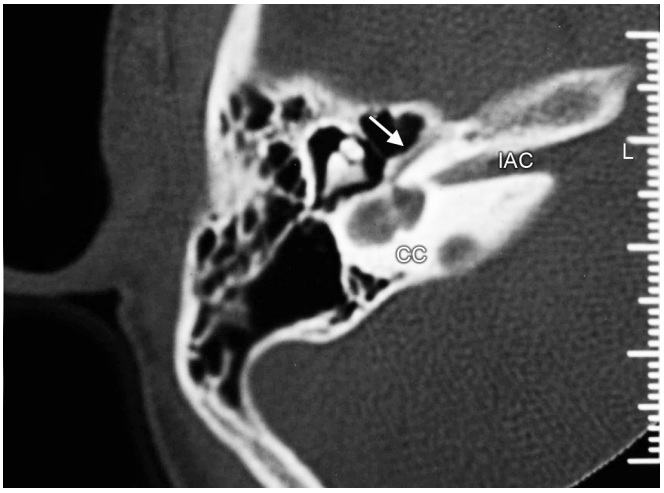



**Fig. 9.4:** Common cavity anomaly represented with an ovoid single structure (CC). Note that the IAC is present and is extending to the midportion of the CC. The facial canal (white arrow) has aberrant course. (IAC: Internal auditory canal; CC: Common cavity).

portion of the IAC fundus. The accompanying SCCs may be enlarged or normal. A CC (Fig. 9.4), on the other hand, is an ovoid or round structure. SCCs or their rudimentary parts may accompany a CC. The IAC usually enters the cavity at its center. The location of a CC may be anterior or posterior to the normal location of the labyrinth. It is very important to differentiate these malformations from each other, because cochlear implantation in a CC may result in acoustic stimulation, but in CAVD, CI will fail with no functional stimulation. In spite of these factors, it may sometimes be difficult to differentiate between the two malformations.

An otocyst deformity is a more primitive malformation than the CC deformity. There is a rudimentary cystic ovoid or round structure that is a few millimeters in dimensions without any internal auditory canal development.

## Audiological Findings

These patients can have detectable hearing thresholds only at low frequencies and at the maximum limits of the audiometer.

## Management

The presence of a CVN is important when discussing management options with the family. High-resolution 3 T MRI with oblique views (either direct or reformats) of the internal auditory canal should demonstrate the presence of a CVN before cochlear implantation. At the present time, there is no test to determine the amount of cochlear fibers in the CVN.[5] If a behavioral audiometric response or language development is present with hearing aid use, a meaningful population of cochlear fibers is assumed to exist and the patient is a candidate for CI. The surgical approach is via a transmastoid labyrinthotomy as described by McElveen.[6] After canal up mastoidectomy, air cells are removed to identify the CC. Originally the position of the labyrinthotomy was best described in the lateral SCC; however, experience in our department has shown that any position along the cavity allows for safe entry into the CC. Therefore, a labyrinthotomy location at the periphery of the CC, away from the facial nerve, is preferred. A straight (nonmodiolar hugging) electrode is preferred, resulting in a lateral position of the electrode. A precurved electrode will have the contacts located medially and may not stimulate the periphery of the CC efficiently.

Postoperative X-rays should demonstrate circular shaped electrode placement that follows the internal curvature of the CC. If there is a cerebrospinal fluid (CSF) gusher, the X-ray should be taken intraoperatively. The presence of a CSF gusher confirms a wide connection between the CC and the IAC. If the electrode is in the IAC, it should be repositioned.

In patients with a very narrow or long IAC where the presence of cochlear fibers is questionable, an ABI may be a more appropriate option from the outset. Additionally, if there is no CVN demonstrable by MRI, ABI is indicated.

The exact location of the neural distribution is not precisely known in CC. Therefore, audiological outcomes cannot be predicted precisely before CI surgery. Initially, the family should be informed that if there is very limited progress with CI, ABI should be done on the contralateral side to provide the best possible hearing stimulation to the child. This decision should be done as early as possible.

## Electrode Choice

Because the exact location of neural tissue in CC is unpredictable, electrodes with contacts on both sides or full ring electrodes should be used. Precurved electrodes with contacts facing the modiolar side will coil within the open lumen of the CC and not likely stimulate the neural elements found along the lateral wall. In case of a CSF gusher, an electrode with a cork type silicon stopper (not available in the United States) may be advantageous in controlling the CSF leakage. The length of the electrode can be calculated by measuring the diameter of the CC and using the formula $2\pi r$ to estimate the perimeter. This roughly determines the length of the electrode that will make one full turn inside the CC.

Beltrame et al.[7] described a special electrode for CI surgery in the setting of a CC. This electrode has a non-stimulating tip which is inserted into one labyrinthotomy and then delivered through a second labyrinthotomy with a microhook.

# INCOMPLETE PARTITION OF THE COCHLEA

## Definition and Radiology

This is a group of cochlear malformations where the external dimensions of the cochlea are similar to that of a normal cochlea but the internal architecture is deficient. Based on our experience at Hacettepe University, incomplete partition of the cochlea accounts for 41% of inner ear malformations. These cases can be further divided into three different types of incomplete partition cases according to the defect in the modiolus and the interscalar septa.

### *Incomplete Partition Type I*

This type was described as a "cystic cochleovestibular malformation" in 2002 by Sennaroglu and Saatci.[3] These represent approximately 20% of inner ear malformations. In this group, the cochlea lacks the entire modiolus and interscalar septa (Fig. 9.5A), giving the appearance of an empty cystic structure. IP-I type cochlea has been reported

to have external dimensions (height and length) similar to normal cases.[8] It is accompanied by an enlarged, dilated vestibule (Fig. 9.5B). Vestibular aqueduct enlargement is very rare. Due to maldevelopment of the cochlear aperture (CA) and absence of the modiolus, there is a defect between the IAC and the cochlea (Fig. 9.5C), and CSF may completely fill the cochlea. The cochlea is located in its usual location in the anterolateral part of the fundus of the IAC.

*Audiological findings*: The majority of IP-I patients have severe to profound SNHL. Hearing aids are rarely sufficient to support oral language development, and virtually all patients with IP-I benefit from CI surgery for hearing habilitation. At Hacettepe University, 35 patients with IP-I have undergone CI surgery. In our patient population, only three patients could use hearing aids unilaterally. Specifically, these children used the hearing aid on the side with moderate-to-severe hearing loss and had profound hearing loss in their contralateral ear.

As it is possible to have cochlear nerve (CN) aplasia in IP-I, some patients may not be a candidate for CI surgery. Four patients with IP-I at our institution have undergone successful ABI surgery.

*Management*: If a patient is diagnosed with bilateral moderate HL, HA can be used for rehabilitation. However, we have not had experience with this as none of the patients have had any residual hearing. For patients with asymmetrical hearing loss (i.e. one side with moderate hearing loss and the other side with profound hearing loss), the best option is to use bimodal stimulation, with a hearing aid on the side with moderate hearing loss and a CI on the contralateral side with profound hearing loss.

It is very important to demonstrate the cochlear nerve with MRI in order for a patient to be a candidate for CI. If the CN is present, then a CI should be pursued, otherwise ABI surgery is preferred.

Two variations may complicate CI surgery in patients with IP-I.

*Gusher*: Although this does not occur in every IP-I patient, the cochlea may be filled with CSF because of the defect between the cochlea and the IAC. In some cases, there may be an egress of CSF as soon as the cochleostomy is made. It is very important to properly seal the leak or the patient will be prone to recurrent meningitis. The surgeon who is operating on patients with an elevated risk of gusher should adopt the principle that it is essential to fully control the gusher prior to completing the surgery. Recent electrodes with a cork type stopper have been used to facilitate this principle. Less severe leakage of CSF, known as oozing, can be usually managed by simply packing the cochleostomy with soft tissue. There are several options for managing and avoiding a CSF gusher:

1. Small cochleostomy: The size of the cochleostomy can be made small enough such that the electrode fits tightly and there is minimal space to place soft tissue around the cochleostomy. This technique, however, may not be effective in controlling the CSF leakage around the electrode
2. Large cochleostomy: The size of the cochleostomy is larger (approximately twice the size of the electrode), and pieces of soft tissue can be placed inside the cochleostomy around the electrode. Although seemingly paradoxical, this is more effective than a small cochleostomy
3. Electrode with a cork type stopper: This electrode has a progressive conical shape and is much more effective at controlling CSF leak than the standard silicon ring at the end of the electrode. This electrode is not yet available in the United States. To make it more effective, it may be passed through a piece of soft tissue prior to insertion into the cochleostomy. Ideally, the cochleostomy should be circular but in reality there may be irregularities. The soft tissue therefore serves the purpose of filling these irregularities around the cochleostomy

   Even with this newer type of electrode, surgical manipulations are sometimes necessary to completely control CSF leakage. Again, the surgeon should not leave the operating room without complete control of the leak. If CSF continues to ooze around the electrode, there will be an increased risk of recurrent meningitis. If full control of the leakage is not accomplished, subtotal petrosectomy (as described below) is the next reasonable option
4. Subtotal petrosectomy: This technique includes complete removal of the skin, blind sac closure of the ear canal, obliteration of the cavity with fat and plugging the Eustachian tube in addition to the procedures mentioned above. By plugging the Eustachian tube the procedure provides additional protection against meningitis. However, it should be emphasized that if the leakage is not fully controlled, complications may still occur

   Once a subtotal petrosectomy is done in a child with a CI, it is very difficult to check the condition of the ear.

MRI cannot be done because of the CI without magnet removal or in cases where the device is approved for 1.5 T MRI scanning with the magnet in place. High-resolution CT cannot differentiate between the fat obliteration and CSF coming from the leakage. If high CSF pressures produce a fistula at the oval window, it may not be possible to detect such a defect. Therefore, we prefer proper control of the leak at the cochleostomy, leaving the ear canal and tympanic membrane intact. During follow-up, any abnormality in the tympanic membrane may alert the surgeon to a CSF leakage. In that situation endaural exploration of the middle ear may be necessary.

5. Continuous lumbar drainage (CLD): In patients with severe CSF leakage, 4–5 days of CLD diverts the CSF from the site and allows for better healing of the cochleostomy site to promote healing. It should be considered in patients with severe CSF leakage.

Electrode choice: We do not know the exact location of the neural tissue in the cochlea. Therefore, electrodes with contacts on the modiolar side may not produce the desired effect. Electrodes with contacts on both sides or full rings may provide better stimulation. In addition, an electrode with cork-type silicon stopper may stop CSF leakage more efficiently.

Postoperatively, these patients should have an X-ray to demonstrate the position of the electrode. If there is severe gusher, the X-ray should be taken in the operating theater. If the X-ray demonstrates that the electrode is in the IAC, the electrode must be repositioned. Electrodes that are modiolar hugging may have a higher likelihood of facial or cochlear nerve damage when they are being removed from IAC for repositioning.

*Facial nerve anomaly*: As there is abnormal development of the labyrinth, the facial nerve may have an abnormal course. As such, the facial recess approach may not provide sufficient exposure for round window insertion. In this situation, an additional transcanal approach may be necessary. This has been done in 3 patients (out of 35) in our department. In cases where this is not possible, subtotal petrosectomy (where the skin is totally removed and the bony external auditory canal is taken down) may provide a better view of the landmarks.

Auditory brainstem implantation: The ABI is indicated in IP-I patients with aplastic CN. Four patients with IP-I and aplastic CN have received the ABI in our department.

Meningitis in IP-I: Meningitis can occur in IP-I patients even prior to their CI surgery or in their nonoperated ear. High CSF pressure filling the cochlea disrupts often thin stapes footplate, leading to a CSF fistula at the oval window and meningitis. Several cases of this have been reported in the literature.[1,9–11]

Usually, these children have recurrent meningitis and high-resolution computed tomography (HRCT) reveals a small opacity in the oval window area. Imaging will also reveal whether the middle ear and mastoid are full of CSF. All patients with IP-I and recurrent meningitis who have normal tympanic membranes but fluid filling the middle ear and mastoid should have an exploration of the middle ear with special attention to the stapes footplate.

It is interesting to note that meningitis is often reported in IP-I cases. IP-III cases almost always have a CSF gusher during CI surgery or stapedotomy but meningitis is very rarely reported in these patients.[1,9] This is most likely due to the fact that the stapes footplate is thicker at birth in these patients and thus it is less likely to develop a defect caused by high CSF pressure.

Management: Meningitis in IP-I necessitates an endaural exploration of the middle ear. Usually, there is a cystic structure of variable size originating from the stapes footplate. It is better to keep the stapes in place and insert a large piece of fascia or muscle tissue through the defect into the vestibule, using the stapes to keep the soft tissue in place. Tissue glue is then used after soft tissue placement to further anchor the tissue. In some cases, it may be necessary to remove the stapes and obliterate the defect with more pieces of fascia and bony tissue. The incus can be inserted into the oval window and may provide a tight seal if all else fails.

### *Incomplete Partition Type II*

In a type II cochlear malformation, the apical part of the modiolus is defective but the basal part is anatomically normal (Fig. 9.5D). This is the type of cochlear anomaly that was originally described by Carlo Mondini and together with a minimally dilated vestibule and a large vestibular aqueduct (LVA; Fig. 9.5D) constitutes the triad of the Mondini deformity. The authors, together with Phelps et al.[9] and Lo,[12] stress the importance of using this particular name only if the above mentioned triad of malformations is present. The apical part of the modiolus and the corresponding interscalar septa are defective. This gives the apex of the cochlea a cystic appearance due to the confluence of middle and apical turns. The external dimensions of the cochlea (height and diameter) are not different from that seen in normal cases.[8] As this study

pointed out, it is not correct to define this anomaly as a cochlea with 1.5 turns.[8] This description should only be used for cochlear hypoplasia.

*Audiological findings*: These patients do not have a characteristic hearing level, as their audiometric threshold testing varies from normal to profound. The hearing loss can be symmetric or asymmetric. The most characteristic audiological finding is the air–bone gap particularly present at low frequencies. Govaerts et al.[13] indicated that the conductive component could not be explained by middle ear impedance problems, such as effusion. Tympanometry is normal in the absence of otitis media and acoustic reflexes are generally present. The cause of the air–bone gap in these children is likely due to a "third window" effect from the large vestibular aqueduct, and can resemble the audiometric findings in superior canal dehiscence syndrome.

These patients can experience progressive hearing loss throughout their lifetime. At birth, they may have normal hearing but usually there is progressive hearing loss over time. The LVA transmits the high CSF pressure to the inner ear and may cause progressive hair cell damage. Pulsation seen during the surgery when the cochleostomy is created demonstrates the high intracochlear pressure transmitted by LVA. Head trauma may exacerbate this hearing loss and these children are advised to avoid head trauma as much as possible. Sudden hearing loss can also be seen. Because of the progressive nature of the hearing loss, these patients usually have good language development. Papsin[14] also reported that children with incomplete partition are typically implanted older than other cases for the aforementioned reason.

*Management*: At a young age, these patients may have near normal hearing and usually do not require amplification initially. With progressive hearing loss, they become candidates for hearing aid. Usually the progression in hearing loss continues, ultimately creating a need for CI at some point in the future. What causes this progression remains unknown. A role for head trauma has been suggested, and these patients are advised to avoid trauma by wearing helmets when playing sports and avoiding contact sports completely.

During surgery, a facial recess approach was successfully used in all 47 patients who underwent CI surgery at Hacettepe University. This standard approach could be used in all patients because the cochlea and labyrinth had normal external dimensions. As a result, the facial nerve does not typically have an abnormal course that would prevent using the facial recess approach.

Out of 47 patients operated on in our department, 22 patients had no CSF leakage, 19 patients had CSF oozing, and 6 patients had a gusher. The majority had strong pulsation at the time of cochleostomy, likely explaining the progressive nature of the hearing loss. Head trauma may cause increase in CSF pressure resulting in progressive or sudden HL.

A gusher is more common in IP-I or IP-III, but it may occur in IP-II as well. This observation demonstrates that there is a defect in the modiolus. A LVA cannot explain CSF leakage. The cochleostomy should be closed completely because there is a risk of recurrent meningitis if CSF leakage persists around the electrode in the cochleostomy.

*Electrode choice*: The basal part of the modiolus is normal. All kinds of electrodes (modiolar hugging, straight) can be used. Because of the risk of CSF leakage and sometimes a severe gusher, electrodes with cork type stopper may be advantageous. The surgeon must be prepared to use the measures as described in the IP-I section to manage the CSF gusher.

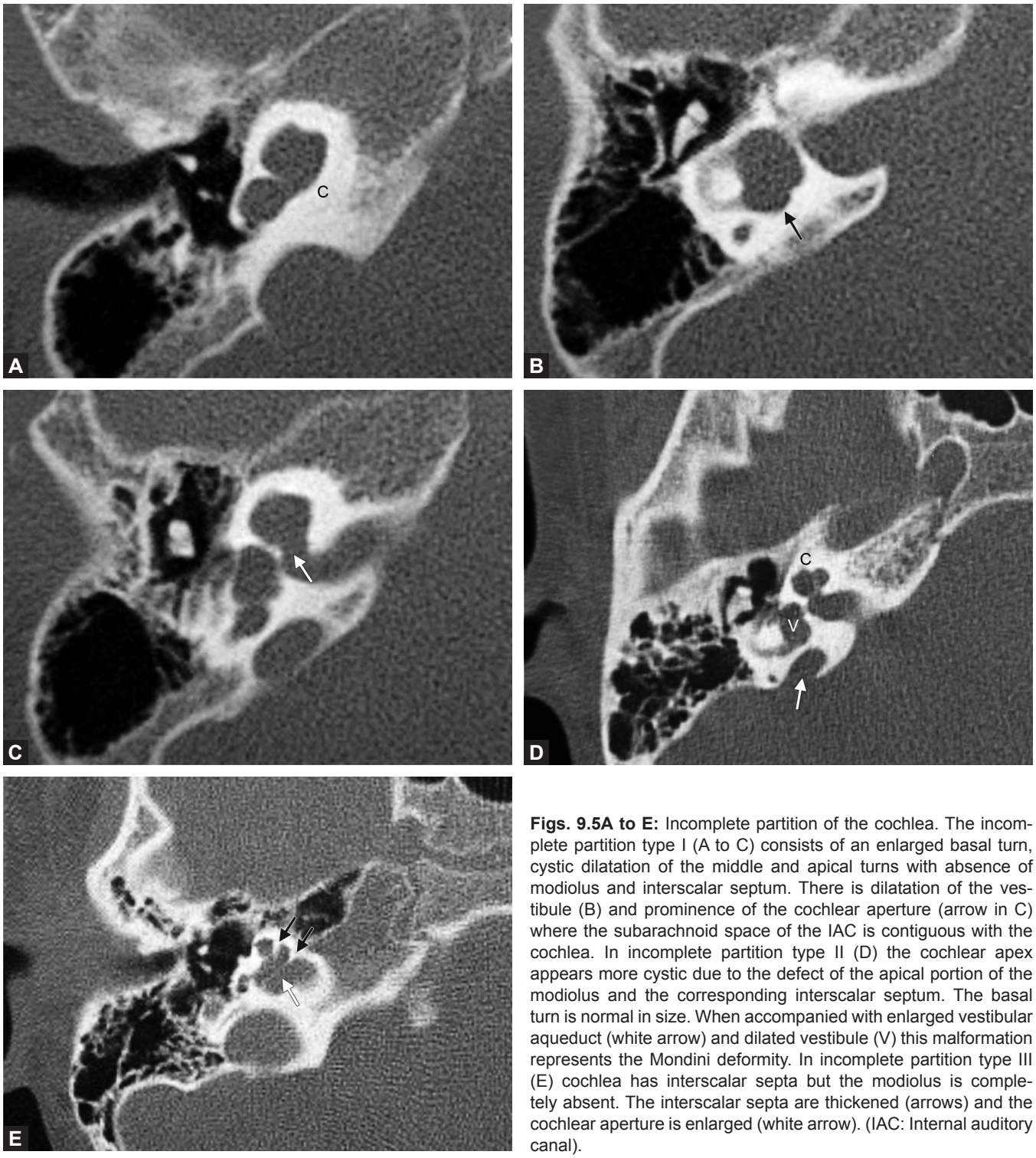
An X-ray can be taken after surgery, as there is a low risk for the electrode to enter the IAC.

### *Incomplete Partition Type III*

The cochlea in incomplete partition type III (IP-III) has an interscalar septa but the modiolus is completely absent (Fig. 9.5E). IP-III cochlear malformation is the type of anomaly present in X-linked deafness, which was described by Nance et al.[15] for the first time in 1971. Phelps et al.[16]described the HRCT findings associated with this condition for the first time, and this characteristic deformity was included under the category of incomplete partition deformities for the first time by Sennaroglu et al. in 2006.[17]

This anomaly is the rarest form of incomplete partition cases. According to the radiological database in Hacettepe University Department of Otolaryngology, IP-III constitutes 2% of the inner ear malformation group.

*Radiology*: Phelps et al.[16] reported that there is a bulbous IAC, incomplete separation of the coils of the cochlea from the internal auditory canal and widened first and second parts of the intratemporal facial nerve canal with a less acute angle between them. Talbot and Wilson[18] later added that the modiolus is absent and there is a more medial origin of the vestibular aqueduct with varying degrees of dilatation.




**Figs. 9.5A to E:** Incomplete partition of the cochlea. The incomplete partition type I (A to C) consists of an enlarged basal turn, cystic dilatation of the middle and apical turns with absence of modiolus and interscalar septum. There is dilatation of the vestibule (B) and prominence of the cochlear aperture (arrow in C) where the subarachnoid space of the IAC is contiguous with the cochlea. In incomplete partition type II (D) the cochlear apex appears more cystic due to the defect of the apical portion of the modiolus and the corresponding interscalar septum. The basal turn is normal in size. When accompanied with enlarged vestibular aqueduct (white arrow) and dilated vestibule (V) this malformation represents the Mondini deformity. In incomplete partition type III (E) cochlea has interscalar septa but the modiolus is completely absent. The interscalar septa are thickened (arrows) and the cochlear aperture is enlarged (white arrow). (IAC: Internal auditory canal).

In addition, Sennaroglu et al.[19] reported that in this deformity the interscalar septa are present but the modiolus is completely absent (Figs. 9.6A to F). The cochlea is located directly at the lateral end of the internal auditory canal instead of its usual anterolateral position. This gives the cochlea a characteristic appearance. From an earlier

study, the external dimensions of the cochlea (height and diameter) were found to be similar to the normal cochlea.[17] Apart from these features it was reported that the labyrinthine segment of the facial nerve has a more superior position in relation to cochlea;[19] the labyrinthine segment is located almost above the cochlea. If the axial sections are followed from top to bottom, the first structure that is identified in these cases is the labyrinthine segment of the facial nerve. In addition, there is a much thinner otic capsule around the cochlea and vestibule. The interscalar septum appears to be thicker than normal.

*Audiological findings*: There may be two types of hearing loss associated with this malformation.

Mixed-type hearing loss: The SNHL component is most likely due to the modiolar defect, whereas the conductive component may be due to stapedial fixation or third window phenomenon. The air–bone gap usually involves high frequencies as well as low frequencies. Snik et al.[20] suggest that the air–bone gap is associated with a third window phenomenon. They reported that because of the congenital malformation, the audiovestibular system functioned more effectively than it normally would, thus leading to better bone conduction levels. Their study revealed that audiological studies were in accordance with pure SNHL and air–bone gap in the audiogram did not signify a conductive hearing loss component.

Profound SNHL: The severity of this type of hearing loss may vary. It is most likely due to the absence of the modiolus, and in this situation, CI surgery is the primary means of restoring hearing.

*Management*: Mixed hearing loss gives the impression of stapedial fixation. Stapedotomy results in a severe gusher and further SNHL, and thus should be avoided. Patients with severe HL are candidates for CI.

Because of the absent modiolous during the surgery of IP-III, two serious problems may occur:

1. Gusher: These patients may have severe gusher during surgery, because of the large defect between the cochlea and the IAC. If it is not properly sealed, the postoperative CSF leakage may lead to recurrent meningitis. Ideally, the size of the cochleostomy should be slightly larger than the electrode in order to allow for soft tissue to be placed around the electrode. Passing the electrode through a tiny piece of fascia and inserting this together with the electrode may further improve the seal at the cochleostomy site

   An electrode with a "cork" type stopper (standard electrode 25 mm) provides for proper sealing of the cochleostomy (to prevent CSF fistula postoperatively) and also makes one full turn around the cochlea.
2. Electrode misplacement into the IAC: Because of the defective modiolus, electrodes with complete rings or contact surface on both sides may provide better stimulation. The probability of the longer electrodes entering the IAC is more than the shorter electrodes. Therefore, an electrode with full rings or contact surfaces on both sides, which will make only one turn around, the cochlea appears to be sufficient.

*Electrode choice*: Modiolar hugging electrodes have a tendency to go toward the center of the cochlea. As there is no modiolus in IP-III, this may result in misplacement into the IAC. The fact that the cochlea is located directly at the lateral end of the IAC rather than the usual anterolateral position may facilitate displacement of the electrode into the IAC during insertion. Longer electrodes may also be misplaced into the IAC. If a modiolar hugging electrode is used and postoperative X-ray demonstrates that the electrode is inside of the IAC, the facial nerve may be damaged when the electrode is removed. Thus, straight electrodes that are 25 mm in length and provide one full turn around the cochlea are preferable.

An X-ray should be taken in the surgery to confirm placement of the electrode. If the electrode is discovered to be in the IAC, it should be repositioned during surgery.

As mentioned before, spontaneous CSF leakage through the oval window is more frequently seen and reported in IP-I, even though both IP-I and IP-III are associated with high volume CSF leakage on cochleostomy. This may be secondary to the thicker stapes footplate that is present in IP-III.

## HYPOPLASIA

### Radiology and Definition

Cochlear hypoplasia represents a group of cochlear malformations in which the dimensions are less than those of a normal cochlea with internal architecture deformities. In cochlear hypoplasia, there is clear differentiation between the cochlea and vestibule and both of these structures occupy their respective locations relative to the IAC. In this regards, they are different than the rudimentary otocyst and CC. In smaller cochlea, it is usually difficult to count the number of turns with CT and/or MRI. But the

definition "cochlea with 1.5 turns" should be used for hypoplasia (particularly type III), rather than for IP-II cochlea. According to radiologic and histopathologic literature, as well as our own radiological data, four different types of cochlear hypoplasia can be identified:

- Type I (bud-like cochlea): The cochlea is like a small bud, round or ovoid in shape, arising from the IAC (Fig. 9.6A). Internal architecture is severely deformed; no modiolus or interscalar septa can be identified
- Type II (cystic hypoplastic cochlea): The cochlea is smaller in its dimensions with no modiolus and interscalar septa, but its external architecture is normal (Figs. 9.6B and C). There is a wide connection with the IAC. The vestibular aqueduct may be enlarged and the vestibule may be dilated (Fig. 9.6C). In this type of hypoplasia, gusher and unintentional entry of the CI electrode into IAC is possible
- Type III (cochlea with <2 turns): The cochlea has a short modiolus and the overall length of the interscalar septa is reduced, resulting in fewer turns (i.e. <2 turns). The internal (modiolus, interscalar septa) and external architecture are similar to that of a normal cochlea, but the dimensions are smaller and number of turns are fewer (Fig. 9.6D). The vestibule and the SCCs are hypoplastic. The CA may be hypoplastic or aplastic (Fig. 9.6D)
- Type IV (cochlea with hypoplastic middle and apical turns): The cochlea has a basal turn which is nearly normal in size and appearance; however, the middle and apical turns are severely hypoplastic and located anterior and medially rather than in their normal central position (Figs. 9.6E and F). The labyrinthine segment of the facial nerve may be located anterior to the cochlea rather than in its usual location.

## Audiological Findings

These patients will present with a range of thresholds on audiometric testing. Decision-making about the amplification options may be difficult, particularly in patients with a hypoplastic cochlear nerve. Patients with mild to moderate hearing loss can be habilitated with hearing aids and have near normal to normal language development. The majority of cochlear hypoplasia patients have severe profound hearing loss where a CI would be a reasonable option.

Some patients have CA aplasia with cochlear nerve aplasia and thus, an ABI would be the best hearing facilitative option. Other patients with cochlear hypoplasia have hypoplastic cochlear nerves. The best option in these cases is to use CI in the better-developed side or the side that is more suitable to CI surgery. If there is limited hearing and language development, an ABI should be considered for the contralateral side.

Some cases of hypoplasia (particularly hypoplasia type IV) may have mixed hearing loss in which the conductive component is due to stapedial fixation.

## Management

### *Cases with Mixed Type of Hearing Loss*

These patients may benefit from stapedotomy. This can be done in childhood if the family is motivated and can result in enhanced oral language development with or without hearing aid usage.

### *Cochlear Implantation*

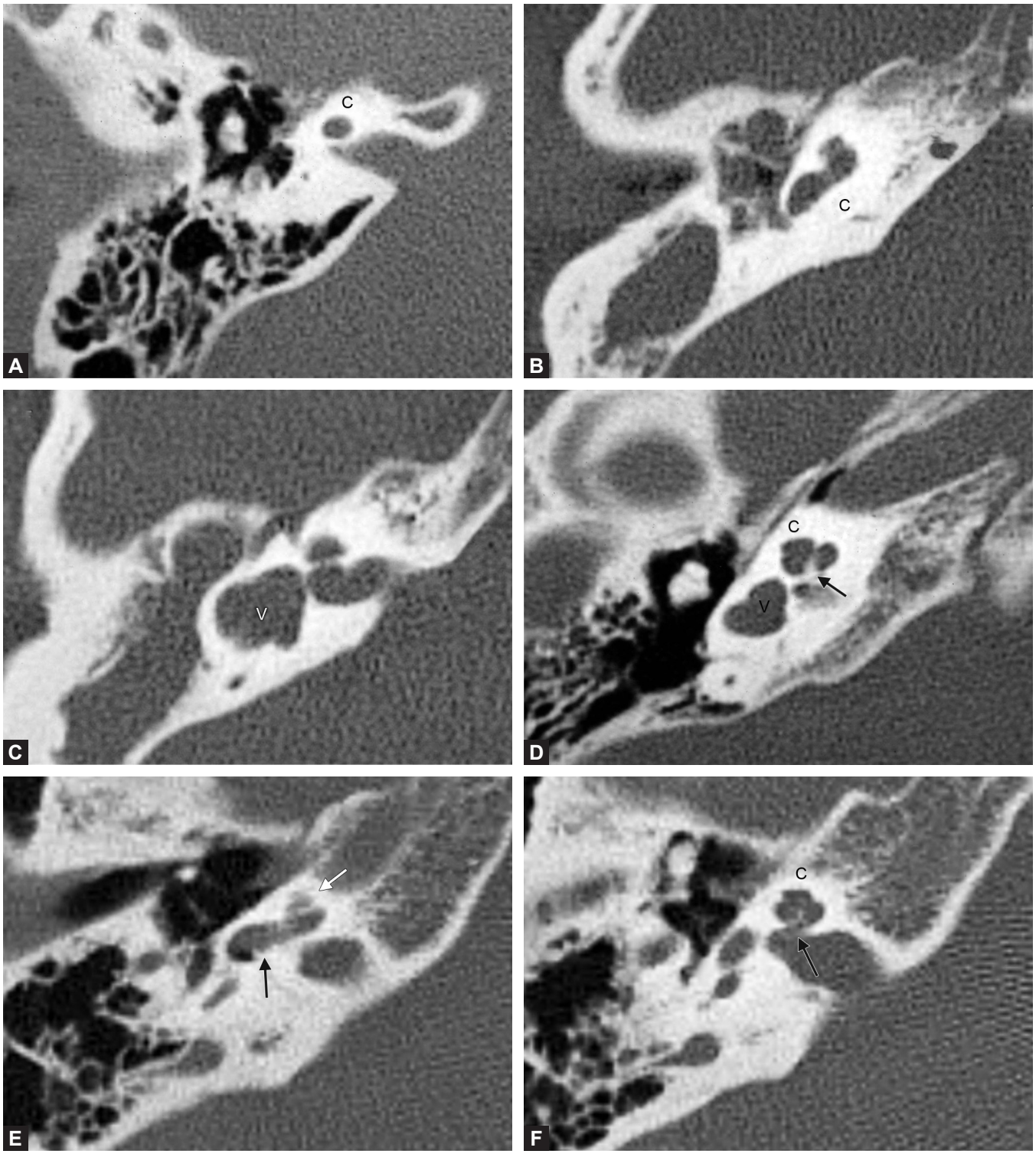
A transmastoid facial recess approach can be used in the majority of these patients. During surgery, facial nerve malposition is to be expected because of labyrinthine abnormalities. We have noticed that if the lateral SCC is not developed properly, the facial nerve may be in an unusual location. In one patient, e.g. we found that the facial nerve was already dehiscent and lying in the area of the facial recess.

If the cochlea is small, the promontory may not have the usual protuberance and it may be difficult to visualize the promontory and round window through the facial recess. In these situations, an additional transcanal approach may be necessary to provide better access to the hypoplastic cochlea.

## Electrode Choice

As the cochlea is smaller than normal, the length and cross-sectional area of the cochlear duct are smaller when compared to that of a normal cochlea. Thinner and shorter electrodes should, therefore, be used. A standard electrode may be too large for the cochlea and it may not be possible to obtain a full insertion.

Hypoplasia type II has the possibility of CSF leakage. A short electrode with a stopper type silicon ring may be used along with other measures for managing a CSF gusher. Because of the possibility that a full insertion may not be obtained, a shorter version of the electrode (19 mm) with a cork type silicon stopper is useful for cochlear implantation in a hypoplastic cochlea (particularly type II).




**Figs. 9.6A to F:** Cochlear hypoplasia can be seen in four types. Type I (A) anomaly is a 'bud like' cochlea where a very small round/ovoid structure is seen instead of a fully developed cochlea. Type II hypoplastic cochlea (B and C) is small in size with no modiolus and interscalar septa. The vestibule may be enlarged (C).Type III cochlear hypoplasia (D) has a short modiolus with shortened interscalar septa. The internal and external architecture however is similar to a normal cochlea. Cochlear aperture is aplastic (black arrow). Type IV cochlear hypoplasia (E and F) is diagnosed when the cochlea has a normal basal turn (black arrow) but hypoplastic middle and apical turns (white arrow).

It should be noted that the anatomy is particularly distorted in type I. Even though CI can be successfully placed into a hypoplastic cochlea, limited language development is expected. During the initial consent, the family should be informed that ABI surgery will most likely be required on the contralateral side in future.

### Auditory Brainstem Implantation

Auditory brainstem implantation (ABI) is indicated for patients with aplastic CA and cochlear nerve aplasia. As indicated before, if the child does not demonstrate significant improvement with CI, ABI should be considered as soon as possible on the contralateral side.

## LARGE VESTIBULAR AQUEDUCT

This describes the presence of an enlarged vestibular aqueduct (i.e. the midpoint between posterior labyrinth and operculum is >1.5 mm) in the presence of a normal cochlea, vestibule, and SCC (Figs. 9.7A and B).

Audiological presentation and management is similar to that of IP-II.

## COCHLEAR APERTURE ABNORMALITIES

### Definition and Radiology

The CA, cochlear fossette, or cochlear nerve canal transmits the cochlear nerve from the IAC to the cochlea. This can be visualized in the midmodiolar view as well as coronal sections on HRCT (Fig. 9.8A).

The CA is considered hypoplastic if there is a narrow opening between the cochlea and IAC (Fig. 9.8B), with a width of <1.4 mm.[21] The CA is considered to be aplastic when the canal is completely replaced by bone or there is no canal on midmodiolar view (Fig. 9.8C).

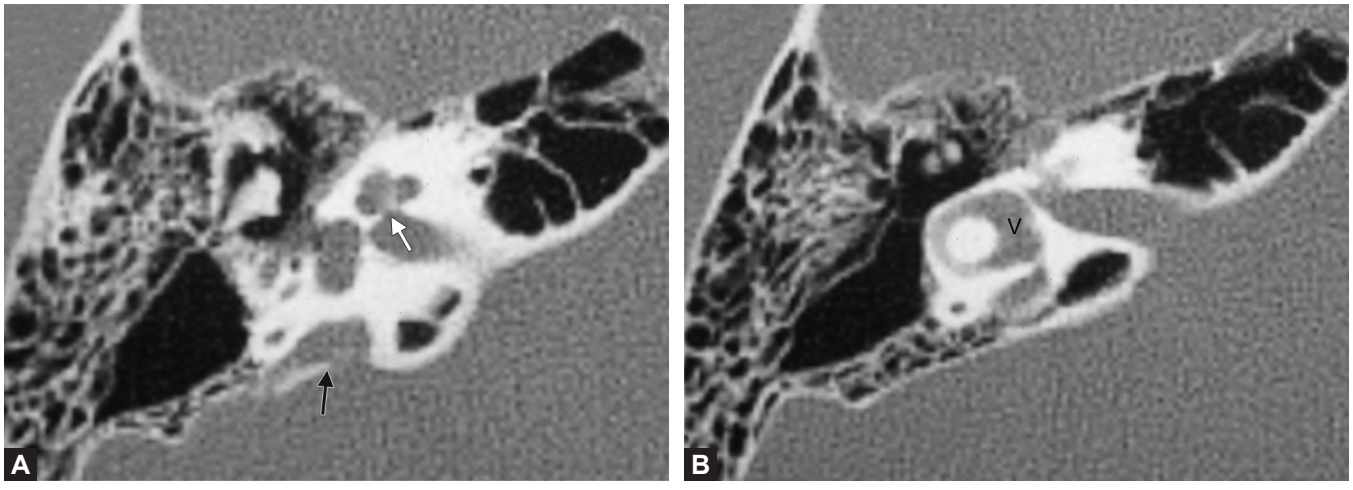
When the CA is aplastic, the cochlear nerve is typically aplastic as well. In situations where the CA is hypoplastic the nerve may be hypoplastic or aplastic.

CA hypoplasia and aplasia usually accompanies cochlear hypoplasia, but it is also possible to see this anomaly in an otherwise normal cochlea.

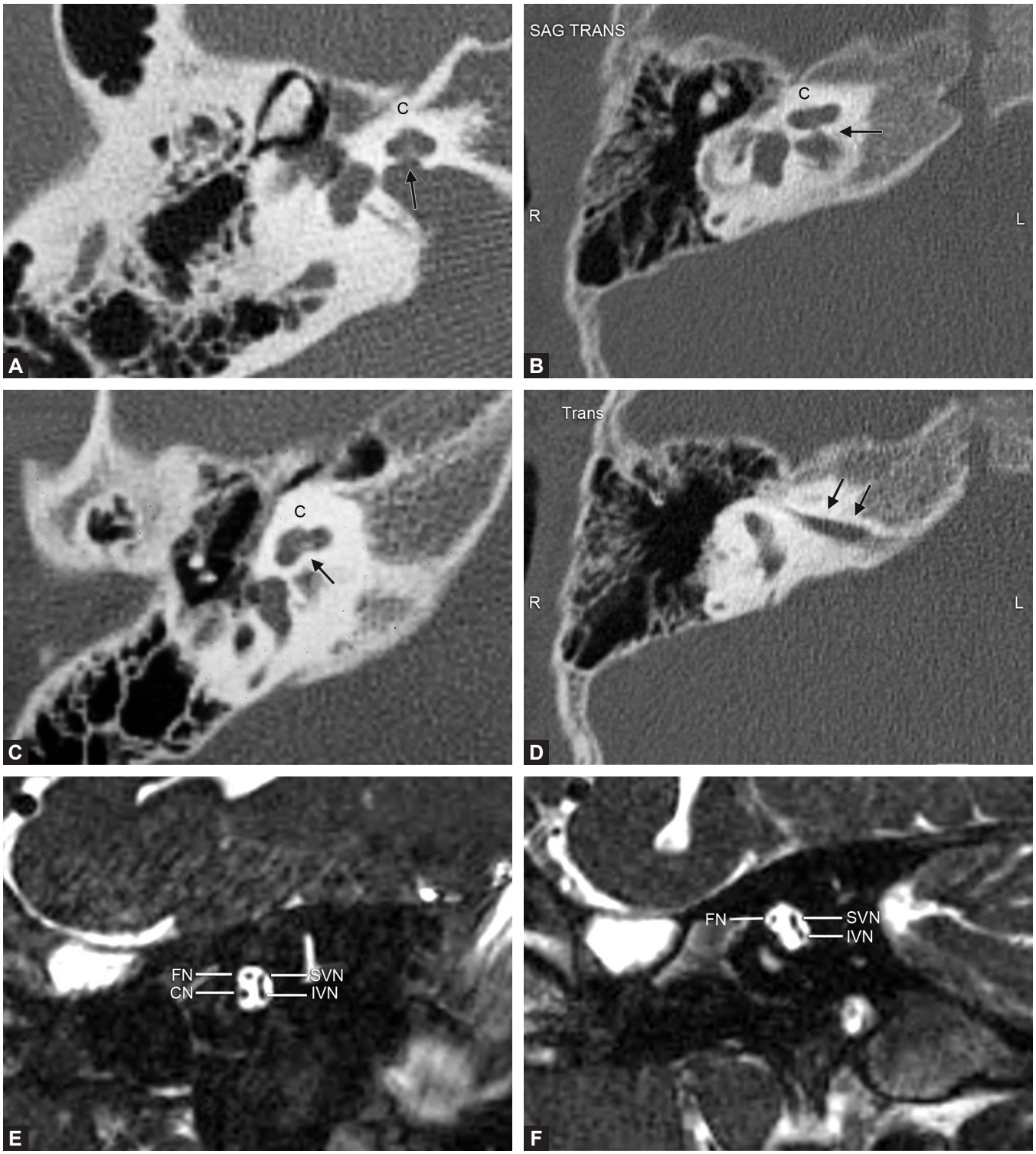
CA abnormalities may be accompanied by a narrow IAC on HRCT. The IAC is considered narrow if the width of the midpoint of the IAC is <2.5 mm (Fig. 9.8D), and can accompany other malformations or with a normal cochlea. In cases of narrow IAC, there is a possibility that the cochlear nerve is aplastic or hypoplastic and therefore imaging with MRI should be obtained. Axial and sagittal oblique high T2-weighted images (i.e. CISS and FIESTA) should be carefully investigated to determine whether CN aplasia or hypoplasia is present. On sagittal oblique MR sections, four distinct nerves can be visualized in the IAC (Fig. 9.8E). In CN aplasia, no nerve can be identified in the anterior-inferior part of the IAC (Fig. 9.8F).

### Audiological Findings

Severe to profound SNHL is usually present. As the cochlea is normal, otoacoustic emissions (OAE) may be present and the child may pass newborn hearing screening if far field auditory evoked responses are not measured. Their hearing loss is typically discovered later




**Figs. 9.7A and B:** A large vestibular aqueduct case has a dilated vestibular aqueduct (A) (black arrow) with normal appearing cochlea (white arrow) and vestibule (B).




**Figs. 9.8A to F:** Normal appearance of the cochlear aperture (arrow) on a transvers CT section from the midmodiolar level (A). Narrowing of the cochlear aperture (arrow) consistent with hypoplasia of the aperture (B). Complete obliteration of the canal (arrow) diagnostic of cochlear aperture aplasia (C). Narrow IAC (arrows) (D). Sagittal oblique MRI of the temporal bone showing a normal size cochlear nerve on the right (E) and absence of the cochlear nerve on the left (F). (FN: Facial nerve; CN: Cochlear nerve; SVN: Superior vestibular nerve; IVN: Inferior vestibular nerve; IAC: Internal auditory canal).

on in childhood based on the family's concerns of lack of sound awareness and language development. If the newborn screening protocol involves OAE and automated ABR, this malformation can be diagnosed during infancy. Diagnostic audiological evaluation will reveal profound hearing loss.

### Management

Hearing aids usually do not provide sufficient amplification in patients with CA hypoplasia and aplasia. In patients with bilateral hypoplastic CA with hypoplastic cochlear nerve, hearing aid trial is necessary. If this does not provide adequate functional hearing, these patients usually become candidates for CI. The family should be counseled that if CI does not provide sufficient hearing in terms of auditory perception, contralateral ABI may be necessary to achieve improved audiologic and language outcomes.

In CA aplasia, ABI is indicated as first-line therapy.

## RESULTS OF IMPLANTATION IN INNER EAR MALFORMATIONS

### Cochlear Implantation

It is difficult to assess audiological results across cohorts from different institutions according to the classification system presented here. Papsin[14] reported that patients with incomplete partition had consistently higher scores than other groups on both open-set and closed-set word testing postoperatively. Children with narrow IACs or cochlear canals performed significantly worse than children with normal caliber IACs and cochlear canals. Additionally, children with hypoplastic cochlea and CC also had worse outcomes. Wermeskerken et al.[22] reported that the ability to develop open-set speech perception in incomplete partition cases is similar to patients with normal anatomy after an average follow-up period of 2 years. Eisenman et al.[23] reported that children with severe malformations performed more poorly than those with mild malformations. Their results indicated that children with malformed cochleae demonstrate significant improvements in their speech recognition skills with a CI in comparison with their preoperative performance with hearing aids. But, the rate of postimplantation improvement was slower than that of children with radiographically normal cochleae. After 2 years there was no difference. Berrettini et al.[24] reported that out of four IP-I cases, two had good results. They concluded that the results of CI in IP-I are variable, but in many cases satisfactory, and are mainly related to the surgical placement of the electrode and residual neural nerve fibers.

Because of the progressive nature of hearing loss, hearing and language outcome with CI is the best in IP-II and LVA groups. In patients at Hacettepe University after 3 years of CI use, we have seen that IP-II and LVA patients have no statistically significant differences in the Meaningful Auditory Integration Scale (MAIS), pattern perception or sentence recognition tests as compared to their age-matched peer controls. Both groups of patients develop spoken language (expressive and receptive) with an increasing rate similar to their peers.

The majority of IP-I and CC patients show significant improvement on postoperative test scores and therefore benefit from CI. Out of six patients at our institution with CC, one patient had excellent word recognition abilities with the CI. The remaining four patients had moderate development, and one patient showed unsatisfactory development. After CI, 70% of IP-I patients had sentence recognition between 70% and100%, whereas 20% of these patients could not complete the test. Children who had at least 70% sentence recognition were also able to develop spoken language by using only auditory inputs. However, in order to develop syntactic elements of spoken language, these patients needed intensive formal therapy programs and visual cues such as speech reading, symbols, and pictures.

Fifty percent of the children with hypoplastic cochlea were able to obtain open set discrimination scores with CI. They developed spoken language similar to other children who underwent cochlear implantation. The remaining 50% of patients with hypoplastic cochlear nerve or type I hypoplasia had insufficient audiologic development and were only able to detect some environmental sounds and differentiate and imitate the pattern changes in words. Some of these patients went on to receive an ABI in their contralateral ear.

### Auditory Brainstem Implantation

There are a limited number of articles regarding the outcomes of ABI in children. Colletti L[25] reported the initial auditory results of ABI in children. All of the 14 prelingually deafened children in this study developed environmental sound awareness, detection of instrumental sounds and lip-reading enhancement after ABI surgery. Three

prelingual children achieved bisyllabic word recognition as well understanding of simple commands. Eisenberg et al.[26] reported the results of a 3-year-old boy who received an ABI 1 year before. They concluded that his audiological results were at the median of the range shown for a small sample of CI children implanted at a similar age. Goffi-Gomez et al.[27] reported their ABI experience in three children with inner ear malformations. All of the patients use their device daily with improvement in their auditory skills. Similarly, Choi et al.[28] reported that in their experience with nontumor patients, all of the children demonstrated an improvement in auditory performance. In our preliminary report with 11 children,[29] we indicated that six children gained basic audiologic functions, were able to recognize and discriminate sounds and could identify environmental sounds such as a doorbell and telephone ring by the third month of ABI use. In the consensus statement written by Sennaroglu et al.,[30] it was indicated that the minimum age at implantation should be between 1 and 1.5 years old and that additional handicaps decreased the likelihood of favorable audiological outcomes with ABI in children.

At the present time, 48 children with various inner ear malformations have received an ABI in Hacettepe University. When the long terms results are analyzed, it may be evident that it is possible to obtain closed and open set discrimination scores with ABI. Of children with more than 1 year of ABI use, 18 patients had 100% pattern discrimination and the remaining 11 patients had scores between 33% and 96%. In terms of multisyllabic words, 11 patients had 100% discrimination score, 8 patients had scores between 25% and 92%. Twelve patients achieved open-set scores above 50%, with two patients achieving 100%.

When different malformations were taken into consideration, patients with CC or cochlear aplasia had the best hearing thresholds with ABI. When we examined the influence of the type of malformation on audiological and language outcomes, again we found that patients with CC deformity have the best scores in all tests. Additionally, patients with CVN identified on MRI were found to have better hearing thresholds than patients with CVN agenesia.

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CHAPTER

# Diagnostic Approach to Common Pediatric Otologic Problems

10

*Adrian L James, Sharon L Cushing, Blake C Papsin*

## INTRODUCTION

Otologic diagnosis aims to identify the relevant features required to establish accurate diagnosis, to assess the severity of the problem and to determine the appropriate timeline for treatment. Ear problems in young children present specific difficulties to the clinician in this regard: not only is the narrow ear canal more difficult to inspect, the child may be unable to provide any description of their symptoms or to cooperate with examination. Furthermore, some pediatric otologic conditions exist or progress in relative silence and may only be discovered incidentally during routine examination or audiometry. A robust diagnostic approach is needed in order to identify these conditions and determine which need further management.

The aim of this chapter is to outline the diagnostic approach to assessment of a child presenting to an otolaryngology clinic with an ear-related problem. Emphasis is given to the differences between the assessment of children and adults, and to the common symptoms and signs that indicate an otologic problem. Considerations for the effective examination and investigation of the child's ear are described. More detailed description of the specific presenting and diagnostic features of these conditions can be found in relevant chapters throughout this volume.

## DIFFERENCES BETWEEN THE APPROACH TO ADULT AND PEDIATRIC OTOLOGIC DIAGNOSIS

Fundamental differences distinguish children from adults in the presentation and diagnosis of otologic disorders. In keeping with other pediatric conditions, the history of the presenting complaint is typically not obtained from the patient but from the parent, potentially leading to misinterpretation of the nature or severity of problems. This difficulty is compounded by seemingly greater tolerance, or less awareness, by children of some symptoms, notably hearing loss. This is particularly true if the onset of such symptoms occurs before the acquisition of the necessary language skills to communicate them. As an example, before newborn hearing screening, profound unilateral congenital hearing loss would often not be identified until most children were over 5 years of age.[1]

In addition to the difficulty of ascertaining symptoms correctly, complete examination and testing can be limited by the child's ability to cooperate. The tympanic membrane cannot be assessed easily when a child is resisting examination and moving, and inflammation cannot be assessed reliably during crying: just as the face becomes red in a crying baby, so does the eardrum! Wax obstruction provides an additional challenge, as tolerance of removal may be limited. Audiometric assessment has to be modified according to the child's stage of development (*see* Chapter 14), with behavioral testing typically not possible until after 9 months of age. Only limited assessment of vestibular function is practical under 4 years of age and sedation or anesthesia typically required for diagnostic imaging up to age around 6 (for CT) to 8 years (for MRI).

Finally, a different spectrum of otologic problems is seen in children from adults with initial presentation of congenital anomalies, and differing acquired pathologies.

Profound prelingual hearing loss provides very specific diagnostic and therapeutic priorities. Acute otitis media (AOM) and otitis media with effusion are much more common, yet classic otologic and neuro-otologic conditions such as otosclerosis, glomus jugulare, Meniere's disease, and acoustic neuroma are very rarely seen in children. Thus, a diagnostic approach specific to conditions of childhood is required. Tips to facilitate general assessment of the child's ear are described below, followed by important aspects of specific presenting complaints.

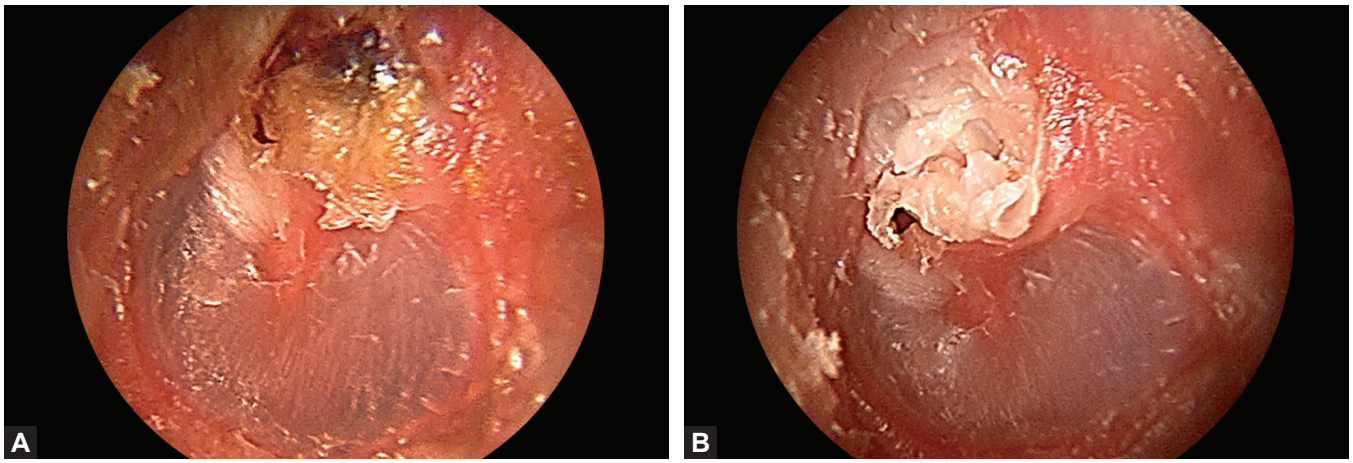
## EXAMINATION OF THE EAR IN A YOUNG CHILD

- Take care not to hurt the child: this may preclude subsequent assessment
- Position the child sitting sideways on the lap of their guardian
- Ask them to embrace the child with one hand holding the child's head to their chest, and the other hand to hold the child's arms to their side, as demonstrated in Figure 10.1. This comforting stable position restrains the child with the ear canal rotated up into an optimal position for examination
- First inspect the external ear for any dysmorphisms including preauricular sinus anterosuperior to the root of the helix or, much less commonly, first branchial sinus anteroinferior to the lobule. Consider checking sites of previous surgical incisions
- An outstanding ear with swelling or redness over the mastoid suggests mastoiditis.[2] This will be tender, but if possible, check for fluctuance that may require drainage, or alternatively for an inflamed postauricular lymph node that will have a more well-defined edge
- Look through the otoscope while positioning it in the ear canal so as to keep it within the lumen and avoid trauma—the bony meatus is sensitive. With care, it may be possible to navigate around wax, so as not to push it into the meatus and obstruct the view. Note the diameter and length of the meatus. In comparison with the tympanic membrane, a false fundus is featureless and laterally placed. Note the presence of wax obstruction, foreign body, purulent secretions, or meatal skin infection
- Always begin with the larger otoscopic speculum that provides a better view. Small speculae are only necessary in a particularly narrow meatus (e.g. neonates or Down syndrome) or to see around wax.

**Fig. 10.1:** This comforting stable position restrains the child with the ear canal rotated up into an optimal position for examination.

### Assessment of the Tympanic Membrane

- Use a systematic approach to examine the entire tympanic membrane. The pars flaccida must be inspected for the presence of retraction or cholesteatoma (Figs. 10.2A and B) and the anterosuperior quadrant must be inspected for an underlying congenital cholesteatoma (Fig. 10.3). Perforation or retraction may involve any part of the pars tensa. The example in Figure 10.4 shows a perforation as well as myringosclerosis that can be distinguished from cholesteatoma by its sharper edge and brighter and more superficial whiteness. Assess for prominent vascularity implying inflammation from infection and the presence of an effusion that may look purulent, suggesting AOM (Fig. 10.5). A serous or mucoid effusion without inflammation implies OME (Fig. 10.6)
- A retracted tympanic membrane requires careful assessment as shown in Figures 10.7A to D. Features to look for in a retraction include the following:
  - Are the limits of the retraction visible?
  - Is desquamated keratin trapped within the retraction?
  - Is there any sign of infection or granulation associated with the retraction?
  - Does the reaction involve any of the ossicles? Which ossicles, and how much contact is there? Is there any ossicular erosion?
  - Does the retraction remain adherent to middle ear structures during pneumatic otoscopy or Valsalva maneuver?




**Figs. 10.2A and B:** Cholesteatoma arising from the pars flaccida of left ear. (A) Cholesteatoma is visible under the anterosuperior quadrant of the pars tensa anterior to the malleus handle. The origin of the cholesteatoma from retraction of the pars flaccida is obscured by dry keratin debris that has the misleading appearance of cerumen. (B) After removal of the dry keratin plug, the pars flaccida defect containing moist white keratin debris is clearly visible. This demonstrates the importance of cleaning and examining the pars flaccida area carefully.

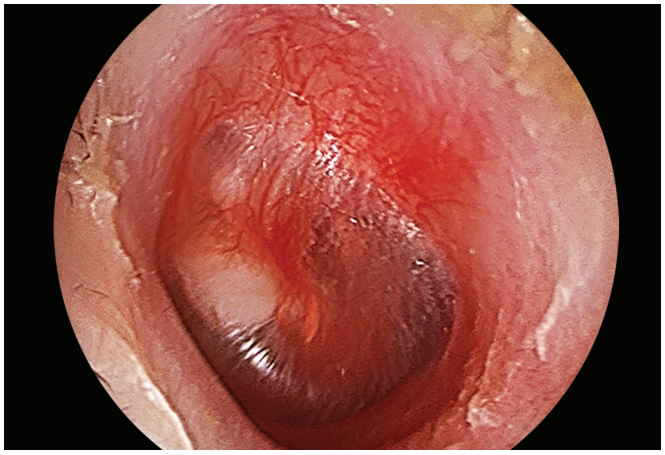


**Fig. 10.3:** Congenital cholesteatoma of the left ear. A rounded white 'pearl' of cholesteatoma is present under the anterosuperior quadrant of a normal tympanic membrane. This area can be partially obscured by the curvature of the ear canal so must be inspected carefully in children.

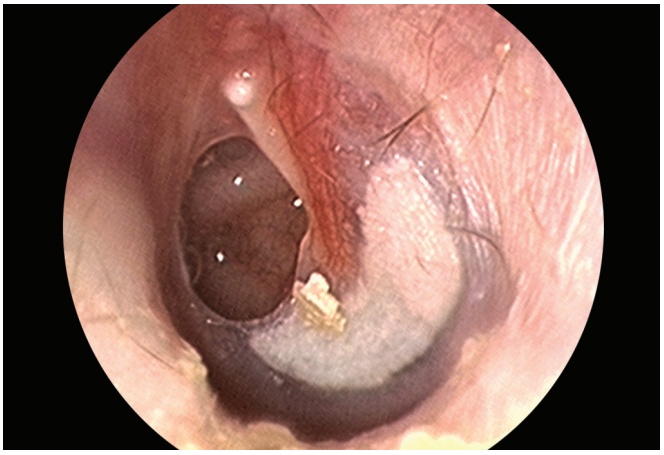


**Fig. 10.4:** Perforation of the anterosuperior quadrant of the right eardrum. There is no sign of infection as the ear is clean and the middle ear mucosa not inflamed. Myringosclerosis is present in much of the remaining pars tensa.

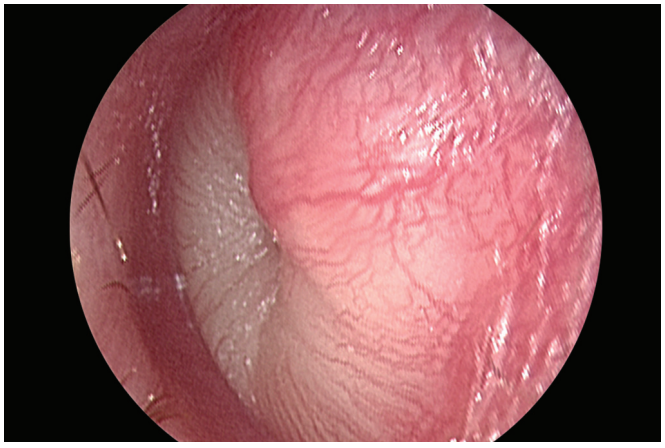


**Fig. 10.5:** Acute otitis media of the left ear. The tympanic membrane is bulging under pressure from a purulent middle ear effusion. Prominent vessels and erythema indicate acute inflammation.

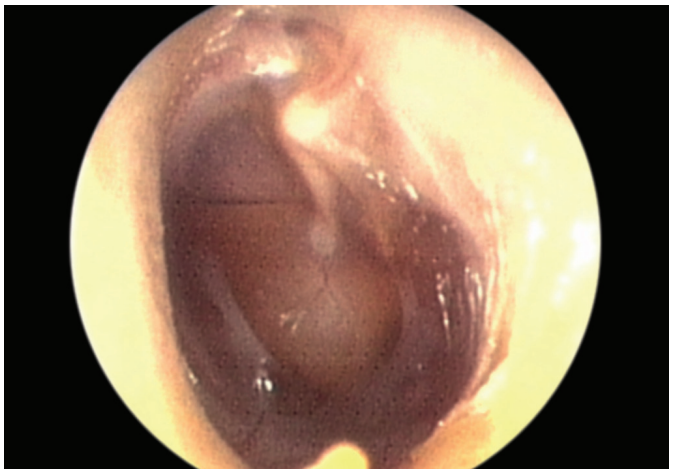
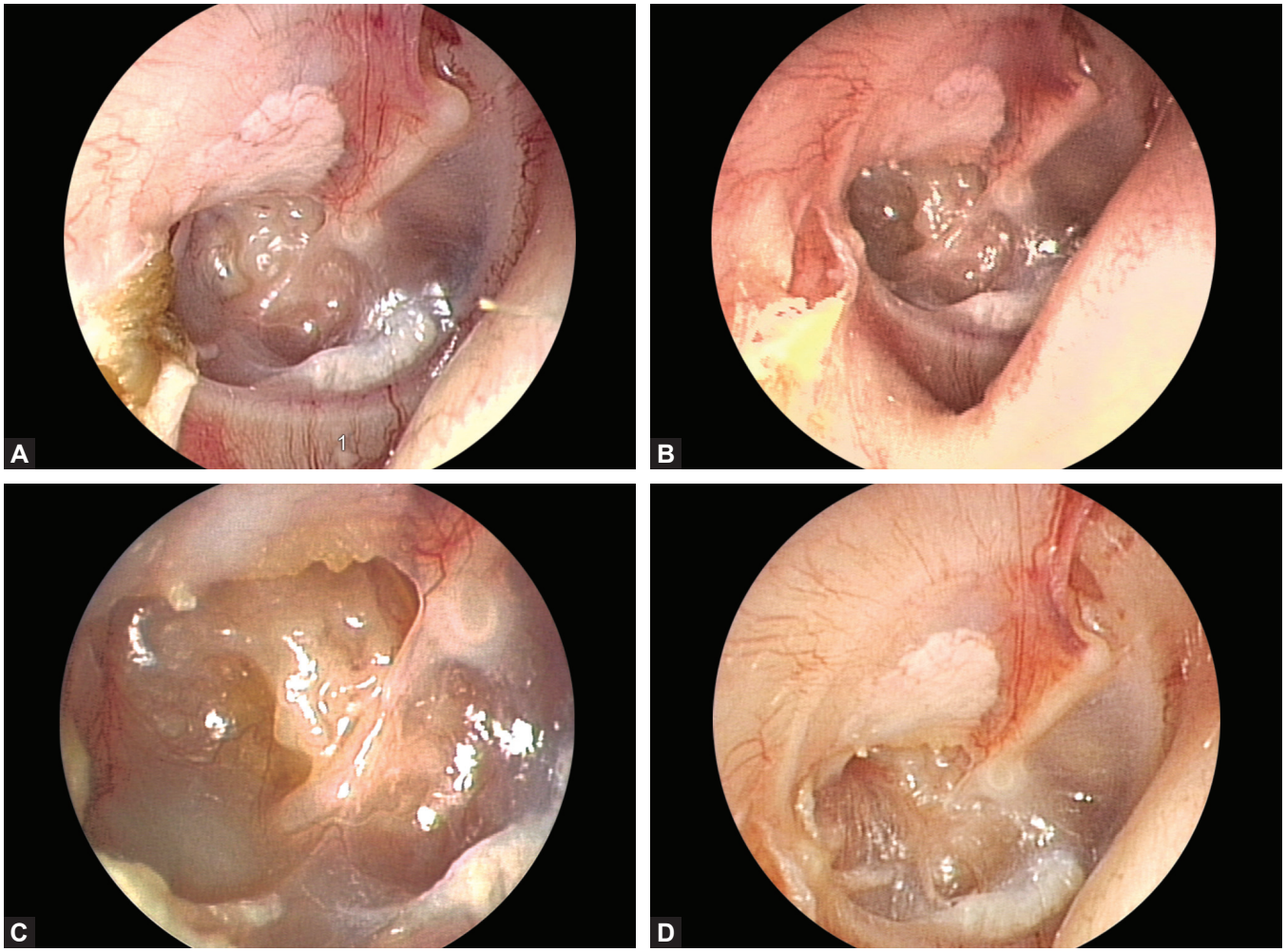
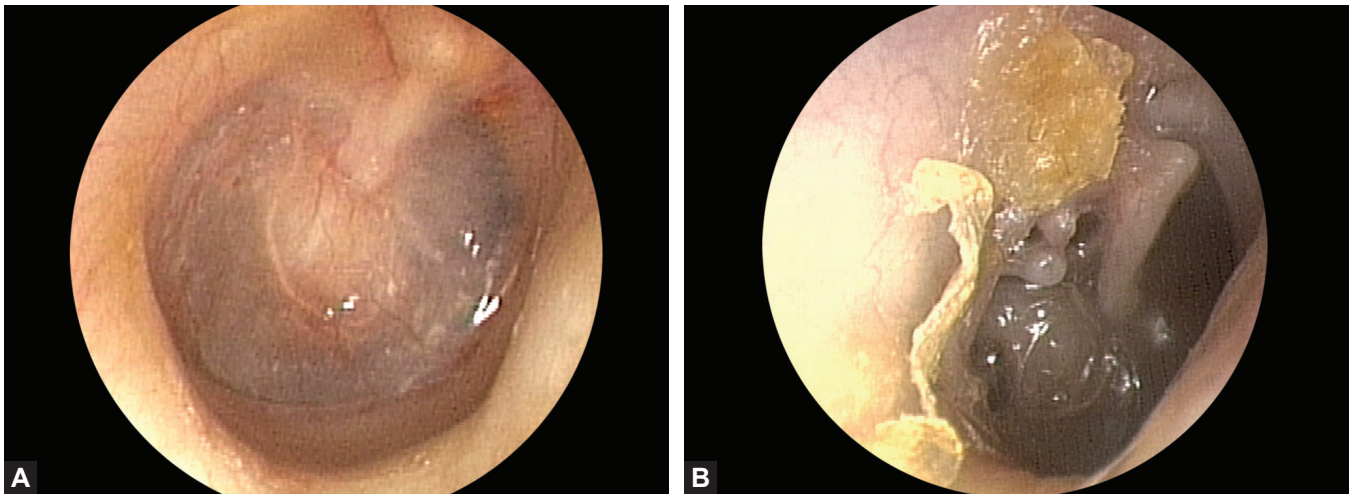


**Fig. 10.6:** Otitis media with effusion of the left ear. A serous middle ear effusion can be identified with certainty in this ear because of the clearly delineated air-fluid level anterior to the handle of the malleus. This allows the subtle difference in color between the air and fluid filled areas to be appreciated.




**Figs. 10.7A to D:** Otoendoscopic images of a right tympanic membrane at different stages of assessment. (A) First inspection shows pars tensa retraction that looks potentially adherent to promontory (centrally) and the jugular bulb (posteroinferiorly). The limits of the retraction in the retrotympanum are not visible and a trail of accumulating keratin indicates a risk that cholesteatoma may be forming. (B) Debridement of the keratin reveals erosion of the meatal skin that can lead to granulation tissue formation. (C) The wide-angle view from the endoscope placed closer to the eardrum shows the retrotympanic retraction is clean. An angled scope could be used to assess the hidden area superiorly. (D) Valsalva maneuver inflates the retraction elevating it off the jugular bulb, but the eardrum remains partially adherent to the promontory.




**Figs. 10.8A and B:** Retraction of the right tympanic membrane in two different ears, showing limitations of staging systems. (A) The pars tensa is touching the promontory. This is classified as Sade stage 4 if the retraction remains adherent to the promontory on pneumatic otoscopy or Valsalva, or stage 3 if not adherent. The response to pneumatic otoscopy or Valsalva maneuver may be inconsistent between observers or different days. (B) In addition to contact with the promontory, this pars tensa is draped around the long process of incus and stapes. The long process of incus is partially eroded and barely in contact with the stapes and the posterior limit of the retraction is not visible. Keratin is accumulating on the adjacent canal wall implying impairment of normal migration. Despite these concerning features, this retraction would also be classified as Sade stage 3 or 4. The diagnosis of progressing tympanic membrane retraction cannot rely upon use of staging systems alone.

  - A drawing or written description can be used to record the status of tympanic retraction. Staging systems are widely used for recording the status of tympanic membrane retraction but the established systems have poor reliability, inadequate sensitivity for noting clinically relevant changes and no correlation with hearing level or indication for treatment.[3] As demonstrated in Figures 10.8A and B, endoscopic photo-documentation is thought to provide a more accurate record.
- Inspection is enhanced by the stereoscopic view with a microscope and by otoendoscopy which can reveal the limits of the anterior recess and retracted areas
- A pneumatic attachment is recommended by many for the assessment of tympanic membrane mobility. This can be difficult in children. The ability of a clinician to identify a middle ear effusion is enhanced equally by pneumatic otoscopy or tympanometry.[4,5]

## Cleaning the Ear Canal

The view must be sufficiently clean to allow inspection of the entire tympanic membrane.[6] Irrigation or mechanical debridement with head light or microscope can be used according to the tolerance of the child:

- *Irrigation*: Usually avoided in the presence of tympanic membrane perforation or retraction, tympanostomy tube or foreign body. Safer than mechanical cleaning on a child that cannot keep still. May leave traces of debris or water that impair accurate inspection
- *Mechanical debridement*: Only feasible if the child keeps still voluntarily or is small enough to be appropriately restrained. Avoid poking the bony meatus or tympanic membrane, as this is usually painful. Suction can be distressingly noisy to children, so the wax curette, alligator forceps, or cotton wool on an applicator are preferable tools when possible. To help keep young children still, an assistant can cradle the head and a parent asked to hold the hands and chest within reassuring sight of the child. Infants may be swaddled effectively
- Complete assessment requires visualization of the entire tympanic membrane. If not possible a repeat visit should be scheduled. Regular application of a ceruminolytic may facilitate cleaning at subsequent follow-up[6]
- General anesthesia may be required to allow sufficient cleaning to make an accurate diagnosis. When possible this should be combined with other interventions that may be necessary such as tube insertion, or in cases where cooperation may be limited, auditory brainstem response testing and hearing aid mold fitting. If however the diagnosis is sufficiently obvious,

it may be more appropriate to proceed directly to surgical treatment so as to avoid the delay and inconvenience of an additional anesthetic (e.g. in management of cholesteatoma).

### General Examination

Examination includes assessment of the general demeanor and health of the child, as well as the remainder of the otolaryngologic examination (including the other ear!). Status of the nose is of particular relevance because of the association between adenoid hypertrophy and otitis media. Flexible nasendoscopy can be tolerated even by young children and should be favored over lateral radiographs for adenoid assessment when possible as it will provide a three-dimensional assessment of the adenoid relative to the Eustachian tube orifice and also facilitate identification of a submucous cleft palate. A bifid uvula or cleft palate may indicate predisposition to middle ear disease, which is even greater when the lip is also cleft.[7]

## PRESENTING FEATURES OF OTOLOGIC CONDITIONS

### Hearing Loss

When assessing hearing loss in children, two important differences from adults must be considered. First that the presentation may be relatively silent as the child may be unaware of the deficit, and second that sound deprivation has irreversible effects on development of auditory neural pathways and consequently speech and language development. The assessment of hearing ability in neonates and young infants relies on the use of objective tests (such as otoacoustic emissions and auditory brainstem response testing) which are used in newborn hearing screening to identify congenital hearing loss as early as possible.[8]

In older children, it is important to ask the parents about severity and time course of hearing loss. Reports that the child can hear but does not "listen" may be indicative of a mild or unilateral hearing loss. Secondary effects of hearing loss on speech and language development, behavior and socialization, and school performance may give important indications of the magnitude of the hearing problem.

While the physician is able to gain a basic impression of hearing and speech ability during conversation with the parent and child, tuning fork tests and informal tests of hearing such as whispering at fixed distances have been shown to have poor reliability in children.[9,10] In order to determine hearing thresholds and to distinguish between conductive and sensory or neural causes, there is no substitute for appropriate audiological tests, especially when conducted by an audiologist experienced in working with children.

When hearing or listening impairment seems out of proportion to audiometric thresholds, disorders beyond the ear should be considered. These include auditory neuropathy spectrum disorder (identified by absent auditory brainstem response in the presence of normal otoacoustic emissions or cochlear microphonic), central auditory processing disorder (for which psychometric tests can be completed), or behavioral disorders (such as autism).

### Otorrhea

Discharge from the ear is indicative of infection, except in rare circumstances such as the clear watery leak of cerebrospinal fluid following temporal bone trauma. The approach to diagnosis aims to distinguish between acute and chronic middle ear infections and otitis externa. History of the complaint is very important as it may not be possible to clear the ear canal sufficiently in a child to make the diagnosis from inspection of the eardrum—at least at the first visit.

Age at presentation gives important diagnostic clues: during infancy AOM with perforation is most likely, in older children chronic suppurative otitis media (CSOM) is most likely (from tympanic membrane perforation or cholesteatoma). Otitis externa seems to be less common than in adults. It is important to elicit a description of the nature of the discharge and how it differs from wax so as not to misinterpret the parental description. Foul smelling discharge is more typical of CSOM, particularly cholesteatoma. Management can be facilitated by understanding whether the infection was provoked by water exposure (e.g. when swimming) or by an upper respiratory tract infection, or whether it occurred spontaneously.

Attention to associated symptoms and timing may help distinguish recurrent acute infections from intermittently discharging chronic infection. It is essential to determine whether otorrhea occurs with or after otalgia. Acute otitis externa occurs with pain and some discharge. If otorrhea occurs after pain, or indeed if

pain subsides when otorrhea starts, AOM should be suspected. Otorrhea without pain or fever is typical of CSOM, cholesteatoma or chronic otitis externa.

Middle ear infection does not always cause sufficient otorrhea to be noticed by the parent or child, even when the tympanic membrane is disrupted.[11] To make an accurate diagnosis, it is vitally important that the entire tympanic membrane is inspected carefully, looking for evidence of infection, perforation, or cholesteatoma. A narrow opening into a pars flaccida cholesteatoma can be missed easily, particularly when partially obscured by waxy keratin debris or pus. If the eardrum cannot be adequately seen after cleaning the canal as thoroughly as can be tolerated, follow-up should be booked to check the child's ear again. Delay in the diagnosis of cholesteatoma may lead to irreversible hearing loss from ossicular erosion and other complications.

## Otalgia

In children, otalgia is most commonly caused by AOM, but diagnosis is not always simple. As outlined in guidelines from the American Academy of Pediatrics[12] accurate diagnosis of AOM can be surprisingly difficult and there is often some degree of uncertainty. A carefully taken history can help to distinguish AOM from the many causes of referred otalgia (Table 10.1).

AOM is most common around 12 months when the infant is too young to describe the cause of his or her distress. At this age, many babies cry out at night, and also may be teething (increased drooling may indicate this cause of otalgia). A short history of distress associated with inflammation of the tympanic membrane and a middle ear effusion are required to make the diagnosis.[12]

**Table 10.1:** Some important causes of otalgia in children

| | | |
|---|---|---|
| - Acute otitis media | | |
| - Acute otitis externa | | |
| - Referred otalgia | - Dental | - Teething |
| | | - Molar abscess |
| | | - Braces |
| | - Tonsils | - Tonsillitis |
| | | - Tonsillectomy |
| | - Temporomandibular joint dysfunction | |
| - Neoplasia | | |
| - (Malingering/attention seeking) | | |

These appearances are not always as clearly seen as in Figure 10.4. The presence of fever, acute otorrhea, and history of a recent cold make the diagnosis more certain. AOM is less common in older children, but diagnosis may be easier to make if a history of otalgia and ipsilateral hearing loss is provided. The degree of certainty of diagnosis, severity of symptoms, age of the child, and frequency of episodes are important criteria to consider when planning treatment.

The presence of otalgia with a normal tympanic membrane and ear canal implies a referred cause.[13] As summarized in Table 10.1, potential dental and oropharyngeal causes must be assessed. Rarely neoplasia may present with otalgia, so caution and thorough assessment must be completed before entertaining the relatively rare diagnosis of a functional cause.

## Facial Palsy

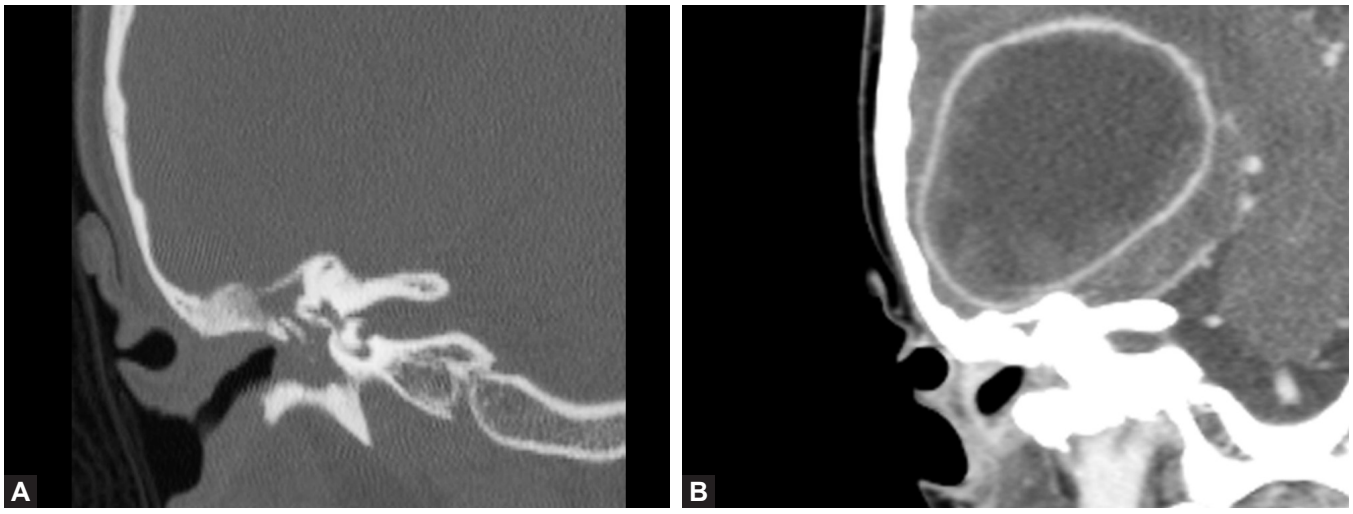
Assessment of facial nerve palsy in children follows the same principles as in adults. Thorough assessment of the ear is important as facial palsy may have an otologic cause such as a complication of AOM, active CSOM, or temporal bone trauma.[14] Presentation with swelling in front of the ear may also be secondary to spread of suppurative middle ear disease, and not imply a parotid cause.

## Headache

Headache is not a typical feature of pediatric ear disease. When associated with suppurative middle ear disease (i.e. AOM, CSOM, and cholesteatoma) it is critically important to consider the possibility of intracranial complications. Children can appear surprisingly well with an intracranial abscess. A contrast-enhanced CT scan may be necessary to make this diagnosis (Figs. 10.9A and B).

## Vertigo and Imbalance

The diagnostic approach to disorders of balance in children aims to distinguish vestibular from other causes. The first challenge is to identify the problem as many children cannot articulate the feeling or sense of vertigo and are often initially thought to be clumsy and uncoordinated. Some may even be misdiagnosed with a behavioral abnormality. Their symptoms can go unrecognized or misdiagnosed for years. Their presentation is variable and depending on the cause can include ataxia,




**Figs. 10.9A and B:** Coronal CT scans of a temporal lobe abscess from cholesteatoma. (A) Using settings optimized for bone, this image shows somewhat rounded soft tissue swelling under the tegmen tympani consistent with cholesteatoma. Without intravenous contrast, the adjacent brain appears normal. (B) The contrast-enhanced scan reveals a large temporal lobe abscess. Contrast material is important in the diagnostic approach for suppurative intracranial complications with CT.

headache, visual disturbances, hearing loss, otalgia, and otorrhea. Other important symptoms include, oscillopsia, drop attacks without loss of consciousness, lateropulsion (sensation of being pushed to one side), and vegetative symptoms (nausea, emesis, and malaise). Learning disabilities can sometimes be a presenting complaint due to poor dynamic visual acuity secondary to deficiency of the vestibulo-ocular reflex. Children with congenital or acquired severe deficits of vestibular function may not experience vertigo but rather have balance deficits that go unrecognized. This is particularly common in children with profound sensorineural hearing loss (SNHL).[15]

Despite such variable presentation, the four focused questions shown in Table 10.2 help to differentiate the pathology in most cases.[16]

Full diagnostic assessment requires examination of static and dynamic imbalance and visual acuity. As outlined in Table 10.3, a large range of testing is feasible in children and may reveal the diagnosis without recourse to more invasive tests of vestibular end-organ function such as vestibular-evoked myogenic potentials and caloric testing. For example, pre- and postrotatory nystagmus can be evoked by rotating the child while seated on a rotating office stool (with the parent if needed to hold a young child) to assess the vestibulo-ocular reflex. Developmental reflexes should be tested when examining infants: floppiness and lack of head control can be early signs of vestibular impairment.

### Tinnitus

When children report noises in their ears, it is appropriate to assess severity and type. Questioning should aim to distinguish between objective causes such as popping or clicking that may imply Eustachian tube dysfunction or, rarely, myoclonus, and pulsatile tinnitus that may imply a vascular cause, from the subjective ringing or humming tinnitus which is more commonly troublesome to adults.[17] Assessment must also consider symptomatology of the patulous Eustachian tube that includes autophony and intrusive sensation of breath sounds in the ear. Chronic sniffing can induce tympanic membrane retraction via a patulous Eustachian tube.[18]

### Hyperacusis

As it is common for young children to find loud noises unpleasant, it is important to determine whether the severity of intrusion into everyday life is sufficient to justify a diagnosis of hyperacusis and supportive therapy.[19,20]

## INVESTIGATIONS FOR PEDIATRIC EAR PROBLEMS

### Audiology

The importance of appropriate audiological assessment of the child with otologic conditions has been emphasized above. Further details can be found in Chapter 14.

**Table 10.2:** Diagnostic approach to assessment of pediatric balance disorders, using four sets of questions. The characteristic answers to these questions indicate likely diagnoses[16]

| | |
|---|---|
| 1. "How does it feel?" | |
| Light headed/faintness | Anxiety |
| | Orthostatic hypotension |
| Whirling/spinning | Peripheral vestibular disorder |
| 2. "What makes it worse?" | |
| Moving | Peripheral vestibular disorder |
| Rolling/bending/look up | Benign positional vertigo |
| Straining | Perilymph fistula |
| 3. "How many episodes and how often?" | |
| Multiple; seconds to minutes | Benign positional vertigo |
| | Benign paroxysmal vertigo of childhood |
| Multiple; >20 minutes to hours | Vestibular migraine |
| | Meniere's syndrome |
| Single; hours to days | Labyrinthitis/vestibular neuritis |
| 4. "Any associated symptoms/problems?" | |
| Change in awareness | Seizure disorder |
| Preceding event | Ototoxic medication |
| | Head/ear trauma |
| Other diagnoses | Otologic disease |
| | Autoimmune disorder |
| | Cardiac disorder<br>Postural orthostatic tachycardia syndrome (POTS) |
| Family history | Migraine |
| | Hearing loss |

## Microbiology

Currently, culture of otorrhea or pus from the middle ear space is generally only helpful for diagnosis when antibiotic resistance is suspected, e.g. after failure of first-line treatment.

## Diagnostic Imaging

Diagnostic imaging can be appropriate as part of the diagnostic approach to otologic conditions. The decision to obtain imaging must be balanced by the need for sedation or general anesthesia in younger children (normally up to the age of around 6–8 years), and by awareness of the long-term impact of irradiation on the developing brain and vulnerable soft tissues such as the lens and thyroid in young people. Use of CT in young children should be reserved to situations in which the results may have sufficient impact on clinical decision making, and not simply to satisfy the diagnostic curiosity of the physician or parent.

Imaging should be considered as part of the diagnostic approach when neoplasia of the temporal bone is suspected (such as histiocytosis or rhabdomyosarcoma) for assessing vascular anomalies (especially prior to surgical intervention) and for assessment of facial nerve palsy if persistent or from temporal bone fracture. SNHL and cholesteatoma are more common reasons to consider diagnostic imaging so are discussed in more detail.

### *Sensorineural Hearing Loss*

At our institution, MRI is now favored over CT as a single imaging modality as it reveals intracranial diagnoses (congenital cytomegalovirus infection, hyperbilirubinemia), cochlear nerve anomalies (congenital aplasia), and intracochlear anomalies (incomplete partition; obliterative labyrinthitis) more clearly than CT and without

**Table 10.3:** Clinical tests of vestibular function for assessment of imbalance in children

| | | |
|---|---|---|
| Static imbalance tests | | |
| Eye movements | | |
| | Spontaneous nystagmus | Vestibular disorder |
| | Pressure-induced nystagmus* | Labyrinthine fistula |
| | Gaze-evoked nystagmus | Central nervous system disorder |
| Dynamic imbalance tests | | |
| Dix–Hallpike maneuver | | |
| | Rotatory nystagmus | Benign positional vertigo |
| Vestibulo-ocular reflex assessment | | |
| | Head thrust test | Vestibulo-ocular reflex anomaly: |
| | | Loss of stationary gaze |
| | | Corrective saccade |
| | Head shake maneuver | Post head shake nystagmus |
| | Dynamic visual acuity | |
| | Rotary chair testing | |
| Vestibulospinal testing | | |
| | Romberg and sharpened Romberg | |
| | Past pointing | |
| | Fukuda stepping test | |
| Gait and gross motor function | | |

*Pressure can be transmitted by tragal compression, impedance testing (Hennebert's sign), or loud sound (Tullio phenomenon).

irradiation. It is important to remember that MRI has restricted utility after cochlear implantation. CT may still be appropriate prior to cochlear implantation to assess candidacy with cochlear nerve hypoplasia or labyrinthitis ossificans and for surgical planning with syndromic anatomical anomalies.

Recent guidelines suggest that CT is not indicated for sudden SNHL in adults.[21] However, it is a more sensitive test than MRI for identifying enlarged vestibular aqueduct that is a common cause of sudden progression of hearing loss in children.[22] In conjunction with MRI, it is useful for identifying cochlear nerve hypoplasia by revealing the diameter of the cochlear nerve canal at the base of the cochlea, and also after meningitis for distinguishing between cochlear ossification or fibrosis when MRI reveals obliterative labyrinthitis.

### *Cholesteatoma*

In most centers, CT is the standard imaging modality in the setting of suspected cholesteatoma despite the fact that it has unreliable sensitivity and specificity for making a diagnosis of cholesteatoma. Keratin accumulation within cholesteatoma is indistinguishable from granulation tissue or effusions, though a convex soft-tissue to air interface is highly suggestive of cholesteatoma. Discharge of purulent contents out of a cholesteatoma sack can leave an air containing space yielding a false negative scan. Bone erosion (e.g. of scutum or incus) may be caused by small retraction pockets, thus providing a false positive scan. The role of CT is not so much in making the diagnosis as in surgical planning, revealing the potential limits of the disease in relation to the patient's anatomy and opportunities for surgical access. Rare complications of cholesteatoma can be revealed (e.g. canal fistula or intracranial pathology) as well as anatomical variations that might predispose to surgical complications (e.g. course of the facial nerve and venous sinuses).

With MRI, non-echo planar diffusion weighted imaging has good sensitivity and specificity for identifying larger cholesteatomas.[23,24] Current resolution and lack of contrast between bone and air limit the utility of MRI in surgical planning, but it can be helpful when diagnosis is in doubt, or to diagnose more extensive occult residual cholesteatoma after previous surgery.

### *Conductive Hearing Loss with a Normal Tympanic Membrane*

CT may help to identify an occult congenital cholesteatoma in the medial epitympanum, more commonly when the hearing loss is unilateral and the child has previously passed newborn hearing screening. CT may also reveal the nature of congenital ossicular fixation and help guide decision-making regarding ossiculoplasty. In cases where such lesions are suspected, a direct coronal CT scan best illustrates the status of the stapes footplate.

### *Complications of Suppurative Middle Ear Disease*

A contrast-enhanced CT scan of the brain must be considered when AOM, CSOM, or cholesteatoma are associated with headache or drowsiness (*see* Figs. 10.9A and B). Fever and malaise are atypical features of CSOM and cholesteatoma and should also raise concern for suppurative intracranial complications.

## Blood Tests and Other Investigations

Blood samples may be difficult to obtain in children and generally do not play a large role in the diagnostic approach to chronic otologic problems of childhood. Testing for genetic mutations is likely to offer more definitive diagnostic testing in the near future and currently has increasing utility in the diagnosis of SNHL. The implementation of more widespread perinatal screening tests is reducing the need for some tests (e.g. congenital hypothyroidism as a cause of hearing loss). Renal function tests can be considered in hearing loss (e.g. Alport's in which SNHL can be associated with deteriorating renal function later in older boys, or branchio-oto-renal syndrome associated with branchial and preauricular sinuses). Thyroid function testing can be considered in the presence of a goiter with SNHL (Pendred's syndrome) but children with this condition are usually euthyroid.

ECG should be considered in assessment of profound bilateral congenital SNHL as a long QT interval is associated with sudden death in Jervell and Lange-Nielsen syndrome. Children with hearing loss should have regular tests of visual acuity to ensure they have no additional sensory impairment. As outlined above, children with imbalance or severe/profound SNHL should have an assessment of vestibular and balance function.

## KEY POINTS

Assessment of pediatric ear problems is made more difficult by the limited history that may be available from the patient and limitations in the degree of cooperation that may be possible with examination and testing.

A thorough diagnostic approach requires the following:

- Careful history taking
- Examination of the entire tympanic membrane
- Debriding the ear canal and drum as necessary
- Collaboration with pediatric audiology
- Being alert to opportunities for early diagnosis for optimum outcome, especially in prelingual hearing loss and also cholesteatoma.

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CHAPTER

11

# Clinical Examination of the Ear

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## INTRODUCTION

The clinical examination of the ear in the pediatric population can be challenging. While teenagers and adults tend to be similar both anatomically and behaviorally, the examination of infants and toddlers requires unique skill and experience in order to obtain a complete examination and make an appropriate diagnosis. The appearances of normal and pathologic disease states may not differ dramatically between children and adults; however, there are often substantial differences in medical history, risk factors, and clinical presentation that may alter the interpretation and management of similar conditions, all of which can impact the clinical outcome.

History is often provided by parents or other caregivers, and as such, the reporting of symptoms can be influenced significantly by the exposure, perceptions, knowledge, interpretation, and quality of life impact on the historian. For example, crying may or may not be a manifestation of ear pain, and, if present, could have any number of causes, none of which would be easily verified or differentiated in infants or young children. Some symptoms such as hearing loss or vertigo may not be noticed by others, and tinnitus would only be known if the child is old enough to perceive and express it.

The difficulties inherent in assessing pediatric otologic problems delineated above only increase the importance of the otologic examination. On the other hand, physical examination, and especially otologic examination, has distinct challenges in the pediatric population. The ear canal is narrow in infants and young children, and may be unusually narrow in a syndromic child. It may be difficult to visualize the ear drum without cleaning the ear canal, which may be very challenging or even impossible in the office. Children with anatomic, cognitive or behavioral limitations require skill and experience in approaching, examining, and testing.

Moreover, the general medical practice climate today emphasizes productivity, resulting in pressure to spend less time with each patient in clinic as well as a higher proportion of scheduled surgeries per patient encounter. These effects may be more pronounced for pediatric otolaryngologists due to the high volume nature of the specialty. Books and training encourage a complete and thorough history taking and physical examination; however, practice pressures "correct" such unrealistic intentions and one of the skills that is often expected to be acquired quickly by both trainees and junior faculty is the ability to spend the shortest amount of time in obtaining a focused history and physical examination while meeting the targeted billing requirements. This creates a conflict between productivity and being able to acquire the necessary elements for decision making while also avoiding assessment errors and medical-legal liability. Therefore, unfortunately today's training should include acquiring fast, efficient, and safe assessment skills. In general, teaching a focused and efficient history taking and physical examination demands a more thorough and complete assessment to be done by the teacher in order to judge and correct what was done by the trainee. Clinicians in training institutions experience the same productivity pressures as any other practitioner, which can limit this critical didactic relationship. Instead, under the present circumstances the teacher often has to rely much more on what the "efficient" trainee gathers, and limit him or herself to verifying some of the most crucial elements.

A similar relationship has become widespread between physicians and mid-level providers, and the same limitations and dangers exist when nurse practitioners and/or physician assistants see patients first, or even on their own.

All of these challenges heighten the importance of other training modalities and materials including books, visual training materials, and special educational activities that do not have the pressure on productivity.

This chapter intends to serve the purpose of providing the important elements helpful or even perhaps crucial in the examination of the ear in the pediatric population. The scope of this chapter does not include medical history as a separate section, which is covered in the previous chapters; however, some relevant elements are mentioned where appropriate.

## FACILITIES AND ENVIRONMENT

### Waiting Room

Otologic problems in children are assessed and managed by a variety of health care professionals in a variety of settings (emergency department, urgent care, family medicine, pediatrician, internist, otolaryngologist, pediatric otolaryngologist). In most cases, a child will be seen in an environment that is only for children. A clinic dedicated to pediatric otologic problems is extremely rare, and does not exist in most centers; therefore, a broad spectrum of pediatric and/or pediatric ENT problems may be seen in the same clinic. Desire to increase or to keep up with decreased reimbursements have created an environment of fast-paced short turnover clinic visits, eroding the patient/parent satisfaction with increase in potential for errors. On the other hand, this planned rapid pace is often not realistic, resulting in prolonged waiting periods up to 1–2 hours past the scheduled appointment. Besides the fact that in an adult clinic the patient is alone or sometimes with just one or two companions, a child always comes with minimum one or two parents and often even more relatives of various ages. These factors all increase the importance of the capacity and conditions of the waiting room. It is extremely important to accommodate this load of waiting people, with adequate space and seating as well as features to keep them busy and less annoyed with a wait. Having toys in a waiting room helps to keep the children busy; however, maintaining the cleanliness of toys can be challenging. Attractive toys in the waiting room or even age appropriate toys given to each child can quickly become fomites, even with the intention of cleaning after use. Instead, solid and easily cleaned stationary toys can be supplemented with visual entertainment options (Fig. 11.1). It is important to have a staff periodically clean the commonly touched surfaces throughout the day, not only at the end of the clinic, for sanitation and also to reassure waiting families of their cleanliness (Fig. 11.2). Similarly, there should be adequate hand sanitization stations in the waiting area with warnings to use hand cleaning before and after touching toys or common surfaces. Ideally, two or more TV monitors targeting different age groups would serve the best. A simple practice is engaging waiting children with coloring pages that can continue to occupy their attention when they

**Fig. 11.1:** Waiting room should be spacious with adequate seating.

**Fig. 11.2:** Toys or items attracting children should have surfaces that can be easily cleaned and sanitized.

continue to wait in the examination rooms. Parents should be encouraged to bring children's favorite toys, which is usually the habit anyway. Recently, these toys are being replaced by portable small electronic game consoles, tablets or smart phones with games or videos, that set invisible chains in keeping patients in their seats.

## Room and Setup

An examination room that meets the needs for children with ear problems should have minimum standard furniture and equipment. The layout and quality of these may vary; however, here are some preferences for practical reasons. One layout that this author finds useful is having the physician stool on wheels in one corner of the room, in between the treatment cabinet and the desk with computer and drawers with documentation and information binders, and the examination chair facing the physician corner (Fig. 11.3). This layout allows the rotation of the examination chair 180° to reach both ears for otoscopy or manipulation, while for a right-handed otologist to easily access the drawers with instruments, material or suction on the right and the desk with the PC and monitor and paperwork on the left. The physician faces both the patient with or without the parent keeping the patient on the lap and the parents or other companions that sit on the other side of the computer table. At the other corner of the room on the other side of the treatment cabinet is the best place for the floor standing microscope or the endoscope tower (Fig. 11.4). On the other side of the microscope an examination table is placed so that the microscope can serve both the patients on the table and on the examination chair (Fig. 11.5). It may not be possible due to the cost or necessary to equip every room with an endoscope tower; however, if there are one or more dedicated endoscope rooms, the remaining rooms, i.e. most of the rooms, can be equipped with a microscope (Fig. 11.6). This setting naturally is describing an environment best for pediatric otologic examination, and may be different for the examination rooms that have a varying weight of need for ear examination. In a handy location, a wall dispenser of various size otoscope speculums should be placed.

Walls can have child friendly posters, as well as pictures or drawings of ears and other relevant anatomical structures. A set of normal and abnormal examination pictures and with a ventilation tube, as well as illustration of the entire ear and related structures from pinna to ear canal, tympanic membrane (TM), middle ear (ME), mastoid, Eustachian tube (ET), nasopharynx, and adenoids is very useful when describing physiology, pathophysiology, and intended treatment options to the patient and the parents.

## Necessary Instruments

The treatment cabinet is an essential element of the examination room (Fig. 11.7). Cabinets may have mounted charging docks on top, as well as containers for frequently used items such as tongue depressors. Drawers should be dedicated to 4×4 and 1×1 gauze, cotton balls, wicks, culture

**Fig. 11.3:** Physician stool is at one corner of the room, in between the treatment cabinet and the desk with computer and drawers with documentation and information binders, and the examination chair faces the physician's stool.

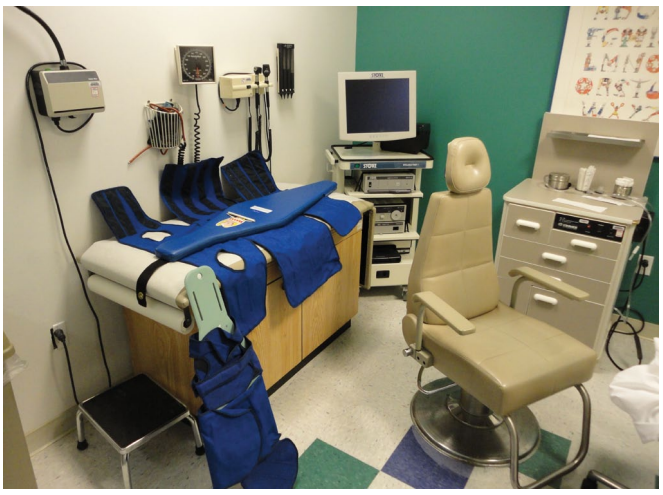


**Fig. 11.4:** The other corner of the room on the other side of the treatment cabinet is the best place for the floor standing microscope or the endoscope tower. Two sizes of papoose are shown used to restrain children if needed for procedures.

**Fig. 11.5:** Microscope can serve both the patients on the table and on the examination chair.

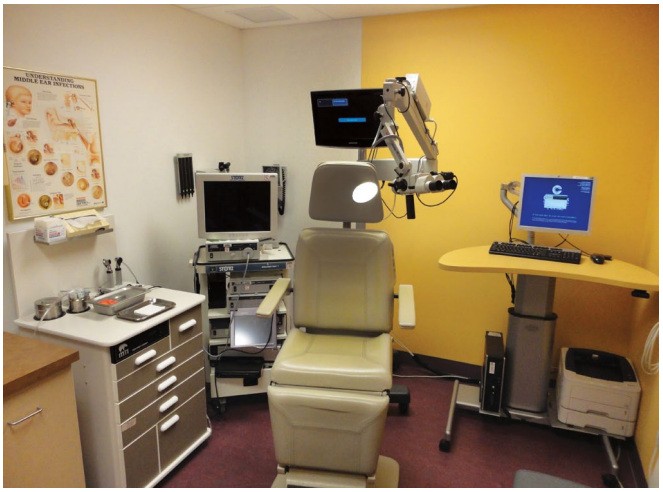


**Fig. 11.6:** Dedicated endoscope rooms may have both the endoscope tower and microscope.

swabs, curettes, additional nondisposable speculum sizes, adequate number of 3, 5, 7 suctions, alligators, right angle picks, and tuning forks (Fig. 11.8). A headlight, Brunning's or Siegel's otoscope sets, Frenzel's glasses, packing material and other equipment, and material that are relatively rarely needed may be kept in a storage room available for all examination rooms.

In addition to the standard commonly used speculum sizes 3, 4, 5, there should be extra-small and extra-large speculums available (Fig. 11.9).The handheld otoscope brand that is most widely available and used in the market is Welch Allyn (Fig. 11.10). The wall dispenser holds the more commonly used sizes of 3, 4, and 5.

The reusable otoscope speculum set that comes with the handheld otoscope has sizes 2, 3, 4, 5, and 9 mm. (Fig. 11.11). These specula are a little thicker; therefore, while the inner diameter is the same, one may achieve a better seal with a speculum in this set. The 9 mm is used when there is a very large canal or using in postmeatoplasty canal-wall-down ear cleaning. The same manufacturer offers SofSpec Extra Comfort Reusable Otoscope Specula. These come as 3, 5, and 7 mm for Pneumatic, Operating and Consulting Otoscopes. The brand has introduced the MacroView Otoscope that comes with the set of Four Reusable Ear Specula for Diagnostic and MacroView Otoscopes of sizes 2.5, 3, 4, and 5 mm. Additional sizes of 2.75 and 4.25 mm speculum are also available to be used for the Diagnostic and MacroView Otoscopes. In addition, for manipulation under microscope, additional small (2, 1.5, 1 mm) and large size (5.5, 6, 6.5, 7, 7.5, 8 mm) metal speculums should be available.

Ear examination often requires cleaning of the external auditory canal (EAC), which is may be a difficult task because of the narrow canal and frequently noncompliant and constantly moving child. In addition, not having proper instruments handy makes this task harder. A set of different sizes of curettes are essential (Fig. 11.12). Round and oval shaped serrated and nonserrated curettes are commonly used in practice. Wire curettes are preferred by some physicians. This author prefers the slightly angled serrated oval-shaped curettes, finding them less traumatic and more effective in loosening and dragging the cerumen out. There should be extra small curettes that can go through the very small speculum sizes as well. Keeping these relatively rarely used specula and curettes separately allows for finding them easily when needed.

## FIRST CONTACT

Physical examination of the ear starts with the first contact with a patient. While the clinician starts the inspection with this first contact, it may or may not be an eye contact, based on the child. Even for children as young as a few months of age, the initial contact and interaction with the clinician has a tremendous effect on realizing the full potential of that patient–clinician encounter. When child's age and cognitive abilities permit, the clinician has to explore the potential path and methods to achieve the goal of developing the most productive and efficient interaction with the child and the family.

A simple first step is displaying a smiling face. A smile is an expression of friendliness universal across cultures

**Fig. 11.7:** Cabinets may have mounted charging docks and containers for frequently used items such as tongue depressors. Drawers are dedicated to gauze, cotton balls, wicks, culture swabs, curettes, additional nondisposable speculums, suctions, alligators, right angle picks, and tuning forks.


**Fig. 11.8:** Cabinet top and drawers are utilized based on the design and preferences of the physicians.

**Fig. 11.9:** Additional extra-small and extra-large speculums should be available.

**Fig. 11.10:** Commonly used pair of otoscopes with pneumatic and surgical heads with disposable or rechargeable batteries are standard tools in clinic.

**Fig. 11.11:** Surgical otoscope head comes with reusable speculum set of sizes 2, 3, 4, 5, and 9 mm. Suitable for most manipulations in wide variety of ear canal sizes.

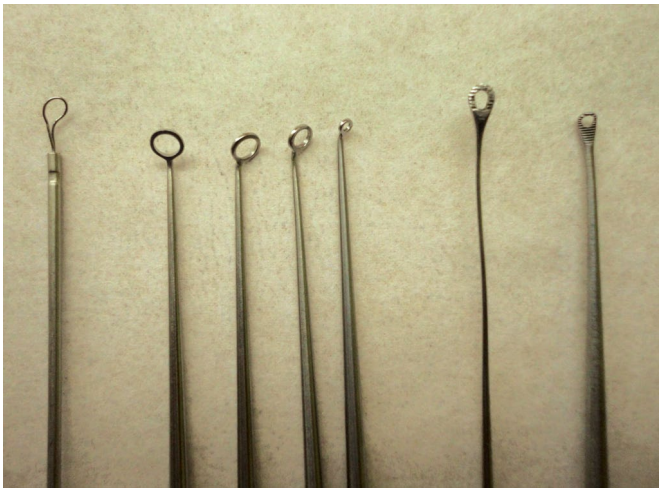


**Fig. 11.12:** A wide range of round and oval shaped serrated and nonserrated or wire curettes should be available in cabinets in each room.

that can ease the interactions to follow. Directing the attention first to the child before the parents and establishing and maintaining friendly contact with the child as long as possible will be very useful throughout the visit and in the future visits. Shaking hands with the patient, in addition to the parents may display the child's importance in the clinician's eye. Hand hygiene may be deferred to just before picking up the instruments and initiating contact with the child for the examination. The child's response to the clinician's attempt to establish contact, will tell a lot to the clinician about the child's character, cognitive and maturity level, past experience with other physicians and the mood that he/she is in at that time. From this starting point, it is the clinician's skill that takes this interaction as far ahead as possible.

There is no single path or method to follow after the initial contact. Clinicians that develop a rich repertoire of interaction scenarios and have the flexibility to change and adapt to the evolving situation will be able to achieve a more efficient and complete physical examination. Gradual introduction of instruments will be useful. Most children are familiar with the handheld otoscope, with good or bad past memories. Especially if the reaction of the child indicates unpleasant previous experience with the otoscope, extra patience and effort with soft and reassuring tones should be attempted.

## INSPECTION

The physical examination starts with inspection of the child. Child's posture, walk, response to sounds and commands, and age appropriate speech and language gives clues on the status of the inner ear. The shape of the head and face may indicate craniofacial malformation, an association or a specific syndrome. Facial asymmetry can be musculoskeletal or neuromuscular, and the latter may give information on the status of the facial nerve. Nystagmus is often not obvious, but the chief complaint and history of present illness would direct the attention of the clinician to the spontaneous nystagmus.

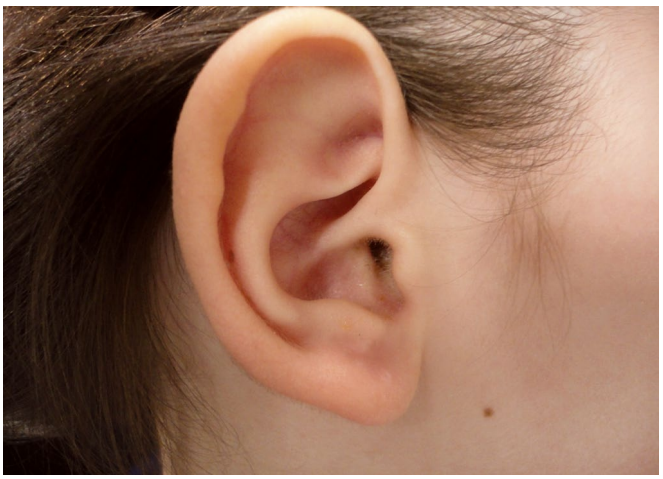


**Fig. 11.13:** Normal auricle.

Inspecting the head also reveals information on the shape and position of the auricle (Fig. 11.13). Periauricular areas need to be inspected for signs of swelling or previous surgery scars. Ecchymotic discoloration over the mastoid process, termed Battle sign, may reflect a skull base fracture. Depression over the mastoid cortex may indicate

a previous mastoidectomy. Asymmetrical protrusion or downward displacement of one pinna would bring attention to postauricular or supra-auricular swelling or abscess and possible mastoiditis. Subperiosteal abscess from acute otitis media (OM) and mastoiditis is more likely to develop more superior to the canal and push the auricle more inferiorly in infants.[1]

Examination of the mouth and palate may reveal cleft palate or submucous cleft both of which predispose the child to otitis media.[2] Bifid uvula may also be associated with increased incidence of ME effusion.[3]

## PALPATION

Palpation of the head and periauricular areas is an essential phase of the initial examination primarily because of being the first contact between the child and the physician for the purpose of examination. Therefore, initial touch should be gentle and not look or feel like part of the examination. To serve the purpose, caressing the head, hair, and cheek should precede the gradual approach to the auricle. It should not be difficult to imagine how annoying it may be to have a stranger touching you first on the auricle with an instant pull and concurrent insertion of the otoscope speculum. This is even more important for children with autism, mental retardation, or cerebral palsy.

Tenderness or swelling around the auricle may be from external otitis or mastoiditis. While the former has circumferential findings, mastoiditis affects the posterior and superior parts of the postauricular region the most. Hematoma of the auricle presents a management emergency.

## OTOSCOPY

Otoscopy is an essential part of the clinical examination of ear. Good visualization provides information on the EAC, TM, and the ME. Findings also provide very important clues on the previous status and history of the conditions in the TM and the ME. A number of methods have been utilized to visualize the EAC, TM, and ME.[4] The tools and techniques aim to straighten the ear canal for direct view, to push away the EAC hair and soft tissues to widen the field of view, to protect the EAC skin from direct contact with and avoid trauma or pain from the instruments used to clean the EAC, to seal the EAC for pneumatic manipulation and change of the EAC pressure to better assess the status and conditions of TM and ME, and to magnify the view for more accurate assessment.

Historically, magnification was not an inherent part of the otoscopic examination. Direct inspection using a head mirror with or without a speculum is still common practice in developing countries. Currently, the handheld otoscope is the standard tool for the otoscopic examination. Otoscope components include a removable speculum, a head into which the speculum fits, a light source coaxial to the line of sight, a magnifying lens opposite to the tip of the speculum, and a hand piece that usually contains a disposable or rechargeable battery.

Otoscopes are used either as closed or open systems. Closed systems allow pneumatic otoscopy, i.e. changing the external ear canal pressure to move the TM. Open systems (or closed systems that can be opened) allow insertion of instruments through the head and the speculum.

Direct visualization of the entire TM with an otoscope often requires straightening of the ear canal. This is achieved by a gentle tug of the pinna in the posterosuperior direction. Only a gentle pull is adequate to get the ear canal angle straightened. Pulling of the auricle with greater than necessary force is not uncommon especially in trainees, resulting in patient discomfort and even pain. A trainee may not realize how uncomfortable this could be. On the other hand, failure to adequately straighten the canal results in using the speculum itself onto the canal to correct the view resulting in discomfort or pain.

Various other otoscope types are available, such as with a larger and rectangular lens, or teaching otoscopes with sidearm viewer, and pocketscopes with smaller lenses. The MacroView Otoscope (Wellch-Allyn) provides approximately twice the field of view and 30% greater magnification than a traditional otoscope. On the other hand, this otoscope is limited to two standard speculum sizes that may hinder the ability to achieve a seal in various size ear canals.

### External Auditory Canal

Discharge from the external ear canal may be obvious on direct inspection or apparent only with otoscopy. Suctioning the ear is unpleasant for the patient and can rarely be done without restraint in very young children. With acute otorrhea in the presence of a ventilation tube, the physician may elect not to get a culture or suction that could alienate a child, and instead consider waiting for the likely favorable response to the course of ear drops. In the case of chronic otorrhea or when there is also otalgia, especially in the absence of known ventilation tube or a perforation, it is necessary to visualize the TM after a good

cleaning with suction. When an older child who cannot be restrained adamantly refuses to be suctioned, alternatives such as drying the otorrhea with a cotton swab may be beneficial.

Swimmers ear can be quite challenging to manage. If the ear canal is completely closed with edema and debris, and there is significant pain, the only way to relatively rapidly help to relieve symptoms is a prolonged and patient cleaning through the bottleneck formed by the middle and outer part of the EAC, remove some of the debris and otorrhea trapped medially and place a wick for sustained delivery of eardrops. This requires cooperation of the child, and otologist's patient reassurance and extremely careful manipulation to sustain the process.

One important finding to note with respect to inflammatory EAC narrowing is fullness and soft, fluctuant bulging of the superior and posterior canal. A subperiosteal abscess formed by eroding through the mastoid cortex may extend from the lateral surface of the mastoid into the canal. Another mechanism for the sagging ear canal is, especially in infants and young children, the development of subperiosteal abscess by extending of pus from the ME into the superior part of the canal where there is no annulus at the notch of Rivinus and extending laterally between the tympanomastoid and tympanosquamous sutures onto the lateral surface of mastoid. A negative CT scan may be misleading, and in this case even there is a subperiosteal abscess that needs to be drained, and a ventilation tube is placed, this mechanism does not definitively warrant mastoidectomy.

Bloody otorrhea in an ear with a history of tubes is almost always related to reactive granuloma formation that responds very well to the antibiotic and steroid combination ear drops. In the absence of history of tube or trauma, bloody otorrhea or polypoid granulation tissue on the TM should alarm the otologist of concerning pathologies including cholesteatoma and neoplasm.

A common EAC problem is cerumen within the ear canal. For optimal visualization of the TM, one study found that cleaning of cerumen was necessary in about a third of young patients.[5] In a child without otologic complaints, if the visible part of the TM appears to be normal and mobile, cleaning of cerumen may not be necessary each time. History of otorrhea, hearing loss, speech delay should all be good enough reasons to remove cerumen for complete visualization of the TM. When not possible, normal tympanometry suggests normal ME function. When not visualized or normal ME status cannot be verified, use of cerumenolytic ear drops or irrigation of the ear canal may be an option. As a principle, neither should be used when an intact TM cannot be verified. Irrigation is relatively commonly used in adult primary care settings, however, rarely in children. TM perforation has been reported with jet irrigation, warranting caution, and gentle irrigation.[6] This author does not remember performing or ordering an ear canal irrigation on a child for over a decade. Instead, removing with a curette is preferred. When intact TM can be verified, use of carbamide peroxide in glycerol (Debrox) over several days to weeks may be an option.

Foreign bodies in the ear canal are often challenging. Most children with a foreign body in the EAC are under 4 years old. Often the otoscopist sees the child after unsuccessful and traumatizing attempts at removal. Prior to any attempt, an effort should be made to assess whether TM is intact and the degree of hearing loss is expected from the foreign body impaction. Removal should be attempted when all the potentially necessary instruments are available. A number of EAC foreign bodies including commonly seen global objects can be removed with a right angle pick with a tiny tip that can get around the object without hurting the canal and drag the object after hooking on or into the object.

Canal wall down cavities require periodic cleaning and should be done by an otologist familiar with the postsurgical anatomy of the patient. This may require prolonged cleaning of the cerumen and debris layer by layer patiently to avoid cavity infections.

Trauma to the EAC could involve just the canal or an underlying head trauma would require relevant attention and workup. Often cleaning attempts traumatize the canal resulting in bleeding and concern on the site of the injury. Cleaning the canal immediately following trauma is for verification of the status of TM and mostly done for documentation purposes. Otherwise, it is quite unpleasant to try to examine and clean a child's recently injured EAC, and therefore, this may be postponed.

## Tympanic Membrane

Inspection of the TM should focus on position, color, degree of translucency, and mobility. Position and size of the light reflex may give more information on the position and the shape of the TM than what is behind. A smooth TM has a single somewhat triangular light reflex wherever the TM is perpendicular to the light source and the eye. The light reflex may not be present due to not having a perpendicular surface area anywhere on the TM.

An absent light reflex may also be due to the absence of a smooth surface from residue or debris remnants on the TM, or due to a thickened, inflamed, or scarred TM. When present, in addition to the observation of change in the position and shape of the light reflex with pneumatic otoscopy, the static shape and position may provide some information on the TM and ME. A bulging TM with a concave surface would have a smaller than usual, even a pinpoint reflex, shifted to a different place on the TM, even to the posterosuperior quadrant. The TM may potentially have more than one light reflex at more than one site of bulging TM. A retracted TM may have a broader light reflex, depending on the degree of retraction, if there is still a distinct area that is perpendicular, compared to the other sites on the TM. Multiple or broken light reflex sites indicate irregular TM surface with possible retraction pockets. As the TM gets atrophic and gradually dimeric, more of the light goes through the TM and not reflected, and the light reflex may disappear.

The TM is naturally slanted medially from posterosuperior to anteroinferior. This may be perceived as retraction of the TM; however, this judgment needs to be based on TM mobility with positive and negative EAC pressure and TM's position referenced to the anchor points. In most quadrants the reference points are either umbo or somewhere along the TM attachment on the manubrium and annulus (except notch of Rivinus where there is no annulus). If the TM fibers are medially positioned in between the central and peripheral anchor points, TM can be described as retracted. Retracted TM does not always imply significant negative pressure, since sequelae from previous infections, ET dysfunction, OM or trauma may weaken the TM structure, resulting in medially positioned TM even with a very mild negative pressure, or adhesion to a surface in the ME may keep the TM in the retracted position in the absence of negative ME pressure. When the TM is retracted, the umbo is typically medially displaced, the manubrium becomes more horizontal and the lateral process of the manubrium becomes more prominent.[7] On the other hand, these changes including more horizontal angle of the manubrium are sometimes present without negative ME pressure, as sequelae of previous infections and effusion and possibly secondary to the shortened tensor tympani tendon.

Bulging of the TM should also be defined as its position relative to the anchor points on the annulus and the manubrium. It is stated that the natural position of the TM is slightly bulging, based on a number of histology slides showing the cross section of the TM not as conical but as slightly bulging outward, displaying doubly curved "seagull" shape.[8] In a normally functioning ET, there is a physiologic reason to have slightly positive pressure at rest giving this appearance. Slightly bulging TM may be physiologic with buildup of gasses in the ME with the changes in breathing and gas consumption during going to sleep and waking up. Change in blood gas composition can result in transmucosal gas exchange into the ME, especially with the changes in rapidly exchanging gases such as carbon dioxide, but this typically does not last long. A patulous ET can result in fluctuating fullness, synchronous with breathing, but this condition is rare in children. Sneezing or nose blowing may open the ET and deliver a gas bolus to keep the TM bulging until it leaks back out passively or gets absorbed to the blood. More commonly, a screaming child may appear to have a bulging and congested appearance masquerading as otitis.

There is varying degree of vascularity of the TM, but normal vascularity comes from the superior part of the EAC where the vascular strip is between the tympanomastoid and tympanosquamous sutures, reaching the TM at the notch of Rivinus on the pars flaccida region of the TM and extend inferiorly along the manubrium. Seeing blood vessels at various density and engorgement may be normal (Fig. 11.14). Hyperemia of the TM should be defined when the TM is red where there are no apparent blood vessels.

Occasionally, there may be one or more bullous lesions on the TM. This could be without a bulging TM

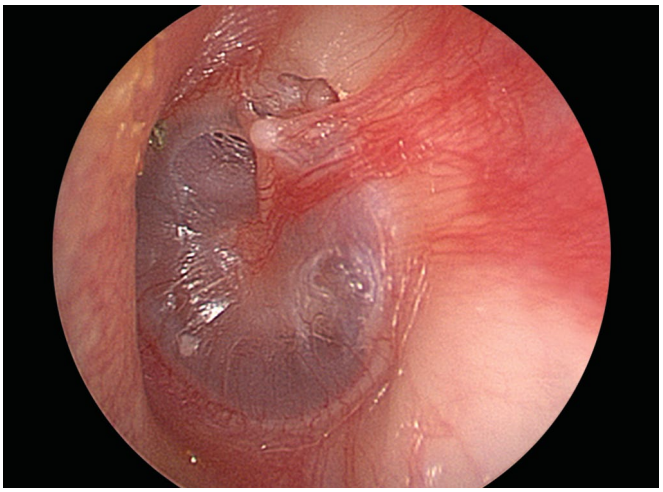


**Fig. 11.14:** Prominent but normal vascularity coming down from superior part of the external auditory canal and extending onto the tympanic membrane along the manubrium. This ear has shallow pars flaccida retraction pocket and some areas of mild atrophy and scarring.

with purulent looking effusion behind, but rather quite painful inflammation of the TM, called bullous myringitis.[9] Bullous lesions on the TM may develop during the perforation of the TM. Sometimes, perforation does not occur instantly through all three layers, but pus may pass through the mucosa and middle layer and for a period of time may dissect the epidermal layer filling underneath as a bulla, just before perforating through this last layer.

Acute OM may present itself with true bulging of the TM. Fullness of the TM is initially apparent in the posterosuperior portion of the parts tensa and the pars flaccida, because these two areas are the most compliant parts of the TM.[10] One other underlying reason for isolated pars flaccida and posterosuperior quadrant bulging should be kept in mind, especially when the rest of the TM does not appear to be bulging or inflamed. A number of mucosal folds and membranes around the ossicles divide ME and attic space into compartments.[11] Rarely, the two small isthmuses between the epitympanum and mesotympanum get blocked with the inflammatory tissues, and purulent effusion trapped above these isthmuses manifests itself as selective bulging of the pars flaccida and posterosuperior quadrant. This presentation may be as severe and worrisome as aditus ad antrum block, presenting with coalescent mastoiditis and its complications. A ventilation tube would not be adequate, since it would not provide drainage of the entrapped pus in the epitympanum and mastoid.

Assessment of EAC and TM trauma should focus on ruling out temporal bone fracture, potential facial paralysis, sensorineural or conductive hearing loss, CSF or perilymph otorrhea, and presence or absence of TM perforation. Assessment of the size and edges of TM perforation may result in need for early intervention, if the edges of the perforation appear to be inverted or displaced unevenly, reducing the chance of spontaneous healing and bringing the risk of cholesteatoma formation.

## Pneumatic Otoscopy

Pneumatic otoscopy should be considered the standard in otoscopic examination.[12] Although not currently widely used by most practitioners, and not even by the majority of otolaryngologists, there is growing awareness and expanding utilization especially among younger physicians.

The TM is semitranslucent and minimally transparent under normal conditions with a degree of normal individual variability (Fig. 11.15). TM thickness and histology or changes resulting from the present or past abnormal

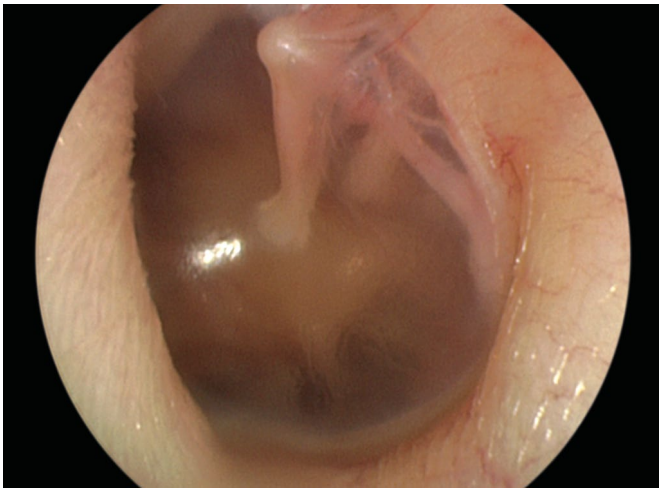


**Fig. 11.15:** Tympanic membrane with normal color, semitranslucency and minimal transparency.

conditions of the TM or the ME impact the translucency and transparency. Pneumatic otoscopy allows assessment of the status of TM and the ME while changing the pressure in the sealed EAC with a squeezable bulb.[13,14]

Misuse of pneumatic otoscopy and resulting misdiagnosis of the ME status is not rare. The most common error is failure to recognize the inability to change the EAC pressure in both negative and positive direction by squeezing and releasing the bulb, resulting in the misdiagnosis of immobile TM, and effusion or infection behind the TM. In order to prevent this error, an otologist should be aware of several important technical details:

1. Choosing the right size speculum is the initial step. While one may get better with experience in guessing the correct size, there are only three commonly used specula 3, 4, and 5 designated by the inner diameter in mm. When it is noticed that the initial choice is not the best for the ear canal, one should not hesitate to change the speculum size. While most pediatric group patients can be examined with a good seal with these three sizes, one should be aware that large ear canals limit the ability to perform pneumatic otoscopy. There is a need for alternative instruments that could get a seal in a larger EAC. For the large ear canals, the Siegel or Brunning speculum set used with microscope is the best option. If not available, tympanometry may be needed to assess the TM mobility
2. Failure to achieve a seal in the ear canal and otoscope head system may be due to suboptimal coupling of the speculum or the lens with the otoscope head. The best method to test the seal of the system is to squeeze the bulb when the tip of the speculum is digitally

**Fig. 11.16:** Otoscope handle grabbed in the palm with the opposing four fingers provide a steady grip. The thumb holds the bulb against the upper part of the otoscope handle while the other hand pulls the pinna gently to straighten the ear canal and keeps the head steady.

occluded.[15] Performing this simple test immediately after inserting the speculum into the otoscope head is a good practice. Especially when using a number of different handheld otoscopes in a number of clinic rooms in various clinical settings, one may run into otoscope heads that do not seal well or at all. Bent otoscope heads and/or worn out or loose lens caps should be repaired or replaced in order to achieve the most basic otoscopic examination standard: pneumatic otoscopy with an otoscope head that can seal. The clinician should be vigilant in checking and demanding this basic otoscopic examination standard in every clinical examination setting

3. There are many ways to hold the otoscope handle and bulb. Of those, this author feels that having the handle grabbed in the palm with the opposing four fingers provides the most steady grip. The thumb holds the bulb against the upper part of the otoscope handle (Fig. 11.16), making the other hand available to pull the pinna gently posterosuperiorly to straighten the ear canal, and to help keep the head steady
4. It is best to insert the otoscope to an ear canal with the bulb half squeezed by the thumb. This half squeezed bulb allows changing the EAC pressure in both positive and negative directions.[8] This is in contrast to earlier teaching to insert the speculum and apply positive pressure after achieving a seal, and after momentarily breaking the seal, releasing the bulb for negative pressure.[13] A concern regarding this teaching is that if the bulb is squeezed after the establishment of the seal, the only possible direction of pressure change is toward positive pressure. If there is negative ME pressure during the examination to start with, and especially if there is significant retraction, squeezing the bulb will result in little medial movement, if any. Furthermore, release of the bulb will not have any effect on pulling the TM more lateral than its original position, resulting in the misdiagnosis of ME effusion, when there is actually only negative ME pressure without effusion.

Pneumatic otoscopy provides extremely valuable and often irreplaceable information regarding the presence or absence of effusion, degree and severity of retraction, atelectasis or retraction pocket, TM perforation and patency of a ventilation tube. For all these conditions, the ability to move the TM by changing EAC pressure is used as the criteria for diagnosis.

One of the common manifestations of chronic and recurrent otitis media and perhaps underlying ET dysfunction is TM retraction, retraction pocket, and/or atelectasis. The retraction pocket or state of retracted or atelectatic TM may be temporary due to the negative ME pressure or more permanent from adhesions of the TM into the ME structures. However, this is usually from some histological changes in the structure of the TM with loosening and weakening of the elastic fibers or partial or complete loss of them. This usually irreversible process may stop progressing in childhood or in adulthood. In the examination of the ear, it is important to have multiple assessments, especially after a cold or allergy exacerbation or an airplane flight to see the ear in its worst condition, and to see if it is improving on its own in time. Keeping track of potential progression and whether there is chronic or intermittent formation of effusion is critical in management.

Pneumatic otoscopy is the clinical method to determine if TM is retracted because of mild or significant negative pressure, whether the retraction is generalized or localized, whether part or entire TM is collapsed on the promontory, or enveloping around the long process of incus and incudostapedial joint, whether any small or large part of the TM that is in contact with the promontory or ossicles, whether there is adhesion, and to be able to see, if there is keratin debris building up within a retraction pocket in an invisible but retractable depth. There should be caution for applying controlled and slowly changed pressure in order to prevent perforation at an atrophic segment of the TM.

Discoloration of the TM may indicate the status of the ME. A general hyperemia with inflammatory appearance, especially with purulent looking effusion and bulging TM, is consistent with acute OM. However, differentiation is not that straightforward, and diagnosis of OM is not based solely on the TM appearance. Still, a clear serous effusion or an amber-colored effusion is more likely consistent with an OM with effusion. Mucoid or mucopurulent effusion without bulging is rather a harder call with respect to acuity of the process. Also, it is also not rare to find ME filled and TM slightly bulging when the child is happily playing in your clinic and even parents are reporting that their child is sleeping well.

## Diagnosis of ME Effusion

Erythema of the TM has been considered a criterion for diagnosis of OM. In a crying baby, visualizing a bulging and red ear drum often leads to this diagnosis. However, these findings may merely be from crying caused by the physical examination itself. Pneumatic otoscopy is a valuable tool to see if the ME is aerated. Even though myringitis, an early phase of OM, is a possibility when erythema is present without an effusion, this condition is rare. When TM mobility is normal, OM diagnosis and administration of any treatment should be avoided. While pneumatic otoscopy is considered invaluable in differentiating the presence and absence of ME effusion, this diagnosis is not simple. Skill and experience is necessary to have a high level of certainty. Even most experienced otologists feel some degree of uncertainty with some ears. TMs are never categorically “mobile” or ”immobile”.

When an otoscopy clearly shows an air fluid level, pneumatic otoscopy does not seem necessary. On the other hand, TMs do not always demonstrate normal translucency, and instead may have thickness from inflammation or myringosclerosis or just scars. It is not rare to have geographic irregular distribution of thick and thin areas or scar bands that may resemble an air fluid level, or air bubbles within the fluid. Changing of the TM position with pneumatic otoscopy usually shifts the air fluid level or position of the air bubbles and verifies the presence of effusion.

Thin, retracted, and deformed TMs that touch the promontory may pose a diagnostic challenge. The whitish surface may often be confused with effusion and even sometimes with a cholesteatoma. The meniscus of fluid at the edges of interface between the surfaces may look like

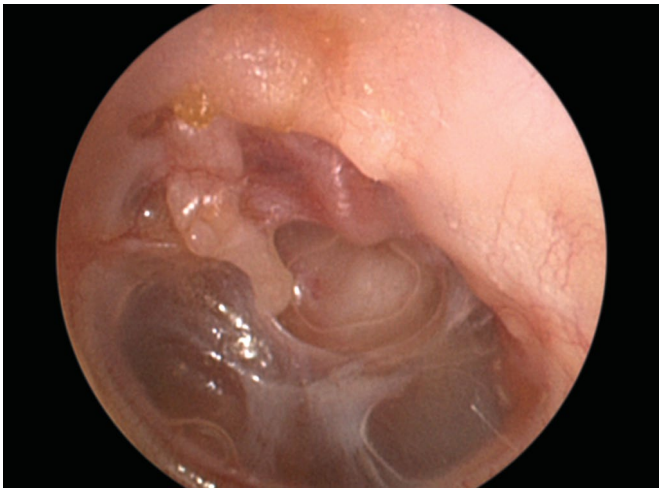


**Fig. 11.17:** A retracted tympanic membrane with atrophic and tympanosclerotic areas. Posterosuperior part is touching the promontory, displaying a round meniscus of fluid at the contact surface, while middle ear is essentially filled with air.

an effusion, but it is caused by a drop of fluid that is often not more than the normal moisture on the mucosa itself (Fig. 11.17). Pulling the TM off of the promontory in part or completely with pneumatic otoscopy will change the size of touching interface area, and cause the meniscus to disappear.

When ME effusion is suspected, several details are critical for diagnosis. In addition to picking the right size speculum and making sure that there is a good coupling and seal between the lens, head, speculum, and ear canal and starting with slightly squeezed bulb, the otoscopist should get used to changing the bulb volume only slightly. If there is a good seal, only a slight squeeze and release should be adequate to move the TM with normal ME pressure, in both directions. Inexperienced otoscopists are more likely to make large pressure changes with the bulb, which may become a habit. Uncontrolled and uncalculated pressure applications lead to significant patient discomfort. If the patient is a child, this contact, which is typically the initial step in the examination, could result in an early loss of chance to build a calm interaction. One reason that feeds this habit is not paying attention to or being able to get a seal with the otoscope. In order to move the TM when there is not a good seal there must be large volume swings in the bulb. When there is no seal, the extent of TM movement is determined by the degree of leak relative to the volume change achieved with the bulb. However, if there is no seal, one cannot get a good feeling of how much bulb movement corresponds to how much normal TM mobility. Having the habit of

performing unsealed otoscopic examinations hinders the necessary experience in developing the sense of normal and abnormal movement of the TM.

First of all, it should be realized that the volume change with maximum displacement of a normal TM from the most retracted to most bulging position is only about 0.2–0.3 mL.[16] Therefore, when the ME pressure is normal, and the TM is in its neutral position, all it is needed to appreciate this degree of displacement is a minimal change in the bulb volume. The pressure required to move a normal TM with normal ME pressure ranged between 10 and 15 mm of water.[17] However, the pressure needed to move the TM when there is ME effusion ranged from 40 to 160, depending on the quality of effusion. Although TM did not move at 200 mm pressure when there was ME effusion, examiners often used excessive pressures up to 500–1000 mm.[17,18] It is the otoscopists skill and experience that develop over years to realize the disproportional degree of volume change in the bulb to move the TM, translating to the confirmation of presence of ME effusion. After reaching the maximum degree of displacement, added displacement will only result in pain and reactive movement of the head that increases the risk of ear canal trauma from the speculum edge. It is the inexperienced otoscopist that results in traumatic pressure of the speculum on the ear canal or pain even bleeding. Role of control of movement, and its impact on accuracy of examination and/or pain will be discussed later in the chapter.

Second, one can always move the TM to a certain degree with exaggerated pressures. Uncontrolled volume swings with the bulb may therefore give the false impression of mobile TM. Theoretically, fluid is non-compressible, and when ME and mastoid cell system is completely filled with fluid, there should be no movement of the TM whatsoever. However, in reality, there is always some degree of movement in the EAC/TM appearance with increased pressure swings. This is usually not a false perception. There are many potential spaces for displacement within the ME cleft that can allow for TM mobility even in the setting of effusion. These may include the presence of some air in the ME/mastoid cell system, displacement of intravascular fluids, compression of the tensor tympani muscle in the semicanal, displacement of fluid in the ET, and compliance of the EAC in young infants.[1] In fact, in the presence of ME effusion, the degree of mobility of TM may even be referenced to the compliance of the EAC soft tissues, and in the absence of effusion, expect much more movement with pressure swings compared to the ear canal tissues. This is equivalent to the admittance with tympanometry at 250 Hz that happens due to the compliance of the EAC and that disappears at 1000 Hz.

An especially important detail with respect to the TM mobility and presence of effusion is the appearance of vascularity on the TM. Positive EAC pressure that exceeds the capillary perfusion would lead to blanching of the TM. Similarly, negative EAC pressure results in engorgement of the vasculature resulting in overall reddening. These changes can be observed in a normal TM; however, this is much more pronounced in the TM with effusion. The key is to notice if the blanching and engorgement of the blood vessels is present at the onset of TM mobility. If there is air with normal ME pressure behind the TM, any significant blanching or engorgement will not be present until the TM reaches the extent of its mobile range as determined by its tissue properties. If, on the other hand, there is effusion filling the ME/mastoid cell system, the blanching and engorgement will be observed before or at the onset of movement of the TM. If this blanching or engorgement happens in one direction only at the onset of a pressure change, the ME pressure can be determined. That is, if the TM blanches with positive pressure only, there is likely negative ME pressure, and vice versa. When an effect is seen with both positive and negative pressure, this suggests a stiff TM and effusion filled ME.

## Otoscopy with Surgical Head

Standard closed head otoscopes can admit an instrument by sliding the lens off to the side, allowing the otoscopist to clean cerumen, suction, or remove a foreign body, still utilizing the lens magnification. However, this approach limits the insertion and manipulation angle, making instrumentation challenging. Handheld otoscopes with a surgical head have a small central lens that rotates which allows instrumentation at a much broader range of angles. It is best to have a second separate handheld otoscope with a surgical head next to a standard otoscope available for each patient encounter. In the presence of cerumen occlusion in the canal, it is often necessary to switch back and forth the otoscopes with the pneumatic and surgical heads, until the full or at least adequate inspection of the TM is possible. It is especially important to have these two handhelds right by the patient when examining and cleaning a restrained child. For a skilled otologist, it is the restraint that annoys both the child and the parents, more than the instrumentation, most of the time. Needing to

change the head on the same handpiece back and forth may lead to frustration of the patient/parent as well as the otologist.

## Otomicroscopy

Microscopes have been used in otological surgery since they were first introduced in the1940s. Use of them in the clinical setting is more recent. However, the binocular microscope is now considered an essential part of clinical examination of the ear. While otomicroscopy is widely used in the clinical examination of adults, it is relatively more rarely used in pediatric practice. There are a number of reasons for this, from cost to lack of necessary training and skill, to the perception that it is not necessary or easy to use in the pediatric population. For many pediatric otolaryngology practices, having a microscope in every office room may be cost-prohibitive.

Microscopic examination requires a relatively steady head. This limits the likelihood of success for routine otomicroscopy in most young children. If needed, some degree of restraining is often required. Routine use of microscopes in the assessment of every patient also reduces the efficiency in the clinic flow, even if stabilizing the head or restraining was not necessary. Microscopic examination takes some time with laying the child on an examination table or reclining the chair and positioning, if needs to be done on both ears sometimes needing to go around or having the patient lay on the opposite direction, depending on the setup of the room.

For most pediatric examinations, visualizing the TM routinely under microscope is not necessary. For many practitioners, most manipulations in the ear canal can be performed competently without using a microscope. On the other hand, a microscope must be available for challenging cases and evaluation of complex otologic conditions. The microscope frees both hands for handling instruments more carefully and sometimes use of two concurrent instruments.

## Pneumatic Otomicroscopy

Microscopic examination is superior to otoscopy in visualization of the landmarks and specific sites and pathologies in detail; however, pneumatic otoscopy is superior to the microscope in assessing ME pressure and TM mobility and identifying the presence or absence of ME effusion.

Specific instruments used with microscope will allow for pneumatic otomicroscopy. Otoscope sets, called Brunning or Siegel, have heads with pneumatic bulb attachment and broad series of speculum sizes that allows seal of the EAC and observe with the microscope through the nonmagnifying glass on the head (Fig. 11.18). Sets also have glasses with magnifying heads that were more commonly used in the era of head mirrors, before handheld otoscopes were available or widely used. Ideal visualization of the TM can be achieved using the microscope with the pneumatic head set sealing the EAC. Naturally, there are limitations as stated earlier for the microscope, where in young children steady head position for sustained stable viewing angle and focus may not be easy or possible (Fig. 11.19).

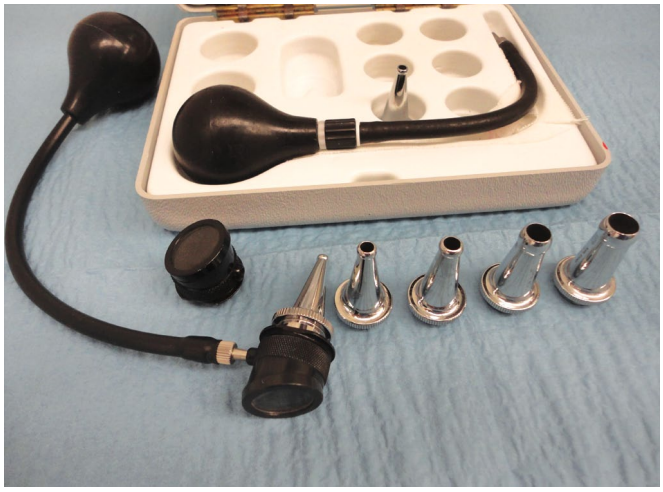


**Fig. 11.18:** Pneumatic otomicroscopy is performed with sets that have heads with pneumatic bulb attachment and broad series of speculum sizes that allow seal of the external auditory canal.

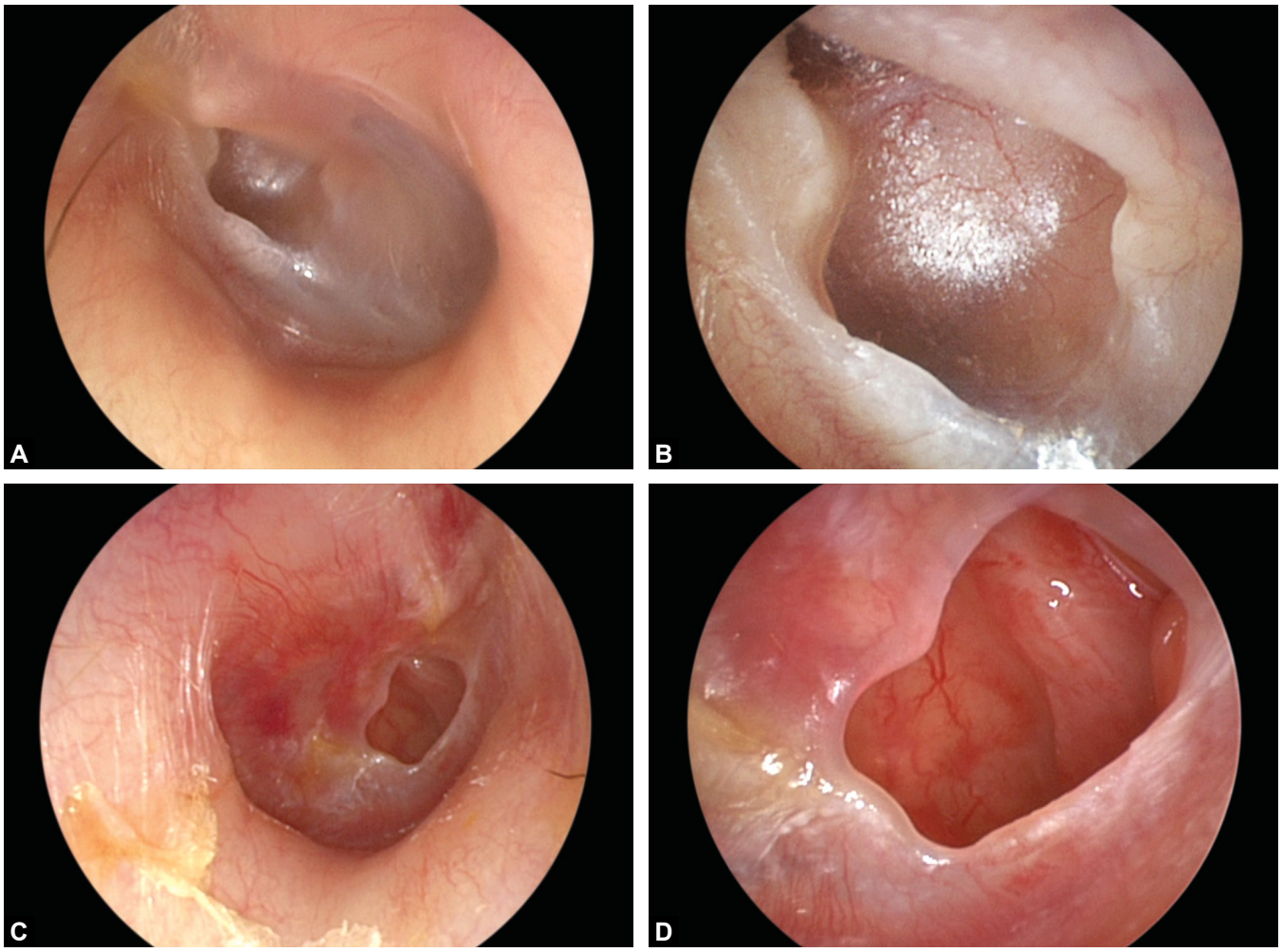
**Fig. 11.19:** A small child sitting on the mother's lap can have manipulation under microscope.

## Otoendoscopy

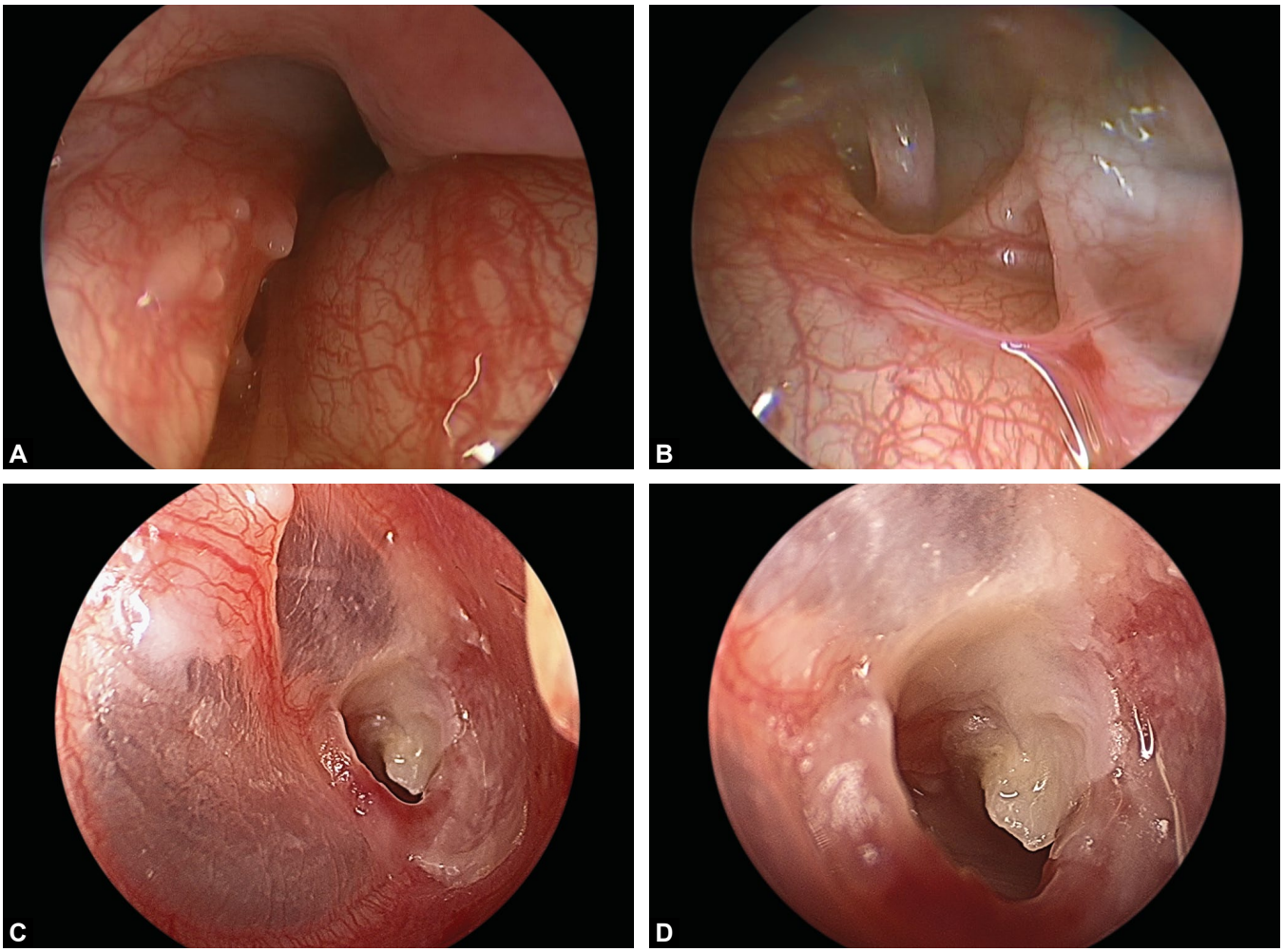
Endoscopy has been applied to otologic surgery for some time. Use of endoscopes in the clinical examination of the ear can be limited, especially in the pediatric population. On the other hand, with a cooperative child, examination of the depth of a retraction pocket or to assess the ME sites that are not directly visible to the microscopic examination may be extremely useful in assessing the ear and the decision making in the management of complex otologic problems (Figs. 11.20A to D).

Patient selection is critical, and the issues related to instrument handling and precautions to prevent trauma and restraint apply to the endoscopic examination of the ear in the office setting. As a rule, otoendoscopy should be used with extreme caution in a child that requires restraining. In an older cooperative child, turning the face of the patient to the monitor brings his attention to the condition of his ears, and enhances the acceptance of any proposed treatment by the patient and the parents tremendously.

Endoscope sizes and the degree of the angled ones vary. In the office a 0° telescope should be preferred, and 30° or 70° telescopes should be reserved for experienced hands on extremely cooperative children (Figs. 11.21A to D). In the absence of specific ear endoscopes, 2.7 mm nasal endoscopes may be used for the same purpose. Technology is rapidly changing and a number of medical instrument manufacturers are developing and marketing smaller and smaller endoscopes with various angles. Currently, decreasing the size below 2 mm seems to decrease the image quality considerably. Short, 6 cm otoendoscopes are excellent for diagnostic imaging, but leave little room for a second instrument if needed. Longer scopes from 16 to 20 cm are more suited to this purpose, but again must




**Figs. 11.20A to D:** Endoscope allows a closer look at a tympanic membrane retraction pocket (A); to visualize potential deeper extension (B); or a perforation (C) to assess better the condition of the middle ear (D).




**Figs. 11.21A to D:** A 70° endoscope visualizing the Eustachian tube orifice (A) and oval window with posterior crus of the stapes (B) A 0° telescope enhances the visualization of the tympanic membrane perforation (C) and skin ingrowth onto the promontory (D).

only be attempted in highly cooperative older patients. Examiners should be aware that heat from the endoscope may result in vertigo due to a caloric response.

## HANDLING OF THE INSTRUMENTS

When there is no need for instrumentation, the examiner's free hand is used for straightening the EAC. When speculum is used with a microscope and when manipulation is planned with the other hand, straightening the ear canal becomes an issue. Common practice is to push the speculum onto the canal to keep the broad visualization of the desired site. However, this can be uncomfortable and could suddenly trigger a series of reactions from more movement to expressing the feeling of pain to crying or even refusal of further examination or manipulation. It is therefore important to reduce the pressure applied on the ear canal by the speculum in addition to the other used instruments.

One technique to straighten the canal when a speculum is inserted without using the other hand is using the third finger to retract the auricle. While the first two fingers hold the speculum, the third is extended under the speculum into the concha and the pinna is stretched gently to achieve the same effect as pulling the pinna with the other hand. It is even more comfortable, because rather than pulling on the helix the tension is placed directly on the concha, which is better tolerated. A right-handed person examining the right ear holds the speculum with the first two fingers of the left hand, and the third finger is brought into the concha and flexed toward the palm to retract in a posterosuperior direction and achieve

**Fig. 11.22:** A right-handed person examining the right ear holding the speculum between the first two fingers of the left hand flexing the third finger placed in the concha in the posterosuperior direction.

**Fig. 11.23:** A right-handed person examining the left ear holding the speculum between the first two fingers while the third finger extends posterior to the speculum pushing the concha in the posterosuperior direction.

an improved directional view (Fig. 11.22). For the same person that examines the left ear, the third finger goes between the speculum and the palm, but this time, instead of flexing, it pushes the pinna in cranial direction, which practically pushes the pinna in the posterosuperior direction (Fig. 11.23).

## Precautions Regarding Instrumentation

Instrumentation in the EACs of infants and children is always challenging. Gentle use of instruments is essential. In an older individual, if any move hurts, the otologist may apologize and continue more carefully. In a small child, there may be no second chance other than going downhill with restraint. However, typically, restraining brings need for more restraining on future examinations. Therefore, ideal pediatric examination is without restraining, when possible. This is impossible for certain ages, presentations and past history of restrained or painful examinations, but the possibility of examination and manipulation without restraint should always be kept in mind and explored. On the other hand otologist should always be prepared for a sudden movement. There is no excuse for a significant iatrogenic trauma in the hands of an otologist caused by a sudden movement when the instrument is in the ear canal. Even most minor trauma can be avoided by an experienced otologist with certain precautions and well developed reflexes.

The best precaution to avoid trauma during an examination of instrumentation of a child's ear is developing a good relationship with the child, if possible. Sometimes, conversation and explaining of what is going to happen and how it is going to be done may make difference even in very young children as young as 2 or 3 years old. Effort should be made to explain that a sudden movement could result in pain, knowing that you cannot rely on this explanation to prevent a movement when pain is experienced. However, often it is the fear of unknown or pain that results in movement. And main goal of such conversation is to reduce the fear. Asking the child to tell you if/when he/she feels any pain coupled with assuring the child that if there is pain you promise to stop doing what you are doing may help reducing the chance of prepain movement.

Next precaution is a specific way of handling the instruments, to have less chance of inadvertent trauma if there is a sudden movement. Focusing into the view inside the speculum reduces the awareness of the movements of the head and the rest of the body. Head movement is not easily noticed when someone is looking at the TM through the otoscope, especially when the other eye is closed. A nonrestrained hand could reach up and pull the otologist's hand or worse, push or hit the instrument of the hand holding it and make an instrument further get inserted into the canal.

In order to trigger the trained reflex of pulling the instrument out of the EAC, there is a need for input. Visual input needs to be used when possible. Keeping both eyes open, even looking through the otoscope with one eye

constantly gives a feedback. Having the hand that holds the speculum or the otoscope touch somewhere on the head when possible will give tactile clue on movement and initiate the reflex to adjust the position or angle or pull out the instrument. The third and probably most important precaution is related to the instrument holding hand. The best technical precaution is to use the hand or fingers as a stopper, keeping stable the distance between the tip of the instrument and the anchor point where the tip of one finger or some part of the hand. When the instrument holding hand is anchored to the edge of the speculum which is lodged in the ear, any movement of the head will not only be felt instantly with the instrument hand, triggering the subcortical/spinal level reflexes, but will move the instrument hand concurrently. Anchoring primarily helps reducing the risk of inadvertent medial movement of the tip but not necessarily prevent rotational movement that could potentially traumatize the sides, i.e. the EAC.

The anchoring practice is essential in general for steady otological surgery, and can be applied to handling of most instruments during surgical manipulation, but it also provides an office technique for less risk for pain and trauma. For most instruments, while the first two fingers (for alligator/scissor group, first and third) are used to hold the instrument, the third (or the second for the alligator/scissor group) usually reaches to the shaft of the instrument for steady handling. The fourth finger can touch the edge of the speculum, and the fifth finger can touch the head, if possible (Figs. 11.24 and 11.25) using these two points to anchor and use as a stopper. Sometimes, using the other hand holding the speculum for the point of anchor may be an option.

Adding an extra stabilizing factor is possible by laying the shaft of the instrument to the edge of the speculum. This technique not only makes the hand and instrument steadier but also results in the movement of instrument concurrently with the speculum when the head of the child moves. On the other hand, this does not necessarily eliminate the risk, and on contrary can increase the lateral rotational movement at the axis of where it is anchored, if the concurrent rotational adjustment of the hand position lags the head's rotational movement, there may be a higher chance of trauma on the side walls.

Similar precautions are applicable to the use of an endoscope in the clinical setting. The diameter and the length of endoscopes may bring varying degree of difficulties. In general, while handling an endoscope in the ear, precaution to rest the second hand that does not hold the endoscope head and camera broadly on the head next to the ear and use the fingertips of that hand to stabilize the endoscope shaft close to the EAC entrance and use the fingers as stopper to prevent any sudden medial displacement with any move is essential.

**Fig. 11.24:** For handling a curette or a similar instrument, while the first two fingers are used to hold the instrument, the third usually reaches to the shaft of the instrument for steady handling, the fourth finger can touch the edge of the speculum, and the fifth finger can touch the head, if possible using these two points to anchor and use as a stopper.

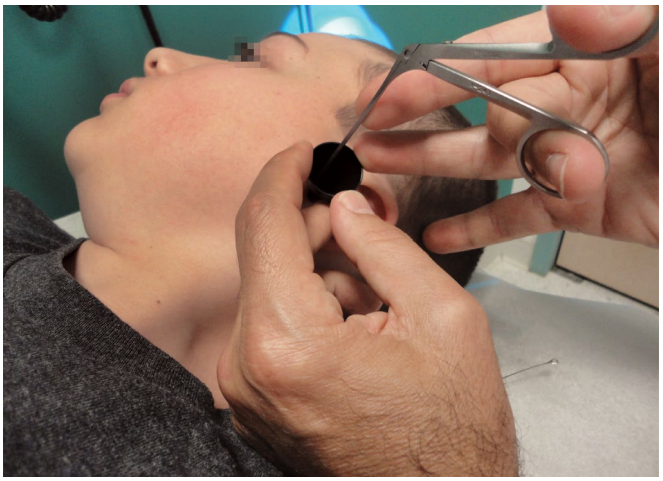


**Fig. 11.25:** For handling an alligator or a similar instrument, first and third finger are used to hold the instrument, the second usually reaches to the shaft of the instrument for steady handling, the fourth finger can touch the edge of the speculum, and the fifth finger can touch the head, if possible using these two points to anchor and use as a stopper.

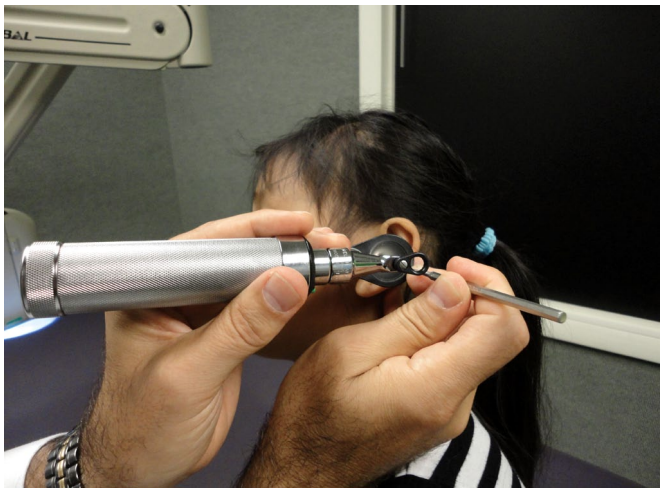


**Fig. 11.26:** When possible from simple examination to all manipulations should be attempted with the child is sitting freely on the examination chair.

**Fig. 11.27:** Most short and simple manipulations can be performed on the parent's lap.

## TO RESTRAIN OR NOT TO RESTRAIN A CHILD

The best restraint is the avoidance of restraint. The more a child is restrained, the more he/she will try to move, get upset, or cry. In the very young, restraining may be unavoidable. In an older child, when possible, all manipulations, starting from the simple examination, should be attempted when the child is sitting freely in the examination chair (Fig. 11.26). All children want to be in control. Starting from the toddlers and preschool age, all children would like to be in charge of what they are doing and what is to be done to them. A practitioner dealing with children should be aware of this and acknowledge it as much as possible. Going the extra length in unrestrained manipulation is only possible with an empathetic and patient approach.

Children should be explained at age appropriate length or detail why the intended manipulation needs to be done and how it is going to be done. If a potentially painful procedure is intended, condition that could cause pain, specifically, their movement should be explained to enforce their effort to stay steady. Their verbal consent needs to be obtained. This assent is not always necessarily a clear verbal approval, but often rather a silent or passive acceptance.

The next option is to not necessarily physically restrain, but to be prepared to restrain with any movement, if that would happen. This requires someone, preferably a family member, being physically close and prepared to hold, if needed. Naturally, the critical differentiation is whether the manipulation can possibly be completed without any restraint throughout the process. If there is such a possibility, it is important to be ready to help stabilizing any potential movement immediately, if that would occur, without a constant tight restraint. The clinician should have a good estimation of the reliability of the family member or other staff in their ability to achieve this task.

If on the other hand, due to the type and extent of manipulation one definitely expects a movement, holding the child tight a little late just when it is needed could limit the unavoidable drama. This applies especially for the short duration of manipulations. Stopping after a very short restraint may reduce the child's reaction. However, when a prolonged, potentially annoying or painful or risky manipulation is planned, and because of the age or the level of cooperation, compliance with this without a restraint is not a possibility, the otologist should plan the best condition of restraint for all these variables. Of the options, when possible, utilizing the parents' help should be prioritized. From the age when restraining is essential, i.e. from newborn period to the age that child thinks sitting on the lap of one of the parents is still acceptable, this option should be tried (Fig. 11.27). The best holding position is having the hand that the head is going to be turned toward, to turn and hold the head against the chest of the parent while the other arm and hand holds or covers both arms of the child over the belly holding the upper body against the chest of the parent (Fig. 11.28). This position is often necessary for even simple otoscopic examination

**Fig. 11.28:** Younger children may gently be restrained on mother's lap by turning and holding the head against the chest while the other arm and hand holds or covers both arms of the child over the belly.

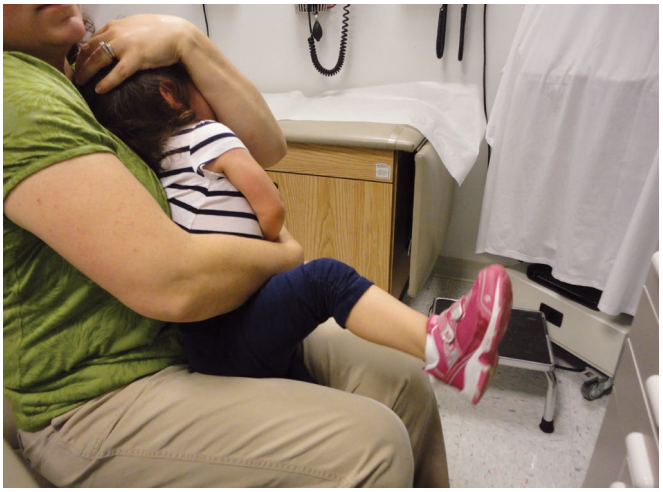


**Fig. 11.29:** When a child starts to move, their legs may need to be restrained between the legs of the parent.

that does not need any manipulation for the infants and most toddlers. For babies, this grasp and stabilization is sufficient, however, for older kids, or the ones that have constantly moving legs, placing the child's legs between the parents' and holding the entire body tight could be necessary (Fig. 11.29). When parents can get good hold of the child, most kids under 4–5 can be restrained like this. This position can always be supplemented with a helper whose role is to help hold the child's head.

Simple otoscopic examination may be performed in a child as young as 2 with the child sitting alone on the examination chair, and it is best to offer the child this option and see if he/she is able to comply. Most young kids may choose to stay where they are, either the seat next to their parent or their lap, but it is always a great start if they agree to come and sit on the examination chair. This, if the examination part goes well, is the first step for unrestrained manipulation, when needed. The second prerequisite in those conditions is good communication. Explaining what is going to happen, and have them accept what you are going to do is essential to build and retain the trust that the child may start to feel in the otologist. In those circumstances, when there is no restraint, instead of hiding, instrument tips should be shown to the child. They are typically afraid of needles or other sharp objects. The curette is the most commonly utilized instrument in the office setting. In this author's experience, most children accept a trial of the use of a curette when they closely see the tip of the instrument and feel it on their skin. Although not as easy, alligator tips can be shown so that they understand that they are not scissors, like what they resemble, and that they are for holding tiny things.

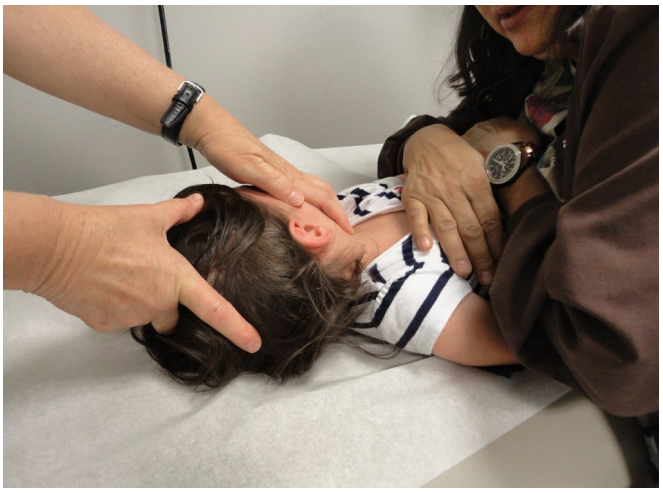


**Fig. 11.30:** A common method of restraining is while one holds the shoulders and below, the other focused on stabilizing the head.

For a prolonged manipulation or work close the TM, in infants, or in young or noncompliant children, restraining on the examination table is more effective and safe. In order to reduce the time under restraint, the otologist should gather all the necessary instruments and material including handheld otoscopes with pneumatic and surgical heads, curettes, gauze, suction, if needed, and extra specula with different sizes. When restraining on a table, a minimum of two helpers should be used. The patient's lower body is stabilized by one, and the head by the other (Fig. 11.30). Arms and shoulders can be held


**Figs. 11.31A and B:** One other restraining technique may eliminate the need for the second helper (A); however, it is not rare to need help to control the legs of the child (B).

by the lower body person who should lean over the child with their body (Figs. 11.31A and B). If the lower body person cannot handle arms shoulders and legs altogether, a third person takes over the legs, pressing the knees on the table, not allowing legs to gain leverage from the table to move the entire body.

When the additional helpers are not available or reliable, swaddling the entire body of baby with a sheet is an option, leaving the head uncovered so that the single helper can control the head. Papoose boards with at least two sizes should be available. These boards have broad Velcro bands that stabilize each section of the body separately for most effective restraint (Fig. 11.32). In noncooperative children older than 3 or 4, who must have the restrained assessment and/or manipulation, the papoose is very useful.

For older or noncooperative children who are strong, the otologist should decide whether or not safe stabilization is possible. It should be realized that, even with the adequate number of helpers, a strong older child may find a way to have a sudden movement that may be adequate to cause significant pain or trauma.

It is crucial to talk with the family members in detail with the greatest sensitivity and empathy. The otologist should develop a high level of skill in assessing the thoughts and concerns of the parents. While the child's level of cooperation is a critical factor, the attitude of the family is of equal importance. There is a need to identify the main decision maker in the family. It is important to explain the reason for restraining, which is performing the procedure in a painless and safe way, with the clarification

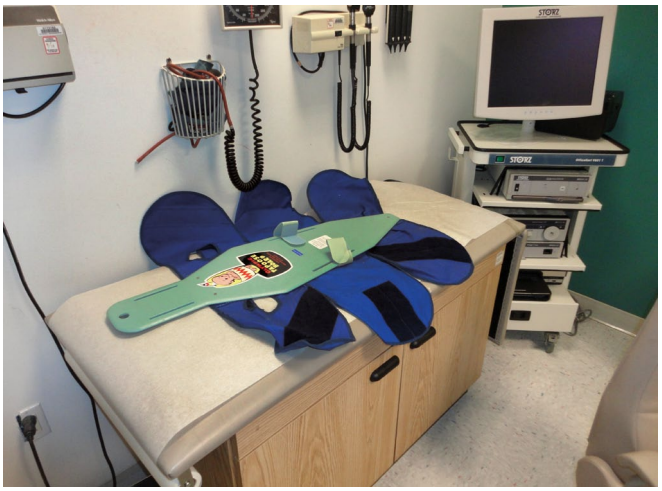


**Fig. 11.32:** When there is a need for prolonged and precise manipulation a papoose may need to be utilized.

that despite the restraining there may be a small risk that pain or trauma may occur. Parents should be aware that at any point they can ask that the procedure is stopped, and also that the otologist may choose to abandon the task when he/she feels that it is no longer possible to complete the intended task, or when continued restraint can no longer be justified. The otologist should be confident enough to abandon manipulation without feeling embarrassed or concerned about being seen as incapable when it is clear that the planned manipulation cannot be achieved.

The comprehension and past experience of the parents, and their past interactions and comfort with the otologist dictate the degree of counseling required.

When families seem overly anxious about any pain or risk, or hint toward medico-legal consequences of such outcomes this may end up shifting the threshold for performing a procedure in the clinic. Whatever the reason, the otologist should respect the decision of parents, and seek alternative options, including examination of ears under anesthesia. If parents do agree to proceed, it is best to ask if they prefer to be in the room. If they are in the room, which should be encouraged unless they strongly prefer to leave, their status of continued acceptance and approval of the ongoing restraint should constantly be monitored.

### Children with Very Narrow Canals

Children and babies with very narrow canals, such as most newborns and most children with Down syndrome bring unusual difficulties in the clinical examination. When this child is referred to a specialty clinic, the question may be a simple one, like whether or not there is an ear infection or effusion, since, typically no one has ever seen the TM before. Preparation for the ear examination starts with preparing the parents. They should understand that answering this simple question may take 5–20 minutes of cleaning under restraint, and even after this prolonged struggle, an answer may not be given with full confidence. But, despite these, every effort should be made to safely and patiently clean the ear canal. All the tools including two handheld otoscopes with very small curettes that can pass through the 3 mm speculum should be placed next to the head. If 2 mm speculum is needed, #3 Fr. suction may work better.

### Children with Cognitive Limitations

Older children with cognitive impairments due to autism, Down syndrome or other syndromes, mental retardation, or cerebral palsy create challenges in the clinical examination of the ear. Sometimes, it is impossible to perform a safe and adequate examination of these children in the clinic. However, it is possible for a hasty approach or impatience to make the examination more difficult or impossible.

The initial step in an encounter with such a child is to stay at a distance and establish trust. By the age that they present to our clinic, such patients have typically been examined by a large number of people with white coats, and it is likely that they did not like most of them. Prolonged conversation between the physician and the parents may allow the child to feel less threatened, seeing the peaceful interaction that is going on. During this period, the physician should assess the child's reactions and gather information about risk or chance of aggressive behavior, the child's past experiences with the ear examination, the child's tolerance and parental expectations and acceptance regarding the pending examination.

This should be followed by the gentle and slow approach to the child, holding his or her hands, and then touching his or her head, constantly talking to the child with a calming voice. Laying one or both hands on the head, close to the ear and keeping it there and well before inserting the otoscope speculum, touching with the fingers, all on and around the pinna usually prevents a big or sudden reaction at first contact. If there is a risk for sudden movement, it would be better to have a family member to be on the other side, gently holding and comforting the child. It must be kept in mind that, sometimes for some reason, the child may react to you, the otoscopist, and if that seems to be the case, one should not take it personally, and explore the possibility of having another person attempt the examination.

Sometimes, from the beginning or well ahead in the examination, it may become apparent that the tasks in the clinical setting will not be achieved, and that restraining may not be an option. Alternatives, including getting a tympanogram, and abandoning the attempt to visualize or clean an ear if there is a reasonable tympanometric curve, or planning to perform this examination or manipulation under sedation or anesthesia should be introduced.

## VISUALIZATION, VIEWING, SHARING, AND DOCUMENTING

Many physical examination tools or instruments for the ear have not changed for decades. The microscope has been used in otologic care for > 70 years, and have been used in office examination of the ear for > 40 years. Endoscopes are relatively new to the outpatient clinics, and even more so to the pediatric clinics. However, viewing the microscopic and endoscopic images in the clinic with a monitor is quite a recent technological advancement. This technology allows the parents to see and better understand the problem, compare one ear to the other or to other reference images, watch any manipulation, and develop a trust (or sometimes distrust) with what they see happening. Images are more and more becoming part of the electronic medical records, allowing direct comparisons of the

conditions, the change in the conditions with time, and the effect of treatment. Photo or video documentation provides an opportunity for medico-legal protection and also brings the risk of being scrutinized. Whether or not we like it, electronic image documentation is not going away, rather its applications continue to broaden. Moreover, having and utilizing these tools in the clinical examination has already become a quality marker and a marketing tool, creating a pressure on providers to expand their technological armamentarium.

## CONCLUSION

Clinical examination of the ear in childhood presents unique differences and difficulties in recognizing, examining, testing, diagnosing, deciding on the clinical management options, and conducting them in the clinic. Other than the surgical and technical difficulties, there are many other important differences that distinguish health-care professionals who assess and take care of ear diseases in children. Assessment and management of acute and chronic ear diseases in children should be done by health-care professionals who are familiar, experienced, and skilled at managing these differences and difficulties in the pediatric population.

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CHAPTER

# 12

# Pediatric Temporal Bone Imaging

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## INTRODUCTION

While imaging in otolaryngology is invaluable in helping with diagnosis and with delineation of surgical anatomy, several considerations are needed when considering imaging in a child. Radiation risks and the need for sedation are among the most critical issues that differ between obtaining radiographic studies in children and adults. This chapter discusses some of the salient points about imaging of the temporal bone in the pediatric population, as well as outline how to decide which type of imaging is preferred based on clinical presentation. Lastly, it will describe how to interpret the studies and how to use them appropriately to help in making a diagnosis.

The initial portion will discuss the various types of imaging used and considerations specific to each type.

The clinical portion is arranged by clinical scenario in alphabetical order and includes:

- Congenital aural atresia and external auditory canal stenosis
- The infected ear
  - The nondraining ear
  - The draining ear
- Facial nerve paresis
- Hearing loss
- Masses, pits, and cysts
- Tinnitus
- Vertigo.

## PART I: IMAGING MODALITIES

Computed tomography (CT) and magnetic resonance imaging (MRI) are the two workhorses of imaging of the temporal bone. The standard technique and protocols most often used for imaging of the temporal bone are first presented. Special considerations for both modalities are then reviewed.

### Computed Tomography

#### *Routine CT Temporal Bone Technique*

The anatomy and pathology of the temporal bone involve small structures; resolution is thus highly important. Collimation is of optimal importance to achieve high resolution.

We routinely use a collimator of 0.6 mm and most commercially available units can be collimated to at least 1 mm. Collimation wider than 1 mm is not usually used, as the resolution is often insufficient.

IV contrast is used for evaluation of vascular pathology, e.g. dissection, for tumors, and may be considered for some types of infections such as coalescent mastoiditis or evaluation for abscesses, but is not routinely used for evaluations for otomastoiditis or hearing loss.

#### *MDCT Reformats*

Multidetector CT (MDCT) provides shorter acquisition times, decrease in tube current load, and improved spatial resolution.[1] Short acquisition is useful in temporal bone imaging in order to reduce motion artifact and in particular in children who require sedation or are imaged postprandially without pharmacologic sedation. Although the radiation dose with multidetector scanners in high-quality mode remains an issue compared with single detector scanners, the improved spatial resolution allows

for high-quality reformats that essentially obviates the need for rescanning the patient in a second coronal plane.[1]

Reformats may, moreover, be obtained in sagittal or oblique planes to improve the detection of pathology in specific clinical settings such as superior semicircular canal (SSCC) dehiscence as discussed below in this chapter under the indication of vertigo and dizziness.

### *Stenver Reformat*

Similar to the method explained above, for making the standard axial and coronal images, the 0.6 mm raw data are brought up on the console viewer in three orthogonal planes: axial, coronal, and sagittal. As above, the technologist scrolls through the sagittal plane until a view of the lateral semicircular canal is obtained represented by the two "dots" of the anterior and posterior limbs. The axial plane is then established by connecting the two dots. The technologist then scrolls through the axial data set until an image of the summit of the SSCC is viewed. The Stenver reformats are then made by tracing a line perpendicular to the long axis of the summit of the SSCC at 0.6 × 0.5 mm intervals. This plane is effectively perpendicular to the roof of the SSCC and displays the roof of the SSCC in cross section.

### *Poschl Reformat*

Similar to the method explained above, for making the standard axial and coronal images, the 0.6 mm raw data are brought up on the console viewer in three orthogonal planes: axial, coronal, and sagittal. As above, the technologist scrolls through the sagittal plane until a view of the lateral semicircular canal is obtained represented by the two "dots" of the anterior and posterior limbs. The axial plane is then established by connecting the two dots. The technologist then scrolls through the axial data set until an image of the summit of the SSCC is viewed. The Poschl reformats are then made by tracing a line parallel to the long axis of the summit of the SSCC at 0.6 × 0.5 mm intervals. The line must be made as parallel as possible to the axis of the summit of the SSCC. A slight obliquity may spuriously obscure a dehiscence by volume averaging with the temporal bone on either side of the summit of the SSCC (Figs. 12.1A to D).

## Cone Beam CT

Cone beam CT is a relatively new technique that uses ultralow dose mA and a cone beam of radiation to scan the entire volume of interest. In the temporal bone, it has the advantages of low-dose imaging, including sparing of the eyes and lenses, and improved resolution of certain structures such as the ossicles, modiolus, and vestibular aqueduct. Cone beam CT, however, requires the patient to be seated and allows for only one ear at a time to be imaged, which may be a concern in infants or young children who may cooperate for imaging for only a short period of time.

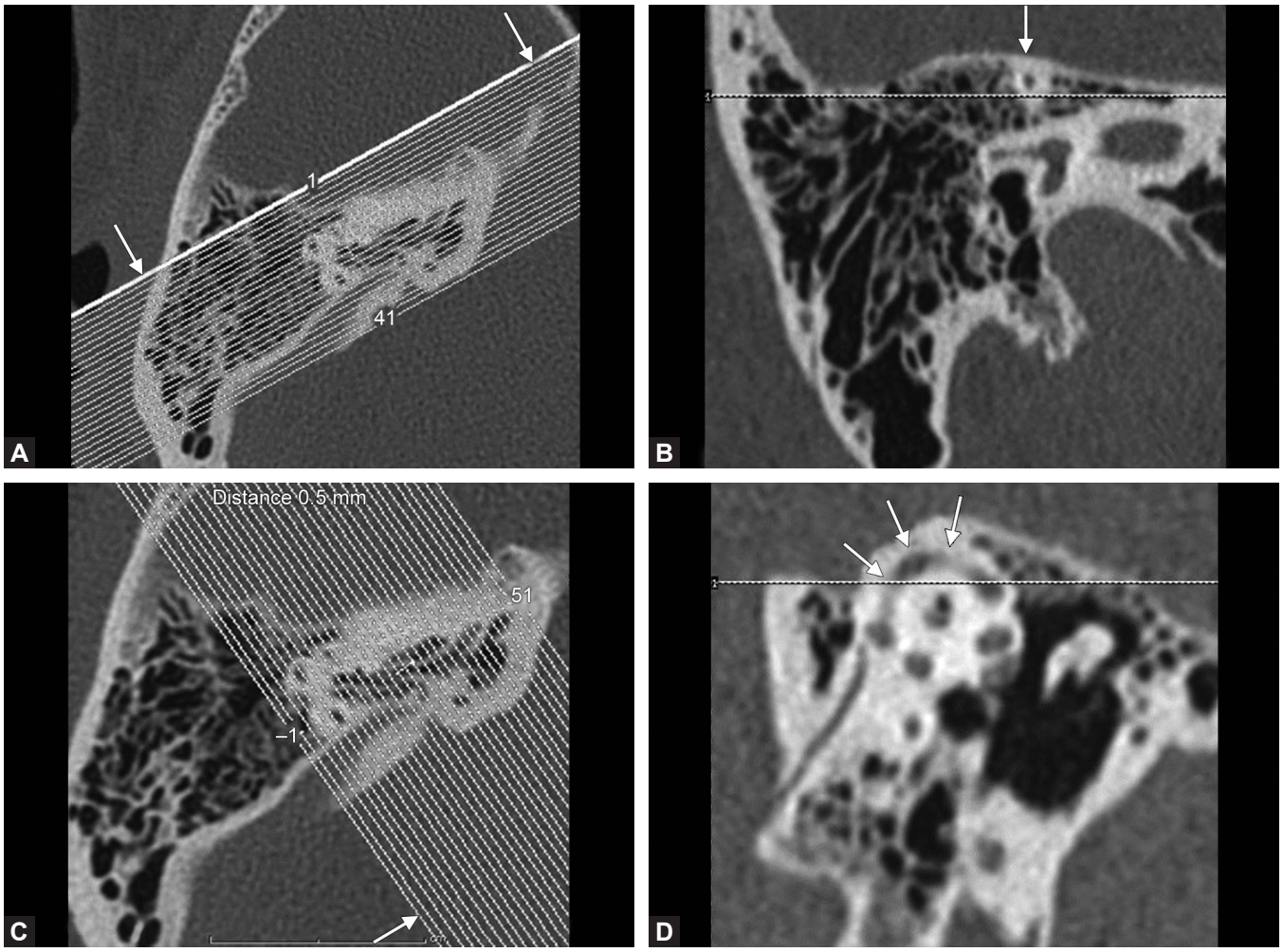
## Radiation Dose Reduction Techniques and Considerations for Pediatric Patients

Compared with most radiography procedures, CT examinations deliver higher radiation dose to patients. The quantity $CTDI_{vol}$ (Volume CT Dose Index) is currently used in CT dosimetry.[2] When a scan is prescribed, the scanner displays the $CTDI_{vol}$ in mGy on the console. However, the dose displayed is not the true dose for the specific patient under examination. Instead, the $CTDI_{vol}$ represents the average dose in the central section of a standardized phantom scanned with the selected protocol.[2a] The head phantom is a cylinder with a diameter of 16 cm and a height of 15 cm.

The effective dose E is used to assess the radiation detriment from partial-body irradiation (e.g. irradiation of only the head or only the abdomen). The effective dose is a weighted sum of the doses to all exposed tissues. $E = \Sigma(w_t \times H_t)$, where $H_t$ is the equivalent dose to a specific tissue and $w_t$ is the weight factor representing the relative radiosensitivity of that tissue. The unit of effective dose is sievert (Sv). The effective dose for a typical CT examination of the temporal bone is about 1 mSv (i.e. 1/1000 Sv). In comparison, the average effective dose from cosmic rays, radioisotopes in the soil, radon, etc., is about 3.11 mSv per year in the United States. The effective dose can be estimated from the dose-length product ($DLP = CTDI_{vol} \times$ scan length), which is also displayed on the CT scanner console. The effective dose for a head study in mSv is approximately 0.0021 × DLP (mGy cm) and approximately 0.0067 × DLP (mGy cm) for a 1-year-old patient.[2]

### *Radiation Risks*

Biological effect of radiation is either deterministic or stochastic. The deterministic effect will not occur unless a threshold dose is exceeded. However, the stochastic effects may occur at any dose level and the probability of occurrence increases with dose linearly according to the linear-nonthreshold dose–response model.[3]




**Figs. 12.1A to D:** Stenver and Poschl reformats in a patient with normal hearing AD. In (A), an axial source image is used as a reference to prescribe a set of 2D reformats that runs parallel to the long axis of the temporal bone in the standard Stenver topographic plane. This reformat runs perpendicular to the axis of the superior semicircular canal and thus provides a clear view of the roof of the superior semicircular canal [single white arrow in (B)]. In (B), the roof of the superior semicircular canal is intact. In (C), a similar axial slice is used to prescribe a set of 2D reformats that run perpendicular to the long axis of the petrous temporal bone in the standard Poschl plane (D). These reformats provide a view of the superior semicircular canal from posterior to anterior (three short white arrows).

For CT of temporal bone, the primary concern for deterministic effect is the dose to the lens. The minimum dose required to produce a progressive cataract is about 2 Gy in a single exposure.[4] If the lens is in the direct X-ray beam, the dose to the lens from CT of temporal bone is in the range of 0.03–0.06 Gy, but it could be as high as 0.13 Gy. If the patient is positioned in such a way that the lens is outside of the direct X-ray beam, the dose is in the order of 0.003 Gy.[5] Although the typical dose to the lens from a single CT scan is much lower than the threshold value for cataract, multiple nonoptimized scans in a short time with the lens in the X-ray beam can result in a lens dose close to the threshold. Every effort should be made to keep the lens outside of direct X-ray beam if it is possible.

Stochastic effects include carcinogenesis and the induction of genetic mutations. Children are inherently more sensitive to radiation because they have more dividing cells and radiation acts on dividing cells. Also, children have more time to express a cancer than do adults.[6]

## *Factors Influencing the Patient Dose*

The CT scanning protocols should be optimized such that the quality of images is sufficient for diagnosis and the patient dose is kept as low as reasonably achievable. To get the best balance of the image quality and patient dose, it is important to understand the effects of imaging parameters on the dose and imaging quality.

Patient dose depends on three group factors: equipment related factors, patient related factors, and application related factors.

The factors in the first group include X-ray beam filtration, X-ray beam collimation, system geometry, and detector efficiency. Although users do not have control of most of these factors, it is important to understand that the *Z*-axis dose efficiency is reduced when the total X-ray beam width becomes very small for MDCT due to the need to keep the beam penumbra out of any detector row.

The dose is strongly dependent on patient size. If the same technique is used to image the heads of an average adult and a newborn, the dose to the newborn is significantly higher.

Imaging parameters such as kVp, mAs (the product of the tube current and the time in seconds per rotation), and pitch (the table travel per rotation divided by the total X-ray beam width) are selected by the operator.

If all other parameters are fixed, the patient dose is proportional to the effective *mAs* which is defined as the *mAs* (*mA* × seconds per rotation) divided by the pitch.

The dependency of dose to *kVp* is more complicated. In general, the dose increases as a power function of kVp ($D \sim kVp^p$) if all other parameters are fixed. The value of $p$ is in the order of 2–3 depending on the type of the scanner.

### *Image Quality*

Image quality is characterized by spatial resolution, contrast resolution, image noise, and other quantities. It is difficult to use a single variable to characterize completely the quality of an image. However, in practice, image noise has been widely used to judge the CT image quality since the detectability of low contrast objects is strongly dependent on the contrast to noise ratio. The standard deviation of an ROI in the image is usually used to represent the noise. In CT, for a given reconstruction kernel, the noise is primarily due to the fluctuation of the X-ray photons reaching the detector. The noise is approximately inversely proportional to the square root of patient dose. To reduce the noise by a factor of 2, dose must be increased by a factor of 4. In general, image quality is better when the patient dose is increased.

### *Strategy for Dose Reduction*

To optimize the CT technique, the image quality required for the specific indication is assessed based on the radiologist's experience. The imaging parameters are then selected based on the patient size and organ type under examination such that the required image quality is achieved while the patient dose is kept as low as possible. Weight or age-based pediatric protocols should be established and special attention should be paid to children under age 2 because their heads are small and under rapid development.

## Magnetic Resonance Imaging

### *Routine Technique*

The standard MRI protocol for evaluation of the temporal bone in adults is detailed below for a 1.5 T magnet:

- The patient is placed in the supine position in the head coil
- Sagittal T1, axial T2, axial FLAIR, and axial DWI images are obtained through the whole brain
- Axial T1-weighted images are obtained through the temporal bone from the arcuate eminence through the mastoid
- Axial CISS (Siemens) or 3D Fiesta (GE) images are obtained through the internal auditory canals (IACs) and pons and are considered key sequences in evaluating children for sensorineural hearing loss (SNHL)
- Gadolinium is then administered
- Axial T1-weighted images are obtained through the whole brain, and high-resolution images are obtained through the temporal bones.

### *Additional Considerations*

Coronal high-resolution T1-weighted images may be useful for more detailed imaging of the temporal bone; the indications for the use of this sequence are reviewed in the indications section of this chapter.

### *MRA*

The most common indication for MRA is in the evaluation for tinnitus. For this indication, MRA is used to evaluate for dural arteriovenous fistulae, aneurysms, vasculopathies such as fibromuscular dysplasia, or arteriovenous malformations.

### *Safety Considerations*

Standard MRI safety considerations obtain in the temporal bone and the reader is referred to publications that list the safety of various prostheses.[7] For those institutions with a busy otology service, the issue of MR compatibility of stapes prostheses, total ossicular reconstruction prostheses (TORPs) and partial ossicular reconstruction

prostheses (PORPs) may arise. These prostheses are listed as well in the standard MRI safety references. Most stapes prostheses do not deflect significantly in a 1.5 T unit.

### *Plain Film Radiography*

Plain film radiographs have limited application to imaging of the temporal bone. A plain radiograph in the Stenver projection, however, may be used for intraoperative or postoperative confirmation of position of a cochlear implant lead. Plain films are used mostly for intraoperative verification of placement of cochlear prostheses. We favor the Stenver projection for this evaluation. The patient is placed in a 45° obliquity contralateral to the implanted ear that places the implanted ear in a position parallel to the film and then in 15° Townes projection. For example, if the left ear has been implanted, the radiographer would turn the head 45° to the right, with the film behind the head of the patient, and shoot a single radiograph with the beam tilted 15° inferiorly toward the patient (Fig. 12.4). Familiarity with this projection and with the proper position of a cochlear implant is one of the few instances in current imaging where plain film radiography is critical as the intraoperative assessment is often made while the patient is still anesthetized on the OR table.

### *Ultrasound*

US may be used for evaluation of periauricular cystic lesions such as first pharyngeal arch anomalies or ultrasound guided biopsies of periauricular lesions.

### *PET*

PET or PET/CT may be used for assessment of temporal bone masses or nodal metastases.

## PART II: REFERRALS AND IMAGING STRATEGIES

This part of the chapter is organized according to the major clinical indications for which a child may be referred for temporal bone imaging. The indications are listed in alphabetical order below. For each clinical indication, the following points are addressed:

- What is the pertinent clinical background?
- What is the first imaging modality of choice?
- What are the clinical questions that the imaging needs to address?
- What is your approach to the interpretation of the imaging?

## Congenital Aural Atresia and External Auditory Canal Stenosis

### *Clinical Background*

Children with congenital aural atresia (CAA) and external auditory canal stenosis (EACS) are often diagnosed just after birth, as this condition precludes examination of the ear and is often accompanied by some degree of microtia. In fact, in only about 5% of cases is atresia noted without coexistent microtia.[8] EACS may present later in childhood due to recurrent bouts of otitis externa or problems with cerumen impaction. Unilateral atresia is more common than bilateral atresia, and bony atresia is more common than membranous.[9]

While CAA and EACS are most common sporadic in nature, they have been described as part of a spectrum of numerous hereditary conditions, including mandibulofacial dysostoses such as Treacher-Collins' syndrome and Nager's syndrome, where associated abnormalities of the mandible are present; branchio-oto-renal (BOR) syndrome, where preauricular pits or cysts, as well as branchial cleft cysts or sinuses are often visible; CHARGE syndrome, where concurrent airway may occur; and facial clefting syndromes, such as Bixler's syndrome, where cleft lip and palate may be present.[10] Vigilance in recognizing the presence of a possible syndrome may lead help with surgical decision making as well as allow for multidisciplinary treatment of patients, both from a clinical perspective and from a radiographic and anesthestic perspective, with regards to safety.

### *Imaging Modality of Choice*

Noncontrast CT scan of the temporal bone

### *Clinical Questions*

- How pneumatized and large are the mastoid and middle ear cavity (MEC)?
- Is the facial nerve at risk for injury?
- Are the oval window and stapes normal?
- Are the inner ear structures normal, i.e. what is the risk of acoustic injury to the inner ear during surgery?
- What is the status of the ossicular chain?
- Is there an associated syndrome or evidence of other extra-auricular malformation that may affect the patient's prognosis?

In cases of aural atresia, imaging plays a primary role in surgical decision making. Multiple studies have demonstrated improved outcomes with atresiaplasty in patients

who score higher on the Jahrsdoerfer criteria,[11] where aspects such as presence of stapes, middle ear and mastoid aeration, facial nerve position, and status of round, and oval windows are given a certain number of points. A similar modified grading system expands on these criteria and again higher scores indicated more favorable outcomes.[12] Patients who are not good candidates by these grading schemes would likely have improved hearing outcomes with bone-anchored hearing aid (BAHA) placement. Imaging may also help to identify underlying genetic abnormalities and find other anomalies that may need to be addressed prior to or at the time of atresiaplasty.

### *Interpretation*

For surgical planning, the pneumatization of the mastoid and MEC should be determined. Evaluate the course of CN VII, paying particular attention to segments that may be aberrant. The AP distance from the posterior margin of the glenoid fossa to the descending portion of the facial nerve should be noted because this space is where the surgically created external auditory canal will pass. Evaluate the status of the middle ear, including the oval window and stapes, as well as possible fusion of the malleus and incus, which is commonly seen. Describe the appearance of the inner ear and the IAC.

The thickness of the skull should be noted, in case a BAHA is a better option. This is typically placed 5 cm posterior to the atretic canal (Figs. 12.2A and B).

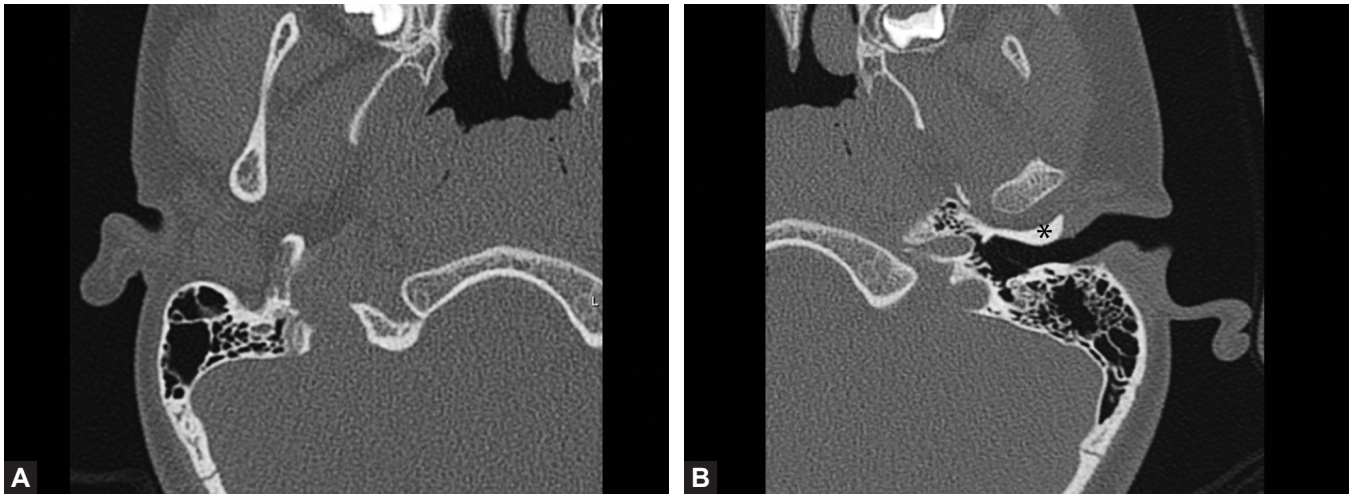
For evaluation of other possible genetic issues, the extra-auricular elements of the scan should be studied. Craniosynostosis may suggest a syndrome such as Apert of Crouzon's syndrome. BOR syndrome may be suggested by presence of cysts/fistulas/sinus tracts in the periauricular region. Zygomatic deficiency and mandibular abnormalities are frequency seen in syndromes affecting the first branchial arch, such as mandibulofacial dysostoses or oculo-auriculo-vertebral syndrome. Orbital abnormalities may be present in syndromes such as CHARGE, BOR, of OAV. Choanal atresia can also suggest CHARGE syndrome, and abnormalities in the maxilla or palate may indicate a clefting syndrome.

## The Infected Ear

There are various presentations of children with an infected ear. These can be divided into the nondraining ear and the draining ear.

### *The Nondraining Ear*

Clinical Background: Children with acute otitis media (AOM) often present with fever, fussiness, possible lethargy, and otalgia. The tympanic membrane (TM) will be bulging and erythematous, indicating the presence of a purulent effusion. In cases of AOM complicated by mastoiditis, a proptotic pinna may be noted, as well as postauricular tenderness or fluctuance, if a subperiosteal abscess has developed. Facial nerve paralysis can also




**Figs. 12.2A and B:** External auditory canal stenosis in a 6-year-old girl with congenital aural dysplasia AD. The right temporal bone (A) is malformed: the external auditory canal has not developed and no aerated passage is seen between the skin and the middle ear cavity compared to the normal aerated left external auditory canal in (B). The tympanic portion of the temporal bone [asterisk (*) in B on the normal side] has not formed. The mastoid is aerated but hypoplastic on the dysplastic side (A).

present in these cases of acute infection. Depending on the extent of clinical suspicion, further workup with imaging may be warranted to determine if surgery is indicated.

### *Imaging Modality of Choice*

- For evaluation of intratemporal complications and initial evaluation for extent of infection: Noncontrast CT temporal bone
- For evaluation of extratemporal complications: MRI brain with gadolinium.

### *Clinical Questions*

- Are there intratemporal (local auricular) complications of AOM such as coalescent mastoiditis, osseous erosion, facial nerve involvement, or suppurative labyrinthitis?
- Are there extratemporal complications of AOM such as sigmoid sinus thrombosis, epidural abscess, or meningitis?

### *Interpretation*

Intratemporal complications should be initially evaluated. Inspect the osseous margins of the mastoid for evidence of demineralization (bone window) and for subperiosteal abscess (soft tissue window) that may reflect a coalescent mastoiditis. Inspect the osseous margins of the facial nerve canal for demineralization that would suggest inflammatory dehiscence. Although dehiscence cannot be definitively determined unless seen intraoperatively, knowledge of possible nerve exposure is helpful for surgical planning. Evaluate for erosion of the walls of the membranous labyrinth that would suggest a suppurative labyrinthitis. Evaluate for middle ear and mastoid opacification, which may suggest AOM or cholesteatoma.

Next, evaluate for extratemporal sequelae of AOM. Inspect the margins of the MEC and mastoid for evidence of epidural or Bezold abscess. Evaluate the transverse and sigmoid sinus for evidence of thrombosis. Evaluate the meninges for evidence of meningitis. Here again, an MRI would be a more sensitive modality (Figs. 12.3A to D).

## *The Draining Ear*

Clinical Background: Children with a draining ear may present with symptoms of acute infection, such as those listed above, or they may present with chronic drainage, with or without otalgia. If the history suggests that the patient initially had an AOM and drainage subsequently began with improvement in symptoms, it is likely that the patient developed a perforation with allowed for drainage. In those cases, imaging is not necessarily indicated, as long as treatment with antibiotics (topical ± systemic) is being continued. If symptoms are not improving, imaging would be indicated to evaluate for those things listed above.

If the patient presents with findings of external auditory canal (EAC) edema with pain on external manipulation, otitis externa is the likely diagnosis. In these situations, imaging is not typically indicated unless the patient is not improving with topical antibiotics, pain is out of proportion to examination, or new symptoms, such as facial weakness, appear. These should make one suspect malignant or necrotizing otitis externa (MOE/NOE), which includes osteomyelitis and may require a prolonged course of IV antibiotics. This would be rare in the pediatric population, as this disease is more commonly seen in diabetics and others with some degree of immunosuppression (i.e. HIV).

A chronically draining ear due to chronic otitis media (COM) can be divided into two main categories: active COM, when the ear demonstrates active inflammation with purulent otorrhea, and inactive COM, where the ear is not constantly draining but bouts of reactivation may occur.[13] Physical examination is paramount in guiding management and need for imaging. Any of the following may be present in COM: TM perforation, retraction, or atelectasis; ossicular chain erosion, middle ear inflammation resulting in granulation tissue and/or adhesions; and cholesteatoma.[13]

### *Imaging Modality of Choice*

- Noncontrast CT of the temporal bone.

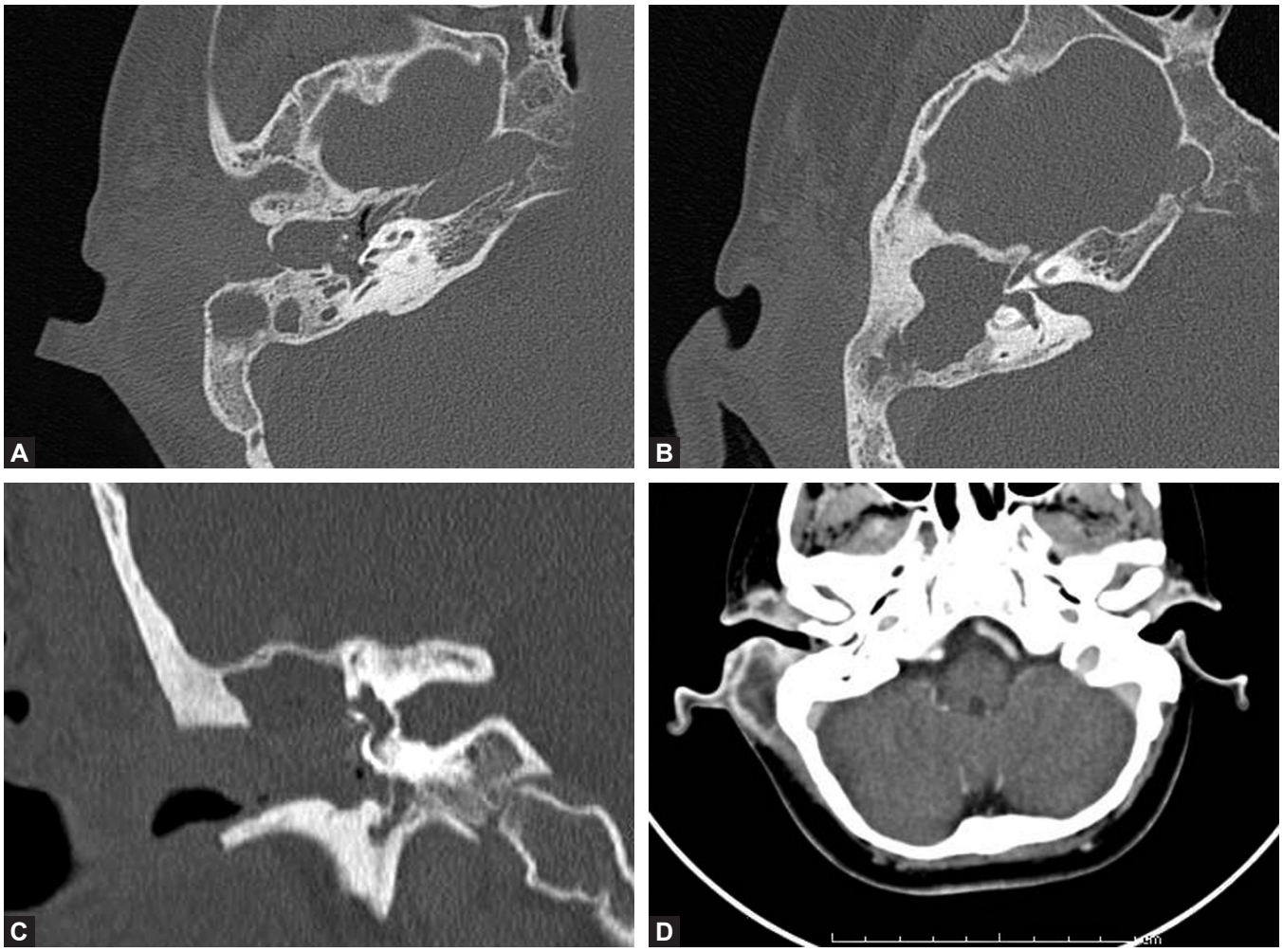
### *Clinical Questions*

When NOE is suspected, the following should be addressed:

- Is there bony involvement or inflammation that extends into the soft tissues inferior to the EAC that would suggest NOE?
- What is the extent and severity of infection?
- Are there any sequelae of infection, such as possible facial nerve involvement?

While the diagnosis of COM ± cholesteatoma is a clinical one, imaging will help answer many questions necessary for surgical planning. In the setting of cholesteatoma, imaging should address the following:

- Is the cholesteatoma limited to the attic or is there further involvement of the mastoid?




**Figs. 12.3A to D:** Coalescent mastoiditis in a 12-year-old boy presenting with draining ear and otalgia, AD. Axial CT images (A and B), coronal reformat (C), and axial postcontrast image (D) show subtotal opacification of the external auditory canal middle ear cavity and mastoid. The walls of the MEC and mastoid are expanded and bulge laterally into the EAC suspicious for a cholesteatoma. The ossicles are markedly eroded. The MEC lesion has eroded through the lateral wall of the lateral semicircular canal. Labyrinthitis ossificans have developed in the basal turn of the cochlea. A rim enhancing subperiosteal abscess has erupted developed from the lateral wall of the mastoid. (MEC: Middle ear cavity).

- Is the mastoid well-pneumatized and aerated?
- Is there ossicular chain erosion?
- Is there dehiscence of major landmarks and structures, such as the facial nerve, tegmen, or lateral semicircular canal?
- Is there external auditory canal erosion?

When cholesteatoma is not present but chronic drainage and/or perforation, retraction, or atelectasis of the TM is the primary issue, imaging should address the following:

- Is the mastoid well-pneumatized and aerated?
- What is the size of the mastoid?
- Is there ossicular chain erosion?

### *Interpretation*

If NOE is the primary concern, the auricle and periauricular soft tissues should be evaluated for signs of edema and fat stranding, suggesting infection. Inflammation extending inferior to the EAC may indicated NOE. Assess the severity of opacification of the EAC. The coronal soft tissue images are keys in evaluating for cartilage involvement that is the site of origin of NOE. Particularly in children, the canal should be evaluated for presence of a foreign body.[14] Bony erosion suggests NOE and may indicate the need for long-term parenteral antibiotics. If there is evidence of skull base

erosion and osteomyelitis, an MRI should be considered to evaluate for intracranial involvement, e.g. abscess or sinus thrombosis.[15]

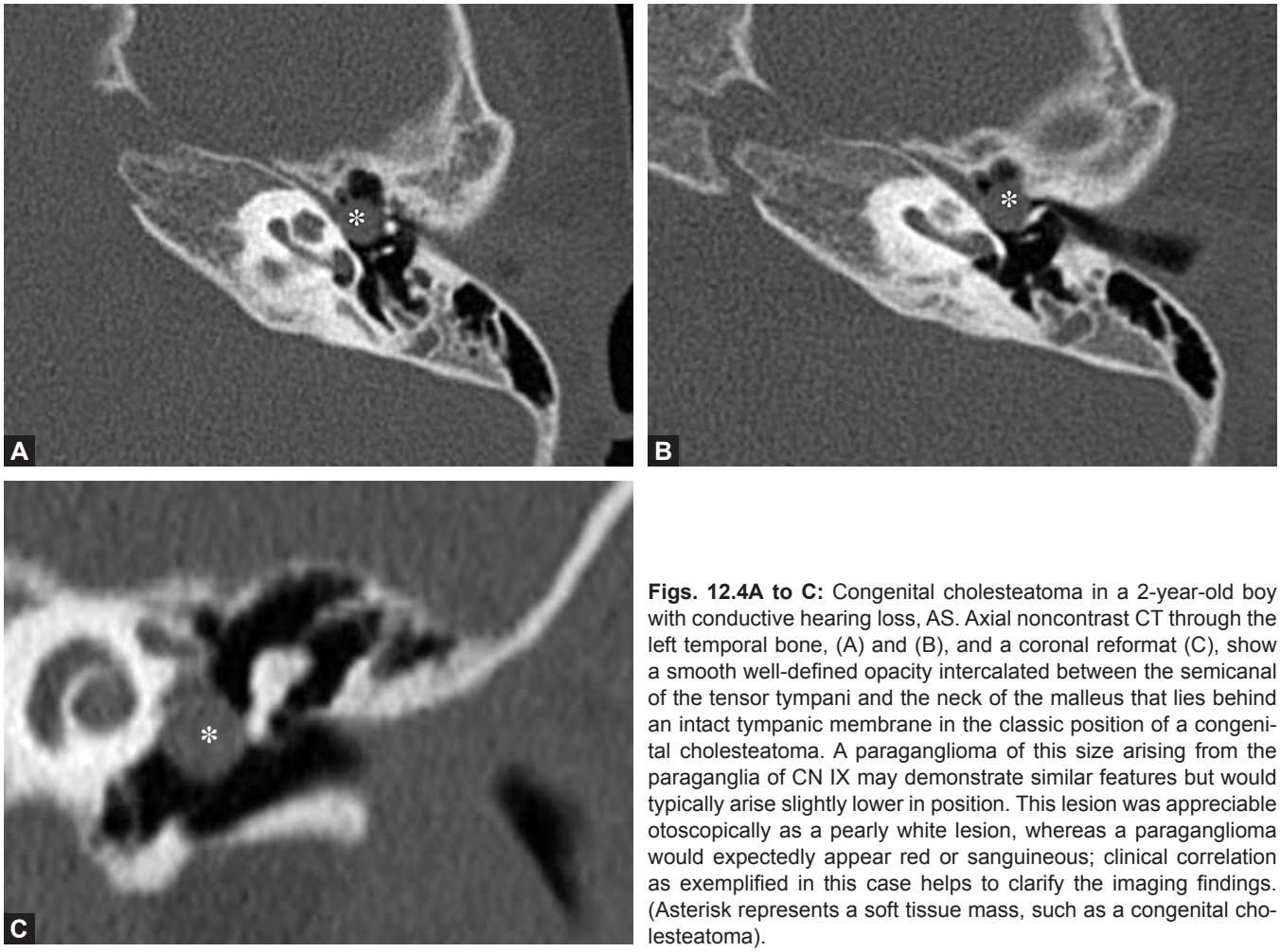
In the case of suspected cholesteatoma or chronic otomastoiditis, the EAC can first be inspected for erosion, as posterior canal wall erosion will likely imply that a canal wall down procedure is needed. Examine for signs of cholesteatoma, including blunting of the scutum, soft tissue in the epitympanum/middle ear/mastoid, and ossicular chain erosion. Be sure to differentiate between a sclerotic mastoid, which has few air cells, and an opacified mastoid, which has air cells that appear to be filled with fluid or soft tissue. Look for surgical landmines, including a high-riding jugular bulb, an anterior sigmoid sinus, a low-lying mastoid tegmen, horizontal semicircular canal dehiscence/fistula, or facial nerve dehiscence (Figs. 12.4 and 12.5).

## Facial Nerve Paresis

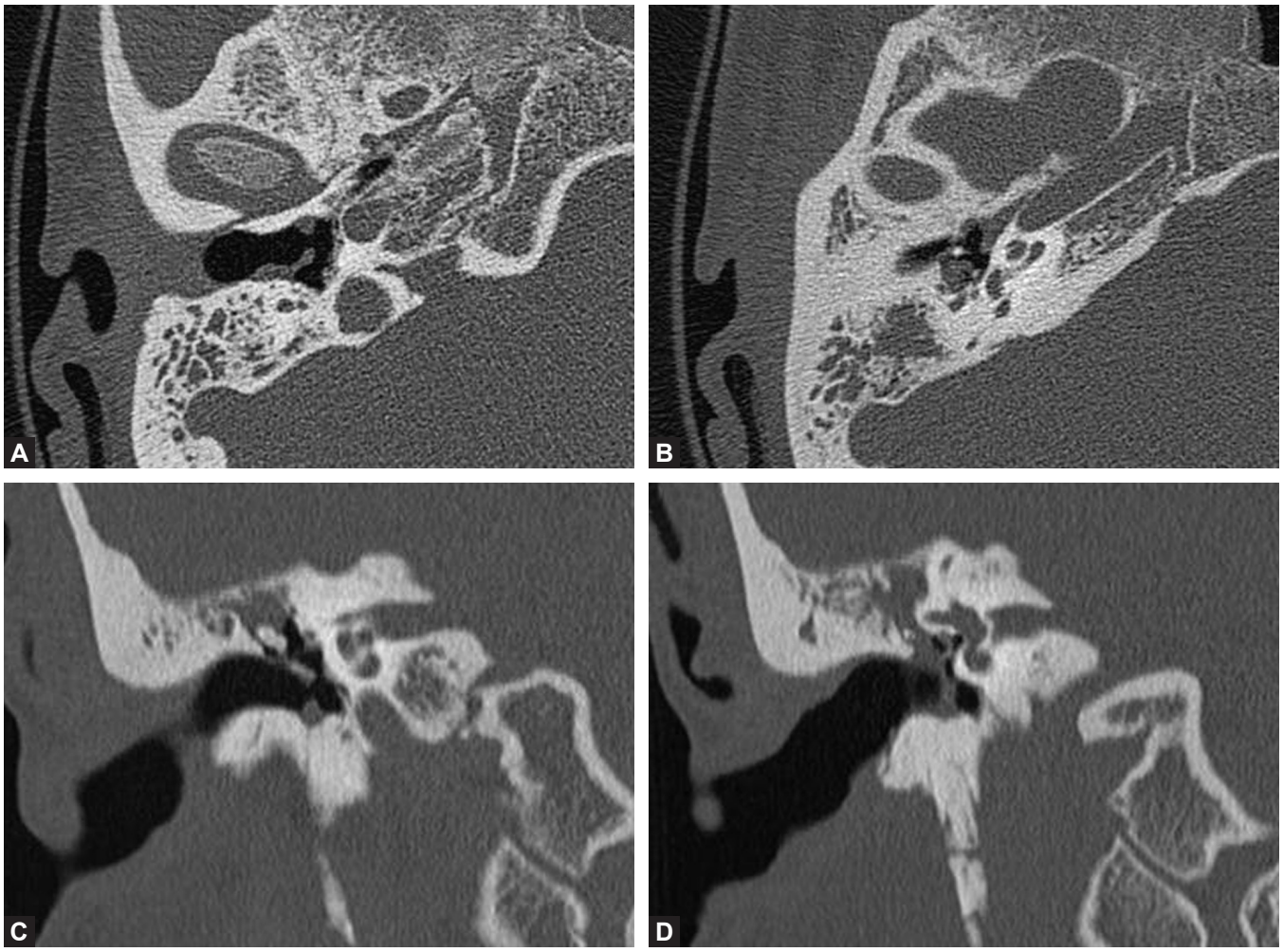
### *Clinical Background*

Children may present with facial paresis or paralysis in a number of different circumstances:

1. Congenital (including Mobius' syndrome, Goldenhar's syndrome, in utero thalidomide exposure)
2. Post-traumatic (including traumatic forceps delivery)
3. Infectious (including AOM, Lyme's disease, Ramsey Hunt's syndrome)
4. Neoplastic (including tumors of parotid, temporal bone, brain)
5. Bell's palsy
6. Iatrogenic (including after parotidectomy, otologic surgery)
7. Melkersson–Rosenthal's syndrome (recurrent facial palsy, orofacial swelling, and fissured tongue).




**Figs. 12.4A to C:** Congenital cholesteatoma in a 2-year-old boy with conductive hearing loss, AS. Axial noncontrast CT through the left temporal bone, (A) and (B), and a coronal reformat (C), show a smooth well-defined opacity intercalated between the semicanal of the tensor tympani and the neck of the malleus that lies behind an intact tympanic membrane in the classic position of a congenital cholesteatoma. A paraganglioma of this size arising from the paraganglia of CN IX may demonstrate similar features but would typically arise slightly lower in position. This lesion was appreciable otoscopically as a pearly white lesion, whereas a paraganglioma would expectedly appear red or sanguineous; clinical correlation as exemplified in this case helps to clarify the imaging findings. (Asterisk represents a soft tissue mass, such as a congenital cholesteatoma).




**Figs. 12.5A to D:** Acquired cholesteatoma in a 12-year-old boy presenting with draining ear and otalgia, AD. Axial CT images (A and B), coronal reformat (C), and axial postcontrast image (D) show subtotal opacification of the external auditory canal middle ear cavity and mastoid. The walls of the MEC and mastoid are expanded and bulge laterally into the EAC suspicious for a cholesteatoma. The ossicles are markedly eroded. The MEC lesion has eroded through the lateral wall of the lateral semicircular canal. Labyrinthitis ossificans have developed in the basal turn of the cochlea. A rim enhancing subperiosteal abscess has erupted developed from the lateral wall of the mastoid. (EAC: External auditory canal; MEC: Middle ear cavity).

In evaluating congenital facial nerve paralysis, other abnormalities may be noted on physical examination, including hemifacial microsomia, additional cranial nerve and neurologic abnormalities, and other systemic issues such as ocular abnormalities or thoracic issues.[16] Post-traumatic injury at birth, such as forceps-assisted delivery or compression by the maternal pelvic outlet, typically has a favorable outcome, but if symptoms persist, other causes, including neoplastic or neurologic etiologies, should be entertained and worked up.[17] With regards to other trauma, such as a temporal bone fracture, presence of sudden onset indicates direct nerve injury, which would push one toward surgical management. Delayed onset suggests edema and may lead the clinician down a different management algorithm. For infectious etiologies, clinical history is paramount, with special attention given to onset, fever, otalgia, otorrhea, exposure/travel, bug bites, etc. In addition, physical examination may demonstrate lesions (vesicles, target lesions from bug bite), other coexisting cranial nerve anomalies (i.e. CN VI or VIII), etc. Neoplastic causes may present with gradual or sudden onset facial nerve weakness, palpable masses, other cranial nerve involvement, and pain. Lastly, while Bell's palsy is a frequently utilized diagnosis, presence of other abnormalities or questionable history should prompt the clinician to consider other etiologies.

### *Imaging Modality of Choice*

- In the post-traumatic setting: Noncontrast CT scan of the temporal bone
- In the non-post-traumatic setting: MRI of brain with gadolinium.

### *Clinical Questions*

The role of imaging in facial nerve paresis varies based on etiology, but should essentially assess the following:

- Congenital: Is the nerve absent or hypoplastic?
- Post-traumatic: Does the fracture occur along the course of the facial nerve?
- Infectious: Is there evidence of otitis media or mastoiditis?
- Neoplastic: Are there any lesions along the course of the facial nerve?

In the case of iatrogenic facial nerve paresis following otologic surgery, imaging may identify where the injury occurred in order to guide further management.

### *Interpretation*

In the setting of post-traumatic facial nerve injury, look for any site of bony disruption of the fallopian canal or free-floating bone fragments along the course of the facial nerve that may be impinging on the nerve. The fallopian canal is most narrow at the labyrinthine segment, and would therefore be the most likely site of compression.

When nontraumatic facial nerve paresis exists, MRI may demonstrate findings such as a brainstem tumor, a demyelinating plaque, facial nerve hypoplasia or aplasia, or abnormal enhancement and/or nodularity along the course of the facial nerve. The parotid gland should also be evaluated to ensure that a tumor affecting the extratemporal portion of the facial nerve is not being missed.

## Hearing Loss

### *Clinical Background*

In children, hearing loss should be thought of from two perspectives: congenital vs. acquired, and sensorineural vs. conductive. When a child presents for hearing loss due to a failed newborn hearing screen, he/she has typically also had a sedated ABR to confirm hearing loss. Once middle ear disease has been ruled out, syndromic and nonsyndromic causes for SNHL are worked up, including but not limited to congenital CMV infection, Usher's syndrome, Jervell and Lange-Nielsen's syndrome, congenital Rubella, and Alport syndrome. Imaging in the process of workup will help elucidate aplasia or hypoplasia of the cochlear nerve, as well as identify other possible temporal bone abnormalities. In addition, imaging may help predict whether the hearing loss may worsen, for example, as in enlarged vestibular aqueduct.

In the case of acquired asymmetric or sudden SNHL in pediatric patients, the incidence and etiologies are not as well documented, but causes may include viral (including EBV, CMV), EVA, ototoxicity, noise exposure, and nonorganic causes.[18] Neoplasms, such as a cerebellopontine angle (CPA) tumor, and inflammatory disorders can be ruled out with imaging. Asymmetric hearing loss is defined as a difference between the two ears in hearing thresholds (>10 dB in three consecutive frequencies or 15 dB in two consecutive frequencies) or a difference in word recognition scores (>15 points difference).

In children who present with an audiogram demonstrating conductive hearing loss (CHL), a good history will provide many clues as to the etiology, including duration that the hearing loss has been present, recurrent infections, history of head trauma, and family history of hearing loss or otologic surgery. Physical examination may also give clues, including middle ear effusion, perforation, retraction, and hyper- or hypomobile TM. Imaging may be indicated if an obvious cause of hearing loss cannot be found on examination.

### *Imaging Modality of Choice*

- For sensorineural hearing loss: MRI of the brain with gadolinium with fine cuts through the IACs (can detect nerve aplasia/hypoplasia) +/- Noncontrast CT scan of the temporal bone (bony abnormalities, including cochlear dysplasias)
- For sensorineural hearing loss for which cochlear implantation is being planned: Noncontrast CT scan of the temporal bone
- For conductive hearing loss: Noncontrast CT scan of the temporal bone.

### *Clinical Questions*

For congenital SNHL:

- Is the cochlear nerve absent or hypoplastic?
- Is the cochlear fossette narrow?
- Is there evidence of an enlarged vestibular aqueduct?
- Is the cochlea properly formed?
- Is the vestibular system properly formed?

For acquired SNHL:

- Is there a cochlear or retrocochlear (CN VIII, brainstem, auditory cortex) lesion?

For CHL:

- Are the external auditory canal, TM, middle ear space, and ossicles normal?
- Is there evidence of otospongiosis or Paget's disease?

### *Interpretation*

For SNHL, inspect the cochlea and inner ear for evidence of dysplasia, abnormal elevated signal on the T1-weighted images that may suggest hemorrhage, abnormal enhancement that may be seen in labyrinthitis, or loss of signal in the membranous labyrinth that may reflect labyrinthitis (ossificans). Trace the cochlear nerve from the cochlear fossette to the brain stem, to identify an abnormal nodule that may represent a schwannoma, abnormal enhancement that may suggest a leptomeningeal process investing CN VIII, and for intactness/presence of the nerve. Hypoplasia or aplasia of the nerve is contraindication to implantation. Look at the IAC and CPA cistern for a mass.

Check the whole brain images for any evidence of disorder of myelination, malformation such as a Chiari I, meningitis, or CNS hypotension or hypertension.[19–24]

For preoperative planning for cochlear implantation in a patient with SNHL, begin by inspecting the thickness of the skull 4–5 cm posterior and superior to the spine of Henle, as this is where the receiver-stimulator portion of the device will be positioned. In children, the bone is often quite thin, and may not allow for drilling of a well in which to place portion of the implant, or may result in dural exposure (intentionally) if a well is drilled. Evaluate the pneumatization of the mastoid, as underpneumatization will likely result in a most challenging mastoidectomy. Also examine the pneumatization of the facial recess and describe the position of the facial nerve with respect to the recess. An aberrant or dehiscent nerve or a laterally positioned posterior genu may lead to injury, and require an alternate approach to the MEC. Check aeration of the middle ear and near the area of the round window niche to determine how difficult electrode insertion may be.

Evaluate the inner ear for evidence of malformation that may reduce the efficacy of the implant or make insertion more challenging. Cochlear malformation may require modification of electrode insertion techniques. Inner ear malformations may raise the risk of meningitis. Labyrinthitis ossificans (LOs) that may be a sequela of prior meningitis may limit the ability of the surgeon to advance the electrode.[25,26] If there is evidence of LO, an MRI should be performed to determine better the caliber of the membranous labyrinth. Evaluate the cochlear fossette (bony canal for CN VIII at the base of the cochlea) for evidence of stenosis that may herald a hypoplastic nerve or dysplasia that may increase the risk for CSF gusher. Check the otic capsule for evidence of otospongiosis or, e.g., Paget's disease that may increase the risk of facial nerve stimulation from the electrode.[27] Evaluate the temporal bone for evidence of COM. Active COM should be addressed prior to placement of the cochlear implant. Again, evaluate the position of the jugular bulb, sigmoid sinus, and mastoid tegmen.

For CHL, EAC narrowing should first be noted. The TM, if visible, may demonstrate perforation, retraction, or thickening. The middle ear space should be evaluated for opacification, which may indicate granulation tissue, cholesteatoma, or a mass. The ossicular chain should be evaluated for possible erosion/discontinuity/fusion. Signs of otosclerosis (otospongiosis) or Paget's disease may be seen at the oval window niche.

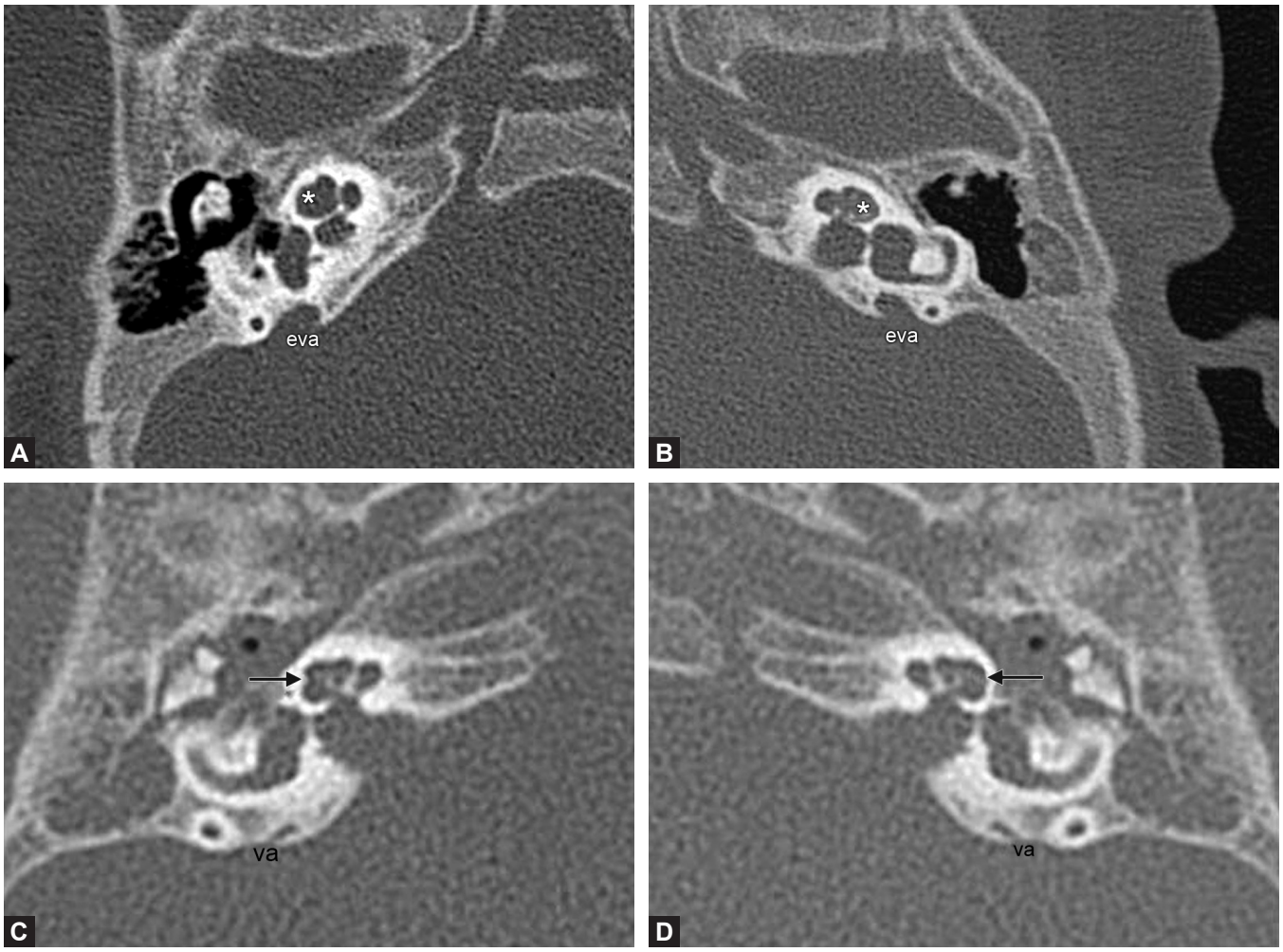
Evaluate the inner ear for evidence of inner ear abnormalities that may produce CHL such as SSCC dehiscence, enlarged vestibular aqueduct, or lateral semicircular canal dysplasia.[28–30] If the standard coronal and axial reformats do not clearly demonstrate intactness of the roof of the SSCC, Stenver and Poschl reformats are used (as described in PART I above) for evaluation for dehiscence of the SSCC (Figs. 12.6A to D).

## Masses, Pits, and Cysts

### *Clinical Background*

Children may present with a variety of lesions in and around the ear. For external lesions, such as preauricular or EAC lesions, accompanying history may include fluctuation in size of a mass, drainage, history of infection, and hearing loss. For lesions that are retrotympanic, accompanying history may include hearing loss, aural fullness, pulsatile tinnitus, and otalgia. Physical examination should note the following:

- Auricular masses: Where is it located in relationship to the tragus? Is there a pit at the skin or is it completely subcutaneous? Are there other masses in the region? Masses in this region may include a preauricular pit/cyst, a first branchial cleft cyst, a parotid tumor, or lymphadenopathy
- EAC masses: Is it soft tissue or bony? Is it unilateral or bilateral? Is it obstructing the TM? Masses in this region may include canal cholesteatoma, exostoses, osteoma, papilloma, or other neoplasm




**Figs. 12.6A to D:** Bilateral cochlear dysplasias and enlarged vestibular aqueducts (EVAs) in 4-month-old boy with bilateral sensorineural hearing loss (SNHL). Axial CT of the temporal bone of the right ear, (A), and left ear, (B), in a child with SNHL are contrasted with the temporal bone CT from an near age matched child with normal hearing (despite bilateral ear effusions) in (C) and (D) (where (C) and (D) are both mirror images of the same left ear replicated for ease of comparison). (A) and (B) are the abnormal right and left ears show bilateral cochlear dysplasias reflected by blunting of the cochlea at the junction of the first and second turns as indicated by the asterisk (*) and in conspicuity of the modioli. Compare the contour of these dysplastic cochleae to the normal sharp angle at the junction of the first and second turns as seen in the normal comparison ears marked by the black arrows. In (A) and (B), the vestibular aqueducts 'eva' are markedly enlarged compared to the normal vestibular aqueducts "va" in (C) and (D).

- Retrotympanic masses: Is it pearly white in nature? Is it vascular appearing or red in nature? Masses in this region may include cholesteatoma, a high riding jugular bulb, glomus tympanicum (paraganglioma), or an aberrant carotid artery.

## *Imaging Modality of Choice*

- Initial imaging to evaluate for possible mass: CT scan of temporal bone with contrast
- Adjunct imaging for soft tissue evaluation: MRI head and neck with gadolinium.

## *Clinical Questions*

- Auricular/EAC masses: When a clear cut diagnosis of a simple preauricular pit is made, imaging is not necessarily needed. However, if there is question of a branchial cleft cyst or neoplasm, imaging can help delineate any tract that may be present, as well as help evaluate the extent of a neoplasm, including nodal metastases
- Retrotympanic masses: Imaging should help determine if the mass is simply a soft tissue lesion or a vascular lesion. In addition, the extent of the mass can be evaluated

### *Interpretation*

For a retrotympanic mass, describe the anatomic relations of the lesion. For a lesion centered in the middle ear/mastoid, determine if there is tegmen erosion or involvement of the middle cranial fossa. Determine the relationship of the mass to cranial nerves VII, IX, X, and XI. Evaluate for involvement of the ossicles, TM, carotid artery, and Eustachian tube orifice. Some of the major clinical considerations are listed below.

For an auricular mass center around the external auditory meatus, erosion of the temporal squamosa or middle cranial fossa should be noted. Evidence of bony erosion, inferior/anterior involvement of the parotid gland, medial extent with or without TM/middle ear involvement, and posterior involvement of mastoid cavity should all be evaluated and noted. Nodal involvement should also be determined.

## Tinnitus

### *Clinical Background*

Children do not typically complain of tinnitus unless elucidated by the parent, but the incidence ranges from 13% to 53%, with a higher incidence in the adolescent population often due to noise exposure. [31] The tinnitus must be separated into pulsatile and nonpulsatile, and accompanying symptoms may include hearing loss, aural fullness, and otalgia. Pertinent physical examination includes otoscopy and auscultation in the periauricular region to evaluate for bruits/blood flow that may indicate a vascular cause.

On otoscopy, fluttering of the TM may be seen in middle ear myoclonus, while a dehiscent jugular bulb may present with tinnitus that extinguishes with turning the head toward the side of the tinnitus. Other causes of pulsatile tinnitus include an arteriovenous malformation, benign intracranial hypertension, or a heart murmur. Imaging can help determine if a vascular lesion is the cause of the pulsatile tinnitus.

In nonpulsatile tinnitus, the quality (pitch, volume) and location (unilateral vs. bilateral) should be determined. In rare instances, imaging may be indicated in unilateral nonpulsatile tinnitus without an identifiable cause to evaluate for a CPA tumor.

### *Imaging Modality of Choice*

- For nonpulsatile tinnitus: MRI of the brain with gadolinium
- For pulsatile tinnitus: MRI/MRA of the brain with gadolinium

### *Clinical Questions*

- Is there a temporal bone lesion present?
- Is the lesion vascular?
- Is the lesion destructive or expanding?
- Is the lesion central or peripheral?

### *Interpretation*

Inspect the external auditory canal and mastoid for evidence of inflammation that may be associated with tinnitus. Check the temporomandibular joint for evidence of degenerative disease that has been reported as a cause of tinnitus.[32]

Evaluate the middle ear for evidence of inflammation such as serous otitis or lesion such as a paraganglioma, hemangioma, or meningioma. Otospongiosis that may cause pulsatile tinnitus from increased blood flow to the promontory may occasionally be seen (if it is florid) as abnormal enhancement or signal abnormality on the CISS, 3D Fiesta, or DRIVE sequence but cannot be excluded by MRI. If any evidence is present to suggest this, CT scan of the temporal bone should be performed as an adjunct study.

Search for a vascular cause that may require review of the noncontrast enhanced CISS, DRIVE, or 3D Fiesta sequence, the contrast enhanced MRI, and the MRA. This search may be divided into arterial causes (carotid artery stenosis, atherosclerosis, aneurysm, aberrancy, persistent stapedial artery), venous causes (dural sinus stenosis/diverticula, dehiscent jugular bulb), vascular impingement (i.e. AICA on CN VIII), and arteriovenous malformations and dural arteriovenous fistulas.

Evidence of inner ear abnormalities, including labyrinthitis and dysplasia, and IAC/CPA cistern tumors should be evaluated.

Evaluate the brain images for evidence of pseudotumor cerebri, Chiari I malformation, or lesion of the fifth or seventh nerves that may be associated with middle ear myoclonus or for a lesion of the triangle of Guillain–Mollaret such as a demyelinating plaque, that may be associated with palatal or middle ear myoclonus.[33–36]

## Dizziness/Vertigo

### *Clinical Background*

In children, a number of etiologies may lead to vertigo, but it is overall a rarely reported symptom. History should help elucidate the cause, as the diagnosis is typically made clinically and does not usually require imaging. Once it is determined that the patient has true vertigo, the timing of the vertigo, as well as presence of hearing loss, should

be categorized. Meniere's disease (episodic vertigo with hearing loss), labyrinthitis (persistent vertigo with hearing loss), benign paroxysmal positional vertigo (episodic vertigo, no hearing loss), and vestibular neuritis (persistent vertigo, no hearing loss) can all be quickly diagnosed with this history. In addition, physical examination may suggest a third window phenomenon (+Hennebert sign, Tullio phenomenon) or middle ear effusion, which can cause episodic vertigo.

In the pediatric population, other causes include peripheral vestibulopathy due to inner ear structural anomalies, such as EVA, migraines, motor/developmental disorders (cerebral palsy, mitochondrial myopathy), CNS structural lesions (Chiari I malformation), and psychogenic vertigo.[37] Vestibular testing is indicated prior to imaging. If history, physical examination, and testing indicate a possible structural or inflammatory cause, imaging is useful.

### *Imaging Modality of Choice*

- If central cause is suspected (i.e. stroke and tumor): MRI of the temporal bone with gadolinium
- If possible third window (SSCC, perilymphatic fistula from cholesteatoma) is suspected: Noncontrast CT scan of the temporal bone.

### *Clinical Questions*

- Is there a central cause (tumor, Chiari I) that may be the source?
- Is there evidence of labyrinthitis?
- Is there evidence of EVA or a 3rd window (perilymphatic fistula, SSCC)?

### *Interpretation*

Check the cerebellum, brain stem, and the supratentorium for evidence of infarct (especially the vestibular nuclei in the medulla), disorder of myelination, malformation such as a Chiari I, or for evidence of neurodegeneration such as spinocerebellar ataxia. In children this component of the evaluation should include a search for evidence of neurodegenerative disorders such as Friedrich ataxia, mitochondrial disorder, or inherited disorder of myelination such as Fabry disease.[38] Check CN VIII, the IAC, and the CPA cistern for evidence of tumor. Abnormal enhancement of CN VIII may confirm nerve pathology such as neuritis or leptomeningeal disease. Evaluate the membranous labyrinth for evidence of labyrinthitis. Lastly, if a CT is done, evaluate for SSCC or perilymphatic fistula if CT is available.

## CONCLUSION

For imaging of the temporal bone in children, CT and MRI of the temporal bone and/or brain are the modalities best suited for the pediatric population. The determination of the modality of choice depends on the clinical indication for the imaging study and the clinical questions that need to be addressed, the age of the patient, and the growing concern for morbidities associated with radiation and sedation, all of which need to be weighed when deciding on the best approach to imaging.

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CHAPTER

# 13

# Histopathology of the Temporal Bone

*Felipe Santos, Alicia M Quesnel, Joseph B Nadol Jr*

## INTRODUCTION

A detailed understanding of the macroscopic to microscopic anatomy of the temporal bone is essential to the otologic surgeon. This understanding is derived from exposure to the three dimension relationships in dissections conducted in the temporal bone laboratory, the study of radiographic imaging including CT and MRI in normal and pathologic disease states and a knowledge base of otopathology specimens that provide an understanding of anatomic relations at the cellular level. This chapter is not a comprehensive overview but rather highlights anatomic correlates from histopathology that inform clinical and surgical decision making. For a comprehensive review of otopathology and temporal bone anatomy, the reader is referred to other texts including Schuknecht's Pathology of the ear, 3rd edn[1] and Anatomy of the temporal bone with surgical implications, 2nd edn.[2]

## MIDDLE EAR AND MASTOID

### The Middle Ear

The tympanic cavity is a mucosal lined space aerated by the Eustachian tube (ET). It houses the ossicular chain. The jugular bulb comprises much of the floor of the tympanic cavity. Along the anterior wall is the carotid canal that can be dehiscent (Fig. 13.1). The roof or tegmen tympani separates the middle ear from the middle fossa floor. The medial wall consists of the sinus tympani, round window, and oval window niche. The dimensions of the middle ear are variable. At term, the antrum and tympanic cavity approximate adult size.

Laterally, the tympanic membrane separates the external ear canal from the middle ear. The tympanic membrane is separated into a pars flaccida and a pars tensa. The tympanic membrane consists of three layers: (1) a lateral epithelial layer, (2) a middle fibrous layer (pars propria), and (3) a medial mucosal layer. The pars propria of the pars flaccida consists of fewer elastic fibers and does not have fibrous tissue arranged in inner circular and outer radial strata like the pars tensa.

The ossicles of the middle ear are the malleus, incus, and stapes. They transmit sound from the tympanic membrane to the inner ear. They are derived from the first and second branchial arches and assume their adult

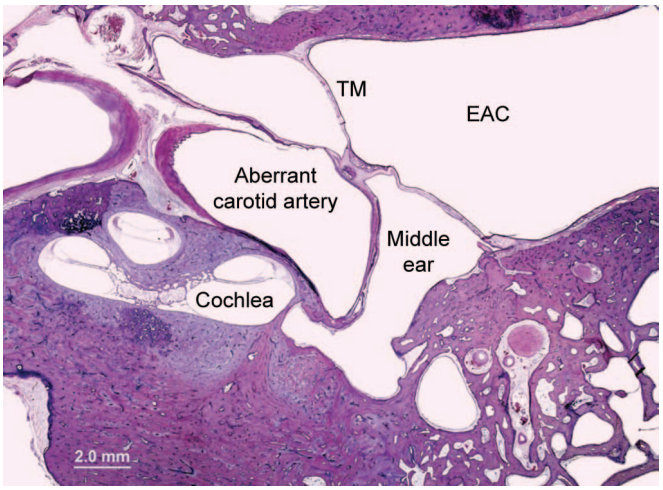



**Fig. 13.1:** A dehiscent carotid canal along the anterior tympanic wall. Tympanostomy tube placement in the anterior inferior quadrant could result in catastrophic hemorrhage. (TM: Tympanic membrane; EAC: External auditory canal).[1] (Courtesy of F Linthicum, House Ear Institute, Los Angeles, CA).

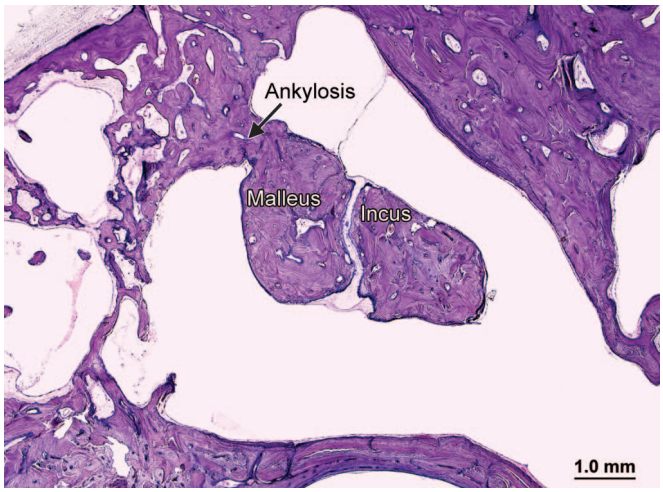



**Fig. 13.2:** Malleus ankylosis can result in conductive hearing loss. The head of the malleus is fixed to the epitympanum.

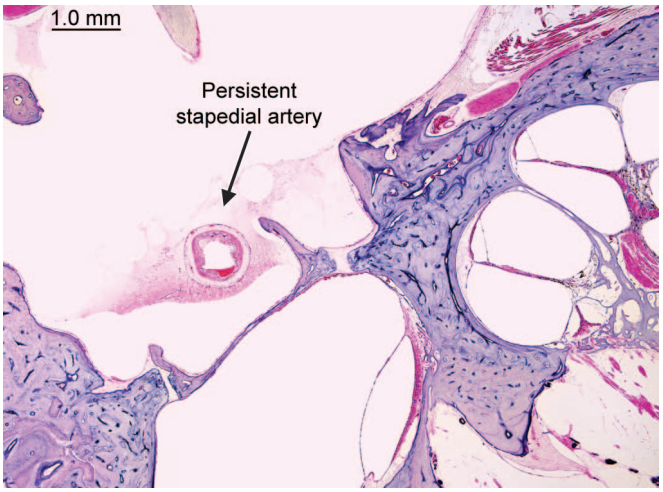



**Fig. 13.3:** A persistent stapedial artery.

configuration by the 20th week of gestation. The malleus consists of a head, neck, lateral process, anterior process, and manubrium. The anterior malleal ligament defines the axis of rotation of the ossicles with the posterior incudal ligament. The malleus is held in place by five ligaments in addition to the tensor tympani tendon, incudomalleal joint, and tympanic membrane. The head of the malleus can ankylose to the epitympanum, resulting in a conductive hearing loss (Fig. 13.2).

The incus consists of a body, short process, long process, and lenticular process. The incudostapedial joint is a diarthrodial articulation. The incus is held in place by the posterior incudal ligament and the medial and lateral incudomalleal ligaments. The incus and malleus have a marrow space that usually regresses following infancy. The ossicles may be pneumatized; this can make them more susceptible to fracture with manipulation.

The stapes consists of a head, footplate, and two crura. The crura are separated by the obturator foramen. This can be closed by a mucous membrane or traversed by a persistent stapedial artery. A persistent stapedial artery is a remnant of the normal embryonic hyoid artery that originates off the internal carotid artery (Fig. 13.3). The stapediovestibular articulation is a syndesmosis. Congenital stapes fixation, characterized by a nonprogressive conductive hearing loss without tinnitus or vertigo, represents roughly one third of ossicular malformations.

## Mastoid

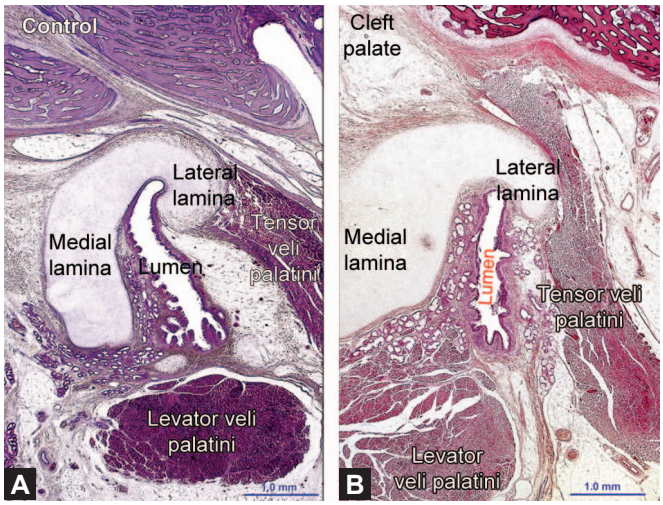
The temporal bone can be divided into different regions, areas, and tracts of pneumatization. The mastoid region is incompletely pneumatized at birth. Diploic bone and marrow are replaced during pneumatization. The mastoid continues to grow for 5–10 years postnatally. As the mastoid grows the tip descends, leaving the stylomastoid foramen in a more protected medial and inferior position to the external auditory canal than at birth. The facial nerve is consequently more susceptible to injury in the mastoid segment in younger patients.

## Eustachian Tube

The ET enables ventilation of the middle ear by communication with the aerodigestive tract. It extends from the lateral nasopharyngeal wall to the medial mesotympanum. The inferomedial portion is cartilaginous and the superolateral portion of the tube is comprised of a bony channel. The ET is closed at rest and three muscles coordinate opening of the pharyngeal end of the ET: tensor veli palatini, levator veli palatini, and salpingopharyngeus.[3] The reader is referred to Chapter 3 for further detail. Cleft palate results in ET dysfunction and anatomical abnormalities of the cartilaginous ET can be seen on histopathology (Figs. 13.4A and B). These histologic differences likely contribute to insufficient opening of the ET and insufficient ventilation of the middle ear cavity.[4] Children born with cleft palate invariably develop recurrent serous effusions, recurrent acute otitis media, and/or chronic otitis media as a result of the poor ventilation of the middle ear cavity.

# THE INNER EAR

The major structures of the inner ear include the cochlea, utricle, saccule, three semicircular canals, endolymphatic




**Figs. 13.4A and B:** Comparison of Eustachian tube orifice anatomy in a normal case and a patient with cleft palate. (A) The normal anatomy of the Eustachian tube orifice on a temporal bone specimen sectioned in the vertical plane. (B) A specimen from a patient with cleft palate is notable for the decreased volume of the lateral cartilaginous lamina, the comparative immaturity of the cartilage, and the straight rather than curved lumen of the Eustachian tube.[1] *Courtesy*: Dr I Sando, University of Pittsburgh School of Medicine, Pittsburgh, PA.

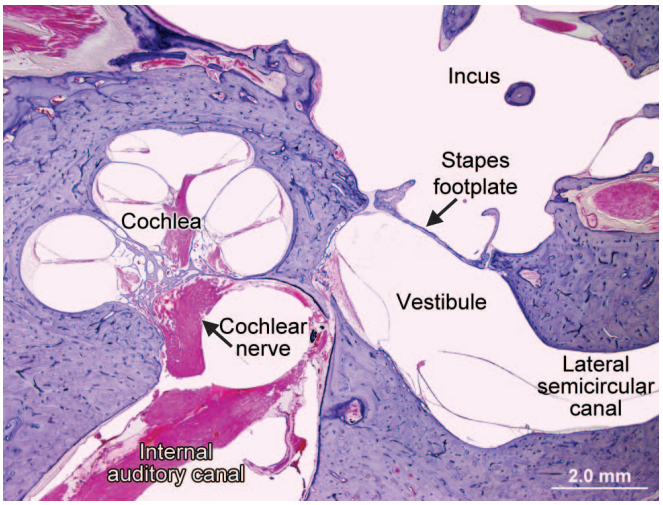



**Fig. 13.5:** Normal anatomy. In a horizontal section through a hematoxylin- and eosin-stained temporal bone at the midmodiolar plane, the size, spatial relationship, and structure of the bony and membranous parts of the cochlea, saccule, utricle, and lateral and posterior semicircular canals can be seen.

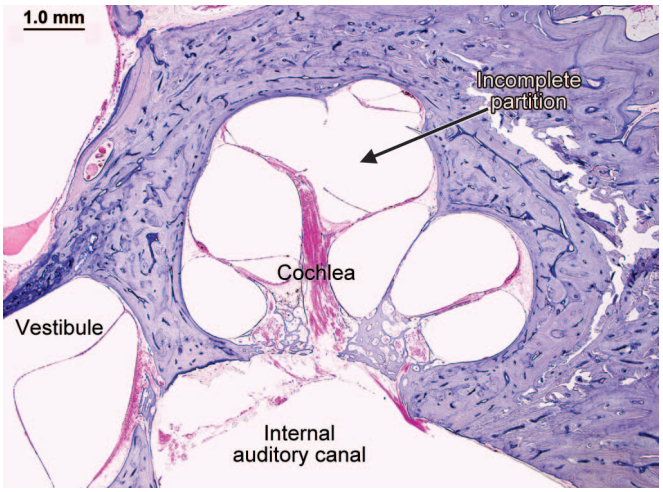



**Fig. 13.6:** Incomplete partition type II. This was previously called the Mondini malformation when associated with an enlarged vestibular aqueduct.

sac, and vestibular aqueduct (Fig. 13.5). The bony labyrinth is fully formed by 22 weeks' gestational age and the inner ear is adult size at that point. The otic capsule bone is formed by endochondral, endosteal and periosteal bone. By 8 weeks' gestation, a cartilaginous model of the otic capsule is formed by mesenchymal condensation.[5,6] Ossification of the cartilage proceeds at multiple ossification centers throughout the petrous bone, and ultimately results in dense otic capsule bone with some remaining cartilaginous islands. These islands are termed "globuli interossei" and are seen in the normal pediatric and adult otic capsule bone (Fig. 13.5). The modiolus is the central bony structure of the cochlea where the spiral ganglion neurons are located, and develops separately from the otic capsule bone. The modiolus is derived from membranous bone, which undergoes ossification between gestational weeks 20–25.[6]

The membranous labyrinth refers to the soft tissue structures, including neural elements, located within the bony labyrinth. The membranous portion of the cochlea includes three fluid filled spaces. The scala tympani and scala vestibuli contain perilymph and communicate at the helicotrema. The scala media, also called the cochlear duct, contains endolymph and is where the organ of Corti resides. The scala media and scala vestibuli are separated by Reissner's membrane. The scala media and scala tympani are separated by the basilar membrane. Deficiencies in the interscalar septae result in cochlear malformations (Fig. 13.6).

The cellular components of the organ of Corti, such as the inner hair cell, outer hair cells, and supporting cells, as well as the stria vascularis, spiral ligament, basilar membrane and Reissner's membrane, are easily examined with light microscopy on a human temporal bone specimen (Fig. 13.7). In temporal bones from patients with

sensorineural hearing loss, there is typically a histopathologic abnormality that can explain the sensorineural hearing loss. The most common abnormalities found include loss of spiral ganglion neurons, loss of outer hair cells and/or inner hair cells, abnormalities of the stria vascularis, and loss of supporting cells. The histopathologic findings in two syndromes with sensorineural hearing loss, Alport's syndrome (Figs. 13.8A and B) and Usher's type I (Fig. 13.9), are shown.

The five vestibular end organs include the saccule, utricle, and three semicircular canals. The vestibular sensory epithelia are located in the macula of the saccule and utricle, and in the cristae of the semicircular canals. There are two types of vestibular hair cells, both with stereocilia and a kinocilium. Type I cells are flask shaped and innervated by an afferent fiber only, and type II are cylindrical and have both afferent and efferent fibers.[8]

The vestibular aqueduct is a bony channel that extends from the posterior fossa to the vestibule. It contains the endolymphatic duct, which terminates at the endolymphatic sac on the surface of the posterior fossa dura. The congenital malformation in which the vestibular aqueduct is enlarged can result in sensorineural, conductive, or mixed hearing loss (Fig. 13.10).

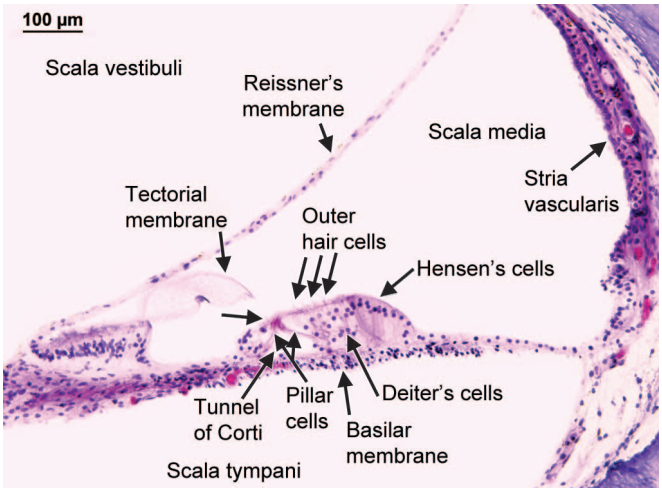
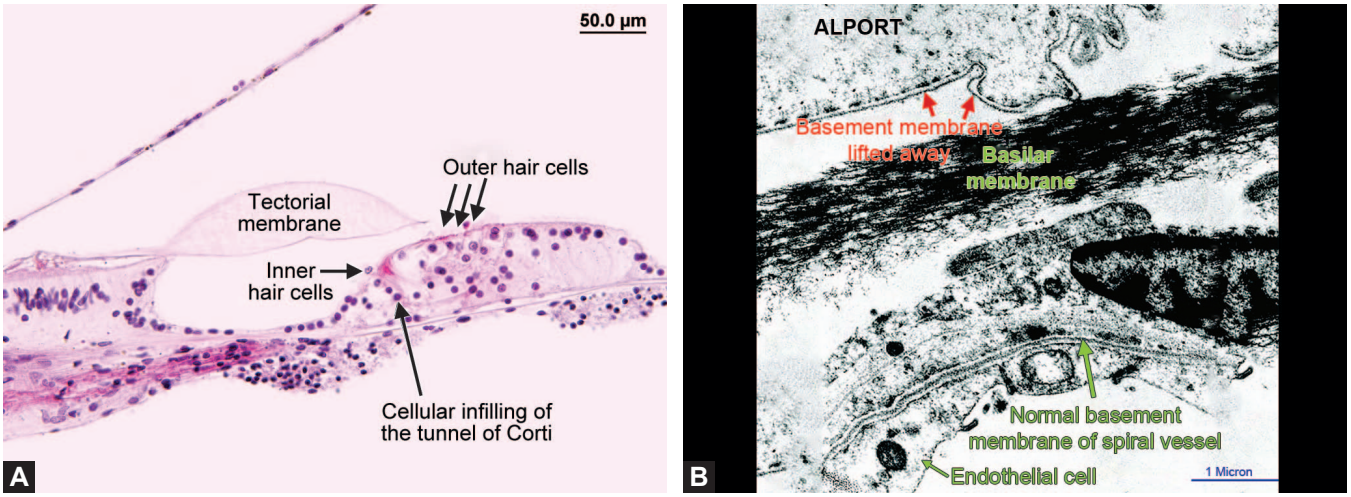



**Fig. 13.7:** The cochlear duct with organ of Corti shown at high power magnification.

## THE FACIAL NERVE

All the neural connections of the facial nerve are established by the 17th week of gestation. The bony covering of the facial nerve (fallopian canal) is complete by term. Dehiscences, particularly in the tympanic segment of the facial nerve and over the geniculate ganglion in the middle fossa, are a common variant of normal. The facial nerve may be more susceptible to iatrogenic injury or disease in these areas as a result of this normal variant (Fig. 13.11).

The intratemporal segments of the facial nerve include the labyrinthine, tympanic, and mastoid segments. The nerve follows a circuitous but constant course in the temporal bone. After the facial nerve exists the internal auditory canal the facial nerve makes its first abrupt posterior turn (first genu) distal to the geniculate ganglion.




**Figs. 13.8A and B:** Alport's syndrome is due to a mutation in the gene that codes for alpha 5 type IV collagen, most commonly X-linked inheritance, and causes glomerular nephritis, sensorineural hearing loss, and ocular abnormalities. The histopathologic findings include (1) absence of the space of Nuel, the space between the outer pillar cell and first outer hair cell in the organ of Corti due to cells obliterating this area (A) and (2) separation of the basement membrane from the basilar membrane in the organ of Corti (B).[1]

The tympanic segment then runs parallel to the petrous ridge above the oval window and makes its second turn (second genu) inferiorly at the sinus tympani. This marks the beginning of the mastoid (or vertical) segment that exits the temporal bone at the stylomastoid foramen. The chorda tympani nerve originates from the mastoid segment near the pyramidal eminence. In infants the chorda tympani may divide distal to the stylomastoid foramen and enter in its own canal.

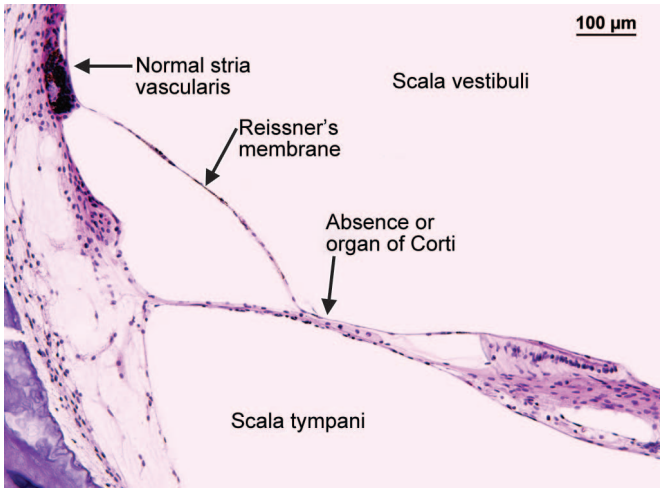



**Fig. 13.9:** Usher's syndrome type I is an autosomal recessive syndrome characterized by congenital profound sensorineural hearing loss and blindness from retinitis pigmentosa. The human temporal bone pathology is notable for complete degeneration of the organ of Corti throughout the cochlea, with the exception of disorganized mounds of cells at the apices.

While uncommon, there are variations in the course of the facial nerve. These include (a) a tympanic segment anterior and inferior to the oval window,[9] (b) a tympanic segment anterior to both the oval and round window membrane,[10] and (c) tripartitions and bifurcations in the tympanic and/or mastoid segments (Fig. 13.12).

## Vascular Anatomy

The course of the carotid artery within the temporal bone is of significant importance to the otologic surgeon. The carotid courses through the petrous bone in a bony canal of 0.5 mm thickness.[11] Up to 1% of carotid arteries may be dehiscent in this area. An aberrant internal carotid artery traverses over the cochlear promontory and results from an enlarged inferior tympanic artery providing the principal blood supply to the intracranial carotid artery. An anomalous course of the carotid or aneurysm may be seen as a pulsating mass along the anterior part of the tympanic membrane.

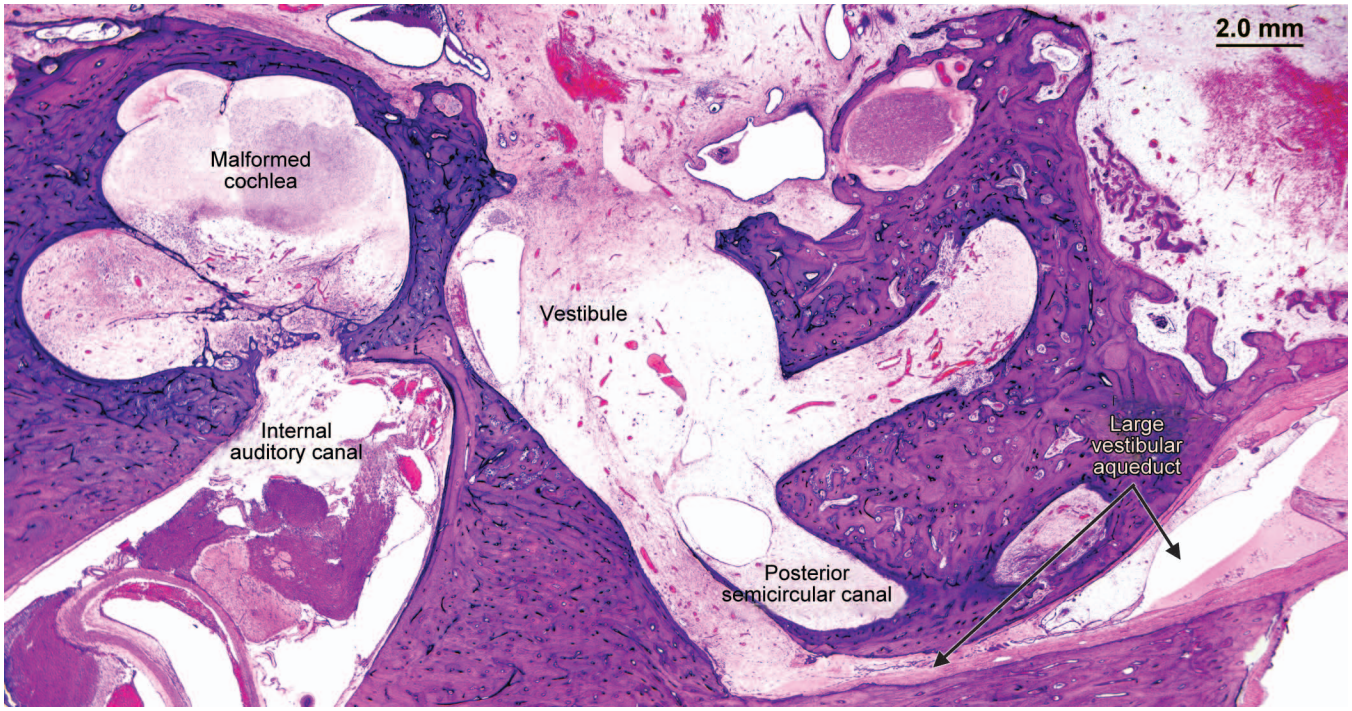



**Fig. 13.10:** Large vestibular aqueduct. This case demonstrates a large vestibular aqueduct, as well as a cochlear malformation with incomplete partition. There was an intense cellular inflammatory process with mature granulation tissue and fibrous tissue filling the cochlea, middle ear, vestibule, and semicircular canals, possibly the result of prior surgery and cochlear implantation.

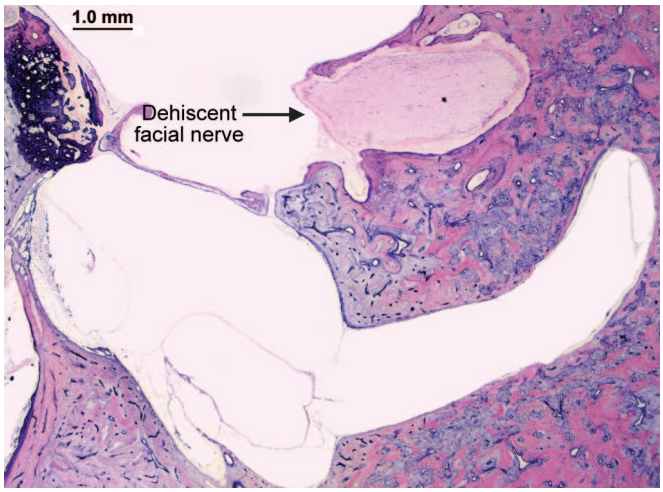



**Fig. 13.11:** Dehiscent tympanic segment of the facial nerve.

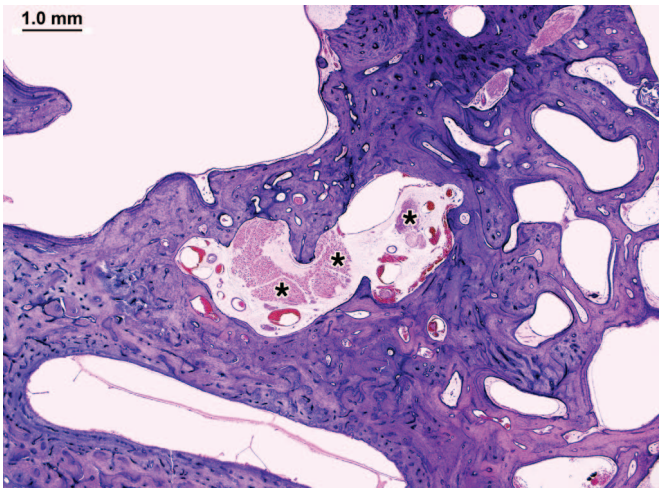



**Fig. 13.12:** Anomalous partitions (indicated by asterisks) of the vertical segment of the facial nerve.

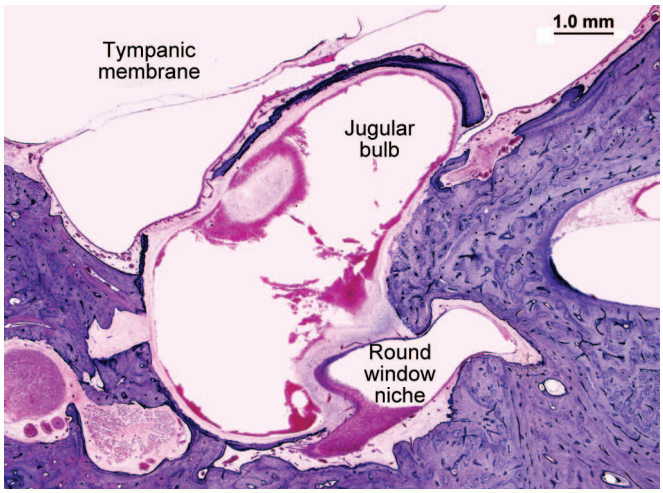



**Fig. 13.13:** A high jugular bulb may preclude an adequate view of the round window membrane during cochlear implant surgery or susceptible to injury with insertion of a tympanostomy tube or elevation of a tympanomeatal flap.

The jugular bulb is variable in position. It may be high in the middle ear and may be seen above the tympanic annulus encroaching the round window membrane. The jugular bulb may be dehiscent in up to 7% of cases[12] (Fig. 13.13).

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CHAPTER

# Newborn Hearing Screening and Audiologic Considerations for Children

14

***Barbara S Herrmann***

## BACKGROUND

Newborn hearing screening is now considered the standard of care in the United States and most developed countries because of the adverse consequences of undetected hearing loss on the linguistic, cognitive, and emotional development of a child. The importance of early identification of hearing loss was recognized by many individuals in the 1950s and 1960s, most prominently by Marion Downs who attempted to institute a behavioral observation based method of screening in the late 1960s.[1] These programs, based on a newborn's startle reaction to various sounds, proved costly due to the variability of newborn behavior. Many infants with normal hearing were referred for more testing and infants with hearing loss were missed. As interest in the early identification of hearing loss grew, the Joint Committee on Infant Hearing (JCIH) was formed in late 1969 composed of representatives from professions involving children and hearing, audiology, otolaryngology, pediatrics, and nursing. After thorough review of existing screening programs, the status of the current clinical techniques available and promising research being started, the Committee published its first statement in 1971.[2] In this statement, it recognized the urgent need for early detection of hearing impairment but could not justify the mass screening of all newborns because of the lack of appropriate test procedures.

As a result, a high-risk approach for identification of congenital hearing loss was suggested in which those infants with factors associated with congenital hearing loss in their medical or family history were identified at birth and enrolled to be tested repeatedly during the first 5 years of life.[2,3] This approach was mandated first in Massachusetts in 1977 and subsequently in other states. Over the next 15 years, studies on childhood deafness, however, indicated that the high-risk approach was ineffective in lowering the age of identification of hearing loss, which remained at an average of 2.5 years in developed countries, for two reasons: (1) 50% of all children born with hearing loss did not have an identifiable risk factor and (2) the high lost to follow-up rate for repeated testing on those children identified with risk factors.[4,5]

During the same time period, physiologic methods of testing hearing that did not rely on a behavioral reaction to sound began to be developed that eventually enabled the accurate testing and diagnosis of hearing loss in the infant. Auditory-evoked response testing using the auditory brainstem response (ABR) began to be used to measure the hearing sensitivity of infants who were at least 30 weeks' gestational age in the late 1970s and early 1980s.[6] Recording the synchronized neural firing from the auditory nerve and central auditory system to brief sounds, the ABR is currently considered the gold standard technique for the measurement of hearing sensitivity in infants.[7] As the testing of infants became possible, the ABR began to be used to screen infant hearing in the survivors of neonatal intensive care units (NICUs) who were recognized as having a higher incidence of hearing loss than well babies. With the successful application of ABR in infant hearing screening, instruments were developed that could be used by individuals with minimal training and knowledge of infant hearing,[8] thus lowering the cost and making more fiscally possible universal screening of all infants. In parallel, another physiologic response from ears with near normal hearing, otoacoustic emissions (OAEs), was also discovered[9] and applied in infant hearing screening.[10]

Newborn hearing screening programs began to be instituted in many NICUs and also in some well-baby nurseries, most notably the Rhode Island Project.[10] The surgeon general, C. Everett Koop, took interest in infant hearing and issued a challenge in 1988 that by the year 2000, all children with hearing loss be identified by 12 months of age, a challenge incorporated in the Health and Human services Healthy People 2000 report.[11] A consensus conference sponsored by the National Institutes of Health on the topic of infant hearing in 1993 concluded with the recommendation that all infants should be screened for hearing loss before discharge from the hospital.[12] This recommendation generated some controversy, most notably sparked by an opinion article by Bess and Paradise in 1994.[13] This article challenged the need for newborn hearing screening based on the lack of data showing the identification before the age of 2.5 years resulted in better outcomes for children than those identified later. This challenge prompted not only controversy but a series of studies, especially by Yoshinaga-Itano and colleagues that tracked the language development of children identified and starting early intervention for hearing loss at different ages.[14,15] These studies consistently indicated that better language outcomes were associated with earlier identification and intervention and that children identified later had a consistent deficit in language that persisted. With this additional evidence, barriers to the clinical implementation of universal newborn hearing screening (UNHS) began to fall, most notably by the endorsement of UNHS by the American Academy of Pediatrics. By 2000 the Joint Committee statement stated "Given the … empirical evidence to date, the JCIH considers that accepted public health criteria have been met to justify implementation of UNHS"[16] with a recommendation that infants not passing the hearing screening be evaluated and diagnosed by 3 months of age and intervention begun by 6 months of age.

This growing body of evidence supported the push in many states to institute statewide infant hearing screening. The first state to mandate newborn hearing screening was Hawaii in 1991, followed quickly by Rhode Island. Over the next two decades, all states and US Territories instituted statewide programs either by legislative action or gubernatorial action. Data from these programs are now compiled by the Centers of Disease Control (CDC) through the Early Hearing Detection and Intervention (EHDI) program.[17] In 2010, 98% of all births in the United States (3,881,046 infants) were screened for hearing loss; 98% of those infants passed the screening. Of the infants not passing the screening, 68% had been evaluated by 3 months of age with an estimated prevalence of congenital sensorineural hearing loss of 1.6 per 1000 births (range 0–4.6). Similar efforts in other developed countries have resulted in newborn hearing screening worldwide.

## SCREENING TECHNIQUES

There are two currently accepted newborn hearing screening techniques using a physiologic response to a sound: (1) the auditory-evoked response using either the ABR or, more recently, the auditory steady-state response (ASSR) and (2) evoked OAEs using either transient-evoked otoacoustic emissions (TEOAEs) or distortion product otoacoustic emissions (DPOAEs). Each of the techniques has its supporters and heated controversy has surrounded discussions regarding which is the better technique to use. Commercially available equipment has been developed for each of the response metrics and how each of these responses can be recorded is detailed elsewhere. Neither of these techniques measures the psychophysical perception of a sound as does the behavioral response, but both require that portions of the auditory system be intact for the responses to be present.

### Auditory-Evoked Responses

The ABR has been used in newborn hearing screening for the longest period of time with the first automated ABR infant hearing screener available in 1985.[8] The ABR reflects synchronized neural electrical activity that is elicited by a transient sound and recorded using surface electrodes on the head.[18] The response is extracted from the ongoing activity of the brain using signal processing techniques, most commonly signal-averaging of the ongoing electroencephalic activity for time window of 10–20 ms after many presentations of either frequency-limited toneburst signals or broadband click signals. Since the presence of the ABR requires the function of the auditory periphery (including the inner and outer hair cells, and auditory nerve) and of the central auditory pathways (up through the level of the upper brainstem), it is a metric of the physiologic integrity of much of the auditory system. For this reason, the ABR is considered the standard technique for the measurement of hearing loss in infants.[7] Most ABR screening instruments use a low-intensity broadband click.

The ASSR is a different auditory-evoked potential that has been more recently developed and is now currently being applied to newborn hearing screening.[19] ASSR analyzes the electroencephalic activity to frequency and amplitude modulated tonal signals with respect to peak detection in the spectral domain as opposed to the amplitude and latency in the time domain used in recording the ABR. Though promising for a more frequency specific measure of auditory screening, the ASSR is 10 times smaller than the ABR, making it more difficult to detect <30 dB HL even in normal hearing individuals. It is also more prone to false detection of artifact as response because of its use of the spectral domain analysis rather than time waveform analysis. The amplitude of the ASSR increases proportionally with the amplitude and frequency modulation of the tonal signals; however, with increased modulation the frequency specificity is similar to that achieved with the toneburst signals of the ABR.

### Otoacoustic Emissions

OAEs are low-intensity sounds that are emitted primarily by healthy normal ears. OAEs are elicited by transient broadband clicks, TEOAEs by the distortion generated in a healthy ear by two tones of different frequencies (DPOAEs).[20] Both TEOAEs and DPOAEs are present in healthy, normal ears and in ears with tonal sensitivity thresholds of 30 dB HL or better. Both are usually detected using spectral analysis of averaged waveforms. TEOAEs and DPOAEs are believed to be generated by the outer hair cells of the organ of Corti, though perhaps not by the same mechanism. Since the outer hair cells are frequently the first to be damaged by conditions causing peripheral hearing loss, OAEs are usually present in ears with normal peripheral hearing and are absent in those with hearing loss >30 dB HL. Thus, OAEs are considered an appropriate metric for identifying infants with hearing loss.

As the clinical application of OAEs increased, it was discovered that a small number of infants (and adults) have present TEOAEs or DPOAEs, and do not have ABRs to low-intensity sounds. These infants and some older individuals have been categorized as having auditory neuropathy/dys-synchrony[21,22] and the damage to the peripheral ear (either to the inner hair cells, the inner hair cell and nerve synaptic junction or to the auditory nerve itself) is sufficient to prevent spoken language development due to poor speech perception. A study of temporal bones from infants who did not pass an ABR infant hearing screening indicated a small number of specimens had present outer hair cells in some areas of the basilar membrane where inner hair cells were absent.[23] Animal models of similar cochlear damage consistently have present OAEs but absent ABRs. Thus although the majority of infants with hearing loss will not have OAEs, a small proportion, estimated to be about 1 in 12,000 births,[24] will pass an OAE newborn hearing screen but not have sufficient hearing to develop speech and language. Because of this issue, the JCIH recommends that ABR be used in the NICU population where the prevalence of auditory neuropathy/dyschrony is greater than in the well-baby nursery.[25]

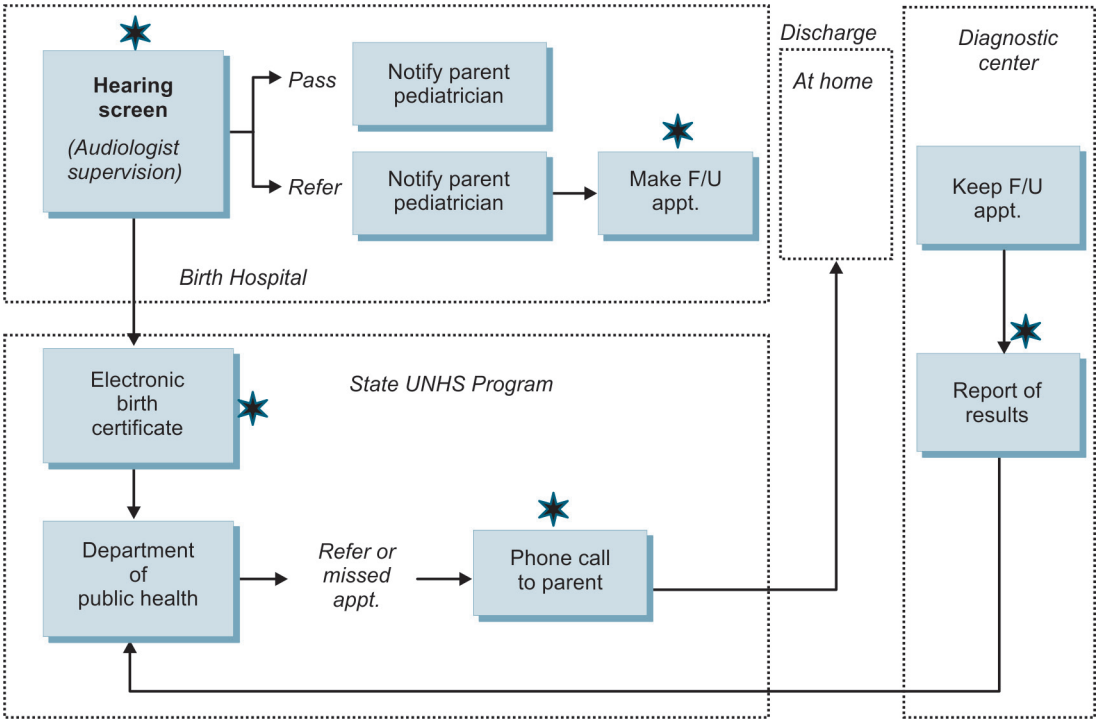
## IMPORTANT CONSIDERATIONS IN UNHS PROGRAM DESIGN

### Overall Design

The success of a newborn hearing screening program depends heavily upon the design and supervision of its implementation. Most states have detailed guidelines regarding the requisite components of a program that include screening personnel, equipment maintenance and calibration, documentation of results within the hospital and to the state, communication to parents and families, and linkage to the follow-up evaluations[26] website that follow the guidelines set out by the JCIH. Each of these components is necessary to have a comprehensive program and the flow of information from one segment to another is critical to the effectiveness of the program. Without careful consideration of overall design, it is not uncommon for many infants to be screened, but because of ineffective monitoring those infants are not diagnosed in a timely manner and consequently do not receive intervention in the initial year of life.

The goal of newborn hearing screening is to identify neonates with hearing loss that will be detrimental to speech and language development, diagnose the hearing loss, and begin appropriate intervention. Flowchart 14.1 illustrates the flow of the UNHS newborn hearing screening program in the state of Massachusetts. The structure of this particular program has resulted in one of the lowest lost to follow-up rates in the country. Screening programs are in birth hospitals and required to be associated with an audiologist for supervision and training (thus providing the nursery with a knowledge base regarding hearing). Hearing is screened in the nursery before discharge from the hospital and the outcome is either pass or refer

**Flowchart 14.1:** Flowchart of universal hearing screening program in the state of Massachusetts as an example of a closed-loop system that helps to minimize the number of infants who do not pass but do not receive a full diagnostic evaluation. Key elements of this system are highlighted by stars and include an audiology supervised hearing screen in the birth hospital, the scheduling of a diagnostic appointment before discharge from the birth hospital, entry of the screening outcome into an electronic birth certificate, contacting the parent after hospital discharge and report of diagnostic evaluation results to the centralized state department tracking the hearing screening of infants in the state.




(did not pass). Results are documented in the medical record and given to the parents verbally and by means of an informational handout containing results and basic information about the importance of hearing to the development of speech. The documentation in the record is transmitted through the discharge summary to the infant's pediatrician. In addition, the results are entered into the electronic birth certificate (EBC) that is maintained by the state's Department of Public Health (DPH). This electronic entry to the birth certificate begins a parallel system of monitoring for completion of the follow-up evaluation and intervention. Infants who do not pass their hearing screening are required to be scheduled for a full diagnostic evaluation at a DPH approved center before discharge from the hospital. This requirement enters the child and family into an audiology diagnostic system making a link between the nursery and the diagnostic follow-up. The usual time between discharge and the follow-up appointment is 3–4 weeks. The DPH department for UNHS screens the EBC data at regular intervals, identifies those infants not passing the screening, contacts the parents after discharge to encourage them to keep the appointment, and provides any assistance necessary. At the completion of the diagnostic evaluation with AER, the diagnostic center submits a data form to the state detailing the results of that evaluation. The DPH links the completion of follow-up diagnosis to the child's UNHS outcome and, if hearing loss is present, links the screening and diagnostic outcome to the state's Early Intervention Department. Babies who do not come to their diagnostic appointments are reported via the same system as a missed appointment, at which point the state again reaches out to the parent (in parallel to the diagnostic center).

In Massachusetts, this closed-loop system from newborn hearing screening to diagnosis and subsequently intervention has resulted in a consistently low rate of lost to follow-up (infants not receiving further testing, diagnosis, and intervention). This low lost to follow-up rate is in contrast to many states that do not directly schedule follow-up appointments before discharge from the nursery nor have established a parallel system of monitoring via the EBC to a state database. Figure 14.1

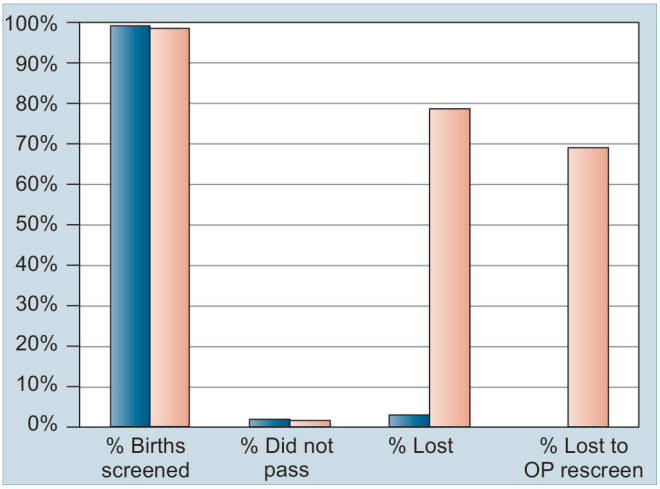



**Fig. 14.1:** Comparison of newborn screening data from Massachusetts (blue) and Texas (brown) which have different program designs. While the states have similar statistics for the percentage of infants screened and the percentage of infants not passing, the states differ greatly with respect to the number of infants not passing the screening that are lost to follow-up for a full diagnostic evaluation. Interestingly, the majority of the infants lost in Texas are lost to an outpatient rescreen; in Massachusetts all screening is done in the birth hospital before discharge and the appointment for the full diagnostic evaluation is made before discharge.

illustrates the lost to follow-up rate reported to the CDC in 2010[27] of two states over the last 10 years, Massachusetts and Texas. Texas does not have direct entry into an EBC for tracking of infants needing services nor a direct link to follow-up through scheduling a diagnostic appointment before discharge. These two elements are very effective in decreasing the lost to follow-up rate that the CDC reported to range from 2.9% to 86.1% and averages 39.3% over the entire country in 2010.

The design of a newborn screening program will also depend upon the health service system that is in place. For instance, in countries with a centralized national health service such as Belgium, newborn hearing screening has been incorporated into the first well baby visit by a visiting nurse in the home about 2 weeks after birth. The screening outcomes are entered and tracked as part of the well-baby health services including the diagnostic evaluations, again creating a closed-loop system that decreases infants who are lost to follow-up.[28]

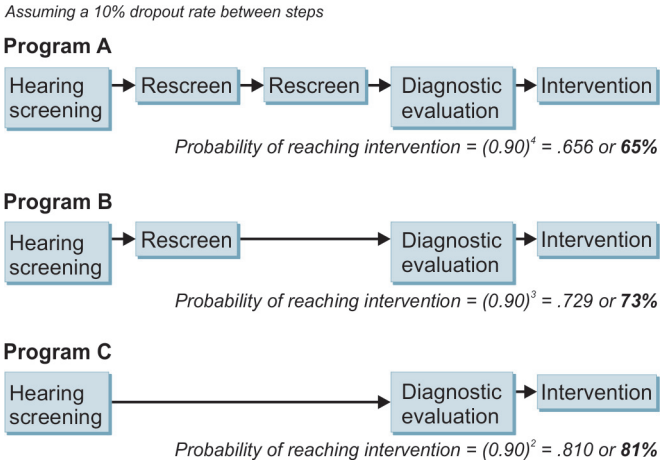
## Multiple Hearing Screens

Within the overall design of the UNHS program are decisions regarding the number of hearing screens before referring an infant for diagnostic testing. As newborn hearing screening programs were being implemented there was significant focus on reducing the number of infants referred for further testing. This concern has merit because of the increased cost in health dollars and the increased anxiety of parents with the additional testing for each referral. Hence, the sensitivity and specificity of a newborn hearing screening technique was critical in lowering cost.[13,29] Some individuals approached lowering the referral rate by rescreening infants who did not pass their initial hearing screening with the argument that reuse of the less expensive screening would eliminate those infants who may not have passed their initial hearing screenings because of a temporary hearing loss at a lower cost than the full evaluation.[10] In many places, this approach resulted in one or more in hospital screens followed by an outpatient screen before referral for diagnostic testing. There are several problems with this approach.

The first problem is that the use of several steps before referral to diagnostic testing increases the probability that the child will be lost to follow-up. If the probability of dropout before follow-up testing is a constant for each step in the design of a UNHS program, then the probability that a baby with hearing loss that does not pass an initial hearing screening makes it through the process to intervention is the product of the probabilities of dropout at each step. Flowchart 14.2 illustrates this principle. Assuming a dropout rate of 10% at each step, the program with the fewest number of steps will have the lowest probability of dropout for the entire program. Using rescreens, especially those scheduled as outpatients only increases the probability of lost to follow-up.

Second, repeated hearing screens increase the chance of a false pass due to the probability of repeated statistical testing.[25] Regardless of the screening technique chosen, all of the automated hearing screening instruments use a statistical test for detection of the response such as an F-test or the calculation of a Likelihood Ratio. Repetition of any statistical test increases the chance of a false identification of significance, which in this application means a response to sound is detected when it does not exist. Hence, repeat screenings only increase the chance of a false result. It is interesting, however, that humans tend to believe the outcome of the screen when it is the one that is secretly hoped for, that is, all testing is stopped when the infant passes a screening even after seven to eight screens that did not pass. For some reason, after multiple tests referring the child, the nursery staff believes the pass outcome.

**Flowchart 14.2:** This flowchart illustrates that increasing the number of steps between hearing screening and intervention increases the probability that the infant will be lost. The calculation illustrated is the overall probability of being lost as the product of the probability of dropout at every stage of the protocol.




Third, mild hearing losses are more likely to be identified with an initial hearing screen in the nursery if the screening is not repeated. Reports are beginning to surface indicating that some screening practices are missing babies with milder but permanent hearing loss.[30] Most screening instruments are set to detect infants whose hearing sensitivity in the 750–4000 Hz range is 30 dB HL or poorer. (For this reason, ABR instruments usually use a stimulus level of 35 dB HL). Some infants have hearing thresholds of 20–30 dB HL and the response detection techniques used are less likely to pass these ears. However, there is an increased likelihood of passing with repeated screens. Additionally, measures of acoustic reflectance[31] have indicated that all infants are born with some middle-ear fluid and most likely vary in the speed by which this fluid is cleared and by the amount of hearing loss, if any, that is caused by the fluid. In normal hearing infants, the fluid does not usually cause a change in hearing sensitivity sufficient to cause the infant not to pass the hearing screening. Infants with hearing sensitivity in the marginal or grey area of 20–30 dB may not pass the initial hearing screen because of a small decrease in hearing sensitivity caused by fluid pushes their thresholds into the range where they do not pass. Once the fluid has cleared, however, this infant with marginal hearing is more likely to pass the hearing screening. An example of this situation is shown in Figure 14.2. This infant did not pass the newborn hearing screening in either ear in the nursery. A diagnostic ABR evaluation at 4 weeks of age estimated the audiogram shown. A repeat recording of the ABR to a 35 dB HL click at the time of the diagnostic evaluation is also shown (the same stimulus used in the newborn hearings screening). The ABR is clearly present and would have been detected upon rescreen. Fortunately for this child, however, the use of a single screen referred this infant for full evaluation that diagnosed the marginal loss and prompted the continued follow-up of this child audiologically, medically, and educationally.

Finally, there is a perception that repeated hearing screenings somehow lower a family's anxiety over the failure to pass a newborn screening without giving any further information about a baby's hearing. A study verifying this perception has not been reported. It is not uncommon, however, for parents whose children have referred on repeated hearing screens to wonder why the definitive diagnostic test was done sooner to give them better information about their child.

## Cross-Disciplinary Collaboration

An important aspect of successful UNHS programs is the cooperation of professionals from several disciplines with the newborn and family to smoothly identify, diagnose, and begin intervention for congenital hearing loss. Beginning with nursery personnel including nursing, screening personnel, and neonatologists/pediatricians, the list of cooperating disciplines grows to include audiologists, otolaryngologists, speech-language pathologists, and educators. For this reason, all these disciplines are represented on the JCIH. Additional services for those diagnosed with hearing loss may also include genetics, ophthalmology, family counseling, and developmental pediatrics. To aid coordination of the contributions of each of these disciplines, the JCIH has described the role of each in contributing to the overall care of the child and support of the family in preventing the difficulties associated with untreated hearing loss in children.[25] Since these professionals often are in different institutions or minimally in different departments, it requires additional effort to coordinate all aspects of the program and support the baby and family in each phase of identification, diagnosis, and intervention.

## The Role of the Otolaryngologist

Pertinent to this chapter is the role of the otolaryngologist. Besides providing support and being a resource to a UNHS

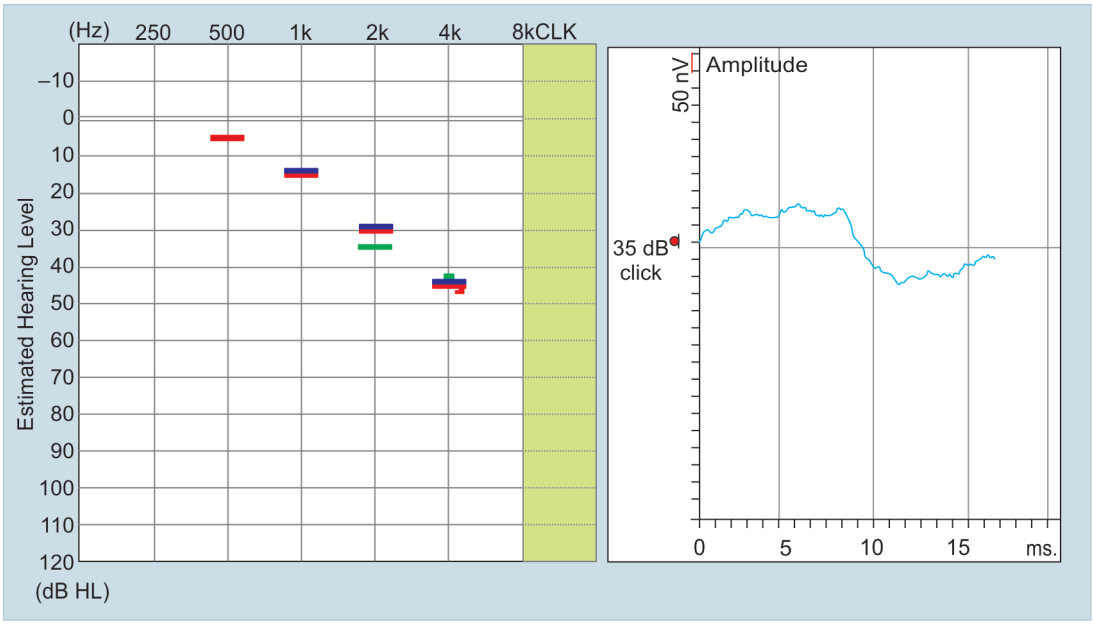



**Fig. 14.2:** Results of the diagnostic evaluation for an infant who did not pass the newborn hearing screening in a single-screen program and was found to have mild hearing loss when evaluated at 4 weeks of age. On the left is the measured hearing threshold sensitivity (red: right ear; blue: left ear; green: unmasked bone) using ABR (shown on the audiogram). On the right is the ABR response to a 35 dB HL click recorded at the full diagnostic evaluation. The clear presence of this response 4 weeks later suggests that the child may have had a slightly greater loss at birth perhaps due to middle-ear fluid which had cleared by 4 weeks of age. This child may have passed a rescreen.

program, the JCIH defines the role of the otolaryngologist in UNHS as the physician who is responsible for the comprehensive head and neck examination and the assessment of structural abnormalities that may be identified on examination or via imaging. The otolaryngologist determines the etiology of the hearing loss, identifies the risk indicators for progressive loss including syndromes associated with hearing loss and other disorders of the head and neck, and determines the need for medical or surgical intervention of ear disease resulting in conductive and sensorineural hearing loss. In addition, the otolaryngologist works with their audiology colleagues in determining the use of appropriate assistive technology such as amplification or cochlear implantation.[25]

## OUTCOMES FOR NEWBORN HEARING SCREENING

As mentioned at the beginning of the chapter, the outcomes of UNHS across the country have been tabulated by the EDHI program of the CDC for over 10 years.[27] Outcomes are tabulated in accordance to the recommendations of the JCIH for number of babies screened, number receiving diagnostic evaluations and also calculates the overall prevalence of congenital hearing loss identified through UNHS (currently 1.6 per 1000 births). These numbers show that most babies in the United States are screened for hearing loss, though the lost to follow-up rate varies drastically from 2.9% to 86.1%, with a national average of 38%. As demonstrated by the Massachusetts UNHS program, this problem is often solved by better design of the overall program and the use of state resources to track those infants who do not follow-through.

Within a single program, outcomes of a UNHS screening program and of the results of follow-up evaluation are the best way to monitor the quality of the program. Figure 14.3 gives an example of the statistics of a newborn hearing screening program over a 1-year period. You can see on this chart that the overall refer rate is calculated each month (with a cumulative total for the program calculated across the months monitored). The results of the follow-up testing on refers are also tabulated. By tracking these statistics, one can monitor any unusual change in referrals beyond the expected rate and address any issues such as equipment problems, need for retraining in a timely manner, need to tighten the linkage to follow-up, etc. Tracking these statistics over years can also highlight any issues or concerns and set expectations.

**Newborn Hearing Statistics**

| | JAN | FEB | MAR | APR | MAY | JUN | JUL | AUG | SEP | OCT | NOV | DEC | TOTAL | % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **All Screenings** | | | | | | | | | | | | | | |
| Total Screened | 319 | 316 | 321 | 322 | 364 | 362 | 400 | 378 | 337 | 283 | 336 | 309 | 4047 | |
| Bilateral Pass | 316 | 315 | 320 | 319 | 364 | 362 | 397 | 373 | 333 | 282 | 329 | 304 | 4014 | 99.2% |
| Right Ear Refer | 2 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 2 | 1 | 9 | 0.2% |
| Left Ear Refer | 1 | 0 | 1 | 2 | 0 | 0 | 2 | 4 | 1 | 0 | 3 | 1 | 15 | 0.4% |
| Both Ears Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 2 | 3 | 9 | 0.2% |
| Total Refer | 3 | 1 | 1 | 3 | 0 | 0 | 3 | 5 | 4 | 1 | 7 | 5 | 33 | 0.8% |
| Follow-Up Appt Made | 3 | 1 | 1 | 3 | 0 | 0 | 3 | 5 | 4 | 1 | 7 | 5 | 33 | 100.0% |
| **Level One Admits** | | | | | | | | | | | | | | |
| Total Screened | 309 | 302 | 306 | 308 | 341 | 350 | 379 | 362 | 322 | 276 | 314 | 287 | 3856 | |
| Bilateral Pass | 306 | 301 | 305 | 305 | 341 | 350 | 376 | 358 | 318 | 275 | 307 | 282 | 3824 | 99.2% |
| Right Ear Refer | 2 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 2 | 1 | 9 | 0.2% |
| Left Ear Refer | 1 | 0 | 1 | 2 | 0 | 0 | 2 | 4 | 1 | 0 | 3 | 1 | 15 | 0.4% |
| Both Ears Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 2 | 3 | 8 | 0.2% |
| Total Refer | 3 | 1 | 1 | 3 | 0 | 0 | 3 | 4 | 4 | 1 | 7 | 5 | 32 | 0.8% |
| **SCN Admits** | | | | | | | | | | | | | | |
| Total Screened | 10 | 14 | 15 | 14 | 23 | 12 | 21 | 16 | 15 | 7 | 21 | 22 | 190 | |
| Bilateral Pass | 10 | 14 | 15 | 14 | 23 | 12 | 21 | 15 | 15 | 7 | 21 | 22 | 189 | 99.5% |
| Right Ear Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.0% |
| Left Ear Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.0% |
| Both Ears Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0.5% |
| Total Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0.5% |
| **Non-nursery** | | | | | | | | | | | | | | |
| Total Screened | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | |
| Bilateral Pass | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | |
| Right Ear Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Left Ear Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Both Ears Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Total Refer | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| **Other** | | | | | | | | | | | | | | |
| Deceased | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Religious Waivers | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Missed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Missed Screened | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| **Total Follow-up** | 2 | 1 | 1 | 3 | 0 | 0 | 3 | 4 | 4 | 1 | 5 | 3 | 27 | 81.8% |
| Normal | 2 | 1 | 1 | 3 | 0 | 0 | 2 | 2 | 2 | 0 | 4 | 3 | 20 | 74.1% |
| Bilateral Sensorineural | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 4 | 14.8% |
| Bilateral Conductive | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 3.7% |
| Bilateral Mixed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.0% |
| Bilateral Unknown | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.0% |
| Unilateral Sensorineural | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 3.7% |
| Unilateral Conductive | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.0% |
| Unilateral Mixed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.0% |
| Unilateral Unknown | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 3.7% |

**Fig. 14.3:** Sample statistics tracking the performance of a newborn hearing screening program over 1 year.

**Table 14.1:** Risk indicators for delayed-onset or progressive hearing loss from the Joint Committee on Infant Hearing 2007 Statement[25]

| |
|---|
| • Caregiver concerns regarding speech, language, hearing or developmental delay |
| • Family history of childhood hearing loss |
| • Neonatal intensive care unit stay of more than 5 days or any of the following: ECMO, assisted ventilation, exposure to ototoxic medications or loop diuretics and hyperbilirubinemia requiring exchange transfusion |
| • In utero infections such as CMV, herpes, rubella, syphilis and toxoplasmosis |
| • Craniofacial anomalies including those involving the pinna, ear canal, ear tags, ear pits and temporal bone anomalies |
| • Physical findings such as white forelock, that are associated with a syndrome known to included sensorineural or permanent conductive hearing loss |
| • Syndromes associated with hearing loss or progressive loss such as neurofibromatosis, osteoporosis and Usher syndrome; other frequently identified syndromes include Waardenburg, Alport, Pendred and Jerveil and Lange-Nielsen |
| • Neurodegenerative disorders such as Hunter syndrome or sensory motor neuropathies, such as Friedreich ataxia and Charcot-Marie-Tooth syndrome |
| • Culture-positive postnatal infections associated with sensorineural hearing loss including confirmed bacterial and viral meningitis |
| • Head trauma, especially basal skull/temporal bone fractures requiring hospitalization |
| • Chemotherapy |

(CMV: Cytomegalovirus; ECMO: Extracorporeal membrane oxygenation).

The most important outcome for UNHS is, of course, the original motivation of preventing the speech and language delays associated with later diagnosis in children with hearing loss. Larger studies of these outcomes are beginning to be reported and are showing the expected effect; that is, identification and intervention of hearing loss before 6 months of age does result in better speech and language outcomes for children.[32,33]

## AFTER NEWBORN SCREENING: OTHER AUDIOLOGIC CONSIDERATIONS FOR CHILDREN

Concern regarding hearing loss in children does not end with newborn hearing screening. Though the exact numbers are not known, timely identification of late-onset hearing loss is the next challenge after UNHS with the same cooperation of disciplines (otolaryngology, pediatrics, audiology, education, rehabilitation) as with newborns. Currently the JCIH[25] addresses this issue through the identification of risk indicators (Table 14.1) for delayed onset of loss and through the monitoring of speech and language skill development for those infants who do not have any identifiable risk indicators for delayed-onset loss. The ideal place for identification of risk indicators and monitoring speech and language is through the medical home of the child, the pediatrician/primary physician within the periodic visits recommended by the AAP. Once referred and diagnosed, the entry into intervention is again the goal to minimize the effects on speech and language and later on education.

The techniques used to test children as they grow change with development of the skills available for response. These differences have been well catalogued and described in many sources including the JCIH statements.[20,25,34] For infants 0–6 months, case history, ABR, OAEs, and tympanometry are recommended components of a diagnostic evaluation. By a developmental age of 6 months, the child is capable of being conditioned to look for a toy or other reinforcing item when hearing a sound using a technique called visual reinforcement audiometry (VRA) for both tonal signals and speech detection. When the child's conditioned response is reliable, VRA replaces ABR for the measurement of hearing threshold sensitivity. By 3 years of age, most typically developing children will play a game such as putting a block in a bucket (play audiometry) to measure hearing threshold; by 5, most typically developing children are capable of raising their hand to a tone with the same reliability as an adult. As children develop spoken language, they become capable of doing tests of speech perception that provide insight into the distortion caused by a hearing loss that complements the information provided by measures of hearing threshold sensitivity.

Suffice it to say, hearing can be tested at any age. Diagnosis and intervention as early as possible will always be in the best interest of the child. Coordination of care and support of families through the process will result in the best outcomes for a child. This process starts with newborn hearing screening and continues through the development of the child and into the adult years. The evidence continues to show that the earliest detection and intervention of hearing loss helps to reduce and even prevent the linguistic, emotional, and cognitive impact that accompanies late-identified hearing loss.

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CHAPTER

# Speech and Language Evaluations of Children with Hearing Loss

15

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## INTRODUCTION

As the framework by which ideas are organized for exchange between people[1] language is important to the socialization of children, their successful engagement in education, and prospects for a productive adulthood. Access to the phonemes or basic units of speech is made possible by the frequency, temporal and intensity coding of the cochlea and central auditory pathway.[2,3] By representing the unique acoustic characteristics of each phoneme, the normal auditory system enables the discernment, recognition, and production of meaningful speech sounds that allow the developing child to illicit human reaction and influence behavior (Table. 15.1).[4,5] In turn, the child's evolving understanding of the world and its expectations are influenced by information received and decoded by the auditory system. An important determinant of long-term success, literacy is also dependent on the ability to decipher phonemes.[6,7] Hearing deficits therefore pose a significant threat to the normal development of language with implications that extend to educational achievement and long-term life opportunities.[8,9]

If the use of spoken language is the treatment goal for a child with hearing loss then access to the speech spectrum must be facilitated using appropriate hearing instruments or devices such as hearing aids and cochlear implants. The evaluation and mitigation of hearing loss without understanding its downstream effects on the child's language milestones, however, limits the development of an appropriate rehabilitation strategy and the ability to monitor outcomes. Whereas the clarity of speech production is often the most obvious manifestation of a hearing deficit, the first priority is to optimize receptive language through early and appropriate intervention,[8–10] so as to fortify the foundation for further language development

**Table 15.1:** Frequency distribution of important speech and language information

| *Frequencies* | *Important speech and language features* | *Communication examples* |
|---|---|---|
| 4,000 Hz | • Grammatical morphemes | • Plural markers (e.g. cat**s** and watch**es**), possessive markers (e.g. mommy**'s**), verb tenses (e.g. trie**s**, walk**ed** ) |
| 2,000 Hz | • Key frequency for speech intelligibility | • Bursts of acoustic energy for plosives (p, b, t, d, k, and g) and affricates (ch and j)<br>• Stridency for continuant sounds (s, z, sh, zh, f, and v) |
| 1,000 Hz | • Suprasegmentals<br>• Vowel discrimination | • Stress, rate and intonation and inflection |
| 500 Hz | • Voice tones<br>• Nasality information | • Differentiation between male, female and child voices<br>• Nasal sound information for /m/, /n/, and /ng/ |
| 250 Hz | • Suprasegmentals<br>• Nasal murmur | • Stress, rate and intonation and inflection<br>• Resonance of the nasal pathways for the nasal sounds |

Information from Ling.[5]

including more fluent speech and good reading skills.[11] Speech and language abilities should be evaluated by a speech-language pathologist (SLP) who has extensive experience and training in hearing loss, management of hearing aids, and management of cochlear implants. A team approach is necessary, however, to effect an optimal rehabilitation strategy and should include close cooperation with an audiologist, otolaryngologist, and educator. Other professionals with special training in auditory rehabilitation, such as teachers of the deaf, are also valuable members of the rehabilitation team, as are parents, the primary teacher of every child. Speech and language skills are evaluated in order to develop a plan for rehabilitation and monitoring. This chapter addresses the purpose of the speech and language evaluation along with the implications of intervention for children with hearing loss.

## THE SPEECH AND LANGUAGE EVALUATION PROCESS

Given the long-term objective of achieving age-appropriate speech and language abilities, tests standardized on typically developing children with normal hearing are used to gauge progress toward this goal.[12] The instruments listed in Table 15.2 are typically used to evaluate the speech and language abilities of children with hearing loss. For a young child, parent report measures are used in conjunction with norm referenced standardized assessments to fully capture the child's speech and language abilities across environments that the clinician may not have the ability to observe. Clinician-directed norm-referenced tests where the child responds to targeted language test stimuli are primarily utilized in older children, however.

Information is first gathered from parents, clinicians, and teachers in order to select appropriate assessments that can be used to characterize the child's unique communication profile. The SLP prepares for the evaluation by reviewing pertinent case history and other available documentation, including audiological reports, previous speech and language assessments, psycho-educational assessments, gross motor and fine motor assessments (i.e. physical therapy and occupational therapy), and education-related documents such as the Individualized Family Service Plan (i.e. special education services for infants and toddlers) or Individualized Education Plan (i.e. special education services for school age children). If possible, it is helpful to directly communicate with providers who are currently working with the child including SLP, audiologist, psychologist, early interventionist, classroom teacher, physical therapist, and occupational therapist. Additionally, the parents and/or guardians are interviewed regarding communication history and current communication behaviors.

Depending on the child's age, assessments are given to evaluate speech articulation and language abilities in the areas of form, content, and use.[13] Form of language comprises syntax, morphology, and phonology. These components provide the structure of language. Syntax specifies how words are organized in sentences. For example, noun–verb agreement or a descriptive word precedes the object of a sentence. Morphology consists of morphemes that are the smallest units of meaning within a word. If one adds an "s" to a noun, e.g., the meaning of the noun changes from singular to plural. In this example, the noun and the grammatical marker "s" are each considered morphemes. Phonology is the sound system of our language. The system is comprised of many individual phonemes or speech sounds that can be manipulated to create words. Content of language refers to the meaning of words and sentences to include nouns, verbs, adjectives, adverbs, concepts, synonyms, antonyms, idioms, and figurative language. Receptive vocabulary is the child's knowledge of word meanings while its counterpart, expressive vocabulary, comprises words that the child uses to impart meaning. A language user who has a strong semantic knowledge base understands and uses a variety of words that are rich in meaning to convey a message. Pragmatics is the social use of language and thereby influences all the other aspects of language. All the above aspects of language are used simultaneously to produce meaningful communication in an effortless manner. Speech articulation abilities overlay how the intended verbal message is communicated intelligibly.

Table 15.1 describes where speech sounds fall across the frequency spectrum.[4] Without sufficient access, gaps in speech perception will be evident and therefore weak or uneven speech and language abilities will be exhibited. Vowels carry 90% of the energy during speech production, whereas consonants account for only 10% of speech energy. However, 90% of the information needed to perceive the differences between speech sounds is carried by consonants.[4] Consonant perception and speech understanding are therefore quite vulnerable to hearing deficits, which predominantly affect the high frequencies (Table 15.1). Hearing at 4000 Hz, e.g. is critical for "s"

**Table 15.2:** Commonly used speech and language evaluation measures

| *Speech production measures (age range)* | *Vocabulary tests* | *Comprehensive language measures* | *Parent-report speech and language measures* |
|---|---|---|---|
| AAPS-3 (1y6m to 18y)<br>GFTA-2 (2y to 21y11m)<br>KLPA-2 (2y to 21y11m) | PPVT-4 (2y6m to 90y)<br>ROWPVT (2y to 18y11m)<br>EVT-2 (2y6m to 90y)<br>EOWPVT (2y to 18y11m) | PLS-5 (Birth to 6y11m)<br>CELF-P2 (3y to 6y11m)<br>CELF-4 (5y to 21y)<br>OWLS II (3y to 21y)<br>CASL (3y to 21y) | SKI*HI (Birth to 5y)<br>MCDI-Gestures and Words (8m to 18m)<br>MCDI-Words and Sentences (16m to 37m)<br>MCDI-Development Inventory III (31m to 37m)<br>Rossetti Infant-Toddler Language Scale (Birth to 3y)<br>CASLLS-Pre-Verbal Level (0m-12m)<br>CASLLS-Pre-Sentence Level (12m-24m)<br>CASLLS-Simple Sentence Level (24m-48m)<br>CASLLS-Complex Sentence Level (4y-8y) |

*Norm referenced measures with normal hearing population.
**Criterion referenced measures.
*AAPS-3: Arizona Articulation Proficiency Scale, 3rd Edition.
*GFTA-2: Goldman-Fristoe 2 Test of Articulation.
*KLPA-2: Khan-Lewis 2 Phonological Assessment.
*PPVT-4: Peabody Picture Vocabulary Test.
*ROWPVT: Receptive One-Word Picture Vocabulary Test.
*EVT-2: Expressive Vocabulary Test.
*EOWPVT: Expressive One-Word Picture Vocabulary Test.
*PLS-5: Preschool Language Scales, 5th Edition.
*CELF-P2: Clinical Evaluation of Language Fundamentals-Preschool, 2nd Edition.
*CELF-4: Clinical Evaluation of Language Fundamentals, 4th Edition.
*OWLS II: Oral and Written Language Scales II.
*CASL: Comprehensive Assessment of Spoken Language.
**SKI*HI Language Scales (compared to deaf population).
*MCDI: MacArthur-Bates Communicative Development Inventories.
** CASLLS: Cottage Acquisition Scales for Listening Language and Speech. (compared to typically developing hearing population).

and "z" grammatical markers that are necessary for the development of plurals, possessives, and some verb tenses. Even mild to moderate high frequency hearing losses can significantly alter normal acquisition of receptive and productive language.

Expressive language develops through listening and manifest as verbalizations that evolve with both receptive language and oral motor coordination. Babies begin speech sound production by vocalizing and crying. These sounds evolve over the next year through exploration of fine motor movements of the vocal tract and further refinement of their oral motor development that shape vocalization to approximate speech sounds that are heard daily.[14–17] For example, the child progresses through a series of babble stages, which precede the production of the first words (Table 15.3). Subsequent production of speech sounds is shown in Table 15.4, reflecting development of oral motor skills and expanding expressive vocabulary.[17] An understanding of these early stages of articulation and phonological skill acquisition is critical to the early detection of abnormal language development before large deficits occur. When there is a delay in the production of early vocalizations, speech sounds or the achievement of appropriate milestones then a number of causes should be considered and ruled out including hearing loss, cognitive learning disorder, and oral motor deficits.

In the case of hearing loss, early intervention with hearing aids or cochlear implants can provide adequate speech input that helps to guide this normal construction and progression of both receptive and expressive language. Appropriate intervention should not, however, await the appearance of deficits in normal speech and language development. In the setting of moderate to severe and progressive hearing loss, the use of a hearing aid may initially be accompanied by normal development of speech and language. The appearance of a plateau or regression of development should prompt strong consideration of cochlear implantation and enhanced rehabilitation.

**Table 15.3:** Pre-linguistic phonological development

| *Babbling stage* | *Examples of associated verbal behaviors* |
|---|---|
| Phonation *(Ages birth to 1 month)* | Crying, coughing, and sneezing; sounds of pleasure |
| Cooing and Gooing *(Ages 2-3 months)* | Vowels and consonant-like sounds produced in the back of the throat; back vowels (i.e. oo, aw, ah) and velar productions (i.e. k and g); responds vocally to speech of others |
| Exploration/Expansion *(Ages 4-6 months)* | Begins babbling using strings of consonants and vowels (CV syllables) varying in pitch and intonation patterns; experiments with speech sounds and verbalization; imitation begins to emerge; squeals with excitement; vocalizes displeasure with intonation; makes non-speech sounds such as raspberries |
| Canonical Babbling *(Ages 7-9 months)* | Engages in vocal play; babbles in reduplicated patterns (i.e. babababa, mamamama); imitates reflexive vocalizations such as coughing and "raspberries"; produces distinct intonation patterns like adult speech; produces a greater variety of speech sounds using lips and tongue |
| Variegated Babbling *(Ages 10-12 months)* | Becomes more imitative of adult speech sounds; continues to use CV syllables in babble; begins to combine a variety of CV syllables resulting in jargon (e.g. "ba-mu-gee-da"); practices words known with inflection; produces adult-like vocalizations including intonation, prosody and rhythm |

Information from Oller[14] and Owens.[24]

## DEVELOPING INTERVENTION GOALS AND MEASURING PROGRESS

The characterization of speech and language delay guides intervention. The results of speech and language assessments are shared with the parents and an evaluation report is generated containing test scores and their interpretation along with narrative describing areas of strengths and weaknesses. Annual evaluations establish a trajectory of improvement of these delays allowing for adjustments of treatment strategy toward further narrowing speech and language. Information from the initial assessment is used as a starting point for establishing intervention goals, making therapeutic recommendations and tracking the development of speech and language skills. Frequency and duration of therapy are driven by the severity of the child's language delays. To monitor speech and language growth more carefully and to modify short-term therapy goals, evaluations can be performed at 6-month intervals or at the therapist's discretion. The clinician should always refer to the administration rules for each specific test regarding time intervals allowed for subsequent testing.

The tracking of speech and language progress on at least an annual basis is necessary in order to monitor expected language growth. In children with hearing aids or cochlear implants, the rate of language growth should be similar to that of a child with normal hearing. Therefore, at least 12 months growth of language should be demonstrated in a 12-month period of time, i.e. month-for-month language growth in a period of one year.[18] Given this growth rate, the goal for a child who received hearing aids or cochlear implants in infancy, is to achieve language-age equivalent scores that are commensurate with the child's hearing age (i.e. length of time with enhanced hearing within the speech spectrum) on all test measures.[12] Not all children may achieve the month-for-month language growth goal, however. Factors that may affect growth rate include age of implantation, cognitive abilities, parental involvement, socioeconomic status, or inadequate intervention services.[8,9]

## THERAPEUTIC CONSIDERATIONS

Once diagnosed and provided with appropriate sensory input through a listening device, the goal of therapy should be to advance the child through the natural language milestones experienced by normal hearing children. Infant and toddler intervention should occur within a natural play environment. Additional emphasis should be placed on coaching and guiding for parents and caregivers how to implement strategies and techniques that facilitate listening and spoken language acquisition. Behaviors that promote language development at home should also be taught, modeled, and reinforced.[8,11,19] Commitment to a longitudinal rehabilitation program consisting of frequent sessions with the child, including the parent or guardian, is therefore critical to achieving rehabilitation goals.

The auditory hierarchy of detection, discrimination, identification, and comprehension serves as a framework for developing intervention goals for children with hearing loss.[20] Each of the levels along the hierarchy builds upon

**Table 15.4:** Developmental age milestones for speech production based on Normative Data from the Arizona Articulation Proficiency Scale (Arizona-3)[17]

| *Age** | *1 ½* | | *2* | | *2 ½* | | *3* | | *4* | | *5* | | *5 ½* | | *6* | | *6 ½* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Vowels* | | | | | | | | | | | | | | | | | | |
| | **æ** | "apple" | ɛ | "red" | | | **eɪ** | "cake" | | | | | | | ɚ | "her" | ɛɚ | "chair" |
| | ʌ | "hut" | ɑɪ | "knife" | | | | | | | | | | | ɝ | "bird" | | |
| | **oʊ** | "comb" | **i** | "tree" | | | | | | | | | | | oɚ | "fork" | | |
| | **ə** | "wagon" | ɑʊ | "house" | | | | | | | | | | | ɪɚ | "ear" | | |
| | **ɔ** | "dog" | ʊ | "book" | | | | | | | | | | | | | | |
| | **u** | "shoe" | | | | | | | | | | | | | | | | |
| | ɪ | "hid" | | | | | | | | | | | | | | | | |
| | ɑ | "father" | | | | | | | | | | | | | | | | |
| *Consonants* | | | | | | | | | | | | | | | | | | |
| | | | **h-** | "house" | **-n** | "train" | **-b** | "cub" | **-t** | "hot" | **dʒ-** | "jam" | **-l** | "ball" | **r-** | "red" | **-tʃ** | "watch" |
| | | | **b-** | "bat" | **w-** | "win" | **-p** | "hop" | **-ŋ** | "ring" | **ʃ-** | "shoe" | **ð-** | "this" | **z-** | "zoo" | θ– | "think" |
| | | | **p-** | "pig" | | | **k-** | "cat" | **j** | "yell" | **- ʃ** | "fish" | | | **-z** | "nose" | –θ | "teeth" |
| | | | **n-** | "nose" | | | **-k** | "cake" | | | **v-** | "vest" | | | **s-** | "sun" | | |
| | | | **m-** | "man" | | | **g-** | "game" | | | **-v** | "five" | | | **-s** | "hiss" | | |
| | | | **-m** | "ham" | | | **-g** | "bug" | | | **l-** | "lake" | | | | | | |
| | | | | | | | **d-** | "dog" | | | **tʃ-** | "chair" | | | | | | |
| | | | | | | | **-d** | "bed" | | | | | | | | | | |
| | | | | | | | **t-** | "tea" | | | | | | | | | | |
| | | | | | | | **f-** | "fish" | | | | | | | | | | |
| | | | | | | | **-f** | "puff" | | | | | | | | | | |
| *Consonant blends* | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | **pl-** | "play" | | |
| | | | | | | | | | | | | | | | **-ld** | "cold" | | |
| | | | | | | | | | | | | | | | **tr-** | "train" | | |
| | | | | | | | | | | | | | | | **gr-** | "gray" | | |
| | | | | | | | | | | | | | | | **st-** | "star" | | |
| | | | | | | | | | | | | | | | **-st** | "nest" | | |
| | | | | | | | | | | | | | | | **-ts** | "cats" | | |
| | | | | | | | | | | | | | | | **-ks** | "books" | | |

*Age in years at which 90% achieve mastery.

the previous level (e.g. you have to be able to detect before you can discriminate). The time spent on each of the levels is dependent on the child's language and learning abilities and it may require the clinician to adjust by moving up and down the hierarchy as different auditory stimuli along the continuum of speech elements (e.g. syllables, words, phrases, sentences, and connected discourse) are worked on.[20] Therapy should not, however, be fragmented but rather comprehensive so that the skills of audition, language, speech, and cognition are being integrated concurrently.[12]

Both didactic instruction and incidental learning have a role in the speech and language therapy of children with hearing loss.[21] During didactic instruction, a teacher or therapist uses a planned structured activity in order to teach specific information and language structures in a systematic way. Older children with hearing loss require some direct teaching of new language concepts and terminology using this approach. As much as 90% of what we know, however, is learned incidentally.[4] For example, we learn how to interact socially by observing and overhearing language through everyday conversations within the home, age-appropriate slang used in peer interactions, and new concepts from listening to the radio or television. A child with hearing loss, however, has more difficulty casually hearing what people are saying or being aware of conversations around them.[5] Because the child with hearing loss does not tune in readily, they may seem distracted or disconnected from events and conversations. Therefore, social rules, novel vocabulary, and language structures often need to be taught directly.

## FINAL THOUGHTS

Speech and language assessments that are administered by a qualified speech and language pathologist provide valuable information that determines the peaks and valleys in the speech and language abilities of children with hearing loss who use hearing aids or cochlear implants. The information gathered from the assessment will assist in determining speech and language growth between assessment intervals, assist with the development of therapy goals, and obtain an understanding of language strengths and weaknesses as they impact the child's performance in the classroom and day-to-day interactions. It is imperative that strong parental involvement, intensive individualized intervention, in addition to appropriate educational placement, take place in order for the child to make the expected language growth. The ultimate outcome for children with hearing loss who have access to the sounds of language via sensory devices is to obtain speech and a language ability commensurate with their hearing peers. Parents who take an active role in their child's educational and therapeutic programming help to attain the best outcomes. The speech language pathologist partners with the parents in guiding them to be the primary language facilitator and advocate for their child.

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CHAPTER

# 16

# Amplification and Classroom Management

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## HEARING LOSS

Hearing loss is the result of cellular dysfunction, structural anomalies, and/or interference of mechanical function by pathology in the ear or auditory pathways. The effect of these anatomical changes is a reduction in the loudness and clarity of auditory stimuli and interference with the brain's ability to spatially organize sound in the environment.[1,2] When the anatomy or physiological response of the body to medical treatment prevents recovery of normal function, the goal of intervention is to maximize the amount of information; the pathways are capable of transmitting and to reduce environmental competition. This may be achieved by using a combination of amplification, auditory encoding devices (such as cochlear implants), assistive listening devices, and management of room acoustics and noise sources. The intervention and combination of devices used is dependent on the degree and configuration of the hearing loss and the age of the patient.

### Effects on Development

Children are particularly susceptible to the life-long detrimental effects of hearing loss. In hearing families and communities, spoken language is the basis of communication. Oral languages rely on the use of complex systems of sound organization for the purpose of encoding meaning. It is the mode by which children in hearing communities are taught by their elders about the world around them and learn about the intricacies of social interactions and relationships within society. When a child has restricted access to the speech sounds at the base of the language, incomplete development of language may result and limit the child's cognitive development.[3,4]

The critical language learning period of the young brain is finite. Early access to auditory stimuli is necessary for the development of the cortical areas governing fundamental auditory processing skills.[3] The brain is most plastic within the first few years of life. After 4 years of age, elimination of extraneous neurons from receptive sensory areas begins. After 7 years of age, the P1 cortical auditory evoked potentials (associated with auditory cortical maturation) no longer achieves normal levels despite introduction of auditory stimulation in congenitally deaf children. Early identification and intervention are crucial in ensuring that adequate acoustic stimulation is received to maximize the developmental potential of the brain.

## SPEECH AND LANGUAGE ACCESS

Adequate hearing sensitivity, in at least one ear, is essential to maintain access to the spectral and temporal fluctuations of speech over distance for normal development of oral language. The loudness of conversation level speech at one meter's distance naturally fluctuates between 55 and 65 dB HL. For every doubling of distance, the loudness decreases by 6 dB. For every halving of distance, the volume increases by 6 dB. A young infant, cradled in a parent's arms, receives the parent's "conversation level" speech at levels fluctuating between 67 and 77 dB HL. For infants with no worse than moderate hearing loss, these levels provide at least some access to the components of speech needed for the initial stages of cortical development. As infants grow, however, their position in relation to their caregivers quickly begins to change. By 1 month of age, they are increasingly placed in portable car seats or baby carriers. By 3 months of age, they become heavier and are placed

on play mats or in play pens located >1 m away. Around 8 months of age children may be crawling across the room, and by 1 year of age they may toddle out the door. When hearing loss is present, small changes in distance may drastically affect a child's access to sound. Amplification of sound may be necessary to ensure adequate and stable access at all times. Significantly better language development occurs when amplification is introduced by 6 months of age when chronic hearing loss is present.[4]

## Amplification

A hearing aid is a device that is composed of microphones, a sound processor, an amplifier, and a speaker. It is used to amplify sounds from the environment and deliver the amplified sound to an ear. The amount of amplification at each frequency is dependent on the selected fitting algorithm, the volume level of the incoming sound, and the amount of hearing threshold decrease at each frequency. The goal of the amplification is to improve access to softer levels of auditory information input.

Decision making in the implementation of amplification in young children revolves around the amount and frequency configuration of the hearing loss, hearing levels in the better ear, the structure of the affected ears, and the gross motor skills of the child. There are no age restrictions on how young an infant may be when beginning use of amplification.[5] Ears, however, must be large enough to allow for the introduction of amplified sound. The curvature of the pinna and the size of the external auditory canal rapidly grow over the course of the first few years of life. An ear mold is a soft plastic insert that is formed to fit the child's ear. It serves as an adapter piece to route amplified sound into the ear canal. The mechanical components of the hearing aid are housed in a small device that sits over the top and behind the ear. An acoustic seal must be maintained to prevent the amplified sound from being detected and reamplified by the microphones of the system. As the child grows, new ear molds are created. The use of ear molds and behind-the-ear style amplification allows for continued access to sound without the need for sending the hearing aid in to the manufacturer repeatedly for re-casing as the ear grows.

In cases where the size of the ear may prevent the use of an ear mold for an extended period of time, and the hearing loss is primarily conductive in nature, a bone-conduction hearing aid may be employed to provide sound directly to the patient's cochleae. A bone conduction hearing aid transmits amplified sound through an oscillator. The device is coupled to the patient's head by snapping it onto a headband or by snapping the device onto a transcutaneous metal post that has been surgically implanted in the patient's skull.

Gross motor development may influence the age of introduction to amplification and the use of monaural amplification that alternates between the ears. Small hands like to grasp, and mouths are the most common portal of exploration. It is frequently easier to introduce amplification as a part of the body prior to the development of aimed intent. Amplification may therefore be provided before neck control is adequate to maintain the head in a position that does not distort the external ear and break the acoustic seal with the ear mold. Hearing aids may be used on one ear alone and alternated between the ears depending on the head position at any given time to ensure that each side experiences stimulation.

The goal of intervention is to maximize the amount of information the auditory pathways are capable of transmitting with the purpose of improving expressive and receptive speech and language. A child needs only one hearing ear in order to learn oral language. In cases of asymmetric hearing loss, amplification may be recommended for the ear with better speech recognition capacity. Amplification of a significantly poorer side can adversely affect the better hearing ear. Children are frequently unable to adjust their positioning within an environment and young children are frequently unable to competently determine when or if amplification may provide any benefit. Amplification of a significantly poorer ear can adversely affect performance in noise and interfere with localization ability.[2,6,7]

Amplification devices do not correct the underlying anatomical weaknesses that cause hearing loss. Alterations in structural orientation or physical characteristics within the ear and cochlea result in the loss of frequency tuning specificity and spectral smearing.[1] Loss of inner hair cells may prevent transmission of the signal to the nerve or result in only partial transmission to the nerve. In cases of neural agenesis, the nerve may not be present or sufficient to transmit complex spectral and timing information to the brain.

## Cochlear and Brainstem Implants

Cochlear and brainstem implants provide an option for encoding sound into controlled electrical signals. These devices employ an external sound processor that uses microphones to receive sounds from the environments.

Sounds are then analyzed and encoded based on spectral and timing information. The code is sent through a headpiece to a surgically implanted internal device. The receiver stimulator of the internal component generates controlled electrical impulses that are transmitted along an electrode array to stimulate neural components within the auditory system. This provides a method of enabling highly impaired systems to have access to sound.

Functional outcomes (or word understanding ability) of implantation cannot be guaranteed and the reduced redundancy of spectral information provided by these devices may not be sufficient to provide normal language acquisition without extensive therapy and support services. Implants are reserved for patients with such severe hearing deficits that either technological restrictions prevent adequate stimulation through acoustic amplification or the level of cellular dysfunction severely limits transmission of acoustically presented information in the better ear.

### Limits of Sound Processors (CI and HA)

The complex array of tuning characteristics in the ear allow the cochlea to encode frequency, intensity, and timing characteristics of an incoming signal with a degree of precision we are as of yet unable to replicate. Hearing aids and implant sound processors are restricted by the limitations of their components. Due to standing sound pressure vibrations/fluctuations in the environment, there is an intensity level below which the vibrations on the microphone diaphragm are not amplified. Signal processing within these devices is reliant on pattern recognizers that selectively amplify or encode fluctuating sounds and suppress steady-state, nonfluctuating sounds. Pattern recognizers are unable to determine which fluctuating sounds and/or which person speaking is important in relation to other sounds in the environment. All fluctuating sounds in the environment are therefore amplified.

## HEARING IN DIFFICULT LISTENING SITUATIONS—THE CLASSROOM

Even hearing aids and cochlear implants that are functioning optimally provide reduced benefit in difficult listening situations. Such situations are those where background noise, reverberation, and/or distance from the sound source are involved. The most typical difficult listening environment for children with hearing loss is the classroom. From preschool through higher education individuals with hearing loss encounter classrooms that are far from ideal listening environments.[8]

Classrooms are difficult listening environments for children with hearing loss, because most are large spaces with many hard, acoustically reflective surfaces. Classrooms also have both internal and external sources of noise that compete with the desired signal. Internal noise sources in classrooms include heating and cooling systems, computers and other equipment, as well as staff and students. External noise sources vary with classroom location but may include human and vehicle traffic going past the room and sound from abutting rooms that carries through walls and ductwork. When audiologists describe a listening situation, they use the term "signal-to-noise ratio" (S/N) to indicate how quiet or noisy the situation is. If the desired signal is louder than the noise/interference, then the S/N is positive by the number of decibels the signal intensity exceeds that of the noise. Conversely, if the noise is more intense than the desired signal, the S/N is negative by the number of decibels the noise exceeds that of the signal. Studies have shown that the poorest, most negative S/N are found in classrooms with the youngest students.[9] People with normal hearing can understand speech in a classroom with a S/N of –6 dB, where the noise is 6 dB more intense than the speech. People with hearing loss typically require an S/N of +12 to +20 dB to understand, and people with normal hearing do at an S/N of 0 dB.[10] Typical classrooms in the United States have been found to have S/N ranging from –6 to 0 dB. These S/N jeopardize the ability of children with hearing loss to access the school curriculum completely.[8]

### Noise Management in Classrooms

Although hearing aids and cochlear implants make many sounds audible for children with hearing loss, they do little, if anything, to improve S/N.[11] To ensure good access to speech in classrooms professionals need to evaluate each classroom for noise levels, ease of listening, and teacher's habitual location during instruction. If a classroom is found to be acoustically poor, there are several options for improving its acoustics. One option is making nonelectronic changes, including putting rubber covers on desk and chair legs, adding carpets and drapes, and installing acoustic panels on the classroom walls. If such changes do not result in an adequate acoustic environment, use of specialized equipment may be needed.[12] The most likely equipment for this purpose in schools is some version of an FM system (Figs. 16.1A to C). When using an FM system,


**Figs. 16.1A to C:** An FM system with a "boot" receiver attached to a hearing aid (A) and an independent ear level receiver (B). The microphone and transmitter are worn by the teacher and may be clipped to clothing (C) or worn as a headset. Room and desktop style speakers are also available.

teachers wear a microphone/transmitter that sends the teacher's voice directly to a receiver. The receiver may be in a set of loudspeakers in the classroom, a personal receiver attached to a hearing aid or cochlear implant, or a receiver integrated into a hearing aid or cochlear implant processor. FM systems using speakers can result in S/N of up to +12 dB if installed and used properly.[11] Personal FM systems can do even better, yielding S/N of between +20 and +25 dB.[11] FM systems can transmit their signals over a variety of available channels to avoid having signals bleed through walls to neighboring classrooms.[13] Many school districts have a contract with a manufacturer to provide FM equipment for any students who need the technology to hear their best in the classroom.

An alternative technology for improving S/N in classrooms is called a "loop system". In loop systems wiring is installed, typically either under carpeting or around the perimeter of the room near the ceiling. Speech from the teachers' microphones is converted to an electromagnetic signal transmitted through the room wiring. Students then typically pick up the electromagnetic signal using telecoils incorporated in their hearing aids or cochlear implants. A limitation of loop systems can be variable signal strength depending on location and orientation of the students' telecoils with respect to the room wiring.

Given the level of general use of technology in today's classrooms, children with hearing aids and/or cochlear implants often need hardware for auditory access to

computers and other equipment. A variety of cables and specialized hardware are available for connecting to a wide range of electronic devices. Audiologists can help to identify hardware that may be helpful for students with hearing loss.

## Additional Factors in the Classroom

Access to appropriate education and the full range of classroom activities for children with hearing loss can be affected by many other factors in addition to classroom acoustics. These include teaching style (traditional, learning groups, etc.), room setup, language skills of the children, availability of a skilled interpreter for students who communicate using sign language, and availability of real time captioning and/or note-takers in secondary education, among others.[14] In their coursework general educators typically receive little information on meeting the needs of students with hearing loss. That makes it important for some professional to be responsible for evaluating classroom, teacher, and student characteristics prior to placement of children with hearing loss in any educational setting. This professional will most likely be an audiologist or a teacher of the deaf/hard of hearing.

In most parts of the United States, there are regional education agencies that provide specialty services such as audiology. In those parts of the country all schools have access to audiologists who provide all of the services mentioned above. In other states, although there are no regional educational agencies, many school districts employ audiologists who can provide such services. In still other states, there are few audiologists employed in schools, and there is no regional structure, so it is more difficult to locate an appropriate professional to evaluate the classroom, teacher, and student to ensure good access to the curriculum.

The goal of evaluating child, teacher, and classroom characteristics for each child with a hearing loss being served by schools is an important one. Hearing loss varies widely in type and degree, and there can be no "one size fits all" approach to classroom management for children with hearing loss. In general it is good to provide all of the intervention needed for each child but no more than is needed for the child to achieve success in school. This means that some children with hearing loss will require only an evaluation of characteristics and needs and preferential seating close to the teacher's location while instructing the class. By the third grade most students with hearing loss can identify the best location in a classroom for hearing and understanding. Some students with hearing loss will need some level of technology and/or supplemental services. Still others may be best served in a specialized educational placement more separate from the general education classroom. Many students with hearing loss will benefit from personnel who can support their social development as well.[15] Finding the right level of support for children with hearing loss is best accomplished by a team of professionals that includes teachers, including teachers of the deaf/hard of hearing, audiologists, psychologists, and speech-language pathologists.[16]

## Role of the Speech-Language Pathologist

While availability of audiologists in the schools varies greatly across the country, almost all schools employ speech-language pathologists. These professionals play an important role in schools for children with hearing loss. Speech-language pathologists evaluate children's communication skills, including both language and speech; they are aware of the effect of teaching style and the importance of multimodality teaching for students with hearing loss; they understand the effects of a poor acoustic environment on learning; and they may have some familiarity with FM systems. Speech-language pathologists can provide vital preteaching of vocabulary that is unfamiliar to children with hearing loss. Then they can supplement classroom content by giving children with hearing loss more chance to use new vocabulary and concepts, and they can post-teach any crucial concepts the children may have missed during the units. Children with hearing loss are also served well by having an adult mentor in school, and in many cases, speech-language pathologists are a good choice for this role.[16] They or school nurses are good choices for the person who keeps spare batteries for younger children using hearing aids in school. Additionally, speech-language pathologists, school counselors, and school social workers can all help with the social aspects in schools. Additionally, children with hearing loss may need support in making friends in the school setting and in meeting other children with hearing loss, and speech-language pathologists, school counselors, and school social workers can all help with the social aspects of the educational setting.

## SUMMARY

Serving the hearing and educational needs of children with hearing loss depends on early appropriate amplification or implantation and communication intervention. This needs to be followed by good access to school curriculum. Such access requires individual evaluation of the needs of the children and characteristics of the classrooms and teachers to ensure that hearing loss is not a barrier to full preparation for a successful adult life.

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CHAPTER

# Multidisciplinary Evaluation of the Pediatric Cochlear Implant Candidate

17

***Margaret Winter***

Cochlear implantation has without question positively impacted the lives of many deaf persons, often providing the only avenue through which spoken language can be used and understood. The majority of adult implant users have communicated through spoken language most of their lives, having had either normal hearing at some point or hearing loss that could be reasonably well addressed through use of conventional amplification. For them, cochlear implants provide better access to sound such that they can continue to communicate, now more easily, as they always have. For older children and teenagers who already communicate through listening and speaking, candidacy criteria and benefits of the device are much the same as for adults. For very young children, however, the implant is the tool through which they learn to listen, to discriminate speech sounds, to understand words and sentences, and to develop spoken language. There is a narrow time window of opportunity in which optimal success is likely to be achieved, and multiple other factors impact a young child's ability to be successful as well. It is unfortunately the case that not all deaf children are candidates for cochlear implantation, and not all deaf children are good candidates where the goal is the development of spoken language. It is essential to keep in mind that the main aim of all those who work with deaf and hard of hearing children should be development of effective communication skills through which a child will succeed socially and educationally. Therefore, careful consideration of the most effective means of communication is an essential element of a candidacy evaluation of a prelingually deaf child.

## THE COCHLEAR IMPLANT TEAM

Pediatric candidacy is best evaluated by a team of professionals who can consider multiple aspects of a child's development and potential to benefit from the device. At a minimum, most teams consist of the surgeon, audiologist, and speech-language pathologist. Additional professionals who contribute greatly to candidacy decisions include a psychologist, social worker, and educators. The psychologist and social worker may be part of an in-house team, or they may be called upon to consult where concerns about a child's cognition or behavior exist or where families may need assistance with practical issues such as applications for social supports, transportation, food, and lodging. An educator may also be part of the in-house team, and the child's teachers and other educational and therapy personnel should always be included in the candidacy evaluation, since even with multiple office appointments the in-house team may not have a clear picture of a child's function in school, parent compliance, consistency of device use, and other factors that teachers will have observed on a regular basis.

In some programs or in some circumstances (e.g. abnormal cochlear anatomy), the surgeon chooses the device. In others, the family makes the selection. Where the child is a determined to be a candidate for a cochlear implant in either ear, the team together with parents will determine whether one or both ears should be implanted. The surgeon or parents may have a preference regarding simultaneous or sequential bilateral implantation.

The surgeon may be the first professional to see a potential candidate, or the child may be referred to the surgeon by the audiologist who has already demonstrated that the child has a qualifying hearing loss and cannot derive sufficient benefit from amplification to develop or maintain development of auditory skills. The surgeon will provide the otologic evaluation and order and interpret imaging. The surgeon may determine that the child is not a candidate medically, in which case the evaluation need not proceed except for parent counseling. If the child is a candidate medically, the surgeon is urged not to make an immediate determination of candidacy without input from all members of the team, since so many factors figure into success with cochlear implantation. The surgeon should provide information regarding risks of the procedure, assume ultimate responsibility for confirming that appropriate vaccinations have been received, and provide reassurance to families fearful of surgery. The surgeon can also be very helpful in explaining or clarifying realistic expectations and emphasizing the importance of parents' role in the habilitation process postimplant. The surgeon should communicate with the programming audiologist immediately after surgery if there were irregularities in the procedure, such as a partial insertion of the electrode array, that may affect the way the audiologist is able to program the device.

The audiologist is responsible for determining the child's unaided hearing loss and benefit from hearing aids. Ideally, children tested at birth under newborn hearing screening programs will have received amplification and early intervention within the first few months of life and their benefit and progress with amplification will be continually tracked before they are candidates for implantation. Unfortunately, not all children presenting as potential cochlear implant candidates have had the benefit of early identification or timely referral to the implant center. Audiologic assessments of pediatric cochlear implant candidates will depend on the child's age, development, and listening experience.

A test battery approach is essential to the most complete understanding of a young infant's hearing abilities. Auditory brainstem response (ABR) and otoacoustic emissions (OAE) testing are the most useful tools for a baby who cannot yet participate in behavioral threshold testing procedures. As the primary measures, they enable the audiologist to identify the type and degree of hearing loss and to make a close estimate of hearing thresholds across the speech frequency spectrum, sufficient to select and fit appropriate amplification. Because these tests are measures of physiologic functions of the auditory system but are not hearing tests per se, it is wise for audiologists also to observe the infant's responses using behavioral observation audiometry (BOA). While not a threshold procedure, BOA allows the child's responses to calibrated sounds to be observed, and responses should make sense with ABR and OAE results. If, for instance, a child startles to loud sound or clearly responds repeatedly to voice or other calibrated stimuli despite an absent ABR response, results of the ABR should be reevaluated.

ABR, OAE, and acoustic reflex measurements in combination are the most sensitive indicators of auditory neuropathy spectrum disorder (ANSD). In ANSD[1] children have normal outer hair cell function, so OAEs are typically present but the children have abnormal hearing nerve function resulting in absent ABRs and absent acoustic reflexes. The exact nature of the disorder is not yet clearly understood. Research indicates that abnormal function of the inner hair cells or dyssynchrony in the firing of the auditory nerve may be responsible. Risk factors include a history of high bilirubin treated by blood transfusion and certain genetic conditions.[2,3] ABR thresholds in ANSD are not necessarily reflective of a child's ability to respond to sound, and often behavioral testing reveals audiometric findings significantly different from what the ABR suggested. Present OAEs usually are consistent with, at most, mild hearing loss, but in ANSD the actual hearing handicap can range from mild to profound even when OAEs are present and robust.

Visual reinforcement audiometry (VRA) is used for behavioral audiologic assessment of older infants and toddlers who are able to sit unsupported and turn toward the source of a stimulus. VRA yields pure tone thresholds to unmasked air and bone conduction stimuli and speech awareness thresholds to voice. As such, it provides more complete information than ABR, but ABR can and should be used to confirm behavioral thresholds where there is any question of reliability.

Between ages 2 and 3 years, typically developing children can learn to perform conditioned play audiometry (CPA). CPA requires the child to wait for a stimulus, then perform a task such as dropping a block into a container or putting a peg into a pegboard as soon as he or she hears the sound. He or she can be taught to ignore masking noise so that an asymmetrical loss can be accurately measured through masked air and bone conduction tests. At this stage, a child who uses spoken language can repeat words

or point to pictures on demand so that a speech reception threshold and a speech discrimination score can be obtained.

Children with developmental delays should be assessed using procedures appropriate for their developmental age rather than their chronological age. The ability of a child to perform some type of conditioned response assists the audiologist in fine-tuning amplification and will be extremely helpful in programming the cochlear implant speech processor if the child receives an implant. If a child is unable to perform any type of conditioned response, challenges in programming will be greater.

A hearing aid trial of 3–6 months, combined with appropriate therapeutic intervention, is generally required unless the child is at risk for cochlear ossification, in which case the hearing aid requirement is waived. The audiologist will assess the appropriateness of the hearing aid fitting through both real-ear and behavioral threshold measures and will assess benefit of amplification through speech perception measures in the auditory-only condition. If hearing aids are not adequately addressing the hearing loss, a trial of more effective amplification may be necessary. For children with ANSD, speech perception measures are especially important, since aided detection thresholds may be deceptive in reflecting the true benefit of amplification.

For young infants who have not yet developed speech, speech perception is usually assessed using parent report scales. Numerous standardized speech perception measures can be used with older children across the age-range who are developmentally able to point to pictures or repeat words or sentences. Tests range in complexity from assessments of pattern perception to comprehension and recall of short passages delivered in the presence of background noise or competing speech.

The speech pathologist assesses the child's overall communication ability, including receptive and expressive language and fundamental speech skills. There are two main goals of the evaluation: to determine whether hearing loss is a factor in any speech or language delay, therefore suggesting stronger likelihood that a cochlear implant would be a benefit, and to establish baseline performance that will guide postimplant therapy and serve as a marker for future progress. As with speech perception testing, the assessments may consist of parent-report instruments or standardized tests requiring the child to point to pictures, respond to instructions, or demonstrate spontaneous language.

With very young children, the speech language pathologist's direct interaction with the child establishes the child's communicative intent, which may be linguistic (words or signs) or prelinguistic (gestures, vocalizations, eye contact). It is important to assess not only the child's auditory-oral skills, if they exist, but also his or her skills in whatever communication mode he or she may be using, such as sign. The evaluation would not be reflective of a deaf child's communication ability if he or she is fluent in sign but is assessed only in terms of his or her oral language facility. Similarly, the speech pathologist should take into account language models in the home; children whose home language is different from his or her instructional language may be fully bilingual, partially bilingual, or may be delayed in both languages such that neither provides a completely effective communication strategy. For comprehensive coverage of the speech language pathologist's role in the evaluation process, see Ambrose et al. (2009).[4]

There is necessarily some overlap in speech perception testing and speech language evaluation for older children, because some aspects of speech perception testing depend upon the child's vocabulary and oral language development. But results of the combination of the two types of assessments can contribute to a greater understanding of a child's skill and potential to benefit from implantation. Speech perception testing is performed in the auditory-only condition, whereas speech language evaluation involves face-to-face communication. A child may have good ability to repeat single words and even sentences but test poorly on overall language measures such as oral expression, grammar, and semantics. Or the child may score well on speech language measures because he or she has made exceptionally good use of even minimal residual hearing but score poorly on speech perception measures where visual cues are not available. It is essential that the testing protocols are truly evaluating a child's abilities, not just pointing to what a child cannot do. Even carefully selected, age-appropriate tests may not achieve this goal if individual differences are not considered. For testing of a child with a developmental delay, measures must be based on their developmental age rather than their chronological age. If a child is unable or unwilling to perform a required task on the most basic of tests, the result should be documented as such, but the clinician can and should probe further to determine what the child actually can do, perhaps with suggestions from parents. Informal assessment can be extremely valuable in determining how stimulable a child may be for development of speech, language, listening, and learning.

An in-house educator or educational counselor can help parents to better understand the individual family service plan (IFSP) and individual education program (IEP) processes, whereby children with hearing loss can access educational services appropriate to their specific needs. A majority of children who receive cochlear implants will require special education, itinerant deaf and hard of hearing assistance, accommodations in the general education classroom, or a combination of these. Families unfamiliar with the IFSP and IEP processes may not yet know how services are established or how they may request them for their children, or that they themselves are indeed an integral part of the IFSP or IEP team.

Inclusion of the child's teachers and speech language or auditory therapists in the candidacy evaluation process helps the in-house team to acquire information about the child's current learning environment and services as well as the options available should the child receive a cochlear implant. A self-contained class for 2-year-olds where American Sign Language is the exclusive mode of communication may be appropriate for the child prior to implantation but will be inadequate after implantation, even if the family goal is to maintain sign skills as well as develop oral language skills. Where a child is in transition between early start services and center-based services, it is important for the implant team to communicate with educational personnel about the intent to provide a cochlear implant so they can make suitable choices for placement.

The psychologist may play a broad role on the implant team, performing cognitive and psychosocial assessments with the pediatric candidate, identifying behaviors of concern, and counseling families with regard to their questions, concerns, and expectations. An interview with parents helps to document parental understanding of their child's hearing loss and the cochlear implant process. Parents and grandparents and in some cases the candidate may be at odds with each other over a variety of issues, including acceptance of the hearing loss, custody issues, fears of surgery, and philosophical differences regarding implantation of young children who cannot yet consent to the procedure. The psychologist can help clarify these issues and present strategies for cooperative decision making, thereby laying a firmer groundwork for success whether or not the child receives cochlear implants.

Direct contact with the child helps the psychologist gain an understanding of the child's general developmental level, communication skills or communicative intent, and interaction with parents. Standardized measures of intelligence can document performance on specific tasks and compare skill levels with those of typically hearing children of the same age, although care should be taken to consider the demands made by the particular tasks on the deaf child's language and auditory skills.

The combination of all assessments enables the cochlear implant team to determine the likely degree to which hearing loss has impacted the child's ability to develop listening, language, and speech production skills and to make informed judgments as to the potential benefits of implantation. A child who has reasonably good access to the speech spectrum with hearing aids but who has developed minimal oral language skills may not be receiving adequate support at home, may be in an inappropriate educational placement, may lack access to effective auditory/oral therapy services, or may for reasons unknown be unable to decode the information from amplification. Any or all of these factors may impact success with a cochlear implant. Conversely a child who has minimal access to auditory information and who has nonetheless developed spoken language skills may reasonably be expected to make good use of information from an implant. Results of the team evaluations inform candidacy decisions and may influence the kinds of supports that need to be put in place to maximize benefit from implantation.

Finally, it is important to note that although they do not perform formal assessments, parents are an integral part of the cochlear implant team. Parental observation of their children's developing communication skills, understanding of successful intervention strategies they can practice at home, and their awareness of likely outcomes with implantation are critical to their child's success. Parents invariably want the best for their child but may not always have the knowledge necessary to provide good language and literacy models at home and advocate for appropriate services at school. The potential of parents as effective teachers can be an important consideration in determining a child's candidacy. The professional members of the implant team can be instrumental in helping parents recognize their value as the most important controllable factor in their children's success.

## CANDIDACY CRITERIA

It is safe to say that the goal of the majority of parents seeking cochlear implantation for their children is the development of functional oral language skills. In some

cases, parents understand that their particular child may be unlikely to learn to listen and speak but wish to proceed with cochlear implantation for whatever other benefits it may provide. Often, these families still remain hopeful that despite poor odds their child may be the exception and will learn to speak. Candidacy decisions depend in part on the goals and expectations of the parents and the criteria set by a specific program. In some cases, a child may not be considered as a candidate in one program but will be a candidate in another. Careful counseling is essential so that parents will understand whether or not their child is a candidate in that particular program, or is not medically a candidate and it could be unwise or dangerous to seek implantation at another center. For families whose children are not candidates, further counseling is imperative to help them pursue other appropriate services or devices that will assist them to develop their most functional communication skills.

Although there are specific, Food and Drug Administration (FDA)-approved criteria for cochlear implantation in young children, over the 25 or so years multichannel cochlear implants have been approved for children the now-conventional applications have outpaced these official criteria. For example, the FDA lists the minimum age for implantation as 12 months, but many clinics in the United States and abroad routinely implant children at significantly younger ages. There is no specific FDA endorsement of bilateral cochlear implantation, but it is now the standard of care for appropriate candidates. Officially, the qualifying degree of hearing loss recognized by the FDA is bilaterally severe to profound, but especially now that bilateral implantation is so common, it has become common as well to provide a cochlear implant for an ear with severe hearing loss where the opposite ear has sufficient residual hearing to continue to benefit from a hearing aid. Technological advances in electrode design and surgical technique are making it possible for successful preservation of low frequency hearing, and new sound processor circuitry combines both acoustic amplification and electrical stimulation to accommodate both aidable residual hearing and absence thereof. It is, then, most common for cochlear implant programs to consider basic criteria through the lens of research findings as well as their own clinical experience.

## Age Considerations

It is well documented that where the goal of implantation is the development of spoken language skills, the best candidates are very young children with minimal length of auditory deprivation,[5] or children who have been successful in developing at least some oral language skills through the use of amplification.[6]

Early identified, early implanted children have been shown to develop speech and language similar to that of children with normal hearing.[7] Though by no means a guarantee of success, these two factors are important predictors of optimal outcomes. Numerous studies have shown that auditory plasticity in children is at its peak only through the infant and toddler years, after which the brain's ability to make the most effective use of new auditory information is significantly reduced.[8] It is generally considered that in good candidates, a reasonable goal for auditory/oral skill development is parallel progress with typically hearing children; that is, children with cochlear implants may be expected to achieve a year's growth in a year's time. In early identified, early implanted children, the age-language gap is minimal, auditory plasticity is at its peak, and age-appropriate oral language milestones may be attained. By contrast, a child who has access to sound for the first time through a cochlear implant at age 5 is 5 years behind in auditory/oral development, and may remain so even with excellent auditory benefit from the implant. An age-language gap of 5 years by age 5 is significant, as the child enters school; the same age-language gap of 5 years by age 11 results in that child's inability to access age-appropriate educational information if he or she has not also developed language through other modalities.

This is not to say that school-age children cannot be good cochlear implant candidates. Children who have had sufficient residual hearing to derive significant, if inadequate, benefit from hearing aids and who have developed spoken language as a functional mode of communication can do well with cochlear implants at any age. Children who demonstrate progression of hearing loss are best implanted before their language development begins to slow and their speech production is affected. Children with sudden loss of hearing are usually excellent candidates.[9] Where a child is old enough to understand the procedures, he or she must be given a voice in the decision making, since children who are not in agreement to proceed with implantation can and will refuse to wear the device. It can be extremely helpful to provide fearful children with contact information for others their age who have had successful experience with their implants. In many cases, children who are initially

reluctant to go forward become enthusiastic about the process once they have been reassured by peers in their same situation.

Children of school age who have minimal auditory experience and have not yet developed spoken language skills may receive more limited benefit from cochlear implantation. There are certainly exceptions, and a benefit of the team approach to assessing candidacy is that each child is considered from multiple perspectives. Important questions to be addressed include whether the child has fully developed communication through another modality such as sign language, through which he or she has been able to achieve educationally. In many hearing families, parents have not learned to sign fluently themselves, thus limiting the ability of their child to engage fully in conversational exchanges at home. These children are not only behind in their oral language experience but there is a significant age-language gap in sign skills as well, which impacts reading, writing, and other academic achievement. Fully developed sign skills may provide a good bridge to learning oral language skills; severely delayed sign skills may not, and the therapy efforts necessary to maximize benefit from a cochlear implant may take away from time more productively spent speeding sign language development. In some cases, parents who are disappointed when their children are not able to learn to listen and speak blame the child because parents lack understanding of complexities of oral language development under these circumstances. This does not mean that school-age children with little auditory experience should never receive cochlear implants. It means that an implant should not be provided without extensive family counseling that stresses a full understanding of the importance of language development and of the reduced likelihood that oral language will become the child's primary communication mode. The exclusive focus for such children should not be auditory/oral therapy. It may well be possible for a late-implanted child with no previous auditory experience to develop functional spoken language skills; it is more likely that with appropriate supports implanted children from this population will always rely mainly on visual language but may also benefit from the auditory information they receive from the implant in terms of sound awareness, speech-reading, and even closed-set speech perception. Without appropriate supports and without full parental understanding of appropriate expectations, children from this population may eventually become nonusers and may be no better off in terms of communication skills than they were before implantation.

Consideration of implantation of children with developmental delays should follow the same guidelines as with older, nonverbal children. While there may indeed be benefits to children with cognitive delays or behavioral disorders, careful assessment of the child's current communication strategies and extensive counseling regarding expectations are essential. Children with developmental delays may derive speech perception benefit from cochlear implantation or may benefit in ways not specifically linguistic, such as improved attention or a general sense of connection to the environment. Benefit from cochlear implantation depends on the type and severity of the developmental delay. The stronger possibility that oral language as a primary or even functional communication mode may not be a realistic goal should be part of the discussion with parents.

While it is not clear why cochlear implants are effective for children with what appears to be a dyssynchrony disorder, a considerable body of literature documents the benefits of cochlear implantation for at least some children with ANSD.[10] Success may depend in part upon coexisting conditions that are more common in children with ANSD than in the general population as well as on the type of auditory neuropathy. When ANSD is a result of cochlear nerve deficiency, outcomes may be poor and preoperative imaging may be critical to predicting reasonable benefit. As is the case for children with the much more common cochlear deafness, children with ANSD who are found to be cochlear implant candidates are best implanted as soon as it can be documented that progress with hearing aids is insufficient or has plateaued or declined, and the same educational and therapeutic supports must be in place for optimal progress to occur.

## Degree of Hearing Loss and Benefit from Amplification

In common practice one of the biggest changes in candidacy criteria is in the degree of qualifying hearing loss. Whereas in 1990, only children with bilateral profound loss and little to no benefit from hearing aids could receive a cochlear implant, it is common now to see implantation of children with much more residual hearing.[11] Qualifying hearing loss may include severe to profound loss in at least the high frequencies (with perhaps even moderate loss in the lows), even when hearing loss in the opposite ear is better and receives good benefit from amplification. For very young children in whom oral language progress cannot yet be measured, more reliance may be placed on hearing threshold levels with appropriately fit

amplification. If aided thresholds in the ear under consideration are outside the long-term average speech spectrum, an implant may be considered with the reasonable expectation that detection levels with the implant will be significantly improved, and, with auditory therapy from an experienced provider, speech and oral language skills will improve significantly as well. For older children with measurable speech perception, clinics may not have a fixed score criterion; rather, the speech perception scores may be one aspect of the determination of how well the child is able to use his or her residual hearing. In school and in social situations, some potential candidates may be seen to do surprisingly well in spite of the severity of their hearing loss; in reality, these children may be working extraordinarily hard to do as well as they do and would be greatly helped by better access to speech information.

## Other Considerations

Care should be taken not to adhere so closely to a set of candidacy criteria that extenuating circumstances are not considered. A child who has poor speech and oral language development and little to no sign skill might, at age 8, not be considered a cochlear implant candidate in some programs. If a diagnosis of Usher syndrome is made; however, the picture changes in that as the child loses his vision he will be unable to use visual forms of language. Provision of cochlear implants and intensive auditory therapy may yet be this child's best avenue for communication. A 17-year-old prelingually deaf young person with minimal benefit from hearing aids, who will not have the option under her current medical coverage to pursue cochlear implantation after age 18, might be considered for a cochlear implant for reasons other than development of spoken language as a primary communication mode. If she is about to complete school and has developed language through another modality, she will not be adversely affected educationally as she learns to make the most of the information the implant provides, even if it is limited. A center's established candidacy criteria should serve as a flexible framework through which decisions are made that lead to best enhancement of communication skills.

## Bilateral Cochlear Implantation

Research and clinical experience support benefits of bilateral implantation, which include improvements in a child's ability to localize and to understand speech in noisy environments.[12,13] As noted above, children who receive simultaneous bilateral cochlear implants are more likely to develop approximately equal skills with each implant than children who receives implants years apart. There are numerous good reasons for beginning with one ear and implanting the second ear at a later date, but the longer the interval between surgeries the less likely skills will be equal between the two ears. While it may seem logical to both implant users and their parents that success with the first implant will automatically lead to success with a second, this often proves not to be the case. Factors that influence success with a second implant include, in addition to length of time between surgeries, the history of hearing aid use and benefit on the second ear, and the speech/language benefit with the first device.

In cases of unilateral implantation, most programs strongly recommend their recipients continue to use amplification on the opposite ear for whatever benefit it may provide. Where there is little residual hearing, children eventually may chose to stop wearing the hearing aid. Thousands of children received only one implant in the 1990s, and many of them are now expressing interest in a second device. Extensive counseling is necessary to help them understand possible and likely outcomes, which can include improved detection without discrimination ability, closed set discrimination only, or open set discrimination approximating the ability of the opposite ear. Consistent use of, and benefit from, amplification contributes strongly to the development of auditory skills after receipt of an implant in the second ear.

## Auditory Brainstem Implants

A relatively small number of deaf children are born without auditory nerves or cochleae. In some cases, an auditory nerve appears to be present, if not normal, on imaging but cochlear implants provide minimal to no benefit. Until recently, there were no options for providing functional auditory stimulation to these children.

The auditory brainstem implant (ABI) was developed for use by teens and adults with neurofibromatosis type 2 (NF2), who have had bilateral acoustic neuromas removed. The surgery usually renders them unable to use cochlear implants. The ABI consists of an electrode array on a small paddle that is surgically placed over the cochlear nucleus in the brainstem.[14] At this time, the ABI is approved by the USFDA only for NF2 patients, but prelingually deaf children have been implanted at centers outside the United States.[15,16] Studies show that some of these children develop auditory and speech perception skills that fall

in the lower range of performance scores achieved by children with cochlear implants.[17,18] Test results using the Categories of Auditory Performance inventory with children implanted by Vittorio Colletti in Verona, Italy, indicate that the best outcomes are seen in children who have normal cognition, compared with children with multiple disabilities that include cognitive delay.[19]

The FDA has recently granted several cochlear implant programs in the United States permission to conduct clinical trials of the safety and efficacy of auditory brainstem implantation of prelingually deaf children. The general criteria for ABIs in this population include severe hypoplasia of the cochleae, agenesis of the auditory nerves, and severe cochlear nerve deficiency.

## AFTER IMPLANTATION

Although it is the audiologist who programs the cochlear implant processor after implant surgery, the job of the team as a whole is not over. Programming cannot be effectively performed in a vacuum; the audiologist depends on information from the child's family, therapists and teachers to know if programming is effective or if there are indications that changes should be made. The appropriateness of the child's educational program and auditory therapy are crucial to maximizing success. Postimplant assessments beginning with the same measures performed preoperatively, graduating to more complex measures as the child progresses, help to guide interventions in therapy and education. Where the child is making month for month progress, the outlook is excellent and parents and providers of service can be assured that strategies being employed are effective. Where the age-language gap is widening, results of assessments enable the team to know when additional supports, strategic changes, or new communication modes should be explored. The child's success in communication and academic achievement continues to be a team effort.

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CHAPTER

18

# Otitis Media

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## INTRODUCTION

Otitis media (OM) is one of the most common infectious diseases in children, particularly in younger children. Approximately 30–35% of all visits for acute illness in the primary care setting in the first 5 years of life are for middle ear disease. Up to 40% of total office visits at 4–5 years of age will result in the diagnosis of some middle ear problem. This includes approximately 10% of children who present at well-child visits and are without any subjective complaint.[1] Studies have shown that nearly half of all antibiotics prescribed in children < 10 years old were for OM.[2] The financial burden for medical and surgical intervention for OM is estimated at $5 billion yearly in the United States alone.[3] But perhaps the impact on the day-to-day lives of families is far greater than any monetary figure. It can be associated with speech, language, and balance difficulties, which can contribute to further learning problems. The parental burden of dealing with a fussy, irritable child who is sleeping poorly can be very frustrating. Also, parents may be forced to miss multiple days of work as day-care settings frequently will forbid children with high fevers to attend; this is in addition to the time missed from work for physician visits.

For the sake of clarity, the following terms and their definitions will be used in this chapter. "Otitis media" will refer to nonspecific inflammation within the middle ear space. "Acute otitis media (AOM)" will refer to acute infection of fluid within the middle ear space, with associated otalgia and an erythematous or bulging tympanic membrane (TM). "Otitis media with effusion (OME)" will be defined as fluid collection in the middle ear space in the absence of signs of acute infection mentioned above. Finally, "middle ear effusion (MEE)" will refer generally to fluid in the middle ear space, whether this fluid is associated with acute infection or not.

## EPIDEMIOLOGY

### Acute Otitis Media

The vast majority of children will have at least one episode of AOM in childhood. Approximately 62% of infants will have AOM by 12 months of age, with this number rising to 84% at 3 years of age, and 95% by age 7. After age 7, children are much less likely to develop AOM.[1] Many children will have recurrent episodes of AOM as well. Up to 20% of infants will have three episodes by their first birthday, and by age 7, 75% of children will have had at least three episodes.

### Otitis Media with Effusion

Determining the incidence of OME is much more difficult because many children will present without any complaints. Furthermore, many episodes of AOM will "become" OME as ear pain and TM erythema and bulging resolve but MEE remains. Identifying the onset and interval to resolution of OME is challenging, as it requires very short observation intervals. This is particularly true given that approximately 65% of OME episodes will resolve in 1 month.[4] Casselbrant et al. found a 53–61% incidence of OME in 2- to 6-year-old day-care children followed monthly with pneumatic otoscopy and tympanometry.

This number dropped to 22% in 5- to 12-year-old school children.[4,5] Lous and Fiellau-Nikolajsen reported a similar 26% incidence in 7-year-olds that they followed for 1 year.[6]

Multiple studies in various countries have looked at the point prevalence of MEE, which includes both AOM and OME, with a great variety of ranges from 1% to 40%. Given the variability in race, sample sizes, age ranges, number of screenings, and screening tools, it is very difficult to generalize these incidence data in a meaningful way. What is clear, though, is that almost all children develop MEE at some point during the first 3 years of life.[7,8]

## Risk Factors for OM

### *Age*

The highest incidence of AOM occurs between 6 and 11 months of age.[9] The incidence decreases yearly after that with the exception of a small bump at 5–6 years of age, correlating with school entry. It is much less common in children 7 years or older. In school-aged children, obesity has also been shown to be a risk factor for AOM.[10] The risk of persistent effusion after AOM also is greatest in the infant and toddler and decrease with age.[11]

### *Prematurity/Low Birth Weight*

There is controversy as to whether OM is more prevalent in premature infants, with conflicting evidence. Gravel et al.[12] and Alho et al.[13] looked at AOM and MEE, respectively, and found no difference between full-term infants and premature or low birth weight infants. Engel,[14] however, did show a higher prevalence of OME in this high-risk population compared with full-term infants. More recently, Bentdal et al.[15] also found a higher relative risk of AOM in premature infants <33 weeks' gestational age (relative risk of 1.37) than full-term infants. They did not find a corresponding tendency in children with low birth weight.

### *Race*

Native Americans and Alaskan and Canadian Inuits have been shown to have a high incidence of OM, particularly OM with chronic otorrhea and/or perforation.[16–18] This is felt to be due to abnormalities of both the anatomic position of the bony Eustachian tube (ET) as well as poor ET function. Hispanic children may also have an increased incidence of OM compared with Caucasian-American children.[19] Early studies indicated that African-Americans had a lower incidence of OM than Caucasian-Americans, but more recent studies have showed an equal incidence up to age 2.[20,21]

### *Gender*

Multiple studies have shown no gender difference between in OME.[22,23] Gender and AOM, however, is less well defined. Some studies report a higher incidence in males versus females,[11] while others show no gender difference.[19]

### *Genetics/Family History*

Family history is clearly a risk factor for recurrent OM. Twin studies of OM show a heritability of 45–64% in males and 74–79% in females.[24–26] Down syndrome, craniofacial abnormalities, and cleft palate are also risk factors for OM. In fact, almost all children with unrepaired cleft palate under the age of 2 years will have OM.

### *Season*

Both AOM and OME are more common in the fall and winter months, paralleling the increase in upper respiratory infections (URIs). It has been shown both in the laboratory and clinically that viral URI predisposes to ET dysfunction and subsequently to OM.[27,28]

### *Day Care*

Day care is perhaps one of the greatest risk factors for AOM and OME, with an odds ratio of at least two reported in more than one study.[29,30] This is most likely related to the increased risk of URI, particularly in the winter months, associated with close contact with a large number of children. In fact, OM incidence is related not only to day-care attendance, but also to the number of children in the day care, with smaller settings experiencing less OM. Having older siblings is also a risk factor for OM, most likely related to increased URI exposure, as with the day-care setting. In fact, Paradise et al. combined number of older siblings and day-care attendance into a "child exposure index" and found correlation with MEE duration.[21]

### *Smoking/Air Pollution*

Multiple studies have shown an association between passive smoke exposure and increased risk of both recurrent AOM and persistent OME. In fact, one study measuring serum cotinine (a metabolite of nicotine) showed a 38% increase in MEE and prolonged OM in those children with

elevated levels.[31] Residential air pollution has also been shown to be a modest risk factor for OM with a relative risk of 1.1–1.3.[32]

### *Breastfeeding*

Breastfeeding is known to have a protective effect against OM versus bottle feeding. The mechanism is not completely clear, but may be related to the immunologic benefit of breast milk, particularly the immunoglobulin secretory IgA. The ideal duration of breastfeeding is less clear. There is evidence that breastfeeding for 6 months leads to a twofold decrease in the rates of AOM and OME.[33] There is also evidence to suggest that that this provides prolonged protection from OM up to 3 years of age. It is unclear whether breastfeeding well beyond 6 months of age offers additional protection.

### *Pacifier Use*

Pacifier use is also a risk factor for OM, with a 10–15% increase in the number of OM episodes in those children who used pacifiers, depending on age.[34] Counseling parents to limit pacifier use resulted in a 29% decrease in AOM from 7–18 months of age.[35] There is evidence to suggest, however, that pacifier use in children <6 months of age does not increase the risk of OM.[36]

### *Atopy/Allergy*

It has long been thought that there may be a connection between OM and atopy/allergy. Current literature does support a link with OME. Allergic patients have an increased risk of both unilateral and bilateral OME as well as a higher degree of hearing impairment with OME than nonallergic patients.[37–39] Interestingly, however, nasal mucosal swelling (as measured by acoustic rhinometry), nasal eosinophilia, asthma, and eczema have not been correlated with OME.[40]

## ANATOMY AND PATHOPHYSIOLOGY

The anatomic structures involved in regulating the middle ear system include the mastoid cavity, the middle ear cavity, the ET, and the nose/nasopharynx, and palate. The ET is perhaps the most important of these structures, particularly as it relates to the development of AOM and OME. The ET serves three important functions physiologically: (1) pressure regulation/ventilation and equilibration to atmospheric pressure, (2) protection of the middle ear from pathogens ascending from the nasopharynx via a gas cushion, and (3) clearance of secretions from the middle ear. The origin of middle ear disease is poor ET function, and inability to regulate pressure. In infants, the ET is shorter and more horizontal than in an adult, and this is one anatomic factor that leads to poor pressure regulation.

ET dysfunction may occur spontaneously, particularly in infants, but is more commonly associated with antecedent events that cause either anatomic or, more commonly, functional obstruction. Anatomic causes include enlarged adenoids, nasal polyposis, foreign body, or tumor. Functional obstruction is associated with inflammation within the nasal cavity and nasopharynx, most commonly from a viral URI in children. Other causes include allergic rhinitis and gastroesophageal reflux disease (GERD). This inflammation leads to edema around the ET orifice, which is located in the nasopharynx, and subsequent inability of the ET to open in its usual passive fashion to regulate pressure. As negative pressure builds, secretions and pathogens can be aspirated from the nasopharynx into the middle ear space, creating MEE. This fluid may persist and not become infected, resulting in OME. If, however, the fluid becomes infected, either with viruses or more commonly bacteria, an AOM develops.

Certain populations have a much higher incidence of ET dysfunction and, subsequently, OM. Anatomically, those children with craniofacial abnormalities, Down syndrome, and cleft palate may have persistent ET dysfunction and difficulties with OM throughout their lives. Immunocompromised children are also at increased risk—this includes those with primary ciliary dyskinesia, immunoglobulin deficiencies, T- or B-cell defects, chemotherapy, or HIV.

## Microbiology

### *Bacteriology*

The most common bacteria isolated in AOM are *Haemophilus influenza* (35–50%) and *Streptococcus pneumoniae* (25–40%). It was hoped that the introduction of the conjugate pneumococcal vaccine PCV7 in 2000 would dramatically decrease the number of episodes of AOM, but the decrease has been reported at a modest 7.8%, with an increase in the number of nonvaccine serotypes and *Haemophilus* infections.[41–43] *Moraxella catarrhalis* is the third most common bacteria (3–20%) isolated, followed by Group A *Streptococcus* and *Staphylococcus aureus* (1–10%).

Also, although neonates and infants usually have the same bacteriologic pattern as older children, gram negatives such as *E. coli*, *Klebsiella*, and *Pseudomonas* are seen with a higher frequency. Anaerobic bacteria such as *Peptostreptococcus, Fusobacterium, and Bacteroides* are more commonly seen in chronic suppurative OM (persistent drainage via a tympanostomy tube or perforation) and in cases of cholesteatoma. A myriad of other bacteria have been recovered from the middle ear in rare cases, including *Mycoplasma*, *Mycobacterium tuberculosis*, Group B *Streptococcus* species, and *Neisseria* and *Chlamydia* species.

Cultures in OME more commonly do not grow bacteria, and this "sterile" culture occurs about a third of the time. Another third of the cultures will grow the three most common AOM bacteria (*S. pneumonia*, *H. influenza*, and *M. catarrhalis*), with *Haemophilus* being the most common. The final third is composed of nonpathogenic bacteria such as the normal skin bacterium *Staphylococcus epidermidis*, as well as viruses.[44]

More recently, the role of bacterial biofilms in the pathogenesis of OM has been debated. A biofilm occurs when a community of bacteria interact together to surround themselves with a polysaccharide matrix, which protects them from a host's immune response. Because of its low metabolic rate, it is also resistant to antimicrobial therapy. Initially, it was thought that biofilms only existed on hard surfaces such as teeth and tympanostomy tubes. But research has shown that biofilms can also be found in the middle ear.[45] These biofilms were identified in 48% of patients undergoing tympanostomy tube insertion even in the face of negative middle ear fluid cultures. Biofilms have also been found in the nasopharynx in children with OM. This suggests that these biofilms may act as a bacterial reservoir for repeated OM via the ET, and may help to explain why adenoidectomy benefits some patients with OM. At this point, the existence of biofilms cannot be disputed. Their exact role in the pathogenesis of OM, particularly as it relates to treatment strategies, has yet to be clearly defined.

### *Virology*

Before the advent of polymerase chain reaction (PCR), the incidence of viral AOM was unknown and largely underestimated, because isolating viruses in culture was technically challenging. Currently, it is thought that viruses alone account for about 20% of episodes of AOM and are present in about 20–30% of fluid in OME. Rhinovirus and respiratory syncytial virus (RSV) are the most common, but influenza, parainfluenza, and adenovirus are also seen.[46] The role of viruses in OM extends beyond their role in the middle ear directly. Viral URIs are often the events that are precursors to episodes of OM. In one study, 70% of episodes of OM were associated with a viral URI, and viruses were isolated from MEE in 77% of these cases.[47] This suggests that mixed bacterial and viral OM is common and perhaps viruses "set up" the middle ear space for bacterial infection, similar to the pathogenesis of sinusitis.

## DIAGNOSIS

### History

The most recent guidelines released from the American Academy of Pediatrics/American Academy of Family Physicians outline the diagnosis of otitis media based on moderate to severe bulging of the TM or new onset of otorrhea not due to acute otitis externa. Alternatively, diagnosis is based on mild bulging of the TM and recent (< 48 hr) onset of ear pain or intense erythema of the TM.[48] Common symptoms of AOM include ear pulling, poor sleep, fever, and irritability, although some children may have no symptoms. OME, as previously mentioned, is the presence of fluid in the middle ear without acute inflammation. This can be more challenging to diagnose and is often not accompanied by any symptoms, particularly in young children. If symptoms are present, the most common ones include hearing loss, fullness, otalgia (especially at night), and imbalance.

### Physical Examination

Physical examination findings of acute inflammation in AOM include a bulging TM (Fig. 18.1), erythema of the TM, or otorrhea associated with spontaneous perforation. The TM may be thickened and dull and purulence may be visualized through the TM. Caution must be taken when assessing redness of the drum, however and the presence of fluid must be confirmed. One study showed the predictive value of redness of the TM alone to be only 7%, and hyperemia of the TM alone is a very common normal finding, particularly in a crying child.[49] OME usually is seen as opacification of the TM with abnormal color, typically pink, yellow, amber, or blue (Fig. 18.2). Bubbles or air-fluid interfaces may be visible and the TM may be in a neutral or retracted position. Pneumatic otoscopy is a critical part of the otoscopic examination, particularly when determining if MEE is present. This involves the application of positive and negative pressure to the TM.

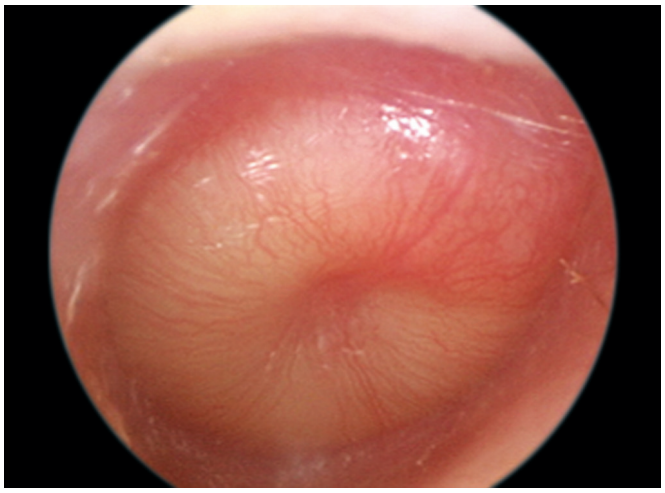

**Fig. 18.1:** Otoscopic examination of acute otitis media.

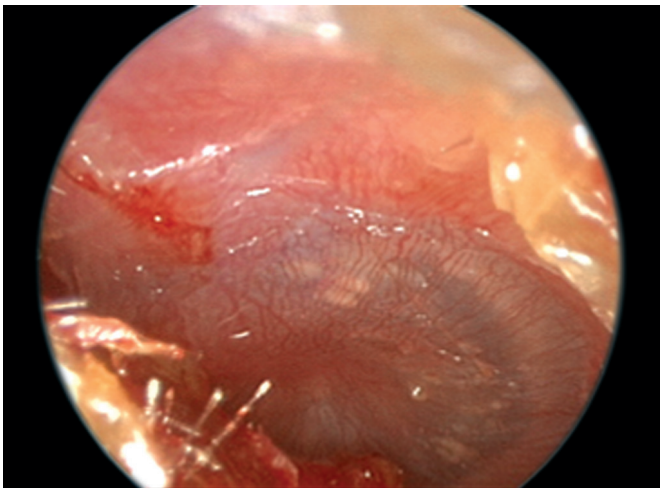

**Fig. 18.2:** Otoscopic examination of otitis media with effusion.

To properly perform pneumatic otoscopy, the largest speculum that adequately fits in the ear canal should be used and an airtight seal must be created within the cartilaginous ear canal. Decreased or absent mobility of the TM is suggestive of fluid and may be used to confirm MEE and OME. Other sources of poor mobility include scarring (myringosclerosis) or thickening of the TM, and obviously a perforation or tympanostomy tube will prohibit mobility. Myringosclerosis is seen as white plaques within the TM, and commonly occurs in a horseshoe pattern centrally around the pars tensa portion of the TM. This occurs with long-standing ear disease, either with or without the previous presence of a tympanostomy tube. Retraction, or atelectasis, of the TM is another common otoscopic finding, and may be associated with OME. In severe cases, hearing loss associated with ossicular chain erosion or cholesteatoma formation can occur. If available, binocular microscopy can also be a valuable tool in examining the TM and assessing for the presence of MEE. One recent study showed an 88% sensitivity and 89% specificity for binocular microscopy in identifying MEE, compared with 68% and 81%, respectively, for pneumatic otoscopy.[50] Obviously, binocular microscopy will not be available in all diagnostic settings and may not be practical in every patient, particularly young children, therefore pneumatic otoscopy remains the gold standard for identifying MEE.

## Ancillary Testing

Immittance testing, or tympanometry, is an audiologic tool that can also be useful in diagnosing MEE. It is particularly useful is young children, those with small ear canals, and those patients in which an airtight seal cannot be obtained for pneumatic otoscopy. Tympanometry involves placing a probe in the ear canal with an airtight seal. The probe emits a tone, and a curve is obtained by plotting the immittance of the middle ear as a function of pressure in the ear canal. A normal, or type A, tympanogram will have a sharp peak, which usually will occur near zero mm water pressure. A flat, or type B tympanogram, is classically associated with MEE, as compliance of the drum is poor. Other sources of flat tympanograms, however, include presence of a tympanostomy tube, or a false positive if a seal is not created with the probe. A type C tympanogram occurs when a peak is obtained, but this peak occurs at a pressure of –150 or greater. This suggests high negative pressure, or a vacuum type effect, in the middle ear, and is much less specific in diagnosing MEE. Tympanometry is highly sensitive, with ranges around 80–90% reported in multiple studies, but its specificity is much lower, reportedly as low as 47%.[50] It is particularly poor in children < 1 year of age, and this may be due to the increased compliance of the ear canal is infants. This can be overcome to some degree by using a 1000 Hz probe tone instead of the usual 226 Hz tone. The role of other supplementary testing, including acoustic reflectometry and ultrasound, is less well defined and not readily available in most physicians' offices.

## Disease Prevention

Modification of the environmental risk factors previously mentioned, such as encouraging breast feeding in the first few months of life and avoiding passive smoke exposure as well as the use of pacifiers, are simple measures that can decrease the incidence of OM. There is only weak evidence that substances such as xylitol and the probiotic bacteria

Lactobacillus prevent OM, and there are not enough supporting data to recommend using the on a routine basis. The role of allergy and GERD in the pathogenesis of OM has not yet been clearly defined, but there is certainly evidence to support their involvement in ear disease. Treating allergy and GERD in those patients who are symptomatic may help prevent further episodes of OM, but there is no clear evidence that treating every child with OM is necessary and it is not routinely recommended. Antibiotic prophylaxis has been shown to prevent AOM, but is largely discouraged because it promotes the emergence of resistant bacteria. The benefit of antibiotic prophylaxis is also small, with nearly a year of antibiotic necessary to prevent only one episode of AOM.

The development of vaccines aimed at the most common causes of OM holds promise. As mentioned previously, the pneumococcal vaccine PCV7 was released in the United States in 2000. Unfortunately, there was only an 8% decrease in total OM episodes with this vaccination, and an increase in nonserotype pneumococcal and *Haemophilus* bacteriology. The true benefit is greater in those patients with recurrent AOM, with a 20% decrease in number of episodes and concomitant 20% decrease in number of children requiring tympanostomy tube placement. It has also resulted in a greater than 80% decrease in invasive pneumococcal disease.[43] More recently, an updated PCV13 vaccine has been released, and it remains to be seen whether this will have a larger impact on total number of AOM episodes. The 23-valent pneumococcal polysaccharide vaccine Pneumovax covers about 90% of pneumococcal infections, but is not efficacious in children <2 years of age, marginalizing its role in preventing OM. Research is ongoing to develop vaccines for nontypeable *Haemophilus* and *Moraxella*.[51,52] The role of maternal immunization with pneumococcal vaccines is also being studied with promising results.[53]

As previously stated, the role of viruses in OM, both directly and indirectly, is significant. The development of viral vaccines has also shown to have a role in decreasing the number of episodes of AOM. The inactivated influenza vaccine reduced the incidence of AOM during flu season by 35%, although the largest benefit is gained in children older than 2, and the efficacy may diminish after 1 year.[54] It does appear that the intranasal live-attenuated influenza vaccine is superior to its inactivated counterpart.[55] Currently, the influenza vaccine is the only viral vaccine that is commercially available for the prevention of OM, but research is ongoing to develop other viral vaccines for OM, with particular attention to RSV.

## MEDICAL TREATMENT OF ACUTE OTITIS MEDIA

There has been controversy for quite some time about the need for antibiotic therapy in all cases of AOM. It has been shown that only a 12% increase in resolution rate was observed in children who received antibiotics versus clinical observation at 2–7 days.[56] Furthermore, the incidence of meningitis, mastoiditis, and other suppurative complications are similar in those treated with antibiotics versus observation (0.17% vs. 0.59%, respectively). In fact, routine antibiotic usage may select out for more invasive, resistant bacteria. A scientific review of the best available studies was performed and new guidelines from the American Academy of Pediatrics and American Academy of Family Physicians were introduced in 2004.[48] This was the first set of guidelines from these academies that included observation as initial management in certain cases of AOM. The factors that are used to determine initial treatment include age, certainty of diagnosis, severity of illness and reliability of the caregiver/follow-up were the factors used to create this recommendation (Table 18.1). Certain diagnosis meets the three criteria mentioned previously in this chapter. Severe illness was defined as severe otalgia or fever >39°C (102.2°F).

### Observation

By definition, the "observation option" refers to observation for a period of 48–72 hours, and limiting management to symptomatic relief. This includes particularly the management of pain, another recommendation from the committee. The most important initial factor in determining whether observation is even an option in a child is the reliability of the caregiver. This not only relates to assurance of follow-up, but also their ability to recognize worsening severity of illness and be able to provide them with prompt access to medical care if necessary. If there are serious concerns with any of these factors, then a physician may choose to initially treat a child with antibiotics empirically. When observation is chosen, a strategy should be in place to ensure that some follow-up occurs. This may include a scheduled clinic or phone follow-up, a parent-initiated visit if there is no improvement at 48–72 hours, or a safety-net antibiotic prescription given to parents to fill if there is no improvement in 48–72 hours. Other exclusion criteria for the observation option include immunodeficiency, genetic abnormalities, craniofacial anomalies, underlying persistent OME, and AOM in the past 30 days.

**Table 18.1:** Criteria for initial antibacterial-agent treatment or observation in children with AOM

| *Age* | *Certain diagnosis* | *Uncertain diagnosis* |
|---|---|---|
| < 6 months | Antibacterial therapy | Antibacterial therapy |
| 6 months to 2 years | Antibacterial therapy | Antibacterial therapy if severe illness; observation option* if nonsevere illness |
| ≥ 2 years | Antibacterial therapy if severe illness; observation option* if nonsevere illness | Observation option* |

*Observation is an appropriate option only when follow-up can be ensured and antibacterial agents started if symptoms persist or worsen. Nonsevere illness is mild otalgia and fever <39°C in the past 24 hours. Severe illness is moderate to severe otalgia or fever ≥ 39°C. A certain diagnosis of AOM meets all three criteria: (1) rapid onset, (2) signs of MEE, and (3) signs and symptoms of middle-ear inflammation.

Adapted from AAP/AAFP Subcommittee Guidelines on Management of Acute Otitis Media, Recommendation 3a, Pediatrics. 2004;113(5):1451-65.

All children under the age of 6 months should receive initial antibiotic therapy for AOM, regardless of certainty of diagnosis or severity of illness. The reason for this is the concern for serious infection in this very young age group and the diagnostic challenge in assessing worsening symptoms or signs of progression to suppurative complications. In children age 6 months to 2 years, initial antibiotic therapy should be instituted if there is a certain diagnosis, or if there is an uncertain diagnosis in the presence of severe illness. If the diagnosis is uncertain and there is nonsevere illness, then observation is an option. This was based on the suggestion in the literature of an increased rate of failure of watchful waiting in this age range. In children greater than age 2, observation is an option even in the presence of a certain diagnosis of AOM, as long as the patient has nonsevere illness. Initial antibiotic therapy should be instituted in the presence of severe illness (Table 18.1).

Although these guidelines are widely accepted, further research may give us a clearer picture of which patients should be treated initially and which can be observed. There have been problems cited with the studies that were used to show high spontaneous resolution rates in AOM. The definition of AOM may have included criteria that allowed inclusion of patients with OME, the antibiotics may have been inappropriate or at an insufficient dosage, and the sickest children and those < 2 years old may have been excluded/underrepresented.[57] All of these factors would make antibiotic therapy appear less efficacious. Another challenge is getting parents to agree to observation, which can be difficult particular given the empiric historic use in AOM. Practitioners have also not universally accepted this into their practice, and one study showed that although 83% of physicians felt observation was a reasonable practice, it was used in only a median of 15% of practices.[58]

## Initial Antibiotic Therapy

The initial antibiotic for an uncomplicated, nonrecurrent AOM is amoxicillin (Table 18.2). Amoxicillin has been shown to be effective against the most common AOM organisms, particularly *S. pneumoniae* and non-Beta lactamase producing *H. influenzae*. The dosage recommendation is the high dose 80–90 mg/kg/day versus the standard 40 mg/kg/day. This higher dose has been shown to be more effective, particularly against the increasing intermediate and highly resistant strains of *S. pneumoniae* that have emerged. In addition, amoxicillin is cost-effective and easy to take, with a low incidence of side effects. In patients with severe illness (severe otalgia or temp > 39°C), or the recommendation is high-dose amoxicillin (90 mg/kg/day)/clavulanate (6.4 mg/kg/day). The challenge in determining appropriate initial antibiotic therapy is the changing landscape of the bacteriology of AOM. Nearly 50% of *H. influenzae* and 100% of *M. catarrhalis* are Beta-lactamase producing, and therefore resistant to amoxicillin alone. But there is also evidence to suggest that AOM caused by these bacteria are more likely to resolve spontaneously, and the combination of *S. pneumoniae* and amoxicillin-sensitive *H. influenzae* still represent the majority of AOM pathogens.

In penicillin-allergic patients without type I hypersensitivity, cefdinir, cefpodoxime, or cefuroxime can be used. Azithromycin or clarithromycin are alternatives in those patients with type I hypersensitivity, although studies suggest increasing resistance rates to these macrolide antibiotics. Other possibilities include erythromycin/sulfisoxazole or trimethoprim/sulfamethoxazole. Clindamycin is also effective if the pathogen is resistant to *S. pneumoniae*. In the case of severe illness or the inability of the patient to tolerate oral medication, intramuscular

**Table 18.2:** AAP/AAFP therapy options for AOM in varying clinical circumstances

| |
|---|
| *At diagnosis when observation is not an option* |
| Recommended: Amoxicillin 80–90 mg/kg/day |
| Alternative for penicillin allergy: Non-type I: cefdinir, cefuroxime, cefpodoxime; Type I: azithromycin, clarithromycin |
| *Clinically defined failure of observation option after 48–72 hours* |
| Recommended: Amoxicillin 80–90 mg/kg/day |
| Alternative for penicillin allergy: Non-type I: cefdinir, cefuroxime, cefpodoxime; Type I: azithromycin, clarithromycin |
| *Clinically defined failure of initial antibiotic treatment after 48–72 hours* |
| Recommended: Amoxicillin/clavulanate (90 mg/kg/day of amoxicillin component, with 6.4 mg/kg/day of clavulanate) |
| Alternative for penicillin allergy: Non-type I: ceftriaxone – 3 days; type I: clindamycin |
| If symptoms are severe (temperature > 39°C and/or severe otalgia) |
| *At diagnosis when observation is not an option* |
| Recommended: Amoxicillin/clavulanate (90 mg/kg/day of amoxicillin with 6.4 mg/kg/day of clavulanate) |
| Alternative for penicillin allergy: Ceftriaxone – 1 or 3 days |
| *Clinically defined failure of observation option after 48–72 hours* |
| Recommended: Amoxicillin/clavulanate (90 mg/kg/day of amoxicillin with 6.4 mg/kg/d of clavulanate) |
| Alternative for penicillin allergy: Ceftriaxone 1 or 3 days |
| *Clinically defined failure of initial antibiotic treatment after 48–72 hours* |
| Recommended: Ceftriaxone 3 days |
| Alternative for penicillin allergy: Tympanocentesis and clindamycin |

Adapted from Pichichero and Casey.[41]

**Table 18.3:** Consistency of guidelines for acute otitis media

| | |
|---|---|
| All recommend as first line | Amoxicillin, mostly at 80–90 mg/kg/day |
| All recommend as second line | Amoxicillin/clavulanate, mostly "ES" 80–90 mg/kg/day |
| Some recommend as second line | Cefdinir 14 mg/kg/day<br>Cefprozil 30 mg/kg/day<br>Cefuroxime axetil 30 mg/kg/day<br>Cefpodoxime 10 mg/kg/day<br>Ceftriaxone 50 mg/kg/day |
| Not recommended by any guideline: Unless pathogen known to be sensitive; patient had severe allergic reaction to penicillin or amoxicillin; or combined with another antibiotic that is effective against additional organisms | Azithromycin<br>Clarithromycin<br>Trimethoprim/sulfamethoxazole<br>Erythromycin/sulfisoxazole<br>Cefaclor<br>Loracarbef<br>Cefixime<br>Ceftibuten<br>Clindamycin |

Adapted from Pichichero and Casey.[41]

ceftriaxone is also an option. The above protocols are designed not only for patients who are treated initially, but also for those in whom the observation option has failed after 48–72 hours. Table 18.3 outlines antibiotic guidelines from a combination of the AAP/AAFP and CDC guidelines.

The optimal duration of therapy for AOM is not completely certain. Evidence suggests fewer treatment failures in younger children with a standard 10-day course, and the current recommendation is 10 days in children <6 years old. A 5- to 7-day course may be appropriate in

children older than 6 years of age without severe disease. Specific antibiotics have been approved for shorter courses even in younger children. Cefdinir and cefpodoxime have been approved for 5-day courses, and azithromycin has been approved for 1-, 3-, and 5-day courses. A recent study showed, however, that high dose amoxicillin/clavulanic acid for 10 days was superior to a 5-day course of cefdinir in the treatment of AOM.[59]

## Antibiotics for Treatment Failures

When initial antibiotic therapy fails, the patient should be started on high-dose amoxicillin/clavulanate if there is no allergy. If they have failed this therapy already, consideration to alternatives such as cefdinir, cefpodoxime, and cefuroxime can be considered. A 3-day course of intramuscular ceftriaxone can also be considered. In those type I penicillin hypersensitivity patients, clindamycin is also an option because of its high (up to 95%) success against highly resistant *S. pneumoniae*.[60] Finally, in the severely ill patient, tympanocentesis can be performed to make a bacteriologic diagnosis for culture-directed therapy.

## Nonantibiotic Therapies

### *Analgesics*

As mentioned previously, the symptomatic management of pain with analgesics is important in patients with AOM, regardless whether or not they receive antibiotic therapy. Multiple options exist, with acetaminophen and ibuprofen the most common and very effective. Topical analgesia with benzocaine has also shown to be effective, though the benefits are very short lasting.[61] Narcotic analgesics such as codeine and its derivatives can also be used, but must be used cautiously particularly in younger children. Lethargy from the narcotic may mask the worsening symptoms of suppurative complications, and respiratory depression is also a side effect that needs to be monitored.

### *Corticosteroids*

Although some small studies have shown short-term benefit with oral or intranasal steroid, the benefits have been marginal. A larger study showed no benefit with oral steroid over antibiotic alone, and steroids are not routinely recommended in AOM.[62]

### *Antihistamines and Decongestants*

Both large individual studies and meta-analysis of studies have shown no benefit in terms of early cure, symptom resolution, duration of effusion, or prevention of complication or surgery with antihistamines or decongestants.[56] They are not routinely recommended in AOM.

### *Alternative Therapies*

Homeopathy, acupuncture, chiropractic treatment, and nutritional supplements have all been used for AOM but there are no data suggesting a beneficial effect of these therapies. These alternative therapies are not currently recommended for AOM.

# MEDICAL MANAGEMENT OF OTITIS MEDIA WITH EFFUSION

## Observation

OME is common in children both with URIs and after AOM, and fluid may persist up to 1 month after an acute episode of AOM in 50% of cases. In a child without speech, language, or learning delays, observation of fluid is recommended for up to 3 months. If a child is at-risk or OME persists beyond 3 months, audiologic evaluation should be obtained. If the child's hearing is normal (<20 dB), continued watchful waiting is recommended. If there is a moderate or worse conductive hearing loss (>40 dB) then surgical intervention is recommended. When the hearing falls in the mild conductive hearing loss range (21–39 dB), the duration and particularly the severity of symptoms related to the hearing loss must be addressed. If there is parental or teacher concern about the child's hearing, surgical intervention may be considered. Otherwise, observation in 3–6 month intervals should occur until the fluid resolves, language delays occur, or structural abnormalities of the eardrum are observed. These recommendations are from the AAP/AAFP clinical practice guidelines for OME, also published in 2004.[63]

## Medical Therapy

Very little evidence exists to support the use of any medical therapy to shorten the duration of OME. The 2004 guidelines conclude that antihistamines and decongestants are ineffective in treating OME and they do not recommend their use, particularly from a risk/benefit standpoint. Antibiotics and corticosteroids are also not recommended. Although there may be short-term benefit to both antibiotics and steroids, these benefits become nonsignificant within several weeks of stopping them. In addition, their side effect profiles lead to a less than optimal risk/benefit ratio. Autoinflation of the ET, described by Politzer, has been shown to have limited short-term benefit

in very small studies, but adherence to the procedure can be difficult in children. No definitive recommendation has been made regarding autoinflation but because of the low cost and absence of adverse effects it may be a reasonable option to consider while awaiting resolution of effusion.[64]

## SURGICAL TREATMENT OF AOM AND OME

### Myringotomy/Tympanocentesis

Myringotomy, or an incision in the eardrum, may temporarily relieve pressure associated with an AOM and allow culture for bacteriology, but has not been shown to be as effective as antibiotic therapy, does not decrease duration of effusion, and does not prevent recurrent AOM. It also has been shown to be ineffective in the long-term management of chronic OME. Therefore, there is little role for myringotomy alone in OM.

### Myringotomy with Pressure Equalization Tube Placement

Myringotomy with pressure equalization tube (PET) placement is the first-line surgical therapy for recurrent AOM, complicated AOM, as well as chronic OME.[63] Children are in general considered candidates for PET placement if they have 3–4 episodes of AOM in 6 months or 4–6 episodes in 1 year. Recently updated guidelines from the American Academy of Otolaryngology also require the presence of effusion at initial visit prior to recommendation of PET placement in recurrent AOM, as well as preoperative audiologic evaluation in all patients prior to PET placement.[65] Studies show that PETs reduce the frequency of AOM episodes by 56% and decrease the duration of OM.[66,67] Although OM can still occur with a PET in place in the form of otorrhea, many of these episodes are not accompanied by any symptoms and can be treated with ototopical antibiotic drops without oral antibiotics. PET placement is also considered in a complicated AOM episode, meaning AOM with mastoiditis, labyrinthitis, facial nerve paralysis, or other complication. The Academy guidelines do not apply to children who have multiple antibiotic allergies/intolerances, immunosuppression or those at risk for, or already with developmental delays.

PET placement is also the most common initial surgical intervention in chronic OME. Indications for intervention, however, are somewhat more controversial. As mentioned previously, hearing loss, particularly as it relates to speech, language, or learning delays is usually the primary factor in determining whether PET placement is necessary. In a child with speech or language delays, particularly those at-risk patients such as those with genetic abnormalities or other developmental delays, prompt PET placement is indicated. Otherwise, OME is observed for 3 months for spontaneous resolution. If the fluid persists and audiologic evaluation reveals moderate hearing loss (>40 dB) or speech or language delays develop, then PET placement is indicated at this time. In the face of a normal audiogram, observation is recommended at 3–6 month intervals until resolution occurs, significant hearing loss develops, or structural damage of the TM is identified—if any of this occurs, PET placement should be considered. In the face of a mild (21–40 dB) hearing loss, a discussion with parents is necessary and either (1) PET can be placed or (2) close observation at 3-month interval scan be continued.

The average length of time a PET stays in place is reported to be between 1 and 2 years. There is minor variation related to the type and model of tube inserted, but most will remain in place for at least 12 months. Postoperative tube otorrhea is common and can be decreased by using saline rinses intraoperatively, a single dose of antibiotic/steroid eardrops intraoperatively, or more prolonged eardrops therapy.[68] An episode of tube otorrhea after the postoperative period is also not uncommon—it may occur spontaneously but is commonly associated with a URI or water exposure. Younger children have otorrhea more commonly associated with URIs, and the typical sinonasal bacteria (*S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*) are usually cultured. In older children, otorrhea is more likely to occur with water exposure, particularly with swimming, and the most common bacterial pathogens are *Pseudomonas* and *S. aureus*. Topical antibiotic therapy has been shown to be at least as effective as and perhaps more effective than oral antibiotics. Oral antibiotics are usually reserved for those patients with severe systemic symptomatology or those that have failed initial topical therapy. Aural toilet (i.e. suctioning) can also help to clear the ear canal and allow the eardrops easier access to the middle ear space. This is even more important in those cases with acutely inflamed, edematous, and narrow ear canals. Chronic or recurrent otorrhea is a rarer problem that can be more difficult to manage. If a patient has failed both topical and oral antibiotic culture-directed therapy in the presence of repeated aural toilet, then consideration can be given to a variety of adjuvant therapies. This could include tube replacement, adenoidectomy, tube removal, intravenous antibiotic therapy, and mastoidectomy. Particularly in those patients with long-standing chronic otorrhea, a CT scan can also be considered to evaluate for the presence of cholesteatoma.

There are other less frequently seen sequelae of PETs. Early extrusion may occur, usually in the setting of an acute otorrhea episode. A tube may become blocked with cerumen, dried blood or dried mucus—this can often be cleared either with ototopical drops or manually in the office setting. Persistent perforation may occur after PET extrusion, with myringoplasty or tympanoplasty necessary to close the hole. A PET may not extrude spontaneously and be retained in the TM – this can be monitored but may eventually need to be removed in the operative setting. Myringosclerosis (scarring of the TM), atrophy of the TM at the prior PET site, and retraction pockets can also occur after tube extrusion. Although these TM abnormalities can also occur without prior PET placement, they have been shown to be more common after PETs.

## Adenoidectomy

25% of children who have had PETs will have a relapse of OM when the tubes extrude or become obstructed.[69] In those instances where repeated PET placement is indicated, there is a role for adenoidectomy, as it decreases by 50% the need for further surgeries (i.e. a 3rd set of PETs). The groups that benefit the most from adenoidectomy are those with chronic OME who are older than age 4 and those with recurrent AOM older than age 2 with a prior history of extruded PETs.[70] Interestingly, the benefit from adenoid removal is independent from the size of the adenoid tissue, suggesting that not only adenoid size, but chronic inflammation, contributes to OM. This may be related to biofilms, but the exact role of biofilms in this setting has yet to be completely elucidated.[71] Adenoidectomy with myringotomy alone was equivalent to PET placement alone in older children, but this is not recommended routinely because it is more invasive than PET placement alone. Adenoidectomy is not recommended routinely with a first set of PETs unless an indication such as chronic adenoiditis or chronic sinusitis coexists.[63] Tonsillectomy is not recommended in the treatment of either AOM or OME, as it has shown very limited evidence of benefit and poses significantly higher risks.

# COMPLICATIONS OF AOM

## Extracranial

### *Acute Mastoiditis*

Acute mastoiditis describes acute infection and inflammation within the mastoid cavity with bony destruction of the architecture of the air cells, or "coalescence". Clinically, the child would have postauricular edema, erythema, and tenderness in the setting of an AOM. There is commonly protrusion of the pinna as well. A CT scan can confirm the presence of coalescence. Management is controversial, but IV antibiotic therapy alone is often the initial choice. If the child shows no improvement within 48 hours, the surgical options include myringotomy ± PET placement and/or simple mastoidectomy. Another management strategy that is commonly employed is to do a myringotomy and PET insertion initially along with IV antibiotics, with mastoidectomy performed if there is no improvement in 48 hours.

### *Subperiosteal and Bezold's Abscesses*

These occur when an acute mastoiditis erodes through the cortical bone either adjacent to the lateral surface of the mastoid cortex (subperiosteal) or through the mastoid tip into the neck (Bezold's sign). This can most commonly via direct bony erosion but may also occur hematogenously through mastoid emissary vessels. Purulence collects in these areas, with resultant fluctuance and erythema. Again, a CT scan can confirm the presence of an abscess and its precise location (Fig. 18.3). Management in these cases includes myringotomy ± PET placement with incision and drainage of the abscess alone or in combination with simple mastoidectomy.

### *Petrous Apicitis (Gradenigo's Syndrome)*

Petrous apicitis occurs when infection spreads from the middle ear and mastoid medially to the petrous portion of the temporal bone, either directly or hematogenously via vascular channels. The classic triad in petrous apicitis is

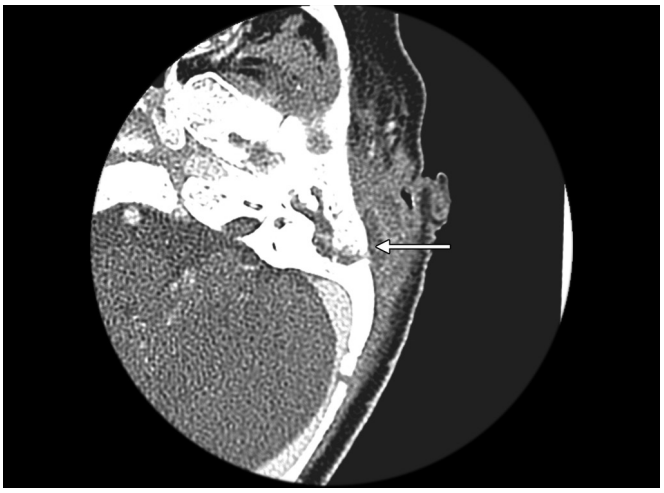

**Fig. 18.3:** Axial CT scan showing acute left mastoiditis with cortical bony erosion and subperiosteal abscess (arrow).

otitis/otorrhea, retrobulbar pain/headache, and abducens nerve (cranial nerve VI) palsy. CT or MRI can usually confirm the diagnosis, and initial management with IV antibiotic therapy alone is often successful.[72] Petrous apicoectomy, typically via a transmastoid approach, is usually reserved for antibiotic failures or infections with complications.

### *Labyrinthitis*

This occurs when inflammation in the middle ear spreads to the labyrinth, which includes the cochlea and semicircular canals. This may be via direct bacterial spread (suppurative labyrinthitis), but is also commonly caused by inflammatory mediators in the absence of the organisms themselves (serous labyrinthitis). Transmission can occur at the oval or round windows, or via microscopic bony labyrinthine defects. The diagnosis is made clinically with acute debilitating vertigo and sensorineural hearing loss in the setting of an AOM. MRI, although not necessary, will also show labyrinthine involvement. IV antibiotics are recommended initially to both treat the infection and try to prevent meningitis. Conversely, labyrinthitis can also be a complication of meningitis – this is in part due to a normal communication channel between the extracranial labyrinth and intracranial meninges, the cochlear aqueduct. Myringotomy ± PET placement drains the fluid and allows for culture-directed therapy, and otherwise vertiginous symptoms are managed in the usual fashion. Serous and suppurative labyrinthitis are treated similarly from a medical standpoint and it is very difficult to distinguish them acutely. In general, however, serous labyrinthitis presents with milder vestibulocochlear symptoms than suppurative labyrinthitis and labyrinthine function is more likely to return in serous labyrinthitis.

### *Facial Nerve Paresis/Paralysis*

The horizontal portion of the facial nerve runs through the middle ear space, and when AOM affects the facial nerve, either through the tiny vascular channels in the normal bony canal or directly secondary to dehiscence of the nerve, facial palsy can occur. This can be a partial weakness (paresis) or complete weakness (paralysis), although more commonly it is partial. Management includes IV antibiotic therapy and wide-field myringotomy versus myringotomy with PET, with culture-directed therapy. A CT scan may be considered to rule out other intracranial or other extracranial involvement. More aggressive intervention is rarely indicated.

## Intracranial

### *Meningitis/Otitic Hydrocephalus*

Bacterial meningitis is the most common intracranial complication of AOM. Transmission of disease from the middle ear can be due to hematogenous spread or directly, via the oval and round windows, cochlear aqueduct, or other bony defects. Symptoms include high fever, altered level of consciousness, vomiting, and neck stiffness. There may be papilledema, Kernig's and Brudzinski's signs, bulging fontanelles, or cranial neuropathies on physical examination. Lumbar puncture is performed to confirm the diagnosis. CT or MRI is usually performed up front to exclude tumor and mass effect, but also may be used to look for other complications. Broad-spectrum antibiotic therapy with myringotomy ± PET for culture is the treatment. Audiologic evaluation of these patients is recommended when neurologic status improves, as sensorineural hearing loss is very common, particularly with pneumococcal meningitis.

Although hydrocephalus is a common finding in bacterial meningitis, another entity has been described known as otitic hydrocephalus. Lumbar puncture demonstrates high CSF opening pressure with normal cytology, thereby excluding meningitis. The pathophysiology is thought to be due to nonobstructing thrombus of the transverse sinus, and MRI is useful to demonstrate the presence of a thrombus. Management includes antibiotic treatment of the underlying AOM, and supportive measures to decrease intracranial pressure.

### *Sigmoid Sinus Thrombosis*

This occurs when a septic thrombus occurs in the sigmoid dural sinus, usually as a result of direct extension of infection from the mastoid cavity. Clinically, it may present with "picket-fence" spiking fevers, headache, and photophobia. Abducens palsy as well as swelling and tenderness over the mastoid process (Greisinger's sign) have also been described. Either CT with contrast or MRI ± venography can make the diagnosis (Fig. 18.4). Management includes IV antibiotic therapy and PET placement ± mastoidectomy. If the choice to perform mastoidectomy is made, the bone directly over the sigmoid sinus should be decompressed. Surgical thrombectomy and anticoagulation are both controversial without strong evidence to support their benefit. This, combined with literature suggesting that recanalization usually occurs spontaneously in 4–6 weeks, suggests that a more conservative approach may be appropriate.[73]

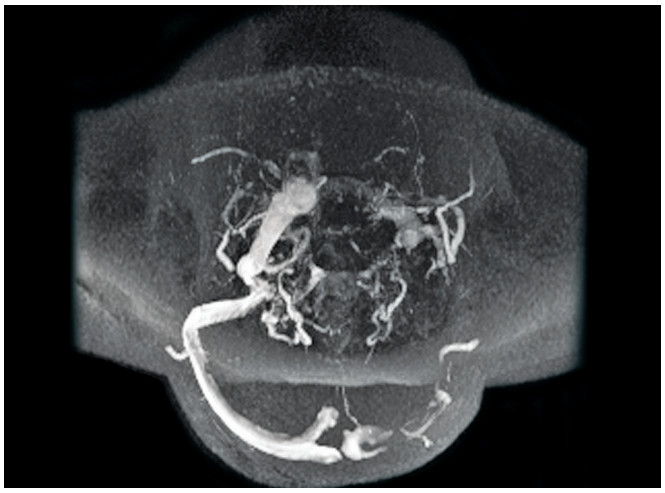

**Fig. 18.4:** MR-venogram showing thrombosis of the left transverse sinus, sigmoid sinus, and internal jugular vein. Comparison can be made to the normal right venous anatomy.

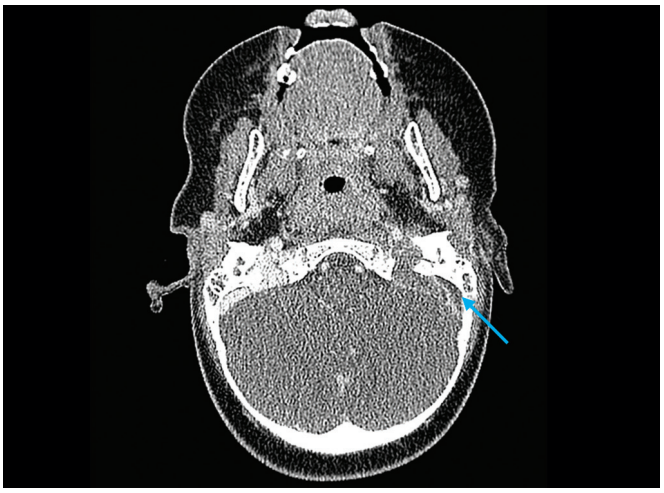

**Fig. 18.5:** Axial CT scan showing epidural abscess (arrow) adjacent to a thrombosed left sigmoid sinus.

### *Intracranial Abscesses (Epidural, Subdural, and Brain Abscesses)*

Intracranial abscesses are defined by the space that they occupy within the cranium. An epidural abscess is located between the bone and the dura mater, a subdural abscess is between the dura and arachnoid maters, and a brain abscess is located intraparenchymally. The mortality associated with subdural and particularly brain abscess is much higher than with epidural abscess. MRI is the imaging study of choice for these abscesses, but most can also be detected with contrast-enhanced CT.

Many epidural abscesses can be managed with IV antibiotic alone, close clinical observation, and interval imaging studies (CT or MRI) for comparison. When an epidural abscess is present in continuity with mastoiditis or sigmoid sinus thrombosis (Fig. 18.5), it may be decompressed via a transmastoid approach. If there is no improvement with antibiotic therapy, or if neurologic status deteriorates surgical drainage either via craniotomy or burr holes, should be performed.

Subdural abscesses tend to spread rapidly through the subdural space, partially contributing to their more aggressive clinical picture. Symptoms include fever, altered mental status, and headache. Neurosurgical drainage is always indicated, while otolaryngologic intervention should be performed if the patient is stable and deferred if the patient is unstable. Other measures to decrease cerebral edema should also be undertaken, as well as seizure prophylaxis.

Brain abscess is a catastrophic complication of AOM, with a reported mortality of as high as 50%.[74] Signs and symptoms may include fever, altered mental status, seizure, and focal neurologic deficits. These focal deficits depend on where within the brain parenchyma the abscess is located. The disease can have an indolent course, making diagnosis all the more difficult. Management is similar to that of subdural abscess.

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CHAPTER

19

# Cholesteatoma

***Kenneth M Grundfast, Jessica Levi***

## INTRODUCTION

The otologic disorder characterized by keratinizing epithelium within the middle ear, cholesteatoma, was first described in 1829 by Cruveilhier.[1] The term "cholesteatoma" was coined by Müller in 1838 to describe this disorder because he thought that the visible mass within the middle ear was comprised of cholesterin and fat.[2] A more apt name would be a keratoma as suggested by Schuknecht but, despite many attempts to refer to the otologic disorder as a keratoma, the word cholesteatoma remains the descriptor of choice even though the keratin mass does not contain cholesterol. The contemporary definition of cholesteatoma is the presence of abnormal squamous epithelial growth medial to the tympanic membrane (TM), typically in the middle ear or mastoid. Cholesteatoma is histologically indistinguishable from a sebaceous cyst or a keratoma lined by stratified squamous epithelium that can occur anywhere in the body. Cholesteatoma is usually found in the middle ear or mastoid, but can be found anywhere in the pneumatized temporal bone. When cholesteatoma has not been detected or treated in an early stage, it can expand, destroying adjacent tissues including bone and the adjacent TM. This may result in TM perforation, otorrhea, hearing loss, semicircular canal fistula, vertigo, labyrinthitis, meningitis, and facial paresis. Congenital cholesteatoma is believed to be the result of an error in embryogenesis typically presenting as a well circumscribed cyst in the anterosuperior quadrant of the middle ear medial to an intact TM. Congenital cholesteatoma can be especially destructive because it often goes undetected for many years and tends to occur in a well pneumatized temporal bone so that the cholesteatoma can infiltrate the many air cells that are present throughout the temporal bone. In contrast to the congenital cholesteatoma that is not a sequela of chronic otitis media, acquired cholesteatoma develops in an ear that has had multiple ear infections and either an eardrum retraction pocket or a perforated eardrum; acquired cholesteatoma tends to occur in a temporal bone that has become sclerotic because of the chronic osteitis that accompanies the many infections and inflammatory processes that are typical of chronic otitis media.

## EPIDEMIOLOGY

Based on a retrospective study, the mean annual incidence of cholesteatoma is 9.2 per 100,000 persons of all ages.[3] Congenital cholesteatoma accounts for 1–5% of cholesteatoma in most published series[4] and is therefore encountered less commonly than acquired cholesteatoma. Recent studies indicate that cholesteatoma may occur more commonly than previously had been known; cholesteatoma was observed in 36% of cadaver temporal bones from patients with otitis media (OM) who had TM perforations and in 4% of temporal bones without TM perforations.[5]

There is no known predisposing factor for congenital cholesteatoma though congenital cholesteatoma seems to be more common in boys by a 3:1 ratio.[6] They are bilateral in 4%.[3] The average age at diagnosis is 4–5 years old.[7] For acquired cholesteatoma, a history of recurrent acute otitis media (AOM) or less often, chronic otitis media with effusion (OME), may predispose one to cholesteatoma

formation. The incidence of acquired cholesteatoma has been decreasing, likely because physicians are better able to recognize and treat the precursors to cholesteatoma formation such as chronic OM and eardrum retraction pockets. Patients who are syndromic or have craniofacial abnormalities may also be at increased risk for formation of acquired cholesteatoma as are patients with a family history of cholesteatoma.[8,9]

## PATHOGENESIS

The two main types of cholesteatoma, congenital and acquired, have very different modes of pathogenesis.

*Congenital*: The original definition of congenital cholesteatoma states that the cholesteatoma develops medial to an intact, normal appearing TM in a child with no history of middle ear disease[10] (Fig. 19.1). However, that original definition of congenital cholesteatoma now seems to be too restrictive and no longer entirely accurate. Nearly all children have a history of at least one episode of OM. Also, congenital cholesteatoma may be overlooked until it has expanded to the point of tympanic membrane perforation with resulting granulation and otorrhea, so that a congenital cholesteatoma that has gone undetected for many years may, at the time of discovery, appear much like an acquired cholesteatoma. Further, because of the typical location in the anterosuperior quadrant and in proximity to the Eustachian tube (ET), in some cases congenital cholesteatoma can cause OME, complicating the diagnosis further.[7] In fact, recent evidence has suggested that congenital cholesteatoma occurs during a time of inflammation.[11] Furthermore, Koltai et al. have shown congenital cholesteatoma can often progress rapidly and behave like acquired cholesteatoma.[12] Most experts accept cholesteatoma as congenital if it occurs in a child with an intact TM and no prior history of otologic surgery.[13] Clues that a cholesteatoma was congenital, especially in the setting of TM rupture are: (1) well pneumatized mastoid visualized on CT scan of the temporal bones (2) location of the nidus of cholesteatoma primarily in the anterior superior mesotympanum and the anterior epitympanum rather that the posterior mesotympanum and fossa incudis.

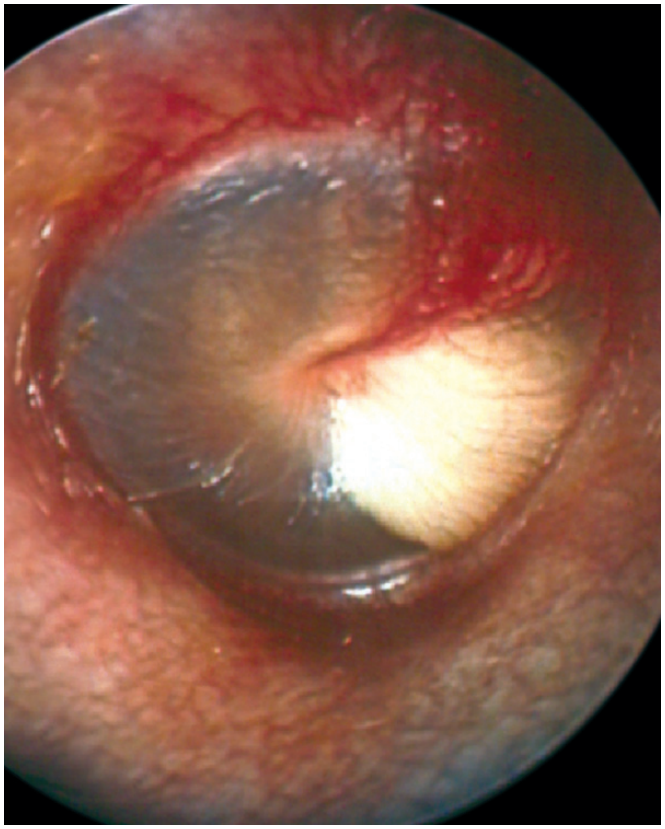

**Fig. 19.1:** Congenital cholesteatoma.

Congenital cholesteatoma is generally identified before the age of 5 and, as mentioned above, usually is located in the anterior-superior quadrant (anterior mesotympanum), and, more specifically, located near the handle of the malleus or the tensor tympani tendon.[14] A congenital cholesteatoma can also be located elsewhere. In a report by Potsic, 18% of congenital cholesteatomas confined to one quadrant were somewhere other than the anterior superior quadrant.[7] In fact, in 50% of cases, they were located in more than one quadrant.[7] There are multiple theories regarding the development of congenital cholesteatoma, the most widely held of which is failure of involution of epithelial rests in the middle ear during embryologic development. Michaels[15] found epithelial cells along the anterosuperior wall of the developing middle ear cleft during weeks 10–33 of gestation and suggested it was these cells that cause cholesteatoma if they do not involute. Other theories include microperforations in the TM that become seeded by epithelium or contamination from the amniotic fluid. Some authors believe epithelial migration or metaplasia may be the source of congenital cholesteatoma.[16]

*Acquired*: Acquired cholesteatoma can be considered to be a sequela of repeated episodes of AOM or OME and often begin as a focal retraction pocket in the posterior superior quadrant of the eardrum (Fig. 19.2). Retraction pockets usually develop in patients with longstanding ET dysfunction and negative middle ear pressure. The pars

flacida and the posterior-superior quadrant are especially prone to retraction pockets. Sites of prior (extruded) tympanostomy tubes are also at risk for retraction pocket formation. Patients with cleft palate are particularly prone to development of this type of cholesteatoma.[17]

The posterior mesotympanum is the second most common location for primary acquired cholesteatoma followed by the anterior epitympanum.[18] Generally, the pocket develops between the pars flaccida of the TM and the neck of the malleus (Prussak's space). The pocket deepens medially and the naturally shed epithelium develops a different migratory pattern. This epithelium can then become trapped and keratin accumulates, forming a cholesteatoma.[19] The cholesteatoma typically expands posteriorly, lateral to the body of the incus. They can also extend to the floor of Prussak's space into the posterior space of von Troeltsch (a pouch lying between the TM and the posterior malleal fold) to enter the middle ear. As this process continues, the sac enlarges and contacts bone, eroding the lateral wall of the epitympanum (scutum).[20] The cholesteatoma continues to grow posteriorly and can enter the aditus ad antrum and then the mastoid. It is in this way that the cholesteatoma can expose the lateral semicircular canal/otic capsule or erode the tegmen tympani (skull base).

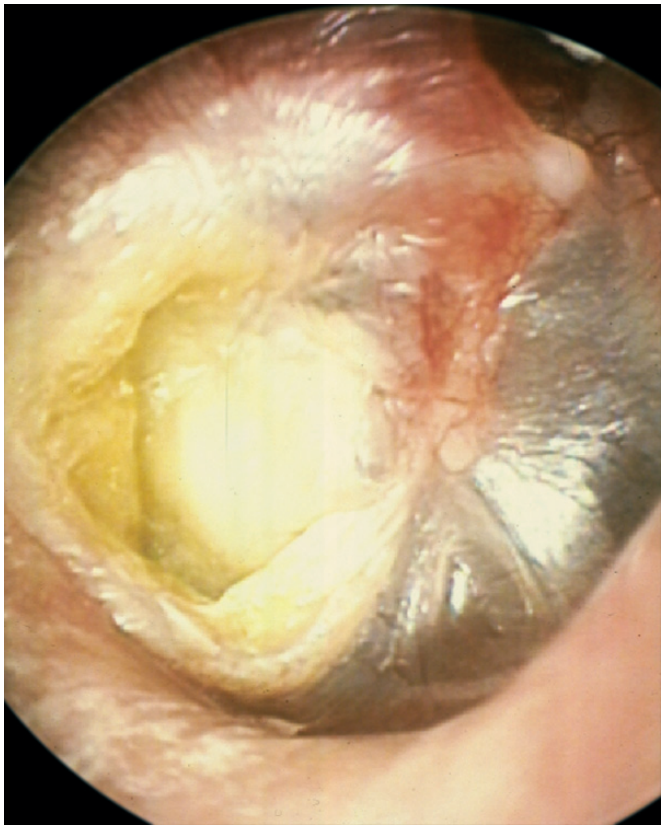

**Fig. 19.2:** Acquired cholesteatoma.

Some believe that acquired cholesteatoma can form from abnormal epithelial cell invasion of the pars flacida via basal lamina disruptions.[21,22] Many authors have shown alterations in epithelial cell markers within the cells of a cholesteatoma,[23,24] which would support this theory. Alternatively, based on work by Wendt in Germany in 1873, Sadé found epithelial cells were pluripotent and could become keratinizing in response to inflammation.[25] Thus, cholesteatoma could form from previously normal columnar middle ear mucosa, which underwent metaplasia (this theory is less accepted however).

Cholesteatoma can also form as a result of tympanostomy tube placement or other perforation in the eardrum (such as due to acute suppurative OM or barotrauma).[26] Weiss found epithelial cells could migrate along a surface by a process that he called "contact guidance".[27] This migration helps explain how epithelial cells move to the middle ear from the surface of the TM to create a cholesteatoma. Cholesteatoma that occurs as a result of some sort of "injury" to the TM are referred to as secondary acquired cholesteatoma.

Regardless of the type, the squamous epithelium of the cholesteatoma is metabolically active and has the potential to erode bone. This bone erosion can occur either by constant pressure creating bony remodeling[28] or by enzymatic activity such as collagenase[29,30] or by enhancing native osteoclastic activity.[31]

## SIGNS/SYMPTOMS

Patients with acquired cholesteatoma usually present with a chronically draining ear.[32] Typically, this is not painful. The otorrhea is generally persistent despite multiple courses of ototopical drops or oral antibiotics. It becomes malodorous when it is infected via an upper respiratory infection or external contamination. Patients may also present with hearing loss (usually due to ossicular chain erosion, most commonly the incus). The extent of the hearing loss is determined by the location of the cholesteatoma and the degree of erosion of the ossicles. Children who have undergone any otologic surgery in the past should be monitored with serial audiograms; any new onset hearing loss should prompt investigation for iatrogenic cholesteatoma.

In some patients, the first sign of a cholesteatoma is drainage from the ear and an aural polyp that can be seen on ear examination. In fact, an aural polyp in a child's chronically draining ear should be considered to be a cholesteatoma until proven otherwise. Children may also present with deep retraction pockets or granulation tissue on the surface of the TM. Retraction pockets are shallow when the full extent can be visualized on otoscopy. The retraction pockets that are most ominous and should be considered to be possible incipient cholesteatoma are those in which the cephalad extent of the retraction pocket cannot be seen on examination with an otomicroscope. When white keratin debris can be seen within the depth of a posterior superior eardrum retraction pocket of indeterminate depth, then this can be considered to be an acquired cholesteatoma.

Dizziness is an uncommon symptom associated with cholesteatoma and may indicate late stage disease. It can occur with lateral semicircular canal erosion or erosion of the stapes footplate. Rarely, cholesteatoma can first become manifest when a complication such as brain abscess or a central nervous system complication has occurred. Pain, headache, or bloody otorrhea may herald some of these complications and should warrant prompt evaluation.

In contrast to the natural history of acquired cholesteatoma, the child with a congenital cholesteatoma that is in early stages of development may manifest few or no symptoms. The affected ear may have a normal otoscopic appearance early in life (Table 19.1). Having said this, early diagnosis of a congenital cholesteatoma can be made by a primary care physician who is a skilled otoscopist and sees on routine physical examination a faint whitish mass medial to an intact eardrum in a child who has had a minimal history of ear problems. As a congenital cholesteatoma enlarges within the mesotympanum, the otoscopic findings become more discernible and, around age three to four years, the diagnosis becomes more apparent when the whitish yellow mass within the middle ear can be seen relatively easily. For children with congenital cholesteatoma, eardrum perforation, ear drainage, and hearing loss usually do not occur until around 5 years of age.

**Table 19.1:** Two kinds of cholesteatoma

| | *Congenital* | *Acquired* |
|---|---|---|
| Age at detection | Average = 3 years<br>Can be 30 years | Average = 8 years |
| Earliest phase | Small sphere medial to intact eardrum | Shallow eardrum retraction |
| Location | Anterior/superior | Posterior/superior |
| Mastoid | Well aerated | Sclerotic, poorly pneumatized |

Cholesteatoma located outside of the middle ear, such as perigeniculate or petrous apex, is more likely to present with progressive facial nerve paralysis or a sensorineural hearing loss.

## DIAGNOSIS AND TESTS

Otomicroscopic examination is the key to diagnosis of cholesteatoma in children. Pneumatic otoscopy is particularly important and can help differentiate cholesteatoma from other ear disorders (see below). Congenital cholesteatoma generally appears as a whitish mass medial to an intact TM. When the pneumatic otoscope is applied, positive pressure forces the eardrum to be pressed onto the surface of a congenital cholesteatoma, making it appear larger (concentrically). When the pneumatic pressure is released, the circular whitish mass appears smaller than when the eardrum was pressed against the mass with the pneumatic otoscope.[14]

The first sign of a developing acquired cholesteatoma is a retraction pocket that does not evert on pneumatic otoscopy.[14] Because most cholesteatomas present later, beyond the retraction pocket stage, the most common sign of an acquired cholesteatoma on examination is granulation tissue or a trail of squamous debris within an eardrum retraction pocket. There is also often granulation tissue in the ear canal and middle ear, and frequently a TM perforation. Pneumatic otoscopy can also help diagnose a labyrinthine fistula, which can result from advanced cholesteatoma (the patient will have vertigo and/or nystagmus with the positive air pressure).

Any child with suspected or known cholesteatoma should have a hearing test. There is a difference in effect on hearing between congenital and acquired cholesteatoma. During early stages, the child with a congenital cholesteatoma can have normal hearing because the cholesteatoma almost always originates near the neck of the malleus and grows toward the anterior mesotympanum and epitympanum, and away from the adjacent ossicles.[14] Having said this, the child with a congenital cholesteatoma that has enlarged into the protympanum can develop ET obstruction leading to OME that causes conductive hearing loss. In these cases, the visualization of the small middle ear mass is obscured by the effusion

and it may go undetected until a myringotomy is done in the ear for the purpose of inserting a tympanostomy tube. In general, a conductive deficit in excess of 35 dB (with a 60 dB maximum) indicates ossicular discontinuity, usually secondary to erosion of the long process of the incus. Potsic found the ossicular chain was involved in 43% of cases of congenital cholesteatoma.[7] The hearing can be normal in some cases as when the cholesteatoma is small or the cholesteatoma itself transmits sound to the stapes.[32] Thus, for the child with a congenital cholesteatoma, hearing impairment may or may not be apparent. In the child with acquired cholesteatoma, hearing impairment often occurs early as the cholesteatoma is developing because the retraction pocket (that is so often the precursor to the cholesteatoma) usually overlies the incudostapedial joint. Therefore, erosion of the incus occurs commonly and this is frequently associated with a mild conductive hearing loss with air/bone gap of approximately 10–15 dB. If a child is too young to cooperate for behavioral audiologic testing, then auditory brainstem response testing can be helpful especially if the child is going to have surgery and there is a need to document hearing threshold in the affected ear.

For children with cholesteatoma, the best outcome is typically achieved with early identification by the primary care physician during routine otoscopic examination. In its earliest stages, congenital cholesteatoma will appear as a faint round or oval whitish mass medial to the anterior-superior quadrant of an intact eardrum. Therefore, pediatricians and family physicians are encouraged to be suspicious of any whitish mass in the middle ear that could be the early sign of an enlarging congenital cholesteatoma and refer appropriately. Having said this, there are various conditions that can be associated with detectable whitish areas in the eardrum and it is advantageous for any physician who examines the eardrums of children to know about the conditions that cause the appearance of whitish eardrum abnormalities that can be seen with an otoscope. Certainly hyaline deposits within the eardrum known as myringosclerosis appear as white densities easily visible in the eardrum. Myringosclerosis can be considered a sequela of OM and often can be seen in children with a history of frequent ear infections or persistent middle ear effusion and in children who have had insertion of tympanostomy tubes in their ears. These eardrum blemishes typically have irregular borders and can be seen to move with the eardrum when positive and negative pressure is applied with a pneumatic otoscope. There are three easy ways to differentiate the otoscopic findings in a child who has myringosclerosis from the findings in a child who has a middle ear mass:

1. *Color*: Myringosclerosis is bright white, cholesteatoma is faint whitish yellow
2. *Borders*: Myringosclerosis has patchy, irregular borders; cholesteatoma has a faint blurred, usually rounded, regular border
3. *Appearance with applied positive and negative pressure*: Myringosclerosis size does not change; cholesteatoma appears to get larger with applied positive pressure and seems to get smaller with negative pressure.

*First, the borders of a whitish density*: When a pneumatic otoscope is used the whitish mass that is a congenital cholesteatoma will appear to enlarge as positive pressure applied with the bulb on the otoscope presses the eardrum against the spherical mass in the middle ear but then seems to get smaller as the eardrum moves laterally, away from the middle ear mass as the pressure is released on the bulb of the otoscope and the eardrum lifts off the middle ear mass. In contrast, the findings are different in the eardrum of a child with whitish areas in the eardrum that are areas of myringosclerosis. In the case of myringosclerosis, the whitish patch moves with the eardrum, neither enlarging nor getting smaller with pneumatic otoscopy. In a child who has had chronic OM and has developed an atrophic flaccid retracted eardrum, the eardrum may rest on the promontory of the middle ear that is actually the basal turn of the cochlea and appear to be a round whitish mass suspicious for cholesteatoma. The perception of cholesteatoma in the middle ear that is actually a flaccid eardrum resting on the whitish round promontory of the middle ear can be differentiated from a middle ear cholesteatoma with adept use of a pneumatic otoscope, because the promontory of the middle ear is located inferior to the umbo of the malleus and a spherical middle ear cholesteatoma is usually located in the anterior-superior quadrant of the middle ear and the promontory of the middle ear is bony hard when palpated with a fine instrument wrapped in cotton while a cholesteatoma mass is soft and can be indented with gentle pressure applied to a small blunt instrument such as a calcium alginate fiber-tipped aluminum applicator (Table 19.2).

In early stages of acquired cholesteatoma, a primary care physician may observe a retraction pocket within the posterior-superior quadrant of the eardrum. An adept otoscopist with excellent diagnostic acumen will use the pneumatic otoscope to assess mobility of the eardrum and will begin to be suspicious if a retraction pocket in

**Table 19.2:** Differential diagnosis of whitish eardrum masses

| | *Myringosclerosis* | *Congenital cholesteatoma* | *Promontory* |
|---|---|---|---|
| Color | Bright white | Dull white/yellow | White or pink |
| Border | Irregular | Distinct | Distinct |
| Number of eardrum opacities | Many | One | One |
| Pneumatic otoscopy | Same size with + and – pressure | Larger with + pressure, smaller with – pressure | No change with pressure, or larger with + pressure |
| Location | Anywhere | Anterior to malleus | Central |
| History of Otitis Media/ETD/ Ear tubes | Yes | No | Yes |

the posterior-superior quadrant of the eardrum becomes adherent to the lenticular process of the incus and cannot be everted with negative pressure applied when pressure that indents the bulb of the pneumatic otoscope is released. This inability to evert a topographic indentation in the eardrum located in the posterior superior quadrant of the eardrum should be considered to be a finding that raises suspicion for presence of a developing cholesteatoma and should prompt the primary care physician to refer the child to an otolaryngologist for evaluation.

Imaging, such as CT or MRI, may be helpful in determining the size and anatomic location of cholesteatoma. Plain radiographs will generally only show a very large cholesteatoma and therefore are not useful. High resolution (≤1 mm slice thickness) CT scan of the temporal bones in the axial and coronal planes is the modality of choice because this imaging study can identify a small cholesteatoma in addition to any bony erosion that may have been caused by the cholesteatoma. This modality is also often helpful in determining the extent of disease, particularly mastoid involvement, which can be helpful in surgical planning.[14] Children with congenital cholesteatoma often have well-aerated mastoids, while those with acquired cholesteatoma usually have mastoid opacification. CT scans are particularly useful to evaluate for complications related to cholesteatoma. Ossicular destruction, erosion of the bone covering the facial nerve, dehiscence of the tegmen, and erosion of the horizontal semicircular canal can all be seen on CT, allowing for appropriate surgical planning.

One limitation of CT is that radiographically cholesteatoma is difficult to distinguish from fluid or granulation tissue. Preliminary studies have demonstrated some ability to distinguish these tissues types using diffusion weighted MRI.[33] MRI is superior to CT in detecting residual or recurrent cholesteatoma behind an intact TM graft. In addition, for some complications, MRI is superior such as evaluation of dural involvement, subdural or epidural abscess, encephalocele, sigmoid sinus thrombosis, or inflammation around the facial nerve.

The characteristic MRI appearance of cholesteatoma is slightly higher intensity than CSF on T1-weighted images and high signal intensity on T2-weighted images. Fat will have high T1 signal and low T2 signal and effusions will have low T1 and high T2 signals. Cholesterol granuloma can appear similar to cholesteatoma but will demonstrate capsular enhancement.

Some surgeons will operate on a cholesteatoma without a CT scan, particularly if the cholesteatoma is small, but many otologic surgeons do routinely obtain a CT prior to cholesteatoma for surgical planning purposes, and especially if the child has manifested worrisome symptoms such as vertigo or facial paralysis.

## COMPLICATIONS

Complications of cholesteatoma include eardrum perforation, secondary infections, hearing loss (conductive or less commonly, sensorineural), or vertigo. Secondary infections can be due to middle ear disease or water exposure. Infection can be caused by *Pseudomonas aeruginosa*, *Proteus* species, *Bacteroides*, or *Peptococcus-Peptostreptococcus*.[34,35] When otorrhea associated with cholesteatoma is malodorous, it is due to these secondary infections. Conductive hearing loss is common and is mostly due to incus erosion, but involvement of any of the ossicles can cause this type of hearing loss. Blockage of the ET can also cause a conductive hearing loss due to OM. Less commonly, patients have a sensorineural loss (in about 1%), usually secondary to a labyrinthine fistula. Cranial nerve involvement is also uncommon, but usually affects the 7th nerve and rarely the 8th. Facial paralysis can develop suddenly with a newly infected cholesteatoma or over time with gradual expansion of a cholesteatoma.

Cholesteatoma can erode semicircular canal otic capsule bone resulting in a labyrinthine fistula and this has been reported to occur in up to 10% of patients with

cholesteatoma.[36] A child with a labyrinthine fistula typically will have vertigo and/or nystagmus on pneumatic otoscopy (positive fistula test). They are less likely to present with sensorineural hearing loss, though this can happen as well. The horizontal canal is the most common site for a labyrinthine fistula. Patients with a fistula are at risk for suppurative labyrinthitis and subsequent profound hearing loss.

Cholesteatoma can erode through the boundaries of the mastoid resulting in intracranial complications such as meningitis, brain abscess compression of the temporal lobe, or venous thrombosis. Infection may also extend along the sternocleidomastoid muscle create a neck abscess (Bezold's abscess). Serious complications occur in <1% of patients. Any patient with cholesteatoma and spiking fevers, headaches or new pain, should undergo a CT scan to evaluate for impending complications.

## TREATMENT

Unless there is evidence of infection such as purulent drainage or erythema in the postauricular area, there is no need to prescribe antibiotics for a child with known or suspected cholesteatoma. Ototopicals, in the form of drops, will surround the cholesteatoma and can often penetrate just beyond the surface, but are not able to eradicate completely an infection especially if there is erythema of the skin of the ear canal and the postauricular soft tissues. In some cases, an acquired cholesteatoma can be managed with periodic otomicroscope examination, and debridement of an eardrum retraction pocket. Operating on a noninfected cholesteatoma is preferable and therefore ototopicals are often used in preparation for surgery.

Surgery is the mainstay of therapy for cholesteatoma; without removal, the cholesteatoma will continue to enlarge. The goals of surgery are to remove the cholesteatoma and provide a safe dry ear while also managing any complications that may have occurred. The secondary goal is for hearing preservation or restoration. In some cases, the goal of a first surgical procedure will be removal of cholesteatoma and ossicular reconstruction to improve hearing is best deferred to a second surgical procedure. The outcome of surgery is based in large part on the extent of disease.

The risks associated with surgery for cholesteatoma include hearing loss, facial nerve injury, taste disturbance, dizziness, cerebrospinal fluid leak, and eardrum perforation.[32] Permanent facial nerve palsy occurs in <1%. The facial nerve can be injured at the pyramidal turn when drilling the mastoid or the horizontal portion can be injured with dissection in the middle ear. Many authors use intraoperative facial nerve monitoring, though it is not proven that this reduces the risk of permanent injury. Facial nerve monitoring may be particularly helpful in cases where imaging shows altered facial nerve anatomy, revision cases, or patients who have had prior facial palsies. Delayed palsies usually recover over a period of weeks. Acute palsies may require reoperation with decompression of the facial nerve after any effects of local anesthetic have worn off.

Dizziness can occur with any middle ear surgery, but in cases where there is a labyrinthine fistula, the incidence is increased. Labyrinthine fistulas pose a unique set of problems. Generally, the desquamated epithelium is removed and the matrix is left intact on the lateral semicircular canal. Some authors recommend a canal-wall-down mastoidectomy at this point. Others advocate for removing the matrix and covering the defect with fascia. It is unclear if removing the matrix increases the risk for postoperative hearing loss.

Other complications can include graft failure or perichondritis. Graft failure occurs in 10-15% of cases, resulting in a TM perforation, which may require an additional procedure. Perichondritis of the conchal or auricular cartilage can also occur.

The only contraindication is a patient who is too sick to undergo surgery. Care must be taken in patients with cholesteatoma in an only hearing ear, but generally, the risks associated with leaving it in place are greater than the risk of additional hearing loss with surgical removal.

## SURGERY

To a certain extent, surgery for congenital cholesteatoma is differs from surgery for acquired cholesteatoma because of the anatomic sites where these types of cholesteatoma typically originate. The key to achieving success in surgery for cholesteatoma is knowing where to expect persistent disease and using a surgical approach that is most likely to expose these anatomic sites. Accordingly, the otologic surgeon should plan to gain access to the site where cholesteatoma is most likely to have begun to develop and where the cholesteatoma is most likely to be hidden from view during surgery. There are many clues to differentiating congenital from acquired cholesteatoma, but simply put those patients with cholesteatoma anterior to the malleus, with minimal history of OM and with a well aerated mastoid on CT scan are most likely to have congenital cholesteatoma.

## Congenital

A small congenital cholesteatoma that is detected early in a child's life usually can be removed, in toto, via a transcanal or a postauricular approach depending on location of the cholesteatoma and preference of the surgeon. In these cases, the small spherical or ovoid mass that is encased in a "matrix" can be fully exposed with a properly designed tympanomeatal flap and teased out of the mesotympanum, intact, using small instruments such as a ball probe or a "whirlybird". If the eardrum is torn during the dissection, it can be repaired with a fascia graft. Many variations of middle ear exploration have been described including one by Levi et al. in which two incisions are made in the TM itself around the cholesteatoma sac, rather than raising a full tympanomeatal flap.[37] These approaches are often appropriate for congenital cholesteatoma; in a review of 172 patients with congenital cholesteatoma, the mastoid was involved only in 23%.[7]

The most common site for congenital cholesteatoma to persist after surgery is anterior to the malleus in the area sometimes referred to as "the cog". To remove a congenital cholesteatoma that extends in a cephalad direction >2–3 mm beyond the level of the scutum the mastoid must be drilled in order to completely remove the cholesteatoma and enable the cog area to be visually inspected. Most experts recommend a complete mastoidectomy though some will perform only an atticotomy. Advances in instrumentation and surgical techniques have led some surgeons to utilize endoscopic surgery removal of these lesions without mastoidectomy. Regardless, the focus needs to be on good exposure of the anterior epitympanum. If a CT scan suggests that cholesteatoma is in the cog area anterior to the head of the malleus or if dissection of a cholesteatoma in the mesotympanum is showing that the cholesteatoma extends anterior and cephalad to the neck of the malleus, then it is advisable to remove the incus and head of the malleus so that the anterior epitympanum (cog) can be carefully inspected. Usually the incus can be sculpted and reinserted in the ear as an incus interposition ossiculoplasty to restore ossicular continuity and maintain or restore good hearing. There is no need to plan second look surgery for all children who have had surgery to remove a congenital cholesteatoma especially if the cholesteatoma is relatively small and contained within a matrix. However, if cholesteatoma is large and the matrix is disrupted before or during surgery and the cholesteatoma has had to be removed piecemeal then risk of persistence of cholesteatoma is higher and it might be advisable to plan a second look surgery to be done 6 months after the initial surgery. Further, whenever the surgeon cannot be sure that all cholesteatoma has been removed, then ossicular reconstruction can be deferred to a second surgery that should be done around 6 months after the initial surgery.

## Acquired

In patients with early acquired cholesteatoma that is developing in a shallow retraction pocket, a simple approach to management is to excise the eardrum retraction pocket. This can be done under mask anesthesia with a cup forceps. Indications for excision of a retraction pocket include the following: when the retraction pocket is progressively deepening or it is indenting the lenticular process or there is granulation tissue forming in the pocket. These are all signs of a developing cholesteatoma and therefore must be addressed. One of three things will happen after a retraction pocket is excised: (1) the ear drum heals normally (this is most common), (2) the ear drum heals but the retraction recurs, or (3) the ear drum does not heal at all, leaving a perforation. If there is a permanent perforation this can be repaired at a later time when there is no longer a risk for cholesteatoma formation. Any patient with a shallow retraction pocket needs to be monitored carefully because the retraction pocket can deepen and progress to develop into a cholesteatoma. Retraction pockets that have been excised must be monitored carefully as well to look for any recurrence before a large cholesteatoma forms. Long-standing retraction pockets lose some elasticity and thus may not revert to a neutral position. Deeper retraction pockets, particularly those adhering to the ossicles, must be resected and replaced with a TM graft. Each surgeon has a different threshold for the various treatment options.

A cholesteatoma that extends beyond the middle ear into the fossa incudus generally requires a mastoidectomy for complete removal. Before the advent of the surgical microscope and the drill, cholesteatoma was typically treated with exteriorization without complete removal. This way of managing cholesteatoma minimized operative morbidity such as facial paralysis, profound sensorineural hearing loss, and dural tears, but often left the patient with a chronically draining ear and progressive hearing loss. During the 1950s and 60s, William and Howard House's Otologic Medical Group introduced canal-wall-up (CWU) and other less extensive procedures to treat certain types of cholesteatoma.

Depending on the size and location of a cholesteatoma an atticotomy rather than complete mastoidectomy may suffice for removing or exteriorizing a cholesteatoma. The usual growth pattern of a cholesteatoma is to extend from the middle ear to the epitympanum and attic and then the mastoid air cells. Thus, there are cases where the lateral wall of the epitympanum (scutum), and cholesteatoma sacs are removed without further entrance into the mastoid air cells.

When a cholesteatoma extends beyond the attic, a complete mastoidectomy must be performed. Generally, the mastoidectomy procedure is performed with postauricular and endaural incisions, but some surgeons prefer an "inside out" approach where bone is removed through the ear canal and the attic is progressively enlarged, essentially starting with an atticotomy.

There are two main types of mastoidectomy: CWU and canal wall down. In CWU mastoidectomy, the posterior portion of the external auditory canal is preserved. Often this requires drilling of the facial recess (a small area bounded by the chorda tympani and facial nerve) to obtain the best access to the cholesteatoma. In a canal-wall-down procedure, the posterior portion of the external auditory canal is drilled down to the level of the vertical facial nerve, marsupializing the mastoid into the external ear canal and leaving one large cavity. Canal-wall-down mastoidectomies often require a meatoplasty to enlarge the external auditory meatus. The meatoplasty facilitates future examination and cleaning of the mastoid bowl. While a canal-wall-down mastoidectomy affords superior access to the cholesteatoma taking down the canal wall is not always necessary.

The most common location for persistent disease in acquired cholesteatoma is between the incus and the facial nerve (medial to the incus). Therefore, the incus often must be removed to visualize the space between the body of the incus and the horizontal portion of the facial nerve just anterior to the second genu of the nerve. As mentioned above, if the incus has to be removed in order to inspect the sites where cholesteatoma is most likely to be present, then the incus can be sculpted and reinserted in the ear sitting atop the stapes capitulum and medial to the umbo of the malleus.

Most experts advocate performing a canal-wall-up procedure when possible. Such procedures have the advantage of maintaining a normal appearance (no large meatoplasty), with easier ability to fit hearing aids and less chronic care. Unfortunately, these patients may be at higher risk of persistent or recurrent disease and therefore may require additional future surgery. Canal-wall-down procedures usually do not require a second look procedure but do require a lifetime of care and yearly cleanings. Osborn et al. suggest the superior hearing outcomes and ease of care in CWU procedures outweighs the possible need for repeat operations (often performed in CWU procedures) in most children with cholesteatoma.[38]

Some patients who undergo a CWU procedure require a planned second look procedure 6 months to 1 year after their initial operation. This is done to examine the surgical site for any residual cholesteatoma and eradicate it prior to formation of a large cholesteatoma. Following CWU procedures, recurrent or residual cholesteatoma can hide medial to an intact eardrum or skin overlying the mastoid cavity.[14] Second look procedures are performed in patients with a large extent of disease at the initial surgery or with disease in difficult areas to eradicate (such as the sinus tympani). Second look procedures are also often done in children with large congenital cholesteatoma that adhere to many middle ear structures. Recent literature has suggested diffusion weighted MRI can effectively differentiate cholesteatoma from scar tissue, granulation and fluid and therefore may represent an alternative to second look procedures in the future. Many otologists also use a second look procedure to perform an ossicular chain reconstruction (OCR) (discussed later).

Canal-wall-down mastoidectomies usually only require one surgery. They afford better visualization of most cholesteatoma, and are thus regarded by many as "safer", especially in inexperienced hands or in patients with very extensive disease. Sometimes the true extent of disease is only realized in the operating room, thus the determination between CWU and canal wall down is made intraoperatively. Any patient undergoing a CWU mastoidectomy should be counseled regarding the possibility of a canal-wall-down procedure, in case there are unexpected findings in the operating room.

Other groups that may deserve canal-wall-down procedures include those patients that are not available to for regular follow-up and disease monitoring. Recurrence in someone with a canal-wall-down defect is more apparent and easier to treat than in someone with a prior CWU surgery. Patients with cholesteatoma that has caused damage to the posterior external auditory canal or those who had prior, failed CWU procedures also may warrant canal-wall-down procedures. Some people also advocate canal-wall-down procedures in patients with ongoing

poor ET function and poorly pneumatized middle ear and mastoids.[39] An only hearing hear may be a relative contraindication to a CWU mastoidectomy.

Special consideration should be given to patients with labyrinthine fistula or facial nerve paralysis. Often, patients with labyrinthine fistulas require canal-wall-down procedures, particularly in an only hearing ear. In these cases, some of the matrix is left in place over the fistula so as not to expose the labyrinth. They can be monitored for cholesteatoma growth via the common cavity. However, in cases where there is a normal contralateral ear, a small fistula, and a large mastoid, the posterior ear canal can be left intact. The matrix is then removed from the lateral semicircular canal and the fistula is patched with fascia. In cases of facial paralysis, a facial recess approach is needed to expose the horizontal and vertical portions of the nerve. Decompressing the nerve may be necessary but the sheath should not be opened.

A radical mastoidectomy is rarely indicated in benign disease such as cholesteatoma unless there is persistent disease around the ET or round window, which the clinician is unable to eradicate after multiple attempts. It is performed by drilling down the posterior ear canal, eliminating the middle ear space and ossicles, and plugging the ET. There is no attempt to preserve hearing.

Cholesteatoma located in other areas, such as the perigeniculate area or petrous apex, require other procedures. In these cases, combinations of the transmastoid, middle cranial fossa, and/or the transsphenoidal approach may be necessary.

## OSSICULAR CHAIN RECONSTRUCTION

The secondary goal of any cholesteatoma surgery is hearing preservation or reconstruction. Many times the cholesteatoma involves the ossicular chain. Because the disease process can be so aggressive and have such serious complications, even seemingly normal structures may need to be removed to allow eradication of disease. Initial hearing results may be worse than preoperative hearing levels, but with a subsequent OCR they are often quite good. Most consider air–bone gaps < 30 dB as an acceptable outcome after OCR. The OCR can be performed at the time of the cholesteatoma resection if it is certain the cholesteatoma has been completely removed and does not involve the ossicles or it can be performed at a later date. If the cholesteatoma is extensive and located at multiple sites in the mesotympanum, epitympanum, mastoid air cells, so that even after careful dissection you cannot be sure that there isn't some cholesteatoma left behind, a second look is recommended. By delaying the OCR to the second look, the reconstruction is not put at risk. That is, if there is any residual cholesteatoma after the first surgery, this can grow to invade or disrupt portions of an ossicular reconstruction In addition, parents are likely to be compliant with the recommendation for second look surgery if they understand that a goal of the second surgical procedure will be improvement in hearing and the best chance for sustained good hearing is when the ossicular reconstruction is done after all cholesteatoma has been removed from the ear. In summary, if there is concern for residual cholesteatoma (such as in the sinus tympani) or there was extensive cholesteatoma at the time of the initial surgery, ossicular reconstruction should be delayed 6–12 months as part of a second look procedure.

Cholesteatoma on the lateral surface of the incus can often be dissected free without removal of the incus, but involvement of the medial surface usually necessitates removal. Cholesteatoma that extends medial to the head of the malleus usually requires both the incus and head of the malleus to be removed (this is often seen with congenital cholesteatoma). Any disease near the stapes should be dissected with the utmost care to avoid footplate dislocation and sensorineural hearing loss. Cholesteatoma on the footplate of the stapes often is difficult to remove and therefore some may be left behind. Aggressive dissection on the footplate can result in sensorineural hearing loss or dizziness and often it is prudent to defer complete removal to a second look procedure, with OCR at that time. Often at the second look, residual cholesteatoma on the footplate will have formed a small keratin pearl which is easier to remove. The ossicles can be reconstructed with bone, cartilage, or prosthetic material. Adhesions can be prevented by placing silastic sheeting over the promontory at the time of the first surgery.

## PROGNOSIS

Timing for the first postoperative visit varies widely depending on surgeon preference and the surgery performed. Some surgeons see their patients on postoperative day 1 to remove the dressing themselves. These patients are often admitted to the hospital overnight for observation. Others wait as long as 3 or 4 weeks before the first postoperative office visit. If a wick is placed at the time of surgery it is generally removed in 5–10 days after surgery. Open cavities

require variable amounts of cleaning over the first few weeks after surgery and most patients are seen in the office every 2–3 weeks. Full epithelialization does not usually occur before 12 weeks. Once the mastoid bowl is healed, the patient should return at least every 6–12 months for cleaning. Follow up should be continued indefinitely as cholesteatoma can recur years later. Kuo et al. found the mean detection time for recidivism was 10.4 years after the initial surgery.[40]

Eradication of cholesteatoma is almost always possible. This may require multiple procedures, however. Congenital cholesteatoma tends to recur less than acquired. Small, well-encapsulated cholesteatoma of either type generally does not recur.[32] Looking at children with congenital cholesteatoma, Potsic and colleagues found recurrence was increased when the extent of disease increased from one quadrant to two or more and increased even further when the ossicles were involved.[7]

The recurrence for acquired cholesteatoma may be as high as 50%.[41] Factors that predispose a patient to recurrence include children younger than 8 years old, or those with ET dysfunction, ossicular chain damage or large cholesteatoma.[42] The facial recess and sinus tympani can be difficult areas to access surgically and thus are often the site of recurrence. In congenital cholesteatoma, recurrence is usually located near the cog.

Canal-wall-down procedures may have a lower recurrence rate than those in CWU (5–10% vs. up to 40%), though it can be difficult to tell if this represents recurrence or merely persistence of disease.[43] On the other hand, Shirazi found similar rates regardless of the procedure performed.[44]

Hearing outcome is largely dependent on whether there is ossicular chain damage, especially to the stapes superstructure, and preoperative hearing levels.[45] Cholesteatoma is a common cause of permanent conductive hearing loss. Death from intracranial complications of cholesteatoma is uncommon and decreasing in incidence because of earlier recognition, more timely surgical intervention, and better antibiotic therapy.

Children should be followed carefully after surgery to monitor for recurrence that can occur many years later. Small pieces of cholesteatoma left behind at the first surgery can grow into larger cholesteatoma (residual disease). ET dysfunction, which may predispose a patient to the first cholesteatoma, may still be present, predisposing to a second one. A patient should undergo otologic and audiologic examination frequently and there should be a low threshold for obtaining a CT scan if recurrence is suspected. Patients who undergo canal-wall-down procedures generally need to be followed for life to ensure the mastoid bowl does not accumulate debris. Patients with a new TM perforation or a newly draining ear should be suspected of having a cholesteatoma. Any unexplained decrease in hearing or new ear drainage should prompt evaluation for recurrence.

## FUTURE

We are just beginning to understand the role of biofilms in many head and neck diseases. In cholesteatoma, there is some evidence that biofilm formation contributes to the erosive nature of cholesteatoma, but the evidence is still limited.[46] With improved perinatal imaging techniques the pathophysiology of cholesteatoma may be elucidated further. In the future, diffusion weighted MRI may aid in diagnosing cholesteatoma at the outset or even monitoring for recurrent disease. Use of otoendoscopes may aid in better eradication with first surgeries, leading to less need for second look procedures or even canal-wall-down mastoidectomies.

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CHAPTER

# 20

# Auditory Neuropathy Spectrum Disorder (ANSD)

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## INTRODUCTION

Auditory neuropathy spectrum disorder (ANSD) is an increasingly recognized hearing disorder with a variety of behavioral presentations, ranging from mild difficulty hearing in background noise to profound hearing loss.[1,2] Unlike traditional sensorineural hearing loss (SNHL), where dysfunction stems initially from damaged or absent outer hair cells, ANSD is characterized by the dysfunction of the inner hair cells, the auditory nerve, or the synaptic region connecting the inner hair cells to the auditory nerve.[2–8] Approximately 1 in 10 cases of identified SNHL are ANSD.[9,10] Often the exact etiology of ANSD remains unknown and genetic testing is unyielding. Predicting the appropriate course of intervention is difficult in infants and young children who are unable to offer behavioral information regarding their sound awareness. Even when hearing thresholds are finally identified in the younger population they are usually not reflective of true speech understanding abilities. In addition, those with ANSD who seem to function successfully in quiet often struggle greatly when listening to speech in the presence of background noise.[1,6,11,12] The wide variety in behavioral presentation also makes speech and language development extremely difficult to predict in infants and children. Frequent assessment of behavioral hearing, combined with periodic speech and language evaluations, seem to be the current gold standard to determine the most appropriate course of intervention on a case-by-case basis. Electrophysiologic assessment beyond the level of the auditory brainstem response (ABR), such as the cortical auditory-evoked potential (CAEP), may also prove to be useful in predicting speech and language outcomes in small children.[13] It is important to gain a better understanding of speech and language outcomes in each individual child, so that the most appropriate form of intervention may be selected, to help the child develop normal speech and language skills.

## PHYSIOLOGY OF ANSD

SNHL is a term that most otolaryngologists are familiar with identifying and most audiologists are familiar with treating, whether it is with hearing aids, speech therapy and/or cochlear implantation. Hearing evaluations were quite routine until the 1990s when hearing professionals began to question why some of their "Deaf" patients could respond to sound. The first report on auditory neuropathy was published in 1996,[6] which described 10 patients with dys-synchronous ABRs and present otoacoustic emissions (OAEs). Soon after Berlin et al.[9] discovered that 1–2% of hearing impaired children in schools for the Deaf in the United States had present OAEs and 10–12% had partial OAEs, indicating normal outer hair cell function in "Deaf" patients. Similar studies confirmed these numbers.[14] A more recent report of ANSD in an "at-risk" population of newborns found that around 5% of patients diagnosed with hearing loss were confirmed to have ANSD.[15] Thus, began the investigation into the physiology of ANSD and consequently the naming of the disorder.

One possible etiology for ANSD involves a dysfunction or absence of the inner hair cells within the cochlea. One row of inner hair cells lies medially within the organ of Corti in the cochlea and totals ~3000 at birth.[16] The inner hair cells are sensory cells responsible for transforming

mechanical energy from the traveling wave in the organ of Corti via stereocilia activation, to chemical signals, to electrical impulses that stimulate type I auditory nerve fibers. In some cases of ANSD, the inner hair cells are damaged or absent at birth.[3] There may also be a problem of the chemical neurotransmitters within the inner hair cells in those with ANSD, resulting in dys-synchronous firing of the auditory nerve. A mutation in the *GJB2* gene (coding for the connexin 26 protein) results in a presynaptic form of ANSD.[17] These patients may present with perception of sound but often have a difficult time understanding the meaning of a message due to the intermittent information traveling from the auditory nerve to the brain. Since the connexin 26 protein inefficiently processes potassium in these patients, inner cell death is inevitable and over time will destroy outer hair cells as well, leading to the "loss" of once present OAEs.[18] A mutation in the otoferlin (*OTOF*) gene also results in a dysfunction of the inner hair cells,[7] and auditory information cannot be appropriately transmitted to the auditory nerve. In these cases, outer hair cell function is preserved, and ABRs will be absent.[7]

Finally, the auditory nerve and/or brainstem auditory pathway nuclei may be dysfunctional in cases of ANSD. Children with cochlear nerve aplasia or hypoplastic nerves, gene mutations resulting in auditory neuron dysfunction, and disorders such as hyperbilirubinemia or progressive demyelinating disorders, will present with a hearing loss that is consistent with ANSD. There have been many cases of cochlear nerve aplasia, both unilaterally and bilaterally, which constitute a form of ANSD where the outer hair cells are working yet there is no behavioral perception of sound.[19] In other cases, magnetic resonance imaging (MRI) has revealed small but present cochlear nerves. This creates cases of ANSD with present and functioning outer hair cells, absent or grossly abnormal ABRs with the presence of a cochlear microphonic (CM), while the remaining nerve fibers deliver some incomplete sound information to the brain. A lack of the protein pejvakin results in a dysfunction in the neurons along the afferent auditory pathways in the brainstem.[20] This higher-up nerve dysfunction results in grossly abnormal ABRs, with intact cochlear hair cell function.[20] Hyperbilirubinemia, one of the biggest risk factors for SNHL and ANSD, has also been identified as a cause for destruction of auditory nuclei in the brainstem and auditory pathway neurons.[21] There are also true auditory neuropathies associated with demyelination of neurons in the brain, such as in Pelizaeus–Merzbacher disease (PMD). Those with PMD have normal neuronal connections in the brain; however, a mutation in the *PLP1* gene leads to abnormal myelination of the neurons which eventually leads to a progressive degeneration around the cortical nerve fibers.[22] Patients with PMD have absent or grossly abnormal ABRs in the presence of normal outer hair cell function, yet they are able to understand speech and language (depending on their level of cognition), though they have difficulty hearing in background noise.

## CLINICAL PRESENTATION OF ANSD

"Spectrum" was appropriately added to the title of auditory neuropathy in 2008,[23] and for good reason. The range of behavioral hearing in this disorder is vast and is inevitably different with every case. Often once behavioral hearing thresholds are obtained, they do not reflect the true ability of the patient to understand speech and language. For example, a patient with ANSD may have a sound awareness threshold in the mild hearing loss range, yet may have no ability to repeat a word spoken to them in quiet when visual cues are denied. From experience testing many children with ANSD in our clinic, we have observed some to exhibit pure-tone hearing thresholds in the moderate hearing loss range, and when presented with narrowband noise, their thresholds may improve to a mild hearing loss range. This may indicate that as more of the nerve fibers are stimulated, the better their sound awareness becomes. But we must be careful when interpreting thresholds with this disorder as they almost always indicate only a level of sound awareness and not speech understanding capabilities. The ability of patients with ANSD to understand speech in quiet and speech in the presence of background noise is still often severely impaired implying that the pure-tone audiogram is not indicative of the ability to understand and develop speech and language.

There are a few instances where, based on etiology, speech perception and speech development can be predicted. For example, those identified genetically with certain otoferlin mutations may initially present with OAEs and profound hearing loss.[4] These patients will not develop speech and language without the intervention of a cochlear implant and intense speech and language therapy. On the contrary, patients identified with unilateral cochlear nerve aplasia usually develop speech and language normally with their unaffected ear. They may require some mild intervention, e.g. the use of a frequency modulation (FM) system in the nonaffected ear, to help them in the classroom, and the extremes of using a hearing aid or cochlear implant are not necessary.

**Table 20.1:** Triaging auditory neuropathy spectrum disorder

| | *Tympanometry* | *MEMRs* | *OAEs* | *ABR* |
|---|---|---|---|---|
| Normal hearing | Type A—normal | Present | Present | Present |
| Sensorineural hearing loss | Type A—normal | Elevated or absent | Absent | Present according to degree of hearing loss |
| ANSD | Type A—normal | Elevated or absent | Present initially may become absent over time | Grossly abnormal or absent |

(ABR: Auditory brainstem response; ANSD: Auditory neuropathy spectrum disorder; MEMRs: Middle ear muscle reflexes; OAEs: Otoacoustic emissions).

Unfortunately, most of the time the etiology of the ANSD is unknown, and it is impossible to predict how an infant or small child perceives sound and consequently how they will develop speech and language. This gives foundation for frequent speech and language evaluations, performed by speech-language pathologists, throughout the first few years of life. By monitoring speech and language development, at a certain point it will become clear as to whether or not the child will develop speech and language, and if intervention is needed. If the child exhibits some sound awareness (i.e. looking when the dog barks) he or she may seem to have appropriate receptive language skills at a very young age. As the child becomes older, the speech and language evaluations will monitor this progress and determine if both receptive and expressive language skills are emerging appropriately per their age range.

If speech and language development does not seem to be progressing as the parents would like, intervention may be warranted. The first form of intervention for ANSD is an FM system, hearing aids, or both used together. An FM system and hearing aids may be more useful for children with ANSD who are able to understand speech and language in quiet, but struggle in background noise.[24] The most extreme form of intervention would be cochlear implantation. In cases where the VIIIth nerve is absent on the MRI, and the absence is confirmed by no ABR, no behavioral response (whenever possible) and no cortical response, cochlear implants are not warranted. There have been approximately five cases in our clinic over the past few years where the VIIIth nerve appears absent on the MRI; however, there is evidence of some neural synchrony on the ABR and/or some behavioral responses to sound with functional sound perception. These rare cases reinforce the need for the cross-check principle[25] not only within the realm of audiology, but also between disciplines, when managing and making recommendations for children with ANSD.

## AUDIOLOGIC ASSESSMENT

A full audiologic evaluation is the best way to differentiate an individual with ANSD from an individual with SNHL, and it can aid in determining his or her ability to understand and produce speech. Specifically, there are three tests within the audiologic evaluation that can diagnose definitively the presence of ANSD: middle ear muscle reflex (MEMR) assessment, OAE assessment, and an ABR evaluation. The results of this "triage" of tests can rule out or confirm the presence of ANSD.[1] A quick reference for these tests and their outcomes in normal hearing patients, those with SNHL, and those with ANSD can be found in Table 20.1.

### Acoustic Immittance

Audiologists, much like otolaryngologists, evaluate middle ear function first and foremost. Audiologists use acoustic immittance to investigate tympanic membrane movement via tympanometry, to determine the presence of normal middle ear function. In the presence of normal middle ear function, i.e. no fluid or middle ear disease, an MEMR threshold search can be performed. MEMRs are evaluated by using a probe attached to the tympanometer to create a pressure tight cavity in the ear canal. Once a seal has been obtained a series of loud beeps (up to 110 dB HL) are presented to the ear. The middle ear mechanically transmits the signal into the inner ear, and then the VIIIth nerve sends the signal to the cochlear nucleus in the medulla. The signal is then transmitted to the ipsilateral and contralateral superior olivary complex which is where the VIIth cranial nerve nuclei are located. A branch of the VIIth nerve connects efferently to the stapedius muscle in the middle ear space. If the VIIth nerve nuclei has enough stimulation (i.e. the sound is loud enough), it will trigger a reflexive contraction in the stapedius muscle. The contraction of the stapedius muscle slightly stiffens the motion of the bones in the middle ear, which lessens

the transduction of sound into the inner ear. Present MEMRs indicate that the VIIth and VIIIth nerves are intact but also that IHCs are functional. In patients with ANSD, the MEMRs will be absent, or in some cases, can be present yet extremely elevated in threshold.[26,27] This is due to the site(s) of lesion in ANSD, indicating a breakdown in the transmission of the auditory signal beyond typical outer hair cell (sensory) hearing loss. However, the MEMR will be absent or elevated in those with traditional severe to profound SNHL, therefore relying on acoustic reflexes alone to determine the presence of ANSD is not possible.

## Otoacoustic Emissions

In addition to evaluating MEMRs, audiologists also evaluate outer hair cell function via assessment of OAEs.[28] These OAEs are the by-product of the contractile properties of the outer hair cells. These properties play a crucial role in amplification and of fine frequency discrimination of sounds reaching the cochlea.[29] When the outer hair cells are present and functioning appropriately, an OAE can be elicited. In patients with ANSD, since the outer hair cells are usually unaffected, OAEs are present. In some cases, OAEs will become absent with time due to over amplification from the use of high-power hearing aids. In those patients with traditional SNHL, OAEs will be absent in the frequency range where more than a mild hearing loss is present. Baffling to many audiologists before the discovery of ANSD were patients with severe to profound hearing loss with present OAEs. Therefore, one hallmark of ANSD is the presence of OAEs with a moderate, severe, or profound hearing loss.

## Auditory Brainstem Response

The final piece of information necessary to make a diagnosis of ANSD is the ABR. This electrophysiologic evaluation requires the use of noninvasive electrodes attached to the head to measure electrical activity along the auditory brainstem, indicating sounds are reaching specific nuclei. This procedure can be performed on patients while they are awake if they are able to be still. In most instances, the ABR is performed on sedated infants or small children who are difficult to test behaviorally. The ABR can be used to estimate frequency-specific hearing thresholds by presenting toneburst stimuli to each ear via insert earphones. To rule out the presence of ANSD, click stimuli are presented to each ear using two different polarities, rarefaction and condensation, to ensure a true neural

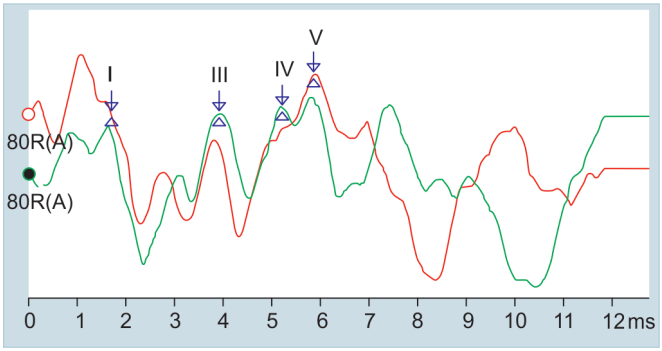


**Fig. 20.1:** An ABR in an individual with normal hearing recorded with both rarefaction (green waveform) and condensation (red waveform) polarities. (ABR: Auditory brainstem response).

response. In those with normal hearing, a normal ABR will reveal the presence and repeatability of waves I–V, when both polarities are overlapping (Fig. 20.1). Those with ANSD have an absent or atypical neural response represented by the ABR. They exhibit what appears to be a mirror image of waveforms when using the rarefaction and condensation polarities, instead of repeatable waves I–V. This mirror image is created by the CM, the gross electrical potential from all of the hair cells in the cochlea, triggered by the simple movement of the traveling wave along the basilar membrane. When the polarities are reversed, the electrical signal from the hair cells in the cochlea will follow the change in stimulus polarity, and the CM will invert. In the past, many audiologists would only use one polarity and run it twice to check for repeatability of morphology. Often the CM can "ring", and if only one polarity is used, a cochlear response may be mistaken for waves I–V. Therefore, it is absolutely pertinent to run two different polarities at high intensities to investigate if there is a true neural response from the auditory nerve and brainstem, or if there is just a response originating from the cochlea.[30] In ANSD, the CM varies in amplitude and duration. It can ring for several milliseconds or be much shorter as shown in Figure 20.2.

## Additional Electrophysiologic Assessment

Several investigators[31] are currently examining cortical auditory function in infants and young children diagnosed with ANSD to better understand cortical maturation, using CAEPs. Present CAEP responses, indicated by a positivity around 80–100 ms (P1) and a negativity around 200 ms (N2), indicate that sound is reaching the primary auditory cortex in the temporal lobe. In addition to identifying

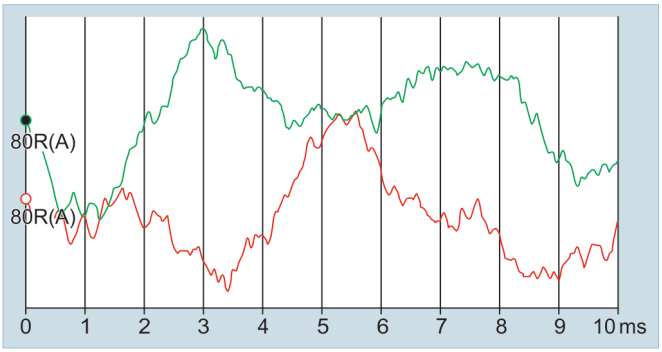


**Fig. 20.2:** An ABR in an individual with ANSD, with only a small cochlear microphonic (CM) and no neural response. (ABR: Auditory brainstem response; ANSD: Auditory neuropathy spectrum disorder).

the presence or absence of a response, the latency of P1/N2 also provides useful information in relation to the processing of the auditory signal in the cortex. The more delayed the latency of P1/N2, the longer it takes for an auditory signal to reach the primary auditory cortex, and therefore the more severely impaired the auditory pathway is presumed to be. Many children with ANSD have been observed to have a present P1/N2 response, although it is delayed in about one third of children.[31] In our laboratory, we have seen 18 children with ANSD for CAEP testing, in which 10 had present CAEPs bilaterally, and 6 had present CAEPs in only one ear, for a total of 89% of children with ANSD exhibiting a present cortical response. Please see Table 20.2 for a further breakdown of CAEPs in our ANSD population. Some investigators[31] are also beginning to investigate cortical auditory development in children fitted with hearing aids or cochlear implants. Speech and language development is almost impossible to predict in children with ANSD, unless a clear site of lesion can be identified and confirmed by behavioral testing, as in cases where the MRI reveals the absence of a cochlear nerve, or genetics testing reveals a specific genetic mutation. In most cases, etiology is unknown and therefore predicting sound perception and speech-language development is impossible. Cardon and Sharma[31] have found, using CAEPs, that the latency of P1 postcochlear implant correlates positively to speech perception measures, i.e. the more delayed in latency the P1 is, the more delayed speech and language perception appears. Through their research, Cardon and Sharma[31] have demonstrated that using CAEPs can provide clinical utility in helping to predict speech and language outcomes in the ANSD population. The CAEP may one day prove significant in predicting the best means of intervention for a child with ANSD based on the presence and latency of the P1/N2 response. Future research is geared in this direction.

## Behavioral Audiologic Evaluation

The staple of audiologic behavioral testing is the audiogram, which uses behavioral responses to map out perception of hearing. A listener is asked to raise their hand or press a button when they "hear the beep", which is usually a simple, single frequency, pure-tone stimuli delivered in a noiseless environment. The presentations are reduced in intensity until the listener can only detect the sound reliably about 50% of the time, therefore obtaining a threshold of hearing. Pure-tone perception is obtained in the low pitches, beginning usually with 250 Hz, up to the high pitches, around 8000 Hz. Ultrahigh frequencies can also be assessed, up to 20,000 Hz. Most patients with SNHL will exhibit an increase in hearing threshold at the frequencies where hearing loss, or cochlear damage, is present. The audiogram is a reliable tool for these patients and usually correlates well with speech understanding.[32] However, for those with ANSD, the audiogram may reflect sound awareness, but does usually not reflect the true ability to understand speech. In theory pure-tone stimuli only stimulate one frequency that may only stimulate one or a few inner hair cells, which concurrently may only stimulate a few nerve fibers. As long as some of those inner hair cells and nerve fibers are working, the tone will be perceived. However, if there is not a complete ability of the inner hair cells or the auditory nerve to capture rapid fluctuations in pitch and intensity, such as in conversational speech, an individual with ANSD might be able to perceive that someone is talking, but will not be able to understand what is being said. Therefore, the audiogram in patients with ANSD should be used in conjunction with other means of speech perception, such as word recognition in quiet and word recognition in background noise.

Word recognition is usually performed in the clinic by audiologists in order to make a comparable comparison to the audiogram. This is a simple task wherein the audiologist presents a list of 25 one-syllable words in quiet, at a clearly audible level, to each ear to get a percent correct score. Word recognition and the audiogram should reflect one another in those with normal hearing. If a patient is identified with SNHL, the words will be presented at a level that will still be clearly audible to them, and if the sound is not so loud that it is distorted, their scores are usually good in quiet. In patients who have ANSD, more often they perform

**Table 20.2:** CAEPs in ANSD

| *Subject ID* | *Age (years)* | *ABR* | *CAEP* | *Delayed P1* | *Delayed N2* | *Abnormal morphology* | *Reduced amplitude* | *Speech development* |
|---|---|---|---|---|---|---|---|---|
| 1 | 9.6 | Absent | Bilateral | Yes | Yes | No | Yes | Age appropriate |
| 2 | 2.2 | Absent | No response | N/A | N/A | N/A | N/A | Delayed |
| 3 | 5.4 | Absent | Right ear only | No | No | No | No | Delayed |
| 4 | 8.6 | Abnormal | Bilateral | Yes | No | Yes | Yes | Delayed |
| 5 | 0.9 | Absent | Bilateral | Yes | Yes | No | Yes | In progress |
| 6 | 0.5 | Abnormal | Bilateral | Yes | Yes | Yes | Yes | In progress |
| 7 | 5.1 | Absent | Left ear only | No | No | No | No | Age appropriate |
| 8 | 1.1 | Absent | Right ear only | No | No | No | No | Delayed |
| 9 | 0.6 | Abnormal | Bilateral | Yes | No | No | No | Delayed |
| 10 | 9.9 | Absent | Left ear only | Yes | Yes | No | Yes | Delayed |
| 11 | 10.4 | Absent | No response | N/A | N/A | N/A | N/A | Delayed |
| 12 | 1.6 | Absent | Bilateral | Yes | Yes | Yes | Yes | Delayed |
| 13 | 1.5 | Absent | Left ear only | Yes | Yes | No | No | Delayed |
| 14 | 0.8 | Absent-left ear; present in the right ear | Right ear only | Absent | Yes | Yes | Yes | Delayed |
| 15 | 6.7 | Abnormal | Bilateral | Yes | Yes | Yes | Yes | Delayed |
| 16 | 4.8 | Absent | Bilateral | No | No | No | No | Delayed |
| 17 | 1.2 | Absent | Bilateral | Yes | Yes | No | No | In progress |
| 18 | 1.4 | Absent | Bilateral | Yes | Yes | Yes | Yes | Delayed |

(ANSD: Auditory neuropathy spectrum disorder; CAEPs: Cortical auditory-evoked potentials).

much worse on word recognition than their audiogram would suggest.[6,12] There are a few patients, however, that will still excel with word recognition, as long as the words are presented in quiet. When speech is presented to the listener in noise, word recognition becomes much harder and almost impossible for those with ANSD.

### Speech Language Evaluation

The variation in clinical presentation of hearing loss in ANSD leads to difficulties predicting speech and language development in infants and young children. Due to earlier identification with newborn hearing screenings, more and more infants are being identified with ANSD shortly after birth. Therefore, the challenge lies in determining if and how these children will develop speech and language skills. Parents are encouraged to have an early baseline speech and language evaluation. Usually these evaluations will consist of parental interviews and observation of the child in the evaluation session. Based on the findings of this initial evaluation, the speech language pathologist will recommend periodic evaluations to track the progress the child is making. The speech language evaluations in the first 18 months of life are the most pivotal in indicating if the child will develop speech and language without any type of intervention.

## ETIOLOGY OF ANSD

### Genetic Links

Manchaiah and colleagues[33] provided an excellent review of the genetic causes of ANSD, and Sininger[10] estimates that up to 40% of ANSD cases may be due to genetic dysfunction. Many nonsyndromic mutations have been reported on in the literature and have a phenotype consistent with ANSD, including otoferlin (DFNB9), pejvakin (DFNB59), and connexin 26 (GJB2). A clinical presentation of ANSD can also be found in many well-known hereditary syndromes involving neurological degeneration, such as Friedreich ataxia, Charcot–Marie–Tooth (CMT) disease, and PMD. Please see an earlier section for more information on these syndromes.

There are a few nonsyndromic mutations that are well reported on in the literature. The protein otoferlin is expressed in the inner hair cells within the cochlea, and when a mutation occurs, the inner hair cells become dysfunctional,[7,33] therefore, impeding a clean chemical signal from reaching the auditory nerve.

### Risk Factors

There are many risk factors and red-flags for infants and children with ANSD. In our experience, and in the literature, two of the biggest red-flags when investigating the presence of ANSD is a birth history including a stay in the neonatal intensive care unit (NICU) and prematurity.[1,10] An estimated 3 out of 1000 infants admitted to the NICU are at risk for being identified with ANSD.[10] There are many reasons a child may be transferred to the NICU after birth, and many of those have been identified in the literature as risk factors for ANSD: low birth weight, brain trauma including anoxia, exchange transfusions, respiratory distress and/or artificial ventilation, ototoxic drugs, and anemia.[1]

One of the two most common risk factors for children identified with ANSD is a history of hyperbilirubinemia.[1,10] The accumulation of bilirubin in children with jaundice has been shown to have a detrimental effect on the auditory nuclei in the brainstem as well as some parts of the auditory nerve.[21] The other most common risk factor for children identified with ANSD is a positive family history of hearing loss.[10] Berlin and colleagues[1] report that approximately 16% of their 260 patients with ANSD have a genetic link, while Sininger[10] estimates up to 44% of children have a positive family history of hearing loss. Although there is a discrepancy in these numbers, it is important to understand that family history of hearing loss should be explored. It is important to note that approximately 38.5% of children identified with ANSD have no accompanying risk factors and a normal birth history.[1] If there is no family history of hearing loss or acquired trauma in these cases, it is almost impossible to determine the etiology of their ANSD.

## MANAGEMENT OF ANSD

Since the behavioral presentation of ANSD varies greatly from one case to the next, the first step in managing this disorder involves close monitoring of the child's hearing and speech abilities. Routine audiologic assessment is crucial in monitoring the degree of sound awareness in those with ANSD, especially in infants. With an increase in newborn hearing screenings, ANSD is able to be identified in infancy, provided the correct protocol of OAEs and ABRs are used, yet infants are unable to indicate what they are hearing and comprehending. Serial audiograms are important in monitoring an infant's sound awareness and localization abilities, as they develop over the first few years of life. However, the meaningfulness of an

infant or child's level of sound awareness is extremely important to assess, and should be frequently monitored via speech and language evaluations. Receptive and expressive language abilities can be explored via routine parental questionnaires beginning in infancy, and through speech and language evaluations as the child ages. The key is to focus on the amount of progress the infant or child is making from one speech and language evaluation to the next. Progress in both expressive and receptive speech and language skills will be the biggest predictor of how and how fast to move forward with intervention for these children.

### Working in an Interdisciplinary Team

At the same time serial audiologic evaluations and speech and language evaluations are occurring, it is often pertinent to involve other areas of medicine, to obtain the full picture of the child and their diagnosis of ANSD. Usually imaging studies are the first course of action recommended by otolaryngologists to investigate possible malformations as the etiology for ANSD. A consultation with a genetic counselor is usually beneficial to find hereditary or nonhereditary mutations or associated syndromes that may be associated with ANSD, such as GJB2-related deafness. An ophthalmology referral is also helpful to rule out any visual problems in the child and to rule out any comorbid progressive disorders, such as Ushers syndrome. A neurology consultation is useful in investigating overall brain function and to investigate the presence of other neuropathies in the body in very young infants and children that may or may not be apparent. A vestibular evaluation is also helpful to assess balance function and to help decide the preferred side for cochlear implantation.

## INTERVENTION

Most children with ANSD will require some sort of intervention in order to develop expressive and receptive speech and language skills. Berlin and colleagues[1] reported that only 5% of their 260 patients with ANSD developed normal speech and language skills without any type of intervention. All children with ANSD who are not showing expected progression of speech and language skills will go through a trial period of amplification, before moving on to more complex interventions such as cochlear implantation.

### Cued Speech

For some parents of children with mild forms of ANSD, the first recommended strategy is to incorporate cued speech into the child's life. Cued speech involves differentiation between phonemes that are similar in appearance by using hand gestures around the face and mouth. It differs from American Sign Language (ASL) in that it is not a language in itself, but rather a manual assistant for any spoken language. Similar to ASL, it does require a certain amount of training to learn the different hand gestures. Cued speech may be beneficial for children who have a milder form of ANSD, with good speech perception in quiet and also in children pre/post cochlear implantation.

### Frequency Modulation Systems and Hearing Aids

Frequency modulation (FM) systems are useful for children who have a milder form of ANSD. Since ANSD is generally a problem of clarity, not volume, the FM system is ideal in providing a clean signal directly to the ear. The FM system consists of a microphone, worn by a speaker, and a receiver, worn by the individual with ANSD. The FM system does not overly amplify the voice of the speaker, but instead allows the message to be clearly transmitted to the individual with ANSD, overcoming background noise. The preferred form of FM system for these children is a personal FM, in which an ear-level receiver is worn by the child. In a classroom, the teacher's voice would transmit through the microphone to the receiver placed at the child's ear. The FM system is especially beneficial in situations with background noise, such as a full classroom. Some children with ANSD benefit from hearing aids paired with an FM system. Most of the time the hearing aids have a mild amount of gain (amplification) in conjunction with the FM system sending a speakers voice directly to the ear. In our experience, about 9% of children with ANSD are successful communicators with an FM system, hearing aids, or both. This is comparable to the literature, which estimates that 15% are successful with traditional amplification.[1]

More commonly, children with ANSD have elevated sound detection thresholds in conjunction with an unclear auditory signal. In these cases, the FM system alone is not enough and amplification is also required for the child to make meaning of sounds and conversation. We recommend the use of a trial period of amplification with loaner hearing aids, as 15% of ANSD patients will benefit from HA.[1] In our clinic, 9% of our ANSD patients who tried hearing aids reported the successful use of hearing aids to develop speech and language. The benefit of the trial period of amplification is to see if hearing aids and FM alone will provide a clear enough auditory signal for the child to

develop speech and language successfully. The hearing aids will be set initially with a very low output. If the low output does not seem to be enough to help the child with sound awareness, and the child is tolerating the hearing aids, then the volume will be increased. Again speech and language development and parental observation will be the most important predictors of success with the hearing aids. A speech and language evaluation should be obtained before and after hearing aid use, to monitor for any help the hearing aids may be providing for the child. After a short trial period with hearing aids, if progress is noted on the speech and language evaluation, and parental observation indicates the child is benefiting from the use of the hearing aids, the child may continue to wear them. Their speech and language development will be closely monitored to assure they are making the appropriate amount of progress in speech development with hearing aids alone. If the child plateaus in speech and language development with hearing aid use, then more aggressive options may be pursued at that point. If the child fit initially with hearing aids is not tolerating them, and little to no progress is made between speech and language evaluations, then the option of a cochlear implant may be more rapidly pursued. While hearing aids may be an option for some children with ANSD, in our clinic, 83% of children who tried hearing aids saw no progression in speech and language development. This is why we do not recommend an extensive hearing aid trial and a few months are usually sufficient to attest the tolerance and progress or lack of thereof in terms of speech and language development.

## Cochlear Implants

The most extreme form of intervention for a child with ANSD would be cochlear implantation. In many cases of unknown etiology, or in the presence of small or dyssynchronous nerve firing, the cochlear implant will send a unified electrical signal to the auditory nerve and provide enough sound for a child to develop speech and language. Once a trial period with hearing aids is exhausted, and speech and language is not developing age-appropriately, a cochlear implant may be recommended. Cochlear implants are a successful means of intervention for many children with ANSD, who do not show improvement with the use of hearing aids.[34,35] Berlin and colleagues[1] estimate that 85% of children who have been implanted showed successful improvement in speech comprehension and language acquisition, while slow progress was observed in 2%, uncertainty in 4% and lack of data in the remaining children because they were recently implanted at the time of the study. So far in our clinic, the majority of children who have been implanted, and for whom follow-up data are available, are also successful users in terms of speech and language development.

The cochlear implant consists of an internal device, an external device, and a sound processor. The internal device contains an electrode array that is inserted into the cochlea. The electrode array bypasses any dysfunction of the inner hair cells and/or the junction between the inner hair cells and the auditory nerve in those with ANSD. The unified electrical signal from the electrode array placed in the cochlea is also believed to better synchronize a dyssynchronous signal in those with ANSD.[36] In children with typical SNHL, the sooner the child can be implanted, the better chance the child will have to gain age appropriate speech, language, and auditory skills. The same is true for children with ANSD. Recent research has shown that children with ANSD implanted at an earlier age have better cortical maturity than children with ANSD implanted at a later age.[31] However, the age at implantation in ANSD varies greatly because of the uncertainty of a specific child outcome.

## Auditory Verbal Therapy

Auditory verbal therapy (AVT) is a crucial step in developing age-appropriate speech and language skills once a child has been implanted. AVT is a type of aural rehabilitation that does not focus on the end product of articulation, but rather emphasizes the pragmatics of language. The child is enriched in language during a therapy session, with the end goal being some form of meaningful communication between the therapist and the child. After receiving a cochlear implant, AVT is mandatory in most centers, so the child learns to listen with the cochlear implant and eventually develops speech and language using the implant. After a few years of AVT, the typically developing child with ANSD using a cochlear implant will graduate from therapy as a successful listener and communicator. AVT is usually not recommended before implantation because the lack of visual cues impairs the child's understanding.

# CONCLUSION

It is estimated that 10% of individuals who present with SNHL loss have ANSD.[9,10] The physiologic dysfunction of ANSD appears to be in the inner hair cells, the synaptic

region connecting the inner hair cells to the auditory nerve, or the auditory nerve itself.[2–8] The gold standard for identifying ANSD clinically is to use a "triage" of tests: OAEs, MEMRs, and ABRs.[1] Unlike traditional SNHL, pure-tone audiograms may not yield a complete picture of functional hearing abilities in those with ANSD, and may indicate more of a sound detection level. Many patients with ANSD will have great functional difficulty listening in background noise.[1,6,11,12] The best tool to measure progression of speech and language development, especially in children and infants with ANSD, are routine speech and language evaluations. The progress made between each speech and language evaluation is pertinent in determining the best course of intervention, in order to develop age appropriate speech and language skills: no intervention, FM system, hearing aids in conjunction with an FM system, or a cochlear implant. Future research is directed at better predicting speech and language outcomes in children with ANSD, using CAEPs.[13]

## CASE STUDIES

### Case Study 1—Susie

Susie began struggling academically, at the age of 7 years, and was referred for a hearing assessment for suspected ANSD. Medical history was significant for many risk factors, including extreme prematurity at 28 weeks' gestation and a prolonged stay in the NICU where ototoxic medications were administered for infection. She required some ventilation assistance after birth for an unknown length of time, and she developed severe jaundice which was treated with phototherapy. Susie reportedly passed her newborn hearing screening in both ears. Upon meeting Susie, she was very friendly and appeared to have age-appropriate articulation. Her audiologic evaluation revealed absent ipsilateral and contralateral MEMRs in the right ear, and partially present yet elevated MEMRs in the left ear. She had partial OAEs bilaterally. Her audiogram showed mild hearing loss in the low to mid frequencies, steeply sloping to a moderately severe hearing loss in the high frequencies; configuration was symmetrical bilaterally. Her word recognition was good in quiet and in noise. Susie's ABR revealed a present CM and some neural synchrony, as indicated by a possible delayed wave V, bilaterally. Due to her elevated/absent MEMRs, partially present OAEs, and grossly abnormal ABR with a present CM, Susie was confirmed to have ANSD. Susie went on to receive a speech and language evaluation that revealed some expressive and receptive speech and language delays, and the fact that Susie relied heavily on lip reading. Susie was fit with bilateral low-gain amplification paired with an FM system. She initially adapted to the amplification well, and used the hearing aids during school and outside of school. After a few months, she no longer tolerated the hearing aids and stopped wearing them. She continues to wear the FM system in school. She is making slow but steady progress academically. Her teachers and her family report that she has "good" and "bad" hearing days, and this is reflected in her ability to retain information. Susie was monitored periodically, every 6 months, and her ANSD remained essentially stable, with good perception of speech in quiet and fair perception of speech in background noise. Susie is certainly the exception when it comes to perceiving speech in background noise. Due to her success with speech perception and her slow but steady academic gain, Susie was not referred for a cochlear implant and was encouraged to continue to use her FM system.

### Case Study 2—Sammy

Sammy was also a late ANSD identification, arriving to our clinic at 5 years of age. Sammy had a history of ongoing ear infections and an active personality, making him difficult to evaluate behaviorally. He reportedly passed his newborn hearing screening in both ears. Around 18 months of age he began to present with some developmental delays and received speech language therapy, occupational therapy, and physical therapy. An MRI study at that time revealed a decrease in myelination in the sensory areas of the brain. A second MRI at 3 years of age indicated a normal amount of myelination and no further concerns for developmental delays. However, speech and language skills did not seem to progress as hoped. Sammy was taken for an audiologic evaluation at an ENT clinic at the age of 4, where he demonstrated normal perception of pure-tones bilaterally. He was unable to picture point for a given word without visualization of the audiologist's mouth. He was referred for a sedated ABR at a local hospital. First, his OAEs were evaluated and were partially present bilaterally. His ABR revealed no neural response at equipment limits of 99 dB nHL with a small CM that reversed with a change in polarity. Due to partially present OAEs and a grossly abnormal ABR with a present CM, Sammy was confirmed to have ANSD. Sammy arrived at our facility at the age of 5 for a CAEP evaluation. The CAEP evaluation revealed present cortical responses with fairly age appropriate latencies bilaterally, with a stronger response in the left ear. Sammy was recommended to have a trial period with hearing aids and an FM system, and his family was also

recommended to implement the use of cued speech. Sammy immediately showed benefit when wearing the hearing aids and requested to wear them daily. A speech language re-evaluation approximately 1 year post hearing aid use revealed some improvement in receptive and expressive speech and language development, although he was still classified as delayed. His articulation had also improved, though he was very difficult to understand to those unfamiliar with him. Sammy continued to be monitored at our clinic every 6 months.

Just before Sammy turned 6, he returned to our clinic for a CAEP evaluation. His parents expressed great concern that his speech and language development had plateaued. They were also deeply concerned that Sammy was not making friends in school due to his inability to communicate effectively. His CAEP evaluation showed a drastic decrease in cortical responses, and a subsequent speech and language evaluation revealed a heavy reliance on facial cues to understand a spoken message. The family was referred to the cochlear implant team for evaluation for candidacy at that time. When Sammy was 6.3 years of age, he received a unilateral cochlear implant. At this time he is mainstreamed in school and is receiving intensive AVT, both in school and outside of school. He is learning to adjust to his implant and he utilizes his amplification on the ear without the implant. Sammy's most recent speech and language evaluation revealed some progress when listening for speech and language with his cochlear implant. However, he will require continued intensive AVT in order to develop age-appropriate speech and language skills, without visual cues.

## Case Study 3—Abby

Abby was referred to our clinic at 6 weeks of age for an audiologic evaluation, due to three prior failed newborn hearing screenings. Abby had no birth complications, no risk factors for ANSD, was born full term, and had no family history of hearing loss. Her parents reported at the time of the ABR that she was startling to loud sounds in the home. Her audiologic evaluation revealed absent MEMRs and partially present OAEs bilaterally. Abby's ABR revealed a robust CM with no neural synchrony, bilaterally, and she was officially diagnosed with ANSD. At 5 months of age, Abby had her first audiometric evaluation in the sound booth, which revealed a speech awareness threshold in the mild/moderate hearing loss range. Abby was referred for genetic testing at that time, for which the otoferlin mutation was negative. She was referred to the cochlear implant team for evaluation for candidacy.

At 10 months of age, Abby was fit with bilateral low-gain amplification. Another booth test again revealed sound awareness in the moderate hearing loss range. At that time, Abby had imaging performed (CT and MRI) that revealed no anomalies in the brain or auditory system. Her first speech and language evaluation was performed at 1 year of age, and revealed a severe expressive and receptive language delay. Abby continued to be monitored periodically with hearing evaluations, which revealed no benefit with the hearing aids. Her parents reported that her hearing seemed to fluctuate, and that she had "good hearing days and bad hearing days". They noticed no difference in her hearing with her hearing aids on. At 18 months, Abby received her right cochlear implant. Immediately after activation, Abby received AVT both in the home and also through our clinic. She made great strides in speech and language acquisition in such a short amount of time that her parents decided to implant her other ear at 2.5 years of age. Abby continues to be enrolled in AVT in our clinic, and she receives AVT in school. She is in a mainstream preschool and continues to make strides in her speech and language skills.

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CHAPTER

# Osseointegrated Implants and Implantable Hearing Aids in the Pediatric Patient

21

*Nikhila Raol, Michael S Cohen*

## INTRODUCTION

Osseointegration is defined as a process whereby clinically nonsymptomatic rigid fixation of alloplastic materials is achieved, and maintained, in bone during functional loading.[1] Osseointegrated implants were first used in otolaryngology in the extraoral setting at Sahlgren's Hospital, Sweden, in 1977.[1] In this setting, bone-anchored hearing aids (BAHA) were fastened to a skin-penetrating attachment. The success was noted to be about 98% in 389 cases, with a success rate of 85% in irradiated bone and nearly 100% in nonirradiated bone, at a follow-up of up to 5 years.[2] In 1996, use of the BAHA in the United States was approved by the Food and Drug Administration.[3] Since that time, routine use has been established in patients with bilateral conductive hearing loss who cannot tolerate traditional hearing aids, single-sided deafness, and congenital ear anomalies with hearing loss. Several types of osseointegrated devices now exist, including the Sophono, SoundBite, or Sonitus, and the Vibrant Soundbridge (VSB). Successful utilization of the BAHA in the pediatric population began in 1983, and FDA approval for the device was established for children over the age of 5 in 1996. This chapter discusses the use of osseointegrated implants in the pediatric population.

## CRITERION FOR IMPLANTABLE HEARING AID PLACEMENT

Indications for bone-anchored hearing device in the pediatric population include (1) congenital aural atresia, (2) congenital microtia, (3) chronic suppurative otitis media, (4) persistent otitis media with effusion, (5) chronic otitis externa, (6) unilateral profound hearing loss, (7) unilateral mixed hearing loss, (8) failure with conventional aids, and (9) trauma to the ear (i.e. traumatic ossicular discontinuity).[4] Mounting evidence suggests that children with unilateral profound sensorineural hearing loss, which presents in 0.1–3% of the pediatric population, get significant benefit from BAHA placement; FDA approval for this indication came in 2002. Implantation is only approved in the pediatric population, however, for age 5 years and over, primarily due to the thought that this would allow for adequate skull thickness to be present (at least 3 mm). However, no consensus exists for the minimum age requirement, and children as young as 14 months old have been successfully implanted.[5] Younger age of implantation has been associated with increased perioperative complications due to thin calvarial bone, such as necessitation of multiple drilling sites[6] and incomplete insertion of fixtures with failure of osseointegration.[7] Exposure of dura mater and/or sigmoid sinus is common, occurring in up to 70.5% of pediatric BAHA cases.[6] Granström has used bone augmentation with expanded polytetrafluoroethylene membranes in children with limited bone thickness (< 2.5 mm) without complications.[8]

### Bone-Anchored Hearing Aids

Prior to the development of the BAHA, children were offered the conventional bone conduction hearing aid. A vibrator attached a headband or in an eyeglass frame was used to conduct sound to the bone (Fig. 21.1). However, the discomfort caused by the pressure needed

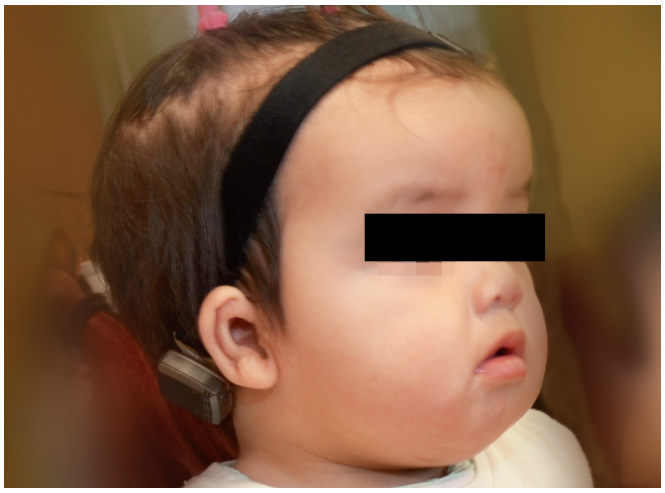


**Fig. 21.1:** The transcutaneous BAHA Softband in a young child, not yet old enough for percutaneous BAHA application.

for sound conduction as well as the sound distortion that occurred due to soft tissue interference prior to reaching the bone made this a less than ideal method for hearing amplification. The BAHA transmits sound energy directly to the cochlea from the external transducer without the damping effect of the intervening soft tissue. This allows for a 10–20 dB HL decrease in audiometric thresholds. When combined with the decrease in discomfort and the cosmetically less conspicuous nature of the BAHA, this leads to increased compliance and ultimately improved outcomes for hearing impaired children.[9]

The Cochlear Baha is comprised of three parts: an osseointegrated titanium fixture (screw), which is implanted surgically in the postauricular calvarium, a percutaneous titanium abutment, and an external sound processor. The sound processor transduces vibrations from air to bone with corresponding intensity, via the percutaneous abutment and implanted fixture. This generates a frequency dependent elastic deformity of the bone cortex.[10] Audiometric criteria for BAHA implantation, as well as the type of hearing aid to be used, are defined by BC thresholds (measured at 0.5, 1, 2 and 3 kHz). A Baha Divino or Baha BP100 can be used for BC thresholds ≤45 dB HL, a Baha Intenso can be proposed for BC thresholds ≤55 dB HL, and a Baha Cordelle II is indicated for BC thresholds ≤65 dB HL with speech discrimination by BC ≥60%. Bilateral BAHA is indicated when the right BC is equal to the left BC with a mean maximum difference <10 dB. BAHA is indicated for single-sided deafness when BC thresholds of the healthy ear are ≤20 dB.[10] In 2009, Oticon introduced the Ponto bone-anchored hearing aid system, similar in composition (three parts) to the original Cochlear Baha. An additional feature of this system is the 10° inclination available for patients with problems due to the skin abutment.

## *Surgical Procedure*

Traditionally in children, a two-stage surgery has been used for BAHA placement. In the first stage, the titanium fixture is implanted into the skull in the superior postauricular region. In the initial description of the procedure, this was done via a U-shaped incision. However, since the 1990s, the linear incision technique has been used, ameliorating the need for a skin flap and therefore avoiding the risk of flap necrosis. After allowing 4–6 months for osseointegration to occur, the second stage is performed, where a skin graft/pedicled flap is placed, along with soft tissue reduction and abutment placement. This allows for a decrease in the skin complications of the procedure. Sleeper fixtures may also be implanted at the time of the first surgery to use in the case of extrusion of the first implant. One stage surgery has been proposed, similar to the procedure in adults, with a three-sided U-shaped incision or, now more commonly, with a linear incision. Studies have shown favorable outcomes for the properly selected patients, including Roman in 1996 without any increase in complication rate,[10] and Tietze and Papsin in 2001, for children over the age of 9 years where at least a 4 mm implant can be used.[9] In addition, excellent outcomes have been shown by Kohan in 2008, who proposed implantation of both a screw and a dormant safety fixture in a single stage after preoperative CT demonstrated adequate thickness of bone,[11] and the Nijmegan group in 2011, who found that children over the age of 10 years did well with two-stage or single-stage surgery via a linear incision.[12]

## *Outcomes and Complications*

The most common complication in pediatric BAHA practice is the periabutment soft tissue reaction, characterized by Holgers et al.[13] (Table 21.1).

An older study by Tjellstrom demonstrated reaction-free penetration in 64% of cases, but this number has improved significantly, with reaction-free outcomes seen in 84–92% of patients.[1,9] This is likely due to improved handling of the soft tissue around the abutment, with skin graft placement if needed at the penetration site. While the exact causative factor in skin reactions is unclear, multiple etiologies have been proposed. Khwaja et al. showed that

**Table 21.1:** Classification of skin reactions

| | |
|---|---|
| 0 | No irritation |
| 1 | |
| 2 | Slight redness |
| 3 | |
| 4 | Red and moist tissue, no granulation tissue |
| 5 | |
| 6 | Red and moist tissue with granulation tissue |
| 7 | |
| 8 | Revision of skin penetration necessary |

From Holgers et al.[13]

keratin may be the culprit, as they were able to demonstrate a foreign body reaction to keratin and keratinocytes at the titanium-bone interface.[14]

Dental implant studies have suggested that microleakage of bacteria between the implant and abutment may be a causative factor,[15–17] while biofilm has been found on implants with failure of osseointegration.[18] The recently-released Cochlear DermaLock abutments have a hydroxylapatite coating on the medial portion of the abutment that is designed to adhere to the surrounding soft-tissue envelope, theoretically decreasing the risk of wound complications. Long-term data on this new abutment design are forthcoming.

Retention of osseointegrated fixtures has been shown to be quite high in both the adult and pediatric population. While fixture survival rates are 90–100% in adults, recent studies have shown pediatric fixture survival rates to be 71–95%.[9] McDermott et al. reported a 14% rate of fixture loss, with a significant trend in children younger than 5 years.[19] A surgical revision rate of 22% and extrusion rate of 5.8% was noted by Granström, with greater skin flap revision needed between 6 and 12 years of age.[8] Zeitoun et al. demonstrated a failure rate of 11.2% of fixtures.[7] Ida et al. identified a complication rate of 46%, with complication assigned to any child requiring revision in the operating room. An 8% extrusion rate was noted, with trauma and infection being the most common causes for extrusion. In addition, longer follow-up, staged procedure, and presence of a craniofacial syndrome were all associated with complications.[3]

Single-stage procedures have become increasingly popular in the pediatric population. Davids et al. demonstrated that two-stage BAHA implantation with a prolonged interval between stages leads to increased survival of implants in children 5 years and younger when compared to older children.[5] However, Ali et al. showed no failure of osseointegration in their study of 30 children who were all implanted in a single-stage fashion, 7 of whom were under 5 years of age.[20] Maximum follow-up was 8 years for these patients. Improvement in audiometric thresholds from preimplantation has been noted to be significant, with thresholds dropping as low as 0–20 dB with a speech discrimination of 100% at 40 dB.[20]

Lowering of audiometric thresholds when compared to conventional bone conduction hearing aids has also been shown; studies by Tietze et al. and Stevenson et al. have shown approximately a 5 dB lowering of the threshold in the speaking range on 0.5–4 kHz. In addition, multiple additional studies have demonstrated subjective improvement in sound quality and speech using patient/parent questionnaires.[21–23]

Increasing literature about the benefit of BAHA implantation for unilateral profound sensorineural hearing loss has shown benefit in adults, with Hol et al. demonstrating improved ability to understand speech in noise and a lifted head-shadow effect,[24] but the pediatric literature remains limited. A study by Christensen et al. demonstrated significant benefit, using the Hearing in Noise Test (HINT) and Children's Home Inventory for Listening Difficulties (CHILD) questionnaires. Preimplant HINT mean scores at the speech-noise ratio were 42%, 76%, and 95% at 0, 5, and 10 dB, respectively, while postimplant HINT mean scores improved to 82%, 97%, and 99%. CHILD scores also improved for both patients and parents. While all ages of implanted children received benefit, the greatest benefits were seen in the teenage group.[25]

## Transcutaneous Bone-Anchored Hearing Device

Sophono developed the Alpha 1 hearing device in 2006 as an alternative to the traditional percutaneous cochlear Baha, and the device received FDA approval in 2011. The indications for implantation are essentially the same as those for the Baha, but the Sophono implant is indicated for patients with bone conduction up to 45 dB, while Baha can be implanted in patients with bone conduction up to 65 dB. The advantages of the device include absence of a percutaneous abutment, minimal skin complications, and lack of need for long-term wound care. A relative contraindication is a patient who might need serial MRI scans. The Sophono Alpha 2 was also recently introduced in 2013, with small enhancements from the Alpha 1.

The Alpha 1 consists of a surgically implanted internal plate that contains two magnets imperviously sealed in a titanium case. The external sound processor has a bone oscillator and uses a metal disk and spacer shim to magnetically couple to the internal portion and deliver auditory signal through the closed skin. The surgery is a single stage procedure that can be performed under local or general anesthesia (Figs. 21.2A and B). Four weeks are given between implantation and placement of external bone vibrating audio processor.[26]

Evidence of effectiveness is limited, but in a series of over 100 patients, including children over 5 years and adults, data suggest that the best outcomes are for patients with conductive hearing loss or single-sided deafness. The only noted complication was skin redness from pressure that was seen in about 4% of patients. This resolved with slight force reduction of the base plates. Early audiometric data in this study shows an average hearing gain in a free field pure tone audiogram of 31.2 ± 8.1 dB, and the suprathreshold speech perception at 65 dB to increase from 12.9% to 72.1% following implantation. The sound attenuation caused by the intact, thinned skin has been measured to be about 10 dB when compared to direct bone coupling (Baha).[27]

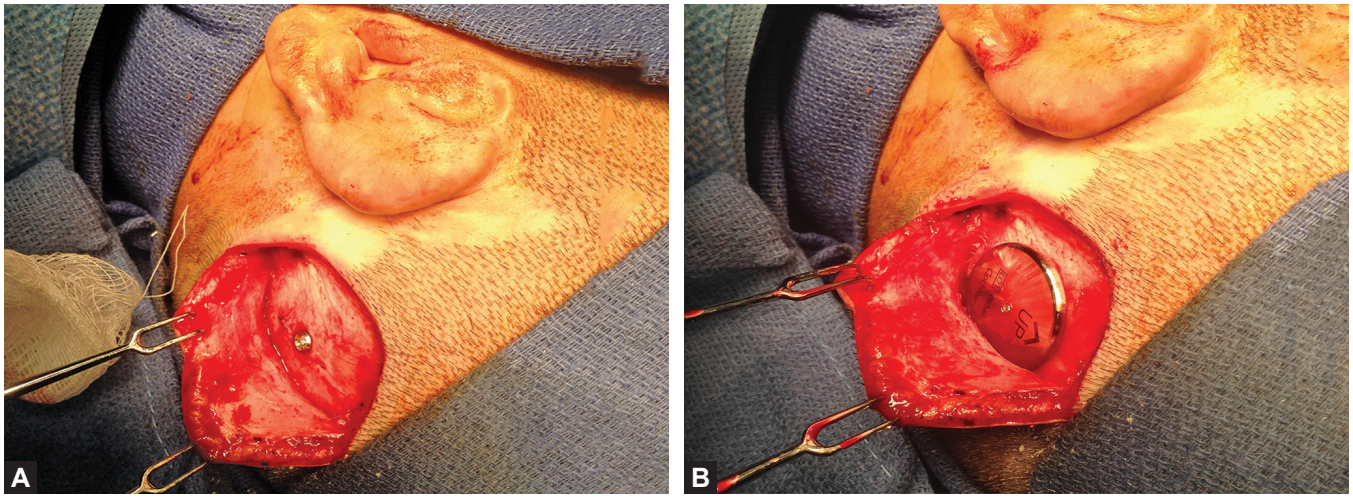
### Intraoral Bone Conduction Device

The SoundBite Hearing System developed in 2010 by Sonitus Medical is another device that amplifies sound via bone conduction, but this has the distinct advantage of not requiring surgical intervention for placement. A microphone is placed in the external auditory canal of the poorer hearing ear, while a removable in-the-mouth device provides direct coupling to the cranium via the teeth.[28]

A study in adults with single-sided deafness demonstrated that the SoundBite was at least as effective as an osseointegrated implant in improving ability to understand speech in noise, with an average improvement of 25% on HINT scores, with one third of the patients improving by over 30%.[28] Another study looking at adults who used the device for 6 months showed similar results with no complications.[28] The primary reason for decreased satisfaction was the comfort of the device in the mouth. With regards to the pediatric population, no literature has been published at this time, but it is conceivable that this device may be used in the older teenage population.[29] Use in the younger children is precluded by the intraoral component, as this could potentially be a choking hazard and would be difficult to fit with a child's mixed dentition.

## MIDDLE EAR IMPLANTS

Middle ear implants, also known as implantable hearing aids, were developed initially for the treatment of sensorineural hearing loss. They provide acoustic amplification and transmission of sound energy by coupling a vibratory element, the floating mass transducer (FMT), directly to the long process of the incus.[30] Because of the difficulty of fixation of the FMT to malformed ossicles in many patients with congenital aural atresia, in 2005, Colletti et al. described another alternative to the BAHA in patients




**Figs. 21.2A and B:** Transcutaneous BAHA surgical site with titanium screw in place (A); same site with magnet now in place (B).

with congenital aural atresia using the round window membrane as the site for the FMT of the MED-EL VSB implantable hearing device. The procedure consists of making a retroauricular incision in the region of hair-bearing skin and creating a large C-shaped flap to preserve the superficial temporal artery. A precisely shaped bony bed is drilled out at the level of the squama temporalis for the demodulator. A transmastoid approach with posterior tympanotomy is used. Reshaping of the fossula of the cochlear fenestra, which is caudal to the subiculum, is done by paring away the anterior and posterior margins of the bony lip of the round window until the edge of the round window membrane can be seen for fitting of the VSB transducer.[31] A study in 2011 which included 14 children, ranging from 2 months to 16 years, demonstrated improvement in air conduction thresholds from 66 ± 12.9 dB to 22 ± 9.1dB, pre- and postoperatively, respectively, in the older children. Free-field auditory brainstem responses in the 4 younger children showed mean preoperative and postoperative AC thresholds of 85.6 ± 14.2 dB and 24.4 ± 8.8 dB, respectively.[32]

## SUMMARY

- Multiple options exist to treat congenital and acquired hearing loss in the pediatric population, including percutaneous osseointegrated implants, transcutaneous implants, intraoral devices, and middle ear implants
- BAHA is the most commonly used device but has the disadvantage of skin complications owing to the percutaneous abutment
- Other devices are being utilized less frequently but many show promise in the pediatric population and are feasible options for audiologic rehabilitation.

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CHAPTER

# 22

# Pediatric Cochlear Implantation

***Aaron D Tward, Michael S Cohen, Daniel J Lee***

## INTRODUCTION

There are few treatments in medicine that have altered patients' lives as radically as the cochlear implant. The cochlear implant is the most successful of all neuroprosthetic devices and provides meaningful sound and speech perception to the majority of infants, children, and adults with prelingual and postlingual deafness. The development of the cochlear implant from an idea to a viable and widely used treatment for hearing loss represents a triumph that required the synthesis of information from the fields of neuroscience, electrical engineering, signal processing, manufacturing, and surgery. At the time of this writing, well over 200,000 cochlear implants have been placed in adults and children worldwide.

## ANATOMY/PHYSIOLOGY

In normal hearing, sound vibrations enter the external auditory canal and vibrate the tympanic membrane. The ossicular chain then conducts the vibrations to the inner ear via the oval window. The inner ear has two portions: the vestibular apparatus, which is responsible for detecting acceleration and balance function, and the cochlea, which is responsible for hearing. The cochlea is a linear tube hollowed out of the temporal bone, which is coiled into two and a half turns. Along the length of the cochlea, there are sheets of soft tissue that divide the space into three key compartments. Reissner's membrane separates the perilymph-filled scala vestibuli from the endolymph-filled scala media (Fig. 22.1). The basilar membrane separates the scala media from the perilymph-filled scala tympani.

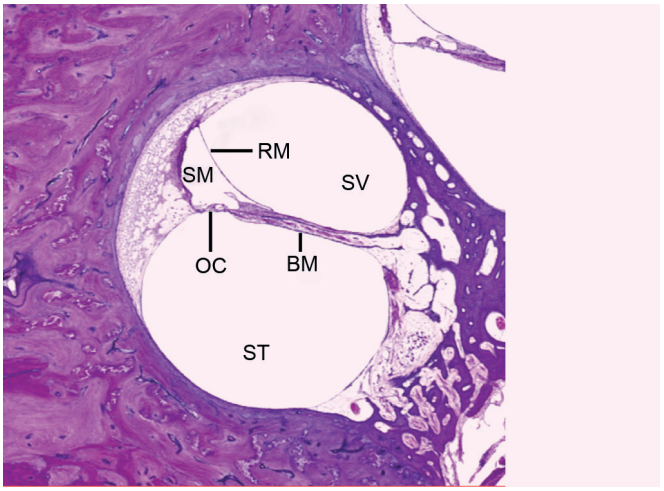


**Fig. 22.1:** Inner ear anatomy. Hematoxylin and eosin stained section of the cochlea. (SV: Scala vestibule; ST: Scala tympani; SM: Scala media; RM: Reissner's membrane; BM: Basilar membrane; OC: Organ of Corti).

Embedded in the basilar membrane, within the scala media, are hair cells, which convert mechanical energy from vibrations of the basilar membrane into electrical energy by depolarizing the hair cells. Once depolarized, hair cells release glutamate at their basolateral membranes that in turn activates spiral ganglion neurons. The spiral ganglion neurons are the first-order neurons of the auditory pathway and their axons travel via the cochlear nerve to the brainstem where they ultimately synapse on second-order neurons found in the cochlear nucleus. The cochlear nucleus is the target of all ascending information originating in the inner ear and these signals are ultimately

transmitted to the auditory cortex via the olivary complex of the auditory brainstem and inferior colliculus (midbrain). The vast majority of sensorineural hearing loss is caused by loss of hair cells. Cochlear implants function by electrically stimulating residual spiral ganglion cells with an electrode placed into the scala tympani, bypassing the absent or dysfunctional hair cells.

## HISTORY OF COCHLEAR IMPLANTATION

The first report that suggested a link between electricity and hearing came from Alessandro Volta in the late 1700s when he inserted two metal rods in his ears and drove a current through them. He observed "a boom within the head" and then described the sound of boiling soup. Subsequently, in 1930, Ernest Weaver and Charles Bray of Princeton University demonstrated that sound is converted to electricity by the peripheral auditory system.[1] They reported that when sound is presented to the ear of a cat, an electrode placed on the ipsilateral auditory nerve detects electrical signals that when amplified and played through a telephone receiver will produce intelligible sounds and speech similar to that presented to the ear. Although they believed the electric signal to have been produced by the auditory nerve, subsequent studies demonstrated this signal to have been generated by the cochlea itself (the cochlear microphonic). In 1957, André Djourno and Charles Eyriès implanted a patient with a device that directly stimulated the cochlear nerve and reported that he was capable of perceiving sound.[2] In 1961, William House and John Doyle implanted a few patients with single gold electrode devices. These patients were able to perceive sound, but the devices would fail as a consequence of tissue reaction to the electrodes.[3] The first multichannel implant in a human was reported in 1965 by Blair Simmons of Stanford and his colleagues at Bell Labs.[4] This implant had five steel electrodes that were implanted in the region of the modiolus. Stimulation of the different electrodes produced percepts of different pitches. In the late 1960s, William House and an engineer, Jack Urban, greatly improved hermetic sealing of the single-channel implant they had developed, thus paving the way for the approval of the single-channel 3M/House implant in 1984. Starting in the 1970s and continuing until roughly 1990, hundreds of children received the single-channel 3M/House implant.[5] With this implant, some children achieved open set speech recognition.

In the 1970s, multiple groups began working on multichannel cochlear implants, including those led by William House, Graeme Clark, Ingeborg Hochmair, Don Eddington, and Michael Merzenich. Ultimately, the first multichannel implant to be approved by the FDA for use in adults was the Cochlear Corporation's Nucleus Mini22 in 1985. Subsequently, the Cochlear Corporation obtained FDA approval for use in children as young as 2 years old. Later multichannel implants from both Advanced Bionics and Med-El were approved in the United States. Over time, the technology of cochlear implants and processing strategies has improved greatly, but the fundamental design of the components has remained similar for many years.

## DESCRIPTION OF MODERN COCHLEAR IMPLANTS

Cochlear implants are comprised of two main components: an external sound processor and an internally implanted receiver/stimulator (Figs. 22.2A and B). A battery powers both the speech processor (worn on the body or behind the ear) as well as the surgically implanted receiver/stimulator via induction. In a normally functioning cochlear implant, sound is first presented to the microphone on the sound processor. This acoustic information is converted to an electrical signal by the microphone and then presented to a digital processor. Using one of a variety of algorithms, the processor then extracts different features of the analog signal, encodes them, and transmits them to the internal receiver/stimulator via the transmitter coil. The induction coil of the internal receiver/stimulator ultimately transmits the signal to a linear array of 16–24 platinum electrodes,


**Figs. 22.2A and B:** Components of a modern cochlear implant. (A) External sound processor; (B) Internal receiver stimulator.

which can be independently activated. These electrodes stimulate fields of spiral ganglion neurons, which alter their pattern of firing in response to the stimulation. The signal encoded in this altered firing is ultimately transmitted to the auditory cortex via the brainstem and inferior colliculus where it is then interpreted as sound.

## CLINICAL CONSIDERATIONS

### Indications and Preoperative Evaluation

Cochlear implants are indicated in children with moderate to profound hearing loss in both ears and who derive minimal benefit from amplification. If there is residual hearing in one ear, the worse ear is generally implanted first and a hearing aid can be used in the better ear (bimodal hearing). These children must also have an inner ear with a cochlear nerve in continuity with the brainstem. The indications listed above guide the components of the preoperative evaluation. Although current devices are approved by the FDA for implantation into children 12 months and older, children as young as 3 months of age have been safely implanted with excellent hearing results.[6]

For children who are capable of conventional pure tone and speech audiometry, a standard audiogram is sufficient evidence of hearing loss. For children who are not capable of conventional pure tone and speech audiometry, auditory brainstem response testing can objectively measure pure tone and click thresholds. In children younger than 2 years of age, cochlear implants are indicated if audiometric testing indicates pure tone averages of 90 dB or greater. For children older than 2 years of age, pure tone averages of 70 dB or greater are sufficient to meet audiometric criteria for cochlear implantation. In addition, a 3–6 month trial of amplification should be attempted to see if any substantial benefit could be obtained. This trial of amplification may be deferred in children with severe to profound sensorineural hearing loss secondary to meningitis as rapid cochlear ossification may prevent the ability to place a cochlear implant if the procedure is delayed. Prelingually deafened children should be enrolled with Early Intervention or programs with similar services to aid in language and speech acquisition.

Noncontrast computed tomography (CT) scan of the temporal bones should be obtained during the preoperative workup in order to assess for cochlear or internal auditory canal anomalies. Particular attention should be paid to the possibility of cochlear ossification, the patency of the cochlear nerve canal, and the width of the internal auditory canal (Fig. 22.3). In addition, even among children with normal cochlear anatomy, CT imaging can aid in surgical planning. For example, identifying a large mastoid emissary vein or narrow facial recess may alter the surgical technique slightly in a way that makes the procedure safer and more efficient.

The addition of high-resolution magnetic resonance imaging (MRI) of the temporal bones with a far T2-weighted sequence such as a constructive interference in steady state (CISS)/fast imaging employing steady-state acquisition (FIESTA) is helpful in assessing the presence and caliber of the cochlear nerve (Fig. 22.4). In addition, the patency of the inner ear can be confirmed by the presence of fluid signal within the cochlea. If the cochlear nerve is absent, an auditory brainstem implant can be considered (*see* Chapter 23). At our institution, all infants with congenital profound hearing loss undergo an MRI scan of the temporal bones under anesthesia before cochlear implant surgery to ensure the presence of a fluid-filled cochlea and auditory nerve.

Active infection with acute or chronic otitis media is a contraindication to cochlear implantation. Infection should be treated with standard care (e.g. antibiotics, tympanostomy tubes, or surgery as needed), and once controlled, consideration can be given to proceeding with cochlear implantation. If the patient is medically unstable or cannot safely undergo general anesthesia, implantation should be postponed until anesthesia is safe. Patients with no cochlea cannot benefit from a cochlear implant, although some auditory benefit has been reported in

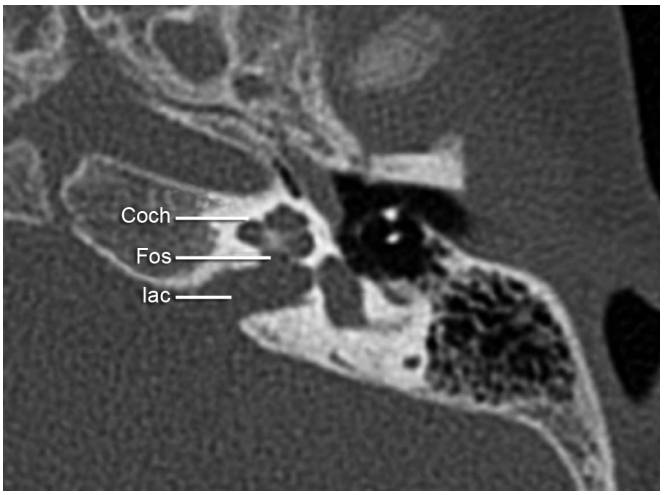


**Fig. 22.3:** Normal bony cochlear anatomy. Axial CT scan of the temporal bone showing two and a half turns of the cochlea, no ossification, and no partitioning defect, and a patent cochlear fossette and internal auditory canal. (Coch: Cochlea; Fos: Cochlear fossette; Iac: Internal auditory canal).

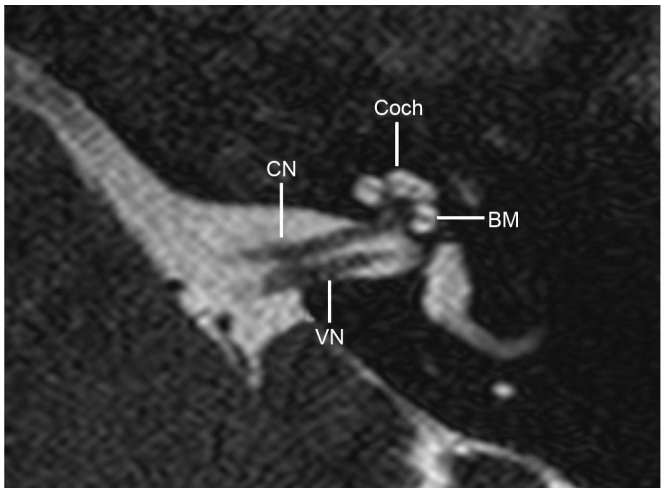


**Fig. 22.4:** Normal cochlear anatomy. Axial FIESTA weighted MRI scan demonstrating the normal appearance of the cochlear fluid spaces and internal auditory canal. (Coch: Cochlea; CN: Cochlear nerve; VN: Vestibular nerve; BM: Basilar membrane).

children with even severe inner ear malformations.[7] The patient's family must demonstrate both the desire and ability to participate in ongoing follow-up with audiologic, educational, and speech/language services in order to proceed with surgery.

In 2003, an increased incidence of meningitis in cochlear implant recipients was reported. This risk was substantially higher among those recipients with an implant and a positioner device.[8] The positioner was designed to be placed into a large cochleostomy after placement of the electrode in order to bring the electrode contacts in closer proximity to the modiolus and therefore the spiral ganglion cells. The positioner device was subsequently recalled with a corresponding decrease in the incidence of meningitis following implantation.[9] Other risk factors associated with meningitis following CI surgery include a history of meningitis, inner ear dysplasia, and an intraoperative cerebrospinal fluid (CSF) leak or gusher encountered following cochleostomy. As a consequence the Centers for Disease Control and Prevention recommends that prior to undergoing cochlear implantation, children who have not previously received vaccination for *Streptococcus pneumoniae* should receive the recommended course of the 13 valent pneumococcal conjugate vaccine (PCV13) (either two or three doses, depending on the age of the child), prior to having a cochlear implant. After the course of PCV13 is complete, children over the age of 2 years should receive a single dose of the 23-valent pneumococcal polysaccharide vaccine, although this need not delay implantation.

## Procedure

After the patient is placed under general anesthesia, facial nerve monitoring is set up on one or both sides (if bilateral simultaneous implantation will be performed). A template of the device may be used to plan the location of the internal receiver/stimulator. If simultaneous or the second side of sequential implantation is planned, then a template can be created with a piece of paper on the first side, and the position of the internal receiver/stimulator on the second side can be planned to match the position on the first side for improved cosmesis. The ear is then prepared using standard aseptic technique and draped. A 4–5 cm postauricular incision is planned approximately 1 cm posterior to the postauricular crease, with care being taken to ensure that the incision does not traverse the body of the internal receiver/stimulator (📻 22.1). The region of the incision is then infiltrated with 1:100,000 epinephrine with or without local anesthetic. The skin is incised sharply and skin flaps are elevated anteriorly and for a short distance posteriorly in the plane superficial to the periosteum of the mastoid cortex. A number 7 shaped incision in the periosteum is created, with the option of a superior releasing incision it the periosteum superiorly. Care should be taken to not place a limb of the incision directly over the device. Using a periosteal elevator, a tight pocket for the device is created, and the depth of the pocket confirmed with a silastic dummy. A well and tie-down holes may be drilled, if desired. A small piece of soft tissue is harvested for later use in sealing the cochleostomy. The periosteal flap overlying the mastoid cortex is elevated, and self-retaining retractors introduced. A simple canal-wall up mastoidectomy is then performed with identification of the short process of the incus, the horizontal canal, and the posterior wall of the bony external auditory canal. Thinning, but not violating, the bone of the posterior wall of the external auditory canal is critical to adequate visualization of the round window niche. A facial recess approach is completed with diamond burrs and copious irrigation to prevent thermal injury to the facial nerve. Once the round window niche is seen, the bony lip overlying the round window niche is carefully drilled away to examine the round window in its entirety. The receiver/stimulator is then inserted into its periosteal pocket and secured. If a round window insertion is desired, a small amount of hyaluronic acid gel can be placed over the round window membrane. The round window is then incised with either a fine tip needle or a sharp Rosen needle. The electrode array is then inserted through the round

window by specifications of the individual manufacturer. No significant resistance should be encountered during insertion. If a cochleostomy is planned, the cochleostomy should be created either 1 mm directly inferior or anteroinferior to the round window membrane in order to ensure scala tympani insertion. The cochleostomy may incorporate the round window itself, or may be separate. The cochlea may be filled with hyaluronic acid if desired. Once the cochleostomy is created, the electrode array is inserted by the specifications of the individual manufacturer. If a ground electrode is present, it is inserted into a periosteal pocket overlying the zygoma. Redundant electrode is then placed in the mastoid cavity, and the periosteal flaps are closed with interrupted absorbable suture. The skin and underlying soft tissue is then closed in a multilayered fashion. If bilateral simultaneous implants are planned, then the head is turned and the procedure above is repeated on the opposite side. Once the operation is complete, a dressing is then placed.

## Special Intraoperative Circumstances

A number of issues may necessitate deviation from the standard, straightforward procedure detailed above, many of which can be anticipated from information gathered in the preoperative workup. In the case of partial ossification of the cochlea, either a narrow electrode array may be selected, or the basal turn can be widened with a drill and the full-length electrode array placed. In the case of complete ossification of the cochlea, multiple cochleostomies may be created and channels drilled for a split electrode. In cases of complete ossification, outcomes do tend to be worse than in those cases without ossification.[10,11]

In cases of cochlear malformations, implantation may be attempted with either a modiolar conforming or straight electrode if at least the basal turn is present, or a straight electrode in cases of severe partitioning defects. One issue that may arise in the context of a cochlear malformation is the presence of an intraoperative CSF leak following cochleostomy or opening the round window. Should this occur, the implant may still be placed and the cochleostomy or round window plugged with soft tissue. The head of the bed may be elevated slightly and the implant placed after the CSF has been given an opportunity to drain, or the implant can be placed through actively flowing fluid. Additionally, a lumbar drain may be placed at the end of the procedure, but the procedure can be safely completed without one. If, however, a postoperative CSF leak persists, a lumbar drain should be placed and the patient placed on bed rest for 3 days in order to resolve the leak. The presence of intraoperative CSF leak does not correlate with worse postoperative outcome.[12]

In cases of the need for replacement of a cochlear implant due to device failure, the old electrode should be left in place in the cochlea until the final moments before the new electrode is placed through the same cochleostomy. Because of the robust soft tissue response to cochlear implants,[13] if the old electrode is removed at an earlier point in the procedure then there is a risk of soft tissue sheath collapse and encountering substantial difficulty in replacing the electrode. If the receiver/stimulator needs to be removed as a consequence of infection or exposure, it is prudent to cut the electrode within the mastoid, leave the electrode in place in the cochlea, and remove the remainder of the device and close the wound. Once a sufficient amount of time to treat the infection and permit healing has elapsed (at least weeks), then in a second stage the old electrode can be removed and a new receiver/stimulator package and electrode placed. Outcomes following revision cochlear implant surgery in children are on average at least as good as those following initial placement.[14]

If during electrode placement resistance is encountered, particularly with a styletted electrode, then insertion should be stopped. The electrode may be pulled back a few millimeters, and an attempt at gentle advancement may be made. Should resistance be encountered again, it is best to accept a partial insertion of the device, rather than forcing the electrode through the cochlea and running the risk of either breaching the basilar membrane or dissecting the soft tissues of the lateral wall.[15]

## Postoperative Care

A mastoid dressing is placed over the surgical site, but may be removed after 48 hours. Particularly with younger children, it may be beneficial to leave a loose dressing on for a longer period of time in order to prevent inadvertent manipulation of the wound or device. Postoperative antibiotics, particularly those which cover gram-positive organisms, may be given for a week after the operation, although there is little evidence to support their routine use. Pain control should be age appropriate with either acetaminophen or opiates as necessary. Children over the age of 2 years may be discharged on the same day as surgery, and children under 2 years of age should be observed overnight for any sequelae of anesthesia.

## Outcomes

Although some variability exists, the majority of children who receive cochlear implants achieve excellent results. Over the long term, most children who receive cochlear implants develop open set speech recognition, use the telephone, are in mainstream schools, and use exclusively oral communication.[16,17] In a recent cost-utility analysis, cochlear implantation was estimated to cause a gain of approximately 10 quality-adjusted life years (QALYs) per implanted prelingually deafened child.[18] The estimated lifetime cost of cochlear implantation was $160,000 per child. As a consequence, the estimated cost per QALY was on the order of $16,000, consistent with a very cost-effective intervention. Further, when indirect costs of nonmainstream schools or additional school services are considered, cochlear implantation in prelingually deafened children is estimated to be *cost-saving*.

Among children who are prelingually deafened, implantation over the age of five substantially limits but does not eliminate the maximal benefit of cochlear implantation (Fig. 22.5).[19] Further, among prelingually deafened children, earlier implantation is correlated with earlier receptive and spoken language improvements and more rapid improvement over time (Figs. 22.6 and 22.7).[20] Children undergoing bilateral cochlear implantation appear to have improved receptive and spoken language development than those who undergo unilateral implantation. The longer the duration between the first and second implants, the worse their language performance.[21] Improved sound localization can be achieved with bilateral as opposed to unilateral cochlear implantation in children.[22,23] Hearing in noise is a particular challenge for children with cochlear implants, just as it is for children with hearing loss who use hearing aids.[24]

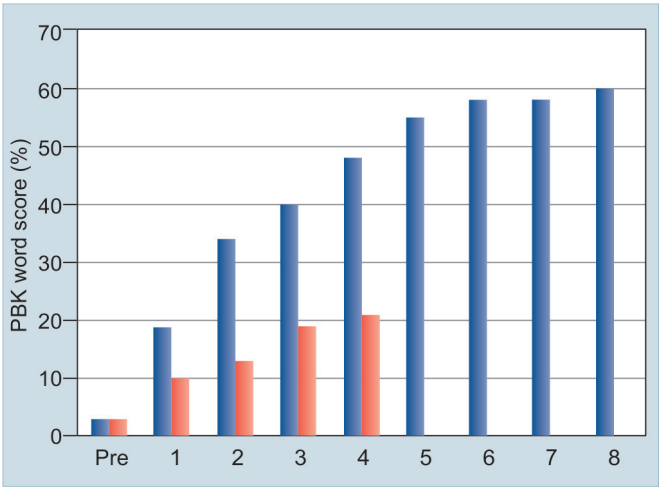


**Fig. 22.5:** Open set speech improvement by age at implantation of prelingually deafened children. Average phonetically balanced kindergarten (PBK) word scores grouped by age of implantation are plotted by number of years after implantation. Blue bars represent the mean scores of children implanted between ages 2-5 (N = 59); red bars represent the mean scores of children implanted between ages 8-13 (N = 18). Pre represents preimplantation scores. Adapted from Harrison et al.[19]

Children with cochleovestibular anomalies show wider variation in hearing outcomes than children without those anomalies.[7,25] Among these children, the best hearing outcomes are obtained in children with either incomplete partition defects or enlarged vestibular aqueduct. Variable outcomes are seen in children with hypoplastic cochleas, and worse outcomes are obtained in children with more severe deformities such as common cavity malformation. Children with developmental delay also tend to have somewhat worse audiologic outcomes than those children without developmental delay; they nonetheless derive substantial audiologic benefit in addition to improvements in intelligence and adaptive behaviors relative to those children with severe to profound hearing loss who are not implanted.[26] Children with auditory neuropathy may also derive substantial benefit from cochlear implantation, but also with more variable audiological outcomes that children with purely cochlear hearing loss.[27]

## Complications

Infection or soft tissue complications following cochlear implantation are uncommon in children with rates reported below 5%.[28] Should a superficial infection occur, antibiotic treatment is typically sufficient to resolve the issue. In cases where the device extrudes and is grossly contaminated, it should be explanted, the infection treated, and the device reimplanted once the wound bed is well healed. Device migration is rare, regardless of the technique of device fixation used.[29] In cases where either no benefit is achieved or when there is initial benefit that is subsequently lost, the device should be interrogated by the patient's audiologist. When the device is found to be malfunctioning this is referred to as a "hard failure". When auditory benefit is lost despite a functioning device, this is referred to as "soft failure".

Additional complications include aberrant nonauditory side effects of stimulation. These can include off-target facial nerve stimulation or vestibular stimulation

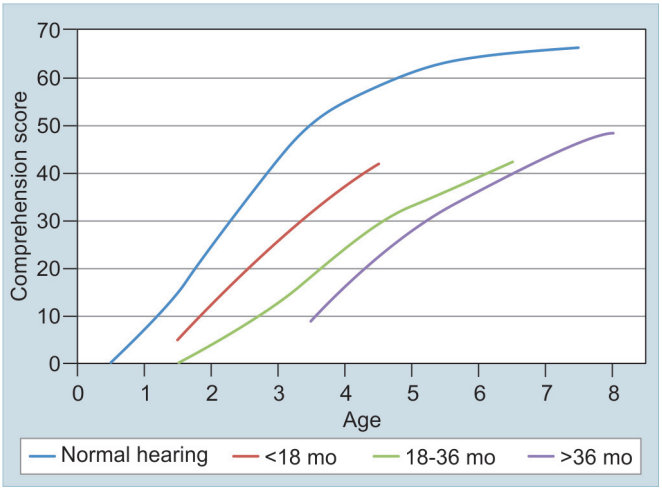


**Fig. 22.6:** Comprehension scores of prelingually deafened children following cochlear implantation before the age of 5. Depicted are nonparametric fits of Reynell Developmental Language Scales Raw scores of language comprehension stratified by age at implantation. Adapted from Niparko et al.[20]

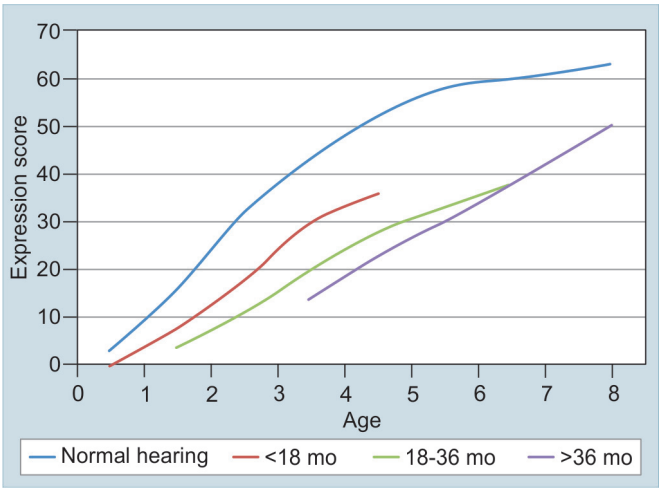


**Fig. 22.7:** Expression scores of prelingually deafened children following cochlear implantation before the age of 5. Depicted are nonparametric fits of Reynell Developmental Language Scales Raw scores of language expression stratified by age at implantation. Adapted from Niparko et al.[20]

and can often be resolved with altering the programming of the device. There may also be failure of the external device to maintain magnetic coupling with the implanted receiver-stimulator. This may require a stronger magnet on the external device, thinning of the skin and soft tissue flap or, least commonly, replacement of a demagnetized internal magnet.

## CONCLUSIONS

In summary, cochlear implants have revolutionized hearing rehabilitation for children with severe to profound hearing loss. Despite the incredible success of these prostheses, there remains a great deal that is unknown regarding the underlying pathology of hearing loss as well as the determinants of outcome following cochlear implantation. With a better understanding of the pathophysiology of hearing and improvements in technology and surgical technique, the coming years are sure to bring substantial progress in hearing rehabilitation for children.

## VIDEO LEGEND

**Video 22.1:** Surgical technique of cochlear implantation.

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CHAPTER

# 23

# Pediatric Auditory Brainstem Implantation

***Aaron D Tward, Daniel J Lee***

## INTRODUCTION

Cochlear implantation has revolutionized the hearing rehabilitation options of children with severe to profoundly hearing loss. Results from commercially available single-channel cochlear implant technology in the 1970s[1] and multichannel cochlear implant technology in the 1980s[2] demonstrated that direct electrical stimulation of the neural components of the auditory system can provide meaningful perception of sound and speech among children and adults with severe to profoundly hearing loss. The primary pathology in the majority of children with severe to profound sensorineural hearing loss lies in the soft tissue components of the inner ear (Organ of Corti), rather than gross malformations of the cochlea or lack of development of an auditory nerve. Therefore, the majority of children with severe to profound sensorineural hearing loss have anatomy that is favorable for placement of a cochlear implant and cochlear implantation is the treatment of choice for these children and their families who desire hearing habilitation/rehabilitation. However, there exists a rare but distinct subset of children with severe to profound sensorineural hearing loss who are unable to benefit from cochlear implantation, either as a consequence of unfavorable cochlear anatomy or lack of a functional cochlear nerve. If hearing rehabilitation with an auditory prosthesis in this subset of patients is desired, then stimulation must necessarily be directed beyond the level of the primary lesion in the auditory pathway to higher centers of auditory processing, such as the cochlear nucleus. The auditory brainstem implant (ABI) bypasses an abnormal, absent, or damaged inner ear and auditory nerve to directly stimulate the second order auditory neurons found in the cochlear nucleus. This device was originally developed by the House Ear Institute for those patients deafened by neurofibromatosis type 2 (NF2), a genetic syndrome resulting in the development of multiple brain and spinal cord tumors, including bilateral vestibular schwannomas. The growth and or removal of these tumors often result in bilateral profound hearing loss that in most cases cannot be helped with the cochlear implant. The ABI was approved by the FDA in the US in 2000 for patients age 12 and over with NF2 and overall outcomes have been modest compared with cochlear implant performance.

A breakthrough came in 2001, when Professor Vittorio Colletti performed the first two non-NF2 infant ABI surgeries in Verona, Italy.[3] Since then, investigators have begun to use ABIs in this population of children for hearing rehabilitation and as of 2013, over 150 infants and children who are deaf from causes not related to NF2 have been implanted. With this novel indication for the ABI, children have the possibility of achieving sound awareness, and in some cases, meaningful speech recognition.

## ANATOMY/PHYSIOLOGY

In normal hearing, sound vibrations enter the external auditory canal, and vibrate the tympanic membrane. These vibrations are then transmitted to the fluid-filled space of the inner ear via the malleus, incus, and stapes and ultimately the oval window. In turn, the basilar membrane of the cochlea vibrates, with the apex of the cochlea being most sensitive to low-frequency sounds and the base of the cochlea being most sensitive to high-frequency sounds.

This property of different frequencies being represented in different positions in space is referred to as tonotopic organization (Fig. 23.1). The inner hair cells sit atop the basilar membrane and convert these vibrations into the rapid release of neurotransmitters at the first neural relay in the auditory system, the ribbon synapse. The ribbon synapse connects the basolateral membrane of the hair cell to the afferent type I spiral ganglion neuron. The axons of the spiral ganglion neurons pass through the modiolus of the cochlea where they coalesce into the cochlear nerve, a branch of the eighth cranial nerve. The cochlear nerve then enters the brainstem near the pontomedullary junction lateral to the entry point of the facial nerve. The axons of the spiral ganglion cells then synapse in either the dorsal or ventral cochlear nucleus. From the ventral cochlear nucleus, neurons project to either the ipsilateral or contralateral superior olivary complex (sometimes by way of the trapezoid body). The neurons of the dorsal cochlear nucleus project either to the ipsilateral or contralateral superior olivary complex or directly to the contralateral inferior colliculus in the midbrain. The inferior colliculus also receives inputs from the superior olivary complex. From the inferior colliculus, projections are then sent to the medial geniculate nucleus and from the medial geniculate nucleus, projections are sent to the auditory cortex. In a similar fashion to the cochlea, the dorsal and ventral cochlear nuclei harbor a tonotopic map (Fig. 23.1), where different nuclei are maximally activated by different frequencies of sound. It is the presence of this tonotopic map that is the driving rationale for use of a multichannel ABI.

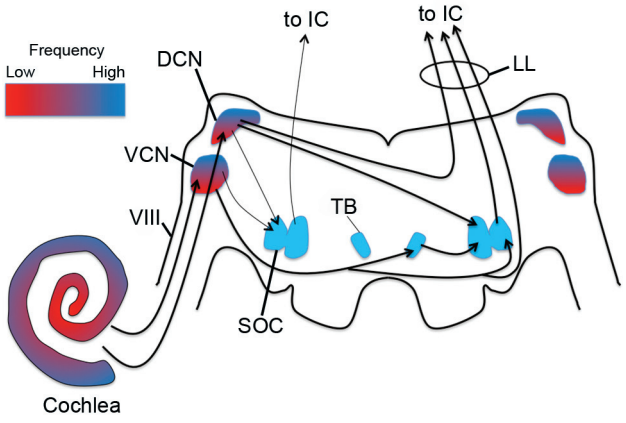



**Fig. 23.1:** Cochlear and brainstem auditory pathways. The cochlear is organized with cells maximally responsive to low-frequency sounds at the apex (red) and high-frequency sounds at the base (blue). This organization is referred to as a tonotopic map. The spiral ganglion neurons of the cochlea project to the cochlear nucleus via the cochlear nerve. The tonotopic map is preserved in the dorsal cochlear nucleus (DCN) and ventral cochlear nucleus (VCN). The neurons of the cochlear nucleus then project either directly or indirectly to the inferior colliculus (IC) via the lateral lemniscus (LL), and after additional relays ultimately to the auditory cortex. (VIII: Cochlear nerve; SOC: Superior olivary complex; TB: Trapezoid body).

## HISTORY OF ABIs

As mentioned in the introduction, the ABI was originally designed to meet the need for auditory rehabilitation in patients with NF2. William Hitselberger and William House performed the first ABI in 1979 on a woman with NF2 immediately after she had her second vestibular schwannoma removed via a translabyrinthine craniotomy.[4] This early generation ABI was a single-channel ball implant with a pair of electrodes placed on the surface of her dorsal cochlear nucleus. Once activated, this patient was able to hear sound and had significant improvement in lip reading. She continued to use the device for at least 20 years. Subsequent work by multiple groups resulted in progressive improvements in the design of ABIs, including the advent of multiple electrodes, transcutaneous stimulation via induction coil, and improved programming strategies.[5] In 2001, the result of the first two pediatric ABI placements in young children with congenital anomalies was reported by Vittorio Colletti and his colleagues in Verona. Both implanted children achieved speech detection and some speech discrimination.[3] In 2013, Colletti performed an ABI surgery in an 8-month-old infant, the youngest performed to date. The largest experience in the world continues to be at the University of Verona, with over 80 ABIs performed in infants and children. Professor Levent Sennaroglu's center in Ankara, Turkey has performed over 50 ABI surgeries in pediatric patients between 12 months and 5 years of age.

The ABI is not yet FDA approved for use in infants and children who are deaf and do not have NF2. With compelling outcome data from Europe, four centers in the United States have established pediatric ABI programs. As of December, 2013, four infants have undergone ABI surgery, in the United States, at New York University, University of North Carolina Chapel Hill, and Massachusetts Eye and Ear Infirmary/Massachusetts General Hospital, and Harvard Medical School. University of North Carolina, Harvard, and House Ear Clinic have approved FDA clinical trials to study outcomes following pediatric ABI surgery. The youngest pediatric ABI recipient in the United States, as of the writing of this chapter, was a 16-month-old male infant with cochlear and

auditory nerve hypoplasia. He underwent uneventful retrosigmoid craniotomy and ABI placement in October, 2013, at the Massachusetts General Hospital, and at 2 months following activation is demonstrating behavioral auditory responses with the ABI.

## DESCRIPTION OF ABIs

The ABI is a modified cochlear implant and consists of an internally implanted receiver/stimulator and an externally worn microphone and speech processor (Fig. 23.2A). Sound is detected by an external microphone, worn either on the body or behind the ear. The signal is then sent to an analog to digital processor that encodes the sound information by one of several processing algorithms. The processor sends the encoded signal to the internal receiver/stimulator via the transmitter coil. The internal receiver-stimulator is composed of an induction coil attached to a ground electrode and an array of 12 (MED-EL ABI, not FDA approved) or 21 disk-shaped platinum electrodes (Cochlear Corp, FDA approved) arranged on a paddle designed to be placed on the surface of the human dorsal cochlear nucleus (Fig. 23.2B). The signal is received by the internal induction coil, activating distinct electrodes (Fig. 23.2C), which are in proximity to or on the cochlear nucleus. Activation of the electrodes electrically stimulates groups of neurons within the cochlear nucleus, and the information is relayed to higher centers in the auditory system. Ultimately, this results in the perception of sound (and varying degrees of speech recognition in some patient cohorts) by the successful ABI user.

## INDICATIONS AND PREOPERATIVE EVALUATION

In general terms, children with severe to profound hearing loss who would otherwise be candidates for cochlear implantation, but for whom cochlear implantation is not


**Figs. 23.2A to C:** The auditory brainstem implant. (A) External processor of an auditory brainstem implant. The transmitter coil contains a magnet in the center that permits it to sit in opposition to the internal induction coil. (B) Internal receiver-stimulator of an auditory brainstem implant. (C) Close-up of electrode array. This array is placed directly on the cochlear nucleus. Each electrode or electrode pair stimulates fields of neurons within the cochlear nucleus.

an option due to unfavorable anatomy are candidates for ABIs. In addition, children with unfavorable anatomy who have had a prior cochlear implant and no significant benefit after 6 months of use with no possibility of revision or contralateral implant can be considered candidates for ABI. At the time of this writing, over 150 children have received ABIs worldwide (V. Colletti and L. Sennaroglu, personal communication).[6–9] As a consequence of increasing interest in the use of ABI in children, a conference on ABI in children and non-NF2 adults was convened in Turkey in 2009. A first consensus statement on the indications for ABI in children was drafted.[10] Two distinct groups of children were identified as candidates: (1) prelingually deafened children with inner ear malformations and/or cochlear nerve hypoplasia or aplasia and (2) postlingually deafened children with cochlear ossification, bilateral temporal bone fractures with cochlear nerve avulsion, or intractable facial nerve stimulation with cochlear implantation. A second consensus meeting on pediatric ABI surgery was held in Ankara, Turkey, in 2013 and the conclusions from this meeting will be published in 2014 following peer review.

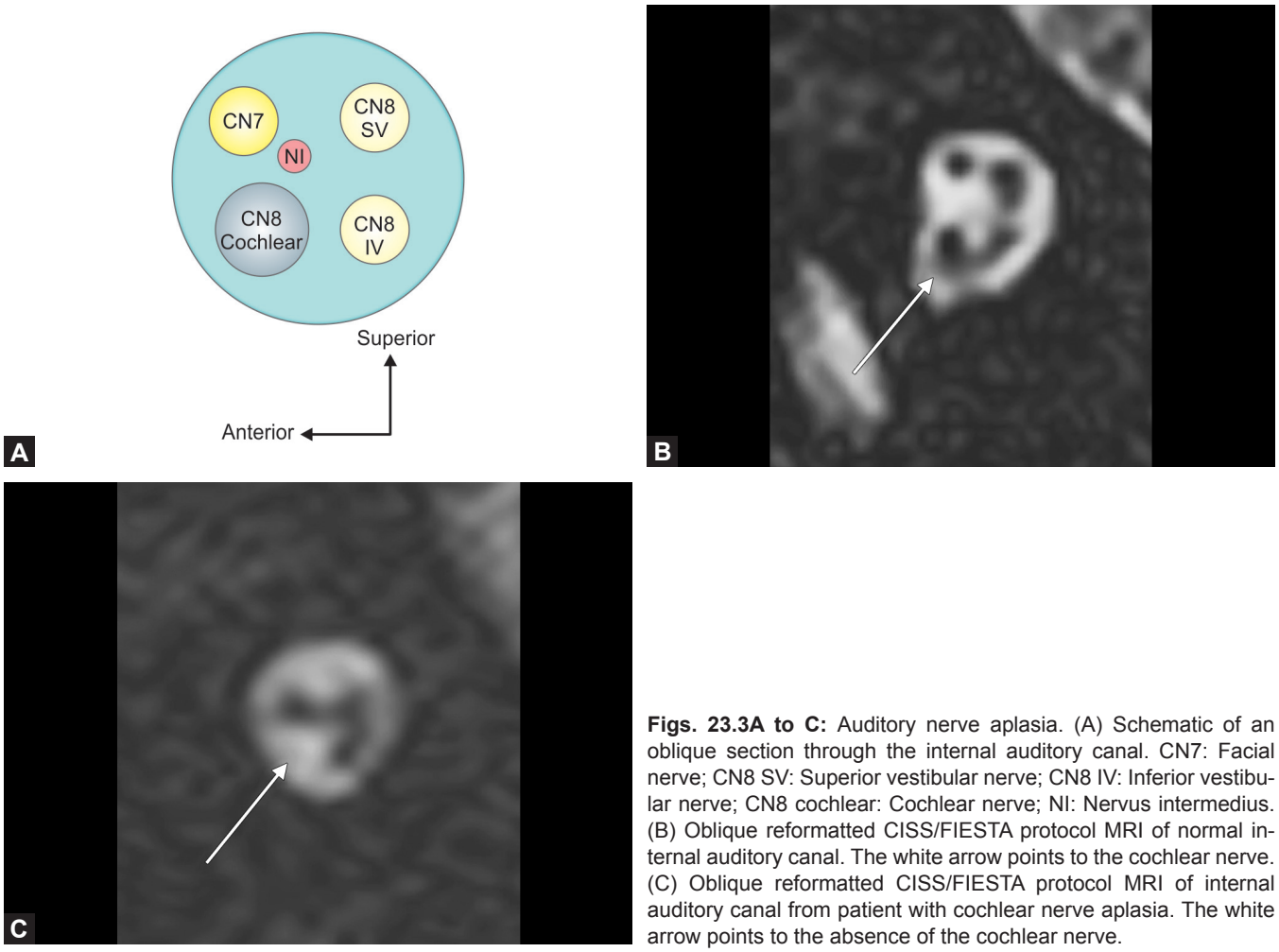
High-resolution imaging and interpretation by an experienced neuroradiologist are critical in the workup of potential pediatric ABI candidates. In particular, a noncontrast high-resolution computed tomography (CT) scan of the temporal bones as well as 3 T high-resolution magnetic resonance imaging (MRI) of the temporal bones including a T2-weighted FIESTA/CISS sequence should be obtained (with direct oblique or reformatted views of the internal auditory canal). A number of factors should be considered that influence surgical planning. First, the gross anatomy of the brainstem should be assessed to evaluate the likelihood that the cochlear nucleus is intact and present along with the vestibulocochlear nerve at the root entry zone. The cochlear nuclei themselves typically cannot be easily distinguished on MRI. The presence and patency of the lateral recess should be confirmed if possible, and attention paid to any structures that might obstruct the lateral recess, including blood vessels or scar tissue. The presence or absence of the nerves of the internal auditory canal may inform the interpretation of landmarks intraoperatively.

In children with complete labyrinthine aplasia, cochlear aplasia, cochlear nerve aplasia, or cochlear aperture aplasia (Figs. 23.3A to C), bilateral temporal bone fractures with cochlear nerve avulsion, or complete ossification of the cochlea with no T2 signal on MRI within the cochlear duct, it is reasonable to consider ABI without first considering cochlear implantation. In cases where there is cochlea, cochlear aperture, or cochlear nerve hypoplasia (< 50% of the diameter of the normal cochlear nerve), or cochlear ossification but with at least a partially patent cochlear duct, then cochlear implantation can be considered as an option, although ABI may still be preferable a priori depending on the particular circumstances of the patient. In cases where it is unclear if there is any functional connection between the cochlea and the brainstem, electrical auditory brainstem response (EABR) testing with cochlear promontory stimulation may be considered. If consistent EABR responses with promontory stimulation cannot be obtained, then cochlear implantation is less likely to provide benefit.[11]

Although data on the subject are limited, it is likely that there is a critical period from birth to age of 3 years after which the ability of the central auditory system to maximally utilize information from an ABI begins to decline. This critical period likely mirrors the critical period for cochlear implantation, or is perhaps even more stringent.[10] As a consequence, among prelingually deafened children, we recommended performing auditory brainstem implantation before the age of 3 years.

A complete medical history and physical is necessary to rule out any comorbidities that would be a contraindication to general anesthesia. In postlingually deaf children, evaluation by an experienced audiologist with audiometry and speech perception testing is necessary. In prelingually deaf children, the audiologic evaluation should include auditory brainstem response testing. A speech-language pathologist and neurodevelopmental evaluation are helpful in assessing the general and domain-specific cognitive abilities of the child. A social work evaluation should be undertaken to assess and reinforce the importance of family support.

Two main factors influence the choice of side for implantation: anatomy and functional evidence of hearing. If there is no evidence of any functional hearing on either side, then the side with the most accessible lateral recess and with any evidence of a cochlear nerve should be selected for implantation. If there is functional evidence of hearing on only one side, such as the presence of ABR at high thresholds, then that side should be selected for implantation as it has a greater likelihood of having a functional cochlear nucleus present.



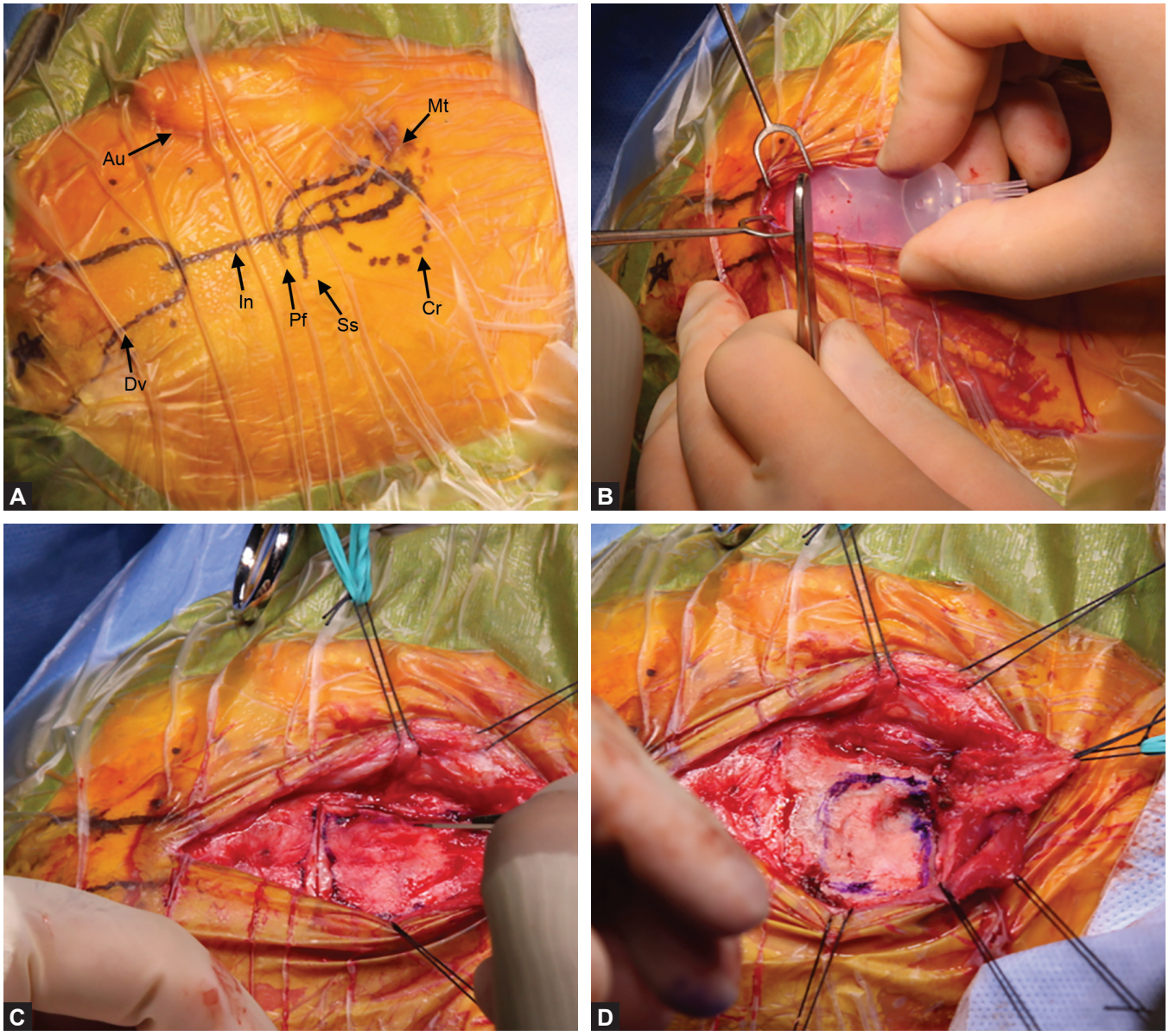

**Figs. 23.3A to C:** Auditory nerve aplasia. (A) Schematic of an oblique section through the internal auditory canal. CN7: Facial nerve; CN8 SV: Superior vestibular nerve; CN8 IV: Inferior vestibular nerve; CN8 cochlear: Cochlear nerve; NI: Nervus intermedius. (B) Oblique reformatted CISS/FIESTA protocol MRI of normal internal auditory canal. The white arrow points to the cochlear nerve. (C) Oblique reformatted CISS/FIESTA protocol MRI of internal auditory canal from patient with cochlear nerve aplasia. The white arrow points to the absence of the cochlear nerve.

## PROCEDURE

The ABI can be implanted via a retrosigmoid or translabyrinthine approach in older children. The retrosigmoid approach is the desired approach for infants and young children without NF2, and has the advantage of preserving vestibular anatomy and function that is present on that side. Due the small size of the temporal bone, the translabyrinthine approach does not provide adequate access to the lower cranial nerves and lateral recess needed to safely guide the electrode in small infants compared to a retrosigmoid craniotomy. After confirming the correct side to be implanted, the child is brought to the operating room and placed under general anesthesia, without the use of long acting paralytics. The patient's head and body are placed in a modified supine position or lateral decubitis position, rotated 45° away from the surgeon. After this, facial nerve monitoring is set up with three subdermal needle electrodes placed and secured in the frontalis, orbicularis oculi, and orbicularis oris muscles, as well as ground and stimulating electrodes placed in the chest. For EABR recording, subdermal needle electrodes are placed and secured in the midline at the vertex of the skull, in the neck over C7, and with a ground over the inion.[12] Monitoring of additional cranial nerves such V, IX, X, and XI may also be established at this point, if desired. An appropriate amount of hair is shaved and the patient is prepped and draped using sterile technique. A device template may be used to determine optimal position of the receiver/stimulator, and the position may be marked on the bone by placing methylene blue through the skin at the end of a needle. An approximately 5–7 cm curvilinear incision is created in the postauricular region (Fig. 23.4A) and a skin flap is elevated in the plane of the temporoparietal fascia, superficial to the periosteum of the mastoid and occipital bones and superficial to the

superficial layer of the temporalis fascia (Fig. 23.4C). An inferiorly based periosteal flap is subsequently elevated (Fig. 23.4D), and the suboccipital muscles are partially detached from the region of the planned craniotomy. A subperiosteal pocket for the device is created superior and posterior to the region of the planned craniotomy and the depth and width are determined by the template (Fig. 23.4B). A well for the device is drilled superior and posterior to the craniotomy site, although this approach is avoided in young infants. At this point, the template is left in the pocket until the ABI is placed.

A 3 × 3 cm craniotomy is created with the anterior limit at the sigmoid sinus, and the superior limit at the transverse sinus (Fig. 23.4D). The sigmoid is fully decompressed to allow for sufficient dural reflection anteriorly in order to minimize cerebellar retraction. Bone wax is placed into any exposed air cells to prevent cerebrospinal fluid (CSF) leak. An incision is created in the dura and the dural flaps are retracted. The cisterna magna is opened, and the cerebellum is decompressed by permitting CSF to drain until flow slows considerably. Using gentle retraction if necessary, the facial, vestibular,




**Figs. 23.4A to D:** Soft tissue technique for auditory brainstem implant (ABI). (A) Surface landmarks of ABI technique. Au: Auricle; Dv: device; In: skin incision; Pf: Anterior limit of periosteal flap; Ss: Sigmoid sinus; Cr: Craniotomy; Mt: Mastoid tip. (B) Insertion of silicone template into tight periosteal pocket. (C) Creation of periosteal flap over craniotomy site. (D) Location of craniotomy site.

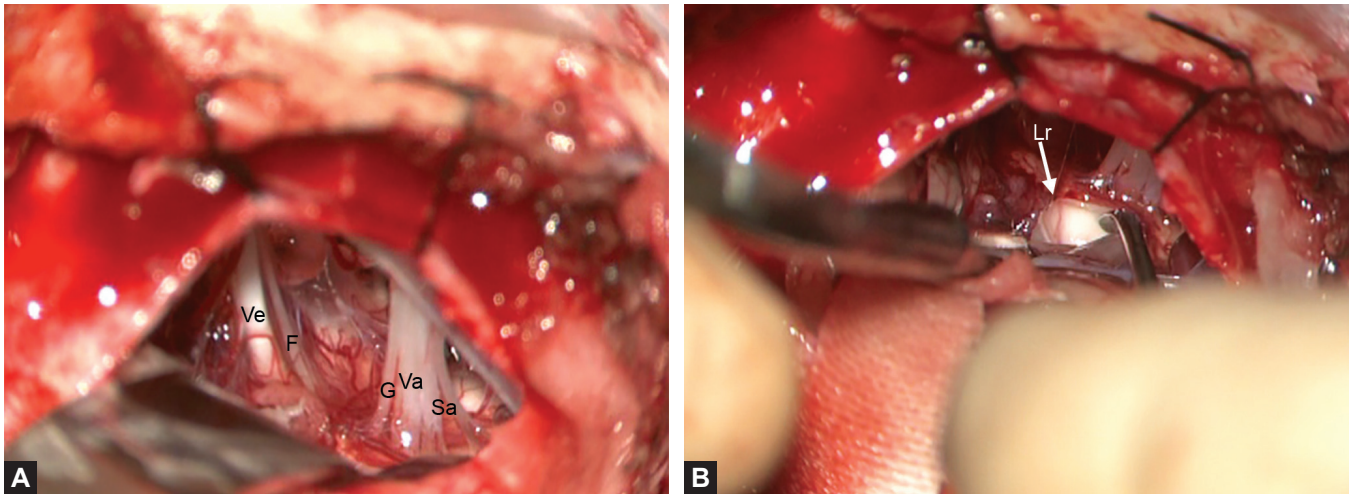
cochlear (if present), glossopharyngeal, vagus, and spinal accessory nerves are identified (Fig. 23.5A). Identification of the seventh cranial nerve is confirmed with stimulation. Using microdissection, the lateral recess is identified (Fig. 23.5B). Key landmarks to identify the lateral recess include the entry points of the glossopharyngeal nerve, the cochlear nerve, and choroid plexus, which may be protruding through the lateral recess. In addition, the cerebellar flocculus may obscure the lateral recess and need to be retracted. Once opened with microdissection, the position of the lateral recess may be confirmed by observing the outflow of CSF. The cochlear nucleus may be appreciated as a bulge protruding into the floor of the lateral recess.

The device is then opened and inspected for any gross manufacturing defects. The magnet is only replaced with a nonmagnetic metallic spacer if routine MRI surveillance is indicated as would be the case in a patient with NF2. The device is placed and secured using a tight subperiosteal pocket technique or using nylon suture tie downs, anchored either to titanium screws or to grooves drilled into the bone. The grounding electrode is placed deep to the temporalis muscle anterior to the craniotomy site in line with the zygoma.

Under microscopic control, the electrode array is then placed on or near cochlear nucleus through the lateral recess. Given the relatively small size of the lateral recess in infants, the Dacron wings of the electrode array are often trimmed to facilitate insertion. An EABR is obtained using bipolar stimulation of electrode pairs across the electrode paddle to confirm proper placement (Fig. 23.6). In general, one to two positive peaks seen in the first 2–3 ms are associated with an auditory response postoperatively. Larger amplitude and long latency responses are generally nonauditory responses. If a consistent EABR cannot be obtained, the electrode array is repositioned until one can be obtained. Once this is confirmed, muscle and/or fat is placed to stabilize the electrode array within the lateral recess. The dura is closed in a watertight fashion with several layers of muscle and bovine collagen dural grafts, and the incision is closed in multilayered fashion with deep layers of absorbable suture and a superficial layer of running, locking, slowly resorbable (Monocryl), or nonresorbable (nylon) suture. A mastoid pressure dressing is then placed.

## POSTOPERATIVE CARE

Patients are monitored in a pediatric intensive care unit with frequent neurological checks for at least one day. A postoperative CT scan is often obtained 6–8 hours after the completion of the procedure to confirm electrode placement and to rule out hemorrhage or hydrocephalus (Fig. 23.7). Postoperative steroids are given and tapered over the course of 4 days. Pain control is achieved with acetaminophen and opiates if necessary. The patients can typically leave the hospital after 3–4 days. The pressure dressings are changed at least once during the hospital stay and parents are encouraged to keep the dressings on for at least 1 week to help reduce the risk of a CSF leak. Wound sutures, if not dissolving, are removed in follow-up 2 weeks after the procedure. As long as there




**Figs. 23.5A and B:** Brainstem anatomy for auditory brainstem implant. (A) Wide exposure of cranial nerves. (Ve: Vestibular nerve; F: Facial nerve; G: Glossopharyngeal nerve; Va: Vagus nerve; Sa: Spinal accessory nerve). (B) Exposure of the lateral recess (Lr). *Courtesy*: L. Sennaroglu, Ankara, Turkey.

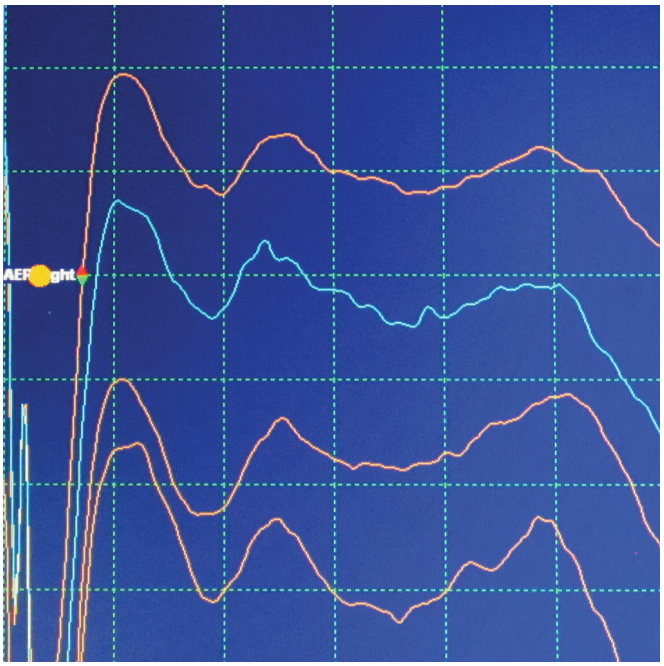


**Fig. 23.6:** Intraoperative auditory brainstem response (ABR). Upon bipolar stimulation of two electrodes, a biphasic response with latency characteristic of brainstem auditory processing was elicited.

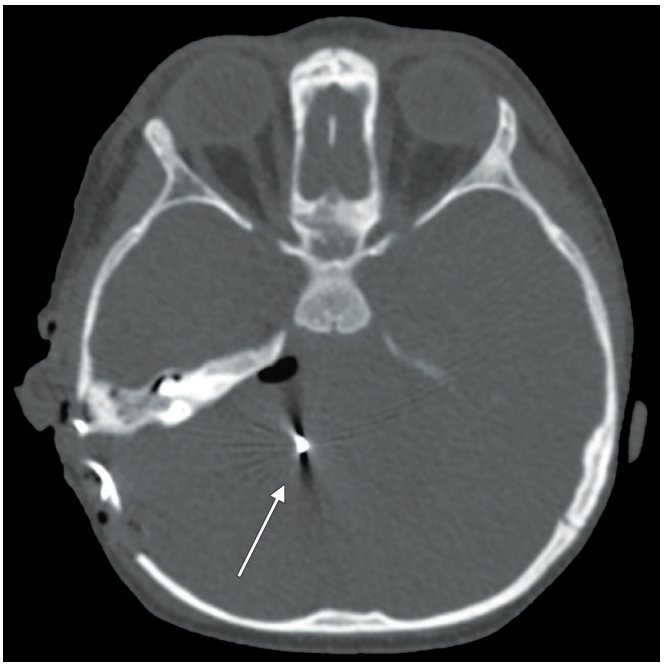


**Fig. 23.7:** Postoperative CT scan after auditory brainstem implantation. An axial noncontrast CT scan was obtained 6 hours following the completion of the operation. The white arrow indicates the electrode paddle in position on the brainstem.

are no wound-related issues, the device can be activated 6–8 weeks after the procedure. We perform the initial activation for infants under dexmedetomidine (alpha 2 agonist/Precedex) intravenous sedation in order to set initial ABI stimulation levels and monitor ABRs and to determine the thresholds required to generate nonauditory side effects such as bradycardia and gag reflex. The ABI can then be more safely activated and mapped in an awake child, with a medical team present, on the following day.

## OUTCOMES

Because we are still in the early days of pediatric auditory brainstem implantation, only a small number of papers have been published by various international groups describing their experience (Table 23.1). In 2007, Colletti reported on the outcomes of 18 children who underwent ABI surgery in Verona, Italy. All of the children used their devices for >75% of their waking hours. On the category of auditory performance scale, the range of scores for these 18 children was from 1 (sound awareness) to 7 (able to speak on a telephone), with an average score of 4 (can discriminate between two sounds).[6] Eisenberg reported the comprehensive evaluation of a child with Goldenhar's syndrome and bilateral cochlear nerve agenesis who had been implanted in Verona at age 3 years, 3 months, and evaluated 6 months and 12 months after ABI activation.[7] At 12 months after activation, this child had Infant-Toddler Meaningful Auditory Integration Scale (IT-MAIS) and Early Speech Perception (ESP) category scores near the median for cochlear implant users at the same point in time following activation. Goffi-Gomez[8] reported on the results of four children implanted with ABI in Brazil. All four children gained sound awareness, and three of the four had significant improvements of IT-MAIS and Meaningful Use of Speech Scale (MUSS) scores. Choi[9] reported on eight children implanted in South Korea. All eight achieved sound awareness, and seven out of the eight children had some sound recognition. Sennaroglu has reported on the outcome of 29 children implanted in Turkey (L. Sennaroglu, personal communication). All 29 achieved sound awareness, and 12 of the children achieved some open-set speech recognition. Some of the diversity of reported outcomes is likely to be a consequence of the different ages of children implanted in these initial efforts, with significantly better results obtained with younger children. In sum , although there exists a range of performance with ABIs in children, almost all children do achieve sound awareness, and a substantial portion achieve a level of performance that is likely to significantly improve

**Table 23.1:** Outcomes after pediatric auditory brainstem implantation

| *Study* | *Sound awareness* | *Daily use* | *Sound recognition* | *Open-set speech* |
|---|---|---|---|---|
| Colletti [6] *N* = 18 | 18 | 18 | 5 | 1 |
| Eisenberg [7] *N* = 1 | 1 | 1 | 1 | |
| Goffi-Gomez[8] *N* = 4 | 4 | 4 | | |
| Choi[9] *N* = 8 | 8 | | 5 | |
| L. Sennaroglu, personal communication *N* = 29 | 29 | 29 | 29 | 12 |
| *Total* | *60/60* | *52/52* | *40/56* | *13/56* |

their cognitive development. Going forward, prospective studies are necessary to better understand the predictors of good performance and optimize outcomes for those children with ABIs.

## COMPLICATIONS

Colletti and colleagues have reported on complications in children following ABI surgery.[13] Among 29 children, major complications were observed in 2/29 children and minor complications in 5/29 children. The major complications were cerebellar contusion, and meningitis, which was treated with antibiotics and resolved. The minor complications included wound seroma/CSF leak, minor infections, balance problems, temporary dysphonia, and non-auditory side effects of stimulation. Sennaroglu has also observed two children with transient facial palsy and five children with CSF leak out of 39 children implanted with ABI. Taken together, these data indicated that auditory brainstem implantation is a relatively safe procedure in children, and has a risk profile that is low, but still somewhat higher than cochlear implantation.

## CONCLUSION

Auditory brainstem implantation in children has opened an exciting avenue of hearing rehabilitation for a group of children with a challenging set of pathologies. Despite the fact that relatively few children have been implanted and prospective studies have not yet sharpened our focus on ways to optimize patient selection and performance, there have been some encouraging success stories among implanted children. Continued and careful research will clarify the safety and success of ABI surgery in this selected cohort of deaf children who are not candidates for the cochlear implant.

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CHAPTER

24

# Balance Disorders in Children

***Michael S Cohen, Richard Lewis, Daniel J Lee***

## INTRODUCTION

Dizziness is a common symptom in children that can be challenging to manage. While dizziness may represent a vestibular disorder, it can also have central neurologic and non-neurologic causes. The term "dizziness" generally refers to an alteration of orientation to the surrounding environment, and it can be difficult for children to describe. Vertigo is defined as the perception of movement, typically spinning or turning, in the absence of actual movement. Children are especially good at compensating for loss of vestibular function and are able to rely on vision, hearing, and proprioception to maintain balance in many cases. A comprehensive approach to management of balance disorders in children will be presented in this chapter.

## PHYSIOLOGY

Vestibular hair cells can be stimulated by rotation, translation, or change in orientation with respect to gravity. This stimulation causes a change in the firing rate of the eighth nerve fiber innervating that particular hair cell, altering the input to the vestibular nucleus. These inputs are integrated in the vestibular nuclei along with visual, auditory, and somatic signals, resulting in compensatory eye movements, truncal control, and spatial orientation.

The vestibulo-ocular reflex (VOR) is a manifestation of the vestibular pathway that keeps the eyes fixed on a target while the head is moving by producing a proportional stimulus to the extraocular muscles in response to vestibular stimulation. The VOR is readily measurable using electro- or videonystagmography, and disturbances of the VOR are apparent in many vestibular disorders.

When an acute loss of peripheral vestibular function occurs unilaterally, there is a loss of resting neural discharge activity in that vestibular nerve and the ipsilateral nucleus. This loss of symmetry between the two nuclei is interpreted by the brain as a rapid head movement toward the healthy labyrinth. "Corrective" eye movements are produced toward the opposite side, resulting in nystagmus, with the slow component moving toward the abnormal side and the fast component moving toward the healthy labyrinth.

## OFFICE EVALUATION

It is important to elicit a chief complaint from the patient in his/her own words. Allowing the child to use his/her own vocabulary can be particularly instructive with regard to his/her subjective experience. History of present illness should include onset, duration, and frequency of episodes, association with other activities, and associated symptoms such as headache, nausea, or vomiting. A history of otologic symptoms such as hearing loss, tinnitus, aural fullness, otorrhea, and otalgia; and neurologic symptoms such as mental status changes, weakness, numbness, dysphagia, dysgeusia, facial weakness, and visual disturbances should be sought. Past medical and surgical history should include gestational age, birth trauma, complications, and history of central nervous system infections. Family history should include presence of migraine headaches, epilepsy, hearing loss, and syndromic illness. A questionnaire sent to the patient before the initial assessment can be useful to organize thoughts about the child's dizziness before the assessment. Children being evaluated for dizziness should have a complete audiologic evaluation, either with age

appropriate behavioral audiometry or with auditory brainstem response testing for children who cannot provide adequate responses with behavioral audiometry.

## Physical Examination

Physical examination should begin with observation of the patient and assessment of his/her general appearance, level of distress, and maintenance of posture. Orthostatic blood pressure measurements should be obtained. Ear examination should include pneumatic otoscopy. The nose, oral cavity, oropharynx, and neck should also be evaluated as part of a complete head and neck examination. Neurologic evaluation with special attention to cranial nerve function should be performed, including visual field testing and fundoscopic examination.

Observation of the child when walking can reveal abnormalities of coordination. Dysmetria may be demonstrated by the finger-to-nose and heel-to-shin tests. Additional abnormalities associated with cerebellar lesions can be assessed by evaluating the patient for dysdiadochokinesia, hypotonia, and decreased deep tendon reflexes.

### *Evaluation of Nystagmus*

Evaluation of nystagmus can best be performed in the office through observation. Frenzel goggles are high-magnification lenses with internal illumination that both reduce visual fixation and magnify the eyes for the observer. These can significantly aid the office evaluation of nystagmus. Alternatively, an infrared video system may be used.

*Spontaneous and gaze-evoked nystagmus*: Spontaneous nystagmus is an involuntary, rhythmic movement of the eyes not induced by any external stimulation. Nystagmus is named by the direction of the fast component. Spontaneous nystagmus is tested by having the patient look straight ahead with and without fixation. Gaze-evoked nystagmus is assessed by having the patient deviate the eyes laterally (no > 30°) with fixation. Nystagmus observed at the extreme limits of gaze, i.e. greater than 30°, is usually physiologic. Nystagmus is often reduced when looking in the direction of the slow component and increased when looking in the direction of the fast component.

*Positional nystagmus*: Positional nystagmus is assessed by examining the patient in each of the following six positions: sitting, supine, supine with the head turned to the right, supine with the head turned to the left, and right and left lateral positions. Persistent positional nystagmus presents without latency and persists as long as the patient remains in the provoking position. Paroxysmal nystagmus has a brief latency, fatigues on repeat provocations, and is usually associated with vertigo. It is often provoked by the Dix–Hallpike maneuver, in which the patient is moved rapidly from the sitting position to a right or a left head-hanging position.

### *Perilymph Fistula Test*

Perilymph fistula testing can be performed by applying pressure to the tympanic membrane either by repeatedly pressing the tragus or by applying positive and negative pressure in the external auditory canal with the use of a Politzer bag or a tympanometer. The patient's eyes are observed using Frenzel goggles. The fistula test is considered positive if nystagmus and vertigo are generated.

### *Head Thrust Test*

The head thrust test is performed by having the patient fix his/her gaze straight ahead. This can be accomplished with an interesting toy in younger children. The examiner then rapidly turns the head to the right or left. In a normal test, the eyes will stay fixed on the object of interest. In cases of vestibular hypofunction, the eyes will remain stationary within the orbit, turning away with the head, and then one or two saccadic movements will bring the gaze back to the object of interest.

### *Motor Function Testing*

The Peabody Development Motor Scale (PDMS), the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP), and the sensory organization test of computerized dynamic posturography (CDP) are valid tools for the evaluation of balance in children.

The PDMS assesses motor development, and is designed for children up to 7 years of age, whereas the BOTMP is appropriate for children from 4.5 years to 14.5 years of age. The BOTMP is generally the tool used after children become able to complete the PDMS gross motor items. The BOTMP takes less time, space, and equipment than the PDMS.

### *Vestibular Testing*

Vestibular laboratory testing is recommended in any child with a history of dizziness in whom a thorough history and physical examination has not established a diagnosis, to differentiate between a peripheral or central vestibular

lesion, and to identify side of lesion in a peripheral abnormality.[1] Because children with severe sensorineural hearing loss (SNHL) may have vestibular abnormalities, vestibular laboratory testing is recommended.[2] This is especially important in infants and young children with delayed motor development.[3] Vestibular laboratory testing assesses both the VOR and vestibulospinal reflexes.

Videonystagmography, having generally replaced electronystagmography, uses infrared goggles to record eye movements in a number of clinical conditions. Spontaneous and positional nystagmus, ocular motor testing, caloric testing, and rotational testing are generally included in the test battery. Only caloric testing gives definitive information about the condition of each labyrinth individually.

Binaural bithermal caloric testing stimulates each ear at 30°C and 44°C using direct irrigation of the ear canal or a closed loop balloon system in patients with a nonintact eardrum. When the irrigation is performed at 44°C the nystagmus (fast component) is toward the irrigated ear, and when using 30°C irrigation the nystagmus is away from the irrigated ear. Several formulas exist to quantify the degree of vestibular response for each side.

Rotational testing is a physiologic test to assess the VOR, as rotation is the natural stimulus to the semicircular canals. Both labyrinths are stimulated simultaneously. Rotational testing uses a specially designed chair to generate physiologic stimuli while eye movements are recorded. Major advantages in children include decreased nausea compared with caloric testing and the ability to seat the child in a parent's lap during testing. Three parameters are derived from the rotational testing; gain measures magnitude of the response (eye velocity) in relation to stimulus, phase measures timing between the response and the stimulus, and asymmetry measures difference in response between sides.

Computerized dynamic platform posturography is a physiologic test of the vestibulospinal and motor systems and assesses balance and posture by modifying visual, proprioceptive, and vestibular inputs under six sensory conditions referred to as the sensory organization test. In conditions I through III, the patient stands on a pressure platform that senses changes in center of gravity. In condition I the visual surround is static, in condition II the patient is blindfolded, and in condition III the background moves in synchrony with the patient's center of gravity, creating the illusion of no visual movement. Conditions IV through VI repeat the visual conditions of conditions I through III; however, the pressure platform is mobile, attenuating proprioceptive inputs. Sway amplitude and speed of sway can be measure in each axial direction or as a composite score. Conditions V and VI, the "vestibular conditions", most reliably isolate the vestibular inputs, and patients with a vestibular loss are likely to lose their balance and fall in these conditions.

Vestibular-evoked myogenic potentials (VEMPs) refer to electrical activity recorded from neck or eye muscles in response to intense auditory clicks or vibrations.[4,5] VEMPs reflect stimulation of the saccule, and may give unilateral information in some cases. VEMPs have been performed successfully in children as young as age 3.[6] Normative data for children may differ from that of the adult population.[7] Elevated amplitudes of VEMPs can be seen in some normal children and should be interpreted with caution.[8]

### *Laboratory Testing*

Laboratory testing may be helpful especially in cases where nonvestibular causes of dizziness are suspected. Complete blood count, serum glucose, and thyroid function tests can reveal common causes of lightheadedness or orthostasis. Additional testing for evidence of rheumatological, metabolic, and autoimmune conditions may be fruitful in select cases.

## Imaging

Imaging studies include computed tomography (CT) with or without contrast enhancement for the evaluation of bony structures of the temporal bone and middle ear. CT is performed to rule out congenital malformations or abnormalities such as infectious processes, cholesteatoma, or temporal bone fractures. Magnetic resonance imaging (MRI) with gadolinium enhancement is the best available imaging modality for clearly demonstrating central lesions and the contents of the internal auditory canal.

# ETIOLOGY

## Prevalence

While estimates of the prevalence of vertigo in children range from 7% to 8%,[9,10] vertigo is the chief complaint of only 0.7% of children presenting to an otolaryngology clinic.[11] These studies suggest that vertigo is not uncommon in children, but is often not brought to the attention of the otolaryngologist. This discordance may be exacerbated by the often vague and ephemeral nature of symptoms. When carefully evaluated, however, balance disorders can be diagnosed in children.

## Central Causes of Dizziness in Children

The majority of children who present with vertigo have a neurologic basis for their symptoms, and in this sense they differ from the adult population. By far, the most common central cause of vertigo in children is a migraine variant, while other central etiologies are relatively infrequent.[10a] Although all children presenting with vertigo do not require imaging of the brain, it is useful to organize the underlying central etiologies of vertigo in two categories, based on the absence or presence of a structural brain abnormality.

### *Central Dizziness without a Structural Brain Abnormality*

Vestibular migraine (VM), previously called benign recurrent vertigo of childhood, is the most common cause of vestibular symptoms in the pediatric population. One large study found that about 40% of all children presenting with vertigo were ultimately diagnosed as having a migraine variant as the cause of their symptoms.[11] VM is a well-recognized but poorly understood disorder. The mechanisms that relate migraine to vestibular symptomatology are unclear, but probably are due to the close juxtaposition and many interconnections between the regions in the brainstem that are thought to generate migraines (e.g. dorsal raphe nucleus) and the vestibular nuclei.[12] Although there have been occasional reports to the contrary,[13] VM is considered a central disorder and in general should not be associated with symptoms, signs, or test findings that clearly localize the pathology to one inner ear.

The diagnosis of VM, which generally follows the criteria first explicated by Neuhauser et al.,[14] has both inclusionary and exclusionary elements. The former generally requires a history of headaches that meet the international headache association (IHS) criteria for migraine,[15] but in children a clear headache history is often absent. Instead, factors that suggest VM include a family history of migraine and a personal history of motion intolerance. If there is a migraine history, then a temporal association between migraine (or related symptoms, such as noise or light sensitivity) and vestibular symptoms is needed to meet the "definite" Neuhauser criteria; if headaches and vertigo episodes are temporally independent, then the diagnosis based on the Neuhauser criteria would be "probable" VM.[14]

The specific characteristics of the vertigo episodes, such as their duration or provoking features, are usually not helpful in making the diagnosis of VM,[15] although vertigo episodes caused by VM are often provoked or exacerbated by changing head position relative to gravity (e.g. turning while in bed). Correlations of vertigo with other known migraine triggers such as foods (e.g. chocolate), sleep deprivation, or hormonal cycles (ovulation or menses) can also be suggestive. As noted above, VM is usually not considered when patients describe symptoms that clearly localize to one ear. The neurologic examination in VM is usually normal and does not display peripheral vestibular or auditory findings. In contrast, central vestibular or eye movement abnormalities are sometimes noted between episodes, although this is more common in adults with VM.[16] Similarly, audiograms and tests of peripheral vestibular function (caloric, rotation, VEMP) are generally normal, although several studies have related increased VEMP thresholds to VM in adult subjects.[17] If imaging is obtained, it is invariably normal. Unfortunately, a specific diagnostic test for VM is not currently available, although recent research suggests that quantitative measures of motion perception may eventually provide a more definitive way to diagnose VM.[18,19]

When a child is diagnosed with definite or probable VM, there are two treatment options to consider. Usually one begins by minimizing migraine triggers, which require lifestyle changes including adequate sleep, regular meals, stress reduction, dietary changes, and aerobic exercise. If this approach is not adequate, then it is reasonable to consider the use of prophylactic migraine medications.[20] It is important to emphasize that abortive migraine drugs such as sumatriptan have not been shown to affect vestibular symptoms,[21] and this approach to therapy is not recommended. However, the decision to use daily preventative medication is difficult in children, and depends on the extent that the vertigo episodes are affecting the quality of life and how the patient and his/her family feel about taking daily medication. The drugs used are not specific for VM, but rather are the typical migraine prophylactic medications, which include Periactin, beta-blockers, calcium channel blockers, tricyclic antidepressants, or antiepilpetic drugs. Treatment is empiric, with the medication chosen based on potential side-effect profiles and on other medical issues in the specific patient. The starting dose is low to minimize side effects, and is raised every 2–3 weeks. It is important to emphasize that a minimum of 2 weeks is needed on a given dose to determine if it is efficacious. Generally, as the dose is raised, the vestibular symptoms will improve, side effects will develop, or a substantial dose will be reached without affecting the vestibular symptoms. In the latter two cases the drug should

be stopped and an alternate drug should be tried. If the patient fails to respond to two or three medications that are tried in this manner, then the underlying diagnosis must be reconsidered. If the patient does respond well, then one could consider tapering and stopping the medication after 6–12 months to determine if it remains necessary. Many children with VM outgrow the vestibular symptoms but they generally develop typical migraine headaches.[22]

Other central causes of vertigo in children who have structurally normal brains are uncommon. Episodic ataxia type 2 is an autosomal dominant calcium channelopathy that presents with recurrent episodes of vertigo and ataxia, which are superimposed on a slowly progressive ataxia.[23] History is notable for a strong family history of similar symptoms and absence of other otologic or neurologic symptoms. Physical examination usually demonstrates central abnormalities such as vertical (e.g. downbeat) nystagmus and abnormal eye movements, and imaging may show atrophy of the cerebellum. The gene responsible for this disorder has been mapped to the CACNA1A gene and this can be tested in clinical laboratories. It is critical not to miss this disorder since the vertigo episodes (but not the progressive ataxia) usually respond very well to medical therapy. For several decades this disorder was treated with acetazolamide, but it is clear that the potassium channel blocker 4-aminopyridine is a more effective form of therapy and is usually well tolerated.[24]

Vestibular epilepsy is quite rare and is thought to reflect abnormal activity in the vestibular region of the cerebral cortex in the temporal or parietal lobes.[25] For this reason, other elements of temporal lobe (e.g. complex partial) seizures, such as reduced level of consciousness, automatisms, or a post-ictal state, may be associated with the vestibular symptoms. EEG may support this diagnosis if it demonstrates epileptiform activity in the temporal lobe, although a normal EEG does not exclude it. EEG monitoring, either inpatient or outpatient using an ambulatory device, increases the probability of capturing epileptiform activity in cases of vestibular epilepsy, but normal results remain nondefinitive, even if episodes occurred during the period of monitoring. Vestibular epilepsy is treated like other temporal lobe seizures with standard antiepileptic drugs.

Psychologic causes of vertigo are relatively common in children, accounting for 6% of all patients in one large study.[11] This can take two forms, either a conscious form that is similar to malingering, where a clear secondary gain (such as school avoidance) can be identified. More commonly, psychogenic dizziness is not conscious but is a form of an anxiety reaction. This diagnosis is considered when the characteristics of the dizziness seem nonphysiologic (e.g. vertigo is present continuously for months), the evaluation is normal, and stressors or a depressive/anxiety disorder is suspected.[26] In this scenario, referral to a psychologist or psychiatrist is warranted, as this problem generally responds well to appropriate behavioral and/or medical therapy.

### *Central Dizziness with a Structural Brain Abnormality*

Two types of structural abnormalities can present with vertigo, either congenital abnormalities or tumors. By far the most common congenital abnormality that presents with episodic vertigo is a Chiari 1 malformation (Fig. 24.1). In this disorder, the caudal brainstem and cerebellar tonsils are located below the foramen magnum, and vertigo and other symptoms are caused by direct mechanical pressure exerted by the bone on these brain structures.[27] Vertigo caused by Chiari malformations is often brief and provoked by Valsalva maneuvers such as coughing or sneezing. In this sense, it can be mistaken for the symptoms of a perilymph fistula or superior semicircular canal (SSC) dehiscence. Other lower cranial nerve symptoms, such as problems swallowing or articulating words, are often associated. Physical examination usually demonstrates downbeat nystagmus, which can be provoked or magnified with a Valsalva maneuver or neck extension, and associated eye movement abnormalities such as gaze

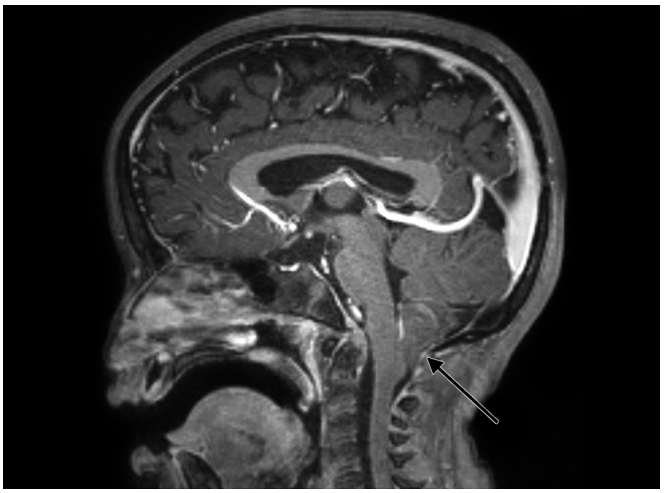


**Fig. 24.1:** Post-contrast sagittal magnetic resonance imaging (MRI) in a 6-year-old patient with dizziness, ataxia, and Chiari malformation. Arrow demonstrates cerebellar tonsils and caudal brainstem present below the foramen magnum.

holding nystagmus and impaired pursuit.[28] MRI displays not only a downward displacement of the caudal brain but also a evidence of "crowding" or pressure of bone on the displaced neural structures. If the symptoms warrant a surgical approach, decompression of the caudal brain by removing surrounding bone can improve or at least stabilize symptoms. One common issue regarding Chiari malformations is that many asymptomatic people have some degree of downward displacement of the cerebellar tonsils, and this becomes a diagnostic issue if people with this anatomic variant develop vestibular symptoms. As a general rule, in the absence of "crowding" on MRI or physical signs of caudal brainstem or cerebellar dysfunction, such as those outlined above, downward displacement of the tonsils is very unlikely to be responsible for vestibular symptoms.

Tumors that present with vertigo are invariably located in the posterior fossa, and can directly affect the brainstem or the cerebellum. Astrocytomas, medulloblastomas, and ependymomas are examples of tumors that can present initially with vertigo.[29] As expected, patients with these tumors rapidly develop other symptoms and signs of brain stem dysfunction, leading to diagnosis with MRI. The one exception is ependymomas, which are located in the ventricle and typically grow very slowly. For these reasons, ependymomas may produce vestibular symptoms for a longer period than other posterior fossa tumors before they are diagnosed with brain imaging.[30]

## Peripheral Causes of Dizziness in Children

### *Head Trauma*

Head trauma can cause an acute episode of vertigo by abruptly affecting the vestibular end organ directly, i.e. a labyrinthine concussion. Although several theories have been proposed, the mechanism of injury in labyrinthine concussion is poorly understood. Pressure waves transmitted directly to the labyrinth through the skull or intracranially via the cochlear aqueduct may cause rupture of the membranous labyrinth or damage to hair cells, hair bundles, or specialized structures in the ampulla or macula. The child usually recovers completely within a short period of time, but, on rare occasions, benign paroxysmal positional vertigo or delayed endolymphatic hydrops may develop. Benign paroxysmal positional vertigo is characterized by nystagmus and associated vertigo elicited by rapid changes in head position from upright to head hanging. It is thought to be caused by canalithiasis and can be treated with particle repositioning.[31] Other mechanisms of vertigo after head trauma include parenchymal injury of the CNS, temporal bone fracture, and perilymphatic fistula.

### *Perilymphatic Fistula*

Perilymphatic fistula is an anomalous connection between the inner ear and middle ear spaces and has been well documented in children.[32] Although perilymphatic fistula is usually associated with hearing loss, it can be associated with vertigo alone.[33] A perilymphatic fistula can be acquired or congenital. The congenital fistulas are associated with abnormalities in the temporal bone, particularly in the area of the stapes, but also in the vicinity of the round window. Acquired perilymphatic fistulae are generally caused by trauma, which may include iatrogenic trauma, barotrauma, penetrating trauma, or other head trauma.

The diagnosis and treatment of perilymphatic fistula consist of exploration of the middle ear and repair of the fistula by packing with temporalis fascia or muscle. At the time of surgery, fluid from the middle ear should be collected and sent for beta-2 transferrin testing, which is considered to be an objective test for the diagnosis of a perilymphatic fistula.[28]

### *Visual Problems*

Visual problems such as refraction abnormalities (myopia, hypermetropia, or astigmatism) or anomalies in ocular convergence (convergence insufficiency or latent strabismus with binocular vision) are a common cause of vertigo in children. The symptoms usually occur in children 6 years or older and are often associated with fatigue and excessive exposure to television, computer, and handheld device display screens. Episodes are usually recurrent and of short duration. The vertiginous symptoms typically consist of a sensation of rotation or displacement of the environment of mild-to-moderate intensity. Headaches occur in nearly 50% of children, particularly when a family history of migraine is present. Neurologic and vestibular evaluations are normal. A complete ophthalmologic examination is indicated. Treatment includes correction of refraction anomalies and comprehensive orthoptic therapy. The sensation of imbalance and dizziness may be due to failure in binocular vision or convergence causing inadequate gaze stabilization during movement and double or blurry vision during fixation. Extensive screen time may unmask a latent ophthalmologic condition.

### *Vestibular Neuritis*

Vestibular neuritis is rarely seen in children younger than 10 years old. It should be considered when a viral syndrome is followed by symptoms suggestive of an acute unilateral peripheral vestibular loss, which is more common in children than in adults.[34] It presents with acute severe vertigo, nystagmus, nausea, and vomiting. The vertigo is worsened by head movements, and patients often prefer to lie down, usually with the affected ear up. There is no hearing loss or tinnitus. Vestibular laboratory testing indicates a unilateral reduced vestibular response to bithermal caloric testing. The symptoms resolve in children within a few days. Management is supportive and symptomatic with early ambulation. A short course of vestibular suppressants such as meclizine may be given, but should be limited as it may delay central nervous system compensation. Corticosteroids, such as prednisone, may shorten the duration of the illness, but no studies of their efficacy in children have been performed.

### *Labyrinthitis*

Acute labyrinthitis is an inflammatory condition that affects the labyrinth and generally leads to both vestibular and auditory symptoms and signs. The etiology of serous (toxic) labyrinthitis is unknown, but bacterial toxins or other biochemical substances in middle-ear fluid are thought to be absorbed into the inner ear through the round and oval windows. Bacterial or suppurative labyrinthitis occurs when bacteria directly infect the labyrinth via the middle ear or from a central route as a sequela of bacterial meningitis. Suppurative labyrinthitis may leave the patient with permanent deficits in vestibular and auditory function. When diagnosed, treatment should be initiated immediately with IV antibiotics and surgical management if appropriate.

### *Meniere's Disease*

Meniere's disease is characterized by a complex of symptoms including dizziness, unilateral hearing loss, tinnitus, and aural fullness. While some patients may have only hearing loss and tinnitus, others may have only vestibular symptoms. The duration of the vertiginous episodes may vary from 30 minutes to several hours, and episodes are frequently accompanied by autonomic symptoms such as pallor, perspiration, nausea, and vomiting. Between these acute episodes, adults and rarely children may have vague symptoms of disequilibrium. Children are more likely to recover auditory function than adults. With time, a reduction in the responsiveness of the involved peripheral vestibular system occurs. Management of endolymphatic hydrops in children includes reassurance and explanations of the condition to the parents in addition to salt restriction and a diuretic.[35] The need for surgical treatment is rare in children.

### *Vestibular Dysfunction in Sensorineural Hearing Loss*

Numerous studies in children with hearing loss have found that the incidence of vestibular hypofunction ranges from 49% to 95% of those tested. Horak et al. compared 30 hearing impaired children and 15 learning-disabled children to a group of 54 normal controls using both vestibular and motor testing. Two-thirds of hearing impaired children had abnormal VOR compared with one-fifth of learning disabled children and 7% of normal controls.[2] Further studies suggest that a component of learning disabilities in the context of hearing loss may be due to deficiencies in reading acuity associated with vestibular dysfunction.[36]

An interesting subpopulation of children with SNHL is those who have undergone cochlear implantation (CI). While numerous studies have evaluated vestibular function following unilateral CI in adults,[37-40] fewer studies have examined the impact of unilateral CI on vestibular function in children. Jacot et al. examined 224 children with profound SNHL prior to unilateral CI and found 50% to have abnormal bilateral vestibular function. Of the patients with existing vestibular function prior to CI, 70% experienced a post-CI worsening of vestibular function. Ten percent of patients developed complete ipsilateral vestibular areflexia.[41] Licameli et al. investigated the prevalence and severity of vestibular impairment in two groups of children with CI and found that 52% had abnormal VOR, 39% had abnormal CDP, and 80% had reduced or absent VEMP in the ipsilateral ear after CI.[42] Cushing et al. performed vestibular testing in a group of 40 children with unilateral CI and found abnormal caloric responses in 50% of patients.[43]

Based on their findings, the above investigators advocate for vestibular testing, when feasible, in any pediatric CI candidate prior to surgery. While no consensus has been reached on the ideal timing and extent of such testing, Jacot et al. suggest a clinical vestibular examination including the head thrust test, bithermal caloric testing, and VEMP.

### *Vestibular Dysfunction in Conductive Hearing Loss (CHL)*

Otitis media is one of the most common diseases in infants and children.[44] Acute otitis media (AOM) occurs at least once in up to 71% of children under 3 years of age and an episode of AOM is followed by persistent middle ear fluid (otitis media with effusion, OME) for at least 4 weeks in 60% of cases.[45] The principal effect of OME on hearing consists of a mild-to-moderate CHL with an average threshold of 27 dB.[46] This degree of hearing loss may delay speech development and be associated with learning disabilities. In addition, Eustachian tube dysfunction with and without middle ear effusion is considered one of the most common cause of vestibular disturbances in children.[47,48] Anecdotal evidence from parents suggests that children with OME often exhibit a high degree of movement disorganization and propensity for falls especially compared with their peers without middle ear disease. Parents further report that their children often begin to walk or become less clumsy after tympanostomy tube insertion. More recently, studies in children have produced evidence supporting both the notion that vestibular, balance, and motor function may deteriorate in the setting of middle ear effusion and that this deterioration is reversed with resolution of OME.

Placement of tympanostomy tubes in children with otitis media has been shown to improve balance. Casselbrant et al. tested 41 children with OME using moving platform posturography before and after insertion of tympanostomy tubes and found a higher speed of sway was in children with OME than in normal children.[49] Golz et al. tested 136 children, 4–9 years of age, using electronystagmography and the BOTMP before and after tube ventilation of the middle ear. Pathologic findings on either study were found in 58% of the children with chronic middle ear effusion, as compared with only 4% of healthy controls. Balance disturbances resolved in 96% of subjects after tympanostomy tube insertion.[50] Casselbrant et al. found that children aged 3–9 years with OME had increased postural sway in response to moving visual scenes compared with age- and gender-matched controls, with statistically significant differences noted at both tested frequencies of surround movement.[51] The above studies indicate that balance-related symptoms in young children may result from OME and that these symptoms often resolve after middle ear aeration returns to normal.

## REHABILITATION OF BALANCE AND MOTOR SKILLS IN THE HEARING IMPAIRED CHILD

As described above, children with peripheral vestibular hypofunction in the setting of a normal central nervous system are likely to compensate well in most environments. Nevertheless, early identification of specific functional deficits can guide rehabilitative efforts. Even when such children have excellent motor skills, strength, and speed, they may be labeled clumsy when they fall or lose balance in conditions with poor or unreliable visual and proprioceptive inputs.[2]

Rine et al. demonstrated a statistically significant improvement in motor development in children with SNHL and vestibular dysfunction treated with exercise intervention. Control patients were subsequently treated with exercise intervention, and demonstrated a comparable improvement.[52] In a preliminary study involving two subjects with SNHL and bilateral vestibular hypofunction, an exercise program using head movements in the setting of complex backgrounds was employed. Both subjects showed improvement in critical print size nearing clinical significance. One subject had an improved dynamic visual acuity score.[53]

With the exception of the above studies, the literature is relatively deficient on the potential for various interventions to improve balance and motor development in SNHL patients with vestibular loss and impaired motor development.

## PEDIATRIC SUPERIOR SEMICIRCULAR CANAL DEHISCENCE

### Introduction

Superior canal dehiscence syndrome (SCDS) was first recognized in adult patients by Minor et al. in 1998,[54] and the first pediatric cases were reported in 2005.[55,56] It can present with a myriad of auditory and/or vestibular symptoms that are associated with a bony defect of the superior canal. High-resolution CT demonstrates a dehiscent area of bone in the region of the arcuate eminence (in contact with temporal lobe dura) or the medial (nonampullated) limb associated with the superior petrosal sinus (SPS-SCD).[57] The etiology of SCD remains unknown, but several hypotheses have been presented. Nadgir et al. suggest that SCD is an acquired condition with an increased prevalence in

older populations.[58] However, others theorize that some patients are born with thin or absent bone overlying the SSC,[56,59-61] and that a "second event" (e.g. skull base trauma, a Valsalva maneuver, or intense acoustic exposure) causes a sudden disruption of the canal defect. The presence of a bony defect in the superior canal at birth is supported by a number of pediatric SCD cases reported in the literature.[57,62-64]

## Embryonic Development

The semicircular canals arise with the budding of the membranous labyrinth from the otocyst. The superior canal develops first, followed by the posterior canal and then the horizontal (or lateral) canal. As the membranous labyrinth approaches adult size, ossification begins at the basal turn of the cochlea and progresses to the semicircular canals (first the superior canal, then posterior, and lastly the horizontal).[65,66] In infants the SSC is initially covered by a thin inner periosteal layer (endosteum). As the child develops, the inner and outer periosteal layers, along with the middle endochondral layer, mature into the trilaminar structure of the otic capsule and continue to thicken to adult thickness by 3 years of age.[59]

Chen et al. suggest that the presence of SCD in the pediatric population may be the result of abnormal development.[63] If SCD is a developmental abnormality, it is possible that superior canal dehiscence is caused by an arrest in the ossification process. However, one would expect the posterior and horizontal canals to be affected more than the superior, as they ossify later.[63] It is also conceivable that the middle endochondral layer and outer periosteal layer may fail to develop and thicken over a section of the canal. If dehiscent, or near-dehiscent, bone is subsequently traumatized, the inner ear may become sensitive to transmitted changes in fluid dynamics and intracranial pressures (resulting in vestibular symptoms).[59] SCD has also been found in patients with other craniofacial or developmental abnormalities (e.g. enlarged vestibular duct),[62,64,67] but there is no evidence to support that these additional anomalies directly cause SCD. An alternative theory is that some patients with SCD are born with relatively low-lying tegmen in relation to the arcuate eminence. Consequently, the superior canal becomes vulnerable to dural pulsations and subsequent thinning of the overlying bone. In patients with SPS-related SCD (a subset of the SCD population in adults and children), the superior canal may not be able to fully ossify during development because the SPS has already developed and may impinge on the canal and block complete ossification.

## Clinical Features

Pediatric SCDS patients can present with similar signs and symptoms as their adult counterparts. They may experience auditory symptoms, vestibular symptoms, or both. Auditory symptoms include hearing loss, autophony, conductive hyperacusis, aural fullness, or tinnitus (may or may not be pulsatile). Vestibular symptoms include disequilibrium, sound- or pressure-induced vertigo (Tullio phenomenon and Hennebert sign, respectively), or chronic dizziness.[57] It is important to note that it may be very difficult for children to accurately identify and verbalize their symptoms. Vestibular symptoms may be even harder for the child to recognize if those symptoms have persisted for the majority of their life. Parents, too, may experience difficulty in distinguishing vestibular symptoms from normal development. Auditory complaints (especially hearing loss) are commonly the presenting symptom as parents tend to notice a lack or delay in verbal development; audiometric testing makes these complaints more objective and easier to track long term.[64] However, children who have a bony defect involving the superior canal and the SPS may have atypical signs and symptoms (*see* Case 2 below).[57] The following are two pediatric SCDS cases from our institution, one with defects of the arcuate eminence (Case 1) and the other with a unilateral defect of the medial superior canal associated with the SPS (Case 2).

### *Case 1*

An otherwise healthy 7-year-old male presented with severe hyperacusis, and dizziness and vertigo provoked by loud noises, coughing, and sneezing. He also reported autophony, tinnitus, and otalgia with loud noise exposure. He denied hearing loss. At the time of presentation, his mother noted that he had extreme sensitivity to loud sounds even as a toddler. The patient was avoiding noisy situations, like the school cafeteria, and had already missed a significant amount of school as a result. His neurotological examination was normal with the exception of the Weber test that lateralized to the right. No spontaneous nystagmus was observed, and he had normal rotary chair and posturography tests. Audiometric testing showed supranormal bone conduction bilaterally and circular VEMPs (cVEMPs) revealed bilateral low thresholds (55 dB

nHL at 500 Hz). CT of the temporal bone revealed bilateral "blue-lined" superior canal defects (very thin bone covering the canal) (Fig. 24.2).

Due to the disabling nature of his symptoms, the patient and his family decided to undergo bilateral transmastoid "resurfacing" (in two stages, right then left ear) with calvarial bone graft and hydroxyapatite bone cement with round and oval window plugging at an outside institution. He initially reported symptom improvement, especially vertigo. His hearing remained stable postoperatively with audiometric testing showing supranormal bone conduction bilaterally (Fig. 24.3). A few months after his second surgery, the patient was hit in the right ear while playing and immediately had re-emergence of his preoperative noise-induced vertigo.

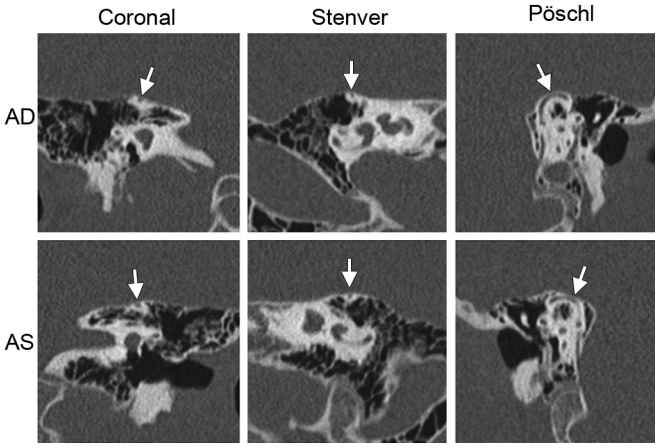



**Fig. 24.2:** Case 1. High-resolution computed tomography (CT). AD, right ear; AS, left ear. All views (coronal, Stenver, and Pöschl) show thinning of the arcuate eminence (peak) of the superior canals bilaterally (arrows), but no clear dehiscence. The tegmen is intact without evidence of dural herniation on either side, and mastoids are well aerated bilaterally.

## *Case 2*

A healthy 15-year-old female presented with vertigo and dizziness and associated nausea that began while playing field hockey.[57] She denied vertigo and dizziness induced by heavy lifting, straining, or loud noise, and did not report any hearing loss, aural fullness, tinnitus, or autophony. There was no prior head trauma. Symptoms subsided after a few days but intermittently re-emerged, especially after exercising. Neurotological examination was unremarkable. The patient exhibited no spontaneous nystagmus or nystagmus elicited with provocative maneuvers behind Frenzel lenses. Her preoperative audiogram revealed low-frequency supranormal bone conduction with an air–bone gap (ABG) in her right ear (Fig. 24.4A), and low cVEMP thresholds (60 dB at 250 Hz, 60 dB at 500 Hz, 65 dB at 750 Hz, and 70 dB at 1000 Hz). Temporal bone CT scan revealed a right-sided superior canal defect involving the posteromedial limb (nonampullated end) contacting the adjacent SPS (Figs. 24.5A and B).

The patient was initially managed conservatively with no surgical intervention, but persistent, exercise-induced vertigo began to severely affect her quality of life. At this point, surgical options were considered, and she and her family decided to undergo a right-sided transmastoid SCD repair. After identifying both limbs of the SSC and the SPS, individual labyrinthotomies were made in the ampullated and nonampullated ends of the superior canal (to isolate

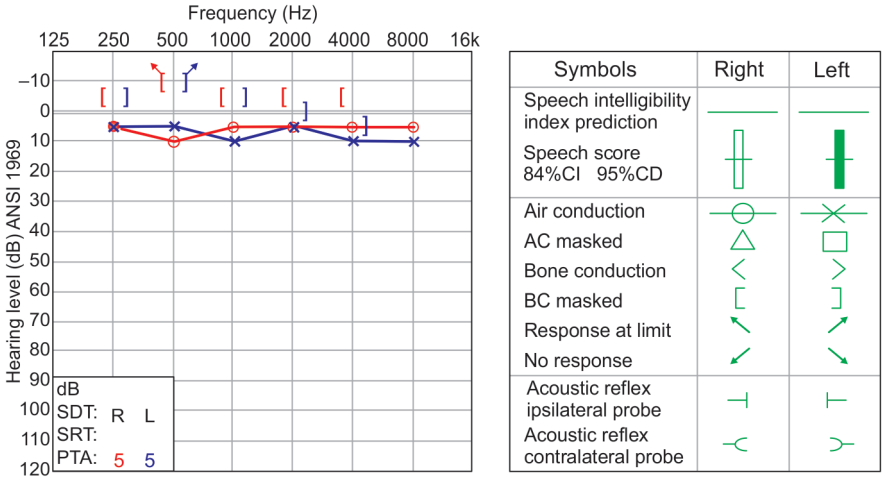
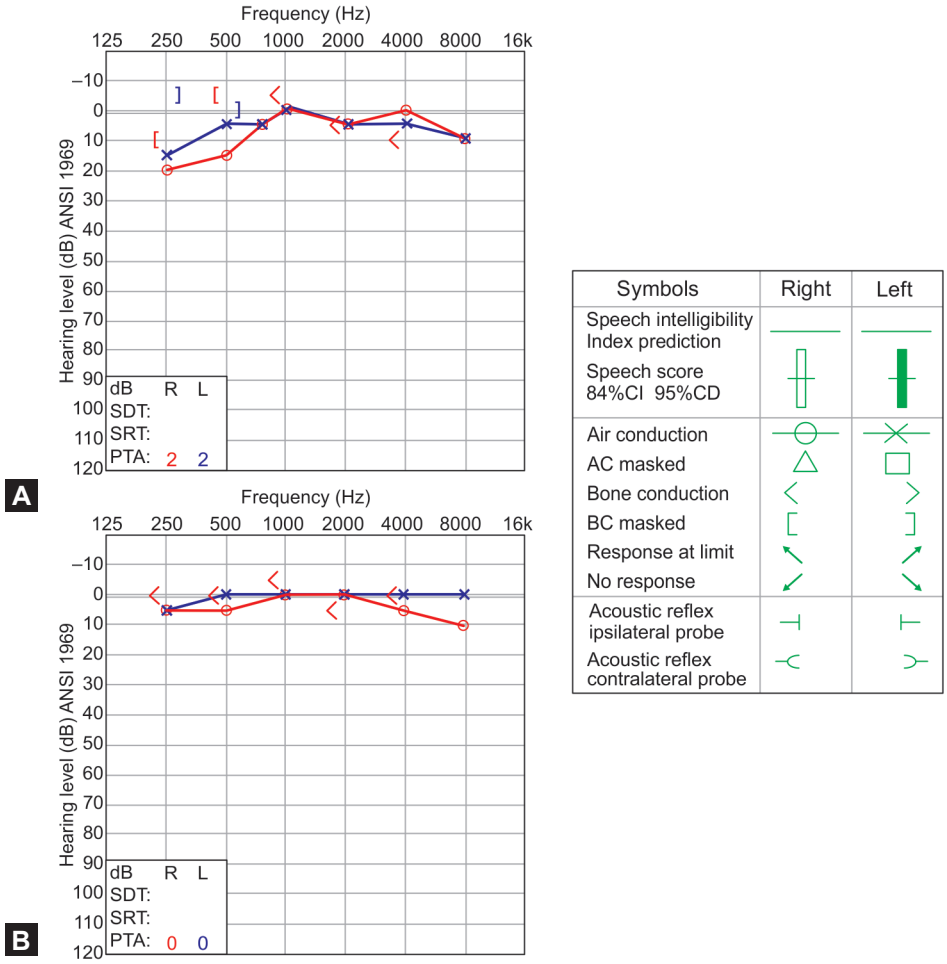



**Fig. 24.3:** Case 1. Audiometric testing, postoperatively. Hearing is within normal limits bilaterally, but there are supranormal bone conduction thresholds at 250, 500, 1000 Hz on the left and at 250, 500, 1000, 2000, and 4000 Hz on the right. These findings were seen before surgery as well. An air–bone gap of 20 dB at 500 Hz is present on the right.



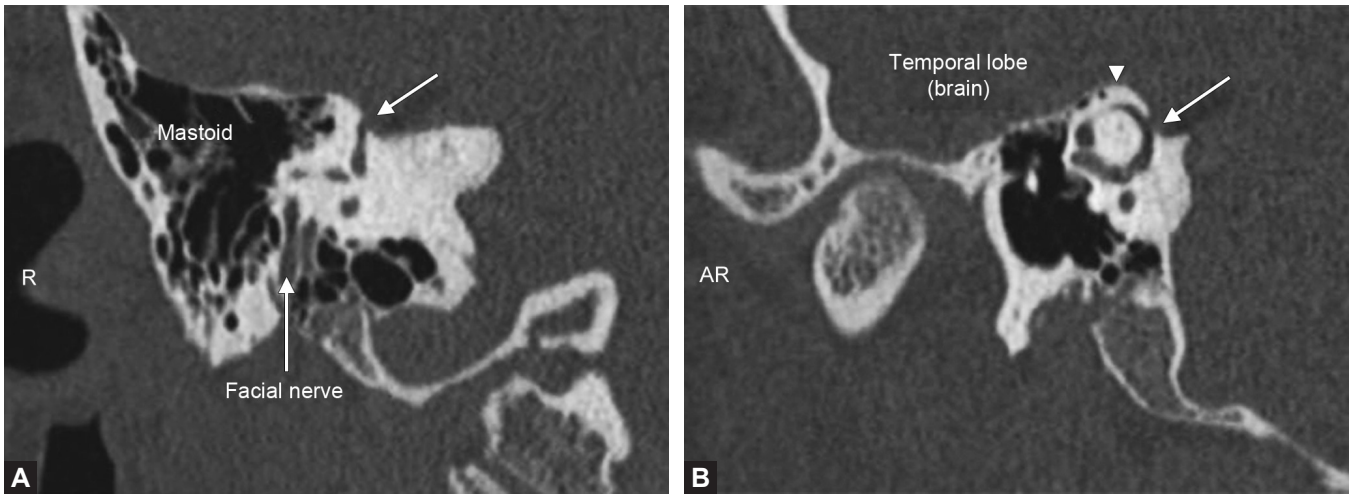

**Figs. 24.4A and B:** Case 2. Audiometric testing. (A) The preoperative audiogram shows supranormal bone thresholds at 500 and 1000 Hz in the right ear with a low-frequency air–bone gap (20 dB at 500 Hz); (B) The postoperative audiogram shows resolution of the supranormal bone threshold at 500 Hz and closure of the air–bone gap. Hearing was normal in the left ear (no superior canal dehiscence in left ear).

the bony defect associated with the SPS). These holes were then occluded with bone wax (Figs. 24.6A to F). The patient experienced mild transient disequilibrium during the first several postoperative days, but subsequently had complete resolution of all pre- and postoperative symptoms.[57] Supranormal bone-conduction thresholds (Fig. 24.4B) and low cVEMP thresholds on preoperative testing also normalized following her surgery.

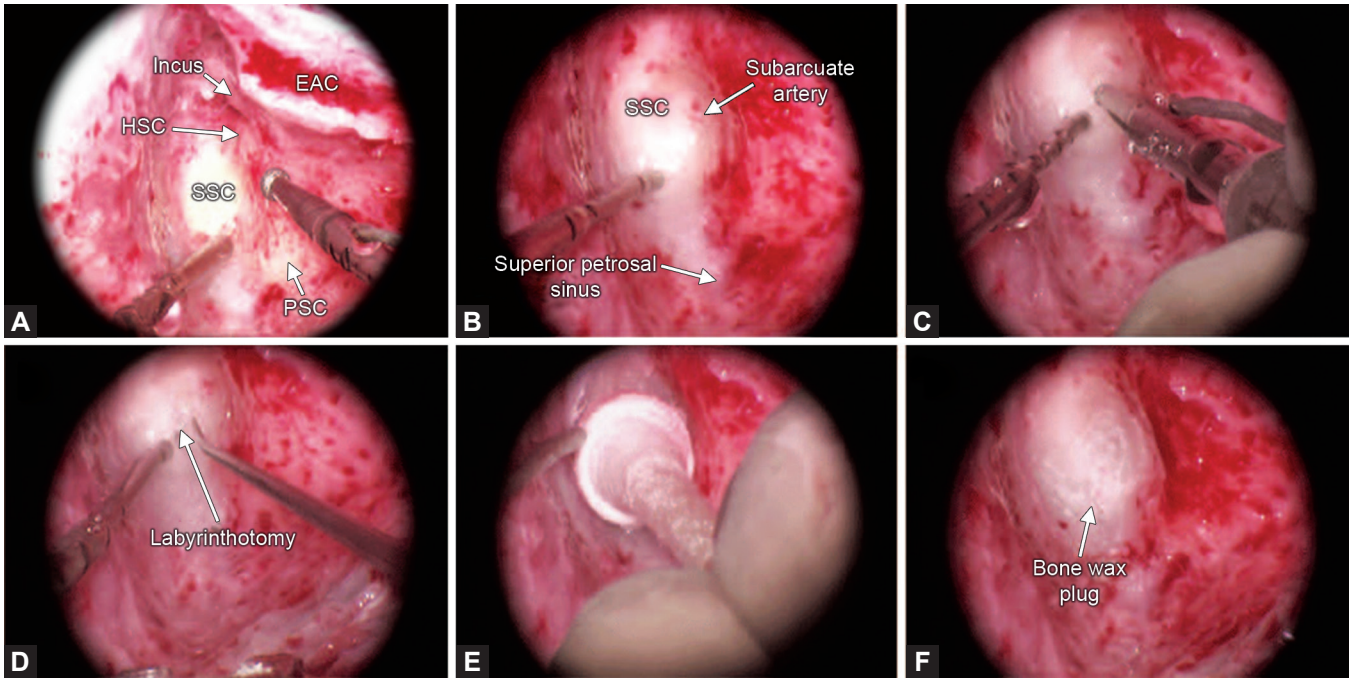
## Diagnostic Testing

High-resolution CT is essential in the diagnosis of anatomic SCD.[67] Furthermore, it is important to have multiple views of the temporal bone to better assess the defect. It can be difficult to visualize the extent of the dehiscence on coronal views, so Stenver (perpendicular to the plane of the SSC) and Pöschl (parallel to the SSC and 45° oblique to the coronal) reconstructions are routinely performed at our institution. In addition, SCD detected radiographically in children < 3 years of age should be considered a normal developmental finding, as the bone overlying the SSC does not reach the average adult thickness until approximately 36 months of age.[57]

Pure tone audiometry is an essential component of the workup and should include bone conduction testing at –5 and –10 dB to exclude the possibility of supranormal bone conduction. Minor et al. reasoned that the dissipation of acoustic energy through the dehiscence can create an ABG and an apparent CHL.[57a] Tympanometry and acoustic reflexes should also be evaluated to exclude middle ear disease or ossicular fixation as a cause of the ABG.[57] These measurements are by no means diagnostic, but hearing should be periodically evaluated to detect any significant change over time.




**Figs. 24.5A and B:** Case 2. High-resolution computed tomography (CT) scan. Right ear of same patient. (A) Coronal view demonstrating a right superior canal dehiscence in the region of the superior petrosal sinus (white arrow) of the right middle fossa. Note that the tegmen is NOT low-lying and otherwise intact; (B) Pöschl view demonstrating right superior canal dehiscence in the region of the superior petrosal sinus (white arrow). Note that the top of the SCC is intact (arcuate eminence) (arrowhead).




**Figs. 24.6A to F:** Case 2. Intraoperative images. Right ear, transmastoid approach. (A) Right mastoidectomy, canal wall up with the superior semicircular canal (SSC) exposed. HSC: Horizontal semicircular canal; PSC: Posterior semicircular canal; EAC: External auditory canal; (B) High magnification view showing the right SSC and the bluish hue defining the prominent superior petrosal sinus in the middle fossa; (C) Careful drilling using a low speed setting and a diamond burr to gently perform a labyrinthotomy, or hole, of the right SCC behind the dehiscence. A second labyrinthotomy is also performed (not shown) in front of the dehiscence; (D) The exposed membranous labyrinth is exposed following labyrinthotomy of the right SCC; (E and F) Plugging of the labyrinthotomy created in the SSC.

A measurement that has been consistently useful in the evaluation of symptomatic SCD is cVEMP testing. cVEMPs may show abnormally low thresholds and elevated amplitudes for patients with SCDS.[68] cVEMPs measure a vestibulospinal reflex mediated through the saccule and the inferior vestibular nerve in which a loud auditory stimulus induces an ipsilateral inhibition to the tonic neck muscle activity recorded on an electromyogram. There is evidence that the threshold to elicit a VEMP response is abnormally low due to an enhancement of endolymph

flow in the labyrinth with a dehiscence.[62] Not all patients (pediatric or adult) have abnormally low cVEMP thresholds; however, Niesten et al. found that patients with a smaller bony defect located further away from the ampulla may not present with lowered cVEMP thresholds (Niesten et al. 2013, in press). Consequently, SCD should not be ruled out solely on the basis of normal cVEMP testing.

### Treatment

Once a diagnosis of SCDS is made, treatment can be conservative or surgical. Conservative management includes observation with interval audiometric testing (hearing aids if appropriate), neurotologic examination, and ensuring that the child meets all developmental balance milestones.[57] This method is preferred due to the age of the patient population.[57,64] Surgical intervention should be saved for those patients with persistent and disabling vestibular and/or auditory symptoms.[64] There are two established surgical approaches to access the superior canal[57]—middle fossa craniotomy and transmastoid—and a number of methods that have been described to repair the bony defect. Both approaches have been used to safely and successfully manage SCD.[57,64] Finally, round window plugging via transcanal tympanostomy is a less invasive option, but has been sparsely described in the literature and has varying outcomes in studies involving small numbers of patients.[69,70] Prospective studies with larger cohorts are needed to determine the ideal surgical approach and repair method in both pediatric and adult patients with SCDS.

## CONCLUSION

Dizziness and vertigo are common symptoms among children. Attention to detail in history taking, thorough physical examination, and appropriate use of ancillary testing will enable the practitioner to navigate the complex differential diagnosis of dizziness and help this important patient population.

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CHAPTER

# 25 Evidence-Based Medicine in Pediatric Otology

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## INTRODUCTION

"Evidence-based medicine" (EBM) was coined in 1992 and defined as "the conscientious, explicit, and judicious use of current best evidence in making decision about the care of individual patients".[1,2] Although criticized as "cookbook medicine" that only incorporated randomized clinical trials (RCTs), it was intended to involve "tracking down the best external evidence with which to answer our clinical questions".[2] This has led to the establishment of "levels of evidence" (Table 25.1) and "grades of recommendation" (Table 25.2) to help practitioners evaluate the strength of the evidence in an individual article, clinical guideline, and other recommendations in an exercise called "critical appraisal of the literature".[3]

Importantly, appraising the medical literature requires an understanding of the types of clinical questions asked and the types of studies that offer evidence to answer these questions. As Table 25.1 shows, RCTs provide Level 1 evidence only for studies of therapy or prevention, etiology or harm; in the absence of Level 1 evidence, other comparative methods (i.e. cohort, case-control, and cross-sectional studies) provide as much evidence as the literature contains for these types of studies. The main concerns with non-RCT study designs are that (1) causality is more difficult to attribute to the intervention or exposure being studied, and (2) observational studies are more susceptible to various forms of bias than RCTs, which are intended to be truly experimental in design. However, due to practical concerns about the ethics of randomization, feasibility of performing randomized studies, and selection bias among participants that leads to limited external generalizability, RCTs do not always provide perfect evidence for clinical questions. Indeed, rigorous observational studies with validation provide Level 1 evidence for all of the other study types shown in Table 25.1 (i.e. prognosis, diagnosis, differential diagnosis/symptom prevalence, and economic and decision analyses). Systematic reviews of multiple controlled studies, regardless of study type, remain the best way of synthesizing good quality studies to evaluate the current medical science for the benefit of patients. When systematic reviews incorporate high-quality primary studies and are able to quantitatively combine results into a meta-analysis, they provide the most reliable evidence from the available medical literature. Unfortunately, if the systematic reviews have only poor-quality studies to evaluate and analyze, the product of those reviews is often a call for better future research.

Several sources are well known for their contribution to EBM and are referenced here as for further information and practice. First is the Cochrane Library (http://www.thecochranelibrary.com), named for Archie Cochrane, a British epidemiologist who published *Effectiveness and Efficiency: Random reflections on health services* in 1972, which pointed out the lack of collective knowledge about the effects of health-care. The Cochrane Library contains several databases, of which the most widely used is the Cochrane Database of Systematic Reviews, the leading source for systematic reviews in medicine. The main limitation with this database is that these systematic reviews include only RCTs. The second is the Centre for Evidence-Based Medicine in Toronto, Canada (http://ktclearinghouse.ca/cebm), which publishes the book *Evidence-Based Medicine: How to Practice and Teach EBM*.[4] This softbound book is recommended to all who benefit from a hard-copy

**Table 25.1:** Oxford Centre for Evidence-Based Medicine levels of evidence (1998, revised 2009)[3]

| *Level* | *Therapy/prevention, etiology/harm* | *Prognosis* | *Diagnosis* | *Differential diagnosis, symptom prevalence study* | *Economic and decision analyses* |
|---|---|---|---|---|---|
| 1a | SR (with homogeneity*) of RCTs | SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations | SR (with homogeneity*) of Level 1 diagnostic studies; CDR† with 1b studies from different clinical centers | SR (with homogeneity*) of prospective cohort studies | SR (with homogeneity*) of Level 1 economic studies |
| 1b | Individual RCT (with narrow confidence interval‡) | Individual inception cohort study with > 80% follow-up; CDR† validated in a single population | Validating** cohort study with good††† reference standards; or CDR† tested within one clinical center | Prospective cohort study with good follow-up**** | Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multiway sensitivity analyses |
| 1c | All or none§ | All or none case-series | Absolute SpPins and SnNouts†† | All or none case-series | Absolute better-value or worse-value analyses †††† |
| 2a | SR (with homogeneity*) of cohort studies | SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs | SR (with homogeneity*) of Level > 2 diagnostic studies | SR (with homogeneity*) of 2b and better studies | SR (with homogeneity*) of Level > 2 economic studies |
| 2b | Individual cohort study (including low quality RCT; e.g. < 80% follow-up) | Retrospective cohort study or follow-up of untreated control patients in an RCT; derivation of CDR† or validated on split-sample§§§ only | Exploratory** cohort study with good††† reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases | Retrospective cohort study, or poor follow-up | Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multiway sensitivity analyses |
| 2c | "Outcomes" research; ecological studies | "Outcomes" research | | Ecological studies | Audit or outcomes research |
| 3a | SR (with homogeneity*) of case-control studies | | SR (with homogeneity*) of 3b and better studies | SR (with homogeneity*) of 3b and better studies | SR (with homogeneity*) of 3b and better studies |
| 3b | Individual case-control study | | Nonconsecutive study; or without consistently applied reference standards | Nonconsecutive cohort study, or very limited population | Analysis based on limited alternatives or costs, poor-quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations |
| 4 | Case-series (and poor-quality cohort and case-control studies§§) | Case-series (and poor-quality prognostic cohort studies***) | Case-control study, poor or nonindependent reference standard | Case-series or superseded reference standards | Analysis with no sensitivity analysis |
| 5 | Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles" | Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles" | Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles" | Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles" | Expert opinion without explicit critical appraisal, or based on economic theory or "first principles" |

*Contd...*

*Contd...*

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RCTs, randomized clinical trials.

*By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.

†Clinical decision rule. (These are algorithms or scoring systems that lead to a prognostic estimation or a diagnostic category.)

‡See note above for advice on how to understand, rate and use trials or other studies with wide confidence intervals.

§Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.

§§By poor-quality cohort study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and nonexposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor-quality case-control study, we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.

§§§Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples.

††An "Absolute SpPin" is a diagnostic finding whose specificity is so high that a positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose sensitivity is so high that a negative result rules-out the diagnosis.

‡‡Good, better, bad, and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.

†††Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a nonindependent reference standard (where the "test" is included in the "reference," or where the "testing" affects the "reference") implies a Level 4 study.

††††Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.

**Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are "significant."

***By poor-quality prognostic cohort study we mean one in which sampling was biased in favor of patients who already had the target outcome, or the measurement of outcomes was accomplished in < 80% of study patients, or outcomes were determined in an unblinded, nonobjective way, or there was no correction for confounding factors.

****Good follow-up in a differential diagnosis study is > 80%, with adequate time for alternative diagnoses to emerge (e.g. 1–6 months acute and 1–5 years chronic).

**Table 25.2:** Grades of recommendation, based on 2009 Oxford Centre for Evidence-Based Medicine levels of evidence[3]

| *Grade* | *Criteria* |
|---|---|
| A | Consistent Level 1 studies |
| B | Consistent Level 2 or 3 studies or extrapolations from Level 1 studies |
| C | Level 4 studies or extrapolations from Level 2 or 3 studies |
| D | Level 5 evidence or troublingly inconsistent or inconclusive studies of any level |

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reference and flashcards, and includes a CD-ROM with additional materials. The website includes information about how to practice and teach EBM, syllabi for practicing EBM, and other resources. Finally, the Centre for Evidence-Based Medicine at the University of Oxford (http://www.cebm.net/) provides additional workshops, conferences and training, as well as online tools and resources that can be used to practice or teach EBM. They publish and update the Levels of Evidence and Grades of Recommendation in Tables 25.1 and 25.2.

Practicing EBM is an iterative process at multiple levels. First, every clinician should evaluate results of new studies for applicability to individual practices and patients as they are published. However, critical appraisal of the literature takes training and practice, and should be incorporated as an element of resident training and continuing medical education. Second, incorporating recent studies into updated systematic reviews usually falls to those who are familiar with the methodology of

systematic reviews. The questions asked in systematic reviews may range from efficacy ("Does the intervention work at all?") to effectiveness ("Does the intervention work in the real world?") and to comparative effectiveness ("How well do interventions work compared to each other?"). Third, professional societies and specialty groups produce or update clinical guidelines to provide their membership with recommendations for the pragmatic application of synthesized studies, especially when wide variations in practice exist.[5] Clinical guidelines from different societies may vary and conflict, however, when those guidelines value one type of outcome over another, or represent standard of care rather than best evidence. Finally, the clinician must again assess the applicability of the guidelines and systematic review results to individual practices and patients. Based on practice and patient characteristics, recommendations from systematic reviews and guidelines may be adopted for many or some patients, but rejected for others due to limitations of the studies included in the systematic reviews, especially generalizability.

The goal of this chapter is to review topics in pediatric otology where there are large controlled studies, or systematic reviews of controlled or high quality studies. It will provide commentary on the applicability of these studies and reviews for clinical practice, and propose topics where pediatric otology could improve the evidence base from which clinicians practice. This review cannot be either exhaustive or completely up-to-date because new studies are presented and published continuously. Nevertheless, this compilation can establish a baseline from which future iterations of EBM in pediatric otology can proceed.

## OTITIS MEDIA

In pediatric otology, the best example of EBM has been in the management of acute otitis media (AOM) and otitis media with effusion (OME), where the sheer prevalence of this disorder has allowed the performance of many RCTs for preventative and therapeutic interventions, resulting in many reviews and generating multiple clinical guidelines. Table 25.3 shows a listing of Cochrane reviews within the past 5 years regarding specific questions in the management of AOM and OME, and the number of RCTs that contributed to the synthesized conclusions.

**Table 25.3:** Cochrane systematic reviews regarding otitis media or otitis media with effusion in children, since 2008

| *Year* | *Title* | *# RCT included (# participants)* | *Results/conclusions* |
|---|---|---|---|
| 2008 | Grommets (ventilation tubes) for recurrent acute otitis media in children[6] | 2 (148 children < 3 years old) | Mean reduction of 1.5 episodes of AOM in first 6 months after treatment; 20–25% incidence of no AOM in first 6 months after tubes vs. 2–10% in no tubes group |
| 2009 | Interventions for ear discharge associated with grommets (ventilation tubes)[7] | 4 (397 children) | Oral amoxicillin clavulanate compared to placebo decreased the odds of discharge persisting 8 days (OR 0.19, 95% CI 0.07–0.49); no benefit of steroids added to topical antibiotic drops |
| 2013 | Autoinflation for hearing loss associated with otitis media with effusion[8] | 6 (404 children, 198 adults) | Autoinflation approximately doubled the rate of improving a composite measure of tympanogram or audiometry at > 1 month. Reasonable to consider autoinflation while awaiting natural resolution of OME |
| 2009 | Pneumococcal conjugate vaccines for preventing otitis media[9] | 7 (46,885 children) | The 7-valent pneumococcal conjugate vaccine has marginal benefit to preventing AOM in infants, but 6–7% reduction may be substantial from public health perspective. Noninfant children with a history of AOM do not benefit when immunized at an older age |
| 2010 | Short-course antibiotics for acute otitis media[10] | 49 (12,045 participants) | Higher risk of treatment failure with short course (< 7 days) antibiotics, OR 1.34 (95% CI 1.15–1.55), absolute difference 3% at one month |
| 2010 | Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children[11] | 10 (1728 children) | Grommets were mainly beneficial in the first 6 months after placement. By 12–18 months of follow-up, there was no difference in mean hearing levels. No effects were found on speech-language development, behavior, cognitive, or quality-of-life outcomes. Tympanosclerosis developed in about one-third |

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| *Year* | *Title* | *# RCT included (# participants)* | *Results/conclusions* |
|---|---|---|---|
| 2010 | Adenoidectomy for otitis media in children[12] | 14 (2712 children) | For the primary outcome of time with OME, adenoidectomy w/tube increases the resolution of OME by 22% and 29% at 6 and 12 months, respectively, over tube alone. For the secondary outcome of AOM, studies were too heterogeneous to pool results |
| 2011 | Antihistamines and/or decongestants for OME in children[13] | 16 (1880 children) | No statistical or clinical benefit. Treated study subjects experienced 11% more side effects (NNT = 9) |
| 2011 | Oral or topical nasal steroids for hearing loss associated with otitis media with effusion in children[14] | 12 (945 children) | No hearing benefit from steroids; higher OME resolution at < 1 month (RR 4.48; 95% CI 1.52–13.23) with oral steroids, but not at > 1 month follow-up. No benefit from steroids in terms of symptoms |
| 2011 | Xylitol for preventing acute otitis media in children up to 12 years of age[15] | 4 (3103 children) | Among healthy children attending day care, reduced risk of AOM in the xylitol group (RR 0.75; 95% CI 0.65–0.88). Among children in day care with respiratory infection, there was no reduction in AOM. Xylitol chewing gum was superior to syrup in preventing AOM among healthy children (RR 0.59; 95% CI 0.39–0.89) but not during respiratory infection, with no difference between xylitol lozenges and syrups |
| 2012 | Zinc supplements for preventing otitis media[16] | 12 (6820 participants) | Among healthy children < 5 years old in low-income communities, there is mixed evidence of for zinc supplementation reducing the incidence of OM |
| 2012 | Antibiotics for otitis media with effusion in children[17] | 23 (3027 children) | Increased complete resolution of OME at 2–3 months ranged from 1% to 45%, whereas complete resolution at > 6 months increased 13% (95% CI 6–19%). No evidence of substantial improvement in hearing or effect on rate of ventilation tube insertion. Adverse events with antibiotics was increased by 3–33% |
| 2013 | Antibiotics for acute otitis media in children[18] | 11 (antibiotics vs. placebo, 3317 children) 5 (immediate antibiotics vs. expectant observation, 1149 children) | Antibiotics reduced pain at day 2–3 and 4–7 days (NNT 20), TM perforations (NNT 33) and contralateral AOM episodes (NNT 11); they did not decrease the rate of abnormal tympanogram at 4–6 weeks or 3 months, or AOM recurrences. Adverse events with antibiotics was increased, NNH 14. No difference in pain, TM perforations, or AOM recurrence for expectant observation |

(RCT: Randomized clinical trial; RR: Risk ratio; CI: Confidence interval; NNT: Number needed to treat; NNH: Number needed to harm; AOM: Acute otitis media; OME: Otitis media with effusion; TM: Tympanic membrane; OR: Odds ratio; OM: Otitis media).

These systematic reviews suggest the following practices, with editorial remarks added in italics:

## Prevention of AOM

- The 7-valent pneumococcal conjugate vaccines prevent AOM in infants on a population level, but may not have a noticeable effect on an individual child[9]
- Among healthy children attending day care, xylitol gum or syrup 5 times/day reduces the incidence of AOM.[15] *Any intervention that requires administration 5 times/day, however, is burdensome to parents and caregivers*
- Among healthy children < 5 years old living in low-income communities, zinc supplementation has a mixed effect on the incidence of AOM.[16]

## Antibiotics for AOM or OME

- There is a higher risk of treatment failure with < 7 day course of antibiotics, with a difference of 3% at one month.[10] *The risk of treatment failure needs to be balanced with the risk of adverse effects, such as diarrhea*
- Antibiotics for AOM reduced pain at 2–3 and 4–7 days, incidence of TM perforations, and contralateral AOM episodes compared to placebo[18]

- Compared to expectant observation, there was no difference from giving antibiotics immediately for outcomes of pain, TM perforations or AOM recurrence[18]
- Antibiotics for OME increases the rate of complete resolution at 2–3 months, ranging from 1% to 45%, but there is no substantial improvement of hearing outcomes or rate of ventilation tube insertion. Antibiotic usage increased the adverse event rate by 3–33%.[17] *In the current age of increasing antibiotic resistance, this practice requires careful consideration of patient factors, such as immunodeficient states, to recommend it.*

## Adjuvant Therapies for AOM or OME

- Autoinflation improved the rate of improving tympanogram/audiogram composite outcome at >1 month for OME[8]
- There was no benefit to using decongestants or antihistamines in children with OME, but a higher rate of side effects.[13] *Use of decongestants and/or antihistamines solely for the treatment of OME ought to be actively discouraged*
- Topical nasal steroids do not improve hearing loss associated with OME; oral steroids have a short-term (<1 month) effect but not a longer-term effect.[14]

## Ventilation Tubes for AOM or OME

- Tubes reduced the number of AOM episodes in the first 6 months after placement, and increased the number of patients with no AOM episodes[6]
- Tubes improved the hearing loss associated with OME in the first 6 months after placement. There is no statistical effect on speech-language development, behavior, cognitive, or quality-of-life outcomes[11]
- Topical quinolone antibiotics were better at clearing the otorrhea associated with tubes than systemic (oral) antibiotics. There was no additional benefit of topical steroids to topical antibiotic drops.[7] *The acute otorrhea in these studies did not include that which was associated with granulation tissue and tubes.*

Table 25.4 lists other notable large studies published in the past 5 years of children with AOM or OME that were not included in the Cochrane reviews. These studies support the practices outlined above, as well as the suggestions below:

- The influenza vaccines, both live attenuated and inactivated, significantly reduce the rate of AOM.[19,24,25] *In the absence of contraindications, receipt of the influenza vaccine ought to be strongly encouraged as a way to prevent AOM*

**Table 25.4:** Non-Cochrane systematic reviews, RCTs, and large clinical studies regarding otitis media or otitis media with effusion that were not included in the Cochrane reviews

| *Year* | *Title* | *Study design* | *# Participants (age of participants)* | *Results/conclusions* |
|---|---|---|---|---|
| 2008 | Effects of influenza plus pneumococcal conjugate vaccination vs. influenza vaccination alone in preventing respiratory tract infections in children: a randomized, double-blind, placebo-controlled trial[19] | RCT, double-blind, placebo-controlled | 579 children (18–72 months) | During influenza seasons, AOM episodes reduced by 57% in those receiving influenza vaccine and 71% in those receiving influenza + Pneumovax vaccines compared to controls |
| 2008 | Tube associated otorrhea in children with recurrent acute otitis media; results of a prospective randomized study on bacteriology and topical treatment with or without systemic antibiotics[20] | RCT, unblinded | 50 children (9–36 months) | Ototopical gtt (hydrocortisone, oxytetracycline, polymyxin B) vs. amox or amox/clav were not different in duration of otorrhea (88% resolved by 7 days). In 33%, oral antibiotics were added to ototopical gtt due to fever or pain |
| 2009 | Recurrence up to 3.5 years after antibiotic treatment of acute otitis media in very young Dutch children: survey of trial participants[21] | Prospective cohort study after RCT | 168 children (6–24 months) | 3 years after randomization, 20% more recurrence of AOM in children receiving amox vs. placebo (aOR 2.5; 95% CI 1.2–5.0). No difference in rate of eventual ENT surgery |

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| *Year* | *Title* | *Study design* | *# Participants (age of participants)* | *Results/conclusions* |
|---|---|---|---|---|
| 2009 | Effect of antibiotics for otitis media on mastoiditis in children: a retrospective cohort study using the United Kingdom general practice research database[22] | Population-based retrospective cohort study | 2,622,348 children (3 months to 15 years) | Risk of mastoiditis was 1.8/10,000 episodes if treated with antibiotics, compared to 3.8/10,000 episodes that were not treated with antibiotics. Number need to treat = 4831 to prevent one episode of mastoiditis |
| 2010 | Comparison between myringotomy and tympanostomy tubes in combination with adenoidectomy in 3–7-year-old children with otitis media with effusion[23] | RCT with 12 month follow-up | 78 children (42–86 months) | No difference in rate of AOM or otorrhea episodes between adenoidectomy + myringotomy vs. adenoidectomy + tympanostomy tube placement |
| 2011 | Pneumococcal vaccination in children at risk of developing recurrent acute otitis media—a randomized study[24] | Randomized, observer-blinded study, high-risk children | 96 children (< 2 years) | Incidence of AOM was reduced 26% in those with PCV7 vaccine, from 4.3 to 3.2 mean episodes, and 50% reduction ventilation tube placement |
| 2011 | The efficacy of live attenuated influenza vaccine against influenza-associated acute otitis media in children[25] | SR of RCTs | 24,046 children (6–83 months) | Live-attenuated flu vaccine (LAIV) reduced any AOM by 38% (10.3 vs. 16.8% placebo). Similar result to trivalent inactivated (TIV) flu vaccine. Influenza-related AOM was reduced by 85% vs. placebo, and 54% vs. TIV |
| 2011 | Ventilation tube treatment: a systematic review of the literature[26] | SR of RCT, controlled trials, and cohort studies | | Grade I evidence for VT improving hearing in SOM for at least 9 months, QoL improved up to 9 months (grade 2). Insufficient evidence for VT decreasing rAOM episodes |
| 2012 | Adjuvant adenoidectomy in persistent bilateral otitis media with effusion: hearing and revision surgery outcomes through 2 years in the TARGET randomized trial[27] | Randomized 3-armed trial | 376 children (> 3.5 years) | Adenoidectomy provided hearing benefit over tubes along at 12–24 months, but not 3–6 months, and reduced by half the number of children meeting 25 dB bilateral hearing loss cutoff for repeat tubes |
| 2012 | Tympanostomy with and without adenoidectomy for the prevention of recurrences of acute otitis media[28] | Randomized 3-armed trial | 300 children (10 months to 2 years) | Primary outcome was intervention failure (2 AOM in 2 months, 3 in 6 months or OME for 2 months), with 13% absolute reduction with tubes alone and 18% absolute reduction with tubes with adenoidectomy. AOM incidence was 1.15 for tubes, 0.91 for tubes with adenoidectomy, and 1.70 for control |

(RCT: Randomized clinical trial; AOM: Acute otitis media; QoL: Quality-of-life; CI: Confidence interval; OR: Odds ratio; PCV: Pneumococcal conjugate vaccine; VT: Ventilation tube; SOM: Serous otitis media; aOR: Adjusted odds ratio; rAOM: Recurrent acute otitis media; SR: systematic review).

- Use of antibiotics in children with OM decreases the incidence of mastoiditis, but with a number needed to treat of over 4800 to prevent one case of mastoiditis[22]
- Adenoidectomy in children older than 3.5 years provides additional hearing benefit in the longer term (12–24 months) over that of tympanostomy tubes alone.[27]

The American Academy of Otolaryngology-Head and Neck Surgery Foundation published the *Clinical Practice Guideline: Tympanostomy Tubes in Children* to provide evidence-based recommendations regarding the appropriate use of tympanostomy tubes in children with AOM and OME, summarized in 12 action statements.[29]

These statements incorporated the evidence summarized in Tables 25.3 and 25.4 pertaining to tympanostomy tubes and summarized other literature synthesized for the purposes of recommending best practices. While the guideline carries the weight of recommendation from the largest otolaryngology specialty organization in the United States, importantly they include the disclaimer that it "is not intended to replace clinical judgment or establish a protocol for all individuals with this condition and may not provide the only appropriate approach to diagnosing and managing this program of care (p. S31)".

The other major publication that deserves notice is the Comparative Effectiveness Review for OME, published by the Agency for Healthcare Research and Quality in 2013.[30] This systematic review addressed Key Questions regarding treatment options for OME that affect the following:

- Clinical outcomes, health utilization, or functional and health-related quality-of-life
- Harms and tolerability among the different treatment options
- Benefits and harms of treatment options in subgroups of children with OME
- Factors affecting health-care delivery or receipt of pneumococcal vaccination.

For these questions of comparative effectiveness, the systematic review of the literature from that publication[30] revealed the following results that were not already mentioned in the Cochrane reviews:

- Longer term tympanostomy tubes were retained for longer duration than other tubes. No other conclusions about the tube design or approaches to insertion could be made. Rates of otorrhea differed by tympanostomy tube type, with a higher probability of otorrhea with longer term tubes. Otorrhea and tympanosclerosis occurred more frequently in ears with tympanostomy tubes than watchful waiting or myringotomy
- There were no differences between tympanostomy tube placement and watchful waiting on language, cognitive development, academic achievement or quality-of-life outcomes during preschool and elementary school
- There is insufficient evidence to support improved quality-of-life outcomes in children who received tympanostomy tubes with adenoidectomy compared to myringotomy plus adenoidectomy
- Adenoidectomy alone was better than no treatment for resolution of OME at 6 and 12 months. There is no additional harm from adenoidectomy except for the rare chance of postoperative bleeding
- There were insufficient studies to compare effectiveness of interventions for subgroups of patients or by health-care factors.

Although tens of thousands of patients are represented by these studies, there are notable limitations to the answers they provide. Foremost, while the outcomes assessed are important to clinicians, they often missed quality-of-life and other patient-based outcomes that are likely very important to children and their parents, and may modify the balance of benefit versus cost/harms. These studies were performed in typically developing children, so that results are not generalizable to children who are considered at risk for speech-language delays and hearing loss, such as those with cleft palate, Down syndrome or neurodevelopmental delays.[30,26]

## HEARING SCREENING

Screening programs are considered feasible and worthwhile from a public health standpoint when all of the criteria below are met:[31]

- The impairment or disease is not immediately or obviously apparent
- The screening test used to identify the impairment or disease is not harmful
- The screening test is inexpensive, yet accurate with high sensitivity and specificity
- There are effective treatments for the impairment or disease
- Early identification of the impairment or disease leads to better outcomes.

Hearing screening appears to meet all of these criteria, and programs for newborn hearing screening (NHS) have been established in most developed and many developing countries. Hearing screening in preschool and school-age children is performed to a varying degree in many states of the United States and other countries, but has not received the same degree of attention as in newborns.

NHS has been legislated in 43 states of the United States, mostly in the late 1990s and 2000s, with the intent of identifying infants with moderate-to-severe bilateral permanent congenital hearing loss. The underlying assumption was that screening would lead to early identification and early treatment/habilitation of hearing loss, which would in turn result in improved speech, language, and educational outcomes. Summaries of the evidence regarding NHS have confirmed the improvement in the early identification of infants with hearing loss and subsequent treatment, thus establishing the *efficacy* of NHS.[32,33] Others have continued to document the challenges of

fitting hearing aids within the recommended time frame (i.e. by 6 months of age) and loss to follow-up after hearing loss was diagnosed.[34] A 2008 systematic review showed that while a good-quality cohort study showed improvements in receptive and expressive language in children identified through NHS compared with those identified later, other observational studies were significantly flawed methodologically by multiple factors, including lack of information on attrition and follow-up.[32] These challenges dilute the overall *effectiveness* of NHS in real-world application.

Preschool and school hearing screening have less evidence to support its routine use in healthy asymptomatic children, despite recommendations from professional organizations[35,36] and awareness that many children with congenital hearing loss are identified after the newborn period.[37,38] A systematic review from 2007 shows that there have been no RCTs of hearing screening in children older than infants and that an observational study of preschool children was inconclusive as to the effectiveness of screening.[39] Intuitively, screening programs ought to identify young children at early stages of hearing loss as they appear. However, there has been insufficient evidence to demonstrate improved identification and outcomes through the implementation of screening programs. Thus, the justification for the cost and effort of hearing screening programs in schools has not yet been established. Because screening programs require considerable time, effort, and expense, further study is needed to establish the effectiveness in preventing or ameliorating poor outcomes due to hearing loss.

## HEARING LOSS

Hearing loss in children is associated with many negative effects, including delayed speech-language development, decreased rates of literacy and high school graduation. Early amplification and rehabilitation of hearing, as soon as the hearing loss is identified, is the standard goal, but the best interventions, protocol, and timeline to maximize benefit and minimize harms have yet to be determined as technology brings new advances to hearing rehabilitation. The Institute of Medicine included the evaluation of comparative effectiveness of different treatments for hearing loss in children and adults among the top 25 in priority in their 2009 recommendations.[40] A search of Medline using the terms "hearing loss, children" or "congenital hearing loss" and "systematic review" over the past 10 years identified 12 articles pertinent to the clinical and economic evaluation of interventions for hearing loss, evaluation of function and health-related quality of life. These articles are listed with results summarized in Table 25.5.

Eight of the 12 systematic reviews pertained to cochlear implantation (CI); one article each addressed boneanchored hearing aids, therapy for cytomegalovirus, auditory neuropathy spectrum disorder, and functional skills and quality-of-life. Overall, unilateral CI in children was found to produce improved outcomes in speech and language, with advantage if occurring prior to 18 months of age over later implantation; there was insufficient data to determine whether CI prior to 12 months of age has an outcome advantage.[42,44,47] Unilateral CI was considered cost-effective, but bilateral CI (simultaneous or sequential) may not be cost-effective, depending on the threshold per quality-adjusted life year.[42,46,48] There were mixed reports on improvements in quality of life among children who received CI.[41] The sole systematic review evaluating boneanchored hearing aids in those with bilateral hearing loss showed mixed results when compared to use of airconduction hearing aids, although there appeared to be audiologic benefits over bone-conduction hearing aids.[49] For congenital cytomegalovirus infection, intravenous ganciclovir protected hearing in symptomatic infants, with trends toward protection when using oral valganciclovir. CI in children with congenital cytomegalovirus infection could improve their language skills, but degrees of improvement were mixed.[50] Similarly, children with auditory neuropathy spectrum disorder could benefit from acoustic amplification and CI but degrees of improvement were mixed.[51] Finally, hearing loss in children is associated with suboptimal level of postural control and motor skills, but overall quantitative degree could not be analyzed.[52]

Several major methodological problems plagued many of the systematic reviews on this topic. First, many of the studies did not specify a research question but instead sought to review the literature for evidence of effectiveness of a particular intervention. Second, the quality of the primary articles was often poor, consisting of uncontrolled case series or retrospective cohort studies, which increased the problem of bias. Unfortunately, poor-quality primary studies leads to poor-quality synthesized evidence. Third, heterogeneity of outcomes precluded synthesis of outcomes so that no quantitative meta-analyses were possible, and only qualitative conclusions of overall effect could be made. To correct these methodological problems does not require that an RCT be conducted for each research question (which might be considered unethical for some

**Table 25.5:** Systematic reviews of studies regarding hearing loss in children

| *Year* | *Title* | *Studies included* | *# Participants (age of participants)* | *Results/conclusions* |
|---|---|---|---|---|
| 2006 | Measuring health-related quality-of-life after pediatric cochlear implantation: a systematic review[41] | 10 cross-sectional studies of children with hearing loss only | 476 (children and adolescents) | Heterogeneity prevented quantitative meta-analysis. Studies that used validated QoL measures showed parent-reported improvements in health utility after CI; lower self-reported QoL in children with HL but not significantly different QoL in adolescents with HL |
| 2009 | Effectiveness of multichannel unilateral cochlear implants for profoundly deaf children: a systematic review[42] | 15 studies, including pre-/post-, cross-sectional, and non-randomized clinical trial designs | 1058 deaf children | Heterogeneity precluded quantitative meta-analysis. All studies reported improved scores on all outcome measures. Five economic evaluations found unilateral CI to be cost-effective |
| 2009 | The effectiveness and cost-effectiveness of cochlear implants for severe to profound deafness in children and adults: a systematic review and economic model[43] | Same as above | Same as above | For prelingually deaf children, the cost-effectiveness ratio for unilateral CI was £13,413 per quality-adjusted life-year, but £40,410 for simultaneous bilateral CI and £54,098 for sequential bilateral CI |
| 2010 | Cochlear implantation under the first year of age—the outcomes. A critical systematic review and meta-analysis[44] | 5 controlled observational studies | 125 children with CI before age 1 year | No quantitative meta-analysis. Only 17 with follow-up of at least 2 years. More rapid development of language skills with earlier implantation, although with wide variation. Robust and reliable outcome measures are lacking |
| 2010 | The effectiveness of bilateral cochlear implants for severe-to-profound deafness in children: a systematic review[45] | 13 controlled observational studies | Children | Heterogeneity precluded quantitative meta-analysis. Middle to high risk of bias. "No robust conclusions could be drawn about the clinical effectiveness of bilateral CIs from the present body of evidence" |
| 2011 | What is the effect of time between sequential cochlear implantations on hearing in adults and children? A systematic review of the literature[46] | 11 case series (6 pediatric) | 122 adults and 223 children | Heterogeneity prevented quantitative meta-analysis. Quality of studies was low. Current evidence suggests a second CI may be beneficial, but effect of time could not be satisfactorily answered |
| 2011 | Systematic review of the literature on the clinical effectiveness of the cochlear implant procedure in pediatric patients[47] | 49 studies (22 related to age at CI, 20 related to bilateral vs. unilateral CI, 7 related to disabilities) | n/a | Not possible to perform meta-analysis due to heterogeneity. CI prior to 18 months has confirmed advantage compared to after 18 months; there may be advantage to CI prior to 12 months. Compared to unilateral CI, bilateral CI has advantages with hearing in noise and quiet, sound localization. CI is also beneficial for children with disabilities |
| 2011 | Systematic review of the scientific literature on the economic evaluation of cochlear implants in pediatric patients[48] | 9 studies (3 prospective, 3 retrospective, 3 cross-sectional) | n/a | Heterogeneity did not allow meta-analysis of cost-effectiveness. Direct cost ranged from €39,507 to €68,235 (2011 values). Cost per quality adjusted life year ranged from $2154 to $16,546 |

*Contd...*

*Contd...*

| *Year* | *Title* | *Studies included* | *# Participants (age of participants)* | *Results/conclusions* |
|---|---|---|---|---|
| 2011 | Bone-anchored hearing aids (BAHAs) for people who are bilaterally deaf: a systematic review and economic evaluation[49] | 12 studies (7 pre-/poststudies, 5 cross-sectional) | Children and adults | Meta-analysis not possible due to differences in outcome measures and patient populations. Some audiologic benefits of BAHA over bone conduction hearing aids; mixed results compared to air-conduction hearing aids; mixed results with bilateral BAHA compared to unilateral. The greater the benefit from aided hearing and > 8 h of usage per day, the more likely BAHAs are a cost-effective option |
| 2011 | Medical and surgical interventions for hearing loss associated with congenital cytomegalovirus: a systematic review[50] | 19 studies (2 RCT, 3 prospective cohort, 8 retrospective case series, 5 case report) | 446 children, 365 with complete audiologic results | No quantitative meta-analysis due to heterogeneity. Intravenous ganciclovir appears to protect hearing in infants with symptomatic CMV; oral valganciclovir trends toward protecting hearing; neutropenia is common. With CI, children improved their language skills beyond their preimplanted state, but degree of improvement was mixed |
| 2011 | Audiologic management of auditory neuropathy spectrum disorder in children: a systematic review of the literature[51] | 18 case reports or case series | 115 participants | No quantitative meta-analysis could be performed. Children with ANSD can benefit from acoustic amplification and CI. "The findings from this review do not resolve the controversies surrounding the audiologic treatment of ANSD in children" |
| 2012 | Postural control, motor skills, and health-related quality-of-life in children with hearing impairment: a systematic review[52] | 17 studies (4 cross-sectional, 1 correlational, 12 no design stated) | Age 5–11 years | Heterogeneity prevented methodological quality assessment and meta-analysis. Children with hearing impairment exhibit suboptimal levels of function in postural control, motor skill performance, and health-related quality-of-life |

(QoL: Quality-of-life; CI: Confidence interval; HL: Hearing loss; ANSD: Auditory neuropathy spectrum disorder; CMV: Cytomegalovirus).

questions, such as the efficacy of CI for profound bilateral hearing loss). Instead, prospective planning of studies to document and account for biases, systematic recording of predetermined outcomes, and increased collaboration among researchers to identify outcomes of interest would improve the quality and level of the evidence we have in this area.

## TYMPANOPLASTY

Tympanoplasty and myringoplasty are common procedures for children with a history of chronic middle ear disease or cholesteatoma, with a wide variety of surgical approaches to the repair of tympanic membrane perforations and conductive hearing loss. A Medline search using the terms "tympanoplasty children" and "comparative study" revealed one randomized study and 11 controlled studies. Two studies of the same study population were excluded. There were no identified systematic reviews pertaining to tympanoplasty for the repair of tympanic membrane perforations. One systematic review evaluated cartilage tympanoplasty or ventilation tubes for the treatment of tympanic membrane retraction pockets using hearing as the outcome; unfortunately, no definitive conclusions could be made regarding efficacy of either of these treatments.[53]

Six of the identified studies compared cartilage grafts with temporalis fascia grafts; results were mixed, with some investigators reporting better perforation closure rates with cartilage and other with temporalis fascia.[54-58]

Four used alternative graft material, including pressed scar tissue, Alloderm, and areolar connective tissue. All studies reported similar success with closure of perforations. One study reported closure rates and hearing improvement in children (age 8–14 years) compared to adults who underwent tympanoplasty, finding no statistically significant difference.[59] Finally, a study of patients (age 2–55 years) with a history of repaired cleft palate compared to age- and procedure-matched controls without cleft palate showed similar closure rates, hearing results, and need for postoperative tympanostomy tube placement.[60] While these comparative studies are helpful to review, a systematic review with a more complete search of the worldwide literature and synthesis of the results would be invaluable to determine whether results were mixed due to the problem of small numbers in studies, differences in technique, or patient factors.

## EDITORIAL COMMENTS

EBM in pediatric otology has gained much scientific basis that aids clinicians to deliver the most benefit and avoid the most harm to children. These four topics—otitis media, hearing screening, hearing loss, and tympanoplasty—were ultimately chosen out of a host of others (e.g. management of aural atresia, assessment of vertigo and balance in children, etiologic workup for hearing loss) that deserve attention and scrutiny. Yet we ought not to be content with the state of EBM in this field and should continue to endeavor to improve the quality of the studies performed, broaden the applicability of studies beyond the typically developing child, and continue to critically review current clinical practices in order to benefit our patients. Future versions of this chapter and other authors will be required to document the progress we make in diagnosis, prognosis, intervention, prevention, and effectiveness studies. Rather than publish more uncontrolled series of cases, we should endeavor to compare results of new and established modes of care. When feasible and ethical, randomized controlled trials should be performed to provide the highest level of evidence by reducing the amount of bias in studies. In order to provide better care for the at-risk or developmentally delayed child, we should collaborate across institutions on larger studies of children who do not fit the criterion of "otherwise healthy". Systematic reviews should be methodologically rigorous, following widely accepted criteria, rather than being an upgraded review of the literature.[4,61] When the opportunity arises to change our understanding of pathophysiology, abandon treatments or procedures that relied on the placebo effect, or advocate for treatments that truly work, we ought to embrace the evidence that produces these changes.

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# SECTION 2

# Pediatric Rhinology

CHAPTER

26

# Pediatric Sinonasal Anatomy and Embryology

***Graham M Strub, Sanjay R Parikh***

The embryologic development of the nose and paranasal sinuses is a complex and dynamic process, beginning at the third to fourth week of gestation and continuing until the age of 18 years.[1] Clinicians who treat diseases of the nose and paranasal sinuses must have an intimate knowledge of the normal anatomy and physiology of these regions, and should therefore have a thorough understanding of both the normal and abnormal embryologic development of these structures. This chapter discusses the embryology of the developing nose and paranasal sinuses and highlights the aberrations of this process that manifest in clinically treatable pathology.

## DEVELOPMENT OF THE PRIMITIVE MIDFACE

The first event in the eventual formation of the paranasal sinuses occurs in the initial yolk sac vesicle, specifically the rotation of the cephalic end of the embryonic disk to form the embryonic head. In this early embryo, the anterior foregut develops with an ectodermally lined membrane, termed the buccopharyngeal membrane, at its anterior limit. At this stage the pericardial cavity lies caudal to this membrane, while the primitive forebrain lies rostrally. The foregut elongates, with its most anterior part becoming the stomodeum. The pericardial sac then rotates around the axis of the buccopharyngeal membrane and brings the cardiogenic region, the eventual transverse septum, and the cranial mesoderm into a ventral position. During this time the ectodermal and endodermal layers of the embryonic disk are separated by a layer of mesoderm that differentiates into the somites, or the "paraxial structures", from which the pharyngeal arches are derived.

It is at this point during the third week of gestation that three primordial facial projections appear: the frontonasal process, the maxillary process, and the mandibular process (Fig. 26.1). The frontonasal process is an ectodermally derived structure within which the nasal olfactory placodes develop. The olfactory placodes form the medial and lateral nasal prominences, and between these prominences proliferating mesoderm creates deepening nasal pits that will eventually become the nares. Between the pits, the medial nasal folds fuse to form the upper lip, premaxilla, and nasal septum. The deepening nasal pits eventually become the nasal sacs, and their posterior walls, or "bucconasal membranes", eventually dissolve and give rise to the posterior choanae.

At this stage, the maxillary process of the first branchial arch grows medially across the inferior border of the nasal pits and fuses with the medial nasal folds of the frontonasal process, effectively closing the inferior aspect of the nasal pits and thus forming the nasal cavities. The outer aspect of the maxillary process also fuses with the lateral nasal processes, forming a solid rod at the nasolacrimal ridge. This rod eventually canalizes to form the nasolacrimal duct, connecting the conjunctiva to the primitive nasal cavity, and assumes an oblique angle as the developing eye migrates medially toward the developing nose. The fusion of the maxillary process with the caudal aspect of the frontonasal process begins the formation of the anterior palate. As the nasal cavities deepen, a ridge along the caudal aspect of the frontonasal process develops and becomes continuous with the partition between the primitive nasal cavities, thus forming the septum. The free edges of the lateral maxillary mesoderm, termed the palatal processes, begin to grow toward each other and

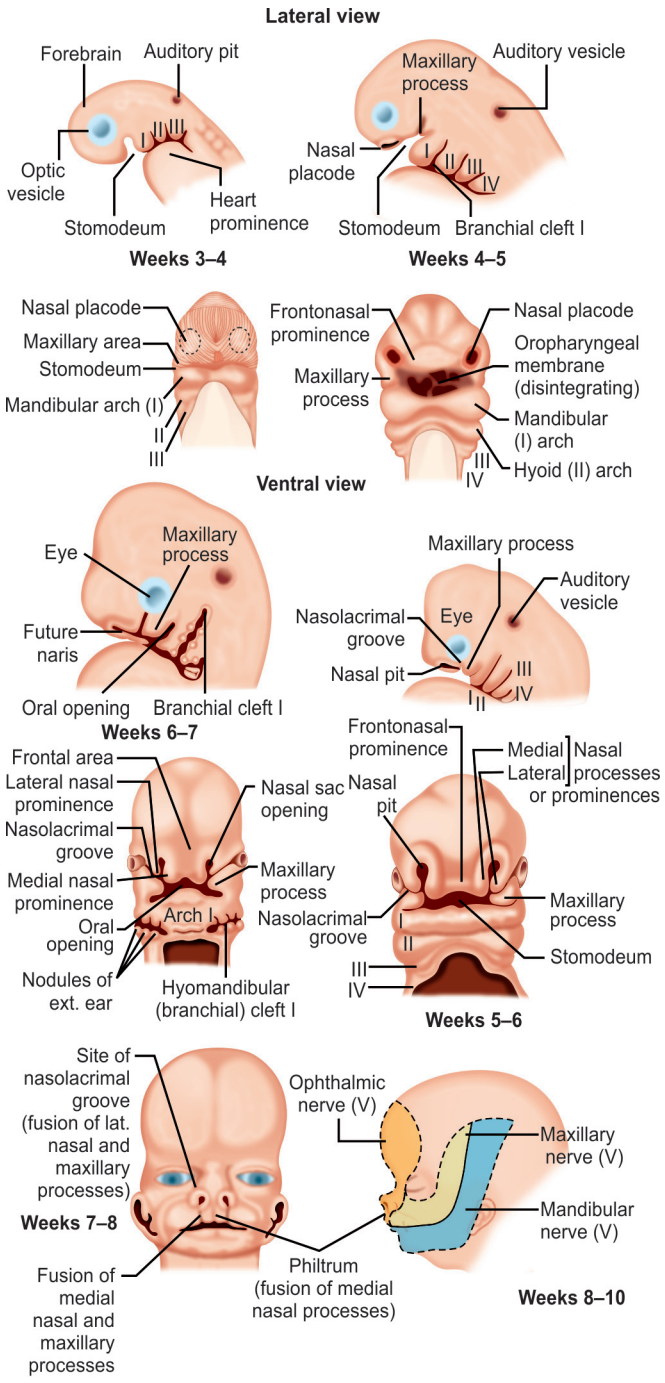


**Fig. 26.1:** Development of the midface structures. At weeks 3–4, the heart prominence, stomodeum, and pharyngeal arches are visible. Development of the nasal placodes and frontonasal process can be seen during week 4. The nasal processes and pits as well as the nasolacrimal grooves are visible at weeks 5–6. By weeks 7–8, the maxillary and frontonasal processes have fused. Adapted from Pansky.[2]

the developing septum, initially growing vertically but then turning to extend horizontally and eventually fusing. This fusion occurs in an anteroposterior direction, eventually forming the soft palate and uvula, and effectively separating the nasopharynx from the oral cavity.

## TURBINATE FORMATION

During weeks 7–8 of development, the lateral nasal walls increase their surface areas and the turbinates and their meatuses begin to form a series of mesenchymal ridges. The first to form is the inferior turbinate and develops at week 7 from the inferior ridge termed the maxilloturbinal. During the eighth week, a series of five to six additional ridges form superior to this, eventually fusing to form three to five ethmoturbinals. The agger nasi cells and the uncinate process are formed from the first ethmoturbinal, while the second and third ethmoturbinals give rise to the middle and superior turbinates, respectively. The fourth and fifth ethmoturbinals regress, although persistence of these structures can occur and results in the formation of the supreme turbinate.

## PARANASAL SINUS DEVELOPMENT

It is at this time, during the third fetal month, that the paranasal sinuses begin to develop. The maxillary, frontal, and ethmoid sinuses develop from evaginations of the lateral nasal wall, while the sphenoid sinus develops from an evagination of the nasal capsule. Only the maxillary and ethmoid sinuses are present at birth (Fig. 26.2).

### Maxillary Sinus

The maxillary sinus is the first sinus to appear and begins as an outgrowth in the lateral nasal wall of the nasal capsule, immediately posterior to the uncinate in the uncibullous groove.[3] It begins as a fluid filled cavity and remains so at birth. The maxillary sinus grows rapidly after birth for the first 3 years, then slows, then rapidly enlarges again between the 7th and 12th year of life. The rapid rate of growth is estimated to be 2 mm vertically and 3 mm anteroposteriorly each year.[4] Pneumatization of the maxillary sinus extends laterally to the lateral orbital wall and inferiorly to the floor of the nasal cavity, bringing the maxillary sinus in close proximity to the maxillary dentition. The adult maxillary sinus is a pyramidal

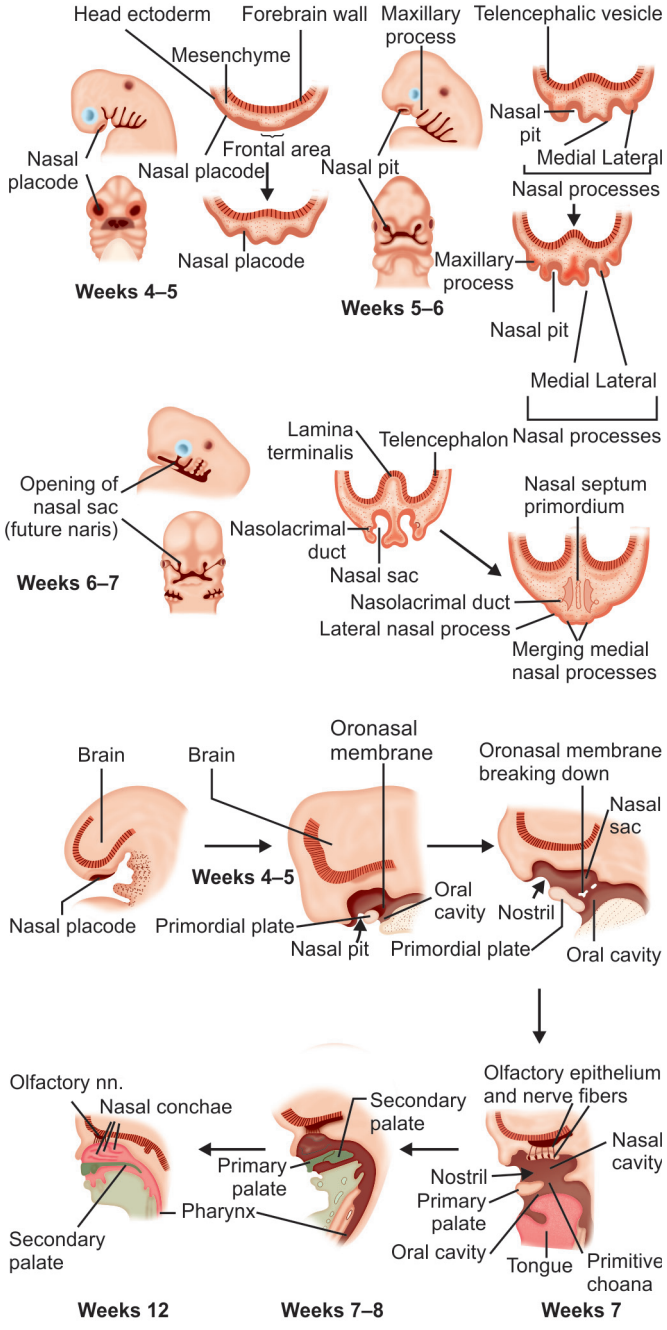


**Fig. 26.2:** Development of sinonasal structures. During weeks 4–5 the nasal placodes and nasal pits are forming, and by week 5 the lateral and medial nasal processes are visible. The nasal sac deepens and the bucconasal membrane breaks down, and by week 7 the nostril, primitive choana, and the primitive primary palate are visible. Development of the palate structures continues through week 8 and the nasal and oral cavities become separated. By week 12, the secondary palate and the nasal conchae have developed. Adapted from Pansky.[2]

structure with dimensions approximately 34 mm antero-posteriorly, 33 mm vertically, and 25 mm horizontally.[4] The boundaries of the maxillary sinus cavity are the orbital floor superiorly, the ascending process of the palatine bone laterally, the maxillary bone anteriorly, and the pterygomaxillary space (containing the internal maxillary artery, sphenopalatine ganglion, foramen rotundum, vidian canal, and greater palatine nerve) posteriorly.[5] Near the anteromedial roof of the maxillary sinus lies the maxillary ostium, an elliptical shaped communication at the merging point of mucociliary flow and draining into the ethmoid infundibulum. Variations in the anatomy of the maxillary sinus occur, including incomplete septi (50%), sinus duplication (2.5%), accessory ostia (25%), and hypoplasia (6%)/aplasia (< 1%).[4] The maxillary sinus receives its arterial blood supply from branches of the internal maxillary artery, including the infraorbital, lateral nasal branch of sphenopalatine, descending palatine, and posterior and anterior superior alveolar arteries. It is innervated by V2 branches including greater palatine, as well as the superior alveolar branch of the infraorbital nerve, and the posterolateral nasal branches.

## Ethmoid Sinus

During the third fetal month, lateral evaginations from the middle meatus begin the formation of the anterior ethmoidal cells, and later evaginations from the superior meatus begin the formation of the posterior ethmoidal cells.[3] The development of the anterior ethmoidal cells occurs anterior to the second ethmoturbinal, while the posterior cells develop posterior to this structure. This accounts for the different drainage pathways from these sinuses; the anterior ethmoids drain through the middle meatus and anterior to the basal lamella of the middle turbinate, while the posterior ethmoids drain posterior to the basal lamella through the superior meatus. The ethmoid sinuses are the most variable sinus structure, and are also fluid filled at birth. They are initially spherical in shape, eventually flattening out and reaching their approximate adult size by 12 years of age. The borders of the ethmoid sinuses include the lamina papyracea laterally, the middle and superior turbinates medially, the face of the sphenoid sinus posteriorly, and the intracranial cavity and cribriform plate superiorly. As the ethmoid sinus cells pneumatize, they can invade adjacent bone, and are subsequently named after the bone invaded. Examples of this concept

include an anterior ethmoidal cell that invades the frontal bone to become part of the frontal sinus, or invading the lacrimal bone to become the agger nasi. Individual ethmoid cells can also be found within the confines of the maxillary sinus or sphenoid sinus. This variability of the ethmoids and their proximity to critical structures such as the orbit and brain make preoperative evaluation with CT scans crucial for safe endoscopic sinus surgery.

Despite this variability, a series of five ethmoid lamellae with their attachments to the lateral nasal wall can serve as a guide during endoscopic sinus surgery. The first encountered (most anterior) is the uncinate process, a sagittally orientated crescent-shaped structure forming the anterior and medial borders of the ethmoid infundibulum. It attaches to the maxilla and lacrimal bone and inferior turbinate at its anterior and inferior borders, respectively. Superiorly the attachment varies, with the most common configuration (70%) attaching to the lamina papyracea laterally and directing frontal sinus outflow medial to the uncinate. The other two attachment configurations, to the ethmoid roof superiorly (19%) or to the middle turbinate laterally (11%), direct frontal sinus outflow through the ethmoid infundibulum.[6,7] The second lamella is the ethmoid bulla, which is the largest of the ethmoid cells and is the most reliable landmark during ethmoidectomy due to its visibility within the middle meatus. Posterior to this the surgeon encounters the third lamella, the basal (or ground) lamella, which serves as the anterior border of the posterior ethmoid cells and is the attachment of the middle turbinate to the lateral nasal wall. The fourth lamella encountered is the basal lamella of the superior turbinate, and the rarely encountered basal lamella of the supreme turbinate lies posterior to this when the supreme turbinate is present (15% of population).[8] The ethmoid sinus receives its arterial blood supply from the ophthalmic artery to the anterior and posterior ethmoidal arteries, as well as the sphenopalatine to nasal branches. They are innervated by V1 to the nasociliary nerve to the anterior and posterior ethmoidal nerves, as well as V2 to the posterolateral branches.

## Frontal Sinus

During the third fetal month, an evagination from the anterosuperior part of the middle meatus forms. This is the frontal recess, which deepens into a small diverticulum that is present at birth. The frontal sinus then forms by either direct expansion of the frontal recess, by pneumatization of an ethmoid cell within the frontal recess, or by pneumatization of an ethmoidal cell from within the ethmoid infundibulum.[9] The mechanism by which the frontal sinus forms will determine the shape and pathway of the drainage tract. The slow process of upward pneumatization then occurs through the frontal bone from the fifth year of life into late adolescence. This pneumatization occurs independently for each side of the frontal bone, so asymmetry between the frontal sinuses is common. The frontal sinus receives its arterial blood supply from the ophthalmic to supraorbital and supratrochlear arteries. It is innervated by V1 to the frontal nerve to the supraorbital and supratrochlear nerves.

## Sphenoid Sinus

During the fourth fetal month the sphenoid sinus begins as an evagination of the posterior nasal capsule. This evagination remains small until approximately 3 years of age when pneumatization into the sphenoid bone begins, extending to the level of the sella turcica by age 7, making it the first paranasal sinus to reach full development. There are three patterns of sphenoid pneumatization: sellar (90%), with pneumatization extending beyond tuberculum sellae; presellar (8%), with pneumatization only up to the tuberculum sellae; and conchal (2–3%), with pneumatization arrest at the initial infantile stage.[9] Dehiscent bone over the optic nerve (5%) or carotid arteries (25%)[10] has been observed and should give the surgeon caution when approaching the sphenoid sinus. The sphenoid sinus receives its arterial blood supply from the posterior ethmoid artery and branches of the sphenopalatine artery. It is innervated by V1 to the nasociliary nerve, as well as the sphenopalatine branches of V2.

# DEVELOPMENT OF SINONASAL MUCOSA

Paralleling the development of the bony and cartilaginous structures of the midface and paranasal sinuses, the mucosal lining that functions in olfaction, air transport, humidification, and purification of air also develops. During the formation of the lateral nasal wall, the sinonasal mucosa exists as a single layer of undifferentiated epithelial cells overlaying the nasal wall mesenchyme. Between 8 and 9 weeks, when the nasal septum and turbinates are developing cartilage, olfactory epithelium appears in the superior nasal cavity and ciliated pseudostratified

columnar epithelium along the nasal septum.[11] By 14 weeks the lateral nasal wall is covered with ciliated respiratory epithelium, and by 16–18 weeks, the maxillary and ethmoid sinuses have ciliated epithelium containing goblet cells. Throughout this time the mucosal lining throughout the paranasal sinuses becomes thicker and more vascularized.[11]

## SINONASAL DEVELOPMENTAL ANOMALIES

The precise coordination of events during embryogenesis of the nose and paranasal sinuses leaves room for several anomalies to develop. These anomalies can occur in isolation or as part of broader syndromes and are of clinical importance to physicians. The most common is choanal atresia, which occurs when the bucconasal membrane fails to rupture during the sixth week of development. Choanal atresia can be unilateral or bilateral and can be either mucosal or bony. Bilateral choanal atresia presents with immediate postnatal respiratory distress due to the fact that newborns are obligate nasal breathers. These newborns typically undergo tracheotomy followed by surgical repair. Choanal atresia occurs in conjunction with several other anomalies in the CHARGE association (coloboma of eye, heart anomalies, choanal atresia, retardation, genital, and eye anomalies) and is due to a microdeletion at chromosome 22q11. Other more rare defects include failure of nasal placode formation leading to absence of a nose. If only one nasal placode forms patients can present with the presence of only one nostril. Facial clefts can occur when the frontonasal prominence fails to merge with the maxillary prominence. Failure of migration of neurons from the nasal placode to the hypothalamus due to a mutation in the *KAL* cell adhesion protein-encoding gene produces Kallmann's syndrome, characterized by anosmia, hypogonadic hypogonadism, micropenis, and unilateral renal agenesis. In addition, there are several congenital masses that can be present within the midface and paranasal sinuses such as dermoids, meningoceles, and encephaloceles. Finally are the anomalies of cleft lip and cleft palate, which are discussed in detail elsewhere in this text.

## CONCLUSION

The development of the paranasal sinuses begins after the formation of the primitive midface structures at month 3 of development and follows a generalized pattern of enlargement and pneumatization. Despite this pattern, there is a great deal of variation between patients and even within the same patient, and therefore, the surgeon must have a sound understanding of the normal embryology and anatomy of these structures, as well as the variations that result in treatable pathology.

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CHAPTER

# 27

# Role of Human Evolution in Rhinosinusitis

***Charles D Bluestone, Jeffrey T Laitman***

## INTRODUCTION

We have recently proposed that both otitis media and rhinosinusitis are unique diseases of humans and consequences of human evolution.[1,2] In this chapter, we show how evolution has been instrumental in making rhinosinusitis a disease of humans, which, if present in animals in the wild, would have been incompatible with survival due to predation. We also posit that an understanding of evolution's role in rhinosinusitis has implications for possible innovative management, albeit somewhat unorthodox, that may have a future role for this commonly encountered malady, especially when chronic, irreversible disease is present.

The impact of evolution on otitis media, which has a similar scenario, is covered in another chapter in this textbook (*see* Chapter 3).

## EVOLUTION'S ROLE IN THE ANATOMY OF THE HUMAN HEAD AND NECK

The three most significant evolutionary changes from our immediate ancestors and other primates are that humans are habitually bipedal, have adapted unique speech, and have a craniofacial skeleton that is substantially different.

## BIPEDALISM, BIG BRAIN, AND "BORN TOO SOON"

The first relevant report published by one of us (CDB) was on evolution's role in the ears, nose, and throat, following a trip to East Africa.[3] During that adventure, it became evident that some animals in the wild, such as elephants, could walk at birth as they had to join a constantly moving herd; any who could not would soon become prey for hungry predators. By contrast, we humans walk at approximately 1 year of age. The conclusion was that humans are born too early or "born too soon." The question is why? Anthropologists have termed human birth to be "secondarily altricial"; some higher mammals are mature ("precocious") at birth, whereas others, such as dogs and cats, are "altricial," i.e. relatively helpless at birth. Humans should be precocious when born but are not.

The reason is that approximately 4 million years ago our hominid ancestors began to walk upright on two legs, i.e. bipedal (Fig. 27.1), after which the female pelvic outlet became smaller. Later, as the human brain enlarged in newborns, we are born about 12 months earlier than ideal—humans should have a 21-month gestational period and not 9 months (Fig. 27.2).[4] Infants triple their birth weight during the first year of life and together with a 23% increase in head circumference, parturition at that age would be impossible. Even at 9 months gestation humans have a difficult delivery through the tight birth canal; we are the only species that requires assistance during birth. Today, with the survival of preterm babies, the impact of evolution on premature birth is that they are "born way too soon," which has even greater problems of birth that is too early. A more detailed discussion of the adaptation of humans to bipedalism and its consequences related to parturition on the ear, nose, and throat are described elsewhere.[3]

In addition to the effect of bipedalism on gestational age, our upright posture had an impact on craniofacial anatomy, e.g. anterior foramen magnum and cranial-base angulation, as described later.

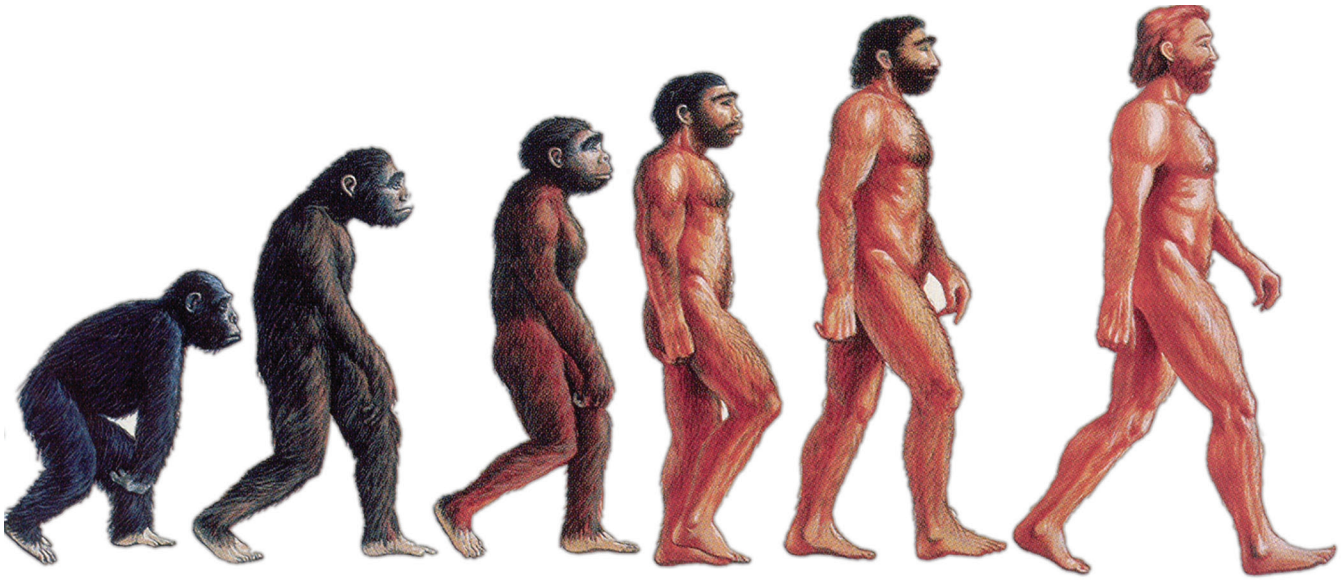


**Fig. 27.1:** Evolutionary changes in locomotor behavior from knuckle-walking chimpanzee-like ancestors to habitual bipedalism in modern humans.
*Source*: From Bluestone et al.[2]

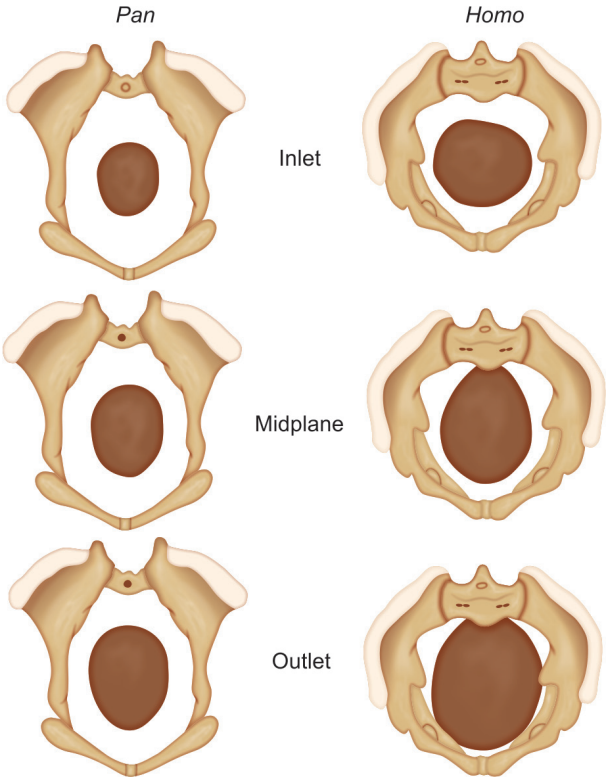
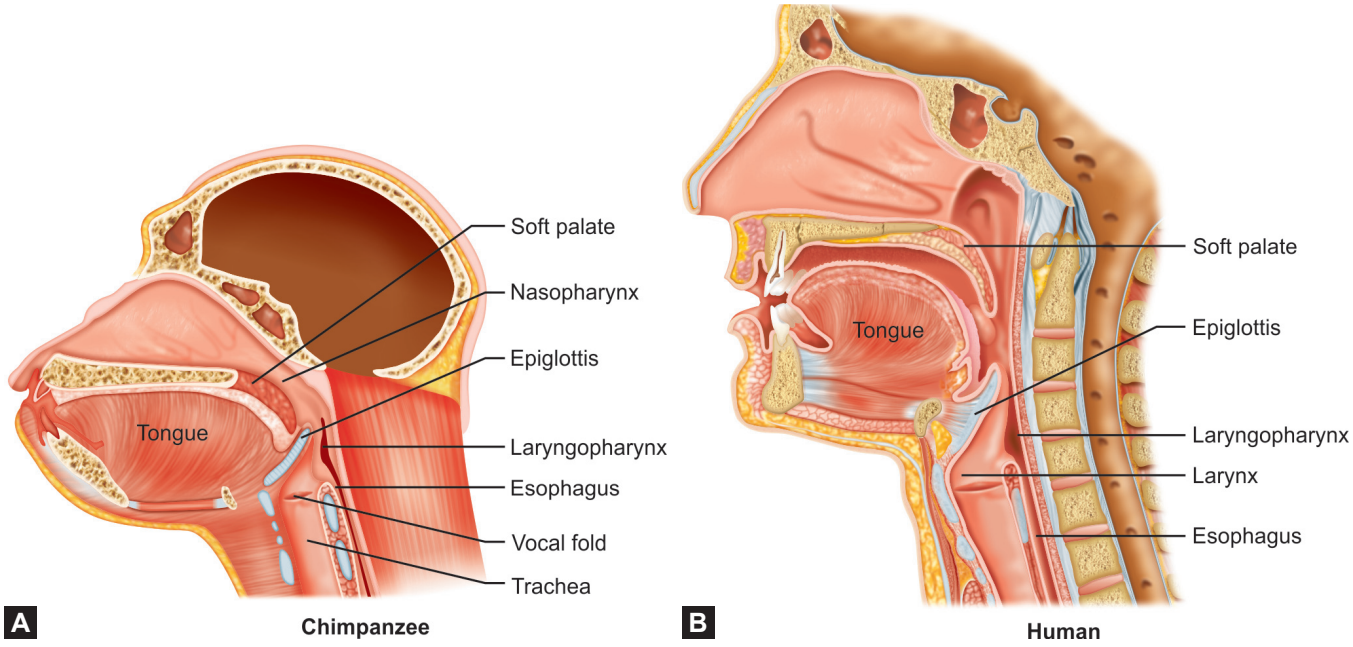


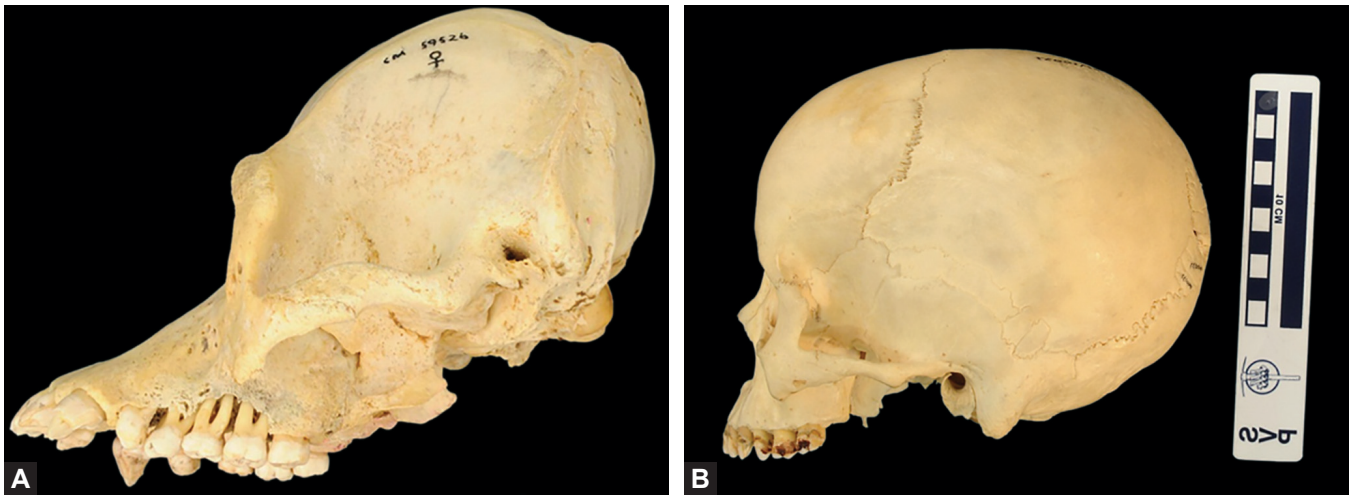

**Fig. 27.2:** Line drawing comparing the pelvic outlet with the brain size (*shaded*) of Pan (chimpanzee) to that of *Homo* (human) at birth. The brain of the chimpanzee easily fits in the relatively large pelvic outlet, but the human brain even at 9 months' gestation has an extremely tight fit.
*Source*: From Bluestone and Swarts.[25]

## ADAPTATION FOR SPEECH

No other species in the animal kingdom is capable of speech, which, in addition to habitual bipedalism and our relatively large brain, is one of our most unique attributes. What anatomic changes occurred during evolution that enabled us to develop speech? An important and significant difference between humans, after the neonatal age, and most other mammals is that the nonhuman laryngeal epiglottis is in contact with the soft palate, which facilitates swallowing while breathing through nose, enabling animals to eat for prolonged periods of time. This is termed the "epiglottic-soft palate lock-up." Human neonates also have a high-riding larynx and "lock-up" that enables them to suck and swallow during nasal breathing; neonates are essentially obligate nasal breathers. After about 2–3 months of age, the larynx in the human begins its structural descent and becomes permanently lower than in the nonhuman primate and reaches the level of the adult larynx after 3–5 years of age (Figs. 27.3A and B). The descent of the larynx elongated the throat and formed our unique two-tube configuration of our narrowed supralaryngeal vocal tract, facilitating speech.[5] As described below, in addition to our lower larynx, humans have lost the prognathism (facial flattening) so prominent in nonhuman primates, and, along with other anatomic differences, is a major factor in the development of human speech.




**Figs. 27.3A and B:** Line drawing in the midsagittal plane comparing the chimpanzee and human showing the shorter palate, oropharyngeal tongue, narrower pharynx, and descended larynx (loss of "epiglottic—soft palate lock-up") in the human when compared with the chimpanzee.




**Figs. 27.4A and B:** Comparison of skulls between the orangutan (Pongo) with its prominent prognathic jaws (A) and human (B), which shows the dramatic facial flattening in the human.
*Source*: From Bluestone et al.[2]

## EVOLUTION'S IMPACT ON CRANIOFACIAL ANATOMY

When one compares the facial profile of the great apes (i.e. gorilla, chimpanzee, and orangutan) with that of humans, the most impressive difference is the ape's prognathic jaw (Figs. 27.4A and B); humans have a relatively flat face. During evolution, humans lost the prognathic jaw (facial flattening) along with a smaller oral cavity, smaller and crowded teeth, and a shorter maxilla, mandible, and palate; impacted third molars are only present in man. The reason humans, and to varying extent our hominid ancestors (i.e. extinct precursors of man), lost the prominent prognathic jaw of the apes, is controversial. Some

have postulated that it is related to selective pressure for speech, whereas others posit it was most likely the result of a change in diet. As proposed by Wrangham,[6] cooking probably started with *Homo erectus* about 1.8 million years ago, which significantly contributed to our being human. With cooking, humans could eat fibrous fruits and tubers and raw meat, which became more rapidly edible and provided much-needed energy for our fast-growing brain. Another hypothesis is that with this change in our diet, a large oral cavity with big teeth suited for prolonged chewing of uncooked food was unnecessary and resulted in facial flattening. One can compare this evolutionary change to the adaptation of the beaks of the 13 different species of Darwin's finches on the Galapagos Islands; their beaks adapted to the specific ecological niche for eating on the different islands. Also, the unique endemic Galapagos marine iguana of these islands developed a flat face, when compared with the land iguana, which adapted to eating algae from the underwater lava rocks.[7]

Other anatomic changes that facilitated speech are an anterior migration of the foramen magnum, acute angulation of the cranial base, a shortened ethmoid bone, and an oropharyngeal tongue. Figures 27.3A and B show that the tongue in the chimpanzee does not encroach on the pharynx, whereas in the human it does, significantly compressing the oropharynx, which has an impact on the upper airway and is related to the pathogenesis of obstructive sleep apnea.

## RHINOSINUSITIS IN OTHER SPECIES IN THE WILD; IMPLICATIONS FOR OTITIS MEDIA

Rhinosinusitis—like otitis media—is also incompatible with survival in animals in their natural environment (*see* Chapter 3). Olfaction, as with hearing and vestibular function, is another special sense that is severely and adversely affected when rhinosinusitis occurs.[8] The sense of smell is critical in most terrestrial animals for recognition, avoidance, and defense against predators.[9] Indeed, if animals in the wild had routinely developed sinusitis, they most likely would have been selected out during evolution. Odor sources from predators have been identified by Apfelbach et al. as coming from the whole animal or from its feces, urine, anal gland secretions, and bedding.[10] Olfaction also aids animals in selecting food that is safe[11] and helps animal mothers in identifying their young. Except for humans (after the neonatal age), most mammals, including our primate relatives, are highly habitual—obligatory in many cases—nasal breathers, and if rhinosinusitis, with its associated nasal obstruction, would have been present they would not only have had poor olfactory function, but they would not have been able to suckle, eat, and swallow while breathing through the nose. Most mammals that are "macrosomatic" (i.e. largely dependent on olfaction for communication with their environment) must keep their nasal airways and olfactory system open to detect the scent of predators. Humans—in contrast to most other mammals, including other primates—are "microsomatic," i.e. less dependent on olfaction.

Thus, rhinosinusitis in most other mammals in a natural setting is probably "rare" in contrast to its frequent occurrence in humans.[12] Although proof is lacking, we hypothesize that if a viral upper respiratory tract infection (URI) regularly occurred in animals, they most likely would not have survived and thus not garnered the evolutionary robustness that would have accompanied acquired immunity.

Indeed, the presumed absence of URI in wild animals could shed light on the etiology and pathogenesis of acute otitis media in humans. In addition to more favorable anatomy of the paratubal muscles (e.g. tensor veli palatini) of the Eustachian tube and its function as present in the Rhesus monkey when compared to humans, lack of viral URI has probably contributed to the probable absence of acute otitis media in animals in the wild; we have never observed spontaneous acute otitis media in the hundreds of monkeys in our laboratory in 30 years. Humans, on the other hand, have relatively poor tubal function and are susceptible to URIs, which has resulted in our high incidence of acute middle-ear infections, especially in infants in day-care environments (*see* Chapter 3).

Chronic middle-ear effusion, also not evident in the monkey, is common in humans, but not necessarily associated with URI. Occurrence of chronic otitis media with effusion has been linked to dysfunction of the Eustachian tube characterized by paradoxical "constriction" during attempts to open (dilate) the tube during swallowing, such as in the infant with an unrepaired cleft, which is thought to be secondary to a functional abnormality of the levator palatini veli muscle.[13] Not only is tubal dysfunction related to the pathogenesis of otitis media but also there is a genetic predisposition.[14] Some populations, such as certain Native Americans (e.g. Inuits, Apaches, and Navajos) and Australian Aborigines, have an extraordinary incidence of otitis media, which undoubtedly is hereditary (*see* Chapter 3).

**Table 27.1:** Presence or absence of paranasal sinuses in Old and New World monkeys

| *Taxa* | *Paranasal sinus* | | | |
|---|---|---|---|---|
| | *Maxillary* | *Ethmoid* | *Frontal* | *Sphenoid* |
| *Cercopithecoidea (Old World monkeys)* | | | | |
| Most taxa<br>e.g. *Papio* (baboon), *Mandrillus* (Mandrill) | No | No | No | No |
| *Macaca* (Rhesus macaque) | Yes | No | No | No |
| *Platyrrhini (New World monkeys)* | | | | |
| Most taxa<br>e.g. *Alouatta* (howler monkey), *Ateles* (spider monkey) | Yes | Yes (in some) | No* | No* |
| *Cacajao* (Uakari) and *Saimiri* (squirrel monkey) | No | No | No | No |

*Recesses that may be homologs of sinuses are variably present.
*Source*: Reprinted with permission from Bluestone et al.[2]

**Table 27.2:** Volumes ($cm^3$) of ethmoid cells and maxillary sinuses of *Homo sapiens* (humans) and pongids (great apes)

| *Species* | *Ethmoid cells* | | *Maxillary sinus* | |
|---|---|---|---|---|
| | *N* | *Mean*† | *N* | *Mean* |
| Homo (humans) | 10 | 4.98 | 10 | 12.33 |
| Pan (chimpanzee) | 10 | 3.26 | 10 | 19.21 |
| Gorilla | 10 | 1.34 | 10 | 41.62 |
| Pongo (orangutan) | 8–7* | 0.54 | 11 | 25.42 |

*Right-left sides; †Mean for right and left sides.
*Source*: Reprinted with permission from Bluestone et al.[2]

## COMPARATIVE ANATOMY OF PARANASAL SINUSES

The anatomy of the paranasal sinuses, or lack thereof, is dramatically different in nonhuman primates when compared with humans. Table 27.1 shows the super family Cercopithecoidea (Old World monkeys) have no sinuses except for one genus, the *Macaca* (Rhesus macaque), in which only the maxillary sinus is present.[15] Platyrrhine primates (New World monkeys) exhibit variations in their sinus anatomy with most reported having maxillary sinuses, some having ethmoids, but only homologs of the human having sphenoid and frontal sinuses; two genera, *Saimiri* and *Cacajao*, have no paranasal sinuses. As shown in Table 27.2, the great apes, the gorilla and orangutan, have the largest maxillary sinuses, but their ethmoids are essentially rudimentary (Fig. 27.5); ethmoids in humans have the largest volume in comparison with the great apes[16] (Fig. 27.6).

It has been proposed the ethmoid sinuses are not a true paranasal sinus and probably only has an olfactory function, whereas the other sinuses do not.[12] Also, as concluded by Marquez et al., the ethmoids are "phylogenetically, embryologically, anatomically, and functionally completely different from all other paranasal sinuses, and only in humans has it taken a key position between all the other paranasal sinuses, controlling their ventilation and drainage."[12] Thus, the ethmoid sinus has key role in the pathogenesis of rhinosinusitis in humans. Also, ethmoid sinusitis is a major factor in impairment of olfaction, whereas the other paranasal sinuses are not.

Animal species that lack or have rudimentary ethmoid sinuses, including the great apes, are unlikely to have olfactory impairment, and when present, are not adjacent to the cribriform plate, the outlet of the olfactory system into the nasal cavity. By contrast, the cribriform plate is in intimate contact with the ethmoid sinuses in humans. In most other mammals, the ethmoid bone is more posterior, and the cribriform plate lies in front for optimum olfactory function, whereas only in humans does the ethmoid bone become pneumatized and exhibit a sinus (probably related to bipedalism, facial flattening, and loss of prognathism); along with anterior migration of the orbits results in deepening of the face. As stated by

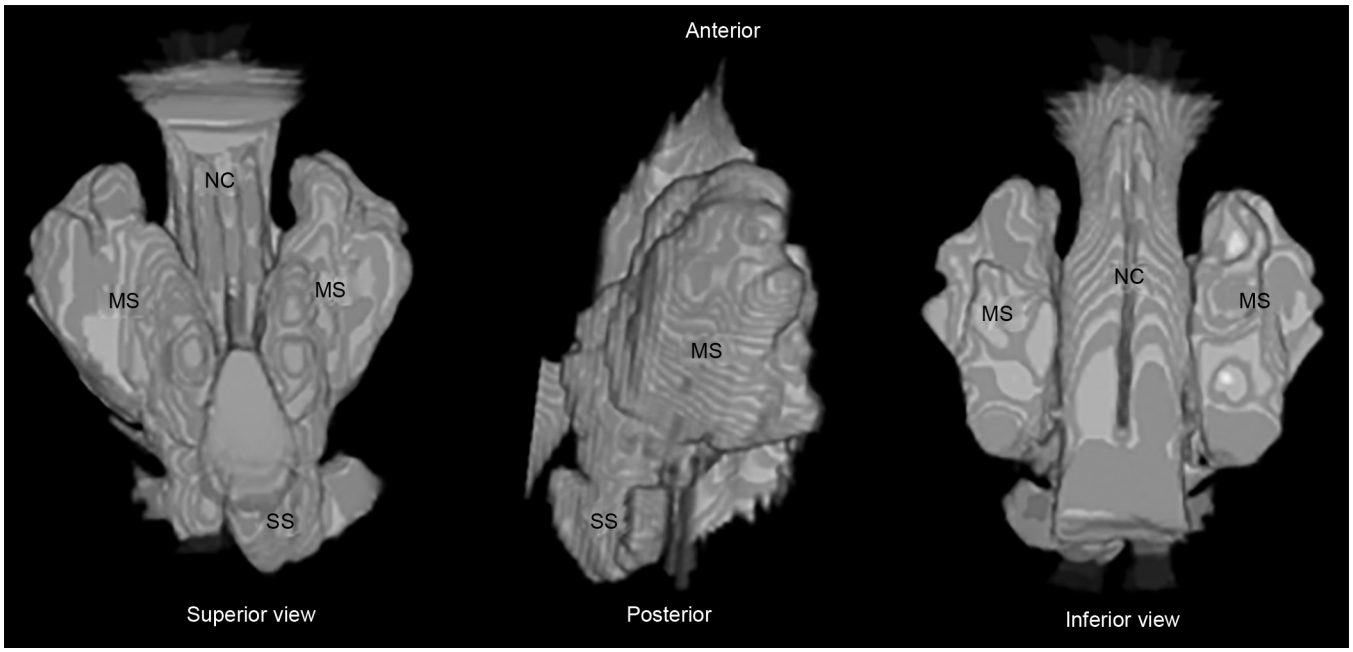



**Fig. 27.5:** Three-dimensional reconstruction of the nasal cavities and paranasal sinuses of an orangutan (Pongo) showing lack of ethmoids in the nasal cavities and large maxillary sinuses. (MS: Maxillary sinus; NC: Nasal cavities; SS: Sphenoid sinus.
*Source*: From Bluestone et al. 2012.[2]

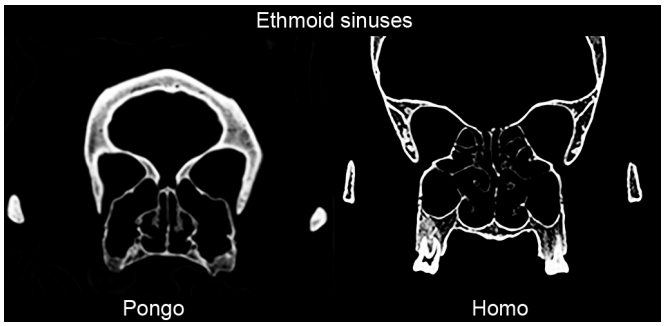



**Fig. 27.6:** Computed tomographic scan, coronal view, of skulls of Pongo (orangutan), left frame, and Homo (human), right frame, showing a lack of ethmoid sinuses in the orangutan compared with prominent ethmoid sinuses (arrow) in the human.
*Source*: From Bluestone et al.[2]

Marquez et al.[12] in "humans the anterior migration of the ethmoid sinus displaced the frontal sinus superiorly that disconnected the frontal sinus from the maxillary sinus and the ethmoids migrated along with the descent of the larynx that contributed to the unique human speech apparatus."

Thus, similar to the effect of evolution on the anatomy of the palate and paratubal muscles of the Eustachian tube, adaptations to bipedalism and speech and loss of prognathism have had a major effect on the anatomy of the paranasal sinuses, especially the ethmoids, which most likely predisposes humans to developing rhinosinusitis when exposed to airborne irritants.

## EVOLUTION'S ROLE IN PARANASAL SINUS AND MIDDLE-EAR DRAINAGE

When humans adapted to habitual bipedalism, there was a significant effect on drainage of the maxillary and sphenoid sinuses, as well as the middle ear. The bipedal posture resulted in the maxillary ostia being high in the medial wall in which drainage into the nasal cavity is by gravity, whereas in quadrupeds, drainage is aided by gravity as a result of the relative anterior tilt characterizing their head position.[17] Although not tested for drainage by gravity, similar anatomy exists in the sphenoid sinus as the ostia are high on the anterior wall. There is a similar impact of upright posture on drainage of the middle ear as it is less likely to drain by gravity into the nasopharynx, because the osseous portion of the Eustachian tube in the middle-ear is high at the level of the neck of the malleus, not in the most advantageous position in the inferior portion of the hypotympanum. In humans, the maxillary and sphenoid sinuses, as well as the middle ear, drainage is dependent on mucociliary transport, which in the middle ear is impaired by negative pressure and inflammation.

## DO THE HUMAN PARANASAL SINUSES HAVE A SIGNIFICANT FUNCTION?

Marquez,[18] in a review of 86 publications in the world literature, reported there were 19 hypothesized functions of the paranasal sinuses in humans over the past 2,000 years, but none reached consensus among researchers. However, production of nitrous oxide (NO) within the paranasal sinuses was the most interesting. As proposed by Lundberg et al.,[19] NO in the upper respiratory tract is produced in the paranasal sinuses and has a role in respiratory physiology, since it enhances pulmonary oxygen uptake due to local vasodilation. High production of NO is unique in humans and most other primates, but much lower in other mammals, such as dogs, rabbits, mice, and rats. In support of this hypothesis, Lewandowski et al.[20] reported that baboons that have no paranasal sinuses were found to have markedly lower concentrations of exhaled concentrations of NO than mammals with paranasal sinuses.

But why have Old World monkeys, except *Macaca*, that have no paranasal sinuses (*see* Table 27.1), survived without sinus NO and why do other mammals that have been identified as having NO require its production from the paranasal sinuses? In addition, nonprimate mammals that have paranasal sinuses (e.g. dogs and rabbits) produce low concentrations of NO and have survived. If some mammals (e.g. almost all Old World monkeys and some New World monkeys) can live without paranasal sinuses, the sinuses probably have no major physiologic function related to the production of NO.

Another possible function for paranasal sinuses is that they provide a biomechanical advantage, but Rae and Koppe[21] reported the hypothesis that sinuses arose in response to biomechanical requirements of skull architecture through dissipating masticatory stress forces related to dietary activities can be rejected. Among the other proposed functions are that they lighten the skull, aid in resonance to the voice, assist in regulating intranasal pressures, warm and humidify air, and are part of normal skull pneumatization. The human ethmoid sinuses, with their relatively small intranasal position (they are not truly a paranasal sinus since they are intranasal), most likely do not play any role in making the skull lighter, but one could argue their position in the nasal airway may be involved in vocal resonance, in addition to the proposed olfactory function and production of NO. The other sinuses also probably don't lighten the skull in the bipedal position of humans. Still another hypothesis is that yawning may activate a ventilator system in the paranasal sinuses for selective brain cooling.[22] Since is there is no consensus on function at this time, most likely the paranasal sinuses in humans exist as primitive retentions, i.e. "evolutionary remains of useless air spaces."[18,23,24]

## DOES HUMAN EVOLUTION HAVE IMPLICATIONS FOR MANAGEMENT?

A reasonable question related to rhinosinusitis, as well as otitis media is since both are probably limited to humans, how does that assumption help otolaryngologists manage patients with these diseases? From our understanding of the consequences of evolution related to otitis media, we learned that there are differences in the anatomy and function of the muscles of the Eustachian tube between the Rhesus monkey and the human that might improve tubal function following repair of the palate in patients with palatal clefts, i.e. levator veli palatini muscle.[25] Are there any implications for management of rhinosinusitis related to evolution?

### Caldwell-Luc Redux?

Given the unfavorable position of the human maxillary ostia due to bipedalism, is there ever a role for the Caldwell-Luc procedure? This old standby was the most common surgical procedure for treatment of chronic maxillary sinus disease for more than a century, but has more recently been replaced by less invasive endoscopic sinus surgery. Since there may be a presumed advantage of gravity drainage of the sinus by surgically making an antrostomy in the inferior meatus of the nasal cavity, there may still be an indication, albeit rarely, for a Caldwell-Luc operation, or modifications of it, when endoscopic sinus surgery of the osteomeatal complex fails to provide a permanent middle meatus antrostomy.[26] Most recently, functional endoscopic balloon dilation of sinus ostia for chronic rhinosinusitis has been become popular, but the efficacy of this new innovation has not had convincing evidence for supporting its use compared with conventional surgical procedures.[27,28]

### Exenteration and Obliteration of Sinuses?

In humans, when a nonvital organ has chronic disease that is irreversible, the organ is deemed useless and removed.

There are a many examples of organs, such as the tonsils and salivary glands, in which other healthy organs continue to function (for tonsils, other lymphoid tissue of Waldeyer's ring; following surgical excision of a diseased parotid or submaxillary gland, the other healthy major and minor salivary glands). Since there is no consensus on the physiologic role of the paranasal sinuses, except for possible production of NO, can a sinus, such as the maxillary, that has end-stage disease, be exenterated and obliterated?

There seems to be a real reluctance to obliterate the maxillary sinus. To date, there are no safe and effective procedures proposed. Yet, there is an example of an obliteration procedure in sinus disease, as when the frontal sinus communication into the nasal cavity cannot be restored following fracture of the frontal bone and its sinuses; in these cases, a fat graft is used for obliteration.[29] Also, there is an operative procedure for placing bone grafts in the maxillary sinus. Maxillary sinus floor augmentation procedure (i.e. sinus-lift) has been a very successful operation to permit tooth implants when there is not enough maxillary alveolar bone for implantation.[30] Can bone grafting techniques used for sinus lift surgery be used to obliterate a maxillary sinus that has failed surgery and has irreversible disease? Another example of an obliteration procedure is for chronic tympanomastoiditis, especially when that ear has no serviceable hearing. The Rambo procedure, using a temporalis muscle flap for obliteration of the tympanomastoid cavity, has been successful in most patients in preventing chronic otorrhea for the more than 50 years since Thomas Rambo first introduced it.[31,32]

If there is any sinus that would have important physiologic functions, it would be the ethmoids, since they are directly in the nasal airway and might be involved in vocal resonance as well as possible production of NO and olfaction. Yet, currently, ethmoidectomy is one of the most common surgical procedures for chronic rhinosinusitis in both children and adults. Thus, obliteration of an offending maxillary sinus is no more detrimental than ethmoidectomy. Candidate patients for obliteration of the maxillary sinuses could be individuals with cystic fibrosis or primary ciliary dyskinesia who have end-stage sinusitis (i.e. irreversible disease), especially since NO concentration is extremely low, or almost nonexistent, in these patients; even in patients without these relatively rare diseases, who have other more common etiologies of chronic sinusitis, NO concentrations have been found to be low.[18] Individuals with cystic fibrosis in whom maxillary sinuses are deemed to have chronic intractable disease, especially prior to lung transplantation, could have the offending sinuses obliterated. Topical daily nasal medical treatment could then be used without the need for repeated treatment of the offending sinuses.

## SUMMARY AND CONCLUSION

Rhinosinusitis, similar to otitis media, is most likely a human disease, secondary to consequences of evolution (i.e. adaptations to bipedalism and speech, and loss of prognathism), which resulted in anatomic differences compared to other mammals, mainly in the ethmoid sinuses and ventilation and drainage of the maxillary and frontal sinuses. In otitis media, the associated special sense of hearing, and more rarely vestibular function, would have been diminished, making survival of animals in the wild unlikely. Similarly, if rhinosinusitis occurred, animals would not have survived during evolution due to the loss of olfaction, another special sense. Although proof is lacking, if animals had developed viral URI during evolution, they would also have been selected out for the same reason and probably developed immunity. Humans have no doubt survived despite development of otitis media, URI, and sinusitis due to our excellent eyesight (another sense organ) and big brain along with protection from predators afforded by our family and social structure.

Because human paranasal sinuses apparently have no agreed upon physiologic function, except for possible production of NO, individuals with irreversible sinus disease might be candidates for exenteration and obliteration of the offending sinus cavity (e.g. maxillary) without loss of any known major physiologic function, as the mucosal lining of the sinus would no longer be capable of any possible function. Although this suggestion is currently unorthodox, indications for an exenteration and obliteration procedure of a sinus, as well as the ideal approach and implant material, should be a subject for future research and clinical goals.

In conclusion, rhinosinusitis is most likely unique to humans and extremely common, especially in infants and young children, and is a consequence of human evolution, as well as immunologic and environmental factors.

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CHAPTER

# 28 Evaluation of the Child with Rhinologic Disease

*Derek J Lam, Carol J MacArthur*

## INTRODUCTION

Expertise in the evaluation of the child with rhinologic disease is a necessary part of the armamentarium for the otolaryngologist treating children. Pediatric rhinologic disease is common; pediatric sinusitis is estimated to complicate the common cold in approximately 5–10% of cases, and children have on average six to eight respiratory infections every year.[1] Most young children will allow very little instrumentation of the nasal cavity or sinuses in the office setting, so the challenge is how to best make a meaningful assessment and come to an accurate diagnosis of the catarrhal child.

## HISTORY

### Nasal Obstruction

Nasal obstruction is perhaps the most common rhinologic complaint in children. A detailed history of the age at onset, duration, chronicity, laterality, and associated symptoms can help to determine the likely etiology of the nasal obstruction and direct further workup or treatment. The differential diagnosis includes infectious etiologies such as viral upper respiratory infections (URIs) and bacterial rhinosinusitis, common inflammatory conditions such as allergic and nonallergic rhinitis,[2–4] allergic fungal sinusitis,[5] asthma,[6,7] cystic fibrosis (CF),[7,8] and gastroesophageal reflux disease (GERD).[9,10] Congenital or acquired tumors and cysts of the sinonasal tract also commonly present with nasal obstruction. These include nasolacrimal duct cysts (NLDC),[11,12] encephaloceles or gliomas, nasal dermoids,[13] vascular malformations,[14,15] antrochoanal polyps,[16] and rare malignant tumors such as teratomas, rhabdomyosarcomas, or esthesioneuroblastomas.[17,18] Nasal polyposis is rare in children except in children with CF; therefore, a history or observation of nasal polyps should prompt a workup for CF if it has not already been done.[7,19–21] A fixed nasal obstruction may be caused by a nasal foreign body, septal deviation, inferior turbinate hypertrophy, choanal atresia/stenosis, pyriform aperture stenosis, and maxillary or midface hypoplasia due to an associated syndrome.[22] This broad differential diagnosis can be categorized based on the age of symptom onset (Table 28.1).

### Rhinorrhea

Rhinorrhea is a nonspecific symptom that is associated with allergic rhinitis and asthma, viral rhinitis, and bacterial rhinosinusitis. Differentiating between allergic and viral rhinitis can often be difficult. Allergic rhinitis is rare in children younger than 2 years old.[23,24] This is because atopic responses to environmental allergies typically develop after two or more seasons of pollen exposure; therefore, a detailed allergy history should be elicited in any child older than age 2 with symptoms of chronic nasal obstruction and rhinorrhea.[4,25] Risk factors for the development of atopy include a significant family history of allergies, especially among first-degree relatives, cigarette smoke exposure, higher socioeconomic class, and being a first-born or only child.[26] Food allergies, most commonly to milk or egg, and atopic dermatitis in infancy are both associated with later development of inhalant allergies, allergic rhinitis, and asthma.[23,27,28]

**Table 28.1:** Age of onset and differential diagnosis for nasal obstruction

| *Age* | *Differential diagnosis for nasal obstruction* |
|---|---|
| Neonate (0–3 months) | Neonatal rhinitis<br>Choanal atresia/stenosis<br>Congenital pyriform aperture stenosis<br>Nasal encephalocele, glioma, or dermoid<br>Nasal hemangioma<br>Nasolacrimal duct cyst<br>Midface hypoplasia |
| Infant (3–12 months) | Adenoid hypertrophy<br>Recurrent viral URI<br>Nasal hemangioma<br>Nasolacrimal duct cyst |
| Toddler (12–24 months) | Adenoid hypertrophy<br>Recurrent viral URI<br>Nasal foreign body |
| Preschool (2–4 years) | Adenoid hypertrophy<br>Recurrent viral URI<br>Recurrent acute rhinosinusitis<br>Chronic rhinosinusitis<br>Allergic fungal sinusitis<br>Allergic rhinitis<br>Nasal foreign body<br>Nasal polyposis (cystic fibrosis)<br>Immunodeficiency |
| Early school age (5–12 years) | Recurrent acute rhinosinusitis<br>Chronic rhinosinusitis<br>Allergic fungal sinusitis<br>Allergic vs. nonallergic rhinitis<br>Adenoid hypertrophy<br>Septal deviation<br>Inferior turbinate hypertrophy<br>Septal hematoma<br>Antrochoanal polyp<br>Nasal polyposis (Cystic fibrosis)<br>Immunodeficiency |
| Teenager (13–18 years) | Recurrent acute rhinosinusitis<br>Chronic rhinosinusitis<br>Allergic fungal sinusitis<br>Allergic vs. nonallergic rhinitis<br>Adenoid hypertrophy<br>Septal deviation<br>Inferior turbinate hypertrophy<br>Septal hematoma<br>Antrochoanal polyp<br>Nasal polyposis (cystic fibrosis)<br>Immunodeficiency<br>Juvenile nasopharyngeal angiofibroma |

## Epistaxis

A report of epistaxis should prompt questions about the frequency, duration, severity, and laterality of the bleeding episodes. The majority of pediatric epistaxis can be attributed to prominent vessels in Kiesselbach's plexus of the anterior septum with thin overlying mucosa that is susceptible to breakdown with either digital trauma or persistently dry air. An association of bleeding with dryer climates is consistent with this etiology. Recurrent epistaxis of significant volume, duration or frequency, especially if associated with syncope, hypotension, or need for blood transfusion, should prompt a more detailed workup for bleeding disorders, vascular anomalies, or vascular tumors. Recurrent epistaxis can be the presenting symptom of an underlying bleeding dyscrasia; therefore, the patient should be asked about easy bruising, frequent or prolonged bleeding episodes in addition to epistaxis, and a family history of hematologic disorders. Symptoms of fixed nasal obstruction or facial pain are suggestive of a nasal mass or tumor such as a juvenile nasopharyngeal angiofibroma.

**Table 28.2:** Chandler classification of orbital complications of sinusitis

| *Chandler class* | *Diagnosis* | *Clinical signs* |
|---|---|---|
| I | Preseptal cellulitis | Eyelid edema and erythema<br>Normal extraocular movements<br>Normal visual acuity |
| II | Orbital cellulitis | Diffuse edema of orbital contents<br>No discrete abscess formation |
| III | Subperiosteal abscess | Subperiosteal purulence of lamina papyracea<br>Lateral and downward globe displacement |
| IV | Orbital abscess | Purulent fluid collection within orbit<br>Proptosis, chemosis, ophthalmoplegia<br>Decreased visual acuity |
| V | Cavernous sinus thrombosis | Bilateral ocular findings<br>Prostration<br>Meningismus |

## Orbital Symptoms

Periorbital cellulitis and abscess are well-known complications of bacterial rhinosinusitis. A history of periorbital edema, erythema, increasing retro-orbital pain, visual acuity changes, or diplopia in the setting of an acute episode of rhinosinusitis should prompt a careful evaluation for possible periorbital abscess. Orbital complications of rhinosinusitis are most commonly described in terms of the Chandler classification scheme (Table 28.2).[29]

However, a more recent classification of orbital complications of acute rhinosinusitis based on a systematic review of the available evidence has been proposed.[30]

## Nasal Pain

Pain is an uncommon rhinologic complaint in children. Report of chronic or worsening nasal pain is suggestive of a severe infection such as complicated bacterial rhinosinusitis or an enlarging or invasive sinonasal tumor. Consideration should be given to nasal endoscopy and computed tomography (CT) or magnetic resonance imaging (MRI) to further evaluate this possibility.

## Assessing Pediatric Sinonasal Quality of Life

The SN-5 is a 5-item questionnaire for assessing health-related quality of life in children aged 2–12 years with persistent sinonasal symptoms. It demonstrated good test-retest reliability, validity, and responsiveness to change when compared with several external constructs.[31] This instrument has been used to demonstrate significant improvement in sinonasal-related quality of life after adenoidectomy or endoscopic sinus surgery.[32] A related instrument is the Pediatric Rhinoconjunctivitis Quality of Life Questionnaire that was developed to measure the quality of life in children ages 6–12 years old with seasonal allergic rhinoconjunctivitis. It has shown good reliability and responsiveness to change.[33]

## Bacterial Rhinosinusitis

Diagnosis of bacterial rhinosinusitis in children relies primarily on a detailed history. It is important to differentiate uncomplicated viral URIs from bacterial rhinosinusitis. Both can be characterized by nasal congestion, rhinorrhea, postnasal drip, hyposmia, cough, fever, and halitosis. Facial pain or headache, while common complaints in adult sinusitis, is less common in children. Acute bacterial rhinosinusitis has been purported to complicate approximately 6–8% of viral URIs, though the exact incidence remains unknown.[34] Viral URIs typically last 5–7 days and have at least begun to improve if not resolve completely after 10 days. There are three general patterns of symptom presentation that are suggestive of a viral URI that has progressed to acute bacterial rhinosinusitis[35,36]:

1. URI with nasal discharge, daytime cough worse at night with symptoms lasting > 10 days
2. URI that is more severe than usual characterized by high fevers for at least 3–4 days with concurrent copious purulent discharge or periorbital edema and pain
3. URI that was improving but suddenly worsens (double sickening)

The duration and specific pattern of symptom presentation has been used to define different categories of rhinosinusitis in children (Table 28.3).[37,38] In addition to these classifications, recurrent acute rhinosinusitis is defined as 3 acute episodes of acute bacterial rhinosinusitis in 6 months or ≥ 4 episodes of bacterial rhinosinusitis in 1 year, each lasting < 4 weeks, separated by intervals of at least 10 days without symptoms.

Thus, a detailed history should include the timing, duration, and severity of symptoms signaling a sinus infection, history of previous sinus infections, antibiotic use, nasal treatments such as steroid or saline sprays, and any previous hospitalizations for sinusitis-related complications. This includes periorbital cellulitis or abscess, Pott's puffy tumor, and meningitis.

Predisposing factors and possible etiologies should be explored. These include frequency of viral URI, daycare attendance or older school-age sibling in the household, allergy history including environmental and food allergies, asthma or eczema, and history of GERD, CF, ciliary dyskinesia, and immunodeficiency,[36,39] Approximately 50% of children with sinusitis also have environmental allergies, and there are known associations between allergies, asthma, and chronic sinusitis.

**Table 28.3:** Classification of bacterial rhinosinusitis

| | *Acute* | *Subacute* | *Chronic* |
|---|---|---|---|
| Symptoms | Purulent nasal discharge or postnasal drip for ≥ 3–4 days<br>High fevers (> 39°C)<br>Cough (worse at night) | Nasal discharge or postnasal drip (any quality)<br>Daytime cough<br>Periodic low grade fever | Nasal discharge or postnasal drip (any quality)<br>Daytime cough<br>Periodic low grade fever |
| Chronicity | Complete symptom resolution during this period | Complete symptom resolution during this period | Persistent symptoms with acute exacerbations and only partial response to antimicrobials |
| Duration | 10 days to 4 weeks | 4–12 weeks | > 12 weeks |

## CLINICAL EXAMINATION

### Head and Neck Examination

A thorough head and neck examination will include an assessment of the overall appearance of the child. The clinical evaluation and examination should be done in a nonthreatening manner for young children, perhaps with the child seated on the caregiver's lap to provide reassurance and for assistance in restraint if necessary. Allowing the child to see and touch the instruments to be used may also help. The facial appearance will often provide clues to the underlying pathology. An open-mouth posture, for example, will indicate that there is nasal or nasopharyngeal obstruction to breathing. Allergic shiners (dark circles under the eyes) will provide a clue that there may be allergic or infectious pathology in the nasal and sinus cavities. The allergic crease (a horizontal crease in the nasal supratip area), or evidence of the "allergic salute" performed in the office, will provide clues to possible allergic rhinitis. Foul odor emanating from the nasal cavity may indicate bacterial sinusitis, and if the odor is putrid and unilateral, indicates a nasal foreign body. Throat clearing or repetitive cough observed in the office may indicate the presence of postnasal drip from allergic rhinitis or sinusitis. A hyponasal voice will also indicate nasopharyngeal of nasal obstruction significant enough to cause alteration in the vocal resonance.

### Neonates and Infants (0–12 Months)

Neonates will more likely have congenital lesions, such as choanal atresia, pyriform aperture stenosis, nasal hemangiomas, NLDC, delivery-related septal deviation, dermoid cysts, gliomas, and encephaloceles (Table 28.1). Unilateral choanal atresia presents with unilateral constant mucoid drainage from one side of the nose. Once this is removed with suction, nasoendoscopy will reveal the atretic plate at the posterior choana (Fig. 28.1). An endoscopic view of the choanal atresia is a nice complementary study to the CT scan in terms of timing of the repair, level of the skull base, septal position and extent of inflammatory changes in the nasal cavity. A 70° telescope can also be used to see the choanal atresia from the nasopharyngeal view (Fig. 28.2). In the neonate, the diagnosis of choanal atresia can be made rapidly and with confidence with the flexible fiberoptic endoscope, even prior to any imaging. Because babies are obligate nasal breathers, bilateral choanal atresia is associated with respiratory distress immediately after birth, with cyclical cyanosis every time the baby stops crying. With a bedside fiberoptic examination, appropriate measures can be taken to stabilize the airway until repair can be scheduled. Pyriform aperture stenosis will present with nasal congestion and difficulty feeding as the narrowed nasal aperture prevents easy nasal airflow during feeds. Anterior rhinoscopy will reveal narrowed nasal vestibules bilaterally and the flexible scope may be difficult to pass, even with nasal decongestion. A single central incisor has been observed in up to 60% of children with pyriform aperture stenosis and is suggestive of possible holoprosencephaly.[40] In such cases one should consider MRI and endocrine evaluation to assess the hypothalamic-pituitary-thyroid axis.[41] Septal deviation can cause nasal obstruction and

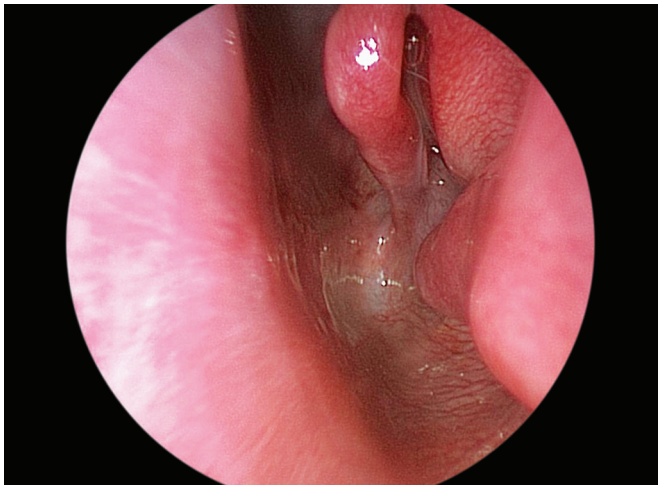


**Fig. 28.1:** Unilateral choanal atresia seen by nasal endoscopy after suctioning secretions to reveal the atresia plate.

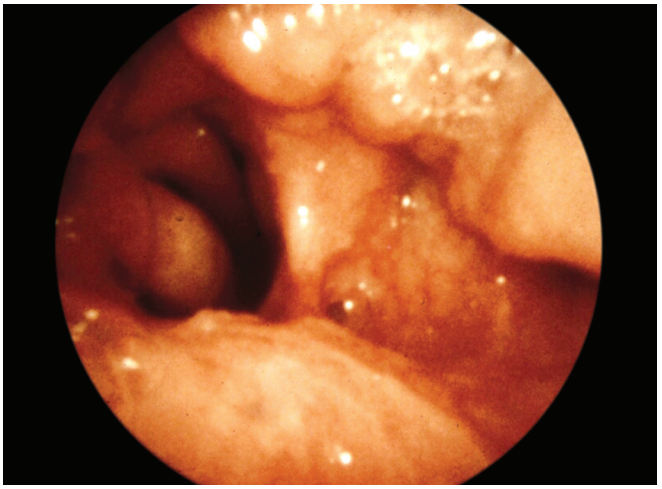


**Fig. 28.2:** Unilateral choanal atresia seen by endoscopy with 70° telescope (nasopharyngeal view).

feeding difficulties (Fig. 28.3). Reduction of the dislocated septum can alleviate the deviation if done acutely in the newborn period shortly after birth. NLDC will present as the triad of epiphora, nasal obstruction, and a cystic lesion inferior to the inferior turbinate (Fig. 28.4). As with choanal atresia or pyriform aperture stenosis, bilateral NLDC can cause significant nasal obstruction, especially with feeding. Congenital nasal masses, such as dermoid cysts, gliomas (Fig. 28.5), teratomas (Fig. 28.6) and encephaloceles will present with unilateral nasal obstruction and a solid or cystic complex mass within the nasal cavity. A midline pit is a clue to the dermoid sinus/cyst (Fig. 28.7). Nasal decongestion and endoscopic examination of the nasal cavity and nasopharynx in infants with nasal obstruction is essential to avoid missing the correct diagnosis in these cases.

Nasal hemangiomas located in the vestibule (Fig. 28.8A) or extending from the alar skin into the vestibule (Fig. 28.8B) can cause significant airway obstruction in an infant and may require treatment. Although hemangiomas are often easily recognizable by their appearance and time course of onset of symptoms, a biopsy sent for Glut-1 immunohistochemical staining will confirm the diagnosis. Ultrasound with color Doppler flow is also helpful to make the diagnosis of infantile hemangioma prior to or instead of MRI imaging.

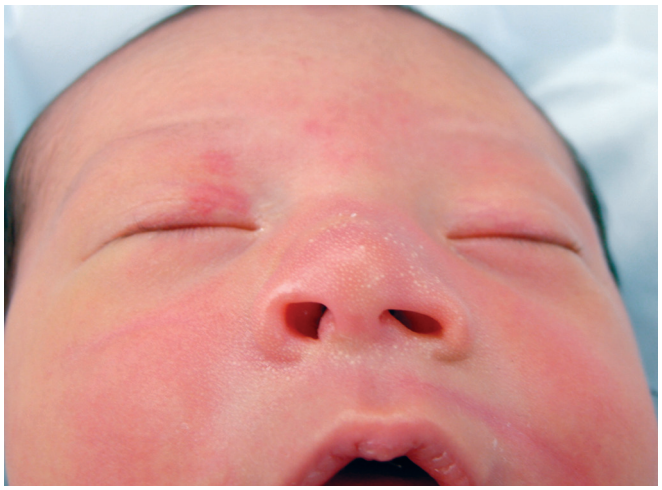


**Fig. 28.3:** Septal deviation in a newborn causing respiratory obstruction and feeding difficulties.

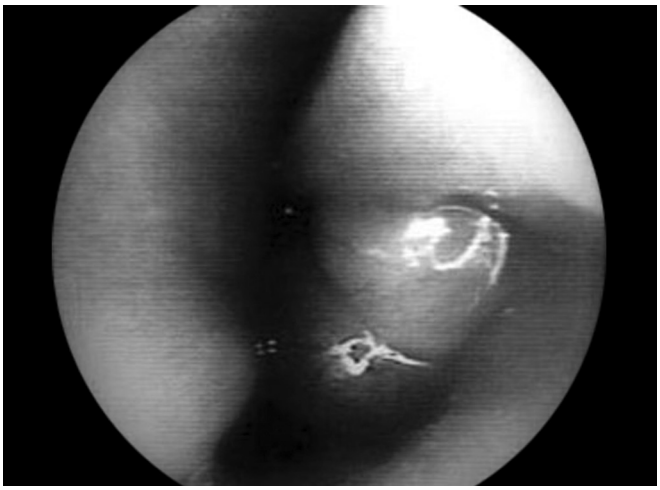


**Fig. 28.4:** Nasolacrimal duct cyst as seen inferior-to-inferior turbinate in the left nasal cavity.

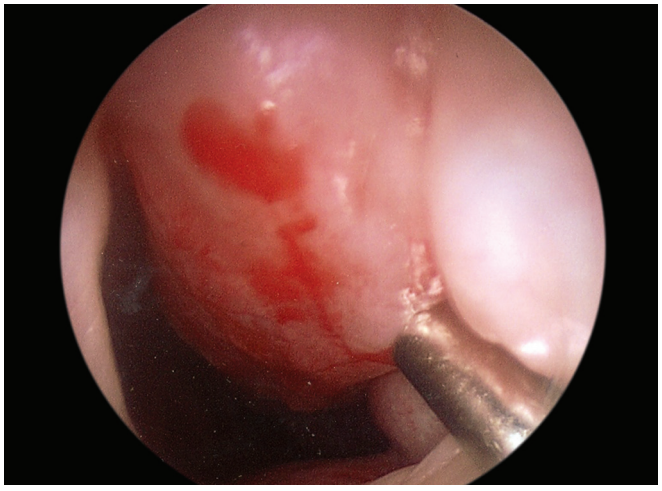


**Fig. 28.5:** Left nasal glioma filling most of left nasal cavity. Presented with unilateral nasal obstruction and feeding difficulty in an infant.

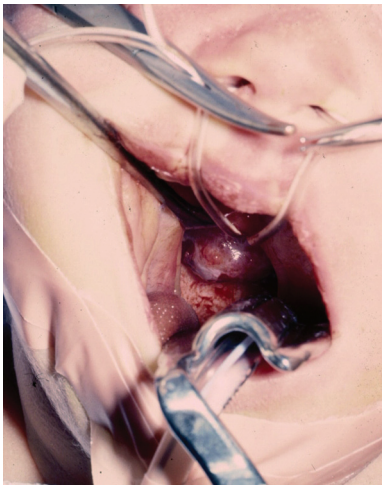


**Fig. 28.6:** Nasopharyngeal teratoma extending into the oropharynx causing complete nasal obstruction and need for urgent management in infancy to re-establish the nasal airway.

In the absence of an intranasal or nasopharyngeal mass, stertor in infants is usually secondary to GERD, until proven otherwise. Nasal endoscopy is often normal in appearance, although the presence of feeds within the nasal cavity can be a clue to GERD causing stertor in the infant.

## Toddlers and Preschool (12–48 Months)

Toddlers and young children will have primarily infectious and inflammatory entities precipitating their visit to the otolaryngologist: enlarged adenoids, viral URI, rhinosinusitis, foreign bodies, polyps, turbinate hypertrophy from allergic rhinitis or smoke exposure, and excoriated anterior nasal septum from epistaxis and nasal digital trauma.

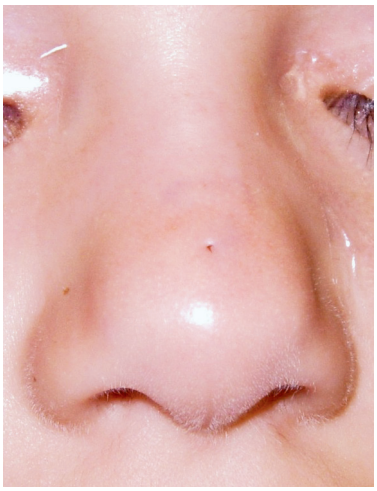
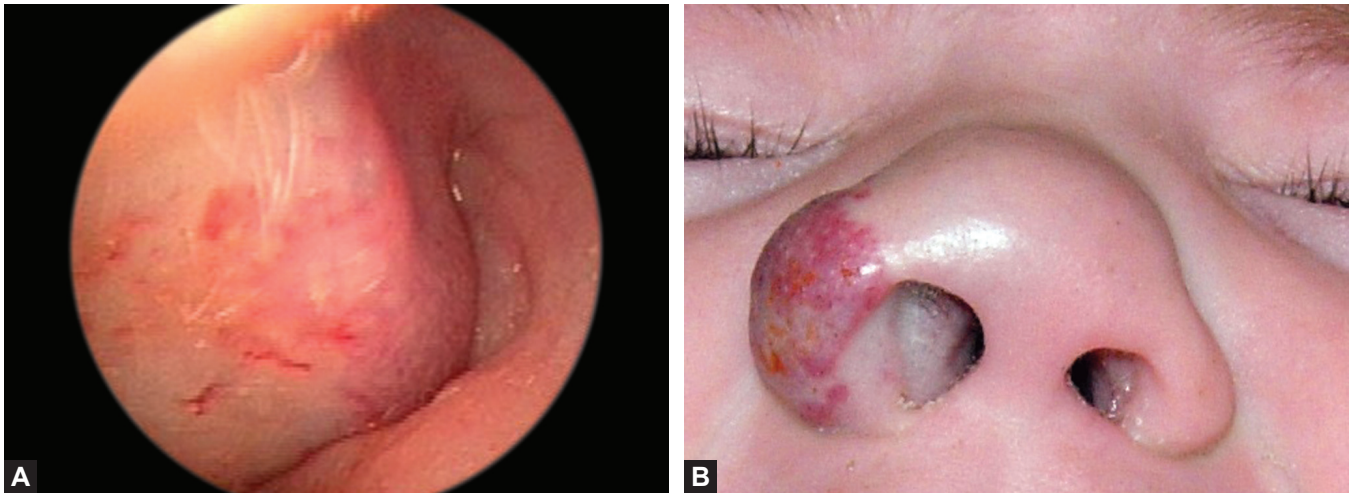


**Fig. 28.7:** Nasal dermoid sinus and cyst with midline nasal dorsal skin pit.

## School Aged Children and Older (> 5 Years)

Pre-teens and teens will also frequently present with infectious and inflammatory conditions as mentioned above. In addition, an intranasal mass associated with epistaxis, especially in males, must be biopsied with a high index of suspicious for juvenile nasopharyngeal angiofibroma. Other nasal and nasopharyngeal tumors can present in this age group as progressive nasal obstruction and discharge. Neoplasms presenting in this anatomic location require a high index of suspicion (Fig. 28.9). Nasal endoscopy and imaging must be obtained to delineate extent of involvement. Trauma can cause nasoseptal deformity, resulting in chronic nasal obstruction as well. This can often be observed with anterior rhinoscopy or nasal endoscopy.

Anterior rhinoscopy can be done on almost any age child with a hand-held otoscope to examine the septum, vestibule, turbinates, and anterior nasal cavity to evaluate for nasal purulence, inflammation, polyps, masses, or deformity. Alternatively, a headlight and nasal speculum can be used, although this can be more difficult than the otoscope in a young, anxious child. Anterior rhinoscopy can be quite informative about the state of the nasal cavity, especially if the otoscope is used to examine the nasal cavity, inferior and middle turbinates and even middle meatus. Examination of the anterior septum and Little's




**Figs. 28.8A and B:** (A) Nasal vestibular hemangioma causing complete unilateral nasal obstruction in infant and feeding difficulties; (B) Nasal alar and vestibular hemangioma causing unilateral nasal obstruction and breathing problems.

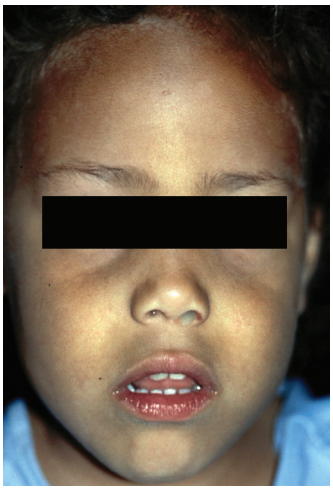


**Fig. 28.9:** Nasopharyngeal rhabdomyosarcoma presenting as unremitting nasal obstruction and discharge.

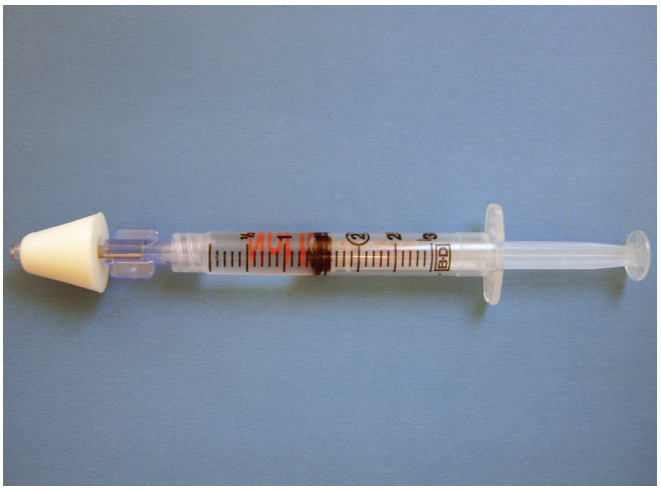


**Fig. 28.10:** The mucosal atomization device (MAD Nasal) can be used to deliver topical anesthetic to the nasal mucosa in any aged child.

area (Kiesselbach's plexus) will reveal a possible source of epistaxis, with prominent vessels, mucosal erosion, and crusting. Identification of prominent vessels in Little's area may target candidate vessels for cauterization, if indicated.

Nasoendoscopy (fiberoptic or rigid telescope) is the next step in the evaluation of the child with rhinologic disease. Examination of the nasal cavity before and after topical decongestion is important to evaluate the condition of the nasal airway before and after is it decongested. Topical anesthesia, such as 4% lidocaine with phenylephrine, applied via atomizer or intranasal mucosal atomization device (MAD Nasal) (Fig. 28.10) is gently sprayed into the nasal cavities. Since the local anesthetic will create anesthesia to the nasal cavity as well as the oropharynx, it may be wise to avoid lidocaine in small infants and patients unable to protect their upper airway from aspiration of secretions.

After topical anesthesia is achieved (usually within minutes), the flexible fiberoptic scope is passed into both nasal cavities, to allow a thorough examination of the nasoseptal mucosa, the turbinates, the nasopharynx, and adenoids. While the flexible fiberoptic scope is versatile and perhaps less uncomfortable for the patient, the rigid rod lens telescope will give the clinician better optics and allow simultaneous instrumentation of the nasal airway, e.g. in suctioning secretions, removing foreign bodies, nasal packing, stents, crusting, examination of postoperative sinus antrostomies, etc. Anatomic abnormalities will be identified that may predispose to infection[42] such as a concha bullosa (will appear as a widened middle turbinate on endoscopy), paradoxical middle turbinate, septal deviation, boggy edematous inferior turbinates (allergic changes), and others; however, the relationship of anatomic abnormalities to pediatric sinusitis is debated.[43]

## Microbiologic Assessment (Cultures)

If the rhinologic examination is being performed for infectious disease of the sinus cavities, middle meatal cultures may be the most accurate for choosing antibiotic therapy, although the reliability in children is debated as well as the most appropriate method.[44–46] A middle meatal culture can be accomplished with a rigid scope and small culture swab (rayon-tipped applicator swab) or endoscopically directed middle meatal aspiration into a culture trap. Nasal cavity cultures may not be as accurate, but can be used to diagnose the etiology of infectious rhinitis in the absence of being able to obtain middle meatal or direct sinus cultures as one could do under anesthesia in the operating room. While the reliability of nasopharyngeal cultures for the diagnosis of acute rhinosinusitis is debated,[46] a recent study shows a high concordance with middle meatal samples in adults.[47] In an immunocompromised child, it is imperative to obtain an accurate sample for culture. Therefore, cultures may have to be obtained from the sinus or middle meatus in the operating room under anesthesia at the time of a sinus endoscopy or other surgical intervention. Cultures should

be sent for bacterial and fungal analysis. If invasive fungal sinusitis is suspected, viable tissue must be sent for frozen section looking for angiogenic spread into the tissues.

## IMAGING

The most common modalities for imaging of pediatric rhinologic disorders are CT and MRI. While plain films have historically been used to evaluate the paranasal sinuses, they have largely been supplanted by CT, which offers far greater detail and precision in evaluating bony anatomy and erosion and soft tissue edema or obstruction. CT scanning with contrast can help to identify abscess collections, while MRI offers superior differentiation of soft tissue masses, inflammatory tissue, and intracranial extension. Depending on the age and temperament of the patient, both may require sedation in order to avoid motion artifact; however, sedation is most frequently needed with MRI scanning due to the small enclosed space and duration and noise of scanning. The primary disadvantage of CT scanning is the exposure to ionizing radiation. This is thought to be a particular concern in children because (1) a child's developing tissues are particularly radiosensitive, (2) the overall radiation risk is cumulative over the child's lifetime, and (3) children have a longer lifetime and life expectancy in which to express the increased risk posed by this radiation exposure.[48] A recent study of the effect of cumulative radiation exposure from CT scanning found significant associations with leukemia and brain tumors in a dose-dependent fashion. Patients who received a cumulative dose of at least 30 mGy had a relative risk of leukemia of 3.2, while in those receiving > 50 mGy the relative risk of developing a brain tumor was 2.8.[49]

### Nasal Obstruction

For imaging studies of congenital causes of nasal obstruction, bony abnormalities such as choanal atresia or pyriform aperture stenosis are best evaluated with a maxillofacial noncontrast CT. In choanal atresia, there is typically narrowing of the posterior nasal cavity with medialization of the lateral nasal wall and thickening of the vomer (Fig. 28.11). The choanal airspace usually measures < 34 mm. In the case of congenital nasal pyriform aperture stenosis, a width of < 11 mm at the narrowest point of the pyriform aperture is diagnostic (Fig. 28.12).[50] Neonatal soft tissue masses such as an encephalocele, dermoid, or glioma are best evaluated with MRI that can help elucidate any intracranial extension. In extensive nasal polyposis, as seen in CF, the CT appearance is typical for demineralization of the medial wall of the maxillary sinuses and ethmoid septations and widening of the nasal cavities (Fig. 28.13).

### Bacterial Rhinosinusitis

Imaging studies including plain films, CT, and MRI are generally not recommended in children for routine evaluation of sinusitis due to their lack of specificity. More than 50% of children with a viral URI demonstrated evidence of maxillary sinus inflammation on plain radiographs, and

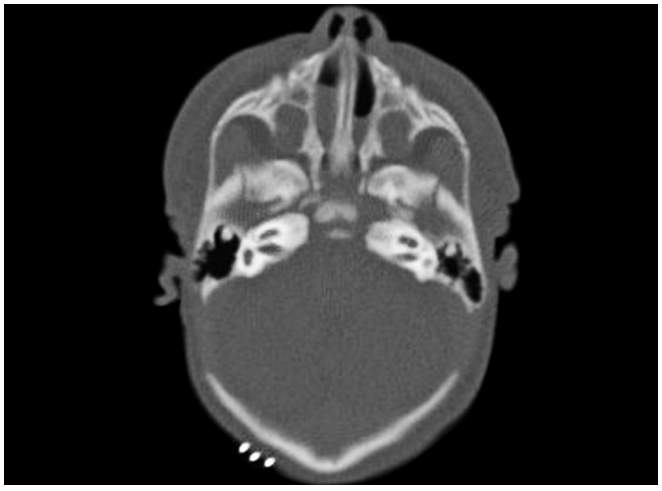


**Fig. 28.11:** Axial CT scan demonstrating bilateral choanal atresia.

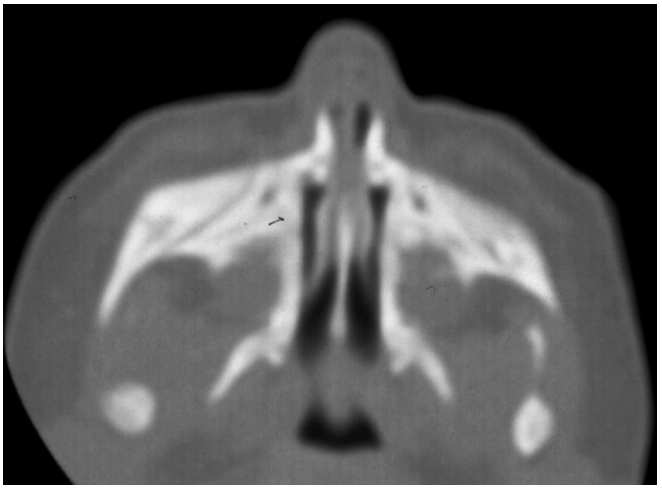


**Fig. 28.12:** Axial CT scan demonstrating pyriform aperture stenosis.

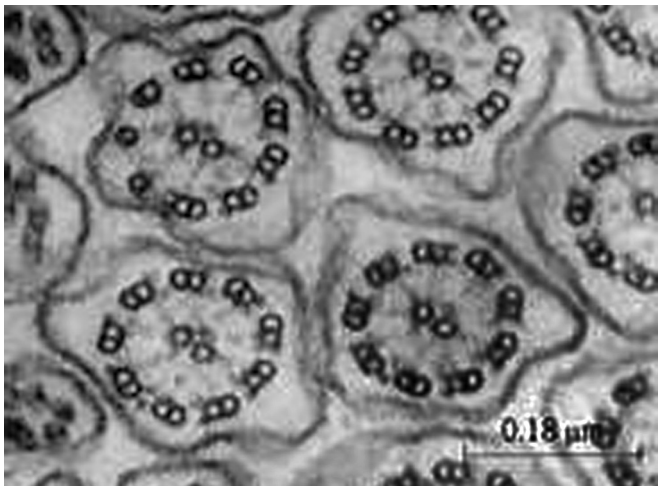



**Fig. 28.13:** The proper ciliary architecture ("nine plus two" central and outer microtubules) shown here on electron microscopic ciliary cross-section.

sinus CTs and MRIs are often abnormal even in healthy children or those with uncomplicated viral URIs.[51–55] Plain radiographs in particular are inadequate for evaluating pediatric sinuses, showing poor correlation with coronal CT scans.[56,57] In 2012, a panel of sinus experts produced a consensus statement on the appropriate use of CT scanning for paranasal sinus disease. This included the recommendation that CT imaging is indicated only when medical management has failed to control the symptoms of sinusitis, for suspected tumor, complications of sinusitis, and prior to sinus surgery. They also stated that pediatric CT imaging is limited by radiation safety concerns and possible need for sedation.[37,58] MRI was the recommended imaging modality for the assessment of immunocompromised patients with suspected invasive fungal sinusitis. CT imaging with contrast has been recommended for evaluating patients likely to have orbital complications of acute rhinosinusitis such as those with proptosis, retro-orbital pain with eye movement, or gaze restriction. MRI is considered the modality of choice for evaluating for intracranial extension of infection.[30]

## MEDICAL ANCILLARY WORKUP

### Immune Workup

Immunodeficiencies can predispose children to an increased risk for rhinosinusitis. While there is conflicting evidence for this in the literature,[59] an immunologic workup should be considered in a child with poor response to aggressive medical therapy or surgical management of their sinus disease. Studies to consider include (a) complete blood cell count (CBC with differential), (b) total immunoglobulin A, G, M, E levels and IgG I-4 subclass levels, and (c) antibody levels to rubella, conjugate *Haemophilus influenzae* type b and pneumococcal polysaccharide antigens. Primary immunodeficiencies diagnosed among patients with chronic/recurrent rhinosinusitis[60] include common variable immunodeficiency,[61] IgA deficiency and IgG subclasses deficiencies (IgG1, 2, 3, 4) and impaired polysaccharide responsiveness (partial antibody deficiency). In patients with humoral immunodeficiencies, sinusitis can be identified in as many as 60%.[62] Immunosuppressed children undergoing chemotherapy will be at greater risk for invasive fungal sinusitis and must be aggressively managed with a high level of suspicion and early biopsy for fungal organisms.[63] Children with absolute neutrophils count < 600 are especially at high risk for invasive fungal sinusitis.[63] Urgent tissue biopsy is indicated in these children and if positive for invasive fungal disease, debridement must be performed emergently under anesthesia, with plans for frequent surveillance and debridement until the disease is controlled.

### Allergy Workup

It can be approached by either measurement of serum levels of total and specific IgE for inhalant allergens, molds and food allergens or by skin testing. Testing very young children with skin prick testing, especially for food allergies, may be less accurate than in adults and older children.[64]

Hyper IgE syndrome (Job's syndrome) is also associated with recurrent sinopulmonary infections, so testing for total IgE levels should be performed when this is suspected, looking for marked elevations in serum IgE of > 2,000 IU/mL.[65] The role of GERD in sinusitis continues to be investigated and debated.[66–69] However, the child with chronic sinusitis who is refractory to medical or surgical management should be considered for a thorough investigation of GERD and a trial of anti-GERD management. An empiric trial of a proton-pump inhibitor may be advised. While each center may approach the child with suspected GERD and sinusitis differently, interventions such as esophagogastroduodenal endoscopy with biopsies for inflammation and eosinophilic infiltrate, 24 h pH monitoring, and esophageal manometry should be considered.

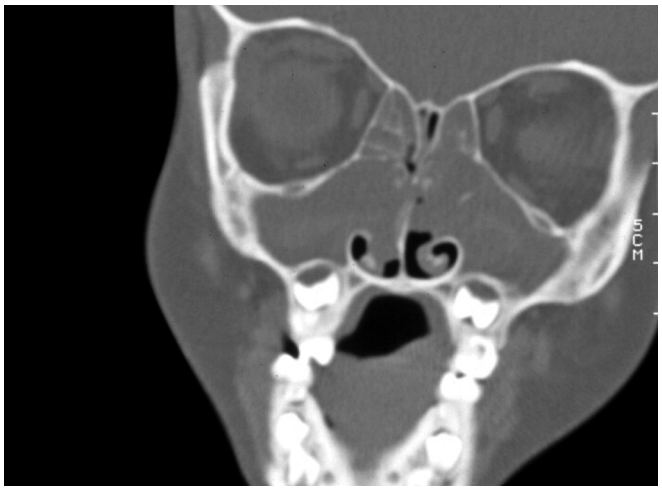


**Fig. 28.14:** Coronal CT in cystic fibrosis patient with classic findings of extensive nasal polyposis.

Ciliary biopsies are a part of the workup of a child with unremitting sinus, ear, and pulmonary disease to evaluate for primary ciliary dyskinesia or Kartagener's syndrome. A nasal ciliary biopsy can be performed in the clinic setting under local anesthesia, but is often difficult to obtain a suitable ciliated epithelial sample in the nasal passage of a child with chronic rhinosinusitis with the associated loss of ciliated epithelium. Obtaining a sample from high in the nasal cavity would be the most likely to yield a good sample. More often, a good, uncrushed sample of ciliated epithelium can be obtained from the bronchus with a bronchial brush biopsy at the time of rigid or flexible bronchoscopy, avoiding the crush artifact from biopsy forceps and obtaining a sample from lower in the respiratory tract where the cells may remain ciliated. The brush is then placed whole into 3% glutaraldehyde (electron microscopy fixative) for fixation and examination by electron microscopy (Fig. 28.14). Diagnosis will be made if the expected 9 + 2 microtubule architecture is altered.

Sweat chloride testing should be obtained in a child with chronic rhinosinusitis, especially with polypoid disease and/or failure to thrive. With a carrier rate of up to 1 in 25 among people with northern European ancestry,[70] CF in its classic form and atypical CF from rare mutations will present to the otolaryngologists' clinic. CF arises from mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. While most children are now diagnosed early in life, some CF genetic mutations produce an atypical CF picture and therefore are not discovered early in life, especially if the mutation primarily causes sinus disease and less fulminant pulmonary and digestive disorders. Sweat chloride testing is considered normal if ≤ 39 mmol/L, intermediate if 40–59 mmol/L, and abnormal ≥ 60 mmol/L, regardless of age. When a borderline sweat chloride test is present, full genetic testing can be obtained for the numerous mutations now recognized in CF.[71] Individuals with sweat chloride values in the intermediate range (30–59 mmol/L for infants under age 6 months; 40–59 mmol/L for older individuals) should undergo extensive CFTR mutation analysis (i.e. expanded panel of CFTR mutations, evaluation for deletions, or gene sequencing). In the presence of 2 CF-causing mutations, a diagnosis of CF can be made. Individuals with no or 1 CF-causing mutation and clinical findings suggestive of CFTR dysfunction (i.e. male infertility, bronchiectasis, or chronic pancreatitis) may be diagnosed with a CFTR-related disorder, depending on their clinical picture or family history, and are at risk for CF. Borderline abnormal sweat chloride testing results should be repeated in infants by age 2–6 months and immediately in older individuals. If sweat chloride values remain in the intermediate range on repeat testing, then further assessment should be performed at a CF care center that can provide basic and ancillary testing to clarify the diagnosis. In atypical CF, the relationship between genotype and phenotype (i.e. sinus, pancreatic, and pulmonary disease) is weak, so close follow-up is important. In the operating room at the time of sinus surgery, identification of significant nasal polyps and the pathognomonic characteristic purulence in the sinus cavities or lower airways seen with CF (extremely mucoid and pasty green/yellow), should alert the surgeon to consider the diagnosis of atypical CF in an older child by sweat chloride and/or genetic mutation testing. Any cultures collected in a CF or suspected CF child should be sent to the microbiology laboratory for special CF bacterial cultures and sensitivities.

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CHAPTER

# 29

# Pathophysiology of Pediatric Rhinosinusitis

***Scott C Manning***

## DEFINITIONS

Young children can suffer six to eight episodes of viral upper respiratory infection per year and up to 5% of these episodes are estimated to become superinfected with bacteria leading to acute rhinosinusitis or contributing to chronic rhinosinusitis (CRS) (*see* Table 29.1 for a list of abbreviations used in this chapter). Pediatric CRS is usually defined as symptoms persisting >12 weeks including some type of congestion and/or rhinorrhea and with endoscopic and/or radiographic evidence of sinus inflammation.[1] Unfortunately, that definition is vague and overlaps with common predisposing conditions such as recurrent viral infection and allergy. Also, chronic unremitting congestion in children implies some type of fixed upper airway anatomic obstruction such as adenoidal or inferior turbinate hypertrophy that may or may not be associated with sinus inflammation. Also, chronic headache, an increasingly common symptom in older children, may be attributed clinically to sinusitis, but more often is a sign of developing migraine or other primary headache diagnosis. From a practical standpoint, a better definition of pediatric CRS is probably recurring symptoms which may include congestion, rhinorrhea, cough and low energy with radiographic or endoscopic evidence of sinus inflammation occurring more than four times in 1 year and lasting more than the expected 10-day course of a viral illness alone.

In an attempt to better understand and treat CRS in adults, researchers are increasingly attempting to categorize patients into "phenotypes"—observed properties resulting from the interaction of genotype with environmental factors and "endo types"—discrete pathogenic pathways often characterized by distinct inflammatory cellular and chemical profiles.[2] The strongest subtyping in adults is between CRS with and without nasal polyps

**Table 29.1:** Abbreviations

| | |
|---|---|
| CRS | Chronic rhinosinusitis |
| CRSwNP | Chronic rhinosinusitis with nasal polyps |
| CRSsNP | Chronic rhinosinusitis without nasal polyps |
| Th 1 | T helper cell 1 |
| Th 2 | T helper cell 2 |
| Th0 | T helper naive |
| CF | Cystic fibrosis |
| CFTR | Cystic fibrosis transmembrane conductance regulator gene |
| AERD | Aspirin-exacerbated respiratory disease |
| AR | Allergic rhinitis |
| AFS | Allergic fungal sinusitis |
| RNA | Ribonucleic acid |
| IL | Interleukin |
| SVCs | Small colony variants |
| STAT3 | Signal transducer and activator of transcription 3 |
| NO | Nitric oxide |
| PCD | Primary ciliary dyskinesia |
| MUC5ac | gene encoding protein mucin 5ac. |
| MHC 1 | Major histocompatibility complex 1 |
| FOX P3 | Forkhead box P3 |
| TGF | Transforming growth factor |
| T-bet | T-box transcription factor |

(CRSwNPs and CRSsNPs), with the former demonstrating a pronounced Th2 skewing (at least in Western patients). Nasal polyps are relatively unusual in the pediatric population and should prompt an immediate evaluation for cystic fibrosis (CF). Interestingly, CF is a complex of diseases in which the causes are known deletions involving the CF transmembrane conductance regulator gene (CFTR). The endo type usually involves primarily an intense chronic Th1 inflammatory response but the CRS phenotypes are highly variable ranging from debilitating recurrent polyposis to few upper respiratory symptoms. The variability of sinonasal symptoms in CF patients illustrates the complex relationship between host and environmental factors with CRS.

Arguably the most relevant subtyping in pediatrics would be CRS with tissue eosinophilia (Th2) versus without (Th1). The former is more often associated with reactive airways disease or asthma and CRS is more clinically important when it triggers or aggravates underlying pulmonary disease. Subcategories in the Th2 category can include allergic rhinitis (AR), asthma-associated CRS, and aspirin-exacerbated respiratory disease (AERD). Examples of Th1 skewing could be CF, and physiologic (immune maturation) or primary immunodeficiency. Better characterization of CRS subtypes will presumably lead to more effective individual treatment regimens.

## THE HYGIENE HYPOTHESIS

The critical period of immune system development is infancy (and prenatal). Antigens interact with antigen processing cells including epithelial dendritic cells and macrophages that in turn release cytokines and other factors that influence Th0 cells (T helper naïve) to differentiate to Th1, Th2, or Th13. Also, pathogens are potent stimulants of the innate immune system's toll-like receptor system (TLR) that recognizes their highly conserved surface pathogen-associated molecular patterns (PAMPs). One basis of the hygiene hypothesis is the idea that TLRs need to be stimulated by certain PAMPs early in life in order to skew Th0 populations away from their in-utero Th2 bias toward Th1 in the adaptive immune system.

Epigenetics refers to the influence of environmental factors on gene expression usually via functional modifications such as DNA methylation and histone modification. These environmentally determined modifications may be permanent for the life of the individual and may even cross over into subsequent generations. Even dietary factors and the gut biome (folic acid, Vitamin B12) can influence epigenetic modifications. The hygiene hypothesis supports the notion that modern living is making the world's current and subsequent generations more "allergic" (Th2 skewed).

While CRS is hard to define, many researchers feel that the incidence is increasing at least in the developed world. The hygiene hypothesis suggests that the pattern of early childhood pathogen exposure could skew the individual to a more inflammatory response and a higher incidence of allergy-type diseases. DP Strachan in Great Britain in 1989 noted that AR and eczema were inversely related to the number of older siblings in the household.[3] He hypothesized that lack of early exposure to certain pathogens could skew the child's immune responses toward Th2 during the early critical period of immunologic maturation. Other researchers have demonstrated increased incidence of AR with smaller family size, especially in boys, and a decreased incidence of asthma associated with a greater number of younger siblings. Additional studies have demonstrated a decreased incidence of AR in children growing up on farms, possibly due to the role of lipopolysaccharides from gram-negative bacteria exposure on immune system development. Also in Great Britain, studies have shown that early exposure to antibiotics, especially cephalosporins and macrolides, can increase the odds of developing asthma, possibly due in parts to alterations in the gut biome and resultant immunoregulatory effects.

The strongest link between an individual pathogen and subsequent Th2 skewing comes from studies demonstrating significantly less allergy in hepatitis A seropositive patients. *Helicobacter pylori* gut colonization has also been linked to decreased incidence of asthma although studies are mixed. Other aspects of a "western" lifestyle with a possible link to Th2 skewing include early introduction of food antigens, high fat diets and vitamin D deficiency (vitamin D inhibits T cell proliferation and induces T regulatory cell hyporesponsiveness).[4]

"Atopic march" refers to the common clinical observation of onset of dermatitis before age 2, then reactive airways disease/asthma shortly thereafter, then AR diagnosed by the early 20s (and increasingly, gastrointestinal inflammation such as gastroesophageal reflux or eosinophilic esophagitis). These patients are increasingly viewed as the result of environmental factors early in life in a genetically predisposed individual causing permanent epigenetic upregulation of the Th2 arm of adaptive immunity.[5]

## UNIFIED AIRWAYS

Asthma has long been associated with CRS both in pediatric patients with and without AR (although allergy testing may be insensitive in young children) and those patients should be considered to be potentially inflamed along the entire respiratory tract.[6] Children with documented AR are likely to demonstrate increased bronchial responsiveness to antigen or irritant stimulation. In one recent prospective pediatric study, chronic and recurrent rhinosinusitis was more prevalent in older children and more likely to be associated with AR, atopy, and asthma versus children with acute rhinosinusitis.[7] Both asthma and bronchiectasis have been found to be associated with higher Lund-Mackay computed tomography sinus scores in adult patients with CRS.[8] And in a recent retrospective study of over 4000 children with a diagnosis of CRS followed in a tertiary center allergy practice, 18% had a diagnosis of asthma.[9]

## ALLERGY

While allergy in detail is the subject of another chapter, the topic has obvious relevance to any discussion of CRS. For one thing, the standard definitions of CRS as symptoms including congestion and rhinorrhea lasting at least 6 months could be entirely caused by AR. In fact, many patients presenting with a diagnosis of CRS have clear sinuses on imaging and not surprisingly derive no benefit from systemic antimicrobial therapy. Studies are mixed regarding causative links between AR and CRS, but there is definitely an association especially in pediatric patients with asthma. One study found that 27% of pediatric patients average age 8 with CRS had AR with skin testing.[9] In another pediatric study, pediatric CRS as opposed to acute rhinosinusitis associated with more AR and adenoidal hypertrophy.[10] And prospective randomized studies of children with CRS have found significant benefits with corticosteroid therapy versus antibiotics alone, but corticosteroids have a generalized immunoregulatory effect on atopic and nonatopic inflammation alike.[11]

From a pathophysiology standpoint, AR could contribute to defects in epithelial barrier defense allowing for more antigen presentation and potentially for easier development of microbial biofilm. AR also has systemic immunoregulatory effects. In adult studies, sensitivity to aeroallergens in general, dust mite allergy in particular and elevated total IgE are all independently associated with CRS, particularly in patients with nasal polyps.[12]

### Localized Allergy

The true prevalence of AR in children with CRS may be significantly underestimated in the current literature due to the relative lack of sensitivity of standard testing in younger patients. Recently the concept of localized mucosal allergy has been introduced, defined as evidence of IgE mediated inflammatory response secondary to nasal antigen challenge.[13] The gold standard in defining this entity is mucosal biopsy after antigen challenge, but pre- and post-challenge rhinometry may be a suitable surrogate for routine clinical studies. Using that technique, a significant percentage of asthmatic CRS patients with negative skin testing are "allergic" defined as reacting to nasal challenge.[14]

### Allergic Fungal Sinusitis

Allergic fungal sinusitis (AFS) is worth mentioning as an extreme example of tissue Th2 response with heavy eosinophilic recruitment to surface epithelium, mucosal sloughing (loss of barrier defense), and buildup of central sinus concretions of eosinophils, Charcot-Leyden crystals (major basic protein) and scattered branching fungal forms all similar to asthmatic plugs (Fig. 29.1). The etiology of the classic form is believed to involve allergic reaction to antigenic fungi usually in the class of dematiaceous (Bipolaris, Alternaria, Exserohilum) or *Aspergillus* species.

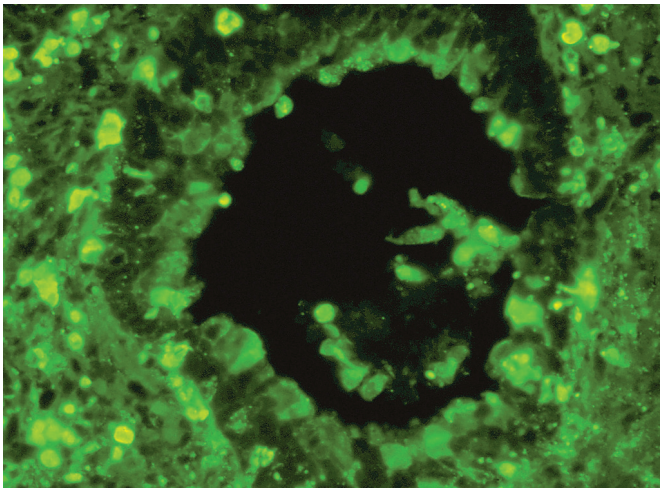


**Fig. 29.1:** Immunohistochemical stain for major basic protein in a mucosal sample from a 12-year-old patient with allergic fungal sinusitis (bipolaris culture). Eosinophils are seen recruited to the mucosal and even sloughing into the mucosal lumen. This illustrates the barrier hypothesis with loss of epithelial integrity potentially leading to a self-perpetuating cycle of further antigen contact, Th2 skewing and upregulated inflammation. (Original photo).

That form of AFS is most commonly located along the 30th parallel of latitude where those types of fungal spores are more commonly present in inspired air. Some authors believe that a phenotypically milder form may be common in all latitudes but prospective studies have not found benefit for treatment for CRS symptoms with systemic or topically antifungal medication.

## Biome

Most CRS researchers no longer believe that microbial infection is the primary cause of CRS and treatment studies generally show no benefit for systemic antibiotics. However, evidence is mounting that patterns of host microbial colonization do indeed have significant effects on host local and systemic immune defense and hyperinflammatory states. Recent advances such as microchip sequencing of 16S ribosomal RNA has led to the realization that all body surfaces are colonized with bacteria that exist in a state of equilibrium via mutual interference secondary to competition for nutrients, blockage of adherence sites, release of antagonistic substances, and many more mechanisms.

As mentioned above, changes in the gut biome (easily modified by antibiotic use and diet) can contribute to Th2 skewing and an increased systemic inflammatory state. Thus, indiscriminate use of antibiotics in early childhood and the practice of routinely using antibiotics in animal feeds may contribute to the perceived increase in CRS in developed societies.

The nasal biome in healthy children usually consists of *Staphylococcus aureus*, *Staphylococcus epidermidis*, alpha and nonalpha hemolytic streptococci, aerobic diphtheroids and anaerobes. Potential pathogens not usually found in healthy individuals include *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Some studies in children have shown more diversity and more bacterial interference in healthy controls, and less diversity and more colonization with bacterial pathogens in sinusitis patients.[15] In another recent pediatric study, adenoid tissue was found to have its own biome including the usual pathogens associated with otitis media (the "pathogen reservoir hypothesis") with evidence of ecologic equilibrium via bacterial interference.[16]

In recent studies of the adult sinus biome, healthy patients showed increased Actinobacteria (*Propionibacterium* species and *Corynebacterium* species) and less staphylococcal species, while CRS patients showed more *S. aureus* and less *S. epidermidis*.[17] While studies of the sinonasal biome are new and results vary probably in part due to differing molecular biological techniques, some interesting conclusions have come to the surface. Healthy sinuses are not sterile, systemic antibiotics (and potentially vaccines) alter the natural ecology and potentially reduce bacterial interference allowing for growth of pathogens and *S. epidermidis* appears to be a competitive antagonist to *S. aureus*. Interestingly, *S. pneumoniae* is felt to be a significant competitive inhibitor of *S. aureus* and the use of polyvalent streptococcal vaccines may have contributed to a possible rise in carrier state frequency of pathogenic staphylococcal species (another hygiene hypothesis example).

Unfortunately, the sinonasal biome story is not as simple as good commensals versus bad pathogens. One recent adult study showed fairly similar bacterial profiles in CRS patients and controls but CRS patients demonstrated increased IL-4, IL-5, IL-8, IL-13, tissue eosinophils and basophils and increased peripheral leukocyte antigen response. Thus CRS patients appear to have a hyperinflammatory response to normal commensals as well as to pathogens. The authors conclude that the microbiome can be thought of as a spectrum referred to as "mutualism" of commensals with beneficial host-bacterial interactions (symbionts) interacting with pathogens with the potential for harming the host. The underlying host level of immune response helps keep the balance but too strong a response (Th2 skewing for example) can lead to inappropriate inflammation and host damage (barrier defense).[18]

## Biofilms

Bacteria in nature usually exist as structured colonies in polymeric matrices fixed to the underlying surface. Epithelial damage and reduced innate immunity presumably can promote biofilm formation and studies have shown a 30–70% incidence of microbial sinus biofilm in patients with CRS. Bacteria in biofilm colonies can evade cellular and complement-mediated cytotoxicity and they have a reduced rate of metabolic activity conferring relative resistance to antibiotics. Biofilm presumably can result in states of constant reinfection as hibernating bacteria re-emerge in a planktonic form and shed. Also, biofilms contribute to the cycle of chronic inflammation partly via the phenomenon of "frustrated phagocytosis" where neutrophils degranulate outside the biofilm structure leading to further surrounding epithelial damage.[12] Microbes that have been demonstrated to cause biofilm in CRS patients include *S. aureus*, *Pseudomonas aeruginosa*,

*H. influenzae* and Alternaria. Biofilm no doubt explains some of the failure of antibiotic therapy for CRS and also the chronicity of the condition.

## MICROCOLONY STAPHYLOCOCCUS/ INTRACELLULAR—INTRAMUCOSAL INFECTION

Bacteria, like all organisms, respond to environmental pressure and one response to antimicrobial therapy pressure can be to undergo transition to a more facultative state with subsequent intramucosal or even intracellular transition (seeking oxidative metabolism). These are presumably the in vivo equivalents of the small colony variants (SCVs) culture from patients undergoing intense antibiotic pressure including those with CF, osteomyelitis, or surgical implant infection. Staphylococcal organisms are the most commonly implicated and studies in adult CRS patients have shown evidence for intramucosal staphylococcal species derived from surface bacteria.[19] Intramucosal *Staphylococcus* has been associated with surface biofilm and may be one more mechanism explaining chronicity and resistance to therapy with CRS[20] (Fig. 29.2).

### Superantigens and *Staphylococcus*

Superantigens are proteins that bypass normal antigen processing and bind directly to the beta-chain of T-cell receptors leading to nonspecific activation of large numbers of T-cells with an immediate release of inflammatory cytokines. The superantigen role for CRS was first proposed for the antigenic fungi (dematiaceous) in AFS, but many bacteria, especially *S. aureus*, are capable of acting as superantigens. The dermatologists implicated staphylococcal species superantigens in the pathogenesis of eczema long ago and otolaryngologists have adapted the strategy of topical antistaphylococcal therapy (mupirocin) for the treatment of CRS.

IgE antibodies to staphylococcal enterotoxins have been identified in up to 28% of nasal polyp adult patients overall and up to 54% of CRS patients with polyps and asthma. Presumably a vicious cycle of more cytokine release, more epithelial barrier degradation, more antigen contact, and more Th2 skewing plays an important role in many patients with CRS. Staphylococcal species colonize up to 30% of patients with noneosinophilic rhinosinusitis, 70% of patients with nasal polyps, and 90% of patients with AERD. The presence of staphylococcal organisms predicts worse outcomes for patients with CRS.[12,21]

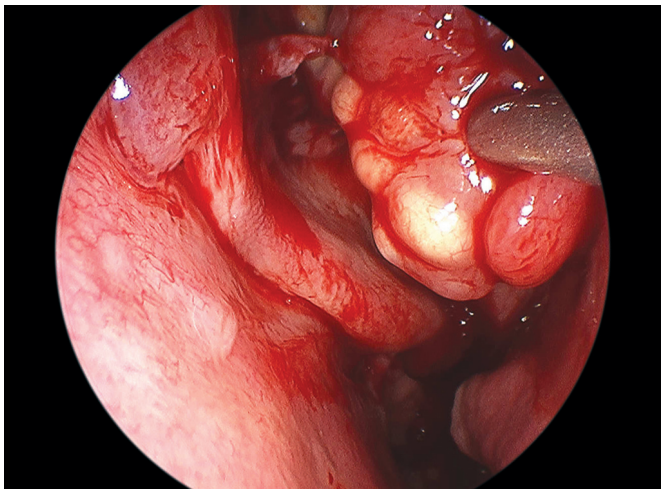


**Fig. 29.2:** A 16-year-old male with pronounced but focal unilateral ethmoid polyposis. After initially poly debridement, intramucosal abscesses became apparent within the left ethmoid. Culture of an abscess open after excision yielded a sensitive *Staphylococcus aureus*.

## BARRIER DEFENSE

The immune barrier hypothesis maintains that epithelial compromise from whatever cause leads to a cycle of microbiological colonization, further epithelial degradation and a self-amplifying cycle of dysfunction immunological response. Epithelial defects can lead to dysfunction of the membrane bound pattern recognition receptors including the toll-like receptors that in turn can cause problems with production of the S100 antimicrobial proteins including STAT3 (signal transducer and activator of transcription 3) a transcription mediator for the IL-6 family of cytokines important in host defense. Establishment of staphylococcal colonization, biofilm, and intramucosal infection can lead to further immune dysfunction as previously mentioned.[22] Eosinophilic inflammation in particular with release of major basic and eosinophilic cationic protein can promote epithelial sloughing. Indoor and outdoor air pollution, cigarette smoke exposure and chemical exposure can also contribute to break down of epithelial integrity.

## PRIMARY IMMUNODEFICIENCY

CRS is probably the most common symptom of primary immunodeficiency in any age group. Immunodeficiency should be suspected when confronted with unusual organisms, context, persistence, or recurrence of disease.

When in doubt, a full immunologic evaluation is appropriate, ideally with the help of an immunologist. For B-cell problems, advances in administration of gamma globulin are broadening the scope of effective therapeutic options especially for CRS.

All children experience a "physiologic" immunodeficiency of childhood in that the immune system develops and does not reach adult levels of function until around age 12. Especially under the age of 7, children are prone to contract viral upper respiratory illness, as much as six to eight times per year, a primary trigger or aggravator of acute or CRS. And children with clinical Th2 skewing such as asthmatics appear often to be slower to develop normal immunoresponse to bacterial pathogens (vaccine nonresponder state). This fact may explain the clinical observation that some asthmatic children seem to rapidly develop purulent rhinorrhea, cough, and asthma exacerbation at the first hint of a viral upper respiratory infection. Fortunately, the majority of even asthmatic children experience normal, though possibly delayed, immune maturation. The current terminology for vaccine underresponse is "specific antibody deficiency to unconjugated pneumococcal vaccine or SAD" and it is usually transient when diagnosed in childhood.[23]

Specific antibody production deficiency cannot reliably be diagnosed under age 2 and the most common age for diagnosing common variable immunodeficiency is age 25. But most of those patients with have a history of unusually persistent and severe respiratory tract infection as children so presumably the condition is underdiagnosed in the pediatric age group. Interestingly, common variable immunodeficiency is often associated with an increased likelihood of allergic disease.

IgA deficiency is common in young childhood but usually transient. X-linked Bruton's agammaglobulinemia presents as refractory bacterial respiratory infections in infancy and young childhood. T-cell problems including severe combined immunodeficiency can present as *Pneumocystis carinii* infection. Neisseria infection should prompt consideration for complement deficiency. Chronic granulomatous infection can present as chronic lung disease, invasive fungal infection, and/or colitis and can be diagnosed via the oxidative burst test.

Although beyond the scope of this chapter, acquired immunodeficiency can contribute to CRS. In a pediatric tertiary care center, children immunosuppressed for transplant or for treatment of lymphoreticular malignancies are at risk for bacterial CRS with the usual organisms or for invasive fungal CRS (Fig. 29.3).

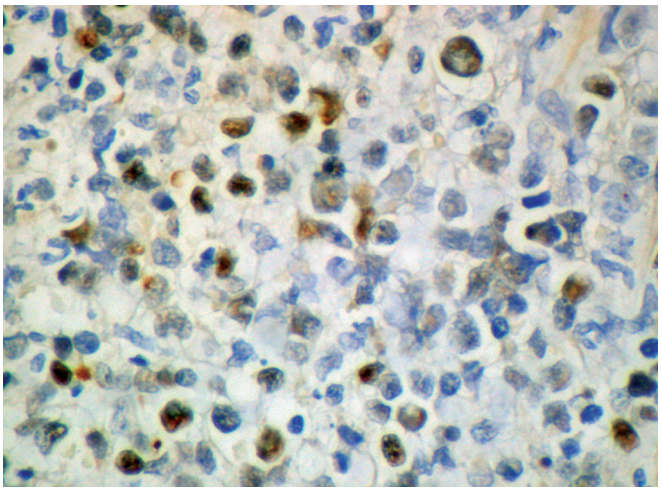


**Fig. 29.3:** A 8-year-old boy on chronic chemotherapy for hemophagocytic lymphohistiocytosis with debilitating sinopulmonary infections refractory to medical therapy. A sinus mucosal sample shows strong intracellular staining for EBER (Epstein–Barr virus RNA transcript). Presumably, viral illness in an immunocompromised host can significantly compromise epithelial immune defense.

## NITRIC OXIDE AND PRIMARY CILIARY DYSKINESIA

Nitric oxide (NO) is involved in many aspects of inflammation and contributes to immune defense, ciliary function, and overall airway ventilation-perfusion matching. A principal source of NO for the upper airways is the sinus epithelium and reduced levels of NO have been recorded in patients with rhinosinusitis, polyposis, CF, and asthma.[24] Reduced levels of NO are often associated in general with eosinophilic inflammation.

Primary ciliary dyskinesia (PCD) is associated with particularly low levels of NO and in fact, very low NO levels combined with chronic lung disease, chronic middle ear effusion, and sinusitis appears to be very specific for PCD, useful when situs inversus (Kartagener's syndrome) is not present (Alsaadi MM, Habib SS). Also, many children with an ultimate diagnosis of PCD have a history of neonatal respiratory distress, sometimes requiring intubation at or shortly after birth. Definitive diagnosis is made via ciliary biopsy with electron microscopy of ciliary ultrastructure. Most disease associated mutations involve the dynein axonemal heavy chain 5 or intermediate chain 1 and clinical molecular testing is becoming more available.[25] PCD is an example of a severe innate barrier immune defense problem that can possibly alter adaptive immunity by increasing antigen presentation early in life.

## Histology

The effects of chronic inflammation over time in CRS lead in general to histologic changes including goblet cell and mucous glandular hypertrophy, chronic inflammatory cell infiltrates, epithelial sloughing and bony osteitis. Studies comparing routine CRS surgical specimens in children versus adults tend to show a high density of submucosal lymphocytes but less percentage of eosinophils, and less basement membrane and submucosal gland hypertrophy.[26] A recent study of pediatric patients with polyps (including allergic fungal sinusitis) versus controls showed an increased mucosal dendritic cell infiltrate in the polyp patients which was associated with vitamin D3 deficiency (T regulatory cell effects).[27] The differences between pediatric and adult CRS histology may reflect differing inflammatory mechanisms or may represent the results of similar inflammatory pathways over greater periods of time. CF patients are characterized by very prominent mucosal goblet cell and submucosal gland hyperplasia with increased glandular MUC5AC (mucin—5a) expression.[28]

## GENES AND GENE EXPRESSION

The classic genetic link to pediatric CRS would have to be the CFTR deletions causing CF. But the literature is expanding rapidly with new information about links between CRS patients and genes involved in pathways of inflammation and immune regulation. The technology for doing genome wide studies is advancing rapidly while the cost, especially using pooled samples from case and control populations, is dropping. Adult CRS pooled sample studies have shown a genetic basis for low circulation CD8 lymphocytes leading to speculation about a possible syndrome-like condition involving major histocompatibility complex 1 (MHC1) deficiency.[29] Other genetic studies of adult CRSwNP patients have shown less FOX P3 (Forkhead Box P3) mRNA and TGF-beta 1 protein (a suppressive cytokine) but higher expression of T-bet (T-Box transcription factor) and IL-5, and IL-13 mRNA compared with controls.[30] Studies of adults with noneosinophilic CRS have found other gene expression patterns with upregulation of innate inflammatory genes for IL-6 and IL-8.[31]

## COMORBID STATES

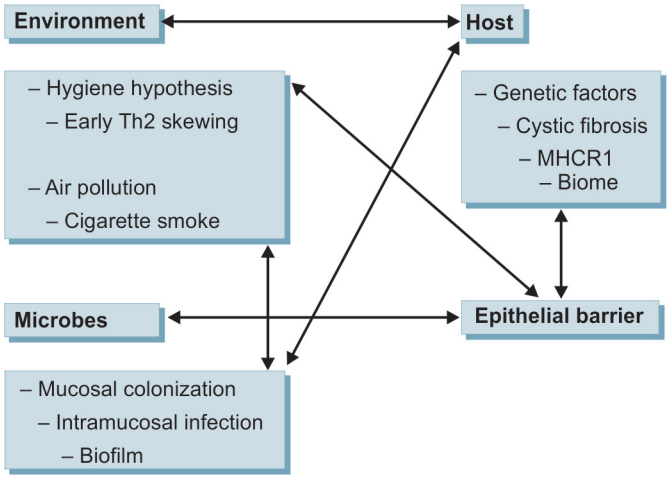
Pediatric CRS is commonly associated with many other conditions, but to date, few causal links have been determined in the associations. The most common comorbidities for younger CRS patients are viral illness, eczema, reactive airways disease, adenoiditis, otitis, and gastroesophageal reflux. For older CRS children, common comorbidities include allergic rhinitis, asthma, eosinophilic esophagitis, and migraine headache. Adenoiditis presumably has some causality based upon studies showing outcome improvement with adenoidectomy and some recent studies suggest a causal link between AR and CRS in adults. In one retrospective pediatric study, gastroesophageal reflux was associated with CRS, asthma, laryngitis, and bronchiectasis, but overall, outcome studies on reflux treatment and CRS have not shown consistent benefit to date (Nation J). A common denominator for many of the above comorbid states is Th2 skewing with tissue eosinophilia (CRS, asthma, eczema, esophagitis, AR).

## CONCLUSION

Long gone are the days when CRS was assumed to be the result of specific microbial infection. Microbes appear to play an important role but mainly by inciting chronic inflammation via colonization of an individual with an inflammatory diathesis as a result of complex genome-environmental interaction potentially starting in utero. CRS is a complicated mixture of conditions with differing symptom expression (phenotype) and mucosal and systemic inflammatory-immune system dysregulation (endo type). The effects of modern living seem to be creating an increasing number of Th2 skewed individuals more prone to be over-reactive to pathogens and allergens (hygiene hypothesis). Staphylococcal bacteria established as mucosal colonies, biofilm, and/or intramucosal infection can incite a more rapid, severe and persistent inflammatory response (super antigen theory) especially when epithelial barrier defenses are compromised. Chronic inflammatory response to established microbial colonization leads to a cycle of further epithelia damage and further microbial establishment (Flowchart 29.1 and Fig. 29.4).

From a therapy standpoint, better understanding of the pathogenesis of CRS has already led to abandonment of the strategy of prolonged systemic antibiotic use (potentially contributing to CRS via negative gut and mucosal biome effects). Topical antibiotics against *S. aureus* (mupirocin) and Th2 modulating therapies (topical steroids, leukotriene antagonists) have become mainstays of CRS treatment as our understanding of the pathogenesis has improved. New treatment horizons include biofilm

**Flowchart 29.1:** Pathophysiology of pediatric CRS (multiple interacting pathways)



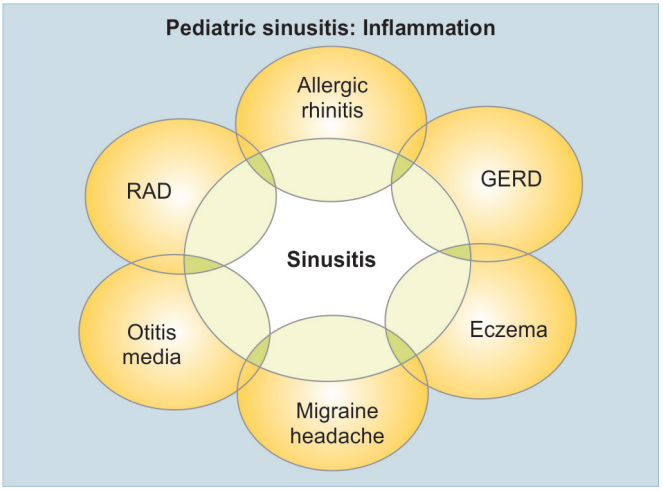




**Fig. 29.4:** Comorbid states of inflammation with pediatric chronic rhinosinusitis. Some associations may be in part causal such as adenoiditis but for others, such as reflux, evidence for causation is lacking.

disruptors, bacterial interference therapy, and more specific (nonsteroidal) blockers of inflammatory pathways. The new era of genetic research is rapidly expanding our understanding of this fascinating condition.

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CHAPTER

# 30

# Pediatric Rhinosinusitis: Diagnosis and Management

*Marianella Paz-Silva, Fuad M Baroody*

## INTRODUCTION

Rhinosinusitis, a complex inflammatory process of the paranasal sinuses, is generally considered a multifactorial problem which, in children, can be precipitated/exacerbated by viral, bacterial or fungal infections, as well as immunodeficiency, cystic fibrosis, allergen exposure, anatomical defects, or mucociliary dysfunction. It is considered a significant health problem around the world.[1,2]

## CLASSIFICATION

Classification of the disease is usually based upon symptoms and their duration and includes both acute and chronic rhinosinusitis (CRS).

### Acute Rhinosinusitis

In children, acute bacterial rhinosinusitis (ABRS) often follows a viral upper respiratory tract infection. The upper airway symptoms generated by these two entities are very similar and include nasal congestion, nasal discharge, and cough. In uncomplicated upper respiratory infections (URIs), fever and other constitutional symptoms (headaches, myalgia) disappear within the first 24–48 h and the nasal symptoms linger for as long as 7–10 days before resolving. It is, therefore, the persistence of these symptoms without improvement beyond 7–10 days that suggests a diagnosis of ABRS.[3] Another clinical presentation in the context of a viral URI that might suggest ABRS is what is often referred to as "double sickening". In this presentation, children experience substantial and acute worsening of respiratory symptoms (nasal discharge, nasal congestion, cough) or a new fever often on the sixth or seventh day of illness, after initial signs of recovery from a URI. Finally, a third clinical scenario that denotes severe ABRS is characterized by the onset of high fever and purulent nasal drainage for the first 3–4 days of a URI. Thus, the duration of symptoms that denote ABRS are usually of < 12 weeks in duration.[1]

### Chronic Rhinosinusitis

In children, CRS is also characterized by the presence of two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior or posterior), with or without cough and/or facial pain or pressure as well as objective signs of disease documented by either nasal endoscopy or computed tomography (CT) scan. The duration of these symptoms is for at least 12 weeks.[1,2]

## PREVALENCE

The exact prevalence of rhinosinusitis in children is difficult to determine and the clinical diagnosis remains very challenging, given the condition's frequent symptomatic overlap with common colds and upper respiratory tract infections that are otherwise widespread among children. Most of the common symptoms consistent with the diagnosis of rhinosinusitis, including cough and purulent rhinorrhea, may affect as much as 40% of the pediatric population at some point during childhood.[1,4]

In a longitudinal study of 112 children aged 6–35 months, 623 URIs were observed over a 3-year period, and episodes of acute rhinosinusitis as defined above were documented by the investigators.[5] Eight percent of the URIs were

complicated by rhinosinusitis, with 29% of the episodes diagnosed because of an increase in the severity of symptoms before 10 days of illness and the remaining diagnosed on the basis of persistent symptoms beyond 10 days. The occurrence of rhinosinusitis in the context of URIs was 7% in the 6–11 month age group and in children over 24 months, and 10% in children who were 12–23 months old. On average, a child younger than 5 years of age has 2–7 episodes of URI per year,[6,7] and a child attending day care may have up to 14 episodes per year.[8] With the incidence rates reported above, the number of acute rhinosinusitis episodes in children every year is sizeable.

To date, several studies have investigated the prevalence of CRS in groups of children with chronic upper respiratory complaints. In 1989, Van der Veken et al. obtained CT scan images of 196 children between 3 and 14 years old, presenting with chronic rhinorrhea, nasal congestion, and cough.[9] They found that within the youngest age cohort there was a predominant maxillary involvement (63%), followed by ethmoid disease (58%) and sphenoid changes (29%). In contrast, in the older age group (13 to 14 years old), the ethmoids were involved in only 10% of the subjects, the sphenoids in none, and the maxillary sinuses in 65% of the study patients.

Another study done by Nguyen et al. in 1993 included 91 new patients between 2 and 18 years of age, presenting with symptoms following at least 3 months of upper respiratory tract infection.[10] CT scans were recorded and reviewed to determine specific sinus abnormalities. The data showed that 36% had no sinus disease, while 63% of the group had chronic sinusitis with clinical signs and positive CT findings. The study likewise found that when symptoms of rhinorrhea, cough, and the absence of sneezing were all present, there was a greater association with CT scan abnormalities. Interestingly, age was the single most important risk factor associated with CRS; CT abnormalities were observed less frequently among the group of 10+ years of age, with only 38% of this group of children having CT abnormalities. Meanwhile, in the group between 2–6 years and 6–10 years, 73% and 74% had CT abnormalities, respectively. When evaluating a series of CT scans in children, the most commonly occurring sinus disease location was the maxillary sinus (99%) followed by the ethmoids (91%).[11]

## QUALITY OF LIFE

Cunningham et al. used parental and childhood generic quality of life questionnaires and administered them in children with recurrent or chronic sinusitis about to undergo sinus surgery.[12] They found that these children had lower quality of life, both by child filled and parental questionnaire compared to a normative, nondiseased population and had even lower quality of life when compared to children with other chronic diseases such as asthma, attention deficit hyperactivity disorder, juvenile rheumatoid arthritis, among others. More recently, the SN-5, a 5 domains survey, has been validated as a measure of sinonasal symptom change over time.[13] The survey addresses sinus infection, nasal obstruction, allergy symptoms, use of medication, emotional distress, and activity limitations; and is filled out by parents to reflect the child's symptomatic distress over the previous 4 weeks. In a prospective study of 32 patients with CRS aged between 2 and 12 years, Terrell et al. showed a correlation between SN-5 scores and disease severity as measured by Lund MacKay CT scan scores.[14] These results suggest that the survey can be used for clinical follow-up, in place of repeated CT scans. Likewise, there is some limited data that show improvements in quality of life as measured by the SN-5 questionnaire for patients with CRS after undergoing procedures such as adenoidectomy or endoscopic sinus surgery.[15]

## DIAGNOSTIC WORKUP AND EVALUATION OF COMORBID CONDITIONS

### History

A careful and detailed history is essential. The lack of ability among young children to adequately communicate their symptoms warrants a reliance on information provided by the parents. The most common clinical symptoms consistent with the diagnosis of rhinosinusitis—as suggested by several studies—are, rhinorrhea, nasal congestion, cough, and postnasal drip.[1,4,16] Sniffling and halitosis have also been reported.[4,11] Children with acute sinusitis might present with additional problems such as fever, purulent rhinorrhea or prolonged upper respiratory infection.[4] On the other hand, in some cases, symptoms of CRS can prove more subtle including malaise, difficulty concentrating, headaches, anorexia, and general fatigue.[2,17]

As mentioned previously, part of the diagnostic challenge might involve differentiating this condition from other symptomatically similar conditions such as allergic rhinitis and upper respiratory tract infections. Thus, the timing ofthe symptoms in relation to the onset of an URI is essential as that is critical for the diagnosis of ABRS.

## Physical Examination

General physical examination should include a complete ear, nose and throat evaluation, including anterior rhinoscopy with or without application of a topical decongestant so as to decrease edema and improve visualization. This can usually be done using the otoscope with the largest speculum. If possible, and tolerated, nasal endoscopy should be performed to evaluate structures such as the adenoids and nasopharynx and to check for signs of mucosal inflammation, polyps, and drainage in the ostiomeatal units. An oral cavity examination may reveal purulent drainage, cobblestoning of the posterior pharyngeal wall, or tonsillar hypertrophy. The finding of nasal polyps in children is unusual and, if seen on exam, should raise the suspicion for cystic fibrosis or allergic fungal sinusitis.

In patients unresponsive to conventional medical therapy, obtaining cultures may be useful in directing further treatment. In adults, cultures obtained from the middle meatus seem to correlate relatively well with cultures obtained from punctures or aspirates of the maxillary sinuses. In children, however, data regarding the usefulness of this approach is limited. In 2010, Hsin et al. obtained 29 paired endoscopically directed middle meatal cultures and 30 paired samples obtained via endoscopically directed middle meatal suction aspiration, and compared them with cultures of maxillary sinus taps obtained under general anesthesia from children (1–17 years) suffering from rhinosinusitis unresponsive to medical treatment.[18] These showed that endoscopic sampling by swab provided a sensitivity of 52%, a specificity of 100%, and a correlation of 66% compared to maxillary sinus taps. Meanwhile, the group where samples had been obtained by suction aspiration provided a sensitivity of 86% and a specificity of 100% and a correlation of 87%, leading the authors to conclude that the aspiration technique might further improve the reliability of endoscopic cultures in children.

Despite this data, most otolaryngologists prefer to reserve this technique for older children more likely to tolerate rigid endoscopy in the office setting. Once general anesthesia has been applied there is no further reason not to rely on the gold standard: obtaining a culture from the maxillary sinus itself via antral puncture.

# COMORBIDITIES

## Allergic Rhinitis

Allergic rhinitis is a common coexistent complaint in patients with rhinosinusitis. The extent of correlation between allergic rhinitis and rhinosinusitis is variable depending on the studies one looks at in the literature. It is certainly useful to evaluate for family history of atopy as well as symptoms of allergic rhinitis and the occurrence of the symptoms during known allergy seasons in one's practice area. If the history is suggestive of the diagnosis, skin or serologic testing might be useful and appropriate therapy recommended.

## Asthma

Asthma is often present in patients with rhinosinusitis and exacerbations of sinus disease are commonly associated with worsening of asthma. Unfortunately, this correlation is not well described in the literature as most studies lack appropriate controls and randomization.[19,20]

## Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD) has also been associated with CRS in several studies.[21-23] In some of these studies, the number of cases with a concomitant diagnosis of sinusitis was significantly higher in the children with GERD (4.19%) compared to the control group (1.35%).[22] In other studies, GERD was documented in a significant proportion of children with CRS and treatment resulted in improvement of CRS and avoidance of surgery.[21,23] Although some evidence supports an association between GERD and CRS, more controlled studies are required to strengthen this association and validate it, and routine antireflux treatment of children with CRS is not warranted.

## Immune Deficiency

Recurrent acute episodes or CRS should raise concerns and can require further investigation as to the potential underlying causes including common variable immunodeficiency (CVID), IgG subclass deficiency, and selective antibody IgA deficiency. Several studies have shown sinus disease in children to be a common manifestation of other underlying immune deficiencies.[4] In 2008, Urschel et al. studied 32 children (between 1 and 17 years of age) presenting with CVID. Their results showed that 78% of participants presented with sinus disease before the CVID was made.[24] Similarly, in a study done with patients referred by primary care doctors and pediatricians due to recurrent rhinosinusitis, Shapiro et al. showed that 56% of them also possessed concomitant immune deficiency, with depressed IgG3 levels and poor response to pneumococcal antigen 7 being most common.[25] It seems prudent

to evaluate immune function in the child with chronic/recurrent rhinosinusitis with an immunoglobulin quantitation and titers to tetanus and diphtheria as well as pneumococcal titers. If responses are abnormal, a repeat set of titers post pneumococcal vaccination is appropriate.

## Cystic Fibrosis

Cystic fibrosis is a genetic disease with autosomal recessive inheritance that affects approximately 1 in 3500 newborns. It is caused by a mutation in the CFTR gene on chromosome 7 that leads to disruption in cAMP-mediated chloride secretion in epithelial cells and exocrine glands. This leads to increased viscosity of secretions resulting in bronchiectasis, pancreatic insufficiency, CRS, and nasal polyposis. The prevalence of chronic sinusitis is very high and nasal polyps occur in between 7% and 50% of affected patients.[26,27] In fact, this is one of the few causes of nasal polyposis in children.

## Ciliary Dyskinesia

The normal movement of mucus by mucociliary transport toward the natural ostia of the sinuses and eventually to the nasopharynx can be disrupted by any ciliary dysfunction or mucosal inflammation. The most common cause of ciliary dysfunction is primary ciliary dyskinesia (PCD), an autosomal recessive disorder involving dysfunction of cilia and present in 1 of 15,000 of the population.[28] Half the children with PCD also have situs inversus, bronchiectasis, and CRS and are known as Kartagener's syndrome. The diagnosis should be suspected in a child with atypical asthma, bronchiectasis, chronic wet cough and mucus production, rhinosinusitis, chronic and severe otitis media (especially with chronic drainage in children with ear tubes). Screening tests for PCD include nasal nitric oxide (lower levels than controls) and in vivo tests such as the saccharin test that documents slower mucociliary transit time. Specific diagnosis requires examination of cilia by light and electron microscopy that is usually available in specialized centers. The most commonly described structural abnormality involves lack of outer dynein arms, or a combined lack of both inner and outer dynein arms.[29] Because chronic nasal inflammation could interfere with the integrity of the cilia, a biopsy from a distant, uninflamed, site such as the carina is preferred to a biopsy of the nasal mucosa or the adenoids.

## Allergic Fungal Rhinosinusitis

Fungi have been implicated in some children with CRS. Allergic fungal rhinosinusitis (AFRS) is thought to be an allergic inflammatory reaction to environmental fungi in immunocompetent patients. This causes a significantly severe form of rhinosinusitis with significant opacification of one or more paranasal sinuses and pressure on surrounding organs leading to findings such as proptosis. The radiologic picture is quite unique[30] and the pathology of the inflamed tissue is characterized by a strong eosinophilic infiltrate of the sinus mucosa. In fact, this is one of the few causes of nasal polyposis in the pediatric age group. The fungi responsible for AFRS are uniform in adult and pediatric populations and include *Bipolaris* species followed by *Curvularia*.[31,32] The exact incidence of AFRS in the pediatric population is not well known, but it tends to occur in older children. The treatment of choice for this entity is endoscopic sinus surgery with debridement of the fungal load and all inflammatory disease followed by anti-inflammatory therapy with intranasal and sometimes systemic steroids.

A multidisciplinary team consisting of allergy, immunology, infectious disease, pulmonary and genetic specialists should be available in order to best evaluate some pediatric patients with medically refractory sinus disease.

# IMAGING

Computed tomography scans have become the standard of choice for supporting the diagnosis of rhinosinusitis. The diagnosis of ABRS is primarily a clinical diagnosis based on symptoms and signs and their duration and imaging is reserved in case complications are suspected such as orbital or central nervous system involvement.[3] In these cases, contrast is used to facilitate visualization of rim enhancement of abscess walls. In uncomplicated CRS, scanning is reserved to evaluate for residual disease and anatomic abnormalities after maximal medical therapy. Abnormalities in the CT scan are assessed in the context of their severity and correlation with the clinical picture and guide the plan for further management that might include surgical intervention. In children with the clinical diagnosis of rhinosinusitis, the most commonly involved sinus is the maxillary sinus (99%) followed by the ethmoid sinus (91%).[11] CT use and applicability has increased as new scanners have become faster and their images have

achieved greater resolution without requiring the use of contrast. These advantages have facilitated the acquisition of these scans in most children without sedation that is still occasionally required in the younger child to minimize motion artifact. CT scans can also provide anatomical guidance for surgical treatments and intraoperative tracking and are useful for identifying potential areas of bony erosion or attenuation. Unique radiologic characteristics can make us suspect other entities such as allergic fungal sinusitis and cystic fibrosis. Magnetic resonance (MR) imaging of the sinuses, orbits, and brain should be performed whenever complications of rhinosinusitis are suspected.

## MEDICAL TREATMENT OF RHINOSINUSITIS IN CHILDREN

The main goal of medical therapy in rhinosinusitis is to reduce the inflammatory process, thus improving sinus drainage and eradicating pathogenic bacteria. An approach that typically combines several agents such as antibiotics, topical or systemic steroids, and irrigations are recommended.

### Antibiotics

Antibiotics are the most frequent treatment administered to children with acute or CRS. Nevertheless, there continues to be a fair amount of controversy as to how to best treat the disease. Acute rhinosinusitis is believed to be largely self-limited, and most practitioners will treat with a 10–14 day course of antibiotics if a child satisfies the clinical criteria for ABRS discussed above. Falagas et al. performed a meta-analysis of randomized controlled trials in order to evaluate antibiotic treatments for acute rhinosinusitis.[33] Three of their studies were done in pediatric patients and their review suggested that antibiotics were associated with faster and better improvements and resolutions of symptoms when compared to placebo. A more recent randomized, placebo-controlled trial not included in the meta-analysis evaluated the efficacy of amoxicillin (90 mg/kg) with potassium clavulanate (6.4 mg/kg) or placebo in children 1–10 years of age with a clinical presentation compatible with ABRS (persistent symptoms, acutely worsening symptoms or severe symptoms).[34] Symptom scores were obtained at multiple time points and the children were evaluated at day 14 from onset of treatment and their condition rated as cured, improved, or failed. Twenty-eight patients in each group completed the study and their average age was around 5 years. Children receiving the antibiotic were more likely to be cured (50% vs. 14%, $p = 0.01$) and less likely to experience treatment failure (14% vs. 68%, $p < 0.001$) than children receiving placebo. Similar to other studies, there were more side effects in the antibiotic treated group compared to the placebo treatment (44% vs. 14% of children, $p = 0.014$). Some studies, however, are not as conclusive. In another study, children with clinical diagnosis of acute rhinosinusitis and upper respiratory complaints lasting between 10 and 28 days were randomized into three groups: one receiving amoxicillin, the second amoxicillin clavulanate, and the third a placebo for 14 days.[35] All three groups improved compared with baseline, and there were no significant differences among the group results, indicating that in uncomplicated cases of acute rhinosinusitis patients are likely to improve regardless of the use of antibiotics.

The most recent clinical practice guidelines based on an evaluation of existing data recommend antibiotic therapy for severe or worsening ABRS because of the benefits observed in randomized controlled trials.[3] In children with persistent ABRS, the recommendation is for either antibiotic therapy or an additional period of observation because some children might improve on their own irrespective of administered treatments. Obviously, the benefits of antibiotic therapy should be weighed in the context of local bacterial resistance trends and other considerations such as drug allergies and negative effects on quality of life of the affected child.

Early studies using maxillary sinus aspiration[36,37] recovered three main pathogens in acute rhinosinusitis, namely, *Streptococcus pneumonia*, nontypable *Haemophilus influenza*, and *Moraxella catarrhalis*. As no recent sinus tap studies have been performed, estimates of the microbiology of ABRS have been based primarily on that of acute otitis media that historically has had a very similar set of organisms causing disease. Taking into account the recent observed changes in the prevalence of causative organisms after the routine administration of the pneumococcal conjugate vaccine, it is currently estimated that *S. pneumonia* and *H. influenza* are currently each responsible for approximately 30% of cases of ABRS in children, with *M. catarrhalis* accounting for 10% and the rest of the cases probably yielding no identifiable organisms.[3] Based on these assumptions and the recent trends of antimicrobial resistance among these organisms, amoxicillin remains the agent of choice for first-line

treatment of uncomplicated ABRS in which antimicrobial resistance is not strongly suspected (resistance is usually suspected in children younger than 2 years, those who attend daycare, and those who have received antibiotics within the previous 30 days).[38,39] Amoxicillin at a standard dose of 45 mg/kg/day in two divided doses is appropriate for children without risks for pneumococcal resistance, while a higher dose of 80–90 mg/kg/day in two divided doses is more appropriate for the children considered at high risk or who live in communities with a high prevalence of nonsusceptible *S. pneumonia*. Amoxicillin clavulanate (using either 45 mg/kg/day or 80–90 mg/kg/day of the amoxicillin component) can also be used in high-risk patients and improves the chances of coverage against *H. influenza* and *M. catarrhalis*. Ceftriaxone at 50 mg/kg/day as a single dose can be useful to initiate therapy for children who have a hard time with PO medications. When patients have a nontype 1 (late or delayed > 72 h) hypersensitivity reaction to amoxicillin, they can be safely treated with cefdinir, cefuroxime or cefpodoxime. Patients with a true type-1 reaction to amoxicillin can also be treated with the above-mentioned cephalosporins, as recent publications have indicated that the risk of a serious allergic reaction to second and third generation cephalosporins in patients with penicillin allergy appears minimal.[40-42] Other options include clindamycin and linezolid (good activity against *S. pneumonia* but lacks activity against *H. influenza* and *M. catarrhalis*). Recent resistance surveillance data suggest resistance of pneumococcus and *H. influenza* to trimethoprim-sulfamethoxazole and azithromycin, to a degree that precludes recommending these agents for the treatment of ABRS in patients with penicillin hypersensitivity.[3] The duration of antimicrobial therapy for ABRS has not been investigated but most recommendations suggest a 10-day course of therapy or treatment for 7 days after resolution of symptoms that, in most cases, would lead to a 10–14 day course of therapy.

Despite the lack of good evidence to support the use of antibiotics for any length of time in children with CRS, in practice, these children are often treated with the same antibiotics listed in the section on acute rhinosinusitis but typically for longer periods of time that vary between 3 and 6 weeks. Because of the lack of data to support this practice, its usefulness must be weighed against the increasing risks of inducing antimicrobial resistance. It is also difficult to ascertain whether what is actually being treated is CRS or acute exacerbations on top of preexisting chronic disease. The exact type of antibiotics used is usually dependent on local resistance patterns that might be different in different countries. Further, it is advisable to always treat with as narrow a spectrum of antibiotics as will likely cover the bacteria that are prevalent in a specific geographic locale.

Intravenous antibiotic therapy for CRS resistant to maximal medical treatment has been studied as a potential alternative to endoscopic sinus surgery. Don et al. retrospectively reviewed 70 children between 10 months and 15 years of age with CRS who were treated with a combination of adenoidectomy, sinus irrigation, and intravenous antibiotics.[43] They report that 89% of the children had complete resolution of symptoms after maxillary sinus irrigation and selective adenoidectomy followed by 1–4 weeks of culture-directed intravenous antibiotics. The most frequently used antibiotics were cefuroxime, followed by ampicillin-sulbactam, ticarcillin clavulanate, and vancomycin. Adverse side effects were also reported including superficial thrombophlebitis (9%), necessity of venotomy (1%), as well as other types of antibiotic side effects such as serum sickness, pseudomembranous colitis, and drug-induced fevers. At least one other study of similar design showed favorable results.[44] The retrospective design, lack of randomization, and lack of placebo arms of these trials limit their value. Furthermore, it is hard to assign benefit to intravenous antibiotic therapy when other interventions were utilized such as irrigation/aspiration of the sinus and adenoidectomy. Therefore, available data does not justify the use of intravenous antibiotics alone for the treatment of CRS in children.

## Intranasal and Systemic Steroids

Studies in adults with acute rhinosinusitis suggest that administering intranasal steroids can result in an additive benefit to antibiotic therapy when compared to placebo.[45,46] Barlan et al. conducted a double-blinded placebo-controlled trial in 89 children with acute rhinosinusitis treated with oral antibiotics.[47] Intranasal budesonide was given to 43 of these patients, while the remaining 46 received placebo saline spray. Their results showed that the budesonide group had greater improvement in cough and nasal discharge symptoms at week 2, although both groups had similar improvements by the end of the study at week 4.

There are no randomized controlled trials evaluating the effect of intranasal steroids in children with CRS. However, the combination of proven efficacy of intranasal corticosteroids in CRS with and without nasal polyps in adults and proven efficacy and safety of intranasal

corticosteroids in allergic rhinitis in children makes intranasal corticosteroids the first line of treatment in CRS.[48-50]

As far as systemic steroids, there is no data to support their use in the context of ABRS in children. In CRS, and since inflammation is a prominent component, the administration of short courses of systemic steroids are commonly used clinically. Significant side effects have precluded the use of prolonged courses. A placebo controlled, randomized, double-blind trial has provided some support for this practice.[51] The trial was conducted in children showing signs and symptoms as well as CT evidence of CRS (a total Lund Mackay CT score suggestive of mild-moderate disease). All the participants were treated with amoxicillin/clavulanate for 30 days, and randomized to receive either oral methylprednisolone or placebo during the first 15 days of treatment. The study showed significant improvements in all parameters (symptoms and CT scores) in both groups when compared to baseline. However, there were significant additional beneficial effects in the steroid group versus placebo related to cough, CT scan scores, nasal obstruction and drainage, and total symptom scores.

## Adjunctive Treatments

Adjunctive treatments are generally used to promote the drainage of secretions and decrease mucosal edema, the most frequently used being nasal irrigations and decongestants. Both have been shown to help in reducing the frequency of rhinosinusitis episodes. Michel et al. in 2005 performed a randomized, prospective, double-blind, controlled study evaluating outcomes, given the degree of mucosal inflammation and nasal patency.[52] They observed the effect of a 14-day treatment (1–2 sprays) with either isotonic saline solution or nasal decongestant in children 2–6 years of age with symptoms of acute rhinosinusitis. Their results showed that both groups experienced improvement in outcomes with no significant differences between the groups. There were no side effects observed with the saline spray, although the decongestant group did use 120% more drug than had been prescribed, demonstrating a worrying potential for these medications to be overused. While no cases of rhinitis medicamentosa were reported in this study, rebound effects are always a risk with these drugs.

A systematic review of the literature was undertaken to evaluate the efficacy of decongestants (oral or intranasal), antihistamines, and nasal irrigation in children with clinically diagnosed acute sinusitis.[53] Of 402 articles reviewed, 44 references were retrieved and were all excluded because they did not satisfy the set criteria. The authors conclude that there is no evidence to determine whether the use of the above-mentioned agents is efficacious in children with acute rhinosinusitis. Nevertheless, it is common clinical practice to recommend a limited (2–4 days) course of intranasal decongestants in cases of severe ABRS to facilitate drainage.

In a more recent publication, erdosteine, a mucolytic agent, was investigated in a randomized, placebo-controlled trial in children with acute rhinosinusitis.[54] Eighty-one patients completed the study and their average age was 8.5 years. Both treatment groups had an improvement in symptoms on day 14, but there were not statistically significant differences between the active and placebo groups. Therefore, there is really no good evidence to support the use of ancillary therapies in the treatment of ARS in children.

As for saline nasal irrigations, a Cochrane review evaluated 8 studies, with 3 of them having been conducted in children. Saline (delivered by several techniques and in different tonicity levels) was evaluated in comparison with either no treatment, placebo, use in conjunction with other treatments, or against other therapies.[55] Results showed that saline, if used as a unique treatment was beneficial in the treatment of the symptoms of CRS. Wei et al. conducted a prospective, randomized, double-blind study comparing daily saline to saline with gentamicin irrigations in children who presented with symptoms compatible with CRS and a positive CT scan to a pediatric otolaryngology office.[56] Forty children were randomized to receive either saline alone or saline with gentamicin irrigations (40 ml to each nostril administered via squeeze bottle) for 6 weeks. The children had a CT scan at baseline and another performed after 6 weeks of therapy and SN-5 quality of life scores at baseline and at weeks 3 and 6 of therapy. Over 90% of the children used the irrigations appropriately and consistently. There were significant improvements in quality of life of the children at 3 and 6 weeks of therapy compared to baseline with no difference between the treatment groups. Furthermore, the total Lund Mackay score at baseline was in the range of 10–12 on a total scale of 24 and this decreased significantly after 6 weeks of therapy to a range between 3.5 and 6 with no significant differences between the groups. These data suggest a benefit of saline irrigation in children with CRS and do not support the addition of an antibiotic.

Clinicians have also tried other treatments for CRS including antihistamines and leukotriene modifiers, especially given their effectiveness in treating allergic rhinitis, but the efficacy of such treatments for chronic sinusitis is not yet well established.

## SURGICAL TREATMENT OF RHINOSINUSITIS IN CHILDREN

Surgical intervention for rhinosinusitis is usually considered for patients with CRS who have otherwise failed maximal medical therapy (including a course of antibiotics, intranasal and/or systemic steroids, and saline irrigations). Children with cystic fibrosis and obstructive nasal polyps, antrochoanal polyps, or allergic fungal sinusitis with obstructive polyps and extensive sinus disease will usually undergo surgery as the initial favored option. In these instances, surgical therapy is targeted at diminishing disease load and improving nasal obstruction and facilitating the administration of topical therapies to the more accessible post surgical cavity. Less commonly, but as importantly, surgery is also used in the context of ABRS with complications such as orbital cellulitis/abscess or brain abscess.[4] The rest of this section will deal with the appropriate surgical approaches that are available to children with CRS who have failed medical therapy.

### Adenoidectomy with/without Sinus Irrigation and Balloon Dilation

The removal of the adenoids in patients with CRS relies on the belief that the adenoids are a bacterial reservoir in the nasopharynx and have been shown to be more likely to harbor bacterial biofilms in children with CRS. Further, in some instances, hypertrophy and/or inflammation/infection of the adenoids themselves (adenoiditis) might be the cause of the presenting symptoms and are hard to distinguish from CRS proper. The benefit of adenoidectomy alone in the treatment of children with CRS has been evaluated by a meta-analysis of nine studies.[57] All of these studies showed that sinusitis symptoms and outcomes improved in 50% or more of the patients after adenoidectomy. Meanwhile, eight of those nine studies were similar enough to undergo meta-analysis, with the results estimating that 69.3% of patients significantly improved after adenoidectomy. Ramadan and Tiu reviewed adenoidectomy failures over a 10-year period and found that children were more likely to fail adenoidectomy if they were younger than 7 years of age or had asthma.[58] Given that adenoidectomy is frequently performed along with maxillary antral irrigation, Ramadan et al. studied 60 children who underwent adenoidectomy for CRS.[59] In this study, postoperative antibiotic therapy was given for 2 weeks and 32 of the children also had a maxillary sinus wash and culture via the middle meatus. The children were followed for 1 year postoperatively and the success rate was 88% for patients who underwent adenoidectomy with a sinus wash compared to 61% for the group undergoing adenoidectomy alone. Interestingly, they also reported that children with a high Lund-McKay CT score and asthma benefited more from adenoidectomy with a wash that from adenoidectomy alone.

Balloon sinuplasty is a common procedure used in adults with CRS and has been shown to be safe in children.[60] In a feasibility study, the cannulation success rate was as high as 91%, and failure was most commonly caused by the presence of a hypoplastic sinus. The majority of cannulated sinuses in children are maxillary. Currently, most surgeons will confirm cannulation of the sinus by using an illuminated catheter. In a nonrandomized, prospective evaluation of children with CRS failing maximal medical therapy, balloon catheter sinuplasty and adenoidectomy were compared.[61] Outcomes were assessed at 1 year after surgery and were based on SN-5 scores and the need for revision surgery. Twenty-four out of 30 patients (80%) who underwent balloon sinuplasty showed improvement in their symptoms compared to 10/19 (52.6%) of the patients who underwent adenoidectomy ($p < 0.05$). As some of the balloon patients also underwent irrigation, it is hard to discern the effect of dilation vs. irrigation from this study. In a more recent study, children with persistent symptoms after adenoidectomy, despite medical treatment, as documented by SN-5 scores and the Lund-Mackay CT score were evaluated.[62] Twenty-six children underwent balloon sinuplasty and it is not clear from the article whether irrigation of the sinuses was performed with sinuplasty. Furthermore, a few children had concomitant anterior ethmoidectomies or revision adenoidectomy. Nevertheless, as a group, surgical success, measured by a predetermined decrease on the postoperative SN-5 score, was achieved in 81% of the children. The reduction in SN-5 scores postoperatively was still significant when the children with hybrid procedures were excluded. Therefore, despite methodological limitations, as mentioned above, this study suggests that use of balloon sinuplasty after failed adenoidectomy might be beneficial.

In sum, most of the available surgical data support adenoidectomy with sinus irrigation as a first step in the surgical management of the child with CRS refractory to maximal medical management. Whether or not balloon maxillary sinuplasty imparts additional benefit to irrigation alone, in combination with adenoidectomy, cannot be established with available data to date.

## Functional Endoscopic Sinus Surgery

Functional endoscopic sinus surgery (FESS) in children is usually more limited than the similar procedure in adults and consists of anterior ethmoidectomy and maxillary antrostomies in most cases with posterior ethmoidectomies and sphenoid and frontal sinus work reserved usually for older patients who show evidence of disease in these sinuses on preoperative CT scans. Early concern over the possible adverse effects of FESS on facial growth were addressed by Bothwell et al. who showed no impact of FESS on qualitative and quantitative parameters of childhood facial growth up to 10 years after surgery.[63] The only meta-analysis reviewing FESS in children was performed in 1998 and showed that using FESS as a surgical approach can be effective in reducing symptoms with an 88% success rate and a tolerably low complication rate.[64] Another study by Change et al. showed that, even using a limited approach to FESS where the surgeon only removed the most obvious obstructions within the child's sinuses, the result was a significant improvement in symptoms such as nasal obstruction, rhinorrhea, postnasal drip, headaches, hyposmia, and chronic cough in more than 90% of patients.[65]

Second look procedures, once common after FESS, are currently avoided given available use of absorbable packing. Ramadan et al. found that the use of corticosteroids during initial FESS might avoid necessitating a second look procedure.[66] Walner et al. after finding comparable rates of revision sinus surgery in children both with and without a second look procedure has likewise suggested that these may not be necessary.[67] The most common findings associated with failure of FESS in children are adhesions, maxillary sinus ostium stenosis, and missed maxillary sinus ostium.[68]

In conclusion, both acute rhinosinusitis and CRS are very common diseases in the pediatric age group and have a significant healthcare burden to both the child and family. The mainstay of management is medical with surgery reserved for treatment failures and complications. The initial surgical approach to the child with CRS should consist of an adenoidectomy with a maxillary sinus wash (with or without balloon dilation) followed by FESS in case of recurring symptoms. It is important to note, however, that most of the data supporting this recommendation stem from observational, not always methodologically optimal, studies.

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CHAPTER

# 31

# Cystic Fibrosis-Related Rhinosinusitis

***Megha Parekh, Kristina W Rosbe***

## INTRODUCTION

Cystic fibrosis (CF) is caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene on chromosome 7, affecting 1 in 3500 newborns. The most common mutation is F508, but at least 1500 different mutations have been identified. This mutation leads to the production of highly viscous secretions and impaired mucociliary transport that can contribute to sinonasal disease, bronchiectasis, pancreatic insufficiency, and focal biliary cirrhosis. Chronic inflammation of the sinuses and nasal mucosa has been reported in 74–100% of CF patients with the incidence of nasal polyposis reported as high as 44% of patients.[1] Multiple factors including genetic, inflammatory, and bacteriologic contribute to the development of chronic rhinosinusitis (CRS) in CF patients.[2]

## PATHOGENESIS

Paranasal sinuses rely on mucociliary transport for effective clearance of secretions, especially in dependent areas that may not spontaneously drain through the natural ostia. Sinonasal mucosa consists of mucus, motile cilia, and respiratory epithelial cells linked by adhesion complexes that include apical tight junctions. Nasal secretions are created by submucosal glands, goblet cells, epithelial cell proteins, lacrimal secretion and vascular transudate. Mucociliary transport promotes clearance of foreign material and bacteria out of the sinuses toward the nasopharynx.

The CFTR gene regulates the CFTR protein. This is a cAMP-activated ATP-gated anion channel that is found across the membrane of cells that produce mucus. The channel transports chloride ions and subsequently the movement of water with direct effects on mucus viscosity. This milieu of tenacious secretions, attenuated mucociliary transport, and upregulated proinflammatory mediators can lead to CRS in CF patients. The pathway to generate hypothiocyanite, an important antimicrobial that selectively kills microorganisms and spares host cells is ineffective in CF, leading to increased proinflammatory cytokines and additional oxidative stress.[3]

## HISTOLOGY

Differences between CF sinonasal mucosa and non-CF patients have been demonstrated at the histopathologic level. Studies have shown dilated glandular ducts and a predominance of mucous glands with a significantly elevated number of plasma cells and mast cells compared to non-CF patients.[4] Ultrastructural changes such as wide mucous cells, cystic dilatation, thicker layers of respiratory epithelium, and a high proportion of goblet cells compared to non-CF samples have also been reported.[5]

## MICROBIOLOGY

The most common organisms found in CF patients with CRS are *Pseudomonas aeruginosa* and *Staphylococcus aureus*.[6] These bacteria commonly colonize the airways of CF patients and create biofilms that are more resistant to traditional antibacterial treatment. Culture samples taken from bronchoalveolar lavages and paranasal cavities during endoscopic sinus surgery show a statistically

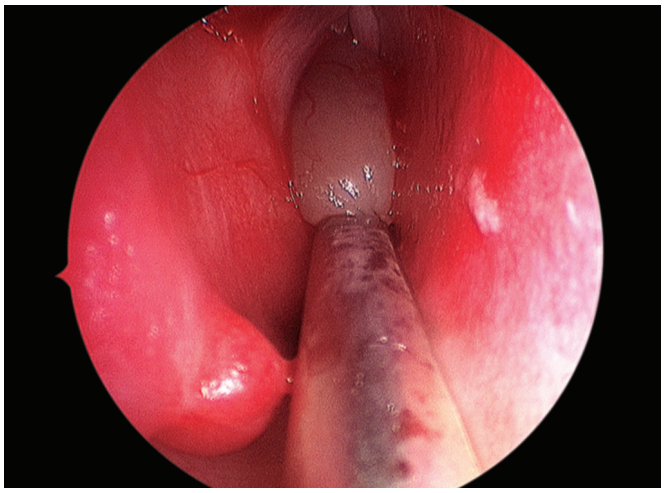

**Fig. 31.1:** Polyp in right nasal cavity.

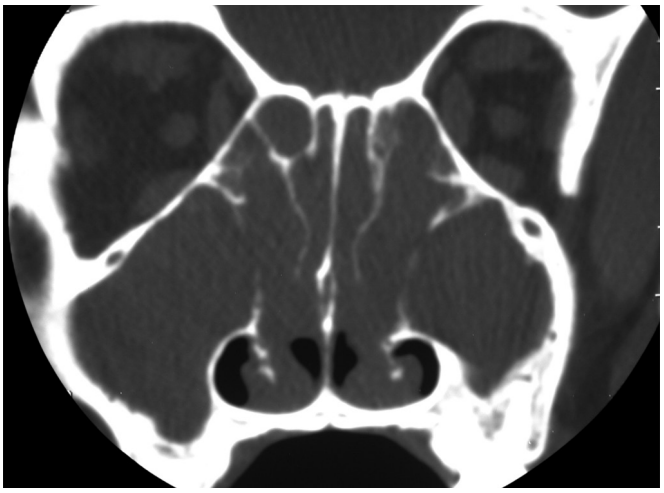

**Fig. 31.2:** Coronal CT scan demonstrating panopacification of the maxillary and ethmoid sinuses.

significant association between paranasal cavity cultures and lower airway cultures for *P. aeruginosa* and *S. aureus* in CF patients. Management of these chronic infections remains challenging due to emerging development of resistance to standard antimicrobial regimens.

## CLINICAL FINDINGS

Symptoms of CRS in CF patients are similar to non-CF patients including nasal obstruction, rhinorrhea, cough, and facial pain or pressure. Some CF patients may also present with reduction of pulmonary function.[7] Young CF patients, who have polyposis, may present with a widened nasal bridge.

A thorough physical examination should include anterior rhinoscopy as well as nasal endoscopy, although this can be challenging in younger patients. Polyps should be identifiable on nasal endoscopy as well as mucopurulent secretions in the area of the middle meatus (Fig. 31.1). There is evidence to suggest that patients who are homozygous for the CFTR-mutation may have a higher incidence of nasal polyposis.[8]

## IMAGING FINDINGS

Historically, the imaging study of choice for CF patients with CRS has been a noncontrast sinus computed tomography (CT) scan. With the increased awareness of cumulative radiation exposure and links to development of malignancy, many centers are developing low-dose radiation protocols, especially for pediatric patients.[9] Some centers are using "cone beam CT", also called digital volume tomography, which can lead to up to an 80% reduction in radiation without loss of resolution compared to standard CT protocols.[10] Other centers have started using magnetic resonance imaging (MRI), although this is traditionally felt to be not as helpful for bony anatomy, takes longer, and therefore may require sedation or general anesthesia for young children. Intraoperative image guidance, especially for revision sinus surgery, is commonly utilized. At our institution, as a tertiary referral center for these patients, our patients often come with imaging that was already ordered by their local physicians. We make every attempt *not* to repeat imaging if at all possible. Almost all CF patients will have abnormal sinus imaging; therefore, a scan should only be ordered for patients who are refractory to medical therapy and in whom, surgical intervention is being considered. Using imaging to monitor CRS or to confirm response to medical therapy is *not* recommended. Symptoms and endoscopic examination should be used to guide treatment.

Characteristic findings on sinus CT include medial displacement of the lateral nasal walls, uncinate process demineralization, and panopacification of the sinuses (Fig. 31.2). There can also be aplasia or hypoplasia of the frontal and sphenoid sinuses.

## MEDICAL TREATMENT

Medical treatment for acute or CRS in CF patients generally includes antibiotics, nasal steroids, and saline irrigations although there are limited outcomes studies on the

efficacy of topical steroids and saline irrigation for CRS in CF patients. A Cochrane review concluded that saline irrigations in non-CF patients improve symptoms and disease-specific quality of life (QoL) scores.[11] Hypertonic saline has been proposed to increase mucociliary clearance, pulmonary function, and decrease inflammation through reduction in proinflammatory cytokines such as interleukin-8 (IL-8), but these effects have not been demonstrated as well in CRS.[12] Culture directed antibiotic treatment is preferable but cultures of the middle meatus, the preferred location, may not be tolerated in younger patients. There is no consensus on duration of antibiotic therapy but longer durations of at least 3 weeks are usually prescribed.[13] Older patients may also be prescribed a course of oral steroids to treat inflammation of sinonasal mucosa. Controlled studies of optimal medical therapy in CF patients are lacking. For those patients with obvious sinonasal polyposis, medical therapy alone may not be adequate.

Nasally inhaled dornase alfa (Pulmozyme, Genentech) is a human deoxyribonuclease that selectively cleaves DNA. This has been proven to reduce the viscosity of pulmonary secretions. Several studies have also examined the use of nasally inhaled dornase alfa and demonstrated an improvement in nasal-related symptoms and nasal endoscopic appearance. There are ongoing investigations of the use of nebulized topical antibiotics and other substances, such as mannitol to rehydrate mucus membranes, for CF patients with CRS.

## SURGICAL TREATMENT

It remains unclear why some CF patients develop symptomatic CRS and/or sinonasal polyposis and others do not. As mentioned previously, extent of radiographic disease may not correlate with symptomatology and should not be used as the sole determinant for surgical intervention. Severity and progression of sinonasal symptoms as well as deteriorating pulmonary function are the most common reasons for surgical intervention. At some centers, CF patients being considered for lung transplantation may be referred for sinus surgery to reduce airway bacterial colonization, although this indication remains controversial. Sometimes, sinus surgery is coordinated at the end of a scheduled admission for a pulmonary "cleanout"—usually a 7–10 day admission for IV antibiotics and aggressive pulmonary toilet to try to optimize pulmonary function.

Goals of sinus surgery in CF patients are generally to remove obstructing polypoid disease, open sinus ostia to promote more efficient clearance, and remove mucopurulent secretions to decrease bacterial colonization (Fig. 31.3).[14] Development and refinement of endoscopic sinus instrumentation has made sinus surgery, even in young patients, possible and safe. Tools such as the straight and angled microdebrider blades allow for relatively fast removal of bulky polypoid disease in the sinuses with less operative time and bleeding compared to prior more traditional methods (📹 31.1). Powerful irrigating systems such as the hydrodebrider can help irrigate out thick secretions and reduce bacterial colonization (📹 31.2 and 31.3). Intraoperative image guidance is also used during endoscopic sinus surgery in CF patients, especially for patients undergoing multiple revision surgeries to confirm anatomic landmarks. Adjuvant medical therapies during sinus surgery such as irrigating with topical antibiotics and/or steroids are being investigated.

Concerns have been raised about alterations in sinus and facial growth of sinus surgery in pediatric patients, but multiple studies have not been able to demonstrate any long-term effects on facial growth.[15,16] Most pediatric sinus surgeons remain conservative, however, in removal of tissue to minimize this potential risk. Hemostatic agents and/or other bioabsorbable products are sometimes placed at the end of sinus surgery to minimize postoperative bleeding and prevent synechiae. Scheduled second look procedures to examine and debride under general anesthesia in children who would not tolerate this type of examination in the office have fallen out of favor.

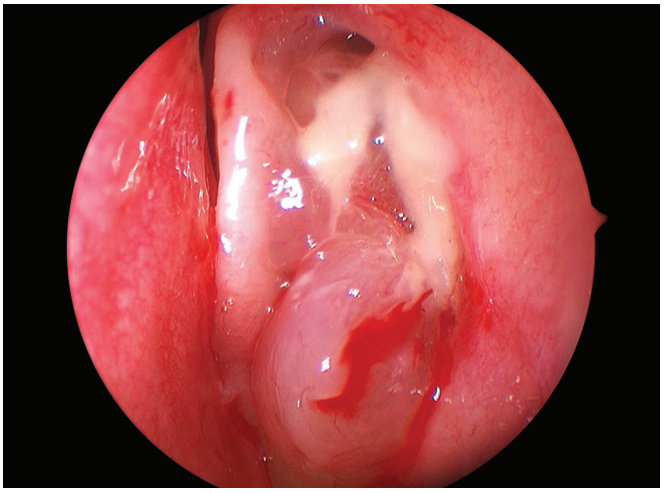

**Fig. 31.3:** Polyp and mucopurulence emanating from left maxillary sinus.

Although there are some studies suggesting that endoscopic sinus surgery is linked to improvement in QoL in CF patients, effects on pulmonary function, hospitalization, and overall medical therapy are less clear and further studies are needed to more fully elucidate the long-term outcomes.[17]

Recent United States Food and Drug Administration (FDA) approval and successful trials of ivacaftor, a CFTR modulator and the first therapy targeting the underlying defect in CF, are promising and may have the potential for significant impact on the future medical care and QoL of patients with CF.[18]

## VIDEO LEGENDS

**Video 31.1** Microdebriding polyp in left maxillary sinus.
**Video 31.2** Hydrodebriding the left maxillary sinus.
**Video 31.3** Hydrodebriding the frontal sinus.

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CHAPTER

32A

# Congenital Nasal Malformations

***Steven M Andreoli, Ken Kazahaya***

## INTRODUCTION

Congenital anomalies of the nasal cavity and nasopharynx include a diverse collection of presentations and pathologies. Although many lesions may be indolent or incidental, clinically relevant lesions routinely present with external findings with cosmetic implications, nasal obstruction, or intracranial communication. Because of obligate nasal breathing during the neonatal period, congenital nasal malformations causing nasal obstruction often result in acute respiratory compromise. The three most common pathologies in this group include choanal atresia (CA), congenital pyriform aperture stenosis (CPAS), and midline nasal masses. Congenital midline nasal masses include dermoid cysts and sinuses, gliomas, and encephaloceles.

## CHOANAL ATRESIA

### Epidemiology and Pathophysiology

CA is a rare anomaly present in <1 per 10,000 births.[1] The majority of CA cases (71%) are mixed bony and membranous atresias, while the remaining 29% are solely bony.[2] There is a nearly equal distribution between unilateral and bilateral cases. Associated abnormalities are identified in 70% of cases, and CHARGE syndrome must be considered.[3]

### Presentation

Secondary to obligate nasal breathing, neonates with bilateral CA routinely present with airway obstruction and respiratory failure. Infants with bilateral CA exhibit paradoxical cyanosis in which respiratory distress is relieved by crying. An oral airway and prone positioning may temporize nasal obstruction. Ultimately, oral intubation is often required prior to surgical intervention.

Unlike bilateral atresia, an indolent presentation is characteristic of unilateral CA. Unilateral chronic obstruction and rhinorrhea are the most common findings in unilateral CA. Because of mucous stasis within the nasal cavity purulent and odorous drainage may ensue raising concern for possible nasal foreign body. As a result of nonspecific symptoms, diagnosis of unilateral CA is made between 2 and 5 years of age.

### Workup

Bilateral CA presents with neonatal respiratory distress. Paradoxical cyanosis raises suspicion for a fixed nasal obstruction. Inability to pass a nasal suction catheter past 3.5 cm is the first finding specific to CA. A mirror placed at the nares will not fog during exhalation. Gold standard diagnosis of CA is made via flexible nasal endoscopy. Following diagnosis, a CT of the midface allows characterization of the atretic plate[4] as seen in Figure 32A.1. The thickness of the bony atretic place, vertical height of the skull base, and medial position of the pterygoid plates are of particular concern for surgical planning.

Unilateral CA is routinely an office based diagnosis. Children with chronic unilateral nasal obstruction and rhinorrhea undergo flexible endoscopy in the outpatient setting. After endoscopic identification of unilateral CA, again CT is recommended to investigate the nature of the atretic plate.

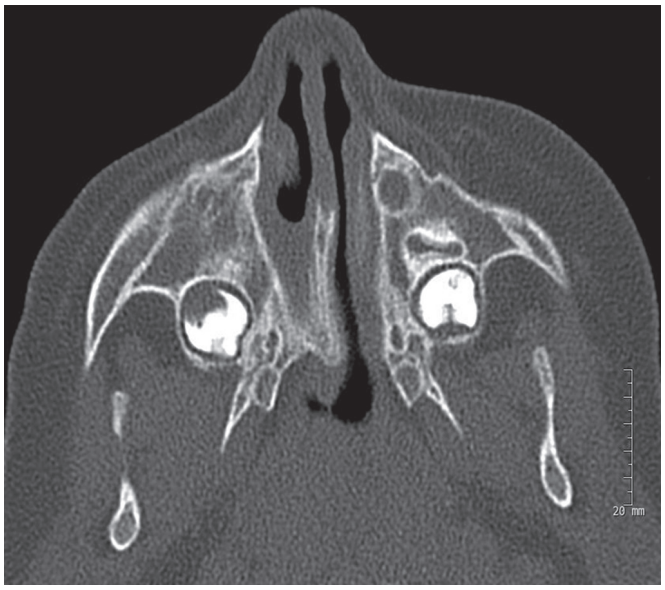


**Fig. 32A.1:** CT demonstrating bright bony and membranous choanal atresia.

## Management

The surgical management of CA continues to evolve. Early surgical management consisted of blind bougienage of the atretic plate with curettage of the vomer and pterygoid plates. This technique placed both the skull base and carotid arteries at risk. Subsequent to blind techniques, the transpalatal approach was applied. This technique offers excellent exposure, but results in palatal arch growth concerns.

Endoscopic techniques have largely supplanted the transpalatal approach. Many technique modifications are reported employing either a 0° transnasal or a 120° transoral approach. Following puncture of the atretic plate, the choanae are widened in all directions using both hand and powered instrumentation.[5] The authors prefer drilling laterally along the pterygoid plate to maximize choanal dimensions. Because of the circular nature of the neochoanae, cicatricial scarring is common. Performing posterior septectomy with resection of the posterior portion of the vomer using a back biting endonasal instruments results in a three dimensional aperture less likely to stenose. In our experience, an anteriorly based mucosal flap is raised on one side and draped across the septal defect to improve mucosalization and decreased granulation tissue.

Postoperative management for bilateral CA remains controversial. Questions remain regarding duration of orotracheal intubation, use of nasal stents, application of topical medications, and revision surgery. Similar to airway surgery, allowing air passage through the reconstructed choanae improves patency. As such, short-term intubation of 1 or 2 days is advocated. In review of nasal stents, there is little evidence to support improved patency with time.[6] In revision cases or cases with narrow choanal dimensions, stents may decrease revision rate. Several topical medications have been utilized attempting to reduce scar formation. Topical mitomycin C prevents fibroblast growth; however, the evidence reports conflicting results about efficacy. Topical nasal steroids may serve to reduce swelling and granulation following surgery; however, significant systemic uptake of nasal steroids can cause adrenal insufficiency.[7] Thus, we advocate a short-term postoperative nasal steroid course followed by saline alone. Revision after bilateral CA repair is unfortunately common. Known predictors of revision surgery include bilateral CA, repair at age < 6 days, prematurity, and associated congenital anomalies.[8]

Surgical management of unilateral CA is met with higher success rates. A similar approach is required, but the ability to use the contralateral side as a landmark facilitates protection of the skull base. Following puncture of the atretic plate similar techniques are performed to drill along the pterygoid plates and a posterior septectomy is performed. As in bilateral cases, an anteriorly based ipsilateral septal mucosa flap is again draped to the opposite side. A lateral flap either superiorly or anteriorly based can also be raised and draped over the exposed pterygoid plate to improve mucosalization. Neither postoperative stenting nor intubation is routinely required.

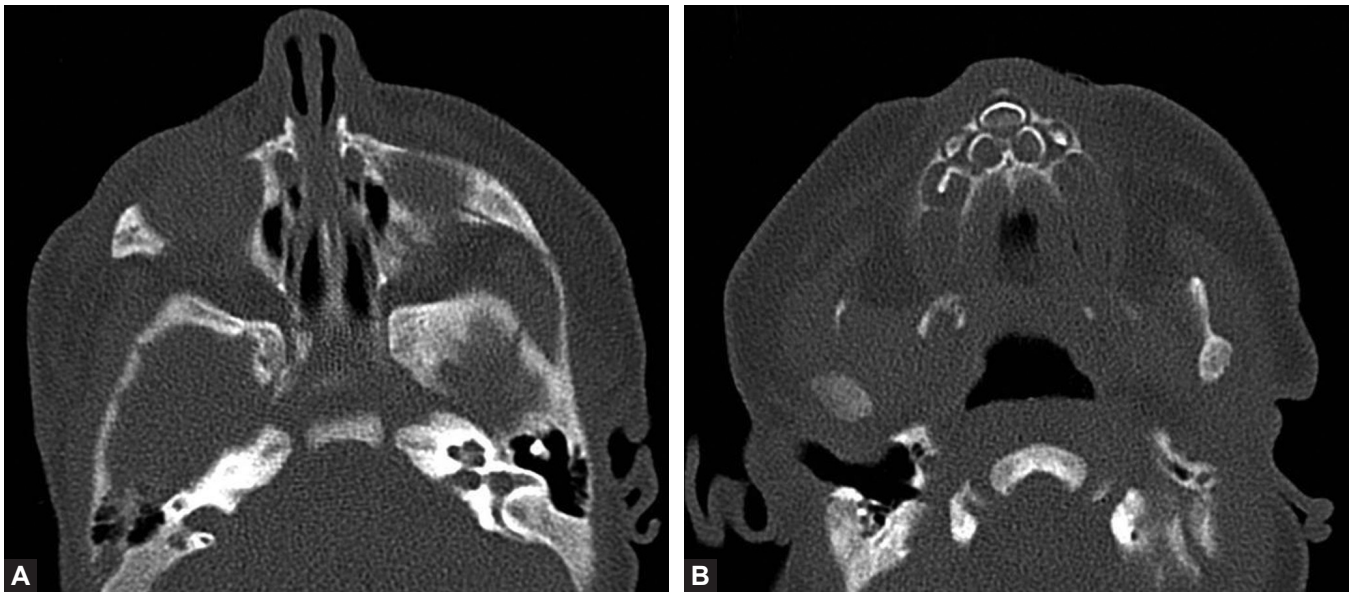
# CONGENITAL PYRIFORM APERTURE STENOSIS

## Epidemiology and Pathophysiology

CPAS results from premature fusion of the medial nasal prominence. Children with CPAS often exhibit complete nasal stenosis. The true incidence of CPAS is unknown. Although not seen in all cases, the associated single median maxillary central incisor is estimated to occur in 1:50,000 births.[9]

## Presentation

CPAS presents with neonatal respiratory distress. Similar to bilateral CA, paradoxical cyanosis is common as crying with oral respiration bypasses the nasal airway obstruction.




**Figs. 32A.2A and B:** (A) CT showing pyriform aperture stenosis, note the associated narrow nasal dimension in the middle nasal vault; (B) Associated solitary median maxillary central incisor.

Conservative airway management is accomplished with oral airway placement. Unlike neonates with bilateral CA, some infants with CPAS are able to maintain a natural airway for an extended period of time. Infants with severe CPAS often require intubation prior to surgical intervention.

## Workup

Anterior rhinoscopy in an infant with CPAS demonstrates narrow nasal vestibules. The lower lateral cartilage is often effaced to the septum. Nasal suction catheters cannot be introduced into the nasal cavity. Inability to pass a flexible endoscope is a common finding with CPAS. CT imaging of the pyriform aperture quantifies the severity of CPAS (Figs. 32A.2A and B). Total diameter < 11 mm is diagnostic of CPAS.[10] In addition to measurement of the pyriform aperture, examination of the mid-nasal and posterior-nasal dimensions is useful in predicting surgical success.[11] CT imaging also detects the presence of an associated midline megaincisor and holoprosencephaly. In patients identified to have holoprosencephaly also require an MRI of the brain.

## Management

Initial management for CPAS revolves around establishing a stable airway. Because of incomplete obstruction, some infants may not require immediate intubation. Enteral feeding is often required in this setting because of poor coordination with feeding in the absence of nasal breathing. For infants with respiratory distress, oral intubation provides a secure airway until surgical management is performed.

The traditional technique for surgical management of CPAS begins with a sublabial approach carried down to the face of the maxilla.[12] Subperiosteal dissection is then performed superiorly into the nose. Because of the extremely narrow dimensions the surgeon must be attentive to remaining midline at all times. A pitfall for surgery is dissection lateral to the pyriform aperture placing the infraorbital nerve at risk. A 0.5 and 1 mm diamond drill are then used in conjunction with either loupe magnification or microscopy to drill laterally against the pyriform aperture. Posterior dissection is carried to the coronal plane of the inferior turbinate head. The medial surface of the burr must be kept off the septum to prevent perforation. In patients with more posterior nasal stenosis, out-fracture of the turbinates can be performed to improve posterior nasal dimensions. Short-term stenting may be useful in preventing stenosis.

More recently, reports have discussed using balloon dilation and stenting as an alternative to the sublabial approach.[13] In select cases at our institution, we have used urethral sounds with nasal stenting. Sequential stenting of the pyriform for several weeks may be sufficient to carry an infant through the obligate nasal breathing period, allow for oral feeding, and obviate the need for alternative alimentation.

## MIDLINE NASAL MASSES

### Epidemiology and Pathophysiology

Three types of midline nasal masses result from faulty closure of the anterior neuropore. The classic differential for a midline nasal mass includes dermoid cysts and sinuses, gliomas, and encephaloceles. The incidence of midline nasal masses ranges from 1:20,000 to 1:40,000.[14] The pathophysiology of the herniated or excluded contents dictates the diagnosis.

During early development, a dural diverticulum extends into the prenasal space.[15] The frontal and nasal bones are segregated by the fonticulus frontalis. With the progression of embryogenesis, the dural projection recedes and the foramen cecum is formed. Incomplete closure of the anterior neuropore results in the spectrum of defects seen with midline nasal masses from the frontal bone and across the anterior cranial base.

Nasal dermoid cysts are theorized to represent failed regression of the dural diverticulum. A stalk projection from the anterior neuropore results in a dermoid sinus tract, which may extend intracranially. Residual attachment to the nasofrontal epithelium results in the pathopneumonic midline nasal dimple and hair tuft. A glioma is neural tissue excluded from the intracranial vault following closure at the foramen cecum. Incomplete closure of the foramen cecum with herniation of neural tissue into the prenasal space or nasal cavity is characteristic of an encephalocele. To avoid complications, differentiation of the midline nasal masses is paramount prior to surgical management.

### Presentation

Dermoids, gliomas, and encephaloceles can range from subtle anomalies to large lesions causing respiratory symptoms. A midline nasal dimple and/or hair tuft are characteristic of a nasal dermoid. Dermoid sinus tracts are lined with epithelium, and keratinous drainage may occur. Dermoid sinus tracts with intracranial extension may result in meningitis or intracranial abscess formation. Encephaloceles, because of the intracranial association, are subject to changes in intracranial pressure. The Furstenberg test, or compression of the internal jugular vein, results in enlargement of the encephalocele as intracranial pressure increases. A glioma presents with a midline prenasal or intranasal mass that may associate with the lateral nasal wall. Unlike an encephalocele, because of complete foramen cecum closure, the Furstenberg test is negative.

### Workup

Physical examination findings with midline nasal masses often narrow the differential. The hair tuft and dimple are characteristic of nasal dermoids. A positive Furstenberg test is diagnostic of an encephalocele. Gliomas and dermoids within the prenasal space have similar examination findings. Radiographic findings characteristic of midline nasal masses were identified in the 1982 by Sessions. In his landmark article, a bifid crista galli was identified as a predictor of intracranial extension.[14] Plain film radiography was used at the time, and may still be used. CT imaging will allow assessment of the bony cranial base. Meanwhile, imaging with MRI offers greater soft tissue characterization and visualization of intracranial involvement and is the imaging of choice for the authors (Figs. 32A.3 and 32A.4).

### Management

Surgical planning for excision of the midline nasal mass hinges on the presence of intracranial involvement. Preoperative imaging allows for anticipation of a CSF leak during excision. Lesions with exclusively extracranial involvement of the prenasal space may be excised via direct midline incision or external rhinoplasty approach.[16] Masses with intranasal extension can be excised with external and endoscopic combined approaches. Lesions with intracranial involvement require coordinated surgery between otolaryngology and neurosurgery. Endoscopic assisted approaches continue to expand our minimally invasive access to the anterior skull base. For lesions with endonasally approachable intracranial extension we have been able to manage without a craniotomy; however external craniotomy continues to be needed for lesions with larger intracranial components.

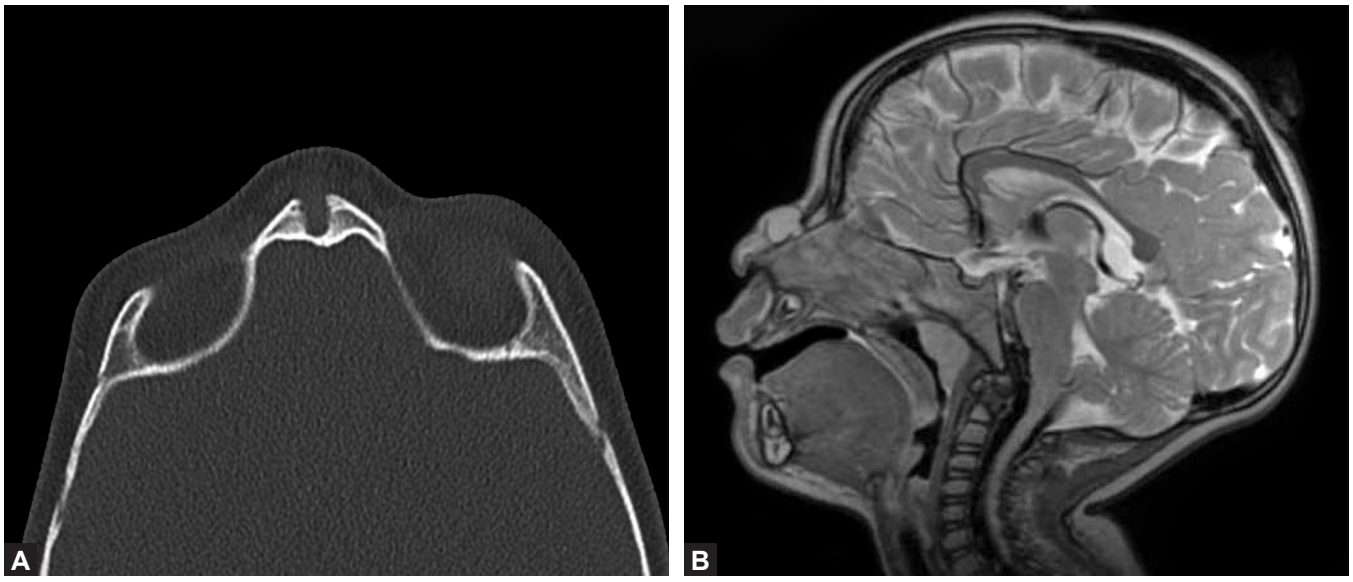
## PROBOSCIS LATERALIS

### Epidemiology and Pathophysiology

Proboscis lateralis (PL) is a rare nasal anomaly affecting 1:100,000 births.[17] There is no known genetic link. PL develops from a failure of fusion or the absence of a medial and lateral nasal process. The embryonic fusion plane between the frontonasal process and anterior maxillary process dictates the position of the proboscis.

### Presentation

PL manifests with a tubular nasal structure originating from near the medial canthus. This structure is analogous




**Figs. 32A.3A and B:** (A) CT showing dermoid cyst extending into the frontal bone; (B) Sagittal MRI with dermoid cyst in the prenasal space with extension through nasal bone.

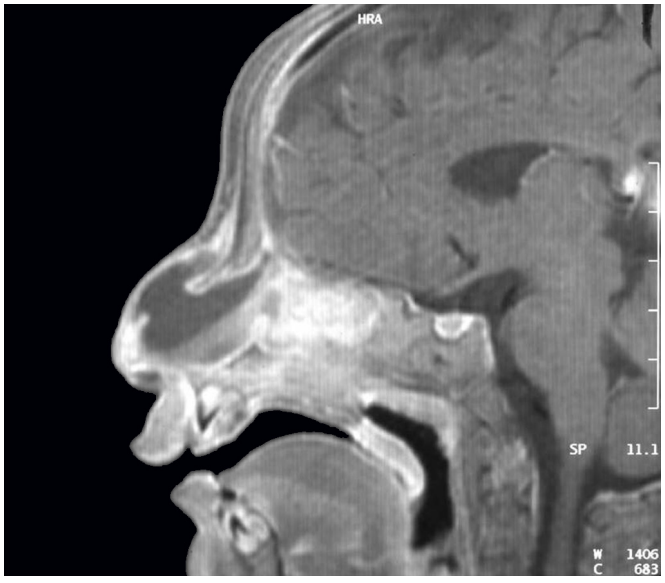



**Fig. 32A.4:** MRI showing large prenasal and intranasal encephalocele.

in appearance and composition to the proboscis of insects. The lining within a proboscis is squamous epithelium.

PL has been classified into four groups based on the associated nasal, ocular, and philtrum findings. The classification system is summarized in Table 32A.1.[18]

**Table 32A.1:** Boo-Chai classification for proboscis lateralis[18]

| *Group* | *Defect* |
|---|---|
| I | Normal nose with supernumerary PL |
| II | PL with ipsilateral nasal defect |
| III | PL with ipsilateral nasal and ocular defects |
| IV | PL with cleft lip and/or palate |

(PL: Proboscis lateralis).

## Workup

PL is evident at birth, and may be diagnosed prenatally on ultrasound in some cases. The contralateral nasal cavity is routinely patent, and airway symptoms are uncommon. Imaging with CT or MRI is prudent to investigate for any intracranial involvement (Fig. 32A.5).

## Management

PL is managed in accordance with the group typing. In patients with group 1 PL and an otherwise normal nose the proboscis can be excised. In patients with ipsilateral nasal defects, the proboscis is used as tissue for reconstruction of the nose.

# ARRHINIA

## Epidemiology

Arrhinia is very rare, with scattered case reports in the literature.[14] There is no known genetic or embryologic cause for arrhinia.

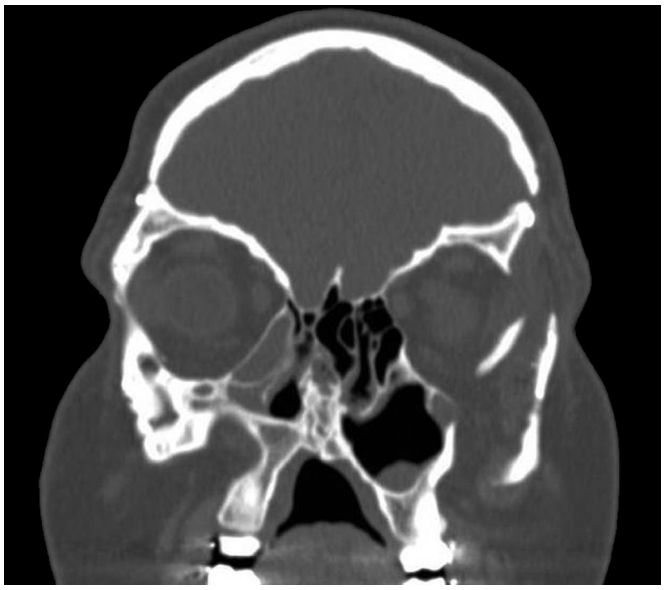


**Fig. 32A.5:** CT of skull base in patient with group II right-sided proboscis lateralis resulting in rudimentary right nasal cavity and paranasal sinuses.

## Presentation

Children with arrhinia have neonatal respiratory distress secondary to obligate nasal breathing. Paradoxical cyanosis would be expected. Management of arrhinia is infancy depends on establishing a secure airway. Because of a complex staged nasal reconstruction, neonatal tracheostomy is expected.

## Workup

Arrhinia is evident at birth. CT imaging of the maxilla and midface are important in understanding the anatomy of the midline face.

## Management

Arrhinia requires a complicated reconstructive course. During this time, a tracheostomy is often required. Management of arrhinia involves establishing a nasal cavity space and creating an external nose. The neocavity is drilled and lined with skin grafts. The external nose is constructed from calvarial bone, cartilage, and regional tissue flaps.

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CHAPTER

32B

# Pediatric Nasal Tumors

***Steven M Andreoli, Ken Kazahaya***

## NASAL TUMORS

Pediatric nasal tumors are comprised of a diverse collection of histologic and clinical presentations. The differential diagnosis includes both benign and malignant neoplasms. Differential diagnoses are outlined in Tables 32B.1 and 32B.2.[1] Attentive workup and diagnosis is integral in appropriate management. Coordinated efforts using a multidisciplinary tumor board is required for children with nasal malignancies.

**Table 32B.1:** Benign neoplasms of the nasal cavity and paranasal sinuses

| |
|---|
| Adnexal neoplasm |
| Ameloblastic fibro-odontoma |
| Benign fibrous histiocytoma |
| Blue nevus |
| Compound nevus |
| Epithelioma adenoides cysticum |
| Giant cell granuloma |
| Hemangioma |
| Inverted papilloma |
| Juvenile nasopharyngeal angiofibroma |
| Langerhans cell histiocytosis |
| Lymphangioma |
| Neurofibroma |
| Ossifying osteofibroma |
| Osteochondroma |
| Port wine stain |
| Spitz nevus |
| Teratoma |
| Xanthogranuloma |

## BENIGN NASAL MASSES

### Juvenile Nasopharyngeal Angiofibroma

#### *Epidemiology and Pathophysiology*

Juvenile nasopharyngeal angiofibroma (JNA) is a rare benign vascular neoplasm of the pterygopalatine fossa and nasopharynx with an incidence of 1:5,000 to 1:60,000.[2] JNAs are found almost exclusively in adolescent males and comprise 0.05% of all head and neck tumors.

These tumors are theorized to originate from the superior aspect of the sphenopalatine foramen; however, the definitive etiology of JNAs is not known. Because of the age and gender predilection, a hormonal pathogenesis has been proposed. Paraganglionic cells within the terminal

**Table 32B.2:** Malignant neoplasms of the nasal cavity and paranasal sinuses

| |
|---|
| Basal cell carcinoma |
| Chondrosarcoma |
| Esthesioneuroblastoma |
| Ewing sarcoma |
| Fibrosarcoma |
| Granulocytic sarcoma |
| Hemangiopericytoma |
| Lymphoma |
| Melanoma |
| Nasopharyngeal carcinoma |
| Neuroblastoma |
| Osteosarcoma |
| Rhabdomyosarcoma |
| Squamous cell carcinoma |

branches of the maxillary artery have also been implicated with deletions identified on chromosome 17 involving both *p53* and *Her-2/Neu*.[3]

The growth of JNAs tends to be bilobed. The intranasal component of the tumor extends medially toward the nasopharynx. Large tumors displace the septum, or may erode into the sphenoid or cavernous sinus. The lateral portion of the tumor spreads toward the pterygopalatine fossa and eventually the infratemporal fossa. Orbital involvement may occur with extension through the inferior orbital fissure. Intracranial extension may occur via erosion through the greater wing of the sphenoid.

### *Presentation*

The most common manifestations of a JNA are unilateral nasal obstruction and recurrent unilateral epistaxis in a teenage male. Growth within the nasopharynx results in Eustachian tube dysfunction and unilateral otitis media with effusion. Although benign, local invasion is common. Tumors with extension into the pterygomaxillary and infratemporal fossa may also exhibit proptosis, diplopia, cranial neuropathies, facial asymmetry, and chronic headaches.

### *Workup*

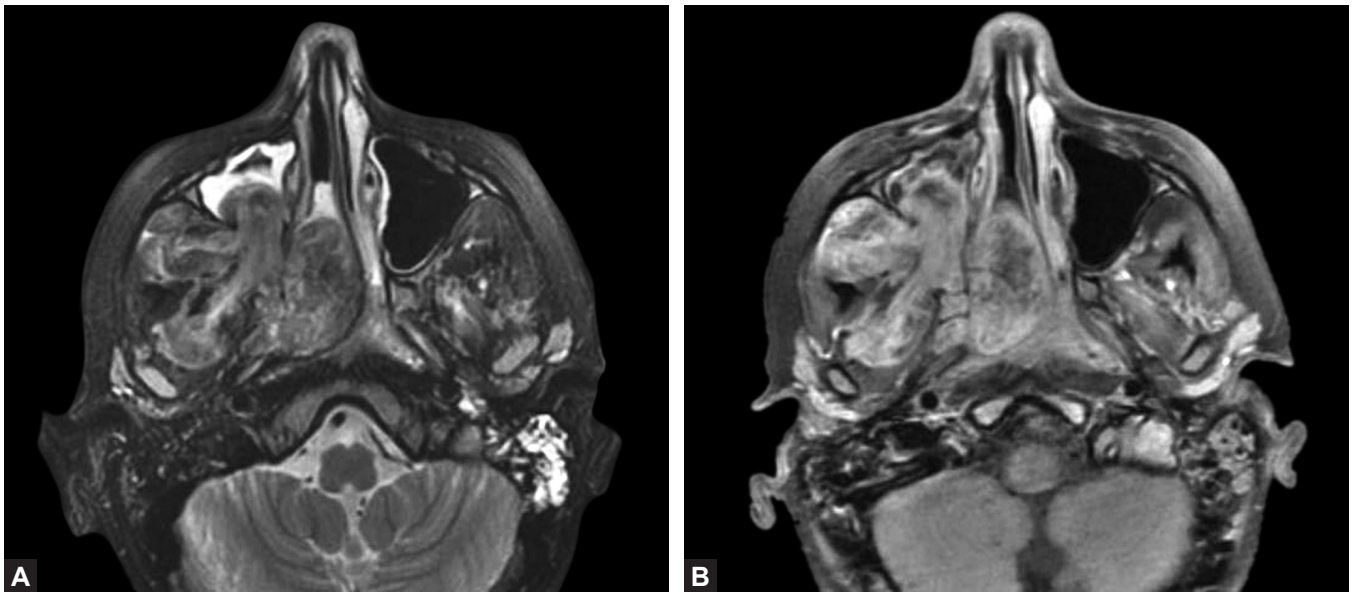
Diagnosis of a JNA begins with careful history and physical examination including flexible or rigid nasal endoscopy. Thorough examination of the nasal cavities and nasopharynx surrounding the sphenopalatine foramen is required. Because of their vascular nature, office biopsy is contraindicated.

Both contrast CT and MRI can define the lateral extent of tumor growth; however, MRI offers improved soft tissue resolution and can provide detailed vascular information (Figs. 32B.1A and B). CT may be required for surgical planning and intraoperative stereotactic navigation. Conventional angiography is useful to identify the feeding blood supply. In a review of cases, bilateral vascular supply was evident in 69% of cases and unilateral vasculature in the remaining 31%.[4] Preoperative angiography also affords the opportunity for embolization that can reduce intraoperative blood loss.

Multiple classification systems have been proposed for JNA, first by Sessions in 1981 and later modified by Radkowski (Table 32B.3).[5,6] Alternative staging is proposed by Fisch separating pterygomaxillary from infratemporal fossa spread. More recently, Snyderman has proposed a new staging system for JNAs that is based on the endoscopic endonasal techniques now utilized.[7]

### *Management*

JNAs are managed with either surgical resection or radiotherapy. Numerous surgical approaches including endonasal endoscopic, lateral rhinotomy, transpalatal, midface degloving, facial translocation, or Fisch infratemporal




**Figs. 32B.1A and B:** (A) T1 precontrast imaging of large right-sided juvenile nasopharyngeal angiofibroma involving the pterygopalatine and infratemporal fossas; (B) Postcontrast imaging of tumor.

**Table 32B.3:** Radkowski modification of the Sessions classification for JNA[6]

| *Stage* | *Description* |
|---|---|
| I | Tumor limited to the nose or sinus |
| II | Pterygomaxillary or infratemporal fossa tumor extension |
| IIIa | Intracranial but extradural tumor extension |
| IIIb | Intradural intracranial tumor extension |

(JNA: Juvenile nasopharyngeal angiofibroma).

fossa have been utilized. In stage I and II tumors, endoscopic surgery is associated with decreased blood loss, operative time, and hospital stay when compared to craniofacial approaches.[8] The authors prefer to ablate the tumor endoscopically using coblation. This technique allows excellent visualization, decreased intraoperative bleeding, and reduced operative time.[9]

Surgical cure rates are comparable despite approach. In a review of 42 consecutive JNAs, recurrence was identified in no endoscopic cases and 17% of craniofacial resection cases. However in this series more stage III tumors were treated with open resection.[10]

Radiation therapy is a surgical alternative in the management of JNA. In a series of 66 JNA patients receiving 30 cGy of external beam, tumor control was achieved in 80% of patient. Recalcitrant disease was successfully managed with additional radiation.[11] A second review of 22 children with JNA demonstrated tumor control in 91% of patients with 30–36.6 cGy of external beam radiation.[12] Residual disease in two children was managed with salvage surgery. Radiation treatment side effects included cataracts, central nervous system syndrome, and secondary basal cell carcinoma.

## Inverted Papilloma

### *Epidemiology and Pathophysiology*

Inverted papilloma (IP) is an uncommon entity in the adult population, and rarely reported in the pediatric literature.[13,14] IPs represent 0.5–4% of all nasal tumors.[15] The ingrowth of epithelium into the subepithelial stroma is characteristic of IP. The etiology for IP is unknown; however, multiple factors have been implicated including allergy, chronic rhinosinusitis with nasal polyposis, and human papilloma virus serotypes 6, 11, 16, and 18.[16] Malignant transformation to squamous cell carcinoma is reported with variable rates.

### *Presentation*

IP presents with a unilateral nasal mass causing obstruction, rhinorrhea, or epistaxis. Less commonly, IP can present with hyposmia or headaches.[17] In large IPs, symptoms may include proptosis, epiphora, and hypesthesia in the distribution of $V_2$.[18] Intranasal examination demonstrates a polypoid mass. The middle meatus is the most common site with attachment to the lateral nasal wall. Septal IP has also been reported in the pediatric literature.[13]

IP has a strong propensity for recurrence with rates reported from 0% to 78% depending on the method of excision, and as such a recalcitrant nasal mass after excision should raise concern for IP. Pediatric recurrence has been reported, but the rate of recurrence is unknown secondary to small case series. In a meta-analysis examining modern endoscopic excision via modified endoscopic medial maxillectomy, recurrence rates were 12% in patients undergoing endoscopic surgery compared to 20% with craniofacial resection.[19]

### *Workup*

Intranasal examination using anterior rhinoscopy demonstrates a mulberry polypoid mass routinely emanating from the middle meatus. Relative to an inflammatory nasal polyp, IPs may demonstrate increased vascularity and be more firm on palpation with nasal instrumentation. Purulent surrounding secretions are common. The extent of the mass should be further investigated using nasal endoscopy. Imaging allows qualification of bony erosion and invasion. Although bony erosion may be better elucidated by CT, MRI is superior for assessing tumor versus inspissated mucus.[20] Preoperative planning and stereotactic navigation may require CT.

Confirmation of pathology is completed with intranasal biopsy. When the origin of the mass is unclear, imaging prior to biopsy is prudent to rule out encephalocele. Depending on the age of the child, office biopsy may be possible. Characteristic pathologic findings include a thick epithelial covering comprised of squamous, respiratory, or transitional epithelium with extensive stroma invasion by hyperplastic epithelium. In cases with malignant transformation, anaplasia with cellular atypia, increased nuclear-to-cytoplasmic ratio, and a loss of structural polarity are noted.

Multiple staging guidelines exist for IP.[21,22] Previous staging systems were not well adopted for comparison of open and endoscopic techniques. As endoscopic

**Table 32B.4:** Cannady classification for IP[22]

| *Group* | *Description* |
|---|---|
| A | IP confined to the nasal cavity, ethmoid sinuses, or medial maxillary wall |
| B | IP with involvement of any maxillary wall (other than medial wall), frontal sinus, or sphenoid sinus |
| C | IP with extension beyond the paranasal sinuses |

(IP: Inverted papilloma).

techniques have evolved and shown similar recurrence rates, a revised staging is proposed and geared toward endoscopic resection (Table 32B.4).[23] In the event of squamous cell carcinoma, tumors are staged based on the American Joint Committee on Cancer guidelines.

### *Management*

IP is primarily managed with surgical approaches. Historically, IP has been managed with open medial maxillectomy via a lateral rhinotomy or midface degloving approach. More recently, endoscopic modified medial maxillectomy has been applied for the treatment of nonmalignant lesions with recurrence rates comparable to craniofacial resection. Intraoperatively, removal of the tumor attachment and drilling the adjacent bone is necessary to reduce the risk of recurrence.

Following surgery routine endoscopic and radiographic surveillance are required for recurrent disease. In patients unable to undergo surgery, successful tumor control can be achieved with radiotherapy.[24] Similarly, patients with identified squamous cell carcinoma may benefit from postoperative adjuvant radiotherapy.

## Nasopharyngeal Teratoma

### *Epidemiology and Pathophysiology*

Teratomas are congenital germ-cell tumors with variable composition of ectodermal, mesodermal, and endodermal components. The most common sites for head and neck teratomas are the neck and nasopharynx.[25] Epignathus refers to a nasopharyngeal teratoma with contributions from all three germ cell layers. The incidence of epignathus is estimated 1:35,000 to 1:200,000 births.[26]

Nasopharyngeal teratomas evolve as endoderm and mesoderm are entrapped with the rostral migration of ectoderm during formation of Rathke's pouch.[27] This process results in a nasopharyngeal collection of all three germ layers.

### *Presentation*

Most cases of nasopharyngeal teratoma are identified prenatally with polyhydramnios secondary to gastrointestinal obstruction. Associated findings may include a nasopharyngeal mass or cleft palate identified on ultrasound. Fetal MRI demonstrates a heterogeneous mass within the nasopharynx projecting into the nasal cavity and/or the oral cavity.

After birth, the growth of a nasopharyngeal teratoma may be dramatic. Fetal respiratory distress is imminent, and prenatal airway preparation is required. Delivery via ex utero intrapartum treatment (EXIT procedure) may allow for intubation or tracheostomy to be performed while the neonate remains on maternal circulation.

### *Workup*

Prenatal workup for polyhydramnios is integral in preventing neonatal respiratory distress. Following delivery, elevated serum alpha-fetoprotein is characteristic of teratomas.

### *Management*

The treatment for nasopharyngeal teratomas is surgical excision. Combined endoscopic and transoral approaches are utilized based on tumor location and extent. Serial AFP measurements may be used for surveillance. Although metastases are not reported, case reports of dramatic recurrence after excision infers malignant behavior in some tumors.[28]

# MALIGNANT TUMORS

## Rhabdomyosarcoma

### *Epidemiology and Pathophysiology*

Rhabdomyosarcoma (RMS) is the most common soft tissue malignancy involving the head and neck in children. RMS is a small blue-cell malignancy that is thought to arise from muscle progenitor cells. The annual estimated incidence of RMS is 6-8 cases per 1,000,000 with a slight predilection for males. There is a bimodal distribution for RMS routinely presenting from 2–6 years and 10–18 years.[29] Head and neck RMS is more common in the younger cohort. Orbital RMS is the most common site for head and neck RMS. However, parameningeal RMS may involve one of several subsites including nasal cavities, paranasal sinuses, infratemporal fossa, pterygopalatine fossa, middle ear, and mastoid.

**Table 32B.5:** Pretreatment staging for Intergroup RMS Study IV—Head and Neck[31]

| *Stage* | *Site* | *T (Invasiveness)* | *T (Size)* | *N* | *M* |
|---|---|---|---|---|---|
| I | Head and neck, excluding parameningeal | T1 or T2 | a or b | N0, N1, or Nx | M0 |
| II | Parameningeal | T1 or T2 | A | N0 or Nx | M0 |
| III | Parameningeal | T1 or T2 | B | N0, N1, or Nx | M0 |
| IV | All sites | T1 or T2 | a or b | N0 or N1 | M1 |
| *T Stage* | | | | | |
| T1: Confined to anatomic site of origin<br>T2: Extension<br>Ta: ≤ 5 cm in diameter<br>Tb: > 5 cm in diameter | | | | | |
| *N Stage* | | | | | |
| N0: Not clinically involved<br>N1: Clinically involved<br>Nx: Clinical status unknown | | | | | |
| *M Stage* | | | | | |
| M0: No distant metastasis<br>M1: Distant metastasis present | | | | | |

(RMS: Rhabdomyosarcoma).

### *Presentation*

RMS typically presents with a painless and enlarging mass. Symptoms are associated with location of the primary tumor. Within the nasal cavities and paranasal sinuses RMS presents with nasal obstruction, serous otitis media, epistaxis, and proptosis. Pain may be associated with orbital or anterior cranial fossa erosion. Central nervous extension may result in meningeal symptoms or cranial neuropathies.[30]

### *Workup*

Following identification of an intranasal mass, imaging with CT and/or MRI is warranted to examine tumor extent. Endoscopic biopsy is necessary for histological confirmation and tumor typing. Histologically, RMS is composed of cells resembling rhabdomyoblasts. Cytologically, cells stain for proteins associated with muscle fibers including desmin, vimentin, actin, and myoglobin. The three histologic subtypes of RMS are embryonal (75% of head and neck cases), alveolar (20% of head and neck cases), and pleomorphic (> 5% of pediatric head and neck cases).

Metastatic disease most commonly involves the lungs, bones, and CNS in parameningeal disease. As such, metastatic workup includes CT chest, bone scan, and lumbar puncture.

The Intergroup Rhabdomyosarcoma Study first reported staging for RMS in 1972. The current staging from Study IV is outlined in Table 32B.5.[31]

### *Management*

Locally isolated and resectable disease is treated primarily with surgical excision. Adjunct chemotherapy is necessary because of assumed micrometastatic disease at presentation. For locally advanced tumors with significant morbidity associated with resection, combination chemoradiotherapy is indicated. Persistent or recurrent disease may be salvaged with surgery. Through the efforts of the IRS protocols, 5-year mortality for parameningeal disease is 69%.

## Esthesioneuroblastoma

### *Epidemiology and Pathophysiology*

Esthesioneuroblastoma (ENB), also referred to as olfactory neuroblastoma, is a rare malignancy of the olfactory neuroepithelium. The incidence of pediatric ENB is 1 per 1,000,000 children.[32] A bimodal distribution exists during the second and fifth generations of life. There is no identified predilection for gender.

### *Presentation*

Symptoms associated with ENB are related to the size and location of the primary tumor. Nasal obstruction is the most common symptom followed by epistaxis and nasal discharge and anosmia. Tumor invasion into surrounding structures may cause neurologic and ophthalmological symptoms. Intracranial involvement is associated with

headaches and nausea. Orbital involvement is associated with proptosis, ophthalmoplegia, and blindness.

### Workup

Intranasal examination demonstrates a red or gray mass emanating from the olfactory cleft medial to the middle turbinate. Because of the possibility of encephalocele from the same location, imaging prior to biopsy is warranted. CT and MRI can be used to delineate bony and intracranial extension, respectively. MRI findings characteristic of ENB include hypointensity on T1 with contrast enhancement and T2 hyperintensity. Intracranial involvement is associated with cyst formation at the tumor–brain interface.[33]

Histological confirmation is required with endoscopic biopsy. ENB is a vascular tumor with propensity for bleeding with biopsy. ENB are small blue-cell tumors that stain positive for S-100 and neuron-specific enolase. Electron microscopy demonstrates true rosettes (Flexner–Wintersteiner rosettes) or pseudorosettes (Homer-Wright rosettes).

Staging for ENB was first reported by Kadish in 1976. Kadish A tumors are localized to the nasal cavity. Kadish B tumors extend to the paranasal sinuses. Kadish C tumors have extension beyond the nasal cavity and paranasal sinuses. Although a TNM staging does exist, Kadish staging remains the common reference in the literature.

### Management

Because of the limited case series management algorithms for pediatric ENB are variable. Endoscopic or endoscopic-assisted craniofacial resection with or without radiation is recommended for tumors with isolated disease.[34] Locally extensive and metastatic disease may benefit from adjuvant chemotherapy, but survival rates from the largest case series have failed to show a clear survival advantage.

## Nasopharyngeal Carcinoma

### Epidemiology and Pathophysiology

Nasopharyngeal carcinoma (NPC) is the most common nasopharyngeal malignancy, representing 33–50% of cases. There is a wide distribution of age at diagnosis; however, pediatric cases are most common during adolescence.

Undifferentiated NPC is endemic to southern China, Southeast Asia, and Alaska. In these cases, there is a strong association with Epstein–Barr virus (EBV). Genetic susceptibility has also been associated with *HLA-A2*, and *HLA-B-Sin2* loci.[35]

### Presentation

Unlike other nasal and sinus tumors, the most common presentation of NPC is a painless neck mass. Associated symptoms include nasal obstruction and discharge, epistaxis, and serous otitis media. Intracranial extension is associated with neuropathies of cranial nerves III, IV, V, and VI.

High index of suspicion in Asian and African American children with a level V neck mass warrants fiberoptic nasopharyngoscopy. Endoscopic examination may vary from a discrete mass to a large mucosalized bulging mass within the nasopharynx.

### Workup

Identification of a nasopharyngeal mass warrants both imaging and endoscopic biopsy. CT and MRI are both useful in workup to identify skeletal and soft tissue involvement. Metastatic workup may include chest and abdomen CT, bone marrow biopsy, and lumbar puncture to evaluate CNS involvement. EBV titers may be prognostic for recurrence surveillance.

NPC is histologically divided into three categories based on the World Health Organization classification. Type I NPC is a keratin producing squamous cell carcinoma. Type II NPC demonstrates a nonkeratinizing carcinoma. Most common in children, type III NPC is an undifferentiated carcinoma with undifferentiated round cells with prominent nucleoli.

### Management

Because of surgical morbidity associated with nasopharyngectomy, the mainstay treatment in the pediatric population is radiotherapy or combined chemoradiotherapy in advanced disease. Surgical salvage may be utilized for locoregional control after treatment failure. Because of a propensity for advanced disease in pediatric cases, 5-year survival rates are reported from 20% to 60%.[36]

## Sinonasal Lymphoma

### Epidemiology and Pathophysiology

Primary lymphoma involving the nasal cavity and paranasal sinuses is rare. Most pediatric sinonasal lymphomas are B-cell non-Hodgkin's lymphomas (NHL). In a review of 208 patients with NHL, 8 (3.8%) children were identified to have maxillary sinus primary disease.[37] Pediatric natural killer (NK)-/T-cell neoplasms, formerly referred to as midline lethal granuloma, are rarer and

represent 1.5% of all lymphomas. There is an increased incidence among Asian and Latin American ethnicities. Case reports of metastases from nonhead and neck T-cell lymphomas have also been reported in the maxillary sinus.[38]

### *Presentation*

Nasal obstruction is the most common symptom in sinonasal lymphoma. Constitutional symptoms including fevers, night sweats, and weight loss are identified in 62% of patients with sinonasal and Waldeyer's ring lymphomas.[39] Intranasal examination reveals a regular and mucosalized mass in B-cell lymphomas, whereas NK-cell lymphoma may manifest with a necrotic and eroding mass.

### *Workup*

Endoscopic biopsy and subtyping is needed in all cases. Imaging with CT of the primary site, chest, abdomen, and pelvis for metastatic workup is warranted. Furthermore, systemic workup including bone marrow aspirate, lumbar puncture, and peripheral blood work is needed for complete staging. The most common staging tool for NHL is the St. Jude or Murphy system that accounts for nodal disease and CNS involvement.

### *Treatment*

Treatment regimens for sinonasal lymphoma are based on the histologic subtypes. Primary therapy for B-cell lymphoma is chemotherapy alone. In invasive NK-/T-cell lymphoma, there is a role for radiation therapy or surgery because of local tissue destruction.

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CHAPTER

# 33

# Pediatric Sinonasal and Anterior Skull Base Surgery

***Dylan K Chan, Sanjay R Parikh***

## INTRODUCTION

Pediatric sinonasal and anterior skull base pathology represents a unique challenge for the otolaryngologist. As in adults, there has been a trend toward development of endoscopic and minimally invasive approaches to pediatric sinonasal disease, but given the anatomic limitations particular to pediatric and especially neonatal disease, knowledge of open approaches remains essential. In this chapter, we address surgical indications and techniques specific to pediatric sinonasal and anterior skull base disorders. These include congenital abnormalities, infectious and inflammatory conditions, and neoplasm.

## CONGENITAL NASAL CAVITY ANOMALIES

### Nasal Dorsal Mass

#### *Preoperative Workup*

A congenital nasal dorsal mass may represent a nasal dermoid, glioma, or encephalocele/meningocele.[1] Such lesions present either as an asymptomatic or infected nasal dorsal mass. Rarely, they present with intracranial infectious complications. Preoperative imaging with computed tomography (CT) and/or magnetic resonance imaging (MRI) is mandatory to evaluate for intracranial extension and can distinguish between a nasal dermoid, glioma, and encephalocele. Bony findings suggestive of intracranial extension include a patent foramen cecum, bifid crista galli, and widened cribriform plate, but any of these features can be present normally, especially in young infants. Soft-tissue characteristics include intrinsic signal characteristics of the mass itself, such as high intensity without gadolinium enhancement on T1-weighted MRI findings for dermoid, or T2 signal intensity for cerebrospinal fluid (CSF)-containing structures, a discrete soft-tissue tract from the mass connecting to the dura, or a frank intracranial mass. Complete absence of any of these concerning findings permits an operative plan limited to resection of the mass itself; any concern for intracranial extension requires preoperative consultation with neurosurgery and preparation of the patient for the possibility of frontal craniotomy for intracranial clearance.

#### *Operative Technique*

The extracranial component may be excised via a direct approach through an incision in the vertical midline or horizontal glabellar skin crease, or through an external rhinoplasty approach. Decision making regarding choice of technique will vary based on pathology and surgeon preference. In general, hidden incisions via intranasal or external rhinoplasty techniques are preferable for benign lesions of the nasal dorsum that may be readily accessible. Malignant or recurrent nasal dorsal lesions may be better suited with a direct incision for maximal exposure. It is unclear if one incision is better than the other to reduce postoperative comorbidities such as recurrence. Cosmetic results will be enhanced with open rhinoplasty techniques for benign pathology such as with a nasal dermoid cyst as long as any associated pit is removed.

The direct approach has the advantage of speed, convenience if a skin pit associated with the dermoid cyst needs to be excised as well, and good visualization; the disadvantage is a visible scar. The external rhinoplasty approach takes longer and may result in irregularities in

redraping of the skin envelope, but overall is cosmetically superior owing to the more-hidden columellar and intranasal incisions. Both techniques permit adequate exposure of the underlying nasal dorsal bone, which must be explored to rule out the presence of a medially directed tract.

If a very limited tract extends through the nasal dorsal bone into the nasal cavity, this may be excised and osteotomies performed via any of the external approaches. Transnasal endoscopic approaches through intercartilaginous and membranous incisions and division of the upper lateral cartilages from the septum have also been described for complete excision of nasal dermoid and subsequent exploration of a dural stalk.[2] Ultimately, biopsy and frozen section of the dural attachment is necessary to determine the necessity for intracranial exploration. Frank intracranial extension subsequently requires a coronal approach and frontal craniotomy. Finally, complete excision of combined intracranial and extracranial dermoid components has been described using a completely endoscopic anterior skull base technique, with reconstruction using autogenous fascia and pedicled nasoseptal flap. If extensive bony work and reconstruction is performed, an external nasal splint can be applied for 1-week postoperatively. Intranasal splints are not required, even if a nasoseptal flap reconstruction is performed.

### *Postoperative Follow-up*

If no intracranial component is seen or suspected upon preoperative imaging and intraoperative exploration of the nasal dorsal bone, clinical observation alone for recurrence of the subcutaneous cyst may be employed. Otherwise, an interval screening MRI at 3–6 months is advisable to evaluate for recurrent disease.

## Nasolacrimal Duct Cyst

Nasolacrimal duct cysts, which may be unilateral or bilateral, occur as a result of membranous obstruction and cystic dilation at the valve of Hasner at the inferior end of the nasolacrimal duct in the inferior meatus. These cysts can lead to significant nasal airway obstruction and respiratory distress in neonates.

### *Preoperative Workup*

Nasolacrimal duct cysts are readily identified on clinical examination, and do not require additional imaging unless there is clinical suspicion for a synchronous lesion. In addition to anterior rhinoscopy, nasopharyngolaryngoscopy should be performed to rule out synchronous lesions, especially choanal atresia. If concomitant ophthalmologic abnormalities other than mild epiphora are noted, an ophthalmology consult should be obtained. In cases of routine nasolacrimal duct cysts, however, such consultation is typically not necessary.

### *Operative Technique*

Treatment of nasolacrimal duct cyst focuses on its decompression and marsupialization; complete excision is not typically required. In the healthy neonate without respiratory distress (usually unilateral), or in those intubated in the intensive care unit (ICU) (often bilateral), this may be done at the bedside. After application of topical anesthetic, the cyst is visualized directly or endoscopically, grasped with a cup or through-cut forceps, and marsupialized and decompressed simultaneously. In situations where greater airway control is desired, or if the cyst recurs after bedside management, the procedure may be done in the operating room under general anesthesia using hand instruments, powered microdebrider, or laser for definitive decompression and marsupialization. Because nasolacrimal duct cysts are typically isolated anomalies at the valve of Hasner at the inferior end of the nasolacrimal duct, the rest of the lacrimal drainage system is typically normal, and marsupialization alone is successful. Lacrimal duct probing is not necessary for primary cases. Should the cyst recur, or should there be continued epiphora even after successful marsupialization, ophthalmology evaluation and treatment should be sought.

### *Postoperative Follow-up*

Babies typically have immediate relief of nasal congestion after cyst marsupialization. Routine clinical follow-up for observation of recurrence can be performed; no imaging is necessary.

## Piriform Aperture Stenosis

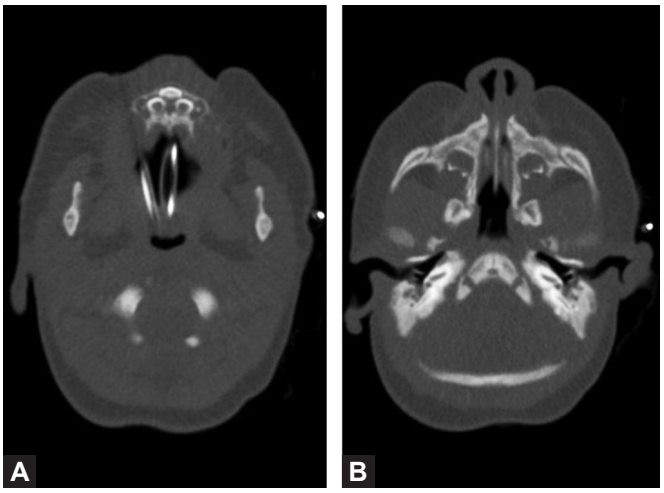
Piriform aperture stenosis is a rare cause of neonatal respiratory failure related to nasal airway obstruction. It refers to bony narrowing at the anteriormost bony margin of the nasal cavity just anterior to the inferior turbinates. Congenital piriform aperture stenosis can occur in isolation, but a significant fraction is seen as part of a spectrum of midline craniofacial developmental defects. This can be as mild as a single central mega-incisor, or as significant as holoprosencephaly.

### *Preoperative Workup*

There are no clear size criteria for operative repair for piriform aperture stenosis. Initial management should be with conservative measures to decrease mucosal edema, including a brief trial of topical decongestant such as oxymetazoline or phenylephrine (no longer than 3 days), topical steroid such as dexamethasone or prednisolone drops (no longer than 1–2 weeks), and nasal saline. Use of a McGovern nipple (a large nipple with the end cutoff) can encourage mouth breathing. These techniques can provide time to allow for growth of the facial skeleton and nasal airway, so as to avoid surgical intervention. However, should the child have persistent symptomatic nasal obstruction causing respiratory distress, failure to thrive, or significant feeding difficulties despite maximal medical management, surgical repair is indicated. Preoperative CT scan is necessary to assess the width of the piriform aperture, single central mega-incisor, and holoprosencephaly (Figs. 33.1A and B). Careful attention should be paid to concurrent dysmorphic features, and genetic analysis considered. The presence of comorbidities does not necessarily change the approach to management, except that children with more significant development abnormalities may have poorer prognosis even after successful management of the piriform aperture stenosis. All parents should be counseled as to the risk of re-stenosis, necessity for stent placement or revision surgery, and nasolacrimal duct injury.

### *Operative Technique*

The piriform aperture is exposed through a sublabial approach. Soft tissue is elevated in a subperiosteal plane to expose the face of the maxilla and inferior half of the piriform aperture without violating the mucosa of the nasal floor. The lateral nasal walls are exposed posteriorly up to and including the nasolacrimal ducts. The lateral piriform aperture and lateral nasal wall bone is drilled to widen the opening; this may be carried out as far as to expose the soft tissue of the nasolacrimal duct without violating it. The nasal spine and anterior maxillary crest may also be narrowed. Controversy exists as to whether intranasal stents are effective in preventing restenosis. Bilateral stenting carries the risk of anterior septal and columellar necrosis. Unilateral stenting is an option to maintain at least a unilateral airway, with the option for delayed treatment of any resulting septal deviation or nasal asymmetry later in life. Stents, when placed, can be fashioned with an uncuffed endotracheal tube with the milled end in the nasopharynx. No smaller than a 3.0 tube should be used, as smaller tubes are very difficult to keep patent. The stent should be secured with a stitch through the membranous septum, ensuring a downward pull on the stent toward the nasal floor so as to avoid the tendency of the stent to ride superiorly and cause pressure necrosis of the alar rim and soft tissue triangle of the nostril. Stents can be maintained for 4–6 weeks with assiduous irrigation and suctioning to ensure its patency. Our preference is for stentless repair, which has the advantage of simplicity of care, avoidance of pressure necrosis, and maintenance of nasal symmetry.




**Figs. 33.1A and B:** Piriform aperture stenosis. Axial noncontrast CT scans at the level of the anterior maxilla (A) and nasal cavity (B) demonstrate a case-specific associated single central mega-incisor (A) and stenosis of the piriform aperture (B).

### *Postoperative Follow-up*

Patients can usually be extubated immediately after this procedure, or shortly thereafter in the ICU. Systemic and topical corticosteroids can reduce edema and promote airway patency. If a stent is used, ample nasal saline irrigation and suctioning of the stent, but not beyond, is necessary. Revision surgery may be necessary should restenosis occur.

## Choanal Atresia

Failure of the bucconasal membrane to canalize in utero leads to either unilateral or bilateral membranous or bony-membranous atresia of the choanal openings.

### *Preoperative Workup*

Bilateral choanal atresia is typically suggested by respiratory failure and cyanosis relieved by crying, whereas unilateral atresia may manifest as mild respiratory distress

in infancy or persistent unilateral nasal congestion and rhinorrhea as an older child. Diagnosis is suggested by a failure to pass catheters through the affected nasal cavity and confirmed by flexible bedside endoscopy and non-contrast CT scan (Fig. 33.2). Given the association of the choanal atresia with other congenital anomalies, particularly cardiac and renal defects in CHARGE, a full preoperative workup for these conditions, including echocardiogram and renal ultrasound, should be performed prior to surgery. Attempts can be made to manage neonates with bilateral choanal atresia with an oral airway or McGovern nipple, but these babies typically require surgery within the first week of life to avoid prolonged intubation. Children with unilateral atresia can be repaired electively at an older age as symptoms dictate.

CHARGE syndrome is a particular challenge; such children often continue to have significant airway obstruction even after successful repair of the choanal atresia and eventually require tracheotomy. Many children with CHARGE have a particularly low roof of the nasopharynx; these children, as well as those without CHARGE that have this anatomic configuration, are at higher risk for restenosis and operative failure. In cases where the anatomy is particularly unfavorable, or other synchronous airway lesions are present that would likely necessitate tracheotomy, one can consider early tracheotomy and delayed repair of the choanal atresia.

### *Operative Technique*

We recommend performing a direct laryngoscopy and bronchoscopy at the time of choanal atresia repair to fully assess the airway. This permits the identification of synchronous airway lesions, which are often associated with CHARGE syndrome, and also provides valuable information should the child have persistent respiratory distress after choanal atresia repair. Children with multiple levels of upper-airway obstruction, gastroesophageal reflux disease, or unfavorable anatomy, particular a small, shallow nasopharynx, are at higher risk for surgical failure.

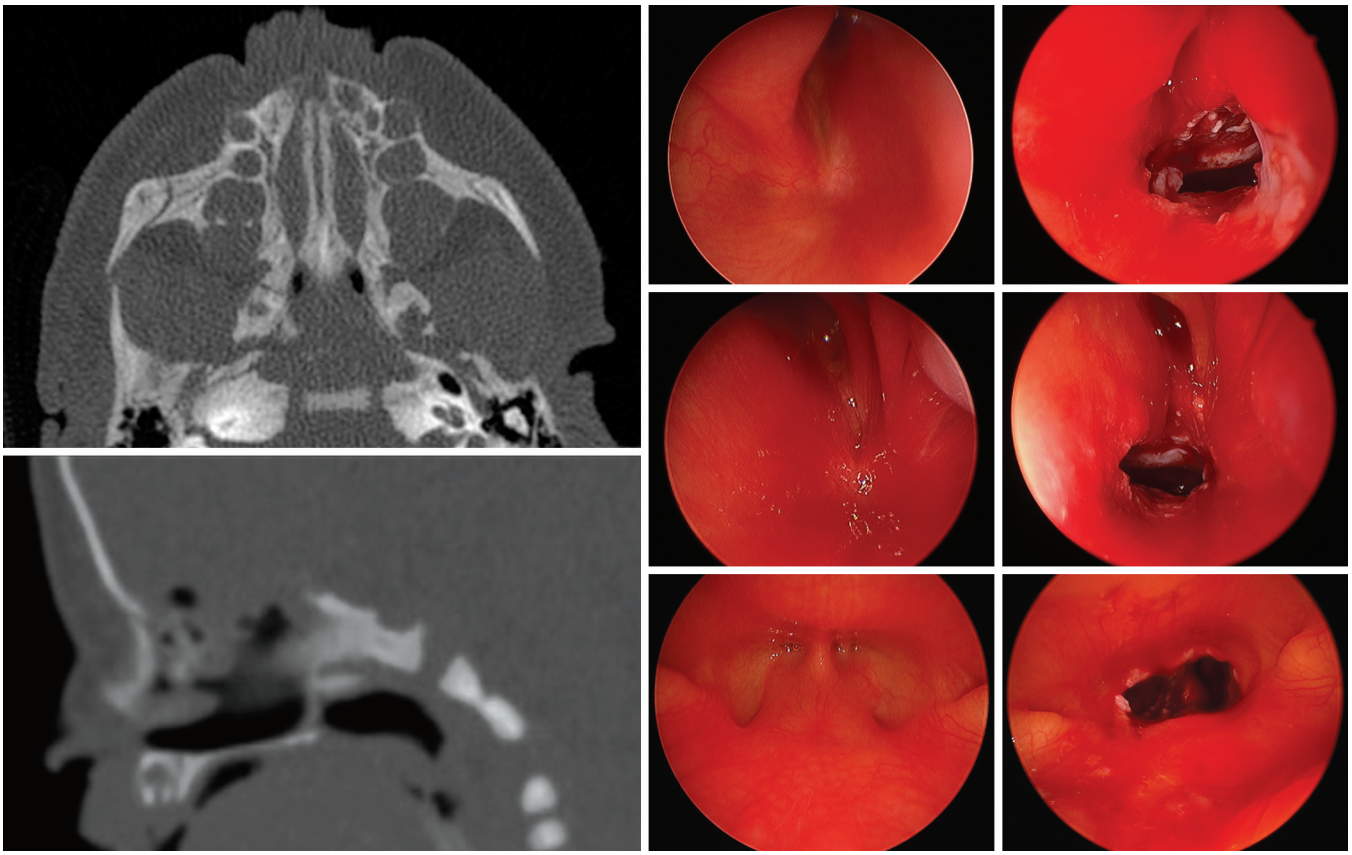


**Fig. 33.2:** Choanal atresia. Axial (top left) and sagittal (bottom left) CT images demonstrating bilateral choanal atresia. Pre- (middle column) and post- (right column) operative endoscopic images of the right (top) and left (middle) choanae from the nasal cavity, and 120° endoscopic views from the oropharynx showing the nasopharyngeal view of the posterior choanae (bottom) are shown.

Transpalatal, sublabial-transnasal, transantral, and trans-septal approaches have been described for choanal atresia repair, but are mostly of historical interest. With the advent of endoscopic instrumentation, endoscopic transnasal approaches have become standard[3] (Fig. 33.2). Image guidance can be considered, but is usually difficult to register with sufficient precision in neonates, and visual landmarks are reliable, so we do not routinely use it. Surgery consists of three phases—visualization of the defect; initial opening of the choana; and widening of the choanal aperture. Visualization is accomplished with a transnasal 2.7-mm 0° endoscope, which is typically an appropriate size for a neonatal nose. A 120° endoscope can also be used through the mouth with appropriate tongue and mouth retraction using a mouth gag to visualize the nasopharynx and posterior aspect of the choanae. The initial opening can be performed under direct visualization with the endoscope using a 7-French suction directed inferior and medial toward the atretic plate, or under visualization from behind with the 120° endoscope and ureteral sounds in the nasal cavity. Once the initial opening is made, it is widened with either standard manual or powered endoscopic rhinologic instruments. The narrowest portion of the choana may be widened by performing a posterior septectomy to achieve a confluent choanal opening, and by using an endoscopic drill to lateralize the medial pterygoid component of the choanae. As with piriform aperture stenosis, intranasal stent placement is controversial, with expert opinions ranging from completely stentless repair to unilateral or bilateral stent placement for many weeks.

### *Postoperative Follow-up*

Postoperative management is similar to that for piriform aperture stenosis, though the presence of intranasal circumferential incisions makes the risk for restenosis and subsequent need for revision surgery higher. Intranasal topical antibiotics, steroids, and saline are important, though caution must be taken with topical steroid drops in neonates, as systemic absorption is significant and can lead to steroid toxicity.

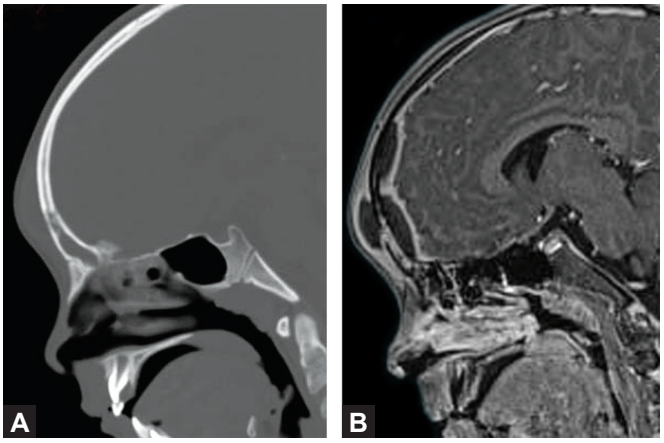
## PEDIATRIC RHINOSINUSITIS

### Acute Rhinosinusitis

Recurrent acute rhinosinusitis is very common in the pediatric population, and rarely requires surgery. However, extension of acute sinusitis into surrounding structures often necessitates surgical intervention. The most common pathways of extension are orbital, frontal subperiosteal, and intracranial. The first two of these are thought to occur primarily as a result of direct extension through bone and are usually found directly adjacent to areas of sinus opacification. Intracranial extension, on the other hand, is thought to occur via diploic veins in the frontal sinus, such that the focus of intracranial involvement may not be directly adjacent to the frontal sinus, but is still likely to be related to frontal sinusitis.

### *Preoperative Workup*

Definitive identification of the involved extra-sinonasal structures is provided by contrast-enhanced CT (for orbital and frontal subperiosteal disease) and MRI (for intracranial involvement) (Figs. 33.3A and B). Ophthalmologic consultation should be obtained for orbital involvement, to assess visual acuity, intraocular pressure, and extraocular movements. Neurosurgical involvement is necessary for extradural and intracranial disease. Discussion can be had with the consulting service regarding the option of initial medical management with intravenous antibiotics, systemic corticosteroids, topical nasal decongestion, and saline irrigation, which can be considered in cases of mild extra-sinonasal involvement, especially if the child is antibiotic-naïve. If any visual or mental status changes are present, however, or if no improvement is noted after 24–48 hours of conservative management, operative intervention is indicated.




**Figs. 33.3A and B:** Acute frontal rhinosinusitis with intracranial epidural abscess. Noncontrast CT (A) and gadolinium-enhanced T1 MRI (B) sagittal images are shown. The intracranial and frontal subperiosteal abscesses were drained directly via frontal burr hole and brow incision, respectively. Endoscopic frontal sinusotomy was performed concurrently.

### *Operative Technique*

The goals of operative intervention are twofold: (1) to irrigate and re-establish drainage pathways within the sinonasal cavity, particularly within the sinuses directly adjacent to the site of extrasinonasal involvement and (2) to directly drain the extra-sinonasal abscess, if present. Computer-guided navigation is a useful aid. The first goal is achieved through routine sinonasal endoscopic techniques for total ethmoidectomy (for orbital involvement) and frontal sinusotomy (for frontal subperiosteal and intracranial involvement). Acute inflammation can make definitive identification of the frontal recess difficult; in such cases, a mini-trephination can be performed and irrigation inferiorly through the frontal recess used to aid in its identification from below. Drainage of an orbital subperiosteal abscess can be achieved endoscopically[4] by removing the lamina papyracea after total ethmoidectomy, or through an external incision, either through the lid for a superior abscess or through a Lynch incision for a medial abscess; in neither case should the periorbita be violated. In general, small (< 6–10 mm), medial subperiosteal abscesses in younger children (< 9 years of age) with minimal proptosis (< 2 mm) and gaze restriction do well with endoscopic drainage alone. Any of these approaches is acceptable for entry through the periorbita and drainage of an orbital abscess unless there is evidence for extension lateral to the vertical plane of the optic nerve; in such cases, direct access to the orbit, such as achieved through a transconjunctival or lateral orbitotomy approach, may be required. A frontal subperiosteal abscess may be simply needle aspirated or drained directly through a small brow incision with placement of a Penrose drain. Intracranial abscesses may be drained concurrently by neurosurgery.

In general, the younger the child, the more difficult it can be to achieve safe endoscopic access due to restricted working area in light of the acute inflammation. Regardless of age, however, we first attempt endoscopic drainage, which restores natural intranasal drainage pathways and treats the source of the infection, and only resort to open approaches should the endoscopic approach fail.

### *Postoperative Follow-up*

The patient should be maintained on intravenous antibiotics and nasal saline irrigations. Use of postoperative systemic corticosteroids and topical steroids and antibiotics may be considered. Duration of intravenous antibiotic therapy depends on the severity and location of the initial infection, with intracranial abscess often requiring consultation with infectious disease and prolonged intravenous therapy with periodic MRI to follow the intracranial component. Typically, so long as continued clinical improvement is noted, the patient may be transitioned to oral antibiotics and discharged home with close otolaryngologic follow-up. Imaging is only obtained as indicated by worsening clinical signs or symptoms.

## Chronic Rhinosinusitis

### *Preoperative Workup*

True chronic rhinosinusitis, especially with polyposis, in a child is relatively unusual; in such cases, one should consider a workup for systemic disorders such as allergy, gastroesophageal reflux disease, primary immunodeficiency, cystic fibrosis (CF), and primary ciliary dyskinesia. Initial medical management with topical nasal steroid, systemic allergy treatment and antireflux management can be attempted. As the most common cause for nasal obstruction and chronic rhinorrhea in children is adenoidal hypertrophy, evaluation and surgical treatment of this should be performed prior to any consideration of more extensive sinus surgery. Only with persistence of symptoms despite maximal medical management and initial conservative adenoidectomy, and radiographic evidence of chronic mucosal inflammation and sinus opacification, should sinus surgery be considered in a child.[5] Conditions such as allergic fungal sinusitis, invasive fungal sinusitis, mucocele, antrochoanal polyp, and Samter's triad do present in children, and should be managed as they are in adults.

### *Operative Technique*

Functional endoscopic sinus surgery for chronic rhinosinusitis in children is largely similar to that performed in adults. Depending on the age of the child, the frontal and sphenoid sinuses may be not developed or underdeveloped, but otherwise the principles of mucosal preservation, restoration, or expansion of natural drainage pathways are consistent with those described in adults. Initial concerns regarding interference with midface growth by sinus surgery, suggested by animal studies, have since been repudiated by prospective studies in children.

### *Postoperative Follow-up*

Straightforward functional endoscopic sinus surgery can be performed on an outpatient basis. Postoperative antibiotics, systemic corticosteroids, and topical nasal saline,

steroid, and antibiotic drops are typically prescribed. Nasal saline irrigations are helpful, but infrequently tolerated by children. Furthermore, most children will not tolerate extensive endoscopy or even minimal debridement in the clinic. Routine "second look" endoscopy under anesthesia for these purposes has been the standard in the past, but is no longer considered to be necessary. Prospective studies have demonstrated a lack of value for "second look" endoscopy.

## Cystic Fibrosis

Children with CF almost universally have evidence of sinusitis on CT or endoscopy, but only a fraction of them have symptoms associated with it that affect their quality of life.[6] Some postulate that sinus bacterial colonization can be detrimental to pulmonary disease both in the context of active pulmonary disease and potential for reseeding after lung transplant, but these associations have not been definitively established. Primary ciliary dyskinesia is also associated with poor mucociliary clearance, and is typically managed similarly to CF with respect to sinonasal disease.

### *Preoperative Workup*

Indications for surgery are controversial, but center on symptom improvement and decreasing overall burden of bacterial disease.[7] Anesthetic complications after sinus surgery are no higher for the CF population compared to non-CF controls, and surgery can be performed on an outpatient basis, though some pulmonologists advocate preoperative pulmonary optimization and postoperative hospital admission. Orbital and intracranial complications of acute sinusitis are rare, though mucocele associated with chronic sinusitis is fairly common.

### *Operative Technique*

Children with symptomatic chronic sinusitis associated with CF will often ultimately require multiple procedures. Disease is typically characterized by profuse polyposis and relatively poorly developed sinus cavities owing to lifelong poor aeration and multiple surgeries. Surgery is directed toward debriding affected tissue and creating large confluent cavities that will be able to drain appropriately despite the impaired mucociliary clearance intrinsic to the disease, as well as to improve irrigation potential. Image navigation is a particularly helpful adjunct given the variable anatomy, especially in revision cases. Limited endoscopic medial maxillectomy (mega-antrostomy, with takedown of the midportion of the inferior turbinate to facilitate gravity-driven drainage of the maxillary sinus)[8] has been described as an effective technique to treat refractory cases. Additionally, some practitioners advocate placement of irrigation catheters in the maxillary sinus at the time of surgery and secured outside the nose, allowing for antibiotic irrigation for a few days following surgery.

### *Postoperative Follow-up*

Follow-up is as for routine chronic sinusitis, except for the high rate of recidivism and requirement for revision surgery as dictated by return of symptoms.

# PEDIATRIC SINONASAL NEOPLASM

With the exception of juvenile nasopharyngeal angiofibroma (JNA), sinonasal neoplasms are exceedingly rare in the pediatric population. For the most part, when they occur they are managed similarly as in the adult. Particular conditions and considerations specific to the pediatric population are delineated here.

## Juvenile Nasopharyngeal Angiofibroma

### *Preoperative Workup*

Diagnosis of JNA is typically made from imaging alone without definitive preoperative biopsy (Fig. 33.4). Given the highly vascular nature of the tumor, type and crossmatch for packed red blood cells is necessary even for small tumors. High-stage tumors, particularly those with involvement of the internal carotid system, should have postoperative ICU monitoring for bleeding and neurologic monitoring. Preoperative embolization by interventional radiology decreases intraoperative blood loss, and should be performed no more than 48 hours prior to surgery, lest collateral vasculature develops. Typically, only contributions from the external carotid system (most typically supply through the internal maxillary artery) can be embolized, whereas internal carotid feeders (usually through the vidian artery) are much more difficult to safely embolize. Residual blood supply after embolization is an important predictor of intraoperative blood loss and postoperative complications. Grading systems by Chandler, Fisch, Sessions, and Radkowski have historically been used to describe extent of disease, but a more recently developed system takes into account both tumor extension and postembolization residual vascularity, and has excellent predictive value for perioperative outcomes for endoscopic resection[9] (Table 33.1).

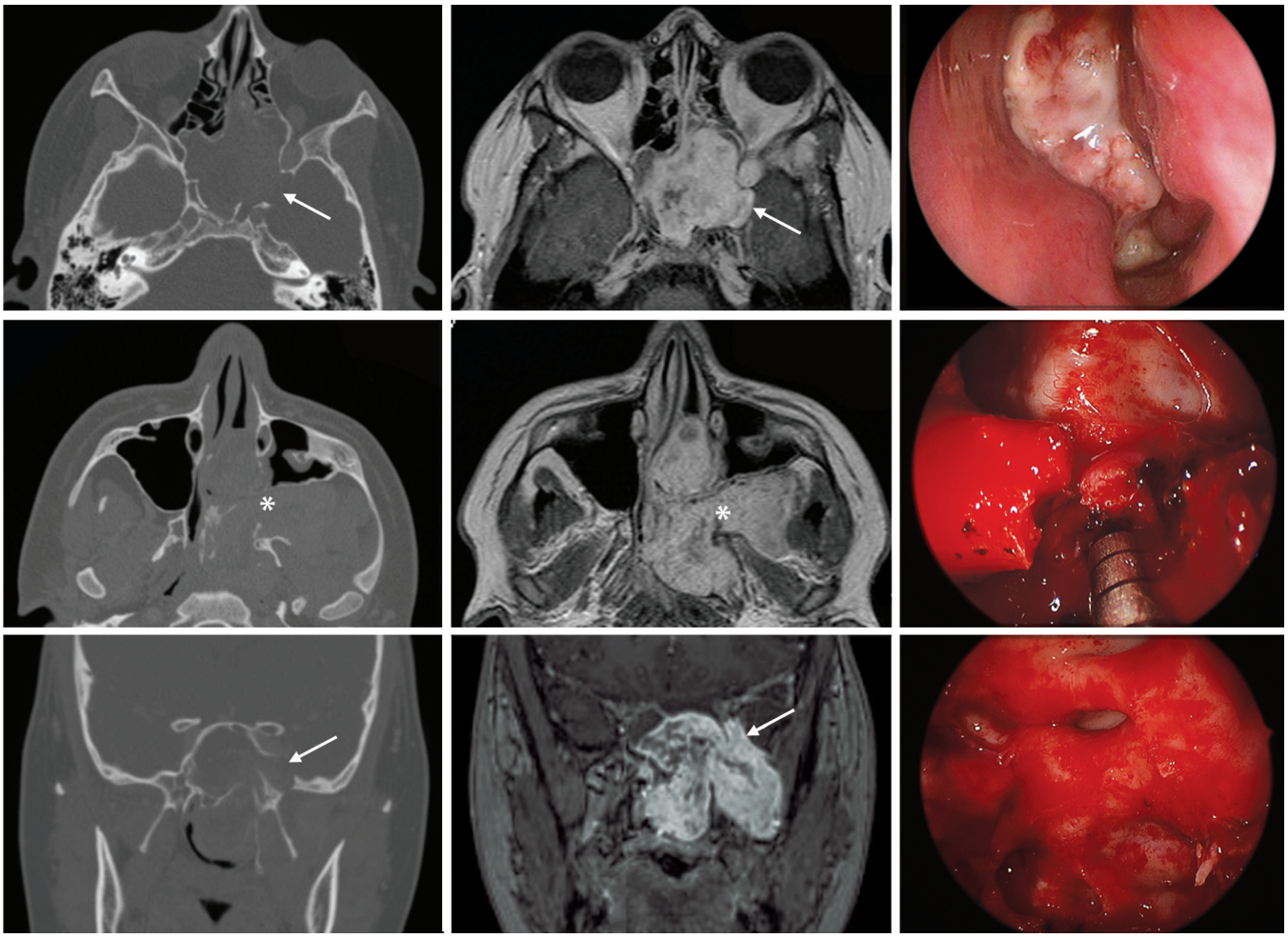


**Fig. 33.4:** Juvenile nasopharyngeal angiofibroma, stage III. Noncontrast CT (left column) and T1 gadolinium-enhanced MRI (right column) axial midorbit (top), axial midmaxillary sinus (middle), and coronal images demonstrate lateral sphenoid skull-base effacement at the medial temporal lobe (arrow), and widening of the pterygomaxillary fissure and sphenopalatine foramen (asterisks). Right column shows endoscopic intraoperative views of the tumor in the nasal cavity (top), lateral sphenoid defect (middle), and opticocarotid recess after tumor removal (bottom).

**Table 33.1:** Staging system for juvenile nasopharyngeal angiofibroma

| *Stage* | *Description* |
|---|---|
| I | Nasal cavity, medial pterygopalatine fossa |
| II | Paranasal sinuses, lateral pterygopalatine fossa; no residual vascularity |
| III | Skull base erosion, orbit, infratemporal fossa; no residual vascularity |
| IV | Skull base erosion, orbit, infratemporal fossa; residual vascularity |
| V | Intracranial extension, residual vascularity; (M: Medial extension; L: Lateral extension) |

Adapted from Snyderman et al.[9]
This staging system provides improved prediction of intraoperative blood loss, need for reoperation, and tumor recurrence, taking into account in particular primarily endoscopic endonasal approaches for resection.

## *Operative Technique*

Historically, JNA was resected using a variety of open approaches tailored to the extent of disease as determined by preoperative imaging. These included lateral rhinotomy, midfacial degloving, transpalatal, transmaxillary, Le Fort I, infratemporal, orbitocraniozygomatic, and subtemporal craniotomy approaches. With the development of improved endoscopic instrumentation and CT and MRI-based intraoperative navigation systems, there has been a trend toward endoscopic-assisted and completely endoscopic approaches[10] (Fig. 33.4). Comparable surgical outcomes in terms of intraoperative blood loss, perioperative complications, and tumor recurrence have been described with endoscopic approaches, with significantly improved length of hospital stay and postoperative

morbidity. General principles of endoscopic sinonasal and skull base surgery and the limits of endoscopic excision are described elsewhere, and apply equally to JNA. Two-surgeon, four-handed technique is recommended for all but the smallest tumors.

Particular surgical considerations are the highly vascular nature of the tumor and its characteristic blood supply pattern. Because of the tumor vascularity, centripetal dissection is recommended, with wide exposure initially and dissection and ligation of major arterial contributions prior to debulking of the mass. If initial debulking may be necessary for exposure, and can be performed with suction electrocautery, bipolar radiofrequency, or powered microdebrider. There are two major vascular pedicles. The first enters laterally from the internal maxillary artery and external carotid through the pterygopalatine fossa and sphenopalatine foramen. This contribution is often embolized preoperatively, but should also be directly ligated intraoperatively. Additionally, infiltration with local anesthetic containing epinephrine through the greater palatine foramen can provide additional hemostasis within the pterygopalatine fossa. For small, stage I tumors without significant lateral extension into the pterygopalatine fossa, the sphenopalatine artery may be exposed at its exit through the sphenopalatine foramen, which is located by incising the mucosa of the lateral nasal wall approximately 1 cm anterior to the basal lamellar insertion of the middle turbinate, elevating mucosa posteriorly, and identifying the crista ethmoidalis. The sphenopalatine foramen will lie just posterior to the crista ethmoidalis. Once the sphenopalatine artery and foramen are identified, a Kerrison rongeur can be used to remove bone of the posterior maxillary sinus wall starting at the foramen and moving laterally. As much of the posterior wall can be removed to identify the lateral extension of the tumor and artery, such that the artery is ligated lateral to the tumor. Alternatively, for larger tumors that clearly extend laterally beyond the sphenopalatine foramen an endoscopic medial maxillectomy with wide exposure and subsequent takedown of the posterior maxillary sinus wall can be performed. Dissection through the fibrofatty tissue usually reveals the artery, which can be ligated with multiple endoscopic clips at its lateralmost extent. Care must be taken to identify and preserve the maxillary nerve ($V_2$), which courses through the pterygopalatine fossa, usually superior and deep to the internal maxillary artery as it travels toward foramen rotundum.

The second major arterial contribution enters posteriorly near the face of the sphenoid through the vidian canal, which can be exposed with a posterior septectomy, contralateral wide sphenoidotomy, and ipsilateral posterior ethmoidectomy and partial resection of the middle and superior turbinates. It is typically not possible to directly ligate these contributions owing to obstruction by the tumor mass, but centripetal tumor removal toward the face of the sphenoid permits controlled dissection and hemostasis as this vascular pedicle is approached within the vidian canal. The endoscopic drill can be used to follow the vidian canal posteriorly to ensure complete tumor removal at this site, which is to most typical for persistent disease. Bleeding in this region is common, and can be controlled with hemostatic foams, packing, and judicious electrocautery.

Additional access may be required for lateral and superior extension toward the infratemporal fossa and superior orbital fissure, respectively. This may be achieved via a sublabial Caldwell-Luc approach, or an anterior septal window, which provides an improved angle of access and instrumentation laterally.

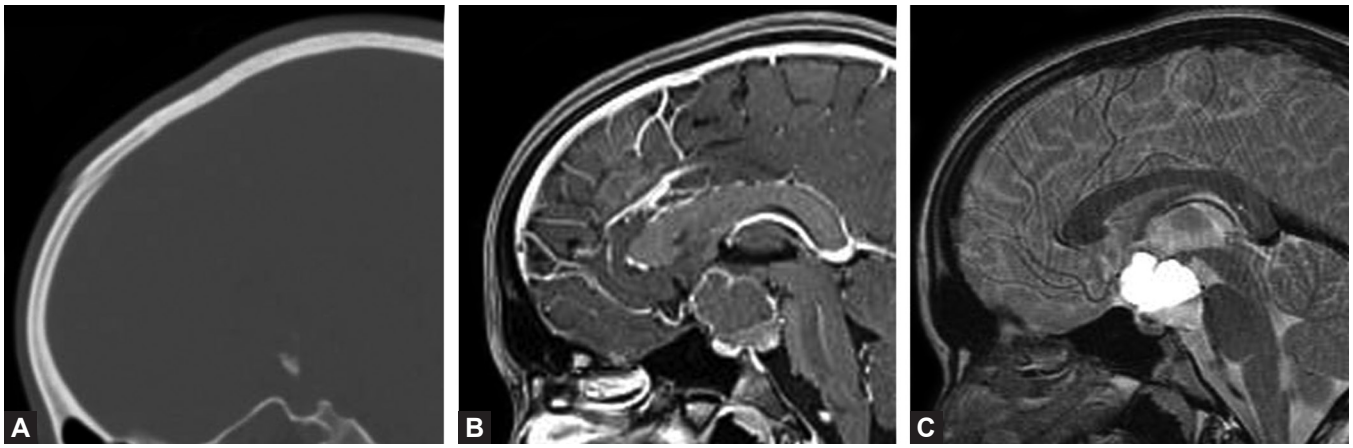
Need for reconstruction of a skull base defect can be predicted somewhat based on preoperative imaging; if it is thought to be necessary, an ipsilateral or contralateral nasoseptal flap should be elevated and placed in the nasopharynx for use or replacement at the end of the case as necessary. Packing of the operative site is determined on a case-by-case basis depending on the concern for postoperative hemorrhage. For stage III and IV tumors, multiple rounds of surgery and embolization may be required.

### *Postoperative Follow-up*

Because of the typically extensive exposure and dissection required for tumor extirpation, saline irrigation and clinic debridement is advocated to maintain sinonasal hygiene and promote remucosalization. Tumor surveillance is typically performed by nasal endoscopy and MRI at 3–6 months after surgery and thereafter as suspicion warrants.

## Other Skull Base Lesions

Skull base pathology is rare in children, and can be classified as neoplastic/cystic (craniopharyngioma (Figs. 33.5A to C), Rathke cleft cysts, chordoma, or pituitary adenoma) or structural (CSF leak, encephalocele or meningocele), and are approached surgically as they are in adults. A major concern with traditional open approaches to the skull base in children is disruption of growth centers and subsequent altered craniofacial development. Thus, pediatric skull base surgery has followed the trend of increasing use of endoscopic endonasal techniques for extirpation




**Figs. 33.5A to C:** Craniopharyngioma. Noncontrast CT (A), T1 gadolinium-enhanced MRI (B), and T2 MRI (C) sagittal images are shown. Drainage of the associated cyst was performed via an endoscopic trans-sphenoidal approach, with immediate relief of optic nerve compression.

and reconstruction, which theoretically can lead to less disruption of craniofacial growth centers compared to open approaches. Endoscopic skull base surgery has particular challenges in children, owing primarily to the small size of the operative field and relative under-pneumatization of the paranasal sinuses; however, the majority of pathology occurs in adolescents, whose sinonasal anatomy approaches that of adults.

Early case series have demonstrated the efficacy and safety of endoscopic skull base surgery in children, with oncologic outcomes, symptom resolution, and complication rates comparable to those achieved with open approaches.[11] In particular, rates of complications such as intracranial infection, CSF leak, major vascular injury, and cranial neuropathy are similar between adult and pediatric endoscopic skull-base surgery, and between open and endoscopic skull base approaches; diabetes insipidus and other endocrinopathies have been suggested to be more frequent with endoscopic compared to open resection of craniopharyngioma, and sinusitis may be more prevalent after endoscopic skull base surgery in children compared to adults. However, given the rarity of these cases, definitive comparisons are impossible to make at this time.

## *Craniopharyngioma*

Craniopharyngiomas are rare benign brain tumors of childhood that arise from Rathke's pouch (the embryologic precursor of the anterior pituitary gland). Although not typically locally aggressive, they may grow indolently adjacent to the pituitary gland with destruction and compression of local neurovascular structures. Presenting symptoms include headache, visual field change (bitemporal hemianopsia), visual acuity change, and diplopia. Compression of the pituitary gland may lead to endocrinopathies. Diagnosis is suspected with imaging in the forms of MRI and/or CT scan and confirmed with biopsy.

The ideal treatment algorithm for a craniopharyngioma is controversial in children with some favoring radical excision with local neurovascular preservation while others favor biopsy followed by narrow field radiation. For either excision or biopsy, transnasal trans-sellar approaches are currently favored although trans-septal techniques are still equally efficacious.

Post-treatment short-term or long comorbidities include headache, CSF leak, visual impairment, and pituitary-related endocrinopathies such as syndrome of inappropriate antidiuretic hormone secretion.

## *Pituitary Neoplasia*

Pituitary neoplasias are rare in childhood and the vast majority are benign in nature consisting of a pituitary adenoma. Such adenomas are typically functional with hypersecretion of an associated hormone. Children often present with the sequelae of increased production of the hormones prolactin, cortisol (Cushing's syndrome), or growth hormone.

Diagnosis is confirmed by sellar exploration with biopsy and excision of adenoma. Approaches to the sella include the classic trans-septal approach and the currently more popular endonasal trans-sphenoidal approach. Sellar exploration and biopsy of the adenoma is often both diagnostic and therapeutic sometimes obviating the need for additional intervention. Patients may be monitored for recurrence by imaging and by regular endocrine evaluation.

### *Congenital Anterior Skull Base Defects*

Congenital defects of the anterior skull base may present in infancy or later in life. As infants are congenital nasal obligate breathers, meningoceles or meningo-encephaloceles may present early in life. Smaller or acquired lesions may present later when patients experience unilateral nasal obstruction, anosmia, or headaches. Rarely, there may be a spontaneous CSF leak related to skull base defect.

Treatment for congenital anterior skull base defects vary depending on the lesion, age of the child, and surgeon preference. Endonasal approaches are advancing for the transnasal removal of protruding nonfunctional dural/brain tissue along with concurrent skull base repair with either autologous or synthetic membranes. Vascular flaps such as the nasoseptal flap have also been demonstrated to be useful for such a repair. In smaller children, endonasal approaches may not be possible secondary to nasal space limitations so traditional subfrontal craniotomy approaches may be appropriate to identify and repair anterior skull base defects.

## CONCLUSION

Surgery in the sinonasal cavity and skull base in the pediatric population presents unique challenges. Nevertheless, a variety of open and endoscopic techniques exist to address the wide range of pathology and anatomy found in children.

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CHAPTER

# 34

# Evidence-Based Medicine in Pediatric Rhinology

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## INTRODUCTION

Chronic rhinosinusitis (CRS) is common in children and frequently encountered in primary care and pediatric otolaryngology clinics alike. CRS can have a significant negative impact on child health and quality of life.[1,2] Management is initially medical, with surgical therapy reserved for cases that fail to respond to maximal medical therapy. Indications for surgery as well as outcomes of surgical intervention are poorly defined, with limited available evidence largely restricted to variable outcome measures and small, nonrandomized, single-institution studies.

## CRS IN CHILDREN: CONSIDERATIONS FOR SURGICAL THERAPY

When considering children as candidates for surgical management of CRS, diagnostic accuracy is a critical first step for the clinician to interpret and apply existing evidence-based treatment paradigms. CRS in children is defined as 12 weeks or more of ongoing symptoms including nasal obstruction or nasal discharge with either facial pressure or cough.[3] CRS should be differentiated from acute rhinosinusitis, acute bacterial rhinosinusitis, recurrent acute bacterial rhinosinusitis, and exacerbations of allergic rhinitis (discussed elsewhere in this text).[4]

There are unique considerations in the pediatric population that should be kept in mind. The impact of the disease on the patient's quality-of-life must be ascertained from the caregiver and patient, and expectations of medical and surgical outcomes frankly discussed. Decision making should be shared among the clinician, the caregiver, and the child when appropriate. When treating children with CRS, it is also important to remain cognizant of possible undiagnosed or untreated comorbid conditions, such as asthma, gastroesophageal reflux disease, allergic rhinitis, cystic fibrosis (CF), primary ciliary dyskinesia (PCD), or immune deficiencies.[3,5-7] The clinician should also ensure that the child's vaccinations are up to date.[3,8]

## INDICATIONS FOR SURGERY

There are no established clinical practice guidelines for surgical management of pediatric CRS, and current practice is based largely on expert opinion, small cohort studies, and individual surgeon preference and experience. Indications include a failure of "maximal medical therapy", which is not well defined but typically includes some medley of saline nasal lavage, prolonged antibiotics, topical and/or oral corticosteroids,[3] antihistamines, and leukotriene inhibitors.

## PATIENT SELECTION AND SURGICAL TREATMENT OPTIONS

Current surgical interventions for CRS primarily consist of adenoidectomy and endoscopic sinus surgery (ESS). Other procedures are largely of historical interest in the United States, including inferior antral windows and the Caldwell-Luc maxillary antrostomy via the supra-canine fossa window.

Following failure of medical management, adenoidectomy is generally employed as first-line surgical therapy, with ESS then performed for persistent symptoms. In 1995, Rosenfeld described a "stepped treatment approach" that proceeded to sinus CT scan and immunological workup only if symptoms persisted after adenoidectomy. If the CT revealed ostiomeatal complex disease, conservative ESS including maxillary antrostomy and anterior ethmoidectomy would then be performed.[9] A 2005 survey of 175 members of the American Society of Pediatric Otolaryngology confirmed that the majority of clinicians use some variation of this algorithm.[10] In some cases, simultaneous adenoidectomy and ESS or ESS alone may be indicated and beneficial rather than the stepwise approach.[11]

These principals apply to treatment of uncomplicated CRS without underlying systemic disease such as CF, PCD, or immune deficiency. In these scenarios, surgical therapy is considered an important adjunct to medical therapy and can be beneficial or even necessary, but is unlikely to result in permanent disease control as monotherapy.[5-7] Approach and outcomes vary in the setting of systemic disease, and are beyond the scope of this chapter.

## EXISTING CLINICAL PRACTICE GUIDELINES

There are several existing clinical practice guidelines that address pediatric CRS in various capacities with no specific recommendations for surgical intervention. The *American Academy of Pediatrics (AAP) 2001 Clinical Practice Guideline: Management of Sinusitis*[12] is geared toward primary care physicians and primarily emphasizes diagnostic criteria for the various categories of rhinosinusitis and appropriate use of antibiotics. There are recommendations to refer to a specialist for surgical management of suppurative complications, but no clear recommendations for surgical intervention for CRS. This guideline also includes indications for imaging in children, with an emphasis on the futility of plain films in the diagnosis of ARS or CRS in children (Table 34.1). The *American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) 2012 Clinical Consensus Statement: Appropriate use of Computed Tomography for Paranasal Sinuses Disease* pediatric sinusitis statements[13] also include recommendations for appropriate use of imaging studies in pediatric rhinosinusitis with no specific surgical guidelines.

Other related guidelines include the American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) Clinical Practice Guideline 2007 for Adult Sinusitis[14] which excludes pediatric patients, and the European Position Paper on Rhinosinusitis and Nasal Polyps 2012[3] which provides medical treatment recommendations for children but does not comment on surgery in the pediatric population.

## MEASURING OUTCOMES IN TREATMENT OF PEDIATRIC CRS

Current outcomes measures for surgical management of CRS include quality-of-life (QoL) assessment tools, radiographic imaging, and nasal endoscopy (Table 34.2). Procedural efficacy is in part difficult to evaluate due to a paucity of standardized outcome measures, with inconsistent reporting of outcomes in the literature. In addition, none of the existing outcome measures account for comorbidities of CRS such as asthma, atopic disease, immunologic disorders, PCD, and CF.

**Table 34.1:** Existing imaging guidelines for pediatric rhinosinusitis

| *Guideline* | *Imaging indications* | *Imaging cautions* |
|---|---|---|
| AAP 2001[13] | Persistent/recurrent infections not responsive to medical therapy<br>Suspected complication of RS<br>Surgical planning | ≤ 6 years old: rarely necessary; symptoms correlate to radiographic studies 88% of time<br>High rate (near 100%) of false positives in children with recent URI |
| AAO-HNS 2012[14] | Failure of medical management and/or adenoidectomy<br>Suspected tumor<br>Suspected complication of RS<br>Surgical planning<br>MRI: immunocompromised patient, concern for invasive fungal disease | CT limited by radiation safety concerns, sedation<br>< 3 years old: not indicated for uncomplicated ARS without appropriate prior management<br>Not indicated for uncomplicated cold of < 10 days duration |

(AAP: American Academy of Pediatrics; RS: Rhinosinusitis; URI: Upper respiratory tract infection; AAO-HNS: American Academy of Otolaryngology—Head and Neck Surgery; ARS: Acute rhinosinusitis).

**Table 34.2:** Outcome measures for evaluating disease severity and surgical effectiveness in pediatric rhinosinusitis

| *Outcome measure* | *Strength* | *Limitation* |
|---|---|---|
| Symptoms | Obtained from caregiver | Nonspecific<br>Subjective<br>Difficult to assess in younger age groups<br>Overlap with other childhood conditions: allergic rhinitis, recurrent viral URIs, chronic adenoiditis, Eustachian tube dysfunction |
| CT | Sensitive and specific in predicting persistent rhinosinusitis in known disease[15] | Radiation exposure<br>Mucosal inflammation can be nonspecific<br>Cost<br>Possible need for anesthesia |
| Nasal endoscopy | Direct visualization<br>Anatomic abnormalities<br>Access for cultures, debridement<br>Avoid radiation | Poorly tolerated in children; pain, bleeding<br>Poor inter/intra rater reliability<br>Second look endoscopy unhelpful[16] |
| Quality of life | Minimal risk<br>Specific to intended outcome (i.e. improved QoL) | Subjective caregiver perceptions may be biased; evaluation by parent proxy<br>Paucity of validated instruments; most common disease-specific instrument in children is the SN-5[15,17] |

(CRS: Chronic rhinosinusitis; URI: Upper respiratory infection; QoL: Quality of life).

## Quality-of-life Instruments

QoL instruments are easily obtained and administered to the caregiver. As CRS is a disease that severely impacts health-related QoL in children, these instruments are useful in specifically addressing the pertinent sequelae of CRS. However, QoL instruments are subject to caregiver interpretation and bias, and there is a paucity of CRS-specific instruments validated for use in children.

The SN-5 is a commonly used CRS-specific instrument that has been validated for use in children. It is a caregiver-completed questionnaire assessing five domains of sinonasal disease on a Likert scale, including sinus infection, nasal obstruction, allergy symptoms, emotional distress, and activity limitations. The SN-5 is specific to pediatric CRS and may be useful in the development of evidence-based guidelines in the future.[2,17]

Other QoL instruments are available that are specific to CRS but not validated for use in children,[18-22] or specific to children and related to but not specifically addressing CRS,[23] such as the S-5 score for acute sinusitis.[24] Finally, many global QoL questionnaires are validated for use in children and may be broadly applied to CRS but lack specificity; one example is the Child Health Questionnaire.[1]

## CT Findings

Several measures of disease severity are based on CT findings alone. CT is useful in children for the assessment of disease recalcitrant to medical management, surgical planning, and to assess for complications of rhinosinusitis; however, its utility as a measure of assessing treatment efficacy is limited by safety concerns over radiation exposure and its high rate of false positives in children with recent symptoms of upper respiratory infection (*see* Table 34.1).[12] CT should be used judiciously in the pediatric population to help guide clinical decision making and surgical planning in properly selected patients.

The Lund–MacKay score, developed for adults, is a scale of 0–24 with 0–2 points for each sinus (0 = no opacification, 2 = complete opacification) and for ostiomeatal complex disease.[25] In children with known paranasal sinus disease, it was found to be 86% sensitive and 85% specific in predicting persistent rhinosinusitis using a cutoff score of ≥ 5 for CRS.[15] However, it fails to account for adenoid disease that is an important component of CRS in children.[9] The Pediatric Rhinosinusitis CT Scoring System was developed for children but has not been widely applied or substantiated. This system scores 0–3 for each side of the paranasal sinuses: 0 if no opacification, 1 if < 50% opacified, 2 if > 50% opacified, and 3 if completely opacified.[26]

## Nasal Endoscopy

Second-look nasal endoscopy has been used in the past to examine and debride the nasal cavity in the 2–4 weeks

following ESS.[27] While this provides direct visualization of the operative site, it is also invasive and may require additional general anesthesia in young children. It has not been shown to impact improvement or resolution of symptoms,[16] and the correlation of nasal endoscopy with symptomatology is unclear.[28,29]

## EVIDENCE-BASED MEDICINE: ADENOIDECTOMY FOR CRS

The adenoid pad contributes significantly to pediatric CRS, and adenoidectomy is generally considered first line surgical therapy for medically refractory disease (Table 34.3). The adenoid pad is often hypertrophied in children causing obstruction of the nasal airway. The adenoid pad has also been shown to serve as a bacterial reservoir,[33] so that adenoidectomy may provide symptom relief even if a small amount of tissue is removed.[9] In Rosenfeld's stepwise approach, a prospective cohort of 41 children with CRS was treated first with antibiotics, followed by adenoidectomy for patients in whom antibiotics failed, and finally ESS if these measures did not provide relief and/or the adenoids were scant. 67% of children in this study experienced improvement of all major symptoms after antibiotics, 75% after adenoidectomy, and 100% after ESS.[9]

A 2008 meta-analysis of adenoidectomy in children with medically refractory CRS found that 69% of patients significantly improved after adenoidectomy when measured by caregiver report of symptoms. The study concluded that adenoidectomy should be considered first-line therapy for pediatric CRS unrelieved by appropriate medical therapy.[30]

## EVIDENCE-BASED MEDICINE: ENDOSCOPIC SINUS SURGERY FOR CRS

ESS with enlargement of the natural drainage pathways of the maxillary and ethmoid sinuses is considered by many otolaryngologists to be definitive surgical intervention for CRS. ESS is more invasive than adenoidectomy with a risk of potentially significant complications (*see* Table 34.3). For these reasons, ESS is reserved by many specialists for disease that is unresponsive to medical therapy and adenoidectomy.

Most trials of ESS for CRS in children are retrospective and single institution, with variable outcome measures used to determine surgical efficacy. Existing studies report success rates of 82–100% with complications of 0.6–1.4% in children.[31,32] There is similarly limited evidence for ESS in adults, with a 2006 Cochrane review concluding that available studies do not definitively demonstrate superiority of ESS to medical treatment.[34]

Several trials compare ESS with adenoidectomy or with combination ESS and adenoidectomy (Table 34.4). Ramadan et al. in a prospective, nonrandomized trial found improvement in symptoms at 12 months in 87% of patients undergoing both ESS and adenoidectomy, compared with 75% and 52% of patients after ESS alone and adenoidectomy alone, respectively ($p < 0.0001$).[11] However, another prospective study using the SN-5 for outcome measurement found no difference in ESS with or without adenoidectomy versus adenoidectomy alone, although both groups experienced improved outcomes compared with patients receiving no surgical intervention.[17] Existing studies are of unclear significance in a nonrandomized and single institution setting.

**Table 34.3:** Advantages and limitations of adenoidectomy and ESS for pediatric CRS

| *Intervention* | *Advantage* | *Limitation* |
|---|---|---|
| Adenoidectomy | 50–80% improvement[30]<br>Simple<br>Low risk<br>Short recovery | Controversy: older children with small adenoid pad<br>May require additional surgery if symptoms persist |
| ESS | 82–100% success rate in selected patients[31,32]<br>Complication rate 0.6–1.4% in experienced hands[31,32] | Higher risk<br>Requires pediatric specialist<br>Multiple postoperative visits<br>Requires preoperative CT<br>No RCTs |

(ESS: Endoscopic sinus surgery; CRS: Chronic rhinosinusitis; RCT: Randomized controlled trial).

**Table 34.4:** Selected studies evaluating ESS outcomes for pediatric CRS

| *Reference* | *N* | *Study* | *Findings* |
|---|---|---|---|
| Rosenfeld[9] | 41 | Prospective, nonrandomized stepwise approach:<br>1. Antibiotics<br>2. Adenoidectomy<br>3. ESS | Improvement in major symptoms at 10–12 months: antibiotics group 67%; adenoidectomy group 75%; ESS 100% |
| Ramadan[11] | 183 | Prospective, nonrandomized ESS vs. ESS + adenoidectomy vs. adenoidectomy alone | Improvement in symptoms at 12 months: ESS + adenoidectomy 87%; ESS 75%; adenoidectomy 52% |
| Chang[35] | 101 | Retrospective | Improvement in symptoms at 23.6 months after ESS: 86% |
| Lusk[36] | 67 | Retrospective<br>Medical therapy vs. ESS | Improvement in pediatric rhinosinusitis CT score at 10 years: medical therapy 69%; ESS 97% |
| Rudnick[15] | 22 | Prospective<br>ESS +/– adenoidectomy vs. adenoidectomy alone | Improvement in SN-5 score at 6 and 24 months: equal for two cohorts |
| El Sharkawy[28] | 81 | Prospective<br>ESS for CRS with allergy, without allergy, and with polyposis | Improvement at mean 28 months in clinical, radiographic and endoscopic findings: predicted by adenoidectomy, second look operation, extent of preoperative disease on CT scan<br>Overall success rate 88% |

(ESS: Endoscopic sinus surgery; CRS: Chronic rhinosinusitis).

## NEW TECHNIQUES

Balloon catheter sinuplasty (BCS) is a new technique that is potentially less invasive than traditional ESS. A preliminary retrospective single institution study demonstrated nonsignificantly improved overall sinus symptoms for BCS compared with ESS, with significant decreases in antibiotic requirement, sinus congestion, and headaches in the BCS group.[37] The use of BCS has not been validated in children and further studies are needed to support its widespread utilization.

## CONCLUSION

CRS can significantly impact health, behavior, and QoL in children. There is limited evidence establishing efficacy of surgical intervention in pediatric CRS, and current practice is largely based on expert opinion and experience. Still, there are widespread reports of symptomatic and clinical improvement, as measured by a variety of outcome measures, following surgery for children who fail maximal medical management. A step-wise approach with initial medical therapy followed by adenoidectomy in refractory cases is most widely accepted. ESS is often used as an adjunct to adenoidectomy or in cases where adenoidectomy fails to relieve symptoms, with promising preliminary results. Further research including well-designed randomized controlled prospective trials and use of validated outcome measures is crucial in delineating the optimal algorithm for surgical management of pediatric CRS.

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SECTION 3

# Pediatric Aerodigestive Care

CHAPTER

# 35 Developmental Anatomy of the Unified Airway

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## INTRODUCTION

Knowledge of the developmental anatomy of the upper and lower respiratory tracts (unified airway) is essential to understanding airway pathology. The signs and symptoms of these disease processes can be attributed to distortion of normal anatomic structures and physiological processes. In this chapter, the embryologic development of the upper and lower respiratory tracts will be described, and the comparative anatomy between the infant and adult airway will be discussed. After this discussion, pathology associated with deviations from this normal development will be highlighted.

## THE LARYNX

The larynx is located at the point where the combined aerodigestive tract separates into distinct airway and digestive systems. Thus, the larynx most importantly acts as a valve that protects the lower airway from aspiration. In addition to this role, the larynx is also involved in respiration and phonation. To effectively carry out these functions the larynx has developed into a complex organ under both voluntary and reflexive neurologic control.

## PRENATAL DEVELOPMENT

After conception, prenatal development is separated into the embryonic and fetal periods. The embryonic period is defined as the first 8 weeks of gestation and the fetal period is defined as the period from 8 weeks gestation until birth.[1] At the completion of the embryonic period, the precursors to all organs are formed. Development in the embryonic period is separated into 23 stages by the Carnegie staging system. In this system, each stage has at least one aspect that is not found in the previous stage. Laryngeal development begins in the fourth week and has eight phases. These phases occur between Carnegie stages 11 and 23 (Fig. 35.1). The mucosa of the larynx develops from endoderm, and the laryngeal muscles and cartilages are derived from the mesenchyme of the fourth and sixth branchial arches.[3]

In the first phase of laryngeal development (Carnegie stage 11), the respiratory primordium forms as a thickening of the epithelium of the ventral foregut. At this point, the lumen of the foregut is patent.

During phase II (Carnegie stage 12), the respiratory diverticulum arises as an outpouching of the patent lumen of the foregut. This portion of the foregut is the primitive pharyngeal floor that will develop into the glottis. The superior extent of the respiratory diverticulum becomes the infraglottic region.[4] Finally, in this stage, two bronchopulmonary buds form off the respiratory diverticulum. These buds later become the lower respiratory tract.

In phase III (Carnegie stages 13–14), the respiratory diverticulum and primitive pharynx migrate cranially and the bronchopulmonary buds migrate caudally.[5] This leads to the formation of the trachea and further separates the upper and lower respiratory tracts. At the same time, the esophagus is also lengthening posterior to the developing trachea.

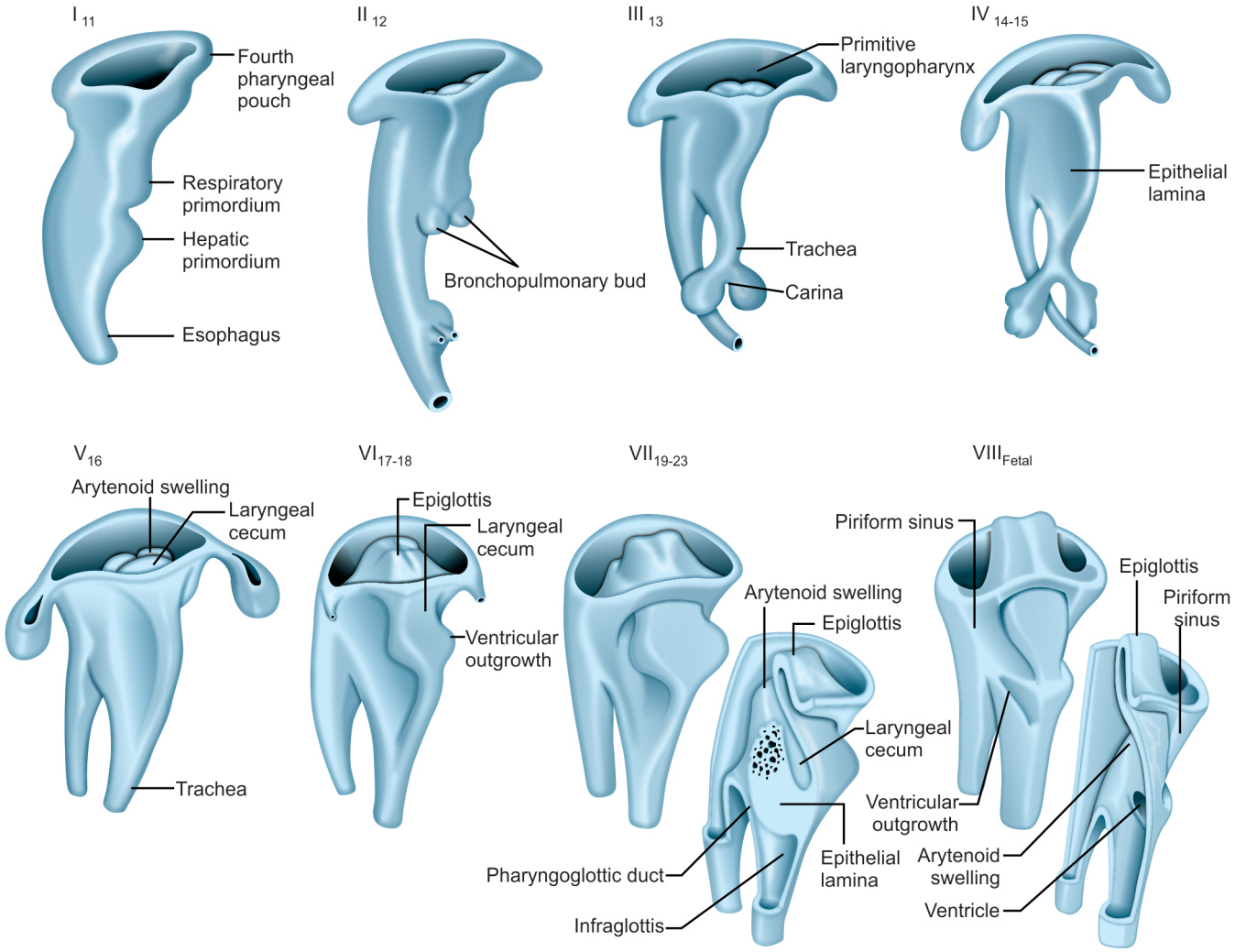



**Fig. 35.1:** The eight phases of laryngeal development within the corresponding Carnegie stages. Adapted from Kakodkar et al.[2]

In phase IV (Carnegie stage 15), the pharyngeal mesoderm, consisting of precursors of laryngeal cartilages, muscles, and arteries, compresses the developing airway cephalic to the respiratory diverticulum up to the level of the fourth pharyngeal pouch.[4] This begins to obliterate the lumen of the airway in this region and forms the epithelial lamina.

In phase V (Carnegie stage 16), obliteration of the primitive laryngopharynx continues from ventrally to dorsally due to the developing epithelial lamina, leaving only a narrow pharyngoglottic duct at the dorsal most extent. During this stage, the arytenoid swellings and epiglottis also become apparent and a depression between these structures called the laryngeal cecum forms. It should be noted that, as mentioned above, the glottis forms from the primitive pharyngeal floor as part of the tracheobronchial anlage. In contrast, the structures of the supraglottic larynx develop more superiorly as part of the buccopharyngeal anlage. This difference in anatomic origin accounts for the different lymphatic drainage patterns found in these two regions of the larynx.

In phase VI (Carnegie stages 17–18), the laryngeal cecum descends further caudally to the level of the glottic region. In phase VII (Carnegie stages 19–23), recanalization of the epithelial lamina begins. This occurs in a dorsocephalic to ventrocaudal direction with the ventral glottis being the last portion to recanalize. This process is due to reorganization and growth of cells as opposed to actual cell loss and is complete by the eighth postovulatory week.[6] During this phase, the recurrent laryngeal nerve is

innervating the transitional area between the laryngopharynx and esophagus, most of the laryngeal muscles are present and the muscular innervation is close to its mature form.[6,7]

In phase VIII (fetal period), the laryngeal ventricles, saccules, and vocal processes of the arytenoid cartilage form. The ventricles are formed by outpouchings of the laryngeal cecum. At this point, recanalization is complete and continuity between the supraglottic and subglottic airway is reestablished. For the remainder of gestation, the larynx continues to grow and its neurologic reflexes are formed. Differentiation of the myenteric plexuses and ganglion cells occurs by week 13, and by week 16, the fetus begins to swallow amniotic fluid. Elastic cartilage forms in the epiglottis and the corniculate cartilages form in the fifth and sixth month. At this point in gestation, fetal breathing and laryngeal movement is present. In a study by Kalache et al., it was determined that there was a linear relationship between gestational age and the diameter of the larynx, pharynx, and trachea on prenatal ultrasound.[8]

## POSTNATAL DEVELOPMENT

### The Adult Larynx

The skeleton of the larynx is made up of the thyroid and cricoid cartilages. The thyroid cartilage is composed of two alae that are fused in the midline and open on the posterior surface. The angle of fusion of the alae in women is more oblique than in men. The cricoid cartilage is the only complete ring in the airway.[9,10] The shape of the cricoid cartilage has been described as a signet ring with the anterior portion measuring 3–7 mm in height and the posterior portion measuring 20–30 mm in height.[1,11,12] Attached to the inside of the thyroid cartilage is the epiglottis. This structure is made of elastic cartilage and functions to prevent swallowed material from penetrating into the airway.

The paired arytenoid cartilages are pear-shaped and articulate on the posterior surface of the cricoid cartilage. At the apex of the arytenoid cartilage lies the corniculate cartilage. Lateral to the corniculate cartilage, within the aryepiglottic fold, lies the cuneiform cartilages.[13] While these structures do not articulate with the arytenoid cartilages, it is theorized that they may provide rigidity to the aryepiglottic fold.[14] In the adult, the inferior aspect of the cricoid cartilage is located at the level of C7.

Ossification of the laryngeal framework occurs throughout development. It should be noted that only hyaline cartilage ossifies so the epiglottis never undergoes this process.[15] The hyoid bone is completely ossified by 2 years of age. The thyroid cartilage ossifies at 20 years in males and later in females. This process starts on the posteroinferior aspect and then extends anteriorly and superiorly. Ossification of the cricoid cartilage occurs beginning on the inferior border and occurs later in life. Similarly, arytenoid cartilage ossification occurs after thyroid cartilage ossification begins.

The muscles of the larynx can be divided into intrinsic and extrinsic muscles. The intrinsic muscles all have insertions and attachments that are contained within the laryngeal framework. The intrinsic muscles of the larynx, which act to abduct and adduct the vocal cords, all attach to the arytenoid cartilages. The extrinsic muscles of the larynx work to elevate and depress the larynx.

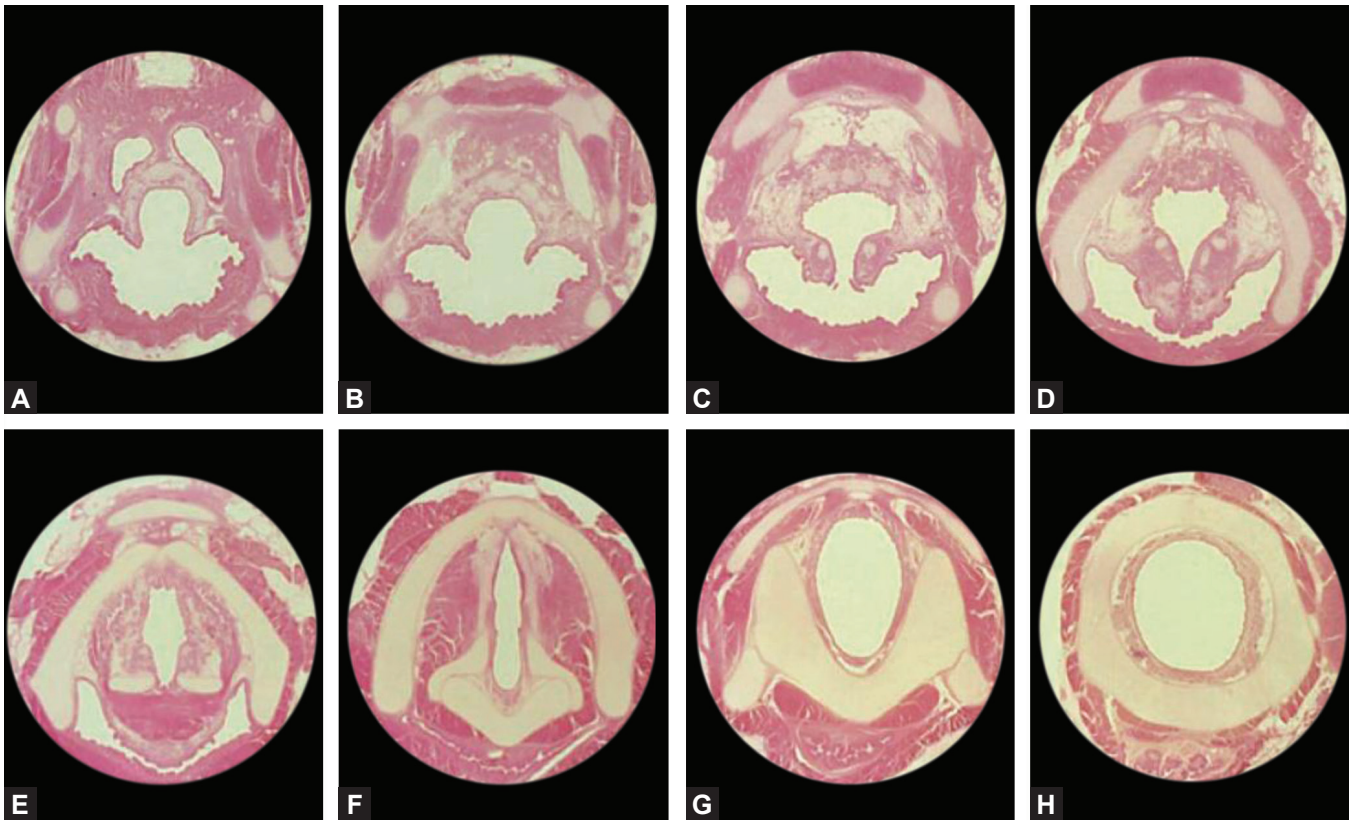
The overall structure of the larynx can be divided into the supraglottis, the glottis, and subglottis. The supraglottic larynx consists of all structures bounded by the epiglottis superiorly and the midpoint of the laryngeal ventricle (the space between the true and false vocal folds). The glottis extends from the midpoint of the laryngeal ventricle to 1 cm below the true vocal folds. Located anteriorly at the level of the laryngeal ventricle lies the saccule. Obstruction of this region results in saccular cysts and occasional airway obstruction. The subglottic airway begins at this point and extends to the lower border of the cricoid cartilage.

### The Infant Larynx

There are several features that vary between the infant and adult larynx (Figs. 35.2A to H). It is essential to understand these differences in anatomy as the presentation of common pathology and the management of the pediatric airway differ due to this varied anatomy.

The position of the infant larynx in the neck with respect to the cervical spine is different than in on adult. At birth, the infant epiglottis is located at the level of C1 and the inferior portion of the cricoid cartilage is at C4. This more superior positioning allows the epiglottis to make contact with the soft palate, facilitating more efficient respiration during feeding. This elevated laryngeal positioning causes the infant to be an obligate nasal breather.[16] As the child grows, the laryngeal framework travels inferiorly.

The infant larynx also varies from the adult larynx with respect to its size and shape. The larynx at birth is one third the size of the adult larynx. Also the proportional size of laryngeal subsites is different in infants and adults.




**Figs. 35.2A to H:** Axial sections through the larynx of an 18-month old from the superior aspect of the epiglottis to the inferior aspect of the cricoid cartilage. (A) At the level of the epiglottis. Note the omega-shape; (B) At the level of the thyroid cartilage. Note the position of this structure posterior to the hyoid bone; (C) The laryngeal saccule as it travels superiorly; (D) Additional depiction of the hyoid location anterior to the thyroid notch; (E) The laryngeal saccule at the level of the false vocal folds. Note the location medial to the thyroid cartilage; (F) The superior portion of the posterior cricoid cartilage; (G) Mid cricoid cartilage; (H) Inferior cricoid cartilage. From Kakodkar et al.[2]

In the infant, the vocal process of the arytenoids makes up about one-half of the glottis. In the adult larynx, this process occupies up to one fourth of the length of the glottis (Fig. 35.3).[18] The soft tissue of the posterior glottis, and the cuneiform cartilages also are proportionally larger in the infant.

The cartilage and submucosal soft tissue of the infant larynx is more pliable than in adults. The looseness of the submucosal soft tissues of the infant larynx can allow for increased edema and loss of airway diameter during states of increased inflammation.[19]

The infant epiglottis is more omega shaped than the adult epiglottis. The thyroid cartilage is flatter in the infant larynx and the superior portion of the thyroid cartilage is posterior to the arch of the hyoid (Fig. 35.4). The cricothyroid membrane is more slit like in infants. Therefore, endotracheal intubation or tracheotomy over a rigid bronchoscope instead of cricothyrotomy is the preferred course for the emergency management of the infant airway. The lumen of the airway at the level of the glottis is pentagonal during inspiration. At the level of the cricoid, the airway is more elliptical with the wider diameter in the anterioposterior direction.[2] The cricoid cartilage is the narrowest portion of the infant airway, whereas the glottis is the narrowest portion of the adult airway.[17] This accounts for the biphasic nature of stridor in infants and young children presenting with croup.

## ASSOCIATED PATHOLOGY

### Posterior Laryngeal Clefts

Posterior laryngeal clefts (PLC) arise secondary to failure of fusion of the posterior cricoid lamina and tracheoesophageal septum, causing an abnormal communication between the larynx and hypopharynx and the esophagus. The incidence of laryngeal clefts is believed to be 1 in 10,000–20,000; however, the incidence is increasing likely

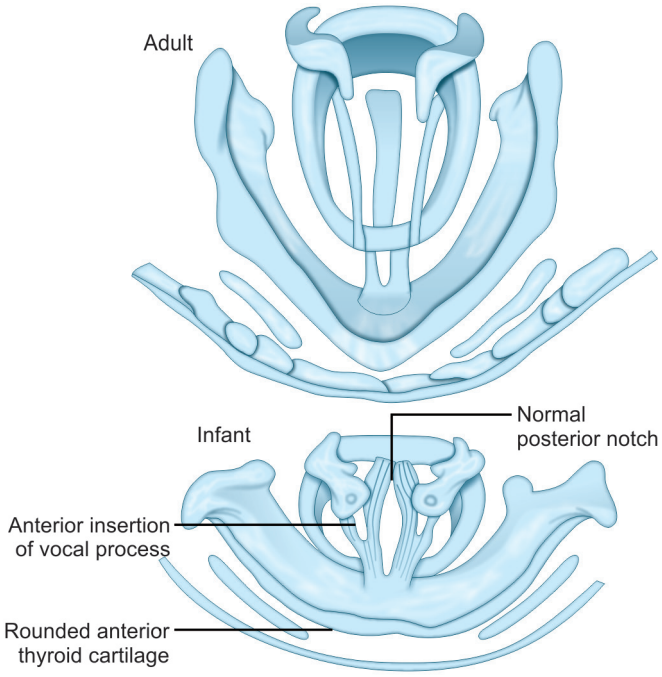



**Fig. 35.3:** Axial view of the adult and infant larynx. Note the relatively large arytenoids and the rounded nature of the thyroid cartilage in the infant larynx when compared to the adult larynx. Adapted from Cunningham.[17]

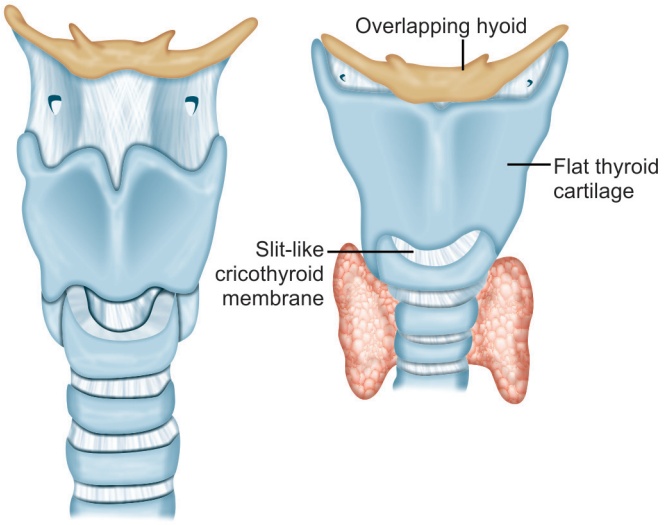



**Fig. 35.4:** Anterior view of the adult and infant larynx. The hyoid bone overlaps the superior portion of the thyroid cartilage and the cricothyroid membrane is slit like in the infant. Adapted from Cunningham.[17]

due to a higher index of suspicion by clinicians.[20,21] Syndromes such as Pallister-Hall and Opitz-Frias syndromes are associated with PLCs.[22]

Patients with PLCs may present with symptoms of choking resulting from aspiration with feeding. Many patients are referred to the pediatric otolaryngologist after a videofluoroscopic swallow study has demonstrated laryngeal penetration or aspiration. The gold standard for diagnosis of PLC is microlaryngoscopy with palpation of the posterior larynx.

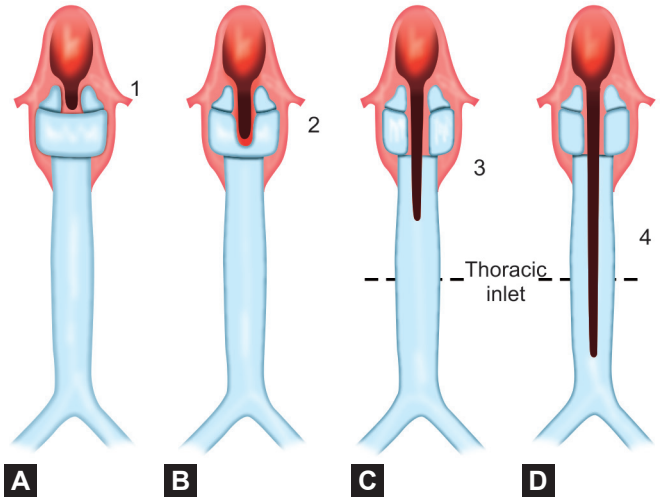
The most widely used grading system of PLC is that described by Benjamin and Inglis (Figs. 35.5A to D).[20] Type 1 clefts represent a defect in interarytenoid soft tissue that does not extend below the level of the true vocal cords. In type 2 clefts, the defect extends into the cricoid lamina below the level of the true vocal cords. Type 3 clefts are defined by extension though the entire cricoid lamina and possibly the cervical trachea. Type 4 clefts extend into the thoracic trachea.

The treatment of PLC is dependent on the severity as many small clefts are asymptomatic and do not require intervention. Most type 1 PLC can be managed medically by managing the dysphagia with thickened feeds but some need to be managed surgically via an endoscopic approach. Bakthavachalam et al. recommended endoscopic repair in patients with severe symptoms or symptoms after age two.[21] More severe clefts can be managed surgically via a transcervical approach.

## Laryngeal Atresias and Webs

Laryngeal atresias and webs occur secondary to failed or incomplete recanalization of the epithelial lamina during phase VI of laryngeal development. In laryngeal atresia, there is complete failure in recanalization of the epithelial lamina. Unless a tracheoesophageal fistula (TEF) is also present to allow for enough respiration to perform tracheotomy, the death rate at birth is high.

Laryngeal webs represent incomplete recanalization of the epithelial lamina and are located anteriorly due to the posterior to anterior direction of the recanalization process. Some webs are thin and may be lysed on intubation of the infant at time of respiratory distress. More commonly, anterior glottic webs are thick and with subglottic extension. Treatment of these thicker webs requires open reconstruction of the anterior commissure or keel placement. Congenital glottic webs have been associated with 22q11 syndrome.[23]




**Figs. 35.5A to D:** Posterior laryngeal clefts. (A) Type 1, with lack of extension into cricoid cartilage; (B) Type 2, with extension into the lamina of the cricoid cartilage; (C) Type 3, with extension through the entire cricoid cartilage; (D) Type 4, with extension into the thoracic trachea. Adapted from Benjamin and Inglis.[20]

## Congenital Subglottic Stenosis

Congenital subglottic stenosis is defined as stenosis of the airway that is present at birth. It is the third most common congenital laryngeal anomaly.[19] Subglottic stenosis can be grouped into two types: cartilaginous or soft tissue. Deformities of the cricoid cartilage and trapped first tracheal rings cause cartilaginous subglottic stenosis. The elliptical cricoid cartilage was first described by Tucker et al. and represents the most common cause of subglottic stenosis by an abnormally shaped structure.[24] When there is an elliptical cricoid cartilage, the transverse diameter of the subglottis is less than the anterioposterior diameter, resulting in a decreased cross-sectional area. The elliptical cricoid has also been known to be associated with a trapped first tracheal ring.[24]

Presentation of subglottic stenosis varies with the degree of airway narrowing. Patients with severe stenosis often present at birth with stridor and respiratory distress, whereas patients with mild stenosis may be asymptomatic or present later in life after recurrent episodes of croup. Diagnosis of subglottic stenosis is made by imaging, endoscopy, and sizing of the airway with endotracheal tubes. A full discussion of the treatment of subglottic stenosis is beyond the scope of this chapter, but in patients with stenosis causing 50% or greater narrowing of the airway surgical management may be required.[25]

## THE LOWER AIRWAY

The lower airway includes the trachea, bronchial tree, and lungs. Knowledge of the developmental anatomy of the lower airway is important because pathology of the tracheobronchial tree can directly affect the upper airway. For example, patients with acquired subglottic stenosis often have this condition secondary to a prolonged intubation due to prematurity and bronchopulmonary dysplasia.

## PRENATAL DEVELOPMENT

Development of the lower airway is separated into five periods: the embryonic, pseudoglandular, canalicular, terminal sac, and alveolar. The first four periods occur entirely prenatally whereas the last period starts prenatally and continues after birth. The initial events in the development of the tracheobronchial tree occur during the embryonic period and are the same as those in the development of the larynx. During Carnegie stage 12, the bronchopulmonary buds form off of the respiratory diverticulum. The location of this lung bud is directed by fibroblast growth factors. During Carnagie stage 13-14, the lung buds migrate caudally. Prior to this migration, there is communication between the lung buds and the foregut (Figs. 35.6A to C).[3] However, when the lung buds travel caudally, two tracheoesophageal ridges form creating a separation between the developing airway from the foregut. These two ridges fuse in the midline to form the tracheoesophageal septum, creating the trachea and lung buds anteriorly and the esophagus posteriorly.

At the time of separation of the airway from the foregut, two outpouchings form at the distal extent of the primitive trachea. These bronchial buds lengthen and become the right and left mainstem bronchi. On the right, three secondary bronchi form. On the left, two form. These secondary bronchi later become the right upper, middle, and lower lobes and the left upper and lower lobes.

The trachea and lung buds continue to migrate caudally until they enter the primitive thorax. Next, the visceral and parietal pleura are formed and the space between the two pleura becomes the pleural cavity.

During the pseudoglandular period, which occurs between gestational weeks 5–16, branching of the tracheobronchial tree continues. In a study performed on rats by Yoshimi et al., this branching is at least partially dictated by homeobox b3 and b4 genes.[26] During this period, the

primitive lung acts more like an endocrine gland and it has no potential for respiration. If a fetus is delivered at this time, it is thus not viable.

The canalicular period occurs between gestational weeks 16-26. During this period, the lumen of each bronchiole enlarges in size and branching of the tracheobronchial tree continues with seventeen subdivisions occurring by the end of the sixth month of gestation.[3] Respiratory bronchioles are formed by the 19th intrauterine week, which then branch to form alveolar ducts.[27] These divisions result in progressively smaller airways that have more intimate connection to an increasing number of blood vessels. This association between the airways and blood supply is what permits the respiratory function of the lung, which is possible near the end of this period.

During the terminal sac period, which occurs between 26 weeks and birth, the terminal sacs, or primitive alveoli, form and capillaries continue to maintain close contact with these airways. Surfactant is produced by the primitive alveoli during this period, which reduces surface tension in the alveoli. Surfactant initially begins to be secreted at 23–24 weeks and its production is sufficient by 28–32 weeks. In the fetal lung, glucocorticoid receptors are present throughout the tissue and stimulation of these receptors induces production of surfactant-associated proteins and may stimulate cell maturation and differentiation.[28]

## POSTNATAL DEVELOPMENT

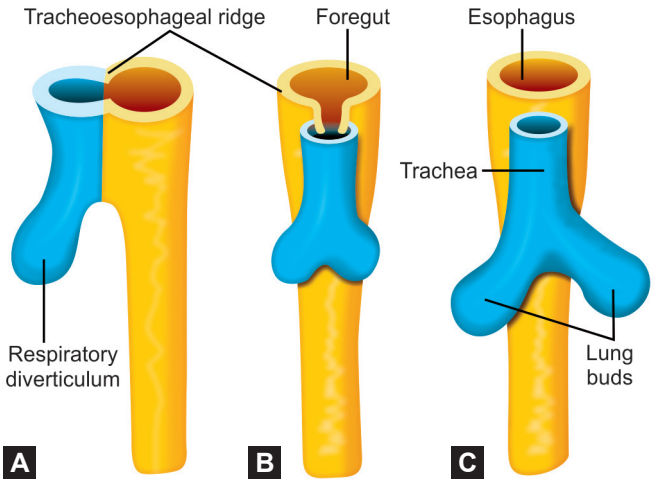
### The Adult Lower Airway

The trachea is the portion of the airway that lies between the inferior aspect of the cricoid cartilage and the carina. The adult trachea's length varies based on gender and height but ranges from 10–14 cm long and is comprised of 16–20 cartilaginous rings.[29] The diameter of the trachea ranges from 12–23 mm, but this diameter varies during breathing and coughing and in changes in head and neck position and intrathoracic pressure.[30] The cartilaginous rings of the trachea are incomplete and the posterior wall of the trachea is membranous. The membranous trachea is made of the trachealis muscle as well as fibroelastic tissue. In the normal trachea, the ratio of the cartilaginous to membranous trachea is 4.5:1.

At the carina, the trachea bifurcates and forms the right and left mainstem bronchus. The right main bronchus has a more vertical course, branching at 25°, whereas the left mainstem bronchus branches at 45°.[22] This accounts for the fact that aspirated foreign bodies are often found in the right mainstem bronchus. Like with the trachea, the mainstem bronchi have incomplete cartilaginous rings.

In normal anatomy, the mainstem bronchi separates into three lobar bronchi on the right and two lobar bronchi on the left. The right mainstem bronchus bifurcates into the right upper lobe bronchus and the bronchus intermedius that then bifurcates into the right middle and right lower lobe bronchi. On the left, the mainstem bronchus bifurcates into the left upper lobe and left lower lobe bronchus. Further branching forms segmental bronchi that are anatomically more variable than that of the lobar bronchi. On the right, the right upper lobe bronchus branches into anterior, posterior, and apical segments. The middle lobe bronchus becomes the medial and lateral segments. The lower lobe bronchus becomes the superior segment, and the medial, anterior, lateral, and posterior basal segments. On the left, the upper lobe bronchus splits into the upper and lingular divisions. The upper division has anterior and apicoposterior segments. The lingular division forms superior and inferior segments. The lower lobe bronchus splints into the superior segment and the anteromedial, lateral and posterior basal segments. Instead of having cartilaginous rings, the lobar, segmental, and more distal bronchi have cartilaginous plates.[31]

With further division, bronchioles and alveoli are formed. At the level of the bronchioles, the airways no longer contain cartilage. Gas exchange occurs at the level of the alveoli, which have intimate association with capillaries.




**Figs. 35.6A to C:** Formation of the tracheoesophageal septum. (A) Lateral view of the formation of the tracheoesophageal ridges; (B) Anteroposterior view of the formation of the tracheoesophageal ridges; (C) Fusion of the tracheoesophageal ridges in the midline to form the tracheoesophageal septum. Adapted from Sadler.[3]

## The Infant Lower Airway

In full-term newborns, the normal trachea is 4 cm long and 4–5 mm in diameter.[32] The trachea in neonates is more complaint than the adult form and it collapses more easily. At the carina, the tracheal bifurcation is less acute in infants than in adults. The alveolar sacs and alveoli are not in their mature form until after birth.[27] This maturation of the alveoli is called the alveolar period of lung development and starts at 8 months gestation and continues into childhood. During this time, intimate associations between alveolar epithelium and capillary endothelium continue to develop and alveolar septa mature. By 1.5 years of age, alveolar septa are in the adult form, where an isolated capillary network and connective tissue stabilize the interalveolar wall.[33]

# ASSOCIATED PATHOLOGY

## Complete Tracheal Rings

Complete tracheal rings are a congenital tracheal anomaly where complete rings replace the normally C-shaped cartilage of the trachea. This results in a narrowing of the normal tracheal diameter and is the most common cause of congenital tracheal stenosis. Complete tracheal rings can be found in only a few rings or it can extend throughout the entire trachea or even into the mainstem bronchi. Slide tracheoplasty has been described as a means of surgical management for this anomaly.[34]

## Tracheomalacia and Vascular or Cardiac Anomalies

Knowledge of the anatomy of the great vessels is important to the otolaryngologist because external compression of the tracheobronchial tree can be due to variations in normal anatomical structures. Tracheomalacia is defined as the narrowing of the tracheal walls and can be defined as primary or secondary. Primary tracheomalacia exists when the defect is due to the trachea itself. In this case, the ratio of the cartilage to membranous trachea may be reduced to 3 to 1 or 2 to 1, and the membranous trachea demonstrates dynamic collapse during respiration. In secondary tracheomalacia, the tracheal walls are narrowed secondary to extrinsic compression, often from vascular anomalies (Fig. 35.7). Similarly, bronchomalacia can be primary or secondary in nature with the secondary form often being secondary to vascular or cardiac anomalies. These anomalies are described below.

### *Aberrant Innominate Artery*

Compression of the trachea by an aberrant innominate artery can be seen on the right anteriolateral wall of the superior portion of the trachea. Compression in this region results in a triangular appearance of the tracheal lumen on endoscopy. If one lifts the tip of the bronchoscope against this area of narrowing, the right brachial pulse will become weaker.

Patients with an aberrant innominate artery may present with symptoms ranging from croup-like cough, expiratory stridor and wheezing, to apneic spells. If obstruction is severe, resulting in apparent life-threatening events, recurrent pneumonia secondary to impaired clearance of secretions, surgical management in the form of innominate arteriopexy may be required. In this procedure, the innominate artery and aorta are suspended from the sternum. In most patients, however, no surgical management is necessary because obstruction is not frequently severe.

### *Double Aortic Arch*

The double aortic arch is rare and is caused by the persistence of both fourth branchial arches and both

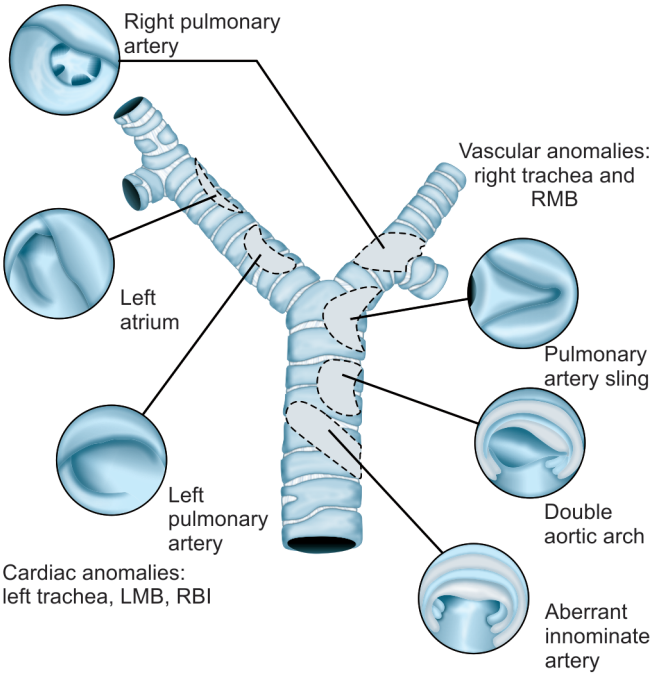



**Fig. 35.7:** Schematic representation of the tracheobronchial tree with the typical endoscopic appearance and location of extrinsic compression of the airways from vascular and cardiac anomalies. Adapted from Kakodkar et al.[2]

dorsal aortas. The result is a complete vascular ring that encircles both the trachea and the esophagus. Typically, the right arch is dominant and posterior to the trachea and esophagus, whereas the left arch is hypoplastic and anterior to these structures. The apex of the right arch is typically more superior to the left arch. The two arches join distally to form the descending aorta, which remains on the left.

Patients with a double aortic arch display symptoms, often at birth, that are secondary to tracheal or esophageal compression. This condition can be diagnosed by esophagram, echocardiography, CT scan, or MRI. It should be noted that both CT and MRI are better at establishing the relationship between the vessels, trachea, and esophagus and are preferred for preoperative planning. After surgery, patients' respiratory symptoms frequently resolve; however, it may take 1–2 years for symptomatic improvement in some patients.[19]

### *Pulmonary Artery Sling*

The pulmonary artery sling is a congenital anomaly where the normal left pulmonary artery is absent. Instead, the left pulmonary artery arises from the right pulmonary artery and travels between the trachea and the esophagus. This results in compression of the right mainstem bronchus and the right side of the lower trachea, which is visible on endoscopy as a slit-like lumen. As with double aortic arch, this results in symptoms of airway obstruction. Treatment of this anomaly involves division and reimplantation of the pulmonary artery and results in an improvement of symptoms.[35]

### *Congenital Cardiac Anomalies*

Compression of the airway can also be caused by congenital cardiac defects that lead to left-to-right shunts and result in pulmonary hypertension. This results in enlargement of the pulmonary arteries, which leads to compression of the left main bronchus. Cardiac defects associated with left-to-right shunts that lead to pulmonary artery hypertension and airway compression include ventral septal defects and patent ductus arteriosis.[35]

Patients with airway compression secondary to pulmonary artery hypertension present with varying symptoms depending on the degree of obstruction. These symptoms are similar to the obstructive symptoms found in the other vascular anomalies above. Treatment of the airway symptoms in these patients involves treating the underlying pulmonary hypertension.

## Tracheoesophageal Fistula and Esophageal Atresia

A congenital TEF is an anomaly, where there is an abnormal communication between the trachea and the esophagus. TEFs may or may not be associated with esophageal atresia, where the esophagus ends in a blind pouch either in its proximal extent, distal extent, or both. The incidence of TEF is estimated to be 1 in 3000–5000 live births. Five types of TEF have been described (Fig. 35.8), with type C being found in 80–86% of cases.[36,37] In type C TEF, proximal esophageal atresia with a distal TEF is found. Type E, or H-type fistulas, are more rare but occasionally go undiagnosed until later in life.[38,39] One proposed mechanism of TEF formation is vascular compromise as the trachea and esophagus are lengthening prenatally.

Patients with TEF and esophageal atresia typically present with feeding difficulties including aspiration, and respiratory difficulties. In the setting of proximal esophageal atresia, polyhydramnios may be found on prenatal ultrasound. Treatment of TEF and esophageal atresia is surgical. Postoperative complications include tracheomalacia, esophageal strictures, recurrent fistulas, and reflux.

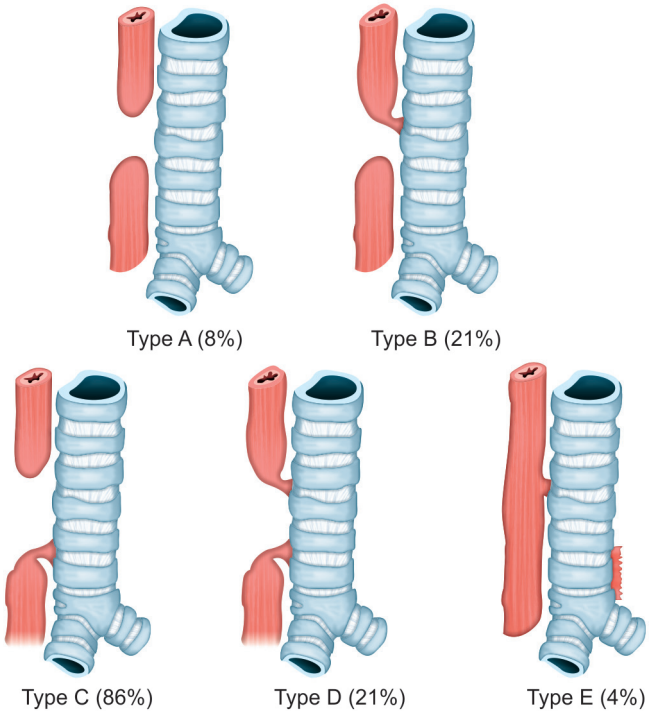



**Fig. 35.8:** The five types of tracheoesophageal fistula. Type C, with proximal esophageal atresia and a distal tracheoesophageal fistula is the most common. Type E, or the H-type fistula may be diagnosed later in life. Adapted from Kakodkar et al.[2]

## SUMMARY

- The unified airway undergoes developmental changes both prenatally and postnatally. Understanding the developmental anatomy of these structures leads to better understanding of the pathology that arises due to deviations from this normal development.
- Development of the larynx occurs in eight stages, seven of which occur during the embryonic period.
- At birth, the infant larynx has several structural differences when compared to the adult larynx. The infant epiglottis is omega shaped and the arytenoid process occupies a larger portion of the infant glottis. The cricothyroid membrane is less developed and the thyroid cartilage lies underneath the hyoid bone in infants.
- Deviations from normal laryngeal development lead to PLC, subglottic stenosis, and laryngeal atresias and webs.
- Development of the lower respiratory tract forms the tracheobronchial tree and promotes maturation of the lungs. Maturation of alveoli continues after birth.
- Congenital cardiovascular anomalies can lead to extrinsic compression of the trachea and mainstem bronchi, resulting in symptoms of airway obstruction.

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CHAPTER

# 36

# Imaging of the Pediatric Airway

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***Robert Liu, Hugh D Curtin, Paul A Caruso***

## INTRODUCTION

While imaging in otolaryngology is invaluable in helping with diagnosis and with delineation of surgical anatomy, several considerations are needed when considering imaging in a child. Radiation risks and the need for sedation are among the most critical issues that differ between obtaining radiographic studies in children and adults. This chapter discusses some of the salient points about imaging in the pediatric population, as well as outlines how to decide which type of imaging is preferred based on clinical presentation. Lastly, it will describe how to interpret the studies and how to use them appropriately to help in making a diagnosis.

The initial portion will discuss the various types of imaging used and considerations specific to each type.

The clinical portion is arranged by clinical scenario in alphabetical order and includes:

- Dysphagia
- Infection
- Nasal obstruction
- Obstructive sleep apnea (OSA)
- Stridor
- Velopharyngeal insufficiency (VPI).

## PART I: IMAGING MODALITIES

The modalities most commonly used to image children with airway disorders are presented in alphabetical order for ease of reference. Special considerations for the different modalities are then reviewed.

### Computed Tomography

CT imaging is versatile and can be useful in a variety of scenarios, including defining the extent of infection, identifying a mass in or adjacent to the airway, delineating vascular anatomy, and clearly demonstrating bony anatomy. In the pediatric population, however, the benefit of CT must be weighed against the risk of radiation exposure.

Diagnostic CT increases the risk of malignancy in exposed children. Standard of care practice aims to reduce radiation dose in the workup of children.

#### *Terminology*

The quantity $CTDI_{vol}$ (Volume CT Dose Index) is currently used in CT dosimetry.[1] When a scan is prescribed, the scanner displays the $CTDI_{vol}$ in mGy on the console. The dose displayed, however, is not the dose for the specific patient under examination. Instead, the $CTDI_{vol}$ represents the average dose in the central section of a standardized phantom scanned with the selected protocol.[2] The head phantom is an acrylic cylinder with a diameter of 16 cm and a height of 15 cm.

The effective dose $E$ is used to assess the radiation detriment from partial-body irradiation (e.g. irradiation of only the head or only the abdomen). The effective dose is a weighted sum of the doses to all exposed tissues. $E = \Sigma(w_t \times H_t)$, where $H_t$ is the equivalent dose to a specific tissue and $w_t$ is the weight factor representing the relative radiosensitivity of that tissue. The unit of effective dose is sievert (Sv). The effective dose for a typical CT examination of the airway using the airway survey

protocol described above is about 1 mSv (i.e. 1/1000 Sv). In comparison, the average effective dose from cosmic rays, radioisotopes in the soil, radon, etc., is about 3.11 mSv per year in the United States. The effective dose can be estimated from the dose-length product (DLP = $CTDI_{vol}$ × scan length), which is also displayed on the CT scanner console. The effective dose for a head study in mSv is approximately 0.0021 × DLP (mGy cm) for an adult and approximately 0.0067 × DLP (mGy cm) for a 1-year-old patient.[1]

### *Factors Influencing Patient Dose*

The CT scanning protocols should be optimized such that the quality of images is sufficient for diagnosis and the patient dose is kept as low as reasonably achievable (ALARA). To get the best balance of the image quality and patient dose, it is important to understand the effects of imaging parameters on the dose and imaging quality.

Patient dose depends on three group factors: equipment related factors, patient related factors, and application related factors.

The factors in the first group include X-ray beam filtration, X-ray beam collimation, system geometry, and detector efficiency. Although users do not have control of most of these factors, it is important to understand that the z-axis dose efficiency is reduced when the total X-ray beam width becomes very small for multidetector CT due to the need to keep the beam penumbra out of any detector row.

The dose is strongly dependent on patient size. If the same technique is used to image the heads of an average adult and a newborn, the dose to the newborn is significantly higher.

Imaging parameters such as kVp, mAs (the product of the tube current and the time in seconds per rotation), and pitch (the table travel per rotation divided by the total X-ray beam width) are selected by the operator.

If all other parameters are fixed, the patient dose is proportional to the effective mAs which is defined as the mAs (mA × seconds per rotation) divided by the pitch.

The dependency of dose to kVp is more complicated. In general, the dose increases as a power function of kVp ($D \sim kVp^p$) if all other parameters are fixed. The value of p is in the order of 2–3 depending on the type of the scanner.

### *Image Quality*

Image quality is characterized by spatial resolution, contrast resolution, image noise, and other quantities. It is difficult to use a single variable to characterize completely the quality of an image. In practice, image noise has been widely used to judge the CT image quality since the detectability of low-contrast objects is strongly dependent on the contrast to noise ratio. The standard deviation of CT numbers of an ROI in the image is usually used to represent the noise. In CT, for a given reconstruction kernel, the noise is primarily due to the fluctuation of the X-ray photons reaching the detector. The noise is approximately inversely proportional to the square root of patient dose. To reduce the noise by a factor of 2, dose must be increased by a factor of 4. In general, image quality is better when the patient dose is increased.

### *Radiation Risks*

The biological effect of radiation is either deterministic or stochastic. The deterministic effect will not occur unless a threshold dose is exceeded. The stochastic effects, however, may occur at any dose level and the probability of occurrence increases with dose linearly according to the linear-nonthreshold dose–response model.[2] Stochastic effects include carcinogenesis and the induction of genetic mutations.

Children are inherently more sensitive to radiation because they have more dividing cells and radiation acts on dividing cells. Also, children have more time to express a cancer than do adults.[3]

The increased risk of malignancy associated with medical CT exposure has received considerable attention starting with analyses based largely on extrapolation from the Hiroshima data and culminating more recently in large scale population studies of children exposed to CT radiation.[3–7] The upshot of this research is the ethical imperative to reduce radiation dose including from diagnostic CT during the workup of children including for pediatric airway disorders.

Mathews et al. studied 10.9 million children between 1985 and 2005 of whom 681,211 underwent a diagnostic CT scan during the study period.[7] 3150 cancers were found in patients who had a CT scan at least one year prior to detection, that is, with a lag period of one year. At a mean follow-up period of 9.5 years, the cancer incidence in the CT exposed group was found to be 24% greater than the non-CT exposed group that yielded an incidence rate ratio (IRR) of 1.24 and an absolute excess incidence rate of 9.38 per 100,000 person years.[7] Incidence risk correlated inversely with age (the younger the patient at time of exposure, the greater the risk) and proportionally

with number of scans and with scans of the chest, abdomen, or pelvis. Lag periods of 5 years yielded IRR of 1.21 and 10 years yielded an IRR of 1.18.[7]

Pearce et al. performed a retrospective study on patients without previous cancer diagnosis who underwent CT in the United Kingdom between 1985 and 2002.[6] They then obtained data on cancer incidence and mortality from the National Health Service (NHS) Central Registry in the United Kingdom between January 1, 1985, and December 31, 2008, in these patients, looked at absorbed brain and red bone marrow doses per CT scan, and determined excess incidence of leukemia and brain tumors in this retrospective cohort. The study began follow-up for leukemia 2 years after the first CT and for brain tumors 5 years after the first CT to avoid the confounding factor of CTs performed related to the cancer detection. Data on 178,604 patients were included in the leukemia analyses and 176,587 patients in the brain tumor analyses. 283,919 CT scans were included in the analysis of leukemia risk (the most common of which, 64%, were head CTs) head and a similar distribution of scan types in the brain tumor analysis. Compared with doses of <5 mGy, the relative risk (RR) of leukemia for patients who received doses of at least 30 mGy was 3.18, and the RR of brain tumors for patients receiving 50–74 mGy was 2.82.[6] For CTs obtained after 2001, 5–10 head CTs in children younger than 15 years result in cumulative doses of 50 mGy to the red bone marrow dose and 2–3 head CTs resulted in cumulative brain doses of 60 mGy. In short cumulative CT doses of 50–60 mGy may triple the risk of leukemia and brain tumors in children.[6]

### *Strategy for Dose Reduction*

In light of the cumulating evidence that CT-associated radiation increases cancer risk, dose reduction strategies are now standard of care for pediatric imaging practices. This effort is often expressed as an ALARA (as low as reasonably achievable) principle.[4]

An important initial step is to consider alternative imaging modalities such as magnetic resonance imaging (MRI) or ultrasound and such consideration de facto is often most efficiently carried out by the ordering pediatric ENT. In the second portion of this chapter, imaging strategies are proposed that favor such alternative modalities whenever feasible.

A second step is to optimize the CT technique; the image quality required for the specific indication is assessed based on the radiologist's experience. The imaging parameters are then selected based on the patient size and organ type under examination such that the required image quality is achieved while the patient dose is kept as low as possible. Weight- and age-based pediatric protocols should be operative at the imaging centers to which the pediatric ENT refers and are considered now to be standard of care.

## Reformats and Reconstructions with MDCT

Multidetector CT provides shorter acquisition times, decrease in tube current load, and improved spatial resolution.[8] Low-image acquisition time (IAT) is useful in pediatric airway imaging in order to reduce motion artifact and in particular in children in the 2 month to 3 year age group who are imaged postprandially without pharmacologic sedation. Although the radiation dose with multidetector scanners in high-quality mode remains an issue compared with single detector scanners; the improved spatial resolution allows for high-quality reformats that essentially obviates the need for rescanning the patient in a second coronal plane.[8] Reformats may, moreover, be obtained in sagittal or oblique planes to improve the detection of pathology in specific clinical settings.

Surface reconstructions of the facial bones, mediastinal vessels, laryngeal cartilages, airway casts, and virtual CT endoscopy are CT reconstruction tools that may aid in diagnosis and surgical planning.

## Fluoroscopy of the Airway and Barium Swallow

Airway fluoroscopy, often in combination with single-contrast barium esophagography, continues to play an important role in the initial imaging workup of the child with difficulty breathing. Because this imaging modality is used to observe the child's breathing over a given period of time, it can help demonstrate dynamic obstruction or narrowing that may be difficult to identify on a static image. This is best done with the neck in hyperextension and arms/hands held above the head. In addition, a barium swallow is useful in assessing a vascular ring or sling which may be compressing the airway.

Fluoroscopy times and total exposure for combined airway fluoroscopy and single contrast barium swallow vary depending on patient age, cooperation, size, and pathology but generally range from 1 to 10 minutes and 10–60 mGy.

## Magnetic Resonance Imaging

MRI is the modality of choice for the initial nonemergent evaluation of head and neck masses, including branchial arch anomalies, hemangiomas, and lymphatic/vascular malformations, which may involve the airway. Although the confined space of the MRI milieu remains a challenge for children usually 2 months to 6 years of age, the superior contrast resolution, noncontrast angiographic techniques, and lack of ionizing radiation (in contrast to CT) present distinct advantages. MRI should also be considered in cases of infection when a patient has already received multiple CT scans within a short period of time, as the bony and vascular anatomy has already been delineated by previous CT.

In addition, it can be used in the form of dynamic imaging (cine MRI) to evaluate functional aspects of the airway. However, given the length of time needed to obtain a proper MRI, the need for sedation becomes a relevant topic in many scenarios. Coordination between otolaryngology, radiology, and anesthesiology is paramount in these situations. Lastly, MRI is useful in identifying brain abnormalities when neurologic abnormalities on head and neck examination are noted.

### *Comments and Caveats*

*Branchial arch anomalies*: A CISS/FIESTA/3D DRIVE sequence may be considered when there is high clinical suspicion for a sinus tract, e.g. pharyngeal cleft sinus tract or fistula; the cutaneous and subcutaneous course of the tract may be best depicted on this sequence that allows for thin section (0.8–1 mm) volumetric acquisitions. A cutaneous marker may be useful to mark the exit site of the tract the scan excursion is then carried axially back to the suspected site of connection usually the external auditory canal, palatine tonsillar fossa, or piriform sinus.

*Hemangiomas*: Laryngeal hemangiomas may be difficult to image and may require high resolution (e.g. 500 frequency × 400 phase matrix) motionless sequences such that targeting of the imaging on the site of obstruction becomes critical for diagnostic imaging. The authors have found three components of the protocol to be critical:

- Discuss the bronchoscopy prior to the MRI and coordinate the findings with the anesthesiologist. Prior to the MRI the site of the suspected obstruction or mass, e.g. subglottic, needs to be discussed with the ENT so that the imaging can be targeted appropriately on this segment of the airway and so that the anesthesia can be planned to avoid compression of the mass by the endotracheal tube in so far as a patent airway can be maintained during the MRI
- Consider pharmacologic paralysis during the MRI. High-resolution sequences are susceptible to motion artifact that may occur from respiration even in a sedated and intubated patient. The authors have found that boluses of paralytics such as vecuronium in intubated patients under the supervision of the anesthesiologist or intensivist managing the airway may provide an adequate temporal window for such high-resolution images
- Targeted imaging: High-resolution images are time costly. The level of the obstruction, e.g. with respect to the vocal folds or carina must be known in advance in order for diagnostic imaging to be obtained through the level of obstruction.

*Vascular malformations*: Characterization of vascular lesions as high or low flow may be helpful for diagnosis i.e. for distinguishing high flow arteriovenous malformations and some hemangiomas from lower flow venolymphatic malformations and for management considerations of embolization and for presurgical planning.[9] A 3D time of flight sequence is thus included into the imaging protocol.

*Fat saturation*: Fat saturation in pediatric head and neck imaging is generally avoided as in the authors' experience the air–bone soft tissue interfaces of the skull base produce artifact that limits the evaluation for perineural tumor and skull base foraminal encroachment and because fat saturation adds several minutes to each additional scan.

*Vocal fold paralysis*: The emphasis on central nervous system (CNS) and craniocervical junction imaging in the above protocol for vocal fold (VF) paresis in children reflects the differences between the results of etiologic studies in adults and children. Ko et al., e.g. studied 161 patients aged 15–85 years (110 patients with unilateral VF paresis) and found iatrogenic causes in 48%, tumor in 12%, neck trauma in 7%, and radiation effect in 6% of cases.[10] Rosin et al., by contrast, studied 51 children with bilateral (29) and unilateral (22) VF paresis. While the leading etiology in the unilateral group was found to be cardiac surgery, 15 of the 29 cases of bilateral VF paresis had neurologic causes.[11] Peripheral neuropathies, both axonal and demyelinating, may results in both unilateral and bilateral VF paresis, are important diagnostic considerations in children, and may, as has been reported in MFN2 mutations, present with CNS manifestations on MRI.[2,12–16]

## Radiography

For certain indications such as the evaluation of stridor in a stable child or the initial evaluation of a child with OSA, plain film radiography continues to play a role in the imaging of the pediatric airway.

## Ultrasound

Ultrasound presents several distinct advantages in the evaluation of pediatric neck lesion that may involve the airway. It is noninvasive, does not produce ionizing radiation, can often be used without sedation even in those age groups where CT and MRI may require anesthesia, and provides for evaluation of vascularity without IV contrast.

## Sedation: What the Ordering Pediatric ENT Needs to Know

Procedural sedation is common in pediatric ENT practice including for diagnostic imaging and the use of procedural sedation has been shown to have increased over the last decade.[17] Below we summarize what the pediatric ENT needs to know with regard to the use of sedation for pediatric imaging:

1. For developmentally normal patients, under 2–3 years of age for CT and under 6 years of age for MRI, you should run requests for imaging through the procedural sedation team (usually composed of appropriate anesthesiology and radiology personnel) for approval before the examination is scheduled, because many of these children will likely require child life assistance or anesthesia. Do not schedule these children routinely as you would other outpatient examinations, even if your electronic ordering system allows it. For developmentally delayed children, all requests for imaging should be reviewed by the procedural sedation team radiology-anesthesiology team
2. General anesthesia (GA) may cause developmental delay in children and examinations such as MRI or CT that require GA should thus be ordered judiciously[18–21]
3. Pediatric ENTs should therefore refer children to medical centers that provide procedural sedation teams.

### *Background*

In light of the growing demand for procedural sedation including imaging studies under GA such as MRI and CT, national consensus guidelines for procedural sedation were published in 1992 and then updated in 2002, 2006, and most recently affirmed in 2012 by the America Academy of Pediatrics, American Academy of Pediatric Dentistry, and American Society of Anesthesiology.[22–25] These guidelines serve as a national standard for procedural sedation.

### *What to Tell the Parents or Caretakers: The Common Questions*

Why does my child need sedation and if so why does it need to be a general anesthetic?

MRI and certain CT examinations require the child to remain still for a certain period of time; this time may range between several minutes, e.g. for CT examinations to an hour, e.g. for some MRIs. Most children, under 3 years of age for CT and under 6 years of age for MRI, experience too much anxiety to remain motionless for the periods of time required to obtain diagnostic imaging. In such settings, anesthesia may be required to ensure that the child does not move during the examination.

What will happen next?

Now that it has been decided that your child will need an imaging study, the procedural sedation team will contact you to discuss how to prepare your child for the examination and what to expect including fasting prior to the study.[25]

### *Effect of Anesthetics on the Developing Brain*

Procedural sedation carries with it a risk for injury to the developing brain: the effect of anesthetic agents including the ones used for procedural sedation such as ketamine, midazolam, propofol, and inhaled agents such as isoflurane have been shown to cause neuronal apoptosis in the dose ranges used for procedural sedation.[26–28] These animal models prompted more recent investigations of the effect of anesthetic agents on the developing human brain. DiMaggio et al., e.g. conducted a retrospective cohort study of 10,450 siblings who underwent surgery before 3 years of age that included an exposed group of 304 children without presurgical history of developmental or behavioral disorder and an unexposed group of 10,146 children. The incidence of subsequent diagnoses of developmental and behavioral disorders was found to be 128 per 1000 person-years in the exposed cohort and 56 per 1000 person-years for the unexposed cohort, and the estimated hazard ratio of developmental or behavioral disorders was 1.6; however, the extent to which the excess risk is causally attributable to anesthesia or mediated by factors such as surgery remained to be determined.[19]

In an attempt to determine the effects of anesthesia versus surgery, Bong et al. studied 100 full-term, apparently healthy children aged 12 years, exposed to general anesthesia for minor surgery before age 1 with an age-matched cohort of 106 nonexposed children. The odds of a diagnosis of learning disability in the exposed group were 4.5 times greater than the nonexposed cohort.[18]

## Procedural Sedation Teams, Child Life, and Alternatives to Sedation

The upshot of such studies for the pediatric ENT or pediatric head and neck imager is the recognition that the ordering of imaging studies under GA should be done judiciously, that (1) there is a clear indication to seek alternatives to GA when feasible, and (2) that referrals for imaging should be made to centers with establish procedural sedation teams.

### *Alternatives to Imaging Under GA Include*

- Alternative modalities such as ultrasound
- Child life specialists that are skilled personnel trained in managing anxious or developmentally delayed children in the imaging suite
- Rapid MRI techniques that may be of sufficient diagnostic yield to obviate the need for a sedated study,[29] and
- Video goggles that may allow certain children to tolerate the enclosed MR environment long enough to allow for diagnostic imaging and have been shown to decrease the need for MR imaging under GA.[30]

### *Procedural Sedation Teams*

The authors' current policy, that we believe to be consonant with national trends, is to require all procedural anesthesia to be managed by a procedural sedation team comprised of anesthesiologists, radiologists, nurses, and child life specialists, under the direction of the anesthesiology department.

The benefits of such procedural sedation teams have been shown to be substantial and referral to institutions supporting such a team is thus an important consideration for the ordering ENT: Ruess et al., e.g. showed that the sedation failure rate dropped from 15% in the 7 months prior to the establishment of a procedural sedation pathway was 15% (19/124) to 1.5% (6/388) ($P < 0.0001$) in the first 25 months after pathway initiation, failures were significantly reduced to. Three (50%) of the six failures after pathway initiation.[31] King et al., e.g., collected data from 5444 sedations, 2148 before, and 3296 after activation of a procedural sedation service activation. The rate of incomplete studies secondary to inadequate sedation decreased from 2.7% before to 0.8% after the procedural sedation-service period. Decreases in cancellations caused by patient illness dropped from 3.8% to 0.6% and rates of hypoxia during sedation dropped from 8.8% to 4.6%.[32]

# PART II: REFERRALS AND IMAGING STRATEGIES

This part of the chapter is organized according to the major clinical indications for which a child may be referred for airway imaging. The indications are listed in alphabetical order below. For each clinical indication, the following points are addressed:

- What is the pertinent clinical background?
- What is the first imaging modality of choice?
- What are the clinical questions that the imaging needs to address?
- What is your approach to the interpretation of the imaging?

## Dysphagia

### *Clinical Background*

Difficulty swallowing in children may manifest as choking/gagging with feeds, recurrent pneumonias, aversion to feeding or refusal of particular types/consistencies of food, and failure to thrive. Particular attention should be given to the consistency of food with which difficulty occurs. If consumption of thin liquids leads to choking or coughing, attention should be given to timing of the symptoms with relation to swallow. When symptoms occur upon initiation of swallow, an anatomic abnormality, such as a laryngeal cleft or a tracheoesophageal fistula, should be considered. If the symptoms are occurring after the swallow or after feeding and are accompanied by arching of the back and discomfort, abdominal pain, food impaction, and emesis, acid reflux or eosinophilic esophagitis may be more likely.[33] In children who present with recurrent pneumonias, silent aspiration may be present, and the parents may not report choking or coughing with feeds. When the history is highly suspicious for reflux, imaging is not immediately indicated. However, if there is question of aspiration or an anatomic abnormality, functional imaging that captures

the act of swallow, such as modified barium swallow, is indicated. Flexible laryngoscopy should be performed prior to imaging, however, to evaluate for VF immobility.

When children have difficulty with swallowing solid consistencies, inflammation from reflux may again be the culprit, but obstructive pathology may also need to be ruled out. These patients may also complain of pain, emesis, and experience weight loss. In these situations, a barium esophagram with small bowel follow through will evaluate the upper digestive tract for any causes of obstruction. Etiologies to consider include neoplasm, stricture, gastric volvulus, and cricopharyngeal spasm.

### *Imaging Modality of Choice*

Modified barium swallow or barium esophagram(s) with small bowel follow-through.

### *Clinical Questions*

1. Is there aspiration occurring, and if so, when is it occurring?
2. Is there evidence of reflux?
3. Is there any suggestion of obstruction?

### *Interpretation*

Single-contrast barium esophagram(s) address these clinical questions well.

The swallow is traditionally divided into oral, pharyngeal, and esophageal phases.

During the pharyngeal phase, as barium transits through the upper esophageal sphincter, attention is given to the laryngeal introitus. If contrast coats the laryngeal surface of the epiglottis but does not cross the vocal folds, this finding is termed penetration. If, however, the contrast passes beyond the vocal folds, this finding is termed aspiration.

If the penetration or aspiration occurs early, e.g. during the antegrade phase of the swallow, an anatomic abnormality such as a cleft or TE fistula should be considered. If the aspiration occurs later, then attention should be made to the esophagus and UES since reflux may result in return of contrast from the esophagus into the pharynx and larynx.

The contrast bolus is then followed through to the lower esophageal sphincter, gastric body, and duodenum to the ligament of Treitz. Failure of passage along this course should raise concern for obstruction including mass, stricture, and malrotation or functional disorder such as delayed gastric emptying.

## Infection

### *Clinical Background*

Pediatric patients with infections that affect the airway may present in a variety of ways. As discussed in the section on stridor, patients may present with acute onset of fever, drooling, inspiratory stridor, and preference for the "sniffing position". These findings suggest epiglottitis, and although rare, can have lethal consequences. In these patients, flexible fiberoptic laryngoscopy is deferred due to possible provocation of an airway crisis; therefore, plain radiography can be useful in these cases but is also often deferred to simple clinical judgment due to the severity of symptoms.

In patients with biphasic stridor, fever, and a barky cough, croup is the most likely diagnosis. These patients often have a prodrome with a gradual progression of symptoms over time. Once again, patients are often treated medically based on clinical symptoms.

When patients present with the history of 1–2 weeks of a viral infection with sudden onset deterioration over a period of hours and fever, stridor, and possible tracheal tenderness, bacterial tracheitis should be at the top of differential diagnosis. Some studies have shown that up to 50% of patients may have concomitant pneumonia, thus a chest X-ray may be helpful in both identifying a tracheal abnormality as well as a consolidation.[34,35]

Cellulitis and abscesses located in the spaces adjacent to the airway, such as the sublingual space, submental/submandibular space, parapharyngeal space, and retropharyngeal space, can have obvious effect on the airway due to narrowing. In sublingual cellulitis or abscess, also termed Ludwig's angina, children may have a history of a dental infection or trauma, and they present with floor of mouth edema and induration, with elevation of the tongue.[36] Imaging is certainly useful in the patients, but the airway must be secured first, followed by CT scan. With infections located in the parapharyngeal and retropharyngeal spaces, neck edema may be seen externally, as well as intraoral edema of the lateral or posterior pharyngeal wall. Limited range of motion of the neck may be noted. In these cases, CT scans are the most commonly used imaging modality, as they can distinguish between cellulitis and abscess, thereby guiding surgical management.[37–39] Lateral radiographs have limited utility in evaluation for retropharyngeal abscesses: a classic radiographic fake-out may occur when a lateral radiograph is obtained in flexion and can produce a radiographic false-positive for

retropharyngeal abscesses. If the radiographic finding seems incongruent with the clinical picture, a CT should be performed to clarify the findings.

### *Imaging Modality of Choice*

While imaging is not used in all of these cases, particularly where the patient is in imminent danger of losing his/her airway, it is useful in cases where the patient is stable:

- Croup, epiglottitis, bacterial tracheitis-plain film radiography
- Deep space neck infection or lymphadenitis-CT scan of neck
- NOTE: Keep in mind that if a patient has had multiple CT scans in a brief timeframe, MRI should be considered to track progression of the infection.

### *Clinical Questions*

1. For radiographs, what is the location of the infection?
2. For CT of the neck, Is there a drainable fluid collection?
3. Is there impending airway collapse not evidenced by the patient's physical state?

### *Interpretation*

Standard radiographic evaluation for airway infection includes lateral and AP radiographs.

The "thumb sign", indicating thickening of the epiglottis, can be seen on lateral neck films in epiglottitis.

Plain film radiographs demonstrating subgottic narrowing and blunting of the subglottic angle on the AP view is also known as the "steeple sign" and is consistent with the diagnosis of croup.

While radiography does not definitively make the diagnosis of bacterial tracheitis, demonstration of irregularity of the tracheal borders and clouding of the air column, sometimes called the "candle-dripping sign", may be seen.

For deep neck infections or suppurative lymphadenitis, a contrast-enhanced CT is performed. Rim enhancing findings that show central hypoattenuation raise concern for abscesses. Lymph nodes may enhance and show central low attenuation and although such findings suggest suppuration, in our experience such nodes may not yield pus upon attempted drainage; when the collection demonstrates irregular margins that extend beyond the expected border of the node, such findings usually indicate drainable collections (Fig. 36.1).

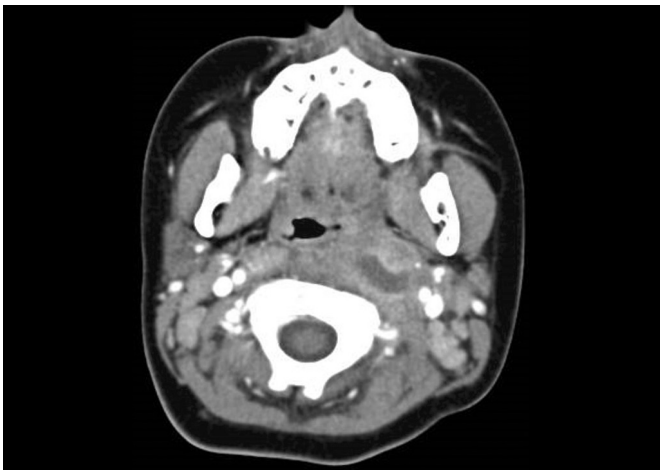


**Fig. 36.1:** Retropharyngeal abscess in a 7-year-old boy presenting with fever and difficulty breathing and swallowing. An axial contrast enhanced CT shows a rim enhancing central low attenuation lesion in the left retropharynx. The lesion lies in the expected local of the left node of Rouviere but the enhancing borders appear irregular and extend slightly outside the borders of the lymph node—findings suggest suppuration.

## Nasal Obstruction

### *Clinical Background*

Etiology of nasal obstruction varies with age at presentation. The pediatric otolaryngologist is often consulted for nasal congestion in the nursery or neonatal ICU. The patients may have difficulty feeding, cyclical cyanosis, nasal flaring, retractions, and desaturations. On physical examination, anterior rhinoscopy may reveal masses if located anteriorly, such as a dermoid, neuroglial heterotopion (so-called nasal glioma), cephalocele, nasolacrimal duct cyst, or neoplasms, such as teratoma, hamartoma, rhabdomyosarcoma, and hemangioma, among many others. In order to distinguish between true obstruction and edema, decongestant may be applied to decrease the swelling. In addition, a 6-french catheter should pass easily through bilateral nasal cavities. If difficulty is encountered anteriorly, pyriform aperture stenosis should be considered. If difficulty is encountered posteriorly (32–35 mm), choanal atresia or stenosis should be on the differential diagnosis. Flexible nasal endoscopy should be performed to evaluate for the site of obstruction more precisely.[40] If narrowing or mass is suspected, imaging is critical in evaluation, with CT being useful for bony anatomy and MRI allowing for improved characterization of a mass. It is important to keep in mind that nasal obstruction can be just one part of a syndrome, such as CHARGE syndrome, Apert syndrome, or Crouzon syndrome.

In the older pediatric population, patients will now be able to describe symptoms, including pain, pressure, and difficulty breathing. If symptoms have an acute onset and have accompanying signs of infection, with physical examination demonstrating pus, acute sinusitis is likely the cause of the obstruction. If physical examination demonstrates a mass, imaging again must be obtained to ensure that this mass has no connection to the brain and to help better characterize the lesion. In additional to those things mentioned above, neoplasms that are also seen in the adult population, such as esthesioneuroblastomas, or benign disease, such as sinonasal/antrochoanal polyps and inverting papillomas, can be seen. In the case of polyps, imaging is helpful in determining the extent of sinus disease and identifying abnormal anatomy for surgical planning.

If a history of trauma exists, a septal hematoma should be evaluated for on physical examination. Septal deviation or nasal bone fracture may also be present, and imaging is not typically necessary in any of these cases as physical examination is adequate for diagnosis.

### *Imaging Modality of Choice*

- For osseous narrowing or obstruction and for trauma or sinus disease, CT maxillofacial without contrast
- For soft tissue masses, MRI face and sinus.

### *Clinical Questions*

1. Is there a mass causing obstruction, and if so, is there connection to the brain?
2. Is there a bony narrowing or atresia?
3. Is there sinus disease?
4. Are there other findings on imaging that may suggest a syndrome?

### *Interpretation*

For CTs in neonates where the clinical findings suggest piriform aperture or choanal stenosis, thin section noncontrast axial images should be performed and reformatted in the coronal and sagittal planes. Piriform aperture stenosis is usually evidenced by an inversion of the normal convex curvature of the frontal process of the maxilla; in piriform aperture stenosis, the frontal process appears concave and curves toward the nasal cavity where it may contact the septum. For choanal stenosis, the distance between the periosteum of the palatine bone along the lateral wall of the choana and the vomer is measured. Traditionally, in normal neonates, the right or left choana measure at least 6 mm and lower measurements raise concern for stenosis. Usually as well the palatal process of the palatine bone appears dysplastic and the vomer appears abnormally thick (Figs. 36.2A to D).

For evaluation for sinusitis, the images are reviewed for abnormal opacity along the walls of the sinuses and nasal cavity. High attenuation opacities raise concern for allergic fungal rhinosinusitis (Fig. 36.3).

Septal hematomas may be subtle radiographically. Interpretation of the images in the context of recent trauma and congestion is important. Hematomas usually arise subperichondrial and thus lie along the anterior cartilaginous septum where they produce an asymmetric bulge that may exhibit hypoattenuation on CT.

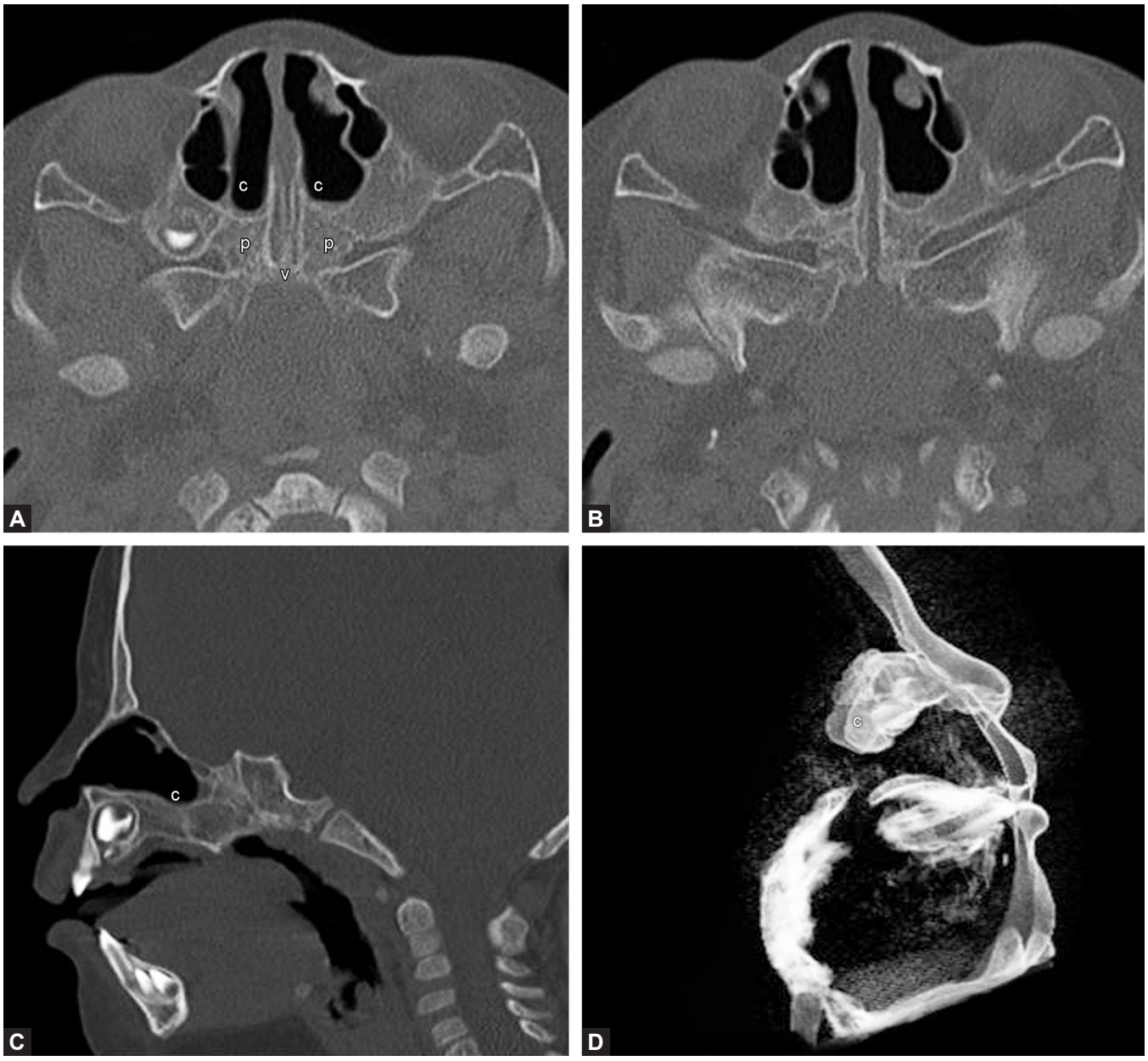
For masses, high-resolution coronal T2-weighted images are favored that allow for evaluation for defects along the anterior skull base and communication of the brain with the sinonasal cavity. Contrast-enhanced MRI may help to distinguish cephaloceles that may demonstrate rim enhancement versus neoplasms that would be expected to enhance confluently (Figs. 36.4 to 36.6).

## Obstructive Sleep Apnea

### *Clinical Background*

Diagnosed in approximately 2–3% of all preschool aged children in the United States,[41] OSA has been become the most common diagnosis for which adenotonsillectomy is performed. Parents may report heavy snoring, pauses in breathing while sleeping, behavior problems, poor attention, memory and cognitive deficits, and poor school performance.[42] Physical examination may reveal enlarged tonsils in many patients. However, some patients may not demonstrate enlarged tonsils but have symptoms consistent with OSA. Because these patients are often younger in age, nasopharyngoscopy may be poorly tolerated and examination can be limited. In this situation, plain radiography can demonstrate adenoid enlargement and has been shown to correlate well with intraoperative findings of adenoid hypertrophy.[43]

In adult patients Riley et al. have described a staged approach to the treatment of OSA where stage I consists of uvulopalatopharyngoplasty, anterior maxillary osteotomy, and hyoid myotomy, and stage II surgery involves mandibular maxillary advancement.[44] In children, however, first-line treatment typically consists of adenotonsillectomy. In patients with persistent OSA following




**Figs. 36.2A to D:** Choanal atresia in a tracheostomy dependent 2-year-old girl. Noncontrast CT axial images obtained at the roof (A) and floor (B) of the nasal cavity demonstrate complete choanal atresia. No aerated passage is seen between the choanae (c) and the nasopharynx (C). The vomer (v) rises abnormally superiorly and is inseparate from the palatine bones (p). The pterygopalatine fossae have formed between the pterygoid bodies and the palatine bones. Sagittal 2D reformat shows the complete osseous plate that closes the posterior nasal cavity. A surface reconstruction air cast (D) shows the aerated nasal cavity back to the choana (c) but no demonstrable aeration between the nasal cavity and the nasopharynx.

adenotonsillectomy, the site of obstruction may be difficult to identify. Drug-induced sleep endo copy may be used help locate where the obstruction is occurring. In addition, the use of static and cine MRI has been shown to be useful in pinpointing areas where narrowing or collapse is occurring.[45–47] For children with suspected craniofacial dysmorphisms, CT may be of use as a guide to surgical management.[48]

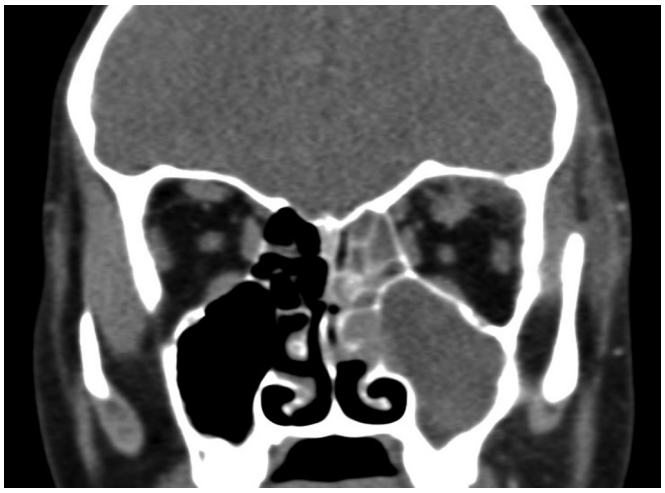


**Fig. 36.3:** Sinusitis. Coronal CT reformat in a 12-year old girl who presented with left facial pain shows complete opacification of the left maxillary and ethmoid air cells consistent with sinusitis. Some of the opacity along the left middle turbinate appears more radiodense (higher in attenuation) that may represent more inspissated or proteinaceous secretions.

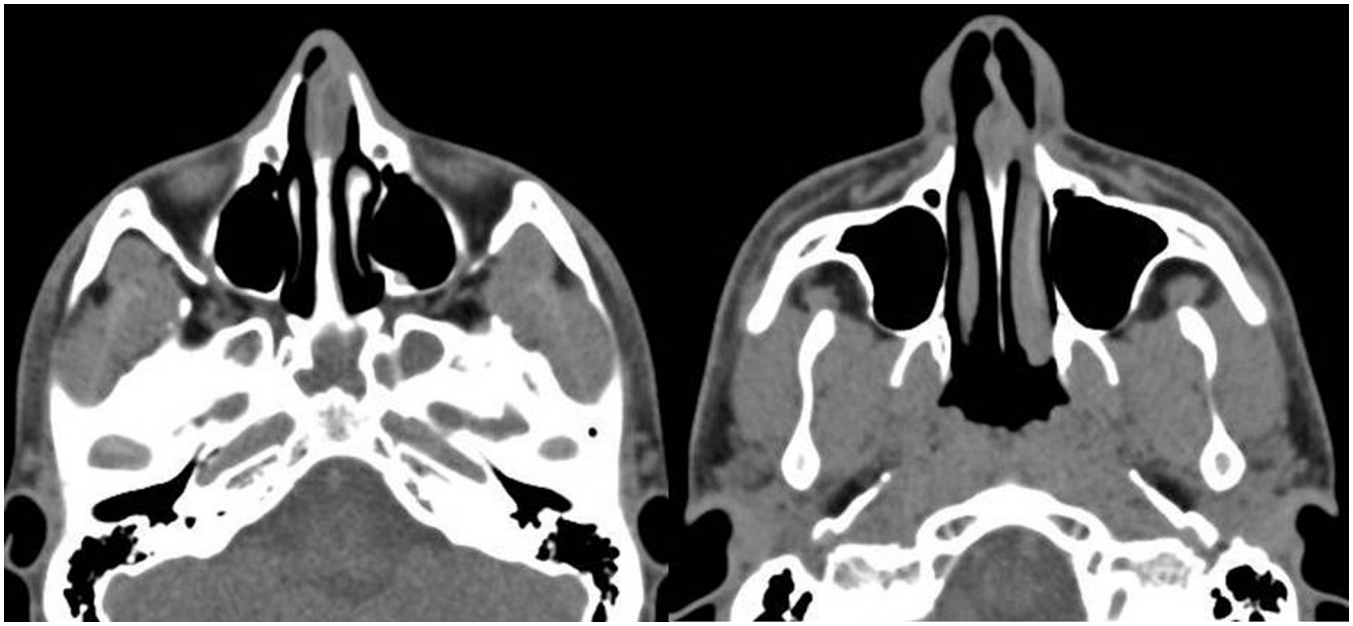


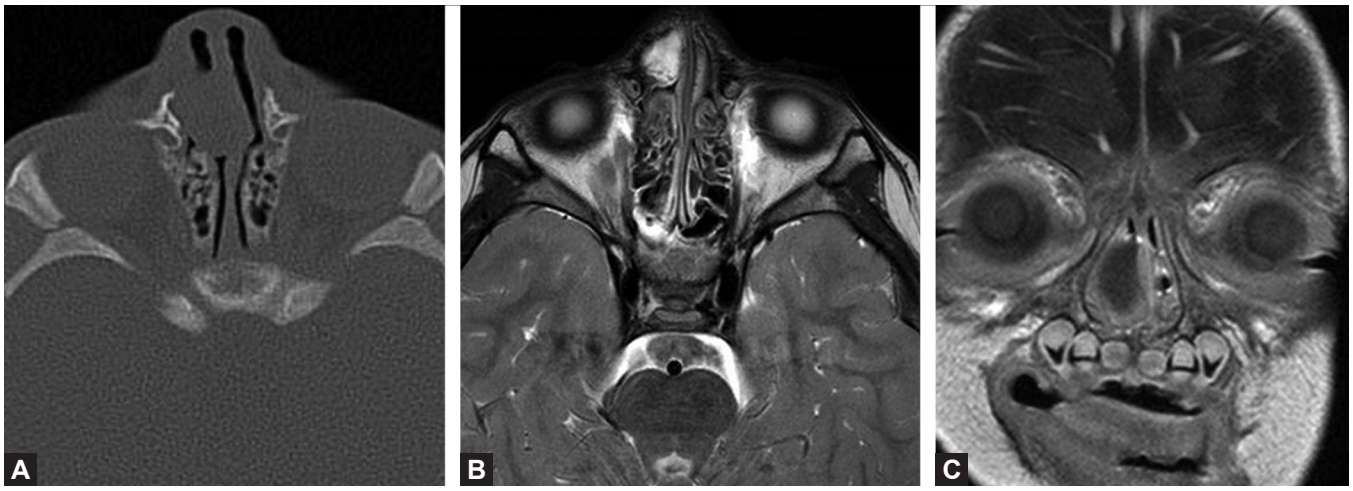
**Fig. 36.4:** Septal hematoma in 16-year-old boy who suffered trauma to the nose 5 days earlier. Two noncontrast axial CT images through the nasal cavity demonstrate abnormal focal expansion at the base of the columella in the cartilaginous nasal septum consistent with a septal hematoma.

## *Imaging Modality of Choice*

- For suspected adenoid hypertrophy, plain film radiography of the nasopharynx
- For persistent sleep apnea following adenotonsillectomy, cine MRI
- For those patients where craniofacial reconstruction is a consideration, noncontrast low-dose CT of the airway.

## *Clinical Questions*

1. Is adenoid hypertrophy the etiology for obstruction?
2. Are there additional sites of obstruction, which are difficult to identify on physical examination?
3. Are there craniofacial dysmorphisms, e.g. long SI dimension of the airway (Abramson Kaban article) that may predispose to OSA and benefit from reconstruction?




**Figs. 36.5A to C:** Neuroglial heterotopion in a 2-month-old boy presenting with nasal obstruction. An axial noncontrast CT (A) shows a round opacity that obstructs the right nasal cavity at the piriform aperture. An axial T2-weighted image (B) and a coronal postcontrast T1-weighted imaged (C) show the lesion centered in the nasal cavity with no demonstrable intracranial connection to suggest a cephalocele.

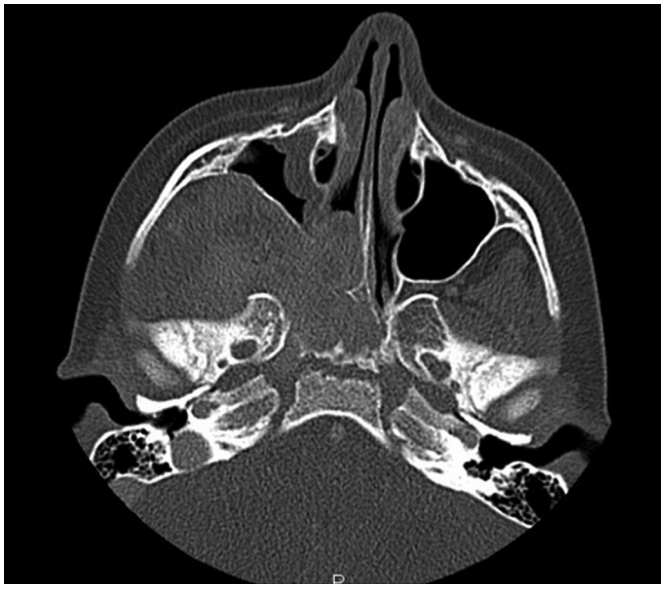


**Fig. 36.6:** Juvenile angiofibroma in a 6-year-old boy presenting with nasal obstruction and epistaxis. Axial contrast enhanced CT in bone algorithm shows a mass centered in the right pterygopalatine fossa that obstructs the right choana medially, erodes the right sphenoid bone posteriorly, and laterally protrudes into the right masticator space.

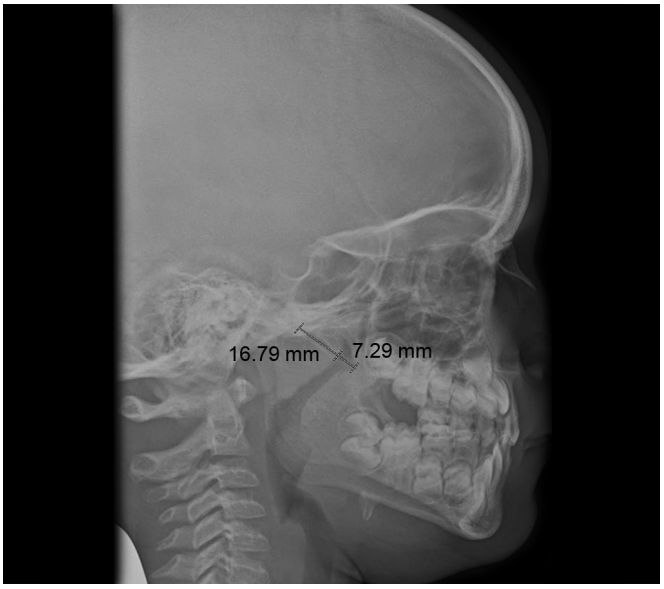
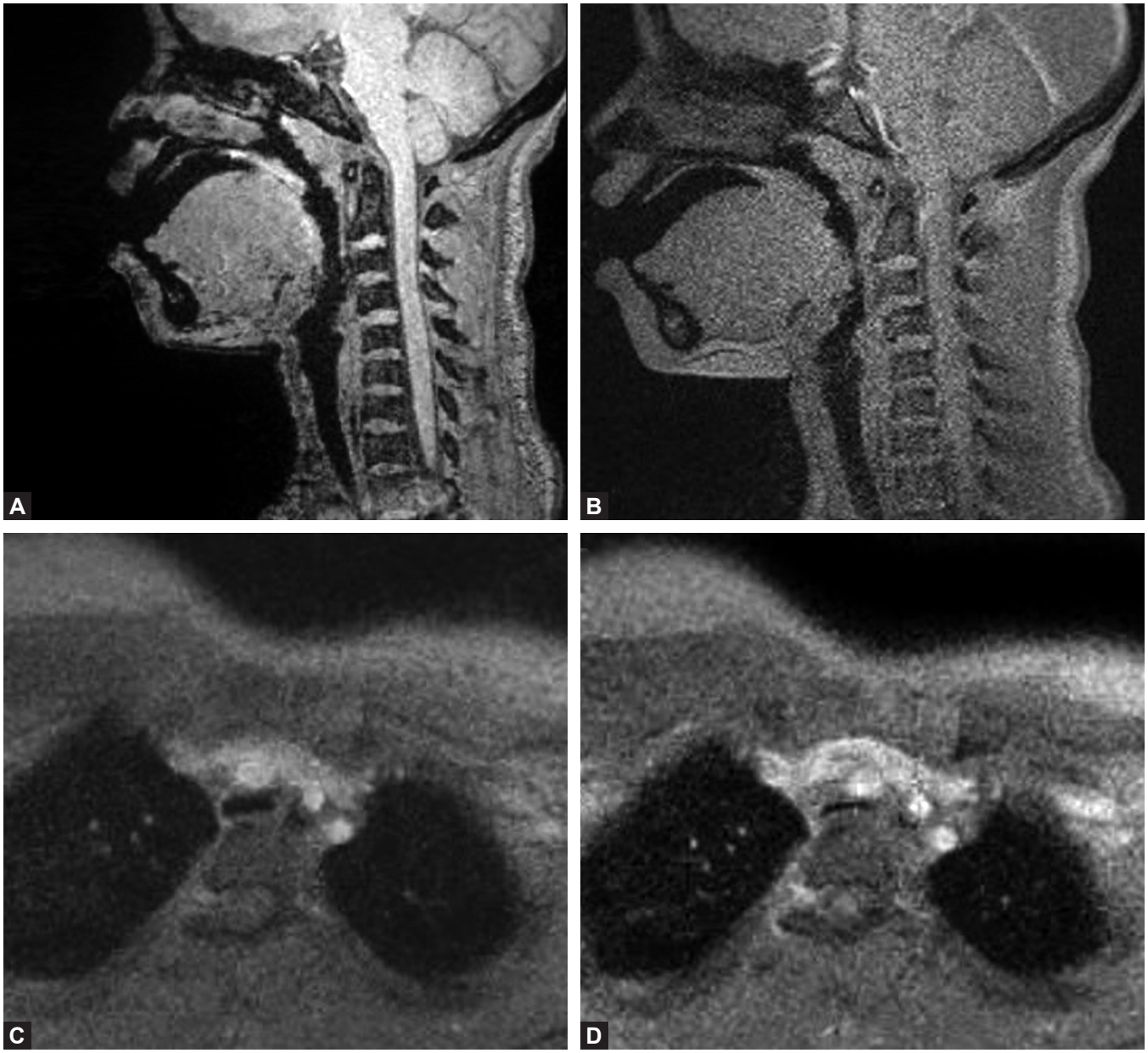



**Fig. 36.7:** Adenoid hypertrophy. Lateral radiograph in a 6-year-old girl with noisy breathing shows a prominent nasopharyngeal pad that measures 17-mm-thick and that narrows the airway to 7 mm AP. The lateral radiograph provides rapid assessment of the caliber of the nasopharyngeal lumen that may be more practical than nasopharyngeal endoscopy in and infant or child.

## *Interpretation*

For adenoid hypertrophy a single lateral radiograph is obtained and the adenoid pad and airway are measured along a line drawn from the posterior nasal spine to the anterior-most aspect of the adenoid pad, and from the anterior aspect of the adenoid pad to the nasopharyngeal base of the spheno-occipital synchondrosis. The adenoid pad is considered normal when it measures about 5–10 mm. At 10–20 mm, there is mild to moderate hypertrophy, and at >20 mm, severe hypertrophy is present, potentially causing nasal obstruction. This is evidenced by the concomitant decrease in the width of the air column as the adenoids enlarge (Fig. 36.7).

When cine MRI is done for persistent OSA, sedation is administered to mimic sleep. Both continuous and intermittent obstruction can be identified during the study. Following anatomic imaging, single sagittal, axial, and coronal slices through the airway can be targeted and reviewed at 1–2 second intervals for movement and collapse during the respiratory cycle. Airway narrowing is most commonly observed at the level of the nasopharynx from the adenoid pad, tongue base from glossoptosis or lingual tonsillar hypertrophy, and along the trachea from tracheomalacia or innominate impression (Figs. 36.8A to D).




**Figs. 36.8A to D:** Cine MRI of the airway in a 12-year-old girl with trisomy 21 and obstructive sleep apnea that persisted after adenoidectomy. (A) a sagittal SPGR at rest and (B) a single sagittal frame from a cinematographic T1-weighted FLASH MRI sequence provides a temporal snap shot of motion of the airway every 0.5 seconds that shows a dynamic collapse of the oropharynx from the tongue base. In (C) and (D), an axial FLASH image obtained through the distal trachea at the crossover point of the innominate artery, the cine MRI shows marked collapse of the tracheal lumen during the respiratory cycle from innominate artery compression. In this study sleep was induced with IV propafol and an oral airway tube that was removed during the cine sequences.

## Stridor and Respiratory Difficulty

### *Clinical Background*

Stridor may present as a manifestation of numerous pathologies, so clinical history is of paramount importance. As a neonate, a child may present with high-pitched inspiratory stridor that has been present since birth or shortly after birth which may be accompanied by failure to thrive, cyanotic or desaturation episodes, and/or difficulty feeding. This history would be consistent with laryngomalacia, and flexible fiberoptic laryngoscopy would be adequate to make the diagnosis. Imaging has been shown to have poor sensitivity for diagnosing laryngomalacia.[49] However, inspiratory stridor may also represent a glottic pathology, such as a VF paralysis. Although this diagnosis is also made with flexible fiberoptic laryngoscopy, imaging is useful in uncovering an etiology, such as an Arnold–Chiari malformation, which may cause bilateral VF paralysis.

As an infant, a child may present with inspiratory or biphasic stridor with a barky cough. The patient may be febrile and appear sick, which point to the infectious etiology of croup. Infants may also present with acute onset inspiratory stridor, fever, drooling, and dysphagia. These symptoms suggest an acute bacterial infectious process, such as epiglottitis. When biphasic stridor is present in conjunction with signs of infection, including high fever, bacterial tracheitis should be considered. Imaging can be helpful in these cases, but should be pursued as long as there is no impending airway collapse.

When an infant presents with stridor that is not associated with infection, other etiologies must be considered. In patients who are diagnosed with recurrent croup who may or may not have a history of previous intubation, subglottic stenosis should be assumed until proven otherwise. Subglottic cysts may also present in a very similar fashion, and may indeed be a precursor to subglottic stenosis. Often, these patients only become stridulous with an upper respiratory infection and have persistent stridor when other symptoms of infection resolve. Imaging plays a limited role here, as direct laryngoscopy serves as the gold standard. Subglottic hemangioma should also be considered, particularly if the patient has any evidence of a cutaneous hemangioma, found in 50% of patients with subglottic hemangioma. While direct laryngoscopy is again the gold standard for diagnosis, imaging may serve to provide additional useful information in providing clues. Lastly, a foreign body, whether airway or esophageal, may cause stridor due to narrowing from intraluminal obstruction or extraluminal compression. These can be seen on plain films and/or fluoroscopy.

Biphasic or expiratory stridor that is coarse in nature should point to a tracheal pathology, whether a fixed lesion, such as complete tracheal rings, or a dynamic lesion, such as tracheomalacia. Dynamic airway imaging, such as fluoroscopy, may be used as an adjunct, but the sensitivity is only in the range of 50–60% and it therefore cannot replace bronchoscopy.[49,50] In addition, a vascular ring may also cause biphasic or expiratory stridor, depending on the location of compression. Bronchoscopy is typically the first step in diagnosis, but imaging, particularly a CT angiogram, is very helpful in identifying the type of anomaly present and whether or not surgery is indicated.[51]

In pediatric patients of any age, stridor may represent a neoplasm in the airway, such as a chondroma, minor salivary gland tumor, laryngotracheobronchial papillomas, or rhabdomyosarcoma, or an autoimmune pathology, such as amyloidosis, Wegener's granulomatosis, or sarcoidosis. In the oral cavity and oropharynx, other masses that may present include thyroglossal duct cyst, lingual thyroid, vascular malformations, foregut duplication cysts, and ranula. Imaging is certainly useful when evaluating a neoplasm but is of limited utility in autoimmune diseases.

### *Imaging Modality of Choice*

- For evaluation of dynamic airway narrowing, airway fluoroscopy/barium swallow
- For possible foreign body aspiration, airway fluoroscopy or left lateral decubitus plain film radiography
- For evaluation of possible vascular compression of the airway, CT angiography of the neck and chest
- For evaluation of a possible mass in the airway, CT of MRI of the neck
- For congenital VF paralysis, MRI brain.

### *Clinical Questions*

1. Is there a mass in the airway?
2. Is there dynamic narrowing of the airway?
3. Is there vascular compression of the airway?
4. Is there a neurologic etiology which may explain VF paralysis?
5. Is there suggestion of an infectious etiology?

### Interpretation

On airway fluoroscopy, the pharynx, larynx, and trachea are studied to evaluate for abnormal collapse during the respiratory cycle, while the pharynx and larynx are often evaluated endoscopically in the office, evaluation of the trachea beyond the vocal folds depends more on the radiographic evaluation. Abnormal collapse of the posterior wall of the trachea during expiration raises concern for tracheomalacia.

On barium swallow, the contours of the esophagus are evaluated for abnormal impressions that may suggest a vascular ring or sling. Normally, along the posterior esophageal wall three impressions are seen: the aortic arch, the left main stem bronchus, and the left ventricle. In a pulmonary sling, where the left pulmonary artery arises anomalously from the right pulmonary artery, the left PA produces an abnormal impression along the anterior wall of the esophagus and the posterior wall of the trachea. In a vascular ring, abnormal impressions are seen along the anterior wall of the trachea and the posterior wall of the esophagus.

CT is useful to survey the entire airway in cases of suspected compression. Although vascular lesions such as hemangiomas may be difficult to detect by contrast-enhanced CT, the rapidity and ease of access of CT makes it the modality of choice for initial imaging of the airway. Vascular rings and slings, narrow segments of the airway, and neoplasms causing mass effect are usually detectable (Figs. 36.9 and 36.10).

MRI is useful for targeted evaluation of compressive airway lesions, in particular for subglottic hemangiomas. We have found MRI to be most useful when the initial bronchoscopic evaluation raises concern for a focal narrowing. MRI often requires sedation and control of respiratory motion by intubation and pharmacologic paralysis to image the airway sufficiently that present relative drawbacks compared to CT. MRI is, however, the modality of choice for suspected central causes of airway compromise such as VF paresis from a Chiari malformation or from suspected myelin disorders (Figs. 36.11 to 36.14).

## Velopharyngeal Insufficiency

### Clinical Background

Children with VPI most commonly present to the pediatric otolaryngologist as part of the multidisciplinary evaluation for treatment, along with the speech pathologist. These children present with hypernasality and have trouble with sounds that require velopharyngeal closure, such as "p", "b", "g", "t", and "d". While much of the diagnosis is made on physical examination with nasopharyngoscopy and with nasometry, imaging can be helpful in uncooperative patients and provide additional information regarding closure pattern. Multiview fluoroscopy allows for visualization of closure in three different planes, but it has been criticized for oversimplification of VPI in one plane, underestimation of the anteroposterior pharyngeal dimension, and the potential to overdiagnose VPI due to speed of radiography when compared to velopharyngeal closure.[52] In addition, due to the radiation exposure, its use has declined in favor of nasopharyngoscopy.[53]

Cine MRI with or without audio has also recently been found to be helpful in more precisely identifying the pattern of closure, specifically looking at motion, bulk, and orientation of the levator veli palatini; however, it is of limited use due to the expense.[53,54]

On clinical presentation, close attention should be given to the possible presence of a syndrome, particularly 22q11.2 deletion syndrome, also known as velocardiofacial syndrome. In these children, a medialized carotid artery may be present, and this may be seen on nasopharyngoscopy. Suggestion of this finding should prompt the physician to obtain vascular imaging to evaluate for this entity, as this may change the surgical plan (Figs. 36.15A and B).

### Imaging Modality of Choice

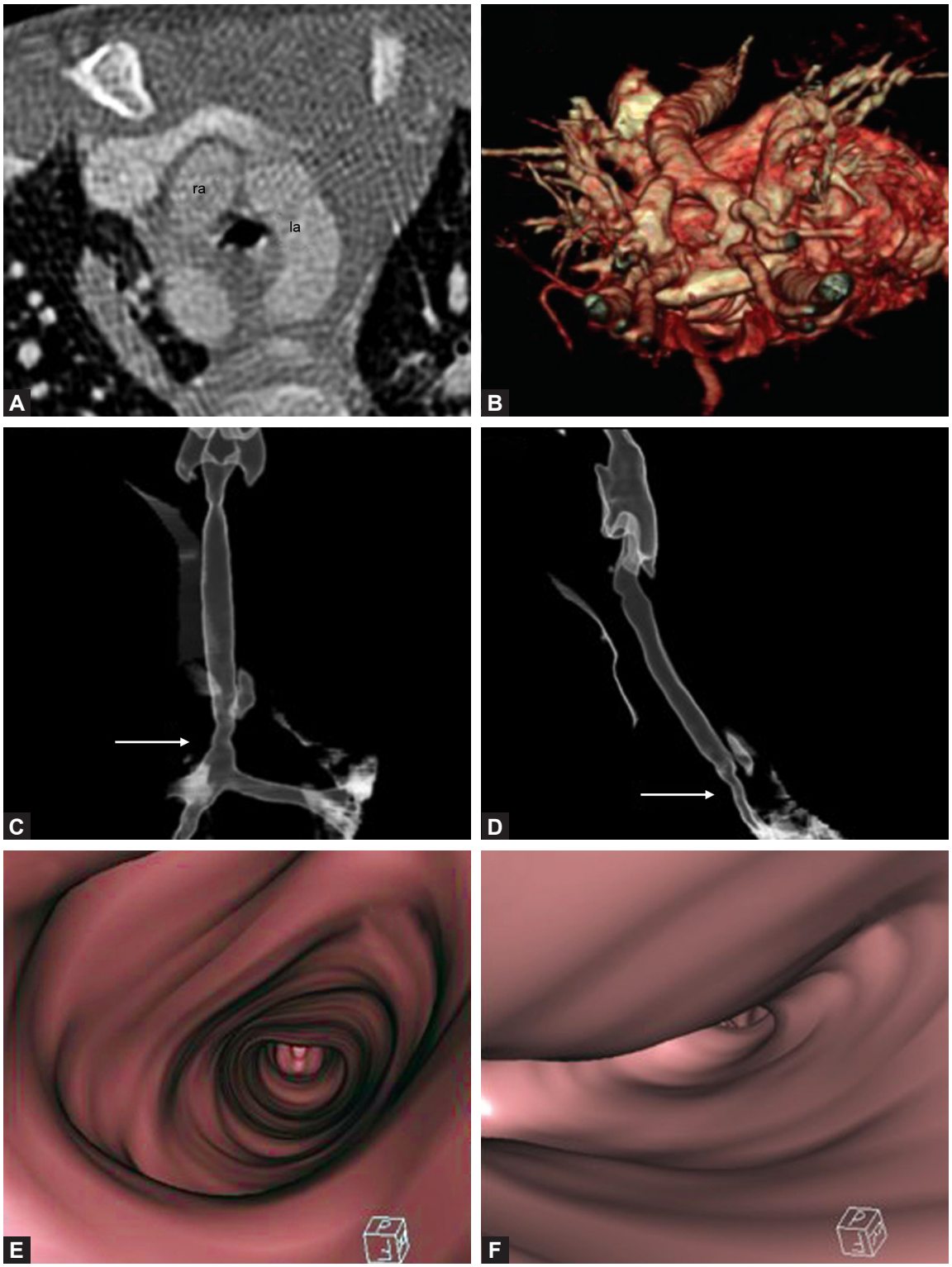
- For evaluation of closure pattern as an adjunct to endoscopy, cine MRI VPI studies
- For evaluation of abnormal vasculature, MRI and magnetic resonance angiography (MRA) of the neck.

### Clinical Questions

1. What is the pattern of closure noted?
2. Is there abnormal vasculature that may alter the planned surgical intervention?

### Interpretation

The cine imaging is coordinated synchronously with voice recordings conducted by the speech pathologist. Silver et al. and Maturo et al. describe the voice recording apparatus constructed of readily available hospital supplies such as a plastic cup held by the patient at his or her mouth during




**Figs. 36.9A to F:** Double aortic arch in a 16-month-old boy presenting with difficulty breathing and stridor. (A) Axial contrast-enhanced CT shows the right aortic arch (ra) and left aortic arch (la) as they form a vascular ring and constrict the trachea. (B) A surface reconstruction shows in a rostrocaudal projection the two aortic arches as the form a circle in the superior mediastinum. (C) (An AP projection) and (D) (a lateral projection) 3D surface renderings of the airway show the abnormal constriction of the distal trachea, white arrows. (E and F) Virtual bronchoscopic fly through renderings of the airway show the tracheal lumen above and at the level of the vascular ring.

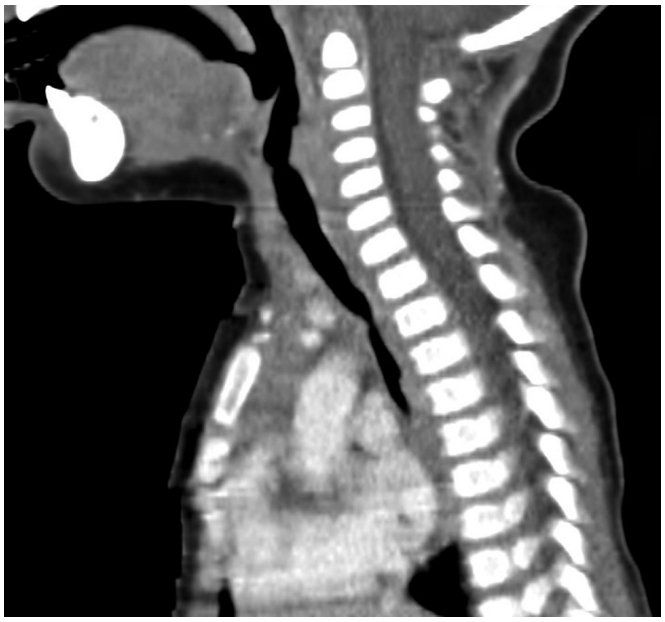
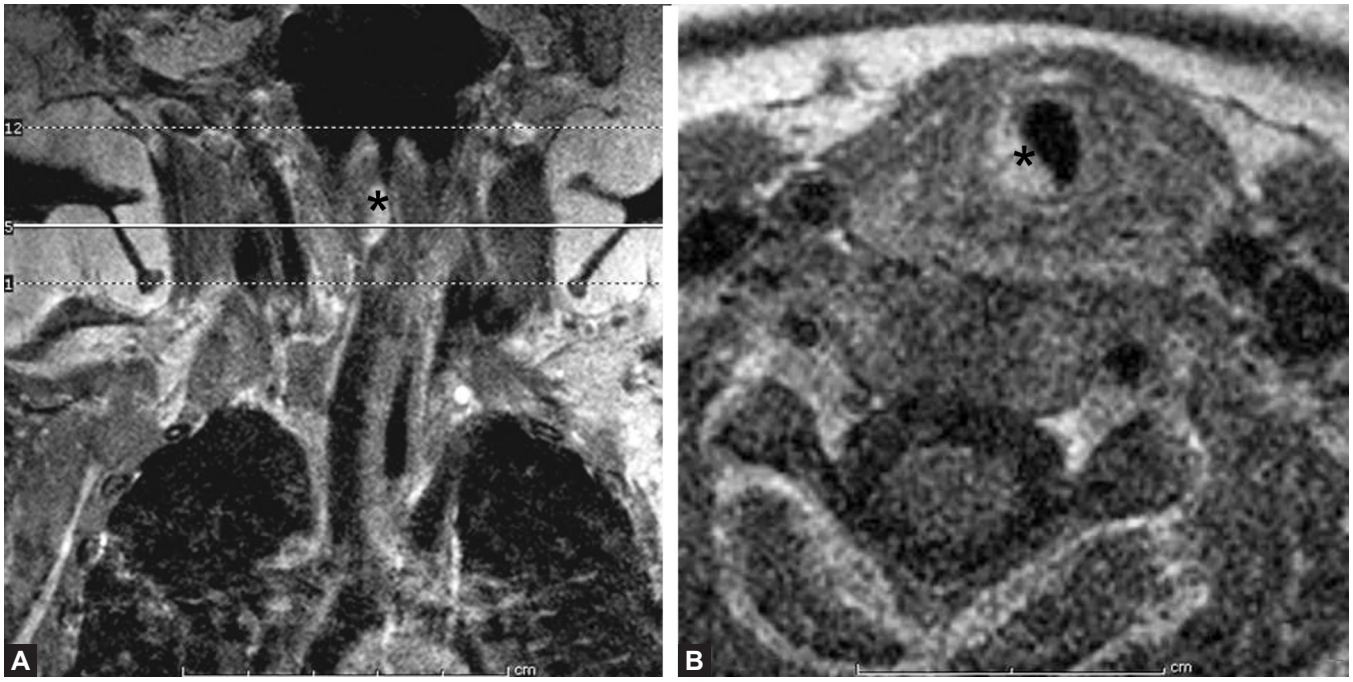
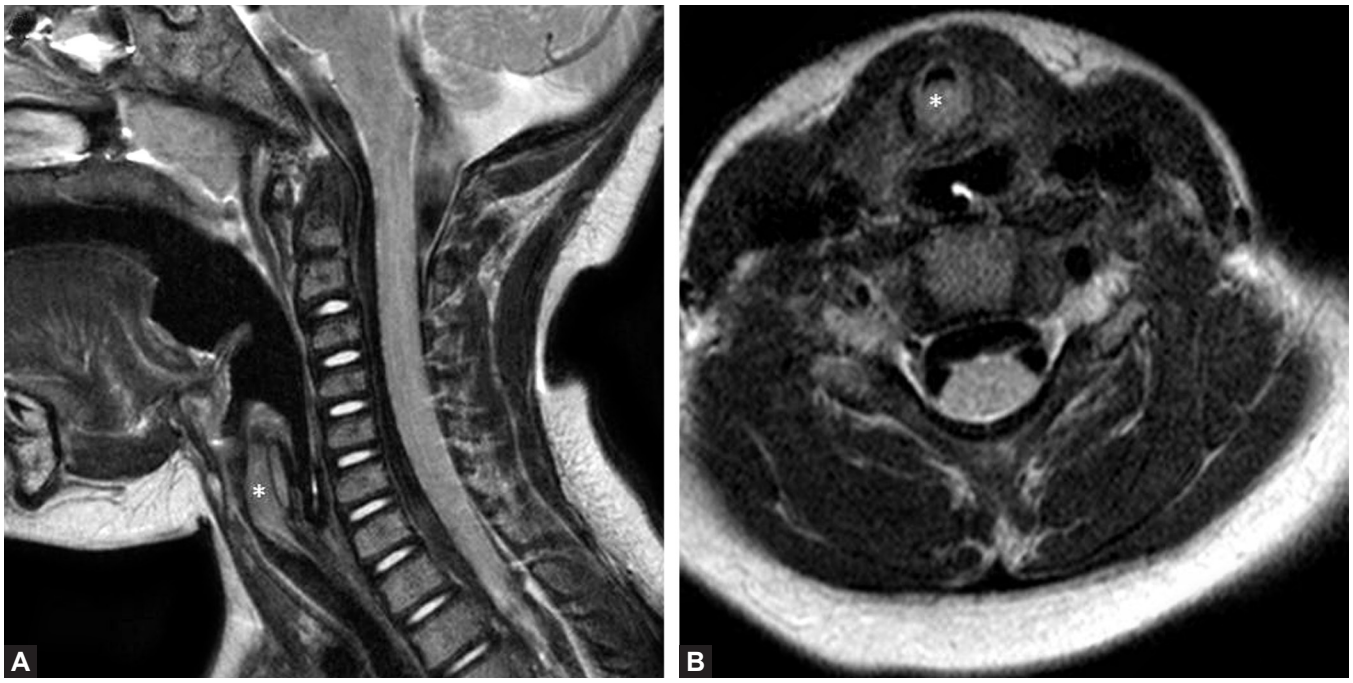


**Fig. 36.10:** Complete tracheal ring in a 1-year-old boy who presented with difficulty breathing. Sagittal reformat from a helical contrast enhanced CT acquisition of the airway shows an abrupt segmental constriction of the tracheal lumen at the T2 level. No extrinsic compressive lesion was seen such that the findings appeared to be most consistent with a luminal abnormality.

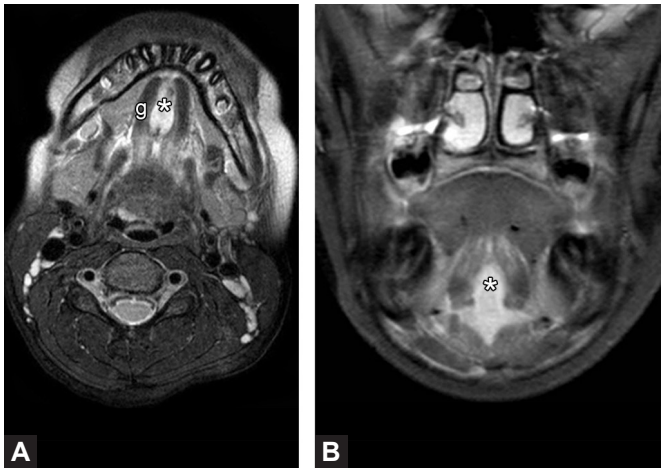



**Figs. 36.11A and B:** Suglottic hemangioma in a 16-month-old girl presenting with difficulty breathing. Coronal (A) and axial (B) post-gadolinium high-resolution T1-weighted images show a subglottic enhancing lesion that protrudes from the right posterolateral wall of the subglottis into the laryngeal lumen. Asterisk (*) indicates a subglottic enhancing lesion consistent with hemangioma.

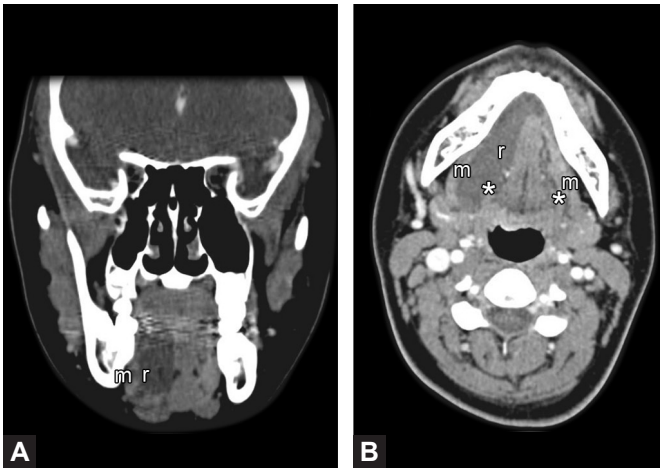
the cine MR imaging and connected via oxygen tubing using hospital tape that is fed through the wave guide, the hole in the wall between MR unit and the technician area, and amplified to a USB preamplified connected to a laptop computer with recording software. Target phrases selected by the speech pathologist similar to those used for videofluoroscopic velopharyngeal studies are used and corecorded with the cine MRI,[53,55] and abnormalities in closure of the velopharyngeal port are evaluated real time during phonation.



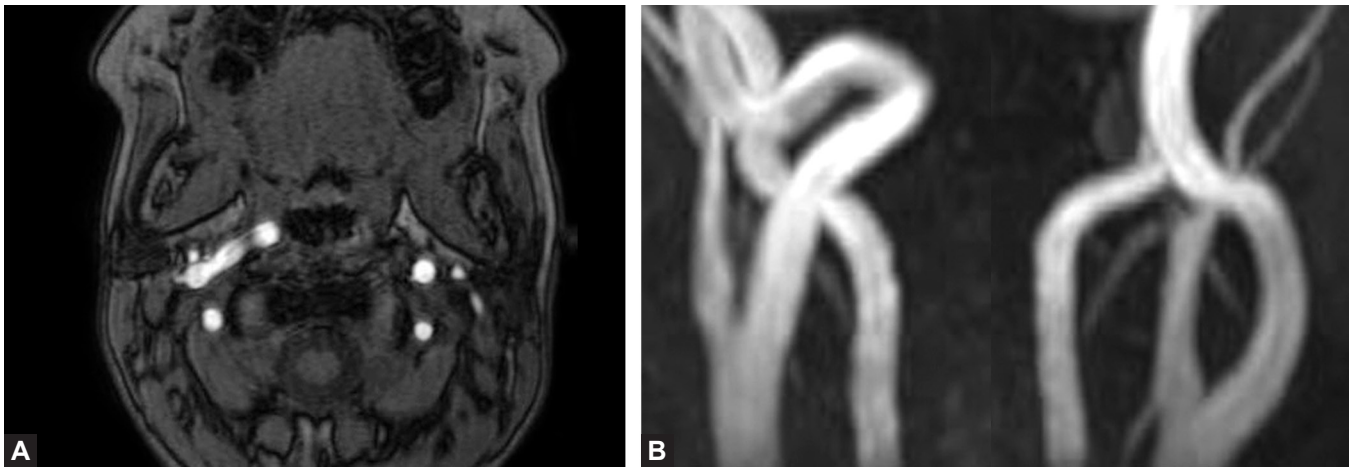

**Figs. 36.12A and B:** Subglottic ectopic thymus presenting in 19-month-old boy with difficulty breathing and subglottic mass on endoscopy. Sagittal T2 (A) and axial T2 (B) noncontrast MR images show a subglottic mass (*) that demonstrates intermediate signal on the T2-weighted images, that narrows the sublottis and proximal trachea, and that protrudes ventrally along the perichondrium of the cricoid cartilage.




**Figs. 36.13A and B:** Foregut duplication cyst in a 1-month-old boy with difficult breathing from glossoptosis. An axial (A) and a coronal (B) T2-weighted images show a well marginated high signal finding in the anterior floor of mouth that splays the geniohyoid muscle (g) and appears clearly separate in origin from the sublingual glands, which thus distinguishes it from a ranula. Asterisk (*) indicates a foregut duplication cyst.




**Figs. 36.14A and B:** Ranula presenting in a child with mouth swelling and pain. Coronal reformat (A) and axial image (B) from a contrast enhanced CT show a well-defined low attenuation lesion consistent with a ranula (r) that expands the right sublingual space between the styloglossus-hyoglossus muscles (*) and the mylohyoid muscle (m). The ranula fills the right sublingual space back to the right submandibular gland that lies along the posterior margin of the lesion.




**Figs. 36.15A and B:** Medial deviation of the internal carotid artery in a child with del22q phenotype most consistent with velocardiofacial syndrome who presented with velopharyngeal insufficiency and had pulsatile finding along the right lateral oropharyngeal wall. In (A) an axial source image from a 3D time of flight MR angiogram shows marked medial deviation of the right ICA that abuts the medial wall of the oropharynx. (B) A maximum intensity projection (MIP) reconstruction shows the medial buckle of the right ICA compared to the normal course of the left.

## CONCLUSION

For imaging of the airway in children, a range of techniques is still useful, including the traditional plain film radiograph of the airway, fluoroscopy, barium swallow, US, CT, and MRI. The determination of the modality of choice depends on the clinical indication for the imaging study and the clinical questions that need to be addressed, the age of the patient, and the growing concern for morbidities associated with radiation and sedation, all of which need to be weighed when deciding on the best approach to imaging.

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CHAPTER

# 37 Preoperative Evaluation of the Child Needing Airway Surgery

*Mary Shannon Fracchia, Jyoti Ramakrishna*

Anesthesia for airway surgery is particularly challenging in the pediatric age group.[1] We know that these children are at an increased risk of compromised airways due to their underlying condition. Hence, the preanesthesia evaluation is crucial in guiding the anesthesiologist on the day of surgery.

A comprehensive visit, ideally in an aerodigestive clinic, or preanesthesia evaluation is necessary prior to airway surgery. The patient is seen by the ENT surgeon and also meets with other specialists (such as pediatric pulmonary or pediatric gastroenterology) who may be performing procedures on the child. At this time, a complete review of history and prior workup, as well as a thorough physical examination, are performed.[2]

For an elective surgery, it is preferable to perform the procedure when the child is not having intercurrent airway symptoms such as an upper respiratory tract infection or wheezing. However, if a patient has recurrent problems with upper respiratory infections, sinusitis, chronic cough, congestion, or croup caused by the underlying airway condition, then performing the procedure to rectify this may have to occur at a time when the airway symptoms are present. It may not be possible to find an optimal time, and risks versus benefits need to be evaluated and discussed with the family. Depending on the level of concern it may be appropriate to discuss with pediatric anesthesia staff ahead of time. Some cases that are determined to be high risk or complex will benefit from meeting the pediatric anesthesia staff for a preoperative visit prior to the day of the procedure.

## SPECIAL CONSIDERATIONS ON PREOPERATIVE HISTORY AND PHYSICAL EXAMINATION IN PEDIATRIC AIRWAY PATIENTS (also *see* Tables 38.1 and 38.2)

### Prematurity

Often, children with airway concerns were born prematurely. Some have been intubated at birth for varying periods. Subglottic stenosis, gastroesophageal reflux, and bronchopulmonary dysplasia are common comorbidities in this population. These children with bronchopulmonary dysplasia and chronic lung disease have decreased pulmonary reserves at baseline and are particularly prone to infection.[2,4] They require chronic respiratory therapies, including oxygen, nebulized steroids, diuretics, and frequent antibiotics.

### Perinatal History

Important points that may have a bearing on surgical outcomes include low Apgar scores or birth hypoxia; maternal diabetes, pre-eclampsia, or drug/alcohol use; perinatal trauma, seizures, prolonged mechanical ventilation, apnea and bradycardia; and sepsis.[2]

### Developmental

Children may have developmental delays as a result of intra- or perinatal events, or an underlying syndrome, and

may not function at their age level. It is important to note this so that the team working with the family on the day of surgery is able to adapt their care appropriately.[2,3]

## Compromised Airway

Laryngomalacia and/or tracheomalacia are other common issue in this population. For instance, surgery might be successful in repairing subglottic stenosis, but the child might not be able to be decannulated because of a floppy airway, known as tracheomalacia.[5] Gastroesophageal reflux can cause inflammation and airway irritability.[7]

In older children, pulmonary function tests are a valuable tool to investigate airway dynamics of a compromised airway. Flow volume loops can differentiate between upper, lower, and fixed airway obstructions and the degree of the compromise. Any child >6 years of age should get a pulmonary function test.

## Aspiration

Many patients with airway problems in early life present with symptoms of feeding difficulties or choking on feeds. Modified barium swallow testing performed with the help of a pediatric radiologist and a speech language pathologist helps preoperatively to assess for evidence of aspiration, especially with liquids. Fiberoptic endoscopic evaluation of swallowing is another test performed at many centers to assess anatomic deficits in the airway that may lead to feeding difficulties and risk for aspiration.[6] Bronchial lavage specimens are often sent for lipid-laden macrophages, the presence of which may indicate microaspiration, although this is known to be an imprecise marker.[7] Aspiration increases the risk of surgery; hence it may be necessary to advise against oral feedings and recommend placement of a gastrostomy tube while delaying airway surgery until such time as this issue is addressed.

## Oxygen Status

From a pulmonary standpoint, many children requiring airway surgery have decreased pulmonary reserves at baseline, especially those who are premature, aspirate, or have a compromised airway. Undergoing general anesthesia during airway surgery will compromise the pulmonary reserve even further. To optimize pulmonary reserve, we need to understand the pulmonary mechanics preoperatively. Before a laryngeal tracheal reconstruction, for instance, we often recommend an overnight oximetry or sleep study with a capped tracheostomy to assess the ventilation and oxygen needs of the child prior to the procedure.[8]

## Medications

A complete list of current medications and doses should be in the chart. Clarifications of which medications should be taken and which held the morning of the procedure are helpful in avoid unnecessary confusion. This also helps in alerting the anesthetist to potential interactions with anesthetic agents.[2]

In particular, a history of steroid use is important. Children with compromised airways and/or premature lungs are usually managed with steroids throughout pulmonary exacerbations. Nebulized steroids typically do not have profound systemic effects but oral steroids do. Children with compromised airways often suffer from episodes of croup treated with dexamethasone. If a child requires more than two courses of steroids in 6 months, the airway reconstruction needs to be deferred. Steroids interfere with healing of wounds and grafts that may be placed during reconstruction.[8]

## Gastroenterological

Gastroesophageal reflux is common in the first few months of life and considered physiological in otherwise normal infants. Gastroesophageal reflux disease or GERD is defined as symptoms or mucosal damage caused by acid reflux. It is often seen at a higher frequency in conjunction with other underlying issues mentioned above such as prematurity, asthma, tracheomalacia, developmental delays, and many genetic syndromes.[7,9] Airway symptoms such as cough and hoarseness may represent extraesophageal manifestations of GERD. Although often a clinical diagnosis, a thorough workup may be mandated including pH probe or impedance measurements and endoscopy. When poor gastric emptying is suspected as a contributory factor, a gastric emptying scan may be of benefit. If reflux is a concern then it should be adequately managed medically in collaboration with a pediatric gastroenterologist prior to surgery and up to 8 weeks postoperatively to aid in recovery.[10] Although concerns have been raised regarding aggressive medical therapy with proton pump inhibitors in the pediatric age group, patients with specific airway concerns often merit aggressive therapy; hence the

risks versus benefits need to be discussed with the family. Occasionally, fundoplication surgery may be necessary if medical therapy fails.[7]

Less commonly, a tracheoesophageal fistula may contribute to airway symptoms. These can be difficult to diagnose on a contrast upper gastrointestinal study, requiring a "tube study" where dye is injected into the esophagus with a nasogastric tube under some pressure; rarely an endoscopic methylene blue injection into the esophagus on the operating table while visualizing the trachea may be necessary.[7]

Eosinophilic esophagitis has recently been recognized to contribute to airway symptoms in children. This is a clinicopathologic diagnosis, which includes a triad of esophageal symptoms such as dysphagia, poor feeding, vomiting, and abdominal pain; lack of response to adequate acid suppressive therapy; and >15 eosinophils/high-power field on esophageal biopsies. It is related to underlying food allergies and often responds to dietary manipulation, rarely requiring treatment with steroids.[11] A team approach, including pediatric gastroenterologists, allergists, and a dietitian, is best for these patients.

## Infection

If the lower airways are chronically infected, this can impair recovery and overall outcomes. Bronchoscopic lavage is often performed to assess for infection. Of specific concerns are methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*, which can be difficult to treat and interfere with wound healing.[12] Obtaining a specimen for culture is helpful to determine sensitivity of the bacteria and guide specific antibacterial therapy.

Human immunodeficiency virus, hepatitis B and C, or other chronic infections must be documented in the patients' chart so that appropriate precautions may be taken.

## Allergies

Drug and latex allergies must be determined and clearly marked on the chart. Asthma from seasonal allergens should be worked up and if possible the peak season avoided when setting a date for surgery.[2] The pulmonologist and allergist need to have the child on a regimen that has airway inflammation well under control. Food allergies and eosinophilic esophagitis (*see* above) are not uncommon, causing irritability of the airways; it is important to obtain a good history and work with a gastroenterologist as well as an allergist to get the inflammation under control prior to any major airway surgery.

## Nutrition

Airway patients often present with nutritional compromise. This could be multifactorial. Poor feeding can result from frequent respiratory illnesses, choking or gagging on feeds, or poor intake related to esophagitis caused by reflux or food allergies. Some children have increased caloric needs due to cardiac or pulmonary issues. Some have neurological impairment or other significant comorbidities that cause impairment of their ability to take oral feeds, often requiring gastrostomy tube feeds. Working with the feeding team, including a pediatric dietitian, and trying to optimize nutritional status preoperatively is important in ensuring the best possible outcome as far as recovery from anesthesia as well as healing from the surgery itself.[13]

## Metabolic

Underlying metabolic diseases can affect how a child may respond to anesthesia.[1] In tertiary care pediatric centers it is not uncommon to have a child with fatty acid oxidation or urea cycle defects, storage diseases, mitochondrial disorders, and other rare conditions presenting for airway surgery. It is necessary to work with the metabolic team to establish guidelines for specific fluid, electrolyte, and medication concerns ahead of time.

## Genetic

Children with genetic syndromes such as Trisomy 21 (Down's), Pierre Robin, and VATER syndrome (or VACTERL association, involving three or more of the following: vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities), to name a few, often require airway surgery. Poor muscle tone, association with congenital defects that affect the airway, and issues such as atlanto–axial joint mobility need to be taken into account. The individual needs of each patient must be kept in mind, with a specific focus on multisystem involvement.[3]

## Endocrine

Every so often, we will be in the situation of performing an airway procedure on a child with type 1 diabetes. Such

children are always scheduled as the first case in the morning. The endocrinologist is consulted ahead of time and a protocol for insulin and fluids is established for each individual patient. Blood sugars are monitored frequently until the time of discharge.[14]

## Hematology

Anemia can contribute to heightened surgical risk. Anemia can occur from a variety of etiologies, ranging from nutritional to a hemoglobinopathy to bone marrow suppression from chemotherapy or other medications. Coagulopathies or clotting disorders may be present and need to be documented, with a plan in place to address them. If transfusion of blood products may be required, this should be discussed with the family and with pediatric anesthesia staff ahead of time and necessary arrangements made.[2]

## Other Organ Involvement

Neurologic and cardiac issues are of special concerns. Muscle tone and seizures may change the anesthetists' approach. Seizure medications should be optimized. A cardiologist may need to clear the patient or give recommendations for antibiotic prophylaxis if a heart lesion is present. The possible need for other specialists, e.g. nephrologist and geneticist, to evaluate preoperatively depends on associated conditions. Many pediatric airway patients have complex multisystem involvement, and a team approach is critical in the success of the surgery.[1-3]

## Anxiety/Psychological

Coming to the operating room is stressful for children as well as for families. It is estimated that 50–75% of children experience significant anxiety before surgery.[15] Some centers offer tours and simulated experiences of what is to be expected so that the child is familiar with the setting when he or she comes in for surgery. Having Child Life specialists available on the day of the procedure has been found to be of great benefit in some centers. Some children have enhanced issues with anxiety due to previous experiences or underlying conditions. It is vital to work with families to help alleviate this. Conversely, many of these children may need to undergo anesthesia several times, so their experience at the first procedure will determine how they react in the future. Talking to the child and explaining the upcoming procedure at their level of understanding often helps things go more smoothly the day of the procedure.[3] However, parents know their children best, and if a parent feels it is best not to alarm the child ahead of time with too much information, one should respect their wishes.

## Autism and Attention-Deficit Hyperactivity Disorder

This growing population of patients is a challenging group to work with. It is important to understand each child's communication skills, level of comprehension, sensory issues, and triggers that cause decompensation. These children may already be on medications to modulate their behavior and mood. A team approach, which includes the primary caregivers, will yield the best results.[3,15]

## Anesthesia Reactions

Although many of these patients are very young, they may have been exposed to anesthesia previously due to comorbidities requiring various procedures. It is important to ask about reactions to anesthetic agents in the past and try and identify which agents were used.[2] History of malignant hyperthermia in the child or a family member would alert the anesthetist to avoid certain volatile anesthetic agents.[16] Also, some children have difficulty when waking up from anesthesia, either due to being disoriented and crying, even screaming inconsolably, or due to nausea and vomiting. If such reactions are known then the anesthetist may be able to modify the protocol to try and avert them.

## Past Surgical History

Patients may have undergone surgery at other institutions for anything from hernia repair to heart surgery. These records should be obtained and reviewed prior to airway surgery.

## Laboratory

Routine lab testing is not indicated as such. However, pulmonary function testing, airway, and chest X-rays, modified barium swallow studies, and allergy testing are often performed, and the results need to be reviewed and documented. Occasionally, a child may be on an anticoagulant where laboratory testing is required and specific guidelines need to be known. Overnight, pulse oximetry and/or a sleep study might also be warranted if the child is on oxygen.

## Consent

Due to the heightened risk of airway surgery when compared with other surgery in this age group, it is even more crucial to meet with the family in a clinic setting to explain the procedure(s) being planned and review risks and benefits before getting signed consent. Families are often anxious and their questions and concerns can be addressed ahead of time in a less stressful environment. Expectations for postoperative care, such as complications and need for admission, can be discussed. There may be circumstances where child custody and legal guardianship issues need to be sorted out so that consent can be obtained from the person who has legal custody of the child. This is best done in advance, since having a fasting child in the preoperative area and not being able to find the person who needs to give permission is an undesirable position to be in.

## Instructions

Written instructions for where and when to arrive and when they can eat and drink prior to the procedure are helpful in assuring a timely procedure and minimizing the need to delay or cancel. A telephone number to contact the team if any questions or issues should arise in the interim is also useful.

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CHAPTER

# 38

# Pediatric Anesthesia for Airway Surgery

***Corey Collins***

## INTRODUCTION

There is an interdependence of the pediatric airway surgeon and anesthesiologist that may be unique to medicine. Beyond the typical reliance between the two specialties, it may be argued that the dynamic and foundational trust needed to ensure smooth, efficient, safe, and effective care is consistently required and tested in the care of the pediatric airway patient. As outlined in this chapter, the clinical approach to pediatric anesthesia for airway surgery builds upon this relationship to encompass risks assessment, clinical judgment, crisis management, communication, and myriad other skills. While no text can delineate such diverse and emotive subjects, this chapter offers an overview of the interplay of our interdependent specialties.

## RISK

Pediatric airway surgery entails risks that must be considered by surgeon and anesthesiologist. Shared knowledge of such risks can improve patient care and outcome through mutual respect for decision-making, predictable clinical challenges, or other concerns.

Though no available datasets accurately quantify specific risks, numerous studies provide insight into the risks associated with a number of pediatric airway surgeries.

For over three decades, Pediatric ENT surgery is disproportionately identified as a risk for perioperative complications, including medical liability closed claims, perioperative cardiac arrests, adverse airway events or unplanned hospitalizations. Such data may indeed reflect a higher risk of complications associated with pediatric ENT surgery and anesthesia, attributable to the inherent pathophysiology of the child with head and neck diseases, the role of airway manipulation and surgery, and the associated challenges of individual clinicians' competencies and expertise when faced with adverse events.

The Pediatric Perioperative Cardiac Arrest registry has collected voluntary data from US centers since 1994 and consistently documents higher cardiac arrest rates (but not deaths) among ENT patients.[1] The interplay of obstructive sleep disordered breathing, young age, and the unpredictable pharmacology related to opioids creates a high-risk scenario for the anesthesiologist caring for these routine cases. The American Society of Anesthesiologists (ASA) database of settled cases from US insurance groups documents that airway events accounts for most claims, and laryngospasm specifically was noted in nearly one-quarter of pediatric cases. Misinterpreted monitoring data, pulmonary aspiration, and unintentional tracheal extubation were quoted as avoidable complications in a number of cases. Over four-fifths of cases involved healthy (ASA PS 1-2) children.[1,2] When complications occur that are attributable to anesthesia care following adenotonsillectomy, liability awards are consistently higher then those attributable to surgical or other causes. Most often these events involve anoxic injuries related to airway management and opioid dosing.[3]

Unplanned intensive care admissions, delayed ambulatory discharge, low parental satisfaction, operating room efficiency, perioperative maladaptive behavior, long-term neurocognitive injury, and other risks may coincide with these more severe clinical events. Postoperative nausea and vomiting increases the likelihood of unplanned admission and significantly delays discharge. Young children may manifest behavioral disturbances for up to 14 days following tonsillectomy. All team members should be aware of these shared risks.

## CENTRAL NERVOUS SYSTEM EFFECTS OF ANESTHESIA

Anesthetic agents are known to induce neurodegenerative changes in neonatal nonprimate mammalian brains via increased apoptotic cell death and additional evidence documents that certain anesthetic agents induce developmental and neurocognitive deficits in primates.[4] Available data in humans, however, are inconclusive and correlation from animal trials to humans is not possible at this time.

Pediatric specialists must balance the risks and benefits of proposed surgery with possible risks of injury related to anesthesia. In pediatric airway surgery, the immediate need for airway protection will likely override possible long-term neurocognitive risks. For example, the child with recurrent papillomatosis cannot be managed with "watchful waiting" regardless of the child's age.

It is important to note that pain and stress produce long-term negative effects on neonatal development and behavior in humans.[5,6] Until significant advances occur, children should continue to receive balanced and effective anesthesia care for necessary surgeries. As recommended by a multidisciplinary clinical panel and the US Food and Drug Administration, clinicians should: "Discuss with parents and other caretakers the risks and benefits of procedures requiring anesthetics or sedatives, as well as the known health risks of not treating certain conditions; Stay informed of new developments in this area; Recognize that current anesthetics and sedatives are necessary for infants and children who require surgery or other painful and stressful procedures".[7]

## CRISIS MANAGEMENT

Crisis management and simulation have been applied to pediatric anesthesiology and otolaryngology.[8,9] Shared training in these areas is encouraging but scientific inquiry into the durable effects of these efforts is early and data supporting the value of such expensive training programs are scant. Nevertheless, simulation has become an element of the maintenance of certification process for anesthesiologists and an increasingly employed method of technical training in US surgical programs.

The shared knowledge of crisis management language, team training, and simulation can positively impact the area of pediatric airway surgery through enhanced communication, trust, resource management, and human factors comprehension. Such an effect has been recommended in the operating room.[10]

High fidelity medical simulation improves team performance in many critical situations including pediatric emergency airway management.[11] While it is likely that the focused team training provided in such simulation may explain some of the benefit, the simulated crisis experience can provide a durable improvement on team member performance. While many surgical teams inherently practice good team behaviors, it is likely that a consistent simulated crisis-training curriculum will further improve performance during rare airway events.

## PREPARATION AND TRAINING FOR PEDIATRIC AIRWAY SURGERY

There is no specific training available to prepare an anesthesiologist for pediatric airway surgery. Current Accreditation Council for Graduate Medical Education (ACGME) requirements for anesthesiology and pediatric anesthesiology do not establish any specific competency component for pediatric airway surgery. Therefore, individual anesthesiologists will have diverse expertise for the management of such cases. Similarly, referral centers will naturally develop institutional expertise with specific techniques and clinical strategies to manage the pediatric airway patient. Teams, therefore, should consider such variables in developing a supporting training environment for new staff and provide appropriate opportunity for orientation to ensure safe patient care and minimize patient and provider risk.

For a variety of reasons, anesthesia for high acuity pediatric airway surgery requires advanced expertise in pediatric anesthesiology. Great Britain, e.g., requires advanced training in pediatric anesthesiology and an annual volume of 200+ pediatric cases to qualify a physician to provide anesthesia for most pediatric cases. Each center will need to consider their local resources and proceed with planning airway surgery in children appropriately.

## PREOPERATIVE PLANNING

Pediatric airway surgery encompasses a wide variety of clinical pathophysiological states, acuity, and complexity. A system to enable efficient case planning, preoperative consultation, equipment readiness, and other time-sensitive issues must be developed locally.

Preoperative medical clearance is often required although few empiric guidelines exist. Consultation with the pediatric anesthesia service in advance of the planned procedure is mandatory for children with structural heart disease, significant dysmorphic syndromes, severe metabolic diseases, and other conditions outlined in Table 38.1. The critical nature of some airway diseases will preclude timely consultation beyond the surgical team; perioperative risks may be significantly increased and consent conversations should document accordingly. Conflict exists in the available literature regarding the importance of preoperative clearance from consultants; e.g., some experts suggest mandatory cardiac echocardiography for children with severe obstructive sleep apnea[12] yet other authors note the lack of clinically relevant findings with such examinations.[13] On balance, clinical judgment, surgical urgency, and individual clinician experience and comfort with each specific child will likely dictate the necessity for referrals and testing.

Current standards in anesthesiology require a preoperative evaluation by the anesthesiologist caring for the child. This mandates a review of records, patient/parent interview, and a physical examination.[14] In high acuity airway cases, specific attention to birth history, previous intubations, critical events, and other important history items is mandatory (Table 38.2).

Examination of the child will focus on the airway, especially quality of respirations, airway anatomy, chest and auscultation, palpation of distal pulses, and visual

**Table 38.1:** Elements of patient history that may impact planned anesthetic

| *Area of interest* | *Significant elements* | *Possible impact on planned anesthetic* |
|---|---|---|
| Birth history | Prematurity | Increased risks of concomitant disease; increased risk of respiratory events; increased incidence of significant medical and surgical history; prolonged endotracheal intubation; possible subglottic stenosis |
| | Low Apgar scores | History of developmental delay; encephalopathy; intrauterine injury |
| | Birth trauma | Neurologic injury; head and neck trauma |
| Pregnancy history | Toxic exposure | Opioid dependence; dysmorphism |
| | Polyhydramnios | Intrauterine renal dysfunction; esophageal obstruction |
| | Oligohydramnios | Fetal hyperglycemia; macrosomia |
| Neonatal history | Apnea/bradycardia syndrome | Anemia; postoperative risk of sudden death |
| | Prolonged endotracheal intubation | Bronchopulmonary dysplasia; subglottic stenosis |
| | Cardiac surgery | Persistent lesions; repaired physiology; shunt |
| Family history | Inheritable disease | Chromosomal abnormalities; dysmorphisms |
| | Anesthetic complications | Malignant hyperthermia; hemoglobinopathies; coagulopathies |
| | Tobacco exposure | Reactive airway |
| Medications | Past and current medications | Compliance with medical therapy; awareness of prior diagnoses; insight into stage of chronic illness |
| | Medications | Interaction with planned anesthetics |
| Surgical history | List of surgical procedures | Complications of surgery; reasons for surgery; impact on chronic health |
| Anesthetic history | Types of anesthesia | Complications with anesthesia; address patient/parent concerns regarding anesthesia |
| Hospitalizations | Reasons for admissions | May reveal undisclosed events or diagnoses; more thorough discussion of chronic illness |
| | Frequent admissions for minor problems | Missed diagnosis; poor access to care; social factors |

**Table 38.2:** Interrelated specialties and possible anesthetic implications

| *Specialty* | *Pertinence* | *Possible impact on planned anesthetic* |
|---|---|---|
| Neurology | Seizure history | Avoid epileptogenic drugs |
| | Communication/development | Appropriate sensitivity to parents and child's abilities; adjust doses of centrally acting opioids |
| | Motor disease/myopathy | Assess risk of MH, hyperkalemia; possibly withhold paralytics |
| Pain management | Current modalities of pain management (e.g. baclofen, methadone, and fentanyl patch) | Accurately prepare for effective analgesic requirements while avoiding harmful drug interactions. Consider tolerance and role on dosing analgesics |
| | History of postoperative pain management challenges | Avoid inefficient and ineffective pain management; improve patient and family satisfaction |
| Metabolic/nutrition | Metabolic disease | Avoid incompatible drugs and hydration solutions |
| | Document nutritional state | Poor nutrition increases risk of adverse drug reaction, inability to tolerate surgical stress |
| | Documents growth and development | Accurate body mass data; better estimation of total body water |
| Nephrology | Renal function | Avoid or reduce doses of renally excreted or nephrotoxic drugs; assess potential hyperkalemia; secondary hypertension |
| Neonatology | Prematurity | Postconceptual age; stigmata of prematurity; life-threatening events |
| Respiratory therapy | Respiratory status | Mode of ventilation; bronchorrhea; oxygen requirement; pulmonary toilet |
| Social work | Family status | Improve communication; prepare for consent discussions; avoid conflict |
| | Guardianship | Identify legal consenting party |
| | Social status of patient and family | Improve family comprehension of health, consent, risk discussion |

examination of the chest and abdomen for evidence of airway obstruction. Other key elements of the physical examination are listed in Table 38.3.

Review of the surgical plan with the surgical team well before induction in the operating room is recommended, even in the most urgent circumstances. The ubiquitous surgical "time out" pauses currently conducted in the United States provides an excellent opportunity for the team to quickly identify and discuss key concerns.

## Current Upper Respiratory Tract Infection

School-aged children will experience between 5 and 10 upper respiratory tract infections (URIs) per year with approximately 4–6 weeks after resolution of symptoms before the risks for perioperative adverse airway events returns to baseline.[15,16] Considerable attention is warranted for the child with a URI scheduled for airway surgery. Despite the considerable literature on the topic, it remains the responsibility of the anesthesiologist and surgeon to decide if the risks of an adverse airway event are balanced by the surgical benefit.[17-20] Associated complications may include laryngospasm, bronchospasm, significant coughing, and arterial desaturation. Respiratory complications are also associated with level of experience of the anesthesiologist.[21]

Certain clinical decisions may decrease risk. For example, avoiding tracheal intubation, extubation of the trachea while deeply anesthetized but with adequate respirations,[18] and avoiding excessive pressure on the tracheal cuff[22] may decrease airway irritation and postoperative bronchospasm, laryngospasm, or arterial desaturation. The supraglottic airway (SGA) may cause less adverse respiratory events.[23]

Children with any of the seven specific risk factors identified by Tait et al. warrant particular consideration: copious secretions, endotracheal intubation in children under 5 years of age, former prematurity, nasal congestion, paternal smoking, history of reactive airway disease, and planned airway surgery.[24] Should an airway procedure proceed in the setting of a recent URI, additional risks

**Table 38.3:** Summary of physical examination findings and possible impact on planned anesthetic

| *Area of examination* | *Specific findings of interest* | *Possible impact on planned anesthetic* |
|---|---|---|
| Airway | Retrognathia; micrognathia; macroglossia; cleft palate | Small oral volume versus large tongue predicts difficult laryngoscopy |
| | Prominent incisors | Possible difficult visualization of larynx |
| | Ankylosed mandible | Limited mouth opening |
| HEENT | Wide-set eyes; malformed ears; cleft lip | Association with cardiac anomalies |
| | Microtia | Associated with difficult intubation |
| | Stridor | Laryngotracheomalacia; vocal fold paralysis; gastrointestinal reflux |
| Cervical mobility | Limited extension; unstable cervical spine | Limited ability to align visual axis with larynx |
| Heart | Murmurs | New murmurs may be innocent or pathologic and often require evaluation |
| | Heave | Right heart overload accompanies pulmonary hypertension; left ventricular outflow obstruction must be evaluated |
| | Thrills | Harsh thrills often accompany serious lesions |
| Lungs | Wheeze | Reactive airway; foreign body; poor compliance with medical management |
| | Rhonchi | Acute lower respiratory infection; poor ventilatory capacity; physical deconditioning |
| Skin | Rash | Viral exanthems; chronic dermatologic disease; preoperative drug eruptions |
| | Cyanosis | Pulmonary/respiratory insufficiency |
| | Lymphatic malformations | May displace airway |
| | Turgor | Dehydration |
| Abdomen | Scars; stoma; feeding tubes | Surgical history; nutritional status; decompress stomach preprocedure |
| Extremities | Clubbing | Chronic hypoxia |
| | Pseudohypertrophy of muscles | Muscular dystrophy |
| | Subcutaneous adiposity | Difficult intravenous access |
| Nervous system | Activity | Assess level of function; focused defects; avoid confusion with postoperative examination findings |
| | Communication | Improve patient recovery; predict ability to assess emergence from anesthetic; predict ability to assess for pain |
| | Motor | Avoid iatrogenic respiratory depression; optimize respiratory mechanics for emergence and postprocedure airway management |

(HEENT: Head, Eyes, Ears, Nose and Throat).

should be explained to the parent and the team should be prepared for a higher likelihood for laryngospasm, bronchospasm, and arterial oxygen desaturation.

## Preoperative Admission

Preprocedure admission for elective airway surgery is most often determined by clinical severity of respiratory distress. There are a number of disease states that may require admission based on medical risks.

### *Insulin-Dependent Diabetes Mellitus*

The diabetic child requires careful assessment of metabolic control before elective surgery. Preferably, consultation is advised well before surgery though if airway surgery is more urgent, admission and consultation with pediatric endocrinology is recommended. Careful adherence to published management guidelines such as the Boston Children's Hospital guidelines is highly recommended.[25]

### *Sickle Cell Disease*

Perioperative complications associated with sickle cell disease include acute chest syndrome, painful crisis, neurologic event, or death. Such complications are typically associated with hypoxia, hypoperfusion, or acidosis. Children having airway surgery may be at higher risk for such events. Strategies to decrease risks preoperatively typically include intravenous hydration and blood transfusion to decrease the hemoglobin S level to < 30%. The impact of such interventions, however, has been poorly documented. A multicenter trial in 1995 documented no benefit to aggressive transfusion and a cohort that included approximately 25% children.[26] While significant practice variability remains, consensus suggests consultation, admission, and management with close communication with hematologic experts, especially in high acuity cases.[27]

### *Complex Congenital Heart Diseases*

Patients with structural heart disease should be referred for preoperative evaluation and possibly extensive testing before airway procedures. Consultant input is mandatory in cases of cyanotic lesions as acute respiratory embarrassment may cause significant perturbations in pulmonary blood flow. Certain lesions or repairs may require standby of invasive cardiopulmonary support.

### *Poorly Controlled Systemic Disease*

Many pediatric diseases add significant perioperative risk if inadequately managed at the time of surgery. Myopathies, seizure disorders, glycogen storage diseases, renal disease, and pervasive dermatologic disease (e.g. epidermolysis bullosa) are but a few examples of conditions that must be evaluated carefully before determination if preoperative admission is necessary. Early and detailed discussions should occur as early as possible for all children with any significant systemic disease.

## Preoperative Testing

Preoperative testing before pediatric airway surgery is only necessary for a small subset of children with significant systemic disease. Very few published reports provide strong evidence for most tests. Testing should be reserved for children with known metabolic derangements, recent clinical exacerbations, or unstable diseases known to add risks.

## Preoperative Preparation

In addition to a standard room preparation dictated by current standards in anesthesiology, specific equipment may be necessary. Medical liability associated with airway mismanagement has taught most anesthesiologists to approach the airway patient with numerous options for airway management available. These include direct laryngoscopy (DL), indirect videolaryngology, SGA devices, fiberoptic bronchoscopy, high-pressure "jet" ventilation, and spontaneous ventilation techniques. All techniques require expertise, training, competency, and preparation.

Pharmacological management of each child will be individualized. Specific goals may include sympatholysis, anesthesia, analgesia, hypnosis, immobility, antisialorrhea, or cardiac support. The armamentarium of available medications changes often. The surgical team may consider review of specific agents to be used to improve awareness of possible complications and the planned pharmacologic state of the patient during the procedure.

Emergency equipment must be available and is described elsewhere in this section. Specifically, options for emergent surgical airway must be immediately available. These will include cricothyrotomy kits, tracheostomy kits, rigid bronchoscopes, or retrograde intubation kits. At a time of crisis, it is important to quickly determine the best option for surgical airway based on the expertise of the physicians and the available resources. Preoperative discussions regarding the "cannot ventilate/cannot intubate" scenario will improve team response and possibly patient outcomes. In many pediatric critical events involving difficult airway management, surgical airways were either delayed or not attempted resulting in poor outcome. Successful surgical airway access requires practice, training. Emergency surgical airway rates are low (< 0.01–2/10,000).[28] Training and practice help, although there is evidence that adherence to published protocols remains unimproved after simulation training.[29]

## Airway Management

Advances in technology have made important changes in the airway management. As costs of fiberoptic fibers and liquid crystal displays have decreased, new devices have come onto the market that permit indirect visualization of the glottis. These proprietary devices use a variety of designs to introduce a camera or fiber optic bundle into the hypopharynx and obtain a visual display of the airway without requiring typical forces involved with DL.

There are three device types routinely used in the United States: devices that are similar in design and use to standard Macintosh and Miller laryngoscope blades; devices that are anatomically curved to match various sized patients that do not permit direct visualization of the glottis or the introduction of the tracheal tube (TT); and anatomical devices with a guide to introduce the TT directly into the visualized glottis. Comparisons with DL are available but no consensus has emerged.

Generally, indirect videolaryngoscopes provide an excellent glottic view, but multiple studies demonstrate time to passage of a TT is longer compared to DL. First attempt success rates are typically higher for these devices. Expert laryngoscopists' success rates are less improved compared to novices and the added time to intubation may increase the rate of oxygen desaturation in patients with low oxygen reserves such as children.[30] The success of these devices in difficult airways or emergencies has increased their use in emergency departments and intensive care units. Holm-Knudsen reviewed the use of the four available devices in pediatric patients and the unique attributes and limitations of each.[31] While success has been reported for each in various settings, most authors continue to recommend awake flexible fiberoptic intubation as the gold standard in the management of the pediatric difficult airway.

### Access Information: IO, Central Lines, Urinary Catheters

In the United States, a majority of pediatric anesthetics are induced by inhalation of anesthetics agents versus perioperative indwelling intravenous lines. While often a safe and reliable option, this method adds important risks should an adverse event occur during or soon after induction. In addition, surgery can only follow the subsequent successful placement of an IV line in all but the most minor of procedures. Occasionally, such access will be quite difficult and mandate alternative access to be considered.

When standard sites for peripheral venous access are unsuccessful, other sites may be considered including the scalp, external jugular, or less commonly, the azygos, gonadal, or inferior epigastric veins. Complications specific to each site should be considered and may be serious.

The advent of an easy to use intraosseous device (Arrow EZ IO; Vidacare, Shavano Park, TX) has made safe, rapid central access readily available for children > 3 kg in weight. While important safety information must be reviewed and considered before its use, this device can provide rapid and definitive access for perioperative or emergency care. Such devices, however, must be replaced within 24 h.

Central venous access may be indicated for long-term access in children having airway surgery. Many children require prolonged sedation after airway reconstruction, for example. Typical sites for central access are the femoral and subclavian veins.

Urinary catheters are rarely indicated following airway surgery unless coexisting diseases mandate careful measurement of urine production and fluid balance. Children are at risk for nosocomial urinary bladder infections following catheterization.

## CASE MANAGEMENT

A brief overview of the major pediatric airway cases follows with a focused discussion of the typical approach to anesthesia management options.

### DL/Bronch/EGD/FOB

Diagnostic endoscopic procedures are often necessary for children exhibiting signs of clinical airway disease. Such signs may include stridor, hoarseness, dysphagia, or chronic cough. While many of these children will have relatively mild disease, there is a consistent risk of more severe occult underlying pathology such as airway tumors, foreign bodies, vascular compressions, or cardiac abnormalities.

Spontaneous ventilation may minimize the risk of a lost airway. An inhalational induction, followed by careful titration of intravenous medications such as opiates or intravenous anesthetics, will provide an adequate depth of anesthesia and permit rigid bronchoscopy without coughing, laryngospasm, or injury to the airway. Brief procedures such as DL may be performed under inhalational anesthesia. The use of suspension microlaryngoscopy will necessitate more profound sympathetic blockade and possibly anti-cholinergic therapy to mitigate a vagotonic decrease in heart rate. If it is clear that there is no significant dynamic or space-occupying lesion threatening the airway, the use of paralytics may be warranted. In such cases, intermittent intubation may simplify the procedure and maintain ventilation and a more routine fashion. The use of SGAs may permit access to the glottis for fibrotic bronchoscopy while allowing positive pressure ventilation as needed. However, such devices do not protect against laryngospasm or aspiration.

## Tracheostomy

Tracheostomies are often necessary to establish definitive airway access in a variety of surgical patients. Anesthetic management will require careful discussion with the surgical team to ensure safe induction of anesthesia, especially in children with known difficult airways. Children who arrived to the operating room intubated must be carefully managed to ensure adequate sedation prior to the onset of anesthesia to avoid dislodgment of the endotracheal tube. Paralytics may be warranted. High-inspired oxygen concentration should be avoided during electrosurgical entry into the airway to reduce the risk for airway fires. Intravenous or inhaled anesthesia may be selected based on concomitant medical concerns. Once the tracheostomy is matured, careful attention must be paid to avoid excessive coughing or breath holding and the child resulting in hypoxemia. There is a risk for immediate subcutaneous emphysema and possible pneumomediastinum or pneumopericardium. In addition, sudden hypoxemia concurrent with tracheostomy will create a challenging diagnostic scenario and is best avoided.

Typically, low-dose opiates are administered (1 mcg per kilogram fentanyl) for sympathetic blockade and antitussive effect. If paralytics are used, they may be administered at any time during the anesthetic; muscle relaxation should be ensured immediately prior to entering the airway.

The newly tracheotomized child will often recover in the pediatric intensive care unit. Transfer to the unit may be facilitated with the assistance of respiratory therapy, especially in children with underlying pulmonary disease or challenging ventilatory requirements.

## Airway Reconstruction

Reconstruction of the pediatric airway is an effective option for a number of indications including subglottic stenosis, tracheal stenosis, or other anomalies as described in Chapter 13. Local anesthetic management techniques have been published,[32,33] although rigorous literature comparing specific techniques, morbidity, or outcomes are lacking.

A careful plan should emphasize the transitions during the induction of anesthesia, airway management, and critical surgical steps. While techniques vary, often a DL will precede oral ETT placement. Ventilatory pressures should be monitored if a costal cartilage graft is obtained to avoid barotrauma and possible pneumothorax. Many children will have a history of chronic pulmonary disease related to prematurity, and peak inspiratory pressures may be elevated. Reduced inspired oxygen concentrations are indicated during electrocautery of the airway to avoid airway fire; any plan to relocate the ETT should be discussed with sufficient time to permit reoxygenation before an ETT is moved to minimize hypoxemia. Some children will be quite sensitive to perturbations in respiratory mechanics and promptly decompensate with the loss of positive end expiratory pressure. Full attention of the team will be required to exclude other causes for acute hypoxemia such as pneumothorax, pneumomediastinum, impaired cardiac preload, or other acute events.

Significant morbidity is difficult to assess and intraoperative events can occur anytime. Although some patients have benign medical histories, many children will have severe systemic disease such as prematurity, velocardiofacial syndrome, or cardiac diseases.

## Juvenile Onset Recurrent Respiratory Papillomatosis

Juvenile onset recurrent respiratory papillomatosis is a rare cause of pediatric airway obstruction and disease. Diagnosis may occur at any age, though 75% of cases are diagnosed by age 5 years and is heralded by hoarseness, stridor, or abnormal cry. Lesions rarely threaten the airway initially though aggressive disease can cause near-complete occlusion of the larynx, spread to the bronchial or pulmonary airways, and undergo malignant transformation to squamous cell carcinoma.[34]

Frequent anesthetics are often needed for debulking procedures. Assessment will focus on the level of airway compromise, though clinical signs of obstruction may be thoroughly masked by a compensating, calm child. Inhalational induction may be considered with preparations in place in case for the urgent lost airway including rigid bronchoscopy and a surgical airway. Avoidance of laryngospasm and frank airway obstruction is important. The use of continuous positive airway pressure (CPAP) hand delivered via the anesthesia circuit is often employed to maintain ventilation despite mild airway obstruction during the induction of anesthesia.

Anesthesia and airway management for respiratory papillomatosis patients has been described using jet ventilation[35,36], intermittent apnea/intubation, or tubeless

spontaneous ventilation[37]. No technique has been clearly demonstrated as superior and benefits to each can be argued. Teams will need to review the plan for airway management including discussion about planned interventions for adverse events. When surveyed, approximately two-thirds of surgeons prefer spontaneous ventilation techniques in the United States and United Kindom.[38,39]

Specific technical papers are available for the different techniques and the complications and benefits of each.[35,36,40] Jet ventilation permits paralysis and a quiet surgical field. Most children will tolerate this technique with stable $pCO_2$ levels and adequate oxygenation. Risks include barotrauma or direct tracheal injury related to the high-pressure (50 psig) oxygen source. Total intravenous anesthesia techniques are required. A number of technical systems have been described including high-pressure/low-pressure cannula techniques, supraglottic catheter placement, or tracheal catheter placement. Intermittent intubation with standard endotracheal tubes also allows the use of paralytics and is generally well tolerated by patients.[41] This technique has been associated with lower laryngospasm and apnea rates with no significant difference in operating time recovery time or post of voice quality. Spontaneous ventilation without an endotracheal tube, while preferred by a majority of US surgeons, may have higher adverse airway events including desaturation and apnea. The technique may be more challenging to learn than those that permit paralysis. Benefits include complete surgical access to the larynx and below, expedient transition from anesthesia onset to surgical start, and reduced trauma to the subglottis and trachea related to catheter placement or endotracheal tube. These techniques may be employed in other tenuous airway cases.

## Foreign Bodies in the Airway

Aspiration of foreign bodies into the pediatric airway is a regular challenge to many pediatric surgical centers. Careful management begins with optimizing the behavioral response of the child to mitigate agitation and possible migration of the foreign body. The child, once assessed, should be brought to the operating room where a calm and controlled inhalation induction should be pursued. Spontaneous ventilation is maintained and respiratory mechanics are supported with the use of CPAP while intravenous access is obtained. Transition to a total intravenous anesthesia (TIVA) technique may be employed to establish a stable plane of anesthesia. Careful assessment of anesthetic depth must be maintained continuously to avoid coughing or dislodgment of the foreign body. Extraction of the foreign body may require considerable time and surgical skill. Often the airway is irritated and prone to reactivity further complicating the anesthetic. Excellent medication among team members will play an important role in surgical success.

## Trauma

Pediatric airway trauma presents exceptionally high risks and warrants considerable preparation, training, experience, and teamwork. While beyond the scope of this overview, management of such patients follows many of similar principles previously offered: definitive communication, a shared plan for airway management with clear roles and alternative strategies to secure the airway, and resource management.[42]

## Burns

Management of the burn child is an area of specific skill and expertise. Airway management is often extremely challenging and subject to significant change during the course of initial resuscitation and subsequent healing. Often the airway is initially managed with intubation followed by tracheostomy and possibly airway reconstruction once the acute phase of injury has resolved. The nature of the burns around the airway will predispose some children to difficult intubation and may mandate awake fiberoptic intubation.

# CONCLUSION

The management of the pediatric airway places many demands on a surgical team. With appropriate training and experience, the full spectrum of pediatric airway patients will receive safe and effective care. The risk for sudden adverse events mandates vigilance and communication to promptly protect the child in distress from catastrophic complications related to airway compromise. A shared commitment to effective and safe patient care provides an excellent framework for the interplay of surgical and anesthesia related issues and can lead to enhanced teamwork and improved care for pediatric airway patients.

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CHAPTER

# Perioperative Intensive Care Management in Airway Surgery

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## INTRODUCTION

The postoperative management of pediatric patients following airway surgery requires a comprehensive understanding of the surgery itself and extensive experience on the part of the surgeon, anesthesiologist, pediatric intensive care physician, respiratory therapist, and the nursing staff for a successful outcome. In the following chapter, we discuss some of the more common issues encountered in postoperative care for pediatric airway procedures from the pediatric intensivist perspective, focusing on operations involving tonsillectomy and adenoidectomy, supraglottic surgeries including supraglottoplasty and laryngeal cleft repair, and intratracheal surgeries including fresh tracheostomy and laryngotracheal reconstruction (LTR). Challenges during the perioperative period are discussed, with the goal to minimize morbidity and lead to successful outcome, and we detail our approach in the pediatric intensive care unit (PICU). More research is needed to determine best practice for pediatric care for many of these operative recoveries.

## TONSILLECTOMY AND ADENOIDECTOMY

The most common airway procedure in children is the tonsillectomy and adenoidectomy for obstructive sleep apnea. Most patients come to attention with classic symptoms of airway obstruction, as well as more subtle signs of behavioral changes and impaired school performance. The majority of procedures are performed with minimal complications. However, severity of upper airway obstruction varies and controversy exists over whether preoperative sleep studies are indicated and whether the use of noninvasive respiratory support measures are indicated prior to surgery. More severe cases with underlying genetic or congenital abnormalities, a severe apnea/hypopnea sleep index (AHI) on a formal sleep study, or the need for noninvasive ventilation prior to surgery are deemed to be at a higher risk for perioperative complications.

Most tonsillectomies and adenoidectomies are performed as outpatient surgeries or with < 24 h postoperative observation.[1] Less is known as to which patients should be admitted to the hospital, either to the general care ward or the PICU. Consensus recommendations state that children < 3 years of age, children with severe obstructive sleep apnea, or children with comorbid conditions such as obesity, sickle cell disease, coagulopathies, congenital heart disease, arrhythmias, and craniofacial abnormalities may require more protracted inpatient care and/or ICU observation.[2] In many centers, the preoperative requirement of noninvasive ventilation requires specialized caregiver skill that requires postoperative PICU monitoring and care. Additionally, we have found age < 2 years, an AHI >24 (whereas AHI > 10 is typically regarded as severe), intraoperative laryngospasm requiring treatment, oxygen saturations < 90% on room air in post anesthesia care unit (PACU) and prolonged PACU stay > 100 min each independently predicted postoperative complications leading to need for PICU care.[3] Overall, determining PICU observation versus ward observation for individuals remains unclear for patients, and should be adapted based on the skill sets of staff in recognizing expected airway complications and the underlying condition of the patient. Better patient selection criteria can potentially lead to more cost-effective care in this population.

Postoperative care is focused on pain control, hydration, and observation for respiratory complications. The use of dexamethasone in the perioperative period is standard of care allowing for pain control, decreased airway swelling, and earlier resumption of diet. One dose between 0.15 and 1 mg/kg is likely sufficient, with no difference in outcome found in varying dosage.[4,5] Additionally, there does not appear to be an association between steroids and postoperative hemorrhage, even in regards to higher dosage.[6,7] Our current practice is to administer one dose of 0.5 mg/kg (max 20 mg) in the perioperative period. Pain is universal after surgery, although the mechanism and best method to treat is unknown. Traditionally, treatment was provided with acetaminophen and codeine. However, codeine should be avoided as a pain medication in children due to varying metabolism and effectiveness in the population, and severe side effects including death following tonsillectomy.[8] Acetaminophen alone may be sufficient. Additionally, consensus recommendations now advocate for nonsteroidal medications, as there is no known increased bleeding risk with these medications.[9] Effective hydration with intravenous fluids (IVF) and prevention of dehydration are also associated with decreased pain.

Respiratory complications can occur intraoperatively, in the post anesthesia recovery unit (PACU) or during postoperative observation.[10] Patients may be sensitive to opiate analgesia and may have prolonged apnea following administration during surgery, requiring noninvasive or invasive respiratory support. For that reason, many advocate for reducing opiate dosages in children with obstructive sleep apnea. Laryngospasm requiring immediate intervention in the OR has been reported, and may require prolonged mechanical ventilation to recover. Additionally, postobstructive pulmonary edema has been reported both immediately in the OR and later in the postoperative period, demonstrated by respiratory distress, frothy sputum production and a chest X-ray (CXR) with diffuse pulmonary edema pattern. Patients require respiratory support with either supplemental oxygen or positive pressure ventilation, which may be noninvasive ventilation such as continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) in older children but younger children may require intubation. High expiratory pressures may be necessary to open the lung and oxygenate. Additionally, diuretics are effective to reduce ventilatory needs. Mechanical ventilation is continued until pulmonary edema resolves and the patient can tolerate decreasing support.

Bleeding is another common complication and although minor bleeding is most common, major bleeding complications can occur.[11] Typically two peaks of bleeding potential occur, in the immediate period and then following eschar formation in 5–7 days postoperatively. Patients with coagulopathies have anticipated bleeding complications and should have presurgical plans with pediatric hematology to prevent complications, such as the use of desmopressin (DDAVP) in patients with von Willebrand's disease. Hemorrhages presenting as outpatients often present to the emergency department (ED) without continued evidence of bleeding and may be observed as inpatients. Those with active bleeding or evidence of clot may require immediate surgical treatment. Young children with active bleeding will require general anesthesia, and securing the airway early with rapid sequence intubation and cricoid pressure to prevent blood aspiration may be beneficial.[12] Fluid resuscitation should occur, and blood products may be necessary depending on extent of bleeding. Major arterial bleeding is possible, and requires endovascular control and possible major vessel ligation.[13] Patients should be managed with a secure airway until bleeding is terminated, and stomach evacuated of blood products.

In our practice, patients requiring preoperative ventilatory support are all managed in the PICU postoperatively. Patients who have intraoperative or PACU-related complications are also transferred to the PICU for management. Consistent with consensus recommendations above, patients deemed high risk for complications are scheduled electively to be admitted postoperatively to the PICU for observation for 24 h. Many patients do not require intervention, so improved patient selection could contribute to improved cost-effective care strategies in the future.

## SUPRAGLOTTOPLASTY

Laryngomalacia is the most common laryngeal abnormality and the most common cause of stridor in infants. The spectrum of disease is diverse, from noisy breathing to life-threatening airway obstruction, for which supraglottoplasty is often performed. Postoperative observation is important to monitor for significant residual stridor or respiratory distress due to failure to remove enough tissue, as well as possible postoperative airway edema secondary to swelling. Comorbid conditions may play a significant role in postoperative complications that usually occur < 10% of the time.[14]

Best practice regarding appropriate patient location for postoperative management remains unknown and institutional practice varies. Some centers bring all patients to the PICU intubated overnight,[15] whereas others monitor all patients in the PICU regardless of intubated or not.[16] One center has shown it is safe to observe the majority of patients on the general care ward despite the presence of major comorbidities without any complications,[17] in contrast to another that demonstrated a 33% reintubation rate.[18] One possible distinguishing characteristic is the surgical technique, with the former study using cold steel versus the latter $CO_2$ laser, creating perhaps more postoperative swelling and risk of complications. The ideal practice thus remains unknown, but it is encouraging that morbidity is low for this procedure and hospital stays can be minimal.

Our practice following this procedure is observation without an endotracheal tube (ETT) in the PICU overnight given potential need for intervention with heliox or positive pressure ventilation if swelling occurs. Heliox is an helium–oxygen gas mixture that provides a lower density gas than room air. In obstructed proximal airways that result in turbulent airflow pattern and poor oxygen delivery, heliox can be beneficial due to its lower density in establishing laminar flow and in allowing oxygen delivery to distal airways. To be effective, however, heliox must be administered at 80:20 or 70:30 helium:oxygen concentrations. Thus, it cannot support children who have large oxygen requirements in addition to airway obstruction. Need for heliox is rare following this procedure but expertise should be available. All patients are administered dexamethasone at a dose of 0.5 mg/kg every 8 h for 3 doses. A proton pump inhibitor or antihistamine is administered for reflux prophylaxis. Patients are typically discharged to home the next day if in no respiratory distress and tolerating oral intake. If there are any residual concerns, patients are transferred to the ward for further monitoring or for advancement of oral feeding.

## LARYNGEAL CLEFT REPAIR

Laryngeal cleft is a rare congenital abnormality in which the posterior elements of the larynx fail to fuse. Diagnosis can be challenging and is based on clinical suspicion as presenting symptoms may be nonspecific including feeding difficulties, cough with drinking thin liquids, wheeze, chronic cough, and recurrent respiratory tract infections. Diagnosis is confirmed through direct endoscopy, with the diagnosis of type 1 clefts increasing. When conservative management fails, endoscopic repair through either suturing or laser techniques may be necessary. Typically postrepair observation occurs in the PICU setting for 24 h, and then patients are transferred to the general care ward for an additional 24 h observation.[19] Postoperatively, patients may have additional swelling with potential risk of airway obstruction. Continuous oximetry and telemetry are necessary and providers skilled in airway management are a must. Availability of heliox at 80:20 or 70:30 helium:oxygen concentrations may be helpful if stenosis is a concern. Dexamethasone is administered to reduce edema in similar dosing of 0.5 mg/kg every 8 h for 3 doses. Ampicillin-sulbactam is administered IV for 24–48 h and then converted to an oral regimen for 10 days. A proton pump inhibitor or anti-histamine is also started and continued for 3–6 months at the discretion of the surgeon.

In our center, we typically utilize a suture repair technique. Disruption of sutures may occur from vigorous crying or coughing, requiring reoperation. For this reason, we attempt to minimize patients' agitation and crying for the first postoperative night and administer an infusion of dexmedetomidine as it preserves normal respiratory drive, yet allows patients to be calm and comfortable.[20] Additional analgesia is provided with acetaminophen, narcotics and benzodiazepines as needed. The following day, the infusion is discontinued, the patient is awakened and allowed to advance their diet and dexamethasone is stopped. One more day of observation for airway obstruction or aspiration occurs on the regular ward, with a swallow study performed for any persistent aspiration concerns either immediately if oral feeds are not tolerated, or routinely a few months postoperatively.

## TRACHEOSTOMY

The major indications for tracheostomy placement in a child are anticipated long-term respiratory compromise from chronic respiratory insufficiency or a fixed upper airway obstruction that is not anticipated to resolve quickly.[21] Whereas in the past fixed obstruction was the most common indication in children, the former indications are increasing reasons for tracheostomy given improved intensive care and survival of patients with chronic neuromuscular and respiratory problems. Risks of the procedure vary based on indication and underlying patient comorbidities. Given the risk of loss of airway control and death, adequate informed consent with families is paramount.

Perioperative care includes preprocedural planning and observation in the postoperative period. A multidisciplinary standard approach to tracheostomy care in adults has potential to decrease morbidity and mortality after this procedure and application of standardization in children is desirable.[22] Overall, areas of consensus in tracheostomy care are emerging and will help defining future research and standardization in children.[23]

Preprocedure planning for the appropriate tube size is critical, with the size of the airway and clinical indication helping guide the decision. Diameter size that is too large can compromise the mucosal wall of the trachea, leading to ulceration and potential fibrosis. The tube should be small enough to allow the child to speak, if possible, but not so small as to lead to hypoventilation, respiratory distress or inability to clear secretions. Use of a cuffed tube will vary by indication, and overinflation of the cuff may lead to vascular compromise of the mucosal wall as well. A cuffed tube will often be necessary in the pediatric patient requiring chronic mechanical ventilation so appropriate sizing is necessary. Unlike adults, children will require progressive larger tracheostomy tubes as they grow, and annual reassessment of size is required. Formulas exist for calculating expected inner and outer diameters based on age.[24] Length is also important to consider, especially in neonates and small infants. Too long a tube may be at the carina or a bronchus, and compromise ventilation. A tube too short may lead to frequent decannulation. Therefore, direct visualization at time of placement may be helpful, and custom lengths may need to be determined if standard lengths are insufficient.

Early postoperative complications include pneumothorax, obstruction, and decannulation. It is critically important to know whether the child can be intubated from the airway above in case of an obstructed or dislodged tracheostomy. If the tracheostomy tube cannot be quickly replaced or is obstructed, oral endotracheal intubation is the best option. Pneumothorax may complicate the initial procedure, especially in neonates and young infants given the proximity of lungs and neck. A CXR is traditionally done after the procedure to evaluate the tracheostomy position and to determine presence of pneumothorax. Recent authors have questioned the utility to the CXR and suggest it may not need to be performed routinely.[25] Subcutaneous emphysema may also be present, but can typically be avoided through loose wound closure techniques and placement of a drain to allow air to track externally. Obstruction of tracheostomy can be best prevented by attention to suctioning needs, providing humidification, and staff awareness of the potential issue, especially in tracheostomy tubes with smaller inner diameters. Accidental decannulation can be a life threatening early complication in children. There may be inability to recannulate, with risks of false tracking the tracheostomy tube through friable tissue or creating alternative tissue planes leading to a life-threatening respiratory emergency. This is best avoided with well-placed stay sutures on either side of the tracheal incision, with sufficient length to be easily located on the chest in an emergency. In the event of decannulation, the stay sutures can be pulled up and out to open the incision clearly and allow safe placement of the tracheostomy tube. If the tracheostomy tube cannot be replaced, an ETT can be placed through the stoma or through the oral native airway to establish airway control. Accidental decannulation can also be prevented through removal of unnecessary tubing or equipment (including the ventilator if no longer required), pain and comfort control as required by age, and staff training to be attentive to a fresh tracheostomy. The use of a tracheostomy tie with an elastic component and hook and loop fasteners through the ends of the tracheostomy tube can also be helpful to ensure appropriate position of the tracheostomy and also help decrease skin erosion.

Hemorrhagic, infectious, and granuloma complications may occur, most often as late complications but additionally early in the perioperative period.[26] Hemorrhage is a life-threatening complication that can occur immediately on tracheostomy cannulation due to injury of the innominate, aorta or carotid artery depending on variability in anatomy. Pressure must be held to decrease bleeding and vascular repair as soon as possible with potential need for assistance from cardiothoracic or vascular surgery. In the ICU, bleeding can occur from pressure from the tracheostomy tube causing erosion into the anterior wall and a tracheo-innominate fistula. In the case of life-threatening bleeding, if the tube is cuffed it can be attempted to be inflated to create tamponade. A cuffed ETT can be inserted through stoma, or a finger can be inserted into the stoma to push anterior to attempt to tamponade bleeding. Immediate surgical intervention is crucial to survival, with overall survival < 25%. Patients with native tracheostomy presenting as outpatients with hemoptysis should prompt an immediate evaluation for potential life-threatening bleeding. This can be performed with a fiberoptic examination and a CT angiogram to evaluate for bleeding sources and potential for tracheoinnominate

fistula. In addition, a granuloma may be a source of irritation and bleeding from either suctioning or tracheostomy tube tip mucosal irritation. Large granulomas can develop and additionally cause life-threatening obstruction. Fiberoptic evaluation can identify and treatment may be with topical steroids or laser/surgical excision. Lastly, infection can also cause hemorrhagic secretions. Chronic intubated patients requiring tracheostomy may have a variety of colonizing flora that can cause tracheitis both acutely and later on as outpatients. Antibiotic prophylaxis during the perioperative period is controversial, although antibiotics are indicated if there is evidence of infection such as with fever, increased or thicker secretions, or irritated tracheal mucosal.

The first tracheostomy tube change is performed by the surgeon to confirm the safety and adequate healing of the stoma. The stay sutures can be removed and future changes performed by dedicated medical personnel or the family once adequately trained. The timing of the first tracheostomy tube change is dependent on the surgeon and the indication for the tracheostomy. In many cases, 3 days is enough time for adequate healing,[27] but practice varies from 4 to 7 days.[28] Our practice is to have all new tracheostomies recover in the PICU with stay sutures. Two replacement tracheostomies are available at the bedside, of the same and smaller size, and an emergent tracheostomy surgical kit is available in unit at all times. Typically at day 5, the surgical team will perform the first tracheostomy change, and remove the stay sutures at that time. Family training for tracheostomy changes then occurs and the patients are transferred to the general care ward until competency in tracheostomy change and cardiopulmonary resuscitation is demonstrated by home care providers and adequate airway supplies are obtained for the patient.

## LARYNGOTRACHEAL RECONSTRUCTION

Laryngotracheal reconstruction (LTR) involves surgical correction of a stenotic airway. Surgical techniques were primary introduced by Fearon and Cotton in 1972 with the aim of expanding stenotic airway segments in children with congenital and acquired laryngotracheal stenosis.[29] Typically this involves cartilage interpositional grafting, with or without a stent, followed either by placement of a tracheostomy (two stage) or placement of an ETT with postoperative sedation and mechanical ventilation for an extended period of time (single stage). Other surgical variations include end-to-end anastomosis and sliding tracheoplasty. Single-stage repair with prolonged intubation creates several perioperative challenges, and patient optimization is critical for successful graft outcome and minimization of morbidities. Our group has previously reviewed management strategies, and here we present a summary approach to typical perioperative issues for the intensivist and surgeon.[30]

### Airway and Respiratory Management

The choice of how to secure the airway postsurgery can vary. Some centers may avoid endotracheal intubation and positive pressure ventilation in older children after end-to-end anastomosis or sliding tracheoplasty. Given the extent of resection, limitation of neck movement may be necessary to avoid tension on the repair with a suture of the chin to the chest. Providers must be prepared to release the stitch for emergency airway management if the airway cannot be secured or visualized, and expert personnel should be available for airway manipulation. A postoperative drain may be utilized to allow any potential air leaks to escape through the skin and prevent pneumomediastinum, pneumothorax, or subcutaneous emphysema.

Although the oral route is generally chosen for endotracheal intubation in the PICU population, some studies have suggested that there may be advantages of using the nasal route.[31] The nasal route postoperatively may provide more secure control of the airway with a decreased risk of inadvertent extubation in the PICU, easier mouth care to prevent aspiration and hospital acquired pneumonia, and decreased sedation requirements from less gagging and oral discomfort, leading to faster recovery and shorter length of stay. Yellen and colleagues have recommended the nasal route, with 21 patients who underwent single-stage LTR nasotracheally intubated for a mean of 8.4 days (range 6–14 days) and a success rate of 95%.[32] Despite reported success and possible advantages, there remain some caveats. The ETT should be one size smaller than typical for patient's age, due to potential nares damage and epistaxis during tube placement. As nasotracheal intubation may be time-consuming, practitioners may choose to initially provide orotracheal intubation and then switch to the nasotracheal route when leaving the operating room (OR). Regardless of nasal or oral ETT, consideration should be given to the use of low profile, low pressure cuffed ETTs,

as uncuffed ETTs may lead to excessive leaks and interfere with effective positive pressure mechanical ventilation in the PICU, and a cuffed ETT may decrease need to replace the ETT in a surgically repaired airway with its inherent dangers.[33] The cuff should be inflated with minimal amount of air necessary to seal the airway, with frequent pressure checks to ensure that pressures are kept ≤ 20 cm $H_2O$ to avoid compromising tracheal perfusion pressure and potentially limiting postoperative subglottic damage. Overall, there are no prospective, randomized trials in either the adult or pediatric population to demonstrate the clinical advantages of the nasal versus the oral route for endotracheal intubation in the ICU setting so use will be dictated by clinical preference.

Airway and respiratory issues often affecting the postoperative course include atelectasis, tracheal secretions, nosocomial pneumonia, air leak syndromes, leakage at the tracheal graft site, and postextubation airway obstruction. Arrival to the PICU should include a CXR to determine ETT position and ensure correct location after travel from the OR, as well as to determine presence of atelectasis and air leaks. Atelectasis should be treated aggressively with positive end expiratory pressure (PEEP) and lung recruitment to minimize pulmonary complications during PICU stay, as its presence my lead to infection, need for high ventilator settings and subsequent longer ventilation, sedation and hospital length of stay until pulmonary status is optimized for extubation. Air leaks may be present on admission from graft harvest site if rib grafts are used, and may require serial observation or immediate drainage with a chest tube. In our institution, we typically utilize a pigtail catheter to drain air if present on arrival to minimize pulmonary compromise. Additional subcutaneous air my be present in the neck and mediastinum and can often be minimized with OR placement of a rubber band drain in the neck incision to allow easy egress of air. A CXR is utilized daily and as needed for clinical changes to confirm no movement of ETT and to assist with optimization of daily ventilation parameters.

Pulmonary secretion management and prevention of atelectasis with chest physiotherapy and endotracheal suctioning are traditional management approaches for prolonged mechanical ventilation. However, their routine use is not supported by evidence-based medicine, and may be detrimental.[34] Rather, our clinical experience suggests that respiratory issues can be decreased by adopting a ventilator strategy that provides for recruitment of atelectatic lung regions, especially early on. The use of lower tidal volumes to prevent the theoretical risks of barotrauma in mechanically ventilated patients has become commonplace and, combined with the use of sedation and neuromuscular blockade, may contribute to progressive atelectasis. In the relatively normal lung after this typically elective procedure, we advocate the use of tidal volumes of 8–10 mL/kg, provided the mean airway and plateau pressures are kept within acceptable ranges, the application of 5–8 cm $H_2O$ of PEEP, and the use of longer inspiratory times of 1–1.5 s, depending on age. Additionally, if so desired, intermittent recruitment breaths can be delivered manually intermittently by disconnecting the patient from the ventilator and providing manual breaths with a resuscitation bag that is attached to a manometer to limit excessive pressures.

Suctioning has many potential adverse effects reported in the literature. These include hypoxemia, bacteremia, lobar atelectasis, mucosal trauma, hemorrhage, bronchoconstriction, lobar atelectasis, decreased cerebral oxygenation, pneumothorax, cardiac arrhythmias, cardiac arrest and even death. Commonly used suctioning methods are open-ETT suctioning and closed system suctioning (CSS). CSS allows suctioning during mechanical ventilation with an in-line multiuse suction catheter system encased in a plastic sleeve. Use of CSS may prevent suctioning-induced hypoxia, atelectasis, and spread of infection between patients and from patients to staff by limiting the spread of aerosolized infectious mucus particles. However, there is a lack of evidence on the optimal suctioning method in the pediatric critical care population.[35] Additional techniques to reduce suctioning complications include reduction of suction pressure, limitation of the depth of insertion of the suction catheter, appropriate preoxygenation, adequate sedation and analgesia and muscle paralysis. We practice suctioning with the CSS and only when clinically indicated, such as with worsening pulmonary compliance due to excessive secretions and/or prior to extubation.

An evaluation of both the upper airway and respiratory function may be helpful in ensuring the appropriate timing of extubation following airway repair. There is no perfect measure to determine extubation readiness in children, and various techniques including leak, negative inspiratory force, and types of spontaneous breathing trials have been examined with varying effectiveness.[36] Overall extubation should proceed when surgical repair allows and typical intensive care extubation criteria are met. The presence of air leak around the ETT may provide a reasonable estimate of extubation success. Gustafson and

colleagues demonstrated that patients without an air leak at 20 cm $H_2O$ or less were twice as likely to fail their initial attempts at tracheal extubation.[31] A pressure support, CPAP or a T-piece trial prior to tracheal extubation may provide additional information regarding readiness for tracheal extubation, although conclusive data in children to support a particular approach is not available.

Upon extubation, immediate concerns are recurrence of airway obstruction, so stridor and work of breathing are monitored closely. Use of periextubation dexamethasone can be helpful to reduce edema caused by ETT, started the day before and continued for 24–48 hours. Respiratory distress after extubation may be categorized as reversible (presence of granulation tissue, mucosal edema, excessive secretions, sedative withdrawal, neuromuscular weakness) or irreversible (prolapsed grafts and/or restenosis of the airway site).[37] A limited trial of noninvasive ventilation may be sufficient to bridge the transition to extubation, especially if sedation, deconditioning and poor muscle tone are contributing to extubation distress. If there is no improvement, surgical evaluation from bronchoscopy is often warranted to determine etiology. In our approach after single-stage repair, the surgical repair is examined under direct visualization by the surgeon with OR bronchoscopy prior to extubation. If repair is deemed adequate, the ETT is downsized by half a size, and the patient is brought back to the PICU with a secure airway. The patient's sedation is then weaned, dexamethasone administered every 8 h for 24 h, and airway assessed for a leak. Extubation occurs in the PICU, with availability of surgeon and pediatric anesthesia as needed. CPAP or BiPAP is utilized to support to the airway, especially if residual tracheomalacia is present from the repair. A bronchoscopy is repeated in one week, or earlier if there are clinical concerns regarding the airway. Most respiratory support can be discontinued within the next 24 h, dependent upon sedation and deconditioning.

## Sedation

The use of continuous sedation following single-stage LTR in young and uncooperative children has been advocated to avoid movement and trauma from the ETT against the fresh graft site and the potentially life-threatening complication of inadvertent tracheal extubation.[38] Neuromuscular blockade may also be necessary to ensure immobility and decrease the risk of graft failure. Unfortunately, sedative use may result in adverse respiratory effects including depressed cough reflex, ineffective clearing of secretions, diminished sigh volumes, and decreased functional residual capacity. Additionally, tolerance and physical dependence may develop, depending on length of infusions, with discontinuation resulting in a withdrawal syndrome complicating the process of extubation. Therefore, optimizing sedation and muscle relaxation protocols are critical to minimizing perioperative issues.

Pediatric sedation and analgesia practice is best titrated to objective scoring measures to minimize oversedation. Pain scores can be obtained through various methods based on a patient's age, using the Face scale or FLACC score for young infants, or numeric scores for older, awake patients. Sedatives can be titrated through a number of scoring methods, depending on unit practice. The COMFORT score combines the scoring of a patient's response or movement in addition to various physiologic parameters, including measurement of alertness, respiration, blood pressure, muscle tone, agitation, movement, heart rate, and facial tension,[39] and can also detail specific ranges of over- or under-sedation with less reliance on physiologic measurements alone.[40] Other sedation scoring systems exist, including the sedation-agitation scale and the Ramsey scale.[41,42] The Ramsey score is limited by the need to disturb the patient, which may paradoxically increase sedation needs. Additionally, none of the sedation scales are valid when utilizing muscle relaxation, and adequate sedation must be inferred from vital sign parameters or during muscle relaxation holidays. Some have advocated use of the bispectral index (BIS monitor) in this situation, but its interpretation and utility in young patients remains investigational.[43] We utilize the COMFORT score for our intubated nonmuscle-relaxed patients, and titrate sedation infusions based on scoring trends to minimize future opiate and sedation dependence.

While sedation in intubated children traditionally requires continuous infusions of sedation, there is increasing interest in intermittent dosing or drug holidays to minimize adverse side effects. In adults, daily interruptions of sedative infusions decrease the duration of mechanical ventilation and the length of stay in the intensive care unit.[44] However, after tracheal repair, the practitioner must balance the safety of the repair and maintaining the endotracheal airway with the side effects of sedatives in children. For this reason, we often sedate young children until it is safe to be awake and potentially extubate. In older children who are cooperative and not likely to remove the ETT, we will utilize intermittent sedation, and potentially allow the child to be awake, maintaining the ETT nasally as

a stent and breathing spontaneously, and therefore minimizing prolonged sedative effects.[45] Clearing the ETT of secretions and ensuring adequate humidification, either through an HME attached at end of ETT or humidified blow by oxygen, are important to minimize obstruction. Spontaneous breathing off the ventilator can also facilitate walking and prevention of deconditioning and oral feeding can also be considered if cleared through a speech swallow evaluation that there is no aspiration with the ETT in place.

To facilitate successful tracheal extubation, avoiding sedative agents that may impair upper airway control and respiratory function is ideal. To accomplish this, switching to shorter acting agents may be beneficial to better control wakefulness at time of extubation. Therefore, it may be beneficial to utilize medications such as propofol, remifentanil or dexmedetomidine for 8–12 h prior to an anticipated extubation attempt. Propofol is short acting and can lead to early awakening on discontinuation, giving more control during this time period. However, the use in children is potentially dangerous given reports of propofol infusion syndrome.[46] Given that the majority of cases occur with high dosing and prolonged infusions, a short-term infusion 8–12 h may be acceptable with appropriate monitoring of acid base and cardiovascular status. Alternatively, the short-acting synthetic opioid, remifentanil, may be used to provide a deep level of sedation with a rapid offset once the infusion is discontinued, with the disadvantage of its cost and the rapid development of tolerance, requiring dose escalation. Our practice is to utilize propofol in children the evening prior to extubation and decrease other sedatives by 50%. In patients in whom propofol is contraindicated we utilize a dexmedetomidine infusion, which is increasingly becoming our preferred option. Dexmedetomidine is a $\alpha_2$-adrenergic receptor agonist that possesses sedative, analgesic, and anxiolytic properties with limited effects on respiratory drive. The short half life of dexmedetomidine allows for easy, quicker recovery, and fewer prolonged sedation-related adverse effects.[47] Adult data have shown dexmedetomidine to be a successful bridge to extubation, and reduce total cumulative sedative use with minimal adverse effects.[48] Following LTR, dexmedetomidine has been utilized successfully as part of the sedative regimen in children.[49]

Additional adjunctive sedatives have been utilized following LTR in attempts to limit tolerance and withdrawal. Diphenhydramine, clonidine, phenothiazines, nonsteroidal anti-inflammatory agents, acetaminophen, and chloral hydrate have all been used in this regard.[50] Given limited effects on respiratory function, they may provide significant benefit particularly when used in rotation with opioids and benzodiazepines. Additionally, the use of nonpharmacologic measures such as reduced stimulation, comforting, and regulation of day–night sleep cycle may reduce the amount of sedative medications.[45]

Given that sedation is often required for a week or longer, the development of tolerance, physical dependency, and withdrawal is expected.[51] The timing of withdrawal may vary according to the medication utilized for sedation and its half life. One strategy suggested for patients receiving long-term continuous sedation is replacing synthetic opioids such as fentanyl with nonsynthetic opioids such as morphine, as the synthetic opioids have increased affinity for the opioid receptor and may lead to a higher incidence of withdrawal.[52] Rotating sedation regimens has also been suggested. Wheeler and colleagues presented preliminary data on a rotating sedation strategy for two patients who required sedation following LTR, rotating a midazolam, fentanyl and dexmedetomidine infusion for a day each until extubation was achieved on day 6. No withdrawal was noted in the rotating regimen versus all patients exhibited withdrawal in the traditional approach, with withdrawal patients requiring longer PICU stay and longer length of time till oral fluids tolerated.

We utilize a time based and standard medication conversion treatment protocol for withdrawal in our patients.[51] If infusions are required for <7 days, the patients have their medications stopped and they are observed for withdrawal, with scoring systems available to objectively quantify the burden of symptoms.[53] Patients requiring infusions for 7–14 days are started on prophylactic replacement therapy on the day of discontinuation, usually with methadone for opiates and lorazepam for benzodiazepines. Therapy is gradually weaned off in 5–7 days, and switched to oral as soon as tolerated.[54] In infusions for rare patients requiring mechanical ventilation and sedation for > 14 days, the weaning occurs over a 10-day period, either in the hospital given need for repeat bronchoscopies, or as an outpatient if appropriate.

## Neuromuscular Blockade

Neuromuscular blockade may be necessary in the immediate postoperative period to minimize movement of the indwelling ETT and disruption of suture lines. Prolonged infusions should be avoided if possible, given the risks of

prolonged weakness and their negative impact on pulmonary clearance. Potential techniques to avoid complications from neuromuscular blockade include monitoring with a nerve stimulator daily to guide the appropriate dosing (allowing two twitches so there is not complete blockade), and discontinuation of the infusion on a daily basis ('vecuronium holiday') to allow for the return of neuromuscular function by allowing the patient to move and only resume blockade if ETT is threatened.[38] Daily evaluation of neuromuscular blockade infusion should occur, with consideration of intermittent boluses instead. Even with appropriate monitoring and drug minimization, patients may have prolonged weakness after discontinuation of blockade. Simultaneous use of corticosteroids for airway edema can also affect weakness and pulmonary toilet. We therefore recommend limiting the use of continuous infusion of blockade to the first 24 h after the surgery with transition to intermittent boluses as needed after this period if ETT safety will allow. Neuromuscular blockade is stopped 24 h prior to extubation attempt to ensure adequate muscle strength. Additionally, limiting the doses of corticosteroids to 24–48 h in the periextubation period can be effective in reducing airway edema as well as preventing worsening of neuromuscular weakness associated with more prolonged administration of corticosteroids.

## Nutrition

Nutrition should be optimized to prevent deconditioning and neuromuscular weakness and facilitate the process of tracheal extubation. Enteral nutrition is the preferred route as it is more physiologic and is associated with decreased infectious complications and decreased length of hospital stay when compared with parenteral nutrition.[55] Enteral nutrition should be started as early as possible in the postoperative period, to improve caloric intake and decrease development of ileus and constipation from prolonged opiate therapy. With gastroesophageal reflux and concerns over damaging the graft site, we typically utilize a proton pump inhibitor throughout the PICU stay. Placement of a nasogastric tube (NGT) may cause concerns over pressure to the graft area if a posterior graft is utilized in the surgical repair. For this reason, the NGT is preferably placed in the OR during the surgical repair so that future placement is not necessary with possible graft disruption. If unable to be placed, our practice is to wait 48 h in the PICU before the NGT is placed, under direct airway visualization while advanced to ensure it enters the esophagus. A nasojejunal tube may facilitate earlier tolerance of feeds, but placement is based on local institutional practice.[56] Regardless of the site of enteral feedings, tube placement should be documented radiographically before initiating feeds. Parental nutrition may be used to supplement or replace enteral nutrition, although the ideal timing to initiate parental nutrition in the PICU remains unknown. Use of parental nutrition requires secure access and may require a central venous line with its attendant infectious risks.

## Infection Prevention

Although there is no evidence-based data for the utility of prophylactic antibiotics in this select patient population, most centers advocate this practice until tracheal extubation is achieved. We typically utilize ampicillin-sulbactam intravenously, while in the PICU to cover for mouth and airway flora. Additionally, these patients carry a high risk of nosocomial infections, particularly if a Foley catheter and possibly a central venous line are utilized. A high index of suspicion should be maintained for infection and ventilator associated pneumonia, with sampling of tracheal secretions for a Gram stain and culture if temperature instability, worsening chest radiography, deterioration in respiratory function, or change in white blood cell count. Maintaining the head of the bed at 30° and oral care may help prevent ventilator associated pneumonia. Blood and urine cultures should be sent for fevers and antibiotic coverage expanded for clinical deterioration. Foley and central venous lines should be removed when no longer clinically indicated. Avoidance of excessive sedation, neuromuscular blockade, excessive laboratory evaluations, and early enteral feeding may facilitate this process. In older patients, we attempt to avoid both a Foley and a central venous line. In younger patients, we attempt to utilize peripheral inserted central catheters to minimize infection risk, and remove Foleys as soon as possible. Laboratory investigations are typically obtained daily for blood gas analysis, and otherwise only obtained for clinical indications to minimize excessive accessing of indwelling catheters and increasing infectious risk.

# CONCLUSION

There are many perioperative challenges after airway surgery based on the type of operation and age of the patient. Many patients have significant comorbidities that require

multidisciplinary care. The ideal type of pediatric unit in which to recover remains undetermined and depends on the surgery and the support required. The perioperative care around single-stage LTR is critical to ensuring a successful surgery with minimal morbidity and requires PICU care. Communication between the surgical and ICU staff can facilitate a smooth recovery and extubation period with minimal morbidity. Further investigation is needed to determine best practice in management and many areas are ideal for standardization, such as antibiotic prophylaxis, feeding regimens, sedation, and withdrawal treatment.

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CHAPTER

40

# Congenital Nasal Masses

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Congenital nasal masses occur at the rate of about 1 in 20,000 to 1 in 40,000 live births.[1] Children often present with either nasal obstruction, an intranasal mass, which does not cause obstruction, or an externally visible cosmetic deformity. In this section, the most common congenital nasal masses will be discussed, including pathogenesis, diagnosis, and management.

## NASOLACRIMAL DUCT CYST

Embryologically, the nasolacrimal duct arises from surface ectoderm located between the maxillary and frontonasal recesses. Beginning in the third fetal month, canalization of the system begins and continues through the sixth fetal month.[2] Also known as a congenital dacryocystocele, a nasolacrimal duct cyst is thought to occur due to a distal obstruction at the valve of Hasner, located at the junction of nasolacrimal duct and the nasal mucosa, and an obstruction proximally at the valve of Rosenmuller, which is the site of entry of the common canaliculus into the lacrimal sac.[3] As a result, distension of the nasolacrimal sac occurs when fluid accumulates in the drainage system. This is opposed to congenital nasolacrimal duct obstruction, where obstruction is only at the valve of Hasner, allowing for tears to flow freely onto the eye due to backpressure. The valve of Hasner is the most frequent site of incomplete canalization, and the incidence of imperforate nasolacrimal ducts in term fetuses ranges from 35% to 73%.[3] However, only about 1.75–5% of these children have persistent obstruction requiring surgical intervention.[4] The typical presentation of nasolacrimal duct obstruction includes epiphora and/or recurrent infections such as conjunctivitis.

Congenital dacryocystocele is a rare variant of congenital nasolacrimal duct obstruction, accounting for only 0.1% of these cases, with 80–90% being unilateral.[5] A significant female preponderance for congenital dacryocystoceles is seen, with an incidence as high as 55–75% reported in girls.[5,6] In addition, the possibility of a genetic bases has been raised by a few reported cases in the literature.[7-9]

Because of the dual site of obstruction, the uninfected dacryocystocele most commonly presents as a blue mass in the medial canthal region. However, in some patients, an intranasal mass causing nasal obstruction may be the only presentation.[10] Other possible presentations include epiphora, eyelash mattering, and conjunctival inflammation. Infection from stasis of lacrimal flow may lead to acute dacryocystitis, periorbital cellulitis, and orbital cellulitis.[4] This secondary infection is at least partially due to the absence of a well-defined fascial layer isolating the lacrimal sac from the orbit in very young children. Nasal obstruction may be secondary to a mass on one side coupled with cyclic vascular congestion on the contralateral side, or rarely, it may be due to bilateral dacryocystoceles.[10]

Endoscopic examination is necessary for patients with suspected dacryocystocele, which may demonstrate a cystic mass protruding from the inferior meatus or simply redundant mucosa at this level (Fig. 40.1).

Computed tomography (CT) scan can be used for confirmation of the diagnosis, although this is not routinely indicated. Expected findings on CT include a medial canthal cystic mass, a dilated nasolacrimal duct, and an intranasal cystic mass. Magnetic resonance imaging (MRI) can also be used if other etiologies need to be excluded, as improved soft tissue detail can be provided (Figs. 40.2A and B).

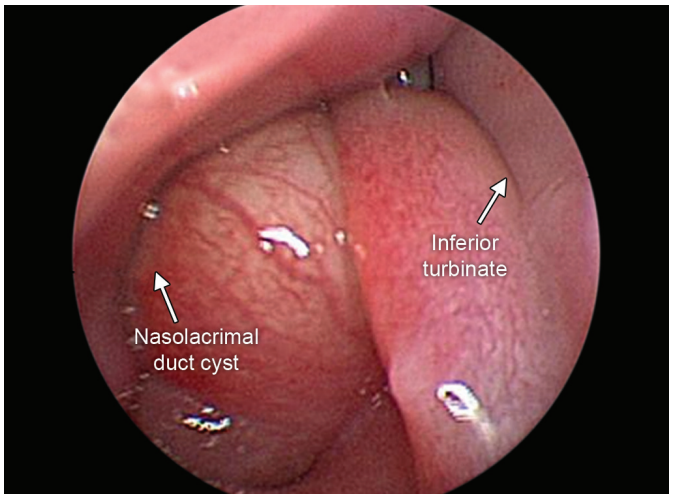
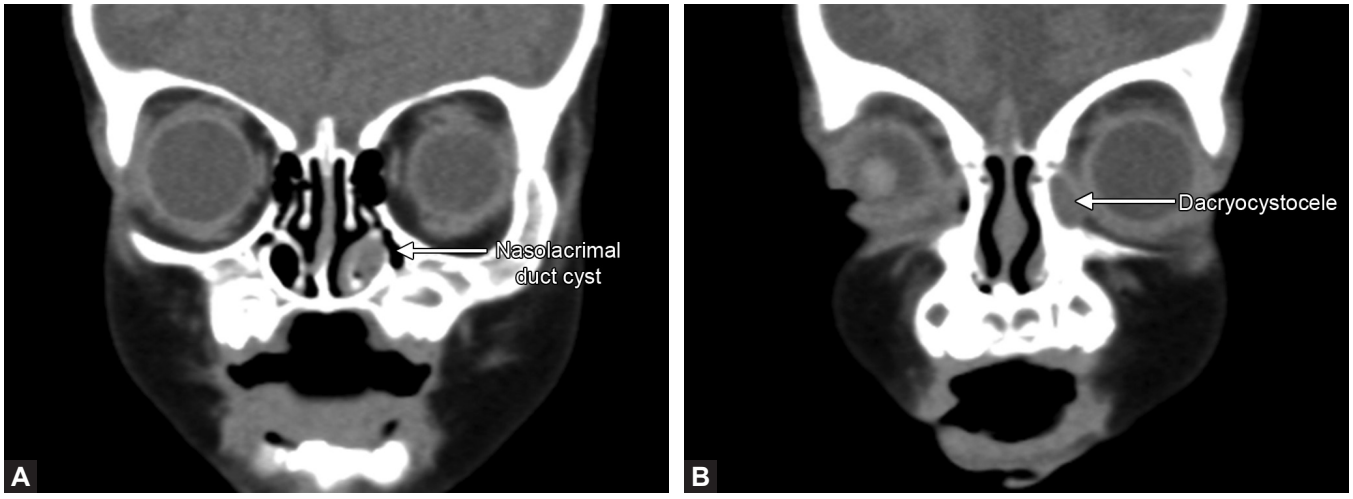



**Fig. 40.1:** Endoscopic intranasal view of large nasolacrimal duct cyst causing nasal obstruction.

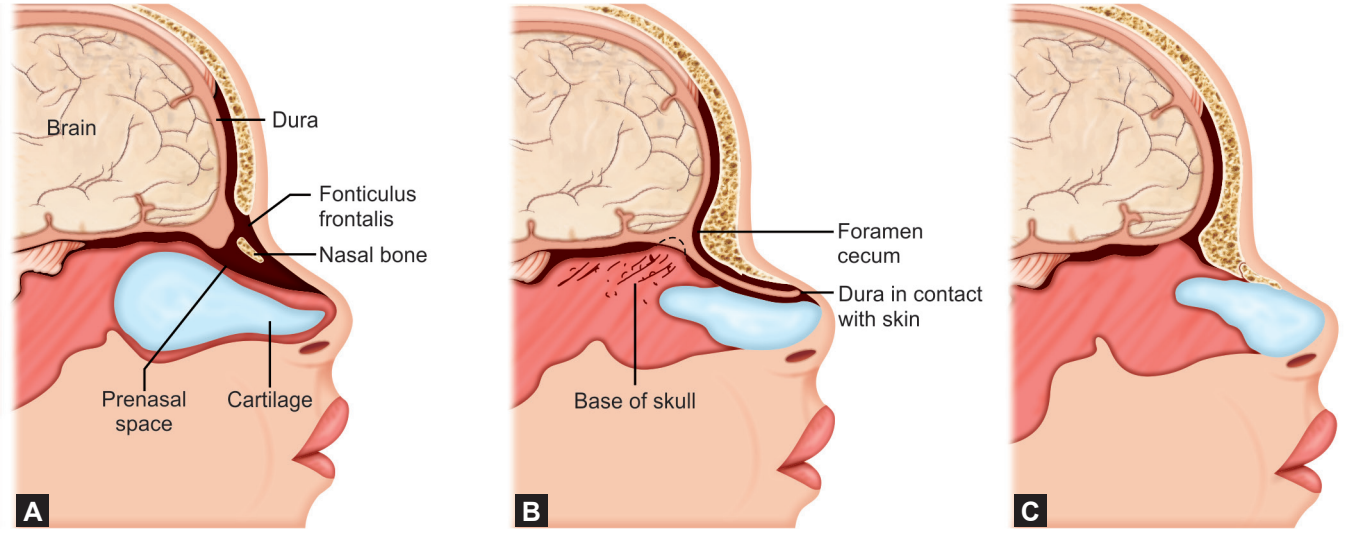



**Figs. 40.2A and B:** CT scan, coronal view, soft tissue window demonstrating obstruction along the course of the nasolacrimal duct. (A) Congenital nasolacrimal duct cyst with a mass seen in the left nasal cavity; (B) Congenital dacryocystocele with a mass seen along the medial wall of the orbit.

Both medical and surgical options exist for treatment. Spontaneous resolution has been shown to occur,[5] and medial canthal massage, warm compresses and antibiotics may hasten this process. With the intranasal component, a warm cloth may be applied over the nasal vestibule, or topical vasoconstrictor nose drops may be applied.[10] Surgical options include cyst decompression via needle aspiration, nasolacrimal probing and irrigation, nasolacrimal dilation using a balloon, and endoscopic dacryocystorhinostomy.[11,12] When only a cystic expansion in the inferior meatus is present, transnasal endoscopic treatment is the senior author's (Dr Christopher Hartnick) preference. In the case of a dacryocystocele that has not previously been treated, a combined approach with endoscopic marsupialization of the intranasal component and simultaneous verification nasolacrimal duct patency by probing and cannulating the duct with intranasal visualization of the probe is performed.[6] A microdebrider may also be used to remove the mass.[10] For revision cases, cannulation of the duct with short-term stenting with a Jones or Crawford tube can be considered.

## NASAL DERMOID

First described in 1817 by Cruvelier when he identified a hair-bearing sinus tract of the nasal dorsum in a child, the nasal dermoid is the most common midline congenital nasal lesion.[13] These masses are created by invagination of surface ectoderm with the formation of an epithelial-lined cyst. However, unlike the epidermoid cyst, this cyst




**Figs. 40.3A to C:** Pathogenesis of dermoid. Note dura contacting skin through foramen cecum with subsequent regression. Adapted from Barkovich AJ, Vandermarck P, Edwards MS, Cogen PH. Congenital nasal masses: CT and MR imaging features in 16 cases. Am J Neuroradiol. 1991;12(1):105-16.

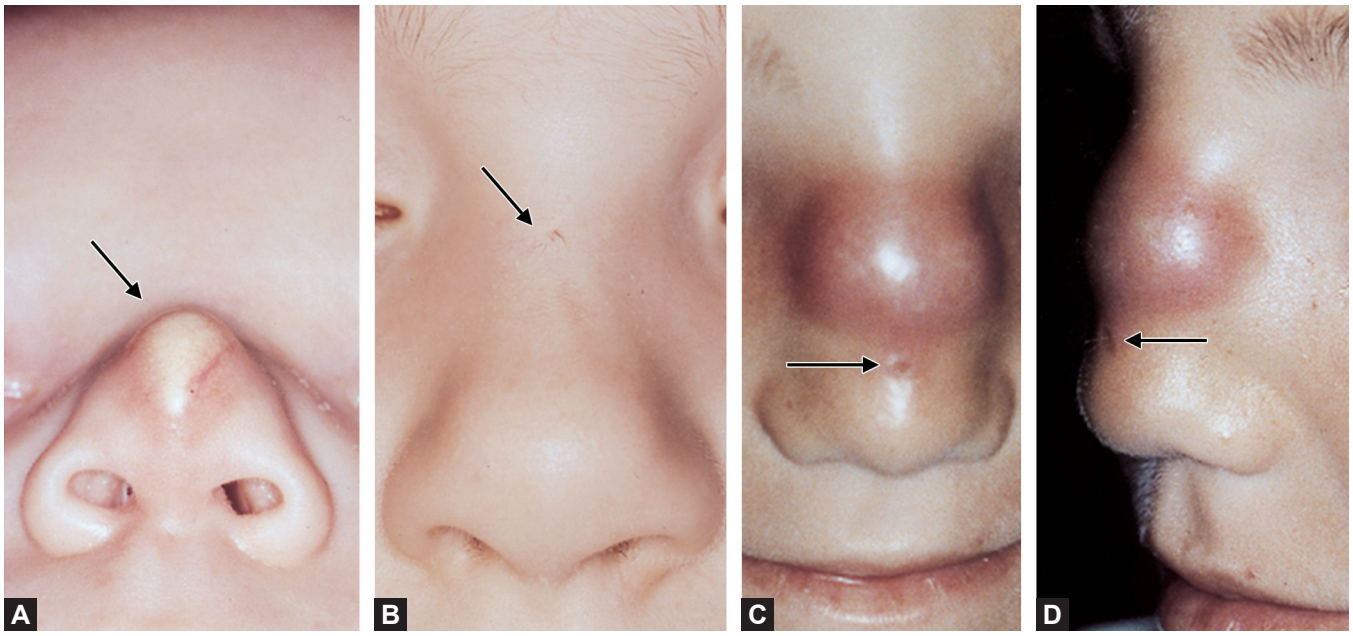
wall also contains hair follicles and supporting adnexa. Between 4 and 8 weeks of gestation, embryogenesis of the midface occurs. The nose has a trilaminar structure, with a superficial layer of ectoderm, a middle layer of mesoderm, and a deep layer of cartilaginous capsule. This cartilaginous capsule originates from the chondrocranium and forms deep to the nasal and frontal bones, which result from ossification of the mesoderm. Each layer is separated by a named space: the fonticulus frontalis temporarily separates the nasal and frontal bones, whereas the prenasal space separates the nasal bone from the deeper cartilaginous nasal capsule.

An extension of dura mater projects through the foramen cecum and temporarily occupies the prenasal space, fleetingly contacting the nasal tip skin. During normal embryologic development, the diverticulum involutes rapidly and the fonticulus frontalis is eliminated with creation of the nasofrontal suture. The prenasal space obliterates and the foramen cecum eventually fuses with the fonticulus frontalis to form the cribriform plate.[14] Abnormal regression of the neuroectodermal tract results in skin elements becoming trapped in the prenasal space and formation of a dermoid cyst or sinus tract, anywhere from the columella to the anterior cranial fossa. In about 5–45% of cases, connection to the dura is found,[15-17] and cases of brain parenchymal involvement has been described.[15] This most often occurs through the foramen cecum or cribriform plate (Figs. 40.3A to C).

Nasal dermoids account for 1–3% of all dermoid cysts and about 4–12% of head and neck dermoid tumors.[18,19] Mean age of presentation ranges from 14 to 34 months, and there is a slight male predominance.[15,17] Association with the Gorlin-Goltz syndrome, or nevoid basal cell carcinoma syndrome, has been reported.[20] In addition, other craniofacial anomalies, such as craniosynostosis, hemifacial microsomia, nasolacrimal duct cysts, cleft lip and palate, external ear deformities, hydrocephalus, and hypertelorism, have been linked with nasal dermoid cysts.[16]

A nasal dermoid cyst generally presents as a noncompressible midline nasal mass which may occur anywhere along a tract from the nasoglabellar region to the columella.[15] Often, a sinus opening with expressible or intermittently draining sebaceous material is also present; hair projecting through a punctum over the nasal dorsum is pathognomonic.[16] Upon examination, the mass does not transilluminate, and there is no enlargement with compression of the jugular veins (i.e. negative Furstenberg's sign)[14] (Figs. 40.4A to D).

Both CT and MRI are important and complementary imaging studies when diagnosing nasal dermoids and determining presence or absence and extent of intracranial involvement. Although CT can clearly show bony anatomy, MRI provides excellent soft tissue detail. CT imaging should be done with cuts no thicker than 3 mm, and findings suggestive of intracranial extension include widening of the foramen cecum, bony defect in the crista




**Figs. 40.4A to D:** (A) Nasal dermoid at tip, black arrow demonstrating mass; (B) Nasal pit, as demonstrated by black arrow; (C and D) Infected nasal dermoid with pit, black arrow demonstrating nasal pit. Reprinted with permission from Rahbar et al.[15]

galli, and a bifid or dystrophic crista galli.[21] On MRI, a high-intensity signal on T1-weighted postgadolinium contrast images in the area of the crista galli in newborns is indicative of a dermoid cyst with intracranial involvement.[21]

The average width of the foramen cecum is about 4 mm but can be as much as 10 mm. Its contents demonstrate soft tissue density on CT and low to intermediate intensity on MRI. The crista galli is on average 3 mm in width, and it has a similar appearance on CT and MRI to bone marrow. As children grow older, the crista galli is replaced by fat, usually by age of 5 but as late as age 14.[21]

Involvement of the neurosurgery team is appropriate when imaging demonstrates an enlarged foramen cecum and a bifid crista galli, indicating intracranial involvement; a combined approach to complete excision can then be accomplished in a single operation.[19,22,23] Imaging done with contrast can help differentiate skull base defects from enhancing lesions, as well as dermoid cysts (nonenhancing) from nasal mucosa (enhancing).[14]

Normal variable anatomy should always be kept in mind when interpreting imaging in cases of suspected dermoid cysts. Neonates and infants may display a midline gap between nasal bones or nonossification of the cribriform plate, which may be mistaken for a sinus tract or connection between the anterior cranial fossa and nasal cavity, respectively.[21] In addition, the fatty changes that develop in the crista galli may be misread as a dermoid cyst.[23,24]

Although timing of intervention remains controversial, surgery is certainly considered the mainstay of treatment for nasal dermoid cysts. Some advocate for removal expediently, but one must consider difficulty of access and decreased tolerance for blood loss in newborns and infants. The senior author does not typically excise these lesions until the age of 1.

Surgical approach must be adequate to allow for the following: (1) access to all midline lesions with medial and lateral osteotomies, (2) repair of skull base defects or cerebrospinal fluid leak, (3) reconstruction of any nasal deformity, and (4) a cosmetically acceptable scar.[23] A number of incisions have been described for removal of a nasal dermoid cyst, including midline vertical incision, which is the most commonly used for a simple cyst, transverse incision, inverted U incision, lateral rhinotomy, and midbrow incisions.[14,15,23,24] The open rhinoplasty is an excellent approach to allow for skull base exposure when a combined single-stage intracranial–extracranial procedure is needed.[13] Successful transnasal endoscopic excision with a small external incision for punctum removal has also been reported. This technique necessitates frozen section

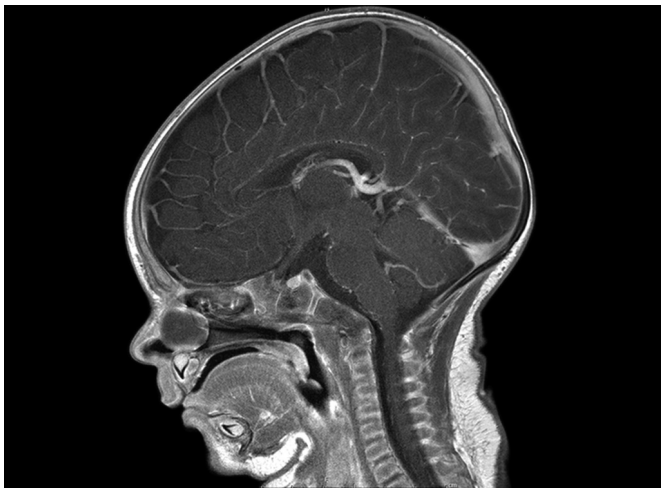


**Fig. 40.5:** T1-weighted postcontrast sagittal image of nasal glioma.

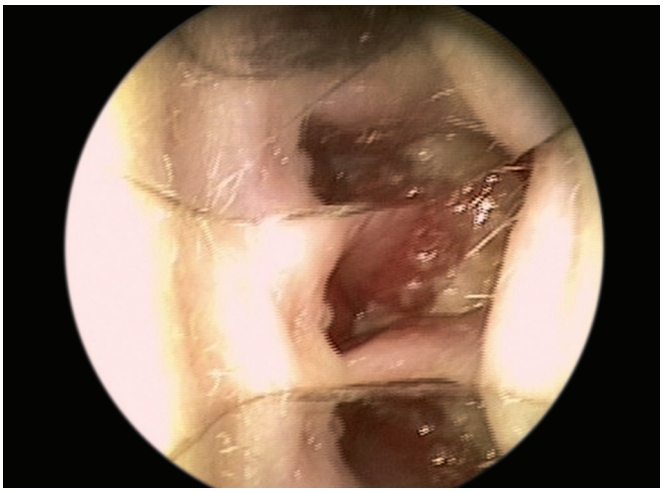


**Fig. 40.6:** Intranasal image of glioma seen on magnetic resonance image.

at the foramen cecum to confirm complete excision.[24] Regardless of technique utilized, complete excision is imperative, as recurrence rates have been shown to be as high as 50–100% when dermal elements are left behind.[14]

## NASAL GLIOMA

Although Schmidt coined the term glioma and gave a complete description in 1900, the initial account was actually given by Reid in 1852. Also described as nasal cerebral/glial heterotopia or encephaloma,[25,26] a nasal glioma is thought to develop due to initial herniation of intracranial tissues into the dural projection through the foramen cecum or fonticulus frontalis with subsequent separation from the brain and degeneration of the stalk, eliminating any cerebral connection.[27] Although it is slightly more common in males, there is no genetic basis nor is there any malignant potential.

Because encephaloceles and gliomas share many characteristics, including pathogenesis and often histopathology, correlation between imaging, surgical findings, and microscopic examination is needed to confirm diagnosis. Although both lesions contain glial tissue, presence of ependymal tissue can identify an encephalocele and rule out a glioma. However, lack of ependymal tissue does not help differentiate one from the other. An absolute lack of cerebral connection combined with the finding of glial tissue on pathology confirms the diagnosis.[27]

About 60% of nasal gliomas appear as an extranasal mass, 30% present with only an intranasal component, and 10% present with a combined lesion.[28,29] Those that present extranasally appear as a firm, smooth, noncompressible mass anywhere along the dorsum of the nose. When there is an intranasal component, the patient presents with nasal obstruction, and examination demonstrates a pale mass in the nasal cavity, at times protruding from the nostril.[27] Like a nasal dermoid, the Furstenberg's test is also negative with a glioma. Most commonly, the lesion originates from the lateral nasal wall near the middle turbinate, or less commonly, from the nasal septum.[30] Again, similar to the nasal dermoid, both high-resolution CT and high-resolution MRI with contrast provide complementary information regarding bony and soft tissue detail.[27] Biopsy of these lesions should be avoided (Figs. 40.5 and 40.6).

Surgical excision is the treatment of choice for these lesions. Because 10–25% of nasal gliomas may have a fibrous stalk extending toward the base of the skull with an associated bony defect (but no connection to the brain itself), neurosurgical consultation may be needed if the imaging dictates as such.[31] Extranasal gliomas require an external incision; ultimately, the approach must provide excellent exposure, allow for exploration of the stalk, and provide a good cosmetic outcome, regardless of the incision. An osteotomy may be needed if the lesion extends deep to the nasal bones to follow the entire stalk. The Boston Children's Hospital experience suggests that an external rhinoplasty incision allows for the best access in these cases. In addition, they suggest that if the mass is too large or in the nasoglabellar area where the external rhinoplasty approach does not provide adequate exposure, the midline nasal or bicoronal incision may be useful.[27]

Intranasal gliomas may be removed endoscopically under image guidance safely; in addition, repair of any

skull base defect can also be done at the same time without need for additional incisions or neurosurgical intervention.[32-34] However, a neurosurgical team should always be aware and available for any of these cases in case complete excision requires frontal craniotomy. Recurrence rates have been shown to be about 4–10%.[35]

## ENCEPHALOCELE

While an encephalocele is a rare entity, it occurs a rate of 1 in 4000 to 1 in 5000 live births. Encephaloceles are classified on the basis of two things: location and contents. The encephalocele is found in the occipital location about 75% of the time and in the frontal location about 25% of the time.[36] Posterior skull base or occipital encephaloceles are more common in females and in North America, whereas frontal encephaloceles are more common in males and in Southeast Asia. The overall rate of occurrence, however, is equal between males and females (Tables 40.1 and 40.2).

Presentation can vary from nasal obstruction to epistaxis to recurrent meningitis. However, in a congenital setting, nasal obstruction or a mass is typically what is encountered. On physical examination, a widened nasal root and increased intraocular distance may be noted.[37] A sincipital encephalocele appears as an external nasal mass, which may present anywhere along the outside of the nose, whereas a basal encephalocele presents as an internal mass with location dependent of site of herniation.[27] Unlike other nasal masses, however, the Furstenberg's test is positive (pulsation and expansion of mass with crying/straining/jugular vein compression) due to intracranial connection. Nasal endoscopy is vital for adequate characterization of the mass (Fig. 40.7).

Preoperatively, neuroradiological and neurosurgical consultations are mandatory. As with nasal gliomas and dermoids, both CT and MRI with contrast are useful and provide complementary information. Of note, contrast is useful to help delineate between and skull base defect and an incompletely ossified skull base, with is often present with young infants.[27] If only one imaging modality can be chosen, however, CT scan allows for better delineation of bony anatomy, making it the modality of choice for preoperative planning[38] (Fig. 40.8).

Surgical excision is once again the mainstay of treatment. This should be done expeditiously to reduce the chance of infectious and cosmetic complications. The procedure always involves a frontal craniotomy for excision of the intracranial component and repair of skull base defect. If an extranasal component is present, the bicoronal incision may be extended down to the bony–cartilaginous junction of the nasal dorsum to allow for excellent exposure. Both orbital osteotomies and hemiorbital advancement have been described to correct hypertelorism for improved functional and cosmetic outcome.[38] For those encephaloceles with an intranasal component, endoscopic excision under image guidance has been shown to have excellent outcomes in experienced hands and avoid external facial incisions. If needed, however, a lateral rhinotomy may be used for exposure.[27] Cerebrospinal fluid leak rates have varied from 17–22% without significant rates of recurrence.[27,38]

**Table 40.1:** Classification based on contents

| *Classification* | *Contents* |
|---|---|
| Meningocele | Meninges only |
| Meningoencephalocele | Meninges, neural tissue |
| Meningoencephalocystocele | Meninges, neural tissue, ventricular system tissue |

## CRANIOPHARYNGIOMA

Craniopharyngioma is a nonglial benign intracranial tumor of the sellar/parasellar region that occurs at a

**Table 40.2:** Classification of frontal encephaloceles based on location

| *Classification* | *Location of herniation* | *Location of mass* |
|---|---|---|
| Sincipital: nasofrontal | Fonticulusnasofrontalis | Forehead or nasal bridge |
| Sincipital: nasoethmoidal | Foramen cecum | Nasal bridge |
| Sincipital: naso-orbital | Medial orbital wall | Orbit |
| Basal: transethmoidal | Cribriform plate | Intranasal |
| Basal: sphenoethmoidal | Between ethmoid and sphenoid | Nasopharynx |
| Basal: trans-sphenoidal | Craniopharyngeal canal | Nasopharynx |
| Basal: sphenomaxillary | Superior and inferior orbital fissure | Pterygopalatine fossa |

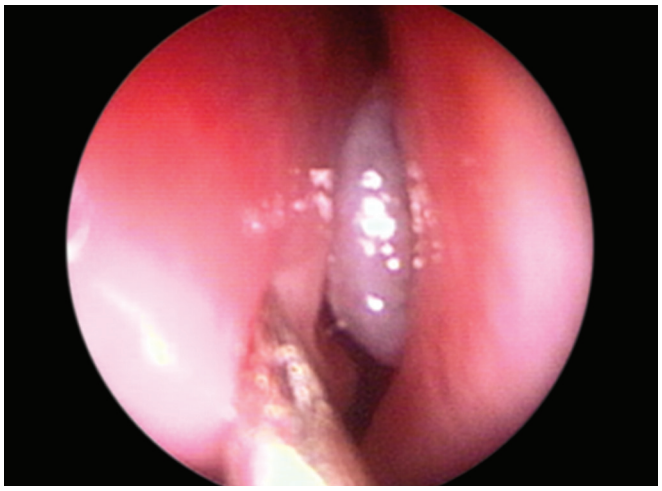


**Fig. 40.7:** Endoscopic view of encephalocele.

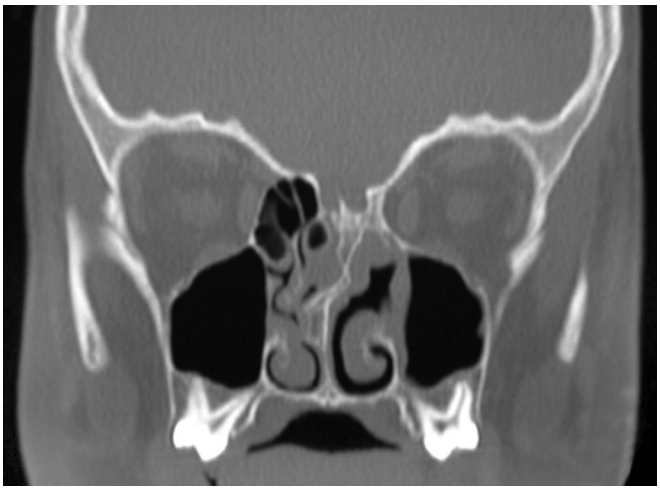


**Fig. 40.8:** Coronal computed tomography demonstrating encephalocele with bony defect at cribriform plate.

rate of about 0.5–2 cases per million persons per year.[39] It represents about 1.2–4% of all intracranial tumors of childhood, and approximately 30–50% of all cases are found during childhood/adolescence.[40] Two major schools of thought exist regarding the embryonal origin: some think that the tumor arises from the ectodermal remnants of Rathke's cleft, whereas others believe that the residual embryonal epithelium of the anterior pituitary gland and anterior infundibulum is the area of origin. Childhood craniopharyngioma typically is of the adamantinomatous histological type, which shows cyst formation and calcifications on imaging, aiding in diagnosis. Although there is a second peak of craniopharyngioma incidence in adulthood (between 50 and 75 years of age), it is of a papillary histological type. In addition, >70% of craniopharyngiomas of the adamantinomatous type express a β-catenin gene mutation, not seen in the papillary type.[41] This suggests that the two types are both histologically and genetically distinct.

Symptoms typically arise from mass effect, including increased intracranial pressure and optic nerve compression, and endocrine derangement, including hypothyroidism, growth hormone deficiency, and hypothalamic dysfunction. Although the symptom complex of headache, visual impairment, pathologic low growth rate, weight gain, and polydipsia/polyuria should point to the possibility of craniopharyngioma in the differential diagnosis, many patients present with one or more of these symptoms years before the diagnosis is made.[42] While growth retardation can manifest very early in the disease process, weight gain, which may lead to extreme obesity due to hypothalamic involvement, usually presents as a late manifestation. Delayed or early puberty may also be seen. Papilledema can be seen in 25–40% of patients due to elevated intracranial pressure. Rarely, ataxia and/or seizures may also be present.[43] No specific findings on an otolaryngologic examination provide additional clues in making this diagnosis.

The most common location of craniopharyngioma is suprasellar with an intrasellar component. Both CT and MRI with contrast are needed to accurately make the diagnosis of craniopharyngioma. While MRI is the gold standard for imaging, the cystic components can have variable signal based on the amount of protein content of the cyst fluid. CT can be used to detect calcifications and therefore confirm diagnosis.[44]

Surgical extirpation in some capacity is part of the treatment of these lesions. For tumors with large cystic components, some have advocated for a two-stage procedure. Initially, an intracystic catheter can be placed for relief of pressure and possibly for instillation of intracystic sclerosing agents. This can be followed by resection.[45] For tumors in surgically favorable locations, complete resection without perturbation of visual, hypothalamic, or pituitary function is preferred. Endoscopic transsphenoidal approaches are becoming increasing popular due to ability to leave the hypothalamus undisturbed.[40] For tumors that are in unfavorable locations, differing opinions exist regarding how much of a role surgical excision should play. While some believe in attempting complete resection, others advocate for planned limited resection, whether biopsy or partial/subtotal resection.

Critics of extensive surgery cite iatrogenic deficits, such as hypothalamic dysfunction, and the high rate of recurrence despite what appeared to a complete resection. While rate of progression of residual tumor after incomplete resection is as high as 71–90%, when radiation is administered after surgery, this rate decreases to about 21%.[46] External beam radiation, proton beam radiation, and intracavitary β-radiation have all been shown to be effective. Due to reasons relating to radiation biology, single-dose stereotactic radiation has been of limited use in the treatment of childhood craniopharyngioma.[42]

## OTHER CONGENITAL NASAL MASSES

Because hemangioma is the most common tumor of childhood, it should always remain in the differential for an intranasal or extranasal mass. In addition, a congenital teratoma may rarely present in the nasal cavity or nasopharynx. This differs from a dermoid tumor in that it contains ectoderm, mesoderm, and endoderm as opposed to only ectoderm and mesoderm.

## SUMMARY

Although congenital nasal masses are quite uncommon, ability to devise a differential and narrow the diagnostic possibilities is important. CT and MRI are both important modalities in characterizing these lesions. Prompt intervention should be undertaken, particularly with an encephalocele, to prevent intracranial complications. Although most of these lesions require complete surgical treatment, additional treatment may be needed to prevent recurrence and/or progression.

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CHAPTER

# 41

# Congenital Lesions in the Oral Cavity and Oropharynx

***Mark Boston, Joseph W Rohrer***

## INTRODUCTION

The oral cavity and oropharynx are complex anatomic regions that begin the aerodigestive tract. Components in these areas arise from all three germ layers that undergo significant migrations to result in a functional oral cavity and oropharynx. The developmental relationships between embryonic cell lines make possible a variety of congenital malformations and anomalies. Variations in embryonic development lead to a wide range of oral cavity and oropharyngeal abnormalities; from minor cosmetic deformities requiring little to no treatment to potentially lethal anomalies. Congenital lesions of the oral cavity and oropharynx may be specific to a particular subsite or may span the entire region and beyond. In addition, other congenital syndromes often manifest with findings in the oral cavity and/or oropharynx.

Congenital lesions of the oral cavity and oropharynx result from failures of migration, trapped ectopic tissues, abnormal proliferation of tissues, embryologic fusion anomalies, and benign or malignant neoplasms. Ectopic tissue, heterotopic tissue, and choristomas are histologically normal tissues present in abnormal locations, whereas hamartomas result from an abnormal proliferation of tissues appropriate to the anatomic site. Embryologic duplications or failures in separation or migration can also lead to congenital abnormalities with impairment or loss of normal function. This chapter presents congenital lesions of the oral cavity and oropharynx by subsites progressing from the oral commissure to the oropharynx with generalized pathologies discussed at the end (Table 41.1).

## EMBRYOLOGY

At approximately 3 weeks' gestation, paired pharyngeal arches begin to develop alongside the pharyngeal foregut (Fig. 41.1). The arches have corresponding pharyngeal clefts lined by ectoderm and pharyngeal pouches lined by

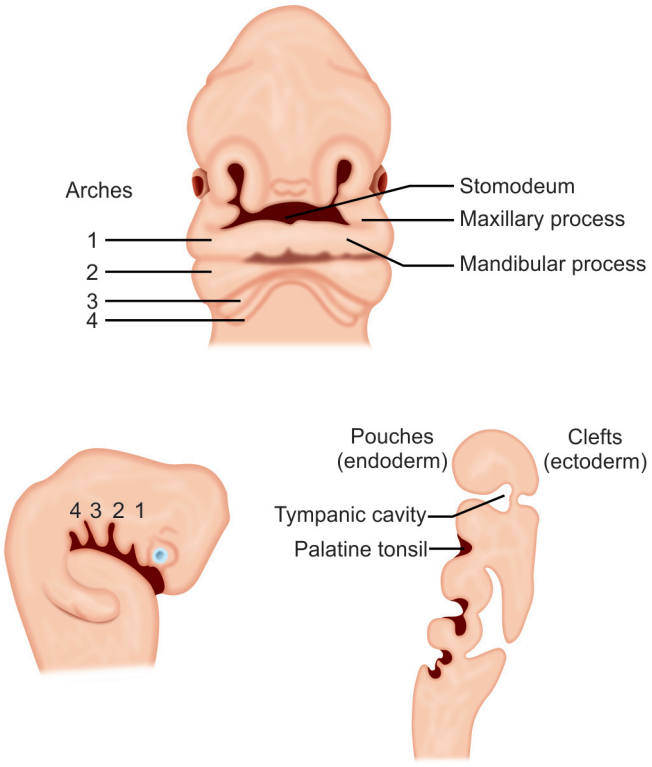



**Fig. 41.1:** Paired pharyngeal arches and their derivatives.

**Table 41.1:** Congenital lesions of the oral cavity and oropharynx by location

| *Anatomic location* | *Lesions* |
|---|---|
| Oral aperture and lips | Microstomia/macrostomia<br>Lip pits<br>Maxillary and mandibular labial frenula |
| Tongue | Ankyloglossia<br>Macroglossia<br>Glossoptosis<br>Geographic tongue/fissured tongue<br>Median rhomboid glossitis<br>Ectopic thyroid<br>Vascular malformations and cysts |
| Mandible/maxilla/gingiva | Facial clefts<br>Micrognathia<br>Nasopalatine duct cyst<br>Midpalatal cysts (Epstein's pearls)<br>Alveolar cysts (Bohn's nodules)<br>Natal/neonatal tooth<br>Cherubism<br>Granular cell tumor (epulis)<br>Eruption cysts<br>Odontogenic tumors |
| Oral cavity | Congenital synechiae<br>Fordyce granules<br>Oral lymphoepithelial cysts<br>Focal epithelial hyperplasia (Heck's disease)<br>Mucocele/ranula |
| Oropharynx | Hairy polyp<br>Second branchial cleft cyst |
| Generalized lesions (multiple sites) | Ephelis (melanosis)<br>Hemangioma<br>Vascular malformations<br>Lymphatic malformations<br>Dysontogenetic cysts<br>Heterotopic cysts |

endoderm. The first pharyngeal arch forms the maxillary and mandibular processes. Extensions off of the nasal placodes form the primary palate with the secondary palate extending from the maxillary swellings. Fusion of the secondary palate takes place at around 10 weeks' gestation.

The first arch muscle derivatives, including the mylohyoid, tensor veli palatini, and muscles of mastication, are innervated by the trigeminal nerve. The facial nerve innervates the second arch derivatives to include the muscles of facial expression. The fourth arch gives rise to the levator veli palatini muscle, which is innervated by the superior laryngeal nerve.

Normal facial skeletal development depends on the accurate fusion of the five facial prominences; the frontonasal process, the paired maxillary swellings, and the paired mandibular swellings.[1] Cleft lip, cleft palate and other, rare facial clefts all occur as the result of improper fusion of the five facial prominences.

The buccopharyngeal membrane, composed of ectoderm and endoderm, separates the primitive mouth (stomodeum) from the primitive foregut. This membrane ruptures around day 24 of gestation, creating an opening that begins the oral cavity. The tongue forms during the 4th week and arises from endoderm covered swellings on the floor of the pharynx (Fig. 41.2). The anterior two thirds of the tongue form from the first pharyngeal arch while the posterior third arises from the second, third, and fourth pharyngeal arches. A median tongue bud (tuberculum impar) develops from the first arch and is overgrown by the lateral tongue buds. These three pharyngeal floor swellings compose the anterior two thirds of the tongue.

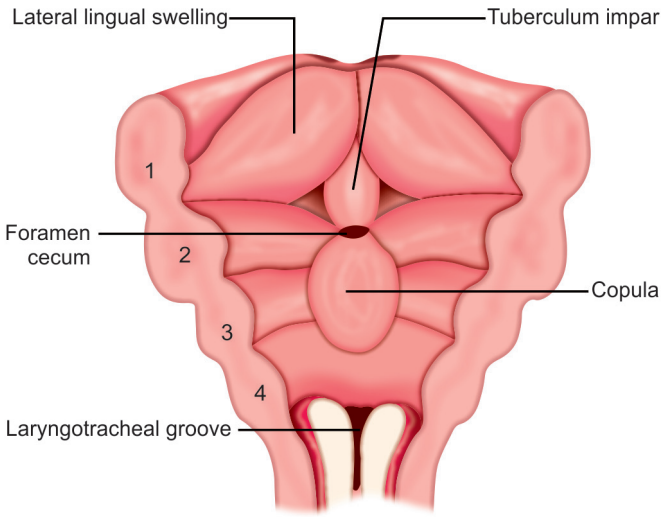



**Fig. 41.2:** Embryology of the tongue and pharyngeal floor.

The second and third arches develop a midline swelling (copula), which is overgrown by swellings from the third and fourth pharyngeal arches (hypopharyngeal eminence) forming the posterior third of the tongue. The occipital somites form the intrinsic musculature of the tongue. All the muscles of the tongue, except for the palatoglossus muscle, are innervated by the hypoglossal nerve. The palatoglossus muscle is innervated by the pharyngeal plexus and the vagus nerve. Separate innervations for taste and sensation versus motor function are explained by these complex tissue migrations.[2]

The thyroid develops in the foramen cecum at the base of the tongue at 4 weeks' gestation and descends along the thyroglossal duct to its final location in the neck by the 7th week.[3] The palatine tonsils develop from the endoderm of the second pharyngeal pouch, and the salivary glands develop from ectoderm invaginating between the maxillary and mandibular swellings (parotid glands), floor of the mouth (submandibular glands), and paralingual gutters (sublingual glands).

## ORAL APERTURE AND LIPS

### Microstomia/Macrostomia

Microstomia is a developmental anomaly resulting in a smaller than normal oral aperture. The most severe form is astomia, a complete failure of the upper and lower lips to divide and can be associated with holoprosencephaly. Other syndromes associated with microstomia are oropalatal dysplasia, Hallermann–Streiff's syndrome, Fine–Lubinsky's syndrome, hemifacial microsomia, trisomy 18, and Freeman–Sheldon's syndrome.[4] Clinical manifestations of microstomia can be barely perceptible to severe. Feeding difficulties are the main concern and both nonsurgical and surgical treatments exist ranging from oral commissure stretching to free tissue transfer.[5]

Macrostomia is an overly large oral aperture. Syndromes associated with macrostomia include Angelman's syndrome, Morquio's syndrome, Noonan's syndrome, Beckwith–Wiedemann's syndrome, Treacher–Collins' syndrome, and Williams' syndrome. Transverse facial clefts, also referred to as Tessier 7 clefts, create an enlarged oral stoma. Lateral facial clefts are rare, reported at 1:5000 births.[6] Surgical repair of lateral facial clefts has been the traditional treatment with combinations of z-plasties, commissure plasties, and local rotational flaps. The goal of surgical treatment is to create a functional oral sphincter with acceptable cosmetic outcomes.

### Lip Pits

Congenital lip pits are perhaps most associated with Van der Woude's syndrome; however, lip pits can also be found in other syndromes such as basal cell nevus syndrome (Gorlin), branchio-oto-renal syndrome, popliteal pterygium syndrome, Kabuki's syndrome, and orofacial digital syndrome.[4] Congenital lip pits typically occur bilaterally on the lower lip in a paramedian position and often contain minor salivary glands. Van der Woude's syndrome has a prevalence of 1:40,000 to 1:100,000 live births with an autosomal dominant pattern with high penetrance and variable expressivity. Cardinal features of the syndrome include lower lip pits, cleft lip with or without cleft palate and isolated cleft palate. Treatment is based on the severity of phenotype and isolated lip pits often require no treatment. Alternatively, the pits may be completely excised if they chronically drain, cause pain, or are cosmetically disfiguring.[7]

### Maxillary and Mandibular Labial Frenula

The maxillary and mandibular frenula attach to the infantile gingiva. After primary dentition erupts the frenula, if attached to far lingually on the gingiva, can cause incisor diastasis and pull at the gingiva leading to gum recession (Fig. 41.3). The absence of the mandibular labial frenula and lingual frenula may indicate a patient with Ehlers–Danlos' syndrome.[8] Patients can be observed until dentition erupts and symptoms develop. Surgical ligation or debulking of the frenulum is curative with orthodontic care as needed to correct dental diastasis.

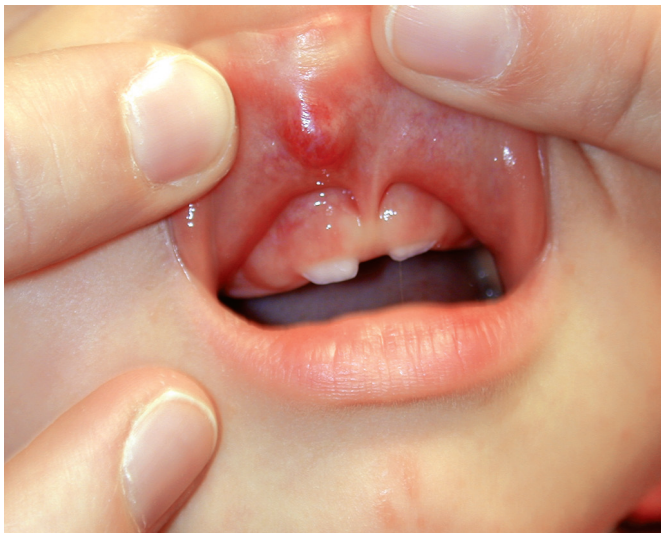


**Fig. 41.3:** Attached upper labial frenulum with diastema of the upper central incisors and an upper lip hemangioma.

## TONGUE

### Ankyloglossia

Ankyloglossia results when the lingual frenulum is short, thick, or is attached too far anteriorly on the tongue. It is reported in 1.7–4.8% of newborns with a male predominance.[9-11] Ankyloglossia may result in feeding difficulties from poor latch, infant fatigue, and maternal nipple pain. Division of the frenulum can take place at the bedside in newborns, but occasionally may require formal frenuloplasty for a broad frenulum or in older children. For children without feeding difficulties, ankyloglossia may cause speech articulation difficulties or cause oral hygiene difficulties from periodontal food collections. Ankyloglossia is more likely to be problematic if the tongue is unable to reach the hard palate or protrude past the mandibular incisors. It may be preferable to delay frenotomy or frenuloplasty in the child without feeding difficulties as spontaneous lengthening can occur over time.

### Macroglossia

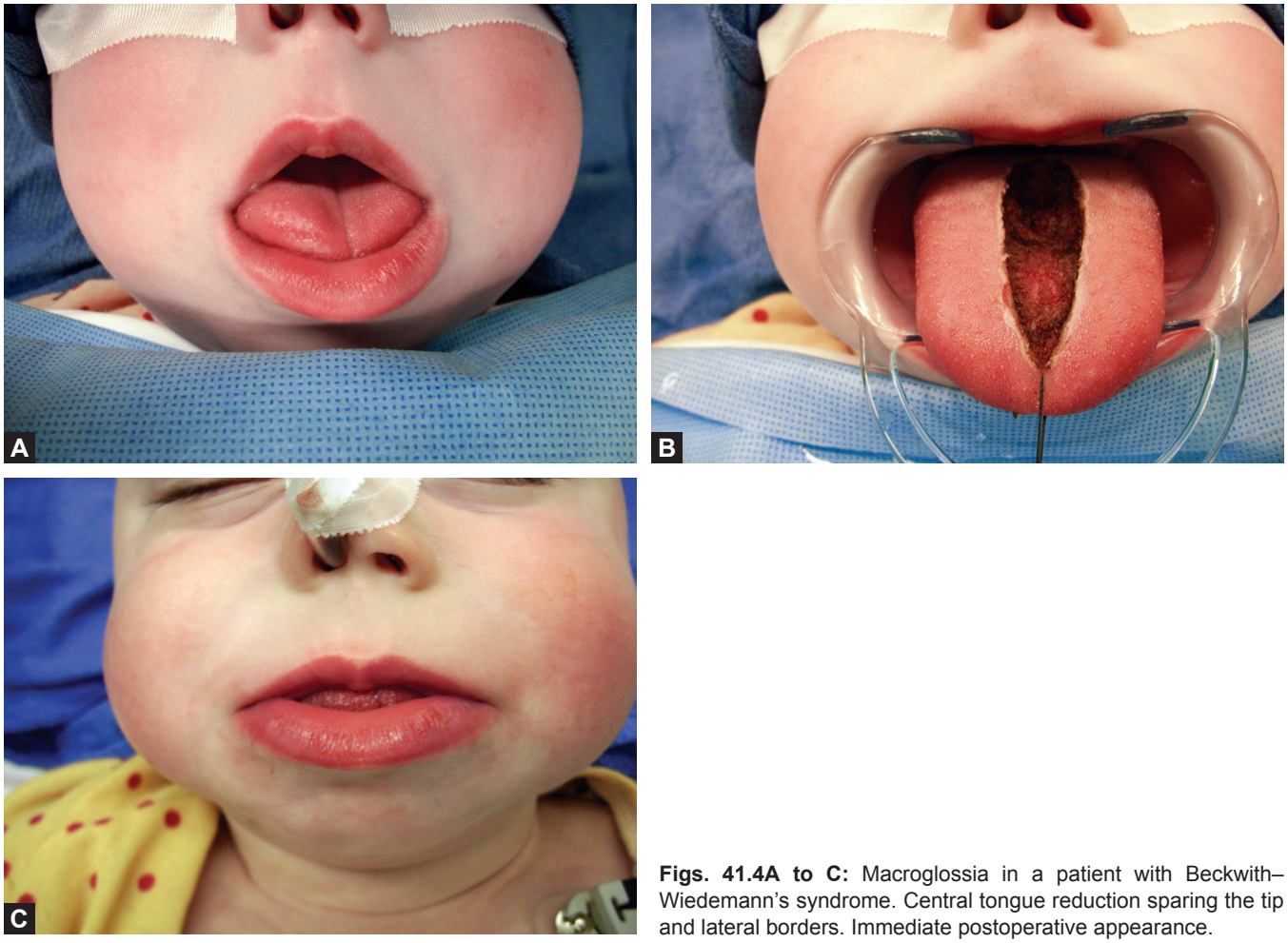
Macroglossia is a disproportionally large tongue that may be either a true enlargement or a relative enlargement due to retrognathism or other facial or oral cavity problems. The spectrum of macroglossia can be mild without sequelae to severe with airway obstruction or feeding difficulties.[12] Vascular malformations, tumors, lymphangiomas, or muscular hypertrophy (Beckwith–Wiedemann's syndrome) can all cause macroglossia.[13] Multiple syndromes have enlargement of the tongue as a feature including Down's syndrome, mucopolysaccharidoses, neurofibromatosis, and Beckwith–Wiedemann's syndrome. Beckwith–Wiedemann's syndrome has an incidence of 1:17,000 births and is associated with macroglossia, anterior abdominal wall defects, visceromegaly, gigantism, and neonatal hypoglycemia.[14] Surgical treatment for symptomatic macroglossia is a partial glossectomy (Figs. 41.4A to C). There are a variety of partial glossectomy techniques all with the goal of reducing bulk while maintaining normal motor function, taste, and sensation. Patients with macroglossia should also be evaluated for the presence of obstructive sleep apnea.

### Glossoptosis

Glossoptosis is defined as posterior displacement of the tongue into the pharynx. Pierre Robin malformation sequence, or Robin sequence, consists of micrognathia, upper airway obstruction, and glossoptosis. An associated syndrome is found in 27% to 82% of children with Robin sequence and include Stickler's syndrome, velocardiofacial syndrome, hemifacial microsomia, Treacher–Collins' syndrome, fetal alcohol syndrome, and other chromosomal abnormalities.[15] Glossoptosis may also be seen in Down's syndrome and other conditions with hypotonia. Surgical treatment of glossoptosis causing upper airway obstruction typically involved glossopexy or tracheotomy; however, mandibular distraction has emerged as an important alternative treatment and is discussed below in the section on micrognathia.

### Geographic Tongue/Fissured Tongue

Geographic tongue, also known as benign migratory glossitis, and fissured tongue (lingua plicata) affect 1.8% and 0.9% of the US population, respectively.[16,17] Both conditions are benign and do not require treatment other than adequate oral hygiene. Deep tongue fissures are associated with Down's syndrome and Melkersson–Rosenthal's syndrome (MRS). MRS is a rare condition marked by fissured tongue, recurrent facial swelling, and facial paralysis.[18] There is no known cause and treatments, including antibiotics, systemic and intralesional steroids, and




**Figs. 41.4A to C:** Macroglossia in a patient with Beckwith–Wiedemann's syndrome. Central tongue reduction sparing the tip and lateral borders. Immediate postoperative appearance.

methotrexate, have been used with varying degrees of success. Those found to have MRS should be screened for Crohn's disease and hairy cell leukemia as associations with these conditions have been made.[4]

## Median Rhomboid Glossitis

Median rhomboid glossitis is a benign condition affecting < 1% of the population. The lesion appears as a smooth, red, depapillated area in the midline of the tongue just anterior to the circumvallate papillae. This area corresponds to the tuberculum impar lending support to a congenital origin of this condition. However, the lesion can also be found off the midline prompting suspicion for noncongenital causes. Candida species have been implicated as a cause of median rhomboid glossitis.[19] Median rhomboid glossitis is usually asymptomatic, but patients may experience pain, burning, or pruritus. Treatment consists of oral hygiene, antifungal troches, and biopsy for any changing or atypical lesions. Surgical resection is rarely indicated.

## Ectopic Thyroid

Failure of normal thyroid migration during gestation results in ectopic thyroid tissue anywhere along the thyroglossal duct tract from the base of the tongue down to the inferior neck. A lingual thyroid is the most common location accounting for 90% of all ectopic thyroid tissue (Fig. 41.5).[20] The incidence of lingual thyroid is 1:100,000 births and females are affected four to eight times more often than males.[3] No additional thyroid tissue is present in up to 80% of cases of lingual thyroid. Lingual thyroids often do not become symptomatic until puberty and symptoms may include hemoptysis, dysphagia, dysphonia, dyspnea, globus, and obstructive sleep apnea. Patients may be euthyroid or hypothyroid. Treatment is unnecessary for

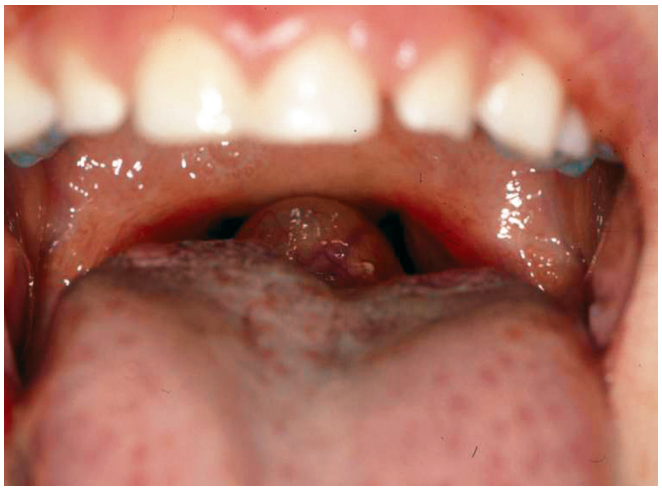


**Fig. 41.5:** Lingual thyroid.

asymptomatic patients. Nonsurgical treatment options include hormone suppression therapy and radioactive iodine ablation. If surgical excision is required, evaluation for additional thyroid tissue in the neck should take place prior to surgery. Scintigraphy with Tc-99, I-131, or I-123 can locate functioning thyroid tissue. Computed tomography, magnetic resonance imaging, and ultrasound can also asses for orthotopic thyroid.[21] Malignancy is rare and, if present, has characteristics similar to thyroid cancer found in the neck.[20] Surgical excision of a lingual thyroid may be performed either transorally or through a suprahyoid neck approach based on visualization. After resection, the patient should be monitored for the need for thyroid hormone replacement.

### Vascular Malformations and Cysts

The tongue is a frequent location of these common lesions. These lesions will be discussed in greater detail later in this chapter. Specific tongue lesions, in order of prevalence, are vascular/lymphatic, mucus extravasation phenomenon, and hamartomatous lesions.[22]

## MANDIBLE/MAXILLA/GINGIVA

### Facial Clefting

Cleft lip and cleft palate are the most common of the facial clefts. Van Der Meulen created an embryologic classification system of facial clefts, whereas Tessier created the most commonly used classification system based on cleft location.[23] The incidence of facial clefting is 0.17% and isolated clefts occur in 66% of these patients.[6] Risk factors for facial clefts include maternal smoking and alcohol consumption, folic acid deficiency, and corticosteroid use. Clefts also have racial variances with rates of 1 in 400 births among Asians and Native Americans to 1 in 2000 births among African Americans. Lateral facial clefts (Tessier 7) occur in 1:3500–5000 births with other Tessier clefts being extremely rare.[24] Clefts are thought to result from a failure of migration and contact of nasal, maxillary, and/or mandibular processes during gestation. Alternative theories include, vascular ischemia leading to developmental arrest, and tethered tissues (amniotic bands) preventing migration. Advances in feto-maternal imaging have made it possible to diagnose facial clefts and airway obstructing masses in utero with near 100% sensitivity.[25] Surgical treatment is based on the type of cleft and associated defects. Maintaining adequate nutrition in children with cleft lip, cleft palate, and lateral facial clefts can be a challenge secondary to incompetence of the oral commissures or oral cavity.

### Micrognathia

Micrognathia occurs as the result of mandibular hypoplasia with the mandibular alveolus positioned posterior to the maxillary alveolus. Stickler's syndrome, hemifacial microsomia, Treacher–Collins' syndrome, Nager's syndrome, and Robin sequence all have micrognathia in their phenotypes. Minor cases may be managed with conservative approaches such as repositioning, prone positioning, and the use of nasopharyngeal airways.[26] Children with micrognathia who require intubation within the first 24 hours of life, who have neurologic deficits, or who experienced intrauterine growth restriction have significantly increased odds of requiring definitive airway surgery.[27] Tracheostomy bypasses the obstruction until the mandible can grow or "catch up". Tracheostomy had been the standard of care until recently when significant advancements in mandibular distraction osteogenesis (MDO) were made. MDO, either intraoral or external, allows for lengthening of the mandibular deficiency and can help avoid tracheostomy or assist with decannulation in many children as anterior advancement of the mandible pulls the tongue forward, improving the airway. Distraction takes place until resolution of the obstruction and is often 15 mm in neonates and further in older children.[28]

### Nasopalatine Duct Cyst

Nasopalatine duct cysts (incisive canal cysts) are the most common nonodontogenic cyst of the maxilla, affecting

1:100 people. The cysts are unilocular and extend between the roots of the central incisors. The cysts arise from epithelial remnants of the nasopalatine duct and extend between the roots of the central incisors. Nasopalatine duct cysts are unlikely to be diagnosed before eruption of dentition. Although most cysts are asymptomatic, some lesions may become painful, drain, become infected, or cause orthodontic misalignment. Symptomatic lesions may require surgical excision and recurrence is rare with complete surgical removal.[29]

## Midpalatal Cysts (Epstein's Pearls)

Midpalatal cysts are epithelial inclusions trapped between fusion planes at the junction of the hard and soft palate and are found in up to 78% of newborns.[30] These small, keratin filled cysts may be present at birth or appear within the first few months of life. They can be found anywhere on the hard palate but rarely occur on the distal soft palate. No treatment is necessary as the cysts spontaneously rupture or regress. They do not cause feeding or respiratory issues.

## Alveolar Cysts (Bohn's Nodules)

Alveolar cysts are epithelial inclusions similar to palatal cysts. Almost 60% of children may present with alveolar cysts at birth. Infants with milia are more likely to present with alveolar cysts than are infants without milia.[30] Most (90%) alveolar cysts present on the maxillary alveolus, and they are more common on the anterior alveolus than on the posterior alveolus.[31] No treatment is necessary as the cysts spontaneously resolve within 4 to 5 weeks.

## Natal/Neonatal Tooth

A natal tooth is a tooth, which is present at birth. Primary dentition does not typically erupt until around 1 year of age. If a tooth erupts within the first 4 weeks of life, it is termed a neonatal tooth and occurs with a prevalence of 1:1000 to 1:3500. Mandibular incisors account for 85% of natal teeth.[32] Natal teeth can cause pain to the mother during breast feeding, or an ulcer in the infant's mouth where the tooth makes contact (Riga–Fede's disease). Natal teeth are the result of displaced tooth germs and are not supernumerary teeth. They are associated with many syndromes to include chondroectodermal dysplasia, Noonan's syndrome, pachyonychia congenita, oculomandibulodyscephaly, and Turner's syndrome. If stable, the tooth can be left in place and filed to remove sharp edges. Natal teeth may be hypermobile but eventually the roots develop and stabilize the tooth. Significantly hypermobile teeth may become an aspiration risk and extraction is recommended.[4]

## Cherubism

Cherubism is a rare, benign, skeletal dysplasia of the maxilla, and/or mandible. The lesions are symmetric, fibro-osseous, multilocular, expansile, and radiolucent, which first become noticeable between 2 to 7 years of age. Diagnosis is made on the basis of the clinical and radiographic findings. Cherubism occurs in three stages: aggressive, nonaggressive, and quiescent. The aggressive phase is seen in young children with rapidly growing lesions that cause tooth root displacement and cortical bone thinning. The nonaggressive phase is typically seen in teenagers and is characterized by slowed growth or stabilization of the lesions. The quiescent phase occurs after puberty when the lesions ossify and begin to remodel with improvement in facial contours. Cherubism has been linked to mutations of the SH3BP2 gene on chromosome 4p16.3.[33] The disease process is self-limiting and resolves spontaneously over time, and observation is the most common treatment. Large, rapidly growing lesions may cause airway obstruction or severe cosmetic deformity and can be treated with surgical curettage and contouring of the involved bone.[33]

## Granular Cell Tumor (Epulis)

Congenital epulis is a rare gingival neoplasm of unknown etiology found in newborns. Based on histological characteristics, it is also known as congenital granular cell tumor. It has an 8:1 female to male ratio and is most commonly found on the anterior maxillary alveolar ridge.[34] The lesions are pink, smooth, and often pedunculated and can be multilobular. Multiple tumors occur in 10% of cases. The lesions, when large, can often be identified on prenatal ultrasound. Large epuli may cause airway obstruction and feeding difficulties. Complete surgical resection is curative though very small, asymptomatic lesions may be observed as they may spontaneously regress.[35] Large tumors obstructing the airway may necessitate the need for an ex utero intrapartum treatment procedure to secure the airway upon delivery. Granular cell tumors can be found in other locations of the oral cavity to include the tongue and floor of mouth, but these are often not congenital lesions and have different immunohistochemical profiles.[36]

## Eruption Cysts

Eruption cysts develop within the mucosa overlying an erupting tooth. Eruption cysts are seen at a mean age of 4.7 years.[37] Eruption cysts present with a 2:1 male to female ratio. Half of all cases occur with secondary dentition, 40% primary dentition, and 10% neonatal teeth. They appear as blue-hued, gingival masses on the alveolar ridge. Eruption cysts may be observed or treated with marsupialization.[38]

## Odontogenic Tumors

Odontogenic tumors are a rare group of neoplasms arising from embryonic tooth structures. They are slightly more common in the mandible (54%) than in the maxilla. The most common of these is an odontoma, which comprises 39% of all odontogenic tumors.[39] Odontomas consist of both epithelial and mesenchymal cells and display tooth tissue differentiation. They have components of dentin, cementum, and pulp. The tumor arises during the normal tooth development and often goes unnoticed until tooth eruption or is found on routine dental imaging. Treatment is complete excision.[40] Ameloblastomas are slow growing but locally invasive bony tumors. They most often occur in the posterior mandible and 15% of cases develop before the age of 16.[40] Ameloblastomas account for up to 12% of pediatric odontogenic tumors.[39] Calcifying, cystic, odontogenic tumors (Gorlin cyst) are painless swellings that can cause displacement of tooth roots. Histologically, they are epithelial lined cysts with a collection of ghost cells.[40]

# ORAL CAVITY/OROPHARYNX

## Congenital Synechiae

Synechiae or adhesions may form in the oral cavity during development. Synechiae may be interalveolar (syngnathia) or from the tonsillar fossa (persistent buccopharyngeal membrane). Syngnathia can occur in connection with cleft palate, although it is seen in isolation as well. Interalveolar adhesions have been linked with multiple syndromes including Van der Woude's syndrome, popliteal pterygium syndrome, orofacial digital syndrome, and cleft palate lateral synechiae syndrome.[41] Surgical division of the adhesions is curative, although postlysis physical therapy may be needed to address temporomandibular joint ankylosis. A persistent buccopharyngeal membrane is the embryonic ectoderm separating the stomodeum from the foregut. When the buccopharyngeal membrane persists after birth, it creates a web spanning from the circumvallate papillae of the tongue to the soft palate and anterior tonsillar pillar. Respiratory distress is unlikely unless choanal atresia is also present. Surgical resection is performed to alleviate feeding difficulties and may need to be done in a staged approach or with radial excisions as circumferential resection may lead to stenosis.[42,43]

## Fordyce Granules

Fordyce granules are ectopic sebaceous glands in the oral cavity. They are similar to adnexal structures typically seen in the dermis and present as white or yellow papules 1–3 mm in diameter. They may be solitary or multiple. A line of Fordyce granules along the boundary between the white lip and vermilion border is classified as Fox-Fordyce's disease. Treatment is reserved for cosmetic concerns, and intraoral lesions do not need to be addressed.

## Oral Lymphoepithelial Cysts

Unlike lymphoepithelial cysts found in the parotid gland of HIV positive patients, oral lymphoepithelial cysts are most often found in the floor of the mouth. They are mobile with a white hue just below the mucosa. Histologically, they present as complete cysts lined with stratified squamous epithelium. It is unknown whether the cysts develop from trapped epithelium or lymphoid crypt obstruction. Surgical excision of these superficial lesions is curative.[44]

## Focal Epithelial Hyperplasia (Heck's Disease)

Focal epithelial hyperplasia is a benign mucosal disease most often seen in Native Alaskan and Native American populations. It has also been seen more prevalently in low socioeconomic groups. It is composed of multiple small painless plaques of the oral mucosa. It has been associated with human papillomavirus types 13 and 32 with virus detected in 80% of lesions. Geographic clustering and interfamilial expression has led many to believe there is a genetic predisposition to the disease. Exophytic lesions may require surgical excision if inhibiting normal occlusion or for cosmetic concerns. Surgery, $CO_2$ laser ablation, cryotherapy, and interferon have been trialed with varying results.[45]

## Mucocele/Ranula

Mucoceles are common lesions seen in the oral cavity. They do not have a true cyst lining and are therefore considered pseudocysts. They result from the collection

of extravasated mucous from minor salivary glands in the oral mucosa. Mucoceles can be marsupialized or surgically excised with the goal of removing the offending minor salivary gland. They are more commonly found in the lower lip and have been associated with trauma.[46] Mucoceles may be seen at birth but are more common in older children.

When the mucocele is located in the floor of the mouth, it is termed a ranula or "little frog". This colloquial name refers to the appearance of the throat of a frog. Ranulas often become larger than other oral cavity mucoceles and often have a blue hue. Ranulas form from the extravasation of mucous from the sublingual gland as opposed to minor salivary glands. Surgical excision of the sublingual gland at the time of resection decreases the rate of recurrence.

A plunging ranula is mucous filled pseudocyst that extends below the mylohyoid muscle. A plunging ranula usually presents as a neck mass and may also have an intraoral component. They are closely associated with the sublingual gland as are ranulas isolated to the floor of mouth. It is thought that plunging ranulas extend from the sublingual gland via a dehiscence in the mylohyoid or that they arise from ectopic salivary tissue elsewhere in the floor of mouth. Plunging ranulas often require a transcervical approach for complete resection and, as with other ranulas, excision of the sublingual gland is performed to reduce the risk of recurrence.[47]

## OROPHARYNX

### Hairy Polyp

Hairy polyp is a very rare ectodermal and mesodermal developmental malformation of the oropharynx and nasopharynx (Figs. 41.6A and B). It most commonly presents with intermittent respiratory distress or feeding difficulties in a neonate. Further examination reveals a pedunculated mass often arising from the tonsillar pillar, soft palate, or nasopharynx. Theories exist that these polyps represent first or second branchial cleft anomalies or very low grade, well-organized teratomas. There is a female predominance. Treatment is surgical excision.[48]

### Second Branchial Cleft Cyst

Second branchial cleft cysts arise from the incomplete obliteration of the embryonic cleft. These can manifest as cysts, sinuses, or fistulas and are the most common or the branchial cleft anomalies. Most often, they present as a neck mass. The tract of a second branchial cleft anomaly, if present, will course between the external and internal carotid arteries, lateral and superior to the glossopharyngeal and hypoglossal nerves, and exit into the tonsillar fossa.[49] Treatment is complete surgical excision.

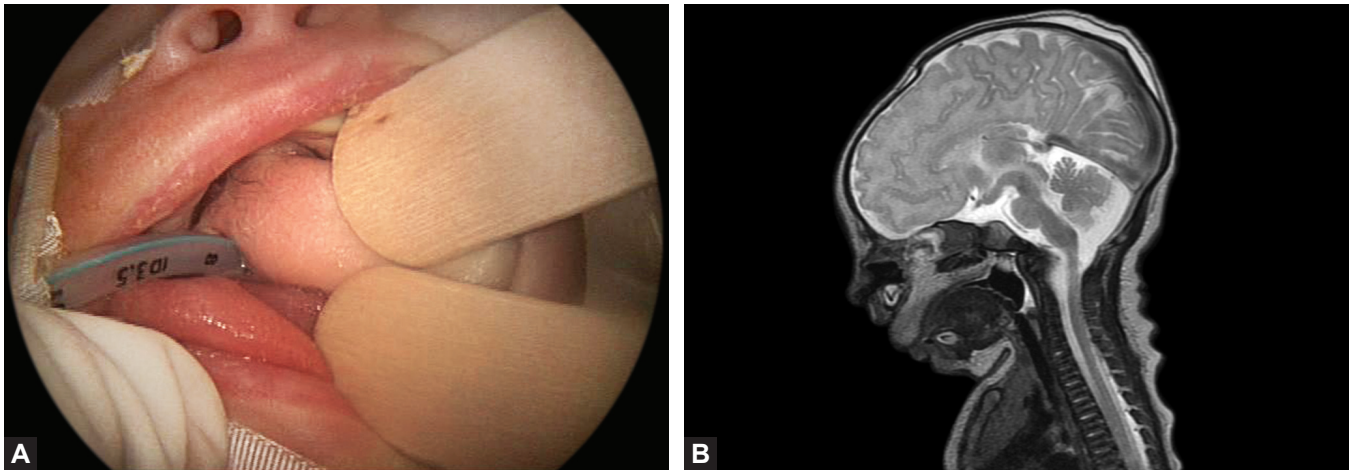
## GENERALIZED LESIONS

### Ephelis (Melanosis)

An ephelis is a well-circumscribed, uniform, pigmented lesion. It can occur in the oral cavity, lip, or tongue and is the equivalence of a freckle on the skin. No treatment is required for this benign lesion.[50]

### Infantile Hemangioma

Infantile hemangiomas are the most common soft tissue tumors in children.[51] The lips, tongue, and buccal




**Figs. 41.6A and B:** (A) Oral hairy polyp in a neonate; (B) T2 sagittal magnetic resonance imaging of neonate with oral hairy polyp. Note attachment of the mass to the skull base and nasopharynx.

mucosa are the most common head and neck sites for hemangiomas (Fig. 41.3). The incidence of head and neck hemangiomas is 4.5% in term newborns and rises to 10% in premature infants weighing <1000 g.[52] Hemangiomas are composed of thin-walled vessels surrounded by endothelial cells that undergo an initial growth phase followed by gradual involution. Observation is the treatment of choice with nearly 50% of lesions resolved by 5 years and 70% by 7 years. Large lesions causing feeding or airway complications, ulcerations, heart failure, or platelet trapping may necessitate aggressive early intervention.

Hemangiomas have been classified as superficial, deep, and mixed and, more recently, as localized or segmental. GLUT-1 is a cellular marker found in infantile hemangiomas, which help distinguish them from other vascular anomalies.[51] The presence of a hemangioma in the "beard" distribution of the lower lip and chin is associated with an airway hemangioma.[53] Rapidly involuting hemangiomas and noninvoluting hemangiomas are often present at birth, whereas infantile hemangiomas may not be noticed during the first few weeks of life.

Traditional hemangioma treatments have centered on intralesional and systemic corticosteroids and interferon injections. Beta-blocker therapy is currently advocated as the treatment of choice with excellent response rates.[51,53] Caution should be used when instituting beta-blocker therapy in children with heart conditions, bradycardia or asthma. In addition, there is a concern for hypoglycemia with beta-blocker therapy as young children have poor glycogen stores.[54] Topical timolol has also been used on small superficial hemangiomas.[55] Laser ablation has been used for superficial lesions, and surgical excision is also performed for nonresponsive lesions or those with life-threatening complications. Early resection following the involution phase can be carried out to improve cosmetic results in areas around the orbits and lips.[51]

## Vascular Malformations

Vascular malformations have a history of significant variability in classification and terminology. Currently, the International Society for the Study of Vascular Anomalies separates tumors (hemangiomas) from malformations. The Hamburg's classification was developed to improve consistency in terminology and is based on the predominant tissue origin of the malformation; arterial, venous, arteriovenous, lymphatic, and capillary.[55] Slow or fast blood flow through the malformation is important in distinguishing among the different lesions as well. Doppler ultrasound is the most cost-effective tool for distinguishing fast from slow flow, whereas magnetic resonance imaging with gadolinium is more effective in evaluating signal characteristics and associations with surrounding structures.

Vascular malformations develop from abnormally formed channels and have an endothelial lining. Unlike hemangiomas, vascular malformations do not regress but rather will expand over time.

Capillary malformations are often called port-wine stains or nevus flammeus. These superficial lesions are often asymptomatic but can be cosmetically problematic when large and located on the face. The pulsed dye laser has been shown to be effective in treating superficial capillary malformations.[56]

## Lymphatic Malformation

Lymphatic malformations (cystic hygromas) may be microcystic or macrocystic. Lymphatic malformations are the most common cause of macroglossia. Macrocystic lesions can be treated with sclerotherapy, whereas microcystic lesions typically require surgical excision or laser ablation. Sclerotherapy agents include OK-432, 100% ethanol, 3% sodium tetradecyl sulfate, bleomycin, and tetracycline. Treatment may not be permanent and recurrence or expansion is common.

## Dysontogenetic Cysts

Dysontogenetic cysts arise from abnormal embryonic development. Epidermoid cysts consist of a stratified squamous epithelium. Dermoids have additional adnexal structures such as hair follicles, sweat glands, or sebaceous glands. Teratomas have the aforementioned but also include mesodermal components. Up to 6.5% of dysontogenetic cysts develop in the floor of the mouth.[57] Teratomas are rare neoplasms in the oral cavity with an incidence of 1:20,000–40,000 live births.[58] Germ cell tumors are frequently grouped with teratomas and are extremely rare in the head and neck.[59]

## Heterotopic Tissue

Choristomas, heterotopias, and hamartomas all represent atypical proliferations of a normal tissue type. Hamartomas represent an overgrowth of tissue found in the anatomical area, whereas heterotopias are normal tissues in an abnormal location. Choristomas are a subset of heterotopias where the lesion is not native to the head and neck. Neuroglial tissues have been found in the tongue and

buccal mucosa and can cause airway obstruction.[60,61] Gastric tissue, as well as respiratory epithelium, have also been described.[62] The two most common locations for oral cavity choristomas are the floor of mouth and the anterior two thirds of the tongue. Surgical resection is curative, and recurrence is rare with complete excision.[63]

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CHAPTER

42

# Infections of the Larynx and Trachea

***Jamie N Andrews, Stephen Maturo***

Acute infections of the respiratory tract are endemic in the pediatric population. Acute respiratory disease is the leading cause of hospitalization in children < 4 years of age.[1] The severity of upper respiratory tract infection may range from mild, self-limited disease to impending airway compromise requiring immediate intervention. Acute infections of the respiratory tract often manifest as stridor, signaling narrowing of the laryngeal inlet, and subglottis. Stridor is the sound caused by abnormal air passage during breathing. It often has a musical, high-pitched quality produced by rapid, turbulent flow of air through a narrowed segment of the upper respiratory tract. A stethoscope placed on the presumed area of obstruction is often helpful in identifying the specific region of narrowing (supraglottis, glottis, subglottis, or proximal trachea). Stridor indicates airway obstruction and is a physical examination finding from which an underlying cause should be sought; it is not a diagnosis. This phenomenon is explained with an understanding of basic fluid dynamics. Airflow typically approximates laminar flow under normal circumstances. Inflammation of the airway results in narrowing of its lumen. As the lumen narrows, the rate of flow increases as explained by the Venturi effect. Bernoulli's principle states that as the speed of a moving fluid (liquid or gas) increases, the pressure within the fluid decreases and vice versa.[2] According to Bernoulli's formula, $1/2\ pv^2 + pgh + p$ = constant (where $p$ = density of fluid, $v$ = velocity of the fluid, $g$ = gravitational acceleration, $h$ = elevation, and $p$ = pressure gradient across the conduit), as the flow velocity increases, there is a drop in the intraluminal pressure. Negative intraluminal pressure promotes airway collapse. This increase in turbulence and collapsibility of the airway is appreciated as stridor.[3]

Children are more susceptible to acute airway compromise due to intrinsic anatomic differences between the pediatric and adult airway. For example, the glottis is the narrowest segment of the adult airway, whereas the pediatric airway is narrowest at the subglottis. The subglottis has a fixed diameter as the cricoid cartilage forms a complete ring that encircles the airway. As the cross-sectional area of a cylinder is proportional to the square of its radius, $A = \pi r^2$ (where $A$ = area, $r$ = radius) even small differences can result in dramatic narrowing of the airway caliber leading to acute airway compromise.[4] Supraglottic swelling classically produces inspiratory stridor. Narrowing at the level of the subglottis typically produces biphasic stridor. Expiratory stridor is caused when narrowing occurs in the intrathoracic trachea or bronchioles.

Although diagnosis is often achieved purely on the basis of physical examination findings, radiographs, laboratory evaluation, and flexible endoscopy often assist in diagnosis. Given the broad spectrum of presentation, clinicians must be adept in diagnosis and management of this disease process. This chapter will discuss the clinical features, diagnosis, and management of croup (laryngotracheitis), supraglottitis, bacterial tracheitis, and retropharyngeal abscesses in the pediatric population.

## Laryngotracheobronchitis

Viral laryngotracheobronchitis (croup) is the most common infectious cause of stridor, accounting for as much as 90% of infectious airways in children.[5] About 3 to 5% of children will experience viral croup at least once in their early development.[6] In patients who experience one episode of croup, 5% will have recurrent episodes.[7] This disease process primarily affects children between the ages of 6 months and 3 years. The peak incidence arises at 18 to 24 months of age, with boys more likely affected by at least a 2:1 ratio.[8] Although croup can occur at any time of the year, it typically occurs in the late autumn and winter months.

## Clinical Features

Patients with viral laryngotracheobronchitis typically present with an upper respiratory prodrome progressing to the characteristic barking cough, hoarseness, and high-pitched inspiratory stridor. The severity of viral croup ranges from mild airway impairment to severe, life-threatening airway obstruction, with the majority of children presenting on the mild spectrum of disease. Biphasic stridor, tachypnea, retractions, cyanosis, and oxygen desaturations are ominous signs, which signify impending airway compromise. Westley et al. proposed a scoring system grading the severity of symptoms, which is based on the level of consciousness, presence, and characteristics of stridor, air entry, and retractions.[9] Although such a classification system has utility in terms of research, the clinical scenario should always dictate management of the patient.

The most common etiologic organism is parainfluenza viruses type 1 and 2, although influenza A and B, respiratory syncytial virus, and *Mycoplasma pneumoniae* are other common infectious causes.[10] Croup transmission occurs mainly by direct contact with exposure to nasopharyngeal secretions.[11] This viral disease primarily involves the glottis and the subglottis, which results in dynamic subglottic narrowing more prominent on inspiration due to increased negative intraluminal pressure resulting in collapse of the subglottic tissues.

## Diagnosis

The diagnosis of croup is primarily obtained by history and physical examination alone. Radiographs are often utilized to confirm diagnosis. Frontal anteroposterior (AP) (high-kilovoltage) soft tissue neck films classically reveal a symmetric narrowing of the subglottic area, or "steeple sign".

## Treatment

The treatment of viral laryngotracheobronchitis depends on the severity of obstruction, with infrequent need for hospitalization (1.5% to 15%) or intubation (1% to 5%).[12] Management strategies for viral croup include humidified mist, racemic epinephrine, glucocorticoids, and heliox. In mild cases, with minimal stridor without increased work of breathing, patients may be managed in an outpatient setting. Historically, patients were treated with mist therapy. The presumed mechanism of action suggests reduced upper airway irritation by loosening thickened secretions, thus facilitating expectoration. Although the administration of humidified mist is often employed in the treatment of patients affected with viral croup, no scientific evidence exists that mist therapy has any effect on reducing subglottic edema or that patients have better outcomes.[13]

In children who demonstrate worsening stridor and increased work of breathing, racemic epinephrine should be administered. Racemic epinephrine is a nebulized solution with a 1:1 mixture of the levo (l) and dextro (d) isomers of epinephrine. Although the racemic mixture is the most common form administered, the l-isomer has been proven to be as effective as racemic epinephrine without increased side effects.[14] L-Epinephrine is administered as 5 mL of 1:1000, with racemic epinephrine administered in a 0.5-mL solution. The α-adrenergic effects of epinephrine work to cause mucosal vasoconstriction, leading to a reduction in subglottic edema. On the basis of a recent Cochrane review, both racemic and l-isomer epinephrine were associated with a clinically and statistically significant transient reduction of symptoms of croup 30 minutes post-treatment regardless of delivery method.[15]

Epinephrine's effect dissipates after 2 to 3 hours after administration, with rebound mucosal edema occurring in some patients. Historically, children treated with racemic epinephrine have been hospitalized for observation given the potential for rebound edema. Thus, if the symptoms of croup are severe enough to warrant the use of racemic epinephrine, then glucocorticoids should be administered to reduce any associated mucosal rebound edema 2 to 3 hours later. The administration of glucocorticosteroids reduces hospitalization.[16-19] Children should be observed closely after administering racemic epinephrine during this time period, and they are often discharged from the emergency department if symptoms resolve.

Nebulized budesonide (2 mg) or oral or intramuscular dexamethasone (dose range 0.15–0.6 mg/kg) is the most commonly used steroids. Oral dexamethasone is

often utilized due to its ease of administration, widespread availability, and lower cost.[20] Chub-Uppakarn et al. studied higher dose corticosteroids versus lower dose corticosteroids (dexamethasone 0.15 and 0.6 mg/kg) and found that both were equally effective in the treatment of moderate to severe croup, and both groups did not suffer adverse reaction from dexamethasone treatment in either group.[21]

The proposed mechanism of action for corticosteroids is that it works to decrease the permeability of capillary endothelium and stabilize lysosomal membranes.[1] This serves to reduce submucosal edema and decrease the inflammatory process. Regardless of its mechanism of action, the use of corticosteroids in the setting of croup has been well established. In a recent Cochrane review, use was associated with lower admission rates, and when hospital admission was indicated, the use of corticosteroids (dexamethasone and budesonide) demonstrated abbreviation of the length of hospital stay.[22]

Heliox, a helium–oxygen mixture, has been used in the setting of severe croup. It decreases the work of breathing by promoting laminar flow through the partially obstructed airway. Currently, no randomized clinical-control trial exists, which demonstrates any clinical reduction in symptoms or that patients have better outcomes. On the basis of a recent Cochrane review, there is a lack of evidence to establish the effect of heliox in the treatment of croup in children.[23]

In as much as 5% of hospitalized children, medical therapy fails and children will develop respiratory failure requiring airway intervention. For atypically presentations, formal endoscopy may be necessary to evaluate for bacterial tracheitis or foreign body. An endotracheal tube placed (nasotracheal or orotracheal) of at least a half size smaller than estimated based on the child's size or age should be used. Although mechanical ventilation can be life saving, it is associated with complications, such as ventilator-induced lung injury, nosocomial pneumonia, and subglottic stenosis.[24] The clinician must balance these risks against the risks of early extubation leading to reintubation. In a study conducted by Kurachek et al., extubation failure, as defined by reintubation within 24 hours of extubation, was independently associated with a fivefold increased risk of death in pediatric patients.[25] Thus, establishing objective criteria in determining the patient's readiness for extubation is critical in reducing complications. Successful extubation of mechanically ventilated patients depends on the patient's ability to sustain unassisted respirations while maintaining adequate gas exchange. This is dependent upon three factors: (1) the ability of the patient to maintain spontaneous, efficient respirations; (2) the effort exerted on the respiratory muscles; and (3) inspiratory drive. Parameters historically assessed to determine readiness for extubation include the air leak test, rapid shallow breathing index (RSBI), negative inspiratory force (NIF), fractional inspired oxygen content ($FiO_2$), volumetric capnography, and maintenance of spontaneous respiration, respiratory rate, and tidal volumes.[26]

The air leak test measures the pressure necessary to generate an audible air leak around the endotracheal tube. Although an air leak test has clinical utility in terms of assessing upper respiratory tract obstruction, it is a poor predictor of extubation success. A study conducted by Mhanna et al. demonstrated a low sensitivity when used as a screening test to predict postextubation stridor in young children (< 7 years old).[27] Another study demonstrated that an air leak pressure ≥ 30 cm $H_2O$ measured in the nonparalyzed patient before extubation was common and did not predict an increased risk for extubation failure.[28] The RSBI was first described by Yang and Tobin in 1991. It quantities rapid shallow breathing as the ratio of respiratory frequency to tidal volume ($f/VT$) and was found to have a sensitivity of 97% and a specificity of 64% in predicting successful extubation. The same study linked extubation failure with decreasing tidal volume to body weight ratio, increasing $FiO_2$, and decreasing mean inspiratory flow.[29] Respiratory muscle strength can be assessed by measuring the maximal inspiratory pressure or NIF. The NIF reflects the strength of the diaphragm and inspiratory muscles, and it is useful in predicting pediatric extubation success.[30] Volumetric capnography has also proven useful in determining a child's readiness for extubation.[31] However, evaluating a combination of variables may serve useful in predicting extubation success. A recent prospective analysis involving 227 mechanically ventilated children found that a spontaneous respiratory rate ≤ 45/min, spontaneous tidal volume ≥ 5.5 mL/kg, and an RSBI ≤ 8 breaths/min/mL/kg body weight were all accurate predictors of successful extubation.[32]

Protocol-based weaning has been proven to result in faster extubation with better outcomes in adults, but evidence of improved outcomes in the pediatric population is lacking. In a prospective trial conducted by Randolph et al., no advantage over clinical weaning was apparent.[33] Shorter weaning (by 12 hours) against historical controls with no increase in overall complication rates was reported in another study.[34]

## ACUTE SUPRAGLOTTITIS (EPIGLOTTITIS)

Acute supraglottitis in children represents an airway emergency. This disease process evolves rapidly and often results in a life-threatening emergency. As supraglottic edema increases, the epiglottis prolapses into the laryngeal inlet resulting in airway obstruction. Prior to the introduction of the *Haemophilus influenzae* type B (HIB) vaccine, children were predominately affected. Since the introduction of the monovalent vaccine for *H Influenzae* type B in 1985, and 2 years later the release of the conjugate vaccine, there has been a precipitous decline in the number of cases of supraglottitis.[35,36] Today, there is a relative decline in children affected with a rise in the proportion of adults affected.[1] The effectiveness of the HIB vaccine has led to an epidemiologic shift in the pathogens responsible for supraglottitis. The most common etiologic organism in the postvaccine era is Group A β-hemolytic streptococci, although *Staphylococcus*, *Klebsiella*, *Moraxella catarrhalis*, *Haemophilus parainfluenzae*, *Pneumococcus*, *Pseudomonas*, and *Candida* are other common infectious causes.[1]

### Clinical Features

Supraglottitis primarily affects children between the ages of 2 and 7 years. Although supraglottitis may occur at any time of the year, it typically occurs in the winter and spring months. The most common signs of supraglottitis are fever, severe throat pain, odynophagia, and respiratory distress. Children often appear toxic, with shallow respirations, retractions, inspiratory stridor, and inability to tolerate their own secretions. Characteristically, the child assumes the "tripod" position, leaning forward, chin up, and mouth open, with hands braced at their side, to maximize air exchange. The child with suspected supraglottitis should be kept under constant observation, preferably with oxygen saturation monitoring. The disease process evolves rapidly (within hours) from mild respiratory symptoms to respiratory distress. On physical examination, the child exhibits inspiratory stridor, increased work of breathing, and drooling. Activity is often limited as all efforts are exhausted in maximizing airflow. Stridor is a late finding that indicates near complete airway obstruction.

### Diagnosis

Although the diagnosis of supraglottitis is obtained by history and physical examination alone, laboratory evaluation, radiographs, and endoscopy can be used to verify the diagnosis. Patients will exhibit an acute leukocytosis on laboratory evaluation. Portable, lateral soft tissue neck radiographs are the single most useful study. Lateral films will reveal thickening and edema of the epiglottis ("the thumb sign") with obliteration of the vallecula. Endoscopy is utilized to confirm diagnosis. Endoscopic findings include diffuse erythema and edema of the supraglottis, epiglottis, arytenoids, and aryepiglottic folds. The normal architecture of the supraglottis is often obscured secondary to edema, and abscess formation over the epiglottis is a common finding.

### Treatment

If acute supraglottitis is suspected, the clinician should avoid over stimulating the child and potentially exacerbating the patient's airway distress. Thus, intravenous (IV) access, blood draws, imaging, and endoscopy should be avoided as this may trigger loss of the airway in an uncontrolled setting. All procedures should be avoided until a stable airway has been established. Establishing a stable airway is the highest priority. Once the diagnosis of supraglottitis is considered, plans for securing a definitive airway should be made as expeditiously as possible. Endotracheal intubation is the preferred method and may be accomplished by either nasal or oral routes. Tracheostomy is rarely necessary, but the surgeon must be prepared to perform a surgical airway if required. The patient is promptly brought to the operating room and using a nonparalytic, spontaneous ventilating, nonirritating, inhalational anesthetic, direct endoscopy is performed visualizing the supraglottic structures. Foreign body aspiration may mimic supraglottitis, thus the airway should be evaluated for the presence of a foreign body if clinical suspicion is raised.

Once endotracheal intubation is successfully attained, blood may be drawn for blood cultures and a complete blood count. Cultures should also be sent of the epiglottis to direct antibiotic therapy. Antibiotic therapy is initiated promptly after the establishment of IV access. Ceftriaxone, ampicillin–sulbactam, or clindamycin are appropriate antibiotic choices. Vancomycin is recommended in patients with a penicillin or cephalosporin allergy. Antibiotic therapy may be modified as blood cultures become available. Patients are then transferred to the intensive care unit for IV antibiotic therapy and ventilatory support. The edema of the supraglottic larynx usually subsides within 48 to 72 hours, allowing safe removal of the endotracheal tube.[1] Extubation can be considered when there is an air leak around the endotracheal tube at < 20 cm $H_2O$.

Extubation should be only performed in a controlled environment with appropriate airway equipment present, and consideration should be given to direct endoscopic evaluation of the airway prior to extubation.

## BACTERIAL TRACHEITIS (MEMBRANOUS TRACHEITIS)

Bacterial tracheitis, also called membranous tracheitis, bacterial croup, or bacterial laryngotracheobronchitis was first described by Jones et al. in 1979.[37] Bacterial tracheitis is thought to arise from a bacterial suprainfection of viral laryngotracheobronchitis. The clinical presentation of bacterial tracheitis is not as rapid as supraglottitis, although it is a potentially life-threatening condition. The most common presenting symptoms are stridor, cough, hoarseness, and fever. The secondary bacterial pathogen most commonly responsible is *Staphylococcus aureus* accounting for 36 to 75% of cases.[38] Cultures also frequently yield *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *H influenzae, Pseudomonas aeruginosa*, and *Streptococcus pyogenes*.[39] Membranous laryngotracheobronchitis affects a wide range of children from those several weeks old to children in their early teenage years with a mean age of 5.2 years.[38] Similar to viral croup, bacterial tracheitis typically occurs in the autumn and winter months when the incidence of viral upper respiratory tract infections are highest. In a recent retrospective analysis conducted by Hopkins et al., bacterial tracheitis was noted to be three times more likely to have caused respiratory failure than viral croup and epiglottitis combined.[40] Early recognition and expeditious intervention are critical to prevent complications arising from this infectious disease process.

### Clinical Features

Patients frequently present with a several day history of upper respiratory symptoms, fever, cough, and evolving stridor. Following a viral prodrome, patients demonstrate a sudden progression of respiratory symptoms, culminating with a harsh, inspiratory, or biphasic stridor with associated respiratory distress. A high fever is common, and patients often appear toxic. Bacterial tracheitis should be considered in any child who presents with acute upper airway obstruction. In contrast to other causes of pediatric upper airway obstruction, bacterial tracheitis does not respond to racemic epinephrine, and the epiglottis appears normal.[41] The only definitive way to diagnose bacterial tracheitis is by direct visualization of the trachea via bronchoscopy.

Patients commonly demonstrate an elevated white blood cell count on laboratory evaluation, although other inflammatory markers such as C-reactive protein may be unremarkable.[37] Blood cultures are frequently negative. Soft tissue AP and lateral plain film radiographs are frequently obtained, which confirm the diagnosis, but can potentially delay treatment and should be avoided in unstable patients. AP radiographs of the neck classically demonstrate the "steeple sign" as noted in viral laryngotracheobronchitis. Lateral radiographs of the neck characteristically demonstrate an irregular, hazy tracheal air column, which indicates soft tissue pseudomembranous detachment. This membranous-like debris is pathognomonic for bacterial tracheitis and is the source of the precipitous decline in the patient's respiratory status. Patients typically have a less severe clinical appearance in comparison with supraglottitis. In fact, a recent retrospective review of 94 patients treated for acute bacterial tracheitis reported a milder course than previously described.[42] Nonetheless, these patients require aggressive medical management and debridement.

### Diagnosis

According to a recent retrospective review, no clinical, radiologic, or laboratory feature was a reliable diagnostic predictor for bacterial tracheitis.[43] Only direct examination via bronchoscopy accurately distinguishes bacterial tracheitis from other forms of acute obstructive upper airway diseases. Bronchoscopy is both diagnostic and therapeutic. Rigid bronchoscopy with laryngotracheal debridement is the cornerstone of therapy. Direct laryngotracheobronchoscopy is performed to remove the adherent thick secretions obstructing the airway. Endoscopic findings are notable for a diffusely infectious process involving the subglottis, trachea, and main stem bronchi. Diffuse mucosal ulceration, copious purulent exudates, and sloughing of pseudomembranous tissue are characteristic findings on endoscopy. Blood cultures are typically negative, but tracheal cultures often yield the etiologic pathogen. Broad-spectrum antibiotic therapy is directed toward the most common pathogens and adjusted according to the tracheal culture results.

### Treatment

Patients often are intubated to assist with aggressive pulmonary toilet. In a multi-institute, retrospective review performed by Tebruegge et al., evaluating 34 patients with bacterial tracheitis, a total of 31 patients (91.2%) required

intubation. Twenty-seven out of the 31 patients (87.1%) were intubated within 24 hours after presentation to the hospital.[38] Recent research also suggests that patients may be effectively managed without intubation. A case series review performed by Shargorodsky et al. evaluated a total of six patients who were diagnosed with bacterial tracheitis who underwent urgent direct laryngoscopy and bronchoscopy with debridement of mucopurulent debris and tissue culture. The mean time to the operating room was 4.2 hours (range 2–7 hours). No patients in their series required urgent intubation, with only one patient requiring intubation postdebridement. All patients received broad-spectrum antibiotics and were kept on acute cardiopulmonary monitoring for at least 48 hours. Patients were then re-evaluated with direct laryngoscopy and bronchoscopy. All patients in their series achieved favorable results and were transitioned to a 10–14 day course of oral antibiotics after discharge.[39]

If intubated, meticulous airway care with frequent saline administration and suctioning of the trachea should be carried out to prevent accumulation of thickened secretions and mucosal debris that may obstruct the airway. Patients are frequently managed with serial examinations of the upper airway with subsequent debridements. In severe cases, repeat rigid bronchoscopy with debridement is required to maintain a patent airway. However, the majority of intubated patients require a relatively short period of assisted ventilation, with a mean duration of ventilation of 3.5 days (range 1–12 days), with 55% extubated within 72 hours.[38] The most common complication of bacterial tracheitis is pneumonia occurring in up to half of all children affected with this disease. Acute respiratory distress syndrome (ARDS) may also develop and is classically diagnosed based on chest X-ray noting bilateral ground-glass pulmonary infiltrates and the need for increased fraction of inspired oxygen ($FiO_2$) to maintain oxygen saturation. Other complications include septic shock, toxic shock syndrome, respiratory failure, and multiple organ dysfunction syndrome.

## RETROPHARYNGEAL CELLULITIS AND ABSCESSES

In the postantibiotic era, retropharyngeal abscesses are an uncommon consequence of upper respiratory tract infections. Suppuration of the retropharyngeal nodal basin, which serves to drain infections in the paranasal sinuses, nasopharynx, and oropharynx results in abscess formation. Other etiologies of infection include traumatic endoscopy or intubation, penetrating foreign bodies, vertebral body osteomyelitis, and dental procedures.[44] The retropharyngeal space is a potential space. It is invested in the deep layer of the deep cervical fascia and extends from the skull base to the mediastinum to the level of the sixth thoracic vertebrae. It is bounded anteriorly by the buccopharyngeal and pharyngobasilar fascia, which invests the superior, middle, and inferior constrictor muscles. Posteriorly, the retropharyngeal space is bounded by the prevertebral fascia. Its lateral limit is the carotid sheath. The retropharyngeal space communicates directly with the parapharyngeal space anterolaterally. This potential space is divided by a median raphe into a left and right compartment. Due to its communication with multiple potential spaces and unobstructed course to the mediastinum, a retropharyngeal abscess can be life threatening. Thus, early diagnosis and treatment are essential to prevent the development of complications.

### Clinical Features

Retropharyngeal abscesses are most common in early childhood with half of patients presenting < 3 years old. Seventy percent of patients who present with retropharyngeal abscesses are < 7 years of age. Infections frequently present with symptoms consistent with an upper respiratory tract infection. As suppuration of the retropharyngeal lymph nodes occur, the patient exhibits neck pain, limited neck range of motion, and frequently dysphagia so severe that the patient may be acutely unable to tolerate their own secretions. Patients commonly are febrile and toxic appearing.

### Diagnosis

Early diagnosis is essential to prevent the development of complications. A complete blood count with differential will characteristically demonstrate a leukocytosis with a leftward shift. If the clinician suspects the presence of a retropharyngeal abscess, a lateral soft tissue radiograph of the neck, in neck extension taken on expiration should be obtained. When the retropharyngeal space at the level of C2 is twice the diameter of the vertebral body, the diagnosis of retropharyngeal cellulitis or abscess is confirmed. If the lateral neck radiograph confirms the presence of soft tissue edema, computed tomography (CT) with IV contrast is useful in distinguishing abscess from phlegmon. CT imaging is also helpful in identifying the

extent of disease, spread to adjacent potential spaces, and mediastinal involvement. CT findings characteristically demonstrate a well-formed ring of contrast enhancement encircling a nonenhancing density.

Although CT imaging of the neck is useful in the diagnosis of deep space neck infections, it has its limitations. Smith et al. noted a 75% positive predictive value in accurately predicting the presence of a discreet collection of pus in patients who demonstrated radiographic evidence of abscess.[45] Based on this study, if a decision to take the patient to the operating room is based solely on the results of CT, a 25% negative exploration rate should be expected. Daya et al. evaluated 54 patients with deep space neck infections and noted a sensitivity of 81% in detecting an abscess by CT scan while CT scan was only 57% specific in identifying abscess.[46] Therefore, the entire clinical picture should be evaluated prior to making treatment decisions and CT findings alone should not determine the decision for surgical drainage.

## Treatment

Early IV antibiotic therapy is indicated when the diagnosis of a retropharyngeal abscess is confirmed. In stable patients, a trial of 24 to 48 hours of antibiotic therapy is appropriate. If the clinical course improves, then outpatient oral antibiotic therapy may be initiated. McCaly et al. evaluated the effectiveness of using IV antibiotics alone to treat clinically stable children with evidence of deep neck abscesses on CT scan. The presence of an abscess was defined as ring enhancement around a nonenhancing density, and a size greater than 1 cm in every dimension. In this series of 11 patients, only one patient did not respond to IV antibiotic therapy and went on to require surgical drainage.[47] These results suggest a 91% response rate to IV antibiotic therapy despite radiographic evidence of abscess on CT scan.

Another study conducted by Cheng and Elden examined 178 pediatric patients and sought to identify risk factors associated with an increased likelihood of medical therapy failure. Risk factors that were statistically and clinically significant in their study included younger patients (< 15 months) and those who had CT imaging findings of a rim-enhancing lesion consistent with abscess formation with size ≥ 2.2 cm. Both clinically findings increased the chances that patients would undergo surgical drainage. The same study noted a 66.3% response rate with IV antibiotics alone.[48] Antibiotic treatment should include coverage from gram-positive bacteria to include *Streptococcus*, *S aureus*, and Group A β-hemolytic streptococci. Abdel-Haq et al. noted a rising incidence in methicillin-resistant *Staphylococcus aureus* (MRSA) infections. In their study of 114 patients, MRSA positive retropharyngeal abscesses were most commonly found in younger patients (age < 3 years) and were associated with a higher complication rate. In fact, all patients in their series who developed mediastinitis were MRSA positive.[49] Clindamycin or ampicillin-sulbactam provides appropriate coverage for a majority of retropharyngeal abscesses. A third-generation cephalosporin such as ceftriaxone may be beneficial if gram-negative organisms are suspected. If the clinical course worsens or fails to improve significantly, surgical intervention should be strongly considered. Oral intubation should be performed, avoiding abscess rupture and subsequent aspiration. A transoral route is the most frequently used approach, allowing adequate exposure to drain the abscess. In cases where the abscess is lateral to the great vessels, or involves multiple spaces, a transcervical approach is frequently employed.[50] Trendelenburg positioning is also helpful in decreasing the potential for aspiration of purulent material. Repeat imaging is rarely necessary as it rarely changes management and exposes the patient to unnecessary radiation.

The retropharyngeal space is divided by a median raphe into a left and right compartment. This has clinical implications, as incision and drainage of a retropharyngeal abscess involves a posterior pharyngeal incision to the level of the prevertebral fascia in a vertically oriented, paramedian plane. The retropharyngeal space communicates directly with the parapharyngeal space anterolaterally. Abscess material often communicates between the two adjacent spaces and is apparent on CT scan. Because both spaces lie medial to the great vessels, both can be successfully managed with an intraoral approach. Additional complications that arise in children with retropharyngeal abscesses include ARDS, mediastinitis, sepsis, and airway obstruction.

# CONCLUSION

Acute infections of the larynx and trachea are common in the pediatric population. These disease processes occur over a broad spectrum of severity, from mild, self-limiting disease to life-threatening airway emergencies. Clinicians must be adept in timely recognition, diagnosis, and expeditious management to prevent complications due to delay in therapy.

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CHAPTER

# 43 Inflammatory and Neoplastic Lesions of the Larynx and Trachea

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## INTRODUCTION

Neoplastic and inflammatory lesions of the pediatric larynx, trachea, and bronchi span a wide range of pathology from the very rare, for example, tracheal malignancies, to the very common, such as inflammatory disorders like laryngopharyngeal reflux (LPR). Symptoms of these lesions and their severity are related to their location and may include cough, voice changes, stridor, or airway obstruction. In this chapter, we highlight the neoplastic and inflammatory lesions found in the larynx and trachea with a focus on the pediatric airway. Table 43.1 offers an outline of the disorders reviewed in this chapter.

**Table 43.1:** Inflammatory and neoplastic processes reviewed in this chapter

| | |
|---|---|
| *Inflammatory disorders* | *Trachea* |
| Laryngopharyngeal reflux | Benign |
| Systemic lupus erythematosus | Granular cell tumor |
| Granulomatous diseases | Fibrous histiocytoma |
| Wegener's granulomatosis | Neurofibroma |
| Sarcoidosis | Hemangiopericytoma |
| Systemic sclerosis | Chondroma |
| Relapsing polychondritis | Malignant |
| Amyloidosis | Mucoepidermoid |
| Stevens–Johnson syndrome | Adenoid cystic carcinoma |
| Rheumatoid arthritis | Rhabdomyosarcoma |
| Epidermolysis bullosa | Carcinoid |
| Cicatricial pemphigoid | |
| *Neoplastic disorders* | *Bronchial* |
| Larynx | Benign |
| Benign | Hamartomas |
| Subglottic hemangioma | Intermediate |
| Neurogenic tumors | Inflammatory pseudotumors |
| Neurofibroma | Malignant |
| Schwannoma | Mucoepidermoid |
| Granular cell tumors | |
| Malignant | |
| Rhabdomyosarcoma | |
| Squamous cell carcinoma | |
| Primitive neuroectodermal tumors | |
| Mucoepidermoid carcinoma | |

## INFLAMMATORY LESIONS

### Laryngopharyngeal Reflux and Gastroesophageal Reflux Disease

Gastroesophageal reflux (GER) is a normal phenomenon that about 44% of the population of the United States experience monthly.[1] It affects both adults and children, and may be associated with acute, chronic or intermittent laryngitis. In adults, symptoms typically follow large or especially fatty meals. GER disease (GERD) is a chronic condition where changes occur in the barrier between the stomach and the esophagus, including relaxation of the lower esophageal sphincter (LES). In children, GER is physiologic and self-limited and often responds to nonoperative treatment. GER has been reported in up to 60% of infants aged 6 months, the incidence declining to 5% by the end of the first year.[2] This early in life GERD predilection is believed to be due to anatomic immaturity of the LES and the predominantly liquid diet of neonates and infants.

GERD has been implicated in the etiology of many extraesophageal disorders including laryngitis.[3] The relationship between laryngitis and GERD is still evolving because of an ever-growing body of literature. LPR is the term given when retrograde flow of gastric contents comes in contact with the mucosa of the upper aerodigestive tract; alternative terms include extraesophageal reflux and supraesophageal GERD. LPR is used interchangeably with GER, but the former is more specific anatomically.

#### *Diagnosis*

Diagnosis begins with a thorough history and physical examination. The symptoms of GERD in both adults and children are described in Table 43.2. Certain medications and foods predispose patients to GERD by relaxing the LES. These items include caffeine, calcium channel blockers, and xanthines. Social behaviors like smoking, alcohol consumption, and poor dietary habits also predispose patients to GERD. Modification of these behaviors and elimination of certain foods from the diet may not only be diagnostic but also therapeutic in adults, older children, and adolescents. In young children, age and neurologic development must also be considered when evaluating a child with GERD. Certain disorders particularly predispose pediatric patients to chronic GERD, including significant neurologic impairment, genetic disorders such as the Cornelia de Lange's syndrome and Down's syndrome, congenital esophageal abnormalities such as repaired esophageal atresia or congenital diaphragmatic hernia, chronic lung disease, obesity, and family history of severe GERD.[4]

**Table 43.2:** Symptoms of gastroesophageal reflux in children and adults

| *Adults* | *Children* |
|---|---|
| Heartburn | Regurgitation and vomiting (70%) |
| Regurgitation | Chronic cough (50%)[87] |
| Chest pain | Epigastric pain and irritability (36%)[88] |
| Dysphagia | Feeding difficulties and feeding refusal (29%) |
| Nocturnal symptoms | Failure to thrive (28%) |
| | Acute/apparent life-threatening event (ALTE) |
| | Bronchospasm and asthma |
| | Sandifer's syndrome |

In infants, GERD and milk allergy may both manifest similar symptoms like regurgitation, vomiting, fussiness, and crying.[5] Both conditions may also coexist, further complicating the clinical picture. Elimination diet and evaluation by a pediatric gastroenterologist may be helpful in differentiating these two diseases.

Barium esophagram and an upper gastrointestinal (GI) series are radiographic studies that allow for identification of anatomic abnormalities of the esophagus, stomach, and duodenum, such as abnormal esophageal configurations, strictures, and hiatal hernia. Esophagogastroduodenoscopy (EGD) allows direct visualization of the upper GI tract to further identify strictures, infections, or inflammatory changes of the esophagus and stomach. Unfortunately, children with GERD infrequently manifest pathological features; therefore, a normal EGD cannot exclude GERD.[6]

Laryngeal findings in LPR and GERD may not always be present and are not very specific for disease. Most typically encountered is posterior laryngeal edema and erythema, particularly involving the arytenoid mucosa. In addition, edema of Reinke's space and diffuse edema of other laryngeal sites to the point of friable mucosa may be present. If there has been recent intubation or airway instrumentation in the context of GERD, granulomas (bilateral tongues of granulation tissue) may be present at the point of injury, most commonly at the vocal processes.

The current gold standard for the diagnosis of GERD is 24-hour pH probe monitoring, although its precision in making the diagnosis is probably not deserving of this description. A distal pH probe is placed 5 cm above the LES, and the proximal pH probe is usually placed 20 cm above the LES, just below the upper esophageal sphincter. A third

pH probe is placed in the pharynx to simultaneously record changes associated with acid escape into the pharynx. As an ambulatory procedure, it allows the patient to resume normal meals and activities. It allows for correlation of reflux events with reflux symptoms as well as measuring the total time that the pH of the esophagus is below 4.0. If this number is above 5% of the total time, it is considered positive. In infants, this number is increased to 9.7% due to expected physiologic reflux.[7] Esophageal impedance is one of the most commonly used tests to diagnose GERD in children today.[8] The test consists of a catheter with multiple electrodes that monitor distension of the esophagus during the passage of food as well as during reflux episodes. The probe also contains a pH probe so acidic and nonacidic events may be differentiated.

### *Treatment*

Whether one is treating GERD or LPR, lifestyle and behavior modifications are hallmarks for treatment of adults, adolescents, and older children. These include avoidance of provocative foods and modifications to eating habits such as eliminating meals just prior to bedtime. In infants, the introduction of thickened liquids like rice cereal and elevation of the crib or bed may be sufficient to treat most GERD. Evaluation of allergy to cow's milk in infants must be ruled out as well prior to moving on to other GERD therapies.

There are several medication choices for the management of reflux, the two most common being histamine-2 receptor antagonists and proton pump inhibitors (PPIs).

Histamine-2 receptor antagonists are the most commonly used acid-suppressive agents in children.[8] These medications are effective in reducing the gastric pH, relieving symptoms of GERD, and resolving esophagitis. Prolonged use, however, may cause tachyphylaxis or tolerance leading to ineffective treatment.[9] In addition, this class of medication is usually weight based and requires frequent dose adjustment as the child grows. Treatment with H-2 blockers fails in at least one third of patients with LPR.[10]

One of the most widely used medications for the treatment of GERD in adults and children are PPIs. PPIs are the most effective antireflux medicine available. Failure typically results from poor compliance, poor timing of medication dosing, or inadequate dose used. Duration of treatment should be approximately 6 months with symptoms of GERD and LPR resolving often in the first few months. Although the side effect profile of PPIs is excellent, otolaryngologists should be cautioned that chronic treatment could be associated with adverse effects such as an increased incidence of *Clostridium difficile* infections. Consultation with a gastroenterologist is recommended in children requiring chronic PPI therapy.[11]

Surgical intervention for GERD in children is indicated for those who do not respond to the above therapies, as well as for those children who manifest failure to thrive, experience acute life-threatening events (ALTEs), have associated severe pulmonary disease secondary to GERD, are neurologically impaired, or have significant complications from GERD such as Barrett's esophagitis.[8] The more common surgical interventions include Nissen fundoplication and percutaneous feeding tube placement.

## Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that usually affects women in their second and third decades of life. However, 20% of SLE cases are diagnosed in the first two decades of life.[12] Pediatric SLE, which tends to be more severe, usually presents in the postpubescent female at the average age of 12 years. The incidence of SLE before the age of 19 years is between 6.0 and 18.9 cases per 100,000 in Caucasian females, but it is higher in African American (20–30/100,000) and Puerto Rican girls (16.0–36.7/100,000). A similar high incidence of SLE is reported in Hispanic, Native American, Pacific Islander, and Asian women.[12]

The SLE follows a relapsing and remitting course and is characterized by an autoantibody response to nuclear and cytoplasmic antigens. SLE can affect any organ system but mainly involves the skin, joints, kidneys, blood cells, and nervous system. Classically, the triad of fever, joint pain, and rash in a woman of childbearing age suggests the diagnosis. SLE may produce laryngeal inflammation in as many as one third of patients. The most common manifestations of SLE are arthritis, malar rash, and photosensitivity.[13] The symptoms of laryngeal involvement range from dysphonia to airway obstruction arising from edema, ulceration, and vocal fold paralysis. As with most other autoimmune diseases, treatment centers on systemic corticosteroid therapy.

## Granulomatous Diseases

Granulomatous diseases of the larynx and trachea had all but disappeared during the 20th century, and only recently, with the advent of organ transplantation, chemotherapy, and acquired immunodeficiency syndrome, have they

re-emerged, mainly in immunocompromised individuals. A granuloma is an imprecise term for any small, nodular, poorly demarcated aggregation of mononuclear inflammatory cells. Such a collection of modified macrophages may resemble epithelial cells and are usually surrounded by a rim of lymphocytes. Granulomas can be caseating with central necrosis or noncaseating. Granulomas arising in the larynx and trachea typically manifest as hoarseness, stridor, and airway obstruction. These granulomatous lesions have a wide breath of presentation on physical examination, ranging from smooth, diffuse swellings to distinct, well-defined nodules. There are numerous etiologies that exist for granulomatous diseases of the larynx and trachea, including bacterial, mycotic, and idiopathic. We review a couple of the most common idiopathic causes below. Infectious causes will be reviewed in separate chapters in this text.

## Wegener's Granulomatosis

Wegener's granulomatosis is characterized by necrotizing granulomatous inflammation and necrotizing vasculitis affecting small-to medium-sized vessels, with larger vessels rarely affected.[14] The disease has a predilection for the upper respiratory tract, lungs, and kidneys, but any organ can be involved. Although usually a systemic disease, rare isolated airway cases do occur, and airway involvement is reported in 15–55% of all cases.[15-17] A recent retrospective chart review of children with Wegener's found that 25% demonstrate airway lesions including vocal fold granuloma, subglottic stenosis, and multilevel stenosis.[18] The etiology of Wegener's granulomatosis remains unknown; the presence of antineutrophil cytoplasmic antibodies (ANCA) in most patients, and its response to immunosuppressive therapy, suggest an autoimmune pathophysiology.[19]

Tracheobronchial Wegener's granulomatosis occurs in <10% of cases.[17] Symptoms include hoarseness, cough, hemoptysis, dyspnea, stridor, and wheezing. Subglottic stenosis is the most common cause of stridor. Subglottic involvement is suspected when pulmonary function testing shows a fixed obstruction and can be confirmed by computerized tomography (CT) and direct laryngoscopy/tracheobronchoscopy. Clinical history and examination may reveal findings of other airway, lung, and kidney manifestations that further support the diagnosis. Laboratory testing for ANCA is confirmatory, keeping in mind that in cases of isolated airway disease, ANCA can be negative 20% of the time.[20] The management of Wegener's granulomatosis is complex and requires a multidisciplinary approach, including otolaryngology, pulmonology, and rheumatology. Medical management includes corticosteroids for systemic disease as well as immunomodulating medications like cyclophosphamide, methotrexate, and rituximab. Endoscopic techniques including balloon airway dilation and laser debulking, as well as the adjuvant use of intralesional steroids and mitomycin C, can help maintain airway patency. Open airway surgery (resection and reanastomosis) for isolated short-segment stenosis is a possibility if endoscopic treatment fails. Tracheostomy may be necessary in some cases.

## Sarcoidosis

Sarcoidosis is a multisystem inflammatory disease of unknown etiology that is manifested by noncaseating granulomas in the affected organ. It is a ubiquitous disease with an incidence that varies according to age, sex, race, and geographic origin.[21] Pulmonary and skin lesions are the most common manifestations of sarcoidosis. Incidence in the head and neck is estimated at 9%.[22] Laryngeal involvement in sarcoidosis occurs in 0.5–5% of cases; isolated laryngeal sarcoid is even more rare.[22,23] Laryngeal sarcoid is extremely rare in children with only three cases reported in the literature.[24-26]

Laryngeal sarcoid typically involves the supraglottis (80–85%) with symptoms that include hoarseness, dysphonia, dyspnea, stridor, dysphagia, globus sensation, and cough. Subglottic involvement also occurs in 20% of cases, whereas glottic involvement is very rare.[27] Direct laryngoscopy reveals a "turban-like" epiglottis, appearing pink with significant edema to the point of obscuring the true vocal folds (Fig. 43.1). Supportive but not pathognomonic findings on laboratory testing include elevated serum angiotensin-converting enzyme, elevated erythrocyte sedimentation rate, and evidence of abnormal calcium metabolism. The diagnosis is made on the basis of the combination of clinical and radiological presentation, evidence of noncaseating granulomas on biopsy, and exclusion of other granulomatous diseases.

The treatment of isolated laryngeal sarcoidosis revolves around maintaining airway patency. Tracheotomy is necessary in the setting of complete airway compromise, and laser resection and balloon dilation are useful endoscopic adjuncts. Oral or parenteral steroids have been used with success in the past for patients with symptomatic laryngeal sarcoidosis. Intralesional steroid injections may help treat localized disease and prevent progression to complete airway obstruction.

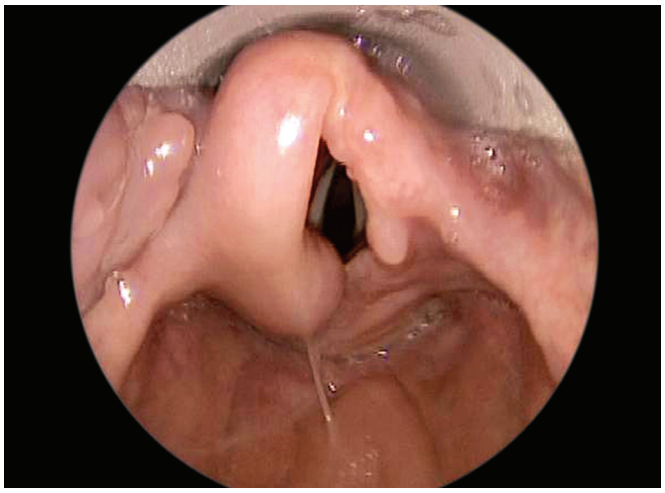

**Fig. 43.1:** Direct laryngoscopy evaluation of "turban-like" epiglottis seen in laryngeal sarcoidosis.

## Systemic Sclerosis (Scleroderma)

Scleroderma or systemic sclerosis, an uncommon disease of uncertain etiology that manifests with thickened, indurated skin with accompanying tissue fibrosis, and inflammation. However, it can occur in a localized form. It is a multisystem disease with relentless progression and can involve the visceral organs, vasculature, and immune system. The American College of Rheumatology's classification of scleroderma requires one major or two minor criteria to make the diagnosis.[28] Major criteria include systemic tightening and induration of the skin and fingers proximal to the metacarpophalangeal joints. These skin changes may not only extremities, but also the head, neck, and trunk. Minor criteria can be sclerodactyly, digital pits or scars, and bibasilar pulmonary fibrosis. Age of onset for this disease is usually in the middle ages, with women more affected than men. The prevalence is reported to be about 240 per million. This disease is exceedingly rare in children with most cases being the localized type. The juvenile-onset systemic sclerosis can overlap as a myositis and the disease tends to be self-limited.[29]

Head and neck manifestations include facial tightness, loss of facial rhytides, inability to open their mouth, sicca syndrome (often leading to poor dentition), hoarseness, and GERD caused by LES incompetence. Involvement in the cricoarytenoid joint has been described as well.[30] Similar to rheumatoid arthritis (RA) of cricoarytenoid joint, these patients have symptoms of pain with phonation, globus sensation, hoarseness, dysphagia, otalgia, and dyspnea. They can present with stridor and potentially respiratory distress. Laryngoscopy examination reveals restricted vocal fold mobility and edematous arytenoid cartilages. If left untreated, the disease process could progress to ankylosis of the joint.

Treatment is symptomatic, and rheumatologists have utilized use of immunosuppressive medications in management of these patients. Since most patients suffer from GERD secondary to the esophageal manifestations, treatment with proton-pump inhibitors is essential and may help cut down on the effects on the larynx. Calcium channel blockers can help with symptoms of the disease like Raynaud's phenomenon but may exacerbate GERD. Airway symptoms secondary to ankylosis may necessitate endoscopic management and potentially tracheotomy depending on severity.

## Relapsing Polychondritis

Relapsing polychondritis (RP) is a severe, episodic, and progressive inflammatory condition involving cartilaginous structures. The ears, nose, and laryngotracheobronchial tree are most commonly involved in the head and neck. Although the etiology is unknown, it is believed to be an autoimmune disease targeted against type II collagen. There is no gender predilection. RP is more common in Caucasians with onset usually in the fifth decade of life, although it can occur at any age. RP in childhood can be a life-threatening condition.[31] The disease can start as acute dyspnea, stridor, and polyarthritis. The diagnosis is made easier when auricular or septal chondritis occurs simultaneously. The frequency of chondritis and systemic manifestations of RP in children is similar to those observed in adults.

There is a known association of RP with other autoimmune disease including RA, Sjogren's syndrome and SLE. Bilateral auricular involvement is the most common otolaryngologic manifestation. Laryngeal disease can occur in about half of cases. When the larynx is involved in RP, inflammation, fibrosis, and destruction of laryngeal cartilage are all possible. In addition to nonspecific constitutional symptoms of fever, malaise and fatigue, symptoms of large airway disease include hoarseness, aphonia, wheezing, inspiratory stridor, cough, pain, and dyspnea.

No laboratory findings are specific for RP. Diagnosis is made clinically with several critical criteria required including biopsy. On laryngoscopy, glottic and subglottic edema and erythema are noted. Treatment varies depending on the severity of disease including the use of nonsteroidal anti-inflammatory drugs (NSAIDs), methotrexate, and systemic steroids. Tracheostomy is reserved for severe or recurrent airway obstruction.

## Amyloidosis

Amyloidosis is a clinical disorder caused by the extracellular and/or intracellular deposition of insoluble abnormal amyloid fibrils that alter the normal function of tissues. It can be systemic or localized. Laryngeal amyloidosis is associated with localized disease primarily affecting individuals (males greater than females by 3:1) between the ages of 40 and 60 years, with a peak incidence in the fifth decade.[32] It rarely presents during childhood, with only a few documented cases.[33] Laryngeal amyloidosis is usually a localized phenomenon that is rarely associated with systemic involvement.[32] Hoarseness is the most common presenting symptom. Clinical findings at laryngoscopy are variable and nonspecific, including diffuse mucosal thickening, submucosal nodules, and less commonly, polyps. The diagnosis is revealed by pathologic examination of tissue samples. Traditionally, treatment has included partial or total surgical excision to maintain a functional laryngeal airway and optimize voice. Life-long follow-up is important with this condition because of its chronic and recurrent nature.

## Stevens–Johnson Syndrome

Stevens–Johnson syndrome (SJS) is an immune complex-mediated hypersensitivity reaction that typically involves the skin and the mucous membranes. Also known as erythema multiforme major, SJS is debilitating and potentially life threatening. SJS is usually triggered by medications, such as sulfonamides, carbamazepine, and phenobarbital. Clinically, patients with SJS present soon after ingestion of the offending drug with symptoms of fever, malaise, conjunctivitis, rash, and severe oropharyngeal mucositis. Mucocutaneous lesions affect the mouth, eyes, skin, genitalia, and occasionally the esophagus. There is a variant of the disease that may involve the larynx. The skin lesions progress to bullae, desquamation, and necrosis, causing secondary skin infections and loss of electrolytes. Diagnosis is made by history, clinical examination, and tissue biopsy. Treatment is mainly supportive, although securement of the airway via endotracheal intubation or tracheostomy may prove necessary in some cases.

## Rheumatoid Arthritis

Rheumatoid arthritis is a chronic systemic inflammatory disease of unknown etiology. It is the most common autoimmune disease, affecting up to 3% of the adult population, with a reported prevalence of 15 to 35 per 100,000 in the pediatric population.[34] Although the hallmark feature is persistent, symmetric polyarthritis that affects the hands and feet, any joint lined by a synovial membrane may be involved, including the larynx in about 25% of cases.

Cricoarytenoid arthritis may present with hoarseness or airway obstruction via posterior laryngeal inflammation, tenderness, and decreased arytenoid mobility. As the disease progresses, it may cause ankylosis and nodules. These rheumatoid nodules may occur anywhere in the larynx or within the vocal folds themselves. Other symptoms are variable but may include globus sensation, stridor, and dysphagia. Cricoarytenoid arthritis should be considered in children with juvenile RA presenting with symptoms of upper airway obstruction. Laryngeal manifestations of RA may be the sole manifestation of active disease.[35] Systemic treatment includes corticosteroids, NSAIDs, or other immunosuppressive agents. Because of their smaller airway dimensions, children with acute onset cricoarytenoid arthritis may require intubation pending the beneficial effect or not of systemic steroid therapy. Surgical rehabilitation of arytenoid function is rarely possible; arytenoidectomy is the treatment of choice for symptomatic ankylosis of the cricoarytenoid joint. Surgical excision is performed for symptomatic rheumatoid nodules as well.

## Epidermolysis Bullosa and Cicatricial Pemphigoid

Epidermolysis bullosa (EB) encompasses a group of inherited disorders characterized by excessive susceptibility of the skin and mucosa to separate from underlying tissues after mechanical trauma. There are three broad categories of EB depending on the anatomic level of separation: EB simplex, junctional EB (JEB), and dystrophic EB.[36] Within each broad category are several subtypes with varying severity. The laryngotracheal manifestations of EB include laryngeal stenosis and stricture; these are most commonly seen within the JEB category (up to 40% by age 6 in one subtype of JEB).[37] Laryngeal compromise can occur as early as the first 12 months of life, requiring the need for careful monitoring for early clinical signs of airway obstruction, even during early infancy. The cumulative risk of laryngeal stenosis or stricture plateaus for both major JEB subtypes by mid-childhood. As a result, the need for continued close surveillance lessens after approximately ages 6 to 9 years. Symptoms include dysphonia (weak or hoarse cry),

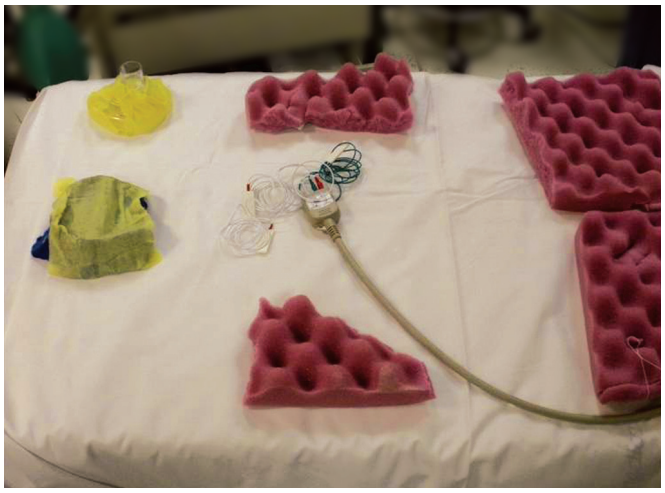

**Fig. 43.2:** Anesthesia considerations and operating room patient positioning in children with epidermolysis bullosa.

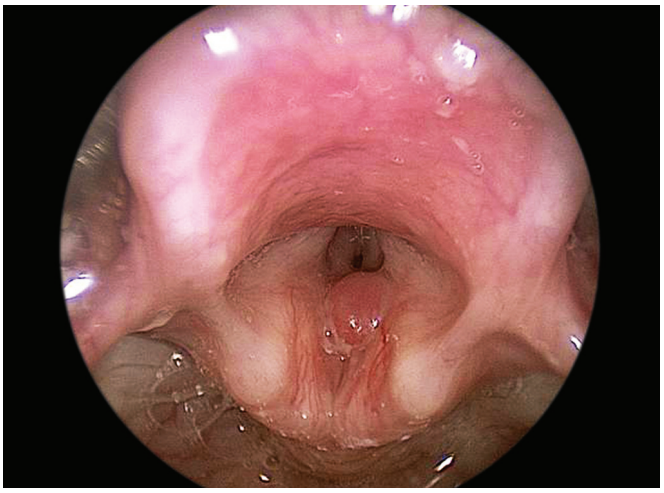

**Fig. 43.3:** Obstructive granuloma present on larynx of child with epidermolysis bullosa.

stridor, and potential significant airway obstruction. Laryngeal involvement is assessed by direct laryngoscopy. The diagnosis of EB is made by skin or mucosal biopsy.

Both the otolaryngologist and the anesthesia team need to take many things into consideration when taking a patient with EB to the operating room (Fig. 43.2). Simple concepts like masking a patient and placement of electrocardiogram (ECG) leads become more complex due to the risk of producing shearing forces leading to bullae formation. Therefore, steps are taken to use excessive amounts of lubricant around and on the contact surfaces of the mask, including the use of petroleum-impregnated gauze. ECG leads are needle electrodes instead of adhesive pads. All pressure points are padded with egg crate padding.

The mainstays of treatment for laryngeal EB include excision of scar and granulation tissue (Fig. 43.3) and concurrent intralesional and systemic steroids. Tracheostomy is reserved for life-threatening airway obstruction, as this procedure brings additional morbidity secondary to the shearing trauma it causes to the mucosa of the trachea and skin of the neck.

### Cicatricial Pemphigoid

Cicatricial pemphigoid (CP) refers to a group of rare chronic autoimmune blistering diseases that predominately affect the mucous membranes and occasionally the skin. Cicatricial scar formation can occur at any site of involvement, including the upper airway, larynx, and esophagus. Unlike EB, CP is rare in children and adolescents, characteristically affecting women over the age of 50 years. Laryngeal involvement occurs about 9% of the time with the symptom of odynophagia being most common.[38] Diagnosis is made by biopsy. Treatment consists of systemic steroid therapy and possible immunosuppressive therapy.

## NEOPLASTIC

### Laryngeal Tumors

#### *Subglottic Hemangioma*

Subglottic hemangiomas are a manifestation of infantile hemangioma, also called infantile capillary hemangioma or hemangiomata. They seldom appear in the airway and comprise only 1.5% of all congenital anomalies of the larynx.[39] These lesions, when large, can result in airway obstruction. There is a female predominance of 1.4:1 to 2.4:1.[40,41] Risk factors for the development of infantile hemangioma include fair skin, white non-Hispanic ethnicity, prematurity, and low birth weight.[41,42] Other possible risk factors include advanced maternal age, multiple gestation, and pre-eclampsia, although all three are potential confounders with prematurity.[41] Chorionic villus sampling has been implicated in infantile hemangiomas as well.[43] There may be a genetic link for a small proportion of these lesions, although this has not been fully elucidated.[41]

In general, infantile hemangioma is the most common tumor of infancy, occurring in 4–12% of infants.[42,44-46] They are true neoplasms in that they have increased mitotic activity and endothelial cell proliferation.[45] They possess characteristic histochemical endothelial vascular markers

that differentiate these lesions from other vascular birthmarks. These markers, which include GLUT-1, merosin, Lewis Y antigen, and FcyRII, are all also present on placental blood vessels.[46] Current theories on pathogenesis expand on these links. One hypothesis is that the lesions are a result of "embolized" placental cells. It is further suggested that a single endothelial progenitor line of cells is stimulated by hypoxia to proliferate in an attempt to normalize relative hypoxemia in tissues. This theory is appealing in that it is supported by much of what we know about the growth phases, location preference, and risk factors for the development of infantile hemangioma.[46]

Infantile hemangiomas demonstrate a characteristic growth pattern. Typically, they are absent or imperceptible at birth and then undergo a rapid growth phase, called proliferation, in which the appearance changes from a pale or mildly pigmented lesion into a larger, often bright red lesion over the course of the first 5 months of life. A prospective study found that 80% of the eventual hemangioma size is reached at a mean age of 3 months though deep hemangioma seemed to follow a growth trend that begins later and continues longer than superficial hemangioma.[46-48] Following the proliferation phase is a second phase, termed the plateau stage, which lasts several months and is characterized by very slow growth. However, recent literature[47] suggests this phase is not one of no or slowed growth but rather a dynamic balance between the proliferation and involution phases. During this phase, the proliferative factors that drove the growth of the neoplasm begin to be outpaced by the factors that drive apoptosis. After usually 1 year of age, the apoptotic factors drive the involution phase, which takes place over the next several years.[47]

Hemangioma may be located throughout the body though 60% occur in the head and neck.[49] Extremities, visceral organs especially the liver and less likely the lungs and intestine, the trunk, and genitals are all other sites though notably the deep skeletal muscle seems to be spared.[49] Cutaneous lesions are classified as focal or segmental, superficial or deep, and single or diffuse.[48] Focal lesions typically occur at embryologic fusion lines between the growth centers of mesenchyme[49,50] and tend to be less aggressive lesions. Segmental lesions, on the other hand, follow dermatomal patterns or developmental segments and have been associated with higher incidence of complications including ulceration and morbidity from other associated sequelae.[47,50]

When present in the airway, particularly in the subglottis owing to it being the narrowest point in the airway in a child, the hemangioma typically becomes symptomatic when it enters the proliferative phase leading to airway obstruction. This complication is seen in 1.4–1.8% of all patients with a diagnosed infantile hemangioma.[51]

*Diagnosis*: The clinical history and a thorough head and neck physical examination, including an in-office flexible fiberoptic nasal laryngoscopy, should be performed in all such patients presenting with airway obstruction. Definitive diagnosis of a subglottic or airway hemangioma is made in the operating room with direct laryngoscopy and bronchoscopy visualizing the lesion and documenting its position, size, and character. Lesions are classically noted to have a bluish hue and are most commonly found on the left.[52] Biopsy is not required for diagnosis, which is usually made on history and endoscopic examination findings. Biopsy has been considered controversial for the theoretical bleeding risk.[53] Shikhani et al. reviewed approximately 10 cases of which one third were biopsied with no bleeding complication.[54] Magnetic resonance imaging (MRI) is preferred over other imaging modalities, if needed to guide therapy; however, its longer acquisition time requires sedation and likely intubation for these infants, and this can potentially increase both the relative complexity of the procedure as well as potential to make a tenuous airway critical secondary to trauma from the endotracheal tube.[50,53] Some authors recommend CT with contrast to better define bony remodeling, critical structure, and presence of invasion. CT has a relatively rapid acquisition time that may allow for evaluation of the unsedated, spontaneously breathing infant.[55] Ultrasound with Doppler imaging has been shown to be useful for superficial lesions to determine extent and vascularity; however, its use in the evaluation of airway hemangioma has been limited. Rossler et al. looked at a small series of infants presenting with stridor using ultrasound to evaluate the lesions then compared those results with later endoscopic findings. They found good correlation in lateral versus midline lesions, although they acknowledge a practical difficulty in performing an airway ultrasound on an infant with symptoms of respiratory distress.[56] Plain films have not been shown to provide value.[53]

Patients with cutaneous hemangioma in the "beard" or trigeminal nerve (V3) distribution are at increased risk of having airway hemangioma and should be carefully evaluated for possible airway complications. Lesions in

this area, which include the chin, anterior neck, lower lip, and preauricular/parotid region were found in approximately 8.5% of patients with head and neck hemangioma in a series reported by Orlow et al. Of these, 63% had some airway involvement and 40% required tracheostomy for airway management.[57] More recently, in a series of 1226 patients by O et al., 29% of those with segmental hemangioma in the V3 distribution were found to have airway involvement.[50] Hemangioma, particularly segmental, in this area should raise suspicion of and evaluation for a potential airway lesion.

*PHACE Syndrome*: One associated syndrome that deserves specific discussion is PHACE [posterior fossa malformations (P), hemangioma (H), arterial anomalies (A), coarctation of the aorta and cardiac defects (C), and eye abnormalities (E)]. This syndrome was first described by Frieden et al. in 1996 in a series of 41 patients.[58] PHACE is important in the discussion of subglottic hemangioma because 52% of patients with PHACE syndrome have airway involvement.[44] While the definition of PHACE continues to evolve, a recent consensus statement released in 2009[59] outlines the current criteria for PHACE and possible PHACE syndrome. Diagnosis of PHACE requires a facial hemangioma > 5 cm plus either one major criteria or two minor criteria. These criteria include anomalies of all the major systems impacted by the syndrome; cerebrovascular, such as anomalies of the major cerebral arteries, abnormalities in brain structure especially the posterior fossa, cardiovascular anomalies, including aortic arch abnormalities, posterior segment ocular abnormalities, and midline defects, such as sternal clefts.[59] Evaluation of patients with suspected PHACE should include additional cardiac, ophthalmologic, and neurologic evaluation.[48] Specific recommendations are for structural brain imaging via MRI with and without gadolinium as well as intracranial and cervical angiography with contrasts enhanced magnetic resonance angiography (MRA) as the preferred method.[59]

*Treatment*: Prior to 2008, the options for treatment of subglottic hemangioma included $CO_2$ laser, tracheotomy, interlesional injection, open surgical excision, and Nd:YAG laser.[40] Then in 2008 there was a serendipitous discovery of propranolol's ability to cause regression of hemangioma in children being treated for severe disfiguring infantile capillary hemangioma.[60] These patients were placed on propranolol due to the concern for right heart failure secondary to shunting of blood into these large hemangiomas. This paradigm shift in treatment ushered in a revolution in the ability to medically manage many cases previously only amenable to surgical management.

Although not currently Food and Drug Administration approved for this indication, it has become first-line therapy for most infantile hemangioma treatment. In 2011, a consensus conference was convened to establish best practices for initiation and use of propranolol for the treatment of hemangioma.[61] Their results were published in January 2013 and include both recommendations for monitoring as well as target dosing strategies based on risk assessment of the specific patient. Relative contraindications to propranolol therapy include sinus bradycardia, greater than first-degree heart block, bronchial asthma, heart failure, cardiogenic shock, and hypersensitivity to propranolol hydrochloride.

Current consensus guidelines recommend a pretreatment ECG and history for relative contraindications.[61] Target dose is 1 to 3 mg/kg/day divided three times a day. Children with comorbidities and those < 8 weeks corrected gestational age are not recommended for outpatient initiation of propranolol. When outpatient initiation is appropriate, patients should be monitored with heart rate and blood pressure at baseline then again at 1 and 2 hours on initial therapy. Parents should be counseled on the need for regular feeds and to discontinue propranolol dosing when the child has restricted oral intake such as with feeds to prevent hypoglycemia.[61]

Special consideration is given to patients with PHACE syndrome when considering propranolol as a treatment as they are at a theoretical higher risk for possible stroke by the lowering of blood pressure as a result of the therapy. While PHACE has a wide variety of arterial anomalies, those thought to be of highest risk are those patients with severe long segment narrowing or nonvisualization of major cerebral or cervical arteries especially when the patients have coarctation of the aorta or other cardiac anomalies.[61] Current recommendations for such patients include a full MRI/MRA evaluation of the head and neck and cardiac imaging with particularly attention to the aortic arch prior to consideration of propranolol therapy. Neurology consultation and follow-up for a careful risk-benefit assessment for the use of propranolol is recommended for those patients whose stroke risk is elevated. If deemed appropriate, then recommendation is for the lowest possible dose with a close titration upward, inpatient initiation, and three times a day dosing to minimize blood pressure changes.[61]

In the literature, there are reports of both late-responders and nonresponders to propranolol treatment. In addition, there are those who are unable to safely tolerate the medication. For these children, the more traditional therapies remain viable options. These include the following systemic steroids—usually oral prednisolone, intralesional steroids like triamcinolone and betamethasone, surgical excision, vincristine, and interferon.[48,62] Oral steroids, once one of the mainstays of treatment, remain a viable option; however, their variable efficacy and significant side effect profile warrant careful consideration. Interferon has been shown effective however with a poor side effect profile including spastic diplegia that does not resolve with treatment cessation. As such, it is only used in a life-threatening situation when it is the only alternative. Vincristine is considered safer than interferon and is generally used for patients with large hemangioma who have developed Kasabach–Merritt syndrome or are nonresponsive to other therapies.[48]

Surgical management may be used in conjunction with any of the medical therapies listed above or as an adjunct to medical therapy if the patient demonstrates only a partial response. Surgical management includes both endoscopic and open procedures, including endoscopic laser, transcervical open excision, and tracheostomy.[62] Tracheostomy was historically used during the proliferative phase of growth and remains an option for acute management of patients with poor or delayed response to medical therapy. Laser excision, particularly with $CO_2$ laser has long been described for airway hemangioma particularly for the ability to obtain microhemastasis. Serial laser sessions are usually performed during the lesion's proliferative phase; however, care must be taken to avoid aggressive laser therapy. In up to 20% of patients undergoing endoscopic laser therapy, subglottic stenosis is the primary complication.[63] Open excision may be performed as a single-stage procedure or as a double-stage procedure in a child with a pre-existing tracheostomy. The open technique uses a midline neck excision at the level of the cricoid cartilage. The laryngotracheal framework is exposed, and a temporary interoperative tracheotomy is placed. The surgeon enters the airway through a vertical incision in the cricoid cartilage. The hemangioma is then excised after a submucosal flap is raised over the hemangioma. For hemangioma that extends into the vocal fold, some tumor is purposely left behind to avoid damage to the vocal cord. Patients then undergo nasotracheal intubation and are left intubated for 3 days to allow healing prior to extubation. In 2002, a paper reporting a series of eight patients with airway hemangioma undergoing open excision found that five of the eight patients needed a cartilage graft as well due to subglottic stenosis identified at the time of the procedure.[64]

### *Neurogenic Tumors*

Tumors of peripheral nerves are seen throughout the body. Rarely, these neurogenic tumors can arise in the larynx and present as a submucosal mass. Neurogenic tumors include neurofibroma, schwannoma, malignant peripheral nerve sheath tumors,[65] and granular cell tumors.[66]

Neurofibromas of the larynx, while very rare, are most commonly associated with neurofibromatosis type 1 though they may occur in isolation. Laryngeal neurofibroma are only very rarely associated with neurofibromatosis type 2. The most common sites of involvement in the larynx include the aryepiglottic folds and the arytenoids.[65,67] This is thought to be a result of the point of origination occurring at the superior laryngeal nerve or the anastomosis between the superior and recurrent laryngeal nerve, also known as the Galen's anastomosis.[68] The tumor arises from the perineural fibrocytes.[69] On histologic analysis, they may be classified as plexiform, diffuse, or both. Plexiform growth pattern is diagnostic of NF1 and is described as a poorly localized pattern along existing nerves. This is contrasted with the diffuse pattern in which the growth occurs slowly as a nodule and symptoms vary in severity based on location and size.[65] Neurofibromas, in contrast with schwannoma, are not encapsulated.[68] Primary symptoms of neurofibroma in children include stridor, dyspnea, and voice changes.[67,68] However, in children under 1 year of age, stridor seems to be the presenting symptom as demonstrated in a series of five patients in the first year of life with neurofibroma of the larynx.[65] Malignant transformation may occur in 10% of neurofibromas, resulting in the malignant peripheral nerve sheath tumors.[70] Treatment consists of complete excision, including possible partial laryngectomy if needed, with close follow-up for possible recurrence as well as care for the other associated NF1 symptoms.[70-72] Preoperative angiography and embolization has been shown to decrease intraoperative blood loss.[72]

Similar to neurofibroma, schwannomas are rare accounting for only 0.1% of all laryngeal neoplasms in all ages. They are most commonly found in women in the fourth to fifth decade of life, but case reports of occurrence

in children also exist in the literature.[70] In contrast to the neurofibromas above, they are only rarely associated with neurofibromatosis, are encapsulated, and grow away from the trunk of the nerve from which it originates.[70] They originate from the Schwann cells, and on pathologic evaluation show the two classically described cellular regions: the Antoni A region of hypercellular palisading nuclei and the Antoni B region of loosely arranged cells in a myxoid matrix.[69] Complete excision with separation from the original nerve is theoretically possible in Schwannoma. Excision is the treatment of choice while incomplete resection can result in rapid regrowth. Malignant degeneration is much less common than in neurofibromas.[69]

Granular cell tumors are similarly rare and their origination from Schwann cells was initially much debated in the literature, although now seems to be widely accepted.[66,73] These tumors seem to be more common in females and predominance in African Americans has been described.[66] Although rare, granular cell tumors do occur most commonly in the head and neck region (>50% of the cases)[73] with approximately 10% of those in the larynx.[74] Approximately, half are located on the true vocal cords.[74] Case reports in the pediatric literature number a couple of dozen.[74] Histologic examination is required to establish the diagnosis with S-100 and vimentin positive staining and polyhedric cells with granular cytoplasm.[66,74] Excision of the lesion is the treatment of choice, but the literature reports a recurrent rate of 8–12% in these patients.[74] Close follow-up is advocated; however, the literature is not clear on the utility of repeated endoscopic examinations in the asymptomatic child.[66] In 2006, Pernas et al. reported on the role of laryngeal tracheal reconstruction (LTR) to allow for wide local excision in one patient with a historical review of the literature. Their patient had undergone two previous endoscopic excisions and returned with symptoms. She underwent a wide local excision via laryngofissure and single-stage LTR. They concluded that LTR was an option for patients with large lesions or those who recur after endoscopic removal.[74]

## *Malignant Laryngeal Neoplasms*

Malignant laryngeal neoplasms are fortunately a very rare entity in the pediatric population, with small numbers of cases reported in the literature. Primary rhabdomyosarcoma, squamous cell carcinoma, primitive neuroectodermal tumors, and mucoepidermoid carcinoma have all been described in small series and case reports.[75-78]

Rhabdomyosarcoma is most commonly of the embryonal type, which develops from the embryonal mesenchyme from which striated muscle arises. As such, it can present anywhere in the body where striated muscle is located. This malignancy accounts for approximately 5% of all malignant tumors in children up to 15 years old. Although approximately 50% of these tumors are located in the head and neck region, they are found in the larynx only about 1% of the time.[78] A case series described five pediatric patients treated with chemotherapy. Adjuvant radiotherapy was used in four of those patients with a follow-up period from 13 to 17 years with disease free survival reported for all patients.[78] Radiation in the prepubescent larynx carries both the risk of secondary irradiation-induced tumor development as well as fibrosis and stunted laryngeal development. Treatment with total laryngectomy has been described.[77,79] Ohlms et al. described one pediatric patient treated with laryngectomy in 1994 with survival at 18 years of follow-up.[77]

Squamous cell carcinoma of the larynx is reported in <1% of all childhood tumors.[80] A review of the literature in 2001 reported 58 known cases.[81] A more recent review in 2010 highlighted at (15:19) translocation in two poorly differentiated squamous cell carcinomas of the airway with a rapidly progressive course.[76] In addition, it has been associated in the past with malignant transformation of recurrent respiratory papillomatosis, especially when radiation had been used for treatment of the lesions.[80] Treatment includes both primary chemoradiation and surgical excision with adjuvant chemoradiation with no clear evidence to recommend either therapy though the psychosocial benefits of laryngeal preservation where possible are highlighted.[77,81]

Primary salivary gland malignancies occur in the pediatric population rarely; however, they account for 10% of all head and neck tumors in children. Of the malignant salivary gland tumors, mucoepidermoid carcinoma comprises approximately one third of all salivary gland tumors. Minor salivary glands exist throughout the upper airway and 0.1% to 1% of all laryngeal tumors are the result of malignant salivary gland tumors in the larynx.[75] Only a very small number of these cases occur in the pediatric population. On physical examination, salivary gland malignancy tends to spread in submucosal fashion without significant mucosal changes; therefore, symptoms may not present until significant tumor growth has occurred. Surgery followed by postoperative radiation therapy with long-term follow-up is recommended. Recurrence > 10 years after primary treatment has been reported.[75]

## Tracheal Tumors

Primary tracheal tumors are infrequent in the pediatric population. In one review of 198 primary tracheal tumors over a 26-year period, only four were in patients under 10 years of age and eight occurred between the ages of 10 and 18.[82] These included granular cell tumor, fibrous histiocytoma, neurofibroma, mucoepidermoid tumor, carcinoid (most common), adenoid cystic carcinoma, and rhabdomyosarcoma. Other tracheal tumors noted in childhood were fibrosarcoma, hemangiopericytoma, and chondroma. This seems to concur with a more recent single institution review of endotracheal and endobronchial tumors in 2011 finding 14 cases between 4 and 18 years old, the most common being carcinoid or mucoepidermoid carcinomas.[83] A 30-year review of the literature for pediatric tracheal neoplasms found only 36 cases reported between 1965 and 1995.[84] In this paper, the authors report 23 of the 36 as benign; the most common was hemangioma (5/23). Of the 13 (36%) malignant tumors, only 1 was carcinoid, instead the most common malignant tumor was malignant fibrous histiocytoma (4/13). In adults, the overwhelming majority of the primary tracheal tumors are squamous cell carcinoma and adenoid cystic carcinoma.[82]

Presentation of a tracheal tumor is based on clinical suspicion in an infant or child presenting with respiratory distress. Tracheal lesions most often present with wheezing or expiratory stridor. Stridor resulting from fixed intrinsic lesions of the airway does not change with position. Unlike a foreign body aspiration that presents with acute onset, tracheal neoplasms likely will present insidiously, perhaps initially being mistaken for reactive airway disease or an upper respiratory illness that does not resolve in due time. Cyanosis, apnea or apparent life-threatening events (ALTE) may initiate the diagnostic work-up after hospitalization. In rare circumstances, difficulty with intubation during unrelated surgery can prompt diagnosis.

Diagnostic evaluation should include a thorough and methodical physical examination. Flexible fiberoptic laryngoscopy will help rule out supraglottic and glottic masses but is limited in assessment of tracheal neoplasms. Radiography including modified barium esophagoscopy, airway fluoroscopy, and, more definitively, CT of the chest can delineate intrinsic versus extrinsic lesions. MRI is also helpful having advantages of good soft tissue evaluation and lack of radiation but likely requiring sedation in a child with an airway lesion. Clinical discretion to anesthetize such a patient is necessary. Definitive diagnosis is made on laryngoscopy and bronchoscopy in the operating room to determine the extent, characteristics, and stenosis of the airway. Pathological specimen of the lesion should be acquired at this time as well to ensure proper diagnosis.

Treatment of tracheal neoplasms is determined by pathological diagnosis. In some circumstances such as hemangioma, the lesion may be medically treated. In others, particularly benign lesions, simple excision (either endoscopic or open) may be all that is necessary. Complex open airway surgery including tracheal resection and reanastomosis may be required for certain larger lesions. In malignant lesions, adjuvant radiation and chemotherapy may be necessary in addition to surgical excision.

## Bronchial Tumors

Primary neoplasms of the bronchus and trachea most commonly present with recurrent pneumonia, cough, and wheezing or asthma unresponsive to treatment. Although tumors in these locations are rare, they have been shown in the literature to be approximately two-third malignant. Sixty-four percent have been found to be malignant on biopsy with pulmonary carcinoid being the most commonly described of the malignant lesions.[83] This rate was similar to a literature review on the subject in 1983.[83,85] In that paper, the same tumor was called a bronchial adenoma. In adults, metastasis is found in 10–30% of pulmonary carcinoid. Slightly fewer pediatric patients were found with metastasis at presentation.[85] Wheezing is thought to be a presenting symptom in part as a result of serotonin released into the airway.[83] Surgical excision is the treatment of choice in these lesions. Mucoepidermoid carcinoma was the second most common malignant lesion. Treatment is surgical excision with prolonged follow-up as when it is found in other areas of the airway. Other bronchial lesions include leiomyoma, adenocystic carcinoma, and bronchogenic carcinoma. In children most bronchogenic tumors are undifferentiated carcinoma or adenocarcinomas.

Of the benign lesions, the two most common are inflammatory pseudotumors, also known as inflammatory myofibroblastic tumors, and hamartomas. Inflammatory pseudotumors are classified by the World Health Organization as intermediate in terms of malignancy.[83] The histologic examination demonstrates a proliferation of reticuloendothelial cells.[85] Hamartomas are commonly found in the adult population but more rarely in the pediatric population. Of note, the triad of pulmonary chondroid hematoma, GI stromal tumors, and extra-adrenal paraganglioma is found in Carney's syndrome, which has been described in female patients.[83,86]

*Disclaimer*: The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

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CHAPTER

# 44 Caustic Ingestions and Foreign Bodies of the Aerodigestive Tract

*Benjamin B Cable, Douglas Ruhl*

## BACKGROUND

Despite a progressive series of regulatory legislation and safety efforts over the last century, potentially hazardous chemical exposure remains to be a serious and relatively common occurrence among the pediatric population. One key contributing factor to this difficult problem is the sheer number of chemicals now available to the average home in the United States. The Household Products Database of the National Library of Medicine currently lists >2,000 widely available products in nine separate categories ranging from cleaning and automotive products to home improvement and pet care products. From this nearly unlimited access to chemical products, the potential for misuse and exposure logically follows. Accidental and purposeful ingestions make up approximately 80% of these cases, whereas dermal, inhalational, nasal, and ocular exposure routes make up the remaining 20%.

In its most recently published data set, the American Association of Poison Control Centers reports >2.3 million poison "exposures" in 2011, 48% of which regarded as children <6 years of age. This overall "exposure" rate is more double than that seen prior to 1987 and has been essentially stable for the last decade. The categories most frequently reported to the National Poison Data System (NPDS), in order of descending frequency, include cosmetic/personal care products, analgesics, cleaning substances, foreign bodies, topical preparations, vitamins, antihistamines, and pesticides. Despite representing a highly disproportionate amount of total exposures, fatalities in children are thankfully rare. Of the total number of reported case fatalities in 2011, <2% of patients were <5 years of age.[1]

When looking specifically at patients <19 years of age, 80% of exposure cases are reported in children <5 years of age. The remainder of cases are nearly equally divided between those from 6 to 12 and those between 13 and 19 years of age. Unintentional ingestions make up the vast majority of cases of those <5 years of age, but intentional ingestion becomes more common in older children. Intentional ingestions outnumber accidental in cases of patients between 13 and 19.[1]

Potentially "caustic" ingestions make up one portion of the overall number of these cases and are defined by exposure to chemicals, which have the ability to interact with and damage organic tissue. Specific data regarding the actual prevalence of pediatric caustic ingestions remain surprisingly rare. Reports by the American Association of Poison Control Centers, via the NPDS, do not delineate caustic agents from noncaustic agents, and the majority of recent literature citations regarding frequency can be directly traced or extrapolated from a single report published >40 years ago.[2] A singular report in 2012, using database queries of International Classification of Diseases, Ninth Revision (ICD9) codes, reported an estimated prevalence of 807 cases in the United States in 2009. The authors point out that this prevalence rate almost surely underestimates the true total number of cases as it deals only with hospitalized patients and requires both accurate coding and accurate reporting to capture cases.[3]

Simplistically, caustic substances are often divided into alkalis and acids. Alkali agents, or "bases", are those chemical substances with the ability to accept a free $H^+$ ion. Historically, the term Lye was used to denote any strong alkali used as a cleaning agent. Today, alkalis can be found in many products, which include drain and oven cleaners

as well as soaps and dishwashing agents. Recent interest in "environmentally friendly" nonphosphate detergents has resulted in the addition of alternate chemical mixtures, which add to the overall pH of available detergents.[4] Practically, alkalis are ingested far more frequently than acids, because they are relatively tasteless and are often more prevalent in the home. Alkalis cause direct damage to the lipoprotein lining of the aerodigestive tract via a liquefactive necrosis. This necrosis occurs as a result of "saponification", which is a term used to describe the direct hydrolysis of triglycerides in cellular tissue. This process is not self-limited and may progress through mucosal, submucosal, and muscular layers of the esophagus and stomach. Intense adjacent inflammation results in small vessel thrombosis and, ultimately, necrotic sloughing between 4 and 7 days after injury.[5]

Acid agents are those chemical substances that have the ability to donate a free $H^+$ ion. As they have a strong and often bitter taste, acid ingestions are reported to make up < 15% of total caustic ingestions.[6] Common acid agents found in the home include pool chemicals, some toilet-bowl cleaners, and battery fluids. As opposed to alkaline agents, acidic agents cause a coagulation necrosis, which results in the formation of an eschar. This eschar may limit overall depth of the resulting chemical reaction. Although this is often thought to be protective within the esophagus, acidic agents are known to have the potential too overwhelm the acidic environment of the stomach and cause severe gastric injury as well as systemic toxicity.

Although "critical pH" levels are often discussed for both acids and bases, the clinical utility of these measurements is questionable. For acids, a substance with a pH < 3 is often cited as having the potential for caustic injury. For bases, a substance with a pH > 12 is cited as having a similar potential for injury.[7] In reality, many factors are likely to be involved in the overall "caustic" nature of an ingested substance. Other factors include strength or concentration of the substance, viscosity, additional adjuvant chemicals present, and time of exposure to the tissue in question. These factors illustrate the critical importance of seeking out the specific identity of the potentially ingested substance and gaining poison control center advice regarding the substances known properties and potential for injury.

## CAUSTIC INGESTION

### Initial Presentation and Evaluation

The three most common presenting signs for children who have ingested a caustic substance are drooling, vomiting,

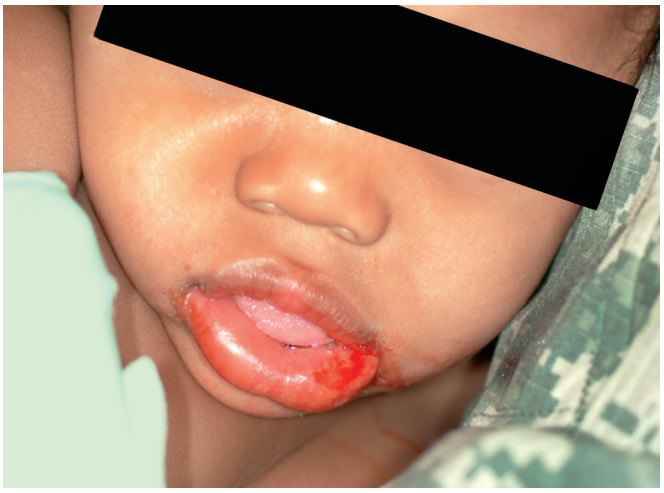


**Fig. 44.1:** Young child with history of caustic ingestion presenting with moderate lip edema and vermilion erosion.

and refusal of further oral intake. Less common signs include lip swelling, tongue erythema, leukoplakia, and oral ulcerations (Fig. 44.1).[8] Although numerous studies have attempted to correlate these presenting signs with the likelihood of deeper esophageal or gastric injury, most show no clear association. In particular, a review of the available literature makes it clear that normal oral and pharyngeal examinations do not rule out a significant distal injury.[9-12]

As always, initial evaluation begins with a detailed history. If at all possible, specific identification of the potentially ingested substance should be made and poison control center contact sought. Details surrounding the actual ingestion event should be clarified if at all possible. Intentional ingestions raise specific concern as the volume of ingested substance is typically larger and the subsequent sequelae possibly more significant.

Physical examination must begin with a broad-multisystem approach. Hemodynamic and airway instability are both unusual but must be evaluated and, if present, aggressively managed in light of exposure to each specific chemical agent. In severe cases, arterial pH disturbances (pH < 7.22 or base excess <–12) have been correlated with life-threatening esophageal injury.[13]

Plain film X-ray examinations of the chest and abdomen are used to rule out free air in the mediastinum and peritoneum.

Patients who present without acute hemodynamic or airway concerns should subsequently undergo thorough physical examinations. In most cases, flexible nasal endoscopy can be completed without difficulty and allows for careful assessment of the nasopharynx, hypopharynx, glottic structures, and esophageal inlet.

## Management

Evidence-based pathways for the management of caustic ingestion have yet to be defined. Historically, initial treatment options for caustic ingestion attempted to modulate the presence of the caustic substance itself and included the induction of vomiting, dilution of the substance with water or milk, and neutralization of the substance with a liquid having the opposite pH of the originally ingested substance. Each of these approaches may impose additional risk and, in most cases, have been abandoned. The induction of vomiting essentially re-exposes the esophagus to the caustic substance and creates an additional risk for aspiration. Dilution, usually in the form of a large volume of water intake, creates a risk for gastric upset and serial reflux of the original substance. Although controversial in animal studies, neutralization attempts have been thought to create exothermic reactions, which may further exacerbate trauma to the aerodigestive tract.[14] Activated charcoal has also been used alone or in combination with these potential therapies but has been shown to be of little value and has also been largely abandoned as a treatment option.[1]

Rather than directly modulate the caustic substance itself, current management focuses on assessing the damage done and tailoring subsequent medical therapy to attempt to avoid the development of complications resulting from this damage.

Assessment of the patient with caustic injury involves observation and consideration for endoscopy. Children with a questionable history of ingestion may be released after only a few hours if completely asymptomatic. All other children should be considered for admission and overnight observation. Children known to have ingested a potentially dangerous caustic agent, and all children with active symptoms should be made nil per os (NPO), admitted for overnight observation, and hydrated with intravenous fluids. Although some controversy exists regarding the need for endoscopy in all admitted patients, most current studies advocate a low threshold for esophagoscopy after 12–48 hours of observation.[8,15] This particular window in time is chosen to allow for the injury to demarcate but not progress beyond the point of possible early intervention. Almost all authors agree that patients with intentional caustic ingestion, irrespective of symptoms, should undergo endoscopy.

A number of grading systems have been proposed for esophageal caustic injury patterns. The most commonly referenced system is defined by Zargar et al.[16] Using this system, a normal esophageal examination is given a Grade 0. Grade 1 injury is defined by mucosal edema and hyperemia. Grade 2a injury is defined by friability, erosions, hemorrhage, blisters, exudates, whitish membranes, and shallow ulcers. Grade 2b injury is defined by Grade 2a findings with deep or circumferential penetration. Grade 3a injury is defined by small or scattered areas of necrosis and Grade 3b by extensive necrosis.

Children found to have a Grade 0 or 1 examination have a low likelihood of complications and can be discharged home after establishing a normal oral intake. Children with a Grade 2 findings may also begin a normal oral intake and can be discharged home but must be followed closely as they have been reported to form esophageal strictures in 50–77% of cases.[8,16] When they do develop, strictures most commonly become apparent between 3 and 8 weeks after injury.[23] Children with Grade 3 injuries will almost certainly develop strictures.[17] If possible, children with Grade 3 injuries should have a nasogastric feeding tube placed at the time of endoscopy. This tube serves as both stent and conduit for feeding. Children with Grade 3 injury require serial dilations, if possible, and can require esophageal resection in specific cases.

Medication management is directed toward minimizing stricture formation. Although a range of medications are frequently used in the treatment of patients with caustic ingestion, none are without controversy. Antireflux agents, including the proton pump inhibitors, tend to be started early after Grade 2 and Garde 3 injuries but no specific evidence exists to support their use. Antibiotics were shown to be of benefit. Benefit in a single animal model >60 years ago and have been subsequently used in most series with Grade 2 and 3 injuries.[18] Despite their widespread use in these cases, no clear evidence of benefit exists. The exception to this paucity of data would be cases where potential perforation and mediastinitis or peritonitis exists. In these cases, antibiotics are clearly indicated.

As distinct from other medications, a broad range of data exists for the use of steroids in patients with caustic ingestion. Most case series have focused on Grade 2 injuries as Grade 1 injuries are unlikely to stricture and Grade 3 injuries are felt to possibly be exacerbated by the use of steroids. Prospective studies of steroid use in Grade 2 patients are mixed in their results.[8,19,20] Two meta-analyses of available data failed to show significant benefit with steroid use.[21,22] Due to the conflicting nature of the original studies and the low incidence of side effects or complications, steroid use in patients with Grade 2 disease continues to be commonly used medical therapy in practice. If used, steroids are often given for 1–6 weeks with a constant dose of 1–2 mg/kg/day of prednisone for the first 7–21 days and then slowly tapered, if longer durations of therapy are chosen.

In most cases, children with Grade 2 findings should undergo fluoroscopic swallow testing before beginning oral intake and being discharged home. Children with Grade 3 injuries and NG tubes in place may also undergo fluoroscopic swallow evaluations before being discharged home.

Children with Grade 0 or 1 findings should both have follow-up examinations to ensure normal dietary intake and swallow function. Children having difficulties with oral intake should generally undergo repeat swallow testing at 3–6 weeks after injury and dilation procedures if strictures begin to develop. All children with Grade 2 or 3 findings should undergo subsequent evaluations of their swallowing function. Most authors advocate fluoroscopic studies to begin during the time that strictures may begin to develop, usually around 3 weeks postinjury. In patients who ultimately develop strictures, 80% will develop within 8 weeks of injury.[23] Again, when evidence of stricture formation begins to develop, dilation procedures can be used as treatment. The development of a long-segment stricture or total obstruction often results in the requirement for a segmental resection or consideration of esophagectomy. Children found to have evidence of stricture development should be considered as candidates for esophageal dilation. While bougie dilation remains an option, balloon dilation techniques have become far more common and are now most frequently cited. Although not proven to be superior to bougie dilation, balloon techniques are often described as having the advantage of avoiding the shearing forces created by the introduction of bougie dilators. Irrespective of technique, frequency of dilation should be based on patient exam and response to initial therapy. Most authors report the need for multiple procedures, accomplished at bi-weekly intervals. Mitomycin-C has been studied as an adjuvant therapy for use at the time of stricture dilation. When used, it is topically placed at concentrations between 0.1 and 1 mg/ml. A recently published review of the 11 publications regarding its use concluded "encouraging" results but cited a lack of prospective evidence.[24]

When compared with the general population, patients with a history of a caustic ingestion are reported to have a thousand-fold increase in the risk of developing esophageal carcinoma, both adenocarcinoma and squamous cell carcinoma. Incidence rates range from 2% to 30% of patients who are followed for long durations of time. Given this concern, serial screening for evidence of dysplasia would seem reasonable.

## HOUSEHOLD BLEACH

Household bleach products are one of the most frequent sources of accidental pediatric ingestion and deserve individual comment. Sodium hypochlorite, the primary chemical found in liquid household bleach, is known to form hypochlorous acid when combined with water. Although potentially caustic in concentrations above 10%, a wide range of studies have shown lower concentrations to be an irritant rather than truly caustic. Current household bleach products are limited to concentrations of 5%. Children who have accidentally ingested liquid household bleach products most often present with vomiting but may also display mild skin irritation, drooling, dysphagia, cough, and abdominal pain. Despite these initial concerning symptoms, serious distal injury is extremely rare. Most children experience a rapid resolution of symptoms and, having undergone a complete examination without significant findings, can be released without further observation. Children with continued symptoms can be admitted for observations but rarely require endoscopy or further intervention.[25] As with any other purposeful ingestions, children with purposeful ingestion of a bleach product should undergo full evaluation with endoscopy. Industrial bleach products are often formulated at higher concentrations and should be considered as caustic.

## FOREIGN BODIES

As long as children will innately be driven to explore their environment, they will put things in their mouth. Despite United States regulations designed to limit small parts in toys and articles designed for use by children <3 years of age, foreign body ingestion remains common. The 2011 Annual Report of the American Association of Poison Control Centers National Poison Data System lists >112,000 calls for foreign body ingestion with >82,000 of the cases occurring in children <5 years of age. This is almost certainly a large underestimate as many, if not the majority, of foreign body ingestion cases do not result in a call to a poison control center. Overall, the peak incidence of foreign body ingestion occurs between the age of 6 months and 3 years. Thankfully, it is estimated that 80% of ingested foreign bodies will pass through the gastrointestinal system without complication. The remaining 20% become lodged in the aerodigestive tract and require either endoscopic or open surgical removal.[26]

Although rarely analyzed together, airway foreign body cases are far outnumbered by gastrointestinal foreign body cases. We will discuss each separately.

## Airway Foreign Bodies

Foreign body aspiration most commonly occurs in children <3 years of age and often reflects a male preponderance. Organic matter is the most commonly aspirated material, although most series demonstrate a wide range of possible objects. In two large reviews of aspirated foreign bodies, vegetable matter made up between 67% and 84% of cases. Nuts were the most commonly encountered material in both series.[25,27] In the acute phase of aspiration, children display gagging and choking that may last for seconds to minutes. As the foreign body lodges and the child habituates, the distress of a small or nonobstructive object subsides and patients may become asymptomatic for an extended period of time. If not directly witnessed, the events may be missed altogether. As a result, studies report between 36% and 60% of cases present >24 hours after aspiration.[25,28] Many present days, weeks, or even months after actual aspiration.

Given the wide window of time for presentation, a high index of suspicion is the single most important factor in diagnosis. In children, virtually any pulmonary symptom that is either atypical or unresponsive to routine therapy should raise the possibility of an aspirated foreign body. Frequent misdiagnoses include pneumonia, bronchitis, asthma, and laryngitis. Classically, an aspirated foreign body "triad" is described. This includes a history of coughing and/or choking with an examination finding both wheezing and unilateral decreased breath sounds. When each part of the triad is evaluated individually, a history of coughing and/or choking is present in >90% of children. Wheezing is reported to be present in >80% of children and unilateral decreased breath sounds in approximately 50% of patients.[25,27,28]

Plain film chest X-ray (CXR) examinations remain the initial study of choice for any child undergoing consideration for foreign body aspiration. CXR results are found to be abnormal in 75–85% of patients, although specific delineation of the foreign body is only visible in the 15% of cases, where the foreign body is radiopaque. More common findings include mediastinal shift due to air trapping, hyperinflation, and atelectasis. Computerized tomographic examinations are felt to have a slightly higher sensitivity. Fluoroscopic examinations have also been used to evaluate for dynamic air trapping. Given our increasing awareness of the recent exponential increase in the overall use of medical radiation and its potentially harmful effects in children, both of these studies should be used only after special consideration and nondiagnostic plain film evaluation.

The majority of aspirated foreign objects lodge in the right main bronchus due to its less acute angle as it departs the trachea. Large case series report just over 50% of all foreign bodies lodging in the right main bronchus. Between 30% and 40% of remaining objects are found on the left main bronchus, whereas the remainder are found in the trachea or larynx itself.[25,27]

If history, physical examination, or radiologic investigation results in the possible diagnosis of an aspirated foreign object, endoscopy should be considered both for definitive diagnosis and treatment.

Rigid endoscopy remains the technique of choice for the evaluation and removal of airway foreign bodies. Close coordination between the surgical and anesthetic teams is imperative to success. While induction with inhalational anesthesia agents remains expedient, anesthetic maintenance is often best achieved with intravenous agents. Anesthesia where the patient maintains spontaneous ventilation can be achieved with highly trained anesthesia providers and is ideal for both diagnostic and therapeutic endoscopy. Intravenous anesthesia ensures a steady level of anesthesia while the airway is instrumented and alternating levels of gas exchange occurs (Fig. 44.2). With spontaneous anesthesia, an endoscope can be directly introduced via a laryngoscope. Without a bronchoscope, the endoscope has a much wider range of motion in the distal trachea and, with head turning, a zero-degree scope can be used to fully evaluate both bronchi and often multiple subsegmental

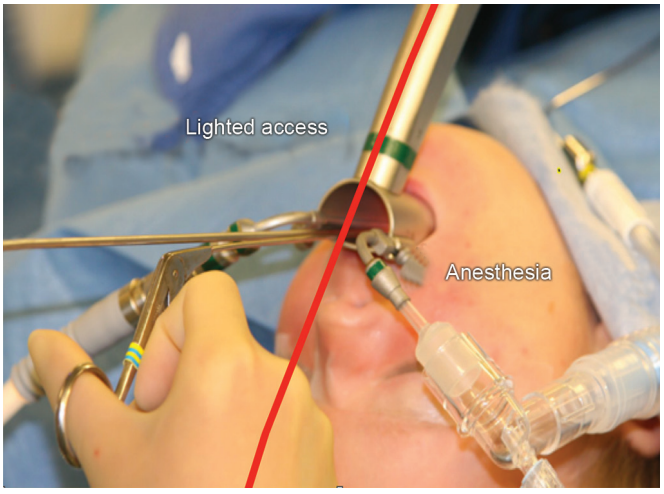



**Fig. 44.2:** Patient undergoing evaluation for airway foreign body using spontaneous anesthesia. Fiberoptic light located on left and anesthesia circuit located on right.

bronchi. If no foreign body is encountered, the procedure can be completed. If a foreign body is identified, it is closely examined to determine the appropriate optical forceps be used for removal. At all times, suction should be available and can be gently carried out using either rigid suction cannulas or atraumatic flexible suctions ranging in size from 4 to 6 French. If the patient continues to achieve spontaneous ventilation, the surgeon has the option to suspend the patient and introduce the optical forceps directly. This allows for continued maximization of movement. If spontaneous ventilation is difficult or intermittent, a bronchoscope is introduced into the airway and the anesthesia circuit attached to the 15-mm port. Optical forceps can then be introduced through the bronchoscope. Once the object is grasped with the optical forceps, it is gently brought to the distal end of the bronchoscope. Sharp points, if present, should be brought into the lumen of the distal bronchoscope but the entire system, bronchoscope and forceps, should then be brought out of the airway as a unit. The glottis provides a second area of constriction and can "strip" a foreign body from the forceps if not passed slowly and with a firm hold. Once a foreign body is removed, a secondary diagnostic examination should be undertaken to ensure complete removal, evaluate for trauma to the airway, and to ensure no additional foreign bodies are present.

Postoperatively, children are observed in a monitored care setting. A postoperative CXR is ordered to rule out pneumothorax. It is common practice to treat patients with perioperative steroids to minimize edema from the procedure.

## Esophageal Foreign Bodies

As with aspirated foreign bodies, the peak incidence for esophageal foreign body ingestion is approximately 3 years of age. As opposed to aspirated foreign bodies, esophageal foreign bodies are most commonly non-vegetable matter with coins being the most common object found in large case-series. In these series, coins make up between 27% and 80% of the total objects encountered. Other objects typically include toy parts, jewelry, hardware, and disk batteries (which will be discussed separately).[29,30]

Children who have ingested a foreign body that has become lodged in the esophagus present with highly variable symptoms that include choking, drooling, poor feeding, dysphagia, odynophagia, chest pain, nausea, vomiting, and respiratory symptoms secondary to tracheal compression. In some cases, children can be entirely asymptomatic.

The CXR evaluation should be ordered for any child with a suspected ingested foreign body. The most common location at which a foreign body lodges within the esophagus is the upper esophageal sphincter or thoracic inlet. This occurs in 60–70% of cases.[30,31] Two secondary areas of narrowing, the mid-esophagus at the level of the aortic arch and the lower esophageal sphincter, each tend to trap remaining foreign objects in equal proportion.

Children with suspected esophageal foreign body ingestion and respiratory symptoms of any kind should undergo endoscopic removal as soon as is practical. Children with inert objects, coins in particular, and without respiratory or severe symptoms can be considered for period of observation. This not only allows for gastric emptying in preparation for general anesthesia but may also allow time for the object to pass. In one large prospective study, 25–30% of coins were found to pass without complication over an 8–16 hour period of time. Of note, proximal coins were found to pass in only 14% of patients, whereas middle and distal coins were found to pass in 43% and 67% of patients, respectively.[32,33] Objects that are found to pass to the stomach most often continue to pass through the gastrointestinal tract without complication. Parents are often asked to screen stools to ensure object passage. Objects not passing by 4–6 weeks should be considered for endoscopic or surgical removal.[31]

Symptomatic objects and objects not found to pass after a period of observation should be removed endoscopically. Evidence supports both rigid and flexible endoscopic techniques. If rigid endoscopy is chosen, a brief diagnostic laryngoscopy and bronchoscopy is often done before intubation. This allows tracheobronchial involvement to be ruled out. Once intubation is completed, the proximal esophagus in small children can often be visualized with firm upward retraction of the overlying skin of the neck. This is most successful in children <1 year of age but may be possible in older children as well. If unsuccessful, an esophagoscope can be introduced and endoscopy used to evaluate the full length of the esophagus. The central lumen of the esophagus should be kept in view at all times and minimal pressure used to pass the esophagoscope. Once located, the foreign body is often surrounded by secretions and debris and must be isolated with gentle suction. Once complete, an optical forceps can be passed and used to retrieve the object. As with aspirated objects, the esophageal object is brought to the distal end of the esophagoscope and the entire unit is removed in unison. Repeat diagnostic endoscopy can be used to confirm object removal and to evaluate any associated mucosal trauma. Children with evidence of

esophageal trauma should undergo subsequent contrast swallow studies to rule out perforation before a normal diet is resumed.

## DISK BATTERIES

Disk batteries represent an especially dangerous hybrid between a potential foreign body and a potential caustic agent. As such, they require special consideration and management. Accidental ingestion of these batteries is becoming an unfortunately more common problem in the pediatric population. During 1985–2009, there was a 6.7-fold increase in the percentage of button battery ingestions with major or fatal outcomes. This was in comparison to two-fold increase of similar outcomes for all human poison exposure during the same time period.[34] Despite this increase in incidence and risk, guidelines for treatment remain to be well established.

Disk battery ingestions have a bimodal distribution with peak frequencies in 1–3 years old and the elderly. The elderly are more likely to ingest smaller, hearing aid batteries that are often confused for medication. Children, on the other hand, are the frequent ingesters of larger, button batteries (Fig. 44.3).[35]

The clinical course of a child with a button battery depends on location of the battery, duration of mucosal exposure, remaining voltage, and chemical composition of the battery.[36] Outcomes are significantly worse for large-diameter lithium cells (>20 mm) and children who are <4 years at the time of ingestion.[35] Lithium-cell batteries have 3 V of electrical charge compared with 1.5 V of other batteries. Significant esophageal injury from lithium batteries can occur within 30 minutes of ingestion.[37] Twenty-five years of retrospective data reported that all deaths related to disk battery ingestion were from 20- to 25-mm lithium batteries ingested in children 1–2 years old.[34]

Four mechanisms of injury have been proposed to account for the damage produced by a button battery lodged in the esophagus: caustic injury due to leakage of the battery contents, electrical discharge and mucosal burn, pressure necrosis, and toxic heavy metal absorption.[36,38-41] It is thought that the alkaline leakage is the major force inciting injury, and battery ingestions are treated as caustic ingestions. Interestingly, lithium batteries do not contain alkali but are associated with significantly worse outcomes.[34] More severe tissue damage may be produced by this type of battery by the flow of electric current through tissue, because they have a higher voltage.[37]

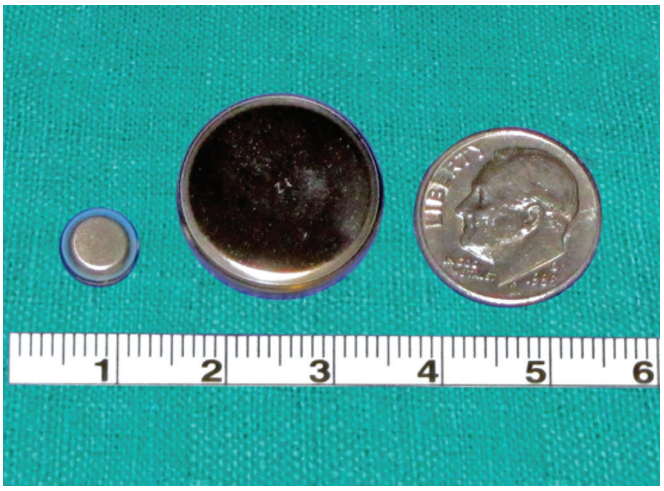
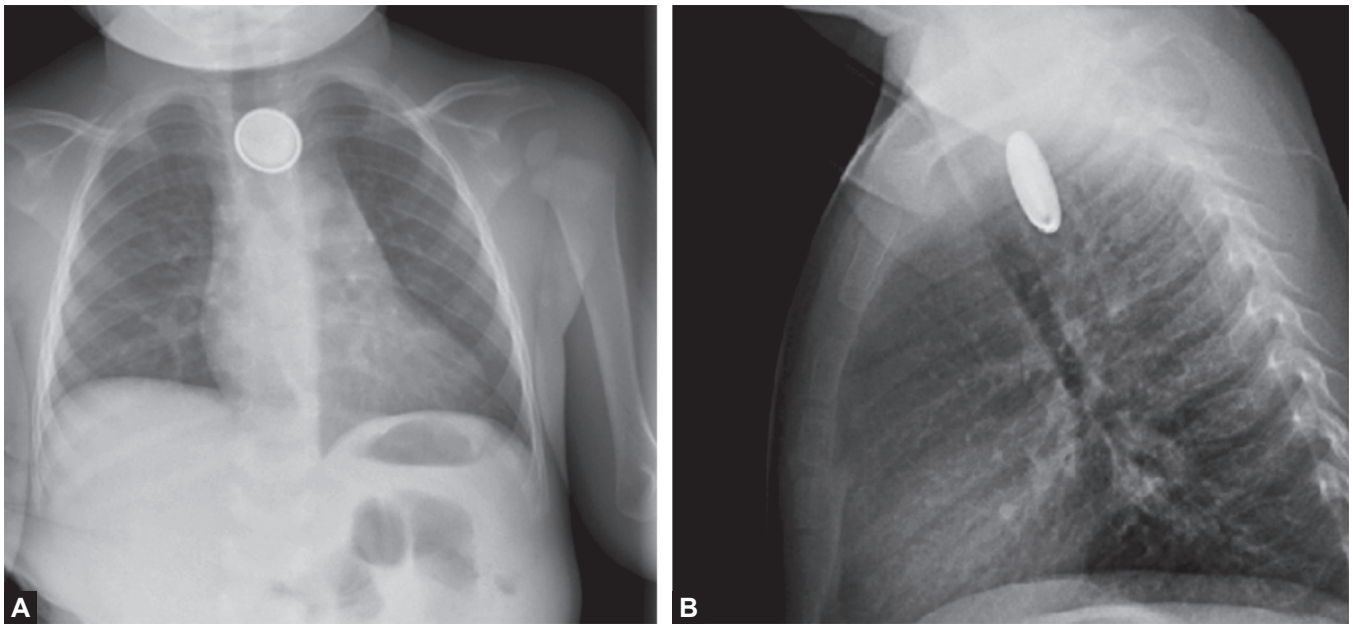



**Fig. 44.3:** Various sizes of common disk batteries.

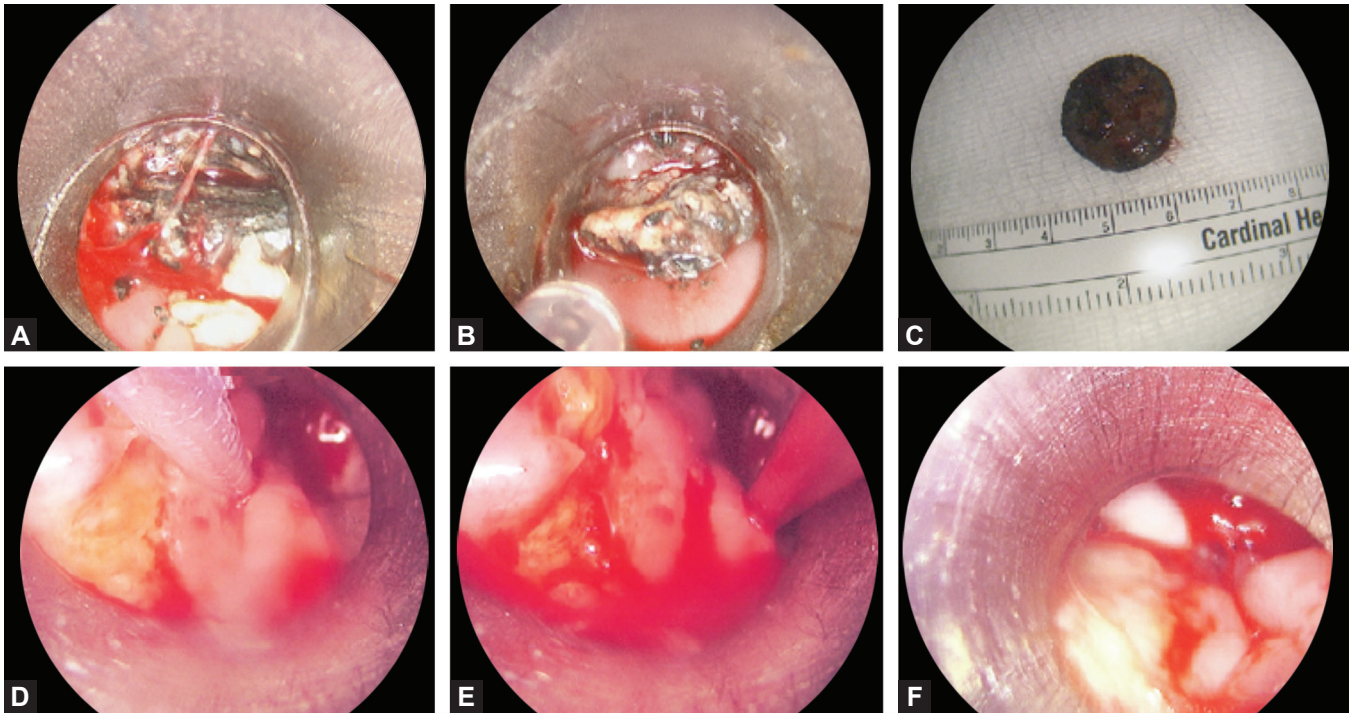
Esophageal injury occurs by flow of a direct current and not by outflow of the alkaline content or compression.[42] No report has demonstrated morbidity due to heavy metal toxicity from battery ingestion; however, it may be prudent to monitor serum levels if a patient ingests a mercury battery as they are more likely to fragment and increase serum levels of mercury.[43] Animal studies have shown the cathode side of the battery becomes increasingly alkaline while the anode side becomes acidic.[44]

Disk batteries are likely to lodge in the same locations as do other esophageal foreign bodies: the cervical esophagus, aortic arch area, and the lower esophageal sphincter. An anteroposterior and lateral chest X-ray is paramount in promptly identifying a battery trapped in the esophagus. The double shadow or "halo" effect is an easily recognized feature of button batteries on radiographs; however, its absence does not rule out its presence (Figs. 44.4A and B).[45] A disk battery can lose its "halo" appearance during the active corrosion process and may actually represent a more urgent situation.

Immediate rigid endoscopy is the foundation in removing esophageal button batteries.[39] Esophagoscopy directly after removal is often difficult to interpret as inflammation is severe and products of the resulting chemical reaction often appear as a thick exudative debris clinging to the esophageal wall. Some authors advocate a second endoscopy one day after battery removal; however, no management standard exists.[39] In data to be published, this author has found a close second-look esophagoscopy, done 2–4 days after initial battery removal, allows for much improved visualization of demarcated injury patterns and an overall downgrade in injury assessment in the majority of cases (Figs. 44.5A to F).




**Figs. 44.4A and B:** Anteroposterior (AP) and lateral plain film X-ray of child with button battery ingestion. Battery demonstrates halo effect on AP view and classic coronal position found in most esophageal ingestions.




**Figs. 44.5A to F:** Serial views of endoscopy during button battery removal. Top row—initial view of esophagus with thick coagulum and apparent circumferential injury. Top right—severely corroded battery after removal. Bottom row—second-look endoscopy done 48 hours after initial battery removal showing partial circumferential injury and limited edema.

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CHAPTER

# 45

# Congenital and Acquired Laryngeal Anomalies

***Gresham T Richter, Abby R Nolder, Ramey Marshell***

## INTRODUCTION

The larynx is the single conduit by which air passes into the tracheobronchial tree and ultimately the lungs. It provides a barrier to aspiration and is the primary means of phonation. Normal laryngeal function is critical to respiration, eating, and oral communication. Thus, congenital and acquired laryngeal anomalies can lead to respiratory compromise, dysphagia, and voice disturbances. Even minor abnormalities can significantly affect laryngeal function. This chapter addresses both common and rare disorders of the pediatric larynx in terms of presentation and management. Many of these conditions require surgical intervention. The treatment goal of pediatric laryngeal disorders is generally to provide a widely patent larynx with normal vocal fold function.

## LARYNGEAL ANATOMY

The larynx is defined by the area involving the most superior part of the epiglottis to the inferior border of the cricoid cartilage. It is subdivided into the supraglottis, glottis, and subglottis. The supraglottis includes the epiglottis, aryepiglottic folds, supra-arytenoid cartilages (cuneiform and corniculate) and tissue, the false vocal folds, and superior half of the laryngeal ventricle (Fig. 45.1). The true vocal folds are the principle structure of the glottis composed of the thyroarytenoid muscle, ligament, and its surrounding mucosa. The glottis includes the sites of vocal fold insertion into the arytenoid and thyroid cartilages as well as 1–2 mm above and below these structures. The subglottis, the narrowest part of the pediatric larynx, includes the area 1–2 mm below the true vocal folds to the lower border of the cricoid cartilage. The recurrent and superior laryngeal nerves, arising from the vagus nerve (CNX), provide the primary motor and sensory neural input to the larynx respectively.

Disorders of the larynx cause site-specific functional problems that are particularly sensitive in the pediatric population. In general, supraglottic anomalies typically lead to inspiratory stridor, airway compromise, and dysphagia. Glottic lesions can lead to biphasic stridor, voice disturbances, and sometime swallowing problems. Subglottic disorders frequently cause significant airway obstruction that is accompanied by biphasic stridor. According to Poiseuille's law [$R \propto (n.L/r^4)$], small changes in the radius of the subglottis will dramatically impact resistance to air entering the tracheobronchial tree.

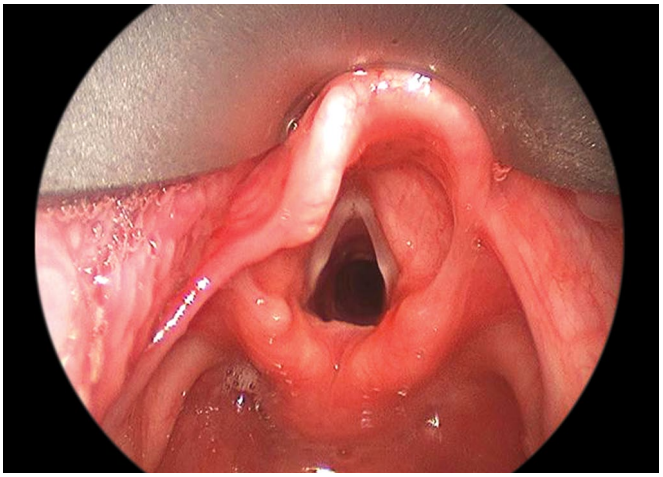


**Fig. 45.1:** Normal pediatric larynx. Endoscopic view of normal pediatric larynx.

# LARYNGOMALACIA

## Background

Laryngomalacia (LM) is the most common congenital anomaly of the pediatric larynx and the most common cause of newborn stridor.[1,2] LM, literally meaning "weak larynx", refers to the collapse of supraglottic structures during inspiration. Reduced laryngeal tone, shortened aryepiglottic folds, and supraglottic redundancy contribute to flaccid inspiratory collapse and airway obstruction in this condition.[3] When present in infants, LM is often accompanied with feeding issues due to discoordination of the suck–swallow–breathe sequence.[4] Stridor is the result of turbulent airflow upon inspiration across abnormally positioned supraglottic tissues. Four to twenty percent of infants with LM require surgical management when the airway and feeding are severely compromised.[5-7] LM may also be present in older children under conditions that impact normal laryngeal sensation and tone. Feeding issues, sleep apnea, and exercise intolerance have been attributed to LM in older children with this condition.[7,8]

## Etiology

The exact etiology of LM remains unclear. Anatomic, cartilaginous, and neurologic theories have been postulated. The anatomic theory implies that anomalous congenital development of the supraglottis leads to LM. This theory suggests that redundant supraglottic laryngeal tissue, high-riding cuneiform cartilages, and foreshortened aryepiglottic folds lead to airway obstruction and stridor. This can be seen in newborns with airway symptoms immediately after birth and often requires surgical correction. Underlying cartilage weakness termed "chondromalacia" has also been proposed as an etiology.

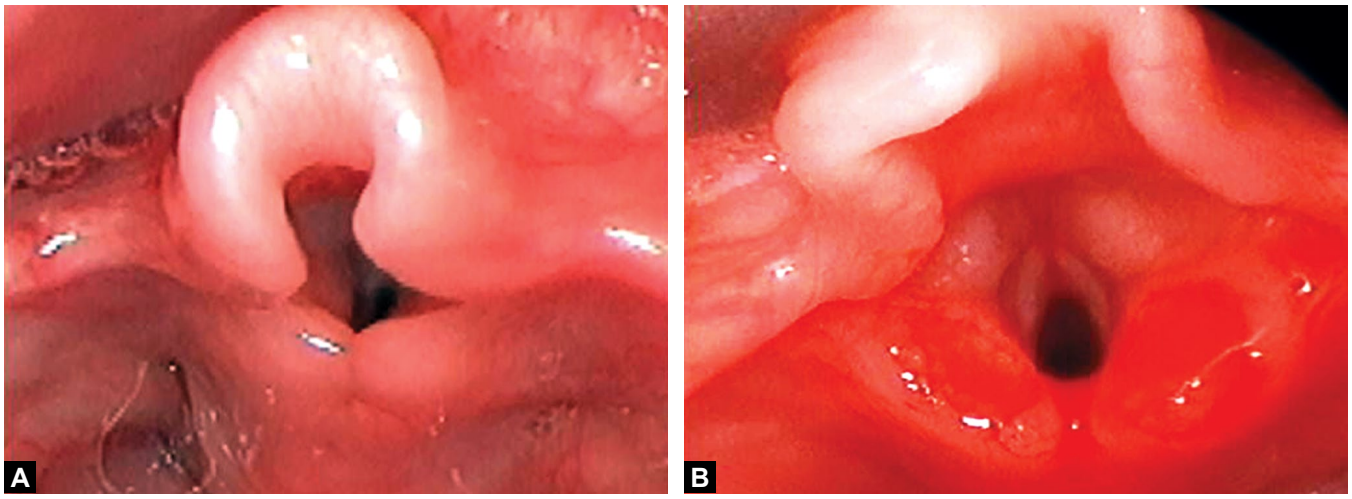
The current prevailing concept, with more evidence, is the neurologic theory of LM. The theory implicates neuromuscular immaturity or weakness as the most likely cause of this condition. Reduced laryngeal tone secondary to inhibited neurosensory input is proposed[4] and thought to be the result of an insult to the central nervous system or sensory fibers of the supraglottis.[9] The association of LM with gastroesophageal reflux disease (GERD) and neuromuscular disorders (cerebral palsy, Chiari malformation, stroke victims) implicates this theory. Neural hypertrophy, as seen in distal gastrointestinal conditions, has been found in supra-arytenoid samples of affected infants.[10]

## Clinical Presentation

The classic presentation of LM is an infant with high-pitched inspiratory stridor that worsens with feeding, crying, supine positioning, and agitation.[11] Symptoms arise during the first 2 weeks of life, increase over several months (especially in the presence of reflux), and peak at 3–6 months of age. Most cases (70–90%) of LM are benign and self-limiting with complete resolution between 12 and 24 months of age.[4,12] Stridor has been reported to resolve in mild to moderate LM by 7–9 months of age.[3,6] Associated manifestations of LM include dyspnea, respiratory distress with accessory muscle use, feeding difficulties, microaspiration, cyanotic spells, perioral cyanosis, obstructive sleep apnea, hypoxia, and failure to thrive.[13] The most common symptoms related to feeding include regurgitation, emesis, coughing, choking, and slow intake. Up to 80% of infants with LM have GERD or laryngopharyngeal reflux (LPR).[4] Older children and adults with evidence of LM frequently have LPR.[8] LM in this population may be the re-emergence of disease thought resolved at infancy. Patients with neuromuscular disorders and weakness (e.g. cerebral palsy) may present with late onset symptoms and a high degree of supraglottic collapse.

### *Diagnosis*

Prompt diagnosis of LM is important to avoid the complications of acute and chronic airway obstruction, such as cyanosis, apnea, failure to thrive, developmental delay, pulmonary hypertension, core pulmonale, cardiac failure, and asphyxiation. With a heightened suspicion, confirmation of LM is made using awake flexible fiberoptic laryngoscopy in the clinic. Supraglottic tissue collapse and obstruction during inspiration is the classic finding. Specific laryngoscopy findings include posteriorly positioned arytenoid cartilages and mucosa into the airway during inspiration, and a shortened distance between the arytenoid and epiglottis (aryepiglottic fold). Shortened aryepiglottic folds and lateral collapse with an "omega"-shaped, or curled, epiglottis are characteristic findings on intraoperative examination with direct microlaryngoscopy (Figs. 45.2A and B). An "omega"-shaped epiglottis, however, may present in up to 50% of normal infants.[4] Pharyngeal dysphagia (oropharyngeal dysphagia, microaspiration) is assessed in patients with LM with coughing and choking during feeds by speech therapy at the time of diagnosis.




**Figs. 45.2A and B:** Laryngomalacia. Intraoperative microlaryngoscopy of an infant's supraglottis with severe laryngomalacia (A) Before; (B) After supraglottoplasty.

Severity of LM is qualified as mild, moderate, or severe and solely based upon clinical symptoms. In general, mild LM is defined by mild inspiratory stridor with no other symptoms and evidence of laryngeal prolapse on flexible laryngoscopy. Patients with stridor, choking, and feeding difficulties in the presence of retractions, but no blue spells represent moderate LM. Severe LM denotes those patients with significant airway obstruction and discoordinated swallowing leading apnea, cyanosis, failure to thrive, or derivations of these symptoms.[14] Severe LM may also be qualified by sleep apnea in an affected infant.[15]

The anatomic appearance of the larynx may contribute to severity but does not necessarily dictate management. Surgical candidates are selected on the degree of airway obstruction and feeding difficulties, rather than the stridor intensity and extent of laryngeal collapse.[14] In patients with moderate to severe symptoms, in whom endoscopic intervention is considered, intraoperative microlaryngoscopy, and bronchoscopy can aid in the diagnosis and determination of surgical intervention. This also allows the opportunity to explore for synchronous large airway lesions, such as tracheomalacia, subglottic stenosis (SGS), and bronchomalacia that accompany LM in > 50% of cases.[16]

## Management

After the diagnosis of LM is made management is determined on the basis of severity of symptoms.[3,14,17]

- Mild LM management includes a 1-month symptom check with flexible laryngoscopy, followed by a 3-month symptom with or without laryngoscopy, until resolution of airway symptoms. Acid suppression therapy may be instituted to prevent disease progression in the setting of an already refluxing patient
- Moderate LM management includes acid suppression medication with a 1-month symptom check followed by symptom checks with or without flexible laryngoscopy every 3 months until resolution. A small percentage of patients (20–30%) with moderate LM will progress to severe disease depending on anatomic variation and control of reflux. This can be determined as early as the first-month follow-up
- Severe LM patients need to be managed with maximum acid suppression, microlaryngoscopy, and bronchoscopy, and supraglottoplasty (Figs. 45.2A and B). Follow-up for these patients with a 1-month postoperative visit is necessary. Recurrence of disease is rare (3–10%) but common in neurologically affected infants and those with uncontrolled reflux.[5,18] Repeat awake laryngoscopy is suggested, but surgical intervention is based upon clinical severity. If doing well then continued follow-ups every 3 months and subsequent weaning of acid suppression therapy is offered.

## Supraglottoplasty

Supraglottoplasty is the process by which the supraglottic larynx is relieved of obstructing collapsible supraglottic structures with preservation of the interarytenoid space. Supraglottoplasty was originally termed "epiglottoplasty" as defined by the reduction of the lateral surface of the

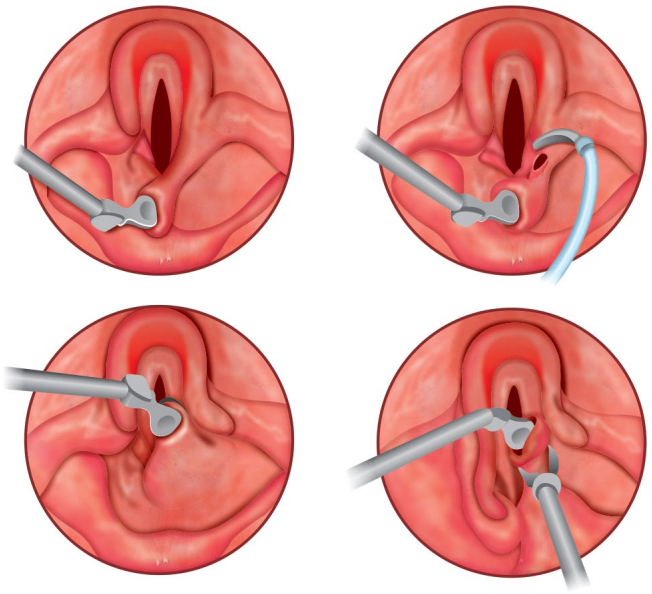


**Fig. 45.3:** Supraglottoplasty. Diagram of cold knife supraglottoplasty technique.[14]
Adapted from Richter et al.[14]

epiglottis in infants with severe LM. This is no longer performed, but the tenants of surgical intervention remain the same. During a supraglottoplasty the aryepiglottic folds are incised and redundant supra-aryteniod tissue is remove with or without the cuneiform cartilage with is often prominent and contributing to obstruction (Fig. 45.3). The procedure is safe, relatively bloodless, and can be performed with $CO_2$ laser or cold knife technique. Reported success rates vary from 79–93% in that a tracheostomy or revision procedure is not required. Infants and children with neurologic or comorbid cardiopulmonary conditions are more likely to fail.[5] Complications are rare. Aspiration improves in the majority of normal infants with severe LM after supraglottoplasty.[19] Patients with "late onset" or "persistent" LM improve with supraglottoplasty when comorbid conditions are not present.[20]

## SUBGLOTTIC STENOSIS

### Background

Subglottic stenosis (SGS) refers to the narrowing of the subglottic airway, a region extending from the undersurface of the true vocal cords to the distal surface of the cricoid cartilage. Subglottic stenosis is specifically defined by an airway lumen diameter of ≤ 4 mm in a full-term infant or ≤ 3 mm in a premature infant.[21,22] Expected internal diameter of the subglottic lumen by age is demonstrated in Table 45.1. SGS is a common cause of airway obstruction and the second most common cause of stridor in infants and children.[23,24] It accounts for more tracheostomies in children <1 year of age than any other laryngotracheal anomaly.[25] Subglottic stenosis can be acquired (95%) or congenital (5%). Although the pathophysiology of each is variable, the accompanying symptoms and ensuing management of the two stenosis types are virtually the same. Congenital subglottic stenosis is typically less severe than the acquired type but may be the underlying cause of acquired disease that is undetected in the presence of injury and inflammation.

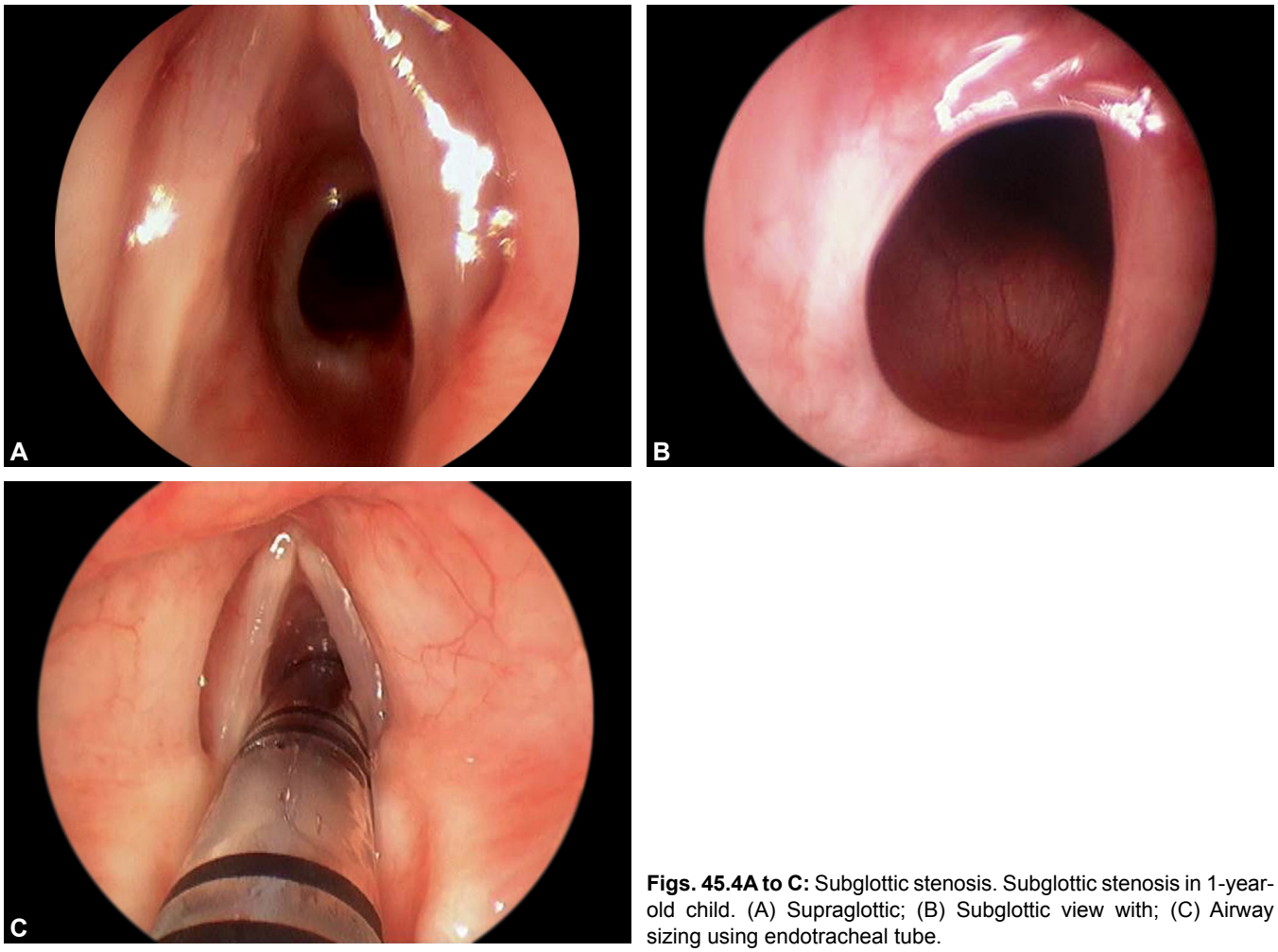
**Table 45.1:** Expected minimal subglottic lumen size-based upon age

| *Age* | *Minimal internal diameter (mm)* |
|---|---|
| 0–3 months | 3.5 |
| 3–9 months | 4.0 |
| 9–24 months | 4.5 |
| 2–4 years | 5.0 |
| 4–6 years | 5.5 |
| 6–8 years | 6.0 |
| 8–9 years | 6.5 |
| 10–12 years | 7.0 |
| 12–13 years | 7.5 |

### Etiology

Acquired subglottic stenosis arises as a consequence of subglottic injury, most frequently secondary to endotracheal intubation. Mucosal injury, ischemia, granulation formation, and subsequent fibrosis lead to the constriction of the already narrowest element of the pediatric airway (Figs. 45.4A to C). Inappropriate endotracheal tube size has been attributed to subglottic injury, but the length of intubation tends to be the most important factor for stenosis formation. Other factors, which may precipitate SGS, especially in the setting of injury, include LPR, infection (respiratory syncytial virus, bacterial tracheitis), and other causes of local inflammatory response.[26] It is important to note that while approximately 90% of acquired SGS results from endotracheal intubation, the reported incidence of subglottic stenosis among intubated patients is now < 1%.[27,28]

Congenital SGS is found in a child without a prior history of airway trauma or endotracheal intubation. The majority of congenital SGS are of cartilaginous origin with anomalous cricoid ring development. The most common




**Figs. 45.4A to C:** Subglottic stenosis. Subglottic stenosis in 1-year-old child. (A) Supraglottic; (B) Subglottic view with; (C) Airway sizing using endotracheal tube.

anomaly is the "elliptic cricoid", which describes a reduced ratio of the transverse diameter relative to the anteroposterior diameter of the cricoid plate. Congenital SGS occurs in an estimated 5% of all subglottic stenosis and is identified earlier than the acquired type, typically in infancy.[29] The only risk factor consistently associated with congenital subglottic stenosis is prematurity.[30] Subglottis stenosis is further classified on the basis of several characteristics, cartilaginous versus membranous, the degree of narrowing, and by histopathology.[23,31] Membranous soft tissue stenosis occurs as the result of submucosal fibrosis, submucosal gland hyperplasia, ductal cysts, or granulation tissue. A soft tissue, or membranous, stenosis commonly is symmetric and circumferential.[26]

## Clinical Presentation

Inspiratory or biphasic stridor is the most common presenting manifestation of SGS. Associated symptoms include retractions, dyspnea, tachypnea, cyanosis, respiratory distress, restlessness, irritability, and feeding difficulties. Newborns with mild to moderate stenosis may remain asymptomatic until 1 to 3 months of age as this correlates with a period of increased activity levels. Both acquired and congenital SGS share similar symptoms. In acquired, a latency period of 2 to 4 weeks after the inciting event of airway injury is common. Severe cases of the congenital type can present with stridor and respiratory distress at birth.[32] Severity of SGS often correlates with symptoms. A fatigued child with suspected SGS with no audible stridor is an ominous sign and needs urgent intervention. The differential diagnosis for SGS includes LM, subglottic hemangioma, and croup.

## Diagnosis

The diagnostic workup of SGS relies on a thorough history and physical examination that is supplemented by both

radiologic imaging and an endoscopic evaluation. Historic clues of significance include continuous "noisy breathing", "wheezing", feeding difficulties, or prior episodes of endotracheal intubation especially in the presence of respiratory syncytial virus.[32] Radiologic evaluation includes anteroposterior and lateral neck and chest X-rays to assess for concomitant respiratory injuries and determination of stenosis location, length, and symmetry.[23] Computed tomography (CT) of the neck and chest in not commonly employed in the diagnostic work-up of pediatric SGS.

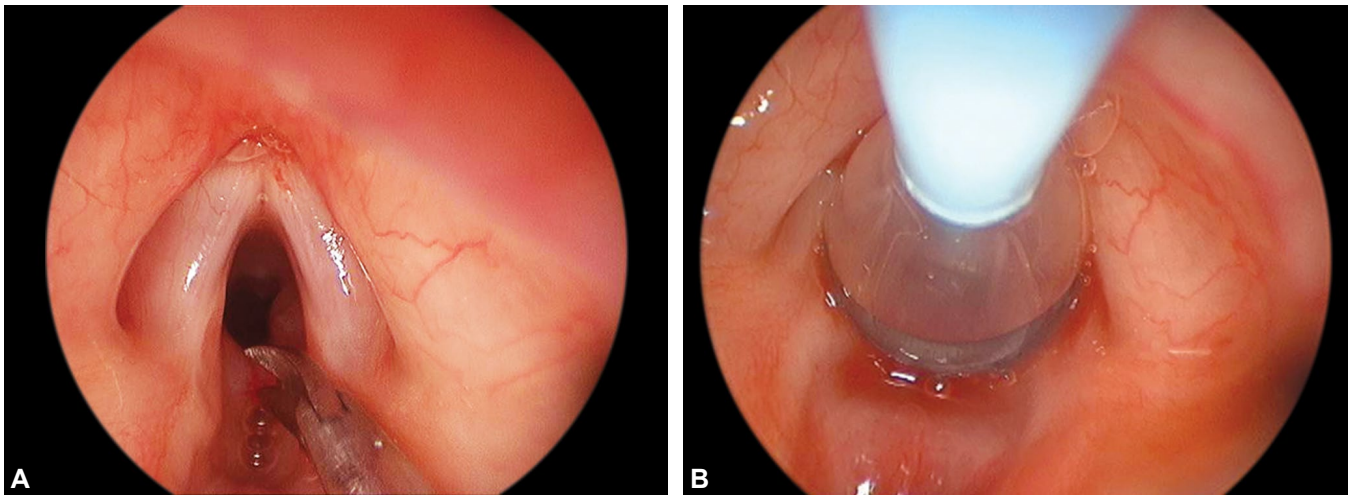
The gold standard for diagnosis of SGS remains to be direct microlaryngoscopy and rigid bronchoscopy. Both procedures require general anesthesia in the pediatric population thus negating the use of CT. During diagnostic laryngoscopy, a subglottic lumen less than the expected size for the child's age is determined to be stenotic.[33] Dynamic and secondary airway lesions, such as concomitant distal stenosis, vocal cord weakness, and tracheobronchomalacia, are also evaluated at bronchoscopy, as they will impact the patient's airway status and success of intervention. Length of stenosis may also be important. A universally accepted staging approach to pediatric SGS is the Myer–O'Connor–Cotton Grading System, which categorizes the degree of stenosis as grade I (0–50% obstruction), grade II (51–70%), grade III (71–99%), and grade VI (complete obstruction). This is determined on the basis of the outer diameter of the expected endotracheal tube for the patient's age (Figs. 45.4A to C). If a leak is present between 10- and 25-cm $H_2O$ with the age appropriate tube, then a stenosis is not present. When a smaller tube is required, then the stenosis grade can be calculated using the formula; actual size/expected size x 100.[33]

The Myer–Cotton staging system roughly correlates with prognosis and surgical outcomes.[34] Some patients may be considered to have a functional SGS in the setting of a flaccid, and not fixed, stenosis. Reflux is associated with the development and severity of subglottic stenosis.[35]

## Management

### *Endoscopic Techniques*

The majority of cases of SGS require surgical intervention. Subtle or mildly symptomatic grade I SGS may be following with nonoperative management and expected improvement with advancing age and size of the child. This is common for congenital low-grade SGS. For acquired and higher grade congenital SGS, surgical management is often required and based upon the degree of stenosis, its anatomic characteristics, and presence of inflammation. Techniques for subglottic expansion are broadly categorized as either endoscopic or open. Endoscopic dilation, with balloons or rigid dilators, is employed for low-grade soft tissue SGS (Figs. 45.5A and B).[36,37] The improved lumen size can then be determined by measuring it with the next larger endotracheal tube. The ensuing inflammation and healing from subglottic dilation will require repeat evaluation and possible dilatation at a later date under general anesthesia. In thick or long-standing fibrotic stenosis, mucosal incisions using cold steel or carbon dioxide laser can be performed in a radial fashion to augment the effect of dilation (Figs. 45.5A and B). Repeat dilatations are often required to achieve continued symptomatic improvement and a less severe stenosis. Intervals between dilatation increase during subsequent visits to the operating room but



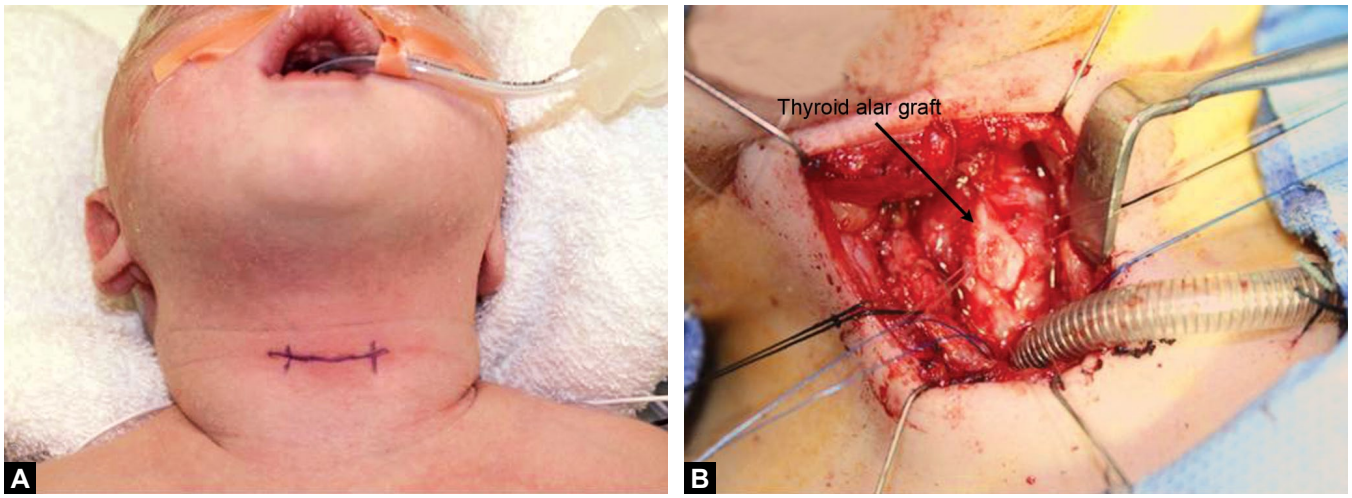

**Figs. 45.5A and B:** SGS intervention. Subglottic stenosis with (A) Radial scar band lysis; (B) Endoscopic balloon dilatation.

are necessary to achieve ultimately a larger, albeit scarred, subglottic diameter. When dilatation repeatedly fails in the persistently symptomatic patient, then open laryngeal augmentation is the next best step in management. Nonetheless, endoscopic dilatation can be employed in the postoperative maintenance of open airway procedures during the immediate and late phases of healing.[38-40]

### *Open Airway Reconstruction*

Endoscopic techniques are not routinely sufficient in treating cartilaginous and long-standing fibrotic stenosis.[41] First describe by Rethi and revisited by Cotton and Seid, the anterior cricoid split (ACS), is used for the relief of acquired or congenital stenosis in infants nonresponsive to endoscopic techniques.[42,43] The ACS is an open anterior neck procedure constituting a vertical midline incision of the anterior cricoid plate, lower third of the thyroid cartilage, and first tracheal rings.[43] The child is intubated with the next size larger endotracheal tube to stent the airway for several days as healing occurs between the opposing cartilage cuts. Although successful, the ACS has been replaced with the use of the thyroid alar graft.[44] A 3–4 mm × 6 mm graft is harvested from the superior lateral thyroid cartilage, and secured between the opposing cut cricoid plates to expand and stabilize the widened subglottic lumen (Figs. 45.6A and B). This laryngotracheoplasty (LTP) was first described by Forte and is best suited for young patients (< 18 months) not requiring more robust cartilage.[44] The ACS and the thyroid alar LTP are beneficial in children who otherwise would require tracheotomy for SGS. Success rates of decannulation are above 80%.[45-47] The primary health of the patient is important for success and the criteria for ACS and LTP with thyroid alar graft are listed in Table 45.2.

In older children with severe SGS (grade III and IV) laryngotracheal reconstruction (LTR or LTP) may be required with more robust cartilage. Autogenous costal cartilage grafts are considered the most effective graft for LTR and can be used to expand both the anterior and posterior cricoid plate, depending upon the degree and location of stenosis.[48] The technique used for LTR includes a horizontal skin incision and vertical split in the stenosis involving the cricoid cartilage, the tracheal rings, and the lower third of the thyroid cartilage. Once the airway is opened, the posterior cricoid plate may also be divided to allow for expansion. The grafts are measured and carved with superior and inferior tapered ends, replicating a boat, and leaving the perichondrium destined for the internal airway surface.[49] The grafts are then secured between the cut cricoid edges (Figs. 45.7A to D). In a single-stage approach, the airway is stented with an age-appropriately sized endotracheal tube for approximately 5 to 7 days. Repeat endoscopy is performed to help monitor the healing and graft coverage in weeks and months after the repair (Figs. 45.8A and B). In more complex patients, with concomitant airway or cardiopulmonary comorbidities, a tracheostomy below the repaired stenosis may be performed.[50] A stent is placed at the repaired subglottis above the tracheostomy and removed several weeks later. This is known as a double-stage LTP. Overall, success of LTP is determined by the ability to decannulate the child to provide normal upper respiratory tract function. Success rates vary depending upon the degree of stenosis.




**Figs. 45.6A and B:** Cricoid split. (A) Approach to anterior cricoid split in 8-month-old infant; (B) Laryngotracheoplasty with thyroid alar graft.

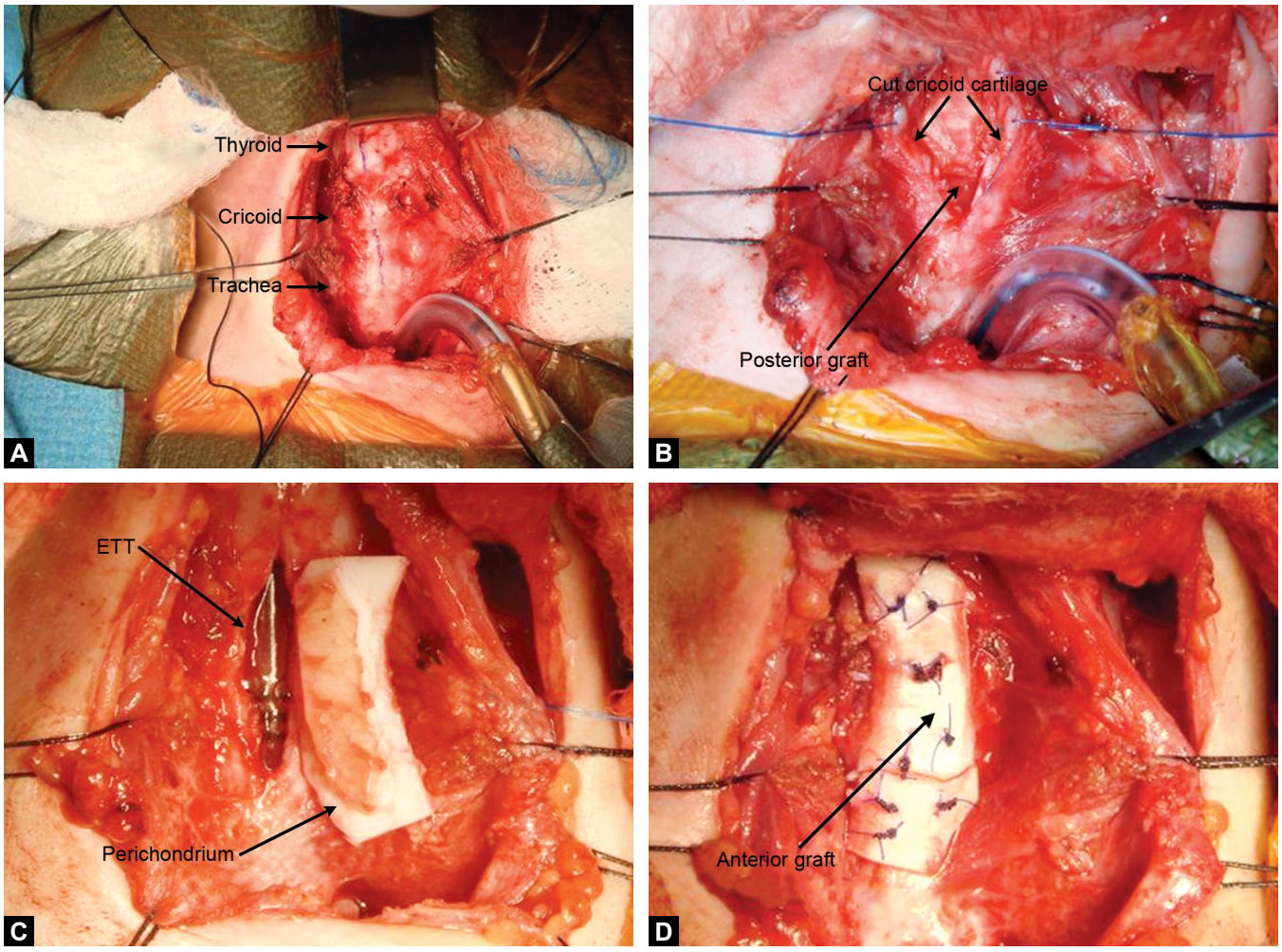
**Table 45.2:** Patient criteria for performing anterior cricoid split with or without thyroid alar laryngotracheoplasty

| |
|---|
| Extubation failure on at least two occasions secondary to laryngeal anatomy |
| Infant weight > 1500 g |
| No congestive heart failure in a month prior to open airway surgery |
| No ventilator support for 1–2 months |
| Minimal supplemental oxygen requirements (< 35% $FiO_2$) |
| Absence of acute upper or lower respiratory tract infections |
| Controlled aerodigestive tract conditions (GERD/LPR) |
| No need for antihypertensives |

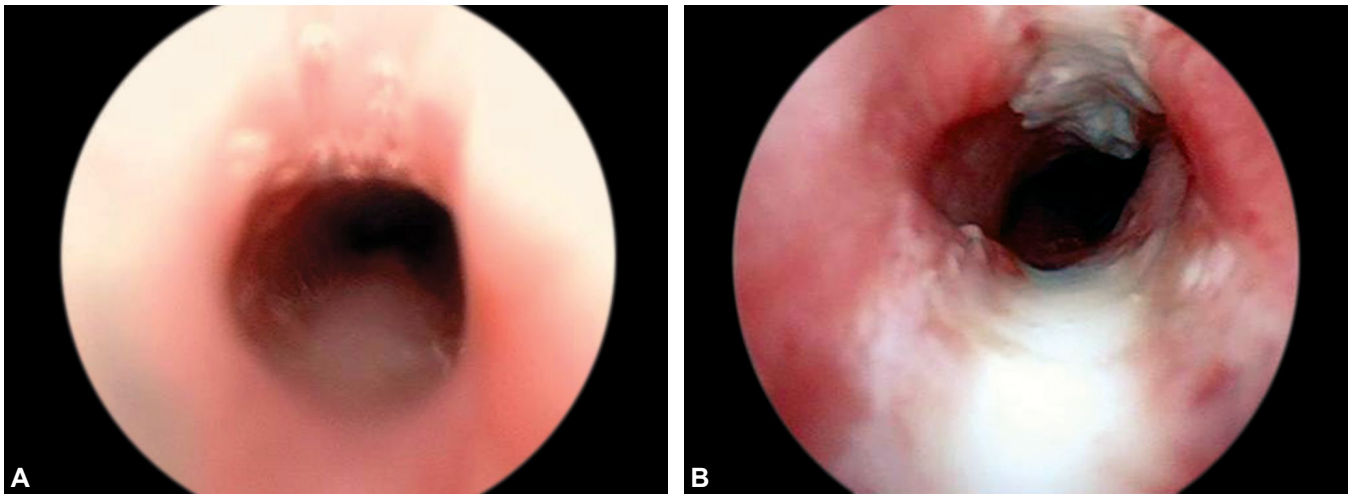
(GERD: Gastroesophageal reflux disease; LPR: Laryngopharyngeal reflux).

Overall, decannulation rates average 80% both single- and double-stage techniques. Multiple operations may be required for high-grade lesions.[34] Voice outcomes are now being analyzed.

Cricotracheal resection may also be employed as an alternative to LTR for severe congenital and acquired stenosis (grades III and IV) that begins at least 2 mm below the true vocal cords.[51,52] This technique involves resection of the anterior arch of the cricoid ring followed by thyrotracheal anastomosis. Although this procedure is particularly beneficial to patients with severe stenosis, it comes with a risk of anastomotic dehiscence, recurrent laryngeal nerve injury (< 5% of cases), and poor voice outcomes.[53] The cervical slide tracheoplasty is also an alternative open airway approach to expanding recurrent or long segment subglottic and tracheal stenosis.[54]




**Figs. 45.7A to D:** Laryngotracheoplasty. Laryngotracheal reconstruction in 3-year-old child with grade II subglottic stenosis. (A) Laryngotracheal dissection; (B) Vertical division of anterior cricoid and tracheal cartilage with posterior cricoid plate costal cartilage graft in place; (C) Anterior costal cartilage in boat shape with perichondrium demonstrated; (D) Anterior graft secured over ETT using 4.0 PDS sutures. (ETT: Endotracheal tube).




**Figs. 45.8A and B:** Postoperative laryngotracheoplasty. Endoscopic view of subglottic lumen in 3-year-old child (A) Before; (B) 7 days after anterior and posterior costal cartilage graft reconstruction. Mucosalization of grafts can be observed (white).

## LARYNGEAL CLEFT

### Background

First reported in 1792 by Richter, the laryngeal (laryngoesophageal) cleft is an anomalous communication between the posterior laryngotracheal complex and esophagus. It is a vertical defect in the septum that normally divides the airway from the esophagus. Although present at birth, a laryngeal cleft may not be detected for several years. Symptoms vary from mild aspiration to severe neonatal distress, depending on the extent of penetration into the airway. Thus, several classification schemes have been proposed with increasing severity associated with deeper vertical penetration. The most widely accepted classification of laryngeal clefts is that proposed by Benjamin and Inglis and later modified by Sandu and Monnier (Table 45.3).[55,56] Symptom severity and morbidity correlates with higher levels of classification.

Tucker and Maddalozzo proposed the Type 0 laryngeal cleft as a defect in the posterior cricoid plate with an intact interartenoid muscle and mucosa.[57]

Laryngeal clefts may be present in 1:10,000–1:50,000 newborns. They approximate 1% of all discovered congenital airway anomalies.[58] Among normal children treated for chronic aspiration this percentage of patients may be as high as 7%.[59] The more shallow the cleft, the greater the frequency in which it occurs. Type IV clefts are exceedingly rare but carry a significantly greater morbidity rate. Syndromes and other anomalies of the aerodigestive tract commonly occur with a laryngeal cleft.

**Table 45.3:** Classification of laryngeal clefts

| | |
|---|---|
| Type 0 | Submucosal cricoid defect |
| Type I | Interarytenoid defect to the level of true vocal folds or below but no defect in cricoid plate |
| Type II | Partial cricoid cleft<br>Below level of true vocal folds but not completely through cricoid cartilage |
| Type IIIa | Total cricoid cleft down to inferior border of cricoid plate completely through |
| Type IIIb | Posterior cleft extending into trachea but not below the level of the sternal notch |
| Type IVa | Cleft extending into intrathoracic inlet down to the carina |
| Type IVb | Extension of cleft into one mainstem bronchus |

### Etiology

Around 3–4 weeks' gestation, the trachea and esophagus share a common lumen as the respiratory tree arises from the ventral foregut. During its propagation caudally the trachea separates from the digestive tract with the simultaneous formation of tracheoesophageal septum. Laryngoesophageal clefts result from the failed fusion of the posterior septal endoderm and/or the mesoderm arising from the 4th and 6th branchial arches.[60] The exact mechanism by which this occurs is unclear. The majority of laryngeal clefts are believed to be sporadic occurrences. No specific toxin or uterine event has been linked to laryngeal clefts. However, syndromes associated with midline defects, including Optiz-G (Frias), Pallister Hall,

CHARGE, VATER, and VACTERL, increase the risk of having a laryngeal cleft. Autosomal dominant transmission of laryngeal clefts has been reported in some families but this is very uncommon.

## Clinical Presentation

Patients with posterior laryngeal clefts may present with copious secretions, aspiration, cyanosis while feeding, inspiratory stridor, choking, and/or recurrent pulmonary infections.[61] Naturally, the deeper the cleft, the more severe the symptoms, the earlier the presentation, and greater the risk of the cleft is to the patient. In cases of Type I clefts, infants may present with a weak cry and stridor. LM may mask the initial symptoms of a Type I cleft. Late identification of shallow clefts may be triggered by chronic aspiration, recurrent pneumonias (16–54%), and chronic cough (27–35%) in the toddler.

Type II–IV laryngeal clefts will invariably present in the newborn with respiratory distress, airway obstruction, and life-threatening pulmonary compromise. Early diagnosis and intervention are paramount for survival in these patients. Type IV clefts carry a 50% mortality rate.

Other aerodigestive anomalies occur in 16–68% of patients with laryngeal clefts. Associated airway conditions include LM, tracheomalacia, bronchomalacia, and tracheoesophageal fistulas (TEF).[59,62] Craniofacial anomalies, genitourinary, and gastrointestinal malformations, GERD, and functional subglottic stenosis are also common in patients with laryngeals clefts.

## Diagnosis

Chest radiographs, barium swallow studies, and esophagrams often predicate the diagnosis of a laryngeal cleft. These studies neither confirm nor deny the presence of a laryngeal cleft but may suggest its presence based upon evidence of acute or chronic aspiration and pulmonary inflammation. The diagnostic challenge occurs when radiographic swallow studies demonstrate persistent laryngeal penetration and aspiration of thin liquids in the normal child.[63] A discreet pattern of aspiration on swallow studies has not yet been correlated with shallow laryngeal clefts. Diagnostic flexible laryngoscopy can be performed in clinic to examine for supraglottic and vocal fold anomalies that may be associated with, or mask, laryngeal clefts such as LM and vocal fold immobility. Functional endoscopic evaluation of swallowing function can be performed in synchrony with flexible laryngoscopy. This endoscopic swallow study allows direct examination of the posterior larynx during the pharyngeal phase of swallowing and may assist in the diagnosis of a cleft.[64]

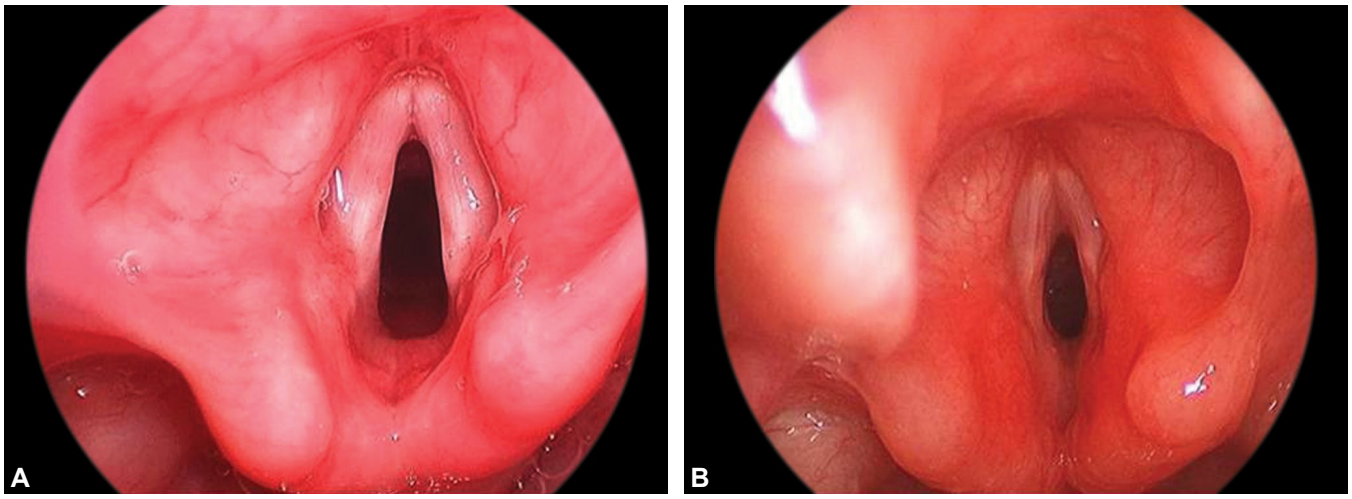
The gold standard for diagnosing a laryngeal cleft is rigid endoscopy with microlaryngoscopy and bronchoscopy under general anesthesia.[61] High-grade clefts (II–IV) are amenable to expedient diagnosis as evident by the defect and redundant mucosa between the arytenoid and cricoid cartilage. The confirmation and depth of a cleft is determined by passing a right-angled probe into the posterior defect. A Type I cleft is not as easily identified and may require additional clinical and diagnostic information to confirm its presence. A missed diagnosis during bronchoscopy with a delayed identification of Type I clefts can occur even in experienced hands. The average age at diagnosis of a Type I cleft is between 2 and 4 years.[65]

Bronchoalveolar lavage can provide evidence of chronic aspiration, by the lipid laden macrophage index, in an otherwise healthy child with a Type I cleft.[66] Similarly, an injection into the interarytenoid space with temporary filler may improve symptoms and swallow study findings if a Type I cleft is present.[67,68] The endoscopic difference between a Type I and Type II laryngeal cleft can be seen in Figures 45.9A and B. LM may also mask the presence of a Type I cleft on rigid diagnostic laryngoscopy.

Examination of the entire tracheobronchial tree and esophagus during endoscopy is important to rule out commonly associated anomalies such as TEF and tracheobronchomalacia.[69] Identifying and passing a thin probe or suction through a small posterior tracheal pouch may diagnose a simultaneous H-type TEF. A genetic consultation should be considered in any patient with a high-grade laryngeal cleft.

## Management

The management of laryngeal clefts consists predominately of endoscopic or open surgical repair. The objective behind any treatment algorithm is to properly diagnose the cleft and prevent the risks of acute and chronic aspiration. Generally speaking, open surgical techniques are employed for Type III and Type IV laryngeal clefts as exposure and access to deep intrathoracic structures is endoscopically difficult. The approach to open repair is largely depending upon the skill and experience of the surgeon. The most common technique is the anterior translaryngotracheal approach. This approach provides exposure of the cleft via a midline vertical incision of the cricoid, trachea, and thyroid cartilages. A complete




**Figs. 45.9A and B:** Laryngeal cleft. Endoscopic view of (A) Type 1; (B) Type II laryngeal clefts. Notice depth of interarytenoid space relative to posterior insertion of true vocal fold to the vocal process.

thyrotomy may be required for adequate exposure. Alternatively, a laryngeal cleft can be accessed by a lateral posterior pharyngotomy incision. The advantage of the anterior approach is a wide-angled exposure and reduced risk to the recurrent laryngeal nerves. The repair is performed in a two-layer closure. Some surgeons offset the suture lines. An interposition graft is frequently employed for long clefts to provide additional support to the repair site. Sternocleidomastoid muscle, fascia, perichondrium, costal cartilage, and periosteum have been used with similar efficacy. Redundant mucosa often needs to be trimmed to prevent postoperative tracheomalacia with posterior laryngotrachea obstruction. The airway is controlled during the procedure with intubation at the inferior aspect of the tracheotomy.[70]

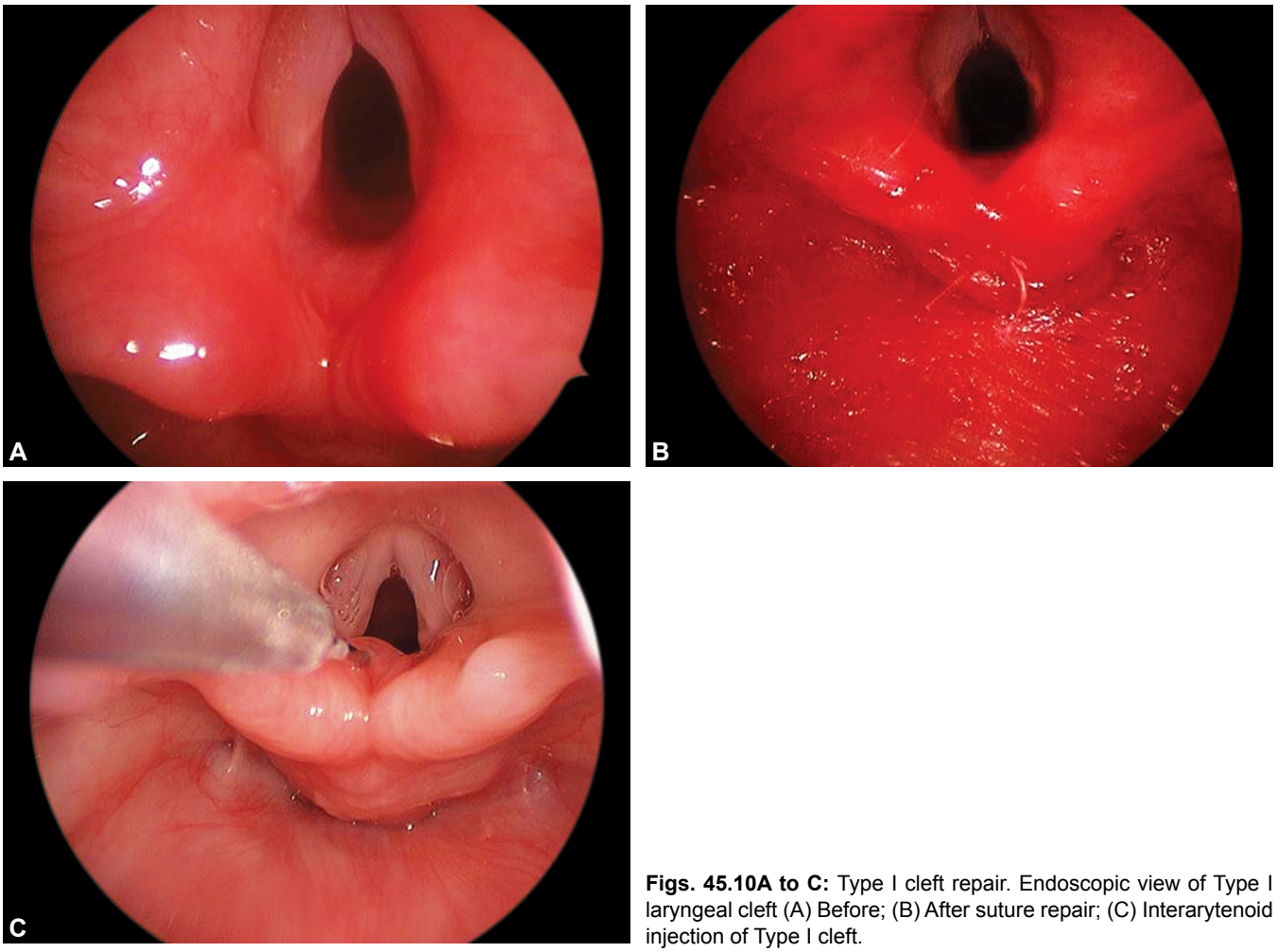
Type I and II, and sometimes Type III clefts, can be repaired endoscopically. Endoscopic repair of a Type III cleft again is dependent upon surgeon skill and the underlying health of the patient. Reflux precautions and medical therapy is preferred to allow for appropriate healing of the tenuous repair. Nissen fundoplication may be required before surgery in patients with severe LPR or recurrent aspiration pneumonia.[69] Type I and II endoscopic repairs have complete closure success rates and improved aspiration above 80%.[62] Type I clefts may be managed initially with thickened liquids, upright feeding, and antireflux medications as symptoms may improve with enhanced age and coordination of swallowing around the shallow defect. Interarytenoid injections, with Gelfoam or hydroxyapatite gel, have gained recent favor to help diagnose a cleft and predict the outcome of future repair (Figs. 45.10A to C).[67,68]

Endoscopic repair is generally performed under general anesthesia with spontaneous respiration. The interarytenoid and cleft mucosa is excised or ablated using cold knife or $CO_2$ laser, respectively. It is paramount to remove every fragment of mucosa prior to suture placement as retained mucosa can lead to recannulation, poor repair, or recurrence of the cleft. Double layer closure has been advocated but single-layer closures is more feasible and as successful using simple interrupted or figure-eight dissolvable sutures (Figs. 45.10A to C). The knots are left extraluminal.

## SUBGLOTTIC HEMANGIOMAS

### Background

Infantile subglottic hemangiomas (SGH) are benign, yet potentially fatal, vascular anomalies arising from endothelial cell proliferation of hemangiopoetic cells of placental or embryonic origin.[71,72] These rare neoplasms account for 1.5% of all congenital laryngeal anomalies. Like their cutaneous counterparts, which occur in 4–5% of all infants, SGH have a 2:1 female to male propensity.[71] They arise within the first few weeks to months of life, undergo a rapid growth phase during the first 6–8 months, and typically stabilize between months 10 and 18.[73] By 5 years of age, most cutaneous and SGH involute. While the inciting factors for proliferation are unknown, the proliferative phase is evident by increased levels of vascular endothelial growth factor and basic fibroblast growth factor. Involution is the result of endothelial apoptosis, angiogenesis downregulation, and tissue inhibitor metalloproteinase invasion.



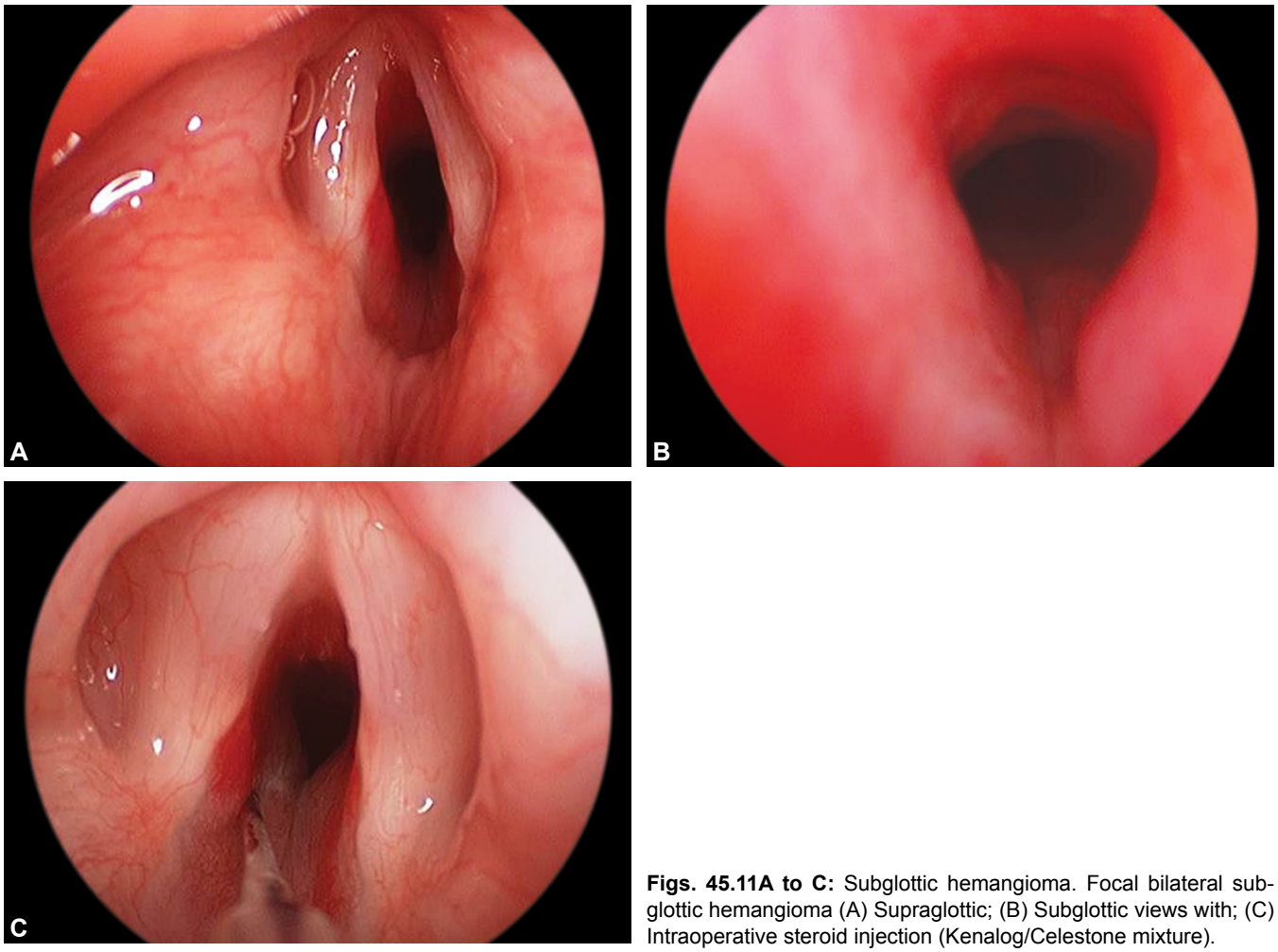

**Figs. 45.10A to C:** Type I cleft repair. Endoscopic view of Type I laryngeal cleft (A) Before; (B) After suture repair; (C) Interarytenoid injection of Type I cleft.

## Clinical Presentation

Subglottic hemangiomas most commonly produce biphasic stridor, although a croup-like cough, cyanosis, and hoarseness may also be present. Airway obstruction is slow and progressive during the first few months of life during the hemangioma's proliferative phase. Upper respiratory tract infections or crying will worsen and intensify these symptoms. Cutaneous hemangiomas are present in approximately 50% of cases, although the reported incidence of SGH in children with cutaneous lesions is only 1–2%.[74] In 50–60% of infants with segmental hemangioma in the beard distribution (trigeminal nerve-V3), an SGH will be present. Importantly, most cases of SGH exhibit symptom resolution after the first year of life once involution begins. However, expeditious diagnosis and treatment is of great importance during the hemangioma's rapid growth within the narrowest part of the newborn larynx.[25]

## Diagnosis

Like other laryngeal anomalies, a thorough history and physical examination should direct the working diagnosis. Awake flexible laryngoscopy in clinic will help rule out other laryngeal anomalies and may demonstrated evidence of a subglottic mass. Direct laryngoscopy and bronchoscopy is required, however, to confirm the diagnosis. A compressible submucosal lesion is consistent with an SGH. Nonobstructive segmental supraglottic and hypopharyngeal cutaneous staining may also be present in patients with segmental facial hemangiomas. An SGH will range in color from blue to red on the basis of the degree of overlying mucosa and vascularity. Focal lesions are most commonly located posterolaterally and can be bilateral (Figs. 45.11A to C). In even mildly symptomatic patients with V3 beard distribution infantile hemangiomas, endoscopic laryngeal evaluation is recommended.[75] If




**Figs. 45.11A to C:** Subglottic hemangioma. Focal bilateral subglottic hemangioma (A) Supraglottic; (B) Subglottic views with; (C) Intraoperative steroid injection (Kenalog/Celestone mixture).

endoscopic evidence is equivocal, biopsy may be required though this carries a risk of hemorrhage. Plain film radiographs of the neck may exhibit the pathognomonic finding of asymmetric subglottic airway narrowing.[72] A magnetic resonance imaging (MRI) will likely yield additional diagnostic support including the extent of paralaryngotracheal disease.

## Management

The majority of SGH will require intervention. In a rare few, SGH may be subcordal and not obstruct the subglottic lumen enough to be symptomatic. Similarly, segmental lesions above subglottis are typically flat and nonobstructive. These lesions may be identified and observed until involution. Tracheotomy is a surgical option for bypassing large SGH as involution is anticipated. However, this approach is rarely employed as less invasive surgical and medical options have emerged.

Treatment options for SGH include pharmacologic, endoscopic, and surgical approaches.[76] Pharmacologic agents include propranolol and systemic or direct intralesional steroids. Potassium titanyl phosphate and carbon dioxide ($CO_2$) laser ablation have good outcomes but require repeat procedures and may pose a risk of subglottic stenosis if perichondrial injury occurs.[77]

Propranolol is a nonselective beta-blocker serendipitously discovered to induce regression of cutaneous hemangiomas at subclinical cardiac doses (2 mg/kg/day). Propranolol is also effective and employed in the management for the majority of SGH.[78,79] Treatment with either propranolol alone or in combination with intraoperative steroid injection has supplanted other treatment modalities for SGH (Figs. 45.11A to C). Open resection of large and obstructive focal SGH may be necessary and successful for lesions nonresponsive to pharmacologic and endoscopic approaches. Extralaryngeal expansion

with LTP using a thyroid alar graft will simultaneously augment the subglottic lumen size.

## CONGENITAL LARYNGEAL WEB

Congenital laryngeal web is a rare entity that can present with dysphonia or aphonia, stridor, or severe respiratory distress, depending on the type and severity of the web. Failure of recanalization of the fetal airway at around 8–10 weeks' gestation is thought to be the embryologic basis for a spectrum of congenital laryngeal anomalies, including webs, stenosis, and atresia.[80] Laryngeal webs can occur in the posterior glottis but more commonly involve a portion of the anterior glottis with extension into the subglottis.[81] The type, severity, and associated symptoms of the laryngeal web dictate the need for surgical management of these congenital anomalies. Cohen devised a classification system (Table 45.4) for laryngeal webs that can be helpful in evaluating and managing these patients.[70]

Laryngeal web should be suspected in a child with hoarseness, weak cry, or aphonia since birth. Cyanotic spells, stridor, and/or dysphagia can also be seen. Flexible fiberoptic laryngoscopy is used for initial evaluation with direct microlaryngoscopy and bronchoscopy to confirm the diagnosis (Figs. 45.12A and B).[70]

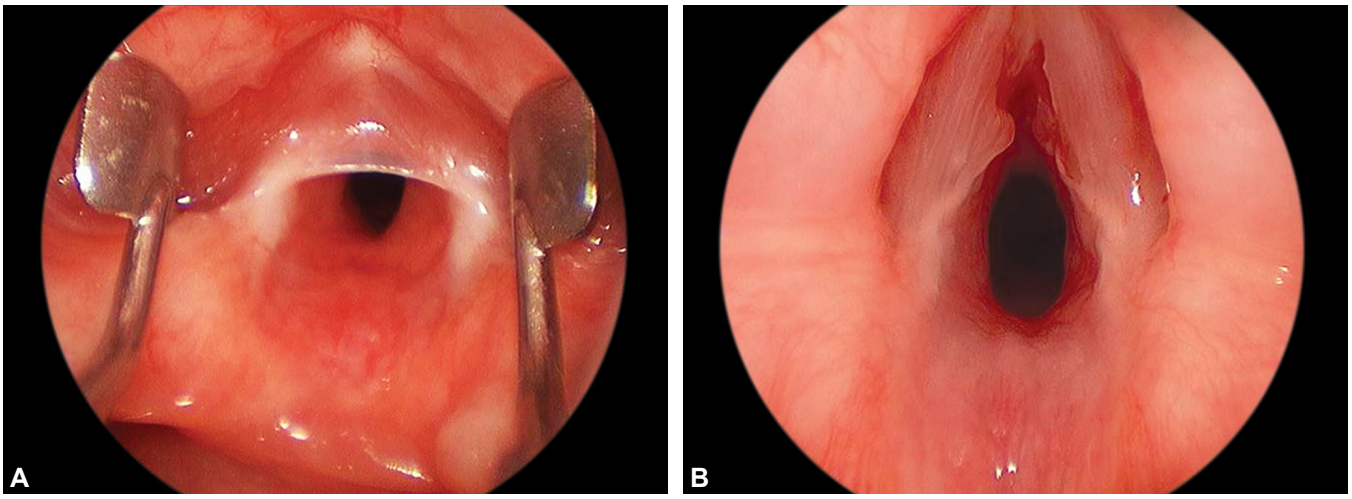
**Table 45.4:** Cohen classification of laryngeal webs

| | |
|---|---|
| Type I | Involves £ 35% of the glottis with minimal or no subglottic extension |
| Type II | Involves 35–50% of the glottis with thick anterior webbing extending to the subglottis |
| Type III | Involves 50–75% of the glottis, often with vocal cord and cricoid abnormalities |
| Type IV | Involves 75–90% of the glottis, with significant vocal cord abnormalities and cricoid narrowing. Usually requires a surgical airway |

A finding of laryngeal web should prompt work-up for other congenital anomalies, including cardiovascular and chromosomal anomalies. Several reports have suggested the association of congenital laryngeal web with chromosome 22q11 deletion, which can lead to various phenotypes such as DiGeorge syndrome and velocardiofacial syndrome (VCFS).[82] Miyamoto et al. presented a series of 17 patients with anterior glottic web who underwent genetic testing by standard fluorescence in situ hybridization analysis. About 11 of 17 (65%) patients were found to have chromosome 22q11 deletion and subsequently diagnosed with VCFS.[83] Cardiovascular anomalies are common among patients with chromosome 22q11 deletion and include atrial septal defect, ventricular septal defect, aortic arch abnormalities, and vascular rings.[82] Based on these associations, it is recommended that patients diagnosed with anterior glottic web undergo genetic screening for 22q11 deletion and if positive should undergo cardiovascular evaluation.

Treatment of laryngeal webs is surgical and ranges from endoscopic microlaryngeal techniques to open laryngofissure and reconstruction with costal cartilage grafting.[80,84] Surgical treatment plans should be individualized to optimize outcomes.

Endoscopic techniques are more often employed in laryngeal web Types I and II and can be delayed until 3–4 years of age if symptoms are minimal.[26] In patients with thin anterior glottic webs (Type I), endoscopic




**Figs. 45.12A and B:** Laryngeal web. Anterior Type II laryngeal web (A) Before; (B) After endoscopic division.

division with cold steel or $CO_2$ laser can be successful in one stage (Figs. 45.12A and B). Type II webs may require a staged procedure with serial dilations with or without keel placement. Endoscopic and open techniques have been used for keel placement. Tracheotomy may or may not be required while the keel is in place.

Type III and IV laryngeal webs often require initial placement of a tracheotomy to secure the airway with delayed surgical reconstruction. Open LTR techniques are used to address the subglottic stenosis component. Laryngofissure is performed with division of the web and the subglottic stenosis. Rib cartilage grafts are used as needed for reconstruction of the cricoid defect. A silastic keel stent is inserted for stenting, or in the case of single-stage LTR an endotracheal tube is left in place for stenting and no tracheotomy is required at the conclusion of the procedure.[80]

Posterior glottic webs usually present with stridor and symptoms similar to bilateral vocal cord paralysis due to poor vocal fold abduction. Management is similar to that of bilateral vocal fold paralysis and includes tracheotomy, repeated division and dilation of the web, arytenoidectomy, and LTR with posterior cartilage graft augmentation.[85]

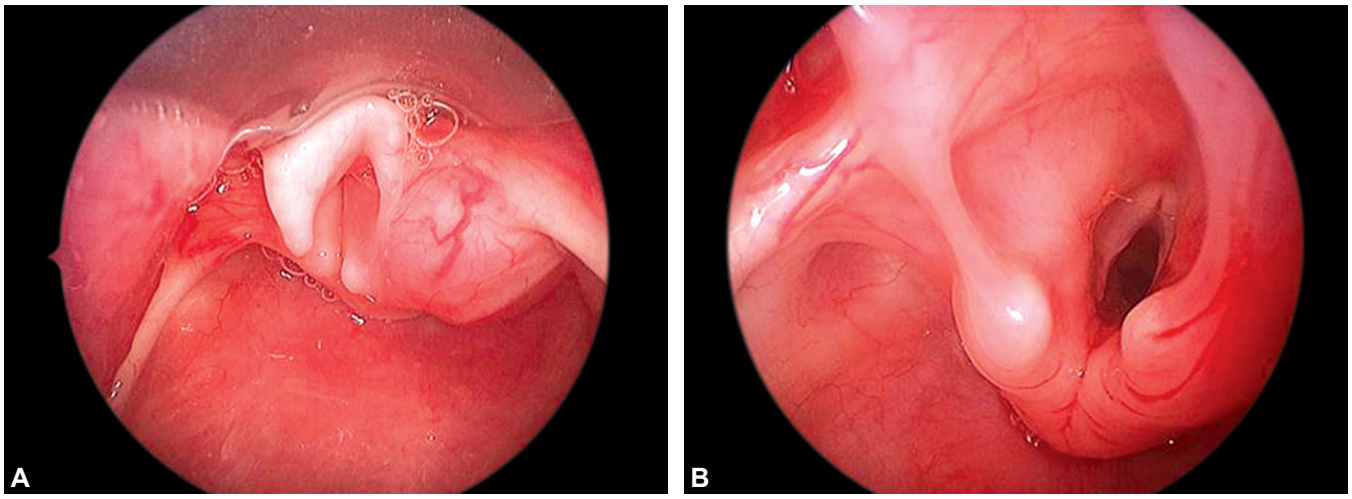
## CONGENITAL LARYNGEAL ATRESIA

Laryngeal atresia represents complete failure of recanalization of the fetal larynx during embryogenesis and presents at birth with aphonia and severe respiratory distress. Congenital high airway obstruction syndrome (CHAOS) is marked by enlarged fluid-filled lungs, dilated distal airways, polyhydramnios, and fetal ascites on prenatal ultrasound and/or MRI and is an indicator of laryngeal atresia.[86] Failure to establish a surgical airway via tracheotomy immediately upon birth can result in death of the infant. Prenatal diagnosis of CHAOS with ultrasound and/or MRI allows for planning of delivery by EXIT (ex-utero intrapartum treatment) to airway, in which a tracheotomy is performed while neonatal oxygenation is maintained by placental support.[87] Infants with laryngeal atresia often have other congenital anomalies including tracheoesophageal fistula, esophageal atresia, renal and/or ureteral agenesis, and duodenal atresia, making morbidity and mortality rates high.[88] Definitive surgical treatment usually involves delayed LTR. However, there has been report of successful endoscopic management of laryngeal atresia.[87]

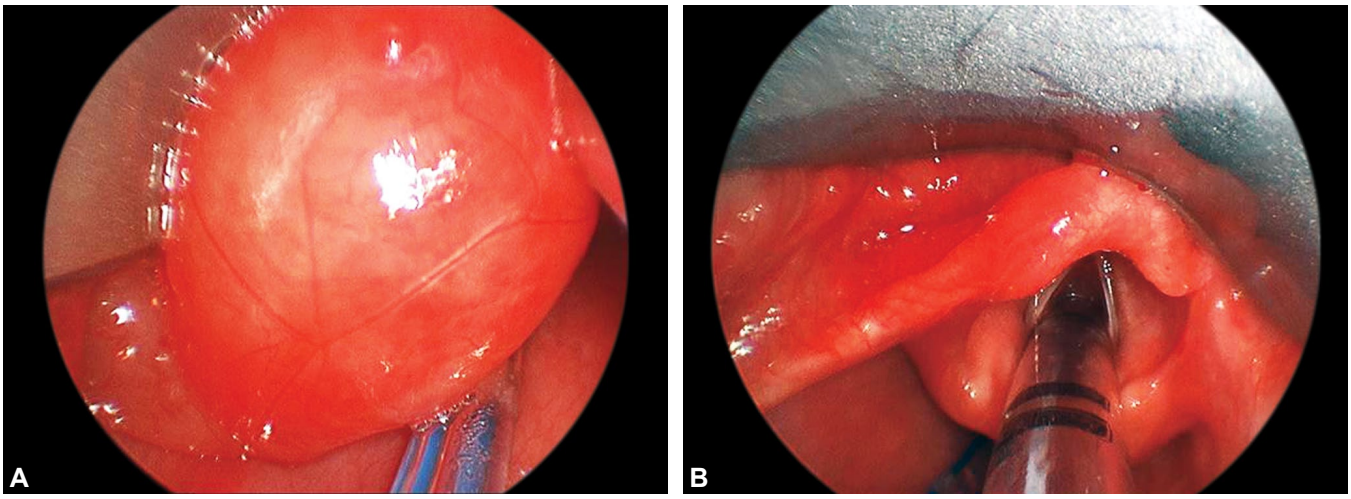
## CONGENITAL LARYNGEAL CYSTS

Congenital laryngeal cysts are a rare cause of stridor, dysphonia, airway obstruction, and dysphagia in infants and children. Several classification systems have been proposed for congenital laryngeal cysts on the basis of the location, extent, histology, and embryologic tissue origin.[71] Surgical treatment depends on the cyst type and severity of symptoms.

Congenital saccular cysts are fluid-filled cysts involving the laryngeal saccule, a small outpouching at the anterior end of the laryngeal ventricle between the false vocal fold, epiglottis, and thyroid cartilage (Figs. 45.13A and B).[89] Saccular cysts are submucosal lesions that can extend laterally into the false fold and aryepiglottic fold or anteriorly into the glottic lumen causing progressive




**Figs. 45.13A and B:** Right laryngeal saccular cyst (A) Before; (B) After endoscopic reduction.




**Figs. 45.14A and B:** Vallecular cyst of newborn airway (A) Before; (B) After excision.

airway obstruction.[90] Diagnosis is made by microlaryngoscopy and the airway is secured, sometimes requiring tracheotomy. Endoscopic aspiration, marsupialization, or excision can be used to treat these lesions; however, recurrence after multiple endoscopic treatments is not uncommon and if encountered necessitates open excision. Radiographic imaging is not necessary for initial diagnosis but may be helpful for surgical planning if open excision is required.[91,92]

A laryngocele is an air-filled dilation of the laryngeal saccule that communicates with the laryngeal lumen.[93,94] Laryngoceles can be classified as internal (medial to the thyrohyoid membrane) or external (extending through the thyrohyoid membrane into the neck). Presenting symptoms include dysphonia, dysphagia, respiratory distress, and neck swelling that may be intermittent and increase with crying.[94] Microlaryngoscopy is diagnostic and radiographic imaging (CT or MRI) is helpful in evaluating these lesions and guiding surgical treatment. Endoscopic marsupialization may be used for small internal laryngoceles while open cervical approaches are favored for larger external laryngoceles.[89]

A mucus retention cyst at the base of the tongue is known as a vallecular cyst (Figs. 45.14A and B). Vallecular cysts are smooth, submucosal lesions that may be present at birth and enlarge with time causing stridor, dyspnea, and dysphagia.[95] Diagnosis is usually with flexible endoscopy in the clinic or microlaryngoscopy in the operating room as part of the work-up for noisy breathing and/or feeding difficulties. The differential diagnosis for a vallecular cyst should also include a thyroglossal duct cyst that arises from the foramen cecum and can present very similarly to a vallecular cyst. Surgical treatment is necessary and can usually be performed endoscopically and sometimes in conjunction with a supraglottoplasty. Endoscopic marsupialization is an option; however, complete excision is favored for large with cold knife or $CO_2$ laser.[96]

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CHAPTER

# 46

# Congenital and Acquired Tracheal Anomalies

***Nathan Gonik, Lee P Smith***

## INTRODUCTION

Few things are more alarming to a parent than a child in respiratory distress. When a physician encounters an airway obstruction, the sense of urgency and concern is shared by everyone caring for that child. Tracheal anomalies often present with distressing features soon after the onset of life. Biphasic stridor, dyspnea, and failure to thrive are hallmarks of this disease spectrum and include pathologies of tracheal stenosis, tracheomalacia, and tracheoesophageal fistulas (TEFs).

The primary concern in treating these patients is establishing a safe airway. Temporizing measures may be necessary and can potentially avert hypoxia and devastating consequences. Without a known diagnosis, attempts should still be made to improve respiration even before completing a physical examination. Prone or lateral positioning with head elevation and neck extension may alleviate compressive and dynamic tracheal obstructions. Inhaled oxygen, nasal continuous positive pressure ventilation or a combination of helium and oxygen (Heliox) may improve respiration and air exchange. Placement of a small endotracheal tube can also facilitate ventilation and possibly bypass known stenoses. Venturi jet ventilation, tracheotomy, and bronchoscopy may be necessary, and the threshold should be low to move the patient to the operating room to evaluate and manage a young patient. Once the airway is secured, definitive treatment can be planned and tailored to each patient's unique pathology.

Major tracheal surgery was once unfathomable. In 1869, Thomas Holmes suggested that an attempt "ought not, I think, be made" to repair a TEF with esophageal atresia (EA).[1] During the 1930s and1940s, reports of successful transcervical and transthoracic approaches to the pediatric trachea began to surface. Techniques popularized by Ladd, Sprague, and Haight were refined and modified with improving survival.[48] With more sophisticated and reliable pediatric anesthesia, the practical indications for pediatric tracheal surgery have vastly expanded. More recently, the focus has shifted toward restraint and trying to identify patients that may be successfully treated endoscopically or without any surgical intervention. Every child and every airway is unique. The same anomaly in two different children may lead to entirely different outcomes. Understanding the anatomy and development of these anomalies will afford the pediatric otolaryngologist the opportunity to choose the best treatment regimens for the individual child's development.

## ANATOMY, PHYSIOLOGY AND EMBRYOLOGY

### Anatomy and Physiology

On a basic level, the trachea houses the column or air entering and exiting the lungs. However, the trachea is more than just a conduit for air. It is an organ tasked with allowing controlled respiration, protection from aspiration, and clearance of secretions. Contained within the visceral compartment of the neck, it continues into the mediastinum surrounded by several important structures. The trachea begins at the inferior aspect of the larynx, extending from the cricoid cartilage to the carina and the

takeoff of the bronchi. The thyroid gland and thymus rest against its anterior surface. The innominate artery also courses across the anterior trachea en route to the right upper extremity. Posteriorly, the trachea rests against the esophagus and vertebral column. It is lined with a ciliated pseudostratified columnar respiratory epithelium with mucous glands dispersed throughout.

The trachea is composed of 15–20 U-shaped cartilaginous rings that are joined posteriorly by a membranous portion encompassing the trachealis muscle. Normal development results in a cartilaginous to membranous (C:M) circumference ratio of 3–4:1.[2,3] Maintaining this ratio affords the trachea some dynamic malleability with normal respiratory airway pressures while still maintaining its patency. If this ratio is too high, the absence of an adequate membranous trachea leaves a narrow, rigid trachea prone to stenosis. With a relative absence of cartilage or widened membranous portion, the weakened trachea may collapse with respiration. Dynamic tracheal motion also helps maintain pulmonary airway pressures and clear secretions during expectoration.

Poiseuille's law delineates that resistance within a column is inversely related to the radius (Fig. 46.1).[4] Small changes in the tracheal caliber can have a significant impact on breathing. This is particularly true in neonates or premature children who may have tracheal diameters of 4–6 mm compared with 17 mm in adults. Even 1 mm of stenosis can lead to 30–45% less surface area and even greater resistance to airflow. Patients generally become symptomatic when the stenosis compromises 30–50% of the airway and dyspnea presents with occlusion of 75% of the cross-sectional area.[4] Aside from caliber, pediatric and adult tracheas have other important differences. Until the larynx descends during the first year of life, the trachea sits higher in the neck and will begin at the level of the second or third cervical vertebrae. During this period, the trachea will end higher in the thoracic cavity, potentially allowing the carina to be pulled up into the neck with appropriate traction.

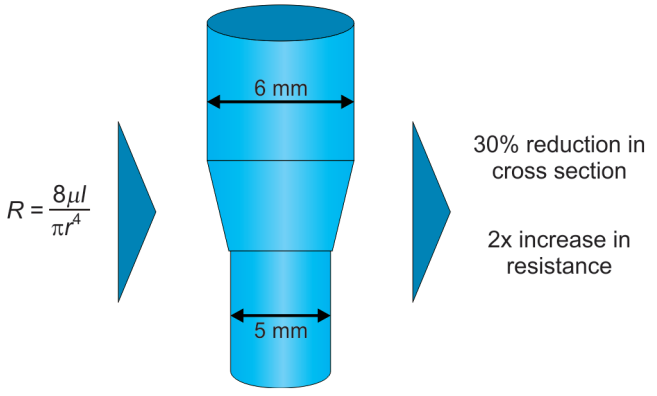



**Fig. 46.1:** Poiseuille's law as it applies to the pediatric trachea. This illustration demonstrates how a change in the tracheal radius affects the flow of air. Resistance is inversely related to radius$^4$. Even a small reduction of the cross-sectional area can lead to a dramatic change in resistance and air flow.

The trachea has a rich blood supply that is fed by branches of the inferior thyroid, intercostal, internal thoracic, phrenic, bronchial, and internal mammary arteries.[2,5] The tributaries off of these vessels join the trachea at its lateral edges to form a submucous plexus. Although it is a robust vascular system with considerable redundancy, tracheal blood supply is vulnerable to disruption. The mean capillary pressure within the venous plexus is 20 mm Hg and intraluminal compression with cuffs or balloons can result in a devascularization injury to the mucosa and cartilage. Strictures can be seen as early as 36 hours after intubation and may propagate expansive inflammatory and fibrotic growths.[2] Also, due to the lateral approach of feeding vessels, when mobilizing the trachea surgically, care must be taken to avoid lateral dissection and devascularization.

## Embryology

Congenital tracheal anomalies are the result of a disruption early in the embryologic development of the airway. The early embryo consists of the three primordial germ layers: ectoderm, mesoderm, and endoderm.[2] Through a series of folds, the endoderm forms a tube that will become the primitive foregut. During the 4th week of embryogenesis a bud forms at the ventral aspect of the foregut that differentiates into the epithelial lining of the airway. As this bud separates from the foregut, it descends from the primitive pharynx caudally, eventually branching into the bronchi and alveoli (Fig. 46.2). Mesoderm migrates along this endodermal tube forming the cartilaginous rings, muscles, and connective tissues of the trachea and esophagus by the 8th week. The mesoderm will eventually surround the trachea and divide it completely from the dorsal foregut. This is a critical point in the development of the trachea. Disruptions in the formation of the tracheoesophageal septum result in the majority of intrinsic congenital tracheal anomalies. As it is difficult to study human embryos at this developmental stage, there is considerable controversy regarding the exact mechanisms of these disruptions.

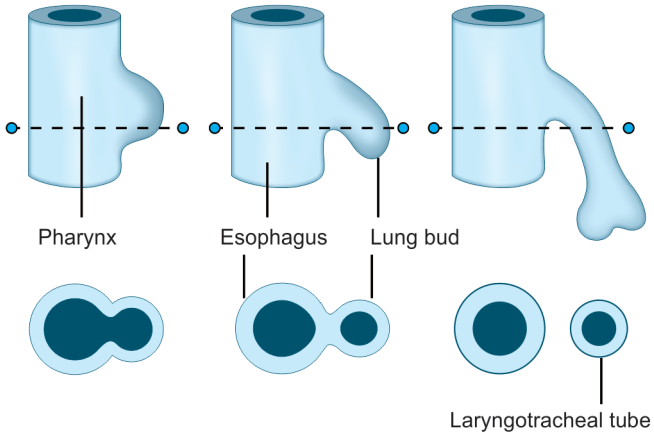



**Fig. 46.2:** Embryologic development of the trachea. This illustration demonstrates the emergence of the tracheal bud from the foregut. As it grows, the tracheoesophageal septum is formed, dividing the trachea and esophagus. This tube extends caudally and will give rise to the bronchi and pulmonary tissue.

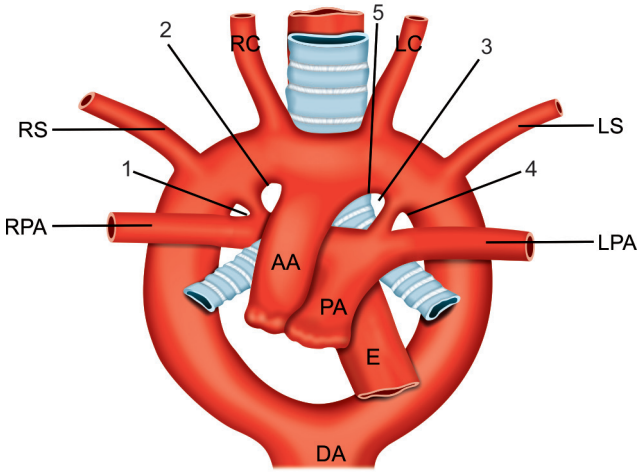



**Fig. 46.3:** Edwards double arch model. Edwards devised a theoretical double aortic arch model that he used to predict vascular anomalies. According to this model, in normal development, there is a break or involution at site #1 and the right ductus will involute. This results in a dominant left arch and a normal branching pattern. A break at #2 would separate the right subclavian artery from the left arch and necessitate an anomalous origin. A break at #3, #4, or #5 will disrupt the left arch, leaving a dominant right arch as well as other associated anomalies.

Classically, it is thought that lateral ridges develop longitudinally along the foregut and fold medially to fuse in the midline creating a septum. These folds have been identified in chick embryos and their disorderly formation and movement cause improper tracheoesophageal separation and fistulous tracts.[6] Other studies in rat embryos have identified areas of programmed cell death at the lateral epithelial edges.[7] Selective apoptosis in these areas lead to reshaping and remodeling of foregut structures, eventually dividing the trachea and esophagus. Other theories focus on the rapid caudal extension of the respiratory bud and the migration of the mesenchyme along these structures. Regardless of the mechanism, it is understood that anomalies disrupting the growth and separation of the tracheal column can result in the development of tracheal stenosis, fistulae, malacia, or agenesis. Errors that occur at the 4th week are likely to cause more drastic changes resulting in tracheal agenesis or EA. Those that occur later in development are more likely to affect peripheral mesodermal structures and result in stenosis and fistulae.

As the trachea is forming, the fetal cardiovascular system is beginning to develop. Initially, the fetus forms a dorsal and a ventral aorta emanating from the aortic sac. The two vessels are connected by six arches bilaterally. During the 4th week of development, the aortae fuse. This results in a single aorta with six joining arches that encircle the primitive trachea and esophagus. Edwards described how the inappropriate or absent involution of these arches can lead to varying degrees of tracheal compression

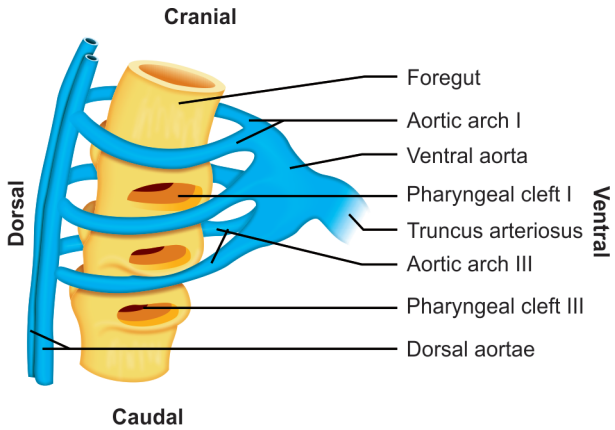



**Fig. 46.4:** The creation of a vascular ring. Depiction of the aortic arches wrapping around the foregut structures as the dorsal and ventral aortae fuse. Without appropriate involution, circumferential narrowing is inevitable.

(Fig. 46.3).[8] In normal development, the 1st, 2nd, 5th, and right 4th arch vessels involute, freeing the esophagus and trachea (Fig. 46.4). Table 46.1 describes the eventual outcomes of each of the six aortic arches after normal development.[9] Errors in 4th arch development lead to the formation of a complete ring, whereas those affecting the 6th arch generally do not cause circumferential compression. The remaining vessels form the normal anatomy consisting of a left-sided aortic arch and descending

**Table 46.1:** Normal aortic arch development

| *Aortic arch* | *Eventual structural outcome in normal development* | |
|---|---|---|
| | *Right* | *Left* |
| 1 | Internal maxillary artery | |
| 2 | Middle meningeal artery | |
| 3 | Internal/external/common carotid artery | |
| 4 | Subclavian artery | Aortic arch |
| 5 | Disappears | |
| 6 | Right pulmonary artery | Ductus/ligamentum arteriosus, left pulmonary artery |

aorta. With normal development, the branches of the mature aortic arch are the innominate, left carotid, and left subclavian arteries from right to left. The right ductus arteriosus should involute and the left ductus runs between the left pulmonary artery and the descending aorta. Displacement or anomalous origins of these vessels can compress the surrounding mediastinal structures.

## TRACHEAL STENOSIS

### Presentation

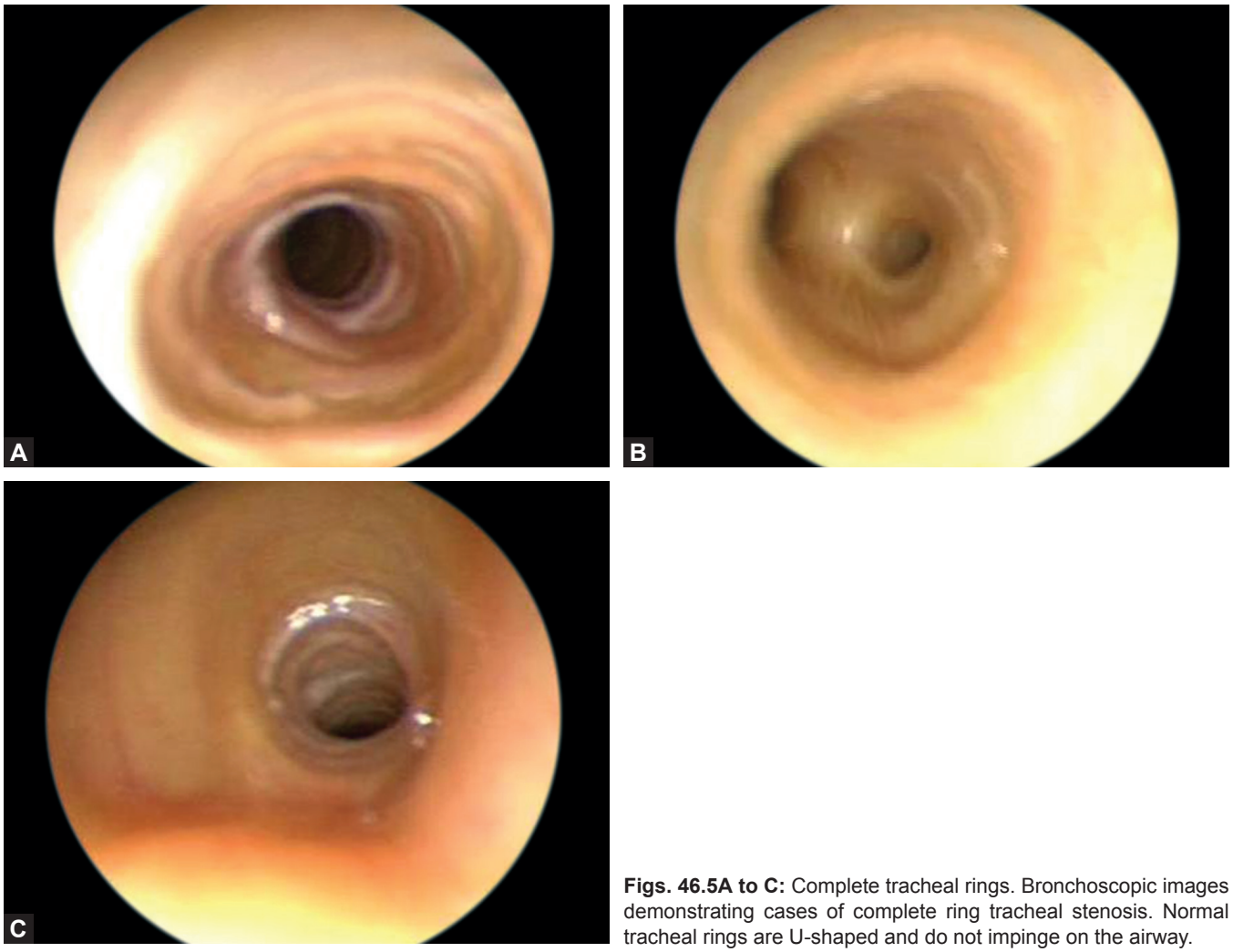
The infant larynx is cone shaped, widening at the glottis, and reaching its apex at the cricoid cartilage. From this point, the airway is generally cylindrical until the division of the bronchi. The trachea may be as narrow as 4 mm at birth and grows proportionately to the child's age and weight, reaching adult dimensions at around 12-14 years old. The term tracheal stenosis encompasses all intrinsic pathologies that create a static narrowing of the cylindrical tracheal lumen. Congenital tracheal stenosis is rare with an incidence of 1 in 64,500 live births and accounts for 1% of all laryngotracheal stenoses.[2] Most of these children are symptomatic shortly after birth with 90% presenting by 1 year of age.[10] Classically, they present with a "washing-machine" breathing pattern characterized by wet biphasic stridor. They may also complain of a dry brassy cough, recurrent respiratory infections, and varying degrees of dyspnea. Still, as many as 50% of cases are identified incidentally while investigating other anomalies (Figs. 46.5A to C). Acquired stenoses have a more variable presentation and are caused by scar formation after prior tracheal trauma. Table 46.2 compares the clinical presentation and management options for congenital and acquired tracheal stenosis and malacia. Stenosis manifests with a higher C:M ratio and a fixed narrowing without external compression. Malacia has a lower C:M ratio and may be caused by external compression. Both pathologies can be congenital or acquired in nature. Recently, the incidence of acquired airway stenosis in intubated neonates has dropped remarkably from 20% to 1–8%.[11] Although the etiology is not entirely clear, it is likely due to multiple factors including newer endotracheal tubes with smaller, softer walls, and using low pressure cuffs or avoiding cuffed tubes when possible. Better patient positioning and reflux management have also likely contributed. Acquired stenoses are still far more common than congenital.

### Classification

It is important to describe each tracheal stenosis accurately. Many classification schemes have attempted to discern between a variety of features. Table 46.3 outlines three classification systems commonly used to describe tracheal stenosis. Each system focuses on a different aspect of the stenosis. While Ho and Koltai's system is more of a binary descriptive model, the others are used to determine the risk and prognosis related to a patient within each subset. In 1964, Cantrell and Guild categorized tracheal stenoses as:

- Generalized—affecting the entire trachea
- Funnel shaped—with tapering of the tracheal lumen until a point of maximal narrowing
- Segmental—with a focal area of tracheal narrowing.[12]

Blumer noted that 20% of cases are generalized, 33% funnel shaped, and 47% segmental.[13] Hoffer et al. later presented a scheme considering the length of stenosis and associated cardiopulmonary anomalies.[14] Utilizing these criteria, they determined that short-segment stenoses have 8% mortality after repair. Long-segment stenoses without cardiopulmonary anomalies had 45% mortality, and any stenosis associated with significant cardiopulmonary anomalies has a mortality rate of 79%. Common cardiopulmonary issues included congestive heart failure, atrial and ventricular septal defects, pulmonary hypoplasia, and vascular slings. Trying to better predict the need and potential benefits of surgery, the Anton-Pacheco classification system utilizes an entirely different approach. Patients were categorized on the basis of the severity of their symptoms. Mild stenoses were defined as those having minimal or occasional symptoms. Moderate stenoses present with respiratory symptoms without airway




**Figs. 46.5A to C:** Complete tracheal rings. Bronchoscopic images demonstrating cases of complete ring tracheal stenosis. Normal tracheal rings are U-shaped and do not impinge on the airway.

**Table 46.2:** Comparison between tracheal stenosis and malacia by cause, pathophysiology, and treatment

| | *Stenosis* | | *Malacia* | |
|---|---|---|---|---|
| | *Congenital* | *Acquired* | *Primary* | *Secondary* |
| Cause | Congenital cartilaginous deformity | Trauma or ischemia | Congenital cartilaginous weakness | Compression or weakness due to another anomaly |
| C:M ratio (cartilage:membranous) | >3 | >3 | <3 | <3 |
| Onset | Shortly after birth | Variable | Shortly after birth | Variable |
| Prognosis | Stenosis may improve with age | Less likely to improve, potentially progressive | Likely to improve with age | Progressive |
| Surgical options (generally) | Open reconstruction | Endoscopic or open | Positive pressure, stenting (internal or external), tracheopexy | Remove source of compression |

**Table 46.3:** Comparison between common tracheal stenosis classification schemes

| | *Cantrell and Guild*[12] | *Hoffer et al.*[14] | *Anton-Pacheco*[14a] | *Ho and Koltai*[2] |
|---|---|---|---|---|
| Comparison based on: | Shape | Length and cardiovascular (CV) anomalies | Degree of symptoms | Multiple |
| Stratification: | Funnel | Short segment without CV anomaly | Mild/minimal symptoms | Congenital versus acquired |
| | Segmental | Long segment without CV anomaly | Moderate/occasional symptoms | Short versus long |
| | Generalized | Stenosis and CV anomaly | Severe/respiratory compromise | Associated anomalies versus none |

compromise. Severe stenoses cause respiratory compromise and are further divided into those associated with and without other congenital malformations. Mild stenoses may not need further treatment, whereas those with moderate or severe symptoms will likely require surgical intervention.[14a] Although there is no unified classification system, Ho and Koltai summarized the themes in each of the schemes discussed above to the following binary descriptors[2]:

- Congenital versus acquired
- Short segment versus long segment
- Associated anomalies versus no other anomalies
- Mild versus severe symptoms.

In describing the anatomy and clinical characteristics of patients with tracheal stenosis, it is best to keep these factors in mind to allow for effective communication and understanding between physicians.

## Preoperative Evaluation

Prior to considering surgical repair, a thorough workup is necessary. It is important to assess the dimensions and location of the stenosis, but first and foremost, a safe method of respiration must be established. Some patients may tolerate room air and others may require supplemental oxygen or positive pressure ventilation. Heliox may be used as an alternative or adjunct to continuous positive pressure ventilation and obviate the need for more invasive ventilation in more severe cases. In severe stenoses, where intubation is not possible or beneficial, extracorporeal membrane oxygenation (ECMO) may be necessary. ECMO should also be considered prior to taking patients to the operating room for endoscopic evaluation or repair. Bronchoscopes may not pass beyond a stenotic area, making ventilation during the evaluation impossible. The 2.5 ventilating bronchoscope is the smallest available at our institution and has an outer diameter of 4 mm. The smallest Hopkins rod telescope has a diameter of 2 mm and may require an apneic examination if it completely occludes the airway during bronchoscopy. Even if a camera can pass through a stenosis, edema or bleeding may exacerbate an otherwise stable situation and make endoscopy distal to the stenosis too risky. The area distal to the stenotic segment can also be visualized through a variety of radiographic methods. Plain radiography can be used as a screening tool to identify areas of stenosis by identifying alterations in the column of air, changes to the cartilaginous framework and areas of hyper- or hypoaeration. Airway fluoroscopy or contrast bronchography can be used to obtain dynamic and static views of the airway distal to a stenosis. This modality has grown out of favor in recent years due to the relatively high dose of radiation and the inability to visualize extralumenal structures. Also, inhaled contrast agents may exacerbate an airway obstruction and induce laryngospasm or bronchospasm. Computed tomography (CT) and magnetic resonance imaging (MRI), however, are now the preferred methods of radiographic evaluation. Both allow for a comprehensive assessment of the inner and outer dimensions of the trachea. They also image the soft tissue structures that surround the trachea and may identify sources of external compression. Both MRI and CT can be digitally reconstructed in three-dimensions to create a virtual bronchoscopy (VB) experience. VB, with a sensitivity, specificity and accuracy close to 90%, is particularly useful in identifying multiple airway anomalies in a single patient.[15,16] Both techniques may require sedation in an infant or young child, and for children with airway challenges, this may represent a significant risk. When deciding between these modalities, one must weigh the radiation exposure produced by CT against the need for prolonged sedation to attain an adequate MRI for analysis.

The workup is completed with an echocardiogram to rule out cardiovascular anomalies. Up to 50% of children with congenital tracheal stenoses have concomitant cardiovascular or pulmonary anomalies. In complete ring deformities, >30% of patients will have pulmonary artery

slings compressing the trachea. This is often referred to as a "ring-sling" deformity.[13] About 20–25% of congenital tracheal stenoses will also have other airway anomalies including a tracheal origin of the right upper lobe (RUL) bronchus or bronchus suis (pig bronchus), a bridging bronchus or absent bronchi.[17] The echocardiography will also help assess a child's ability to tolerate an invasive surgery by identifying any congenital heart defects, congestive heart failure, or signs of pulmonary hypertension. As described in Hoffer's classification, these factors strongly influence the success of repair.

## Treatment

### *Conservative Management*

Traditionally, conservative management had been reserved for patients too unstable for open surgery. Newer evidence suggests a role for watchful waiting in a subset of patients who would otherwise be candidates for surgery. Rutter et al. (2004) demonstrated that 5 out of 10 patients with complete rings had adequate tracheal growth to alleviate symptoms and avoid surgical reconstruction.[18] Cheng et al. observed 11 mild–moderate stenotic patients and concluded that short-segment stenosis with <60% obstruction could be managed conservatively.[19] By 9 years old, most achieved a normal age adjusted tracheal caliber. In those who do not improve adequately, surgery should be technically easier and produce better results in an older patient. These benefits must be weighed against the risk of leaving a child with poor exercise tolerance and pulmonary reserve for a considerable portion of their childhood. Also, if unable to phonate effectively, children may experience significant psychosocial, communicative, and educational delays that can persist into adulthood.

### *Surgical Management*

When surgery is necessary, the intervention needs to be tailored to the patient and their particular stenosis. Tracheal resection has traditionally produced good results, but it has always been limited by the need for a tension-free closure. Initially, success was possible for resections up to 20–25% of the trachea. With superior and inferior release maneuvers, 30% of the tracheal length can be excised successfully.[2,13] Under tension, the suture line is at risk of early dehiscence, an emergency, which may necessitate an expedient return to the operating room, or a late and progressive scar. To overcome these limitations and repair long-segment stenosis, a variety of tracheoplasty techniques have been attempted.

In 1982, Kimura presented his series of costal cartilage grafts.[20] Idriss et al. soon followed with a series of pericardial patch tracheoplasties.[21] Both of these techniques allow the expansion of the entire length of the trachea with long-term survival rates above 80%.[22] Table 46.4 lists open approaches to tracheal stenosis. Each tracheoplasty technique has its own advantages and disadvantages. While mortality rates are similar between the approaches, the slide tracheoplasty is thought to result in fewer returns to the operating room for removal of granulation tissue. Mortality rates are as reported by Backer et al.[72] Pericardial patches are pliable, allowing for an airtight closure. This pliability also allows for paradoxical airway collapse with inspiration requiring that the patch be suspended to surrounding structures and prolonged stenting after the initial surgery. Costal cartilage is more rigid allowing for better resistance to negative pressure collapse, but airtight seals are often difficult to establish and stenting may also be required. Histopathologic postmortem studies have shown that both of these mesenchymal autologous grafts will eventually regress and be replaced by fibrosis and scar tissue.[17,23] This scar formation will often extend dramatically into the lumen of the trachea requiring frequent reoperation and debridement. To address some of these challenges, Tsang et al. proposed the slide tracheoplasty in 1989.[24] Grillo later modified the technique to the operative approach most commonly utilized today.[25] Unlike resection, in a slide tracheoplasty, no tissue is removed. The stenotic segment is bisected longitudinally and the cut edges are brought together in an interlocking fashion. This, in effect, doubles the circumference of the stenotic section and quadruples the cross-sectional area. Consequently, the length of the trachea will also be shortened by half the length of the stenosis. As there is no autografted tissue or circumferential suture line, there is considerably less risk of scarring or restenosis and these patients may require fewer returns to the operating room.[26] Mortality with this procedure is between 9% and 21% and generally better than the other techniques.

For mild to moderate stenoses, endoscopic management is also possible. Jackson or Maloney rigid dilators have been used for decades with variable results. Endoscopic techniques rely on minimizing epithelial damage so that the mucosa can heal before the fibrosis extends and proliferates intraluminally. Rigid dilators generate shearing forces upon insertion, which may abrade the mucosa. With the recent introduction of endoscopic balloon dilators, the trachea can be distended with primarily radial forces, minimizing epithelial damage. Hebra et al.

**Table 46.4:** Comparison of tracheal resection and tracheoplasty techniques

| | *Resection* | *Pericardial patch* | *Costal cartilage* | *Slide tracheoplasty* |
|---|---|---|---|---|
| Advantages | • Less risk of granulation or fibrosis<br>• Single-site surgery<br>• No implant | • Airtight closure<br>• Same surgical access as repair<br>• Can treat long-segment stenosis | • Rigid tissue<br>• Can use multiple pieces of the same rib to treat long-segment stenosis<br>• Rib graft is commonly used in other pediatric procedures | • Only native, vascularized tissue is utilized<br>• No circumferential scar<br>• Can treat long- or short-segment stenosis<br>• Less reoperation for restenosis and scarring |
| Disadvantages | • Exclusively for short-segment stenosis<br>• Need for neck flexion postoperatively<br>• Mortality 8%[72] | • Frequent reoperation for stenosis<br>• Tissue flaccidity can lead to inspiratory collapse<br>• Mortality 23%[72] | • Frequent reoperation for stenosis<br>• No airtight closure<br>• Graft is difficult to work with due to warping and rigidity<br>• Mortality 27%[72] | • Shorter trachea may cause bronchomalacia<br>• Mortality 20%[72] |
| *Effects* | | | | |
| Postoperative tracheal length | Length of remaining normal trachea | Normal | Normal | Shorter by half the length of the stenosis |
| Postoperative tracheal circumference | Normal | Normal | Normal | Double the circumference of the stenotic segment |

described a 15-year experience with balloon dilations for tracheal stenosis. In his series, 90% of patients had short-term relief and 54% had sustainable airway expansion.[27] Ossoff et al. described similar success utilizing laser assisted balloon dilation.[28] These approaches are ideal for short-segment (<1 cm) stenoses. Shapsay described similar success in moderate to severe stenoses. In congenital and complete ring stenoses, endoscopic management is more controversial. In theory, fracturing complete rings with a balloon may allow expansion of the tracheal framework underneath intact epithelial surfaces. Several series have highlighted the increased risk of tracheitis, perforation, and mediastinitis as well as higher mortality rates with this approach.[29] In some cases of short-segment complete rings where a child may not tolerate an open approach, balloon dilation may still be appropriate but a high index of suspicion should remain for complications and leaks.[30,31]

A rare variant of congenital tracheal stenosis, tracheal sleeves, bear mentioning because their management is distinctly different. There are <25 reported cases in the literature, and they are all in patients with cranial synostosis syndromes.[32] Apert's, Crouzon's, and Pfeiffer's syndromes are the most common. These tracheas, described as "stovepipes", can be C-shaped or complete circles and have no vertical interruptions between cartilaginous rings. This long, rigid tube of tracheal cartilage often extends to and incorporates the cricoid cartilage. On endoscopy, a smooth intraluminal surface with the absence of dynamic movement suggests the presence of this anomaly. While not inconsistent with life, the mean age of survival is 3 years old. Patients will often have other respiratory anomalies as well as upper airway collapse secondary to craniosynostosis dysmorphisms.[33] Even with a normal caliber, the rigidity of the trachea will impair secretion clearance. In a review of all published cases, Lertsburapa et al. (2010) found that placement of tracheostomy tube allowed for better clearance of secretions and prolonged survival.[32] Interestingly, the presence of a normal trachealis and a C-shaped sleeve did not improve the prognosis. There is no effective open or endoscopic approach to expand the trachea beyond its natural growth.

## TRACHEOMALACIA

### Presentation

Similar to tracheal stenosis, tracheomalacia can involve short segments or extend through the entire tracheobronchial tree, and it can be either congenital or acquired. However, stenosis and malacia represent distinct pathologies (Table 46.2). Tracheomalacia is caused by a weakened cartilaginous structure that flattens the trachea,

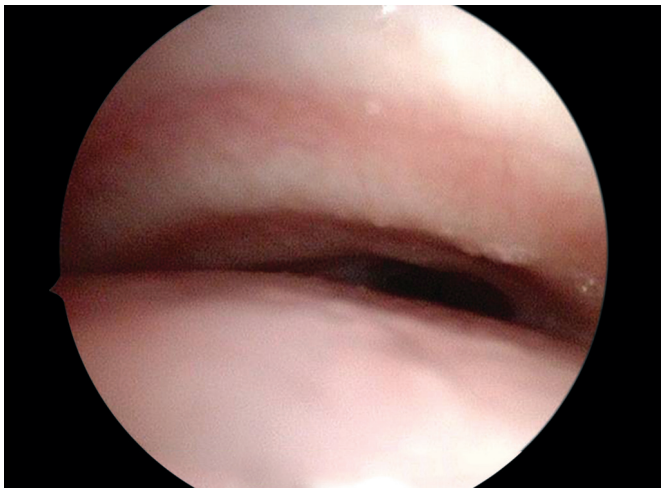


**Fig. 46.6:** Primary tracheomalacia. This is an image demonstrating dynamic tracheal collapse due to tracheomalacia. The anterior cartilaginous structure is weakened allowing the posterior membranous trachea to advance anteriorly and obstruct the airway.

widening it posteriorly (Fig. 46.6). The expanded membranous portion then advances anteriorly producing a C:M ratio closer to 2:1.[3,10] Tracheomalacia may be the result of inherently weak cartilage or cartilage deformed by pressure from mediastinal and cervical structures. The natural course of tracheomalacia also differs considerably from that of stenosis and varies according to the etiology.

Tracheomalacia is the most common bronchoscopic finding in children admitted for unexplained respiratory failure. It has an incidence of 1:2600 live births, but despite being relatively common it is often a missed diagnosis. Malacia manifests with variable symptoms and resembles other respiratory ailments. Children may not be diagnosed until after having been previously treated for asthma, laryngomalacia, or recurrent respiratory infections. If not identified early, many patients will experience the sequelae of prolonged courses of steroids, antibiotics, and mechanical ventilation.

## Classification

Tracheomalacia is classified into primary and secondary etiologies. Primary malacia is due to an inherent defect in the tracheal cartilage. Infant tracheas may have soft, collapsible cartilage due to high estrogen levels, nutritional deficiencies, collagen synthesis disorders, or prematurity. In this setting, a collapse of up to 20% of the tracheal lumen is considered benign or normal.[3,34] When the trachea collapses to 50% of its cross-sectional area it is more likely to become pathologic.

Secondary malacia occurs when a separate anomaly or process causes the trachea to collapse.[35] Vascular rings and thyroid goiters can cause secondary malacia by exerting direct external pressure on the trachea. Even after the compressive elements are removed, the trachea may not recover completely as the deformed cartilage needs time to strengthen. The presence of TEFs or their repair can also weaken the trachea and cause secondary malacia.

## Preoperative Evaluation

The differential diagnosis for tracheomalacia is the same as that of stenosis, and much of the diagnostic workup is the same with slight variations. The gold standard for assessment is rigid or flexible bronchoscopy during spontaneous ventilation. It is important that the child is breathing independently so that any dynamic component to the collapse can be observed. Radiographic modalities including MRI and CT are important in identifying sources of compression. Newer cinematic MRI sequencing allows for the dynamic imaging of the trachea during respiration, but it is limited in its availability and the need for sedation. As an initial screening test, plain or magnified tracheal roentography and a barium swallow will screen for and identify many forms of external compression including up to 90% of vascular rings. When vascular compression is anticipated, angiography and echocardiography can assess the aberrant anatomy and screen for other cardiovascular defects. Sixteen percent of patients with vascular anomalies, as a whole, will have concomitant cardiac issues.[43,44] Other associated congenital anomalies may include 22q deletions, EAs and fistulae, vertebral deformities, horseshoe kidneys, hiatal hernias, and imperforate anus. Karyotyping and other ancillary tests should be reserved for cases where there is increased suspicion for a syndrome or relevant comorbidities. Finally, it is important to keep an open channel of communication with the intensivists and cardiologists to medically optimize children prior to surgery.

## Treatment

### *Primary/Intrinsic Tracheomalacia*

Primary tracheomalacia may be caused by immature and weak cartilage that is unable to sustain structural integrity against respiratory pressures. Given time, most cases will resolve between 18 months and 2 years of age.[10,34] As such, conservative measures are preferred in most cases. Placing the child prone or in a sniffing position with the head

of bed elevated may be adequate to improve symptoms and normalize the work of breathing. If these measures are not effective, a clinician could consider supplemental oxygen or continuous pressure appliances. When these efforts are inadequate and the child is failing to thrive, surgical options should be considered. Tracheotomy can facilitate ventilation with positive pressure to maintain patency of malacic segments, but it may not bypass distal compression. Tubular plastic and metallic stents have been used to reinforce the structural integrity of malacic areas with varying success. Although they are clearly able to limit both primary and secondary malacic collapse, they are prone to dislodgement and granulation. Also, they tend to disrupt normal ciliary clearance and as the child grows they may need to be dilated, removed, or replaced to accommodate the growing airway.[36,37] Internal stents should be reserved for severe cases and surgeons should exercise caution when considering their use because of significant risk of morbidity and mortality. Extralumenal approaches are also possible. The soft tissue surrounding the trachea can be lifted anteriorly and sutured to the sternum in a tracheopexy or aortopexy.[38,39] Others describe success in extraluminal stenting with absorbable plating systems or cartilagenous grafts.[40] Recently, a resorbable extraluminal stent was custom printed for a patient with severe bronchomalacia and used successfully.[41]

### *Secondary Tracheomalacia*

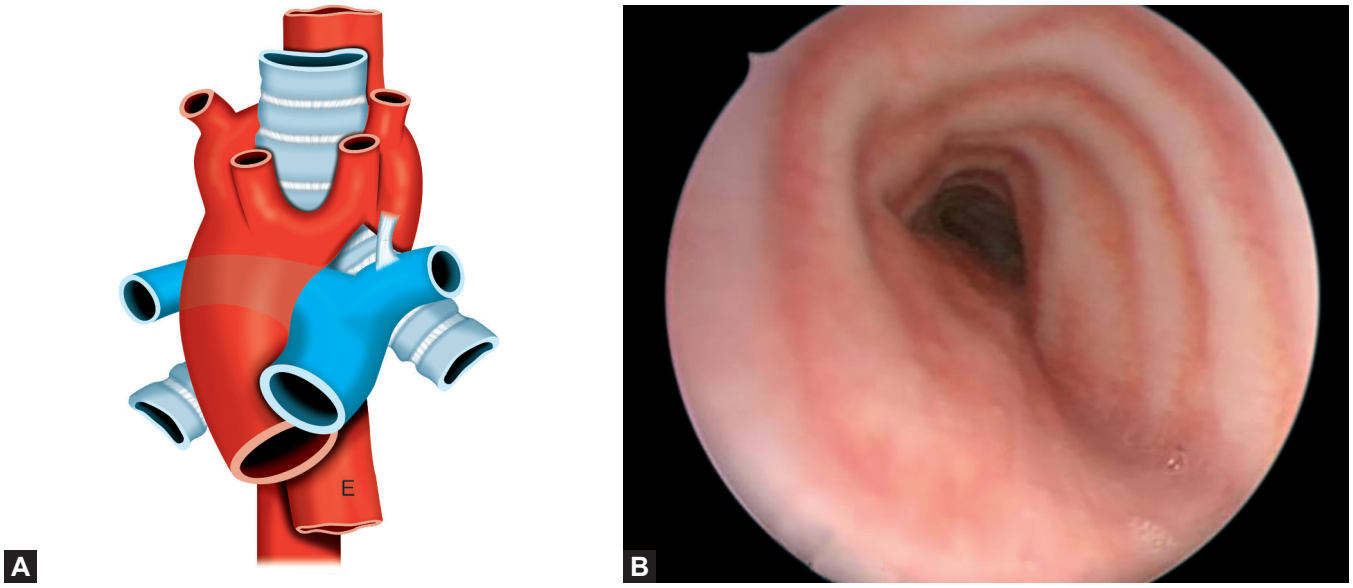
When another structure is pressing on the trachea and causing respiratory symptoms, it generally has to be removed. Unlike intrinsic malacia, as the child grows, this fixed obstruction is likely to further impinge on the airway and weaken the cartilagenous support. These structures can originate from cardiovascular, bronchogenic, thymic, thyroid, or lymphatic sources. Vascular anomalies are present in 3% of individuals but only rarely cause tracheoesophageal compression.[42] As discussed previously in this chapter, normal development of the cardiovascular system requires the selective involution of primitive aortic arches. Ultimately, this will allow for a predominantly left-sided aortic channel instead of the circumferential system that results from the early fusion of the primitive aortae. If maintained, this vascular circle will compress the visceral contents of the neck, impairing the function of the trachea and/or esophagus. Complete circumferential vascular anomalies are often called "rings" and are symptomatic in 70–90% of patients.[43] Noncircumferential vascular anomalies are termed "slings" and have a more variable presentation. Table 46.5 describes the relative frequencies of symptomatic aortic arch anomalies causing tracheoesophageal compression. Double aortic arches are the most common symptomatic anomaly. Innominate artery slings are common incidental findings, but they are rarely symptomatic.

**Table 46.5:** Relative frequency of vascular anomalies in children

| | *Frequency* |
|---|---|
| Double aortic arch | 43% |
| Isolated innominate artery compression | 15% |
| Right-sided arch with aberrant subclavian | 11% |
| Right-sided arch with left ligamentous arteriosum | 11% |
| Pulmonary artery sling | 7% |
| Isolated aberrant subclavian artery sling | 5% |
| Double aortic arch with atretic left arch | 5% |

*Complete vascular rings:* The double aortic arch was first identified by von Siebold in describing a case of cyanosis in a neonate in 1837.[42] It was more than a hundred years before the first successful surgery for a complete ring was performed by Gross in 1945.[44] Vascular rings represent only 1% of congenital cardiovascular issues and pose a unique clinical scenario. Children often present early in infancy with progressive symptoms of stridor, cyanosis, and dysphagia. Ninety percent of these anomalies will be detected by barium esophagram, but they cannot be ruled out entirely without additional imaging, usually MRI/MR angiogram.[42,45] Further complicating the scenario, intubation or tracheotomy may not provide relief and may worsen symptoms by placing a tube against the narrowed segment of trachea or compressing the great vessels through the tracheal wall.

*Double aortic arch*: Double aortic arches account for 48-55% of vascular rings (Figs. 46.7A and B).[42,43] Almost 90%[42] of these patients will be symptomatic and require surgical correction. The anomaly is the result of a persistent right fourth aortic arch in the presence of a normal left arch. The right arch passes behind the trachea and esophagus, whereas the normal position of the left arch places it anteriorly. The circle is completed when the two arches join at the normal left descending aorta. In 80% of double arches, the right side is dominant. Determining this laterality is critical in deciding which side can be ligated without causing cerebrovascular or generalized ischemic injuries.




**Figs. 46.7A and B:** Tracheomalacia due to a double aortic arch. (A) Illustration depicting the double aortic arch pathology. The left and right arches encircle the trachea and esophagus (E) constricting the lumen of the airway. Reproduced with permission from Hernanz-Schulman.[64] (B) Bronchoscopic findings in a child with extrinsic tracheomalacia due to a double aortic arch. Note the posterior and anterior deformities in the tracheal wall.

*Right-sided aortic arch rings*: One in 1000 individuals have benign right-sided aortic arches. Most of these are solitary anomalies without a concomitant left arch and they are rarely pathologic.[43] In 22% of ring deformities, a right-sided arch passes posterior to the trachea. The ring is completed with the combination of the left subclavian artery anteriorly and the ductus or ligamentum arteriosum laterally (Fig. 46.8). This combination is more likely to become problematic when the aortic arch lies completely to the right of the vertebral column and the subclavian has to travel further to reach the left side of the body. A right arch can also create a ring if there is a mirror-image arch branching pattern and a retroesophageal ligamentum arteriosum or if the descending aorta passes retroesophageally while the arch compresses anteriorly. Even more rare, a left aortic arch can produce a ring anomaly when it is associated with a right descending aorta.

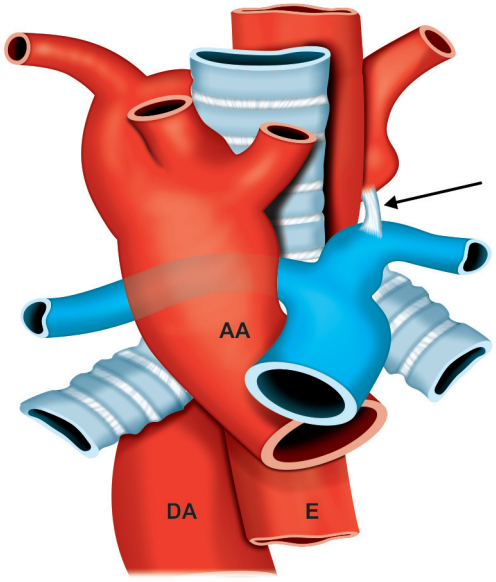
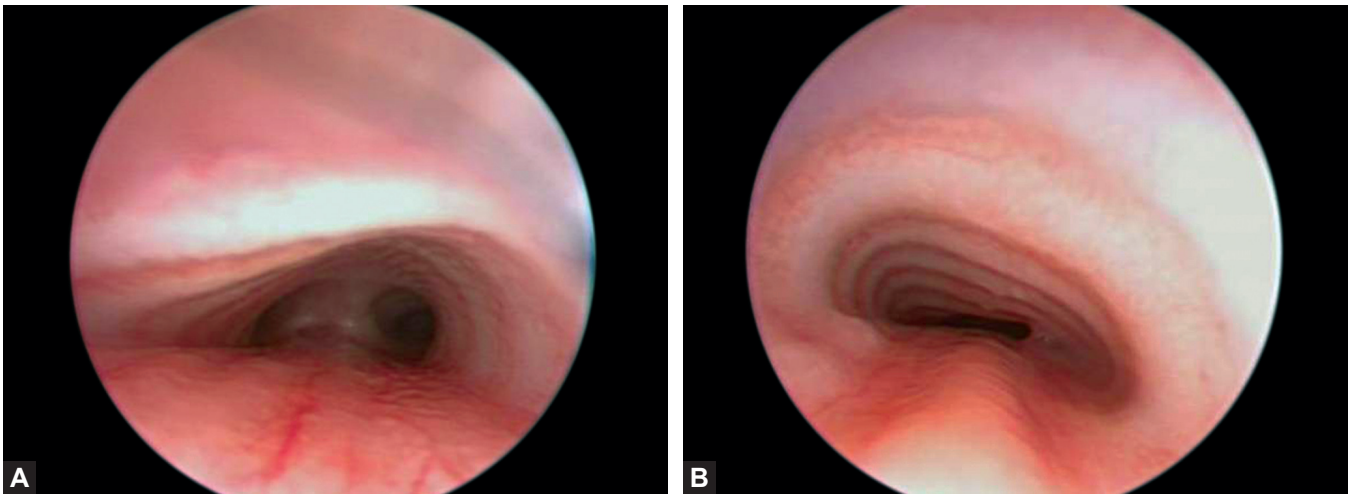



**Fig. 46.8:** Right-sided aortic arch ring anomaly. Illustration depicting a vascular ring compressing the trachea and esophagus (E). It is caused by a right aortic arch in combination with an aberrant right subclavian and left ligamentum arteriosum (arrow). (AA: Ascending aorta; DA: Descending aorta). Reproduced with permission from Hernanz-Schulman.[64]

*Vascular slings*: Vascular slings are more common than rings but have a more variable presentation. Compression by an aberrant innominate is identified in up to 20% of bronchoscopies in infants with dyspnea.[42] An anterior or V-shaped pulsatile tracheal deformity is typical (Figs. 46.9A and B). The diagnosis can be confirmed by lifting the tip of bronchoscope against the malacic segment and observing a decrease in the pulse pressure in the right arm due to occlusion of the brachiocephalic artery. Traditionally, a more distal origination of the innominate artery is thought to lead to increased tension as the vessel crosses the trachea. However, 90% of children with an




**Figs. 46.9A and B:** Innominate artery sling. Bronchoscopic images depicting anterior tracheal wall deformities and malacia due to innominate artery compression. Note the inverted "V" deformity and flattened cartilaginous framework.

innominate sling have a normal origination and 95% of children with congenital heart disease have a distal innominate without any symptomatic compression.[43] When encountered incidentally, it is difficult to determine its true effect on respiration. If ignored, some children may go undiagnosed until their teenage years with symptoms of exertional dyspnea, stridor, and/or recurrent tracheobronchitis.

The pulmonary artery sling is the most common symptomatic non-ring vascular anomaly. It is caused by a developmental failure in the sixth aortic arch. As a result, the left pulmonary artery forms as a collateral of the right pulmonary artery. It then passes between the trachea and esophagus and wraps around the right mainstem bronchus causing compression.[42] If the left ductus arteriosus joins the common pulmonary artery trunk, a true vascular ring can be formed.[45] In 50% of cases, the pulmonary artery sling is associated with complete tracheal rings. Inversely, 30–65% of complete ring stenoses will have a pulmonary sling.[45] Due to the frequency of this combination of pathologies, Contro coined the term, "ring-sling" deformity to describe the association.[46] Ninety percent of these patients will not survive without surgery and when possible, it is best to address both anomalies in a single operation.

An aberrant right subclavian artery is another relatively common vascular anomaly that is rarely symptomatic. It can be identified in 1:200 healthy individuals. In this scenario, the right subclavian has its own division off of the distal aortic arch or descending aorta. It then courses posterior to the trachea and esophagus to reach the right upper extremity. When symptomatic, children are more likely to have dysphagia than respiratory complaints.

Aside from aberrant great vessels, other vascular phenomena can cause airway compression. In cases of normal anatomic configuration, large aneurysms or vascular tumors can crowd mediastinal structures. Also, dilation of pulmonary vessels due to pulmonary hypertension or congestive heart failure can cause tracheobronchial malacia. This is manifested most often where the left pulmonary artery crosses the left mainstem bronchus or where the right pulmonary artery crosses the right bronchus intermedius. Engorged mediastinal vessels may cause compression of the left lateral tracheal wall and deviate the airway to the right. Despite marked bronchoscopic findings, these children are generally dyspneic due to their cardiac issues and treatment is usually medical, addressing the heart disease.

## TRACHEOESOPHAGEAL FISTULA

### Presentation

Thomas Gibson aptly and eloquently documented a case of EA and TEF in 1697. He described "an infant that would not swallow, the child seemed very desirous of food, and took what was offered it in a spoon with greediness; but when it went to swallow it, it was liked to be choked... and it fell into struggling convulsions".[1] Untreated EA with TEF is a fatal condition due to the inability to protect the respiratory tract from alimentary material and failure to ingest adequate nutrition. Prenatal diagnosis is only possible in 10% of cases.[47,49] Polyhydramnios and an absent stomach bubble suggest an ineffective fetal swallow, but they are nonspecific findings. After birth, coughing or

frank regurgitation of meals is typically observed. Suspicion is further heightened when a nasogastric tube coils and fails to pass into the stomach. Children with solitary TEF without atresia (or H-type TEF) may present with failure to thrive, varying degrees of respiratory difficulty, or recurrent pneumonias due to aspiration. In these cases, the presentation may be more insidious and a definitive diagnosis may not be made until later in childhood or even adulthood.

The EA with TEF requires expedient care but is rarely a true emergency. When on a ventilator, a distal fistula can create an urgent scenario if the endotracheal tube rests above a sinus tract leading to the stomach. Pressurized air from the ventilator may build in the stomach and intestine increasing the risk of reflux or even perforation. Care must be taken to assure proper endotracheal tube placement and a soft abdomen. Gastrostomy may also be necessary to provide a safe outlet for excess and trapped air. However, a gastrostomy may also make the fistulous tract the path of least resistance and divert air away from the lungs necessitating early division of the fistula.[1,50]

## Genetics

Tracheoesophageal fistulas are a relatively common anomaly found in 1:3000–3500 live births.[7,51] Most cases are sporadic without a significant family history. Despite a low twin concordance rate (2.5%), a twin gestation is a risk factor for EA/TEF in a single fetus. Not considered an inherited trait, up to 50% of EA/TEF patients will have other congenital anomalies and 10–20% of cases are related to known syndromes. Table 46.6 details the relative frequencies of other congenital anomalies associated with tracheoesophageal fistulas and esophageal atresia.

The EA/TEFs have been associated with multiple chromosomal anomalies and individual gene mutations. They are core components of the VACTERL or VATER associations that include, vertebral, anal, cardiac, tracheoesophageal, renal, and limb defects. VACTERL accounts for up to 10% of TEF cases.[7,47,52] An additional 3–7% are seen together with trisomy 18 (Edwards syndrome). CHARGE association (coloboma, heart abnormalities, atresia choanae, retardation of growth and/or development, genitourinary, and ear defects), trisomy 21 (Down's syndrome), trisomy 13 (Patau syndrome), and trisomy X have also been associated with EA/TEF. Anomalies in chromosomes 2-10, 12-15, 17, 18, 21, 22, y, and x and mutations in many individual genes have also been seen in conjunction with EA/TEF. Sonic hedgehog (SHH) and nkx gene mutations, among others, have been implicated in inappropriate formation of the tracheoesophageal septum during early in embryogenesis.[7,53]

**Table 46.6:** Frequency of anomalies associated with tracheoesophageal fistulae and esophageal atresia

| *Anomaly* | *Frequency (%)* |
|---|---|
| None | 52 |
| Congenital heart disease | 19 |
| Gastrointestinal | 13 |
| Genitourinary | 10 |
| Imperforate anus | 9.4 |
| Musculoskeletal | 8.6 |
| Face or palate | 5 |
| Central nervous | 3.3 |
| Down's syndrome | 2.6 |
| Larynx, trachea, lung | 1.5 |
| Diaphragm | 1.6 |
| Vascular | 1.0 |
| Liver, spleen | 0.8 |
| Other | 4.1 |

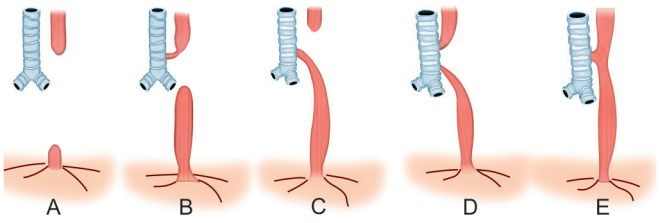
## Classification

Two commonly used classification systems for TEF are those of Vogt (1929) and Gross (1953) (Figs. 46.10A to E).[54,54a] Table 46.7 compares TEF/EA classification systems. The classification systems by Vogt and Gross are cited extensively in the literature. It is helpful to understand how their classification systems overlap. Table 46.7 describes the anatomic findings associated with the types of EA/TEF that they subdivide. Kluth later compiled an atlas detailing 96 variants of this disease spectrum.[54,55] There have been numerous other classification schemes that we could discuss; however, it is easier and more generalizable to describe these anomalies anatomically. There are three primary manifestations. The vast majority of cases (80–90%) are manifested by proximal EA with a distal TEF. About 7–10% will have isolated atresia without fistulae and 2–4% will have TEFs without an atresia (H-type fistula). Other manifestations include atresia with proximal and distal fistulae and atresia with only a proximal fistula.[1,50]

In 1962, Waterston et al. developed a classification system that attempted to predict survival and surgical success. His criteria included: birth weight, presence of

**Table 46.7:** Comparison of tracheoesophageal fistula (TEF) classification systems

| *Gross*[54] | *Vogt*[54a] | *Anatomic description* | *Relative frequency* |
|---|---|---|---|
| — | 1 | Esophageal agenesis | Rare |
| A | 2 | Normal superior and inferior esophagus with absent middle portion. No TEF | 7–10% |
| B | 3a | TEF connecting to proximal esophageal pouch only | Rare |
| C | 3b | Proximal esophageal pouch with TEF connecting to the distal esophagus and stomach | 80–90% |
| D | 3c | TEFs connecting both the proximal and distal pouches to the trachea | Rare |
| E | — | H-type fistula with patent esophagus and TEF | 2–4% |




**Figs. 46.10A to E:** Gross classification system of esophageal atresia (EA)/tracheoesophageal fistula (TEF). Illustration of the Gross classification system for TEF/EA pathologies described in Table 46.7.

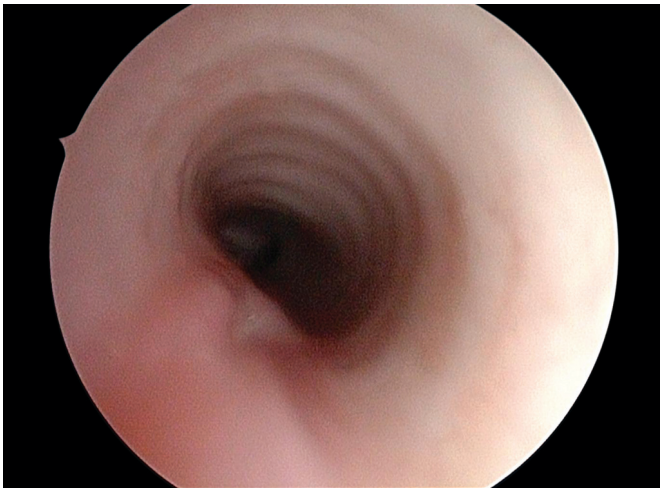


**Fig. 46.11:** Bronchoscopy of a child with a tracheoesophageal fistula. The small dimple on the posterior wall may be missed even if the index of suspicion is high. Gastric dyes like methylene blue may be needed to find a fistula if initial attempts fail.

pneumonia, and other anomalies.[56] With improved surgical success, Spitz later revised the classification as follows:[1]

- I: >1500 g at birth with no cardiovascular anomalies (98% survival)
- II: < 1500 g or major cardiovascular anomalies (82%)
- III: < 1500 g and major cardiovascular anomalies (50%).

For this classification, major cardiovascular anomalies include cyanosis requiring palliative or corrective surgery and noncyanotic children requiring therapy for heart failure. For higher risk patients in the latter groups, surgery should be delayed until patients are nutritionally and medically optimized.

## Preoperative Evaluation

Only 10% of patients with EA will be identified prenatally.[49] The remainder will be identified clinically after birth. The workup and treatment of atresia is outside of the scope of this chapter, and the remainder of this section will focus on the management of TEF. The gold standard for identification of a TEF is by direct visualization with bronchoscopy and esophagoscopy (Fig. 46.11). This may include the use of methylene blue or other dyes to visualize small sinus tracts. Alternatively, a barium esophagram, especially in the prone position can identify small fistulas that might be missed otherwise. Push esophagrams, performed via a nasograstic or orogastric tube with pressure to distend the esophagus may be needed to identify H-type fistulas, which can often be missed with a passive swallow technique.

Although 50% of patients with EA/TEF will have other associated anomalies, 90% of solitary TEFs will be isolated findings in otherwise healthy children.[1,50-52] Some associated conditions may be otherwise incompatible with life. Palliation rather than invasive surgical correction may be indicated in these cases. A trisomy 18 karyotype or high-grade intraventricular hemorrhage, for instance, may prompt this discussion.

## Treatment

Open surgery via a transthoracic or transcervical approach is classically the gold standard treatment. However, there

is significant morbidity implicit in these approaches.[1,47] Fistulae above T3 can usually be accessed through a horizontal cervical incision. Those below T3 are easier to reach via a right thoracotomy. Further complicating the operation, comorbid conditions, like heart failure and vascular anomalies may alter the position of structures within the mediastinum making safe dissection more challenging. Recently, thoracoscopic approaches have been described with success and complication rates similar to open surgery.[57,58]

Endosopic options offer a less invasive alternative for treating isolated H-type fistulae. Many techniques have been described including using blunt or mechanical mucosal stripping, laser,[59] and electrocautery fulguration.[60] In a review by Richter et al., 37 cases of endoscopic fistula repair were identified.[61] Eighty-one percent of patients had successful closure of the fistula with endoscopic techniques; half of these successes required multiple endoscopic revisions. Results may also be improved with the use of a tissue sealant histoacryl or fibrin glue. Large patent fistulae are less likely to close with endoscopic management, and success is reported with lumens as wide as 6 mm. Conversely, pinpoint fistulae may not be canulatable precluding endoscopic management.

## Complications

Survival for EA is now better than 90%, and the most common cause of death is related to other comorbidities.[44] For solitary fistulas, 100% survival is expected. Still, there are reports of life-threatening airway swelling after endoscopic closure.[62] As a rule, patients should be observed following endoscopic approaches to H-type fistula repair to evaluate for airway compromise, mediastinitis, or perforation. If intubation is necessary, care must be taken to secure the endotracheal tube beyond the fistula.

After the initial postoperative period, aspiration may not be related to refistulization. Developmental defects in the tracheoesophageal septum may result in poor peristaltic function and chronic esophageal reflux. Eighty-five percent of patients will have some microaspiration 12 months after repair and 1.5% of patients will continue aspirating into adulthood.[47] Aside from aspiration, gastroesophageal reflux is common in these children and can increase scarring at a site of fistula repair leading to stenosis. Also, the congenital or surgical defect in the membranous trachea may result in secondary/extrinsic tracheomalacia causing further respiratory symptoms.

# OTHER TRACHEAL ANOMALIES

## Tracheal Agenesis

Tracheal agenesis is considered incompatible with life. It has an incidence of 1:100,000 live births.[63] Most cases are diagnosed prenatally with polyhydramnios, fetal ascites, and enlarged, hyperechoic lungs. Some cases are not realized until after birth when a child presents with an absent cry, severe respiratory distress, inability to intubate, and possibly a failed tracheotomy.[54] Floyd et al. classified three types of agenesis[65]:

1. Partial tracheal agenesis with a short segment of distal trachea connected to the esophagus via a TEF
2. Complete agenesis with a normal carina and bronchi emerging from the esophagus
3. Complete agenesis with individual bronchi branching from the distal esophagus

To date, no child has lived beyond 6 years old with tracheal agenesis. Temporizing measures include placement of a tracheotomy tube in an individual bronchus, esophageal stenting and ventilation, and tracheal substitution. Even with successful reconstruction of the trachea with cadaveric or autografted tissue, children still have challenges clearing secretions. Recently, attempts have been made to seed decellularized tracheal matrix with autografted fetal stem cells. A single case report in 2013 has gathered considerable media and scientific attention.[66] Although this offers hope for a previously incurable condition, it remains to be seen if long-term success is truly possible in these children.

## Congenital High Airway Obstruction Syndrome (CHAOS)

The term CHAOS was coined by Hedrick et al. (1994) in describing a series of airway obstructions encountered at birth that were previously considered unsalvageable.[67] One cause of CHAOS is laryngeal atresia, which may present similar to tracheal agenesis, except that beyond the stenotic or atretric portion of the airway, a formed and patent trachea exists. Laryngeal atresia is the result of failed recanalization, similar to the suspected mechanism of congenital subglottic stenosis.[68] Other causes of CHAOS include cervical masses and laryngotracheal cysts that compress the airway. CHAOS is diagnosed prenatally by identifying large fluid filled lungs, a flattened diaphragm, and a dilated tracheobronchial tree on ultrasound. The etiology may be better established after obtaining a maternal-

fetal MRI. Prenatal diagnosis affords the opportunity to perform a tracheotomy or initiate ECMO in a controlled environment using an EXIT (ex utero intrapartum treatment) procedure. During an EXIT procedure, the baby is partially delivered via cesarean section and the airway is secured while the child is still receiving maternal–fetal circulation. Due to the rarity of this disease spectrum and the difficulties facing these children after birth, only a few cases of successful airway reconstruction have been reported.[69] Others will survive and remain chronically tracheotomy dependent.

## Tracheobronchial Branching Anomalies

The incidence of tracheobronchial branching anomalies varies from 1% to 3%.[4] They are more common in patients with other congenital anomalies. In a review of 580 bronchoscopies by Sanchez, 30% of patients were asymptomatic and these anomalies were incidental findings. The remaining 70% presented with chronic cough, recurrent infections, bronchiectasis, or stridor, and there was a high-preoperative suspicion for an anomaly. The most common airway affected is the right upper lobe (RUL) bronchus. RUL anomalies include improper angulation, supernumary bronchi, or absent segmental bronchi. A bronchus originating from the trachea was also seen in 23% of branching anomalies. Most tracheal bronchi are accessory branches to the upper lobe.[70] Occasionally, the entire RUL will originate from a tracheal bronchus. This branching pattern is often called a "bronchus suis" (pig bronchus). The placement of this anomaly is fairly consistent, and the bronchus is usually found 2 cm above the carina on the right lateral tracheal wall. Other accessory bronchi that form during embryogenesis may not develop into functional respiratory units. Nonfunctional tracheal appendages represent 0.5% of tracheal anomalies but can be found in 1% of individuals on postmortem examination.[71] These diverticula represent inherently weak areas of the trachea and bronchi. Usually asymptomatic, they may become clinically relevant if a patient requires mechanical ventilation. Intubation trauma and increased airway pressure may cause an outpouching of the airway lumen at these sites forming a tracheocele or bronchocele. When symptomatic, these may require endoscopic drainage or open surgical resection.

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CHAPTER

# 47

# Surgery for Subglottic and Tracheal Lesions

***Derek J Rogers, Christopher J Hartnick***

## INTRODUCTION

Chevalier Jackson was one of the first to recognize and report subglottic stenosis in children as a complication of high tracheostomies performed for infectious processes.[1] The most common etiology of subglottic stenosis gradually became endotracheal tube trauma, as the surgical techniques for tracheostomy evolved and antibiotic therapy for inflammatory airway disease improved.[2] Prolonged nasotracheal intubation for management of the premature respiratory system became commonplace after the work of McDonald and Stocks in 1965.[3] Although prolonged nasotracheal intubation revolutionized neonatal critical care, a significant increase in acquired subglottic stenosis resulted. With refinement in techniques, the incidence of subglottic stenosis in intubated premature infants has dropped from as high as 20% in the 1970s.[4] The estimated incidence from the late 1980s to the late 1990s was about 2% of all surviving neonates intubated >48 hours.[5-7] Congenital subglottic stenosis due to malformed cricoid cartilage, incomplete recanalization, and/or hypertrophy of submucous glands is a frequent congenital laryngeal anomaly. Other common subglottic lesions include cysts and hemangiomas.

Tracheal stenosis has been a known cause of upper airway obstruction for over a century. Similar to subglottic stenosis, acquired tracheal stenosis due to intubation trauma or tracheostomy is most common. The reported incidence of tracheal stenosis after intubation and tracheostomy is estimated to be 0.6% to 21% and 6% to 21%, respectively.[8-10] Congenital tracheal stenosis is rarer, with an estimated incidence of 1 in 64,500.[11] It is usually caused by complete tracheal rings and may be associated with vascular compression of the airway. Other commonly encountered tracheal lesions include suprastomal granulomas in the tracheotomized patient and persistent tracheocutaneous fistulas in those who have decannulated. Benign and malignant neoplasms of the trachea are quite rare in children.

Although the clinical presentation and diagnostic evaluation of both subglottic and tracheal lesions share many similarities, the treatment options for these two entities differ considerably. Both entities may be approached via endoscopic or open routes and often require some form of temporary stenting. Subglottic and high-tracheal stenosis may be treated similarly; however, lower tracheal lesions and long-segment tracheal stenosis mandate different surgical techniques.

## SUBGLOTTIC LESIONS

### Subglottic Stenosis

The most common characterization of subglottic stenosis is to differentiate it into congenital and acquired etiologies. Congenital subglottic stenosis results from incomplete recanalization of the primitive laryngopharynx and can range from mild cricoid shape disturbance to complete failure of recanalization. Congenital subglottic stenosis is the third most common congenital laryngeal anomaly after laryngomalacia and vocal fold paralysis.[12] Acquired subglottic stenosis is defined as any form of laryngeal stenosis not congenital in nature and is most often a result of trauma from endotracheal intubation. Although

prolonged nasotracheal intubation in premature infants has shown the largest rise in the incidence of subglottic stenosis, one must realize that even short-term intubation may result in the same condition.[13] It remains unclear why some children develop subglottic stenosis from endotracheal intubation and others do not. When the pressure caused by an endotracheal tube exceeds capillary pressure, this leads to ischemia, edema, necrosis, and ulceration within the first several hours to days of tube placement.[14] Secondary infection may ensue, causing perichondritis and even full-thickness cricoid destruction.[15] Three weeks of healing occurs, and most children recover without lasting effects. Yet, in some children, the initially soft stenosis becomes markedly inflamed and develops into a firm, fixed scar. This appears to be a multifactorial process related to gastroesophageal reflux disease (GERD), undiagnosed congenital narrowing, type and size of endotracheal tube, and systemic factors.[16,17] One should remember that other etiologies of acquired subglottic stenosis include inflammatory/autoimmune conditions, uncontrolled GERD, external laryngeal trauma, surgery (especially tracheostomy above the second tracheal ring), and external beam radiation.

### *Clinical Presentation*

Since subglottic stenosis affects specifically the larynx, patients present with effects on airway, swallowing, and/or voice. In children who are not intubated, biphasic stridor and exertional dyspnea are frequently present. The children often suffer from multiple croup-like illnesses, especially during the winter months. During the episodes of respiratory distress, suprasternal and intercostal retractions are common. Many children have dysphagia, aspiration, and other feeding difficulties. Hoarseness or breathiness may be present, depending on the degree and location of the scarring. Often, children have a prior history of endotracheal intubation. Multiple failed extubation attempts with an appropriately sized endotracheal tube and an absence of an air leak below 25 cm $H_2O$ may signal the presence of subglottic stenosis. These children often undergo tracheostomy due to failed extubation.

### *Diagnostic Evaluation*

A thorough history and physical examination is needed in children with possible subglottic stenosis. The history should include gestational age, Apgar scores, and number and duration of intubations. One should note any other medical problems such as bronchopulmonary dysplasia, congenital cardiac disease, neurologic status, craniofacial dysmorphisms, and genetic or syndromic conditions. Providers should have a low threshold for obtaining an echocardiogram, as many of these children have congenital cardiac disease. The vocalization and feeding histories are important, including dysphonia and aspiration symptoms with or without recurrent pneumonia. The physical examination should determine any dysmorphic features or craniofacial anomalies. A flexible fiberoptic laryngoscopy should be performed in stable patients to assess for any other lesions and to evaluate vocal fold mobility and the dynamics of the supraglottis.

*Imaging*: The most important reason for obtaining imaging in any child with potential subglottic stenosis is to rule out low tracheal stenosis prior to induction of anesthesia and to allow for appropriate preoperative planning in the event the airway is lost distally. If a low tracheal lesion is identified, thoracic surgery consultation and consideration for extracorporeal membrane oxygenation (ECMO) should be entertained. High kilovoltage lateral and anteroposterior neck and chest films usually provide adequate visualization of the upper airway and evaluate any pulmonary pathology simultaneously. Airway fluoroscopy is another means of imaging, which provides dynamic information such as tracheomalacia. High-resolution computed tomography (CT) of the neck and chest with virtual bronchoscopy has gained popularity recently. By using this imaging modality, one could possibly better evaluate the entire airway preoperatively, resulting in improved planning. If the high kilovoltage chest film shows mediastinal widening, a CT may also be necessary to rule out a mediastinal mass, which could result in compression of the great vessels and immediate drop in preload during induction of anesthesia. Ultimately, one must weigh the risks of airway obstruction during the scan and increased radiation dose before choosing CT.

*Swallow evaluation*: A modified barium swallow, or videofluoroscopic swallowing study, may be obtained with both a radiologist and speech-language pathologist present to evaluate dynamic swallowing mechanics. This study may provide information regarding potential aspiration risk in children with severe subglottic stenosis after the stenosis is corrected. A modified barium swallow can be combined with a traditional barium swallow and/or airway fluoroscopy to assess for mediastinal anomalies such as vascular rings or slings. Additional data may be gained from a fiberoptic endoscopic evaluation of swallowing (FEES), such as determining laryngeal sensation. FEES may also

be used in children with oral aversion to identify subclinical aspiration because it requires a smaller bolus. The goal of preoperative swallowing evaluation is to help predict which patients may experience prolonged postoperative dysphagia requiring intervention. The type of surgical intervention and timing may be tailored to improve surgical outcomes. Hypopharyngeal pooling, persistent residue, and poor oral motor skills associated with premature spillage into the hypopharynx predict a poor postoperative swallowing course.[18]

*Voice evaluation*: Parents of a child with subglottic stenosis initially focus on a safe airway and swallowing, successful decannulation, and some sort of functional voicing. Once a safe airway is established and the child begins to grow, parents become more concerned with voice quality. Approximately 50% of children who undergo airway reconstruction for subglottic stenosis have a significant risk of developing voice disorders.[19] The patient, his or her parents and caregivers, speech language pathologist, and otolaryngologist must work in close coordination.[20] A wide variety of voice disorders and laryngeal dysfunction may result after airway reconstruction. Detailed documentation must be kept regarding communication ability and condition of the larynx. Of utmost importance is the patient's potential for voicing before and after airway reconstruction.

*Multidisciplinary involvement*: Children with airway anomalies require the care of multiple specialists. A multidisciplinary aerodigestive clinic represents an effective means of bringing the team of specialists together in one location. A pediatric otolaryngologist, gastroenterologist, pulmonologist, and speech-language pathologist should be intimately involved in the care of these patients. Constant discussion between the various specialists ensures the appropriate use of medications, imaging studies, pulmonary function tests, and speech and language therapy. In addition, good preoperative teamwork allows better coordination and decision making during and after operative interventions.

*Triple endoscopy*: Triple endoscopy represents the most thorough way to evaluate a child with suspected subglottic stenosis and consists of direct laryngoscopy with rigid bronchoscopy (DLB) by the otolaryngologist, flexible fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) by a pulmonologist, and esophagogastroduodenoscopy (EGD) with biopsies by a gastroenterologist. The DLB defines the static anatomy of the airway. The flexible bronchoscopy evaluates dynamic pathology such as tracheomalacia and assesses for signs of aspiration or other bronchopulmonary disease. The lipid-laden macrophage index (LLMI) developed by Colombo and Hallberg[21] has traditionally been used as a measure of chronic aspiration or pulmonary disease with cutoffs of anywhere from 85 to 104. However, Reilly et al. found recently that a wide variability existed between the range of the LLMI and the diagnosed pulmonary disease.[22] One should also screen for methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in the BAL and other body sites, as preoperative treatment of MRSA-colonized patients may reduce the likelihood of postoperative infections, graft loss, and dehiscence.[23] The EGD searches for GERD and/or eosinophilic esophagitis. The gastroenterologist may place a pH probe (with or without esophageal impedance), if deemed appropriate.

Rigid bronchoscopy with a Hopkins rod telescope provides excellent visualization and documentation of the airway, but it may underestimate the degree of dynamic airway collapse. The child should ideally be evaluated in a light plane of anesthesia allowing spontaneous ventilation, enabling the evaluation of dynamic airway disorders such as laryngomalacia and tracheomalacia. Once subglottic stenosis is identified, it should be described in detail and graded (Fig. 47.1). One should note the thickness, firmness, shape, and length of the stenosis. The Myer-Cotton grading system is most often used to document the degree of subglottic narrowing (Fig. 47.2). The airway is sized in relation to an age-appropriate endotracheal tube. For children aged 2 to 12 years, the age-appropriate endotracheal tube size is estimated by adding 16 to the child's age in years and then dividing this sum

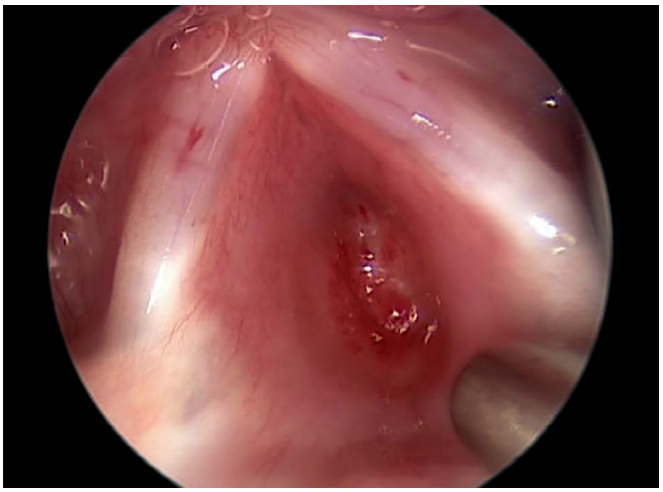


**Fig. 47.1:** Intraoperative photo demonstrating complete grade 4 subglottic stenosis.

| Classification | From | To |
|---|---|---|
| Grade I |  No obstruction |  50% obstruction |
| Grade II |  51% obstruction |  70% obstruction |
| Grade III |  71% obstruction |  99% obstruction |
| Grade IV | No Detectable Lumen | |

**Fig. 47.2:** Myer-Cotton grading system for subglottic stenosis. Reproduced with permission from Myer CM III, O'Connor DM, Cotton RT. Proposed grading system for subglottic stenosis based on endotracheal tube sizes. Ann Otol Rhinol Laryngol. 1994;103: 319-23.

by 4. The surgeon records the endotracheal tube size, which allows an air leak between 10 and 25 cm $H_2O$ and relates this to the expected size in the form of a percentage. If the patient has a tracheostomy, the distal trachea and bronchi should be visualized through the stoma.

Evidence continues to mount regarding the deleterious effects of GERD in the airway.[24,25] Animal models demonstrate that gastric acid applied to both injured and intact mucosa is associated with delayed healing and histiologic damage.[26-28] Reports have also shown esophageal biopsies consistent with GERD in 50–68% of patients with subglottic stenosis.[17,29] Despite these reports, a direct cause–effect relationship between GERD and poor surgical outcome in subglottic stenosis has yet to be determined. However, it would seem reasonable to treat known GERD in patients with subglottic stenosis before and after surgery.

Eosinophilic esophagitis has been discovered recently to adversely impact patients with subglottic stenosis. Esophagitis unresponsive to traditional GERD regimens associated with food allergies or generalized atopy is suspicious for eosinophilic esophagitis. Esophageal biopsy typically shows >15 eosinophils per high-power field at any one biopsy site within the esophagus.[30] The child must have been on a 6-week course of an appropriate dose proton pump inhibitor (PPI), or, if the child has not been on a PPI, a pH probe placed during the endoscopy must show no clinical GERD pH abnormalities. A case of a failed laryngotracheal reconstruction (LTR) thought to be due to previously undiagnosed eosinophilic esophagitis was described in 2002.[31] Another report suggested eosinophilic esophagitis is an important cause of upper airway symptoms and must be carefully considered in the workup and treatment of children with subglottic stenosis.[32]

## Treatment

### *Tracheostomy*

A tracheostomy represents an effective method to bypass a severe subglottic stenosis. Often, it is performed in younger infants to allow time for them to grow before they undergo a formal airway reconstruction. A tracheostomy is occasionally needed emergently in children with subglottic stenosis. Although this is a life-saving procedure, tracheostomy-related mortality rates range from 0.5% to 3.6%, and the procedure is not without significant and frequent complications.[33-35] Potential complications vary from mild bleeding or small suprastomal granuloma to catastrophic plugging or accidental decannulation. A practice pattern survey by the American Society of Pediatric Otolaryngology found that most surgeons make a vertical skin incision, remove subcutaneous fat, mature the tracheostoma, use stay sutures in the trachea, and secure the tracheostomy tube with ties.[36]

Surgical procedure: Ideally, the patient will be intubated with a small endotracheal tube passed through the subglottic stenosis. If the stenosis is too narrow, the tracheostomy will need to be performed with the child spontaneously ventilating and being masked. Remove any feeding tube from the esophagus so that the esophagus is not mistaken for the trachea during the dissection. A shoulder roll is placed under the patient to expose the necessary surgical landmarks.

A vertical skin incision is made at the level of the cricoid. A cervical lipectomy is accomplished to provide better visualization and decrease the dead space between the skin and the trachea. The strap muscles are divided vertically in the midline. The airway is skeletonized from the cricoid cartilage down to the fourth tracheal ring (Fig. 47.3). In many children, the thyroid cartilage telescopes under the hyoid and the thyroid notch will not be palpable as in adults. One must ensure the innominate artery and/or lung apices are not encountered when isolating the trachea distal to the thyroid gland. The thyroid isthmus is divided with bipolar cautery. Next, 4-0 Prolene sutures are placed through the tracheal cartilage at the level of the second and third tracheal rings on both sides to establish distal airway

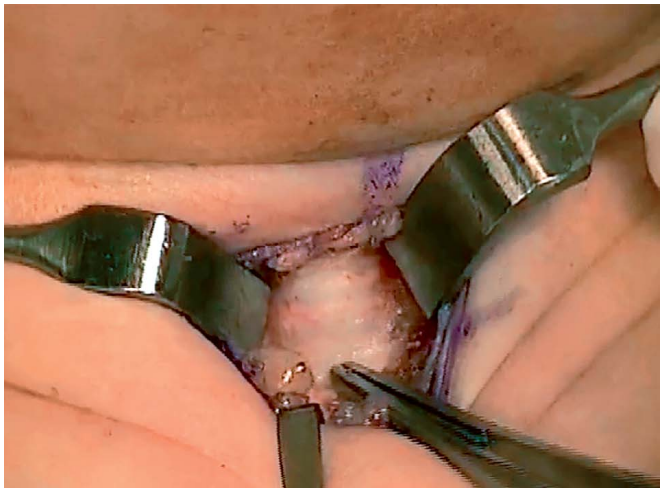


**Fig. 47.3:** Trachea is skeletonized down to fourth tracheal ring. Reproduced with permission from Gallagher TQ, Hartnick CJ. Pediatric tracheotomy. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73: 26-30. Copyright 2012 Karger (Basel, Switzerland).

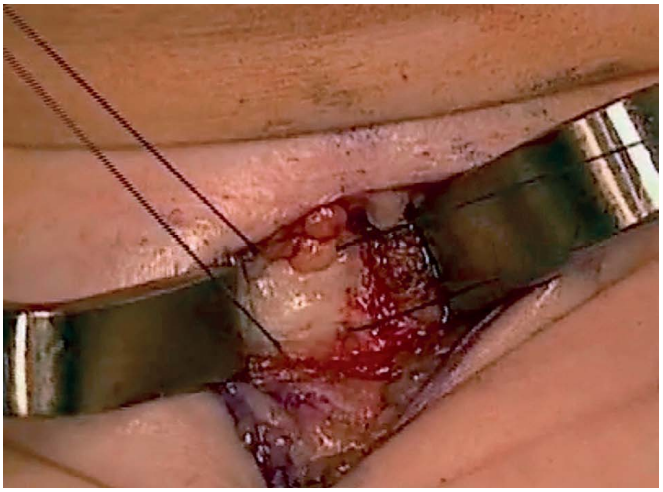


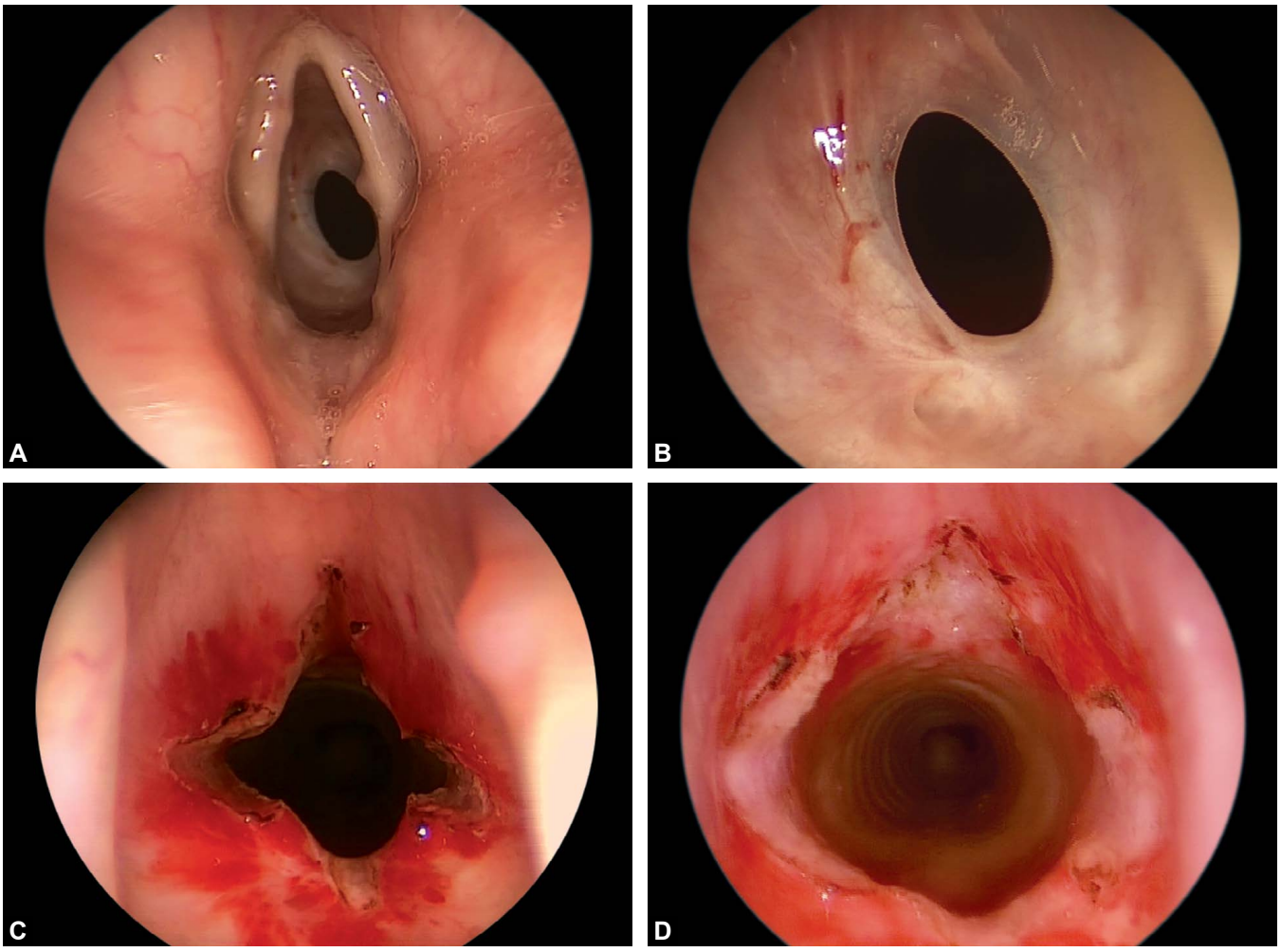
**Fig. 47.4:** Stay sutures are placed using 4-0 Prolene. Reproduced with permission from Gallagher TQ, Hartnick CJ. Pediatric tracheotomy. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:26-30. Copyright 2012 Karger (Basel, Switzerland).

control (Fig. 47.4). After communication with the anesthesiologist, a median vertical incision is made through the second and third tracheal rings with a scalpel, cutting from caudal to cephalad. The tracheostomy is then matured with 4-0 Monocryl vertical half-mattress sutures (usually two sutures placed inferiorly suffice). Maturing the tracheostoma greatly enhances safety during the first week after tracheostomy by allowing easy recannulation and preventing a false passage. The concern for persistent tracheocutaneous fistula due to maturing the tracheostoma has been refuted.[37] The endotracheal tube is withdrawn, and an age-appropriate sized tracheostomy tube is placed. The tracheostomy tube is secured with ties. The stay sutures are marked "left" and "right" and taped to their respective sides of the chest. The shoulder roll is removed, and a flexible fiberoptic tracheoscopy is performed through the tracheostomy tube to ensure there is adequate distance from the tip of the tracheostomy tube to the carina. The patient is transferred to the intensive care unit (ICU), and a humidified trach-collar is used along with frequent suctioning to prevent obstruction of the tracheostomy tube. The first tracheostomy tube change is performed by the otolaryngology service at 3 to 7 days postoperatively.

*Endoscopic techniques*

The use of endoscopic techniques for the treatment of subglottic stenosis represents an attractive option because it avoids a neck incision and may not require grafting or stenting. Early, soft subglottic stenoses and thin, web-like stenoses may be better served with this method. The carbon dioxide ($CO_2$) laser is frequently used to make radial incisions in the scar (Figs. 47.5A to D). The stenosis is then dilated with either uncuffed endotracheal tubes or a balloon. Due to the significant shear forces created during dilation with traditional bougienage techniques, balloons have been developed.[38] The balloon should be one specially designed for airway stenosis, which expands radially with equal force in all directions. The size of the balloon is estimated by using the outer diameter of an age-appropriate sized endotracheal tube. Studies have shown adequate results using $CO_2$ laser for early or mild subglottic stenosis, although multiple procedures are usually needed.[39-41] One report showed that a tracheostomy or cricoid split was avoided in 7 out of 10 infants with acquired subglottic stenosis by using endoscopic balloon dilation.[42] An animal study in rabbits found that balloon dilation actually causes cricoid fractures.[43] Endoscopic techniques are also employed after open airway reconstruction to prevent restenosis of the intraluminal soft tissue once the cartilage framework has been enlarged.

Mitomycin-C is an alkylating antineoplastic antibiotic with the ability to inhibit fibroblast proliferation and activity by blocking DNA and protein synthesis. An animal study[44] and human studies[45-48] have shown good preliminary results using mitomycin-C to limit restenosis. However, a randomized, double-blind, placebo-controlled



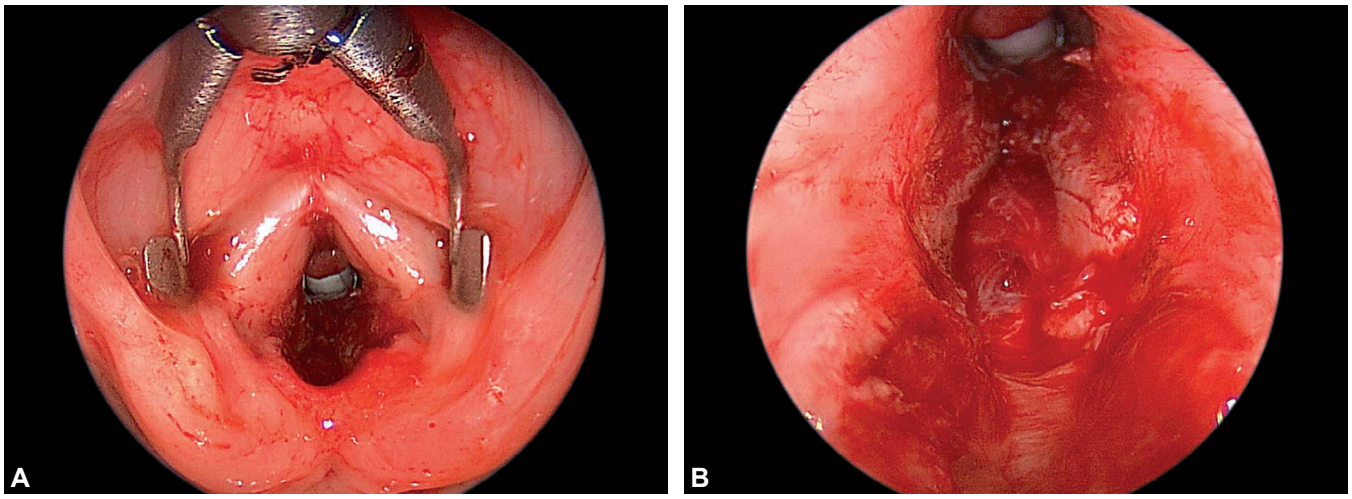

**Figs. 47.5A to D:** A thin subglottic stenosis is treated with endoscopic $CO_2$ laser and balloon dilation.

trial of a single topical dose of mitomycin versus isotonic sodium chloride showed no difference when applied to the pediatric airway after LTR.[49] Intralesional steroids such as triamcinolone may be used to help prevent restenosis. A particularly potent topical antibiotic and steroid combination medication is Ciprodex (ciprofloxacin/dexamethasone), which in small studies and anecdotally has been quite effective in limiting granulation tissue and decreasing edema while the airway remucosalizes.[50] Larger prospective studies are needed to more objectively assess its efficacy. Ciprodex may also be nebulized by placing 1 mL in 1 mL of physiologic saline with two to three treatments per day for up to a week.

General contraindications to endoscopic surgery for subglottic stenosis include:[51]

1. Firm, circumferential scarring
2. Scar tissue >1 cm in vertical length
3. Interarytenoid and/or posterior commissure scar
4. Severe bacterial tracheitis after tracheostomy
5. Excessively exposed perichondrium or cartilage after $CO_2$ laser treatment
6. Combined laryngotracheal stenosis
7. Failure of multiple previous endoscopic treatments
8. Significant diminution of cartilage framework

Although the entities listed above are the traditional contraindications, more substantial endoscopic procedures are being developed. In 2003, Inglis et al. described an endoscopic posterior cricoid split with placement of a posterior costal cartilage graft in patients with mild to moderate posterior glottic or subglottic stenosis.[52] A subsequent study of 28 children who underwent endoscopic posterior cricoid split showed that 25 were decannulated or never required tracheostomy.[53] Studies have now shown that endoscopic anterior cricoid split and balloon dilation is also a feasible procedure for pediatric subglottic stenosis.[54,55]




**Figs. 47.6A and B:** A $CO_2$ laser is used to perform a posterior cricoid split while leaving the interarytenoid musculature intact. Reproduced with permission from Modi VK. Endoscopic posterior cricoid split with rib grafting. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:116-122. Copyright 2012 Karger (Basel, Switzerland).

*Endoscopic posterior cricoid split*: Endoscopic posterior cricoid split is indicated for subglottic stenosis of Myer–Cotton grade 3 or less. It is also effective in treating bilateral vocal fold immobility and posterior glottic stenosis. The procedure depends on adequate endoscopic exposure and is contraindicated in severe transglottic stenosis, grade 4 subglottic stenosis, and tracheal stenosis.

Surgical procedure: After laser precautions are undertaken, a Lindholm laryngoscope is inserted into the vallecula and placed on suspension. A laryngeal spreader is placed in an inverted fashion to retract the false vocal folds and secured to the suspension apparatus with a rubber band. A straight laryngeal suction is used to push the interarytenoid muscles posteriorly and rotate the posterior cricoid lamina inferiorly and anteriorly. The posterior cricoid lamina is then divided with the $CO_2$ laser without lysing the posterior perichondrium or damaging the underlying esophagus (Figs. 47.6A and B). A costal cartilage graft is harvested and sculpted in a T-shaped fashion with perichondrium on the lumen side. The dimensions are approximately 1 cm in length with 5 mm width of perichondrium and 1 mm flanges. A rescue suture of 5-0 Prolene is placed through the superior aspect of the costal cartilage graft (Fig. 47.7). Laryngeal forceps and a curved angle probe are used to insert the graft, and the rescue stitch is then removed (Fig. 47.8). Stenting is accomplished with an endotracheal tube (preferably nasotracheal intubation) for 7 to 10 days.

The patient is transferred to the pediatric ICU for airway observation. A repeat DLB is performed at approximately 7 to 10 days postoperatively to check healing at that time before extubation. Corticosteroids are given before extubation and continued for a few days.

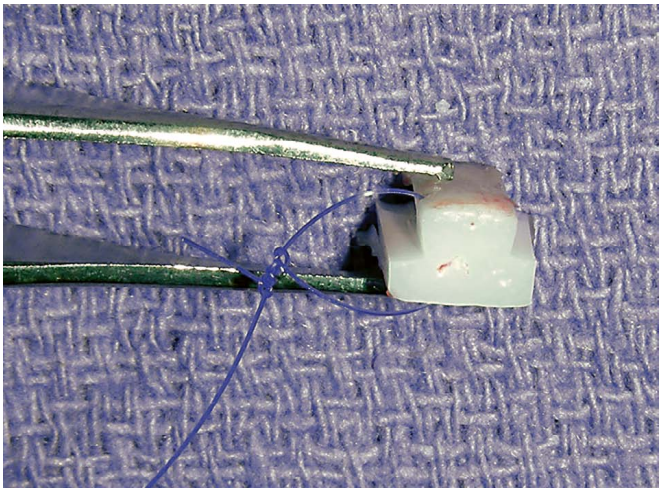


**Fig. 47.7:** Costal cartilage graft with perichondrium on luminal surface and 5-0 Prolene suture placed. Reproduced with permission from Modi VK. Endoscopic posterior cricoid split with rib grafting. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway Surgery. Adv Otorhinolaryngol. 2012;73:116-22. Copyright 2012 Karger (Basel, Switzerland).

*Open techniques*

*Anterior cricoid split*: Anterior laryngotracheal decompression via anterior cricoid split in neonates who failed extubation in the absence of glottic or supraglottic pathology was introduced in 1980 by Cotton and Seid as a means of avoiding tracheostomy.[56] The procedure relies on the fact that a moderate increase in subglottic diameter may enable extubation, and an early subglottic

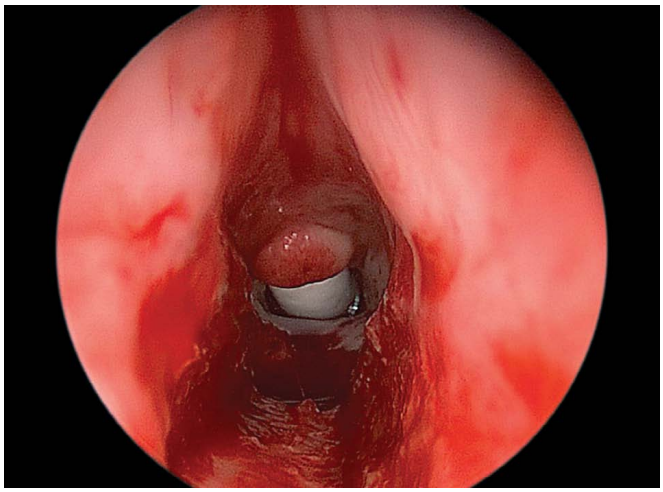


**Fig. 47.8:** Posterior cricoid split with costal cartilage graft in place. Reproduced with permission from Modi VK. Endoscopic posterior cricoid split with rib grafting. In Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:116-22. Copyright 2012 Karger (Basel, Switzerland).

injury may simply need time to heal. The purpose of an anterior cricoid split is to avoid tracheostomy and allow time for the subglottis to heal and grow. Criteria have been established for anterior cricoid split in neonates (Table 47.1).[57] If the animal work indeed proves that balloon dilation produces an endoscopic cricoid split, this surgical method may be tried before an open anterior cricoid split.

Surgical procedure: A horizontal skin incision is made over the cricoid cartilage, the strap muscles are divided vertically in the midline, and the laryngotracheal skeleton is exposed from the thyroid notch to the third tracheal ring in an intubated neonate. A vertical incision is made through the first two tracheal rings, the anterior cricoid, and the lower portion of the thyroid cartilage below the anterior commissure (Figs. 47.9A to D). The airway is left open with the endotracheal tube visible, and 4-0 Prolene stay sutures are placed through each side of the exposed cricoid in case of accidental extubation. The skin is closed loosely over a passive rubber band drain.

The child remains intubated for 7 to 10 days, where the endotracheal tube serves as the stent. Extubation is then attempted, and if the child fails, a tracheostomy tube is usually placed. Corticosteroids are given before extubation and continued for several days thereafter.

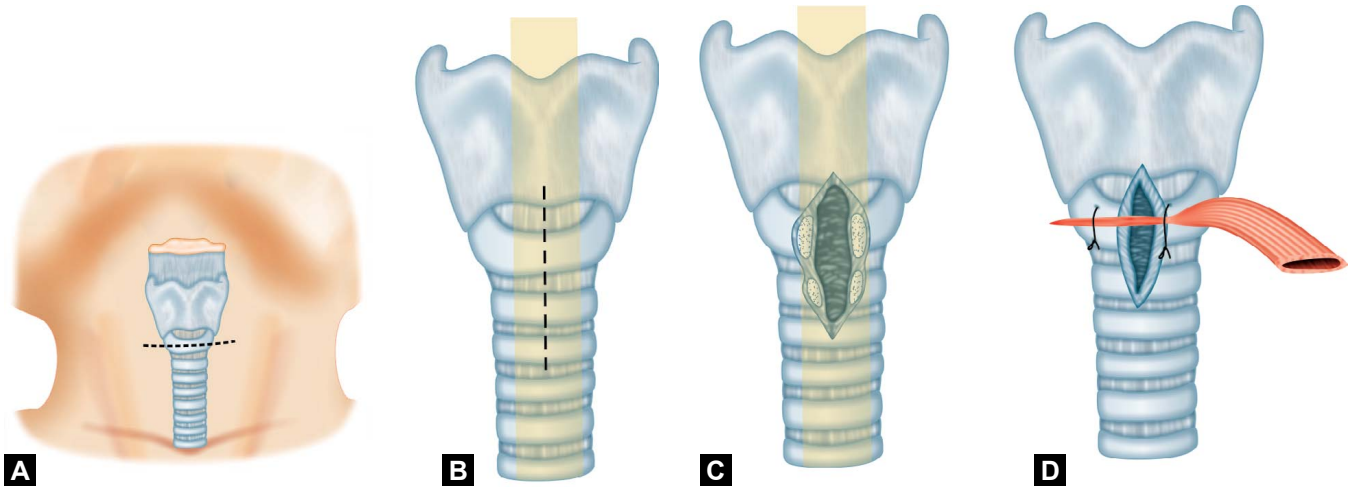
*Laryngotracheal reconstruction*: LTR still represents the most definitive and versatile treatment modality for pediatric subglottic stenosis. Rethi hypothesized that

**Table 47.1:** Criteria for anterior cricoid split in neonates

| |
|---|
| Extubation failure at least twice due to subglottic pathology |
| Weight > 1500 g |
| No ventilatory support for at least 10 days |
| Supplemental oxygen requirement < 35% |
| No congestive heart failure for at least 1 month |
| No acute upper respiratory tract infection |
| No antihypertensive medications for at least 10 days |

incising but not excising the mature scar of subglottic stenosis coupled with stenting to maintain expansion during healing was adequate in adult war victims.[2] Fearon and Cotton adapted this concept when they described vertically dividing the cricoid ring and placing cartilage grafts in between the cricoid lamina.[58] Decannulation rates for LTR now approach 90%.[59]

Although the basic steps are the same for every LTR, each procedure is tailored to the specific patient. The patient must not have tracheostomy dependence due to chronic pulmonary disease or neurologic impairment requiring oxygen dependence. LTR is particularly indicated in combined glottic and subglottic stenosis and when the subglottic stenosis is too close to the vocal folds to allow a safe plane of superior dissection for a cricotracheal resection (CTR). The first decision is to determine whether to perform the reconstruction in two stages (double-stage) or in one stage (single-stage). The traditional method is to perform a double-stage procedure, defined as leaving the tracheostomy in place while the airway heals. Double-stage LTR remains the safest option and is good for patients with high-grade stenoses, tracheal obstruction, significant tracheomalacia, and craniofacial or vertebral anomalies. Gustafson et al. found that the placement of both anterior and posterior grafts, an age of < 4 years, a pre-extubation air leak of > 20 cm, sedation for > 48 hours, and moderate to severe tracheomalacia were associated with a greater risk for reintubation.[60] Hartley et al. reported that the duration of stenting (intubation in single-stage LTR with anterior costal cartilage graft) was not correlated with the reintubation rate.[61] If any lack of confidence exists in the postoperative ICU management of airway patients, a double-stage LTR should be performed. Single-stage LTR consists of removing the tracheostomy or avoiding a tracheostomy altogether at the time of surgery. If the postoperative ICU management is known to be adequate and the patient does not have the above



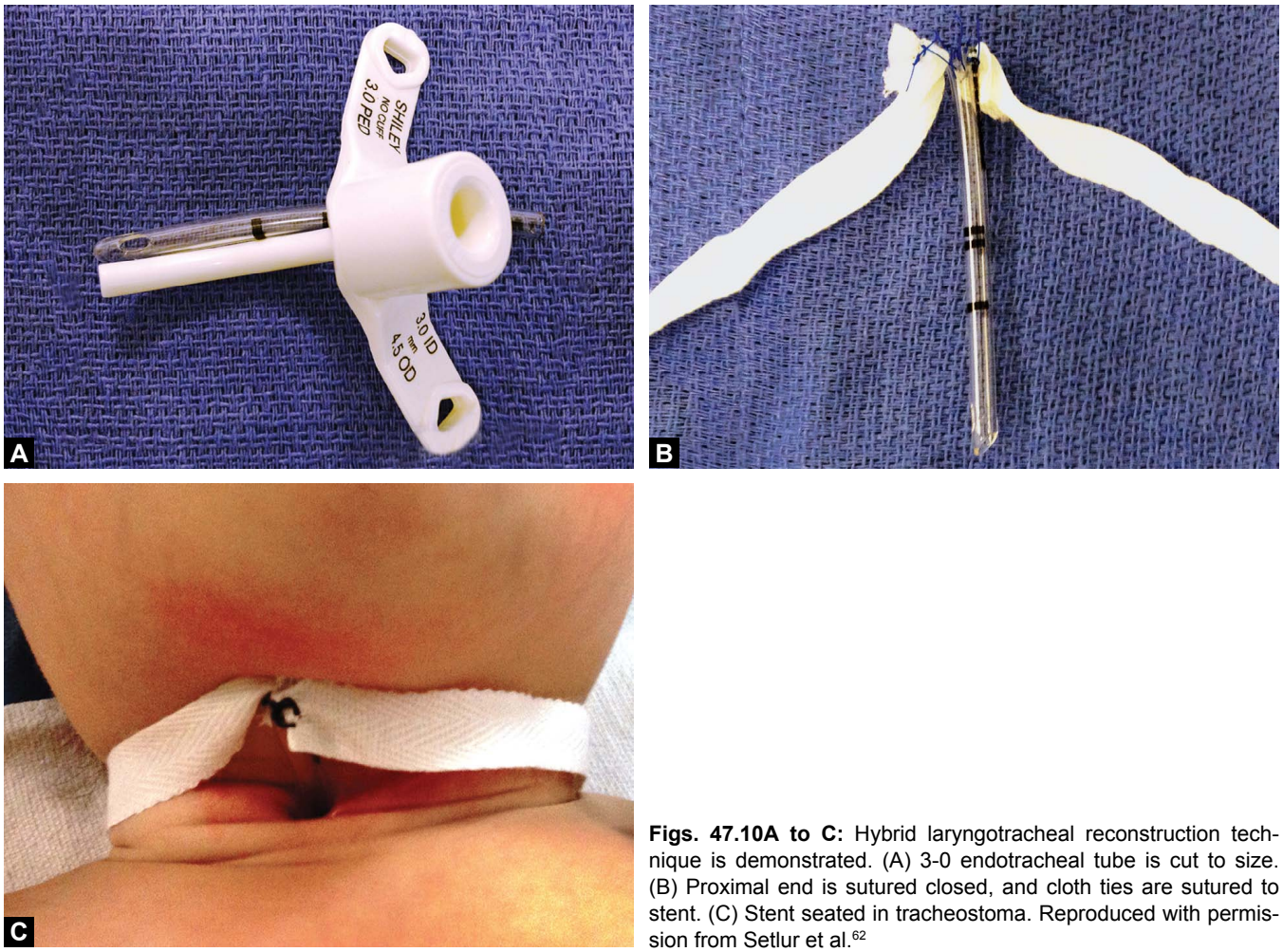

**Figs. 47.9A to D:** Diagram depicting the anterior cricoid split procedure. (A) Horizontal skin incision is made over the cricoid; (B) and (C) vertical incision is made from caudal aspect of thyroid cartilage down through the first tracheal ring; (D) Wound is closed over a passive drain. Reproduced with permission from Zalzal and Cotton.[51]

conditions, one should consider a single-stage LTR. More recently, a hybrid LTR (or 1.5-stage LTR) has been developed to combine the benefits of both double- and single-stage LTR.[62] A 3-0 uncuffed endotracheal tube is cut to the length of an age appropriate tracheostomy tube, sutured closed at one end, and placed in the stoma instead of the tracheostomy tube (Figs. 47.10A to C). A hybrid LTR is ideal for patients who would benefit from the placement of a long-segment but short-term stent in the airway; it essentially allows a single-stage LTR to become applicable to patients with higher grade or more complex stenoses. Alternatively, one could use a 3-0-capped tracheostomy tube in the stoma instead. Using this varied technique helps prevent scarring and granulation tissue that may form at the junction between the suprastomal stent and the tracheostomy tube in a traditional double-stage LTR.

Children usually do not undergo formal LTR with costal cartilage grafting until 1 year of age. This allows time for the ribs to enlarge, the patient to gain weight, and the lungs to mature. Any cardiac issues should be optimized by this time. The children are also less likely to require a tracheostomy for ventilatory support. Although the most common goal of LTR is decannulation or prevention of a tracheostomy, some children require airway reconstruction to allow for a safe, intubatable, emergent airway. Other children with grade 4 subglottic stenosis may undergo LTR to provide them with a voice.

Cartilage graft options: The most common choice of cartilage graft in pediatric LTR remains autogenous costal cartilage. A large amount of cartilage exists, and it is rigid yet easily trimmed to the appropriate shape and dimensions. Costal cartilage should always be used for the posterior cricoid graft. For the anterior graft, a few additional options exist; however, costal cartilage is frequently employed here as well. Auricular cartilage can be used successfully in lower grade stenoses and may epithelialize faster than costal cartilage.[63-65] Thyroid ala cartilage may work effectively in grade 2 or 3 subglottic stenosis[66,67] and has shown good functional voice outcomes.[68] Another advantage of this technique is the avoidance of a chest incision. Survival of cartilage grafts has been shown on gross and histologic examination in a rabbit study.[69]

Stents: Stents are necessary to stabilize the cartilage grafts after a cricoid split and prevent immediate scar contracture.[51] The larynx and trachea will move with breathing, swallowing, and any attempt at phonation. In a single-stage LTR, the nasotracheal tube itself functions as the stent. A few options exist for stenting in a double-stage LTR. One option is to also use a nasotracheal tube as the stent as in single-stage LTR. Next, one can cut off the end of an age-appropriate sized Montgomery T-tube and suture the cephalad portion closed with permanent suture to help prevent aspiration. Another option is to use the Montgomery T-tube in its original form, which works well in combined glottic and subglottic stenosis in patients aged $\geq 5$ years. One must be quite careful if choosing this option because if the T-tube clogs, it may be difficult to remove and




**Figs. 47.10A to C:** Hybrid laryngotracheal reconstruction technique is demonstrated. (A) 3-0 endotracheal tube is cut to size. (B) Proximal end is sutured closed, and cloth ties are sutured to stent. (C) Stent seated in tracheostoma. Reproduced with permission from Setlur et al.[62]

re-establish a patent airway. An Aboulker stent is a cigar-shaped Teflon prosthesis, which effectively counteracts scar contracture and stabilizes a reconstructed airway; however, granulation tissue may form at either end of the stent.[70] More recently, Monnier helped develop the LT-Mold suprastomal stent (not yet FDA approved), which is made of soft silicone designed to limit granulation and improve healing by conforming to the internal laryngeal contours.[71] Stents used after a double-stage LTR usually stay in place for about 1 to 2 weeks.

Surgical procedure: If the patient does not have a tracheostomy, it is ideal to intubate with a small endotracheal tube at the start of the case. The neck and chest should be prepped and draped, and the proposed skin incisions are marked (Fig. 47.11). In some cases, it may not be certain whether LTR or CTR is the best option until the laryngotracheal complex is opened. It would be prudent to wait and harvest cartilage later (if needed) in this circumstance. Moreover, costal cartilage may be too small to adequately carve and insert in infants aged <1 year. If it is already certain that autogenous costal cartilage grafts will be used, this is harvested first as a "clean" procedure.

The costal cartilage is usually harvested from the right side for a right-handed surgeon. A 4-cm horizontal skin incision is made in the inframammary crease and taken down to the 5th or 6th rib (Figs. 47.12A and B). The bony–cartilaginous junction is identified (Fig. 47.13). The cephalad and caudal edges of the rib are carefully cauterized to reduced bleeding. These edges are then incised sharply with a scalpel. A Cottle elevator followed by a Freer elevator is used to dissect posteriorly in a subperichondrial plane. Approximately 2 cm of costal cartilage is harvested from a straight section, maintaining the lateral perichondrium on the graft and leaving the medial perichondrium intact to protect the pleural and lung.

The wound bed is filled with sterile saline, and a Valsalva is performed to 30 cm $H_2O$ pressure to ensure the pleura was not violated. The wound is closed in layers over a rubber band drain. The costal cartilage is sculpted to the appropriate dimensions, according to the child's airway. The dimensions of the anterior graft vary depending on the degree of airway distraction needed once the stent is in place.

A horizontal neck incision is made above the tracheostoma over the cricoid in a double-stage LTR, or an elliptical incision including the tracheostoma is made for a single-stage LTR. The strap muscles are divided vertically in the midline, and the laryngotracheal cartilages are skeletonized from thyroid notch to two tracheal rings caudal to the tracheostoma. Positive control is gained of the distal trachea by placing 4-0 Prolene sutures bilaterally through the tracheal cartilage (caudal to the tracheostomy if present). Then, 4-0 Prolene sutures are placed on both sides of the proposed anterior cricoid split. If laryngofissure is planned, the vertical midline is marked, and a horizontal hash mark is made with electrocautery to facilitate accurate reapproximation upon completion of surgery (Fig. 47.14).

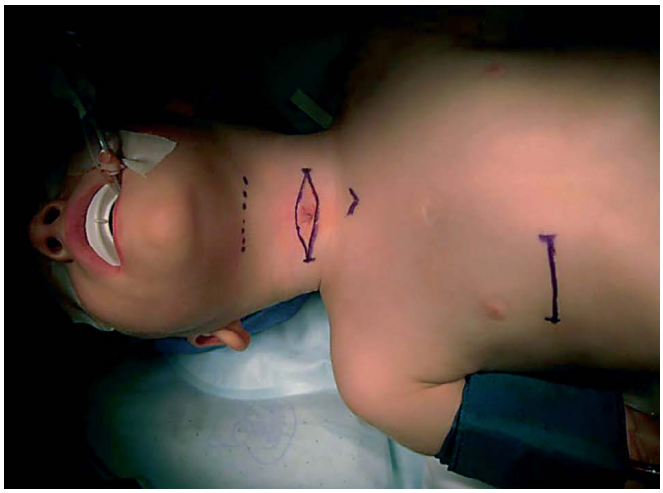
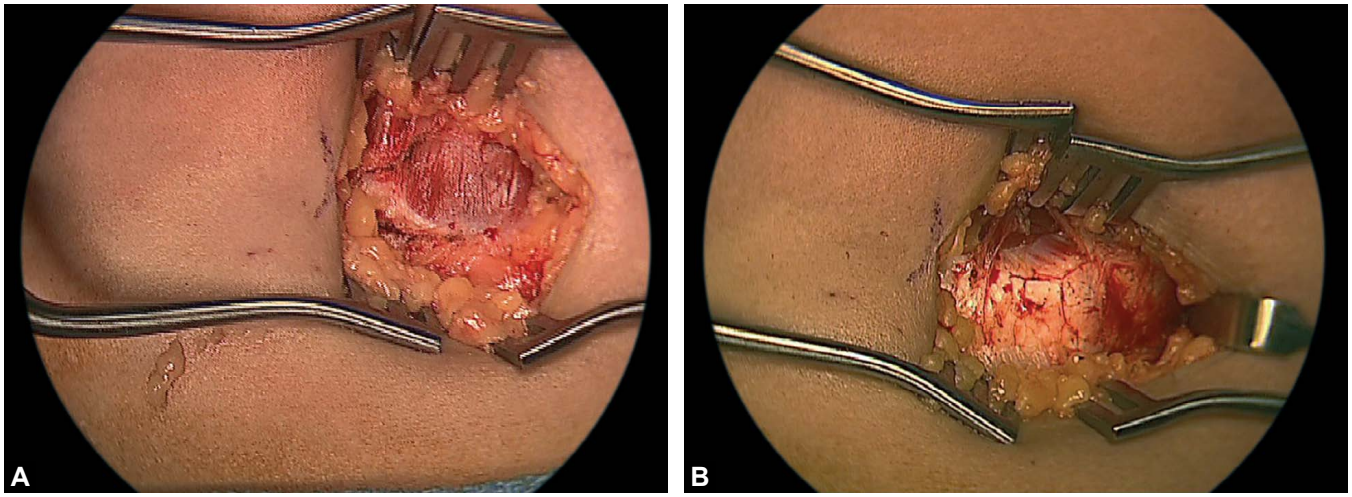


**Fig. 47.11:** Neck and chest landmarks and proposed incisions are marked. Reproduced with permission from Gallagher TQ, Hartnick CJ. Laryngotracheal reconstruction. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:31-38. Copyright 2012 Karger (Basel, Switzerland).

The anterior cricoid lamina is divided with a Beaver blade. A fine hemostat is placed in the lumen of the airway and used to distract the cricoid split. The incision is carried cephalad to the thyroid cartilage and caudally down to the first tracheal ring (and through the tracheal ring if it is involved in the stenosis). The patient is extubated, and the distal trachea is intubated with an age-appropriate sized endotracheal tube. If a laryngofissure is deemed necessary as is the case for most moderate to severe stenoses, a Beaver blade is used to divide the thyroid cartilage in the midline from caudal to cephalad while leaving the inner perichondrium intact initially. Some stenoses may allow visualization with only a partial laryngofissure that stays caudal to the anterior commissure. Many stenoses require a complete laryngofissure (Fig. 47.15). Endoscopic assistance with an assistant using a telescope via direct laryngoscopy




**Figs. 47.12A and B:** (A) Muscle layer exposed. (B) Perichondrium exposed. Reproduced with permission from Gallagher TQ, Hartnick CJ. Costal cartilage harvest. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:39-41. Copyright 2012 Karger (Basel, Switzerland).

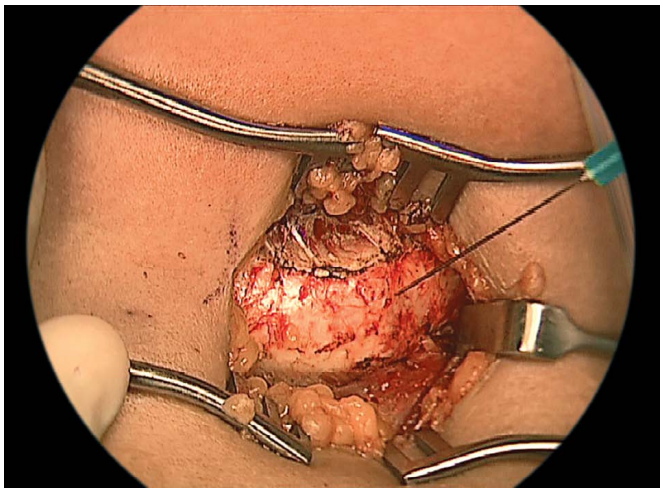


**Fig. 47.13:** The bony-cartilaginous "blue line" is located. Reproduced with permission from Gallagher TQ, Hartnick CJ. Costal cartilage harvest. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73: 39-41. Copyright 2012 Karger (Basel, Switzerland).

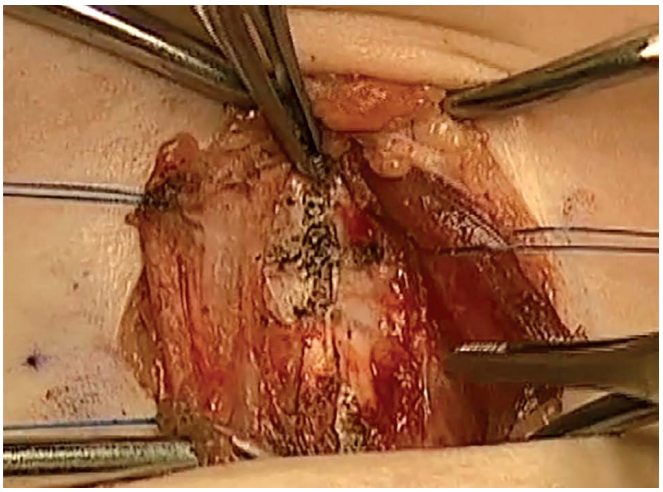


**Fig. 47.14:** A cruciform mark is made on the thyroid cartilage to facilitate accurate reapproximation. Reproduced with permission from Gallagher TQ, Hartnick CJ. Laryngotracheal reconstruction. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:31-38. Copyright 2012 Karger (Basel, Switzerland).

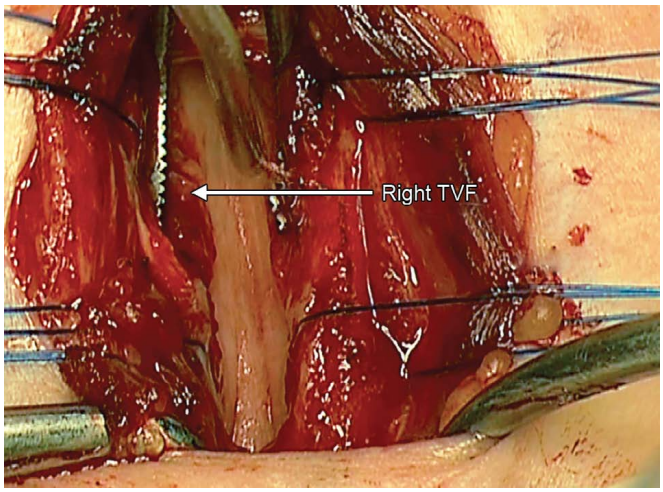



**Fig. 47.15:** View after complete laryngofissure and anterior cricoid split. The right true vocal fold is marked by the white arrow. Reproduced with permission from Gallagher TQ, Hartnick CJ. Laryngotracheal reconstruction. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:31-38. Copyright 2012 Karger (Basel, Switzerland).

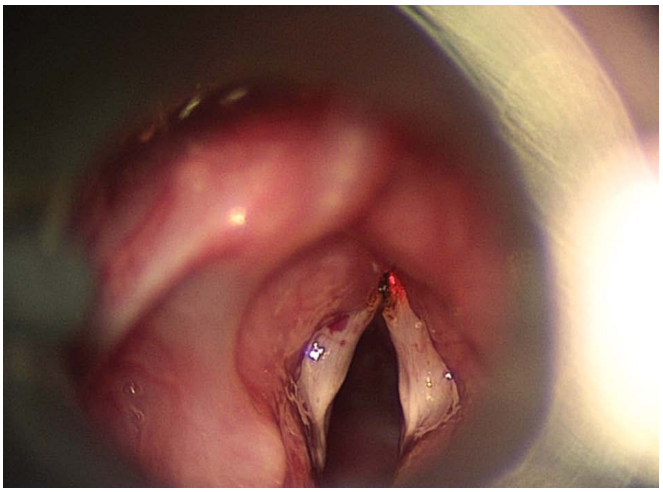


**Fig. 47.16:** Endoscopic $CO_2$ laser anterior laryngofissure.

may ensure accurate division of the anterior commissure, provided the patient does not have a grade 4 stenosis. Alternatively, in patients with adequate exposure, an endoscopic $CO_2$ laser anterior laryngofissure may be performed during suspension microlaryngoscopy before the neck or chest is opened, which ensures precise division of the anterior commissure and assists in accurate reapproximation of the true vocal folds after the reconstruction (Fig. 47.16).[72]

Next, the surgeon must decide whether to perform a posterior cricoid split. Most severe stenoses, congenital elliptical stenoses, or posterior stenoses require both an anterior and posterior cricoid split. If only the anterior cricoid is split, it is akin to enlarging the roof of a house without enlarging the foundation (Fig. 47.17). If a posterior cricoid split is deemed necessary, the mucosa overlying the posterior cricoid lamina is infiltrated with epinephrine. The posterior cricoid lamina is carefully divided down through the posterior perichondrium with a Beaver blade, while using a right-angled hemostat to apply posterolateral countertraction. The posterior cricoid lamina will release and convert from a "V-shaped"

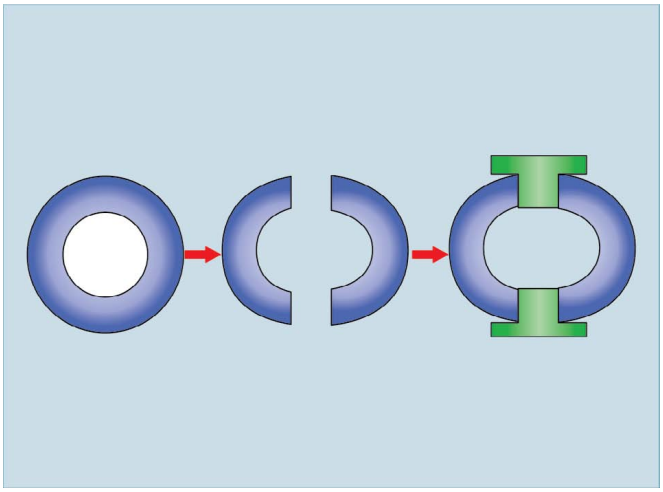


**Fig. 47.17:** Diagram of anterior and posterior cricoid split with grafting.

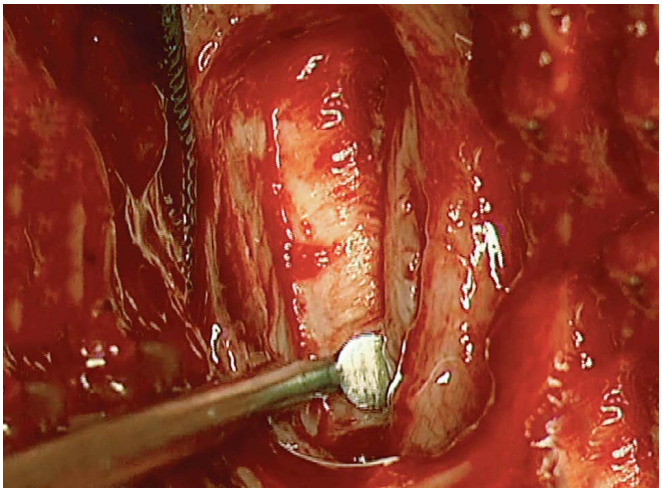


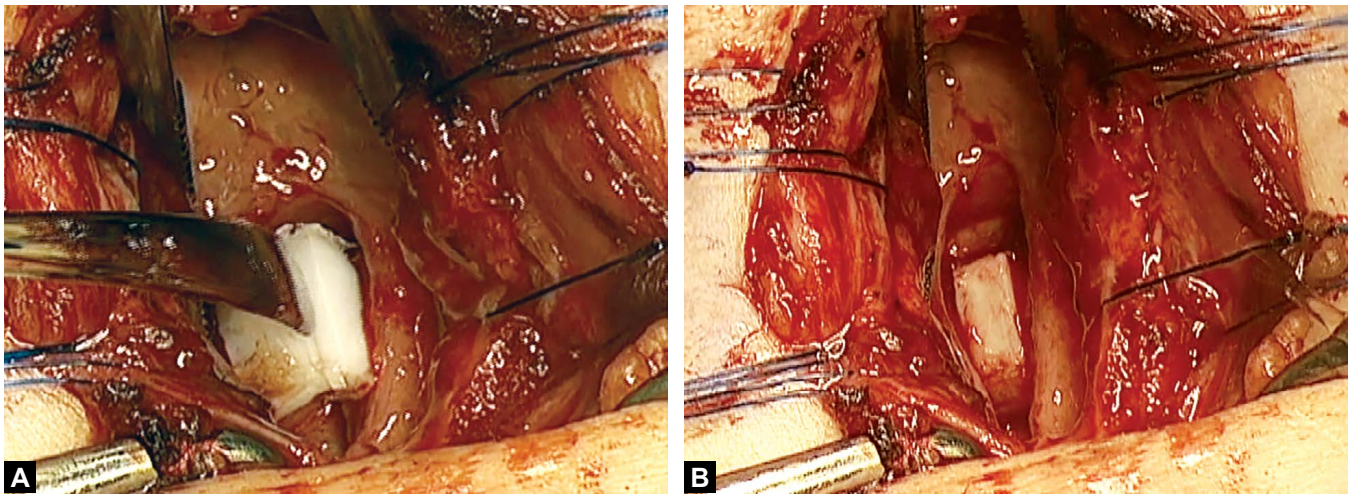
**Fig. 47.18:** The posterior perichondrium is elevated off the posterior surface of the cricoid using an otologic round knife. The oblique fibers and raphe of the posterior cricoarytenoid muscle are seen deep to the round knife. Reproduced with permission from Gallagher TQ, Hartnick CJ. Laryngotracheal reconstruction. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:31-38. Copyright 2012 Karger (Basel, Switzerland).

incision to a "U-shaped" one, and the esophageal musculature will now be visible. A medium-sized otologic round knife is used to undermine the posterior cricoid along the split to allow room for the posterior cartilage graft (Fig. 47.18). The posterior cartilage graft is secured into position by sliding the cartilage flanges underneath the divided cricoid lamina (Figs. 47.19A and B). For a double-stage LTR, a stent is then placed so that the caudal portion abuts the tracheostomy tube and the cephalad portion sits just above the true vocal folds to limit scarring and aspiration. The stent is secured by placing a 2-0 Prolene suture through the strap muscles, tracheal wall, stent, contralateral tracheal wall, and contralateral strap muscles. The suture is tied over an 18-gauge angiocatheter and left in the subcutaneous tissues on the patient's right.

If a laryngofissure was performed, it is closed prior to airway sizing and anterior cartilage graft placement. The previously made horizontal hash marks are lined up, and the anterior commissure is reapproximated with a submucosal vertical mattress 4-0 Monocryl suture placed far-to-far and near-to-near. If this is a revision LTR with vertically misaligned true vocal folds, the anterior commissure should be realigned during this step. The remainder of the thyroid cartilage is closed with 4-0 Vicryl simple interrupted sutures. For a single-stage LTR, the airway is then sized by placing an age-appropriate nasotracheal tube past the reconstruction. If needed, an anterior cartilage graft is trimmed to appropriate size and sutured into position with 4-0 Vicryl horizontal mattress sutures (Fig. 47.20). Fibrin glue is placed over the reconstruction, a rubber band drain is placed, and the wound is closed in layers.

The postoperative management depends both on the patient's age and the type of LTR. For double-stage LTR, the patient is awoken at the end of the procedure and transferred to the ICU for overnight observation. A chest film is obtained to rule out pneumothorax and to check the position of the endotracheal tube (if placed). A modified barium swallow is performed before feeding to assess aspiration risk. The stent is then removed in the operating room one week later, and follow-up DLB is performed as necessary. For patients aged 3 years or younger undergoing a single-stage LTR, they remain nasotracheally intubated in the ICU for 3 days (anterior graft only) to a week (posterior graft). Paralysis and sedation with medication holidays are implemented. The patients are extubated in the operating room after corticosteroids are given and sedation is weaned the prior day. Once extubated, they undergo swallow evaluation to determine the appropriate diet. A second DLB is performed at 2 weeks postoperatively, and balloon dilation may be utilized if needed. For patients >3 years undergoing a single-stage LTR, paralysis may not be necessary if they tolerate their nasotracheal tube awake. Patients are placed on reflux medication for 3 months.

*Cricotracheal resection*: Even in the most experienced hands, LTR may require revision. Common reasons for failure include collapse in the region of the anterior cricoid split and excessive granulation due to the lack of




**Figs. 47.19A and B:** A Freer elevator is used to secure the posterior graft into position by sliding the flanges under the cricoid. Reproduced with permission from Gallagher TQ, Hartnick CJ. Laryngotracheal reconstruction. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:31-38. Copyright 2012 Karger (Basel, Switzerland).

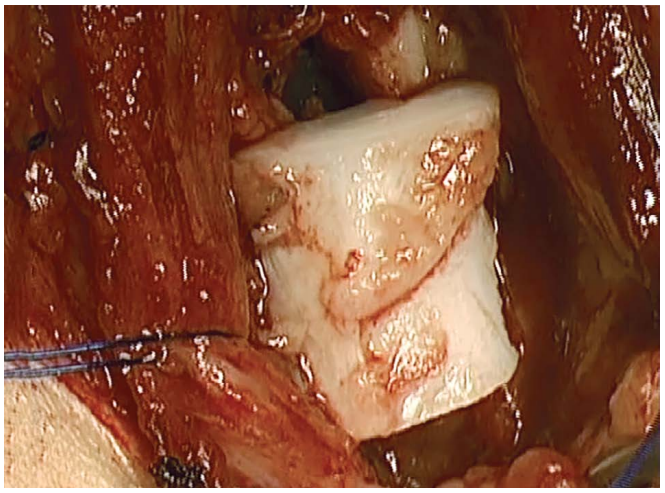


**Fig. 47.20:** An anterior cartilage graft (if needed) is sutured in place after placing an age-appropriate sized nasotracheal tube. Reproduced with permission from Gallagher TQ, Hartnick CJ. Laryngotracheal reconstruction. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:31-38, Copyright 2012 Karger (Basel, Switzerland).

mucosal covering of the cartilaginous grafts. In 1974, Gerwat and Bryce described the CTR procedure in children.[73] Monnier et al.[74,75] advanced the procedure in the 1990s and early 2000s, and others continue to modify it for unique laryngotracheal stenoses.

A CTR is indicated for symptomatic subglottic stenosis that is isolated from the true vocal folds by at least 3 mm. For purely subglottic lesions, the procedure may be combined with a posterior cricoid split and costal cartilage graft, known as an extended CTR. A CTR is a good option for persistent subglottic stenosis after a previous LTR. Similar to the LTR, a CTR may be performed in either a single-stage or double-stage fashion depending on the aforementioned factors for LTR staging. Monnier et al. found that up to five tracheal rings may be resected in a pediatric CTR.[76] Walner et al. reported that up to 3 cm of trachea could be resected.[77] A CTR is more technically challenging than LTR and carries an additional <3% risk of recurrent laryngeal nerve injury and 5% dehiscence rate of the anastomosis.[74]

Surgical procedure: A shoulder roll is placed to achieve effective neck extension. A bougie esophageal dilator is inserted to allow for identification of the esophagus during elevation of the posterior trachea. The patient's family should be counseled regarding the possibility of conversion from CTR to LTR, and both the neck and chest should be prepped and draped as explained in the LTR section (*see* Fig. 47.11). A transverse neck incision is made over the cricoid, or centered around the tracheostoma if planning a single-stage surgery. As in LTR, CTR may be double staged. However, two normal tracheal rings must exist between the tracheostomy and the stenosis. The strap muscles are divided vertically in the midline, and the laryngotracheal complex is then skeletonized from hyoid down to the fifth tracheal ring. If the patient does not have a tracheostomy, it may be beneficial to perform a temporary one through the third and fourth tracheal rings or lower if feasible. This permits full access to the subglottis and proximal trachea while maintaining ventilation through the distal trachea. If performed, the

tracheostomy is intubated with a cuffed endotracheal tube. Two 4-0 Prolene sutures are placed through both sides of the trachea caudal to the tracheostomy to gain positive control of the distal airway. Next, two 4-0 Prolene sutures are placed through both sides of the proposed anterior cricoid split. A suprahyoid muscular release is performed to release the laryngeal skeleton at its cephalad aspect. The cricothyroid muscle is dissected off the anterior cricoid with bipolar cautery, taking care to avoid the cricothyroid joint and recurrent laryngeal nerve. The ends of the cricothyroid muscle are tagged for later suture reapproximation. An anterior cricoid split is performed with a Beaver blade and carried cephalad to the thyroid cartilage and caudal to the first tracheal ring.

The extent of the stenosis is evaluated by direct inspection. If the stenosis involves the first few tracheal rings, they are divided as well. A formal LTR is performed instead if the stenosis is within 3 mm of the true vocal folds. The cricoid is dissected free of the adjacent tissue in a subperichondrial plane to protect the recurrent laryngeal nerve. The anterior face of the cricoid is removed piecemeal laterally to the 3 and 9 o'clock positions (Fig. 47.21). The trachea is then intubated directly. An otologic 4-mm diamond drill is used if needed to remove the remaining cricoid ring laterally so that only a flat posterior cricoid plate remains (Fig. 47.22). If a significant posterior stenosis exists, a posterior cricoid split with autologous costal cartilage graft is performed (extended CTR). The posterior cricoid mucosa is injected with epinephrine and then elevated off the posterior cricoid lamina with a bipolar and Freer elevator. The involved tracheal rings are removed from the proximal segment. If two sturdy tracheal rings do not exist between the tracheostomy and the distal trachea stump, the tracheostomy is resected. A short segment of the distal trachea stump is dissected 360° around in a subperichondrial plane to prevent injury to the recurrent laryngeal nerve; this provides the necessary mobilization while limiting disruption of the tracheal blood supply. Temporary 4-0 Prolene retraction sutures on both sides of the distal tracheal stump facilitate exposure and allow easier dissection during this step. When elevating the trachea posteriorly, one palpates the esophageal dilator posteriorly while looking down the tracheal lumen to ensure the membranous trachea is not transected anteriorly.

The shoulder roll is then removed. Tension sutures of 2-0 Prolene are placed submucosally around the first two tracheal rings of the stump and through the thyroid cartilage superiorly on both sides of the airway. The sutures are pulled (but not tied yet) to ensure no tension at the future anastomosis site. A nasotracheal tube is placed from above, spanning the anastomosis. In a single-stage CTR, the tracheostomy is removed, and the tracheostomy is sutured closed with 4-0 Vicryl suture. The posterior cricoid mucosa is sutured directly to the posterior tracheal mucosa with simple interrupted 4-0 Vicryl sutures

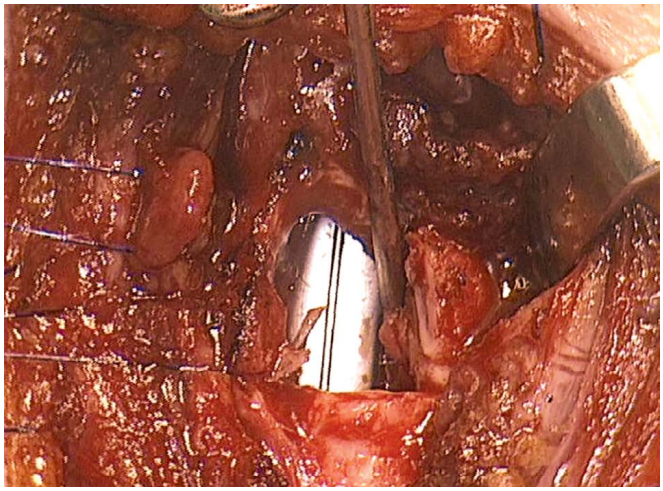


**Fig. 47.21:** Anterior cricoid is resected in a piecemeal fashion. Reproduced with permission from Gallagher TQ, Hartnick CJ. Cricotracheal resection and thyrotracheal anastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:42-49. Copyright 2012 Karger (Basel, Switzerland).

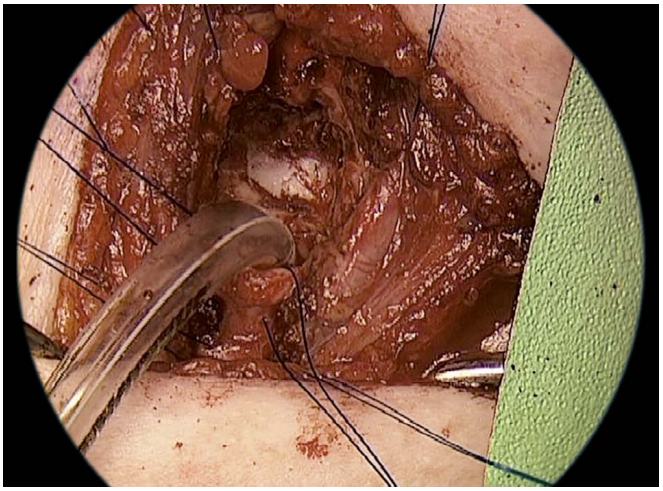


**Fig. 47.22:** Only a flat posterior cricoid plate remains after drilling down the remaining lateral shelves. Reproduced with permission from Gallagher TQ, Hartnick CJ. Cricotracheal resection and thyrotracheal anastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:42-49. Copyright 2012 Karger (Basel, Switzerland).

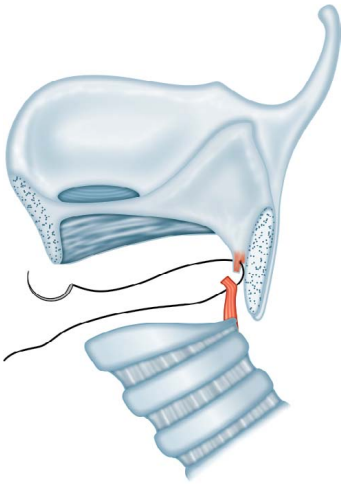


**Fig. 47.23:** Posterior tracheal mucosa is sutured directly to the posterior cricoid mucosa if enough remains. Reproduced with permission from Gallagher TQ, Hartnick CJ. Cricotracheal resection and thyrotracheal anastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:42-49. Copyright 2012 Karger (Basel, Switzerland).

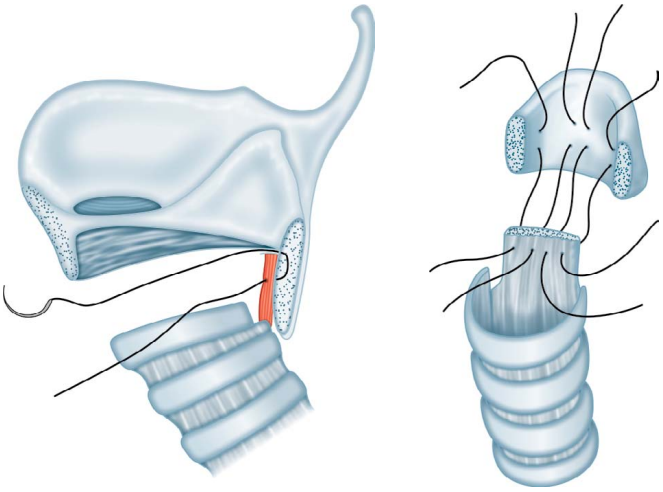


**Fig. 47.24:** Sutures incorporate the posterior cricoid cartilage if inadequate mucosa remains. Reproduced with permission from Gallagher TQ, Hartnick CJ. Cricotracheal resection and thyrotracheal anastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:42-49. Copyright 2012 Karger (Basel, Switzerland).

from 3 to 9 o'clock (Fig. 47.23). If little posterior cricoid mucosa remains, the sutures should also incorporate the posterior cricoid cartilage (Fig. 47.24). The sutures are not tied until they have all been thrown (Fig. 47.25). The 2-0 Prolene tension sutures are then tied. The anterior mucosa is reapproximated with 4-0 Vicryl sutures in an interrupted and extraluminal fashion. All sutures are thrown first before tying them. The cricothyroid muscle is reapproximated with 4-0 Vicryl sutures (Figs. 47.26A to C). Fibrin glue sealant is placed over the laryngotracheal complex. A passive drain is placed, and the wound is closed in layers. Large Prolene chin-to-chest sutures are used to prevent head extension (Fig. 47.27).

Depending on the age of the patient and tension of the anastomosis, the patient may be extubated and transferred to the ICU. Some patients may require up to a week of sedation and paralysis for immobilization and optimal healing. Corticosteroids are not used because they may inhibit critical wound healing at the anastomosis. Broad-spectrum intravenous antibiotics are started. Once extubated, flexible laryngoscopy should be used to evaluate vocal fold mobility. Balloon dilation should not be employed until 6 weeks after the CTR. A modified barium swallow is performed to assess the aspiration risk. If crepitus/subcutaneous emphysema occurs during the first few postoperative days, the patient should return to the operating room for reintubation and inspection of the anastomosis. Antireflux therapy is initiated for at least 3 months.

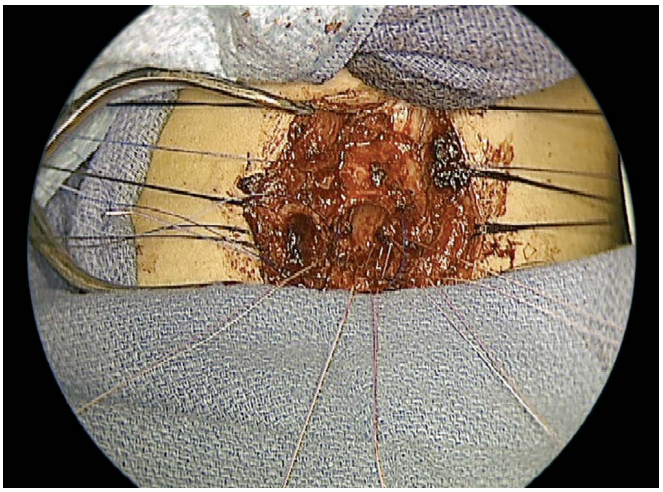
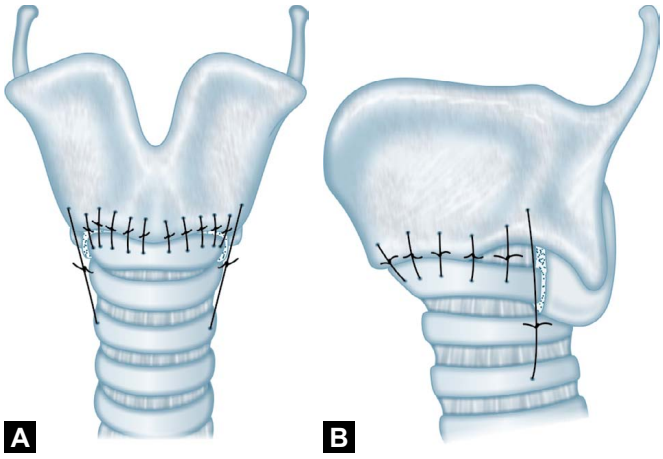
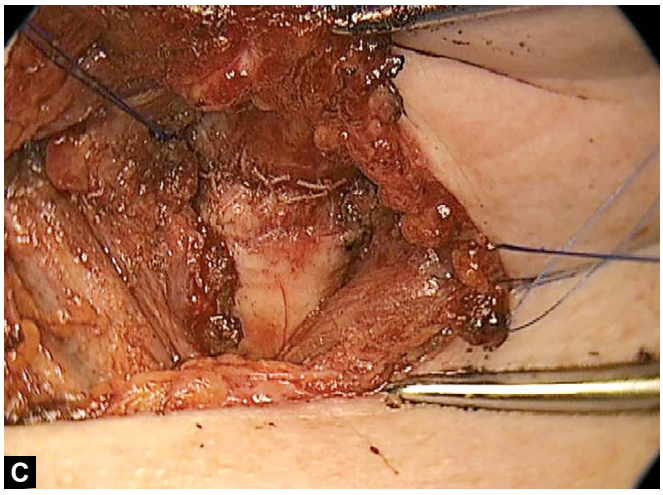


**Fig. 47.25:** Sutures are all thrown and neatly arranged before tying them. Reproduced with permission from Gallagher TQ, Hartnick CJ. Cricotracheal resection and thyrotracheal anastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:42-9. Copyright 2012 Karger (Basel, Switzerland).

## Subglottic Cyst

A subglottic cyst is a rare entity that may present quite similarly to subglottic stenosis (Figs. 47.28A and B). The cysts occur most often in preterm infants with a history of intubation. The estimated incidence of subglottic cysts is 1.9 per 100,000 live births.[78,79] They frequently recur and may be an early sign of a developing subglottic stenosis.




**Figs. 47.26A to C:** Diagram of the completed anastomosis. (A) Anterior. (B) Lateral. (C) Intraoperative. Reproduced with permission from Gallagher TQ, Hartnick CJ. Cricotracheal resection and thyrotracheal anastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:42-49. Copyright 2012 Karger (Basel, Switzerland).

Halimi et al. found that the mean age at diagnosis for subglottic cysts was 8 months.[80] Treatment options include needle aspiration and/or marsupialization with microlaryngeal instruments, microdebrider, or $CO_2$ or Thulium lasers.

## Subglottic Hemangioma

A subglottic hemangioma is another rare, albeit life threatening, cause of pediatric stridor (Figs. 47.29A and B). During DLB, it typically appears as a soft, compressible, submucosal, erythematous, or purplish mass in the posterolateral subglottis. It usually presents by the first few weeks of life with biphasic stridor and has a 1:2 male-to-female ratio.[81-83] Large subglottic hemangiomas require treatment to prevent significant airway compromise during the unpredictable involution course. Although corticosteroids have historically been the main medical treatment, considerable side effects are associated with prolonged use.[84] Propranolol continues to evolve as the current primary medical treatment modality. At our center, patients are admitted for observation by the pediatric hospitalist or cardiology service and undergo the following protocol: a propranolol dose of 0.5 mg/kg is given, and blood pressure and heart rate are monitored hourly for 4 hours. If the patient tolerates the initial dose, then approximately 12 hours later they should be administered a second dose at 1 mg/kg, and blood pressure and heart rate should be monitored for 4 hours. If the second dose is tolerated, then the patient should be discharged on a dose of 2 mg/kg divided into two doses per day. Methylprednisolone at a dose of 1–2 mg/kg daily is given for the first 3 days. Other propranolol protocols for the treatment of infantile subglottic hemangioma have been developed.[85] For large, symptomatic lesions that fail to respond to medical therapy, surgery may be necessary. The lesion may be bypassed with a tracheostomy until it involutes. Some subglottic hemangiomas may be treated endoscopically with laser ablation, or they may be excised via an open approach.[83,86]

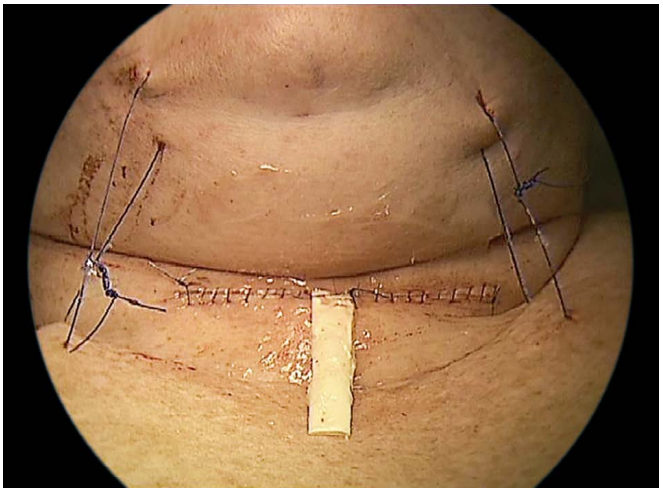
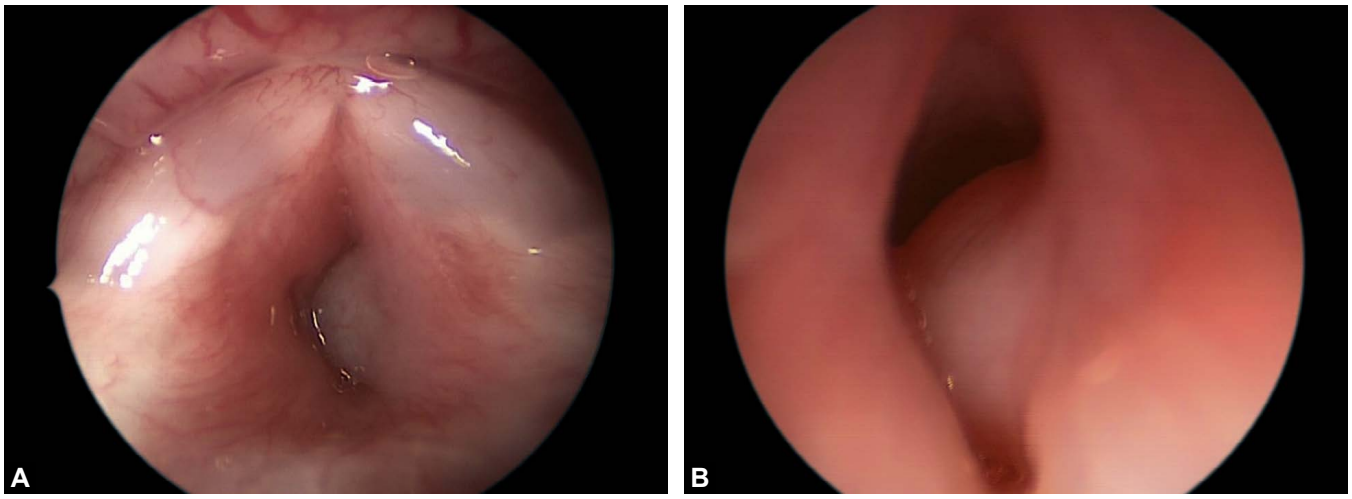


**Fig. 47.27:** Wound is closed over a passive drain, and chin-to-chest sutures are placed to limit neck extension. Reproduced with permission from Gallagher TQ, Hartnick CJ. Cricotracheal resection and thyrotracheal anastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:42-49. Copyright 2012 Karger (Basel, Switzerland).

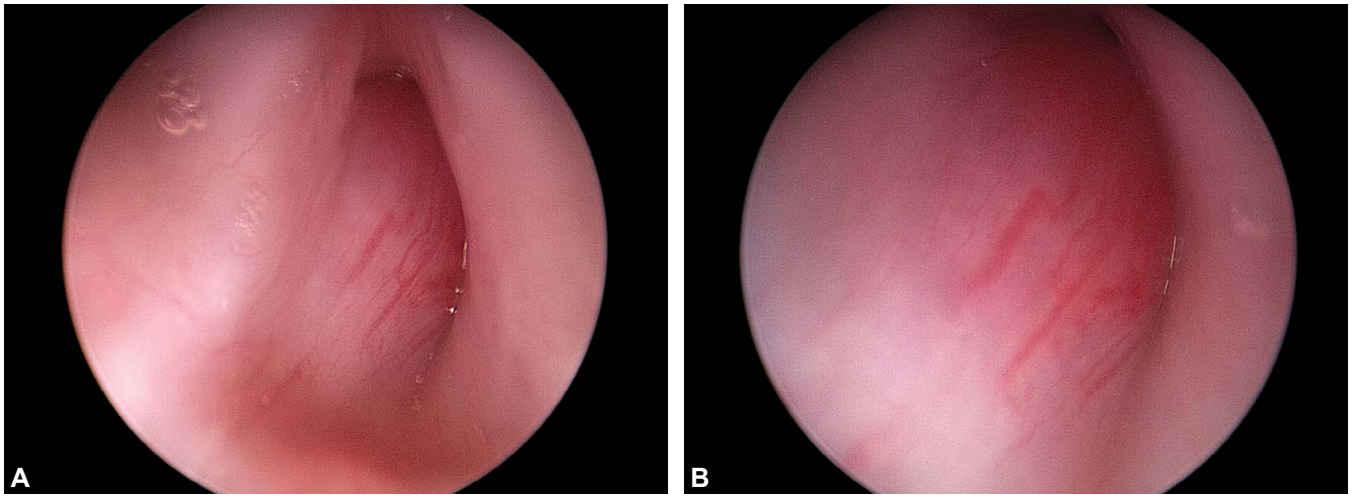
# TRACHEAL LESIONS

## Tracheal Stenosis

As in subglottic stenosis, tracheal stenosis is classified as either congenital or acquired. Congenital tracheal stenosis




**Figs. 47.28A and B:** Intraoperative photo of a subglottic cyst.




**Figs. 47.29A and B:** Intraoperative photo of a subglottic hemangioma. Note the increased vascularity.

is most commonly due to complete tracheal rings and may be associated with vascular compression of the airway. Complete tracheal rings have been divided into the following patterns: complete rings that are patent proximally but progressively narrow to a tiny distal ring near the carina; a long-segment "stove-pipe" section of similar-sized tracheal rings; a short-segment stenosis in the midtrachea; and complete rings associated with a bronchus suis, or pig bronchus (Fig. 47.30).[87-89] Similar to subglottic stenosis, acquired tracheal stenosis results most often from intubation trauma. Other acquired etiologies include tracheostomy, tracheocutaneous fistula excision (resulting in A-frame deformity), intraluminal mass, autoimmune/inflammatory disease, and external trauma.

### *Clinical Presentation*

Congenital tracheal stenosis will typically present in the neonatal period. Infants demonstrate worsening respiratory distress, biphasic or expiratory stridor, retractions, apnea, cyanosis, and sometimes dying spells. Children with tracheal stenosis have been described as having "washing machine respiration" due to adherent secretions at the site of the stenosis.[88] If the infant grows faster than the stenotic airway, the stenosis may deteriorate into a critical obstruction after a few weeks of life.[90] Some children with complete tracheal rings present later in life because moderate obstruction may accommodate growth without causing respiratory distress.[89] Acquired tracheal stenosis may present more insidiously months to years after the insult.

### *Diagnostic Evaluation*

A thorough history and physical examination is completed first with particular attention to the same areas discussed in the aforementioned section regarding subglottic stenosis. All children with suspected congenital tracheal stenosis should undergo echocardiogram because up to half will have cardiac anomalies. A preoperative flexible laryngoscopy may not be safe if the child is in significant respiratory distress.

*Imaging*: As in subglottic stenosis, patients with suspected tracheal stenosis may be imaged with high kilovoltage lateral and anteroposterior neck and chest films.

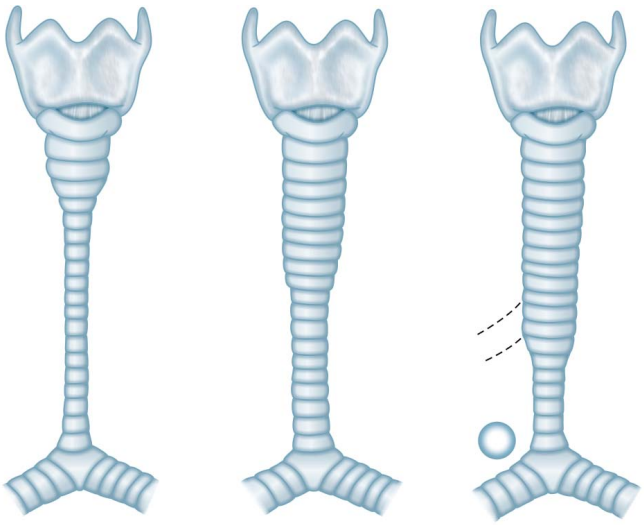
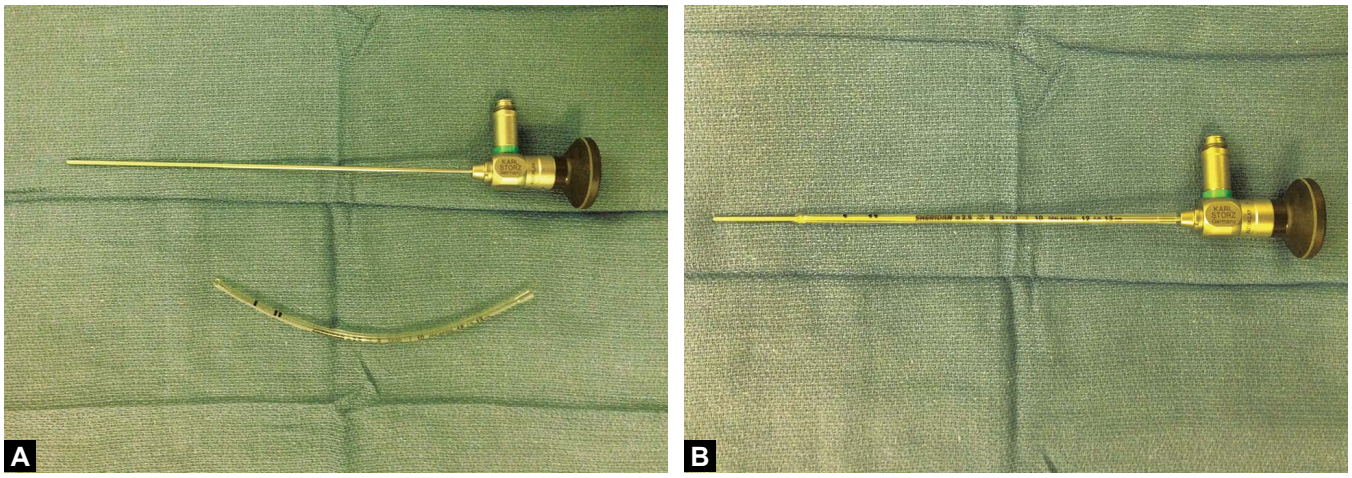


**Fig. 47.30:** Various forms of congenital tracheal stenosis. Reproduced with permission from Grillo HC. Congenital and acquired tracheal lesions in children. In: Grillo HC (ed), Surgery of the trachea and bronchi. Hamilton, Ontario: BC Decker Inc, 2004.

However, in the stable child, spiral CT (virtual bronchoscopy) or magnetic resonance imaging (MRI) with contrast of the neck and chest provides detailed information regarding the dimensions of the airway and stenosis, and it simultaneously assesses for cardiac and vascular anomalies. The sensitivity and specificity of CT virtual bronchoscopy compared with rigid bronchoscopy in the evaluation of tracheal stenosis has been reported as 92% and 100%, respectively.[91] Effective preoperative imaging facilitates contingency planning for the upcoming DLB and other operative interventions, such as the potential need for cardiopulmonary bypass, ECMO, or thoracotomy.

*Direct laryngoscopy with bronchoscopy*: DLB in a patient with suspected tracheal stenosis presents several unique challenges. The goals of endoscopy are to determine the location and type of the stenosis (complete tracheal rings or not) and to estimate its smallest diameter, thickness, and length. When possible, the bronchi should also be assessed for compression or stenosis. The DLB ideally will be used in conjunction with the preoperative CT or MRI to provide a roadmap of the airway.

One should set up a size 2.5 rigid bronchoscope. A 1.9-mm telescope loaded with an uncuffed 2.5 endotracheal tube is used initially, which potentially allows immediate intubation after evaluating the airway (Figs. 47.31A and B). Alternatively, a 3.0 uncuffed endotracheal tube can be loaded on a 2.7-mm telescope to improve optics if the stenosis is less severe. If the tracheal stenosis is too small to accommodate a 1.9-mm telescope, one should not force past the stenosis. This could easily convert an otherwise stable airway into a critical one. If the stenotic region is accidentally traumatized, intravenous dexamethasone and topical oxymetazoline should be used.




**Figs. 47.31A and B:** A 1.9-mm telescope is loaded with a 2.5 endotracheal tube.

When the stenosis is too narrow to pass a 1.9-mm telescope, a few options exist. A tracheostomy is obviously rarely helpful in tracheal stenosis because the smallest complete rings tend to be more distal. The 2.5 rigid bronchoscope also has an outer diameter of 1.9 mm but may be able to traverse the stenosis in an emergent situation. A smaller, flexible bronchoscope may represent the best means of evaluating distal to the stenosis. Hayashi et al. have developed a "stereovision" flexible bronchoscope that uses two lenses to more accurately measure the diameter of a tracheal stenosis.[92] Many times it is best to intubate with a 2.0 or 2.5 endotracheal tube so that further planning may occur and ECMO or cardiopulmonary bypass may be arranged. Another option particularly useful in older patients is to make a custom endotracheal tube by suturing a smaller endotracheal tube to the end of a larger one to create a long, narrow-diameter endotracheal tube (Fig. 47.32). In an emergency, the 2.0 endotracheal tube may be wedged into the proximal portion of the stenosis to allow positive pressure ventilation. The DLB may need to be aborted if the stenosis is quite small, and the patient is in stable condition.

## Treatment

### *Endoscopic techniques*

Endoscopic surgery for tracheal stenosis is similar to that of subglottic stenosis, and the same aforementioned contraindications for subglottic stenosis apply to tracheal stenosis. Stenoses that are web-like or lower grade are potential candidates for endoscopic treatment. The $CO_2$ laser can be used to make radial incisions in the stenosis followed by balloon dilation. Ciprodex and mitomycin-C have been used to limit granulation and to aid healing. However, although endoscopic procedures have evolved into achieving a cricoid split with a balloon, most congenital tracheal stenoses will require open surgery due to the length of the stenotic segment and potential dire complications from purely endoscopic treatment. Balloon dilation of complete tracheal rings with endotracheal stenting has been described, but the complications may be life threatening.[93-95]

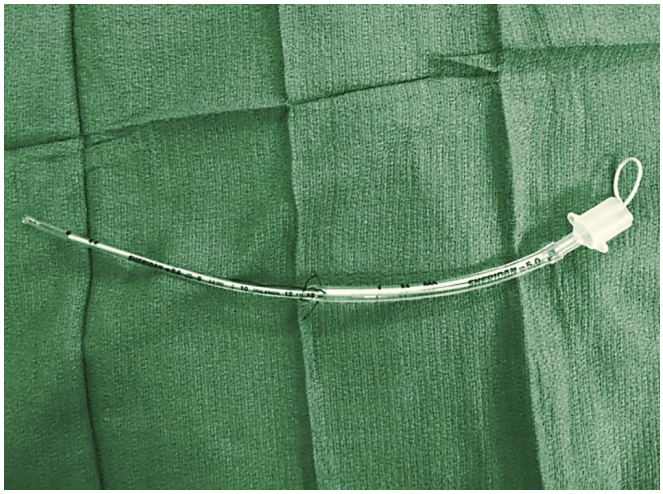


**Fig. 47.32:** A modified endotracheal tube is fashion by suturing a smaller diameter tube to the end of a larger diameter tube, which forms a long, narrow-diameter tube. Reproduced with permission from Gallagher TQ, Hartnick CJ. Tracheal resection and reanastomosis. In: Hartnick CJ, Hansen MC, Gallagher TQ (eds), Pediatric airway surgery. Adv Otorhinolaryngol. 2012;73:50-7. Copyright 2012 Karger (Basel, Switzerland).

*Stents*: Experience with endotracheal stents in the pediatric population remains more limited compared with adults. Stents are divided into either hollow silicone or expandable metal varieties. Nicolai conducted a comprehensive review and determined that endotracheal stents should be used as a last resort, complications should be anticipated, and the stents should be removed as soon as their therapeutic effect in no longer being achieved.[96] Although it seems appealing to use endotracheal stents, they should be placed only after extremely careful thought.[50] Expandable metal stents are touted for their ability to allow mucociliary clearance through the stent, but they are associated with stenosis at either end of the stent and granulation tissue within the stent.[97] These stents tend to become incorporated into the tracheal wall and may be quite difficult to remove.[98] Silicone stents present their own set of complications. They may migrate or become occluded due to biofilm formation within the lumen of the stent. Successful use of absorbable polydioxanone stents has recently been reported.[99] Further research is needed to develop better stenting technology to prevent the complications of current designs.

### *Open techniques*

*Tracheal resection and reanastomosis*: It is only indicated for short-segment stenosis. It is typically employed for tracheal stenoses occluding the lumen >50% for a length of ≤3 cm, or involving approximately four to five tracheal rings.[77,100] It is also indicated for patients who have failed endoscopic interventions for tracheal webs or stenoses and are not amenable to observation, positive pressure ventilation, tracheostomy, or stenting. GERD should be medically controlled prior to surgery. Children with tracheostomy tube dependence due to pulmonary or neurologic disease are not surgical candidates. As stated earlier,

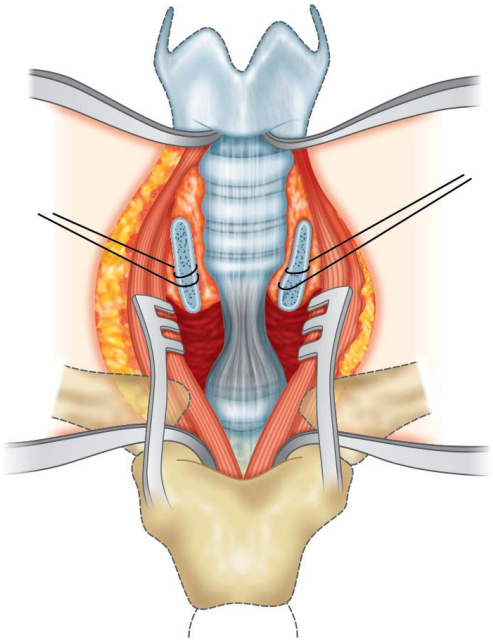


**Fig. 47.33:** The airway is skeletonized from hyoid to distal cervical trachea, exposing the stenotic segment. Reproduced with permission from Grillo HC. Tracheal reconstruction: anterior approach and extended resection. In: Grillo HC (ed), Surgery of the trachea and bronchi. Hamilton, Ontario: BC Decker Inc, 2004.

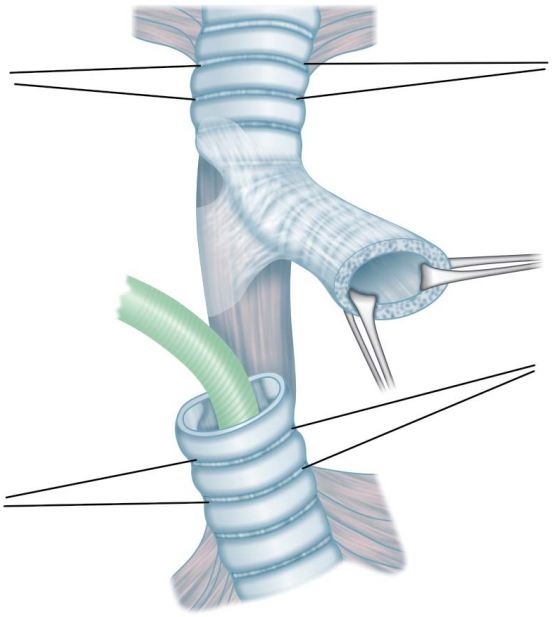


**Fig. 47.34:** The endotracheal tube is withdrawn, and the patient is intubated through the distal tracheal segment. Note the sutures through both the tracheal segments maintaining proximal and distal control of the trachea. Reproduced with permission from Grillo HC. Tracheal reconstruction: anterior approach and extended resection. In: Grillo HC (ed), Surgery of the trachea and bronchi. Hamilton, Ontario: BC Decker Inc, 2004.

these patients may require ECMO, cardiopulmonary bypass, and/or thoracotomy, so appropriate preoperative planning is mandatory.

Surgical procedure: A shoulder roll is placed for neck extension. DLB should be repeated to assess for any changes since the last airway evaluation. The skin is prepped from the chin to the umbilicus. A bougie esophageal dilator is placed to make the esophagus palpable during the later dissection. A transverse skin incision is made over the cricoid, or an ellipse is made to excise the stoma if a tracheostomy is present. The strap muscles are divided vertically in the midline, and the laryngotracheal complex is skeletonized from the hyoid caudally to the distal cervical trachea (Fig. 47.33). Some tracheal stenosis may require exposure down to the mainstem bronchi. The suprahyoid muscles are released. A small hypodermic needle is used to locate the external level of the stenosis while performing rigid bronchoscopy.

Next, 4-0 Prolene sutures are placed below the level of the stenosis on both sides of the trachea to provide distal airway control. The trachea is incised vertically with a Beaver blade, and the stenosis is inspected to determine the number of rings needed for resection and whether the stoma needs to be included in the resection. If less than two tracheal rings exist between the stoma and the stenosis, the stoma should be excised as well. Piecemeal resection of the stenotic trachea ensues in the subperichondrial plane to avoid injury to the recurrent laryngeal nerves; the nerves are not identified in the dissection. The endotracheal tube is withdrawn, and the distal tracheal stump is intubated (Fig. 47.34). The endotracheal tube is intermittently replaced during dissection of the posterior stenosis off of the palpable esophagus beneath. The patient should be spontaneously ventilating during this procedure. A short segment of the distal trachea stump is dissected 360° around in a subperichondrial plane to mobilize this segment while limiting disruption to the tracheal blood supply. When elevating the trachea posteriorly, one should palpate the esophageal dilator posteriorly while looking down the tracheal lumen to ensure the membranous trachea is not transected anteriorly. Rarely, additional releasing maneuvers such as bronchial or annular ligament release or a Relan maneuver may be required to achieve a tensionless closure.

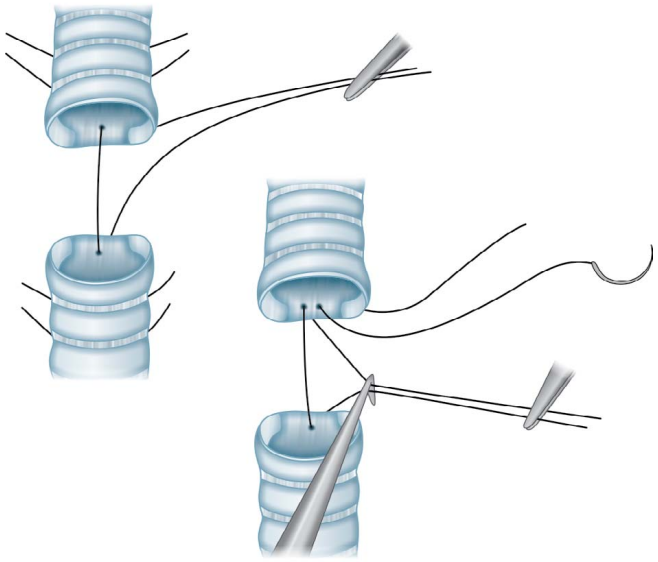


**Fig. 47.35:** The posterior tracheal anastomosis is accomplished with five 4-0 Vicryl sutures placed in a buried, extraluminal fashion. Sutures are tied after all of them have been thrown. Reproduced with permission from Grillo HC. Tracheal reconstruction: anterior approach and extended resection. In: Grillo HC (ed), Surgery of the trachea and bronchi. Hamilton, Ontario: BC Decker Inc, 2004.

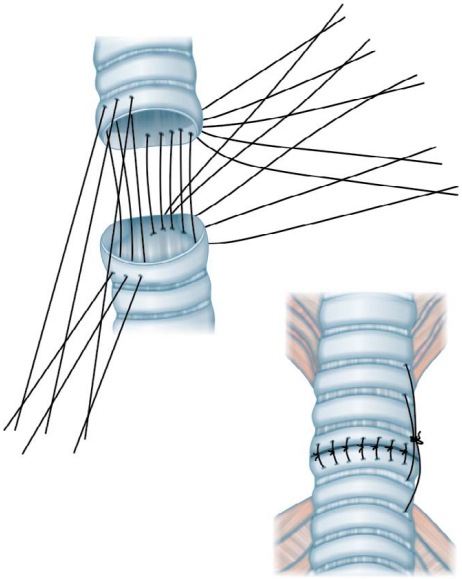


**Fig. 47.36:** The anterior tracheal anastomosis is completed with five 4-0 Vicryl sutures in a simple, interrupted fashion. No sutures are tied until all have been thrown. The 2-0 Prolene tension sutures in the lateral trachea are then tied. Reproduced with permission from Grillo HC. Tracheal reconstruction: anterior approach and extended resection. In: Grillo HC (ed), Surgery of the trachea and bronchi. Hamilton, Ontario: BC Decker Inc, 2004.

The shoulder roll is then removed to facilitate reapproximation of the tracheal segments. Two 2-0 Prolene tension sutures are placed (but not tied yet) in the trachea at the 3 and 9 o'clock positions. These sutures must span at least two tracheal rings and be placed submucosally. The posterior trachea is anastomosed with 5 buried extraluminal 4-0 Vicryl sutures starting in the midline and working laterally; the sutures are not tied until all of them have been thrown (Fig. 47.35). The patient is then intubated either nasotracheally or orally past the anastomosis. Nasotracheal intubation is performed if significant tension exists on the anastomosis. The anterior trachea is reapproximated with five simple, interrupted 4-0 Vicryl sutures, which are not tied until all have been thrown (Fig. 47.36). The 2-0 Prolene tension sutures are then tied. Fibrin glue is placed over the tracheal anastomosis, and the wound is closed in layers over a Penrose or rubber band drain. Large Prolene chin-to-chest sutures are placed bilaterally.

Some patients may be extubated in the operating room, depending on their age and the tension of the anastomosis. Others will require up to a week of sedation and possibly paralysis for proper immobilization. Prophylactic intravenous antibiotics are given for 7 days, and antireflux therapy is commenced for 3 months. These patients are not given intravenous steroids until at least a week postoperatively, when appropriate healing of the anastomosis has been confirmed on repeat DLB. Balloon dilation should not be employed until 6 weeks after the tracheal resection. Flexible laryngoscopy should be used to evaluate vocal fold mobility once extubated. If crepitus is felt in the postoperative period, the patient should return to the operating room for DLB and intubation.

*Slide tracheoplasty*: Although more common isolated airway lesions such as subglottic stenosis or short-segment tracheal stenosis are managed well with open airway surgery, long-segment tracheal stenosis remains more challenging and can be associated with higher mortality rates. Numerous techniques have been developed to treat long-segment tracheal stenosis, including costal cartilage or pericardial patch tracheoplasty, tracheal resection, and tracheal autograft. However, slide tracheoplasty has become the standard treatment for infants or children with long-segment tracheal stenosis and complete tracheal rings.[88] Tsang et al.[101] first described slide tracheoplasty in 1989, and Grillo et al.[87] popularized it in the 1990s. Macchiarini et al. found that slide tracheoplasty in animals doubled the circumference of the trachea and

quadrupled the cross-sectional area while not inhibiting tracheal growth.[102] Additional advantages include the use of only native tissue, and the operated site contains normal ciliated respiratory epithelium immediately after surgery. Slide tracheoplasty is especially indicated when the stenosis involves more than two thirds of the trachea. The presence of a bronchus suis may be a contraindication in distal tracheal stenosis because of inability to mobilize the trachea sufficiently.

Surgical procedure: Concomitant cardiac anomalies may be repaired simultaneously with slide tracheoplasty, but they are repaired before the tracheoplasty. Cardiopulmonary bypass is utilized if the stenosis involves the distal third of the trachea and if there is a concomitant cardiac lesion requiring thoracotomy. One may use ECMO for an isolated low- or mid-segment stenosis, where cannulation of the distal trachea with an endotracheal tube or jet ventilation may not be possible. Selective ventilation of one lung may also be possible.

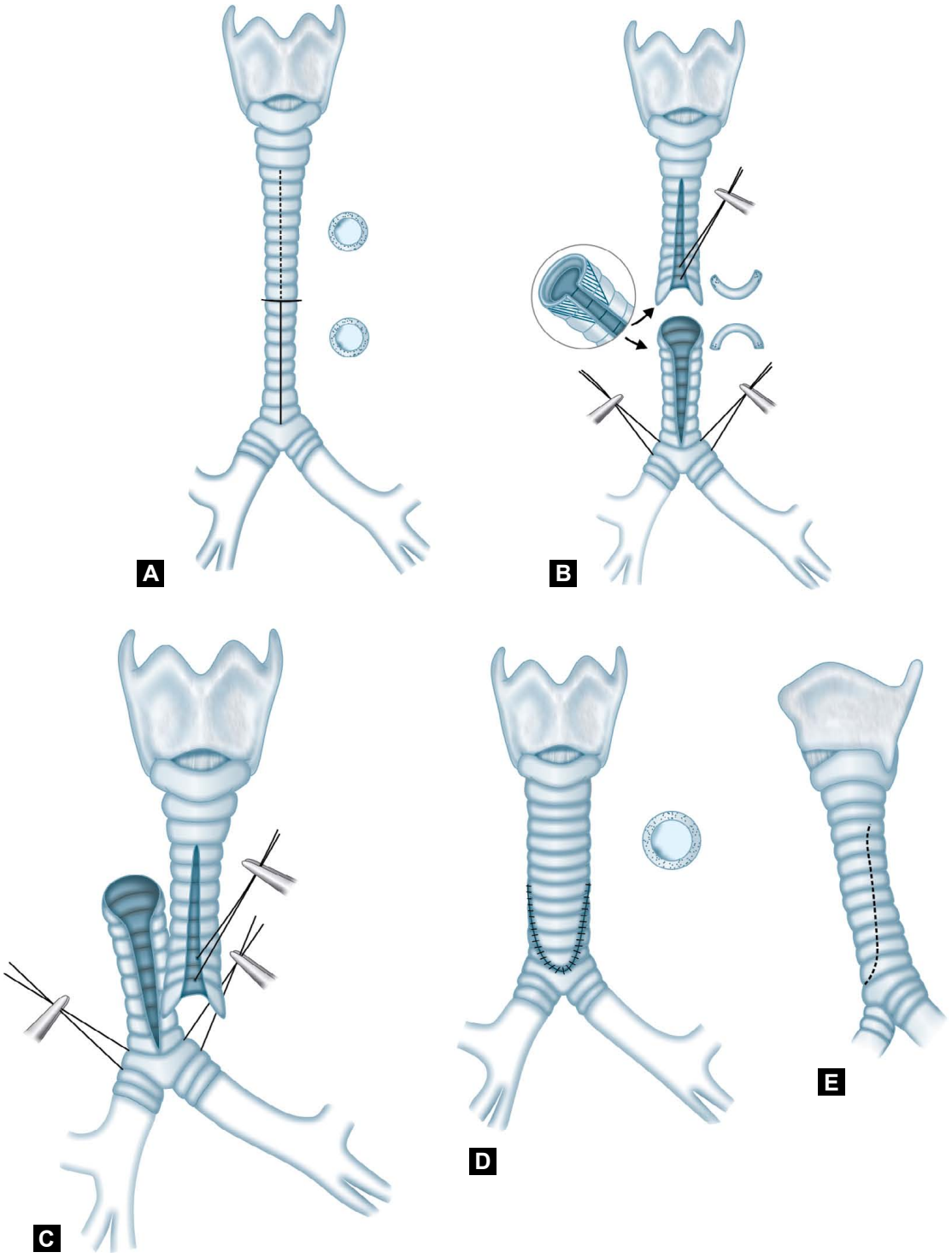
The cardiac repair (if necessary) is accomplished first. A shoulder roll is placed to aid in neck extension. A bougie esophageal dilator is inserted to make the esophagus more prominent during the later dissection. A low collar neck incision is made. In the rare event that the child has a tracheostomy, the incision includes the stoma. The strap muscles are vertically divided in the midline, and the laryngotracheal complex is skeletonized from the hyoid caudal to the distal trachea below the level of the stenosis. The suprahyoid muscles are released to allow mobilization of the proximal trachea. ECMO or cardiopulmonary bypass greatly facilitates exposure of the distal trachea, because the innominate artery may be retracted away from the trachea. A hypodermic needle is used to locate the external level of the stenosis while performing rigid bronchoscopy. The needle is also used to assess the dimensions of the stenosis to determine how long to make the incisions in the proximal and distal tracheal segments. The trachea is dissected 360° subperichondrially around the midpoint of the stenosis before transecting it at this level.

The proximal end of the trachea is dissected circumferentially in a subperichondrial plane to permit a vertical division of the posterior wall through the entire length of the stenosis (Figs. 47.37A to E). The distal end of the trachea requires less peritracheal dissection before performing a vertical division in its anterior wall along the entire length of the stenosis. The right-angled corners produced by these divisions are trimmed from the proximal and distal tracheal segments. The segments are then overlapped, ensuring the proximal segment is placed anteriorly. The anastomosis is accomplished using simple, interrupted 5-0 Vicryl (infants and children) or 4-0 Vicryl (adolescents). The sutures are placed full thickness through the trachea approximately 3 mm apart, with the knots tied extraluminally. The suturing begins proximally and progresses in parallel succession distally, and the final suture is placed at the distal end of the anterior wall of the upper tracheal segment. All sutures are thrown before being tied. Before the sutures are tied, the patient is nasotracheally intubated under direct vision. Fibrin glue is applied to the trachea. A leak test is performed by flooding the surgical field with saline and conducting a Valsalva to 20 cm $H_2O$. The patient is taken off ECMO or cardiopulmonary bypass. If cardiopulmonary bypass was used, the chest is closed by the cardiothoracic surgeon. The neck is closed in layers over a passive drain. Chin-to-chest sutures are placed to prevent inadvertent head extension for the first week. The bougie dilator is removed from the esophagus, and a nasogastric tube is inserted.

Depending on patient's age and the degree of tension on the anastomosis, the patient may be extubated at the conclusion of the procedure. The patient may require nasotracheal intubation for up to 7 days with sedation and/or paralysis for appropriate immobilization and healing. Intravenous corticosteroids should not be used for at least 1 week after surgery. A DLB is performed at 1 week postoperatively. Balloon dilation should not be employed until 6 weeks after the slide tracheoplasty. A flexible laryngoscopy should be performed to ensure vocal fold mobility. Empiric reflux therapy is used for 3 months.

## Suprastomal Granuloma

The formation of a suprastomal granuloma is one of the most common complications of pediatric tracheostomy. Approximately 4–80% of pediatric tracheostomies develop a suprastomal granuloma.[103-105] The etiology remains unknown, but granuloma formation may be due to trauma, secretions, or chronic infection.[106] A child < 2 years of age with a tracheostomy should under surveillance DLB every 6 months. Bleeding from the tracheostomy or difficult tracheostomy tube change warrants a DLB. A survey in 2011 of American Society of Pediatric Otolaryngology members regarding surgical techniques for suprastomal granuloma treatment reported the following: skin hook and eversion (68%), microdebrider (35%), and laser




**Figs. 47.37A to E:** Diagram of slide tracheoplasty. (A) Extent of stenosis is carefully evaluated. Circumferential subperichondrial dissection is performed only at the midpoint of the stenosis, where it is then divided transversely. The proximal stenotic segment is vertically incised posteriorly, and the distal stenotic segment anteriorly for the full length of the stenosis. (B) The right-angled corners produced by these incisions are removed from the proximal and distal segments. A stay suture placed at the tip of the superior flap and traction sutures at the tracheobronchial angles (or within the mainstem bronchi) are helpful. (C) The proximal and distal segments are slid together. Simple, interrupted sutures are placed along the entire oblique circumference of the tracheoplasty (some surgeons use a running suture here). (D) Anterior and (E) lateral views of the anastomosis. Reproduced with permission from Grillo HC. Repair of congenital tracheal lesions. In: Grillo HC (ed), Surgery of the trachea and bronchi. Hamilton, Ontario: BC Decker Inc, 2004.

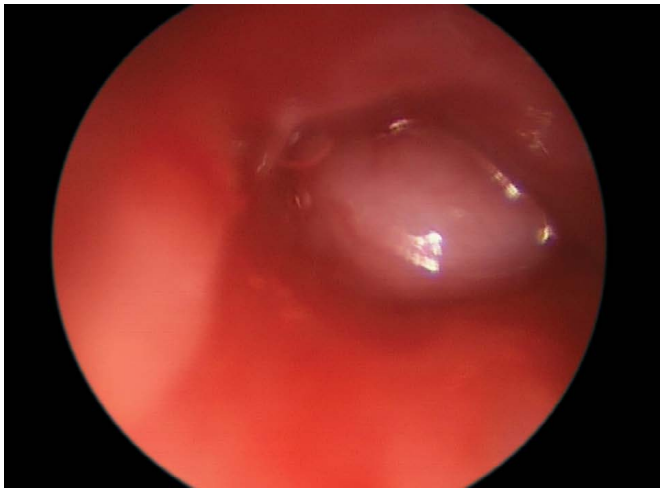


**Fig. 47.38:** Completely obstructing suprastomal granuloma in a small trachea.

(14%).[107] Although these methods are effective in many cases, it is essential that the airway surgeon know how to perform an open excision of a suprastomal granuloma. Some granulomas are too large or firm to be removed safely through the stoma, or the child's airway may be too small to accommodate endoscopic techniques (Fig. 47.38).

### *Surgical Procedure*

After induction of anesthesia through the tracheostomy tube, a DLB is performed to evaluate the airway. The tracheostomy tube is replaced with an endotracheal tube through the stoma. A shoulder roll is placed to extend the neck. A small horizontal neck incision is made just superior to the stoma. Low oxygen settings are used during any electrocautery to reduce the risk of airway fire. The trachea is identified, ensuring to stay superior to the stoma tract. If the stoma tract is violated, the patient should be treated as if they have a fresh tracheostomy. A small vertical incision is made in the trachea, taking care not to divide the cricoid. The granuloma is grasped with a fine hemostat or right-angled clamp and removed using fine scissors or scalpel. A repeat DLB is performed to ensure complete removal of the granuloma. The trachea is closed using interrupted 3-0 Vicryl sutures. Fibrin sealant is applied to the trachea, and the wound is closed in layers over a passive drain. The tracheostomy tube is then replaced.

The patient is observed overnight, and the drain is removed on the first postoperative day if no subcutaneous air is present. A chest film is obtained immediately after surgery to ensure there is no pneumothorax. A suture removal kit is placed at the bedside in case expanding subcutaneous emphysema develops, and the incision needs to be opened. Routine tracheostomy care resumes in 1 week.

## Tracheocutaneous Fistula

Another common complication of pediatric tracheostomy is a tracheocutaneous fistula. The incidence of persistent tracheocutaneous fistula after decannulation ranges from 3.3% to 43% and may be related to the duration of cannulation, age at tracheostomy, and technique used for the tracheostomy.[108,109] A persistent tracheocutaneous fistula may cause significant morbidity to include recurrent aspiration, respiratory infection, difficulty in phonation, weak cough, skin irritation, social discord, intolerance to submersion, and inadequate cosmesis.

Several methods exist to close a tracheocutaneous fistula, including primary closure in layers, fistulectomy and primary closure in layers, fistulectomy with healing by secondary intention, and monopolar cauterization of the tract. However, a fistulectomy with primary closure in layers definitively removes the fistula, affords the patient good cosmesis, and avoids the need for further wound care. The timing of tracheocutaneous fistula closure remains controversial. Most agree that a waiting period of 3 to 6 months after decannulation is reasonable. If concern for obstructive sleep apnea exists, a polysomnogram should be obtained preoperatively with the fistula occluded. Most importantly, one should ensure that the tracheocutaneous fistula is not a result of persistent airway obstruction causing a path of least resistance.

### *Surgical Procedure*

A DLB is performed before excising the fistula to rule out other obstructive airway pathology and to determine if the patient would be a difficult intubation. The patient is intubated from above. A shoulder roll is placed to extend the neck. An ellipse of skin encompassing the tracheocutaneous fistula is incised. Blunt dissection is performed along the fistula tract down to the trachea. The fistula tract is followed into the trachea and then sharply divided. One should consider dividing the fistula vertically to facilitate the dissection into the trachea. The trachea is then reapproximated with simple interrupted Vicryl sutures. Fibrin sealant is placed over the trachea, the wound bed is flooded with saline, and a Valsalva is performed to 30 cm $H_2O$ to check for an air leak. The wound is closed in layers over a passive drain.

The patient is extubated and transferred to the ICU. A tracheostomy set and age-appropriate sized tracheostomy and endotracheal tubes are placed at the bedside. The neck is followed closely to ensure no subcutaneous emphysema, which may necessitate opening the incision. On the first or second postoperative day, the drain is removed and the patient discharged home.

## Neoplasms

Tracheal neoplasms are exceedingly rare. Aggressive respiratory papillomatosis may spread to the trachea (Fig. 47.39). Roby et al. found only 14 patients between 1993 and 2009 at their tertiary care children's hospital had endotracheal or endobronchial neoplasms; of these, 64% were malignant and 36% were benign.[110] In contrast to this report, Desai et al. reviewed the English literature over a 30-year period and found only 36 cases of a tracheal neoplasm; of these, 64% were benign and 36% were malignant.[111] Possible benign tumors include papilloma, hemangioma, fibroma, adenoma, and granular cell tumor. Tracheal papillomas may be treated with microdebrider or potassium-titanyl-phosphate laser. Malignant tracheal tumors consist of carcinoid, mucoepidermoid carcinoma, adenocystic carcinoma, fibrosarcoma, lymphoma, and other even rarer tumors. One should ensure the tumor is intraluminal and not originally extraluminal with extension into the trachea. The treatment of malignant tracheal neoplasms may necessitate tracheal resection and reanastomosis or slide tracheoplasty.

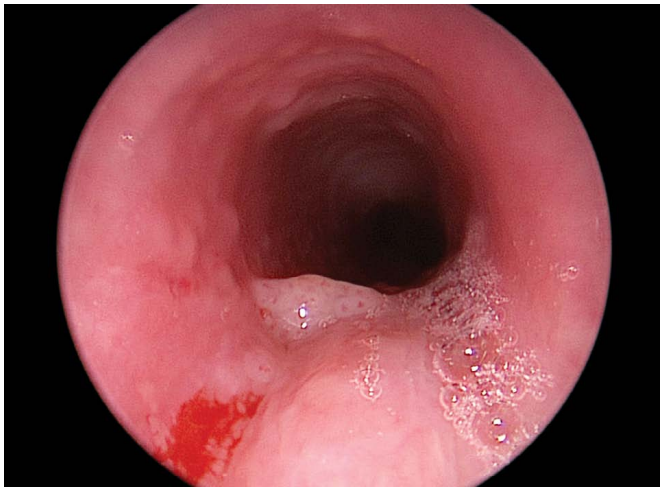


**Fig. 47.39:** Papilloma in the midtrachea.

# COMMON COMPLICATIONS AFTER AIRWAY RECONSTRUCTION

## Laryngotracheal Reconstruction

One should be prepared for a couple common complications following LTR. A pneumothorax is possible during the costal cartilage harvest. If a small rent is made in the pleura, it is repaired with chromic sutures, and the donor site is closed over a passive drain. However, a larger rent or pneumothorax may require a pigtail catheter or a formal chest tube. Another important point to emphasize is that most LTRs require repeated DLBs with dilation postoperatively. The cartilage framework may be enlarged, but the intraluminal soft tissue still needs to heal properly. The patient may require a DLB every 1 to 2 weeks for the first month to stabilize healing. Typically, the airway is dilated with uncuffed endotracheal tubes the first 2 weeks and then using airway balloons thereafter. Ciprodex is applied to the subglottis at each DLB.

## Cricotracheal Resection/Tracheal Resection and Reanastomosis/Slide Tracheoplasty

Restenosis is also common after tracheal resections and tracheoplasties. Just as in LTR, patients may need a DLB with dilation every 1 to 2 weeks for the first postoperative month. The anastomosis is gently dilated with uncuffed endotracheal tubes for the first 6 weeks. After 6 weeks, airway balloons may be used to dilate the trachea. Ciprodex is applied to the anastomotic site at each DLB.

Dehiscence of the tracheal anastomosis is another potential complication. A passive drain should be left in place for the first week to allow egress of any minor tracheal leak. One should follow the patient's neck examination closely for any signs of subcutaneous emphysema. Should significant subcutaneous emphysema and airway distress suggesting a large dehiscence occur while the patient is not intubated, a flexible fiberoptic intubation may be necessary. The appropriate lumen will need to be intubated, as one will lead to the carina and the other to the mediastinum. Once the airway is secured, the patient will need to return to the operating room for repair of the anastomosis.

A potential complication unique to tracheal resections and tracheoplasties is vocal fold paralysis, which may be

either unilateral or bilateral. The incidence of recurrent laryngeal nerve injury in CTR is <3%.[74] Unilateral vocal fold paralysis may not require intervention if there is good apposition of the other vocal fold. If aspiration and dysphonia are diagnosed, the paralyzed vocal fold may need to be medialized. However, one should wait at least a year before performing any permanent procedures for vocal fold paralysis because function may still return. For bilateral vocal fold paralysis, the patient may require a tracheostomy. One could consider a cordotomy or posterior cricoid split with costal cartilage graft in an attempt to avoid a tracheostomy.

## HIDDEN AIRWAY LESION

Despite thorough awake fiberoptic laryngoscopy and DLB in the operating room, not every airway lesion may be clearly identified on initial examination. The most common missed lesions are usually dynamic, such as laryngomalacia and tracheomalacia. Dynamic airway lesions become evident with increased airflow after successful relief of the primary obstructive lesion. Synchronous lesions usually do not require operative intervention. However, Rutter et al. reported that five children with synchronous lesions manifesting after successful airway reconstruction required surgical intervention, including four patients needing a tracheostomy.[112]

## MULTILEVEL OBSTRUCTION

Although many children present with an isolated airway lesion, some may demonstrate a major concomitant lesion. For example, an infant may suffer from both congenital subglottic stenosis and long-segment tracheal stenosis. It may be beneficial to approach these children in a step-wise fashion. No true roadmap exists for these extremely complicated airways, and each treatment plan should be individualized to the child.

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CHAPTER

48

# Cough in the Pediatric Patient

***Daniel P Hsu***

## BACKGROUND

Cough is the most common specific complaint seen by primary care physicians in the United States, accounting for >2.5 million visits annually.[1,2] The evaluation of cough can be a frustrating endeavor. Cough is a normal physiologic response, and the vast majority of cough falls into a normal or expected category. Cough is an ill-defined entity, and patient or parental perception often dictates seeking medical evaluation. The provider evaluating cough has many challenges. History often poorly reflects the frequency and duration of coughing. Intensity of cough is often poorly characterized and based upon subjective parental report. Individual variability in a patient's cough receptor sensitivity exists. There are no well-established criteria for normal coughing in children. One study showed that cough frequency averaged 11.3 events per 24 hours, with a range of 1 to 34.[3] Chronic cough is defined as a persistent cough that lasts for >4 weeks in children (<15 years old), or >8 weeks for older adolescents and adults.[4] Evaluation of children with chronic cough is a common reason for medical consultation not only in the primary care clinic, but also in the pediatric subspecialty and otolaryngology clinics.

## PATHOPHYSIOLOGY

Cough is a normal physiologic response and an important component of the lung's mucociliary clearance function. Cough is defined by three physiologic phases: inspiratory, compressive, and expiratory.[5] The inspiratory phase is characterized by a deep inhalation to increase lung volume. As the chest wall dimensions increase in a vertical and horizontal plane, the muscles of expiration begin to contract. The diameter and length of bronchi also increase during this phase. The second phase is the compressive phase and begins with closure of the glottis. This facilitates the increase in intrathoracic pressure as the expiratory muscles actively contract. Airway pressure may reach as high as 300 mm Hg. The final phase of cough is the expiratory phase, which is the phase where the functional effect of cough is manifested. The phase begins with opening of the glottis, resulting in the release of the intrathoracic airway pressure. Relaxation of the diaphragm allows abdominal pressure to contribute to the intrathoric pressure. The abdominal pressure along with an increase in expiratory muscle contraction increases the dynamic pressure on the airways. This leads to turbulent flow within the airways that creates a shearing force to remove mucus from the airway lining. The culmination of the expiratory phase leads to the desired result of a cough, which is the expelling undesired material from the airways of the lung.[5-8]

The cough pathway begins with activation of a cough receptor, located throughout the upper respiratory, lower respiratory, and gastrointestinal tracts.[8] Afferent signals travel primarily via the vagus nerve to the cough center in the medulla. The medulla coordinates the complex actions required to generate cough, after receiving signals from afferent sources. In addition, the cough reflex can be activated at a higher cortical level, as cough can be initiated voluntarily. The efferent pathways, primarily through the vagus and phrenic nerves, trigger the musculature involved in the cough mechanism.[5-8]

## CLASSIFYING CHRONIC COUGH

The differential diagnosis for chronic cough is extensive. Classifying different categories of chronic cough is challenging. One classification system categorizes chronic cough into three broad groups: normal/expected cough, specific cough, and nonspecific cough.[3] A thorough history and physical examination will often provide clues to an expected cough or specific cough diagnosis. The patient with a nonspecific cough provides a diagnostic challenge that warrants a stepwise evaluation. This chapter will discuss specific cough diagnoses and the approach to a nonspecific cough.

## SPECIFIC COUGH DIAGNOSES

### Rhinitis, Environment, Recurrent Viral Illness

#### *Recurrent URI*

Upper respiratory infections (URIs) are among the most common cause of pediatric acute care visits. The typical URI is a self-resolving infection in children with duration of no >10 to 14 days. However, up to 13% of URI may have an apparent duration of >15 days.[9] The daycare setting increases the frequency of URI experienced by children, with many caretakers reporting 6 to 12 respiratory infections in a 1-year period.[10] This frequency of URI can be distressing for a parent, often seeking medical evaluation for a "chronic cough". History will often elucidate recurrent URI from other causes of chronic cough. The typical URI will have a peak of symptoms within the first 2 days, with a gradual resolution of symptoms. The symptoms are confined to the upper respiratory tract and should not manifest with respiratory distress. The cough is often more distressing to the caretaker than it is to the patient. During respiratory illness season, it is not uncommon to have URI occur in close sequence. With specific questioning, the caretaker will generally recall a few days where the child was asymptomatic between URIs. Review of systems will be otherwise unremarkable in these children and reassurance is all that is required.

#### *Bronchiolitis*

Bronchiolitis is a clinical syndrome of children <2 years of age, characterized by a classic cough with varying degrees of respiratory distress. Acute symptoms tend to peak slightly later than URI, generally between days 3 and 5 of illness. The acute symptoms may be severe enough to require hospitalization, particularly in high-risk groups (e.g. history of premature birth, cardiac disease, chronic respiratory disease, and neuromuscular disease). The most common infectious etiology is respiratory syncytial virus, although many other viruses may cause bronchiolitis. The duration of cough related to bronchiolitis tends to be longer than URI, with median duration of 15 days and 25% of patient with symptoms lasting >21 days.[11] Beyond the acute period, chronic cough associated with bronchiolitis should be similar to URI. The child will have a normal evaluation with unremarkable review of systems and physical examination. There is an association between asthma and respiratory syncytial virus bronchiolitis, although it is unclear whether a child with a genetic predisposition to asthma is more likely to develop bronchiolitis or the infectious bronchiolitis leads to airway remodeling with subsequent development of chronic asthma.

#### *Postinfectious Cough*

Postinfectious cough is a prolonged cough lasting >3 weeks that most often occurs after an URI. Lower respiratory inflammation is likely involved in a postinfectious cough, although the specific mechanism is unknown. Extensive airway epithelial disruption, bronchial hyper-responsiveness, and increased cough receptor sensitivity have all been suggested.[12] There is no specific etiologic agent, and many infectious organisms have been associated with postinfectious cough. Adenovirus, parainfluenza viruses, respiratory syncytial virus, and *Mycoplasma pneumoniae* have all been implicated in postinfectious cough.[13] Many other viral etiologies are likely sources, and coinfection with several viruses is also likely. *Bordetella pertussis* infection has a classic presentation with a convalescent phase that involves a prolonged duration of cough. Serologic testing can be performed for diagnostic purposes only, as no specific treatment is available. Although early treatment of *B. pertussis* with a macrolide may limit symptoms and decrease the spread of infection to others, there is no recommended treatment of any etiology of postinfectious cough.

#### *Upper Airway Cough Syndrome*

Upper airway cough syndrome (UACS) is a more recent term to describe what was previously described as post nasal drip. UACS is considered a more appropriate term

as irritation and inflammation of the posterior nasopharynx may contribute to the pathophysiology rather than solely from posterior drainage of nasal secretions. There is no specific history or physical examination finding. In addition to cough, common complaints include an irritation or tickle in the throat.[14] No specific radiographic or laboratory testing has been found to be useful. Data in pediatric patients are lacking, and consideration for UACS in children is extrapolated from adult literature.

### *Environmental Irritants*

Overwhelming evidence exists regarding the effects of environmental tobacco smoke (ETS) exposure on the respiratory health of children. It has been associated with an increase in respiratory infections, decrease in pulmonary function, and increase in chronic cough.[15-22] These sequelae along with the lifelong cardiorespiratory conditions and increased risk for lung cancer categorize ETS exposure as a significant public health concern. The exact pathophysiology for chronic cough and ETS exposure is not entirely clear. Increased cough receptor and higher neuronal pathway excitability has been postulated.[20] ETS is an irritant that can also trigger acute respiratory symptoms in any patient with underlying chronic respiratory disease.[19] Other environmental irritants to include urban pollution, indoor molds, nitrogen dioxide gas, and wood burning stoves have all been implicated in causing chronic respiratory symptoms in children.[20,22] Reduced exposure to the irritant or removal from the environment should lead to an improvement in symptoms.

### *Hypersensitivity Pneumonitis*

Hypersensitivity pneumonitis (HP) is a disease caused by inhalation of an antigen that provokes a diffuse immune response. Many antigenic sources have been implicated and can be categorized into fungal/bacterial, animal proteins, or chemical.[23] Most commonly described sources of HP include frequent handling of birds and exposure to molds in a farming environment. HP may present clinically in three different patterns (acute, subacute, and chronic). Acute symptoms will present similar to any viral illness with fever, respiratory symptoms, and malaise occurring within hours of exposure. The subacute category is characterized by respiratory symptoms (e.g. cough and wheezing) that occur for weeks to months, with or without fever, and may involve weight loss. Signs and symptoms of chronic HP are similar to subacute HP; however, seeking medical attention is delayed for months to years due to the insidious nature of chronic HP. Chronic HP is characterized by progressive dyspnea on exertion. No specific testing is diagnostic of HP. A high index of suspicion with exposure risk is critical in the diagnosis. Chest radiograph is often nonspecific, and high-resolution computed tomography (CT) of the chest may show a diffuse interstitial pattern. Serologic studies positive for antigen specific immunoglobulin G can help support the diagnosis. Bronchoalveolar lavage will frequently show a lymphocytic predominance.[23,24] Exposure avoidance is the most important aspect of treatment, although acute treatment with oral steroids or chronic treatment with inhaled steroids had been attempted with mixed results.[23]

## Classic Infections

### *Tuberculosis*

Tuberculosis (TB) is a globally endemic disease, primarily located in the countries of Africa and Asia. Although TB infection is reported primarily in adults, children are also susceptible to TB infection and account for up to 11% of cases globally.[25] It is important to differentiate infection from disease. The majority of patients will not develop clinical disease, with 90% developing latent TB infection. There is a 10% lifetime risk of developing disease. However, infants and children are at a higher risk of progression to disease compared with adults. Children also have a higher risk of extrapulmonary TB and mortality.[26] The symptoms of TB in children are similar to adults. Patients may develop nonspecific constitutional symptoms, cough, low-grade fevers, and night sweats. Failure to thrive may be observed in children. Younger children may not expectorate, increasing the challenge of recovering organism in laboratory culture. First morning gastric aspirates are often required to improve recovery of organisms.

### *Fungal*

Endemic mycoses are generally asymptomatic infections that may occur in normal hosts. Histoplasmosis is a fungus found in soil that is common in the Mississippi and Ohio River Valleys. Blastomycosis is found in the Ohio River Valley up to the Great Lakes region. Coccidioidomycosis is found in the desert southwest environment. Each of these endemic mycoses can lead to infections in normal hosts. Patients infected with endemic mycoses generally have mild constitutional symptoms but may develop a subacute infection with a prolonged cough.

In rare circumstances, the infection may become more invasive and disseminated. The subacute infections may mimic that of TB and should be considered if the patient has been to the corresponding geographic location. Infections with endemic mycoses are generally self-resolving, rarely requiring treatment.[27]

### *Pertussis*

Pertussis, commonly known as "whooping cough", has become more prevalent over the past few decades with disease primarily found in two primary age groups: infants < 5 months and children > 10 years. Infants appear to be at higher risk due to incomplete immunization, whereas older children are at risk due to waning immunity. Classic pertussis can be divided into three distinct phases: catarrhal, paroxysmal, and convalescent. The catarrhal phase may last up to 2 weeks and is characterized by prodromal symptoms. The paroxysmal phase is distinguished by a paroxysmal cough, post-tussive emesis, and inspiratory "whoop", which can last up to 6 weeks. The convalescent phase is the final phase, with slow resolution of respiratory symptoms over a 1- to 2-week period.[28] Diagnosis can be established by culture, although the sensitivity decreases greatly after only a few weeks into the symptoms. Treatment with macrolide antibiotics does not change the course of disease and is primarily utilized to decrease spread of infection to others. The disease is generally self-resolving in older children and adults, without the need to provide intensive medical care. Infants are at risk for acute respiratory compromise and may require hospitalization. Supportive treatment is provided until the resolution of the disease process. The most effective strategy to limiting the morbidity and mortality associated with pertussis is awareness and vaccination programs.

## Recurrent Bacterial Infections

### *Cystic Fibrosis*

Cystic fibrosis (CF) is the most common life-limiting genetic disease in Caucasians.[29] It is inherited in an autosomal recessive pattern and causes disease in multiple organ systems. The primary cause of early morbidity and mortality is the recurrent pulmonary infections that lead to end-stage lung damage. The underlying pathophysiology of the lungs is secondary to mucus obstruction, recurrent infections, and an exaggerated inflammation of the airways. The interplay of these three main components leads to bronchiectasis. Respiratory symptoms are not typically present at birth in patients with CF. There is a wide spectrum of respiratory disease severity in CF. As the disease process progresses in the lungs of CF patients, clinical symptoms will begin to manifest. The presenting symptom is often a chronic recurrent cough. A moist cough may occur due to the presence of mucus in the airways. Some patients will present with recurrent pneumonias, although chest radiographs are often normal early in the disease. Infectious organisms, such as *Pseudomonas aeruginosa, Staphylococcus aureus, Haemophilus influenzae, Burkholderia cepacia, Alcaligenes xylosoxidans,* and *Stenotrophomonas maltophilia*, may be obtained via deep pharyngeal throat culture or from sputum. These bacteria thrive in environments with poor mucus clearance, and recovery of any of these organisms should warrant diagnostic testing for CF.

Sinus disease is also a common feature of CF. Radiographic studies often show complete opacification of the sinuses in patients with CF, although many patients will be asymptomatic. The bacterial organisms within the sinuses are similar to the bacteria found in the CF airway. There is also a higher incidence of nasal polyps in patients with CF.

The CF impairs the exocrine function of the pancreas, primarily production of lipase, rendering the patient pancreatic insufficient. It is estimated that 85% of patients with CF are pancreatic insufficient. Gastrointestinal manifestations are often the first presenting features seen in CF. Meconium ileus, noted soon after birth, is a hallmark feature that is essentially pathognomonic for the diagnosis, although the majority of patients with CF do not present with this manifestation. Cholestasis may occur early in life, leading to an increased direct hyperbilirubinemia. Pancreatic insufficiency leads to the inability to absorb fat adequately and subsequently CF patients present with steatorrhea and failure to thrive. The fat malabsorption also can lead to poor absorption of the fat soluble vitamins (A, D, E, and K) and the symptoms associated with these vitamin deficiencies. Patients who present with any of these gastrointestinal findings should undergo evaluation for the diagnosis of CF.

Male infertility is also a hallmark of the disease due to obstructive azoospermia. Congenital bilateral absence of the vas deferens is the primary cause. Female patients with CF can become pregnant, although thickened secretions within the reproductive tract may impair normal fertility. An increased incidence of CF mutations among male clients at assisted reproductive centers has been shown.[30]

The gold standard diagnostic test for CF is the sweat chloride test. Due to the inability to resorb chloride in the sweat gland, the chloride concentration in sweat samples will be elevated in patients with CF. Genetic mutation testing may be an alternative diagnostic test, when the quantity of sweat obtained is insufficient, or the level of sweat chloride concentration is of an indeterminate level. Newborn screening has become universally adopted within the United States. Although each state has a variation in the screening tests, CF newborn screen is a two-tiered process that involves screening for an elevated immunoreactive trypsinogen as the first tier. The second tier involves either repeat testing for the elevated immunoreactive trypsinogen, or a limited genetic mutation panel. It is important to consider that newborn screen does not rule out the diagnosis of CF.[31]

The CF is a life-limiting genetic disease with a wide clinical spectrum of symptoms, involving multiple organ systems. Sinopulmonary disease and failure to thrive are key features of the disease that should lead to consideration of CF as a diagnosis. Patients diagnosed with CF should be referred to a certified CF center for further medical care.

### *Primary Ciliary Dyskinesia*

Primary ciliary dyskinesia (PCD) is a genetic disorder that is characterized by abnormal ciliary function. This abnormal ciliary function leads to primarily sinopulmonary and otologic disease. PCD is also characterized by sperm dysmotility.[32] In the 1930s, Kartagener described a triad of chronic sinusitis, situs inversus, and bronchiectasis, which is now known as Kartagener syndrome.[33] It has since been discovered that the underlying ciliary ultrastructure defect in PCD leads to the syndrome first published by Kartagener. It has been suggested that normal ciliary function is critical to visceral organ axis of orientation in utero, which explains the estimated 50% of patients with PCD also having situs inversus. Conversely, it is estimated that 10% of patients with situs inversus will also have PCD.[34] PCD is primarily inherited in an autosomal recessive pattern.

Patients with PCD will often present with a moist cough due to the mucociliary clearance defect in the airways. These patients are susceptible to the same bacterial organisms that occur in CF patients. Ultimately, bronchiectasis will occur in patients with PCD from the recurrent pulmonary exacerbations. Chronic rhinitis and sinusitis are frequently seen in PCD. Frequent otitis media with effusion is also a hallmark of the disease. Many patients with PCD undergo placement of one or more sets of tympanostomy tubes prior to the diagnosis being made.

Testing for PCD involves evaluation of the ciliary ultrastructure from endobronchial or nasal epithelium specimens. Electron microscopy can determine if the normal "9+2" arrangement of microtubules, and the presence of inner and outer dynein arms are noted. Abnormalities in these regions of the cilia are the most common defects noted. However, obtaining a wide sample of respiratory epithelium is important to observe for consistent axis of orientation of the cilia. Random orientation of the cilia has been shown to be a cause of PCD. Moreover, the wide sample of epithelium is important as it is not uncommon to find abnormal cilia in any given sample. The overall pattern of ciliary structure and orientation is important when considering the diagnosis of PCD. Other tests that may confirm the diagnosis of PCD include video analysis of ciliary beat pattern, nasal nitric oxide (low levels in PCD), and genetic testing. The saccharin taste test has been utilized as a screening test for PCD, but it is not recommended in children.[32]

### *Immunodeficiency*

Over 100 primary immunodeficiency syndromes have been described since Bruton reported for X-linked agammaglobulinemia (XLA).[35] Primary immunodeficiencies may involve any component of the immune system, although antibody deficiency is the most common. Of the antibody deficiencies, IgA deficiency is the most common. IgA deficiency does not lead to clinical symptoms in all patients, although it may be associated with recurrent upper and lower respiratory tract infections. Common variable immunodeficiency (CVID) is an autosomal dominant disorder with incomplete penetrance. It is characterized by low levels of circulating antibodies. B-cell numbers are normal; however, they are unable to differentiate into antibody producing plasma cells. T-cell defects can also be seen with CVID. XLA is characterized by essentially nonexistent levels of antibodies as well as B cells. Selective antibody deficiency occurs due to an ineffective response to polysaccharide vaccinations, with normal serum levels of antibodies.[36] These antibody deficiencies may not lead to symptoms in the first 6 months of life, as maternal antibodies that cross over from the placenta will be protective during that time. The clinical presentation of antibody deficiency includes a spectrum of recurrent sinopulmonary infections, particularly with pyogenic bacteria.[37]

T-cell immunodeficiencies are characterized by susceptibility to invasive opportunistic infections with viruses or fungi. Antibody deficiencies are commonly seen with T-cell defects, as B-cell function is dependent on T cells. DiGeorge syndrome and severe combined immunodeficiency (SCID) are examples of T-cell disorders. DiGeorge syndrome is associated with dysmorphic features, cardiac, thymic, and parathyroid issues. Viral and fungal pneumonia may occur in a minority of patients, as the T-cell deficiency is variable. SCID is associated with more severe infections of the sinopulmonary, gastrointestinal, and mucocutaneous systems. These patients often present with failure to thrive and chronic diarrhea in addition to the opportunistic infections. Patients may present with clinical symptoms soon after birth.[37]

### *Chronic Rhinosinusitis*

Chronic rhinosinusitis is characterized by persistent rhinorrhea, nasal congestion, and cough that lasts > 12 weeks.[38, 39] The symptoms of chronic sinusitis are similar to symptoms seen in acute sinusitis, although chronic sinusitis symptoms may be less severe. It has been postulated that the cough noted with chronic sinusitis may be related to UACS. Chronic sinusitis is discussed in further detail in a separate chapter of this book.

### *Congenital Thoracic Malformations*

Congenital thoracic malformations encompass a group of pulmonary lesions that are identified initially by radiologic methods; however, classification of these lesions requires pathologic evaluation after resection.[41] This group of lesions include cystic pulmonary adenomatous malformation (previously known as cystic congenital adenomatous malformation), bronchogenic cyst, pulmonary sequestration, and congenital lobar emphysema. Due to advances in radiologic modalities, many of these lesions are discovered antenatally. Some of these antenatally discovered pulmonary lesions will regress spontaneously before birth and require no intervention. Persistent lesions may have late complications to include malignant transformation and recurrent infection. Controversy exists regarding surgical excision of asymptomatic lesions. Cough and dyspnea are a key finding in the symptomatic congenital cystic lung lesions and must be considered in the differential of chronic cough.[42]

## Noisy Breathing Associated with Cough

### *Asthma*

Asthma is one of the most common reasons for pediatric outpatient visits. Asthma accounts for 12.8 million missed school days, 3% of all pediatric hospital admissions, and 2.8% of all emergency department visits in the United States.[43] The underlying pathophysiology of asthma is characterized by inflammation, airway obstruction, and airway hyper-responsiveness that lead to clinical symptoms. The clinical presentation of asthma varies by patient, with wheezing as the hallmark feature. However, other common symptoms include cough, shortness of breath, and chest tightness. Asthma is an episodic disease with varying degrees of severity. Some patients may display symptoms only with exercise or exertion, whereas other patients may have symptoms on a daily basis. Despite the chronic pattern of symptoms, any patient with asthma can experience an acute exacerbation that may require emergency care.

Although most patients with asthma do not present with cough as their sole symptom, a chronic recurrent cough may be a key symptom that identifies asthma.[44] It is not uncommon for children or their caregivers to underrecognize symptoms. Children may not "know any better", as the symptoms they feel are normal for them. Parents may also believe their child is "nonathletic" or "does not like sports" when the child struggles with athletic activities or chooses not to participate.

The diagnosis of asthma may often be challenging due to the wide variability in clinical presentation. There are several historical clues that will suggest the diagnosis. Wheezing, coughing, tight chest, and shortness of breath are frequently mentioned symptoms of asthma. History may reveal common triggers for respiratory symptoms (Table 48.1). There may be a history of atopic disease (allergic rhinitis and eczema). Family history for asthma or atopic disease may also be discovered. Prior use and response to bronchodilators, inhaled corticosteroids, or oral corticosteroids suggests the diagnosis of asthma. However, it should be noted that a history of nonresponse to medications, particularly bronchodilators, does not rule out asthma. Symptoms of asthma are frequently more severe at night.

Physical examination of the chest is frequently normal at the time of evaluation unless the child is experiencing an acute exacerbation. In that situation, diminished

**Table 48.1:** Common asthma triggers

| |
|---|
| Exercise |
| Weather changes |
| Extremes of ambient temperature |
| Seasonal allergens (e.g. molds, grass, trees) |
| Perennial allergens (e.g. dust mites, animals, cockroaches) |
| Respiratory infections |
| Strong odors (e.g. smoke exposure, cleaning agents) |
| Strong emotions |
| Food or medications |

breath sounds, expiratory or inspiratory wheezing, coughing, crackles, accessory respiratory muscle use may all be characteristic signs. A thorough physical examination should be performed to provide clues to other disease. Extrapulmonary evaluation may reveal signs of atopic disease (e.g. "allergic shiners", transverse nasal crease, enlarged nasal turbinates, posterior pharyngeal cobblestoning, dry skin patches). Other findings, such as digital clubbing, nasal polyps, heart murmurs, and poor growth may suggest other diseases besides asthma.

Pulmonary function testing (PFT) may be helpful if a child is able to perform the test adequately. It is important to note that normal PFT does not rule out asthma. Evidence of airway obstruction may be seen in the PFT. Reversible airway obstruction noted by PFT performed after a bronchodilator provides supportive evidence for asthma. Reversible airway obstruction may be seen even if the baseline PFT is normal. No specific laboratory tests are required in the diagnosis of asthma, although an elevated total IgE or allergen- specific IgE may be seen. Other laboratory signs of atopic disease may include an elevated eosinophil count in the differential of a complete blood count. Chest radiograph is often normal or nonspecific in asthma. Signs of hyperinflation may be seen. Imaging may reveal abnormalities that warrant further evaluation for other diseases.

Asthma is one of the most common respiratory diseases of childhood. Although there is no specific testing to confirm the diagnosis, there is a classic pattern of signs and symptoms that support the diagnosis. Asthma is one of the leading diagnoses in the evaluation of nonspecific cough.

### *Spasmodic/Recurrent Croup*

Spasmodic croup and recurrent croup are interchangeable nomenclature for a disease entity that is incompletely understood. The patient who presents with an acute episode of spasmodic croup is often indistinguishable from viral croup (infectious laryngotracheitis). Both entities present acutely with a "barking seal" cough and hoarseness. It may progress to include inspiratory stridor and respiratory distress. Rarely, a patient may develop respiratory failure.

Viral croup typically presents as an acute febrile illness associated with a prodrome of symptoms of an URI. The most common infectious agents are the parainfluenza viruses. Given the infectious etiology, it is uncommon for children to develop viral croup more than once a year. Viral croup may occur in patients 3 months to 6 years of age, although peak incidence is between 7 and 36 months of age.[45] The key feature that differentiates spasmodic from viral croup is the recurrent nature of the episodes. Spasmodic croup may occur several times per year and may occur frequently enough in close succession to be considered in the differential diagnosis of chronic cough. Although spasmodic croup can present with coryza, it often occurs suddenly without a viral prodrome. Spasmodic croup almost exclusively occurs at night. There may be a history of atopic disease, family history of spasmodic croup, or gastroesophageal reflux reported. Spasmodic croup has also been reported to occur up to 11 years of age.[46]

Spasmodic croup should be considered a diagnosis of exclusion. Other etiologies of upper airway obstruction should be considered especially in patients outside the typical age range. The frequency and severity of episodes may also warrant further evaluation for other etiologies. One author suggests elective endoscopy in moderate or severe recurrent croup. "Moderate recurrent croup was defined as (1) 3 or more episodes occurring in 1 calendar year, (2) 2 or more episodes occurring in at least 2 consecutive years, or (3) multiple episodes in 1 or more years that required emergent outpatient intervention for airway obstruction".[46] Severe recurrent croup was defined as any patient requiring hospitalization for management.

Treatment for acute exacerbation of spasmodic croup is the same as the treatment for viral croup. Corticosteroids and nebulized racemic epinephrine are the standard treatments for patients with croup who present with stridor. Home remedies (e.g. exposure to warm humidified air or cold air) have little supportive data; however, they are commonly recommended for initial therapy prior to seeking medical care.

Spasmodic croup is not a well-understood disease entity that should be considered in the differential diagnosis of chronic cough. Other treatable causes of upper airway obstruction should be ruled out before the diagnosis of spasmodic croup is given. Spasmodic croup appears to self-extinguish with time.

### *Vocal Cord Paralysis*

Vocal cord paralysis (VCP) is the second most common congenital anomaly of the larynx.[47,48] VCP can be divided into bilateral and unilateral. Clinical onset of symptoms and type of symptoms may distinguish between bilateral and unilateral VCP prior to visualization. Bilateral VCP often presents with stridor and dyspnea. The causes of bilateral VCP can be categorized as "neurologic, traumatic, iatrogenic, or idiopathic".[47] Neurologic causes of VCP include disorders, such as an Arnold–Chiari malformation, that lead to insult of the vagus nerve in the region of the brainstem. Traumatic causes of VCP are generally related to birth injury or intubation that affects the recurrent laryngeal nerve. Iatrogenic causes of VCP include surgical complications that also cause injury to the recurrent laryngeal nerve. It is believed that idiopathic causes of VCP are secondary to infection. Although chronic cough from dysphagia and aspiration may be associated with bilateral VCP, it is more common in unilateral VCP.

The causes of unilateral VCP may be similar to bilateral VCP, although post-surgical complications are the most common cause of unilateral VCP.[49] The patient's age at time of diagnosis is often later in unilateral VCP. Unilateral VCP also generally presents with poor phonation, hoarseness, and dysphagia with aspiration.

Diagnosis of VCP is generally confirmed by flexible endoscopy of the larynx. VCP in children may spontaneously resolve with time, and conservative therapy is an option. VCP and surgical treatment will be discussed in further detail in other chapters. It is important to consider VCP in the differential diagnosis of chronic cough.

### *Anatomic Abnormalities of Airway*

Anatomic abnormalities of the airway can lead to a chronic cough. Disorders such as tracheoesophageal fistula, laryngeal cleft, and cleft palate may cause chronic cough from dysphagia and aspiration. Other anatomic abnormalities, such as a laryngomalacia, tracheomalacia, bronchomalacia, airway hemangioma, subglottic stenosis, are generally associated with noisy breathing. Abnormal airway anatomy will be discussed in further detail in other chapters.

## Digestive Tract-Associated Disease

### *Dysphagia and Aspiration*

The coordination of sucking, swallowing, and breathing is a complicated mechanism that normally develops in utero. The protection of the airway from aspiration into the lower airways relies on normal anatomic structures and neuromuscular innervations. The epiglottis is the primary structure of the larynx that guards the airway during the process of swallowing. The superior and inferior laryngeal folds have the ability to strongly constrict to support the defense of foreign material attempting to invade the airways. The sensory innervation of the larynx consists of physical, chemical, and thermal receptors. Proper functioning of these receptors and pathways are critical to triggering the motor components of the nervous to cause laryngeal muscle contraction. The sensory innervation is also crucial in the cough reflex arc that expels foreign material that has inadvertently encroached upon the lower airway.[50]

Causes for dysphagia and aspiration can be grouped into two broad categories, congenital or acquired.[51] Most underlying diseases, associated with dysphagia and aspiration, are readily apparent. Prematurity is one of the more common causes of dysphagia, if coordinated swallowing and breathing has not yet developed. Prolonged feeding time associated with developing suck and swallow mechanism may lead to fatigue, with subsequent weakening of the airway defense against aspiration. Although less common, this may occur in term newborns. Dysphagia and aspiration is not limited to the newborn period, as some children continue to have a dysfunctional swallow during infancy and into toddlerhood. These patients present a diagnostic challenge, as the history and physical examination may be otherwise unremarkable.

Diseases that affect the physical structure of the oral pharyngeal region can affect normal swallowing. Isolated defects such as cleft palate or choanal atresia may cause dysfunction of proper swallowing. Other defects such as laryngeal cleft and tracheoesophageal fistula may create a pathway that bypasses the normal physical defense mechanisms of the airway. Head and neck tumors may also impinge on respiratory and digestive tracts leading to dysphagia. Some abnormalities, often associated with genetic syndromes, that present with micrognathia or macroglossia may impair normal swallowing. Neuromuscular diseases are commonly associated with dysphagia and aspiration and will be discussed in a separate section.

The diagnosis of dysphagia should be suspected by history. Obvious anatomic abnormalities of the oropharynx, premature birth, cerebral palsy, or neuromuscular weakness are risk factors for dysphagia and aspiration. A child without obvious physical abnormalities presents a more challenging diagnostic dilemma. A history of coughing, choking, or sputtering with feedings may be reported. Other historic information that may suggest dysphagia include prolonged feeding time, frequent breaks during feeding, increased work of breathing during or after feeding, nasopharyngeal regurgitation, or stertor. A child with recurrent pneumonias, generally not in a singular location, may also suggest dysphagia with aspiration as an etiology. A video fluoroscopic swallow study (VFSS) is the test of choice in the evaluation for dysphagia. The VFSS is performed by a speech pathologist in conjunction with a radiologist. Different consistencies of barium, starting with thin liquids, are provided during the testing. An evaluation of the swallowing mechanism, to include correct bolus formation and proper swallowing, is assessed. The VFSS may demonstrate abnormalities such as aspiration, laryngeal penetration, reflux, residue, or delayed swallow initiation.[52] Flexible laryngoscopy should be considered in the evaluation of dysphagia as it may uncover a laryngeal anomaly. A chest X-ray should be performed, if not previously obtained, to evaluate for possible pulmonary infiltrate or evidence of chronic lung injury.[53] The treatment of dysphagia depends on the severity of findings on the VFSS, identified laryngeal anomalies, or the severity of respiratory symptoms. Use of specialized low flow nipples for bottle feeding and thickening of feeds may be sufficient if the swallowing dysfunction is expected to improve, and there is no concern for respiratory sequelae. In the extreme spectrum of disease, the patient may not be safe to take feedings by mouth and may require a gastrostomy tube to deliver enteric nutrition. Speech therapy is helpful in improving swallowing function.

### *Gastroesophageal Reflux*

Gastroesophageal reflux is the passage of stomach contents back into the esophagus. Gastroesophageal reflux disease (GERD) is GER associated with symptoms or complications.[54] There is evidence to suggest that GERD is a common cause of chronic cough in adults[55]; however, the issue is much more controversial in children. One study showed that acid reflux did not have a temporal relationship with cough.[56] Another study used intraluminal impedance with pH monitoring and concluded that there may be a temporal relationship with acid or nonacid reflux and cough.[57]

The majority of studies linking GERD with chronic cough in children are case reports or case series. Cough is one of the more common symptoms reported in children with GERD, with it more commonly reported in children aged 1 to 5 years old compared with older children.[54]

One of the main reasons that the association of GERD with chronic cough remains controversial is the lack of a gold standard testing for GERD. There are many tests that may be performed in the evaluation of GERD, to include pH monitoring, multiple intraluminal impedance, barium contrast radiography, nuclear scintigraphy, and upper gastrointestinal endoscopy. Bronchoscopy with bronchoalveolar lavage, for the measurement of lipid-laden macrophage index, can be utilized to support the diagnosis of aspiration. However, there are concerns for either poor sensitivity or specificity with any of these tests.

There are two proposed mechanisms for GERD related to chronic cough. One possible mechanism involves reflux to the level of the larynx, with possible aspiration of the reflux. The other mechanism involves triggering the cough receptor in the distal esophagus, with subsequent vagally mediated bronchospasm.[58] It is possible that both of these mechanisms play a role in GERD-related chronic cough.

The diagnosis of GERD is challenging. History may reveal a child who tends to eat bland foods and avoid spicy or acidic foods. Emesis is common in the infant; however, this tends to improve with time. A chronic cough, after meals or at nighttime, may be consistent with the diagnosis of GERD. Physical examination findings are generally unremarkable. Low weight may be discovered if GERD is severe enough to cause failure to thrive.

An empiric trial of GERD medications to include H2 blockers or proton pump inhibitors may improve the chronic cough.[59] GERD is not a common cause of chronic cough; however, it should be considered in the differential diagnosis.

## Miscellaneous Causes of Chronic Cough

### *Retained Airway Foreign Body*

Foreign body aspiration is a common cause of morbidity and mortality in children. Data from the Center for Disease Control estimated that over 17,000 children < 14 years of age were treated in an emergency department for choking-related events in 2001.[60] The most common age group for foreign body aspiration is between 1 and 3 years of age.[61,62] This is consistent with the developmental milestones of that age group, where exploration of the world frequently

involves putting items into the mouth. Toddlers are the highest risk age group, although foreign body aspiration can occur at any age.

A child who presents with acute respiratory distress, witnessed aspiration, choking, gagging, coughing paroxysm should alert a provider to have a high level of suspicion for foreign body aspiration.[63] Aspiration of a radiopaque object can make the diagnosis simple, as the object will be seen on chest radiograph. However, many episodes are not witnessed or reported by an adult caretaker. A child may not have acute respiratory distress, or the initial signs of an airway foreign body may resolve quickly. A high index of suspicion is often required to make the diagnosis in these situations.

A retained foreign body in the airway may present with chronic recurrent coughing or wheezing. It may lead to recurrent pneumonia, hemoptysis, and ultimately could lead to bronchiectasis. Although most airway foreign bodies are removed within 3 days of the event, almost 20% are not diagnosed immediately and removal is delayed for >30 days.[62] A stable patient with a retained foreign body in the airway may be misdiagnosed with asthma. Perceived improvement with inhaled corticosteroids and bronchodilators may further delay the diagnosis, especially if asthma is a comorbid condition. Toddlers will often experience frequent lower respiratory tract illnesses, including bronchiolitis, which may also complicate the medical evaluation.

The diagnosis of a retained foreign body requires a high index of suspicion. Repeated questioning about an aspiration event is often required, as the adult caretaker may not recall an event immediately. In some situations, the adult caretaker may purposely withhold information for fear of being investigated for child neglect or abuse. Recurrent wheeze, cough, or shortness of breath may be seen; however, these symptoms are not specific. A history of sudden onset of respiratory symptoms in the absence of URI, and without prior recurrent respiratory symptoms consistent with asthma, should heighten the index of suspicion. Persistent focal wheeze or asymmetric breath sounds may be discovered. Chest radiograph may reveal air trapping or focal atelectasis, although it is often normal. Serial chest radiographs may reveal repeated infiltrates in a singular region of the lung, when an airway foreign body has been retained for a prolonged period of time without removal. Although the foreign body can become lodged in any airway, the most common location is the right mainstem bronchus. This is most likely due to airway anatomy with the right mainstem bronchus being a straighter path from the trachea compared with the left mainstem bronchus.

Further radiologic examination is generally unnecessary when investigating a possible airway foreign body. In particular, if a CT requires sedation of the patient, the sedation may lead to respiratory compromise. CT has also been shown to miss airway foreign body.[64] Rigid bronchoscopy is the diagnostic and therapeutic procedure of choice. Flexible bronchoscopy will allow for visualization of an airway foreign body; however, retrieval devices do not fit through the channel port of a pediatric-sized bronchoscope.

### *Neurodevelopmental Disorders*

Neuromuscular diseases encompass a wide spectrum of disorders, often with unclear etiology, that lead to arrested or delayed development. Neuromuscular disorders can be broadly categorized into diseases that originate from the upper motor neurons versus lower motor neurons.[65] Discussion of specific neuromuscular diseases is beyond the scope of this chapter; however, any child with a history of chronic neuromuscular weakness must be considered at risk for chronic cough from several factors. One key risk factor for chronic cough is dysphagia, with aspiration. Several factors in patients with cerebral palsy such as intellectual disability, poor head control, and seizures were found to be associated with a higher risk for dysphagia.[66] Evaluation of dysphagia is discussed in a separate section of this chapter. Another risk factor for chronic cough is the respiratory muscle weakness that may develop in certain neuromuscular diseases.[67] This may lead to poor cough and airway clearance, which will increase the risk for lower respiratory tract infections and pneumonia. Decreased tidal volume breathing may lead to atelectasis with chronic respiratory insufficiency complicating normal mucociliary clearance from the airways. With time, other factors such as kyphoscoliosis and obstructive sleep apnea further challenge the patient's respiratory system leading toward chronic respiratory insufficiency and potentially respiratory failure.[67]

### *Habit Cough*

Habit cough is a diagnosis of exclusion that encompasses cough that occurs without an underlying organic condition. It is primarily seen in the pediatric population, with 90% of the cases reported under 18 years of age.[68] Other

**Table 48.2:** Habit cough characteristics

| |
|---|
| Generally not present while patient is asleep |
| "Barking" or "honking" cough |
| Chin to chest position |
| Cough diminishes with pleasurable activity |
| Negative evaluation for organic cough |
| Inconsistent response to respiratory medications, antibiotics |
| "La belle indifference" |
| Secondary gain |
| Often has a preceding respiratory infection |

terms have been utilized to characterize this condition, including functional cough, psychogenic cough, cough tic, operant cough, and involuntary cough syndrome.[68] Habit cough can be frustrating to diagnose and treat. It can be a comorbid condition associated with a true organic cause of cough. Patients will often have many primary care or specialty clinic encounters before the diagnosis is made.

There is no consensus on a definition for habit cough, although classic features appear to suggest the diagnosis (Table 48.2).[69] Habit cough has a loud "honking" or "barking" quality. The cough may be accompanied by a "chin to chest" positioning. The cough often diminishes when the patient is doing a pleasurable activity. The patient will often exhibit "la belle indifference", appearing unaffected or unconcerned about the cough. The cough is frequently more distressing to the parent or teacher of the patient. One key characteristic is the absence of cough while the patient is asleep. Although other disease entities may have absence of cough while asleep, this finding is almost universal in children with habit cough.[70] One literature review of 17 articles and a total of 153 patients noted that the cough disappeared when the patient was asleep in all patients with habit cough.[68] The onset of habit cough frequently follows a respiratory infection. It has been postulated that coughing from a respiratory illness leads to a "learned" effect, where the patient continues to cough for months to years because of the development of a subconscious model for coughing.[69] Habit cough also often has an association with secondary gain, or psychological conflicts.[68]

Many cases of habit cough are misdiagnosed initially. Treatment for asthma with bronchodilators and corticosteroids is often prescribed. Patients may also receive over the counter cough medications and antibiotics. The response to medications is generally equivocal. Diagnostic evaluations with radiographs, PFT, serology, and endoscopy are ultimately negative. Other diagnoses may be difficult to differentiate from habit cough. In particular, the psychologically derived etiologies of cough will also present with negative diagnostic evaluation. Psychogenic cough is a term that has fallen out of favor due to the stigmata associated with it. However, it likely represents cough due to somatization of an underlying psychiatric disorder. Conversion disorder and mixed anxiety and depressive disorder are the most common psychiatric diagnoses associated with cough.[70] Psychosocial stressors associated with anxiety, depression, or abuse may also lead to cough somatization. Disorders within the tic spectrum should also be carefully considered. The tic spectrum of disease includes transient tic disorder, chronic motor or vocal tic, and Tourette syndrome. Although tic coughs may not sound as "honking" or "barking", it may be very difficult to differentiate habit cough from tic cough. The presence of motor tics along with vocal tics (i.e. chronic cough) for >1 year suggests the possibility of Tourette syndrome and warrants a referral to child neurology or child psychiatry for further evaluation.

Treatment for habit cough is nonpharmacologic. Suggestion therapy has been described with the major points detailed.

"The major elements of the suggestion therapy sessions were as follows:

1. Expressing confidence, communicated verbally and behaviorally, that the therapist will be able to show the patient how to stop the cough.
2. Explaining the cough as a vicious cycle of an initial irritant, now gone, that had set up a pattern of coughing, which caused irritation and further symptoms.
3. Encouraging the suppression of cough to break the cycle. The therapist closely observes for the initiation of the muscular movement preceding coughing and immediately exhorts the patient to hold the cough back, emphasizing that each second the cough is delayed makes further inhibition of cough easier. Utilizing the distractor as an alternative behavior to coughing is emphasized.
4. Repeating expressions of confidence that the patient was developing the ability to resist the urge to cough.
5. When some ability to suppress cough is observed (usually after about 10 minutes), asking in a rhetorical manner if they are beginning to feel that they can resist the urge to cough, e.g. "You're beginning to feel that you can resist the urge to cough, aren't you?"

6. Discontinuing the session when the patient can repeatedly answer positively to the question, "Do you feel that you can now resist the urge to cough on your own?" This question is asked only after the patient has gone 5 minutes without coughing".[68]

The key feature in treatment is to enable the patient to feel a sense of control over the cough. Other successful treatments have been described. One approach involves wrapping a patient in a bed sheet tightly and reinforcing that this would stop the cough. Another method is to have the patient take small sips of water when the urge to cough is present. These methods have been shown to extinguish the cough relatively quickly.[68]

### *Cardiac*

Although cardiac etiologies for chronic cough in children are not particularly common, it should be considered in the differential diagnosis. Chronic cough from a cardiac etiology is generally related to congestive heart failure that develops from specific cardiac abnormalities that will increase pulmonary venous pressures. This back pressure in the pulmonary venous system may lead to pulmonary edema. A productive cough may have a clear color, although occasionally hemoptysis may be present. Pulmonary arterial hypertension is a condition characterized by remodeling of the pulmonary arteries, which can lead to right-sided heart failure. This condition manifests with shortness of breath and dyspnea on exertion. However, compression of the airways by dilated pulmonary vessels may trigger the cough reflex. In general, other associated signs and symptoms will be evident on history and examination making a cardiac etiology evident.

### *Interstitial Lung Disease*

Childhood interstitial lung disease (ILD) is a diverse group of conditions that are characterized by inflammation of the pulmonary interstitium and alveoli.[71] This heterogeneous group do diseases can be broadly categorized as intrinsic lung disease, ILD associated with systemic disease, or other primary disorders. Examples of intrinsic ILD include cryptogenic organizing pneumonia, nonspecific interstitial pneumonia, desquamative interstitial pneumonia, and lymphoid interstitial pneumonia. ILDs associated with systemic disease are conditions commonly associated with rheumatology such as systemic lupus erythematosus, Sjogren's syndrome, or dermatomyositis.[72] ILD presenting in infancy generally falls under a different set of diseases to include neuroendocrine cell hyperplasia of infancy, pulmonary interstitial glycogenosis, and surfactant dysfunction disorders.[73]

The diseases that have been grouped under ILD have a broad clinical presentation and prognosis. Tachypnea is often the initial respiratory symptom seen and may be the only clinical finding at presentation.[71] Other symptoms include cough and dyspnea with exertion. Hypoxemia may be a noted at baseline in more severe disease, although it may only present during times of exertion. Other clinical manifestations include acute respiratory distress, hemoptysis, inspiratory crackles upon lung auscultation, digital clubbing, or cyanosis. Infants may present with failure to thrive.[71] ILD associated with systemic diseases will generally have nonpulmonary manifestations and laboratory results that are consistent with the systemic disorder.

### *Medication*

Several medications have been well described as a cause of chronic cough. Angiotensin converting enzyme inhibitors are the most commonly described medications that can induce cough. The mechanism has not been completely elucidated, but it may involve bradykinin and substance P. The onset of cough may occur within hours, but it may be delayed for several weeks to months. There may also be a predisposing genetic susceptibility.[74]

Other medications such as nonsteroidal anti-inflammatory drugs and beta-blockers may lead to acute bronchospasm. Chronic use of inhaled medications may also lead to bronchospasm, which can be a reaction to the propellant or other inert component of aerosolized medication.[75]

### *Arnold's Ear-Cough Reflex*

Arnold's ear cough reflex is a rare cause of chronic cough in childhood.[76] Only 4.2% of patients in one study clinically demonstrated the reflex, which is triggered through the auricular branch of the vagus nerve.[77] There are case reports of chronic cough associated with stimulation of the ear canal by wax and cholesteotoma.[76] This rare cause of chronic cough is a diagnosis clinicians should be aware exists, although it is unlikely to be encountered.

## APPROACH TO NONSPECIFIC CHRONIC COUGH

The approach to evaluation of chronic cough should focus on the history and physical examination. History

obtained from the family should focus on the duration of cough symptoms to determine if the patient meets the criteria for chronic cough. Careful attention to the pattern of symptoms and asking if there was any period of time where the child has been asymptomatic can be helpful in determining if the cough is expected as due to recurrent URI. Moreover, a history of evolving symptoms with a classic presentation such as pertussis may provide insight into further evaluation for the patient. Timing and relationship of cough to other events, such as drinking liquids, will help point toward a specific etiology such as dysphagia or aspiration. Symptoms while asleep versus awake may assist with narrowing the differential diagnosis such as habit cough. Response to empiric trials of medications (e.g. bronchodilators, antibiotics, inhaled, or oral steroids) may provide clues to the diagnosis. Past medical history focused on the frequency of sinopulmonary infections, otitis media, specific locations of past pneumonias, pattern of rhinitis, unusual skin infections, GER symptoms, growth and development, eczema, and thoracic abnormalities are important points to question. A thorough review of systems may also point toward a specific diagnosis. Family history of asthma and atopic disease, CF, ciliary dyskinesia, and infertility may indicate higher likelihood of corresponding diseases. An environmental history should be obtained to determine possible risks such as ETS and animal exposures. There may be key clinical features that suggest the possibility of a specific cough (Table 48.3), which would dictate targeted diagnostic testing and evaluation. The age of the patient is also an important consideration when developing a differential diagnosis. For example, one might be more concerned for a retained airway foreign body in a toddler compared with an older child.

A child with a nonspecific chronic cough should obtain a chest radiograph if not previously performed. Findings such as a right-sided aortic arch might indicate an associated vascular anomaly. Anatomic abnormalities such as a pulmonary cyst may be discovered with a screening chest radiograph. Simple spirometry should be obtained in children who are able to perform the maneuver. Spirometry may show evidence of airway obstruction. Obtaining a postbronchodilator spirometry may also show reversible airway obstruction, even if the prebronchodilator spirometry is normal. Although spirometry does not rule in or rule out asthma, it may provide evidence to support the diagnosis. Laboratory testing to include a complete blood count with leukocyte differential to look for a peripheral eosinophilia, total IgE level, and antigen specific IgE. Positive tests would support atopic disease and allergic rhinitis, which have a high association with asthma.

**Table 48.3:** Key features suggestive of a specific etiology of chronic cough

| |
|---|
| Poor growth |
| Steatorrhea |
| Hemoptysis |
| Dyspnea |
| Hypoxemia/cyanosis |
| Weight loss/night sweats |
| Dysphagia/aspiration |
| Feeding difficulties |
| Cardiac abnormalities |
| Chest pain |
| Recurrent otitis media |
| Chronic sinusitis |
| Recurrent pneumonia |
| Productive or moist cough |
| Digital clubbing |
| Honking cough occurs only while awake |
| Opportunistic infections |
| Associated with stridor |

An empiric trial of a bronchodilator, typically delivered as a metered dose inhaler with a spacer, should be tried. A decrease or temporary resolution of cough suggests airway hyper-reactivity that is consistent with asthma. It is important to ensure that patients and parents have the proper expectation regarding bronchodilator response. Many parents will report that the bronchodilator "did not work". However, detailed questioning often reveals that cough subsided for hours, before returning. This is consistent with the duration of action of a bronchodilator. It is also important to ensure proper delivery and technique of any aerosolized medication. A month trial of inhaled corticosteroid could also be considered for an empiric trial of medication. Other medications to consider are antihistamines and nasal corticosteroids for suspicion of allergic or nonallergic rhinitis. An empiric trial of a proton pump inhibitor could also be considered for cough related to GERD. It is generally advisable to avoid multiple simultaneous trials of medications, which may complicate diagnosing the etiology of the cough.

A CT of the sinuses might be considered in the evaluation of chronic cough, although caution should be

exercised in interpreting a CT that reports evidence of sinusitis. It has been reported that children may have abnormal sinus CT results without reporting any symptoms consistent with acute or chronic sinusitis.[77] Other noninvasive testing to consider are immune screening with immunoglobulins, CH50, and antibody levels for *Haemophilus influenzae*, tetanus, and diphtheria. Pertussis antibody testing may also assist with determining an etiology of the chronic cough. Sweat testing for CF may also be considered.

Beyond the initial noninvasive testing or empiric trials of medications, consultation with pediatric pulmonologist, otolaryngologist, and allergist/immunologist should be considered. More invasive procedures such as a flexible bronchoscopy with bronchoalveolar lavage and endobronchial biopsy may be helpful in determining an etiology for the chronic cough.

## SUMMARY

The child who presents with a chronic cough can be a diagnostic dilemma. A comprehensive history and physical examination will generally guide the diagnostic evaluation. A detailed history may determine the etiology of the chronic cough without further testing. Specific causes of chronic cough that are highly suspicious based upon the history and physical examination often have testing that will confirm the diagnosis. The evaluation of a nonspecific cough requires a deliberate approach that may require consultation with pediatric subspecialty providers. Noninvasive testing and empiric trials of medication can be considered before consultation is requested.

The views expressed herein are those of the author and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army and Department of Defense, or the U.S. Government.

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CHAPTER

# 49

# Pediatric Esophageal Disease

***Jennifer Setlur***

## INTRODUCTION

Esophageal disease is an increasingly recognized contributor of airway symptoms in children. Both gastroesophageal disease (GERD) and eosinophilic esophagitis (EoE) should be considered when a child presents with aerodigestive symptoms. Although awareness of esophageal disease has increased in recent years, it remains an underdiagnosed entity in many children. This is typically the result of poor or inadequate testing and work-up, which can generate adverse surgical outcomes. Because esophageal disease can be hard to detect owing to the lack of a single, easy test, a team approach involving otolaryngologists, pulmonologists, gastroenterologists, and speech pathologists is useful in ensuring the proper diagnosis of treatment. This chapter will focus on the symptoms, diagnosis, and treatment of GERD as it affects the airway. EoE will also be reviewed, given the growing recognition of its impact on the airway.

## GASTROESOPHAGEAL REFLUX DISEASE

Esophageal disease in children can lead to some confusion among providers from different disciplines. To clarify, gastroesophageal reflux (GER) refers to the passage of gastric contents into the esophagus, whereas GERD refers to the clinical signs and symptoms that result from GER. Otolaryngologists will frequently point to and encounter laryngopharyngeal reflux (LPR) disease, which refers to the manifestations in the larynx and pharynx due to reflux disease.[1,2] In adults, LPR is viewed as a distinct entity from GERD. Symptoms of LPR include cough, sore throat, hoarseness, and throat clearing; there may be very few complaints of classic GERD symptoms, such as heartburn or abdominal pain. Dysfunction of the upper esophageal sphincter (UES) generates LPR, whereas problems with the lower esophageal sphincter (LES) generate GERD.[2]

Although for adults the literature tends to separate LPR from GERD, the distinction remains uncommon in children. Instead, the impact of reflux on the airway is referred to as extraesophageal reflux disease. Children who present for aerodigestive evaluation may have symptoms involving the larynx, pharynx, esophagus, and airway or any combination thereof. This makes defining disease with the correct and most accurate terminology difficult. To simplify, here we will use GERD to refer to the airway manifestations of reflux disease, although extraesophageal reflux disease may be more accurate.

In the infant population, most will have some degree of GER, but few will have true GERD. Over 50% of infants up to the age of 4 months can exhibit reflux as part of their normal physiology.[3] Reflux resolves in the majority of infants by the age of 1 year, but 5% of children will go on to develop GERD.[4] Over 40% of the children who do develop GERD will also have airway manifestations.[5]

Reflux disease is not exclusively the result of acidic gastric contents in the upper aerodigestive tract. The term "acid reflux" refers to contents with a pH < 4, weakly or nonacidic reflux has a pH between 4 and 7, and frank alkaline reflux has a pH > 7. Both acidic and nonacidic reflux can cause airway symptoms with similar frequency, and some studies will suggest that nonacidic reflux is present more in children with airway symptoms than acid reflux.[6,7] One possible explanation is that bile acids have been shown to have proinflammatory effects.[8] As indicated on esophageal pH probes, most reflux episodes after

meals in children are not associated with drops in pH; reflux episodes can last up to 2 hours after feeds.[9,10] The concern in very young infants then is that of nonacidic reflux, as the rate of physiologic reflux is higher, and feeds occur in short, frequent intervals.

## AERODIGESTIVE TRACT STRUCTURE AND FUNCTION

Normal swallowing function is accompanied by relaxation of the LES, but relaxation in the absence of a swallow over time can lead to GERD. Adult specialists will frequently identify esophageal dysmotility in association with GERD, but in children this connection is less well understood due to the lack of normative data. What is known in children is that GERD can lead to esophagitis, which, in turn, affects esophageal musculature; ultimately, this can generate dysmotility.[11]

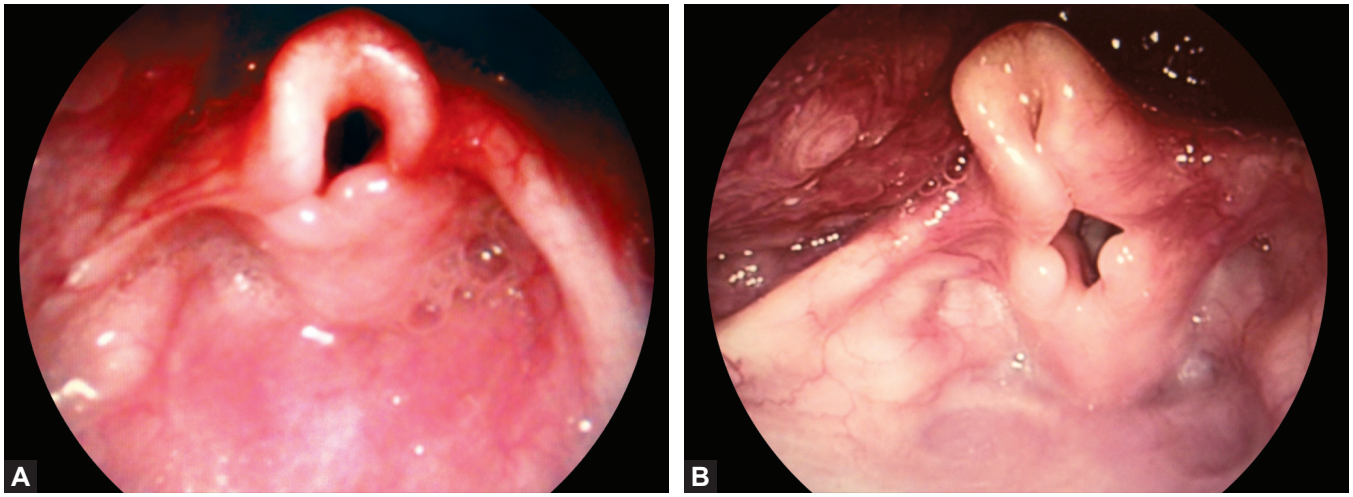
Anatomic distinctions in the pediatric population increase the risk of reflux. In newborns and young infants, the esophagus sits at a more obtuse angle to the esophagus, and the intra-abdominal esophagus is shorter. Perhaps, the biggest factor is a neurologically immature LES with increased transient relaxations. Some infants may have abnormal or decreased laryngopharyngeal sensation, which makes them less able to detect laryngeal penetration from and aspiration of gastric contents.[12] The literature has not conclusively shown that airway manifestations of GERD are higher in preterm infants versus term infants primarily because of variation in research methods. Although there is a trend toward a higher incidence of airway manifestations in preterm infants, most babies will see their symptoms resolve by the age of 2 years.[13-15]

There are multiple pathways by which gastric contents affect the airway mucosa, and this is augmented by the fact that the laryngotracheal mucosa is extremely sensitive to gastric acid.[16] Not only can acid damage and eventually scar and narrow the airway, it can also worsen irritation from other causes, such as endotracheal intubation. In addition to the structural damage, functional disruption can also occur as a result of reflux. Cyanotic spells or apparent life-threatening events (ALTE) can result from acid-generated laryngospasm.[17] Reflex mechanisms such as laryngospasm and bronchodilation are seen as responses to reflux stimulation of the lower esophagus, and these reflexes may also contribute to airway manifestations of GERD in addition to the direct effects of reflux on the airway.[8,18,19]

## SYMPTOMS AND INITIAL PRESENTATION OF GERD

Reflux in infants is most commonly detected by spitting up, burping, frank emesis, back arching or discomfort, and dysphagia. In older children, pain, discomfort, and nausea are the more common complaints.[4] Some children may have a more worrisome history to include failure to thrive, hematemesis, anemia, or recurrent pneumonia.[20] Airway manifestations in children can include laryngomalacia, hoarseness, vocal cord nodules, subglottic stenosis, recurrent croup, asthma, apnea, and ALTE.[1,21]

Laryngomalacia represents a delay of maturation of the supporting structures of the larynx and is both the most common cause of congenital stridor and the most common congenital lesion of the larynx. It may affect the epiglottis, the arytenoid cartilages, or both (Figs. 49.1A and B). Providers will often associate laryngomalacia




**Figs. 49.1A and B:** (A) Prolapse of the arytenoids into the airway in laryngomalacia; (B) Infolding of the immature epiglottis.

with GERD in some capacity, but the exact association is not entirely clear. What is known is that infants with laryngomalacia have a higher incidence of GER, presumably a result of the more negative intrathoracic pressures necessary to overcome the inspiratory obstruction.[22] Also known is that mucosal changes of the larynx in children with laryngomalacia are consistent with those mucosal changes seen in the esophagus of children with GERD, but a clear cause and effect relationship has not been demonstrated.[23] Because of this treatment of laryngomalacia with medications aimed at reducing reflux has not been proven as an effective therapy. Laryngomalacia most likely comes from neurologic immaturity, and factors such as anatomic variations and GERD may worsen the severity.[24]

Reflux-associated voice changes may be the result of either chronic laryngitis or vocal cord nodules (Fig. 49.2). True vocal fold nodules are the most common cause for prolonged hoarseness in the pediatric age group.[25] Nodules are primarily the result of vocal abuse, but studies have suggested other causes such as genetic predisposition, behavioral factors, and environmental factors.[25] Reflux as a direct cause of nodules has not been studied extensively in the pediatric population. Research in adults with nodules has shown that pharyngeal reflux is more prevalent in patients with nodules when compared with a group of control patients, suggesting an association between GERD and nodules, although not necessarily a causative one.[26] Most children will benefit from treatment with voice therapy and decreased vocal abuse; few will have true GERD in need of treatment with reflux medication. In contrast, chronic laryngitis is the result of LPR, and this is a well-defined association. In these patients, examination of the larynx shows mucosal edema and erythema of the supraglottis and glottis.[27] Some children may suffer from LPR and have voice changes but fail to have these examination findings. In these patients, a trial of reflux medications may be helpful for both diagnostic and therapeutic approaches. Patients who fail such a trial may benefit from further work-up for conditions such as nonacid reflux, with pH probe and impedance testing, or EoE, with esophagoscopy and biopsies.

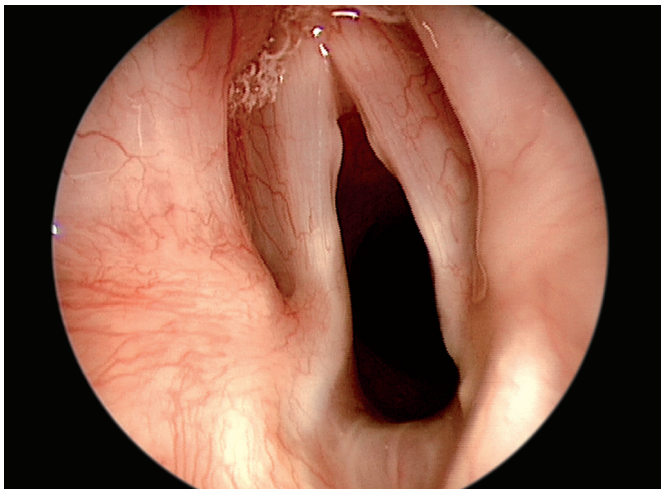


**Fig. 49.2:** Bilateral true vocal cord nodules.

In addition to its functional effects on the larynx, GERD has also been implicated in playing a role in the development of subglottic stenosis. This is largely based on studies done in animals.[16,28,29] Much speculation has surrounded the effect of GERD on postoperative outcomes after airway reconstruction.[30-33] Evaluation of children for reflux disease preoperatively is generally recommended, and the use of antireflux medications postoperatively is a common practice given their relative safety.

Children who present with chronic cough and recurrent croup may suffer from GERD, and a carefully taken history can aid in the diagnosis. For instance, cough that worsens when the child is supine may suggest GERD as the cause. In older children, the chief complaint may be that of cough associated with a foul taste in the mouth, or discomfort in the throat or stomach. Children being evaluated for recurrent croup should also be evaluated for GERD, as there is a high incidence of reflux in this group.[34,35]

Reflux disease may not only impact the upper airway, but the lower airway as well. There is evidence that symptoms of reflux disease are more common in children with asthma, which is the most common pediatric pulmonary condition in the United States.[36,37] In addition, asthma symptoms tend to be more severe in children with known GERD, and the proposed pathway of disease is inflammation of the lower airways due to reflux.[37] Once the lower airway is inflamed, work of breathing increases ultimately generating negative pressure on the LES allowing for more reflux. The link between GERD and asthma is one that is well established, but it may not be necessary for every asthmatic child to be evaluated for GERD. Instead, evaluation should be reserved for children with asthma who present with frank reflux symptoms, those who have persistent asthma symptoms despite good medical management, and others who have atypical airway symptoms not classically associated with asthma.

Occurrences such as ALTEs and nonobstructive apneas can be quite worrisome to families and practitioners alike. Over 50% of ALTE cases will have a defined cause, with the

most common cause being GERD.[38] Although this is the most common cause, careful multidisciplinary evaluation should still be performed to identify other causes, such as neurologic disturbances, infection, respiratory problems, and cardiovascular abnormalities, which could lead to mortality if not detected early. Nonobstructive apnea in association with GERD is not well understood, but we advocate for the evaluation of GERD in these patients as reflux is a treatable condition that could prevent poor patient outcomes.

## DIAGNOSIS

Accurate diagnosis of GERD starts with a careful history, and usually starts with empiric treatment that can be diagnostic and therapeutic. Specific and extensive testing should be reserved for refractory or atypical cases. For the child who presents with a primary airway complaint, a history or work-up aimed at detecting GERD may not be the first step that a provider takes. Instead, the initial focus is on the airway, making sure that it is protected and secure. Only then does one move on to the underlying cause of airway-related symptoms, focusing on underlying anatomic abnormalities or other problems like reflux disease.

Airway symptoms such as cough or noisy breathing in association with feeding problems, spitting up may suggest reflux. When reflux is suspected on the basis of the history, evaluation should next focus on the physical examination. In addition to a general examination of the head and neck, one should note the presence and quality of noisy breathing and signs of respiratory distress or increased work of breathing; a fiberoptic examination of the upper aerodigestive tract should be included. This allows for the provider to evaluate the structure and function of the larynx and pharynx. If a diagnosis remains unclear, then the assessment should move on to other testing, such as a barium swallow, upper gastrointestinal (GI) series, pH probe testing, impedance monitoring, and endoscopy as these are the commonly employed studies used to diagnose GERD in children.

The relative disadvantage of tests such as barium swallow or upper GI series is that they are snapshots of the esophagus and are usually done in the upright position. Because reflux events can occur up to 2 hours after feeds, they may not reveal these delayed reflux events.[39] Instead, we advocate for the use of pH probes, which remain in place for a 24-hour period. The "gold standard" for diagnosing GERD is the dual channel 24-hour pH probe; despite this, standardization across centers is lacking and false negative rates can be as high as 20%.[40]

The main cause of these false negatives is the inability of these probes to detect short episodes of reflux.[41] Despite its shortcomings, it remains the most sensitive and specific test when compared with other available modalities. The presence of dual channels means that pH fluctuations at the level of the LES and UES can be detected; this presence of a probe near the UES is particularly useful in children with airway manifestations of reflux, as they may only have pH changes near the UES with no changes seen near the LES.[42]

The Bravo pH-monitoring system is likewise useful and can be used over a 24-hour period or even up to 96 hours if needed. Whereas the standard pH probe is placed through the nose and must remain there for the duration of the test, the Bravo probe is placed endoscopically and is a small gel cap that sits on the wall of the esophagus (Fig. 49.3). Because it goes virtually undetected by the child, evaluation of reflux in the setting of his or her normal activities can be done. Both the Bravo probe and the standard pH probe send information to an external monitor, which is especially useful since one can record symptoms such as voice changes, cough, or wheezing that can then be compared with objective reflux events based on the pH recorded. The BRAVO probe is particularly helpful for the child with paradoxical vocal fold motion (PVFM) to determine if gastric reflux is the causative factor. The Bravo has the disadvantages of being too large for younger children and the lack of a dual probe. Newer devices, such as the Dx-pH Measurement System, are coming to market and can provide pH measurements not

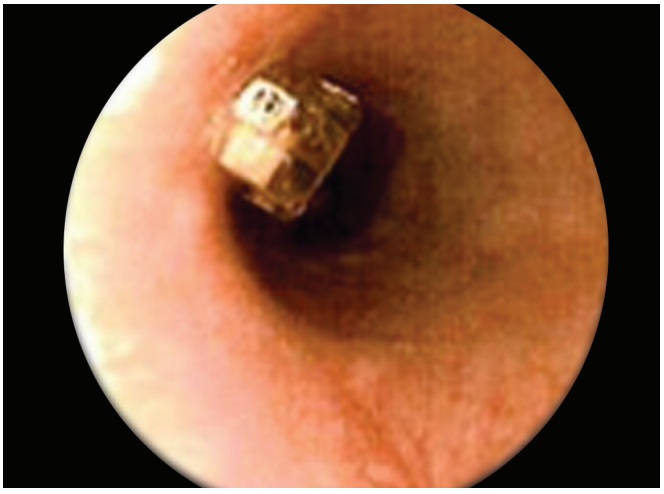


**Fig. 49.3:** Bravo probe sitting on wall of the esophagus.

only in the esophagus, but also in the extraesophageal regions like the pharynx. Such a probe uses a transnasal catheter that sits posterior to the uvula and detects the pH of liquid, frank refluxate as well as aerosolized refluxate that may be present.

Impedance testing, or multichannel intraluminal impedance (MII), is an exciting tool to diagnose reflux gaining in use, as it can overcome some of the limitations of standard pH probe testing. A six-channel probe is placed transnasally, and the impedance, or opposition to electrical current, is measured among the channels. As the ionic concentration increases, impedance decreases as the two are inversely related; therefore, air has higher impedance than acidic refluxate, which has a higher ion content.[11] Because of its multiple channels, the direction of impedance change can be measured, so one can differentiate a reflux even from a swallowing event. It allows the detection of reflux independent of the pH, which can be helpful in evaluating patients who suffer from nonacid reflux as this can be difficult to diagnose. The standard pH probe can only detect pH changes of at least 1 point and to a value lower than a pH of 4 or higher than 7.5, which means it cannot detect weakly acidic or weakly alkaline changes.[10,11,41] Although there are many advantages of MII, the major disadvantage is the lack of standardization in the pediatric population and the inability to detect very small differences in acidity; the latter is being overcome by combined MII–pH probes.[43] In addition, the data analysis has proven time consuming, but hopefully this will change as newer software is made available.

For the very difficult to diagnose child with aerodigestive complaints, a multidisciplinary approach is best. Examination with rigid laryngoscopy and bronchoscopy, flexible bronchoscopy, and flexible esophagogastroduodenoscopy should be pursued. At the laryngeal and upper airway level, GERD can produce edema of the supraglottis (arytenoids), postglottic region, vocal cords, and subglottis. Other findings may include vocal cord nodules and erythema, effacement of the laryngeal ventricles, and frank subglottic narrowing.[1] Evaluation more distally, along the trachea, may reveal mucosal erythema and cobblestoning, as well as blunting of the carina. Many of these findings depend on the interpretation by the endoscopist, so there can be variation among providers when compared with testing with pH probe, but the combination of visualized findings with objective measures improves testing sensitivity.[1] Examination with flexible bronchoscopy not only allows the detection of dynamic changes, like trachomalacia, but also allows for bronchoalveolar lavage. The specimen should be sent for measures of lipid-laden macrophages, as this can reveal aspiration that perhaps is clinically undetected. A lipid-laden macrophage index, or LLMI, of >100 has been shown to have a high degree of sensitivity for aspiration, although it does not reveal if the source of aspiration is reflux or a swallowing problem.[44,45] After airway evaluation, examination of the upper GI tract should next, to look for changes such as ulceration or erosion, and to obtain biopsies. Tissue is then studied for microscopic changes of GERD and eosinophilic esophagitis.

For the patient with symptoms refractory to medical management, esophageal manometry may be necessary. This can be helpful to assess esophageal peristalsis as well as the activity at the level of the LES, since achalasia and other motor disorders may mimic GERD.

## TREATMENT

Perhaps the most important first step in the treatment of GERD-related airway manifestations is to correctly identify that GERD is the cause of the symptoms. Once this has been done, then treatment typically begins with lifestyle changes. Avoidance of spicy or caffeinated foods, remaining upright after feeds, and thickening feeds are commonly used in the initial management of GERD. For older children in whom obesity is present, enrollment in a weight loss program is helpful, as excess weight is linked to increased rates of GERD.

Medical therapy is next, and begins with proton pump inhibitors (PPIs). Much of what is known about the effects of PPIs on GERD in children is taken from data obtained from the adult population. PPIs are first-line as they have been shown to produce quicker healing and symptom resolution, when compared with histamine blockers.[46,47] When compared with histamine blockers, PPIs are more effective in the treatment of extraesophageal symptoms of GERD.[48] Duration of treatment is an active area of investigation, and early studies suggest a trial of therapy between 3 and 6 months.[48] Patients with symptoms refractory to the standard PPIs may be best served by referral to a gastroenterologist. These specialists are likely to consider adding prokinetic agents to the therapeutic regimen after anatomic obstruction is ruled out. When PPIs have little or no effect on symptoms, non-acid reflux should be considered, particularly since non-acid reflux can play a role in airway disease. Currently, in the United States, metoclopramide is approved to augment GI motility. As a dopamine antagonist, it increases the pressure

at the LES and improves gastric emptying. Unfortunately, because dopamine receptors are present in the central nervous system (CNS), pronounced side effects may include drowsiness, restlessness, and, most importantly, dystonic reactions and extrapyramidal movements, especially in infants < 6 months of age. Other agents, namely, cisapride, have been withdrawn from the commercial market due to the increased risk of cardiac arrhythmias. As an alternative to metoclopramide and its CNS effects, specialists have turned to the macrolide antibiotic erythromycin, which stimulates motility by direct effect on the motilin receptors of the intestines.

The GERD that persist despite maximum medical management may require surgical intervention, the most common of which is a fundoplication.[49] This is a safe and effective procedure and complications such as esophageal obstruction, wrap breakdown, and esophageal stricture are uncommon.[49,50] The ability to perform the fundoplication laparoscopically has improved outcomes compared with the open technique.[51,52] While the effects of surgery on acid reflux have been well demonstrated, its effects on nonacid reflux are not yet established but remain a growing area of interest.

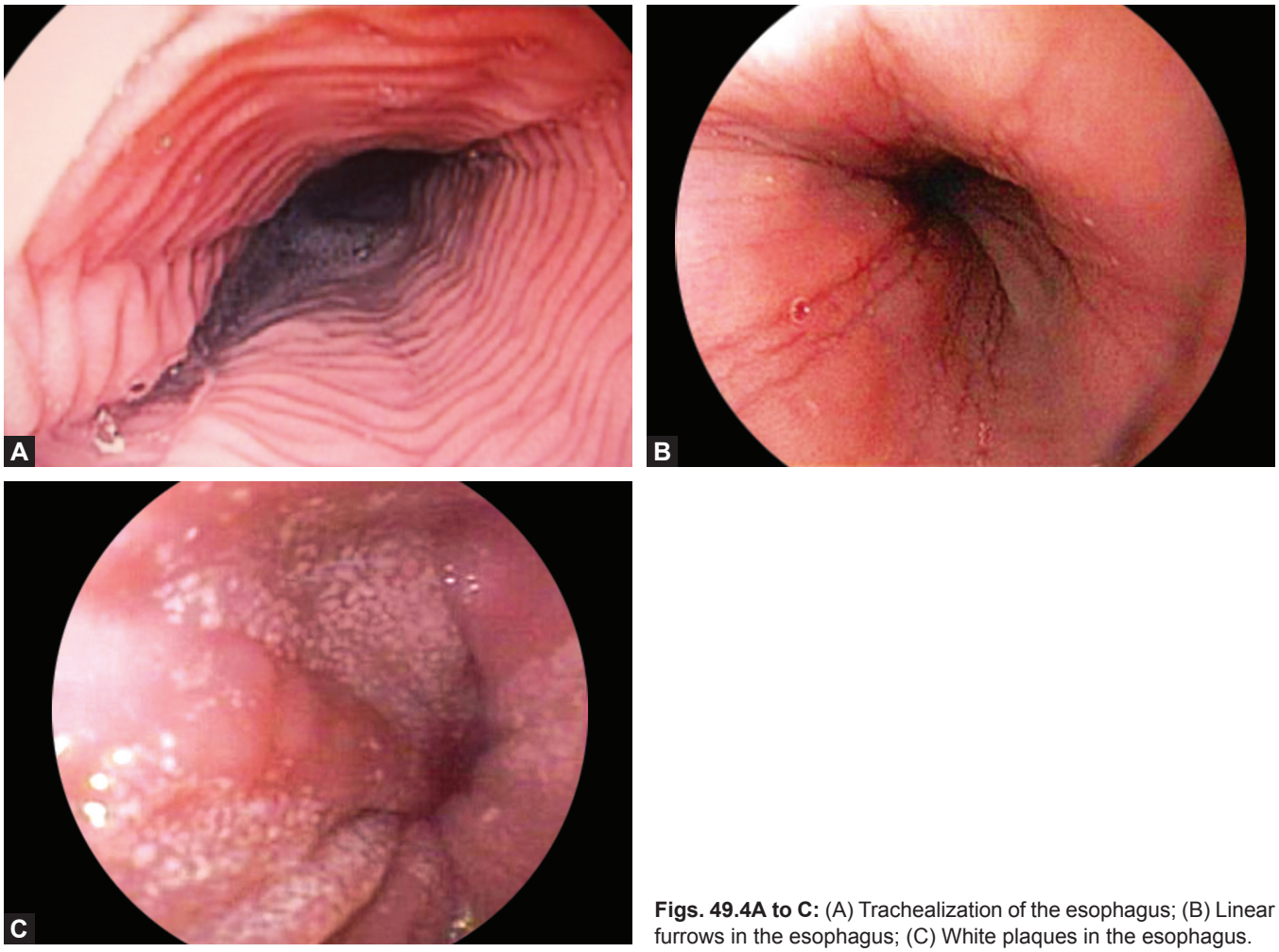
## EOSINOPHILIC ESOPHAGITIS

Eosinophilic esophagitis is a relatively new and increasingly common diagnosis for patients who present with symptomatology similar to those with GERD but who do not respond to targeted therapy. It is a clinicopathologic condition and three criteria must be met to make the diagnosis of EoE: clinical symptoms of esophageal dysfunction, an esophageal biopsy with ≥15 eosinophils per high-power field (HPF), and exclusion of other causes of esophageal eosinophilia.[53] It is important to note that biopsies should be obtained after a 6-week trial of PPIs at the maximum dose has been administered. If a trial of medical therapy is not possible (for example, due to contraindications to PPIs or severity of symptoms prohibiting a trial of medicine first), then biopsies should be done simultaneous with a pH probe to document the absence of GERD. Initial suspicion for EoE is raised when there is a nonresponse of symptoms to high-dose PPIs, or negative pH study. Thereafter, a biopsy is pursued, demonstrating increased eosinophils in the esophageal mucosa; the gastric and duodenal mucosa must also be sampled to confirm the eosinophilia is confined to the esophagus. The latter is key in making an accurate diagnosis of EoE, since GI eosinophils can be seen in GERD, inflammatory bowel disease, parasitic infection, scleroderma, immunosuppressed state, and with the administration of certain medications.[53,54]

The incidence is approximately 1 in 10,000 children per year, with a male predilection and an average age of diagnosis of 8 years.[55] The most common EoE symptoms are heartburn and regurgitation, and recurrent emesis, abdominal pain, food impaction, and dysphagia may also be seen.[56] Less common findings are failure to thrive, chest pain, and diarrhea. Children may also present with food refusal, as they may be too young to verbalize a complaint of dysphagia.[53]

Extraesophageal manifestations of EoE may be part of the patient's initial presentation. In the airway specifically, EoE has been linked to otitis media, recurrent croup, adenoid hypertrophy, and sinusitis, but it is unlikely that the sole symptom of EoE is airway related; a thorough review of symptoms is imperative.[56,57] The prevalence of EoE in the population of children with aerodigestive symptoms refractory to initial medical management has been demonstrated by one group to be 3.72% (unpublished data). It has also been implicated in subglottic stenosis.[58,59] It remains unclear why or how EoE impacts the airway. One possibility is the result of airway exposure to gastric contents in the setting of persistent dysphagia and recurrent emesis associated with EoE. Airway symptoms associated with EoE have been reported as wheezing, stridor, dyspnea on exertion, recurrent croup, and hoarseness.[60] In one study, 6.25% of children who presented with croup and cough were found to have > 15 eosinophils per HPF.[61]

When EoE is suspected clinically, evaluation with esophagogastroduodenoscopy is required. Esophageal rings ("trachealization" of the esophagus), linear furrows, and white plaques are characteristic endoscopic findings of EoE, but they are not specific for this diagnosis, and significant variations can exist between observers (Figs. 49.4A to C).[62-64] Some cases may exhibit mucosa that is pale or has decreased vascularity, and friability may be seen with passage of the scope. Long-standing disease in older children and adults may be associated with strictures. Up to 10–20% of EoE patients may have normal mucosal appearance on endoscopy.[62] Testing with pH probe, radiographic studies, and impedance testing may also be used, but they are not necessary to make the diagnosis of EoE. Instead, they should be employed to evaluate the patient for other conditions of the upper digestive tract. Examination of the upper airway in EoE




**Figs. 49.4A to C:** (A) Trachealization of the esophagus; (B) Linear furrows in the esophagus; (C) White plaques in the esophagus.

patients may reveal findings to that of patients with GERD, including laryngeal edema, erythema, airway narrowing.

The approach to obtaining biopsies is an active area of discussion, because a single biopsy samples only a tiny fraction of the mucosal surface.[64] The general consensus is to obtain multiple biopsies from multiple locations, obtaining specimens from both suspicious looking regions and normal mucosal areas. More than 15 eosinophils per HPF must be seen, but other histologic findings such as eosinophilic microabscesses, eosinophil degranulation, and basal zone hypertrophy.[56]

Several evidence-based treatment options for EoE exist for the adult population, and this has been applied to children as well. It should be noted that there are no medications specifically approved for the EoE treatment, so all are used off-label.[65] The main goal of therapy is to improve symptoms and normalize the esophageal mucosa; symptoms will recur once therapy is stopped, due to the chronic nature of the condition. Short courses of oral steroids can be helpful in the initial control of symptoms, as they decrease eosinophil counts, but they should not be relied upon long term.[66] Local steroid delivery, with medications formulated to treat asthma such as fluticasone and budesonide, can be swallowed to coat the esophagus. They have a safe profile and the main adverse effect is local, which can include candida esophagitis.[67-69] Because of the strong association between EoE and allergic diseases, leukotriene antagonists have been studied, but results are equivocal.

Diet modification is the mainstay of nonpharmacologic treatment of EoE. It can be difficult for both child and caregiver, and close follow-up with a nutritionist is imperative. Several approaches to dietary changes exist, including elimination of the most highly allergenic food groups, an elemental diet, and targeted elimination therapy.[65] Another nonpharmacologic therapy, useful in older children who suffer from esophageal narrowing, is serial esophageal dilation to avoid food impaction. The

risks of multiple procedures include mucosal rents, mucosal perforations, and postoperative chest pain requiring hospitalization; as knowledge of EoE increases, so does the safety profile of therapeutic esophageal dilations.

Information about the prognosis and progression of disease is lacking in children, but information from the adult population suggests that EoE is a disease with periods of quiescence and relapse.[65] It is thought that because the rest of the GI tract is spared, chronic changes to the esophageal muscle and mucosa occurs over time, generating not only strictures, but abnormal motility as well.[70-72] Development of premalignant or malignant lesions has not been documented, in contrast to long-standing GERD. Whereas in adults, a follow-up endoscopy is recommended 8 weeks after the initiation of therapy, similar recommendations do not yet exist in children.[65] It is generally accepted that endoscopy should be symptom triggered in children, in an effort to limit the number of procedures they undergo.

## FUTURE DIRECTIONS

The airway and digestive tract were once thought to be separate in structure and function, but current understanding suggests that they should be viewed as a more unified upper aerodigestive tract. Although this is being increasingly recognized, children who present with airway manifestations of GERD, nonacid reflux, and EoE can be difficult to diagnose and treat. Previous research efforts were focused primarily on establishing whether there was a causal relationship between GERD and airway symptoms. Focus is now shifting toward airway symptoms in the setting of nonacid reflux and EoE and toward determining pediatric test standards, diagnostic, and therapeutic protocols through prospective, controlled studies. The approach to the child with airway manifestations of esophageal disease may be best done by a multidisciplinary team composed of otolaryngologists, pulmonologists, gastroenterologists, and speech pathologists. These teams are becoming more common at academic centers. Combining the efforts of specialists from different departments can improve research efforts and will ultimately lead to improvements in patient care for children with airway manifestations of esophageal disease.

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# SECTION 4

# Pediatric Head and Neck

CHAPTER

50

# Developmental Anatomy

***Robert Chun, Michael E McCormick***

## NORMAL DEVELOPMENT OF THE LIP

The craniocaudal axis of the embryo is established early in the embryonic period, and the process of neurulation begins at about 21 days. Neurulation involves the "rolling up" of the neural plate, a process which will effectively divide this tissue into the neural tube and the nonneural ectoderm. As the neural folds are closing, the neural crest cells emerge from the junction of these two tissue types. Neural crest cells then undergo an epithelial-to-mesenchymal transition, a process that is thought to involve the presence or absence of bone morphogenetic proteins (BMPs).[1]

In the developing face, the neural crest cells then migrate from the dorsal neural tube to the paired branchial arches and facial prominences. These neural crest cells in the first pharyngeal arch will give rise to the maxillary and mandibular prominences, which have begun to surround the primitive stomodeum by the 5th week of gestation. The cephalic portion of the neural tube gives rise to the midline frontonasal prominence. The ventral forebrain then induces thickening of the ectoderm at the lateral edges of the frontonasal prominence into the nasal placodes.[2] During the 5th week, the nasal placodes will invaginate into the nasal pits, which now separate the medial and lateral nasal prominences.

The maxillary prominences grow medially and compress the medial nasal prominences during the 6th week. The medial nasal prominences will fuse with each other in the midline during the 7th week to form the intermaxillary segment. This tissue will eventually develop into the primary palate, four upper incisors, medial upper lip, philtrum, columella, and nasal tip.[1] At this same time, the lateral nasal prominences are fusing with both the medial nasal prominences and the maxillary prominences. The groove between the lateral nasal prominence and the maxillary prominence will detach from the overlying ectoderm and canalize into the nasolacrimal duct and sac. The lateral nasal prominences will give rise to the nasal sidewalls and ala. The maxillary prominences will develop into the cheeks, lateral upper lip, and the secondary palate (Table 50.1).[3]

**Table 50.1:** Facial contributions of neural crest—derived prominences

| *Facial prominence* | *Anatomic structure* |
|---|---|
| Frontonasal prominence | Forehead, nasal bridge |
| Medial nasal prominences | Nasal tip and columella, philtrum, medial upper lip, primary palate, four upper incisors |
| Lateral nasal prominences | Nasal sidewalls and ala |
| Maxillary prominences | Cheeks, lateral upper lips, secondary palate |

## NORMAL DEVELOPMENT OF THE PALATE

The secondary palate begins to develop at the end of the 5th week from neural crest cells of the maxillary prominences. The palatine shelves are two outgrowths from the maxillary prominences that grow inferiorly during the 6th week along either side of the tongue. The shelves then rotate to a more horizontal position above the tongue. Beginning at 8 weeks of gestation, the palatine shelves

begin to fuse in an anterior-to-posterior direction, starting at the primary palate (intermaxillary segment) and incisive foramen. At the same time, the nasal septum will fuse with the newly formed palate. The epithelial linings of the palatal shelves partially slough off, leaving only the basal layers, known as the medial edge epithelium (MEE). The midline epithelial seam is formed by the fusion of the MEE layers and is then resorbed, leaving a continuous mesenchymal layer within the palate. The process is complete by the 12th week with fusion of the uvula.[1,2]

## Abnormalities in Development of the Lip and Palate

Failure of the establishment of a medial-to-lateral axis can result in holoprosencephaly (HPE). BMP signaling abnormalities have resulted in HPE-like phenotypes in animal models. In humans, HPE occurs in 1 in 10–20,000 live births and is the most common structural malformation of the forebrain. The phenotypes vary in severity and include cyclopia, cebocephaly, midfacial hypoplasia, and cleft lip with or without palate.[1]

Missteps in any of the series of fusions during the formation of the lip and palate can produce any of a number of pathologic conditions. Median facial clefts result from a failure of fusion of the medial nasal prominences in the midline. Oblique facial clefts, such as those described in the Tessier classification, have a complicated and debated embryologic origin, as evidenced by their diverse presentations. Abnormalities in neural crest migration have been implicated. Another simplified explanation is a failure of the mesoderm of the lateral nasal prominences and the maxillary prominences to fuse.

Cleft lips occur from a failure of fusion of the medial nasal prominence primarily with the maxillary prominence. If the medial and lateral nasal prominences fail to fuse as well, the cleft lip will extend between the columella and nasal ala (complete cleft lip). A complete cleft lip extends into the nasal aperture or has a thin bridge of skin (Simonart's band) connecting the cleft and noncleft sides of the lip.[2] Classically, Simonart's band has no orbicularis oris muscle fibers within it, and the presence of muscle tissue likely suggests an incomplete cleft lip. Incomplete cleft lips involve a variable amount of the height of the upper lip. Complete cleft lips are often associated with a cleft of the alveolus on that side as well. Bilateral cleft lips occur when the intermaxillary segment has failed to fuse with either maxillary prominence, often resulting in a hypoplastic and everted premaxilla.

Clefting of the palate occurs in varying degrees and can be unilateral or bilateral. They are classified according to their location relative to the incisive foramen, a classification, which relates back to their embryologic origins. In a unilateral cleft of the secondary palate, the noncleft side of the palate is fused with the nasal septum. Since fusion of the secondary palate progresses from anterior to posterior, the severity of clefts of the secondary palate depends on when the fusion was interrupted. Complete clefts of the secondary palate extend to the incisive foramen, and they result from a complete failure of fusion on that side. Developmental interruptions that occur late in the fusion process result in less severe clefts. Submucous cleft palates have deficient palatal musculature with intact mucosa. Often, there is a bifid uvula or a bluish area in the midline where the muscle is deficient (zona pellucida). A notch can often be palpated in the posterior hard palate as well.[2]

Special mention should be made of the cleft palate seen in children with Pierre Robin sequence (also known as Robin sequence). In these situations, the cleft is U-shaped as opposed to V-shaped. The prevailing theory on the embryogenesis is that micrognathia and a posteriorly displaced tongue physically prevent the midline fusion of the palatal shelves on both sides. This abnormality occurs both in syndromic and isolated nonsyndromic forms.

# EMBRYOLOGY OF THE BRANCHIAL ARCHES AND POUCHES

The five or six pairs of branchial arches are composed of ectoderm, mesoderm, and endoderm; from these germ layers, the structures of the head and neck are formed. Externally, the arches are separated by branchial clefts, of which only the first branchial cleft further develops into the external auditory canal. The pharyngeal pouches are endodermally lined pouches of the pharynx associated with branchial arches. The branchial cleft, arches, and pouches form the muscles, bones, nerves, and vessels of the head and neck.

## Derivatives of Branchial Arches and Pharyngeal Pouches

The first branchial cleft eventually forms the external auditory canal and the tympanic membrane. The body of the mandible is derived from the first arch as well as the malleus (excluding the manubrium), the incus (excluding the long process), and the muscles of mastication. The primary motor and sensory innervation is from the

trigeminal nerve. The first pharyngeal pouch forms the middle ear mucosa as well as the tympanic membrane with the first branchial cleft.

The styloid process, the manubrium of the malleus, the long process of the incus, stapes (excluding the footplate), and the hyoid bone (superior part of body and lesser cornu) are derived from the second arch. The muscles of facial expression as well as the anterior belly of the digastric muscle, the stylohyoid, and stapedius muscle are derived from the mesoderm of the second arch. The facial nerve innervates the second arch structures. The second pouch forms the lining of the palatine tonsil.

The third arch forms the inferior part of body and greater cornu of the hyoid bone as well as the stylopharyngeus muscle. The glossopharyngeal nerve innervates the stylopharyngeus muscle. The inferior parathyroid is derived from the superior third pouch, whereas the thymus is from the inferior third pouch.

The fourth through sixth arches form the cartilages of the laryngeal framework in addition to the laryngeal muscles and cricothyroid muscle. The recurrent laryngeal nerve innervates the muscles of the larynx. The superior parathyroid glands are derived from the fourth pouch as well as the calcitonin-secreting parafollicular cells of the thyroid.

## Abnormalities of the Branchial Clefts and Pouches

Residual openings or incomplete closures of descending tracts can lead to branchial anomalies. A branchial sinus has a single opening, a fistula has an opening to both the skin and pharynx, and a cyst is an enclosed dilation without any connection. The second through sixth anomalies will have a skin opening lying in the lateral neck anterior to the sternocleidomastoid muscle (SCM). In general, branchial cleft anomalies will lie superficial to derivatives of the caudal arch. For example, the second branchial fistula will lie superficial to the common carotid artery of the third branchial arch.

The first cleft has anomalies ranges from preauricular cysts or pits to first arch anomalies. Work classified an ectodermally derived duplication of the external auditory canal as a type 1 first cleft anomaly and type 2 first cleft anomaly including both ectoderm and mesodermal derivatives (cartilage).[4] A type 2 first cleft anomaly lies inferior to the ear usually originating in the submandibular space. Both first cleft anomalies are intimately involved with the facial nerve of the second arch.

A second branchial cleft anomaly will lie anterior to the SCM, and its associated fistulous pathway will end in the tonsillar fossa (📷 50.1).

The fistula will lie superficial to the common carotid artery, and a derivative of the second arch and fistulous path will go between the internal and external carotid artery. The third arch derivatives will pass posterior to the internal carotid artery.

A fistulous pathway of the third cleft ends in the thyrohyoid membrane, whereas the fourth cleft ends in the piriform sinus (📷 50.2).

The third cleft fistula will lie superficial to the vagus and recurrent laryngeal nerve. A fourth branchial cleft anomaly will pass between the superior and recurrent laryngeal nerves. Recurrent thyroiditis is also associated with fourth cleft anomalies.

## Thyroglossal Duct Cyst

The thyroid gland begins at the foramen cecum of the base of tongue descending anteriorly in the neck through the mid portion of the hyoid bone to its paratracheal destination. Remnants of this descending tract will result in a thyroglossal duct cyst. Removal of the cyst and the tract including the mid portion of the hyoid bone (Sistrunk procedure) will decrease the recurrence rate to 10–15%.[5] It is imperative that the normal thyroid cartilage is identified and preserved and not mistaken for the hyoid bone in a Sistrunk procedure (📷 50.3).

Rarely will the thyroglossal duct cyst be the only functioning thyroid tissue for the patient; therefore, an evaluation for normal thyroid tissue should be performed prior to surgery.

# NORMAL DEVELOPMENT OF THE LARYNX AND TRACHEA

Just like the majority of organogenesis, the embryonic period of laryngeal development occurs during the first 8 weeks of gestation. The primitive gut tube develops early in embryogenesis from endoderm incorporated during lateral in-folding of the embryo. It is during the 3rd week that the respiratory diverticulum appears as an outgrowth from the ventral portion of the foregut (laryngotracheal groove).[6] This diverticulum will elongate toward the caudal end of the embryo as two lateral furrows develop on the sides of the laryngotracheal groove. These furrows will fuse in the midline in a caudal-to-cranial direction to form the tracheoesophageal septum, formally

separating the respiratory and digestive tracts. As this septum thickens by proliferation of the cells within it, a single lung bud forms and divides into right and left lung buds in the 4th and 5th weeks.[4] The respiratory epithelia and glands of the larynx and trachea develop from the ventral endoderm lining the laryngotracheal groove; the bronchi and lungs will develop from the more caudal endoderm.[7]

At this same time, the neural crest-derived pharyngeal arches are migrating toward this area and will give rise to a number of structures in the region, including the muscles and cartilages of the larynx. The exact destiny of the fourth through sixth branchial arches remains unclear, but together, they contribute to the remainder of the laryngeal skeleton, including the thyroid, cricoid, arytenoid, corniculate, and cuneiform cartilages. The more cranial thyroid cartilage is believed to form from fusion of two plates derived from the 4th branchial arch. The more caudal cricoid cartilage arises from two cartilaginous centers from the sixth arch, which will fuse in the ventral midline in the 7th week. Dorsally, fusion of the cricoid occurs during the cranial progression of the tracheoesophageal septum. The tracheal cartilages are believed to be formed from the lateral splanchnic mesoderm.[5,8]

The intrinsic and extrinsic muscles of the larynx are also formed from the mesodermal elements of the fourth through sixth arches, and both motor and sensory innervation are provided by vagus nerve.[5] The motor control for these muscles originates in the nucleus ambiguous of the medulla and travels with the vagus nerves until leaving via either the superior or recurrent laryngeal nerves. These two nerves are apparent approximately by the end of the 5th week.[4]

The hypobranchial eminence appears in the 3rd week and is a product of the mesoderm of the second, third, and fourth pharyngeal arches. The caudal portion of this develops into the epiglottis, which becomes evident by the 6th week. The arytenoid swellings begin to appear in approximately the 5th week of gestation and have their origin in the fourth to sixth branchial arches. The arytenoid swellings grow and differentiate into the arytenoid and cuneiform cartilages. The growth of the aryepiglottic folds toward the epiglottis completes the supraglottic development. These three growing tissues (hypobranchial eminence, paired arytenoid swellings) initially compress the sagittal laryngeal lumen into a T-shaped opening.[3] As the supraglottis develops further, the laryngeal aditus is temporarily obliterated by the fusion of the epithelial lamina by the 8th week.[6] Recanalization will occur toward the end of laryngeal development, restoring connection of the respiratory tract with the primitive pharynx during the 10th week. The embryology of the vocal cords will be discussed elsewhere in this text.

## Abnormalities in Development of the Larynx and Trachea

The most common congenital abnormality of the larynx is laryngomalacia, but the exact pathophysiology involved with this condition is still unclear.[9] Embryologically, there appears to be no difference in the development of the supraglottic structures in infants with and without laryngomalacia. Histologic studies have shown normal cartilaginous structure in infants with laryngomalacia. Immature neuromuscular control resulting in poor tone of the supraglottic structures is most likely responsible for this clinical condition.

As discussed previously, the tracheoesophageal septum arises from cellular proliferation that occurs in a caudal-to-cranial direction. Interruption of this proliferation can result in a laryngeal or laryngotracheal cleft or a tracheoesophageal fistula. The intimate codevelopment of the trachea and esophagus can be seen in the fact that >90% of tracheoesophageal fistulas are associated with esophageal atresia. These abnormalities have been identified as early as the 5th or 6th week of gestation.[4]

Laryngeal webs of varying severity occur because of a failure of the recanalization of the airway. The most common location is the anterior glottis between the vocal folds, and these webs can be thin or thick. Less common areas for laryngeal webs are the posterior glottis, subglottis, and supraglottis. About one third of children with laryngeal webs have other anomalies of the respiratory tract, such as subglottic stenosis.

## LARYNGEAL WEB AND ATRESIA

Complete failure of recanalization results in laryngeal atresia (📻 50.4).[4] This is often fatal unless immediately recognized after birth or if there is an anomalous connection between the respiratory and digestive tracts (e.g. tracheoesophageal fistula) that is allowing the passage of air into the lungs.[7]

Congenital subglottis stenosis is the third most common congenital anomaly of the larynx, behind laryngomalacia and vocal cord paralysis.[7] This condition results from incomplete canalization of the cricoid cartilage

during laryngeal development. During development, the cricoid cartilage begins as a slit with thick lateral walls. As the lateral cricoid condenses, the subglottic airway becomes more patent. Interruption of this process will result in the typical elliptical appearance of congenital subglottic stenosis.[3]

Tracheal atresia and agenesis are extremely rare conditions that are almost uniformly fatal. They likely result from a failure of canalization of the developing airway. Complete tracheal rings are thought to arise from disproportionate growth of one or more tracheal cartilages (📹 50.5). More than half of patients with congenital tracheal stenosis have another congenital malformation in any of a number of organ systems, including cardiac, genitourinary, and gastrointestinal.

Primary tracheomalacia is extremely rare and is thought to be the result of a congenital immaturity or weakness of the tracheal cartilages. Secondary tracheomalacia is a product of abnormal development of the great vessels and the resulting compression on the trachea. Examples include aberrant innominate artery, double aortic arch (📹 50.6), and pulmonary artery sling. The details of these conditions are discussed elsewhere in the text.

## VIDEO LEGENDS

**Video 50.1:** Second branchial cleft fistula turned inside out coming from the tonsillar fossa.

**Video 50.2:** Fourth branchial cleft sinus with purulence coming from the pyriform sinus opening.

**Video 50.3:** Complication from attempted Sistrunk procedure with removal of thyroid cartilage and not hyoid bone.

**Video 50.4:** Laryngeal atresia.

**Video 50.5:** Complete tracheal rings.

**Video 50.6:** Tracheomalacia secondary to a double aortic arch.

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CHAPTER

# 51

# Adenotonsillar Disorders: Hypertrophy and Infection

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## INTRODUCTION

Tonsillectomy, with or without adenoidectomy, is one of the most common surgical procedures performed on children in the United States. The incidence of tonsillectomy has dramatically decreased since its peak in the 1950s due to more strict surgical indications and the advent of large evidence-based studies looking at the efficacy of tonsillectomy.[1] At its peak in 1959, 1.4 million tonsillectomies were performed in the United States, decreasing to 500,000 in 1979. A low point was reached in 1985 when 340,000 tonsillectomies were performed.[2,3] The current incidence of tonsillectomy in children <15 years of age in the United States has been estimated at 530,000 annually.[4]

The primary preoperative indications for surgery have changed in recent years. In the past, chronic infection of the tonsils or recurrent streptococcal pharyngitis had been a primary surgical indication for adenotonsillectomy. However, in recent decades, airway obstruction, sleep apnea, and sleep-disordered breathing (SDB) have become the most common preoperative indications for surgery in young children.[3]

The effects of SDB on school performance and behavior of children have become more apparent in recent years. Specifically, children with SDB or overt obstructive sleep apnea (OSA) may show significant improvement after tonsillectomy and adenoidectomy.[32]

Finally, the basic technique of tonsillectomy and adenoidectomy has evolved significantly over the centuries with the recent development of new technologies and operative techniques. Their application to tonsil and adenoid surgery will be discussed, as well as updated concepts in the perioperative management of pediatric tonsillectomy patients.

### Anatomy/Embryology

Waldeyer's ring begins to take form in the respiratory tract during the fifth month of gestation. The ring is composed of the lingual tonsils, adenoids, and palatine tonsils. These structures are a combination of epithelial, lymphoid, and mesenchymal cells.[5] Epithelial crypts grow down into epithelial connective tissue, which are then infiltrated by lymphoid cells in the fourth month of gestation.[5] By the seventh month of gestation, the adenoid pad is first seen. The palatine tonsils are derived from the second pharyngeal pouch and are seen in the seventh month of gestation.

### Adenoids

The adenoids form the central part of the ring of lymphoid tissue. The adenoid is composed of lymphoid tissue, with its apex pointed toward the nasal septum and its base toward the roof and posterior wall of the nasopharynx. The adenoid is covered by a pseudostratified ciliated columnar epithelium that is plicated to form numerous surface folds. The adenoid develops as a midline structure by the fusion of two lateral primordial growths that become visible during early fetal life and continue to grow until the fifth year of life, often causing some degree of nasal airway obstruction.[6]

The blood supply and drainage are from the ascending pharyngeal artery, the ascending palatine artery, the pharyngeal branch of the maxillary artery, and the artery

of the pterygoid canal. Venous drainage is to the pharyngeal plexus, which communicates with the pterygoid plexus and then drains into the internal jugular and facial veins. The nerve supply is from the pharyngeal plexus. The efferent lymphatic drainage of the adenoids is to the retropharyngeal and pharyngomaxillary space lymph nodes.[6]

## Tonsils

The palatine tonsil represents the largest accumulation of lymphoid tissue in Waldeyer's ring and, in contrast to the lingual and pharyngeal tonsils, it constitutes a compact body with a definite thin capsule on its deep surface. Tonsillar crypt formation occurs when the endodermal epithelial cells form a wedge of epithelial cells in the surrounding mesoderm.[7]

The tonsillar fossa is composed of three muscles: the palatoglossus muscle, which forms the anterior pillar; the palatopharyngeal muscle, which is the posterior pillar; and the superior constrictor muscle of the pharynx, which forms the larger part of the tonsillar bed. The glossopharyngeal nerve lies just deep and lateral to the tonsillar fossa. This nerve can be easily injured if the tonsillar bed is violated. Transient post-tonsillectomy loss of taste over the posterior third of the tongue and referred otalgia can result from injury to this nerve.[8]

The arterial blood supply of the tonsil enters at the upper and lower polls. There are typically three arteries at the lower pole: the tonsillar branch of the dorsal lingual artery, the ascending palatine artery, and the tonsillar branch of the facial artery. At the upper pole of the tonsil, the ascending pharyngeal artery enters posteriorly, and the lesser palatine artery enters on the anterior surface. Venous blood drains through a peritonsillar plexus surrounding the tonsillar capsule. The plexus drains into the lingual and pharyngeal veins, which, in turn, drain into the internal jugular vein.[8]

The nerve supply of the tonsillar region is through the tonsillar branches of the glossopharyngeal nerve. The transient postoperative otalgia that patients my experience is likely due to the tympanic branch of the glossopharyngeal nerve. Lymphatic drainage courses through the jugulodigastric or tonsillar nodes located behind the angle of the mandible.

# IMMUNOLOGY OF THE ADENOIDS AND TONSILS

B lymphocytes comprise 50% to 65% of all adenoid and tonsillar lymphocytes. Conversely, 70% of the lymphocytes in peripheral blood are T cells. The immunoreactive lymphoid cells of the adenoids and tonsils are found in four distinct areas: the reticular cell epithelium, the extrafollicular area, the mantle zone of the lymphoid follicle, and the germinal center of the lymphoid follicle.

Adenoids and tonsils are responsible for inducing secretory immunity by regulating secretory immunoglobulin production. Both the adenoids and tonsils are favorably located to mediate immunologic protection of the upper aerodigestive tract as they are exposed to airborne antigens. There are 10 to 30 crypts in the tonsils, and they, lined with stratified squamous epithelium, are able to trap foreign material and transport it to the lymphoid follicles.

The tonsil produces antibodies as well as B cells that migrate to other sites around the pharynx and periglandular lymphoid tissues to produce antibodies. Immunoglobulins (Igs) produced by the adenoid include IgG, IgA, IgM, and IgD.[9]

Involution of the tonsils begins after puberty, resulting in a decrease of the B-cell population. Tonsil-specific disease, such as recurrent tonsillitis, result in chronic inflammation of the reticular crypt epithelium and subsequent replacement by stratified squamous epithelium. These changes lead to reduced activation of the local B-cell system and decreased antibody production. Adenoid hyperplasia and chronic adenoiditis do not result in similar histologic and immunologic changes.[10]

Adenoids and tonsils are active immunologic organs that generally reinforce the mucosal immunity of the entire upper aerodigestive tract. The immunologic role of these organs should be considered before a patient undergoes adenoidectomy or tonsillectomy; however, it is clear that no major immunologic deficiencies result from these procedures.

# BACTERIOLOGY

Healthy children up to 5 years of age can harbor known aerobic pathogens. Ingvarsson et al. revealed that *Streptococcus pneumoniae* was recovered in 19% of healthy children, *Haemophilus influenzae* in 13%, group A *Streptococcus* in 5%, and *Moraxella* (*Branhamella*) *catarrhalis* in 36%.[11]

Many organisms can induce inflammation of Waldeyer's ring. These include aerobic, as well as anaerobic bacteria, viruses, yeasts, and parasites. Some of the infectious organisms are part of the normal oral pharyngeal flora, whereas others are external pathogens. Because the oropharynx is colonized by many organisms, most infections of Waldeyer's ring are polymicrobial. These

organisms work synergistically and can be demonstrated in mixed aerobic and anaerobic infections.[10]

Another feature of mixed infections is the ability of organisms resistant to an antimicrobial agent to protect an organism susceptible to that agent by the production of an antibiotic-degrading enzyme that is secreted into the tissues. Because of the polymicrobial nature of most infections around Waldeyer's ring, it is often difficult to interpret data derived from clinical samples obtained from mucosal surfaces and to differentiate between organisms that are colonized and those that are invaders.

## VIRUSES

Rhinovirus, influenza virus, parainfluenza virus, adenovirus, coxsackievirus, echovirus, reovirus, and respiratory syncytial virus are the most common viral pathogens in pharyngitis. Viral pharyngitis is usually mild in presentation with patients complaining of a sore throat and dysphagia. Most patients will have a fever with erythema of the pharyngeal mucosa. The tonsils may be enlarged, but frequently there is no associated exudate.

Management of viral infections is nonspecific and symptomatic. Antibiotics are helpful in cases of secondary bacterial infection.

### Epstein–Barr Virus

Epstein–Barr virus (EBV) induces the mononucleosis syndrome. The most common method of transmission is oral contact. Symptoms usually consist of high fever; general malaise; large, swollen gray tonsils; dysphagia; and odynophagia. Petechiae located at the junction of the hard and soft palate are also seen commonly in EBV. Often, these patients have hepatosplenomegaly as well.

Diagnosis of EBV is confirmed by laboratory studies. Serologic studies include monospot and serum heterophile antibody titers. Only 60% of patients with infectious mononucleosis have a positive test within the first 2 weeks after onset of the illness; however, 90% will have a positive test 1 month after onset. More recently EBV-specific serological assays have become the method of choice for confirmation of acute or convalescent EBV infection.[12] Management of this condition is largely symptomatic. Recovery may take weeks to months, and antibiotics are used only to treat secondary bacterial infections. Rarely, oropharyngeal obstruction from severely enlarged tonsils can be life threatening and should be managed promptly with the insertion of a nasopharyngeal airway and short-term high-dose steroid therapy. If the obstruction is severe and unrelieved by these measures, a tonsillectomy may need to be performed.

### Candida

Candidiasis can result in severe pharyngitis. The classic presentation is white plaques on erythematous oral pharyngeal mucosa. Removal of these plaques may reveal a raw, bleeding surface. Management is with topical nystatin or fluconazole.

### Vincent's (Ludwig's) Angina

Vincent's angina is secondary to bacterial infection with *Spirochaeta denticulate*. Patients present with complaints of high fever, headache, sore throat, and physical findings of cervical lymphadenopathy and a membrane on the tonsil that, when removed, reveals an ulcer that remains confined to the surrounding tissue and usually heals in 7 to 10 days. Management is with penicillin. Local treatment in the form of oral hygiene is helpful. This condition may be confused with trench mouth, which is caused by the same organisms, but the oral cavity ulcers in trench mouth include the gums and oral mucous membranes.[13]

### Streptococcal Tonsillitis/Pharyngitis

Group A streptococcus is the most common bacterial cause of acute pharyngitis. While acute tonsillitis is a nuisance, adequate treatment is very important as a result of the link of streptococcus to acute rheumatic fever and poststreptococcal glomerulonephritis. Although the incidence of rheumatic fever has decreased, all groups of β-hemolytic streptococcus have been associated with rheumatic fever.[14]

Acute streptococcal tonsillitis is a disease of childhood, with a peak incidence at about 5 to 6 years of age. Acute tonsillitis is manifested by fever, odynophagia, dysphagia, and otalgia. Examination will reveal erythematous enlarged tonsils, a tonsillar membrane or purulent exudates, and possible jugulodigastric lymph node enlargement.

The diagnosis of acute tonsillitis is usually made on the basis of clinic presentation. As a result of the related illnesses, group A β-hemolytic streptococcal (GABHS) pharyngitis should be verified or ruled out by microbiologic tests in patients who appear to have this illness. A throat swab and/or throat culture is the gold standard for diagnosis.[15]

One of the major problems in the use of throat cultures in everyday medical practice has been the delay in obtaining results. These can range from 18 to 48 hours, delaying appropriate management; however, a delay of this length will not increase the development of rheumatic fever. Nevertheless, it can be difficult for physicians to convince parents of the wisdom of withholding antibiotics, especially if their children are ill. If group A streptococcal pharyngitis is treated early in the clinical course, the period of communicability is reduced. Management is thus initiated before culture results are available and unfortunately may not be terminated even when negative results are obtained. Development of rapid tests for the detection of the group A streptococcal antigen has therefore presented a useful advance.[16]

Even if optimally obtained and processed, throat cultures are not without flaws. Throat culture cannot reliably differentiate acute from chronic infection. The management of all patients who have positive cultures results in over management. There are occasional false-negative results (approximately 10% of cases), but a recent report has stated that these patients are most likely carriers who do not require treatment. Studies have reported that a single throat culture is 90% to 97% sensitive and 90% specific for GABHS growth.[17]

Penicillin is still the management of choice in most cases. Clinical failure of penicillin should lead to the suspicion of β-lactamase-producing organisms. This could be a result of these organisms acting as pathogens themselves, so-called "direct pathogens", or by these organisms protecting susceptible pathogens from the effects of β-lactamase antibiotics, so called "indirect pathogens". In these cases, an alternative to the use of penicillin is to use a penicillin plus a β-lactamase inhibitor such as clavulanic acid (i.e. Augmentin).[18] Antibiotic therapy within 24 to 48 hours of symptom onset will result in decreased symptoms associated with sore throat, fever, and adenopathy 12 to 24 hours sooner than without antibiotic administration. Ten full days of therapy are necessary, as studies have shown that children receiving 10 days of therapy have lower clinical and bacteriologic recurrence rates than children receiving only 7 days of therapy.[19]

### PFAPA Syndrome

Periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome was first described by Marshall et al. in 1987. They described a fever syndrome according to its most characteristic symptoms: periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis.[20] Children usually present between the ages of 5 and 8 years old. Fevers are usually >102° F and usually last between 3 to 7 days. These fevers also recur every 3 to 6 weeks. The fever cycle is usually associated with one of the other symptoms of aphthous stomatitis, pharyngitis, and cervical adenopathy, with pharyngitis the most common related symptom. Rarely, all three symptoms may be present with each fever.

In the majority of cases, an otolaryngologic physical examination and lab work-up does not reveal any significant pathology. Occasionally, the tonsils are erythematous, prompting throat cultures, which are almost always negative for group A β-hemolytic streptococcus. Rarely, blood work will show an elevated white blood cell count or erythrocyte sedimentation rate. The diagnosis of PFAPA syndrome should be considered a diagnosis of exclusion.[21]

Treatment of PFAPA syndrome includes both medical and surgical options, with surgical intervention gaining momentum as the treatment of choice among pediatric professionals. Oral antibiotics have shown to have no effect on symptomatology. Antipyretic agents may help reduce high temperatures; however, they are often not able to induce a consistent afebrile child. Oral corticosteroids have a dramatic effect on reducing the fever cycle. Oral prednisone or prednisolone (1 to 2 mg/kg) within a few hours of the beginning of the fever cycle has been shown to significantly reduce or halt the fever cycle within several hours. The current gold standard for treatment of PFAPA syndrome is tonsillectomy. A recent study showed resolution of PFAPA in 97% of children.[22] Several other studies have supported the treatment of adenotonsillectomy, showing an immediate cessation of fever cycles and significant differences in symptomatology of PFAPA when compared with control patients.

## COMPLICATIONS OF TONSILLITIS

### Nonsuppurative

Scarlet fever is a result of the production of endotoxins by streptococcal bacteria. This condition presents with an erythematous rash, lymphadenopathy, fever, and erythematous tonsils and pharynx. The membrane that is present over the tonsils is usually more friable than that seen with diphtheria. Management of this condition is with intravenous administration of penicillin G.

Poststreptococcal glomerulonephritis may be seen after both pharyngeal and skin infections. The typical

patient develops nephritis 7 to 10 days after a streptococcal infection. Penicillin is the treatment of choice; however, there is no evidence that antibiotic therapy improves the clinical condition. A tonsillectomy may be necessary to eliminate the source of infection.

## Suppurative Infections

Peritonsillar abscess (PTA) most commonly occurs in patients with recurrent tonsillitis or in those with chronic tonsillitis who have been inadequately treated. The spread of infection is from the superior pole of the tonsil with pus formation between the tonsil bed and the tonsillar capsule. This infection usually occurs unilaterally and the pain is quite severe, with referred otalgia to the ipsilateral ear a few days after the onset of tonsillitis.[23] Drooling is caused by odynophagia and dysphagia. Trismus is frequently present as a result of irritation of the pterygoid musculature by the pus and inflammation. There is gross unilateral swelling of the palate and anterior pillar with displacement of the tonsil downward and medially with reflection of the uvula toward the opposite side.

Treatment options include needle aspiration in cooperative patients. Most children will require general anesthesia for drainage of the abscess in the operating room. If there has been a previous history of tonsillitis, a quinsy tonsillectomy may be performed.[24]

Imaging for PTA is based on a case by case or institutional protocol. Children presenting with classic clinical presentations of PTAs do not require a computed tomographic (CT) scan.[23] However, some cases of smaller PTA or cases in which there is concern for spread across fascial planes should have imaging with contrast.

### *Parapharyngeal Space Abscess*

An abscess in the parapharyngeal space can develop if infection or pus drains from either the tonsils or from a PTA through the superior constrictor muscle. The abscess is located between the superior constrictor muscle and the deep cervical fascia and causes displacement of the tonsil on the lateral pharyngeal wall toward the midline. Involvement of the adjacent pterygoid and paraspinal muscle with the inflammatory process results in trismus and a stiff neck.

Patients with parapharyngeal space infections must be treated quickly as the abscess can spread down "Lincoln Tunnel" into the mediastinum. Clinically, this may be confused with a PTA, and, if indicated, a CT scan with contrast should be obtained.[25]

Initial management of lateral pharyngeal space infections should be with aggressive oral or intravenous antibiotic therapy. Surgical intervention will often be required for those patients that fail medical management. An intraoral approach is possible but does carry with it the problem of inadequate exposure if severe bleeding should arise. An external approach to the parapharyngeal space is achieved by dissection between the submandibular gland and the anterior aspect of the sternocleidomastoid muscle. Using this approach, exposure is ideal, the abscess can be drained, and the area can be irrigated.[25]

### *Retropharyngeal Space Infections*

Retropharyngeal space infections occur most commonly in children <2 years of age. Children often present with irritability, fever, dysphagia, and muffled speech. Physical examination usually reveals unilateral posterior pharyngeal swelling.

A transoral approach is recommended for incision and drainage of retropharyngeal space abscesses. A small vertical incision is made in the lateral aspect of the posterior pharyngeal wall at a point between the midline of the pharynx and the medial aspect of the retromolar trigone.

# CHRONIC ADENOTONSILLAR HYPERTROPHY

## Etiology

Chronic adenotonsillar hypertrophy in children is the most common indication for adenotonsillectomy in the United States. Typically, the tonsils and adenoids are very small at birth and progressively enlarge over the first to fourth years of life as a result of increased immunologic activity. In addition to chronic bacterial infection, secondhand smoke exposure also has been implicated as a cause of adenotonsillar hypertrophy in children.

## Airway Obstruction

Pediatric OSA, confirmed by polysomnography, is reported to have an incidence of 1–3%. The obstructive apnea is almost always associated with hypertrophy of the tonsils and adenoids. This obstruction is worse when the patient is supine and asleep due to the effects of gravity and the relaxation of surrounding nasopharyngeal and oropharyngeal soft tissue. The obstruction can result in a mildly

compromised airway, which results in snoring as well as apnea and desaturation. The apnea typically is short and usually associated with a brief arousal wherein the patient will reposition and open the airway.

Before the syndrome of OSA was widely recognized, children sometimes presented with pulmonary hypertension and cor pulmonale, failure to thrive, and developmental delay. While these comorbidities are still diagnosed, they are less common than daytime sleepiness and behavioral difficulties. Behavioral difficulties may include hyperactivity [attention deficit hyperactivity disorder (ADHD)], inattentiveness in the classroom, problems with academic performance, and difficult behavior.[26]

The American Academy of Pediatrics in their most recent clinical practice guidelines recommends that all children should be screened for snoring, and that those children found to have a significant snoring history should undergo an overnight polysomnogram to differentiate primary snoring from OSA syndrome (OSAS).[27] More than one apneic event per hour is considered abnormal. However, apnea is rarer in children than in adults and often the diagnosis is made on the basis of other disturbances, but there is considerable debate about how to measure these other disturbances.

Guilleminault et al. introduced the idea of the upper airway resistance syndrome in 1982. This syndrome included children who had clinical symptoms consistent with OSAS but did not have polysomnographic evidence of sleep apnea or hypopnea. This group is among many researchers that now feel the term "benign snoring" should be used with suspicion. A large proportion of these children may have undiagnosed clinically significant sleep disorders. Because of this lack of clarity in the literature about what exactly defines clinically significant sleep apnea, a broader term has been used—SDB.[26] SDB thus represents a continuum and includes all children with snoring who are felt to have clinically significant symptoms related to a sleep disorder—from those with frank apnea to those diagnosed with upper airway resistance syndrome.

## Attention Deficit Hyperactivity Disorder (ADHD)

Numerous articles in the literature have shown a significant relationship between SDB and the symptoms of ADHD. One study looked at the relationship between the symptoms of SDB and problem behavior including hyperactivity and inattention. The study enrolled 3019 5-year-old children. They used a limited questionnaire to evaluate for symptoms of SDB as well as problems with behavior. Symptoms of SDB were present in 25% of the children. They found a strong association between parent reported sleep problems and the parent reported incidence of inattention, hyperactivity, and aggressiveness.[28,29]

The pathophysiology of ADHD is unknown; however, there are suggestions that an abnormal sleep pattern may be one major factor. Stimulants have been shown to improve behavior in patients with ADHD. Stimulants are felt to work because ADHD is a disorder caused by hypovigilance rather than hypervigilance. As a result, if the sleep obstruction was removed it should follow that the quality of sleep would improve and therefore symptoms of ADHD would diminish.[30]

There has been some recent literature to suggest that adenotonsillectomy in children with SBD or formal OSAS will improve the behaviors associated with ADHD when compared with control groups.[31]

## Neurocognitive Development

Sleep, particularly in children, can be a very active process and may play a key role in proper brain maturation. There have been multiple reports indicating that children with a childhood history of snoring and SDB may suffer in their neurocognitive development. Children with OSAS, SDB, or even "simple snoring" could be at a disadvantage in comparison with their classmates with regards to attention span, memory, and standardized test scores.[32] The exact mechanism is not clear at this time; however, the central nervous system continues to develop from birth until late adolescence. Episodic hypoxia, hypercapnia, and sleep fragmentation could place this development more susceptible to injury.

## Enuresis

Enuresis is another indicator of severe underlying airway obstruction in children. Weider et al. described enuresis related to chronic adenotonsillar hypertrophy and significant airway obstruction that was relieved by adenotonsillectomy. In their study, all patients with secondary enuresis (developed later during childhood) responded to adenotonsillectomy, whereas 24 patients with primary enuresis (congenitally present) did not respond to surgery, possibly as a result of other neurologic factors.[33] A proposed cause of enuresis is poor nocturnal regulation of antidiuretic hormone release that is related to disorders of rapid eye movement (REM) sleep.

## Growth Problems

Children with chronic adenotonsillar hypertrophy and airway obstruction may also present with failure to thrive related to abnormal regulation of growth hormone. Decreased REM sleep may also result in decreased growth hormone production in children. Children with OSAS and with growth hormone deficiency have seen normalization of these levels after adenotonsillectomy.[34]

## Cardiopulmonary Complication

Cor pulmonale, or right heart failure, is related to chronic upper-airway obstruction. This results in chronic hypercapnia and hypoxia and eventual right ventricular dilation. Adenotonsillectomy and relief of the upper airway obstruction will eventually reverse this condition.[35]

## Craniofacial Growth

Adenotonsillar hypertrophy and upper-airway obstruction has been shown to affect craniofacial growth patterns in children. Chronic mouth breathing as a result of adenoid hypertrophy has been shown produce malocclusion and maxillofacial growth abnormalities. Adenoid hypertrophy also results in so called "adenoid facies" in children. This consists of longer facial height as well as a retrognathic mandible.[36]

Adenotonsillectomy has been shown to reverse some of these findings. As a result of this relationship among upper-airway obstruction, adenotonsillar hypertrophy, and craniofacial growth disturbance, children undergoing ortho-dontic procedures for malocclusion who show evidence of adenotonsillar hypertrophy and mouth brea thing should have an otolaryngologic evaluation prior to surgery.[37,38]

# HISTORY OF TONSILLECTOMY AND ADENOIDECTOMY

Roman physician Aulus Cornelius Celsus in 50 AD first described a technique of enucleation tonsillectomy using a combination of finger dissection and extraction with a hook and bistoury utilizing a vinegar wash to control bleeding.[39,40] In the later Middle Ages, a technique of removing the tonsils by tying a ligature at its base and allowing it to necrose became an accepted technique, although it was associated with significant discomfort.[39,41] In the 18th century, Benjamin Bell developed a uvulatome, a device designed to quickly amputate a diseased uvula, which later inspired Physic (1768–1837) to modify the instrument to allow a quick and safe alternative technique for tonsillectomy that was more tolerable than the suture ligature technique that was popular at the time. Fahnestock[40] later modified the Physic tonsillotome to accommodate a prong or fork, to literally spear the tonsil to promote clean amputation of the tissue (Fig. 51.1). Until the late 19th century, these surgical procedures were all done without the advantages of general anesthesia.

The anatomy of the faucial tonsils had been studied for centuries; however, Rudolph Albert von Kölliker (1817–1905) of Austria was the first to demonstrate the significance of the microanatomy and lymphatic network of the tonsils. The fine intracellular structure of the tonsils was further elucidated by William Hiss in the later 19th century,[40] and the arrangement of lymphoid tissue around the pharyngeal region was described by Heinrich Wilhelm Gottfried von Waldeyer-Hartz (1836–1921), today known as Waldeyer's ring.

With the introduction of general anesthesia in the late 19th century, surgical procedures became much more tolerable, with increased safety and lower rates of complications. With the utilization of general anesthesia, more delicate and careful surgical dissection of the tonsil was now possible and speed was not of the utmost necessity for a good surgical outcome. In 1912, Samuel J. Crowe became chairman of the Department of Laryngology and Otology at Johns-Hopkins University, appointed by the famous general surgeon, William Halsted. Crowe published a significant study evaluating 1000 consecutive tonsillectomies performed between 1911 and 1917 in his

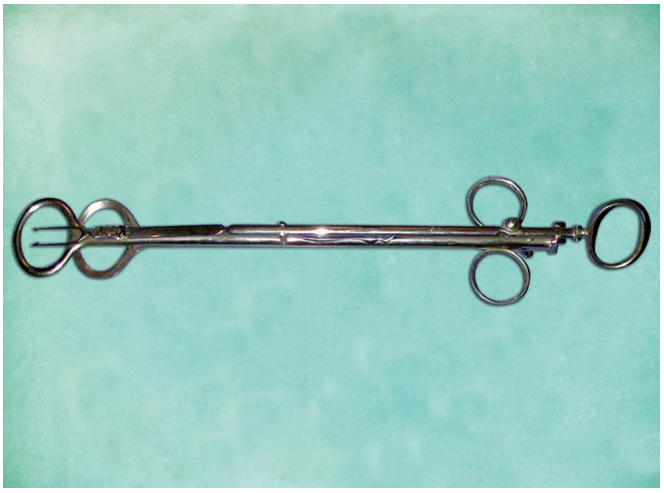


**Fig. 51.1:** Fahnestock tonsillotome.

paper entitled "Relation of Tonsillar and Nasopharyngeal Infection to General Systemic Disorders". He provided a detailed description of his meticulous, sharp dissection technique, utilizing the Crowe–Davis mouth gag for surgical exposure. He described a very low complication rate, which compares favorably with modern tonsillectomy studies (Figs. 51.3A and B).[42]

Advances in adenoidectomy developed much later, with the first described procedure performed by a Danish physician, Wilhelm Meyer in his 1868 publication "Adenoid Vegetations in the Nasopharyngeal Cavity".[43] Meyer described his technique of posterior rhinoscopy to diagnose adenoid hypertrophy and recommended a technique of adenoidectomy utilizing a ring knife.[43] Jacob Gottstein, in 1885, described the first modern adenoid curette.[43]

The introduction of modern technology into surgical techniques has developed rapidly over the last century. With the introduction of electrocautery as an aid to the surgical removal of tissue in 1928 by neurosurgeon Cushing and Bovie, it was just a short time before this new technology was applied to tonsillectomy, leading to quicker operations with minimal intraoperative bleeding.[44] The $CO_2$ laser was developed in 1960 and applied to otolaryngology in 1970 as an adjunctive procedure with microlaryngoscopy. Later, the $CO_2$ laser was applied to tonsillectomy, and subsequently other lasers were developed, which have also demonstrated efficacy in tonsillectomy, including the KTP (potassium-titanyl-phosphate) and Holmium lasers.[45,46] Other technologies, which will be discussed later in this chapter that have been developed in recent years and applied to tonsillectomy include radio frequency ablation (coblation tonsillectomy), harmonic scalpel, and microdebrider intracapsular tonsillectomy.

## SURGICAL INDICATIONS FOR TONSILLECTOMY AND ADENOIDECTOMY

Indications for tonsillectomy and adenoidectomy performed together are different than conditions where adenoidectomy alone is under consideration. Therefore, the indications for these two procedures will be discussed separately. The disease processes and indications for surgery vary based on the patient's age group. Very young children predominately have problems with airway obstruction and sleep apnea related to adenotonsillar hypertrophy, although chronic infection may play a significant role. Older patients (in addition to airway obstruction) have a higher incidence of infectious processes, including chronic tonsillitis, chronic recurrent streptococcal pharyngitis and PTA. In cases of PTA, (quinsy) tonsillectomy may be considered in lieu of incision and drainage or needle aspiration, especially in young children who may not tolerate an office-based procedure under local anesthesia (Table 51.1).

It should be noted that in the majority of cases when tonsillectomy is performed, adenoidectomy is performed simultaneously. The majority of surgical indications are categorized under problems related to infection or obstruction; however, suspected neoplasia, although very rare, may be considered in selected cases. When neoplasia is suspected, the tonsils should be sent to pathology for detailed histologic analysis. Routine indications for surgery do not warrant histologic evaluation.[47]

**Table 51.1:** Surgical indications for tonsillectomy

| |
|---|
| *Infection* |
| Recurrent, acute tonsillitis, or pharyngitis (GABHS)<br>7 or more episodes/year<br>5 or more episodes/year for 2 years<br>3 or more episodes/year for 3 years |
| Cardiac valvular disease associated with recurrent streptococcal tonsillitis |
| Recurrent febrile seizures |
| Chronic tonsillitis that is unresponsive to medical therapy associate with:<br>Halitosis<br>Persistent sore throat<br>Tender cervical lymphadenitis<br>Recurrent, symptomatic tonsilloliths |
| Streptococcal carrier state unresponsive to medical therapy |
| Peritonsillar abscess |
| Tonsillitis associated with abscessed cervical nodes |
| Mononucleosis with severely obstructing tonsils that is unresponsive to medical therapy |
| *Obstruction* |
| Pathologic snoring and chronic mouth breathing |
| Obstructive sleep apnea or sleep disordered breathing |
| Adenotonsillar hypertrophy associated with:<br>Enuresis<br>Growth retardation or failure to thrive<br>Poor school performance<br>Behavioral problems<br>Cor pulmonale<br>Dysphagia<br>Speech abnormalities<br>Craniofacial growth abnormalities<br>Dental occlusion abnormalities |

Although younger children may present with chronic infections relating to the tonsils and adenoids, airway obstruction tends to be more common due to a smaller airway when compared with older children. Typically, children with obstruction related to tonsils and adenoids will present with a history of excessively loud snoring at night. They may also have a history of chronic mouth breathing and possibly may have developed craniofacial and dental manifestations of airway obstruction commonly known as the "adenoid facies".[48,49] A detailed history may help elicit the severity of the child's snoring. Observation of an audio or video tape demonstrating the child's breathing pattern at night may be helpful in determining the severity of airway obstruction. Snoring that is intermittent that may be exacerbated with upper respiratory tract infections and that does not cause significant disturbance of sleep may be managed by observation. Severe or pathologic snoring is more worrisome. The parents will often relate a history of pauses in the breathing pattern, gasping for breath intermittently at night, a very restless sleep pattern with frequent wakening during the night, failure to thrive, enuresis, daytime somnolence, inability to focus during the daytime and attention issues at school affecting school performance. In some cases, descriptive terms such as "snores like an adult", or "snores like a freight train" are used by the family to describe pathologic snoring. When this type of breathing pattern has been present for long duration (at least 6 months), in the presence of enlarged tonsils and adenoids, surgical intervention may be beneficial. In very young children with excessive adenotonsillar hypertrophy, in addition to airway obstruction, dysphagia and poor oral intake may result in food aversion, leading to failure to thrive. Several studies have shown that adenotonsillectomy in appropriately selected patients may improve SDB and problems associated with SDB, i.e. behavioral and neural cognition problems, enuresis, and failure to thrive.[50-52]

In cases where the degree of nocturnal airway obstruction is not apparent by history, a sleep study may be warranted. Conversely, in cases with a history of excessive pathologic snoring without corresponding physical findings consistent with significant adenotonsillar hypertrophy, a sleep study would be warranted to determine if OSA is occurring at night.

In cases of snoring, it is important to perform a nasal examination to evaluate other causes of nasal obstruction including turbinate hypertrophy, which in severe cases may cause and pathologic snoring and obstruction sleep apnea without adenotonsillar hypertrophy. In cases of inferior turbinate hypertrophy, medical therapy and possibly surgical intervention may be beneficial.

In 1996, the current standards and indications for pediatric polysomnography were outlined by the American Thoracic Society. When sleep studies are warranted in the assessment of nocturnal airway obstruction in children, it is important to utilize a sleep lab experienced in accommodating children and interpreting pediatric sleep data. Definitive pediatric standards for the results of polysomnograms in children are variable, but in general, apneic events numbering greater than one apnea/hypopnea events per hour are considered significant and may warrant surgical intervention in the presence of adenotonsillar hypertrophy. Other factors evaluated during polysomnography, include oxygen desaturation as measured by pulse oxymetry and end-tidal $CO_2$ levels. SDB may be categorized by episodes of recurrent partial or complete airway obstruction during sleep, resulting in irregular ventilation and disruption of normal sleep patterns.[53,54] Although enlarged tonsils and adenoids are the most common cause of sleep disorders and breathing in children, it is likely that the severity of the SDB may be related to a combination of factors in addition to adenotonsillar enlargement, including factors such as craniofacial anatomy and neuromuscular tone. Therefore, children with relatively small tonsils may still manifest significant airway obstruction in the presence of craniofacial anomalies or hypotonia. It is not unusual in children with neuromuscular disorders, such as those with cerebral palsy, to have significant obstruction at night (SDB or overt OSA) resulting from hypotonia combined with mild to moderate adenotonsillar hypertrophy. Surgical intervention to remove the tonsils and adenoids may improve the airway significantly; however, persistent obstruction at night is possible due to underlying hypotonia.

## CHRONIC INFECTIONS

Patients with chronic recurrent tonsillitis, chronic tonsillitis, or chronic recurrent group A β–hemolytic streptococcal pharyngitis (GABHS) may benefit from tonsillectomy. Some of the symptoms seen may include a sore throat, foul taste in mouth, or halitosis that is often associated with chronic streptococcal infections. Numerous studies have demonstrated the efficacy of elective tonsillectomy in helping children with recurrent sore throats and recurrent GABHS.[55,56] Factors that may be taken into account

in the presurgical evaluation of children with recurrent throat infections include the severity of each episode, responsiveness to medical therapy, and quality of life issues such as missed school days, chronic sore throat, recurrent tonsilloliths, and halitosis. Conditions when tonsillectomy should be considered include patients with cardiac valvular disease, a history of febrile seizures associated with acute infectious episodes, poorly controlled diabetes, and possibly patients with intraventricular shunts who may be at risk for shunt or central nervous system infections with acute episodes of pharyngitis. These underlying conditions may lead to life-threatening situations in the presence of severe pharyngotonsillar infections.

Tonsillectomy may be considered in cases of PTA. In children with a PTA and a prior history of recurrent pharyngitis or tonsillitis, quinsy tonsillectomy is an excellent treatment option. Although incision and drainage or needle aspiration in an outpatient setting in the presence of PTA is an acceptable option, younger children may not tolerate this procedure utilizing local anesthesia. If general anesthesia is required for the drainage of a PTA, quinsy tonsillectomy is the most definitive approach. In cases of recurrent PTAs, quinsy tonsillectomy is recommended.[57-59]

Clinical guidelines for physicians to utilize when evaluating patients for adenotonsillectomy were published by the American Academy of Otolaryngology-Head and Neck Surgery as the "Clinical Indicators Compendium of 1995"[60] and was updated in 2011 as the "Clinical Practice Guideline-Tonsillectomy in Children".[61] The recent guidelines were composed by a multidisciplinary team of physicians including pediatric otolaryngologists, general otolaryngologists, and pediatricians to provide clinicians with evidence-based guidelines as to which children are the best candidates for tonsillectomy. Secondary objectives of these guidelines were to recommend optimal perioperative management of children undergoing tonsillectomy drawing on evidence-based research with the ultimate goal of reducing inappropriate or unnecessary variations in care. A brief summary of the guidelines is as follows:

1. Tonsillectomy may be warranted in children with seven or more episodes of throat infections in a year, or five or more episodes per year in the past 2 years, or three or more episodes a year in the past 3 years
2. Children who may benefit from tonsillectomy, who do not fulfill the above criteria may include, but are not limited to, children with multiple antibiotic allergies or intolerance, PFAPA syndrome or a history of PTA
3. In children with SDB, comorbid conditions that may improve after tonsillectomy include growth retardation, poor school performance, enuresis, and behavioral problems
4. Tonsillectomy may improve health in children with abnormal polysomnography in the presence of adenotonsillar hypertrophy and SDB
5. SDB may persist or recur after tonsillectomy and require further medical or surgical management
6. Advocating for pain management follow tonsillectomy and educating caregivers about the importance of optimal pain management and frequent reassessment of pain
7. Clinicians who perform tonsillectomy should determine their rate of primary and secondary post-tonsillectomy hemorrhage at least annually.

These practice guidelines should be individualized as they are applied to a particular patient or clinical situation before deciding on the potential benefits of surgical intervention.

## INDICATIONS FOR ADENOIDECTOMY (TABLE 51.2)

Adenoid hypertrophy or chronic infection of the adenoids may require adenoidectomy. In situations where the tonsils themselves are small and not involved with the disease process, or in cases where the tonsils have already been removed, adenoid enlargement will lead to nasal obstruction, chronic mouth breathing, excessive snoring, poor olfaction, and possibly OSA.[62] Young children with a history of chronic rhinitis or sinusitis may also benefit from adenoidectomy, since many of the symptoms of chronic sinusitis in young patients may be related to chronic adenoiditis.[63] Adenoidectomy may obviate the need for more extensive sinus surgery in young children with a history of recurrent sinusitis. In children with chronic, purulent rhinitis, adenoidectomy may be beneficial in situations where there has been a poor response to medical therapy. Nistico et al.[64] demonstrated that biofilms were prominent in adenoid tissue removed from patients with a history of chronic sinusitis. Adenoids removed for airway obstruction without a history of sinusitis revealed less significant biofilm coverage of the mucosa. This study suggested that biofilms may lead to the adenoids acting as a reservoir for bacteria, particularly resistant bacteria in cases of multiple antibiotic therapy, and their surgical removal may lead to reduced episodes of rhinitis and sinusitis in this patient population.

**Table 51.2:** Surgical indications for adenoidectomy

| |
|---|
| *Infection* |
| Purulent adenoiditis |
| Chronic sinusitis in young children |
| Adenoid hypertrophy associated with:<br>Chronic otitis media with effusion<br>Chronic recurrent acute otitis media<br>Chronic otitis media with perforation<br>Otorrhea or chronic tube otorrhea |
| *Obstruction* |
| Adenoid hypertrophy associated with excessive snoring and chronic mouth breathing |
| Sleep apnea or sleep disturbances |
| Adenoid hypertrophy associated with:<br>Cor pulmonale<br>Failure to thrive<br>Dysphagia<br>Speech abnormalities<br>Craniofacial growth abnormalities<br>Occlusion abnormalities<br>Speech abnormalities |
| Other |
| Suspected neoplasia |

Large obstructive adenoids may lead to hyponasal speech (rhinolalia clausa) that may improve after adenoidectomy. However, patients with hypernasal speech [velopharyngeal insufficiency (VPI) or rhinolalia aperta] should not be considered for adenoidectomy, since this may worsen the condition. However, in unusual cases, excessive tonsillar hypertrophy may impede palatal movement, which may improve hypernasal speech after tonsillectomy.[65]

In patients with cleft palate, or submucous cleft palate manifesting a bifid uvula, who have adenoid enlargement and nasal obstruction, conservative adenoidectomy may be performed with the upper portion of the adenoid pad is removed to open the posterior choanae of the nose, but the lower aspect of the pad is left intact to allow good velar closure avoiding postoperative VPI.

Patients with significant nasal obstruction and suspected adenoid hypertrophy, who have symptomatology of underlying inhalant allergy, may benefit from antihistamine therapy and intranasal steroids to improve symptomatology. When suspected, allergy evaluation is warranted to determine candidacy for immunologic desensitization or appropriate avoidance measures for the offending antigenic agents. Demain and Goetz[66] demonstrated that aqueous nasal beclomethasone therapy may lead to improvement in nasal obstruction secondary to adenoid hypertrophy. They confirmed their results with pre- and post-therapy flexible nasopharyngoscopy in select patients.

Although the role of adenoidectomy and the treatment of otitis media is not been definitively proven and has been somewhat controversial, several studies have demonstrated the efficacy of adenoidectomy in improving the course of severe otitis media in children.[66-71] Adenoidectomy should be considered in children undergoing primary ventilation ear tubes placement who have symptomalogy and a diagnostic evaluation confirming adenoid hypertrophy by radiography, nasopharyngoscopy or intraoperative nasal endoscopy. Patients who have required multiple sets of ear tubes may also be candidates for adenoidectomy regardless of adenoid size or symptomatology.

## PREOPERATIVE ASSESSMENT

Before adenotonsillectomy is undertaken, it is important to determine if the patient has any underlying medical conditions that may affect their intraoperative or postoperative course and to determine whether ambulatory outpatient surgery is warranted or if overnight admission for observation is necessary. An undiagnosed bleeding diathesis may lead to significant morbidity and possible mortality; therefore, it is crucial to elicit this information from the patient history. Any suggestion of an undiagnosed bleeding disorder in the patient or the possibility of a family history warrants a hematologic evaluation consisting of coagulation studies and a von Willebrand screening profile.[72] In 1999, the American Academy of Otolaryngology—Head and Neck Surgery developed a consensus statement that recommended preoperative coagulation evaluation only when bleeding disorder is suspected.[60] This approach has been confirmed by Manning et al.,[73] Close et al.,[74] and Jones et al.[75], reviewing large series of patients who underwent preoperative coagulation studies. Close et al. demonstrated that excessive bleeding associated with tonsillectomy was not typically the result of an identifiable coagulapathy.[74] It should be noted that other studies do exist demonstrating a higher incidence of abnormalities on preoperative coagulation screening suggesting a possible benefit for preoperative hematologic screening.[76,77] The current general consensus is that routine preoperative coagulation screening is not recommended unless the medical history suggests risk factors for an underlying coagulopathy, i.e. easy bruising, prolonged

bleeding after cuts and abrasions, or a family history suggesting hereditary coagulopathy.[60] Ultimately, the utilization of preoperative coagulation screenings should be left to the discretion of the surgeon.

Patients with a history of severe airway obstruction based on history or confirmed by polysomnography secondary to adenotonsillar hypertrophy may require chest radiography, electrocardiography, and possible cardiology consultation preoperatively. Patients with cor pulmonale and hypercapnea from long-term airway obstruction may require close observation in the postoperative period in an intensive care setting. Mechanical ventilation may be required to avoid postobstructive pulmonary edema. Polysomnography may be warranted when severe airway obstruction is suspected, but it is not clearly elicited by parental history.

Patients with other underlying medical conditions, such as asthma, congenital heart disease, or seizure disorders should be evaluated by their medical specialists preoperatively and cleared for surgery. Postoperative inpatient observation may be warranted in some of these cases. African American patients should be screened for sickle cell disease preoperatively, and female patients of reproductive age should undergo preoperative pregnancy testing. Patients with some forms of velocardiofacial syndrome (22 QL.2 deletion syndrome) may require preoperative angiography or other imaging studies to determine the presence of abnormal medially displaced carotid arteries, which may be at risk and damaged during tonsillectomy.[78]

## INPATIENT VERSUS OUTPATIENT TONSILLECTOMY

In appropriately selected children, it has demonstrated that outpatient tonsillectomy can be performed safely with reported postoperative observation times varying between 136 minutes to 8 hours.[79-83] During the postoperative period, patients need to obtain adequate intravenous hydration and be monitored for adequate ventilation, oxygenation, and oral intake before discharge. Patients with excessive nausea and vomiting, inadequate oral intake, or poor oxygenation may require longer observation periods or conversion to inpatient admission. In the preoperative assessment it is very important to appropriately select patients who are at risk for postoperative complications who will require postoperative inpatient observation (Table 51.3).

**Table 51.3:** Relative indications for admission after tonsillectomy

| |
|---|
| Under 3 years of age |
| Severe obstructive sleep apnea |
| Bleeding diathesis |
| Craniofacial abnormalities |
| Underlying medical conditions:<br>Diabetes mellitus<br>Seizure disorders<br>Cardiovascular disease<br>Poorly controlled asthma |
| Patient lives long distance from the hospital |
| Social situation not conducive to close observation at home |

Children < 3 years of age may be more susceptible to postoperative complication as has been demonstrated in numerous studies,[84-87] including airway obstruction, poor oxygenation, and inadequate oral intake. Patients with excessive body mass index (BMI > 95%) should be considered candidates for inpatient observation after surgery due to risk of airway obstruction and complications of postobstructive pulmonary edema, as well as children with underlying conditions, such as cardiovascular disease, asthma, seizure disorders, and craniofacial disorders. In addition, patients who live excessive distances from the hospital or whose home care situation is not consistent with close postoperative observation may benefit from inpatient observation.

## TONSILLECTOMY AND ADENOIDECTOMY

### Surgical Technique

In 1917, Crowe et al.[88] described a meticulous sharp dissection technique for extirpation of the tonsils, and for decades afterward this became the preferred modality for tonsillectomy. With the advent of electrocautery (diathermy) in the early 20th century, this adjunctive surgical modality allowed quick, precise, and safe control of bleeding for vessels in the tonsillar fossa. Later in the 20th century, the use of electrocautery to actually dissect out the tonsil, in addition to controlling hemostasis became the preferred technique. For those surgeons feeling that electrocautery resulted in higher increased postoperative pain, sharp dissection combined with ligatures to control bleeding vessels remained a surgical option.

In addition to monopolar cautery, bipolar cautery, using electric current, which passes through the tissue between the tips of a cautery forceps, has been described as a technique resulting in minimal blood loss and decreased postoperative pain compared with monopolar cautery.[89]

In recent decades, other new technologies have been introduced as potential modalities for tonsillectomy including: $CO_2$ or KTP laser, bipolar radio frequency ablation (coblation), Harmonic scalpel, Liga Sure technique,[90] and intracapsular tonsillectomy. In addition, the guillotine tonsillectomy technique is still utilized in many places and has demonstrated a low complication rate.[91,92] This technique is frequently used in children without the benefit of general anesthesia in China.[93]

The results of a study group in 2002 looking at new technologies in tonsillectomy have been published looking at issues such as cost-effectiveness, patient safety, and supporting evidence as to the efficacy of these new technologies.[75]

### *Electrocautery Tonsillectomy*

Electrocautery uses electric current to coagulate blood vessels and to cut tissue. In monopolar electrocautery, the electric current passes out from the tip of the instrument and is safely dispersed to a grounding electrode with a large surface area, usually placed on the patient's thigh. In bipolar electrocautery tonsillectomy, the electric current is passed through tissue between the fine tips of a pair of bipolar forceps. Other types of cautery devices such as the Erbe constant voltage electrocautery may be used, but it does not appear to have significant benefits over traditional cautery techniques.[94]

Endotracheal tube fires or other oral or airway fires may occur in the presence of electrocautery when high concentrations of oxygen are leaking around the endotracheal tube. Therefore, it is important to take precautionary measures to prevent air leakage utilizing a moistened hypopharyngeal throat pack and a cuffed endotracheal tube, in addition to using lower oxygen concentrations for ventilation (< 40%).[95] Other electrocautery-related complications include perioral or intraoral burns and nasopharyngeal stenosis, which may occur from excessive cauterization on the nasopharyngeal surface of the palate and with inadvertent trauma to the posterior tonsillar pillars. It is important to be aware of the location of the electrocautery tip at all times so that it does not contact other surfaces in the oral cavity or metallic instruments, such as the mouth gag or a metal suction handle.

The authors believe that electrocautery tonsillectomy is an excellent surgical technique and results in acceptable postoperative discomfort with minimal blood loss when the device is set on a low wattage setting.

### *Bipolar Radio Frequency Technique (Coblation Tonsillectomy)*

Coblation technique utilizes a radio frequency bipolar electric current that passes through a normal saline medium, which creates a plasma field of sodium ions that subsequently disrupts molecular bonds without using excessive heat. These energized ions result in vaporization of tissue at a relatively low temperature of 60°C by breaking down intracellular bonds. With the low-heat production generated by this device, reduced postoperative pain from thermal injury has been reported.[96-98] Coblation may be utilized for complete tonsillectomy or for intracapsular tonsillectomy (tonsillotomy), where the tonsil is vaporized while leaving a thin layer of lymphoid tissue to protect the underlying constrictor muscle.

A bipolar cautery is incorporated into the tip of the wand to allow bipolar cauterization if bleeding is encountered. The tip of the coblation wand is also bendable, allowing its placement into the nasopharynx for coblation adenoidectomy.

### *Harmonic Scalpel Tonsillectomy*

The harmonic scalpel, which utilizes ultrasonic energy, cuts and coagulates tissue resulting in minimal thermal trauma and tissue damage. Electrical energy is converted from a generator into mechanical vibratory energy through a transducer consisting of piezoelectric ceramics, resulting in a back-and-forth vibratory motion of the blade at a frequency of approximately 55,000 cycles per second (kHz). The device can cut tissue at low or high power settings and is able to coagulate bleeding tissue, but it has difficulty coagulating briskly bleeding vessels. Harmonic scalpel technology was initially utilized in laparoscopic surgery and was later adapted to tonsillectomy.[99-101] Although studies have demonstrated the efficacy of harmonic scalpel,[101] advantages over more traditional surgical techniques have not been demonstrated. Significant cost of the disposable hand pieces is also of concern in this era of cost-conscious medical practice.

### *Intracapsular Tonsillectomy (Tonsillotomy)*

Intracapsular tonsillectomy typically utilizes powered instrumentation (microdebrider technology) to excise and ablate tonsillar tissue while leaving the peritonsillar capsule intact and without creating mucosal cuts in the tonsil pillars to excise tissue upon extirpation of the tonsils. Hemostasis is obtained with suction monopolar cautery applied directly to the residual lymphoid tissue. The electrocautery may also be used to ablate residual bulky lymphoid tissue of the tonsillar fossa. When this technique is utilized, postoperative pain is decreased compared with traditional tonsillectomy techniques, and postoperative, immediate, and delayed bleeding seems to be significantly reduced.[102-104] The tonsil is exposed utilizing a Herd retractor and the bulky tonsillar tissue is sequentially shaved with the microdebrider to a point well behind the levels of the anterior and posterior tonsillar pillars. Care must be taken not to violate the tonsillar capsule where significant bleeding and possible damage to the great vessels may occur.

This technique is ideal for very young children, typically < 3 years of age, with large obstructive tonsils, a history of SDB or OSA, without a significant history of chronic tonsillitis or recurrent streptococcal pharyngitis. In cases where chronic tonsillar infection is an indication for surgery, traditional complete tonsillectomy is preferred. In very small children with a low-reserve blood volume, intracapsular tonsillectomy is an excellent technique with its decreased risk of postoperative bleeding. However, there is a risk of tonsillar regrowth in a small number of cases and the need for complete tonsillectomy may be required if tonsillar regrowth becomes symptomatic[105] or a history of recurrent streptococcal pharyngitis becomes a problem later in childhood. In addition, with the decreased postoperative discomfort in very young children this technique reduces the chance of postoperative dehydration.

The microdebrider may also be utilized for adenoi dectomy, using an angled microdebrider blade, visualizing the nasopharynx in the typical fashion with a nasopharyngeal mirror. The safety and efficacy of microdebrider adenoidectomy has been demonstrated,[105,106] with this technique allowing more precise, rapid, and safe removal of adenoid tissue. Power-assisted adenoidectomy has demonstrated improved results over curette adenoidectomy when looking at time of surgery, intraoperative blood loss, and better control of depth of resection.[107] Higher increased surgeon satisfaction, utilizing powered instrumentation for adenoidectomy, has also been demonstrated.[107]

### *Description of Surgical Technique*

The description for a monopolar electrocautery tonsillectomy and microdebrider adenoidectomy will be described. Although numerous techniques and technologies have demonstrated efficacy for tonsillectomy and adenoidectomy, the authors feel that monopolar cautery tonsillectomy and microdebrider adenoidectomy is an excellent technique, which allows complete removal of the tonsil with minimal blood loss and acceptable postoperative discomfort.

Before anesthesia is induced, the patient should have no solid foods by mouth for 8 hours prior to surgery; however, the patient may drink clear liquids until 3 hours before surgery. Preoperative sedation with midazolam hydrochloride (0.5–1 mg/kg) approximately 30 minutes prior to surgery may be utilized for patients with excessive preoperative anxiety. Anesthesia is induced by mask ventilation, with subsequent intravenous access. Preoperative corticosteroids are given (typically 0.5 mg/kg of dexamethasone). Perioperative corticosteroids may reduce airway edema and improve immediate postoperative recovery;[108] however, there is no evidence that one dose of corticosteroids will improve the overall recovery time of children undergoing tonsillectomy.[109,110] In the past, intravenous antibiotics (typically ampicillin) were given with a postoperative 7-day course of oral amoxicillin. Telian et al. demonstrated the efficacy of perioperative antibiotics for tonsillectomy,[111] but more recently there have been recommendations against perioperative antibiotics due to lack of evidence of their efficacy in the postoperative course of pediatric tonsillectomy patients.[61] Peritonsillar infiltration with long-acting local anesthetics may improve immediate postoperative discomfort and possibly decrease intraoperative blood loss in patients undergoing sharp dissection tonsillectomy.[112]

After anesthesia has been induced, the patient is placed in the Rose position (Fig. 51.2), and the patient is suspended with a Crowe-Davis mouth gag to expose the oropharynx. A red rubber catheter is used to retract the soft palate, placing it through the right nares to retract the soft palate to better visualize the upper aspect of the tonsils and to allow better exposure of the nasopharynx. After the catheter is placed, a moistened pack is placed in the hypopharynx to occlude any potential oxygen

leaking around the endotracheal tube into the pharynx to minimize the risk of intraoperative fire. The hard and soft palate are examined and palpated to rule out evidence of a submucous cleft palate. Complete adenoidectomy in the presence of a palate defect could lead to the postoperative complication of VPI. In these situations, a conservative adenoidectomy is warranted where the upper aspect of the adenoid pad is removed to open up the choanae, leaving the lower aspect of the adenoid pad to allow good velar closure and reduce the chance of postoperative hypernasality.

Typically, the adenoidectomy is performed first, visualizing the nasopharynx with a mirror. In the past, adenoid curettes had been utilized with either straight or curved handles (Figs. 51.3A and B), but in recent years the authors have converted to the microdebrider adenoidectomy technique. An adenoid curette placed in the nasopharynx for adenoidectomy is demonstrated in Figure 51.4A. When adenoid curettes are utilized, the curette is seated above the adenoid pad, adjacent to the posterior choanae and nasal septum, allowing complete curettage of the adenoid pad. After the adenoid has been resected, a nasopharyngeal pack is placed until suction cautery hemostasis can be performed. If adenoid vegetations are noted encroaching upon or into the choanae, smaller curettes are available that will reach into the choanae to remove this tissue. In microdebrider adenoidectomy, the angled blade is utilized, with its oscillation rate set at a maximum of 1500 rpm. The nasopharynx is visualized with the mirror, and the adenoids are debrided under direct visualization, taking care to avoid damage to the torus tubarius of the Eustachian tube and also taking care not to debride too deeply into the prevertebral fascia, which may result in increased post-operative pain and possibly a stiff neck (Fig. 51.4B). When the adenoid tissue has been completely removed, a nasopharyngeal pack is placed until suction cautery hemostasis can be performed.

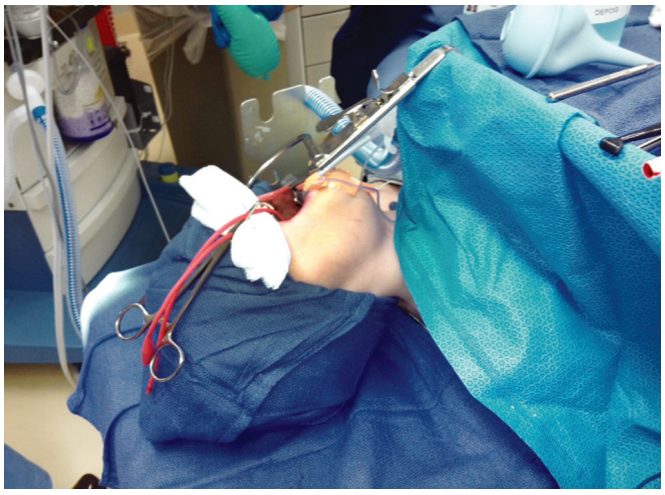
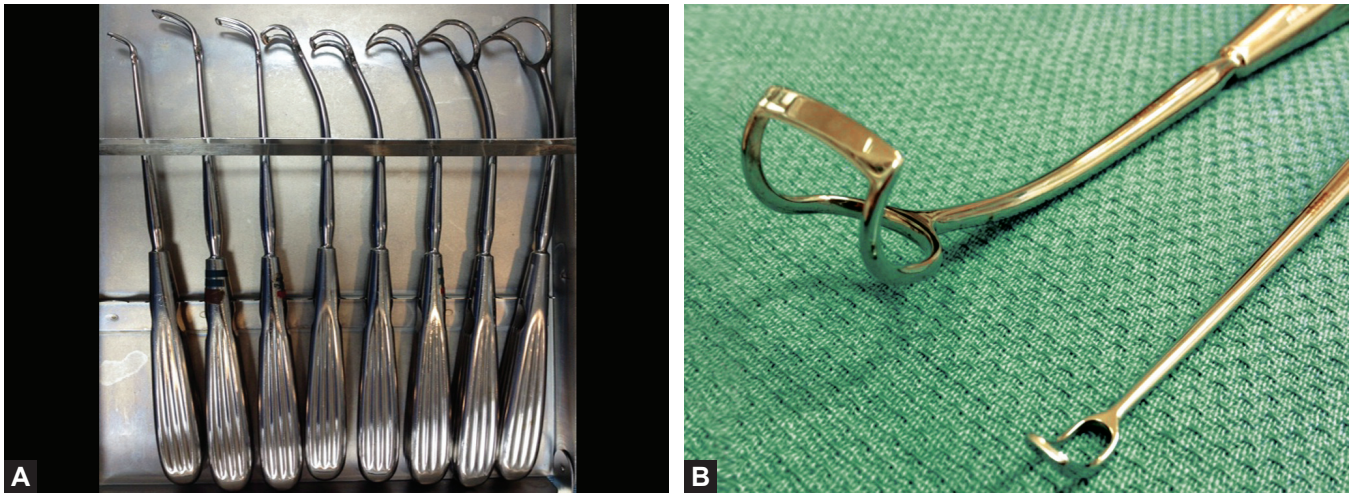
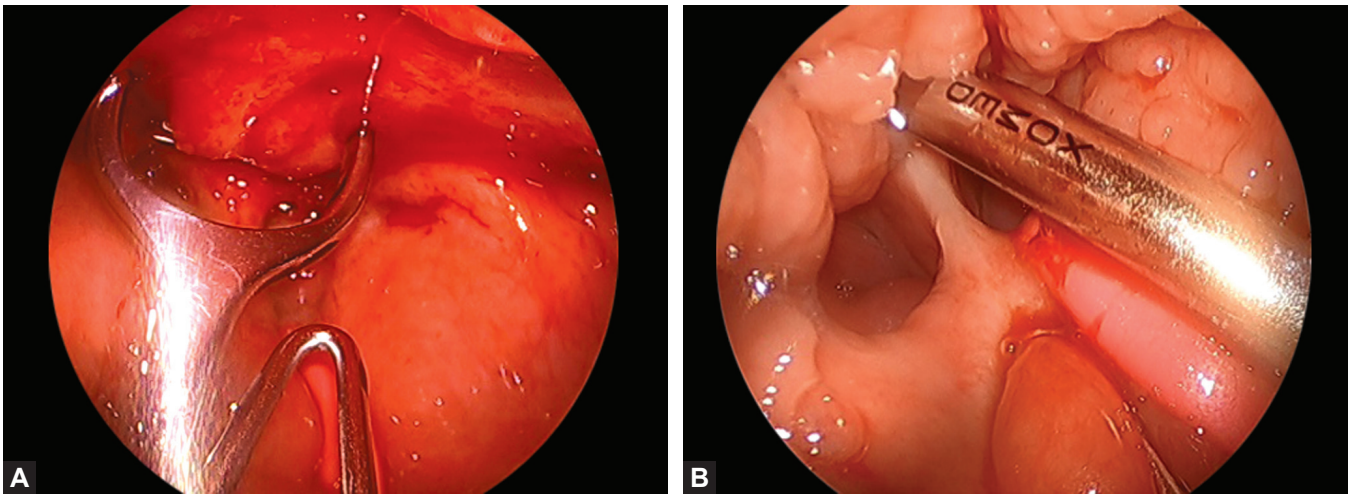


**Fig. 51.2:** Patient suspended for tonsillectomy and adenoidectomy with a Crowe-Davis mouth gag in the Rose position.

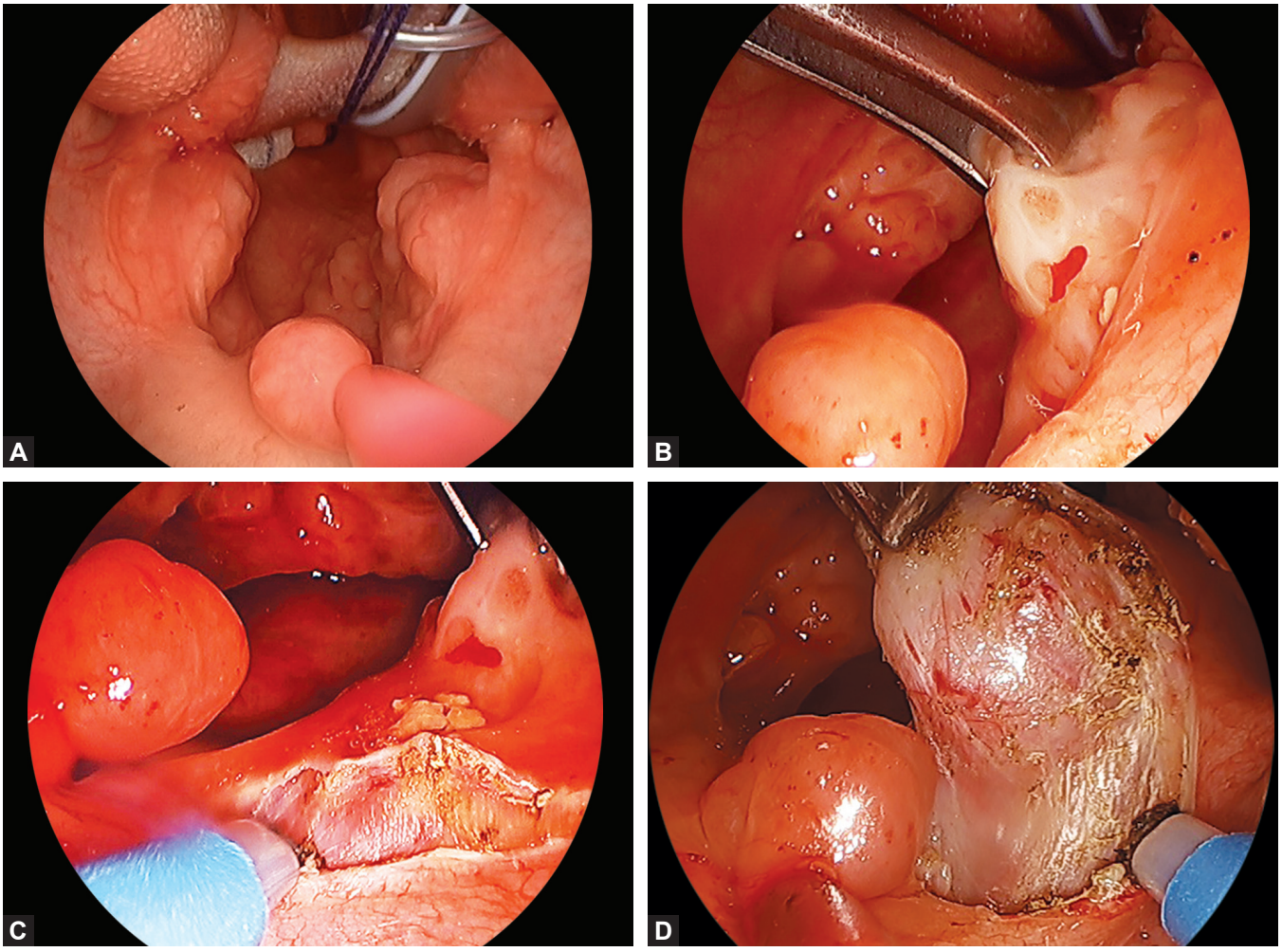
At this point, the monopolar cautery tonsillectomy is performed (Figs. 51.5A to E). Typically, the monopolar electroautery is set on 10–15 watts. The tonsil is grasped with an Allis clamp and retracted medially, exposing the superior pole, which is incised with the electrocautery using the cautery blade tip (we prefer a blade tip to a sharp needle point). The tonsillar tissue is carefully dissected in the avascular plain between the capsule and tonsil bed. Vessels that are encountered are cauterized. When the tonsil is completely mobilized superiorly, the dissection




**Figs. 51.3A and B:** Adenoid curettes.



**Figs. 51.4A and B:** (A) Adenoid curette set in position for excision of adenoid pad; (B) Microdebrider blade positioned for excision of adenoid pad.



**Figs. 51.5A to D:** Monopolar cautery tonsillectomy. (A) Exposure of tonsils and oropharynx for tonsillectomy and adenoidectomy. Note the moistened hypopharyngeal throat pack, the red rubber catheter to retract the soft palate, and the tongue blade of the Crowe–Davis mouth gag; (B) Tonsil grasped with Allis clamp; (C) Incision made with blade cautery tip at the superior pole to identify the tonsillar capsule and the associated avascular plane for dissection; (D) Dissection in the avascular plane.

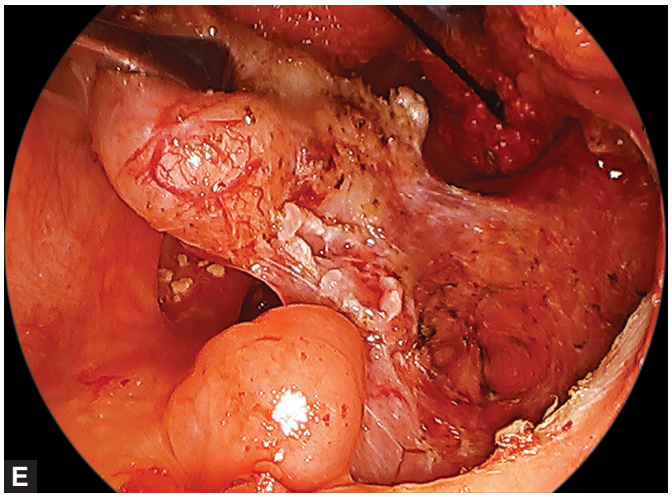
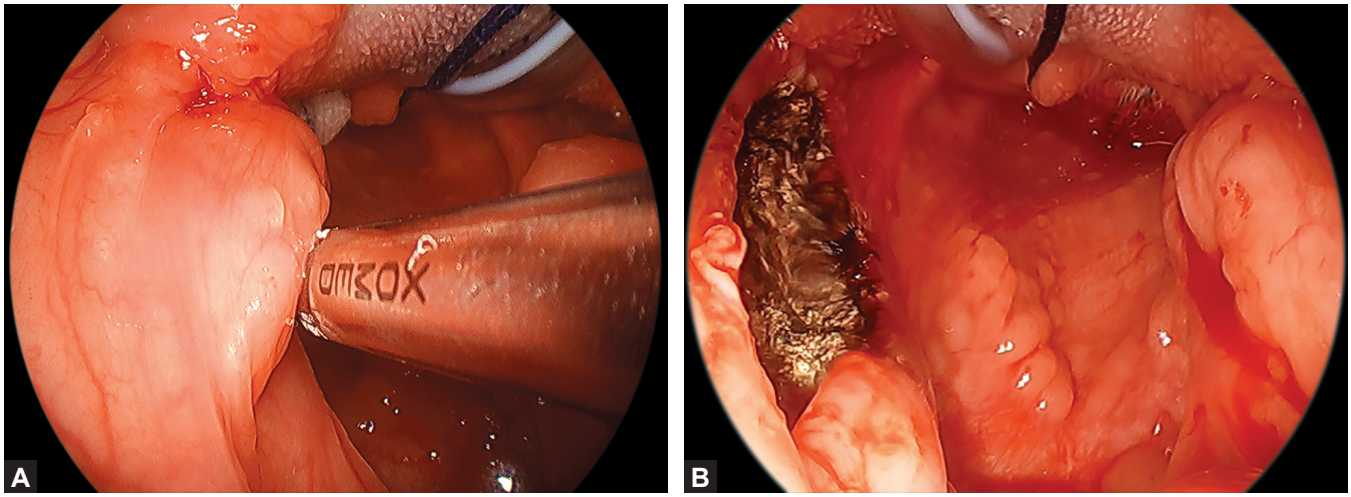



**Fig. 51.5E:** Tonsil pedicled at the inferior pole before amputation with the cautery.




**Figs. 51.6A and B:** (A) Microdebrider blade in place for intracapsular tonsillectomy; (B) The tonsil bed is dry after intracapsular tonsillectomy and monopolar suction cauterization for hemostasis.

continues toward the inferior pole in the avascular plain amputating the tonsil with the cautery at its attachment inferiorly. If sharp dissection technique is used, an incision of the superior pole mucosa is made with a scalpel blade and blunt dissection utilizing a Thompson dissector or a Fischer knife is performed. A tonsil snare can be utilized to amputate the tonsil at the inferior pole. If significant bleeding is noted at the time the tonsil is completely removed, a pack may be placed in the fossa before monopolar suction electrocautery hemostasis is performed. Care must be taken to preserve the surrounding tissue, particularly the posterior tonsillar pillar. If this is significantly damaged or inadvertently excised, nasopharyngeal stenosis or VPI may result. In addition, care must be taken to avoid touching metallic objects in the mouth with the cautery (i.e. mouth gag, tongue blade, or a metal suction), which could lead to intraoral burns. The electrocautery blade should be guarded with a nonconducting material, with only a small part of the metallic blade protruding at the end. Hemostasis is now obtained utilizing suction electrocautery in the tonsillar fossa and then the nasopharyngeal pack is removed and hemostasis is obtained in the nasopharynx using suction monopolar electrocautery. Figures 51.6A and B demonstrate the placement of the microdebrider for intracapsular tonsillectomy.

After hemostasis has been obtained in the tonsillar fossa and nasopharynx, irrigation of the nasal cavities and oropharynx is performed. The hypopharynx is suctioned, evacuating secretions and residual blood, and at this

point, it is recommended that the stomach is suctioned with a flexible suction catheter. The patient is subsequently awakened, extubated, and taken to the recovery room.

## PERIOPERATIVE MANAGEMENT

Postsurgical morbidity is a significant clinical issue for children undergoing tonsillectomy and adenoidectomy, and management of these issues in the postoperative period may have a significant influence on the long-term recovery of the patient. Conditions to be addressed in the days after surgery include emesis, decreased oral intake, pain and bleeding.[113,114] Prophylaxis to prevent or decrease the incidence of these issues has long been the mainstay of postoperative management.

### Opioids

The most commonly encountered issue in the postoperative period is pain, which can preclude resumption of a regular diet. Decreased oral intake can lead to readmission for rehydration or it may precipitate postoperative hemorrhage. Opioids are used in the postoperative period to mitigate these risks, allowing the patient to maintain an adequate oral diet.

Opioids have significant potential side effects, including nausea, vomiting, constipation, excessive sedation, and respiratory compromise.[115] Excessive sedation is of particular importance, as patients undergoing adenotonsillectomy for OSA are already at an increased risk for a reduction in respiratory drive. It is estimated that up to a third of cases of OSA patients may have persistent obstructive symptoms after surgery, thus compounding the respiratory depression for the patient taking opioids for postoperative pain relief.[116]

Traditionally, surgeons have often used codeine to control pain in the postoperative period. The activity of codeine depends on its conversion to morphine by the cytochrome P-450 isoenzyme 2D6 (CYP2D6).[117] It has been discovered that the gene encoding CYP2D6 has many genetic variations, which can affect the amount of codeine that is converted to an active form in children. An estimated 75–92% of the population has the normal range of CYP2D6 activity. However, 5–10% of the population are at the lower range, resulting in poor metabolism, and therefore, the patient may receive little to no morphine or analgesia from the prescribed codeine. On the opposite end of the spectrum, ultrarapid metabolizers can convert codeine into large amounts of morphine.[117] Ultrarapid metabolizers account for 1–15% of the population and seem to vary by ethnic group, with the highest percentage of ultrametabolizers being of Middle Eastern and North African descent. These patients are at particular risk for the toxic effects of morphine and life-threatening decreased respiratory drive. Due to this risk, the US Food and Drug Administration (FDA) has recently added a black box warning to the drug's label stating that codeine is contraindicated for this use in children.[118]

The use of hydrocodone, oxycodone, and morphine in the postoperative period has not been found to be related to cases of pediatric death or life-threatening respiratory depression after the use of these drugs.[118]

There is some debate as to whether to administer medications that control postoperative pain as needed (PRN) or on a regularly scheduled basis. Administration of medication on a fixed schedule is more commonly employed, although there is little evidence that this method is better than a PRN method.[119] The only exception is one recent study, which found time-dependent dosing of acetaminophen with hydrocodone more effective than PRN dosing around the clock.[120]

### NSAIDs

Nonsteroidal anti-inflammatory drugs (NSAIDs) work by reducing the production of prostaglandins by interfering with cyclo-oxygenase. A reduction in cylco-oxygenase causes a decrease in swelling and pain. NSAIDs have been used as an alternative to opioids, thereby avoiding the side effects of nausea, vomiting, and respiratory depression.

Surgeons have been reluctant to use NSAIDs in the perioperative period due to their antiplatelet effects, which may theoretically increase the rate of postoperative hemorrhage.[121] There have been conflicting studies on NSAIDs and the risk of postoperative hemorrhage.[122-124] The difficulty in investigating this topic involves the rarity at which postoperative hemorrhage occurs and the large number of participants required to provide an adequate number of events to give a significant result.[125] The latest review found results that did not exclude an increased risk of bleeding associated with NSAID use. The authors stated that they could not draw any conclusions about the effect of NSAIDs on bleeding.[126] The only NSAID that has been shown to increase the risk of postoperative hemorrhage is ketorolac. The rate of bleeding with ketorolac ranged from 4.4% to 18%, and therefore, ketorolac use should be avoided in tonsillectomy patients.[127,128]

## Local Anesthetics

To decrease perioperative morbidity, intraoperative local injection of anesthetic to the tonsillar fossa has been used. A recent Cochrane review assessed the effect of preoperative and postoperative injection of local anesthetic on pain after tonsillectomy. The randomized controlled trials found no evidence that these injections decreased postoperative pain.[129] Topical agents such as oral rinses, mouthwashes, and sprays have also been used in an attempt to decrease postoperative pain. The research on these agents was associated with a risk of bias in most studies, the reporting quality poor, and the data inadequate to permit comprehensive and reliable conclusions.[130]

## Steroids

Without prophylaxis, the reported incidence of postoperative vomiting in children undergoing tonsillectomy ranges from 40% to 73%.[131-134] A systematic review on pediatric patients undergoing tonsillectomy showed that a single dose of intraoperative, intravenous steroids reduced postoperative emesis by half. The review also found that children who received an intraoperative dose were also more likely to return to a soft/solid diet by day 1.[135]

Systemic steroids have been shown to be as efficient as 5-HT3 antagonists (i.e. ondansetron, metoclopramide) and droperidol in reducing postoperative nausea and vomiting. Their use is increasing and currently recommended in the American Academy of Otolaryngology-Head and Neck Surgery Foundation guidelines for tonsillectomy in children.[136,137]

There had been concern regarding an increased bleeding risk associated with administration of systemic steroids,[138] although a recent meta-analysis on dexamethasone and tonsillectomy bleeding found no increased risk of postoperative bleeding with the use of steroids.[139] Associated risks of a single-dose dexamethasone in nondiabetic patients appear minimal. A single dose of corticosteroid, even a large one, has been considered to be virtually without harmful effects.[140]

## Postoperative Antibiotics

Early randomized controlled trials suggested improved recovery after tonsillectomy when antibiotics were used in the postoperative period.[141] It was presumed that antibiotics worked by reducing bacteremia or through an anti-inflammatory process.[142] However, more recent studies refute these findings. A recent systematic review from 2012 suggests that although individual studies vary in their findings, there is no evidence to support a consistent, clinically important impact of antibiotics in reducing the main morbid outcomes after tonsillectomy (i.e. pain, need for analgesia, and secondary hemorrhage rates).[143] A Cochrane review from 2010 found that perioperative antibiotics were not associated with a reduction in significant secondary hemorrhage rates or total secondary hemorrhage rates. It found "no evidence to support a consistent, clinically important impact of antibiotics in reducing the main morbid outcomes after tonsillectomy".[144] Any putative benefit of antibiotics needs to be carefully weighed against the risk of possible emergence of resistant bacteria and adverse events, such as rash, allergy, and possible gastrointestinal upset or diarrhea.

## Acupressure

Various nonpharmacological techniques have been examined in trials as alternatives to antiemetic drugs. The P6 acupoint has been associated with decreased postoperative nausea and vomiting. This acupoint lies between the tendons of the palmaris longus and flexor carpi radialis muscles, 4 cm proximal to the wrist crease.[145] Acupoints can be stimulated by acupuncture, electroacupuncture, laser acupuncture, transcutaneous electrical nerve stimulation, acupressure, and capsicum plaster.

A Cochrane review of P6 stimulation for the prevention of postoperative nausea and vomiting concluded that there was no evidence of difference between P6 acupoint stimulation and antiemetic drugs in the risk of nausea, vomiting, or the need for rescue antiemetics.[146] However, for numerous reasons, P6 stimulation has failed to achieve widespread popularity as compared with pharmacological methods.

# COMPLICATIONS OF TONSILLECTOMY AND ADENOIDECTOMY

## Complications

Complications from adenotonsillectomy surgery can be classified into intraoperative, early postoperative, and late postoperative complications. In the intraoperative period, patients can experience trauma to the teeth, soft palate, pharyngeal wall, larynx, or difficult intubation; laryngospasm; laryngeal edema; hemorrhage; aspiration; respiratory compromise; endotracheal tube ignition;

and cardiac arrest. Injury to nearby structures has been reported, including lip burn, eye injury, and fracture of the mandibular condyle.[130] In the early postoperative period, complications include nausea, vomiting, pain, dehydration, hemorrhage, referred otalgia, postobstructive pulmonary edema, VPI, and nasopharyngeal stenosis. Complications have been found to be more common in patients with craniofacial disorders, Down syndrome, cerebral palsy, major heart disease, or bleeding diatheses and in children <3 years with polysomnography-proven OSA.[147-151]

During the postoperative period, approximately 1.3% of patients experience delayed discharge during the initial hospital stay for the above-mentioned reasons. Up to 3.9% of patients have secondary complications requiring readmission.[152] The most common reasons for readmission in the early postoperative time period or prolonged initial stay included pain, vomiting, fever, and tonsillar hemorrhage. In addition to these common causes of morbidity, many unusual and rare complications of tonsillectomy have also been described. More rare complications, which may or may not require hospitalization, include postobstructive pulmonary edema, atlantoaxial subluxation (Grisel's syndrome), taste disorders (hypogeusia, ageusia, dysgeusia, and phantogeusia), persistent neck pain (Eagle's syndrome), and nasopharyngeal stenosis.[153]

## Hemorrhage

Hemorrhage is the most common serious complication of adenotonsillectomy. When bleeding occurs in the operating theater, the initial step is often packing of the tonsillar fossa to apply pressure. Upon removal of the packing, any residual bleeding can usually be controlled by electrocautery on a low wattage setting. More significant bleeding may necessitate clamping and then ligating the bleeding artery or placement of a pack in the tonsillar fossa and oversuturing of the tonsillar pillars to provide constant pressure of the fossa.[154] Care must be taken to avoid accidently ligating the lingual or maxillary arteries near the inferior tonsillar pole. Also, the internal carotid artery lies in close proximity to the tonsillar fossa, and damage to this structure can cause a pseudoaneurysm and massive bleeding.[155] In severe cases, ligation of larger arteries through an open-neck exploration may be necessary. However, this should be an extremely uncommon step.[154]

Postoperative hemorrhage can be categorized into primary or secondary. Primary occurs within the first 24 hours after surgery and is thought to be due to a reopening of vessels. Secondary hemorrhage occurs after the first 24 postoperative hours and is thought to be due to sloughing of the surgical site eschar. Reported postoperative hemorrhage rates requiring treatment vary from 2% to 10%, and bleeding requiring reoperation from 1% to 5.5%, although variable rates have been reported with different surgical techniques.[79] Regardless of technique chosen, careful attention in the preoperative clinic and in the operating room will enable the surgeon to achieve intraoperative hemostasis and will lead to acceptable postoperative hemorrhage rates. The National Prospective Tonsillectomy Audit, performed in the United Kingdom in 2005, investigated the occurrence of postoperative hemorrhage in 33,921 patients undergoing tonsillectomy in England and Northern Ireland over a 14-month period in 2003–2004. The study demonstrated that there was a higher risk of postoperative bleeding with increasing patient age, male gender, and those with a history of recurrent acute tonsillitis (3.7%) and previous PTA. The rate was highest in quinsy patients (5.4%) compared with patients with pharyngeal obstruction and OSA (1.4%).[152] When postoperative bleeding is minimal, it is often managed at home with observation and it is not reported by the patient. However, more than minimal bleeding brings the patient to clinic or hospital for re-evaluation and often requires intervention in the form of hospitalization, transfusion, cauterization, or surgery. All patients must be informed as to how to handle a postoperative tonsillectomy hemorrhage with instructions to return to the nearest hospital. It has long been assumed that tonsillectomy hemorrhage was the main cause of death in the postoperative period, but a recent study refutes this point. A study of 55 cases of death or anoxic brain injury in patients who underwent tonsillectomy and associated procedures found that most of these events involved either suspected overdose of narcotic medication or an unexplained post-tonsillectomy death. Bleeding as the cause of death was rare. Neurological or cardiopulmonary impairments were relatively common in this cohort, with a less clear role for obesity. These data suggest that death after tonsillectomy most often occurs quietly and unexpectedly.

## Postobstructive Pulmonary Edema

Postobstructive pulmonary edema can occur following surgery of the upper airway. Controversy exists over the exact physiology, but it is likely due to acute obstruction

during emergence from anesthesia.[156,157] Obstruction can be caused by laryngospasm, a blood clot, or swelling and edema of the tongue and upper airway caused by surgery.

Previous studies have identified patient risk factors for respiratory complications after adenotonsillectomy. Young age, morbid obesity, hypotonia, craniofacial abnormalities, and severe OSA as determined by polysomnography have been identified as risk factors for acute airway obstruction after tonsillectomy.[158] High-risk patients should be observed closely after surgery with pulse oximetry. These patients may also benefit from prophylactic use of a nasopharyngeal airway and a nasal decongestant such as oxymetazoline to provide an improved nasal airway for several hours after the removal of a mechanical stent.[159] However, some patients may require prolonged mechanical ventilation, especially those with persistent hypercapnia until $PCO_2$ values return to normal.

## Velopharyngeal Insufficiency

Velopharyngeal insufficiency is a rare complication, which is most commonly associated with adenoidectomy. Patients with an occult submucous cleft or history of cleft palate are at particular risk of VPI postoperatively and should not undergo adenoidectomy unless absolutely necessary. If such a situation does arise, these patients should undergo a partial adenoidectomy, thereby allowing the soft palate full closure with the posterior and lateral pharyngeal walls. Patients with a history of hypernasal speech or nasal regurgitation are at particular risk of developing VPI postoperatively. A referral to a speech language pathologist (SLP) in these patients is required preoperatively. SLP can be particularly helpful in the estimated one in 1500 to one in 10,000 otherwise healthy patients who develop VPI in the postoperative period.[160-162] Most cases of postoperative VPI are transient and will resolve with time without treatment. However, severe cases may require surgical intervention. Options for surgical intervention include a pharyngeal flap, sphincteroplasty, or posterior pharyngeal wall augmentation depending on where the closure defect is located.

## Nasopharyngeal Stenosis

Nasopharyngeal stenosis is an obliteration of the normal communication between the nasopharynx and the oropharynx resulting from the fusion of the tonsillar pillars and soft palate to the posterior pharyngeal wall.[163] This surgical complication results when there is excessive excision of posterior tonsillar pillars, undermining the posterior pharyngeal wall and excessive electrocautery. Other known risk factors include performing surgery during an acute episode of pharyngitis or purulent sinusitis, revision adenoid surgery with removal of lateral pharyngeal bands, and keloid formation.[164] This is a very difficult surgical complication to remedy and the best treatment option is prevention. Careful operative technique, judicious use of electrocautery, and adequate preoperative evaluation are essential to prevent nasopharyngeal stenosis.[165] Various treatment modalities have been used to correct this stenosis including of skin flaps, local mucosal flaps, stents, skin grafts, scar incisions, and $CO_2$ laser.

## Atlantoaxial Subluxation

Atlantoaxial subluxation can be caused by traumatic and nontraumatic (Grisel's syndrome) causes, resulting in subluxation or dislocation of the C1 vertebra on the C2 vertebra, or the atlantoaxial joint. Patients may complain of neck pain and limited neck mobility, and they usually present with torticollis. The pathognomonic position of the head is described as having the head tilted 20° toward and the chin rotated 20° away from the side of the inflammatory process and in slight flexion.[166] The underlying mechanism for nontraumatic subluxation post-tonsillectomy and adenoidectomy is believed to be from local tissue inflammation from infection or surgical trauma. This can result in decalcification of the C1 ve tebra and laxity of the anterior transverse spinal ligament.[167-171] Suspected cases warrant an urgent CT scan and magnetic resonance imaging to diagnose decalcification (which may be associated with osteomyelitis) and ligamentous inflammation, respectively. Neurosurgical consultation is also advised to prevent development of neurologic deficit.[168-170] Treatment of nontraumatic atlantoaxial subluxation involves decreasing the inflammation, reducing the atlantoaxial subluxation, and resolving the infectious process with antibiotics that cover potential oropharyngeal pathogens. Up to 15% of patients may develop permanent neurologic sequelae ranging from radiculopathy to quadriplegia.[172] Early recognition and intervention can prevent substantial morbidity and mortality such as Grisel's syndrome, spinal cord compression, and irreversible neurologic sequelae.[167-171] Patients with Down's syndrome are at particular risk of traumatic atlantoaxial subluxation due to increased ligamentous laxity and possible bony deformities of the cervical spine.

Particular attention is required when manipulating the cervical spine during surgery.[149] Prior to surgery the American Academy of Pediatrics and the Special Olympics both recommend screening radiography.[173] Flexion–extension cervical spine radiographs that demonstrate an anterior atlantodental interval >4–5 mm are considered abnormal, and further imaging is recommended.

## QUALITY-OF-LIFE DATA

Children with recurrent tonsillitis and SDB show significantly lower scores on several quality of life subscales, including general health, physical functioning, behavior, bodily pain, and parental impact as compared with healthy normal children.[174] Stewart et al.[174] found that these patients' scores were comparable with the scores for children with asthma and juvenile rheumatoid arthritis. Subscales related to emotional impact, behavior, and parental impact of the child's disease were worse for the children with tonsil and adenoid disease.

Resolution of symptoms of SDB seems to be related to obesity. A recent meta-analysis[60] showed that resolution of SDB in obese children occurred only in 10–25% of patients.

Controversy exists as to whether surgery improves quality of life for patients with recurrent tonsillitis. Paradise et al.[175] investigated tonsillectomy with or without adenoidectomy versus nonsurgical therapy for severely affected children (seven or more documented episodes of tonsillitis in the year before enrollment, five or more episodes in each of the 2 preceding years, or three or more in each of the 3 preceding years). The authors found a significant decrease in the number and severity of infections in the surgical groups during the first 2 years of follow-up. The differences in the third year favored the surgical group, but the results were not statistically significant.

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CHAPTER

# 52

# Pediatric Deep Neck Space Infections

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## INTRODUCTION

Head and neck space infections are relatively common in the pediatric population. Although most are easily treatable, disastrous complications can result, necessitating appropriate recognition and management. Relative to the adult population, there are key differences in regard to etiology, anatomy, and microbiology in pediatric deep neck space infections.

## ANATOMY

The real and potential spaces of the head and neck are defined by the superficial and deep fascial layers, which delineate their boundaries. A thorough understanding of this anatomy is necessary for an accurate diagnosis. This knowledge guides treatment of deep neck space infections.

The superficial cervical fascia is the enveloping fascia of the platysma and muscles of facial expression incorporating the superficial musculoaponeurotic system. It descends from the zygomatic process to the axilla and subcutaneous tissue over the pectoral region.

The deep cervical fascia consists of three layers: superficial, middle, and deep. The superficial layer of the deep cervical fascia completely surrounds the neck and is the investing fascia of the superficial musculature. A potential space exists between the superficial cervical fascia and the superficial layer of the deep cervical fascia, which allows for skin mobility over deeper neck structures. The superficial layer of the deep cervical fascia attaches to the spinous processes of the cervical vertebrae posteriorly. Superiorly, it attaches to the nuchal line, the skull base at the mastoid process, zygoma, and mandible. It descends inferiorly to the clavicle, acromion, and scapular spine. The superficial layer of the deep cervical fascia splits at the mandible and overlies the masseter laterally and the medial surface of the medial pterygoid, creating the masticator space.

The middle layer of the deep cervical fascia is subdivided into visceral and muscular divisions. The muscular division envelopes the infrahyoid strap muscles, attaching superiorly at the hyoid and thyroid cartilages and inferiorly at the sternoclavicular complex. The visceral division envelopes the thyroid, trachea, esophagus, pharynx, and larynx, attaching superiorly at the skull base, hyoid, and thyroid cartilages. Inferiorly, this visceral division is contiguous with the pericardium. The buccopharyngeal fascia is the portion of the middle layer of deep cervical fascia superficial to the pharyngeal constrictors when approached from a transcervical route. Condensations of this fascial layer form a posterior midline raphe that joins with the alar fascia and divides the retropharyngeal space vertically in the midline. The pterygomandibular raphe is another condensation of the buccopharyngeal fascia that attaches superiorly to the hamulus and inferiorly to the mylohyoid line of the mandible.

The deep layer of the deep cervical fascia is composed of both the prevertebral fascia and alar fascia. The prevertebral fascia lies anterior to the bodies of the vertebrae and extends the length of the vertebral column from the foramen magnum to the coccyx. It envelops the paraspinous muscles, covers the scalene muscles, and attaches to the transverse processes of the vertebrae. The alar fascia lies between the prevertebral fascia and the buccopharyngeal fascia and extends from skull base to mediastinum, defining the posterior extent of the retropharyngeal space. The danger space is the space between the two layers of deep cervical fascia.

The carotid sheath is the main neurovascular conduit in the neck and is formed from a condensation of all three fascial layers. It extends from the skull base to the thorax and contains the internal jugular vein, carotid artery, vagus nerve, and ansa cervicalis.

The fascial planes effectively subdivide the neck into compartments. Infections in each compartment have unique clinical implications and differentiating features. These compartments can communicate with each other and with adjacent areas, opening a route of spread of infection within and outside of the neck. The spaces can be subdivided into regional groups: facial, suprahyoid neck, infrahyoid neck, and those that travel the length of the neck.

## Facial Spaces

### *Canine Space*

This is the space between the levator anguli oris and anterior maxilla, and infections in this area are most often a result of an infected canine tooth. Occurring in the subperiosteal plane, canine space infections present with swelling overlying the medial maxilla and effacement of the nasolabial fold. Treatment involves addressing the underlying dental pathology. Infection can spread through the ophthalmic vein system to the cavernous sinus, leading to cavernous sinus thrombosis. This has classically been attributed to the valveless nature of these veins, but a cadaveric study demonstrated valves within the ophthalmic and facial veins leading the researchers to hypothesize that the presence of a communication and the cranial directionality of the flow are responsible for facilitating the spread of infection.[1]

### *Buccal Space*

The buccal space is bounded by the superficial cervical fascia laterally, the buccinator muscle on the deep aspect, the modiolus anteriorly, and the attachment of the buccinator to the pharyngeal constrictor posteriorly at the pterygomandibular raphe. This space contains the parotid duct, facial artery, and buccal fat pad. Most buccal space infections are odontogenic in origin, but oral mucosal granulomatous disease can also be a contributing factor in buccal space infections. Buccal space infections can spread to adjacent spaces including masseteric, parapharyngeal, temporal, and periorbital and can also lead to a cavernous sinus thrombosis via venous extension through the transverse facial vein.

### *Parotid Space*

The parotid space is formed by the superficial layer of the deep cervical fascia. It encompasses the parotid gland, intraparotid lymph nodes, retromandibular vein, posterior facial vein, and external carotid artery. The parotid space communicates medially with the prestyloid parapharyngeal space through an incomplete medial fascial border. Infections here can be the result of parotitis or lymphadenitis, as well as spread from the parapharyngeal space. This space also contains the extracranial facial nerve as it runs through the superficial lobe of the parotid gland, and severe infection or inflammation can cause a facial paresis.

### *Temporal Space*

The temporal space is bounded superiorly by the temporal line, inferiorly by the zygomatic arch, laterally by the temporalis fascia, and medially by the outer table of the calvarium. It contains the temporalis muscle and infections of this space present with pain and trismus. This space is sometimes considered to be the superior part of the masticator space as it is directly contiguous.

### *Masticator Space*

The masticator space is the large space in the lateral face bounded laterally by the superficial layer of the deep cervical fascia overlying the masseter and medially by the same fascia medial to the medial pterygoid. It sits adjacent to the parapharyngeal space anterolaterally. It can be subdivided by the mandibular ramus into the masseteric and pterygoid spaces. Contents of the masticator space include the aforementioned muscles, the ramus, and posterior body of the mandible, inferior alveolar nerve, internal maxillary artery, and buccal fat pad. Infections in the masticator space are most often odontogenic and usually arise from the third molars.

## Suprahyoid Neck Spaces

### *Peritonsillar Space*

The peritonsillar space is the space bounded laterally by the capsule of the palatine tonsil, medially by the superior pharyngeal constrictor muscle, anteriorly by the palatoglossus muscle, and posteriorly by the palatopharyngeus muscle. It contains loose areolar connective tissue (Fig. 52.1).

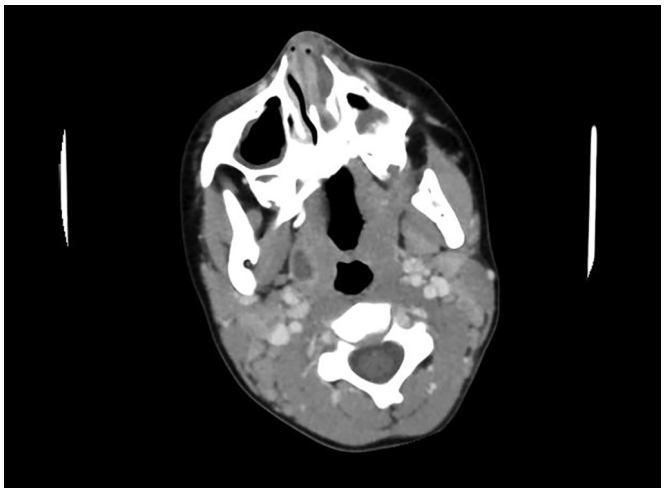

**Fig. 52.1:** Right peritonsillar abscess in an 8-year-old child.

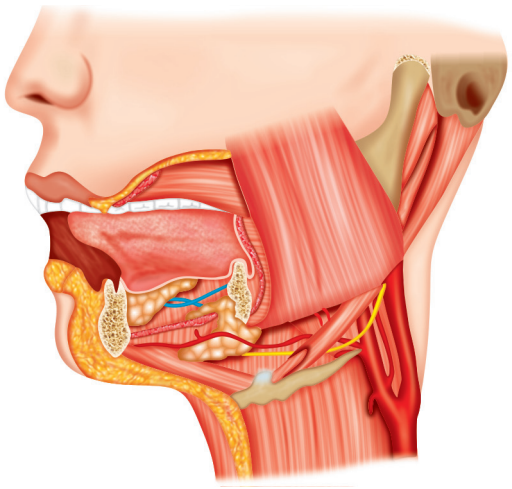

**Fig. 52.2:** Submandibular and sublingual spaces.

## *Submandibular Space*

The submandibular space is the space that lies between the mylohyoid muscle medially and the platysma and mandible laterally. The anterior belly of the digastric defines the anterior limit of the space, whereas the posterior belly of the digastric and stylomandibular ligament marks the posterior extent. The floor of the submandibular space is the superficial layer of deep cervical fascia. The submandibular space contains the submandibular gland and lymph nodes, facial vein and artery, and hypoglossal nerve. It communicates directly with the sublingual and parapharyngeal spaces posteriorly around the free edge of the mylohyoid (Figs. 52.2 and 52.3).

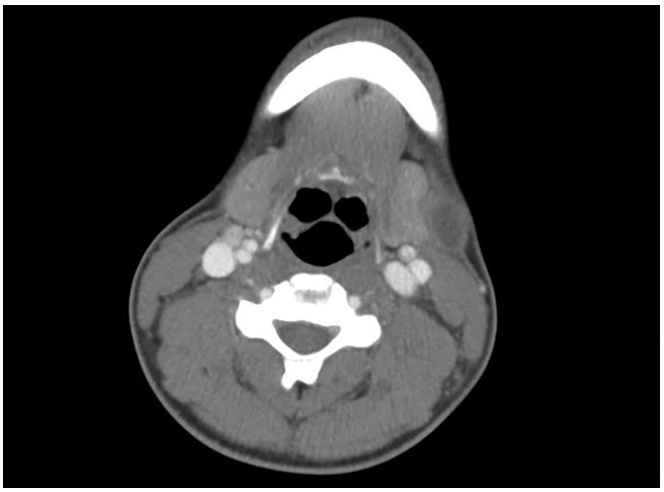

**Fig. 52.3:** Left-submandibular space infection in an 18-year-old.

## *Sublingual Space*

The sublingual space can be considered a subcompartment of the submandibular space. It lies deep to the mucosa of the floor of the mouth. The inferior and lateral border is the mylohyoid muscle, and the anterior border is the lingual cortex of the mandible. It is a paired space that communicates with the contralateral sublingual space deep to the lingual frenulum. This space is otherwise bounded medially by the genioglossus and geniohyoid muscles. The sublingual space contains the sublingual gland, the deep lobe of the submandibular gland, Wharton's duct, the hypoglossal and glossopharyngeal nerves, and lingual artery. Infections in this space are often odontogenic in nature and are defined by the mylohyoid line, which represents the insertion of the mylohyoid muscle on the lingual cortex of the mandible. The apices of teeth anterior to the second molar lie superior to the mylohyoid line, and thus infections of these teeth usually involve the sublingual space. Bilateral sublingual space infections, classically known as Ludwig's angina, can rapidly result in airway compromise. The sublingual space communicates with the parapharyngeal and submandibular spaces at the posterior border of the mylohyoid.

## *Parapharyngeal Space*

The parapharyngeal space sits in a location central to other suprahyoid neck spaces and can be conceptualized as an inverted four-sided pyramid. Superiorly, the base of the pyramid is the skull base including the foramen lacerum, jugular, and hypoglossal foramens. The apex

lies at the greater cornu of the hyoid bone. It is bounded posteriorly by the prevertebral fascia and anteriorly by the medial pterygoid and pterygomandibular raphe. The lateral border is the parotid gland, mandibular ramus and lateral pterygoid, whereas the medial border is the buccopharyngeal fascia covering the superior pharyngeal constrictor.

The parapharyngeal space is divided by the styloid process into muscular and neurovascular compartments. The prestyloid, or muscular, compartment contains fat, stylopharyngeus and styloglossus muscles, lymph nodes, deep lobe of the parotid, internal maxillary artery, inferior alveolar, lingual, and auriculotemporal nerves. The poststyloid compartment contains the carotid artery, internal jugular vein, sympathetic chain, and cranial nerves IX–XII, as well as occasional salivary tissue.

The parapharyngeal space communicates with or sits adjacent to the retropharyngeal, submandibular, masticator, and peritonsillar spaces. The carotid sheath passes through the posterior aspect of parapharyngeal space (Fig. 52.4).

## Infrahyoid Neck

### *Anterior Visceral Space*

The anterior visceral space is enshrouded by the visceral division of the middle layer of deep cervical fascia. It extends from the thyroid cartilage inferiorly toward the superior mediastinum. The anterior visceral space contains the pharynx, esophagus, larynx, trachea, thyroid/parathyroid glands, recurrent laryngeal nerve, and level VI lymph nodes.

## Full Length of Neck

### *Retropharyngeal Space*

The retropharyngeal space lies between the buccopharyngeal fascia (middle layer of deep cervical fascia) anteriorly and alar fascia posteriorly. These two fascial layers condense in the midline to form a vertical raphe. It contains fat and lymph nodes, which are felt to atrophy during childhood (but can manifest in adulthood with metastatic cancer from the upper aerodigestive tract). The space extends from the skull base superiorly to the mediastinum at approximately the level of the second through fourth thoracic vertebrae. The space is bounded laterally by the carotid sheath. The retropharyngeal space contains areolar connective tissue and lymph nodes. Infection can occur from direct spread from parapharyngeal space or lymphatic drainage from the nasopharynx (Figs. 52.5 and 52.6).

### *Danger Space*

The danger space sits between the retropharyngeal and prevertebral spaces and extends from skull base to diaphragm. It is bounded posteriorly by the prevertebral

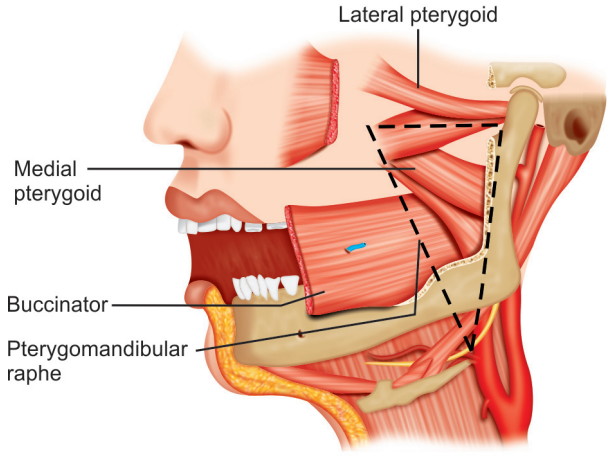


**Fig. 52.4:** Parapharyngeal space.

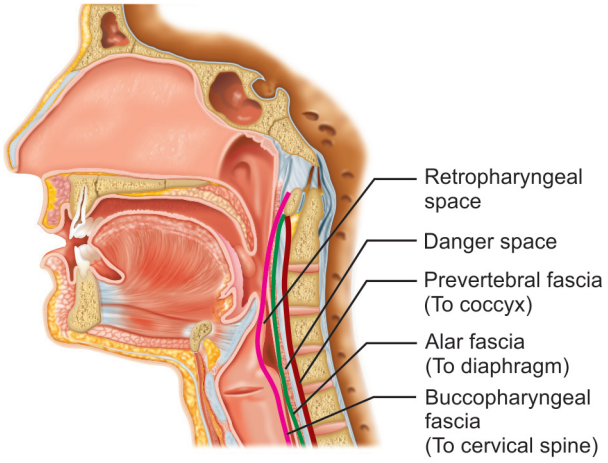


**Fig. 52.5:** Cross-sectional imaging of the prevertebral deep cervical fascia layers and graphic representation of a retropharyngeal space infection.

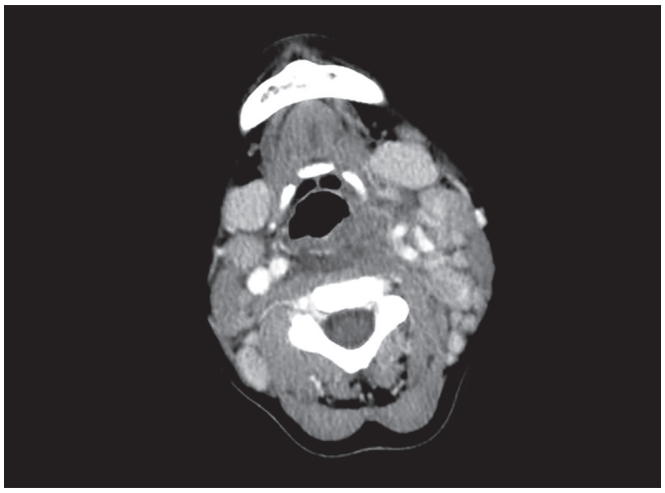

**Fig. 52.6:** Axial computed tomographic image of a developing retropharyngeal infection.

fascia and laterally by the transverse processes of the vertebral bodies. It is a potential space filled with loose areolar connective tissue.

### *Prevertebral Space*

The prevertebral space is the space bounded by the prevertebral fascia anteriorly, the vertebral bodies posteriorly, and the transverse processes laterally. It extends from the clivus to coccyx. It contains muscles, the vertebral artery and vein, phrenic nerve, and brachial plexus.

### *Carotid Sheath*

This space runs the full length of the neck. It is a fascial conduit composed of condensation of all three layers of deep cervical fascia. The carotid sheath contains the great vessels as well as the cranial nerves IX through XII and the sympathetic trunk. This space is not usually relevant in children with the exception of carotid pseudoaneurysms and the syndrome of septic thrombophlebitis of the internal jugular vein.

## MICROBIOLOGY

The microbiology of deep neck space infections is well defined and follows naturally from the common sources of infection. Infections usually arise from adjacent or hematogenous spread from infected tonsils or pharyngeal tissues or from suppurative cervical lymphadenitis complicating upper respiratory tract infections. Infected branchial cleft cysts and odontogenic infections are less common but should remain on the differential. The predominant organisms are the aerobic gram-positive organisms, especially staphylococcal and streptococcal species with *Staphylococcus aureas* being the chief pathogen; a finding that has grown more common over the last decade.[2] Group A β-hemolytic *streptococcus*, *Streptococcus pyogenes*, cogulase negative staphylococcus, and *Haemophilus influenzae* are other important organisms. Anaerobic organisms including *Prevotella*, *Porphyromonas*, *Fusobacterium,* and *Peptostreptococcus* are also important in the setting of odontogenic infections and due to their presence in normal oropharyngeal flora. A sizable minority (25%) of infections will exhibit a polymicrobial culture result, although it is likely that the majority of deep neck space infections are polymicrobial. This discrepancy in reported rates is due to the fact that appropriate methods to isolate anaerobic organisms are often not utilized.[3] The majority of deep neck abscesses contain β-lactamase producing bacteria.[4] The increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) warrants careful consideration when choosing initial antimicrobial therapy and monitoring response to treatment. Several studies have documented this growing trend. One study found that the rate of pediatric neck abscess demonstrating MRSA increased from 2.4% in the years 2000–2004 to 20% in the years 2005–2010.[5] Another study showed that the overall prevalence of MRSA in children requiring surgical intervention at a tertiary care hospital was 49% between 2004 and 2009.[2] This study identified age <16 months old (10-fold increased risk) and lateral neck location as risk factors for community acquired MRSA. Another series by Cheng and Elden demonstrated age <15 months old as a risk factor for MRSA.[6] Nontuberculous mycobacterial infections should also be considered. Atypical mycobacterial infections are the most common cause of chronic cervical abscesses and occur in younger children (age 2–5) most commonly in the level I and II cervical lymph node basins.[7]

## CLINICAL PRESENTATION

Children with a deep neck space infection will often present with characteristic signs and symptoms including neck mass or swelling, neck stiffness, drooling, dysphagia, odynophagia, trismus, changes in voice, cough, otalgia, fever, and decreased oral intake. Laboratory findings may include an elevated white blood cell count with an increased percentage of neutrophils, including the immature band forms. Inflammatory markers such as

erythrocyte sedimentation rate and C-reactive protein may also be elevated. A C-reactive protein >9 mg/dL has been reported to have a 67% probability of serious bacterial infection in children <3 years of age.[8] Procalcitonin is an acute phase reactant that has shown some potential to predict sepsis and thus may become another useful marker,[9] although the data are too limited to recommend its routine use at this time.

Initial rapid assessment should first and foremost focus on airway stability and potential threats to the airway. Acute airway distress is a rare but dangerous presentation of a deep neck space infection and one that first responders, primary care providers, emergency room providers, and otolaryngologists should be prepared for. This presentation will alter the acute management of the patient with stabilization of the airway being paramount. It is important to recall that in the pediatric patient, rapid deterioration and changes in the clinical picture can occur, turning a nonemergent situation into one that can be life threatening.

Once airway safety is established, further examination should include a thorough examination of the head and neck including intraoral and oropharyngeal examinations. This may be difficult in younger children, especially those who are uncomfortable, in pain and have limited jaw opening. Examination of the oral cavity should include assessment of dentition to assess for a potential odontogenic source of infection. Oropharyngeal examination may reveal asymmetric tonsils indicating peritonsillar or parapharyngeal space infections. Swelling of the posterior oropharynx may indicate a retropharyngeal or parapharyngeal process; this will often be asymmetric due to the presence of the midline raphe in the retropharyngeal space.

Neck examination should focus on obvious swelling, mass, limitation of range of motion and any overlying erythema. The clinical finding of fluctuance in an area of lymphadenitis is often used an indicator to pursue additional or initial imaging or progress to intervention. This finding however is less accurate than often taught. It is not predictive of whether fluid will be found on needle aspiration.[10]

## IMAGING

The decision on whether or not to image is always an easy one. Any child in distress should not be transported to the radiology suite; however, portable plain films may be done at the bedside. In the nontoxic child with no evidence of airway compromise but findings consistent with deep neck space infection, deferring the radiologic evaluation is reasonable pending the clinical response to antibiotics. As discussed below, it is not clear from the literature which imaging findings should prompt early operative intervention versus trial of antibiotic therapy. Therefore, we reserve computed tomography (CT) for those children who present with evidence of complicated infection, concern for early airway involvement, or who have failed 48–72 hours of empiric antibiotic therapy.

### Plain Radiography

The lateral soft tissue neck film is often used as a screening examination in children in which there is a reasonable suspicion of retropharyngeal space infection (Fig. 52.7). It has been reported to have a sensitivity of approximately 83%, which in the same series was compared with a CT sensitivity of 100%.[11] Thickening of the retropharyngeal space to >5 mm at C2 or >½ the width of the vertebral body in the sagittal plane is one indicator of possible infection. Caution should be taken to interpret this finding in the correct clinical setting, as a radiograph timed during swallow can give a false-positive image. In addition, an adequate image requires good neck extension, which may be limited by pain-induced torticollis. A child who is actively crying is also difficult to image with this technique. The lateral neck film can also be used to screen for epiglottitis and adenoid hypertrophy. Chest radiography can be used to diagnose concomitant cardiopulmonary issues.

### Computed Tomography

The CT has long been the imaging modality of choice for imaging in deep neck space infections. Its advantages

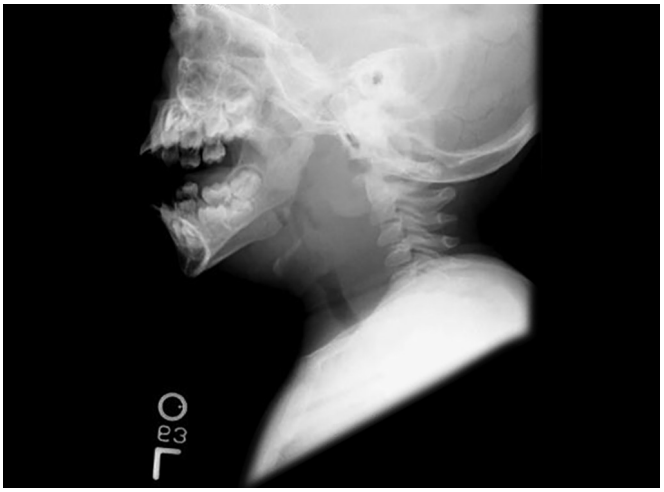

**Fig. 52.7:** Prevertebral soft tissue thickening on plain film.

include quick scan time, excellent resolution, ability for multiplanar reformation, resolution of bony structures, ability to administer contrast for assessment of enhancement, and identifying involvement of anatomical structures (Fig. 52.8). However, there are some problems seen with the use of CT. It is prone to artifact from dental devices or hardware. In addition, risk estimation models have suggested a defined attributable excess mortality to radiation exposure from CT imaging, although epidemiological data are lacking.[12] This risk appears to increase with decreasing age. Intravenous contrast carries the risk of nephrotoxicity and allergic reaction. Like any intervention, the risk must be balanced with the possible benefit. However, it is clear that the overuse of CT should be avoided.

There have been concerns raised regarding the utility of CT to accurately predict an abscess with one study showing a sensitivity of 81%, specificity of 67%, and positive predictive value of 89% in children with retropharyngeal and parapharyngeal abscesses.[13] Appearance on CT is not predictive of need for surgical drainage[14] as CT correctly predicts only 71% of abscesses discovered on subsequent surgical exploration[15] and the false-positive rate may be as high as 15–32%.[16]

The CT scans are useful when surgical intervention is planned as they can act as a "roadmap" for the surgical approach. This allows the surgeon to plan the approach to minimize the risk to major neurovascular structures and to optimize the amount of dissection, which must take place. With regard to retropharyngeal and parapharyngeal abscesses, CT findings will also dictate whether the approach is via a transcervical or transoral route based on location relative to the great vessels.

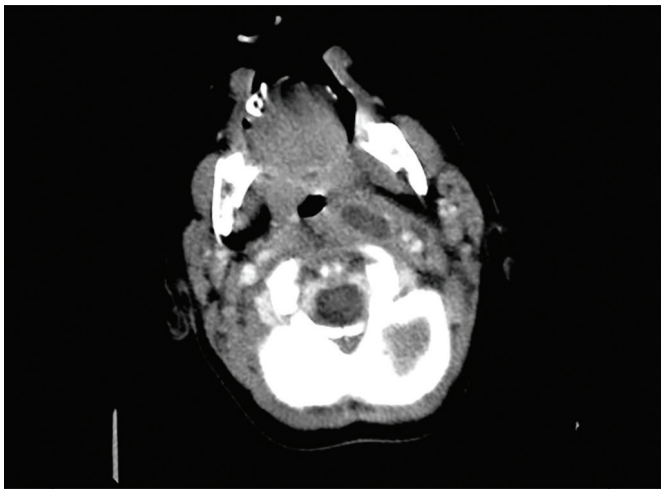

**Fig. 52.8:** Axial computed tomographic image of a left parapharyngeal space infection in a 1-year-old child.

## Ultrasound

Ultrasound is gaining traction as a primary imaging modality for various applications within the head and neck. It is safe, able to be performed at the bedside or in the operating room, and easily learned. Head and neck surgeons are most familiar with its utility in assessing lesions of the thyroid, but it has becoming more apparent that as experience and familiarity increase, so does the clinical utility. For superficial infections, ultrasound has a greater sensitivity but lower specificity when compared with CT.[17] One study showed that in 97.6% of inflammatory neck masses, ultrasound performed by radiologist provided sufficient information about the lesion negating the necessity for a CT scan.[18] There exists limited evidence to support the use of ultrasound in imaging of deep neck space infections and even less to define parameters for its use. Limitations exist including the inability of ultrasound to look beyond bone and air-filled structures, variability between examinations and examiners, decreased familiarity with ultrasound images, the limited utility of static ultrasound images for later review, the inability to assess for evidence of potential airway compromise, and no contrast enhancement. Ultrasound can be used to visualize most of the neck with the exception of the superior retropharyngeal, medial masticator, and the parapharyngeal spaces. Children are especially amenable to ultrasound examinations due to their smaller neck sizes. We propose that ultrasound imaging in the radiology suite is potentially less useful than bedside and intraoperative ultrasonography in the hands of the otolaryngologist. As otolaryngologists become more familiar with this powerful tool, we anticipate that it may supplant CT as the primary imaging modality in the initial assessment of many deep neck space infections. CT scans will continue to be useful for defining airway compromise, assessing infections medial to the great vessels, and providing a surgical roadmap in cases where the approach is potentially complicated.

# TREATMENT

## Medical

Corticosteroids are often used to suppress the inflammatory response and improve the symptoms associated with deep neck space infections. Clinical experience has shown that administration of corticosteroids can improve trismus, torticollis and oral intake, and decrease inflammatory edema that may threaten the airway. However,

steroids also can artificially suppress the clinical picture, masking progression of infection. Steroids cause an elevated white blood cell count secondary to neutrophil demargination, limiting the utility of trending white blood cell counts during corticosteroid use. There are no data that we are aware of to support or not to support this practice.

Mounting evidence suggests that empiric antibiotic therapy may be a viable alternative for deep neck space infections that would otherwise be treated surgically.[19] Clinically, a cutoff abscess size of 1.0 cm is often used to determine whether an attempt at medical therapy should be made. This cutoff has been used in the literature[20]; however, it is not clear from the literature whether there is a defined size at which medical therapy is less likely to work. McClay et al. looked at children with CT evidence of abscess between 1.0 and 3.0 cm in maximum dimension who were treated with empiric antibiotics. Ten of eleven children responded, and only one progressed to surgical drainage.[21] Freling et al., after retrospectively reviewing 76 pediatric and adult patients, suggested that abscess size < 3.5 cm with < 50% rim enhancement may deserve a trial of IV antibiotic treatment.[16] In a series by Cheng and Elden, 66% of children who presented with retropharyngeal or parapharyngeal space infections will improve with antibiotics alone. Those children who failed medical therapy tended to be younger (< 51 months), have a higher WBC count, be admitted to the ICU, demonstrate complete rim enhancement on CT, and have an abscess > 2.2 cm.[6] It seems logical that larger, multiloculated abscess would be less likely to respond to antibiotic therapy than small, unilocular fluid collections. Children who present in airway distress, sepsis, or with neurovascular compromise should not be considered for sole antibiotic therapy. Also, the literature does not address whether initial medical or surgical management results in decreased rate of severe complications.

Initial choice of antibiotic therapy must take into account the increasing prevalence of community acquired MRSA as well as the high rate of polymicrobial, mixed aerobic and anaerobic infection, and the high prevalence of β-lactamase-producing organisms. Empiric therapy may include clindamycin as a sole agent or clindamycin with a second- or third-generation cephalosporin. Clindamycin has excellent oral bioavailability and distributes well into soft tissue. It has the added effect of inhibiting staphylococcal and streptococcal virulence factors.[22] Amoxicillin–clavulanate is often used in the outpatient setting as initial therapy; however, it is not effective against MRSA. Similarly, ampicillin–sulbactam is not an ideal choice in the inpatient setting. Trimethoprim–sulfamethoxazole and doxycycline are reasonable choices for outpatient therapy in the setting of risk factors for MRSA but do not provide the breadth of coverage of clindamycin. Other options include a second- or third- generation cephalosporin with metronidazole. Vancomycin, with or without a third-generation cephalosporin, is reserved for toxic patients or when the local resistance patterns suggest a high level of resistance of staphylococcal species to clindamycin. Ultimately, initial therapy should be guided by local antibiotic resistance patterns. There are reports in the literature of clindamycin failure in patients in whom initial culture results showed staphylococcal and S*treptococcus agalactiae* isolates susceptible to clindamycin. This has since been found to be related to inducible resistance, which can be assessed with the D-zone test. All isolates demonstrating erythromycin resistance should be assessed for inducible resistance. Not all strains of staphylococcus resistant to macrolides demonstrate inducible resistance, but those strains with D zone positivity should be assumed to be resistant to clindamycin and alternate agents should be used. Currently, many laboratories utilize automated bacterial identification and antibiotic susceptibility systems, which reflexively assess for inducible resistance if macrolide resistance is identified, and report the isolate as clindamycin resistant if this is positive. In recent reports, the prevalence of inducible clindamycin resistance in isolates from soft tissue infections has been shown to be between 1.3% and 35%, although neither of these studies were specific to pediatric head and neck infections.[23,24] Walker et al. reported 35% of methicillin-susceptible *Staphylococcus aureus* isolates and 14% of MRSA isolates from pediatric neck abscesses resistant to clindamycin.[5] Johnigan et al. in 2003 reported six of seven patients with erythromycin-resistant clindamycin-sensitive isolates, suggesting that this may become an relevant clinical conundrum as these patients are susceptible to developing clindamycin resistance during therapy.[25]

## Surgical

The indications for surgery versus observation or needle aspiration are not always clear. Certainly, when there is an abscess in the setting of airway compromise, sepsis, or morbid complication such as mediastinitis, then surgery is necessary, even lifesaving. However, most children do not have such a severely ill presentation, and it is not always clear when to proceed.

### *Needle Aspiration*

Needle aspiration, with or without catheter drainage, has been shown to be a viable option in pediatric patients with uniloculated neck abscesses[10,26] Potential advantages include minimal or no scar, mitigation of the risks of open surgical drainage, and ability to perform under local or with minimal sedation in older children. Another series of 35 patients showed that in patients with suppurative cervical lymphadenitis, needle aspiration successfully treated all of them with no complications.[10] Several required repeat aspiration. Topical anesthetic agents are ideally placed prior to the procedure. Toddlers and young children may require conscious sedation, whereas older children and adolescents can often be calmed with behavioral techniques.

### *Incision and Drainage*

Open approaches to deep neck space infections can either be via a transoral or transcervical route, dictated by the involved space and the extent of the abscess.

Infections of the peritonsillar space can be treated with transoral needle aspiration or incision and drainage. In the older cooperative patient, this can be tolerated in the clinic or emergency room setting. Retropharyngeal space abscesses and parapharyngeal space abscesses medial to the great vessels may also be accessed transorally. A simple mucosal incision followed by blunt dissection into the abscess cavity will suffice. Transoral approaches are not amenable to drain placement, although an ellipse of mucosa may be taken to slow closure of the wound.

The transcervical approach is the traditional approach for most deep neck space infections, especially suppurative lymphadenitis of the lateral cervical lymph nodes, parapharyngeal space abscesses lateral to the great vessels, and abscesses of the submandibular space. The incision is oriented parallel to relaxed skin tension lines. In the neck, this involves a horizontal incision preferably in a skin crease if one is visible. The incision should be made as small as possible while assuring it is long enough to facilitate safe exploration and drainage. Dissection and identification of normal structures may be difficult secondary to infection and inflammation. Preoperative imaging is helpful to guide the surgical approach. When possible, blunt dissection is used to minimize potential insult to neurovascular structures. When the abscess cavity is located, purulent material should be sent for aerobic and anaerobic cultures. The cavity should be explored with finger dissection to break up loculations. Curettage of the abscess "rind" may facilitate blood flow to the cavitated area and aid in diagnosis of atypical infections. After the cavity is thoroughly irrigated, a surgical drain may be placed to prevent repeat accumulation of infected fluid and allow for gas exchange. A passive drain such as a Penrose or rubber band drain is usually sufficient. A closed suction drain may be appropriate in a particularly large cavity to prevent hematoma, seroma, or purulent fluid accumulation. This drain is usually left in place 24 to 72 hours and removed after the patient demonstrates clinical improvement.

## COMPLICATIONS

The vast majority of deep head and neck space infections are managed without significant life-threatening complications. The complications that can arise, however, are potentially devastating and need to be on the radar of every clinician caring for these patients. One review noted that the major complication rate was just under 10% and that predisposing factors included younger age, retropharyngeal abscess, and *Staphylococcus aureus* infection.[27]

Airway compromise is the most immediate of the complications related to pediatric deep neck space infections. Because children often decompensate rapidly, a high index of suspicion must be had. Signs of impending airway compromise, such as tachypnea, stridor, retractions, lethargy, require swift intervention to secure the airway. Intubation with an appropriately sized tube is the preferred method of airway management, but tracheostomy may be necessary and lifesaving. The controlled setting of the operating room is the preferred location for airway management if the child can be safely and expeditiously transferred from the clinic or emergency room.

Mediastinitis is another known complication of deep neck space infection. It has been attributed to the virulence of MRSA isolates that are seen in ever-increasing numbers.[27,28] Children with mediastinitis will clinically worsen despite appropriate antibiotic therapy and can quickly develop cardiovascular compromise. Surgical drainage of the mediastinum in combination with prolonged appropriate antibiotic therapy is necessary for appropriate control. A transcervical approach may often be sufficient, especially in infections that do not extend inferior to the tracheal bifurcation.[29] If a transcervical approach is not deemed to be sufficient, a video-assisted thoracoscopic surgical approach or midline sternotomy approach may be necessary. Mortality rates are not well defined, but the literature would suggest that it is less in children than in adults.[28]

Septic thrombophlebitis of the internal jugular vein, also known as Lemierre's syndrome, is another rare complication of deep neck space infections, with an incidence of <2.3 per million.[30] Primarily associated with infections of the tonsils, pharynx, and lower airways, this syndrome presents with a septic picture, facial swelling, and pain in the setting of recent infection. *Fusobacterium necrophorum* is the primarily pathogen responsible, but other organisms have been implicated including MRSA.[31] Diagnosis can be made by evidence of a filling defect on contrast-enhanced CT or ultrasonographic evidence of a thrombus in the internal jugular vein. Treatment consists of systemic antibiotics. The role of anticoagulation is controversial.[32] Anticoagulation is often used in cases of septic thromboses at other anatomic sites, but the low incidence of Lemierre's syndrome prevents adequate data.[33] Ligation and resection of internal jugular vein are reserved for refractory cases that demonstrate persistent embolic phenomena or progression of the thrombosis. Mortality is between 4% and 18%.[30]

Carotid pseudoaneurysm or rupture is a dangerous but extremely rare complication. Signs and symptoms include a pulsatile neck mass, Horner's syndrome, compromise of cranial nerves IX–XII, cervical ecchymosis, or even bright red blood from the nose, mouth, or ear. Treatment is primarily endovascular but may also require immediate surgical ligation of the carotid.

## CONCLUSION

In summary, deep neck space infections are commonly encountered by otolaryngologists who treat children. Understanding the anatomy and microbiology facilitates appropriate treatment decisions, limiting the potentially devastating complications of these infections.

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CHAPTER

53

# Overview of Neck Masses

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## INTRODUCTION

The majority of neck masses in children are benign or inflammatory lesions. This is vastly different from adults, in whom a neck mass is considered malignant until proven otherwise. The differential diagnosis of a neck mass in a child typically falls into one of three main categories: congenital, inflammatory, and neoplastic (benign and malignant). The location of the mass in the neck can also further narrow the list of possible diagnoses (Table 53.1).

A review of 446 pediatric neck masses at a tertiary center in 1988 reported congenital lesions (54%) as the most common, followed by inflammatory lesions (27%), then malignant neoplasm (11%), and benign neoplasms (8%).[1] Neck masses were found to be malignant in approximately 1 in 10 patients. However, the incidence of inflammatory lesions was probably underestimated in this study, as only masses that required surgical excision or biopsy were included in the study. Reactive lymphadenopathy is extremely common in children, and rarely requires biopsy. Malignant neck lesions are rare in children, but it is important to be vigilant in children with risk factors for malignancy. Five to ten percent of malignant tumors in children are reported to originate in the head and neck area.[2]

**Table 53.1:** Diagnosis of pediatric neck mass by category and location

| *Type/location* | *Midline* | *Anterocervical* | *Posterocervical* |
|---|---|---|---|
| Congenital | Thyroglossal duct cyst<br>Ectopic thyroid<br>Dermoid cyst<br>Vascular malformation<br>Thymic cyst | Branchial cleft anomaly<br>Vascular malformation<br>Hemangioma<br>Fibromatosis colli<br>Transverse process of C2 | Vascular malformation<br>Hemangioma |
| Inflammatory | Lymphadenitis thyroiditis | Lymphadenitis<br>Sialadenitis<br>Atypical mycobacterium<br>Tuberculous<br>Traumatic (nodular fasciitis, hematoma) | Lymphadenitis |
| Neoplastic (benign & malignant) | Thyroid<br>Parathyroid teratoma | Lymphoma<br>Sarcoma/fibrosarcoma<br>Carotid body tumor<br>Metastatic (rhabdomyosarcoma, neuroblastoma) | Lipoma<br>Lymphoma<br>Sarcoma/fibrosarcoma<br>Metastatic (rhabdomyosarcoma, neuroblastoma) |

The importance of a thorough history and physical examination in a child with a neck mass cannot be overstated. Radiologic tests are helpful adjuncts in establishing a diagnosis, but they should never replace the clinical history and examination. A systematic approach is essential in the assessment of a pediatric neck mass. Certain caveats of the history and clinical examination can provide clues to the etiology of the mass, and direct diagnostic studies required to confirm the diagnosis.

## HISTORY

Although the history may not provide the exact diagnosis, it can help differentiate the lesion into one of the categories described above. Paramount elements of the history include:

1. Age of onset
2. Duration of symptoms
3. Mass-related symptoms
4. Presence of systemic symptoms.

A neck mass present at birth is congenital, although some remain unnoticed until acutely infected, resulting in a sudden increase in size in early childhood. Such masses include lymphatic malformations, thyroglossal duct cysts, and branchial cleft cysts. Malignant lesions are more often encountered in older children. The mean age for diagnosis of branchial cleft cyst is reported as 3.6 years, whereas that of lymphoma is 11.7 years.[1] It is important to appreciate that the age of presentation for many pathologies overlap.

Rapid growth of a lesion over a 24- to 48-hour period associated with fever may be suggestive of an infectious process, such as reactive lymphadenitis or neck abscess. Hemorrhage into a congenital lesion caused by trauma may also have a similar presentation. Steady growth of the lesion over a period of 4 to 8 weeks should be concerning for malignancy, such as lymphoma, especially if systemic symptoms of fatigue, weight loss, and night sweats are also present. Slow or fluctuating growth is usually more suggestive of a benign or inflammatory process.

If an inflammatory etiology is suspected, a recent history of infection elsewhere in the body, foreign travel, and sick exposures should be obtained. Cervical reactive lymphadenitis usually presents after gradual regression and resolution of a treated primary infection in the head and neck. Pain at the site of the mass, dysphagia, and limited neck motion may all suggest an inflammatory component. A history of exposure to cats, farm animals, insects, and individuals with tuberculosis is important in evaluating for uncommon infective and granulomatous processes including cat scratch disease (*Bartonella henselae*), primary tuberculosis, atypical mycobacterium, and tularemia.

A thorough family history is important to evaluate for genetic and familial disorders associated with cervical masses. Benign congenital cysts are seen in branchio-oto-renal syndrome.[3] The familial MEN II (multiple endocrine neoplasia) syndromes are associated with medullary thyroid carcinoma.[4] Certain individuals may have a higher risk of malignancy, and this should be elicited in the history. Immunocompromised status, history of previous cancer, and ionizing radiation treatment may predispose to malignancy.

## PHYSICAL EXAMINATION

A complete physical examination is essential in any child undergoing assessment for a neck mass. Otologic, nasal, and oral examinations can be easily performed. A "strawberry tongue" and perilimbic sparing conjunctival injection may be signs of Kawasaki's disease.[5,6] The skin should be closely inspected for any cutaneous lesions and primary infective sites. If malignancy is suspected on the basis of history and physical characteristic of the mass (solid, firm, fixed, multiple matted nodes), flexible fiberoptic nasopharyngoscopy and laryngoscopy should be performed to examine the nasopharynx, hypopharynx, and larynx. One sixth of children with a malignant neck mass have a primary lesion in the nasopharynx, oropharynx, or hypopharynx. Focused examination of other body sites (groin, axilla, and abdomen) should be performed for the presence of lymphadenopathy or other systemic processes involving these regions. Splenomegaly may be found in a child with infectious mononucleosis, whereas a heart murmur may be present in Kawasaki's disease.

Examination of the mass in the neck should focus on following features:

1. Size
2. Location
3. Multiplicity
4. Tenderness
5. Color (erythema, purple)
6. Consistency (cystic, solid, fluctuating)
7. Mobility (firm, fixed to overlying skin or deep tissues)
8. Skin changes (fistulae, pits)

Midline neck masses raise the suspicion for a dermoid lesion or thyroid anomaly. Lateral neck masses are more likely to be vascular malformations, branchial cleft anomalies, or lymphadenopathy. Branchial anomalies may manifest as a tract or sinus opening with its position in the neck being a clue to its embryonic origin.[7] Reactive lymph nodes secondary to an oropharyngeal infection are most typically found in the anterior cervical triangle. Such nodes are also usually tender to palpation. Solid masses found in the posterior triangle of the neck are more likely to be associated with malignancy than those found in the anterior triangle. Another area of concern is the supraclavicular region; the most frequent diagnosis of a supraclavicular mass is lymphoma, which accounts for one third of all supraclavicular masses.

The mass should be examined to determine consistency and relationship to surrounding structures. The majority of congenital lesions are cystic, whereas malignant lesions are firm and fixed. Lesions closely adherent to overlying skin may suggest a benign etiology such as pilomatrixoma or nodular fasciitis, or an inflammatory etiology secondary to atypical mycobacterial infection. A purplish hue overlying the skin is also suggestive of atypical mycobacterium infection.[8]

## DIAGNOSTIC STUDIES

Once the likely etiology (congenital, inflammatory, neoplastic) is determined by history and clinical examination, further diagnostic testing can be used to confirm clinical suspicion. It has been shown that in cases of reactive lymphadenopathy, the majority of laboratory tests performed are normal. This questions the cost-effectiveness of such tests in an era of increasing health costs and emphasizes the essential role of clinical history and examination in determining which investigations are necessary.

### Laboratory Studies

Laboratory testing should be lesion specific. A complete blood count with differential is beneficial in cases of inflammation or where malignancy is suspected. In cases suggestive of atypical cervical lymphadenitis, serology testing for Epstein–Barr virus, toxoplasmosis, and *Bartonella henselae* (cat-scratch disease) are indicated. In refractory lymphadenitis and when the clinical history of travel indicates it, serology for cytomegalovirus, tularemia, brucellosis, *Borrelia* (Lyme disease), mumps, coccidioidomycosis, and histoplasmosis should also be considered. A purified protein derivative skin test should be performed in suspected atypical mycobacterial lymphadenitis or tuberculous lymphadenitis. If such a lesion is actively draining, material can also be sent for acid-fast bacillus stain and culture.[8]

Thyroid function tests may be required specific to a suspected thyroid lesion. Liver and renal function tests may be necessary in cases of suspected systemic involvement. Urinary collection for vanillylmandelic acid should be performed if neuroblastoma is suspected.[9]

## RADIOLOGIC STUDIES

Ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are the main radiologic studies that can assist in the diagnosis of neck masses.[10] They should never replace the clinical examination. Imaging may be helpful in delineating the extent of a lesion and assisting in surgical planning. The decision of which mode of imaging is most appropriate is often based on the availability of the study, skilled personnel to read the studies and the provision of pediatric anesthesia and nursing to provide sedation or anesthesia in the case of MRI.

### Chest Radiograph

Plain chest radiographs have largely been replaced by more advanced imaging techniques in the evaluation of a child with a neck mass. However, they are still very helpful in certain cases. In cases suspicious of malignancy, they can help identify pulmonary metastatic disease, and in lymphoma, they can demonstrate mediastinal hilar lymphadenopathy. Cavitatory pulmonary lesions may also be identified in children with chronic granulomatous neck disease.

### Ultrasound

The advantages of ultrasound in the pediatric population are that it is readily available, relatively inexpensive, does not expose a child to radiation, and can usually be performed without the need for sedation or anesthesia. Ultrasound is useful in being able to determine the size of a lesion and characterize the echogenicity of the lesion as cystic, solid, or complex. It can also determine the borders of a mass and help define its relationship to surrounding structures, such as the great vessels.[11]

In cases of lymphadenopathy, it can help determine the size and multicentricity of nodes and determine if an abscess is present. Lymphatic malformations appear as multilocular cystic masses with cyst walls of various thickness. In thyroglossal duct cysts, ultrasound can confirm the presence of a normal thyroid gland. Fibromatosis colli of infancy has a characteristic appearance on ultrasound, depicting its intrinsic relationship to the sternocleidomastoid muscle. In select cases, ultrasound can also be used to perform needle-guided aspiration of neck abscess and needle or tru-cut guided biopsy of neoplasms.

## Computed Tomography

The CT can accurately delineate between solids and cystic lesions, but it is in its ability to establish location relative to other anatomic structures that it remains superior to ultrasound. Vascularity of a mass can also be determined when contrast is used, as can the relationship of the mass to the great vessels. Likewise, thrombus in the internal jugular vein can be identified as a nonenhancing area within the vessel. Neck abscess can also be clearly defined as an area of low attenuation with rim enhancement with contrast. CT is the superior mode of evaluation in evaluating osseous involvement of possible malignant lesions. A major disadvantage of CT imaging is exposure to radiation and the need for sedation in smaller children.

## Magnetic Resonance Imaging

The MRI is vastly superior to CT in the provision of precise soft tissue detail. Also, there is no radiation exposure. It can be very helpful in the differentiation of vascular from lymphatic malformations in the neck. Magnetic resonance arteriography can also be used to assess the vascularity of lesions, such as glomus tumors, and the integrity of the great vessels secondary to mass effect (carotid stenosis, venous thrombosis). The main disadvantage of MRI is that its soft tissue clarity is affected by motion. Thus, young children require sedation or even general anesthesia while undergoing an MRI.

In some cases both CT and MRI are necessary to complement each other and provide maximum soft tissue and bony detail.[12]

## Positron-Emission Tomography

The use of positron-emission tomography (PET) in children with neck masses is largely limited to the assessment of the extent of malignant tumors and in determining their response to treatment. The radionucleotide tracers used in PET rely on glycolytic metabolism, which is the preferred mode of metabolism in tumor cells. Such tumor types include rhabdomyosarcoma, neuroblastoma, and lymphoma.[12]

## Fine Needle Aspiration

Fine needle aspiration (FNA) is widely used in adults in the assessment of neck masses; however, its use is limited in children. Its use is highly dependent on the availability of an experienced cytopathologist and their comfort level in being able to differentiate malignant from benign lesions. FNA can provide preliminary histopathologic diagnosis and better determine the need for a future definitive operative procedure. However, in most cases, general anesthesia is required to perform an FNA on a child, and thus the preferred option of taking a formal open biopsy or even tru-cut biopsy should be considered.[13] In cases, where surgical access to the mass is difficult, FNA and tru-cut biopsy can be performed under radiologic guidance.

## Incisional/Excisional Biopsy

Surgical excision or incisional biopsy may be necessary to establish the diagnosis, particularly if malignancy is suspected. A biopsy is indicated when the diagnosis continues to remain unclear from laboratory and radiologic studies, and if there has been no significant resolution of the mass on medical therapy. Biopsy should be performed earlier if malignancy is suspected. A history of rapid or progressive growth, fixation of the mass to skin or deep neck structures, supraclavicular location, and weight loss or prolonged fever in a child with a neck mass where diagnosis is uncertain warrants biopsy.

Biopsy may be incisional or excisional based on the size and location of the mass and the presumed diagnosis. Excision biopsy, if possible, is performed in cases where surgical excisional is the likely definitive treatment. These are most likely congenital lesions. In the majority of inflammatory lesions, incisional biopsy is performed to get a diagnosis. An exception would be in cases of atypical mycobacterium, where complete surgical resection if possible is recommended.

In cases of suspected malignancy, coordination of procedures requiring general anesthesia among a multidisciplinary team should be performed such as incisional biopsy, central venous line insertion, bone marrow aspirate, and lumbar puncture. Frozen section is recommended at the time of surgical biopsy in such cases, not to make a definitive diagnosis, but to ensure sufficient tissue for pathologic analysis has been obtained.

## CONCLUSION

The differential diagnosis of a pediatric neck mass includes a wide array of congenital, inflammatory, benign, and malignant lesions. The clinical history and physical examination are extremely important in placing the mass in one of these categories and should dictate which diagnostic tests are required to confirm the diagnosis. The majority of neck masses in the pediatric population are congenital or inflammatory in origin, requiring a thorough understanding of embryology and anatomy of the cervical region. The clinician should never overlook a diagnosis because it is less common at that particular age, as considerable overlap may exist. Malignancy represents 11% of all neck masses in the pediatric population and must always be ruled out. A mass that does not respond to treatment or has associated systemic symptoms or unusual findings should be promptly biopsied via a percutaneous or surgical route.

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CHAPTER

# 54

# Congenital Cystic Neck Masses

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## INTRODUCTION

Head and neck masses in children are common and can be congenital or acquired. Inflammatory lymphadenopathy and congenital lesions represent the most common head and neck masses.[1-3] Congenital head and neck masses are the result of misguided embryologic events and developmental remnants that persist after birth. It is therefore imperative that surgeons have a thorough understanding of the relevant embryology and anatomy underlying each type of lesion to achieve correct diagnosis and complete surgical excision. Although the majority of these lesions become evident in childhood, they may present at any time. Thyroglossal duct cysts (TGDCs) are the most common of the congenital head and neck masses, followed by branchial cleft anomalies, teratomas, dermoid cysts, vascular malformations, and lymphatic malformations. In this chapter, we will discuss some of the common cystic congenital head and neck masses, including TGDCs, teratomas, dermoid cysts, and branchial cleft anomalies.

## THYROGLOSSAL DUCT CYSTS

Thyroglossal duct cysts (TGDCs) are the most common congenital lesions located in the neck. A TGDC results from deviation in the normal embryologic development of the thyroid gland. During the third and fourth week of fetal development, epithelium on the floor of the pharynx, in an area that later becomes the foramen cecum of the tongue, invaginates to form a tubular structure known as the thyroglossal duct. The duct then extends anteroinferiorly, close to or through the hyoid bone, to eventually lie at or just below the cricoid cartilage. The distal end of the duct becomes bilobed and further differentiates into the thyroid gland. During the thyroglossal duct descent, the hyoid bone is concomitantly undergoing anterior fusion. The tract usually passes anterior to the hyoid and then hooks around its inferior border to lie in a concavity on its posterior surface before continuing its descent (Fig. 54.1). We have found that when the TGDC tract could be identified in surgical specimens, it was anterior to the hyoid in 72% of cases and posterior in 28%.[4]

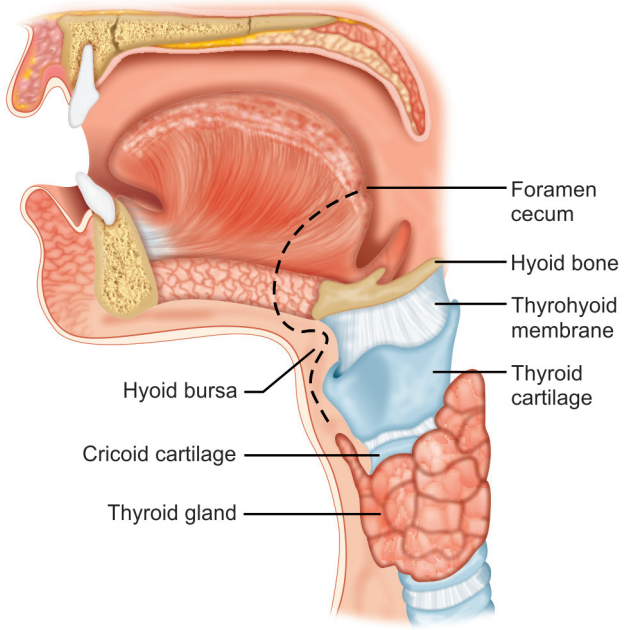



**Fig. 54.1:** Course of the thyroglossal duct. Thyroglossal duct cysts can occur anywhere along this pathway from the foramen cecum to cricoid cartilage.

Thyroid development is complete by the eighth week of gestation. Between the 8th and 10th week the thyroglossal duct obliterates, leaving the foramen cecum at the base of tongue proximally and the pyramidal lobe of the thyroid gland distally. In theory, if viable epithelium of the thyroglossal duct persists, TGDCs can occur anywhere along the duct's natural course from the foramen cecum to the cricoid.

The majority of TGDCs are detected in the first two decades of life, but they can present at any age. TGDCs usually appear as midline cervical masses that either lie directly above the hyoid bone or just below it. Their location, however, may vary; approximately, one third will present as submental or low cervical masses. Less than 1% of TGDCs are located off of the midline. On physical examination, TGDCs appear as smooth, round, firm masses that are approximately 2 cm in diameter (Fig. 54.2). They may move upward during swallowing or tongue protrusion as a result of their intimate relationship with the hyoid. There is no sex predilection.

The diagnosis of TGDC is made after a detailed history and physical examination complimented by radiologic studies. Ultrasonography can identify the cyst and confirm the presence of normal thyroid tissue.[5,6] On ultrasound the TGDC appears round, is hypoechoic, and avascular with Doppler (Figs. 54.3A to C). If a normal thyroid gland is identified and the patient is clinically euthyroid, no further testing is required. If normal thyroid gland is not found, additional evaluation with thyroid function tests and a radionucleotide thyroid scan can assist in determining the activity of ectopic thyroid tissue. In rare instances, a TGDC can represent the patient's only thyroid tissue and thus removal would require the patient to be on lifelong thyroid hormone supplementation.

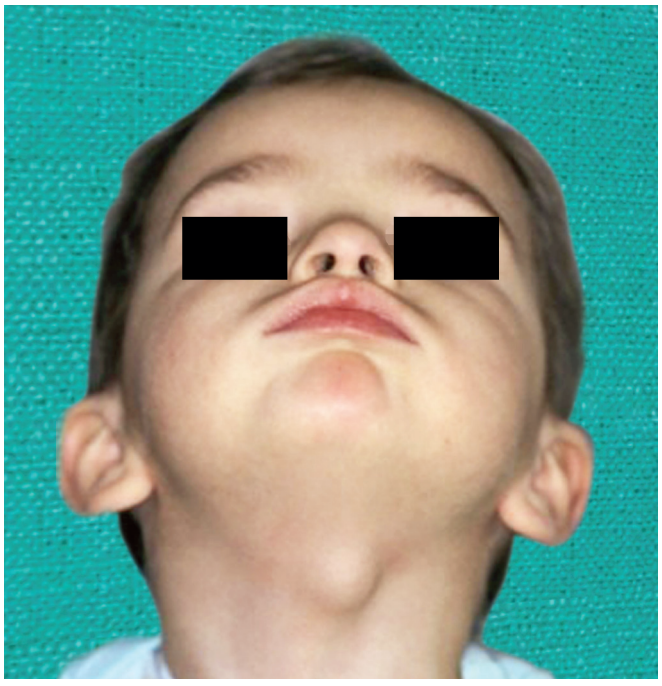


**Fig. 54.2:** Typical clinical appearance of a thyroglossal duct cyst.

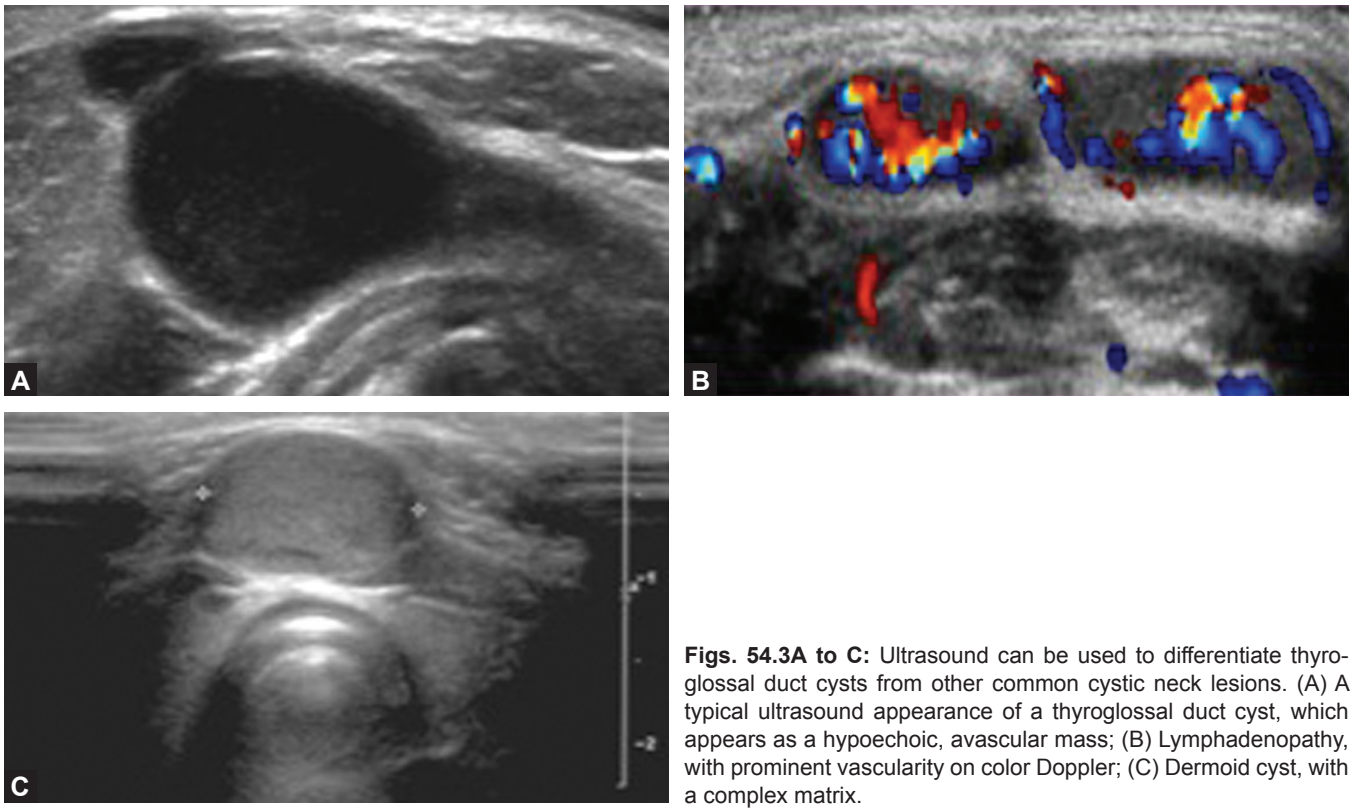
The TGDCs are lined with squamous or respiratory (pseudostratified columnar ciliated) epithelium. Thyroid follicles were present in approximately 46% of specimens where the thyroglossal duct could be identified[4] Malignancies have been reported in TGDCs after excision and histologic analysis, but they are extremely rare.[7] Because of the histologic makeup of TGDCs, malignancies can be either squamous or thyroid in origin.

Timely surgical excision is the mainstay of treatment for TGDCs as they are prone to infection and ulceration. During an acute infection, a large incision and drainage is not recommended due to the increased risk of recurrence following a later complete excision of the cyst. Instead, antibiotic therapy with needle aspiration to decompress the cyst is advised.

Surgical approaches to the TGDC have been developed primarily to avoid complications associated with chronic infection, which usually results in cutaneous fistula. Historically, simple cystectomy or incision and drainage resulted in recurrence rates of > 50%.[8,9] In 1893, based on embryologic principles, Schlange proposed excision of the cyst as well as the central portion of the hyoid bone, thereby reducing recurrence to 20%.[9]

In 1920, Sistrunk first described the procedure that is commonly performed today for excision of the TGDC. Like that of Schlange, his operation was also based on the principles of embryology and included resection of the central hyoid. Sistrunk's procedure differs in that it includes resection of the central hyoid as well as a cuff of lingual musculature oriented toward the foramen cecum. This has proved to the most efficacious way of eliminating recurrences.[10,11] In an extensive review, Mondin et al. performed a meta-analysis of TGDC recurrence rates following Sistrunk's procedures in 950 patients.[7] They reported a recurrence rate of 6.6%.

Reports of recurrent TGDC have noted association with incomplete surgical resection, young age, recurrent infections, intraoperative rupture of the cyst, and histopathologic considerations such as multiplicity of tracts in the suprahyoid region.[9,12,13] In our experience, recurrence




**Figs. 54.3A to C:** Ultrasound can be used to differentiate thyroglossal duct cysts from other common cystic neck lesions. (A) A typical ultrasound appearance of a thyroglossal duct cyst, which appears as a hypoechoic, avascular mass; (B) Lymphadenopathy, with prominent vascularity on color Doppler; (C) Dermoid cyst, with a complex matrix.

can be classified into two categories: (1) that which is suprahyoid and (2) that which is infrahyoid or which involves the bone itself. The presence of multiple suprahyoid microscopic tracts cannot be predicted and can only be addressed with wider resection of the lingual musculature, which is usually accomplished at revision surgery. Complete resection of the middle third of the hyoid bone can be accomplished through an understanding of the posterior hyoid space (PHS) at the time of initial surgery.

The thyrohyoid membrane is classically, but erroneously, depicted as inserting on the inferior margin of the body of the hyoid bone. In actuality its primary insertion is into the pre-epiglottic tissues, where it then reflects and secondarily inserts on the posterior superior rim of the hyoid bone (Fig. 54.4). This has the net effect of creating a cavity between the thyrohyoid membrane and the posterior aspect of the hyoid bone, which we refer to as the PHS. Its boundaries are ventrally, the posterior aspect of the hyoid; dorsally, the thyrohyoid membrane; superiorly, the secondary reflection of the thyrohyoid membrane and its insertion on the superior rim of the hyoid; inferiorly, the caudal rim of the hyoid; and laterally, the lateral aspect of the hyoid bone (Fig. 54.5).

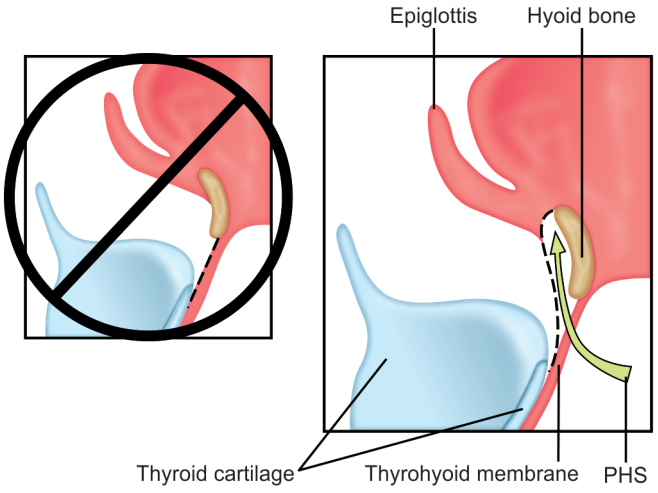



**Fig. 54.4:** Schematic drawing of the base of tongue and upper laryngeal area. The dotted line demonstrates the primary insertion of the thyrohyoid membrane on the pre-epiglottic tissues and its reflection onto the superior rim of the hyoid bone. Arrow indicates posterior hyoid space.

Identification of the PHS allows the surgeon to accurately ascertain the dimensions of the hyoid bone in both the anterior to posterior and caudal to cephalic planes.

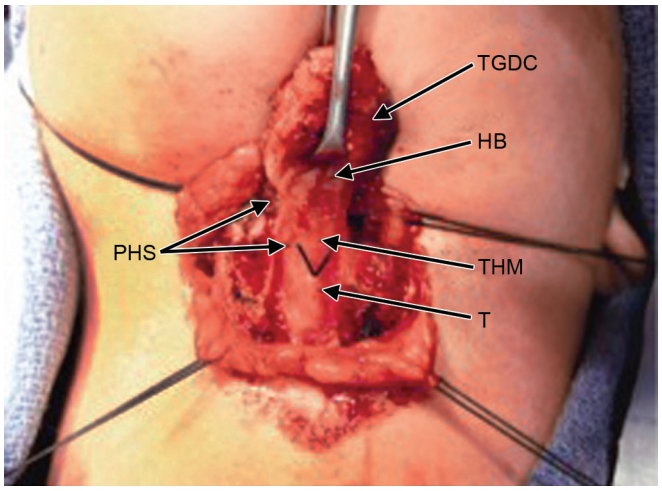



**Fig. 54.5:** Intraoperative photo demonstrating the hyoid bone after transection; the posterior hyoid space is unroofed. The secondary reflection of the thyrohyoid membrane creates a hinge. Note the THM is intact after transection. (HB: Hyoid bone; PHS: Posterior hyoid space; T: Thyroid cartilage; TGDC: Thyroglossal duct cyst; THM: Thyrohyoid membrane).

This maneuver ensures adequate and complete resection of the middle third of the hyoid bone and allows removal of all tissue in the PHS cavity anterior to the thyrohyoid membrane and adherent to the hyoid bone. This is critical in assuring complete removal of TGDCs.

Minor complications associated with the Sistrunk's procedure such as wound infection, seroma, and stitch abscess have been reported to have an incidence between 20% and 30%.[8] Major complications, although rare, have been reported and are limited to neurovascular injury, violation of the airway, and postoperative hematoma causing airway compromise. Exposure of the thyroid cartilage and identification of the thyrohyoid membrane as well as the PHS preclude inadvertent entry into the airway. Transection of the hyoid bone medial to the tendon of the digastric muscle prevents injury to neurovascular structures. Postoperative placement of a drain minimizes the risk of hematoma formation.

## TERATOMAS

Teratomas are a group of tumors that contain all three germ layers (ectoderm, mesoderm, endoderm). They occur in 1:4000 births, with approximately 1% to 3.5% affecting the head and neck. Although for the most part these lesions are benign, malignant lesions have been described infrequently in the literature.[14]

Three theories have been proposed for the origin of teratomas. Acquired implantation suggests that skin or mucous membrane, with its associated mesodermal component, is traumatically implanted into deeper tissues. Congenital inclusion theorizes that incomplete closure of embryogenic fusion lines results in the capture of germ layers into ectopic areas. The third theory proposes that totipotential rest cells from two or three germ layers become isolated and begin independent growth in a disorganized manner.

Teratomas have been categorized into four groups: (1) true teratomas, (2) teratoid tumors, (3) epignathi, and (4) dermoid cysts. True teratomas are composed of all three germ layers with differentiation to the extent of identifying structures such as teeth and hair within them. Teratoid tumors are also composed of three germ layers but are poorly differentiated. Epignathi are similar to true teratomas; however, they display differentiation to the extent of reduplicated fetal parts such as limbs. Lastly, dermoid cysts, the most common teratoma of the head and neck, are composed of only ectodermal and mesodermal derivatives.

Teratomas are rare in the head and neck region and are usually recognized in infancy or early childhood. The most common site of presentation is the cervical region, followed by the nasopharynx.[15] Teratomas in the neck present as large, firm masses (Fig. 54.6). Those found in the nasopharynx are usually pedunculated and skin covered and arise from the soft palate or fossa of Rosenmuller. Teratomas show mixed echogenicity on ultrasound and focal areas of low attenuation and high intensity on computed tomography (CT) and $T_1$-weighted magnetic resonance imaging (MRI). Due to their location and often large size, teratomas in the head and neck frequently present with airway obstruction and respiratory compromise. Timely establishment of an airway via intubation, cricothyrotomy, or tracheotomy is essential even before the diagnosis of teratoma can be made. Once the airway is secured, surgical excision is the treatment of choice.

Teratomas develop in the midline or lateral neck during the second trimester and can rapidly expand. If significant growth occurs before birth, this can result in esophageal and airway obstruction in utero. Esophageal obstruction can lead to polyhydramnios and pulmonary hypoplasia.[16] Large teratomas can be diagnosed on prenatal ultrasound studies, which may lead to further evaluation with MRI. If airway obstruction is suspected, a coordinated multispecialty approach for the delivery of the infant is

necessary. An ex utero intrapartum treatment procedure is arranged to allow for the maintenance of uteroplacental circulation while establishing a secure airway. A timely surgical excision is then the mainstay of treatment.

## DERMOID CYSTS

Dermoid cysts are the most common teratoma in the head and neck. Approximately, 7% of dermoid cysts are found in the head and neck.[17] Unlike true teratomas, dermoid cysts contain only ectodermal and mesodermal elements. They consist of epithelium-lined cavities filled with skin appendage elements such as hair or sebaceous glands. Dermoid cysts occur as a result of entrapment of epithelial components along embryonic fusion lines.

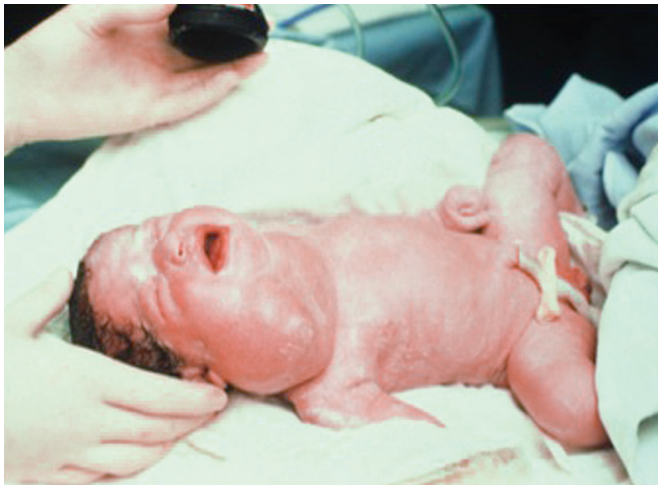


**Fig. 54.6:** Infant with a large cervical teratoma.

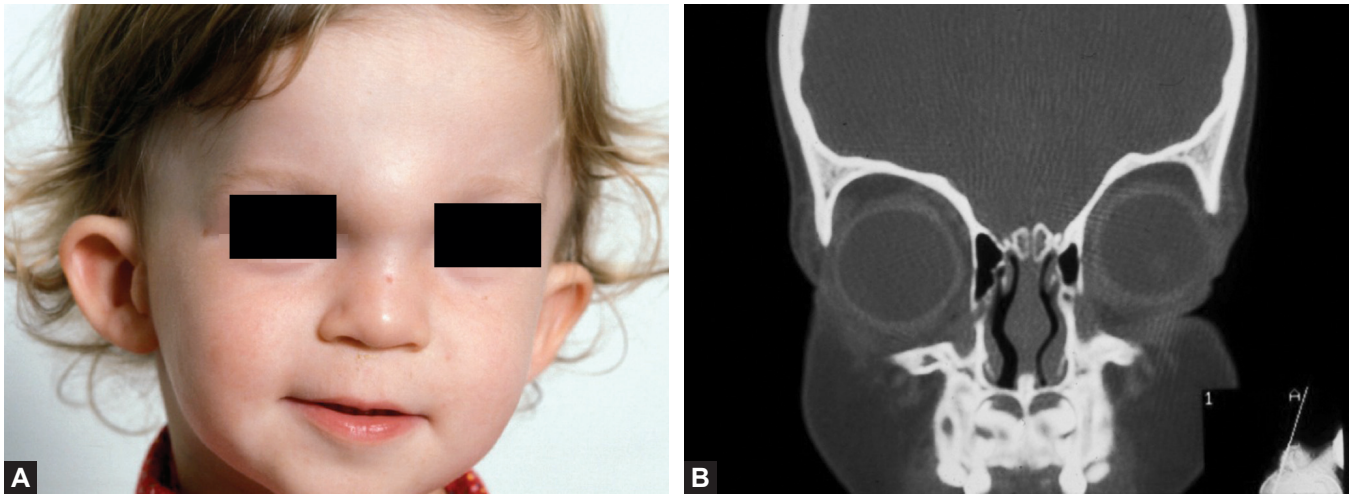
In the head and neck, dermoid cysts are found in the orbit (50%), floor of mouth (23%), neck (14%), and nose (13%). Because nasal and orbital dermoid cysts may have intracranial extension, they should routinely be evaluated with a CT scan or an MRI prior to excision. Although imaging studies are helpful for preoperative planning, diagnosis of dermoid cysts is ultimately made on pathological examination of the specimen.

When infected, lesions with intracranial extension predispose the patient to meningitis or intracranial abscess. Most nasal dermoids have a sinus tract that opens to the skin in the midline anywhere from the glabella to the columella (Figs. 54.7A and B). Cervical dermoids typically present as painless superficial masses that move with the skin. They will gradually enlarge but rarely become infected. Surgical excision is recommended to establish pathological diagnosis, prevent subsequent infection, and ameliorate a cosmetically deforming lesion. With complete surgical excision, recurrence is uncommon.

## BRANCHIAL ANOMALIES

Congenital masses of the laterocervical region are most commonly related to aberrations in the development of the branchial apparatus. A complete understanding of branchial anomalies (BAs) therefore demands study of the underlying embryology of the cervical region.

Development of the branchial apparatus begins in the second week of gestation, and by the fourth week four well-defined pairs of arches are evident.[18] Each arch is composed of mesoderm, which contains a dominant




**Figs. 54.7A and B:** (A) Child with a nasal dermoid cyst. Note the fistulous opening along the nasal dorsum; (B) Coronal computed tomographic scan of the same patient, which demonstrates intracranial extension through the cribriform plate.

**Table 54.1:** Branchial arch derivatives

| *Arch* | *Nerve* | *Muscle* | *Skeletal structure* | *Artery* |
|---|---|---|---|---|
| 1 | Trigeminal (V) | Muscles of mastication, mylohyoid, anterior digastric, tensor tympani, tensor veli palatini | Malleus, incus, portion of mandible | Maxillary |
| 2 | Facial (VII) | Muscles of facial expression, stapedius, stylohyoid, posterior digastric | Stapes, styloid, lesser cornu and upper body of hyoid | Stapedial |
| 3 | Glossopharyngeal (IX) | Stylopharyngeus | Greater cornus and lower body of hyoid | Common/internal carotid |
| 4 | Superior laryngeal | Pharyngeal constrictors, cricothyroid | Laryngeal cartilages | Subclavian (right), aortic arch (left) |

artery, cranial nerve, cartilage bar, and group of muscles (Table 54.1). Arches are separated by ectoderm-lined clefts externally and endoderm-lined pouches internally. In humans, four arches persist and ultimately develop into the structures of the head and neck after remodeling and obliteration of the intervening clefts and pouches.[19] This transformation of the branchial apparatus occurs according to a well-defined pattern and dictates the anatomic relationship of BAs to the nerves, arteries, and muscles of the head and neck.

The first branchial cleft gives rise to the external auditory canal, and along with the first branchial pouch, contributes to the formation of the tympanic membrane. It is the only branchial cleft with a well-defined derivative in the head and neck. Branchial clefts 2, 3, and 4 merge into an ectoderm-lined depression known as the sinus of His. This sinus is typically obliterated during remodeling of the branchial apparatus, and incomplete obliteration of this structure is felt to give rise to most BAs.[20] The first branchial pouch, in addition to its contribution to the tympanic membrane, also gives rise to the middle ear cavity and Eustachian tube. The second branchial pouch forms the palatine tonsil and mucosal lining of the tonsillar fossa. The pyriform sinus is derived from both the third and fourth branchial pouches; the third pouch additionally gives rise to the inferior parathyroid glands and thymus, whereas the fourth pouch gives rise to the superior parathyroid glands.

The BAs comprise 20% of congenital neck masses in children and are the second most common congenital lesion after TGDCs.[19,21,22] BAs can present as cysts, sinuses or fistulae, and are the result of incomplete obliteration of branchial clefts and pouches during embryogenesis.[23]A cyst develops from entrapped remnants of clefts or pouches with no external or internal connection and therefore retains secretions. A cleft sinus maintains an external connection to the skin, whereas a pouch sinus maintains an internal connection to the aerodigestive tract. A fistula arises from incomplete obliteration of both a branchial cleft and pouch, which results in a cavity that communicates with both the skin externally and the aerodigestive tract internally without an interposing mesoderm plate. BAs are named for their arch of origin; their tract will always course deep to the derivatives of their own arch and superficial to those of the next.

The BAs are typically lined with either stratified squamous or respiratory epithelium, reflecting their origin from ectoderm-lined clefts or endoderm-lined pouches, respectively.[18] Cysts have also been known to contain lymphoid tissue, sebaceous glands, salivary, thymic, thyroid, and parathyroid tissue.[23-25]

The prevalence of BAs is equal among males and females.[23,24] Although present at birth, most lesions will not manifest themselves until infancy or early childhood; rarely, initial presentation is delayed until adulthood. Fistulae and sinuses are often evident earlier in life due to associated mucoid secretions and higher propensity for infection.[23,26] Cysts may have a more occult presentation, appearing as soft, fluctuant neck masses at variable locations within the neck. The most common complication of these lesions is infection, often with subsequent abscess formation. In these cases, it is imperative to rule out a communication with the aerodigestive tract to minimize the chance of recurrence after surgical removal.

Diagnosis of BAs can often be made on the basis of history and physical examination, especially when an obvious cleft sinus or fistula opening is identified in the lateral neck (Fig. 54.8). However, the differential diagnosis of a lateral neck mass in the pediatric population is broad and should include lymphadenitis, hemangioma, lymphangioma, laryngocele, sialadenitis, thyroid nodule, thymic cyst, lymphoma, and fibromatosis colli.[1] Malignancy, while rare in the pediatric population, should be a foremost consideration in the adult presenting with a cystic neck mass.

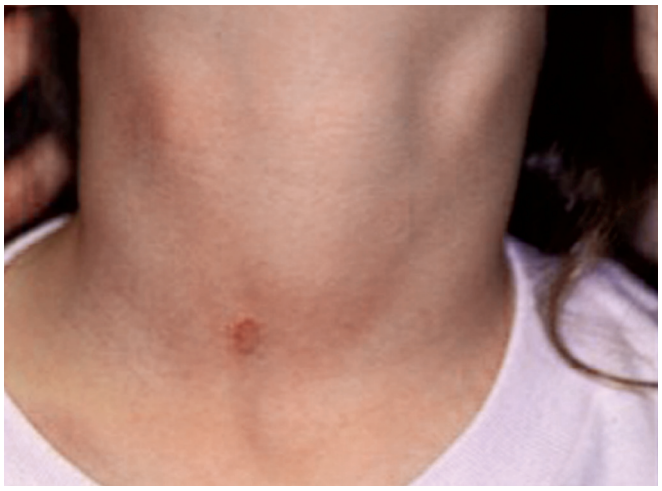


**Fig. 54.8:** Child with a second branchial cleft fistula, as evidenced by fistulous opening anterior to the sternocleidomastoid muscle.

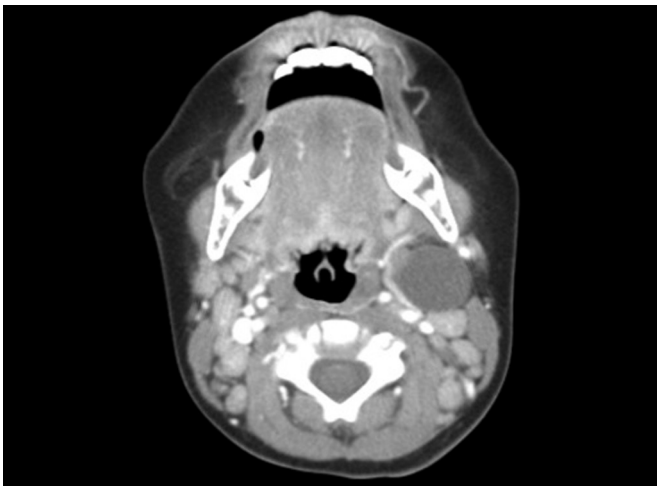


**Fig. 54.9:** Computed tomographic scan showing a second branchial cleft cyst.

Imaging studies can be helpful in differentiating BAs from other lateral neck masses, but they are not without their limitations. CT is the most common modality used, as it can help clearly define the anatomy of a BA in relation to the surrounding normal structures. On CT, BAs typically appear as well-defined, thin-walled lesions filled with homogenous low-attenuating material (Fig. 54.9). In the case of recurrent or acute infection, however, they can be hyperattenuating with a thick, irregular, and enhancing rim.[27] We have previously shown CT to be 81% accurate in the diagnosis of branchial sinuses but only 50% accurate in the diagnosis of branchial fistulae, as imaging typically fails to demonstrate the entirety of the tract.[23,28] Furthermore, CT exposes the child to radiation and often requires the use of sedation in the pediatric population.

On ultrasound, BAs typically appear as well defined, anechoic, or hypoechoic masses with posterior enhancement.[29] Ultrasound is efficient, avoids sedation and radiation exposure, and, with the addition of color Doppler, can help differentiate BAs from lymphadenopathy. However, ultrasound has little utility in defining the tract of a sinus or fistula, and the sonographic appearance of BAs is known to be somewhat variable in the adult.[30] Some authors advocate the use of CT fistulography with barium swallow to define the course of a third or fourth branchial fistula or pouch sinus.[31] However, it is critical that this study not be performed during a time of acute inflammation, as scarring or edema of the fistulous tract will prevent passage of the contrast material and lead to false-negative results. It is currently our practice to use a single imaging modality, either CT or ultrasound, to confirm the diagnosis of a BA when it is in doubt. We do not routinely perform CT fistulography, barium swallow, or direct laryngoscopy and have not found an increased recurrence rate when these studies are not used.[23]

Complete surgical excision is the definitive treatment for BAs. Watchful waiting is not advised, as spontaneous regression does not occur and recurrent infection is common. In our experience, recurrences after surgical resection are most commonly seen in the setting of multiple infections.[23] Our practice is to delay elective surgery until the child is 1 year of age, and after any acute infection has resolved. We have found that failure to identify an epithelial-lined tract on the surgical specimen is the most sensitive predictor of recurrence; this further underscores the need to search for a fistulous tract during surgical dissection, even if one is not found on preoperative imaging studies.[23]

## First Arch Anomalies

First branchial cleft malformations are uncommon; historically, they are reported to account for < 10% of all BAs, but more recent reports suggest this number may be as high as 25%.[32,33] There is nearly a 2:1 female to male predominance.[34,35] They are true duplications of the external auditory canal and have been further classified by Work into Type I and Type II lesions (Fig. 54.10). Type I lesions are cystic and strictly ectodermal in origin, are found medial to the concha and typically extend lateral to the facial nerve to end in the postauricular crease. Type II lesions, which are more common, contain both ectoderm

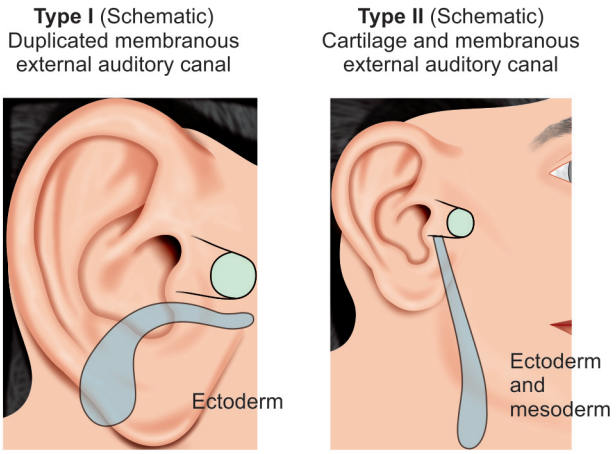



**Fig. 54.10:** Schematic diagram depicting Type I and Type II first branchial cleft cysts.

(skin) and mesoderm (cartilage) and can present as cysts, sinuses, or fistulae. Type II lesions can occur anywhere superior to the hyoid, typically near the angle of the mandible, and are known to have an intimate association with the facial nerve.[36] Most Type II tracts will lie superficial to the main trunk of the facial nerve, but it is not unusual for the tract to course deep or even split the upper and lower branches.[34] Both Type I and Type II lesions are always lined with keratinizing squamous epithelium, in keeping with their ectodermal origin. It is important to note that first BAs have no relationship with preauricular pits and sinuses.

Clinical presentation can vary given the potential for auricular, parotid, and cervical involvement.[24] As such, misdiagnosis is common, and an average of 4 years has been reported between time of initial presentation and definitive treatment.[37] A high index of suspicion and thorough physical examination are therefore required to adequately diagnose these malformations in a timely fashion. In a retrospective study by Triglia et al., 44% of patients with a first brachial cleft anomaly had an obvious fistula in the external auditory canal, and 10% had an asymptomatic membranous attachment between the floor of the external auditory canal and the tympanic membrane.[35] This underscores the importance of careful otoscopic examination when a first branchial arch anomaly is suspected.

The surgical approach to a first branchial cleft anomaly should utilize intraoperative facial nerve monitoring in conjunction with a standard parotidectomy incision and facial nerve dissection. It is rarely necessary to carry the dissection > 1–2 cm beyond the pes anserinus of the facial nerve. Occasionally, the incision needs to be extended into the neck for more complete exposure. If the tract leads into the cartilaginous portion of the external auditory canal, it is our practice to resect a small portion of cartilage and pack the canal for several weeks. Incomplete resection will invariably lead to recurrence. In the series reported by Ford et al., patients required an average of 2.4 operations before achieving cure.[37] Similarly, repeated incision and drainage will also lead to scarring that can make subsequent surgery a challenge and put the facial nerve at risk.

## Second Arch Anomalies

Second branchial cleft anomalies are the most common, accounting for > 90% of BAs.[24] They can present as blind sinuses, solitary cysts, vestiges associated with cartilage remnants, or complete fistulae. Complete fistulae are rare, but when they occur, they are usually right sided and with a female predominance.[28] Bilateral second cleft fistulae should alert the physician to the possibility of an underlying genetic syndrome, such as Branchio-oto-renal syndrome. The fistulous tract opens anterior to the sternocleidomastoid muscle, then penetrates the platysma muscle, and courses lateral to the great vessels. It passes deep to all second arch structures, including the external carotid artery and the posterior belly of the digastric muscle, before terminating in the tonsillar fossa. The tract remains superficial to all third arch structures, including the internal carotid artery and the glossopharyngeal nerve. It is important to note that the caudal two thirds of the fistulous tract demonstrate a clear association with the internal jugular vein, as knowledge of this anatomic relationship can circumvent vascular injury at the time of surgery.[28] Second branchial sinuses follow the same course as the fistulous tract but end blindly, whereas cysts are isolated entities that can be found anywhere along the path described (Fig. 54.11).

Surgical resection requires a lateral neck exploration, including exploration of the carotid sheath up to the lateral pharyngeal wall. The lateral aspect of the hyoid bone, the cartilaginous derivative of the second arch, is used to identify the base of the tonsillar fossa; the fistulous tract is followed cephalad to the hyoid, into its pharyngeal opening and suture ligated. Although many authors advocate a "step-ladder" incision first described by Bailey in 1933, it is our practice to approach these lesions through a single transverse cervical incision (Figs. 54.12A and B).[38]

## Third Arch Anomalies

Third BAs are rare, accounting for only 2–8% of all BAs.[32,37] They are most commonly diagnosed in early childhood as acute suppurative thyroiditis or neck abscess, and approximately 90% occur on the left side of the neck.[25] The tract is similar to that of second tract anomalies, in that it also starts anterior to the sternocleidomastoid muscle. However, the tract of third cleft anomalies passes deep to structures of the third arch, including the internal carotid artery, superior constrictor muscles, glossopharyngeal nerve, and the greater horn and body of the hyoid bone. The tract loops around the hypoglossal nerve and passes through the thyrohyoid membrane, above the internal branch of the superior laryngeal nerve, to terminate in the base of the pyriform sinus (Figs. 54.13A and B).[24]

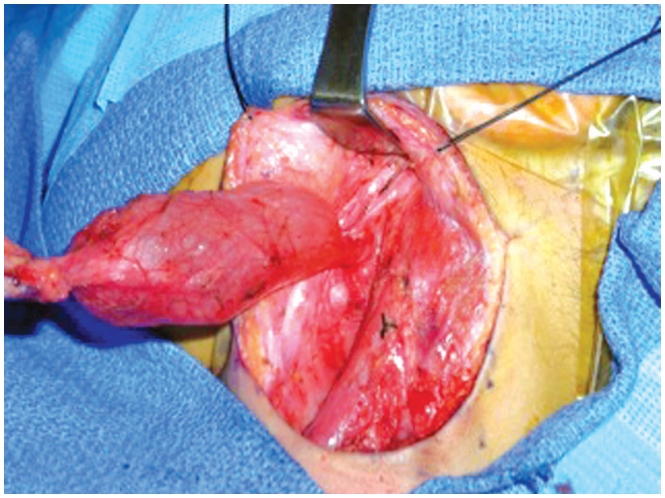
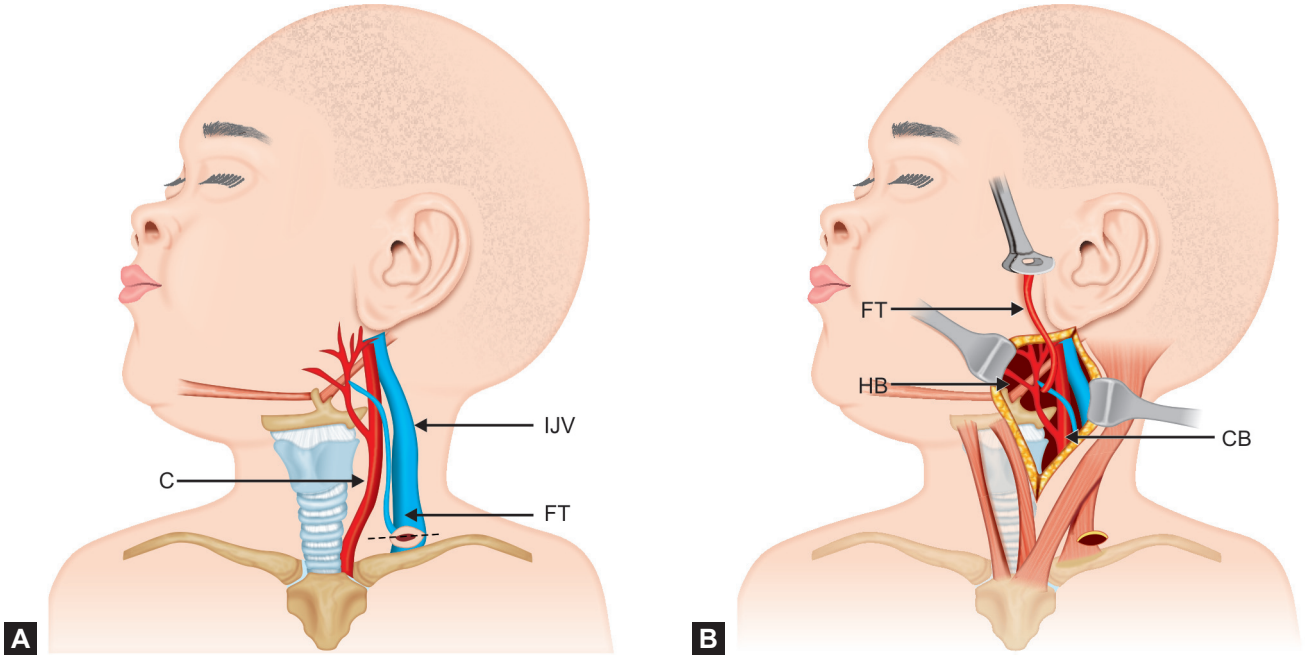


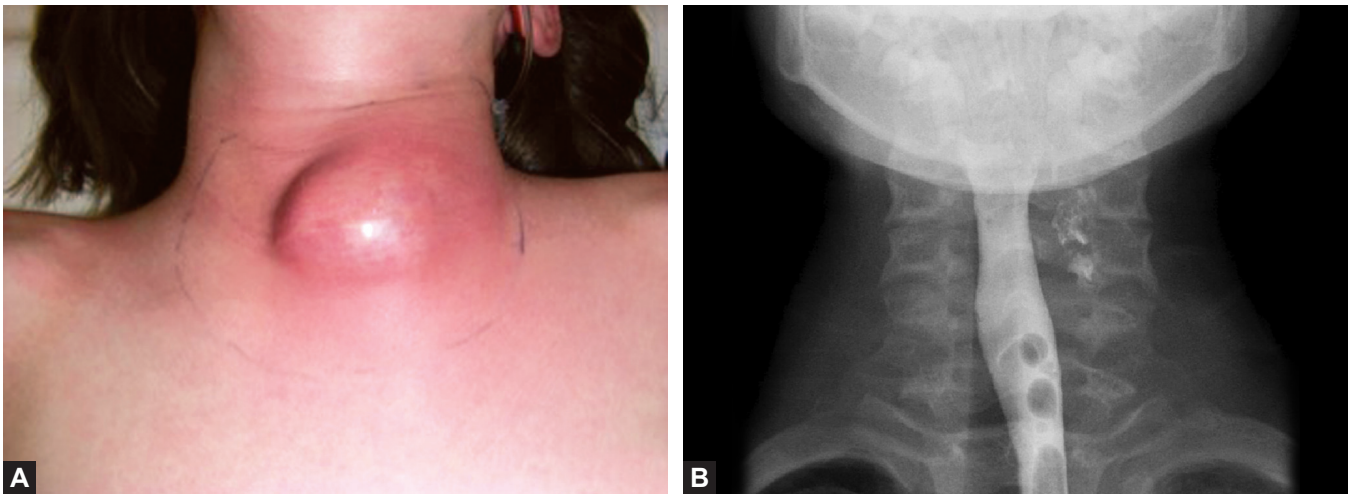
**Fig. 54.11:** Intraoperative photograph of a second branchial cleft cyst, with fistulous tract seen extending between the internal and external carotid artery.

Although early surgical resection is typically the rule in the management of BAs, a systematic review by Nicoucar et al. suggests a higher rate of complications in children under the age of 8, and it therefore may be prudent to delay definitive surgery until later in childhood.[25] Recurrent infections can be managed with antibiotics and incision and drainage when indicated, although the risk of recurrence after this procedure is high.

Transoral obliteration of a pyriform sinus opening has been increasingly reported in the literature and potentially represents a minimally invasive means of treating third and fourth cleft fistulae in the younger patient population.[39,40] Reported recurrence rates after endoscopic cauterization are similar to those seen with open neck exploration,




**Figs. 54.12A and B:** (A) Schematic drawing illustrating the relationship of the caudal portion of the second branchial cleft fistula tract to the internal jugular vein (C: Carotid artery; FT: Fistula tract; IJV: Internal jugular vein); (B) Schematic drawing illustrating the dissection of the second branchial cleft fistula tract. Note: It should be amputated above the hyoid bone (FT: Fistula tract; HB: Hyoid bone; CB: Carotid bifurcation).




**Figs. 54.13A and B:** (A) Child with a third branchial cleft cyst; (B) Esophagram demonstrating extension to the left pyriform sinus.

although numbers are still small due to the overall rarity of these anomalies.[25] It is currently our practice to search for a fistulous opening and cauterize this if present, but we do not advocate cauterization as the sole treatment for BAs. While this practice can lead to a scarring down of the fistulous tract, the lesion itself still remains, as does the theoretical risk for secondary infection. Rather, we advocate tracing the fistulous tract superiorly and amputating it nearly flush with its pharyngeal communication. An exception to this rule occurs in the case of recurrent lesions, in which further surgery is expected to lead to significant morbidity. In this instance, we have used cauterization alone with no evidence of recurrence to date, although the long-term success of this method remains to be seen.

## Fourth Arch Anomalies

Fourth arch anomalies were first described by Sandborn and Shafer in 1972 and are exceedingly rare, although there is recent evidence that their incidence may be somewhat higher than previously reported.[41,42] All reported cases have been left sided, possibly reflecting the more complex anatomical development of the branchial tract on that side.[43] Many authors group fourth and third arch anomalies under the umbrella of "pyriform sinus malformations", but they are anatomically distinct entities. The fourth arch tract originates in the apex of the pyriform sinus, which differentiates it from the third arch tract that originates more cephalad in the base. The fourth arch tract exits the aerodigestive tract through the cricothyroid membrane beneath the superior laryngeal nerve, as opposed to the third arch tract that exits via the thyrohyoid membrane and above the superior laryngeal nerve. From this point the tract of fourth arch anomalies courses inferiorly in the tracheoesophageal groove, posterior to the thyroid gland. On the left it makes a loop around the aortic arch, but on the right this loop occurs around the subclavian artery. The tract then courses superiorly, deep to the common carotid artery, to make a second loop around the hypoglossal nerve before exiting the skin anterior to the sternocleidomastoid muscle.[44]

The presentation of fourth arch abnormalities has been reported to vary based upon patient age.[42] Neonates often present with respiratory distress, whereas older children have the more "classic" presentation of acute suppurative thyroiditis or neck abscess, as seen with third arch anomalies. Cutaneous fistulae are not seen until later in childhood, which suggests that the tract may progress and migrate with age. Misdiagnosis is common given this variable presentation, and barium esophagogram and direct laryngoscopy have been demonstrated to have the highest positive predictive value.[42] As previously discussed, barium esophagram can often lead to false-negative results in the acute phase, and direct laryngoscopy has been advocated to assist in the diagnosis through identification of an opening in the pyriform sinus apex.[32] Treatment options are similar to those discussed for third arch anomalies. Complete surgical resection of the fistulous tract typically requires hemithyroidectomy and often resection of a small portion of the lateral thyroid cartilage, and therefore risks the recurrent laryngeal nerve.

## Thymic Anomalies

Thymic tissue is an uncommon source of pediatric neck masses, but it should be considered in the differential diagnosis. The thymus is primarily derived from the third branchial pouch, with minor contributions from the fourth branchial pouch. Beginning in the sixth week of gestation, the thymus descends into the anterior mediastinum along paired thymopharyngeal ducts, deep to the thyroid gland and sternocleidomastoid muscle.[45] Thymic rests may be deposited anywhere along this path from the angle of the mandible to the midline of the neck, between the common carotid artery and the vagus nerve.

Thymic cysts are uncommon, accounting for only 2% of congenital neck masses.[43] The origin of thymic cysts has been debated in the literature, although they most likely arise from persistence of the thymopharyngeal duct or from cystic degeneration of Hassall's corpuscles.[46] Thymic cysts often mimic second branchial cleft cysts or lymphatic malformations. Imaging, particularly MRI, can be helpful to differentiate these anomalies. Thymic cysts most commonly present as a painless neck swelling, often on the left side of the neck, and a male predominance has been reported.[47] These cysts are found more frequently in the lower neck, and within the carotid sheath. The definitive diagnostic test is histopathological examination, which reveals the pathognomonic Hassall's corpuscles. Excision is the preferred treatment, but the presence of mediastinal thymic tissue should be confirmed prior to surgery to avoid inadvertent removal of the only thymic tissue in a young child, which has the potential to result in serious immune dysfunction.

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CHAPTER

# Lymphatic and Vascular Abnormalities of the Head and Neck

55

***Milton Waner, Teresa O***

In the mid-1980s, Mulliken and Glowacki published their landmark paper recognizing two distinct groups of congenital vascular lesions, hemangiomas and vascular malformations.[1] With this, our understanding of these lesions emerged from the "dark ages". Their "biological" classification has since been modified into what is now the ISSVA (International Society for the Study of Vascular Anomalies) classification of congenital vascular lesions. The importance of correctly identifying a vascular lesion cannot be overstated since the natural history and treatment of these lesions is so different.

The ISSVA classification divides vascular lesions into two groups, vascular tumors and vascular malformations. Vascular tumors include infantile hemangiomas (IHs) and other tumors, whereas vascular malformations are true developmental anomalies.

## VASCULAR TUMORS

### Infantile Hemangiomas

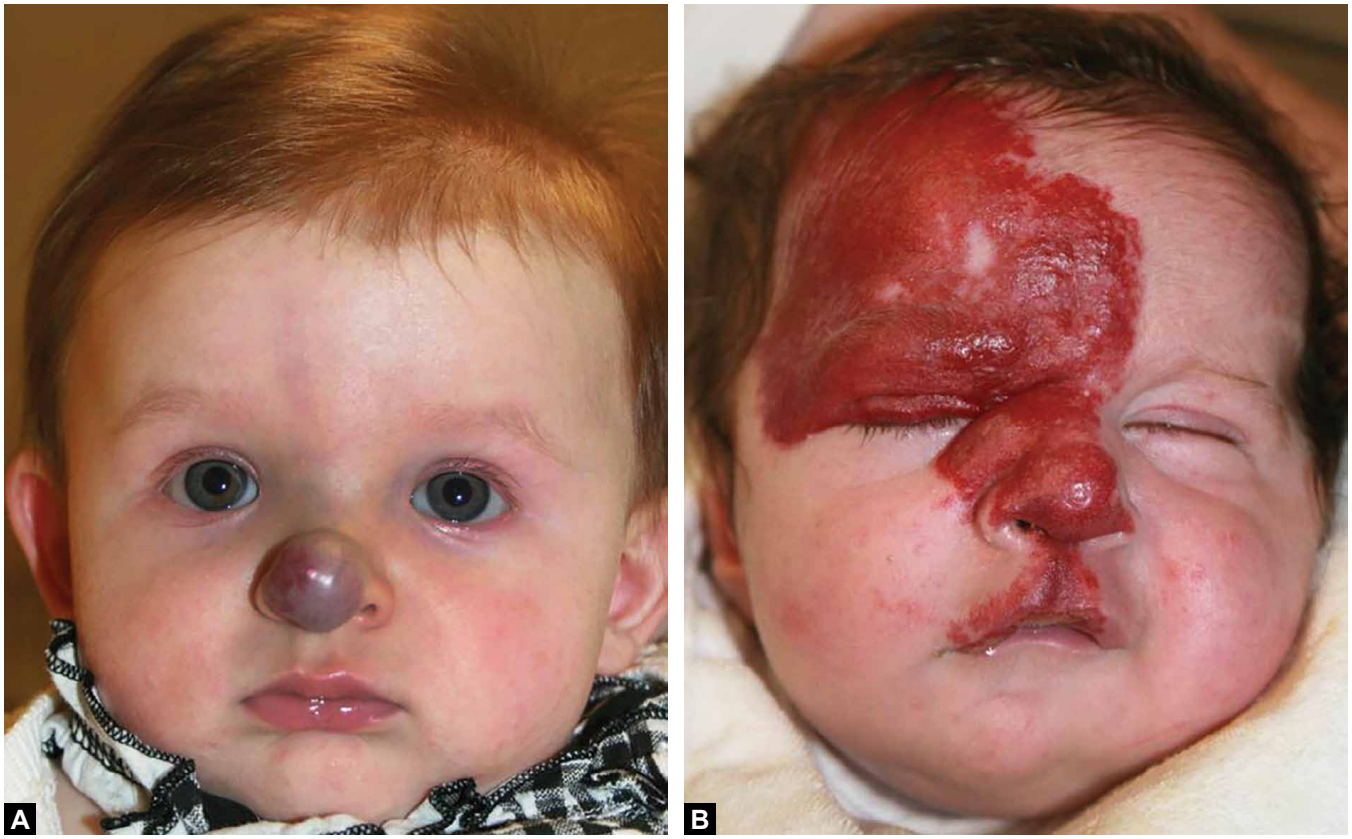
These are by far the most common vascular lesions, occurring as commonly as 1:10 live births. Hemangiomas are more common in females (by a ratio of 3:1), fair skinned infants, premature, and low birth weight infants.[2-4] They are usually not present at birth and present in the first few weeks of life. They grow rapidly at first, but this growth rate slows by about 6 months of age. This is followed by a quiescent period that then merges into a period of involution.[5]

Two distinct types of hemangiomas are recognized, focal and segmental[6] (Figs. 55.1A and B). Focal lesions, as their name implies, grow as solitary tumors, whereas segmental are dermatomal in their distribution and may grow as confluent lesions involving the entire dermatome or as islands of hemangioma distributed across the dermatome. These types of hemangioma appear to be identical both histologically and immunohistochemically, but they are strikingly different in their behavior (Table 55.1). Focal hemangiomas typically make their appearance by the second or third week of life, proliferate for 7 to 8 months, and then involute after a quiescent period of about a year or two. Involution may last anywhere from 4 to 12 years. Segmental hemangiomas on the other hand present at or soon after birth but proliferate for a longer period of time. This may last 12 to 18 months and in some cases, 36 months or even longer. They ulcerate much more frequently (35%), and this may lead to extensive necrosis and tissue loss. Subsequent scarring is almost inevitable.[6]

All hemangiomas involute.[1,7] The process begins anywhere between the ages of 12 months and 3 years and lasts up to 12 years. The number and diameter of vessels decreases and eventually the hemangioma is replaced with a fibrofatty stroma. The hemangioma will physically appear softer, less vascular and begin to shrink.

**Table 55.1:** Focal and segmental infantile hemangiomas

| | *Focal* | *Segmental* |
|---|---|---|
| Appearance | By 2nd or 3rd week of life | At or soon after birth |
| Proliferation | For 7–8 months | For 12–18 months (in some cases, 36 months or even longer) |
| Response to propranolol | Variable | Excellent |
| Ulceration | 8–12% | 35% and may lead to extensive necrosis and tissue loss |




**Figs. 55.1A and B:** Focal and segmental hemangiomas. A child with a focal nasal tip hemangioma (A) and a child with a segmental V1 and frontonasal hemangioma (B).

About 30% of children with segmental IHs will have PHACES syndrome. This is a constellation of abnormalities associated with segmental IHs.[8]

The term PHACES is an acronym for:

- Posterior fossa structural malformations
- Hemangiomas (segmental)
- Arterial anomalies (e.g. agenesis, hypoplasia, and stenosis of vessels)
- Cardiac defects
- Eye abnormalities
- Sternal and other midline abnormalities.

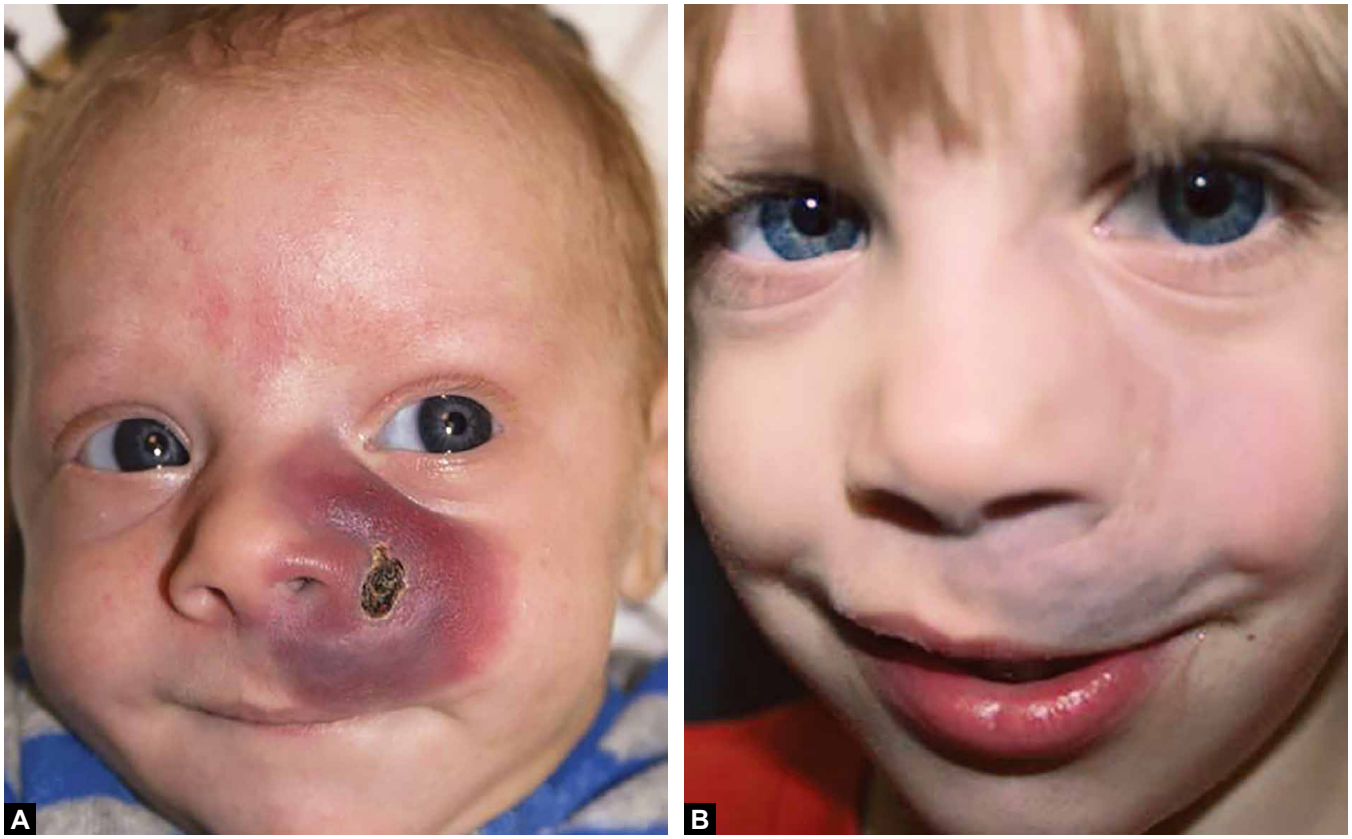
One or more of the above must be present to qualify for the diagnosis of PHACES syndrome.

## Rapidly Involuting Congenital Hemangioma (RICH)

These are congenital vascular tumors that are fully formed at birth. RICHs usually present as firm, highly vascular masses. This vascularity often imparts a purplish discoloration to the otherwise hypopigmented skin (Figs. 55.2A and B). They are high-flow lesions and may precipitate high-output cardiac failure either in utero or after birth. Once the child is born, these lesions begin to involute. This process is usually complete by 18 months of age, and they usually leave extensive atrophy in their wake. The end result is an atrophic indentation. RICHs are GLUT 1 negative.[9]

## Noninvoluting Congenital Hemangiomas (NICH)

These lesions are also fully formed at birth but unlike hemangiomas and RICHs, NICHs never involute. Instead, they are stable over the lifetime of the patient. Observation over the first few months of life will often help distinguish between a RICH from a NICH. A RICH will become softer and may even begin to shrink, whereas a NICH will remain unchanged. NICHs present as firm vascular masses, often more diffuse/segmental in their distribution (Fig. 55.3). The overlying skin is almost always a purplish discoloration, and the lesion feels spongy on compression. These lesions are high flow, and this is evident radiologically as well as on ultrasound. NICHs are also GLUT 1 negative.[9]




**Figs. 55.2A and B:** A rapidly involuting childhood hemangioma (RICH). Note the lesion fully developed at birth (A). A hallmark of this lesion is its rapid spontaneous involution (B).

## Tufted Angioma (+/– Kasabach-Merritt Syndrome)

Tufted angiomas are rare vascular tumors, which may present as a solitary tumor or an erythematous violaceous plaque that may be present at birth or present over the first year of life.[10,11] Spontaneous involution may occur; however, the frequency of this is not documented. Histological examination reveals a proliferation of endothelial cells for-ming lobules with a typical "shotgun" distribution.[12]

Tufted angiomas may be associated with Kasabach–Merritt syndrome (KMS). Clinical findings of KMS include thrombocytopenia, hypofibrinoginemia, and a coagulopathy.[19]

## Kaposiform Hemangioendothelioma (+/– KMS)

Kaposiform hemangioendothelioma is a rare tumor of childhood often associated with Kasabach-Merritt phenomenon and occasionally lymphangiomatosis. Lesions are slightly raised usually covered by cutaneous echymotic hemorrhages.[13] The consistency is usually a firm, brawny edema (Figs. 55.4A and B). If KMS is present, clinical findings include thrombocytopenia, hypofibrinoginemia, and coagulopathy.[12]

These lesions are CD31, CD34, and FLI1 positive and GLUT1, LeY negative, Compared with Kaposi sarcoma's, which are HHV-8 positive.

## Spindle Cell Hemangioendothelioma

These lesions present as superficially located mass, some with Maffucci syndrome.[14] Histology characterized by cavernous blood filled spaces and spindle cells.[15]

## Diagnosis

A diagnosis is almost always made on the basis of history and physical examination. IHs are usually not present at birth and proliferate during the first few weeks of life. A second growth period is often seen around 4–6 months of age. In about 30% of cases, the hemangioma may be

present at birth in the form of a hypopigmented macule or a macule of fine telangiectasia. Regardless of whether or not they were present at birth, all hemangiomas proliferate during the first year of life. Focal hemangiomas grow as well defined lobulated masses and occur in sites of predilection. The hemangioma may be superficial, deep, or compound. A superficial lesion invades the dermis and looks like the classical "strawberry birthmark". A deep lesion will vary from a bluish hue to no discoloration, depending on the depth of the lesion. Segmental hemangiomas are more diffuse and involve one or more of the dermatomal segments. The segment may be densely involved or just sparsely involved, but the growth is diffuse and not tumor like. Thirty percent of head and neck segmental hemangiomas are associated with PHACES syndrome. A thorough physical examination, a cardiological assessment, and a magnetic resonance imaging (MRI) are nece-ssary to investigations to make this diagnosis.

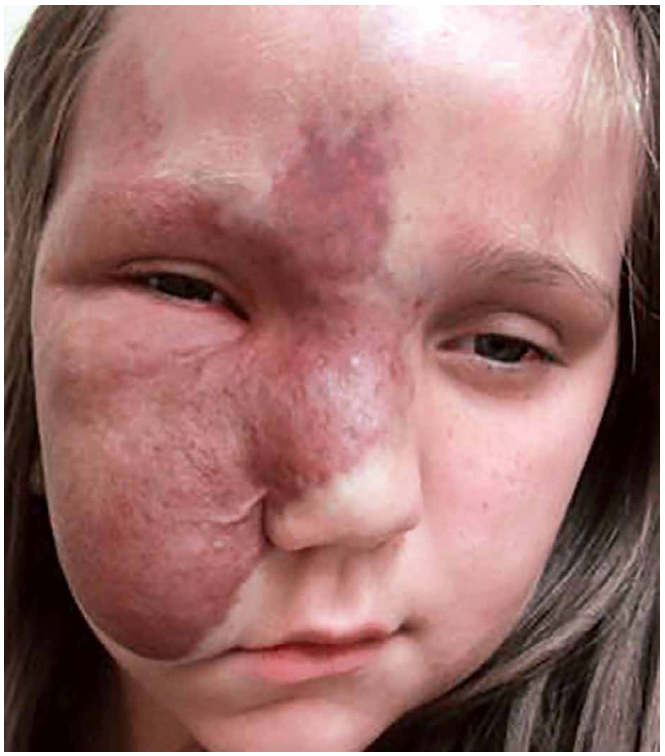
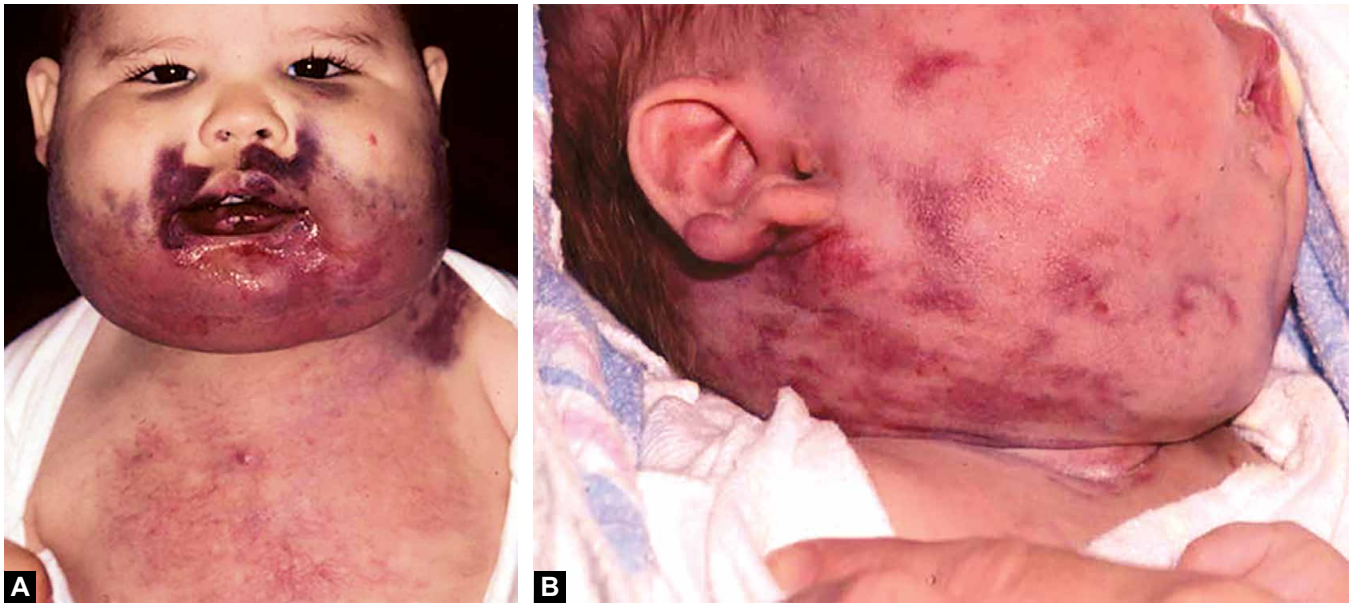


**Fig. 55.3:** A child with a right midfacial noninvoluting childhood hemangioma (NICH). These lesions neither proliferate nor involute.

The RICHs are all present at birth and fully formed. They are often surrounded by hypopigmented skin, but the overlying skin is unmistakably a bluish vascular hue. They never proliferate but instead, slowly involute over a period of 18 to 24 months. NICHs are also present at birth and are clearly vascular but never proliferate and never involute. Kaposiform hemangioendotheliomas are firm tumors that are usually also present at birth. The parotid gland is a common site for these. If KMS is present, ecchymoses are present in the skin overlying the tumor. A complete blood count will demonstrate a low platelet count.

A biopsy is only rarely necessary, but all hemangiomas are GLUT-1 positive. None of the other lesions are GLUT-1 positive, and they have their own unique characteristic.




**Figs. 55.4A and B:** Two patients with Kaposiform hemangioendotheliomas. Both patients have Kasabach-Merritt syndrome. Note the ecchymoses overlying brawny edema.

GLUT-1 is a glucose transporter protein that is highly expressed in most embryonic and fetal endothelial cells. This protein is however lost in all endothelial cells except at blood–tissue barriers such as the placenta and the central nervous system.[16] This finding led to the theory that hemangiomas are derived from placental tissue.[17-19] The current belief is that hemangiomas are stem cell tumors and that the glucose transporter protein is retained due to the fact that these are primitive embryonal tumors. [20-21]

Radiological features of hemangiomas are consistent. They are high-flow, lobulated parenchymatous lesions with intermediate intensity on T1-weighted images and increased signal intensity on T2-weighted images. These lesions retain gadolinium.

## VASCULAR MALFORMATIONS

Vascular malformations are true congenital developmental malformations of the vascular system. They are therefore always present at birth. They do not proliferate, nor do they involute. Instead, slow steady with advancing age is seen. Certain factors such as hormonal changes and trauma can also influence the rate of expansion. Unlike vascular tumors, vascular malformations expand due to hypertrophy of existing structures and not cellular hypertrophy as is the case with hemangiomas.

Vascular malformations are subdivided according to their vessel type. In accordance with the previously mentioned ISSVA classification, there are:

1. Capillary malformations
   a. Port-wine stains (PWSs)
   b. Telangiectasia
2. Venous malformations (VMs)
   a. Common sporadic
   b. Familial cutaneous and mucosal VMs
   c. Glomovenous malformations
   d. Blue rubber bleb nevus syndrome
   e. Maffucci syndrome
3. Lymphatic malformations
4. Fast-flow vascular malformations
   a. Arteriovenous malformations (AVMs)
   b. Arteriovenous fistulae
5. Complex-combined vascular malformations (mixed malformations)

Recent advances in genetic research have demonstrated the importance of genetic mutations in the etiology of these lesions.[22,23] This is a field that was until recently uncharted and in which major advances are expected.

## Capillary Malformations

Port-wine stains are by far the most common examples of vascular malformations. They occur in 1 in 1,000 live births.[24] PWSs present as macular, cutaneous vascular stains which vary in color from a light pink to a dark purple (Figs. 55.5A and B). PWSs are vascular, and therefore, the color will vary during the course of a day, depending on the blood flow through the lesion. They are dermotomal/segmental in their distribution and are caused by dilatation of the postcapillary vessels in the dermal plexus. The absolute number of vessels is not increased.[25,26] This dilatation results from an absence of autonomic innervations, which causes a loss of venomotor tone.[25,27] The net effect of this loss is vasodilatation, which is progressive over the lifetime of the patient. The PWS will therefore darken as the patient gets older.

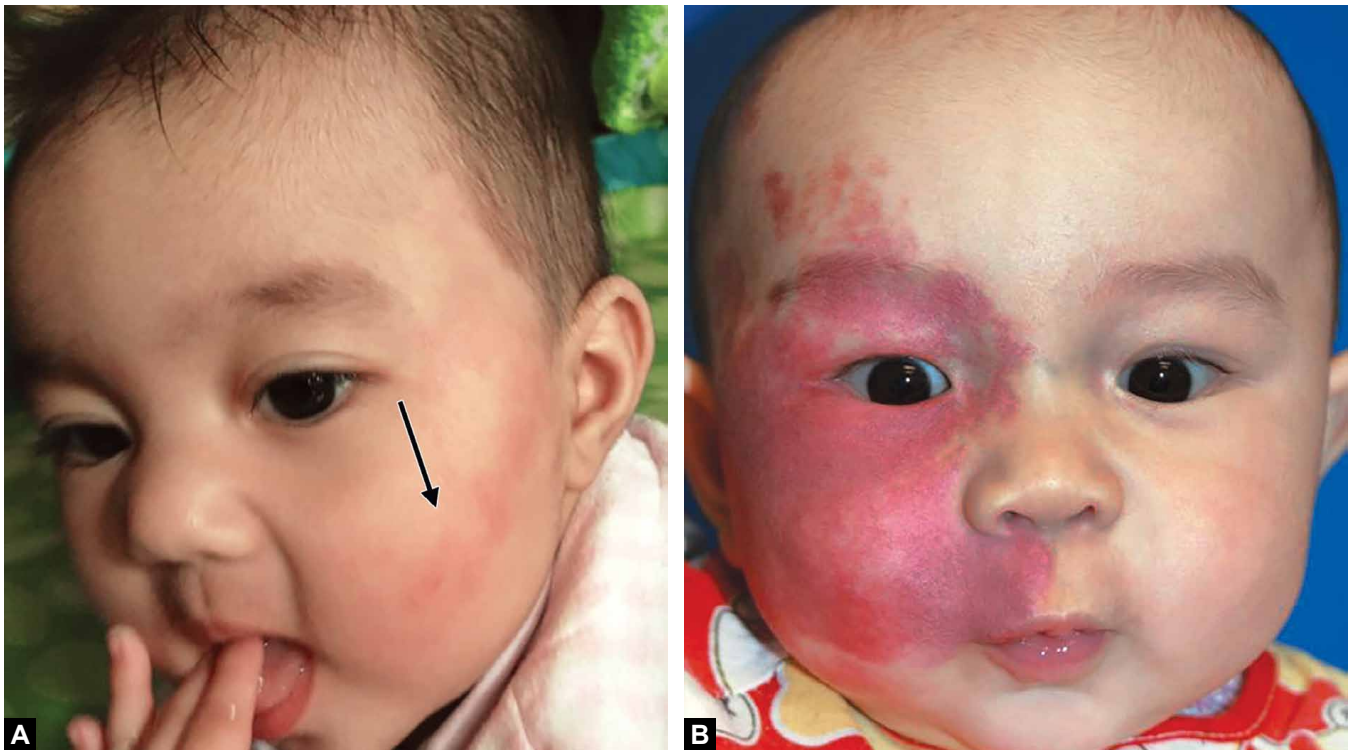
Within the dermatome, the distribution of the vascular stain can vary from being a confluent lesion that involves the entire dermatome (Figs. 55.6A and B) to a geographic lesion made up of scattered islands of staining within an otherwise normal dermatome. In addition to darkening, as the patient ages, around 10% will form nodules or cobblestones, which are made up of focal collections of ectatic vessels (Figs. 55.7A and B).[28]

Sixty percent of PWSs patients develop soft tissue overgrowth, which may affect all or part of the involved dermatome (Figs. 55.7A and B). This involves all of the layers of the dermatome, including bone. Although the cause of this is unknown, we believe that there is a growth signal abnormality wherein the signal to stop growing is absent. The involved tissue therefore continues to grow unabated throughout the life of the patient. This can lead to severe disfigurement.

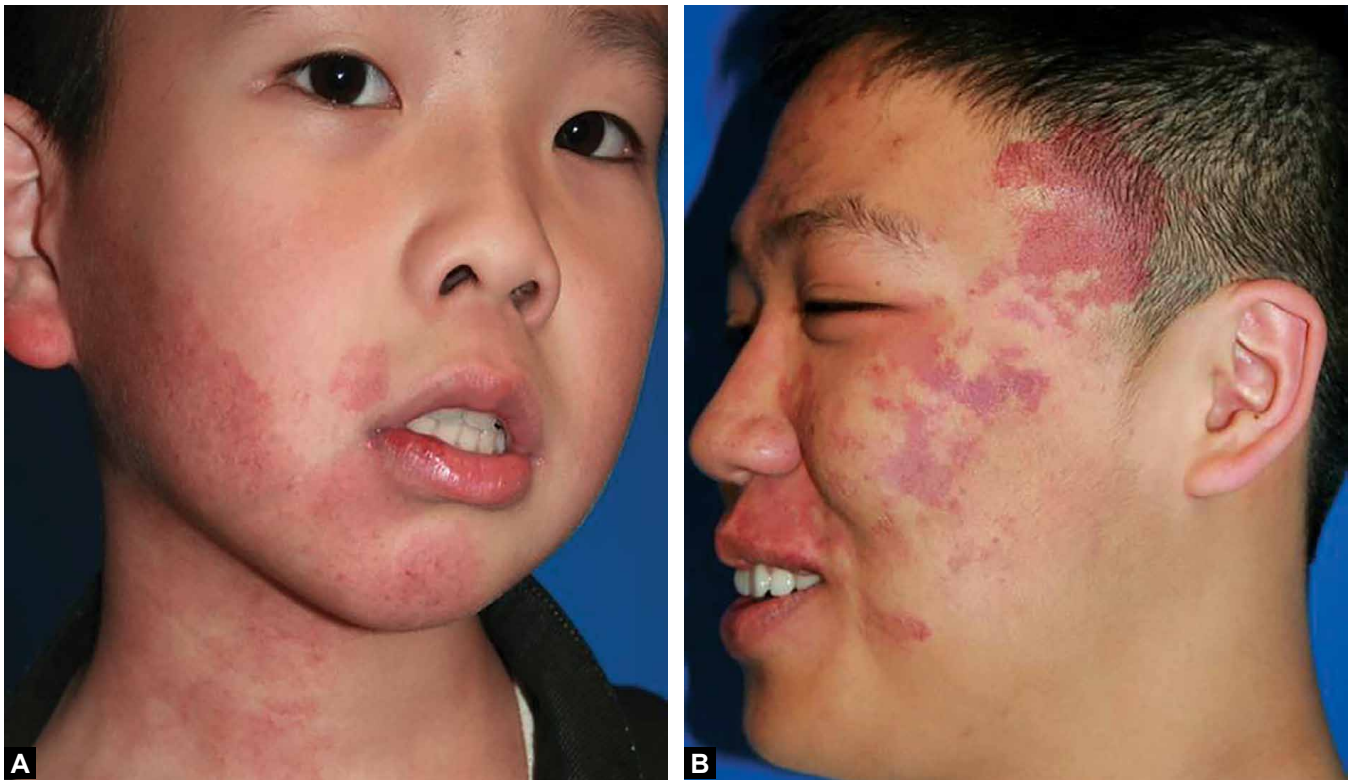
The PWSs may also involve ocular structures, and if left untreated, this may in some cases lead to blindness.[29,30] Patients with lesions involving one or both eyelids (V1 alone or V1 and V2) should be seen by an ophthalmologist for evaluation and follow-up. These patients may develop glaucoma, which, if detected early and treated aggressively, will prevent blindness.

### *Syndromes Associated with Port-wine Stains*

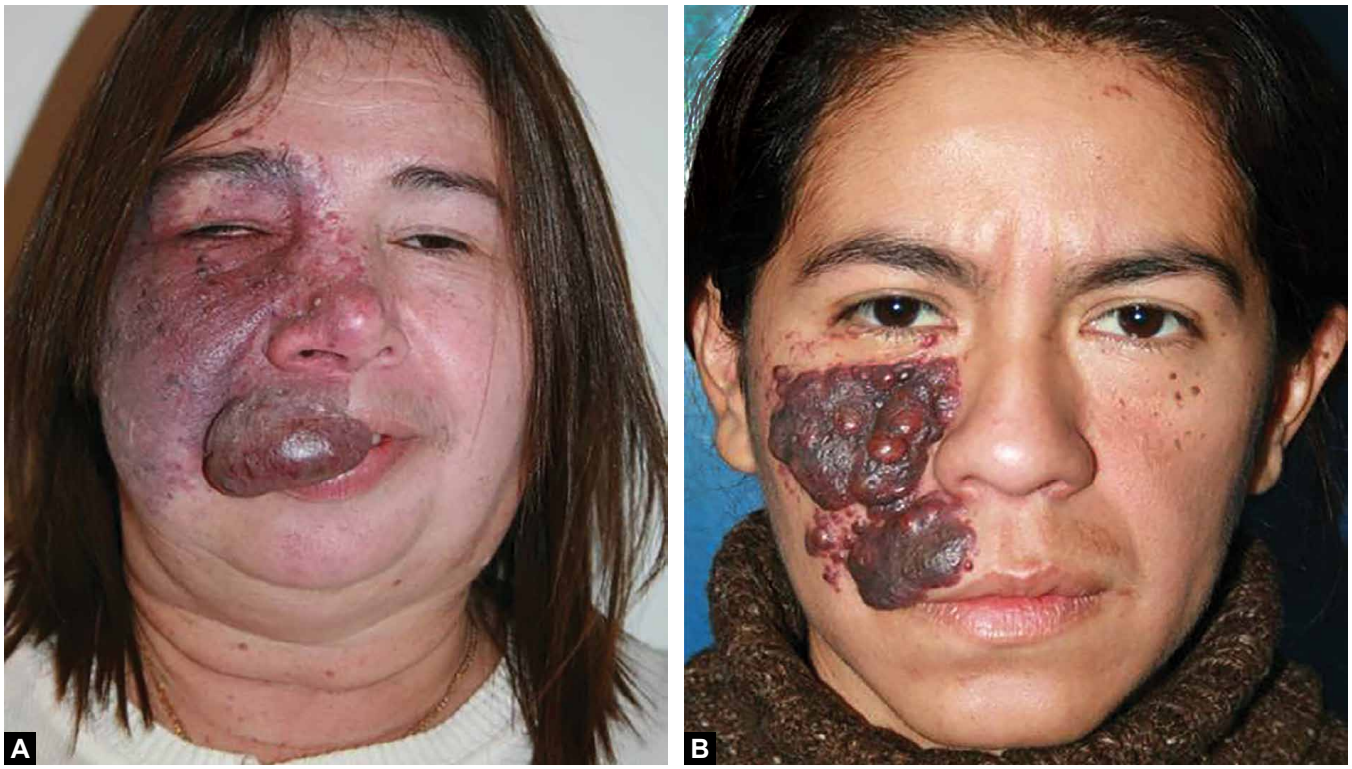
*Sturge-Weber syndrome:* Between 6% and 10% of patients with V1 PWSs will have Sturge-Weber syndrome (SWS).[29,31] The PWS may involve multiple dermatomes of which the VI involvement is part of an extensive lesion or the PWS may involve the VI dermatome alone. This syndrome refers to a triad of findings consisting of a PWS in the




**Figs. 55.5A and B:** Two patients with midfacial port-wine stains. (A) An infant with a very faint (Grade I) geographic lesion (arrow). (B) A confluent (Grade III) lesion.




**Figs. 55.6A and B:** Confluent and geographic port-wine stain lesion. (A) A patient with a confluent V3 and cervical port-wine stain. (B) The patient has a V2 geographic port-wine stain.




**Figs. 55.7A and B:** (A) A patient with soft tissue hypertrophy of the upper lip. (B) A patient with cobblestones and soft tissue hypertrophy. (Reproduced with permission from Waner M et al. Surgical management of vascular malformations. In: Persky MS et al., eds. Vascular lesions of the head and neck: diagnosis and management. New York, NY: Thieme; 2015:102-14).

V1 distribution, a leptomeningeal vascular malformation (ipsilateral), and a choroidal vascular lesion of the eye.

The SWS is characterized by contralateral seizures, hemiplegia or hemiparesis, cerebral atrophy, and mental impairment.[32,33] Developmental delays occur in about half of these patients. Ocular manifestations include glaucoma, choroidal vascular lesions of the eye, coloboma, cataract formation, iris heterochromia, and myopia.

*Capillary malformation–arteriovenous malformation*: This is a rare autosomal dominant lesion caused by a mutation of the RASA1 gene.[23] These patients present with small multifocal capillary malformation that resemble a PWS overlying AVM. These lesions are not segmental in their distribution, and the flow rate of blood through these capillary beds appears to be high.

## Lymphatic Malformations

Lymphatic malformations (LMs) (also known as lymphangiomas and cystic hygromas) result from an abnormality of lymph flow across an area.[34,35] This may be due to an overdevelopment or an underdevelopment of lymph tissue in an area. The net result of this is a slowing of the flow rate of lymph, which results in focal or diffuse edema of the involved area. The clinical manifestation of this is a focal or diffuse mass (Fig. 55.8). If the disease process extends to skin and/or mucosa, this manifests as small lymph and or blood-filled vesicles (Figs. 55.9A and B). These patients can have devastating consequences, including craniofacial distortion, severe functional abnormalities including airway obstruction and dysphagia.[36] Tongue and/or floor of the mouth disease can lead to glossoptosis, and multiple vesicles often leak lymph or a mixture of blood and lymph. LMs can also lead to craniofacial bony distortion, which is due to a mass effect of the malformation and/or bony overgrowth.[37,38] These patients often have dental hygiene issues and an open bite, which, in turn, will lead to drooling, feeding difficulties, and poor speech intelligibility.

Lymphatic malformations are frequently diagnosed in utero. A large craniofacial lesion will alert the treating physician that an airway obstruction is likely and that an exit tracheostomy may be necessary.[39]

## Venous Malformations

Venous malformations (VMs) are a heterogeneous group of disorders that are the result of a developmental error in

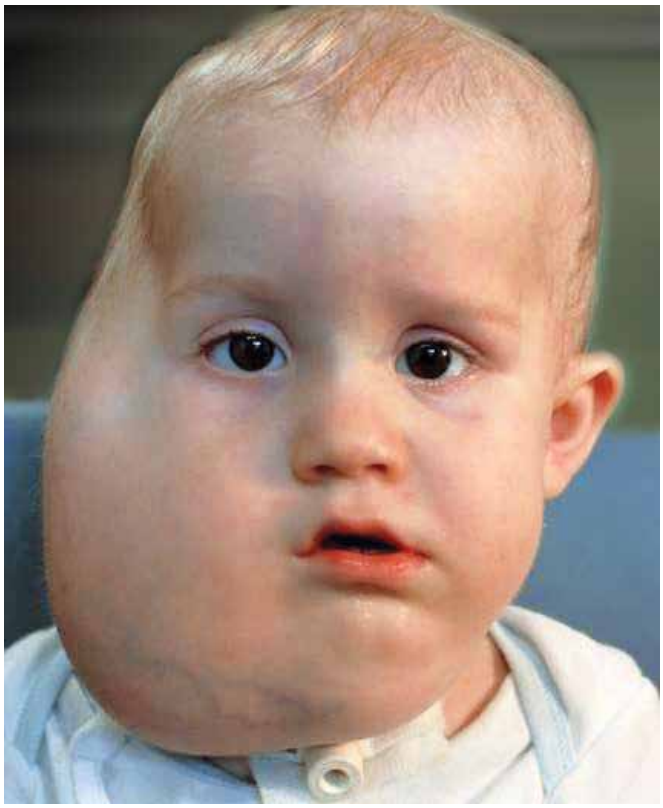


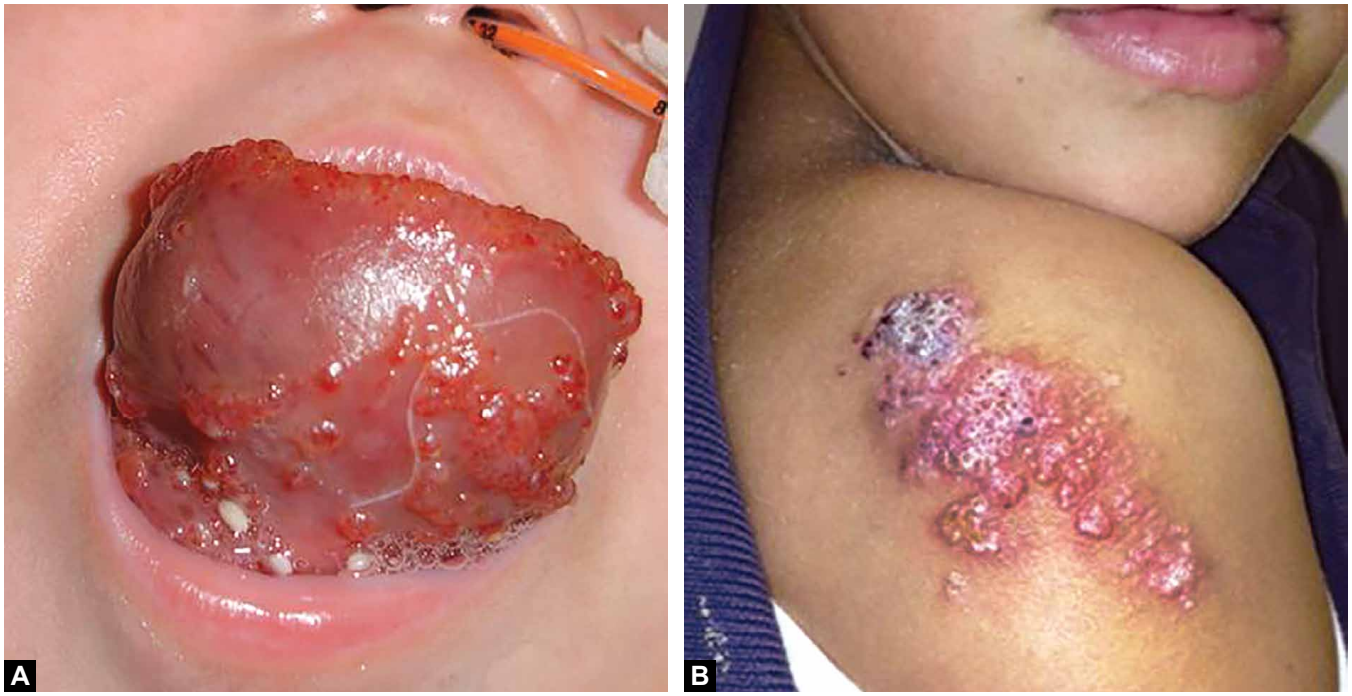
**Fig. 55.8:** A child with a diffuse, microcystic lymphatic malformation.

the development of the venous system. The veins in a typical VM are numerous, thin walled, and dilated. During surgery, these areas appear as honeycombed complexes of thin walled veins that can bleed profusely. The flow rate of blood through this system is significantly slowed and whether this or some other factor is responsible, intravascular clotting may take place. Phleboliths form and these can become inflamed and tender. If the amount of intravascular clotting is extensive, a consumptive coagulopathy may result and this is known as localized intravascular coagulation (LIC).

The VMs may be focal or diffuse, and in 90% of cases, they are solitary (Fig. 55.10). These are sporadic in nature. In 10% of cases, there is a familial factor; 80% of these are Glomuvenous malformations and the remaining 20% are cases of cutaneomucosal VMs (CMVM).

Glomuvenous malformation is an autosomal dominant condition in which glomus like cells are found along the vessel walls of the malformation. These lesions are typically superficial and involve cutaneous and subcutaneous structures. They are painful to palpation in about 50% of cases. CMVMs are multifocal autosomal dominant small (< 5 cm) and involve the head and neck in 50% of cases.

The VMs are typically bluish, soft, compressible lesions that expand when in a dependent position. Phleboliths are




**Figs. 55.9A and B:** (A) Child with macroglossia and diffuse involvement of her tongue with microcystic LM. Note the vesicles on the tongue, a manifestation of mucosal involvement. (B) A child with cutaneous manifestation of a lymphatic malformation, also known as lymphangioma circumscriptum.

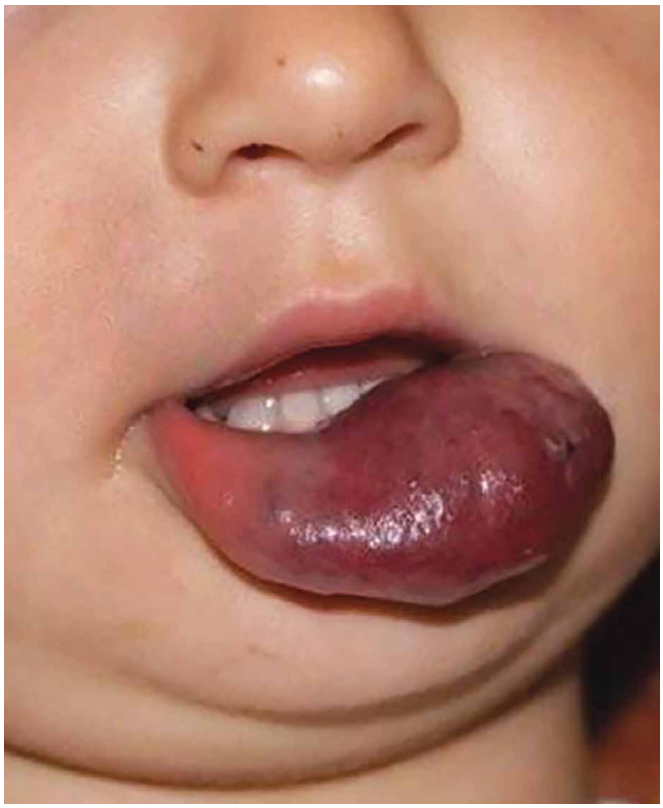


**Fig. 55.10:** A child with a venous malformation of her lower lip. This was initially misdiagnosed as a hemangioma.

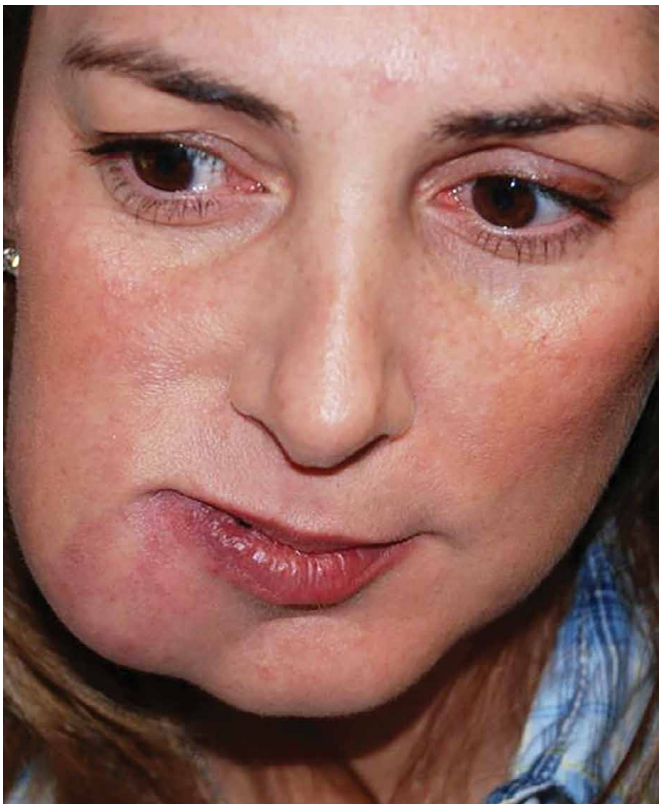


**Fig. 55.11:** A patient with a focal arteriovenous malformation involving a choke zone between the facial artery and the mental branch.

commonly palpated within these lesions and their presence is a diagnostic feature of a VM. A VM involving the face or scalp, with a transcalvarialdural communication with an intracranial sinus is known as sinus pericranium.

Blue rubber bleb nevus syndrome is a rare condition in which multiple small (<2 cm) cutaneous lesions as well as gastrointestinal lesions are present. Severe gastrointestinal bleeding is the major complication associated with this syndrome.

### *Arteriovenous Malformations*

The AVMs are congenital vascular anomalies in which there is abnormal shunting from the arterial side to the venous side of the circulation in a specific area. This takes place across an abnormal capillary bed in which we believe the normal regulatory mechanisms have been lost. This loss of regulation is either due to a loss of the normal precapillary sphincters that control the flow of blood across a capillary bed, or the autonomic control of these sphincters. Loss of this regulation results in continuous shunting of blood across a capillary bed. It is this constant perfusion, which brings about the clinical changes. Constant perfusion results in slow expansion of the capillary bed otherwise known as the nidus. This, in turn, causes venous dilatation and arterial hypertrophy, which are secondary changes. It is important to recognize the difference between the nidus, which is the site of the primary pathology and the secondary changes, which result from the shunting but are not the site of the primary pathology. Any proposed treatment should be directed at the nidus rather than the secondary changes.

The AVMs may be focal or diffuse. Focal lesions commonly occur in "choke zones", which are areas between angiosomes (Fig. 55.11).[40] An angiosome is the three-dimensional blocks of tissue supplied branches of a single-source artery. As an expansion of this theory, we believe that the capillary beds within these choke zones are the primary sites of the nidus. Autoregulation of the flow through these capillary beds is probably most likely to be deficient, and this becomes the nidus of an AVM.

Clinically, AVMs present as firm vascular masses. Although they may not be apparent at birth, they are

always present. Over the lifetime of the patient, they slowly increase in size. Despite the high perfusion rate, tissue ischemia occurs and this in turn may cause ulceration of the overlying skin or mucosa, which puts the patient at risk for infection and bleeding. The vascular mass may or may not pulsate and if the flow through the nidus is considerable, a fluid thrill may be evident within the nidus.

## THE TREATMENT OF HEMANGIOMAS OF THE HEAD AND NECK

### Indications for Treatment

The recognition that focal hemangiomas occur in sites of predilection and that these lesions follow patterns of presentation will facilitate a discussion concerning guidelines for their intervention. Segmental hemangiomas also follow patterns of presentation and their behavior is also often predictable.

As a rule, one should only consider treating a lesion when doing so will offer a distinct advantage to conservative management. Several factors must be considered:

1. An infant's healing environment differs greatly from that of an older child. Infants and very young children produce less TGF-β induced collagen, and therefore less scar tissue. In contrast, older children produce copious amounts of TGF-β induced collagen and hence more scar tissue. In infants, the ratio of TGF-β and TGF-β2 to TGF-β is lower and the collagen quality is fine and reticular with less cross-linking and is laid down more rapidly. The advantages of operating on an infant are therefore obvious. An incised wound in an infant will be more likely to heal with little to no scar tissue than the same wound in an older child. This factor should also influence the timing of any planned surgery or laser treatment.
2. Mesenchymal stem cells are more readily mobilized during the healing process of an infant than in an older child. This also translates into less scarring and underscores the value of treating at a younger age.[41-43]
3. The anatomic location and size play an important role in the decision whether or not to treat. A 2 cm hemangioma on the tip of a child's nose will pose a different problem to the same size lesion at the back of the child's neck.

Lesions to consider for treatment:

- Any facial or clearly exposed hemangioma (60% of IHs involve the central face)
- Any lesion that is unlikely to involute completely and in whom intervention will result in a more favorable outcome
- Any complication warrants treatment. Complications include ulceration, functional impairment, cardiac failure, and disfigurement
- Airway lesions
- Periocular lesions warrant special attention due to their propensity to cause amblyobia.

Once a decision to intervene has been made, the choice of modality will then be made. Three factors are important in this determination.

- The lesion subtype, focal or segmental
- The stage of the disease, proliferating or involuting
- The depth of the lesion, superficial, deep, or compound.

The choice of treatment is best undertaken by a multidisciplinary team. This should include the following specialties: pediatric dermatology, pediatric hematology oncology, interventional radiology, pediatric otolaryngology, head and neck surgery, plastic surgery.

### Medical Treatment

#### *Propranolol*

Propranolol was first introduced in 2008 as a therapy for hemangiomas.[44] Prior to this it was used in the pediatric population to treat hypertension. Since 2008, propranolol has become an extremely popular drug, rapidly surpassing all other modalities. In fact, in the vast majority of centers, propranolol has become the first line of therapy.[45,46] Propranolol is a nonselective β1, β2 antagonist. Its exact mechanism of action is still unknown. The medication is well tolerated and major side effects are limited to bronchospasm and hypoglycemia[47-50] (*see* Table 55.1). There is no consensus on the need for monitoring after the initiation of treatment. Some centers routinely admit children for 24–48 hours, and others do not. All agree that a cardiac evaluation is necessary to exclude a contraindication prior to commencement of therapy. When starting treatment, the therapy should ramp up over a 5-day period to the full dose of 2–3 mg/kg/day divided into three doses.

The duration of treatment will be determined by the type of lesion and its response. In general, segmental hemangiomas have a longer growth period, which can last up to 36 months. To prevent rebound growth, therapy should be continued until this no longer occurs. This may take anywhere between 12 and 36 months. Focal hemangiomas

behave differently and proliferation is, for the most part, done by 10 months of age. Treatment beyond this age is seldom necessary. There is no physiological reason to taper doses when stopping. One simply stops.

The efficacy of propranolol has been extensively reported. Most authors agree that the response rate approaches 100%; however, closer analysis of these articles calls into question the definition of "response". While almost all lesions "respond" showing a reduction in size and discoloration of the overlying skin, the number of lesions that do not completely disappear and require other forms of treatment such as surgery or laser treatment is around 50%.[51] Furthermore, our own experience indicates that the response of children with segmental hemangiomas appears to be greater than that of focal lesions. These data are unpublished at the time of writing this article.

The mechanism of action of propranolol is still under investigation. It appears that the mechanism involves one or more of the following: B adrenergic receptor blockade, which prevents local vasodilatation within the hemangioma, vascular endothelial growth factor and basic fibroblast growth factor inhibition, which prevents endothelial cell proliferation and endothelial apoptosis.[52-55]

Topical beta-blockers have also been reported to be effective in treating very superficial hemangiomas and are considered by some to be an alternative.[56] Several case reports have been published and all report encouraging results however there are valid concerns regarding the bioavailability of the drug in neonates and infants. Timolol gel-forming solution (Timolol GFS), the more popular form, appears to be up to 10 times more potent than propranolol.[57,58] Although precise correlates have not yet been determined, each drop of topical timolol may represent between 2 and 8 mg of oral propranolol. When applied near a mucous membrane or to an ulcerated surface, significant amounts may be systemically absorbed.[59]

Presently, studies are exploring the use and efficacy of selective B1 antagonists.

### *Systemic and/or Injectable Corticosteroids*

Although some physicians still advocate for the use of oral corticosteroids,[60] their role has been significantly relegated by the advent of propranolol. Steroids were the mainstay of IH treatment, and their efficacy was reported to be between 30% and 60%, but their numerous side effects preclude their use as a first-line therapy. These include cell-mediated immune suppression, adrenal suppression, cushingoid features, growth retardation (which lasts as long as the child is on steroids and in some cases appears to be permanent), gastrointestinal irritability, hypertension, and hypertrophic obstructive cardiomyopathy. Steroids are now rarely prescribed and are only used in cases where propranolol is contraindicated.

Intralesional steroids became popular in the mid-1980s due to their reported diminution in systemic side effects. They were especially useful in treating ocular hemangiomas, but the occasional case of central retinal artery occlusion tempered our enthusiasm. Nowadays, propranolol has replaced this form of therapy. Intralesional steroids are still useful for focal hemangiomas that respond poorly to propranolol and as an adjuvant in the treatment of airway hemangiomas.

### *Vincristine*

Systemic vincristine is a microtubule-disrupting agent that inhibits angiogenesis.[61] This drug became popular in cases of steroid failure, or as an adjuvant to steroids where their long-term use was becoming problematic. Vincristine was also useful in treating kaposiform hemangioendotheliomas.[62,63] Side effects include a drug-induced peripheral neuropathy, constipation, hyponatremia, and hair loss. Nowadays, vincristine is rarely used but still remains useful in cases where propranolol is contraindicated.

## Laser Treatment

The development of lasers that were able to selectively destroy vascular tissue below intact skin led to widespread use of these lasers in the early nineties. They still remain useful for the treatment of superficial hemangiomas or the superficial component of a deep lesion.[64-66] The laser most widely used is a pulsed dye laser (PDL). Unfortunately, light at this wavelength (595 nm) is rapidly attenuated in human skin and has an effective therapeutic depth of only 1–2 mm.[64-67] Nd:YAG lasers are in the near-infrared spectrum and will penetrate deeper. They are therefore more effective for the deeper components,[68] but the therapeutic range for these lasers is narrow and in inexperienced hands there is a higher risk of scarring. This has precluded them from widespread use.

### *Laser Treatment of Superficial Hemangiomas*

Superficial proliferation of hemangiomas will replace the papillary dermis with hemangioma. Natural involution in these instances will almost always leave an atrophic scar.

The advantages of early treatment of superficial hemangiomas, especially where there has been replacement of the dermis with hemangioma are significant. Early treatment can reduce or eradicate a superficial dermal hemangioma (Figs. 55.12A and B) and if treated early enough, this will allow the return of normal dermis and prevent atrophic scarring so commonly seen after involution. This is presumed to be due to the ability of an infant's skin to mobilize stem cells during the healing process. Repeated treatment every 4–6 weeks has produced excellent results.

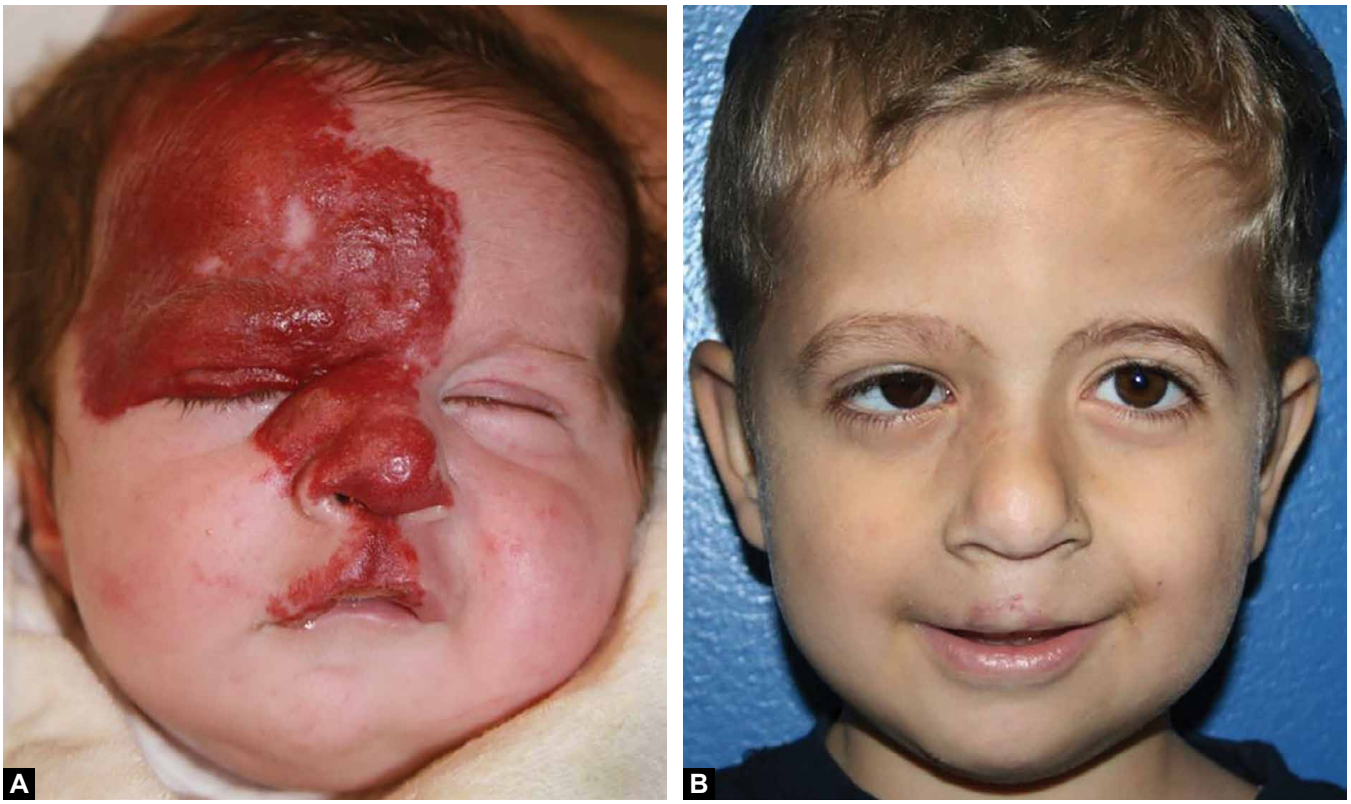
Oral propranolol is also effective in these cases but may not be warranted if the lesion is small or the parents of the child object to a systemic therapy. Topical beta-blockers have been reported to be effective in treating very superficial small hemangiomas (2-3 mm) and are an alternative to systemic propranolol.[69] These agents were developed for topical use in ophthalmological disorders. The bioavailability of the drug is unknown in neonates and infants, and therefore, care must be taken near mucous membranes or ulcerated lesions. Laser treatment therefore still remains a viable alternative when treating superficial proliferating hemangiomas.

Repeated laser treatments can be effective in treating superficial hemangiomas.[70] During the proliferative phase, treatments every 4 to 6 weeks are recommended. Parameters vary from center to center, but the end point of a successful treatment should be a purpuric color change, which will dissipate over the course of 10 to 12 days. Treatment with a PDL is painful and so for smaller lesions, treatment can be administered as an office procedure with topical anesthesia. For larger lesions and in older children, general anesthesia is preferred. Propranolol combined with pulse dye laser has been found to be synergistic.[71]

### *Laser Treatment of the Superficial Component of a Compound Hemangioma*

Lasers can be effectively used to treat the superficial component of a compound lesion especially if the deep component has been or will be surgically removed.[64,66] Once again, a purpuric end point is preferred. Several treatments spaced at 6 weekly intervals are usually necessary to achieve an acceptable end point.

Occasionally, after several treatments a telangiectatic pattern of larger vessels persists. These vessels can be seen




**Figs. 55.12A and B:** A child with a segmental V1 and frontonasal hemangioma before and after several laser treatments. This child was also treated with a course of propranolol.

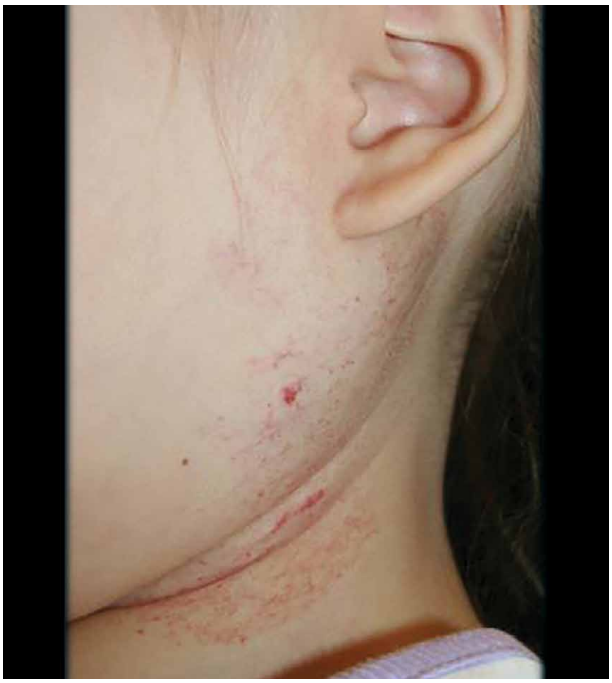


**Fig. 55.13:** A child with an involuted hemangioma. All that is left is telangiectasia.

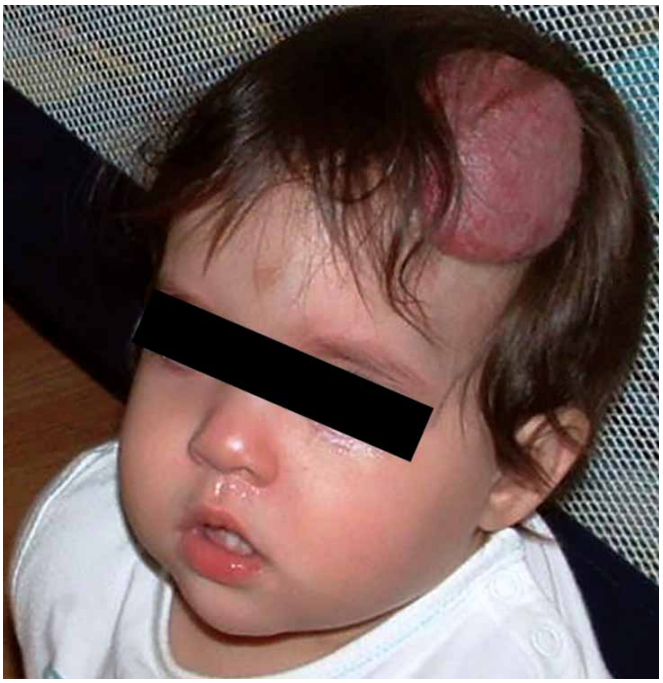


**Fig. 55.14:** An infant with a large scalp hemangioma in whom the overlying skin is alopecic. This cannot be corrected with propranolol but with surgical excision, one is able to remove the hemangioma and approximate hair bearing skin on either side of the lesion.

as discrete vessels, and due to their larger size, they require a greater thermal load to obliterate them. This can be done with either a diode laser or a Nd:YAG laser (in conjunction with dynamic skin cooling). Intense pulsed light emitting devices can also be used.

### *Quiescent or Involuting Hemangiomas*

Once systemic treatment has commenced or is completed, superficial vascular ectasias often remain. The incidence of this has not been published, but it is frequent enough to warrant discussion. This is most effectively treated with a PDL. Occasionally some of the telangiectasias that persist are larger vessels in the range of ≥200 μm (Fig. 55.13). In these cases, far more thermal energy is needed to destroy these vessels and a diode laser with a smaller spot size (1 mm) or a Nd:YAG laser with cooling may be effective.[72]

## THE SURGICAL MANAGEMENT OF HEMANGIOMAS

The indications for surgery are not uniform and vary from center to center. In general, indications for surgery include:

1. Failed conservative therapy. This category includes patients who have had no treatment. Their hemangiomas have been allowed to proliferate and then involute naturally. At some point, it may become obvious that the lesion is unlikely to involute adequately. Alternatively, the child may have reached a level of maturity where it is obvious that he or she is aware of the lesion and is psychologically affected by it.
2. Failed medical therapy. Despite the enormous success of propranolol, a significant percentage of patients require some other form of therapy to complete their treatment and obtain the best results. In many instances, propranolol will fail to shrink a hemangioma completely. Surgery is therefore indicated. In some cases, residual telangiectasia will remain, requiring laser treatment. Alternatively, a complication or functional disturbance will need to be corrected.
3. Surgery is likely to provide the best outcome. In some cases, especially when dealing with focal hemangiomas, treatment with propranolol is unlikely to correct a defect or problem. In these instances, surgery may provide a better outcome (Fig. 55.14).
4. Complications. Ulcerated hemangiomas may be severely painful, bleed, and become secondarily infected. In addition to this, once they have healed, they invariably leave a significant scar. Timely surgical intervention will obviate the need for weeks to months of

medical therapy and is likely to provide a better outcome than medical treatment aimed at healing the ulcer (Figs. 55.15A and B).

Airway hemangiomas require close monitoring, and surgery may be necessary to maintain an adequate airway.

Eyelid hemangiomas are often treated with propranolol but this may fail to relieve visual axis obstruction soon enough to prevent amblyopia.

Congestive cardiac failure sometimes complicates very large hemangiomas, and these lesions may need to be removed urgently.

For the purpose of simplicity, the surgical management will be discussed by anatomical sites:

- Lip
- Orbital/paraorbital
- Nasal
- Cheek
- Forehead and scalp
- Parotid
- Airway

## Hemangiomas of the Lip

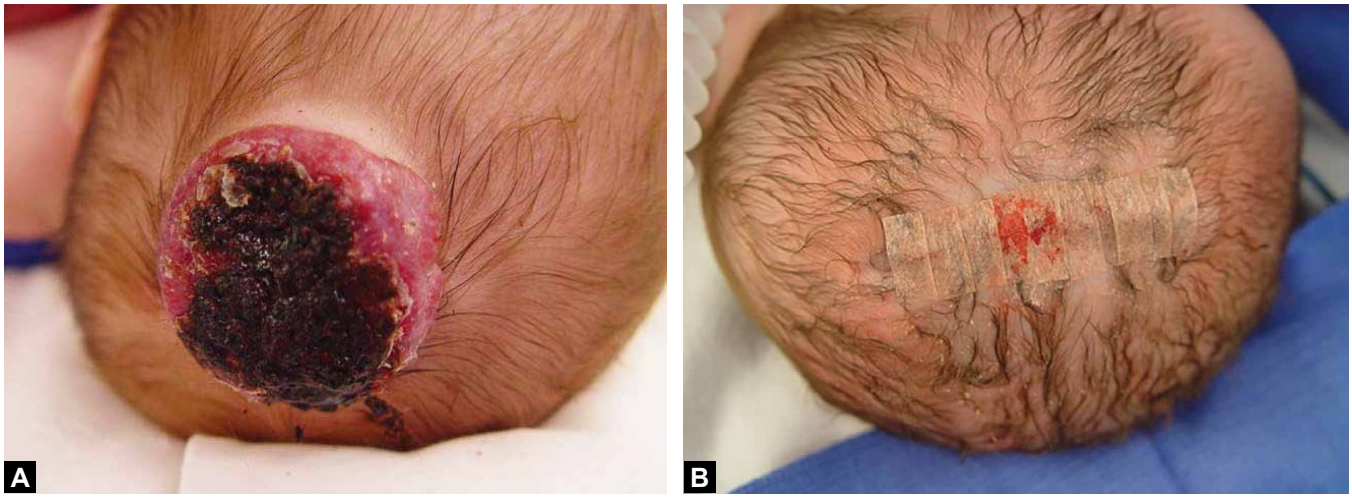
The indications for treatment of a lip hemangioma may be functional, medical, and/or cosmetic. A hemangioma of the lip may prevent oral competence, which in turn will cause drooling, affect speech and feeding. There is a high incidence of ulceration in segmental lesions, which may lead to pain, bleeding and act as a site for infection. Lip hemangiomas can also be extremely disfiguring.

As with all anatomical sites, lip hemangiomas may be focal or segmental in their distribution, and there are distinct patterns of involvement with both types.[73] The anatomical extent and distortion of each lesion can be predicted. With this in mind, we have developed surgical guidelines for their management.[73] Segmental hemangiomas may involve the maxillary, frontonasal, or mandibular segments. The lower lip is the most common site of both focal and segmental lip.

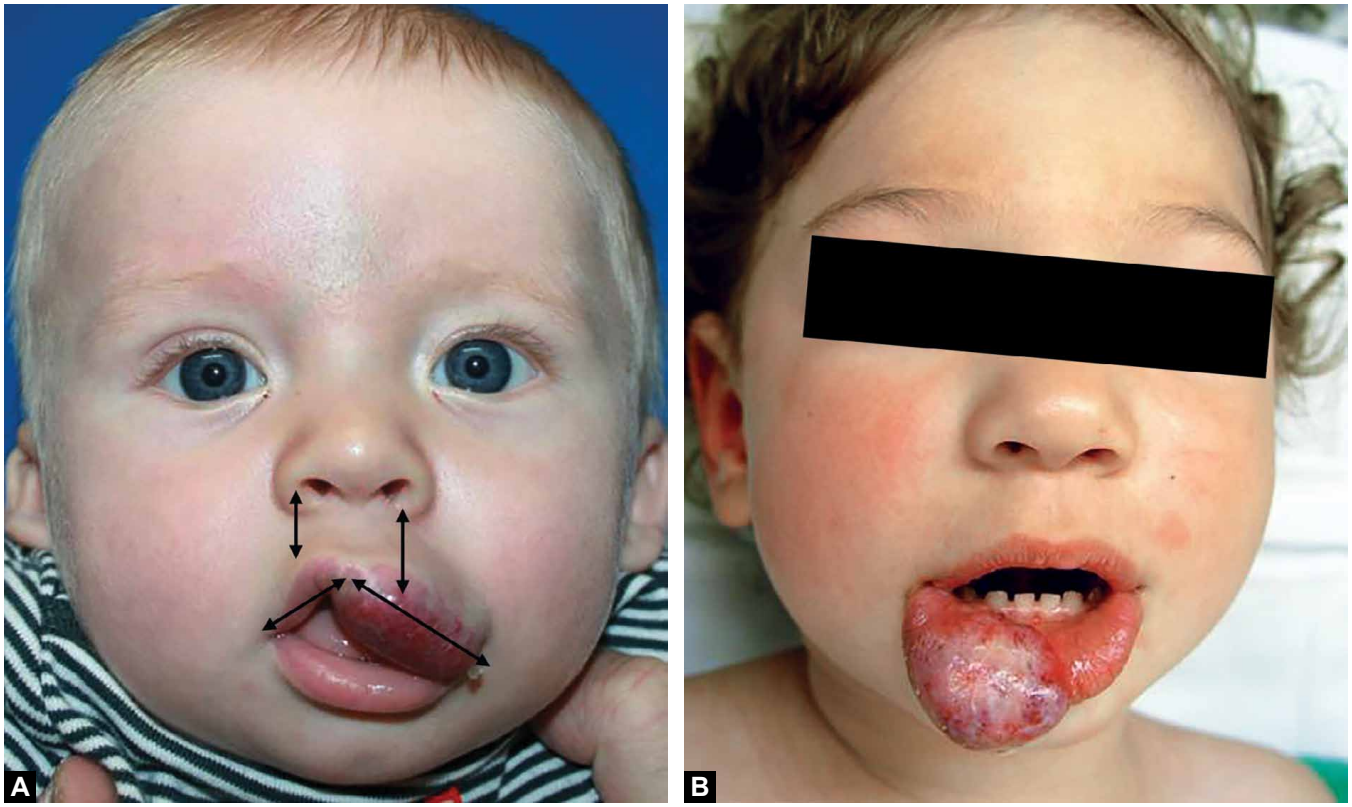
- Both the upper and lower lips may be elongated in their vertical or horizontal dimension (Figs. 55.16A and B).
- The lip may be inverted or everted, which may lead to oral incompetence.

These dimensions can be corrected and the surgical approach will depend on the site of the hemangioma. Hemangiomas frequently act as a tissue expander (especially in focal lesions) and thus, >30% of the lip can be excised without causing microstomia. In general, incisions are placed along boundaries of facial subunits (alar groove, philtrum, vermiliocutaneous junction (VCJ), wetdry mucosal margin). This usually provides easy access to the lesion, and any redundant tissue can then be removed with an acceptable cosmetic result.

Lower lip focal hemangiomas are the most common focal lesions and tend to involve the lateral aspect of the lower lip. These lesions will frequently lengthen and evert the lower lip. The lip can be lengthened by as much as 50%, depending on the size of the hemangioma. These lesions can almost always be resected via a wedge excision (Figs. 55.17A to D).




**Figs. 55.15A and B:** An infant with an ulcerated hemangioma, before and immediately after surgical excision. The need for analgesia and wound care is obviated.




**Figs. 55.16A and B:** (A) An infant with a focal upper lip hemangioma. Note that the lip is lengthened. In both its vertical and horizontal dimensions. (B) Child with a lower lip focal hemangioma that has resulted in significant lengthening of the lip.

Propranolol has made the most impact on the treatment of segmental hemangiomas. With early treatment, most of the deformities can be prevented. However, all too often treatment is delayed and devastating functional as well as esthetic abnormalities will result.

Frontonasal segmental lesions are the most difficult since they distort the philtrum. The vertical height of the upper lip is usually lengthened. These can be approached via the VCJ and/or the posterior border of the columella and the nasal sill.

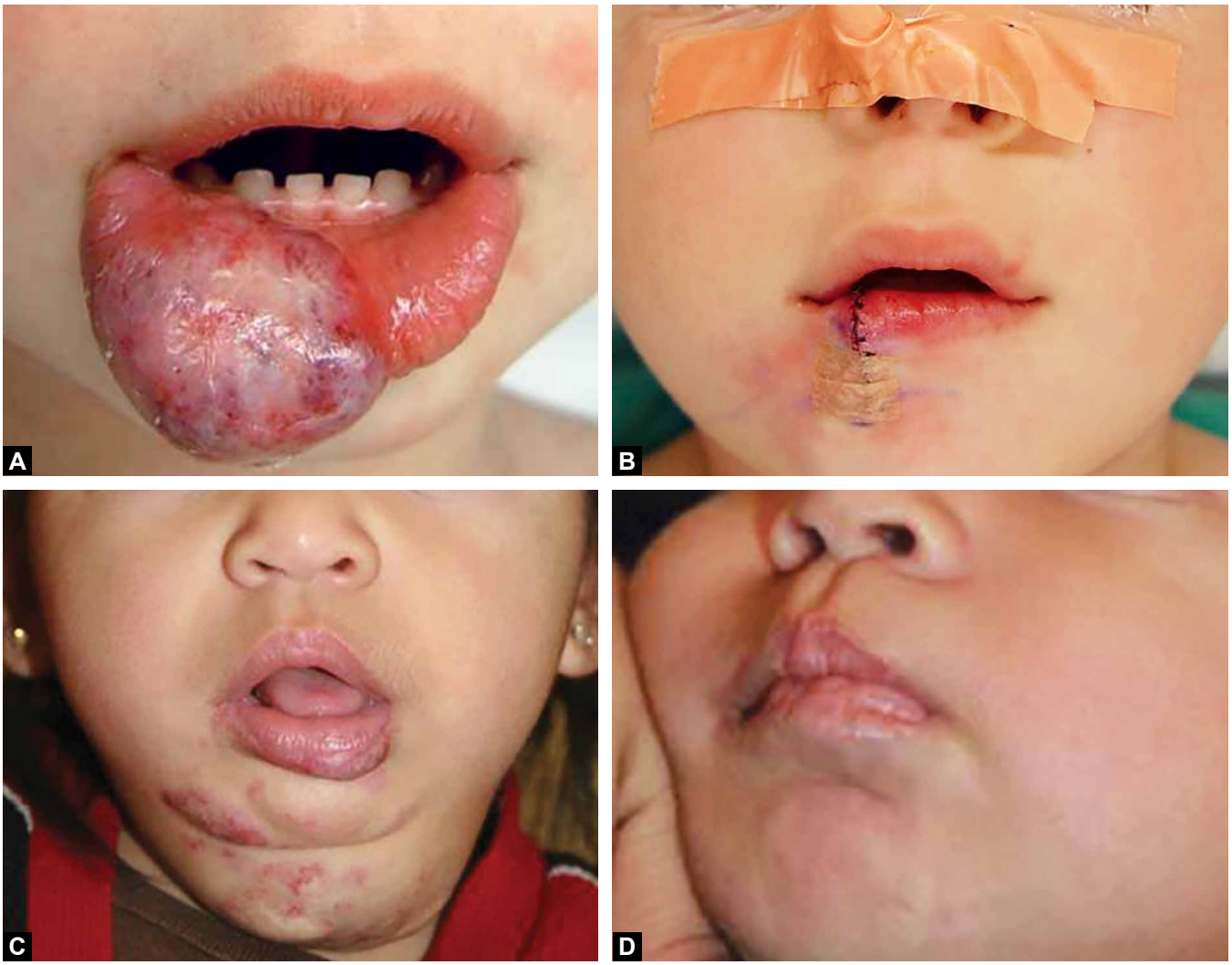
Maxillary or V2 segmental lesions elongate the hemilip and invert the VCJ. The hemilip can be shortened via a wedge resection. The incision begins along the VCJ, extends up the philtrum and across the base of the nasal sill and around the nasal alum.

The most common segmental hemangioma involves the entire lower lip (mandibular segment). Since ulceration is frequent, the VCJ is usually distorted and the concavity between the VCJ and the labiomental crease is obliterated. These lesions also lengthen the lower lip. A wedge resection of the lower lip will correct the horizontal lengthening (Figs. 55.17A to D). An incision along the VCJ and vermillion advancement will correct the inversion as well as the convexity below the VCJ. A specially modified suture technique will help recreate the natural sulcus of the lower lip (Figs. 55.18A to H).

Each of the above procedures may be performed in a staged approach to prevent over-resection and over correction. Both the PDL and the $CO_2$ laser with fractional delivery options are useful in correcting atrophic scarring and residual cutaneous hemangioma.

## Eyelid/Orbital/Periorbital Hemangiomas

Orbit, eyelid, and conjunctival hemangiomas constitute a special category owing to their anatomic location. These periocular hemangiomas threaten visual development through a number of mechanisms.[74-77] They also significantly impact facial expression and psychological development. While evaluation and management follow principles common to all IHs, unique challenges in these cases strongly influence clinical decision making.



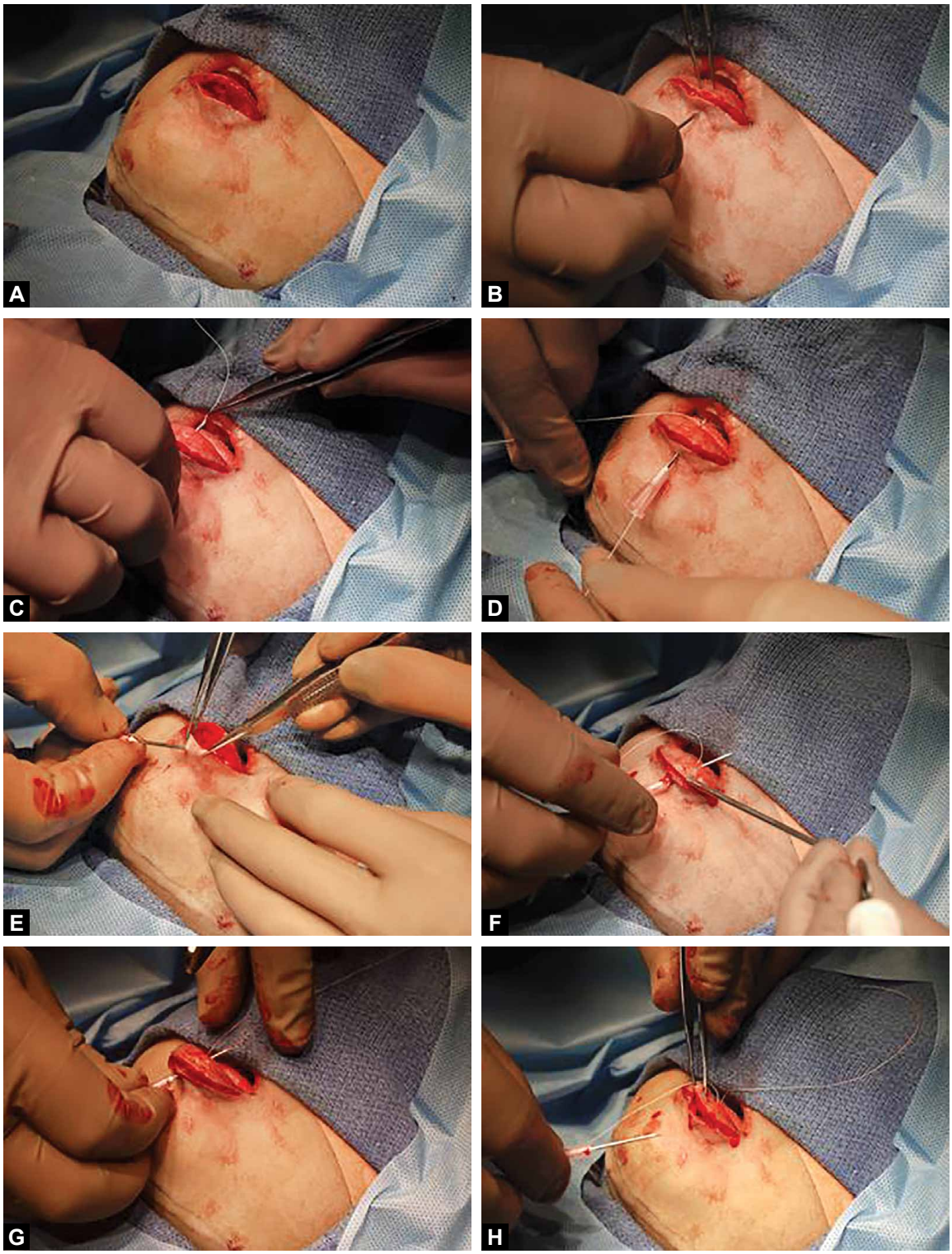

**Figs. 55.17A to D:** A wedge resection is used to correct the lip length discrepancy and at the same time, remove the offending hemangioma. Propranolol treatment would not have resulted in this degree of correction.

The complex management decisions in a patient with periocular hemangioma should be approached in two distinct steps. One must first decide whether or not to treat the child. Once a decision to treat is reached, the most appropriate modality should be chosen.

### *Indications for Treatment*

Beyond the common factors influencing this decision, the threat of permanent visual loss (amblyopia), permanent spectacle dependence (astigmatism), strabismus, permanent eyelid deformity (blepharoptosis, irregular lid contour, entropion, trichiasis, mydriasis), and orbit distortion must be weighed when deciding whether to continue observation or to intervene. The most serious cause of amblyopia is deprivation of visual stimuli by direct visual axis obstruction. In cases of complete obstruction, they should be treated with the urgency of a severe, unilateral congenital cataract. Cases of partial obstruction should be managed according to the amount and frequency of visual axis obstruction. Head positioning may not be appreciated since the contralateral eye remains unaffected.

Astigmatism, pathologic warping of the cornea, can be caused by upper or lower eyelid hemangiomas. Although amblyopia due to astigmatism can be treated with contralateral patching regimens, a child with uncorrected astigmatism will require lifelong spectacle or contact lens correction. The astigmatism can be reversed with early intervention, best before 9 months of age. Beyond 13 months of age, there is little evidence to suggest reversibility of astigmatism.




**Figs. 55.18A to H:** A surgical evacuation of the subcutaneous space is undertaken (A). Following this, an 18-G needle is inserted through all layers to the mucosal side (B). A strand of 5-0 Vicryl is passed from the mucosal side all the way through (C and D). The needle is then withdrawn until the tip is intradermal (E). At this point it is redirected through the dermis and then back through all the layers to the mucosal side close the previous suture (F). A 1-mm segment of dermis is ensnared by this suture. The needle is then withdrawn completely while the suture end is removed from the needle (G). The two strands can then tied in the mucosal side, thereby obliterating the dead space and everting the lip (H).

Strabismus may result from mechanical obstruction of extraocular muscle (EOM) movements, direct EOM invasion, or may be associated with a remote hemangioma in the same eye. Medial rectus involvement is most common and most obvious, producing esotropia. Superior oblique involvement is common in typical superonasal eyelid and orbit cases, but the strabismus is subtle and requires tilt-testing or forced ductions to diagnose.

Permanent eyelid deformity results from direct invasion, vascular steal, or prolonged pressure of adjacent structures. Most sensitive are levator palpebrae superioris, tarsus, eyelash follicles, and lamina papyracea. Levator muscle can be salvaged with early treatment, but prolonged invasion produces a fatty, atrophic muscle akin to true congenital ptosis. These cases require the less effective frontalis suspension surgery to bypass the levator muscle. Tarsus, lash follicles, and the bones of the orbit also respond well to early intervention as the ongoing anatomic destruction or deformity can be arrested at a very early stage. Preservation of tarsus ensures eyelid margin stability while maintenance of the bony socket prevents globe displacement, enophthalmos, and facial asymmetry.

### *Treatment Alternatives*

Alternatives available to treat periocular hemangiomas mirror general treatment options, but again special regional factors must be considered. Urgency, laser safety, and the luxuriant vascularity of the region all influence the treatment method selected.

Topical hemangioma treatments around the eyes have met with limited success, partially due to painful irritation (imiquimod)[78] but also to fear of topical effects on the conjunctiva and cornea. Topical steroids, for example, carry the risk of glaucoma and cataract formation. Intralesional steroid injection had been an important local treatment introduced in the 1970s, but numerous reports of retinal artery occlusion followed.[79,80] This is thought to be caused by retrograde injection of steroid particles into arterioles, which are then redirected down the retinal arterial tree. With improvements in systemic medications and surgical techniques, many now feel that intralesional steroids are contraindicated in periocular hemangiomas.

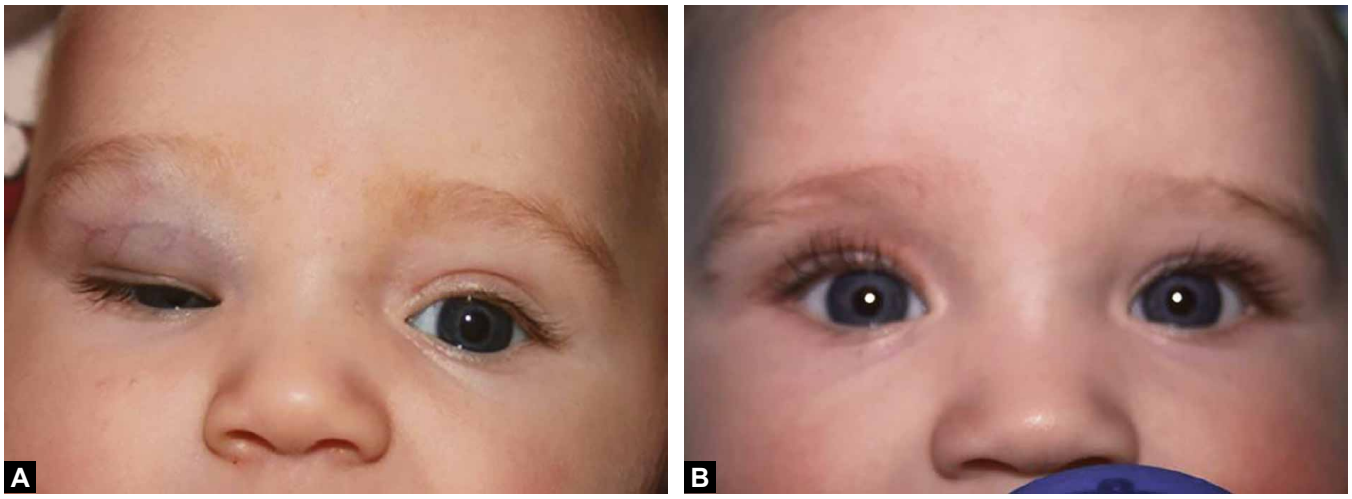
Both systemic and topical beta-blockers have supplanted corticosteroids as the mainstay of systemic treatment,[56,69,81-83] and doubtless an enormous benefit to many patients. Nonetheless, a "propranolol paradox" has become increasingly common in the treatment of periocularhemangiomas. Many of the effects of periocular hemangiomas are time dependent and can be effectively and thoroughly treated if addressed early (see above, "Whether to Treat"). The rise of propranolol has unfortunately delayed referral to an appropriate subspecialist in some cases, increasing sequelae, and limiting treatment alternatives. For example, a year-long course of propranolol will usually improve an eyelid hemangioma considerably, but the resultant eyelid is frequently elongated horizontally, sectorally ptotic, and sectorally void of lashes. Medical treatment also significantly prolongs amblyopia treatment through patching and chemical penalization.

Laser treatment can be very effective in treating superficial periocular hemangiomas, and some authors describe excellent results for conjunctival hemangiomas as well. Conjunctival and iris hemangiomas respond very well to topical beta-blocker treatment. The common glaucoma eye drop, timolol, has been used most frequently and with good success. Again, prolonged topical steroids are to be avoided.

Surgical removal of periocularhemangiomas has improved dramatically over the past decade with more sophisticated more techniques and instrumentation; several surgeons are now able to remove these lesions safely and quickly. Still, surgery is the most idiosyncratic of all the treatment options, so different geographic regions have to make decisions accordingly. Surgery is rapid and definitive; if it can be offered safely by experienced surgeons, it is often the optimum way to treat periocular lesions. Early surgery effectively eliminates the risk of amblyopia, decreases amblyopia treatment times, and dramatically improves the chances for EOM, eyelid, and orbit preservation. Nevertheless, orbital hemangiomatosis is not amenable to surgery. As with other areas, a multidisciplinary team within and beyond ophthalmology serves the patient best.

### *Focal Eyelid Hemangiomas*

The most common site appears to be an upper medial lid lesion. These hemangiomas compress the globe and cause a medial ptosis. Often, only the tip of the iceberg is visible and an MRI will reveal a large lesion extending along the medial orbital wall posteriorly to the equator of the eye. The superior oblique is almost always intimately related to this lesion and will need to be identified and preserved during surgery. A lid crease incision with careful dissection and preservation of the superior oblique should be undertaken.




**Figs. 55.19A and B:** An infant with an extensive focal upper eyelid hemangioma. This lesion involved the middle third of the eyelid and extended medially into the orbit along the medial wall of the orbit to the origin of the medial rectus muscle. This child had ptosis and asymmetric astigmatism. The lesion was surgically removed via a lid crease incision.

Hemangiomas involving the mid-upper lid can also be approached through a lid crease incision (Figs. 55.19A and B). In these cases, the hemangioma frequently extends down to the distal extreme of the eyelid, and the lash follicles will be encountered. These should of course be preserved.

Higher brow lesions are also common and should be removed via a sub-brow incision. These lesions are usually restricted to the brow and do not enter the orbit.

Lower lid lesions are also common. The greatest challenge with these lesions is to prevent an ectropion. In most cases, there is enough tissue expansion to prevent this. Occasionally, a rotation flap such as a Tenzil rotation flap will need to be employed.

### *Segmental Eyelid Hemangiomas*

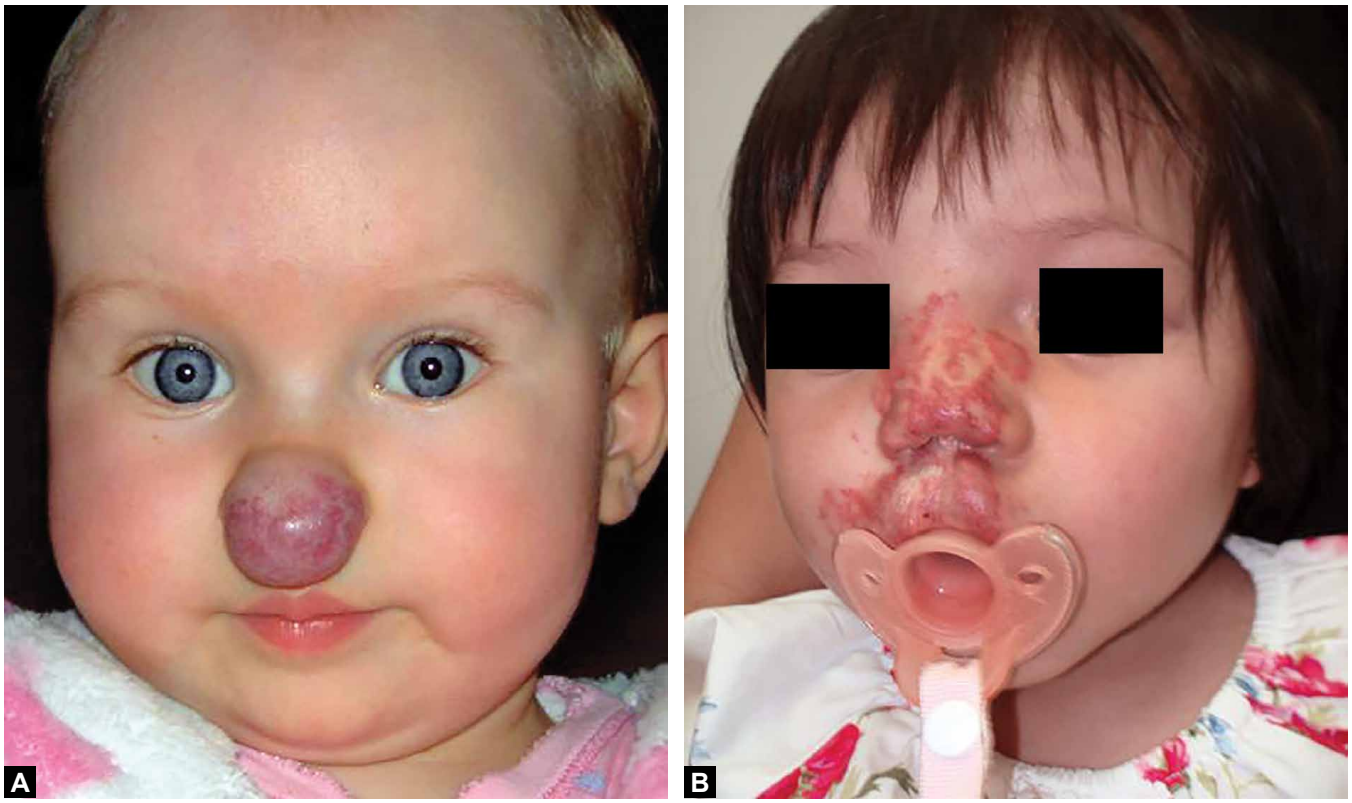
The upper lid is most commonly involved, as part of a V1 segmental lesion. Involvement of the upper lid frequently includes skin, subcutaneous tissue, orbital fat, and the levator muscles. These lesions can also extend all the way to the apex of the orbit. Early intervention with propranolol is essential. Delayed intervention will lead to extensive levator infiltration and ptosis. Despite this, surgical correction of an upper lid ptosis is often necessary. This may include debulking of the lid as well as a levator advancement/shortening.

## Nasal Hemangiomas

About 15% of facial hemangiomas occur on the nose.[6] The majority of these lesions are focal and involve the nasal tip. The nose may also be involved as part of a segmental hemangioma (Figs. 55.20A and B). Both frontonasal FN or V2 segmental hemangiomas may also involve the nose, and in these cases, more than one nasal subunit is usually affected. Left untreated, most of these children experience social ridicule from both society at large and the medical profession. Terms such as “Harlequin nose” and “Cyrano nose” are frequently used to describe these lesions. Early intervention is thus clearly indicated. Prevention of these deformities with timely medical therapy is preferable and in many cases, if started early enough, no further treatment is necessary. If this has not happened or the lesion has failed to respond to propranolol, surgical treatment may be necessary.

The timing of surgical intervention is important. One should not intervene until proliferation has ceased and the lesion is in its quiescent phase. This would mean not earlier than the 10th month and up to at least 18 months of life for a segmental lesion. While it is tempting to wait until the child is much older, this should be discouraged for two reasons. The psychosocial trauma inflicted upon these children can be avoided with early intervention, and the likelihood of scarring is diminished when surgery is performed around 1 year of age as opposed to 5 or even 6 years of age.

Nasal tip hemangiomas have many features in common. They almost all distort the nasal tip by displacing the lower lateral cartilages laterally and rotating them outward.[84] The overlying skin is usually not involved. Most of these lesions are midline, but a minority may involve




**Figs. 55.20A and B:** (A) An infant with a focal nasal tip hemangioma. (B) An infant with a segmental frontonasal hemangioma. The hemangioma ulcerated, and this resulted in loss of the entire columella as well as extensive scarring.

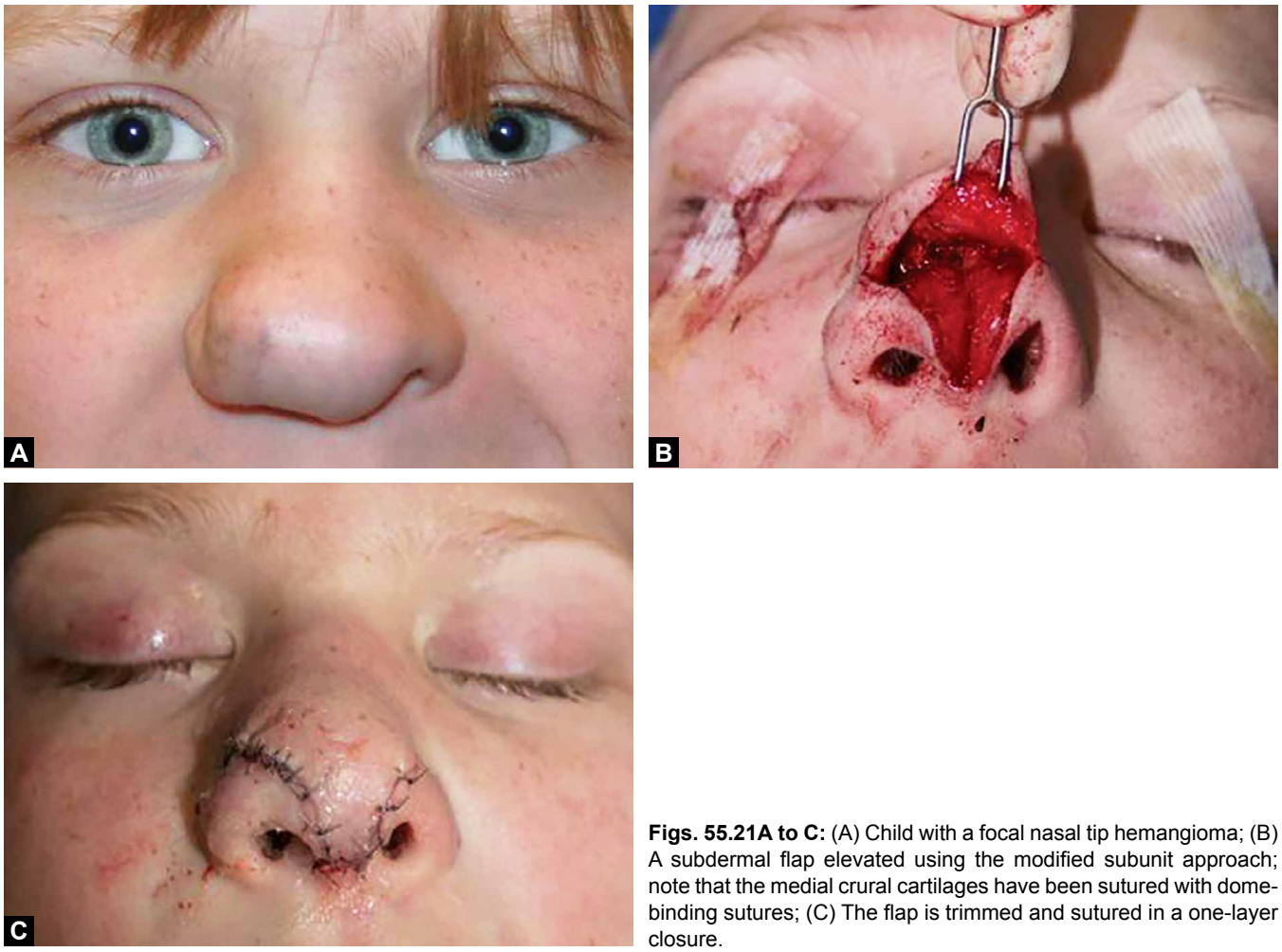
one side more than the other. Many surgical approaches have been described. Of these, we prefer the modified subunit approach as described by Waner et al.[84] An incision extending across the columella and then up just past the soft triangle to the space between alae and the nasal tip. This approach allows access to the lower lateral cartilages as well as the ability to trim excess skin (Figs. 55.21A to C). Two or three dome binding sutures as well as a columella transfixion suture will be needed to correct the deformity of the nasal tip. In cases involving more than one subunit, an extension of this incision may be necessary. Laser treatment of the overlying skin may precede or follow the surgical resection. If the skin is extensively infiltrated, raising a flap will be difficult if not impossible. In these cases, laser treatment, aimed at eradi-cating the cutaneous component, should precede surgery.

## Hemangiomas of the Cheek

Surgery is usually indicated for focal lesions that have failed conservative treatment or have never been treated. Mid-cheek lesions are the most common and are usually found lateral to the nasolabial fold. Most of these lesions are compound, and although they are cutaneous in origin, they frequently extend down to the fascial layer overlying the buccal fat space. Facial nerve involvement is not uncommon and therefore facial nerve monitoring is highly recommended. These lesions can be removed through an elliptical incision, encompassing involved skin and parallel with relaxed tension lines of the face. If the degree of skin involvement is too extensive to remove without facial disfigurement, some involved skin can be left in one of the flaps. This can be treated with laser at a later stage. Extensive mobilization of the flaps is essential before closing and unless one is removing a proliferating lesion, truncation of the lesion may be necessary to avoid a contour deformity. The remaining lesion will, over time, become fibrofatty tissue.

## Hemangiomas of the Forehead and Scalp

As with all other anatomical sites, both focal and segmental hemangiomas can involve the forehead. Focal lesions are usually paramedian or involve the midforehead on one side or the other. They are usually compound lesions that extend up to and frequently involve the forehead muscles.




**Figs. 55.21A to C:** (A) Child with a focal nasal tip hemangioma; (B) A subdermal flap elevated using the modified subunit approach; note that the medial crural cartilages have been sutured with dome-binding sutures; (C) The flap is trimmed and sutured in a one-layer closure.

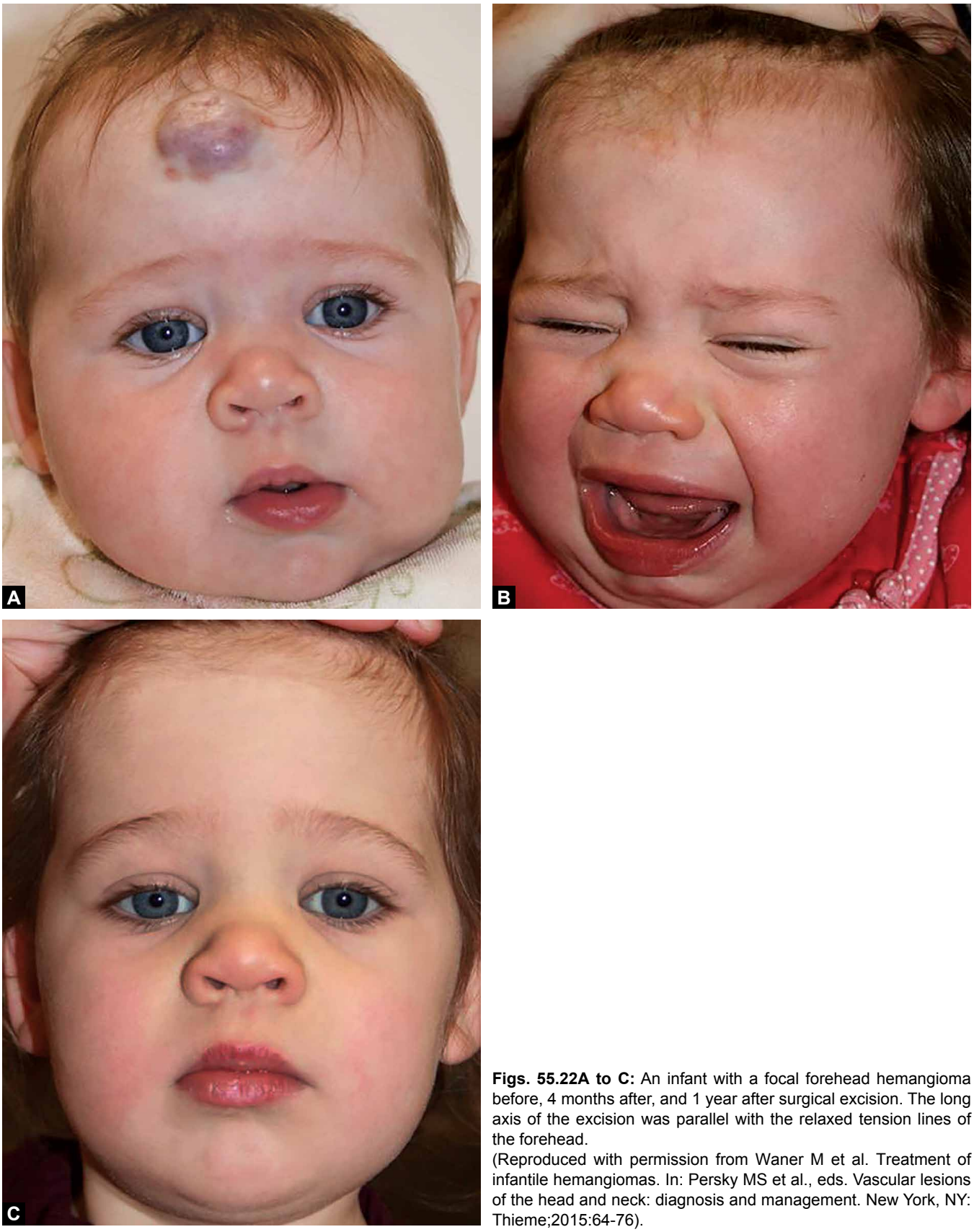
Frontonasal segmental as well as V1 segmental hemangiomas can also involve the forehead.

In general, early treatment with propranolol with or without concomitant laser treatment is preferred for both segmental and focal hemangiomas. Surgical resection may be necessary for focal lesions. Since the relaxed tension lines of the forehead are horizontal, the axis of surgical resection ideally should be parallel to them (Figs. 55.22A to C). This may result in displacement of the brow if the lesion is compound and the vertical dimension of the superficial component is >2 cm. Tissue expansion caused by the mass of the hemangioma will often avoid brow and/or hairline displacement. In cases where there is a large hemangioma and brow displacement is likely, the placement of a tissue expander should be considered. At times, a vertical incision may be necessary. Even this will heal well in young children and be barely noticeable. During surgery, preservation of the forehead muscles is essential to a good outcome.

Scalp hemangiomas can grow to very large dimensions and when they involute, they almost always leave an area of alopecia overlying a soft doughy mass. An important consideration when planning treatment is the fact that in infants <4 months of age, the absence of a thick fibrous galeal layer will leave the skin of the scalp extremely lax. The galeal layer develops around 4 to 5 months of age and the skin loses its laxity.[85] Because of this, it is much easier to remove very large scalp lesions before 4 months of age. This should clearly be weighed against the added anesthetic risks seen in this age group.

## Parotid Hemangiomas

Parotid hemangiomas are the most common benign salivary gland tumors in children. Interestingly, the parotid gland appears to be the only major salivary gland that may be affected by hemangiomas.[86] This is most likely related to the embryological origin of these glands. The parotid




**Figs. 55.22A to C:** An infant with a focal forehead hemangioma before, 4 months after, and 1 year after surgical excision. The long axis of the excision was parallel with the relaxed tension lines of the forehead.
(Reproduced with permission from Waner M et al. Treatment of infantile hemangiomas. In: Persky MS et al., eds. Vascular lesions of the head and neck: diagnosis and management. New York, NY: Thieme;2015:64-76).

gland is ectodermal in origin, whereas the submandibular and sublingual glands are endodermal in origin. Since hemangiomas appear to be ectodermal lesions, this could possibly explain the absence of hemangiomas in submandibular and sublingual glands. Minor salivary glands are also frequently involved, especially in the mandibular V3 segmental distribution. These minor salivary glands are also ectodermal in origin.

Both focal and segmental hemangiomas may involve the parotid gland. Focal lesions usually involve the entire parotid gland, with or without involvement of the overlying skin. V3 segmental hemangiomas may also involve the parotid gland. These are usually bilateral and the overlying skin is also frequently involved together with the lower lip.[87] All segmental V3 patients should be evaluated laryngoscopically since almost one third of these patients will have airway involvement. In addition to this, there is a high association with PHACES syndrome.

### *Treatment of Parotid Hemangiomas*

Parotid hemangiomas may be extremely disfiguring. Segmental lesions may also ulcerate, and the likelihood of airway issues is significant. Massive parotid hemangiomas may lead to excessive shunting, which, in turn, may cause congestive cardiac failure. For all these reasons, parotid hemangiomas should be treated. Propranolol is the first line of therapy. The likelihood of response with segmental hemangiomas is high. Unfortunately, not all focal lesions respond completely (Figs. 55.23A to C). Treatment failures or residual disease after the cessation of propranolol should be treated surgically. Since hemangiomas are extremely vascular, this surgery can be very challenging. Facial nerve monitoring is strongly suggested and caution must be exercised by the surgeon, because the positions of the branches of the facial nerve are frequently displaced, and the perineurium is frequently infiltrated by hemangioma, which makes neural dissection more challenging. Preoperative embolization may reduce the vascularity of the hemangioma and facilitate surgical excision.[86]

Intralesional corticosteroid injection using a combination of triamcinolone (40 mg/mL) and betamethasone (6 mg/mL) has been used successfully to treat parotid hemangiomas.[88] This may be an option where propranolol is contraindicated or has failed. Despite the fact that corticosteroid is injected locally, systemic absorption is still significant and the side effects commonly seen with systemic corticosteroids may therefore occur.

Pulsed dye laser treatment is helpful in treating the superficial component of a compound hemangioma as an adjuvant to propranolol and surgery.

## Airway Hemangiomas

The term "subglottic hemangioma" has been used to refer to all lesions involving the airway. Both focal and segmental hemangiomas may involve the airway[89] (Figs. 55.24A to C). The most common site for a focal lesion is the subglottis, but the pattern of involvement for a segmental hemangioma is completely different. Segmental involvement is typically more diffuse and involves both supraglottic as well as subglottic structures. Hypopharyngeal and tracheal involvement is also not uncommon, but involvement of these areas is usually quite benign. At least one third of patients with a V3 segmental cutaneous pattern also have airway findings.[90] It is therefore imperative that all patients with this distribution of disease should undergo endoscopy.

Given the fact that the term "subglottic hemangioma" is an oversimplification, a more appropriate term is "airway hemangiomas", which includes both focal and segmental lesions.[89]

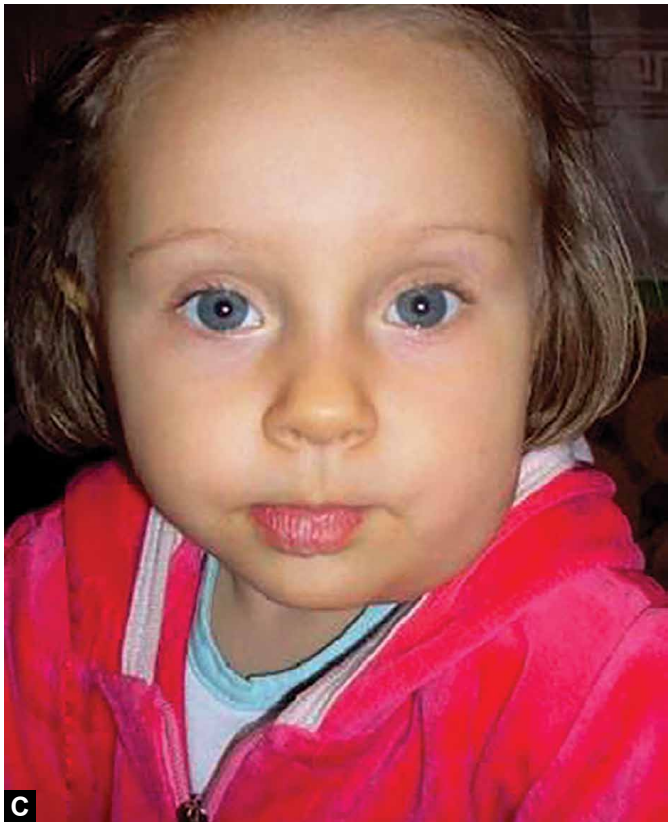
### *Focal Airway Hemangiomas*

Oral propranolol is the first-line therapy. Response is usually rapid and in most cases, intubation and/or tracheotomy can be avoided. Corticosteroids may be used as adjuvant therapy in cases of airway obstruction. In these instances, steroids are used in short pulses, whereas propranolol treatment sustained until 9–10 months of age. It is especially important to monitor the child for hypoglycemia when steroids and propranolol are used in tandem.

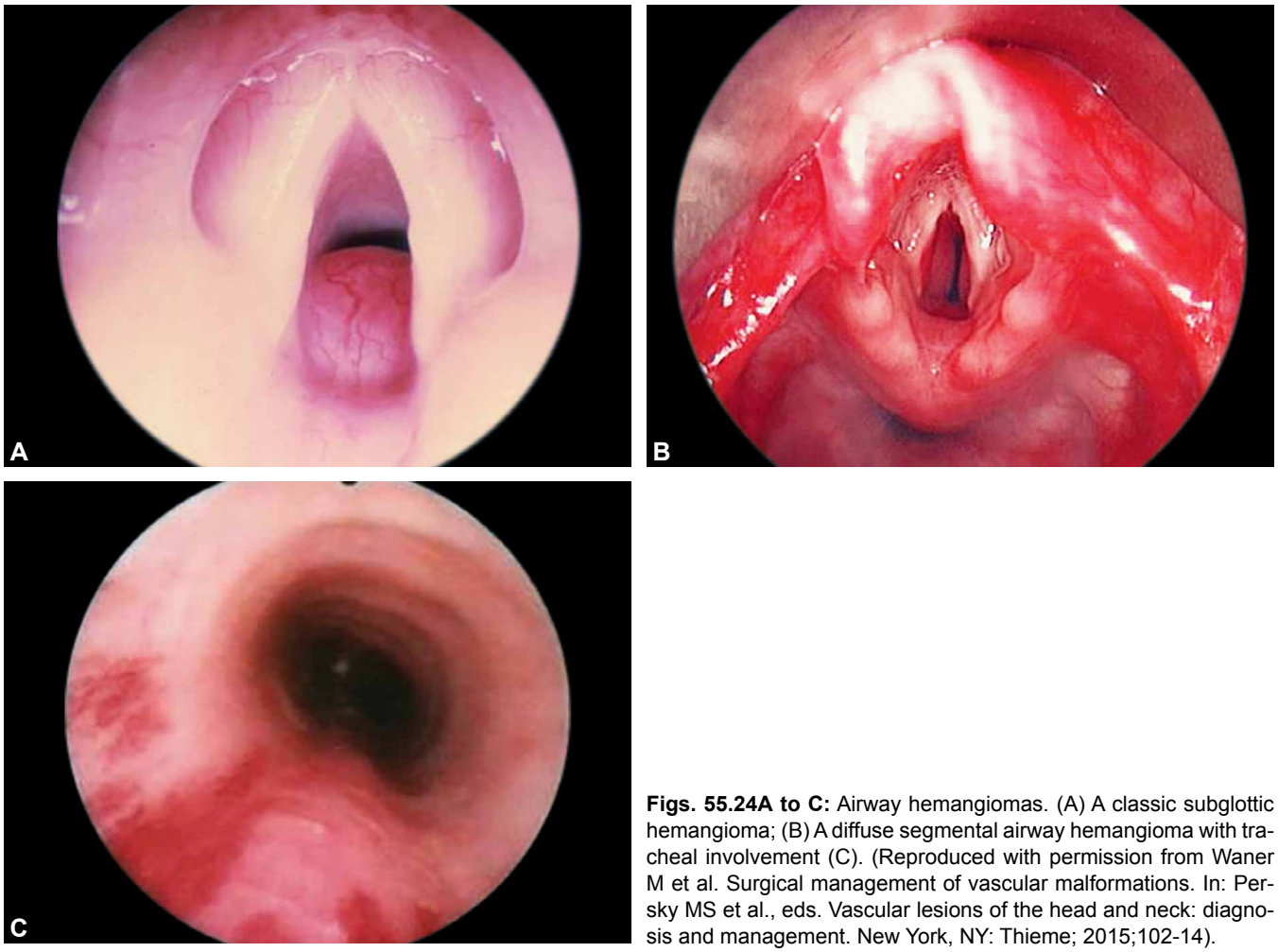
If propranolol is contraindicated or fails to produce an adequate effect, other treatment options should be considered. These include intralesional corticosteroid injection, $CO_2$ laser ablation, and surgical resection. The treatment bias will be determined by the experience of the surgeon.

### *Segmental Involvement*

Segmental airway involvement will vary from diffuse mucosal staining to extensive bulky disease and airway obstruction. Tracheal staining is also not uncommon. Since there is no way to predict which patients will progress, all patients with nascent disease should be closely followed clinically and with serial direct laryngoscopy/bronchoscopy procedures. For those who warrant treatment, propranolol is the drug of choice and it appears that the vast majority of patients will respond. Tracheostomy is therefore much less frequently performed.


**Figs. 55.23A to C:** An infant with a parotid hemangioma before, 5 months after, and 11 months after treatment with propranolol. Note that the hemangioma responded dramatically but not completely to propranolol. A small residuum remains that will need to be surgically removed to correct facial symmetry.




**Figs. 55.24A to C:** Airway hemangiomas. (A) A classic subglottic hemangioma; (B) A diffuse segmental airway hemangioma with tracheal involvement (C). (Reproduced with permission from Waner M et al. Surgical management of vascular malformations. In: Persky MS et al., eds. Vascular lesions of the head and neck: diagnosis and management. New York, NY: Thieme; 2015;102-14).

## TREATMENT OF VASCULAR MALFORMATIONS

The treatment of vascular malformations is a multidisciplinary endeavor, and the participation of several specialties is essential for the best outcome. Since many of the conditions cannot be "cured", the goal of treatment is to improve facial symmetry and a patient's quality-of-life. Very small lesions may be "cured" but larger, more diffuse lesions may be "inactivated" and may require "maintenance therapy" throughout a patient's lifetime.

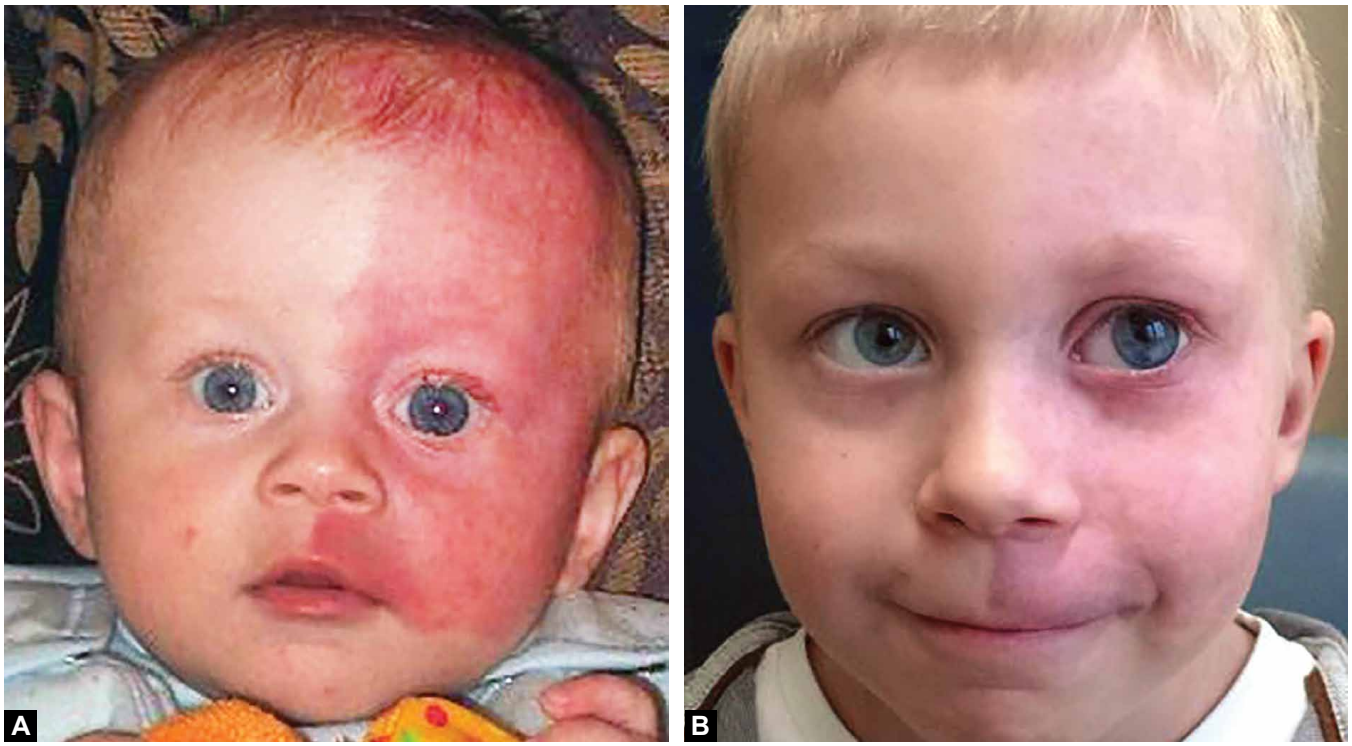
### Port-wine Stains (Venular or Capillary Malformation, PWS)

The PWSs or capillary malformations are dermatomal/segmental vascular lesions characterized by ectasia of the vessels in the papillary and reticular dermis. About 30% will form cobblestones and in a small percentage soft tissue hypertrophy in all tissue layers including skin, subcutaneous fat, muscle, and even bone.

#### *Laser Treatment*

Serial laser treatment is the mainstay for the treatment of PWSs. PDLs have proven efficacious in their management and are therefore the most widely used laser for the treatment of PWSs[72,83] (Figs. 55.25A and B). A small percentage of patients will have complete clearance of their birthmark. The vast majority of patients will lighten considerably. Twenty to thirty percent of patients will have resistant lesions, which will only marginally improve.[91]

The best age to begin treatment remains unresolved. Some groups advocate for early treatment, whereas others have found no advantage. Despite treatment and regardless of how well they respond, all PWSs will eventually recur.[92]



**Figs. 55.25A and B:** A child with a left-sided confluent port-wine stain before and after multiple pulsed dye laser treatments. All treatments were done under general anesthesia. This child has left-sided glaucoma, but no evidence of Sturge-Weber syndrome.

Alexandrite lasers (755-nm) have been used for resistant lesions; however, their therapeutic index is narrower with higher risk of scarring. The laser preferentially targets deoxyhemoglobin found in venous vessels, which may explain its efficacy for darker lesions.[93] The PDL on the other hand targets oxyhemoglobin.

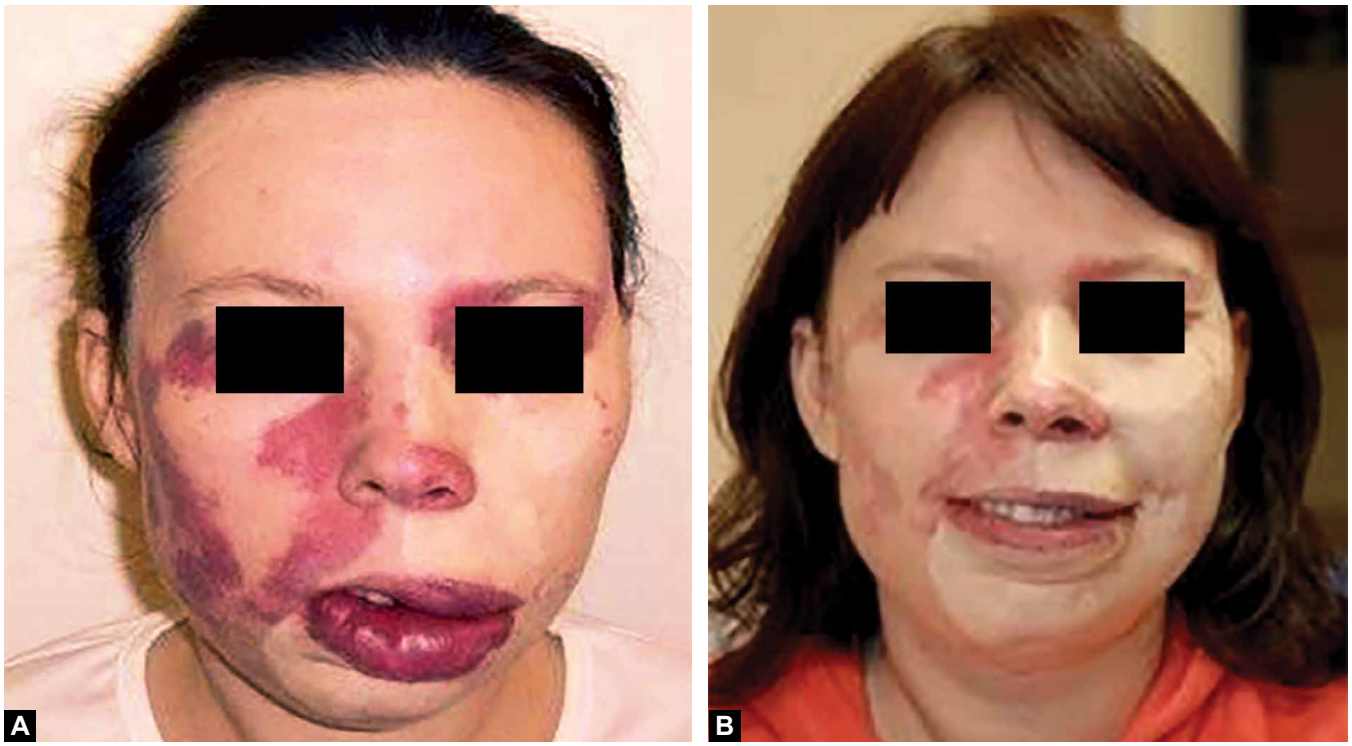
## Photodynamic Therapy

Photodynamic therapy (PDT) has been studied extensively in China. A two-step treatment is used consisting of an intravenous injection of a porphyrin-based photosensitizer, followed by irradiation of the affected area with coherent or noncoherent light. The porphyrin drug is a photosensitizer and is thus activated by light at a particular wavelength. Once activated, the photosensitizer generates oxygen-derived free radicals, which damage/destroy endothelial cells in PWS vessels of all sizes. Patients are required to avoid direct sun exposure for a period of 2 weeks after the treatment. During this interval, they are extremely photosensitive and exposure to direct sunlight can be harmful. Studies have shown that PDT is as effective for treating light PWS and more effective for darker PWS.[94-96] The main reported side effects include hyperpigmentation and scarring. In one series, a 5-year follow-up showed no recurrence.[95]

## Surgical Management

A proportion of patients with PWSs experience soft tissue hypertrophy within the affected area.[28] This hypertrophy may involve all or part of the affected dermatome and both mesodermal and ectodermal elements are involved. The upper lip and maxilla are commonly involved with skeletal hypertrophy together with muscle and subcutaneous fat hypertrophy. Cobblestone or soft tissue nodule formation is more common than soft tissue hypertrophy. These nodules are made up of coalesced ectatic vascular tissue. In early cobblestones, the lesion is clearly vascular and empties on compression. At this stage, it may be treated with a PDL or Nd:YAG laser. An established cobblestone, however, is more fibrous and less compressible and will not respond to laser treatment.

Soft tissue hypertrophy and established cobblestones are treated surgically. Our preferred surgical approach is a zonal, problem-oriented approach.[97] Incisions are placed along the boundaries of facial subunits or in the direction of the relaxed skin tension lines.




**Figs. 55.26A and B:** An adult with a right VII and VIII confluent port-wine stain. This patient also has upper and lower lip soft tissue hypertrophy. She was treated elsewhere with full thickness skin grafts. We resected the excess soft tissue from her upper and lower lips.

The most commonly affected areas are the upper and lower lips. The affected lip is usually elongated in the vertical and the horizontal dimensions and thickened in the anteroposterior dimension. The length is usually addressed through a full-thickness wedge resection and the thickness, through a wet/dry margin or a VCJ debulking procedure. It is often necessary to remove a wedge of muscle together with submucosal or subcutaneous tissues (Figs. 55.26A and B).

The cheek is accessed through a nasolabial incision, and the forehead can be approached through a coronal flap or a suprabrow incision. In these instances, subcutaneous fat is usually reduced, leaving the muscles and their respective nerves intact. The nasal tip is often deviated to the opposite side with enlargement of the nasal vestibule and thickening of the ala. A traditional rhinoplasty may be performed as well as repositioning of the nasal ala. Maxillary and/or zygomatic bone may be thinned to improve symmetry.

Staged procedures spaced 4–6 weeks apart are common since correction in more than one vector is needed. It must be remembered that if the patient is still growing, a repeat procedure should be anticipated.

These procedures aimed at improving the patient's quality of life. Despite the fact that it is likely that a repeat procedure may become necessary, this should not discourage the surgeon from intervening early. Removal of disfiguring tissue will improve the patient's self-esteem and therefore his or her quality of life.

## VENOUS MALFORMATIONS

When deciding when and how to treat a patient with a VM, one should keep in mind the natural history of the disease. VMs will naturally increase in size over the life of the patient. The rate of expansion varies. "High-grade" or "active" lesions expand more rapidly, whereas others expand in a more benign fashion. Trauma, hemorrhage, sepsis, hormonal fluctuations (puberty and pregnancy), and thrombosis will all result in a more rapid expansion. Advancing age results in a thinning of the supporting connective tissue, which also leads to more rapid expansion.

The following modalities have a role in the management of VMs: laser treatment (neodymiun:yttrium aluminium garnet, Nd:YAG laser), sclerotherapy (transcutaneous or transmucosal), and surgical resection.

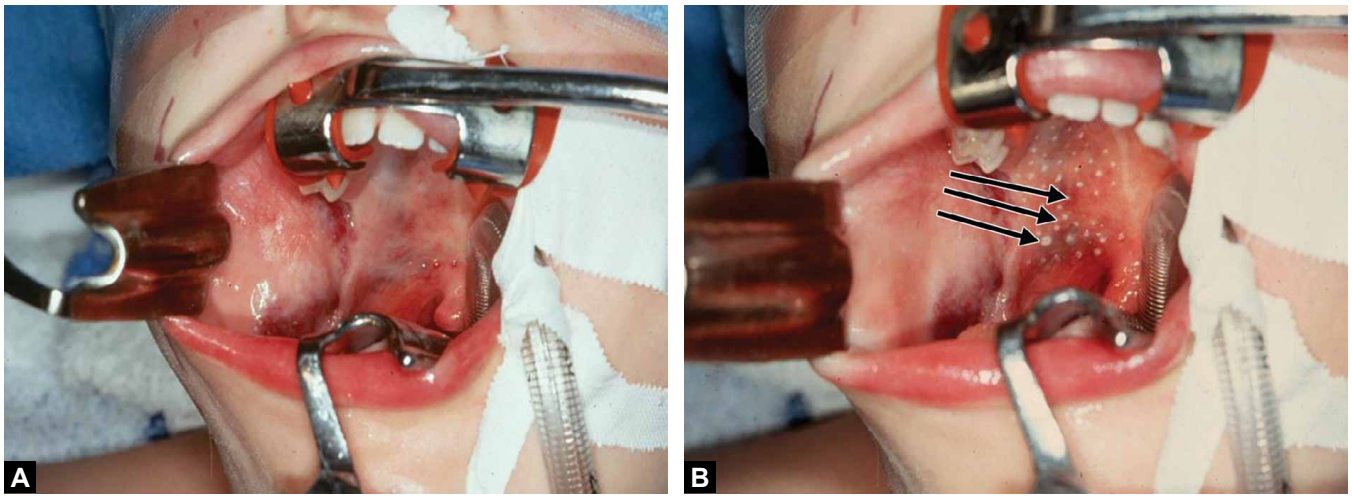
The choice of modality will depend on the depth of the lesion and its anatomical location. In general, superficial lesions and the superficial component of a compound lesion are treated with an Nd:YAG laser.[98,99] Deep lesions can either be treated with sclerotherapy as a primary modality, or sclerosed preoperatively and then surgically removed 24 hours later.[100-102] In anatomical locations where surgery will add significant morbidity, sclerotherapy is advocated. It is important to realize that although sclerotherapy may seem innocuous, it carries significant morbidity and mortality and may require several treatments.[103,104] The risks and benefits of each modality should be carefully weighed before selecting a treatment plan.

## Laser Treatment

Near-infrared light (800–2500 nm) is useful because in the 800–1200 nm range it is weakly absorbed by hemoglobin and will penetrate to an effective depth of at least 1–2 cm. Since VMs are usually at a much deeper level than PWSs, PDLs, which emit light at 595 nm are not effective. Light at 595 nm is highly absorbed by hemoglobin and thus the effective depth of penetration of light at this wavelength is only 1–2 mm. An Nd:YAG laser (1064 nm) is the most appropriate laser for treating VMs. Certain diode lasers also emit light in the 800–1200 nm range and can also be used provided that they provide sufficient power.[98,105] When used transcutaneously, the newer Nd:YAG lasers are capable of producing a larger spot size with dynamic surface cooling. The cryogen coolant cools the skin surface and in so doing prevents thermal necrosis of the overlying skin. The laser pulse proceeds the coolant by about 40 s. The end point should be vasoconstriction or darkening due to intravascular coagulation of the lesion. No blanching of the overlying skin should be allowed as this will lead to necrosis and the risk of scarring. For mucosal disease, a bare fiber is preferred. The fiber should be held about 1 mm from the treated surface and a grid or "snowstorm" pattern of treatment spots spaced 5–8 mm apart should be delivered (Figs. 55.27A and B).[105]

The Nd:YAG laser or diode laser treatment at appropriate parameters is effective as a primary treatment for superficial lesions or the superficial component of compound lesions. By treating skin or mucosa, a layer of intentional subcutaneous or submucosal scarring is produced which will enable the surgeon to raise a mucosal or skin flap during surgery. Laser treatment should precede surgery by about 6 weeks to achieve this.

Our preferred method for treating laryngeal disease consists of using a 600-μ quartz fiber, taped to a zero degree telescope in such a way that the fiber extends beyond the telescope for about 2–3 mm. In this way, the fiber tip can be seen through the telescope. We usually employ laryngoscopic suspension and deliver the laser pulses with the fiber/telescope apparatus under direct vision. Each pulse should be directed at vascular tissue from a distance of about 3 mm from the surface. This will enable the light to scatter through the lesion and effectively coagulate it. Vasoconstriction should be evident after each pulse. It is important not to deliver too many pulses during one treatment session since treatment invariably produces edema, which will reach a maximum during the first 18 to 24 hours




**Figs. 55.27A and B:** (A) Right intraoral buccal and soft palate mucosal venous malformation; (B) Immediately after Nd:YAG laser treatment. Arrows indicate points of laser impaction on mucosa and demonstrate the snowstorm pattern for treatment.

post-treatment. The patient should be admitted postoperatively for observation, and steroids should be administered intraoperatively as well as postoperatively for 4 days.

## Sclerotherapy

Sclerotherapy may be used as a primary or adjuvant treatment for VMs.[103,104] Intramuscular VM with no overlying contour deformity may be treated with primary sclerotherapy to inactivate the disease. However, once the lesion is expanded, sclerotherapy alone will not shrink the lesion. Surgical excision will be required to remove disease and correct facial symmetry.

Eyelid and orbital lesions may be treated with a combination of laser, sclerotherapy, and surgical resection. Recently, bleomycin has been used to treat orbital lesions with minimal swelling and good effect.[106]

## Surgical Resection

Lesions of the head and neck are best treated according to their anatomical site. We have divided these lesions into facial and cervical lesions. Facial lesions may be focal or diffuse. Focal lesions are best considered by their anatomical location as well as their depth. Diffuse lesions are generally treated in a staged manner, and during each stage, the area being treated is approached in accordance with its depth and anatomical location. In general, superficial lesions and the superficial component of a complex lesion are treated with an Nd:YAG laser as described previously.

Facial lesions may involve one or more of the following spaces:

- Parotid space
- Masseteric/temporal space
- Buccal fat space
- Premaxillary / premandibular space

The approach to each of these spaces should be considered separately as each space has its distinct anatomical considerations.

### *The Parotid Space*

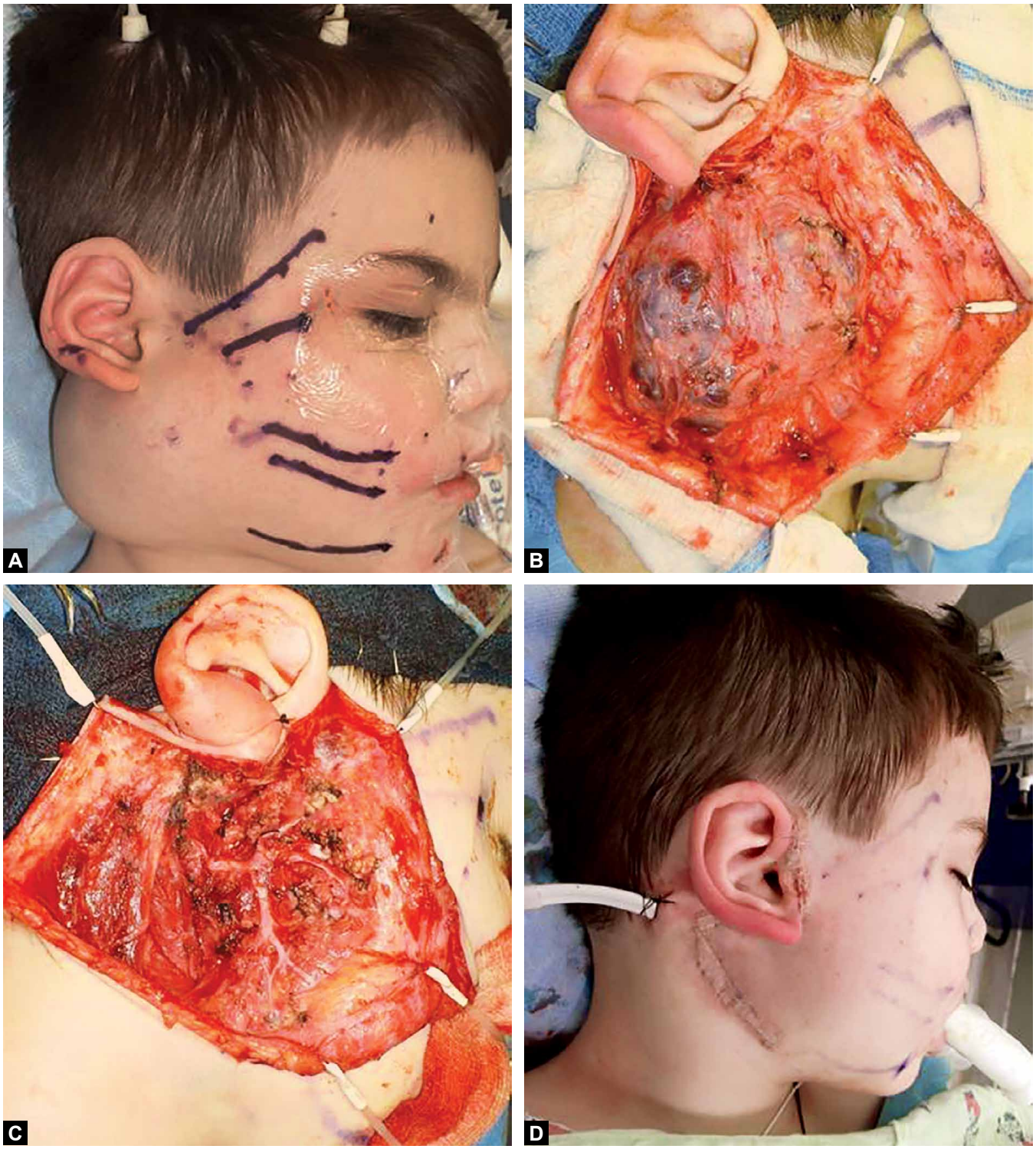
The parotid space contains the facial nerve and its branches as well as the superficial temporal vessels. Small focal lesions of the parotid may be sclerosed or surgically removed. There are no firm guidelines for this decision, and we believe that the preference of the multidisciplinary team is the over-riding factor. Focal lesions may be completely removed or even cured. Diffuse lesions within the parotid can be extremely difficult to resect without intraoperative hemorrhage, which, in turn, may lead to facial nerve damage. We may treat these primarily with sclerotherapy or if a decision is made to proceed with surgery, the lesion should be sclerosed 24–48 hours preoperatively to reduce intraoperative blood loss and facilitate facial nerve dissection. The surgical approach should be via a parotidectomy incision. The facial nerve main trunk can be found at the stylomastoid foramen and then traced forward. Alternatively, the individual branches can be found distally, anterior to the parotid gland, over the fascia on the masseter, and then traced in a retrograde fashion to the stylomastoid foramen. We prefer this approach in cases where there is diffuse parotid disease since one finds the branches in a disease-free area. The parotid gland is then removed in the same way as in tumor dissection (Figs. 55.28A to D).

### *The Masseter*

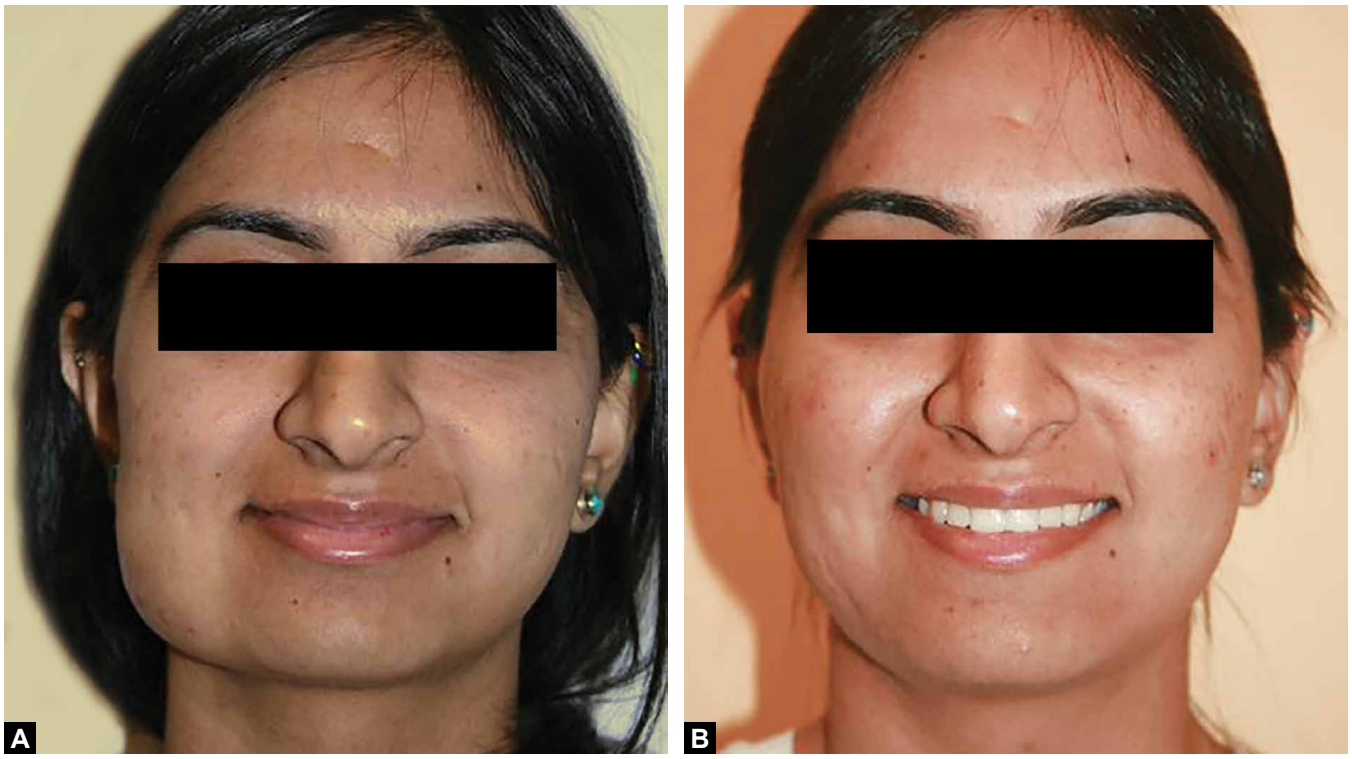
Focal VMs of the masseter are not uncommon. These lesions have been erroneously referred to as "intramuscular hemangiomas". In general, sclerotherapy will not reduce the size of the lesion. Therefore, if the lesion protrudes and is disfiguring, it should be surgically resected (Figs. 55.29A and B). An extended parotidectomy incision is made with extension along the cervical crease. The flap is raised over the parotidomasseteric fascia overlying the parotid and then over the masseter. The facial nerve branches will be found in the fascial layer on the surface of the masseter. These branches can be dissected and carefully elevated, thereby exposing the masseter. The muscle is then removed from its inferior attachments on the mandible and its superior attachment to the zygomatic arch. The remaining soft tissue defect is corrected with an autologous fat graft.

### *The Buccal Fat Space*

The buccal fat space is a common site for VMs. This space is enclosed by an investing layer of fascia. The facial nerve branches are within the superficial layer of this fascial layer. VM may involve a portion of the space or the whole space. More commonly, the lesion extends to the masseter or the premaxilla. The surgical approach to the buccal fat space is similar to that of the masseter. An extended parotidectomy incision with elevation of a flap will expose the masseter as well as the buccal fat space. The facial nerve branches can be found on the surface of the masseter or in the fascia of the fat space. The fascia between the facial nerve branches should be incised and the buccal fat can be teased out and removed. In most cases, we prefer not to sclerose the malformation preoperatively because in this case, the edema may make the dissection more difficult.




**Figs. 55.28A to D:** A child with a parotid venous malformation (A) preoperatively showing the markings from facial nerve mapping. The lesion had been sclerosed 24 hours previously to diminish intraoperative blood loss and facilitate facial nerve dissection. The flap is elevated (B) and the facial nerve branches are located anterior to the parotid gland. The nerves are then dissected out, and the venous malformation is removed piecemeal. The skin flap is then replaced (D).
(Reproduced with permission from Waner M et al. Surgical management of vascular malformations. In: Persky MS et al., eds. Vascular lesions of the head and neck: diagnosis and management. New York, NY: Thieme; 2015;102-14).




**Figs. 55.29A and B:** An adult with a masseteric venous malformation before and after surgical resection of the lesion.
(Reproduced with permission from Waner M et al. Surgical management of vascular malformations. In: Persky MS et al., eds. Vascular lesions of the head and neck: diagnosis and management. New York, NY: Thieme; 2015;102-14).

This space may also be accessed via an intraoral approach, but we prefer not to use this approach due to the fact that it is extremely difficult to locate the facial nerve.

### *The Premaxilla/Premandibular Space*

Lesions of these anterior spaces commonly involve the adjacent lip as well. They can be approached through an intraoral approach. Preoperative sclerotherapy followed within 24–48 hours by surgical resection is our usual approach. During surgery, resection of the sclerosed mass is undertaken. If the sclerotherapy was complete, this will include the entire lesion. Since VM is commonly intramuscular, it may also be necessary to remove muscle during surgery. The extent of muscle removal is usually not be sufficient to impact function (Figs. 55.30A and B).

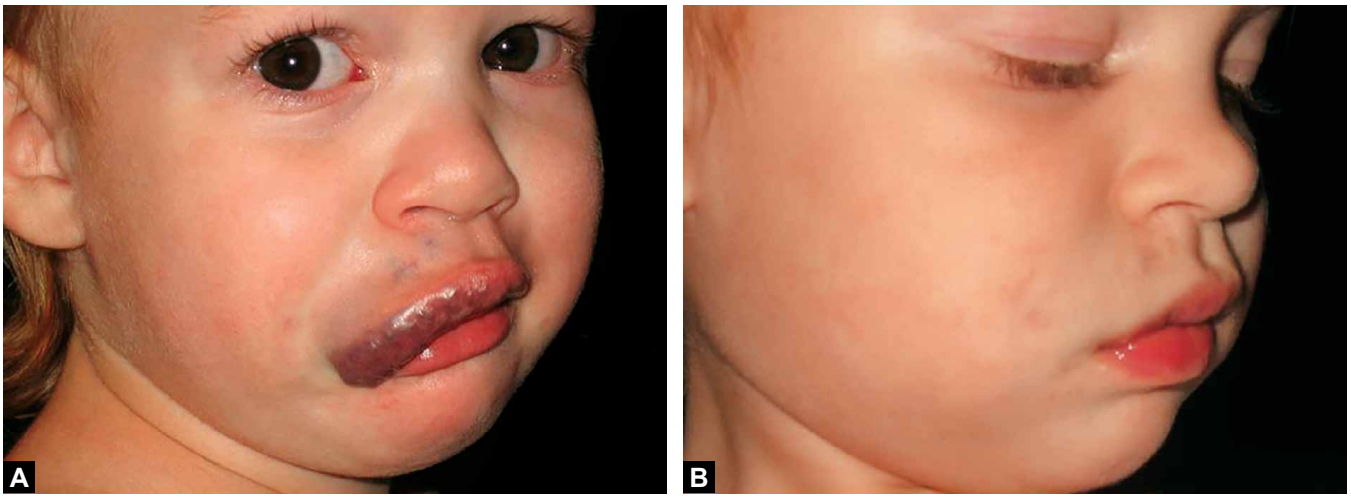
### *Cervical Lesions*

Cervical lesions can also be removed surgically. These dissections are more familiar to the head and neck surgeon and should therefore pose very little difficulty. Preoperative sclerotherapy can also be advantageous and is our preferred approach.

## Coagulation Abnormalities

Localized intravascular coagulation is a coagulation disorder associated with vascular lesions, especially VMs.[107] Microthrombosis occurs within the VM, which, in turn, results in a chronic consumptive coagulopathy. This is a chronic condition, which is usually well compensated for by the patient. Any increase in consumption could potentially stress the system and the patient will decompensate. This may happen postsurgery, sclerotherapy, trauma, or after prolonged immobilization. If the consumption is severe, this could lead to disseminated intravascular coagulation. These patients typically have an elevated D-dimer level due to the chronic consumption. The degree of D-dimer elevation appears to correlate with the size of the VM.

The LIC decompensation can usually be prevented and/or treated with low molecular weight heparin.[107,108] This should be started 2 days prior to any form of treatment, which may produce coagulation and should be continued for several days post procedure. The timing of treatment is empirical and to date, there are no data to confirm this.




**Figs. 55.30A and B:** A child with a venous malformation of her premaxillary space and her upper lip. She was treated with an Nd:YAG laser 6 weeks preoperatively. This was followed with preoperative sclerotherapy and surgical resection.

## Glomuvenous Malformation

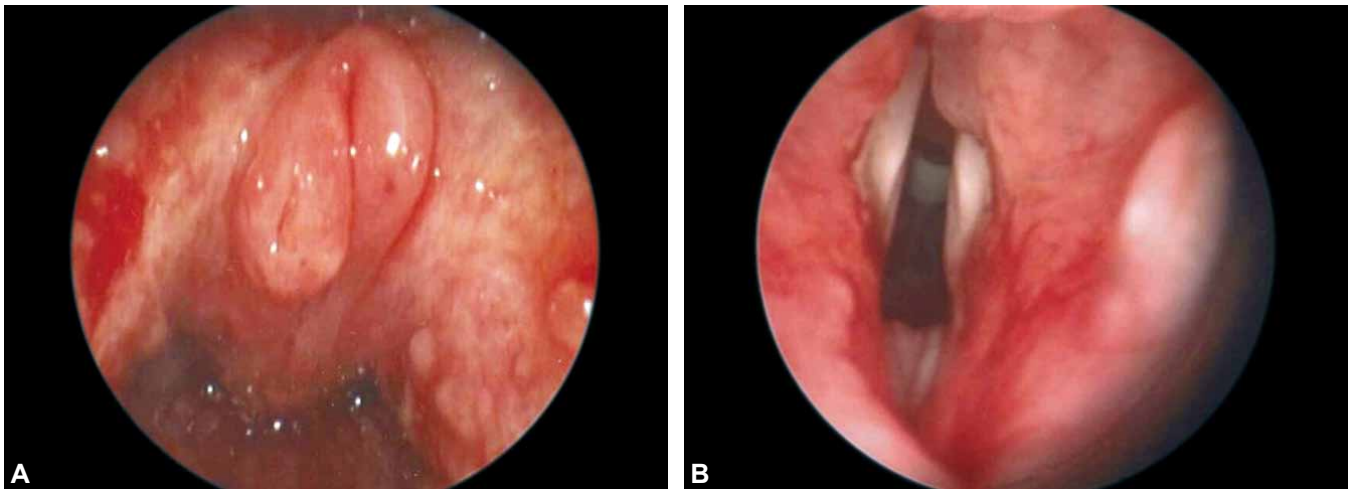
Glomuvenous malformations are low flow vascular malformations that affect the epidermal, dermal, and subcutaneous fat layers. They are often dermatomal or segmental, and they can be treated with a combination of laser (Nd:YAG) and surgical excision. Depending on the cutaneous extent of the lesion, the incisions should be placed along facial subunits or relaxed skin tension lines.

## Lymphatic Malformations

The LMs are congenital abnormalities of the lymphatic system in which the flow of lymph across the affected area is retarded. The degree of retardation varies from case to case and even within the same patient during certain incidents. A high-grade lesion is one in which there is a marked abnormality. The flow of lymph in these cases is significantly slowed, and these patients will manifest with the clinical features of an LM at birth. In low-grade lesions, there may be no clinical manifestation of the LM until some event later in life causes an increase in the production of lymph. This may be the result of trauma, a viral infection, or hormonal changes, and this may not occur until the second or third decade of life. An intermediate lesion usually manifests within the first 18 to 24 months of life.

The clinical presentation of a lymphatic malformation is a firm, flesh colored, or bluish mass. These lesions do not fill in a dependent position and are not compressible. The most characteristic feature of LMs is that they are prone to exacerbations and remissions, and these are usually associated with upper respiratory infections. This feature is not seen with other vascular malformations and will differentiate LMs in the differential diagnosis. During exacerbations, the lesion becomes swollen, inflamed, and tender.

The natural history of an LM is to expand over time and frequently cause severe disfigurement. Mucosal and/or skin involvement results in the presence of vesicles. These are commonly seen on the tongue and mucosa but can also involve the overlying skin of an LM. The vesicles are usually filled with lymph, which is transparent. LMs, whether they are mucosal or deep, have a variable concentration of veins in the walls of their cysts. During an exacerbation, bleeding into one or more of these cysts may occur resulting in a reddish or purple discoloration of some of the vesicles. Hemorrhage into a large cyst may cause an expansion of the lesion, and this in turn will cause a variable degree of pain.[109] Tongue and/or floor of the mouth involvement frequently causes glossoptosis. In evaluating a patient with glossoptosis, it is important to differentiate between frank macroglossia and glossoptosis due to floor of the mouth disease. Oral cavity, floor of the mouth, and parapharyngeal disease causes deformation of the mandible and/or the maxilla. This appears to be due to the mass effect of the lesion on bone. An increase in the angle of the mandible, and an open bite will result from the mass effect. An open bite deformity is seen in severe cases. These children have difficulty with chewing and their alimentation often needs to be supplemented in order for them to keep up with their caloric demands. They commonly drool and their speech intelligibility is severely compromised. LMs are therefore among the most challenging of lesions.




**Figs. 55.31A and B:** An infant with typical supraglottic lymphatic malformation involvement. The omega-shaped, edematous epiglottis is typical. Note the left supraglottic disease with normal appearing cords.
(Reproduced with permission from Waner M et al. Surgical management of vascular malformations. In: Persky MS et al., eds. Vascular lesions of the head and neck: diagnosis and management. New York, NY: Thieme; 2015;102-14).

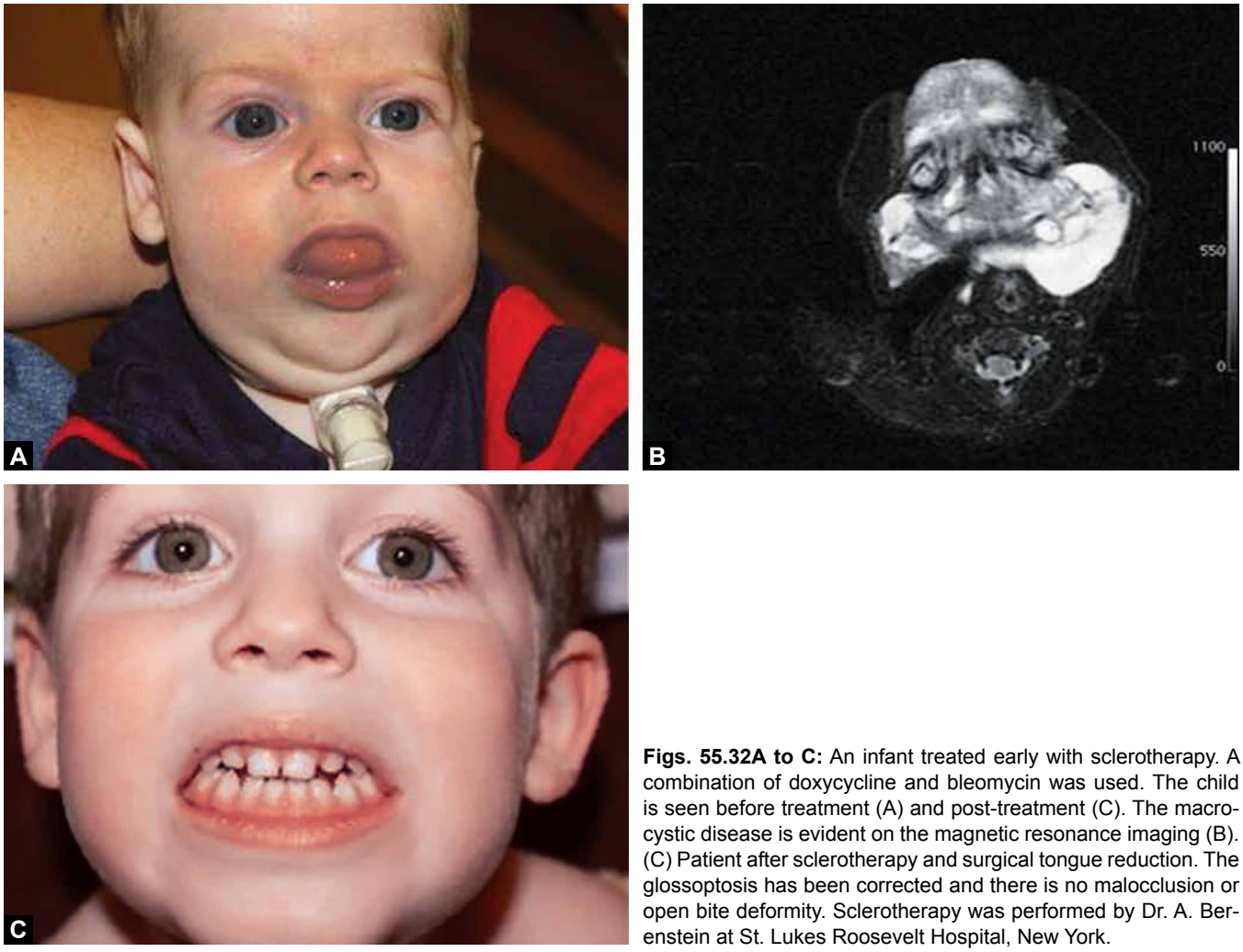
Almost half of the patients with head and neck LM will have airway involvement. An analysis of these cases determined that the airway involvement was always supraglottic.[110] No cases with glottic, subglottic, or tracheal disease were seen (Figs. 55.31A and B). This is presumably due to the paucity of lymph tissue in these areas. Many of these patients will have tracheotomy[37] and an increasing number of these are done as exit procedures (Figs. 55.31A and B).

The radiological features of lymphatic malformations are unique. They are multiseptated cystic masses that are "soft" lesions and therefore invaginate between structures. The cyst sizes vary from small to intermediate to large. This appears to be largely dependent on the consistency of the surrounding tissue. Furthermore, a cyst may vary in size, depending on whether the MRI was taken during an exacerbation or quiescent period. Much has been made of whether or not the lesion is "macrocystic" (>2 cm) or "microcystic".[111] This merely refers to the likely response of a lesion to sclerotherapy with Picibinal (OK432). Smith et al. found that macrocystic lesions responded best, hence the distinction. LMs are prone to internal hemorrhage, and one commonly finds fluid–fluid levels due to separation of the blood and lymph within a cyst. This is a diagnostic feature of LMs. Gadolinium staining is limited to the capsule or the septae and is therefore not as intense as in other vascular malformations.

The management of lymphatic malformations is multidisciplinary. Sclerotherapy, surgery, and mechanical ablation (laser ablation, coblation, or radiofrequency ablation) are all useful and are often all used in a single patient. Sclerotherapy has become the first line of treatment for LMs.[111,112] A number of agents are popular and include OK432, doxycycline, 98% ethanol, sodium morrhuate/ethiodol (3:1), and sodium tetradecyl/ethiodol (3:1). Of these, OK432, doxcycline, and bleomycin are the most widely used. It has become clear that macrocystic lesions (cysts >1–2 cm) respond best to sclerotherapy. In our institution, doxycycline is the preferred agent with or without bleomycin (Figs. 55.32A to C). The advantage of bleomycin is that it causes minimal post injection swelling and can therefore be used in the retro-orbital space or around the airway. In addition to this, bleomycin appears to be effective in treating microcystic lesions. Extensive experience with OK432 in treating macrocystic lesions has also been encouraging. In one series, it was found to be much more likely to be successful than surgery with considerably less morbidity. In addition to this, long-term control of macrocystic lesions treated with OK-432 was excellent. A meta-analysis of data on sclerotherapy shows that inconsistent presentation of data and inconsistency between case series hinders the development of uniform guidelines for the management of these difficult lesions. In over 60% of papers, the reduction in size of the LMs is not clearly defined.[113]

### *Surgical Resection*

For most extensive lesions, surgery is used in conjunction with sclerotherapy. Surgical resection is useful in reducing the size of the lesion, and in some cases, surgical resection




**Figs. 55.32A to C:** An infant treated early with sclerotherapy. A combination of doxycycline and bleomycin was used. The child is seen before treatment (A) and post-treatment (C). The macrocystic disease is evident on the magnetic resonance imaging (B). (C) Patient after sclerotherapy and surgical tongue reduction. The glossoptosis has been corrected and there is no malocclusion or open bite deformity. Sclerotherapy was performed by Dr. A. Berenstein at St. Lukes Roosevelt Hospital, New York.

can completely eliminate disease. This is especially true with macrocystic cervical lesions. While these lesions also respond well to sclerotherapy, surgical resection is a single-stage treatment, whereas multiple rounds of sclerotherapy are usually necessary to accomplish the same. When dealing with cervicofacial lesions, surgical removal is often incomplete. In these instances, control with sclerotherapy should be undertaken rather than repeat surgery. Where it is contemplated that both surgery and sclerotherapy will be needed, it is preferable to perform surgery first since operating in a field that has been previously sclerosed is extremely difficult. The fibrosis caused by sclerosing agents distorts surgical planes and makes it difficult to define and preserve important structures. This is especially true in the parotid gland. Sclerotherapy will distort the perineural anatomical plain and embed the facial nerve in a block of fibrosis making it extremely difficult to dissect out the nerve.

The surgical approach to disease involving the various areas of the face should be the same as those mentioned in the approach to VMs.

In cases of glossoptosis, a determination should be made as to whether this is due to frank macroglossia or due to disease involving the floor of the mouth, which may also cause tongue protrusion. Where the latter is the dominant cause, treatment of the floor of the mouth with sclerotherapy is indicated. If this is unsuccessful, surgery may be necessary. On the other hand, where there is true macroglossia, a tongue reduction is indicated. Two procedures have been described, a wedge resection and a keyhole procedure. We prefer a wedge resection since one is able to determine precisely how much tissue should be removed.

Mucosal involvement of the tongue is commonly symptomatic and disfiguring. Symptoms include pain, especially when acidic food or carbonated drinks are consumed.

These patients also have frequent lymph seepage as well as bleeding from the vesicles. The presence of these vesicles is therefore an indication for intervention. Several modalities are available. $CO_2$ laser ablation has been used extensively in our institution, but good results have also been reported with coblation.[105,114] No direct comparison of these two modalities has ever been undertaken. Both of these treatments are however temporary and only address the superficial vesicles. This will improve the quality-of-life in these patients, but it must be understood that this is temporary. These patients can be symptom free for a variable period, lasting anywhere from 1 to 5 years. However, in most cases, there is a deep component as well, and this will still persists since laser treatment will only ablate superficial vesicles. These vesicles will invariably recur. Recent work with intralingual injections of bleomycin clearly treats the deeper component and appears to provide more lasting relief. Further work is necessary to verify this.

### *Sclerotherapy*

The use of sclerosing agents is essential in the treatment of lymphatic malformations. This form of therapy is evolving. In earlier times, absolute alcohol was used as a sclerosant. More recently, agents such as doxycycline, OK-432, and, more recently, bleomycin are being used with good results and fewer side effects. Bleomycin is the most recent entry into this field and appears to have significant advantages. Unlike the other sclerosants, treatment with bleomycin is followed with little or no post-treatment edema. This is especially useful for areas such as the orbit and airway. Its main disadvantage is that it has a maximum lifetime dosage and risk of pulmonary fibrosis when this dosage is exceeded.

Sclerotherapy is performed by the percutaneous/transmucosal cannulation of the cyst, followed by drainage and the injection of a sclerosant into the cyst, which will destroy the cyst wall. Since larger cysts are more easily targeted, larger or macrocysts (>2 cm) respond best. Microcysts are naturally more difficult to target and respond poorly. As a consequence of this, lymphatic malformations are commonly referred to as either macrocystic or microcystic. This "classification" is purely based on their differential response to sclerotherapy. In reality, the size of the cysts can vary from month to month, depending on whether the lesion is active or quiescent. In addition to this, we believe that the size of the cysts is likely to be related to the anatomical location of the lesion and hence, the surrounding tissue. Cervical lesions are more likely to be macrocystic, whereas facial lesions are more likely to be microcystic. Having said this, most head and neck lesions are made up of both macrocysts and microcysts.

Since sclerotherapy appears to be noninvasive when compared with surgery, it has become more popular and is often the first line of treatment for lymphatic malformations. However, a meta-analysis of published data showed significant inconsistencies when reporting outcomes of treatment. Multiple treatments are the norm and the outcomes are variable. While sclerotherapy is able to reduce the bulk of a lesion, surgery is frequently necessary as an adjuvant to sclerotherapy. However, when surgery is performed after sclerotherapy, the normal tissue planes are adherent and anatomical landmarks are usually very difficult to find. This makes facial nerve preservation during parotid surgery a real challenge. For this reason, we advocate surgery as the first line of therapy. Residual disease can then be sclerosed and since surgical resection has reduced the volume of disease, this will, in turn, reduce the number of sclerotherapy events.

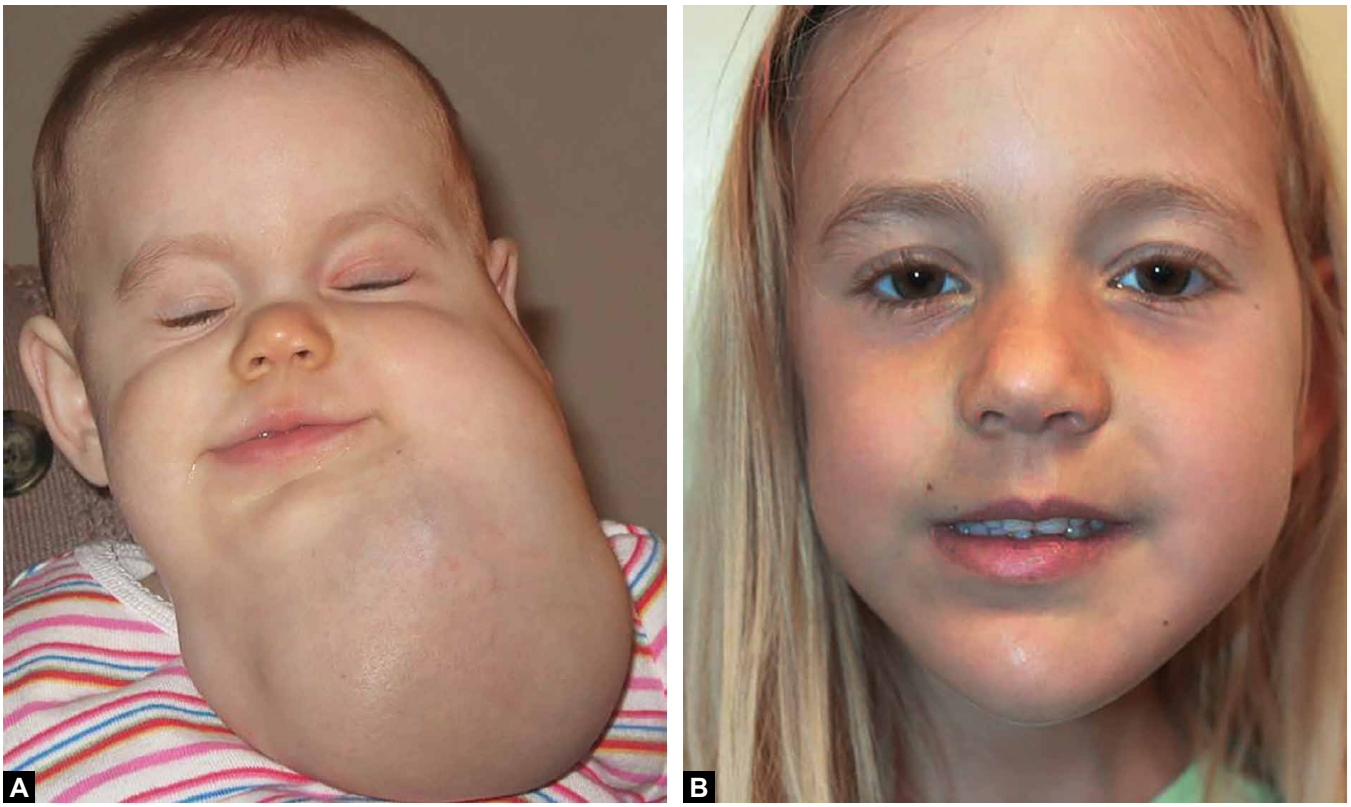
Lesions of the orbit and retropharyngeal or parapharyngeal lesions are however best treated with sclerotherapy as a primary treatment and bleomycin should be used in these cases since it produces the least amount of postoperative edema.[115,116]

Large "macrocystic" cervical lesions can be treated with either sclerotherapy or surgery as a primary treatment but mixed cervicofacial lesions are best treated with surgical debulking followed with sclerotherapy to sclerose the residual disease (Figs. 55.33A and B).

*Special considerations:* After surgery, the healing response in LMs is exaggerated. An excess of scar tissue forms. Surgical excision is followed by corticosteroid injection 4–6 weeks later to quell the response (combination of betamethasone 6 mg/kg and triamcinolone 40 mg/kg, 1:1).

## Arteriovenous Malformations

The AVMs are among the most challenging lesions to treat. They may be focal or diffuse, high grade, or low grade. Low-grade lesions may only present during the second, third, or fourth decade of life, whereas high-grade lesions are obvious at birth. The underlying abnormality appears to be an absence of the normal regulation of blood flow across a capillary bed. Instead of regulated blood flow across the capillary bed, there is continuous shunting of blood across the capillary bed, which, in turn, leads to progressive dilatation of the capillary vessels. A number of




**Figs. 55.33A and B:** An infant before and after surgical resection and several rounds of sclerotherapy. She had mixed macro- and microcystic disease. Surgical debulking removed the large mass and sclerotherapy was used to treat the small amount of remaining disease. At the time of this publication, she has been disease free for 18 months.

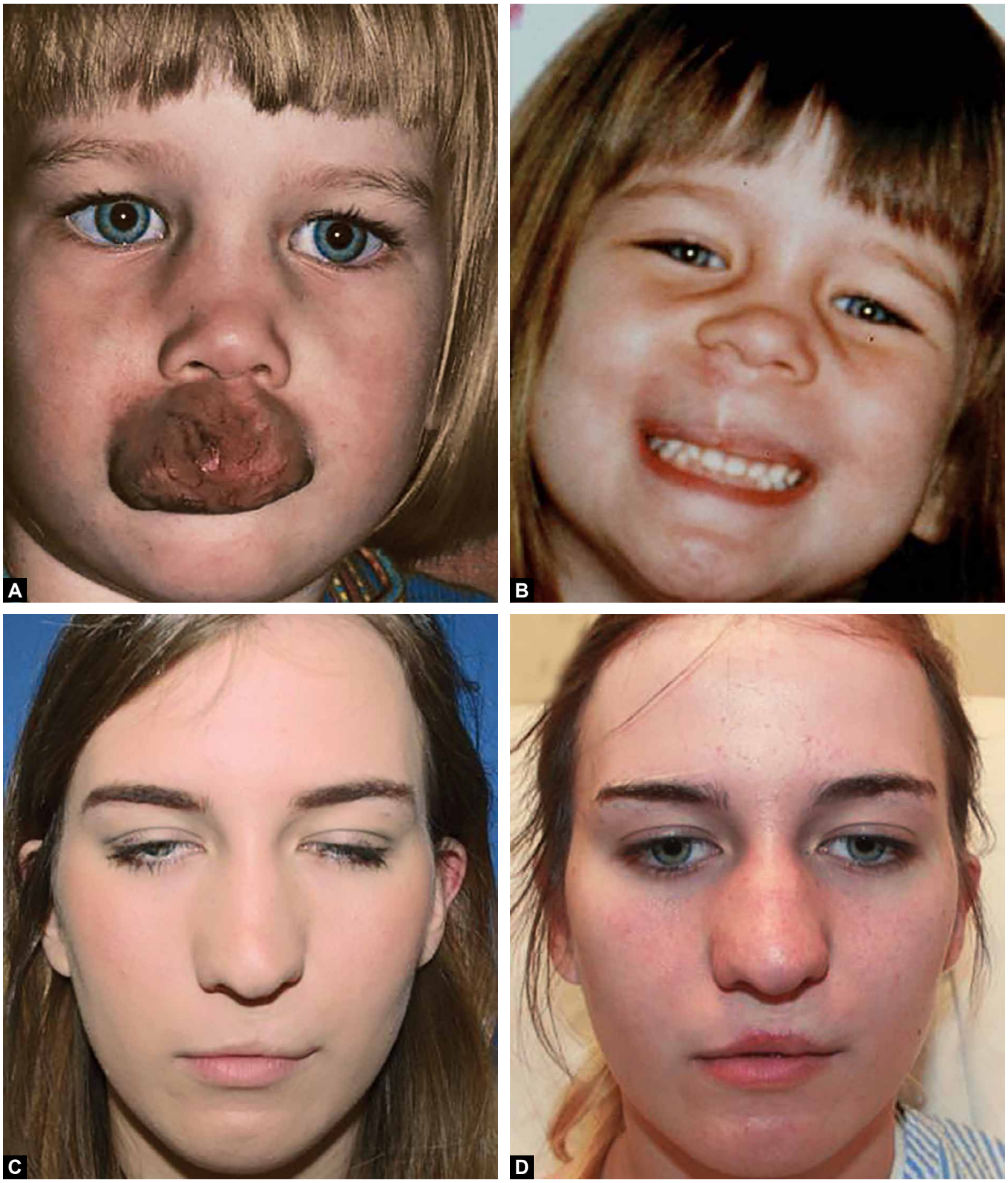
"secondary" changes occur such as venous dilatation and arterial hypertrophy, which accommodate the increased blood flow across this AVM. Over time, as the capillary bed dilates, the volume of blood shunting across this area will increase, which, in turn, leads to further "secondary" dilatation of the surrounding vessels, and in time, this could lead to flow reversal upstream and a steal syndrome.[117]

The underlying pathology, i.e. an abnormal capillary bed is known as the "nidus", and treatment should be directed at the nidus. The dilated vessels surrounding the nidus are secondary changes, and it is not necessary be treat them. Once the "source" of the shunting is eliminated, these secondary changes will begin to reverse. When a surgeon is faced with a large lesion, it is often difficult to differentiate between the nidus and the secondary changes. Combining the findings of an angiogram with an MRI is helpful in this regard. The area of shunting is the nidus.

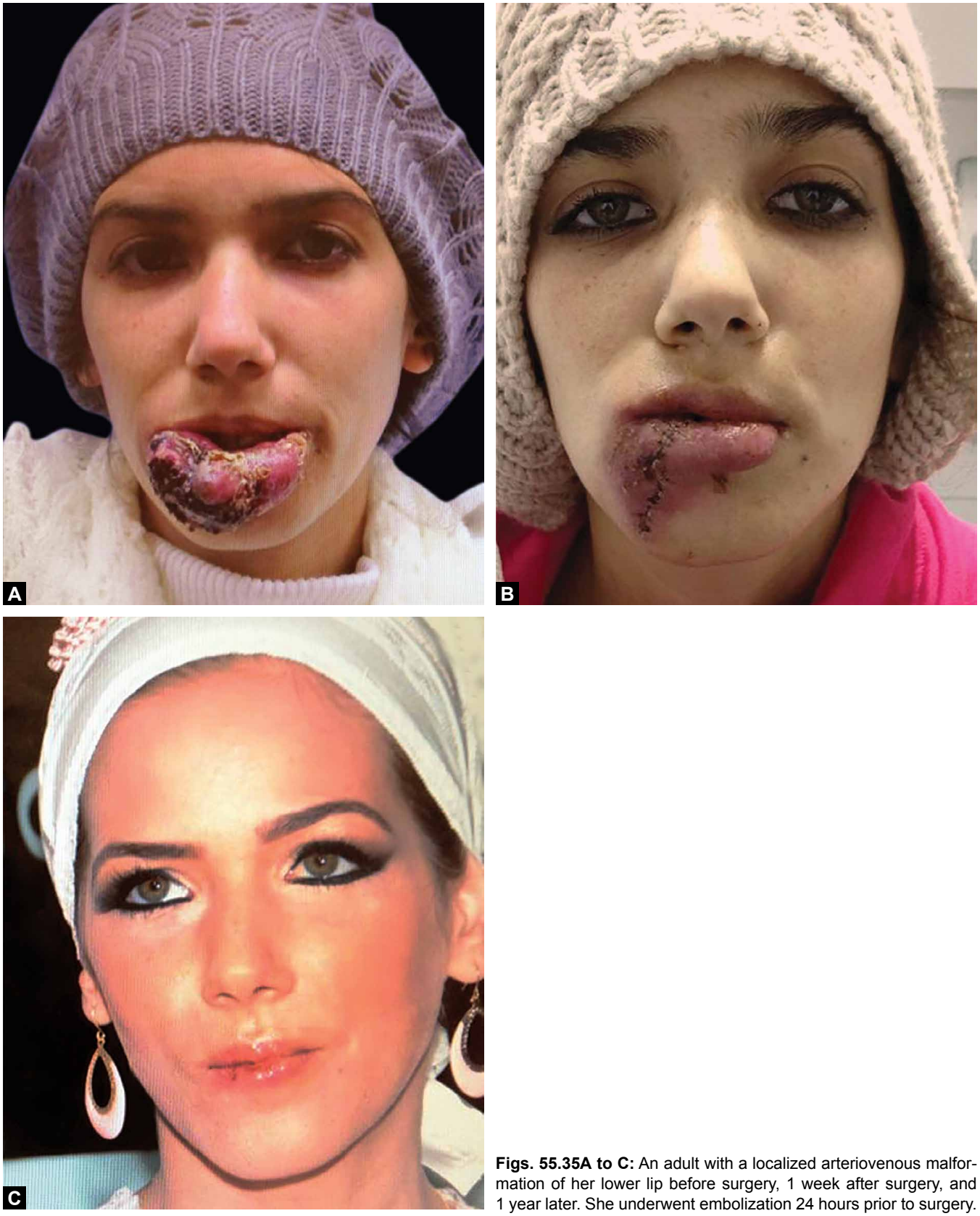
Treatment of AVMs is best approached in a multidisciplinary setting. The participation of both an interventional radiologist and a surgeon are essential, and both embolization and surgical resection are necessary treatment modalities.[118,119] In general, preoperative sclerotherapy, followed by surgical resection of the nidus is advocated. When treating localized or focal lesions, this may be curative (Figs. 55.34 and 55.35). In more diffuse lesions, a "cure" is unrealistic. In these cases, an attempt should be made to improve the quality of life of the patient. This is usually accomplished by staged surgical procedures, usually preceded by embolization and surgical resection (Figs. 55.36A and B). Addressing problem areas that have ulcerated and are bleeding, as well as improving the appearance of the patient is our objective.

Surgical resection can be extremely challenging, and preoperative embolization will decrease or eliminate intraoperative bleeding. The choice of embolic agents depends on the experience of the interventional radiologist and whether or not embolization is being performed as a primary or preoperative treatment.

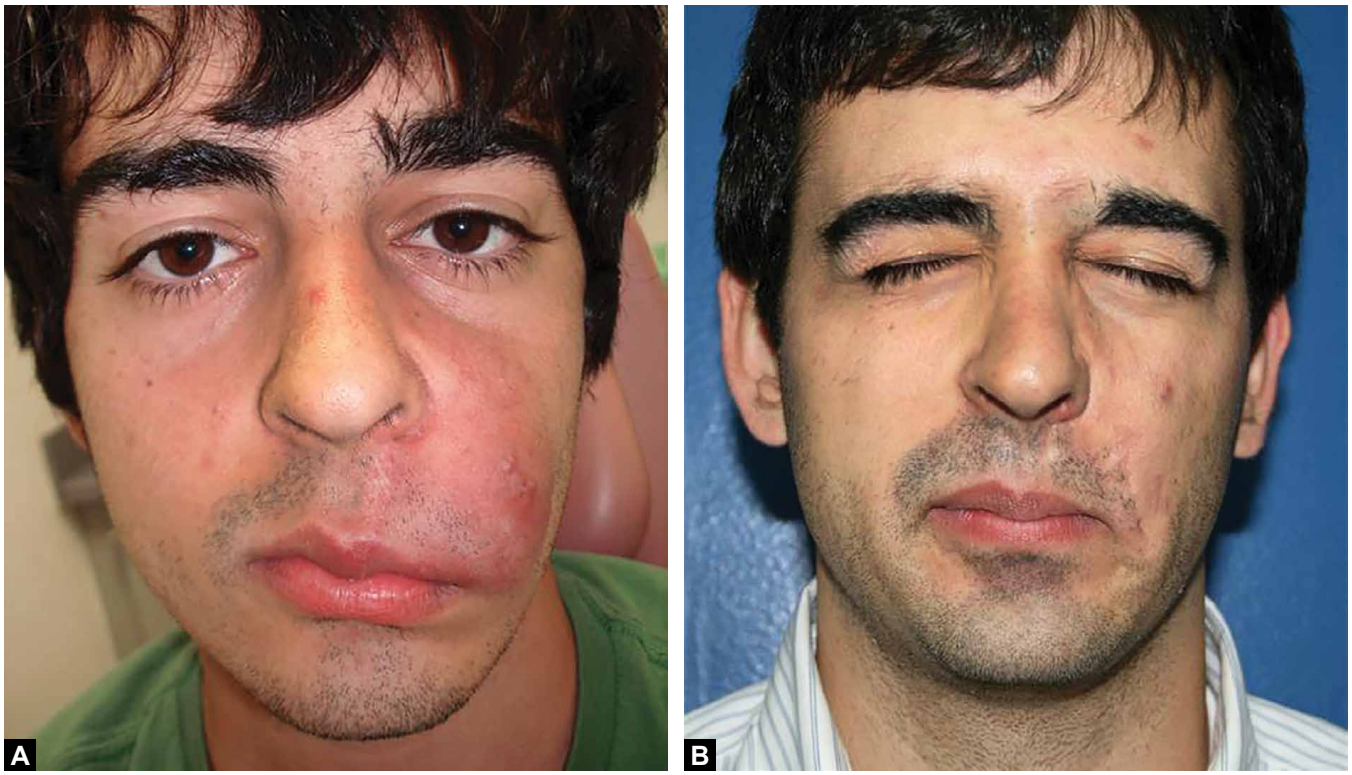
Our preference for surgery is based on our belief that elimination of a nidus with conventional interventional radiological techniques is rare. There are a small number of successful reports of nidus elimination after embolization




**Figs. 55.34A to D:** A 4-year old with a localized arteriovenous malformation of her upper lip (A). Although it appeared that the entire lip was involved, this was not so. She underwent resection of the nidus only (B) and remained disease free until 18 years of age (C). She returned for minor esthetic surgery prior to attending college (D).




**Figs. 55.35A to C:** An adult with a localized arteriovenous malformation of her lower lip before surgery, 1 week after surgery, and 1 year later. She underwent embolization 24 hours prior to surgery.




**Figs. 55.36A and B:** A patient with a diffuse arteriovenous malformation of his midface. The lesion extent corresponded with the area of erythema. This was removed in a piecemeal fashion. Each surgery was preceded with embolization/sclerotherapy. In the photo on the left, about 6 years has transpired since his last procedure without recurrence.

with absolute alcohol, but the morbidity and mortality of absolute alcohol should preclude its use in the head and neck by all except those with extensive experience with this agent. However, even in the most experienced hands, there is a risk of necrosis of overlying skin and even cardiopulmonary collapse if a bolus finds its way into the central circulation.

Surgery is also challenging. Intraoperative blood loss, especially in a child can be significant. The preservation of important structures can be compromised by the profuse hemorrhage and skin necrosis probably due to venous congestion of the skin flaps is sometimes seen. The exact incidence of this has not yet been determined, but it is believed to be significant.

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CHAPTER

56

# Pediatric Skull Base Lesions

***Katie L Pricola, Derrick T Lin, Benjamin S Bleier, William T Curry Jr***

## INTRODUCTION

For clinical and treatment purposes, the skull base is defined as that region of the cranium that extends from the orbital rims and frontal sinus to the foramen magnum posteriorly. The skull base is characterized by thick bone that protects the contents of the orbit, the middle and inner ears, the cranial nerves, and the vascular inflow and outflow to the brain (Fig. 56.1). Congenital, infectious, traumatic, and neoplastic pathologies can affect portions of the skull base and require surgical intervention. Skull base surgery is a complex and potentially morbid endeavor that requires expert understanding of head and neck anatomy, neuroanatomy, otology, and ophthalmology.

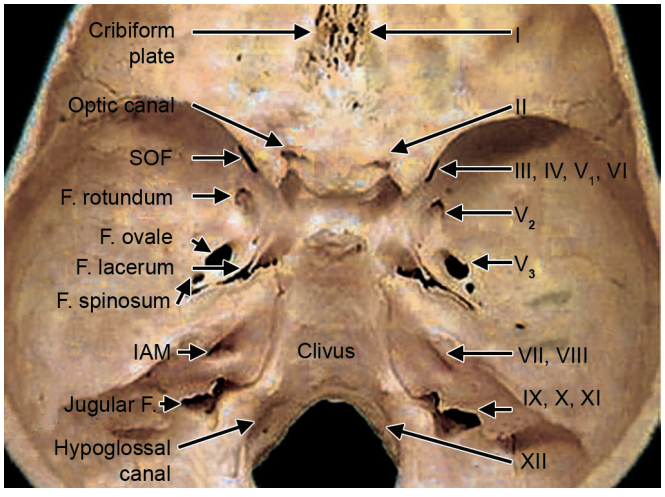



**Fig. 56.1:** Superior view of the skull base with the brain, meninges, vasculature, and cranial nerves removed. Roman numerals denote the foramina through which the cranial nerves pass. (F: Foramen; SOF: Superior orbital fissure).

The field continues to evolve and is marked by its multidisciplinary nature, despite the relatively tight geographic space. Head and neck surgeons and otologists frequently collaborate with neurosurgeons and ocular surgeons. Modern techniques in reconstruction, including autologous tissue transfer and free flap repair, have allow more extensive resections and better quality of life after surgery. The evolution of endoscopic technology and surgical skills over the past decade has also allowed deeper surgical access to the skull base with less removal of bone and less disfigurement than was required in earlier generations.

It is beyond the scope of this chapter to review every possible skull base lesion that can present in children. Here, we focus on presentation of the most common surgical lesions of the pediatric skull base and review the pathophysiology, presentation and diagnostic criteria, staging, treatment options, outcomes, and recurrence rates.

## JUVENILE NASOPHARYNGEAL ANGIOFIBROMA

Juvenile nasopharyngeal angiofibroma (JNA) is a rare tumor, which predominantly affects adolescent males with an average age of 15 years. JNA accounts for 0.05–0.5% of all head and neck tumors. It is a histologically benign, locally aggressive, and extremely vascular lesion.[1,2]

### Pathophysiology

The JNAs are derived from myofibroblasts and primarily located in the nasopharynx.[3] They are a nonencapsulated, irregular network of blood vessels in a matrix of fibroblasts.

The tumors are most commonly supplied by the internal maxillary artery with reports of feeders from the external carotid, internal carotid, common carotid, and ascending pharyngeal arteries as well.[4]

As noted, tumors arise in the nasopharynx, and though histologically benign, they exhibit locally aggressive behavior with spread through pre-existing bony apertures causing tissue destruction and bony remodeling. Local invasion corresponds with the direction of spread. Anterior spread expands into the nasal cavity, lateral spread is into the pterygopalatine fossa, and superior extension leads into the cranial vault.[5,6]

Intracranial spread is reported in 10–30% of cases.[2,7,8] The most common location for intracranial spread is into the middle cranial fossa (8.6% of patients) through the ethmoid and sphenoid sinuses with erosion into the sella and planum sphenoidale.[9]

Tumor can also spread through the maxillary, ethmoid, and sphenoid sinuses into the infratemporal fossa. In some cases, orbital invasion through lamina papyracea/superior wall of maxillary sinus or through the inferior orbital fissure has been identified.[10,11]

## Presentation and Diagnosis

Children present most commonly with epistaxis followed by nasal obstruction and less commonly with nasal discharge, pain, sinusitis, vision loss, facial deformity, facial pain, or proptosis.[8,12,] On gross inspection, a purple/red nasal mass is usually apparent (Fig. 56.2).[13] Office nasal endoscopy or nasopharygoscopy may be performed, but biopsy is contraindicated given risk of life-threatening hemorrhage.

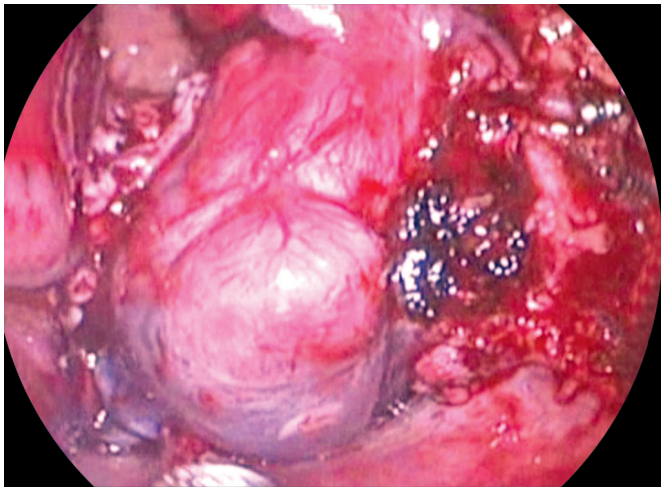


**Fig. 56.2:** Intranasal endoscopic view of a juvenile nasopharyngeal angiofibroma. Note the lobulated hypervascular appearance. The mass fills the cavity.

The diagnosis can almost be made on physical examination alone, although both computed tomography (CT) and magnetic resonance imaging (MRI) are routinely used. CT shows tumor classically involving the nose and pterygopalatine fossa. Anterior bowing of posterior maxillary wall (Holman–Miller Sign) is considered pathognomonic of JNA. MRI shows a contrast enhancing mass, occasionally dumb-bell shape, again located in the nasopharynx, and pterygopalatine fossa.[14] MRI also further delineates important relationships between the tumor and the carotids, cavernous sinus and the pituitary gland.

## Staging

Staging for JNA describes the anatomic compartments in which the tumor resides and has relevance for surgical approach and resectability. The two most commonly cited systems are those of Radkowski and Andrews.[15,16]

The Radkowski[15] staging system is the most widely cited and describes tumor with respect to anatomic location. Stages IIIa and IIIb denote tumor with intracranial spread.

| Radkowski staging[15] | |
|---|---|
| Ia | Tumor limited to nasal cavity and nasopharynx |
| Ib | Tumor in nasal cavity with paranasal sinus extension |
| IIa | Tumor with minimal extension through sphenopalatine foramen, into medial pterygomaxillary fossa |
| IIb | Tumor with full occupation of pterygomaxillary fossa, displacing posterior maxillary wall anteriorly, orbital erosion, displacement of maxillary artery branches |
| IIc | Infratemporal fossa, cheek, posterior, to pterygoid plates |
| IIIa | Minimal intracranial extension |
| IIIb | Extensive intracranial extension with or without cavernous sinus |

| Andrews JNA stage[16] | |
|---|---|
| I | Tumor limited to the nasal cavity and nasopharynx |
| II | Tumor extension into the pterygopalatine fossa, maxillary, sphenoid, or ethmoids sinuses |
| IIIa | Extension into orbit or infratemporal fossa without intracranial extension |
| IIIb | Stage IIIa with small extradural intracranial (parasellar) involvement |
| IVa | Large extradural intracranial or intradural extension |
| IVb | Extension into cavernous sinus, pituitary, or optic chiasm |

Additional staging systems not elaborated on here—Chandler et al.[17] and Sessions et al[18]—apply similar grading schema with varying degrees of intracranial extension defining stages III and IV.

Snyderman et al. recently published an endoscopic staging system, which prioritizes the impact of route of skull base extension as well as residual vascularity after embolization. All systems have implications for surgical accessibility and approach.[19]

## Treatment

The gold standard of treatment remains surgical resection, although the literature is rife with unresolved discourse regarding whether the best approach is open or endoscopic.

Regardless of planned method of surgical resection, preoperative embolization 24–72 hours prior to resection should be considered.

### *Surgical Approaches*

Open surgical approaches in the literature for JNA include lateral rhinotomy, transpalatal, transmaxillary, midfacial degloving, Le Fort I, Denker, and infratemporal craniotomy surgical excision.[20-24]

A 2011 series from the Barrow Neurological Institute reported 22 patients from 1992 to 2009 who underwent radical craniofacial procedures. The surgical procedure involved a transbasal combined with transmaxillary approach that involves a bifrontal craniotomy with additional removal of supraorbital bar and nasal orbital complex as well as an LeFort I procedure with or without palatal splitting. The authors noted that a gross total resection (GTR) was achieved in 17/22 patients. The overall series recurrence rate was 18% with a fairly high complications rate: 23% of patients had cerebrospinal fluid (CSF) leak, 14% suffered infection, 10% incidence of bony defects, 10% had meningitis, and 4% endured either chronic drainage, epistaxis, sinusitis, or nasal congestion.[25]

Numerous institutional case series have been published with a range of estimates as to the mandatory degree of resection, rates of recurrence as well as complications.[9] In a 2013 review, Boghani et al. consolidated this information and separately analyzed individual and aggregate data for a total of 1047 reported cases.

Based on 60 patients with information available with regard to stage, there is a 6.7% average overall rate of recurrence with endoscopic resection. This can further be broken down into 3.4% for Radkowski stage I, 10.7% for stage II, and 0% for stage III. Based on 150 patients for which only aggregate data was available (not accounting for stage), the authors found a 4.7% overall rate of recurrence with the endoscopic approach.

Based on 44 patients with staging information available, there is an 18.3% average overall rate of recurrence; 7.7% for Radkowski stage I, 22.2% for stage II, and 25% for stage III. Based on 518 patients for which no staging information is available, there was a 22.6% overall rate of recurrence with open surgical approaches.

This recurrence rate for combined open/endoscopic approaches was noted to be 20.6%. The morbidity associated with endoscopic surgery has been reportedly less with an average of 0.5 L estimated blood loss from surgery compare with the 1.5 L average for open approaches.

Bleier et al. have published a contemporary series of cases of all Andrews' stages. All stage I and stage II tumors were fully resected endoscopically, as was an Andrews stage IIIa lesion. Tumors in stages IIIb and higher were resected via lateral rhinotomy, alone, or in combination with a craniotomy. GTR was achieved in all but one with residual tumor in the cavernous sinus.

### *Adjuvant Therapy*

Radiation therapy is the mainstay of treatment for large, nonresectable tumors with recurrence rate noted to be 15% at 5 years, and an average of 3 years required for complete involution of tumor.[26]

Given the aggressive local nature and mass effect often precluding the use of radiation or the utility of radiation when more immediate relief is necessary, there is a demand for systemic chemotherapeutics. The majority of trialed agents and future therapeutic targets rely on the hormone receptor theory and the angiogenesis model.

The hormone receptor theory rests in the epidemiology of this disease, which most commonly affects males during adolescence/puberty. Multiple studies have looked at androgen and estrogen responses with controversial and conflicting results. Flutamide (antiandrogen) has been shown to be effective in 87% of cases for presurgical volume reduction when given as pretreatment in postpubertal males; there is no notable reduction when given as pretreatment in prepubertal males.[27]

There is significant interest in angiogenesis inhibition as therapy for JNAs given their hypervascular nature. Currently, there are no existing approved therapeutics.

# ESTHESIONEUROBLASTOMA

## Pathophysiology

Esthesioneuroblastoma, otherwise known as olfactory neuroblastoma, is an extremely rare entity with a total of 120 cases reported in the pediatric literature.[28-36]

Esthesioneuroblastoma is a neuroectodermal tumor thought to arise from the basal layer of olfactory epithelium lining the nasal septum, cribriform plates, and nasal turbinates by a poorly understood mechanism. Histologically, it is composed of small round blue cells with the appearance of primitive neuroectodermal tissue and occasional Homer Wright rosettes[37] (Fig. 56.3A).

## Presentation and Diagnosis

Unlike JNA, there is no gender predominance with equal numbers of males and females affected. The most common presenting symptoms are unilateral nasal obstruction and occasional epistaxis. In a large case series, 76% of patients presented with symptoms of nasal obstruction, 42% with epistaxis, 30% with headache, 10% with visual disturbances, and 8% with exophthalmos.[38]

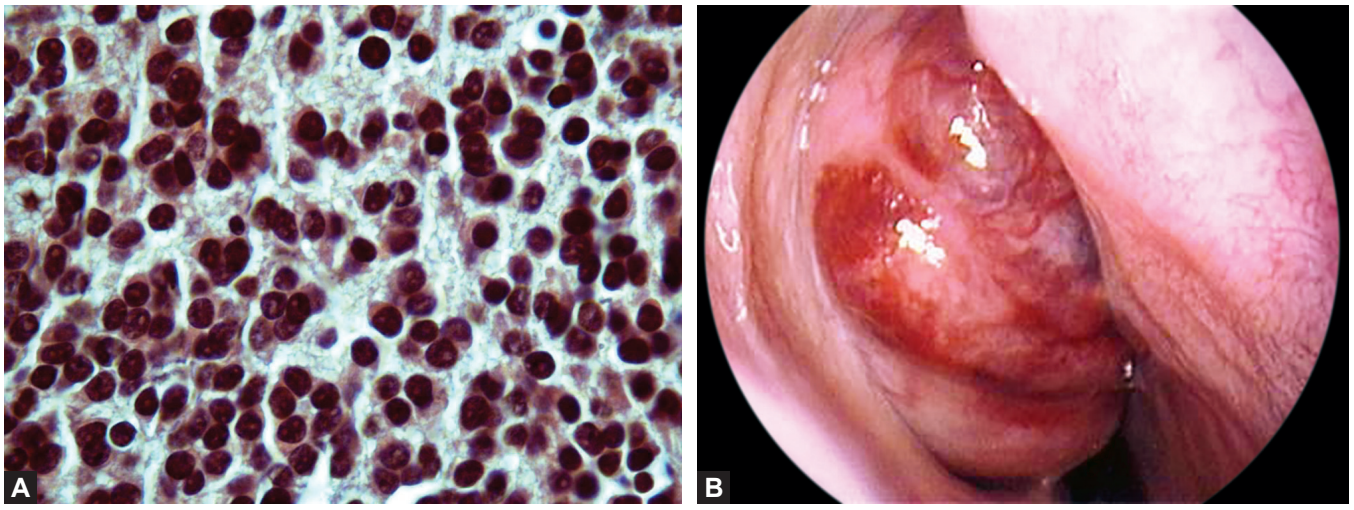
On clinical examination, the tumor appears as a homogenous, friable, soft tissue mass in the nares (Fig. 56.3B). Standard workup includes CT and MRI. CT details bone destruction and integrity of the lamina papyracea, cribriform plate, and ethmoidal air cells. MRI is used to assess for intraorbital and intracranial involvement. Tissue diagnosis is necessary to distinguish the tumor, which typically stains positive for S100, chromogranin, a synaptophysin and negative for cytokeratin, desmin, vimentin, actin, GFAP, UMB45, and common leukocytic antigen.[39]

## Staging

| Kadish staging[40] | |
|---|---|
| Stage A | Disease confined to nasal cavity |
| Stage B | Disease confined to nasal cavity and one or more paranasal sinuses |
| Stage C | Disease extending beyond the nasal cavity or paranasal sinuses, including involvement of the orbit, base of skull, intracranial cavity, cervical lymph nodes, or distant metastatic sites |

The TNM staging system, as proposed by Dulguerov et al. has also been employed.

| TNM staging[40] | |
|---|---|
| T1 | Tumor involving the nasal cavity and or paranasal sinuses, excluding the sphenoid and superior ethmoids |
| T2 | Tumor involving nasal cavity and/or paranasal sinuses, including the sphenoid with extension to or erosion of the cribriform plate |
| T3 | Tumor extending into the orbit of protruding into the anterior cranial fossa, without dural invasion |
| T4 | Tumor involving the brain |
| N0 | No cervical lymph node metastasis |
| N1 | Any form of cervical lymph node metastasis |
| M0 | Metastasis |
| M1 | Distant metastasis |




**Figs. 56.3A and B:** (A) Hematoxylin and eosin staining of an esthesioneuroblastoma from an 8-year-old patient. Note the sheets of small round blue cells with occasional rosette formation. (B) Endoscopic view of an esthesioneuroblastoma within the nasal cavity.

## Treatment

These rare pediatric tumors are treated empirically on the basis of the adult experience given insufficient number of patients to power a randomized trial.

The gold standard of treatment is craniofacial surgical resection with goal of negative margins. Dulguerov et al. recommend resection of the ipsilateral cribriform plate, crista galli, olfactory bulb, and associated dura as well as the lamina papyracea and portion of the orbital periosteum (assuming no orbital involvement).

Radiation has been used nearly universally though with most consistent use in patients with incomplete resections and positive margins. Chemotherapy has been used in cases of nonresectable, recurrent, or metastatic disease.[29] More recent cases series in the literature suggest that adjuvant chemotherapy is being used much more commonly with VAC-Adria (vincristine, doxorubicin, cyclophosphamide) and IE (ifosfamide and etoposide) among other trialed chemotherapeutics.[32]

## Outcomes and Recurrence

The largest cohort of pediatric esthesioneuroblastoma is reported from Mayo Clinic, where a total of 49 patients were treated between 1951 and 1990.[41] Five-year survival rates for all comers were 69% with 80% for low-grade and 40% for high-grade tumors. This is comparable with historic 5-year survival rates published in the late 1970s, which report 75% for stage A, 60% for stage B, and 41% for stage C.[42]

Other large case series have combined both the adult and pediatric experience. The University of Virginia treated 50 patients aged 9–77 years from 1976 to 2004, using a standardized institutional protocol involving neoadjuvant radiation with or without chemotherapy prior to craniofacial resection. Sixty-six percent of the treated patients had Kadish stage C disease. Patients with Kadish A or B esthesioneuroblastoma underwent preoperative radiation followed by craniofacial resection; Kadish C patients underwent preoperative chemotherapy and radiation. Rates of disease-free survival were 86.5% at 5 years, 82.6% at 15 years with an overall 34% rate of recurrence in their patient population. Of note, the majority of patients in the series were 40–60 years old.[38]

MD Anderson recently reported their results on 70 patients treated from 1992 to 2007, of which 77% had T3 or T4 disease at initial presentation and 38% were Kadish stage C. Almost all patients underwent surgical resection (90%) and two thirds of patients underwent postoperative radiation with or without chemotherapy (66%). Overall rates of recurrence in this series was 48% and overall median survival was 10.5 years, although surgery alone had a median survival of 7 years while surgery and radiation was reported as 18 years.[43]

Broich et al. retrospectively applied the Kadish system to 945 patients in the literature. Of the patients reported from 1924 to 1997, 18% had stage A, 32% had stage B, and 49% had stage C disease. Of the patients with a minimum 5-year follow-up, survival rates for combined therapy, surgery, and radiation therapy were 72.5%, 62.5%, and 53.8%, respectively.[29]

Dulguerov et al. published the largest, most recent meta-analysis of the literature, which evaluated 5-year survival rates based on all treatment modalities as they were applied from 1990 to 2000. Twenty-six studies with a total of 390 patients were analyzed with 12% stage A, 27% stage B, and 61% stage C with mean survival rates of 72%, 59%, and 47%, respectively. Overall local recurrence rate was 29% and regional recurrence rate was 16%. Five-year survival rates were extrapolated as follows: overall survival 45%; surgery alone 48%; surgery and radiotherapy 65%; radiotherapy alone 37%; combination of surgery, radiotherapy, and chemotherapy 47%; radiotherapy and chemotherapy 51%; and chemotherapy alone 40%. The data analyzed, however, were in the aggregate, and treatment modalities were not subgrouped based on stage.[39]

# SARCOMAS

Sarcomas of the head and neck are rare entities even among sarcomas, comprising ~10% of sarcomas. From 1970 to 2004, MD Anderson treated a total of 1161 head and neck sarcomas (combined pediatric and adult numbers), of which 15% were osteosarcoma, 6.5% chondrosarcoma, 9.6% malignant fibrous histiocytoma, 3.6% fibrosarcoma, 5.2% dermatofibrosarcoma protuberans, 12.9% rhabdomyosarcoma (RMS), 2.8% leiomyosarcoma, 11.6% angiosarcoma, 2% hemangiopericytoma, 5.1% neurogenic sarcoma, 2.4% liposarcoma, 4% synovial sarcoma, 1.1% Ewing's sarcoma, and 17.8% unclassified. Thirty-two percent of these tumors were invasive to the skull base.[44]

## Rhabdomyosarcoma

Rhabdomyosarcoma is the most common soft tissue tumor in children.[45] Thirty-five percent of RMSs arise in the head and neck[46] and >50% of head and neck RMA cases are invasive of the skull base.[44]

## Pathophysiology

In the head and neck region, two histopathologic subtypes of RMS predominate: embryonal and alveolar. Embryonal RMS (ERMS) typically affects patients <10 years old and is typically associated with orbital disease. Histologically, it is composed spindle-shaped cells.[47] By molecular genetic testing, ERMS displays loss of heterozygosity at the 11p15 locus, the location of the IGFII gene, with loss of maternal genetic information, and duplication of paternal genetic information.[48,49]

Alveolar RMS (ARMS) typically affects children >10 years of age. Histologically, ARMS is composed of small, round, densely appearing cells lined up in a matrix resembling pulmonary alveoli.[47,50,51] By molecular genetic testing, there is a translocation, t(2;13)(q35;q14), which fuses two transcription factors PAX3 and FKHR as well as a variant t(1;13)(p36;q14), which fuses *PAX7* with FKHR.[52]

## Presentation and Diagnosis

More than half of pediatric cases of RMS occur in children < 6 years with the remainder ranging in age from 10 to 18.[53]

Pediatric RMS of the head and neck can be parameningeal, nonparameningeal, and orbital in location. Parameningeal disease is defined by location in the nasopharynx, the nasal cavity, paranasal sinuses, infratemporal fossa, pterygopalatine fossa, and middle ear and often presents with nasal or sinus obstruction accompanied by mucopurulent or sanguineous discharge. Nonparameningeal tumor involves the cheek, parotid, and nose and typically presents as a painless enlarging mass. Orbital tumors present with proptosis and ophthalmoplegia.[54]

The Hospital for Sick Children treated a total of 48 patients with RMS from 1972 to 1998, 29 of which had nonorbital tumors, 20 parameningeal, and 9 nonparameningeal. In this series, age at diagnosis was 5 years on average with a range from 3 months to 12.5 years. Embryonal tumors were three times as prevalent as alveolar, consistent with previous reports in the literature.[55]

Diagnosis is made on the basis of the physical examination findings combined with CT and MRI evaluation. Children with parameningeal disease should undergo lumbar puncture to determine presence or absence of leptomeningeal spread.[56]

## Staging

Staging for RMS has historically been by group and is based on extent of surgical resection.[55]

**Intergroup Rhabdomyosarcoma Study (IRS) surgical-pathologic grouping[58]**

| | |
|---|---|
| Group I | Localized disease that is completely resected<br>IA—confined to muscle or organ of origin<br>IB—contiguous involvement, with infiltration outside the muscle or organ of origin; regional nodes not involved |
| Group II | Compromised or regional resection<br>IIA—grossly resected disease with microscopic residual<br>IIB—regional disease, completely resected, in which nodes may be involved and/or resected |
| Group III | Incomplete resection or biopsy with gross residual disease |
| Group IV | Distant metastatic disease present at onset |

A TNM staging system for RMS exists, and its prognostic value has been validated, retrospectively, via the Intergroup Rhabdomyosarcoma Study (IRS) II data set.[46]

**IRS TNM staging system[46]**

| *Stage* | *Site* | *T* | *Tumor size* | *N* | *M* |
|---|---|---|---|---|---|
| I | Orbit<br>head and neck (nonparameningeal)<br>GU-nonbladder/nonprostate | T1 or T2 | a or b | N0 –N2 | M0 |
| II | Bladder/prostate<br>Extremity<br>Head and neck (parameningeal) | T1 or T2 | A | No or unknown | M0 |
| III | Bladder/prostate<br>Extremity<br>Head and neck (parameningeal) | T1 or T2 | a<br>b | N1<br>N0, N1, or Nx | M0 |
| IV | All | T1 or T2 | a or b | N0 or N1 | M1 |

T1 = confined to anatomic site of origin.
T2 = extension and/or fixation to surrounding tissue.
a = <5 cm in diameter.
b = >5 cm in diameter.
N0 = no LN involvement.
N1 = LN involvement.
Nx = unknown LN involvement.

## Treatment

The gold standard of treatment for sarcoma, among all subtypes, remains surgical resection. General principles that universally apply include goal of en bloc surgical

resection with wide surgical margins, which requires multidisciplinary surgical teams, including neurosurgery, plastic surgery, otorhinolaryngology, and ophthalmology. The purpose of en bloc resection is to avoid leaving extracapsular disease; malignant cells extend beyond the tumor pseudocapsule and require a 2–3 cm margin. Extracranially, this is much more feasible given the requisite resection of skin, subcutaneous tissue, bone, and truly anything adjacent to tumor. In the head and neck, this is difficult to achieve technically given proximity of critical neurovascular structures to tumor with the additional morbidity of causing significant postoperative deformity. Sarcoma surgery in the head and neck is performed with the goal of minimizing deformity. Tumor involving the scalp and face requires excision down to periosteum with frozen sections taken to verify negative margins and extent of tumor determines need for mastoidectomy, craniectomy, maxillectomy, and rhinectomy as needed to achieve this. Tumor involving the parotid gland may require sacrifice of the facial nerve, and tumor involving the orbit may require a minimum of lid resection up to complete orbital exenteration. Reconstructive surgery is required to abrogate deformity and restore function from resection. Reconstruction is often necessary to facilitate subsequent adjuvant treatment with radiation with both rotational and free flaps to cover open defects.[44] Generally speaking, the approach toward adjuvant treatment in sarcomas has been radiation treatment for locally recurrent disease, primary treatment for intermediate to high-grade tumors or subtotally resected tumors, and as preoperative cytoreduction for tumors without anticipated gross-total resection. Chemotherapeutic treatment has been reserved for high-grade sarcomas and in conjunction with radiation for nonresectable disease.

Pediatric RMS requires a multimodal approach from the time of diagnosis. Results from IRS-I–III have consistently established that outcomes are enhanced by the addition of adjuvant therapy, as surgery alone is associated with overall survival rates ranging from 8% to 20% while patients on chemoradiation protocols enjoyed long-term survival at rates of 25–83%.[57–59] IRS-I enrolled 699 patients from 1972 to 1978, not previously treated, < 21 years of age with rhabdomyosarcoma or undifferentiated sarcoma.

IRS-II enrolled 999 patients from 1978 to 1984 and IRS-III enrolled 1062 patients from 1984 to 1991, both utilizing the same enrollment criteria and clinical grouping as with IRS-I. In each protocol, patients from all groups of disease were treated with multidrug chemotherapy, and additionally all patients in groups II–IV were treated with radiation therapy as well.

**Results from IRS-I[58]**

| *Group* | *5-year disease-free survival, %* | *5-year overall survival, %* |
|---|---|---|
| I | 80 | 81–93 |
| II | 65–72 | 72 |
| III | 69 | 50 |
| IV | 52 | 20 |

**Results from IRS-II[57]**

| *Group* | *5-year disease-free survival, %* | *5-year overall survival, %* |
|---|---|---|
| I | 80 | 70 |
| II | 69–88 | 74–79 |
| III* | 74–78 | 66 |
| IV | 53 | 27 |

*Of note, central nervous system (CNS) prophylaxis was given to patients with parameningeal disease, which increased overall survival to 67% from 45% in IRS-I.

The IRS-III showed improved outcomes in group I with respect to 5-year progression-free survival (PFS) of 83% and improved group III 5-year PFS of 62%; otherwise, there were no significant differences from IRS-II.

The IRS-IV results have further defined failure-free survival (FFS) based on group and stage (refer to above for group and stage designations).[59-61]

**Results from IRS-IV[59,60]**

| *Group* | *3-year FFS, %* | *Stage* | *3-year FFS, %* |
|---|---|---|---|
| I | 83 | I | 86 |
| II | 86 | II | 80 |
| III | 73 | III | 68 |
| IV | < 30 | | |

Accordingly, patients can be stratified into low- and high-risk populations.[59-62]

**Risk assessment based on IRS II-IV[59-62]**

| *Low risk (88% 3-year FFS)* | *Intermediate risk* | *High risk (20% 3-year FFS)* |
|---|---|---|
| Stage 1, group I/IIA | Nonmetastatic ERMS stage 2, stage 3, or group III (73% 5-year FFS) | Stage 4 |
| Stage 2, group I | ARMS stages 1–3, groups I–III (5-year FFS of 65%), | Group IV RMS (ERMS >10 years of age and ARMS of any age) |
| Stage 1, group III (orbit only) ERMS | Patients <10 years of age who have metastatic disease | |
| Stage I, group IIB/IIC | | |
| Group III (non-orbital disease) | | |

Adjuvant treatment, namely, the specific chemotherapy regimen, is based on the above risk stratification as determined by Children's Oncology Group (COG) studies.[63,64] To date, there are no therapeutic trials based on tumor molecular genetics.

### *Outcomes and Prognosis*

Over the past few decades, substantial improvement in survival has been attributed to the collaborative effort between the IRS Group, COG, and COG Soft Tissue Sarcoma (COG-STS) Group. Prognosis is based on stage, group (extent of resection), age, and primary tumor. Survival is best with group I tumors and worst with group IV.[65,66] Overall, survival is improved with multiagent chemotherapy and radiation. Current side effects of treatment include infection and infertility often due to cyclophosphamide[62] and endocrine dysfunction, cataracts, retinopathy, and changes to dentition associated with radiation.[67]

Overall treatment guidelines based on the above trials are summarized below.

## Osteosarcoma

Osteosarcomas are tumors derived from osteoblastic tissue with bone-forming tumor cells. Ten percent of osteosarcomas occur in head and neck,[68] although this is more typical of the adult population. Head and neck osteosarcoma usually occurs in third or fourth decade of life; pediatric osteosarcoma is more common in the extremities.

Head and neck osteosarcoma may involve the mandible, classically the posterior body of the ramus, the maxilla–alveolar ridge, palate and sinus floor, and secondarily the skull.[69,70] Patients may present with dental pain, tooth loss, or painless mass. Treatment is not standardized although consists of aggressive surgical resection with multiagent chemotherapy including cisplatin, doxorubicin, and methotrexate.[71] Given the infrequency of pediatric head and neck osteosarcoma, there is a paucity of literature specific to its treatment and outcomes.

## Ewing's Sarcoma

Ewing's sarcoma is an aggressive, poorly differentiated tumor, typically found in the long bones in children and accounts for 4% to 6% of all primary bone tumors. Ewing's sarcoma of the bones of the skull or face is extremely rare (skull > mandible and maxilla) and occurs in 1–4% of cases[72,73] with a total of 23 cases of sinonasal Ewing's sarcoma reported in the literature.[74-87]

### *Presentation and Diagnosis*

Patients in our institution presented with nasal congestion, orbital swelling, oculomotor dysfunction, diplopia, and headaches. On physical examination, findings include proptosis with vascular-appearing mass noted on endoscopic nasal examination. CT shows heterogeneous mass with calcifications and erosions.[86,87]

### *Histology*

Tumor cells are positive for vimentin and CD99 and focally for epithelial membrane antigen, and negative for keratin, desmin, muscle-specific actin, myogenin, myoD1, and FLI-1. Ewing's sarcoma has a characteristic chromosomal translocation in the EWSR1 gene at 11;22 and EWS/FL11 fusion transcript, which can be ascertained by fluorescence in situ hybridization analysis.[88]

### *Treatment*

Given the rarity of this disease entity in the head and neck, reported standardized treatments are lacking; however, our institution reported our experience using multimodal treatment. Prior to initiating treatment, patients are evaluated by a multidisciplinary team including neurosurgery, otolaryngology—head and neck surgery, radiation oncology, and medical oncology. The current protocol at our institution for patients with resectable disease where surgery would not cause significant morbidity is a combination of chemotherapy followed by surgical resection. For unresectable disease patients are treated with chemotherapy followed by proton beam radiotherapy. For some patients, subtotal resection (STR) prior to proton beam radiotherapy is used to help reduce the required proton treatment volume or to alleviate obstructive symptoms.[87] Proton beam therapy is preferred in sinonasal and skull base malignancies in favor of sparing critical adjacent structures such as the globe, optic nerve, lacrimal gland, pituitary, and intracranial structures.[89]

In our institutional experience, one patient with obstructive symptoms, after five cycles of vincristine, doxorubicin, and cyclophosphamide as well as alternating ifosfamide (IF), etoposide (ET) and moderate response, patient underwent preradiation surgical debulking endoscopically followed by 8 weeks of proton beam radiation therapy to a total dose of 45 GyE. In a second patient, treatment was initiated with vincristine, doxorubicin, and cyclophosphamide, alternating with VP-16 and IF. Chemotherapy was followed by a course of proton beam radiation therapy to a dose of 45 GyE. Both patients remained

disease free at 1 year post-treatment with reported symptoms of sinus congestion from mucus secretions and mucocele, respectively.

### *Outcomes*

The prognosis for Ewing's sarcoma has improved over the last 10 years due to disease recognition and improved multimodal treatments. For patients with Ewing's sarcoma of the head and neck, tumors arising in the maxilla or mandible have had the best overall prognosis.[86] Overall, the use of chemotherapy and radiation therapy has improved disease-free survival. In 1981, the Cooperative Ewing's Sarcoma Studies (CESS-81) compared three treatment regimens: surgical resection, primary radiation therapy, and combination surgery and radiation therapy. Five-year survival rates were 54%, 43%, and 68%, respectively. A follow-up study in 1986 looking at 3-year follow-up by the same group (CESS-86) showed no statistical difference within the treatment groups (62% to 67%), and at that point advocated radiation alone in cases where surgery would lead to significant morbidity.[90] The role for adjuvant chemotherapy was validated when the Intergroup Ewing's Sarcoma Study (IESS)-II reported a disease-free survival rate of 68% with their protocol using adjuvant vincristine, doxorubicin, and cyclophosphamide (VAC).[91] The use of neoadjuvant IF and ET has been shown to be effective in patients who have relapsed after treatment with VAC; however, the addition of IF and ET to the VAC regimen has not been shown to have any additional advantage.[92] Given the evidence, therapy has been standardized to some extent to include initial chemotherapy followed by either surgical resection, radiation therapy, or a combination of both, depending on the location of the tumor at initial presentation and surgical resectability.[90]

## Chordoma

Chordomas are primary tumors of the spinal cord or clivus that originate from the primitive notochord and occur anywhere along the path of the notochord. In adult chordoma literature, the majority of tumors occur in the sacrococcygeal (50%) region and mobile spine (15%) with only 35% occurring at the skull base.[94] Chordoma in the pediatric literature is nearly exclusive to the skull base,[95,96] and pediatric chordomas account for ~5% of all chordomas in the literature. To date, there are approximately 152 cases of pediatric chordoma reported, the largest series of which was published out of Massachusetts General Hospital (MGH) with 73 patients aged 1–18 years.[97] This series is composed of patients who underwent protein beam radiation between 1981 and 2003.

### *Histology*

Histologically, chordomas are composed of three distinct subgroups as reported by MGH—conventional, chondroid, and "atypical"—cellular chordomas or poorly differentiated chordomas.[97] Conventional chordomas have a lobular arrangement of vacuolated cells—physaliphorous cells—that grow in cords within a mucinous matrix.[98]

Chondroid chordomas contain a mixed appearance of conventional chordoma with areas resembling neoplastic hyaline cartilage. Atypical tumors in the MGH series were one of two subgroups. Some of these tumors were highly cellular with a solid growth pattern with confluent sheets of tumor cells in the absence of extracellular matrix. Those tumors that had some areas with appearance similar to that of conventional chordoma were designated cellular chordomas, whereas tumors with sheets of small irregular cells and an epithelial appearance were designated poorly differentiated chordoma. All tumor subtypes stain positive for cytokeratin, epithelial membrane antigen, S100 protein, and vimentin.[97]

### *Presentation and Diagnosis*

Chordomas are extremely rare tumors in patients < 30 years old with a total of 153 chordomas in patients < 20 years old reported in the literature as of 2013.

In one large pediatric series out of the Mayo Clinic (12 patients from 1902 to 1982), presenting symptoms included diplopia, headache, occipital cervical pain, difficulty swallowing, dysarthria, and ataxia with cranial nerve VI and XII palsies apparent on examination.[95] In the MGH series, symptoms were cited as pain, neurological dysfunction, nasopharyngeal obstruction, and failure to thrive.

In a review of the literature stratifying by age, children < 5 years old were reported to present with elevated intracranial pressures long tract signs, hemothorax, kyphosis, nasal obstruction, and neck masses more often than their > 5-year-old counterparts who more often presented with diplopia and headache.[96]

The tumor is negligibly more common in males with 45.6% female and 54% male occurrences, although age bears a profound impact. Age < 5 years is associated with more aggressive histology, atypical chordoma pattern (65%), and higher rates of metastasis (58%). Patients aged

5–20 years had more benign histology and lower rates of metastasis (8.5%). Seventy-eight percent were identified as classic chordoma.[96]

In the largest single institutional series (MGH), 73 pediatric chordoma patients were diagnosed between 1981 and 2003, 31 males and 42 females. Of the 73 cases, 58% were conventional chordoma, 23% were chondroid chordoma, and 14% were highly cellular with a solid growth pattern, and no myxoid matrix or lobular architecture.

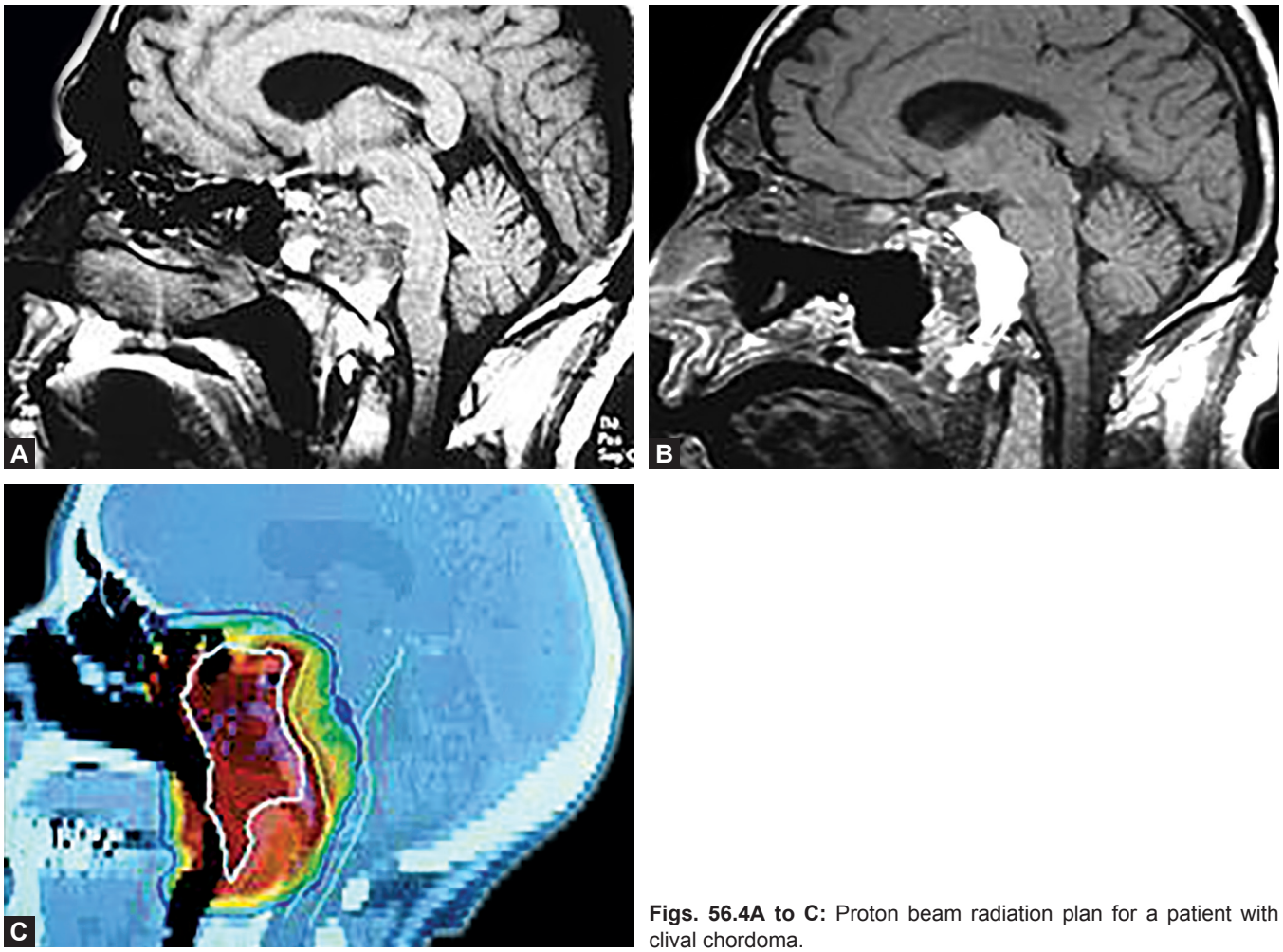
### *Treatment*

Treatment is empiric without randomized trials; however, surgical resection accompanied by radiation has been the most common reported approach. Forty-six of the 79 patients in the literature were treated with some form of adjuvant radiation with more recent avoidance of radiation noted only after radical resection.[96]

Surgical extirpation is generally limited by inaccessibility of the tumor as well as intimate relationship of tumor to vital structures. Given this, patients are standardly treated with postoperative radiation, either conventional or proton beam, the latter of which was favored in the MGH series. Pediatric skull base chordomas treated with proton beam radiation had better survival than chordomas in adults.[97] (Figs. 56.4A to C).

### *Outcomes and Prognosis*

In the MGH series, the survival rate was 81% (1–21 years, mean age of 7 years), and all but 1 patient with poorly differentiated chordoma died of disease. Fourteen patients had tumor progression after proton beam therapy and subsequently died, 83% of patients with poorly differentiated chordomas died, and the 1 patient still alive at 1-year post diagnosis had evidence of lymph node metastasis. Outcomes in conventional chordoma and chondroid




**Figs. 56.4A to C:** Proton beam radiation plan for a patient with clival chordoma.

chordoma were more favorable with only 14% and 18% of patients who died of disease, respectively.[97] This report substantiates the literature that suggests "atypical chordoma" or poorly differentiated chordoma as a distinct entity associated with a very poor prognosis.

## Chondrosarcoma

Chondrosarcomas most typically of the long bones and pelvis with a < 10% occurrence in the head and neck, based on the adult literature. The incidence of head and neck chondrosarcoma in the pediatric population is exceedingly rare with 68 total cases reported in the literature. The largest reported case series of pediatric head and neck chondrosarcoma was published in 2000. Gadwal et al. reviewed 14 patients aged < 18 years old with head and neck chondrosarcoma, a case total which represented 4.67 % of their total institutional chondrosarcomas.[99]

### *Presentation and Diagnosis*

Based on the Gadwal et al. study and review of the literature, average age at presentation is 11 years (3–18 years) with an even ratio of male to female patients. Presenting symptoms most commonly included mass lesion, followed by nasal obstruction/congestion, epistaxis, sinusitis, headache, vision changes, pain, proptosis, hoarseness, and fatigue.

Most common site for tumor was the maxillary sinus, followed by mastoid, with additional cases of tumor in the nasopharynx, orbit, skull base, neck, and nasal cavity.

Diagnostic workup included imaging (plain film, CT, and/or MRI) with calcification and boney destruction the most consistent finding.

Histologically, the tumor is composed of irregular, binucleated, and multinucleated cells within lacunar spaces and exhibit loss of normal cartilage architecture.

Three chondrosarcoma subtypes have been identified, classic, dedifferentiated, and mesenchymal. The classic subtype is the least aggressive while mesenchymal tends to be more aggressive and histologically high grade with small round blue cells, scant cytoplasm, and more mature hyaline cartilage.[100]

### *Treatment*

Almost all patients undergo surgical resection, although postoperative treatment with radiation and chemotherapy is more varied. In the Gadwal series, five patients underwent radiation and two underwent chemotherapy with a 100% reported survival rate for all cases in their series. As with chordoma, treatment is empiric and consists mainly of surgical resection followed by radiation.[95,101] Due to the need for high-radiation dosages, these tumors were historically considered radioresistant. Anecdotally, chondrosarcoma is more responsive to radiation than chordoma with improved response to proton beam radiation that has been more recently reported.[102,103] Currently, there are no standard chemotherapeutic protocols,[104] although there has been some reported effects with trials of vincristine[105] as well as with other drugs trialed in varying combinations—hydroxyurea, 5-fluorouracil, cisplatin, vinblastine, bleomycin, preoperative cyclophosphamide, vincristine, doxorubicin, dacarbazine, methotrexate, ifosfamide, actinomycin-D.[106-108]

### *Outcomes*

Given the small sample sizes with varied treatment regimens, it is difficult to predict prognosis. Disease-free survival in literature is 48% (mean of 7 years) with a 31% mortality rate (mean 2.2 years).[99]

# SELLAR LESIONS

## Craniopharyngioma

Craniopharyngiomas are histologically benign tumors that account for 50% of pediatric suprasellar tumors[109] and 1.8–4.4% to 10% of pediatric brain tumors.[110,111]

To understand the anatomic develop of craniopharyngioma, as well as the numerous other sellar lesions that can be seen in children, it is worth briefly reviewing pituitary development. The anterior adenohypophysis is derived from Rathke's pouch and is composed of the pars tuberalis, which surrounds the infundibulum, the pars intermedia, which communicates with the neurohypophysis and the pars distalis. The posterior neurohypophysis is essentially an extension of the hypothalamus and becomes the pituitary infundibulum and posterior lobe of the gland.

There are three distinct subtypes of craniopharyngiomas—adamantinomatous, papillary, and mixed. The adamantinomatous is more common in pediatric cases. These tumors are believed to arise from remnants of Rathke's pouch or the craniopharyngeal duct and more specifically, originate from squamous embryonic rests. Histologically, these lesions are similar to adamantinomas or ameloblastomas, which is the tooth producing tissue of the jaw. Grossly, the cystic portions of these tumors

contain desquamated epithelium, keratin, and cholesterol giving it the characteristic "machine oil" appearance. Dystrophic calcification, fibrosis, inflammation, cholesterol clefts, and finger-like projections invading the hypothalamus are other classic features of the adamantinomatous craniopharyngioma. On MRI, adamantinomatous lesions tend to be sellar/suprasellar in location, lobular in shape, mostly cystic with a T1 hyperintense cyst, and commonly have vascular encasement and calcification.[112]

Papillary craniopharyngiomas are more common in the adult and are thought to result from metaplasia of squamous cell rests, remnants of the stomodeum that give rise to oropharyngeal mucosa. Grossly, the cysts contain thick, yellow fluid and overall these tumors tend to be better encapsulated.[113] On MRI, papillary lesions tend to be suprasellar in location, round in shape, mostly solid with T1 hypointense cysts.[112]

### *Presentation and Diagnosis*

Tumors have a bimodal distribution for peak age at presentation—5–14 years and 50–74 years and equally affect males and females.[114] These tumors can arise anywhere along the developmental path of Rathke's pouch, including the nasopharynx, sphenoid bone, intraventricularly, and most commonly in the infundibulum where squamous epithelial rests occur.[115] The majority (95%) of tumors have a suprasellar component, 40-53% have intrasellar involvement, and 30% extend into anterior and middle cranial fossa.[116]

Tumors are expansile and may adhere to the pituitary stalk, invade the hypothalamus, and can cause local compression of optic chiasm, optic nerves, and pituitary.[117]

More than half of patients present with symptoms of local mass effect—headache, vision changes, and or endocrine dysfunction.[118]

Once patients present, they usually undergo MRI, CT, or both. MRI is the gold standard modality of choice and shows tumor in relation to the chiasm, optic nerves, pituitary, hypothalamus, and Circle of Willis as well. MRI also determines the extent of intrasellar/suprasellar extension, presence of intraventricular and/or posterior fossa extension as well as how solid versus cystic the tumor appears. This information is critical to surgical planning and approach. Calcification can best be noted on CT, and historically skull films would best show sellar enlargement as well as suprasellar calcification, although plain films are no longer routinely obtained.[117]

In addition, ophthalmologic and endocrine evaluations are necessary. Neuro-ophthalmolgy is necessary for formal visual field and visual acuity testing as well to detect the presence of papilledema or optic atrophy. Endocrine evaluation of basic laboratories, including growth hormone, IGF-1, prolactin, AM cortisol, thyroid panel, follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, estradiol, is performed. The most important part of the endocrine workup is assessing thyroid and cortisol status as these need to be known and addressed preoperatively.[117]

### *Staging*

Multiple grading schema have been proposed, which reflect anatomic location. Hoffman et al. described grade based on intrasellar, prechiasmatic, and retrochiasmatic location.[119] The Samii grading scale below provides more detailed information that namely affects surgical approach.[120,121]

| Samii grade | Location[120,121] |
|---|---|
| I | Purely intrasellar or infradiaphragmatic |
| II | Intracisternal +/– intrasellar component |
| III | Tumor extends to lower ½ of III ventricle |
| IV | Tumor expanded to upper half of III ventricle |
| V | Tumor extends to septum pellucidum or lateral ventricles |

### *Treatment*

The gold standard of treatment remains controversial. Given that there is neither standard nor any Class I evidence to support treatment strategies, we will list the treatment options and then review some of the larger case series and literature reviews with respect to PFS, morbidity, mortality profiles associated with each approach.

### *Surgery*

In prior decades, GTR was held as the gold standard of treatment. Utility of this treatment approach has fallen out of favor somewhat, and aggressive surgical debulking is described in cases where decompression to relieve visual disturbance and or obstructive hydrocephalus are necessary. However, in some centers it is still the standard of care with excellent outcomes, particularly when there is either no or limited hypothalamic involvement. The mostly widely cited morbidity associated with GTR is the higher postoperative rates of endocrinopathy. Other risks with radical resection include hypothalamic injury and epilepsy.

Subtotal resection with postoperative radiation has becoming increasingly favored in the literature with STR encompassing an array of surgical approaches from craniotomy with partial tumor resection +/– omaya reservoir placement if there is a large cystic component to burr hole placement with stereotactic placement of omaya reservoir for conscious cyst drainage postoperatively. There are also some centers that, in place of radiation, use intracystic chemotherapy. Bleomycin had been the agent of choice but has been abandoned due to drug side effects; some centers are trialing intracystic alpha interferon. STR with serial MRI is another surgical option.

### Radiation

In modern case series, all patients are being treated with radiation regardless of surgical strategy. The major concern with treating pediatric patients with radiation has been predominantly an issue with the long-term complications, whereas surgical complications are usually apparent in the short term.

Risks associated with radiation include optic neuropathy and/or necrosis, endocrinopathy beyond that of the initial tumor burden (radiation-induced can occur months to years subsequent to radiation), secondary malignancy—4 out 626 patient in literature with a reported lethal secondary malignancy—high-grade glioma.[122]

In addition, there is a risk of decreased IQ though this has anecdotally been associated more with the dual affect of radiation and hydrocephalus.[123]

Vision can also be at risk from cyst progression and hydrocephalus exacerbated by radiation. Lastly, though, radiation increases the risk of surgical morbidity of subsequent surgery required given gliosis, fibrosis, and disruption of anatomic planes.[122]

### Case Series

*UCSF:* The University of San Francisco (UCSF) treated 32 patients from 1956 to 1974 and followed them for 5 years subsequently.[124]

For eight children treated with GTR, 38% rate of recurrence, 88% 5-year survival. Eighty-six percent were noted to have panhypopituitarism and 63% had diabetes insipidus (DI).

For four patients treated with STR alone, there was a 50% 5-year survival; however, this treatment arm was abandoned in favor of STR and radiation by the treating physicians who saw better results with radiation. In 12 patients treated with STR and radiation, there was no statistic on recurrence, an 88% 5-year survival; 83% were noted to have panhypopituitarism and 50% had DI. In eight patients who had biopsy/cyst aspiration and radiation, again no statistic on recurrence though a 100% 5-year survival; 75% were noted to have panhypopituitarism and 25% had DI and panhypopituitarism. In this series, 84% of tumors were cystic. Seven patients died, five of whom had cystic tumors. The poorest prognosis was for age <5 years regardless of treatment with 60% 5-year survival versus 88–100% in all other age groups.

*Boston Children's Hospital:* Boston Children's Hospital treated 37 patients from 1972 to 1981 and followed them for both recurrence and functional independence at least 10 years out from treatment.

The first treatment group consisted of eight patients who were treated with GTR and radiation. At 10 years, 25% were independent, 37.5% were independent with some difficulty, and 25% were partially dependent; 1 patient died secondary to hypothalamic crisis, and 87.5 % had DI. Four recurrences occurred between 3 and 12 years after initial treatment, 2 of which responded to subsequent reirradiation, 2 required re-excision.

The second treatment group consisted of six patients treated with STR and radiation. At 10-year follow-up, 67% were independent, 17% fully dependent, 1 patient died due to progressive tumor growth refractory to multiple efforts at resection as well as reirradiation, and 66% of patients suffered DI.

The third treatment group consisted of 21 patients treated with biopsy, with or without cyst aspiration and radiation. At 10 years, 76% were independent, 9.5% were independent with some difficulty; 9.5% were partially dependent, 1 patient died secondary to a radiation-induced brain stem glioma, 1 patient recurred requiring injection of intracavitary bleomycin as well as reirradiation and ultimately a course of chemotherapy, and 5% of the biopsy and radiation group suffered DI.

The overall recurrence rate for the series was 14% with four out of five recurrences in the GTR and overall mortality rate was 8% with one death in each treatment group.

Intellectual achievement was universally impacted in the Boston experience though in group III slightly more than half of the patients were performing at their grade level versus only 50% of group I and less than half of group II.[125]

*St. Jude's Children's Research Hospital:* St. Jude's Children's Research Hospital treated 28 patients between 1997 and 2003 with equivalent doses of radiation regardless of surgical extent (extensive, moderate, minimally

invasive) and evaluated cognitive function across groups. At 3 years PFS for all comers was 90%. After radiation, 70% required growth hormone (GH) supplement, 90% thyroid replacement, 40% had hypogonadism, and 75% needed cortisol supplement. Factors found to contribute to lower IQ in the St. Jude experience—aged <7 years, shunted hydrocephalus, recurrent cysts requiring multiple drainage procedures, extensive resection, DI.[123]

*Toronto:* The Hospital for Sick Children treated 126 patients from 1975 to 2011. Fifty patients were treated from 1975 to 1989, 43 patients from 1990 to 2001 and 33 patients from 2001 to 2011.

Across the decades, patients presented with headache (68–86%), visual disturbance (58–79%), growth hormone deficiency (24–40%), and 33–66% of all patients had documented pituitary imbalance of any type. The higher rates of pituitary dysfunction were noted in the 1975–1989 patient sample and those patients underwent mainly GTR with only 10% of patients treated with partial resection. From 1990 to 2001, of the 43 patients treated, 86% had GTR, 12% had STR, and 2% had cyst decompression (CD) with intracyctic chemotherapy (ICC). Of the 33 patients treated from 2001 to 2011, the majority of patients (60%) underwent CD with or without an additional treatment modality- 27% had CD, 12% had CD and radiation and 21% had CD and ICC. The next largest treatment arm was the 27% of patients who underwent STR—18% STR, 9% had STR and radiation. And the minority of patients, 12%, had GTR.

The institution quotes 54% recurrence rate in the most recent decade as compared with 34% and 30% in 1975–1989 and 1990–2001, respectively, however, concluded that it is not statistically significant and support using radiation as first-line therapy as well as for recurrence with standard surgical approach of biopsy or STR rather than GTR given similar rates of recurrence.[126]

### *Summary*

Based on the UCSF experience, 5-year survival is equivalent across treatment arms regardless of extent of resection with higher rates of pituitary dysfunction in GTR group. Based on the Boston experience, there appears to be a higher risk of functional dependence and pituitary dysfunction after GTR. Based on the St. Jude's experience, radiation treatment in combination with any extent of surgery affords high rates of PFS with radiation effects on cognitive decline attributed to additional factors like age, repeated and extensive resections, comorbid hydrocephalus, and DI. Finally the Toronto experience over 4 decades similarly supports less extensive surgery combined with adjuvant therapy. When 109 studies with 531 pediatric craniopharyngioma patients were reviewed in a meta-analysis out of UCSF, the authors found that across all institutions there was a 35% recurrence rate for GTR, 65% recurrence for STR, 50% recurrence for STR and radiation, 41% recurrence for biopsy or CD and adjuvant treatment. There was no significant difference between PFS at 1 and 5 years between GTR and STR and radiation.[127]

## Germ Cell Tumors

Germ cell tumors (GCTs) are an umbrella group of tumors thought to originate from germ cell rests. These tumors are more common in the Asian literature. The different subtypes are further defined on the basis of the histology and anatomic location.

Seventy percent of GCTs are germinomas, with the rest composed of nongerminomatous GCTs (NGGCTs)—embryonal carcinoma, yolk sac tumors (endodermal sinus), choriocarcinoma, mixed tumors, and teratomas.

### *Presentation and Diagnosis*

Tumors can be pineal and/or suprasellar in location, with the majority found in the pineal region. In males, the pineal region is most commonly affected, and conversely in females the suprasellar region is more common. The tumor may be centered in the pituitary stalk with or without hypothalamic or pituitary involvement. More expansive lesions involve basal ganglia, and occasionally there is involvement of the thalamus, brainstem, cerebral, and cerebellar hemispheres.[128,129]

Presenting symptoms are most commonly secondary to elevated intracranial pressure, particularly in the pineal region tumors. Patients present with headache, nausea, vomiting, hypothalamic-pituitary dysfunction, and visual disturbances. Occasionally, they exhibit precocious puberty from tumor secreting B-hCG.

The gold standard of diagnostic workup includes MRI to determine extent of tumor; however, there is often microscopic spread that cannot be appreciated on MRI. If GCT is suspected, serum and CSF testing are performed for alpha fetoprotein (AFP) and B-hCG. AFP will be positive in yolk sac tumors and teratomas with endodermal sinus tissue. B-hCG will be positive in choriocarcinomas, teratomas, and embryonal carcinomas; germinomas may have low-level B-hCG. The most indicative results are in

NGGCT with both high levels of AFB and B-hCG. If marker testing is equivocal, biopsy is necessary for diagnosis. In addition, evaluation for CNS dissemination requires a cranial–spinal screening MRI and CNS cytology.

### *Treatment*

Germinomas are extremely chemotherapy and radiation responsive; NGGCTs vary in response in relation to some of their mixed tissue with teratomas being the most treatment resistant. For germinomas, the role of surgery is generally biopsy to obtain tissue diagnosis and symptomatic relief with treatment of hydrocephalus. The treatment of hydrocephalus can be challenging given risk of tumor dissemination, thus endoscopic third ventriculostomy is preferred where possible. Craniospinal radiation has been the mainstay of treatment, although whole ventricular radiation has also used for focal appearing tumor. The role for chemotherapy in germinomas varies across institution and is most commonly used for cytoreduction to decrease radiation fields/doses to limit later radiation side effects. Regimens include agents used for extracranial disease—cisplatin, carboplatin, etoposide, cyclophosphamide, bleomycin.[130]

The First International Central Nervous System Germ Cell Tumor Study Group trial attempted a treatment arm using chemotherapy without radiation but despite good initial response, there were high rates of relapse.[131]

Craniospinal radiation alone remains an acceptable treatment modality with the MAKEI series, quoting 90% 5-year PFS.[132]

However, there is no single standard treatment algorithm. A recent single institution retrospective analysis quoted an 86% 10-year overall survival and 74% PFS at 99 months for germinomas across all treatment arms though with a shorter time to relapse with chemotherapy alone or radiation alone as compared with chemotherapy followed by whole brain, whole ventricle, or craniospinal radiation.[133]

The NGGCTs are more resistant to treatment with lower rates of disease-free survival as compared with germinomas and as a result are more aggressively treated universally with chemoradiation and often more extensive surgical resection. Survival rates in the literature for NGGCTs vary from 25% 5-year survival with resection and radiation alone[134] to 56% 3-year survival in poor prognosis tumor and 100% 10-year survival in good and intermediate prognosis tumors treated with multimodal therapy.[133]

Trials of preradiation chemotherapy, postradiation chemotherapy have had the best results using platinum-based chemotherapeutics and craniospinal radiation with or without surgical resection with 4-year survival improvement from 25% to 74% with addition of chemotherapy.[134]

**Therapeutic classification of germ cell tumors[135]**

| | |
|---|---|
| *Good prognosis* | Pure germinoma<br>Mature teratoma |
| *Intermediate prognosis* | Germinoma with elevated levels of B-hCG<br>Extensive/multifocal germinoma<br>Immature teratoma<br>Teratoma with malignant transformation<br>Mixed tumors composed mainly of germinoma or teratoma |
| *Poor prognosis* | Choriocarcinoma<br>Yolk sac tumor<br>Embryonal carcinoma<br>Mixed tumors composed mainly of choriocarcinoma, yolk sac tumor, or embryonal carcinoma |

## Rathke's Cleft Cyst

Rathke's cleft cysts arise in region of pars intermedia between the adeno- and neurohypophysis and represent benign cystic remnants of Rathke's pouch/craniopharyngeal duct. Based on autopsy series, the incidence is estimated to be 11%.[136] The majority of these cysts are suprasellar in location and on MRI are well circumscribed, nonenhancing lesions. These lesions are usually followed with serial MRIs as long as they are asymptomatic though if large enough they may become symptomatic relative to mass effect on infundibulum, pituitary gland or optic chiasm.

## Pituitary Adenoma

Pituitary adenomas are rare in the pediatric population and account for 1–10% of all childhood brain tumors and 3–6% of all surgically treated adenomas.[137,138] The two largest case series have come out of Cleveland Clinic with 20 patients treated from 1981 to 2005 and UCSF with 150 patients treated from 1970 to 1999.

### *Presentation and Diagnosis*

The most common presenting symptoms are headache and vision changes and less commonly menstrual irregularities, galactorrhea, and Cushing-related symptoms of

weight gain, hirsutism, fatigue, and labile mood.[139] These tumors are slightly more common in females[139] with an average age at presentation of 15 years and a range of 8–19 years.[139,140]

Diagnostic workup consists of a neuroendocrine and neuro-ophthalmologic evaluation as well as MRI. Occasionally, patients will need to undergo preoperative venous sinus sampling to determine the laterality of the secreting tumor to determine the plan for surgical resection.[140] Treatment is determined on the basis of the subtype of tumor, which we will detail further.

Prolactinomas are more common in older patients, and the most common in the UCSF series comprising 52% of their patients with an average age of onset 14 and female:male ratio of 4.5:1. Prolactinomas are traditionally treated with dopamine agonists (cabergoline, bromocriptine) with surgery considered for patients intolerant of or with tumors resistant to these medications. Surgery can be used as an adjuvant to medication; debulking reduces the level of prolactin produced, which decreases the dose of dopamine agonist required for treatment. With medical management there is usually always some residual tumor and patients remain on medications indefinitely. Radiation is not used for prolactinomas given its high risk, low reward; radiation takes years to decrease prolactin secretion and carries the standard risk of pituitary injury from radiation.[140]

Growth hormone-secreting tumors are larger, commonly macroadenomas and are also more common in older patients with average age at onset 13–15 years (11–18)[139,141,142] and an male:female ratio of 2:1.[140] These children occasionally present with precocious puberty. Treatment for GH-secreting adenomas is usually surgical resection and though radiation reduces GH secretion in 60–80% of patients, it again takes years for this effect to be realized and carries the additional risk of impairing normal pituitary function. Systemic treatment with somatostatin analogs may help with normalizing GH and IGF-1 levels.[140]

Adrenocorticotropic hormone-secreting tumors are smaller, commonly microadenomas and more common in younger patients with an average age at presentation ranging from 8 to 14 years (range of 10–17)[139,141,142] and with a female:male ratio of 2.3:1.[140]

Nonsecreting tumors are the most common of all adenomas to expand beyond the sella, tend to be large in size, have a male:female ratio of 3:1 and may present with vision impairments. The surgical goal is usually decompression of optic nerves and chiasm.[140]

Incidental adenomas, which do not fit into the aforementioned categories are usually followed; however, based on the UCSF experience indications for surgical intervention include evidence of impaired anterior pituitary function, extrasellar extension, >1 cm in size, headache associated with tumor expansion, rapid growth, and both symptomatic and asymptomatic vision decline on formal ophthalmologic evaluation.[140]

Recurrence rates after surgical resection vary based on institution and surgeon; UCSF quotes 10%, Cleveland Clinic estimates 17%, and Mayo Clinic quotes 35% in their experience with 36 patients treated from 1975 to 1988.[141]

### Other Sellar Lesions

Craniopharyngiomas, germinomas, pituitary adenomas, and Rathke's cleft cysts are some of the more common lesions of the sellar region. However, a few other lesions within the differential diagnosis include glioma, ganglioglioma, PNET, Juvenile pilocytic astrocytoma, optic pathway gliomas, hypothalamic hamartomas, lipomas, arachnoid cysts, dermoid cyst, meningiomas, and third ventricle lesions, including choroid plexus papilloma and ependymoma expanding caudally into the suprasellar cistern.

## CHOLESTEATOMA

### Pathophysiology

Cholesteatomas are keratin filled lesions that develop from retained epithelial cell rests.[143,144] Cholesteatomas are considered congenital if the tympanic membrane is intact, there is no otorrhea, and no prior otologic intervention. Congenital cholesteatomas arise from congenital rests of tissue trapped in the temporal bone. Less than 5% of all cholesteatomas are congenital.

The more common acquired cholesteatomas occur after birth and are usually associated with chronic middle ear disease. Distinct from congenital, these are not thought to arise from epithelial rests, but rather from injury to aberration of the tympanic membrane. This includes retraction pocket cholesteatomas that result from previously diseased, chronically inflamed invaginating tympanic membrane that creates a pouch within which sloughing surface epithelium is retained, eventually forming a cholesteatoma. Other etiologies of insult include otitis media or abnormal epithelial migration secondary to tympanic membrane perforation, invasion of superficial epithelium into middle ear through tympanic membrane perforations, and iatrogenic injury after tympanoplasty.

## Presentation and Diagnosis

Congenital cholesteatomas are present at birth and continue to grow with an average age at diagnosis of 4–6 years (0–18 years); increasing severity of disease is associated with later age of diagnosis. More than 80% of congenital cholesteatomas are asymptomatic[145]; 50% of patients have history of acute or chronic serous otitis media.[145,146]

Lesions are usually found incidentally on examination and appear as spherical white cysts behind intact tympanic membrane, which can later be seen as bulging white mass in middle ear space.[147] Lesions may also be found incidentally on CT or during myringotomy procedures. Hearing loss and middle ear effusions are signs of later stage disease, and there is substantial risk of continued growth with invasion of middle ear ossicles, mastoid, and temporal bone if left untreated. Evaluation consists of physical examination as well as CT. CT is routinely used for work-up otic infections in older children, conductive hearing loss, and tympanic rupture.

## Staging

The two standard staging systems for cholesteatomas are the Nelson staging and Potsic staging. Nelson staging is divided by the presence or absence of ossicle involvement.[146] The Potsic staging is divided on the basis of the anatomic location of disease by quadrant.[148] The lowest risk of recurrence is with single-quadrant disease.[148]

| Nelson staging[146] | |
|---|---|
| Type 1 | Middle ear without ossicle involvement |
| Type 2 | Ossicle involvement |
| **Potsic staging[148]** | |
| Stage 1 | Single quadrant |
| Stage 2 | Multiple quadrants |
| Stage 3 | Ossicular involvement |
| Stage 4 | Mastoid extension |

Potsic stage 1 occurs most frequently in children aged < 3 years[149] in the anterior superior quadrant most commonly (85%) followed by the posterior superior quadrant (65%).[149]

## Treatment

The gold standard of treatment is surgical resection with the goal of preservation or restoration of hearing, maintenance of normal anatomy, and complete removal of squamous epithelium.

## Operative Planning

Three basic middle ear approaches for surgical resection are the transcanal tympanoplasty, endaural tympanoplasty and postauricular tympanoplasty. Each of these approaches can be further elaborated upon depending on the extent of disease. For disease limited to anterior mesotympanum, tympanoplasty alone may provide adequate visualization for resection. For superior disease in the attic/antrum, additional anterior, and posterior atticotomies in association with transcanal or postauricular tympanoplasty may be necessary. Posterior disease with ossicular involvement requires mastoidectomy if the exposure through the middle ear approach is inadequate.[150] When mastoidectomy is necessary, the decision then remains is whether to do a canal wall up or canal wall down procedure. With congenital cholesteatomas preserving the posterior external auditory canal wall is more common; however, canal wall down mastoidectomy may be required if there are pre-existing canal wall defects, labyrinthine fistula, or a sclerotic mastoid.[151] With canal wall down mastoidectomy, the disease region is exteriorized by removal of the posterior ear canal wall, which both improve surgical exposure and facilitate postoperative surveillance in the outpatient setting. Canal wall up is preferred if possible to preserve middle ear hearing and function, but it is associated with higher rates of recurrence and usually requires a planned second-look surgery.[152]

## Outcomes and Recurrence

Disease recurs in approximately 30% of patients. The best surgical outcomes are associated with stage 1 disease with 5% recurrence rates, followed by stage 2 with 24% recurrence, whereas stage 3 and stage 4 have 44% and 64% rates of recurrence, respectively.[149] Extent of disease at time of resection plays a role in recurrence and residual disease; higher rates of recurrence are associated with removal of disease-affected ossicles and more so if disease is noted medial to malleus or incus, abutting incus or stapes, enveloping stapes or eroding the ossicles at the time of resection.[149]

# ENCEPHALOCELE

Encephalocele is a postneuralation mesenchymal breach in which there is extracranial herniation of neural tissue. Encephaloceles are classified on the basis of location of the boney defect, anterior versus posterior, with further

subdivisions within each class describing the path of the herniation. Almost all encephaloceles are sporadic, with an unknown incidence given that most result in spontaneous abortions. Anterior defects are further classified as sincipital or basal, and posterior are subdivided into occipital, occipitocervical, and parietal. Sincipital encephaloceles are subdivided into frontoethmoidal, frontonasal, nasoethmoidal, naso-orbital, and orbital or interfrontal. Basal encephaloceles include spheno-orbital, sphenomaxillary, sphenoethmoidal, transethmoidal, and sphenopharyngeal. Occipital encephaloceles are divided into supra- and infratorcular. Parietal encephaloceles include interfrontal, interparietal, anterior, and posterior fontanelles.

Anterior encephaloceles are less common in the Western World and are associated with other craniofacial deformities including widening of the nasion, cleft lip and cleft palate, and craniosynostoses. There is also a reported increased incidence of lipomas in the corpus callosum. With both anterior and posterior encephaloceles there may be concomitant microcephaly and/or hydrocephalus.

Posterior encephaloceles are more common in the Western World and are more likely to have seizure and hydrocephalus. They often present with associated brainstem and cerebellar abnormalities and occasionally cortical dysplasia. Although typically sporadic, there is some association between occipital encephaloceles and Meckel–Gruber syndrome, which corresponds with additional extracranial developmental dysfunction.

Diagnostic workup includes physical examination and imaging. On examination the masses engorge with valsalva maneuvers, particularly with the anterior defects. MRI is obtained to assess for integrity of neural tissues as well as to evaluate for hydrocephalus. CT aids with planning for craniofacial reconstruction. The gold standard of treatment is elective surgery with the goal of repositioning herniated neural tissue +/– resection of nonviable tissue, repairing the dural defect and preventing CSF leak, and reconstructing the craniofacial bones with plastic surgery. Posterior defects can be approached extracranially while anterior defects require intracranial exploration often requiring a bifrontal craniotomy but can also be approached endoscopically.[153]

## MENINGIOMAS

Pediatric meningiomas comprise 0.4–4.6% of pediatric brain tumors[154-156] with demographic features that vary considerably from their adult counterparts; male predominance is nearly universally noted in the literature. Of the clinical series in the literature ranging from 15 to 35 years of retrospective analyses, patient ages ranged from 5 months to 20 years with the majority in their late teens, males were more commonly affected (54–71%) and rates of concomitant neurofibromatosis (NF) ranged from 6% to 41%, and prior radiation exposure ranged from 8% to 40%.[156-161]

### Presentation and Diagnosis

Most common presenting symptoms are increased intracranial pressure (20–41%), headache (40–45%), vomiting (29.7%), weakness (21–35%), seizures (20–35%), and cranial nerve palsies (14%).[155-158,160]

The MRI with gadolinium is the gold standard for imaging. Historically, however, the diagnosis was often made based on plain film and angiography with hyperostosis and or boney erosion noted in 30% of patients with subsequent angiography in ~50% of patients.[157]

Tumor location is most commonly intracranial (89%) and supratentorial with convexity (16–58%) most frequently cited followed by parasagittal, intraventricular, falcine, and anterior and middle cranial fossa. Skull base location was noted as high as in 16–49% of patients in Brazil and India, respectively.[156,157,160] The exceeding majority of cases are WHO Grade I (64–96%), followed by Grade II (4–26%), and most infrequently Grade III (0–9%).[156-160]

### Treatment

The gold standard of treatment is surgical resection and re-resection for recurrence. The technical limitation to surgical resection in this population is the large, highly vascular tumors in children with lower blood volumes as well as the general morbidity associated with long surgical times, blood loss, and transfusions. The surgical goal is GTR with rates of 60–86% achieved in the literature.[157]

Adjuvant treatment remains controversial as with other pediatric tumors, although the co-association of NF increases the risk of secondary malignancies postradiation. In the literature, radiation has been used in patients with recurrences refractory to multiple resection regardless of grade as well based on atypical pathology.[157,160,162]

### Outcomes and Prognosis

Recurrence rates have been quoted as anywhere from 0% to 100%. The largest North American case series of 87 pediatric meningiomas reported a mortality rate of

10.6% and a recurrence rate of 19.4%. Overall, recurrence was highly associated with degree of resection—GTR 26–57%, STR 33–100%, as well as histologic subtype and NF status. One series estimated a 10-year PFS of 30% for Grade III, 92% Grade II, 70% Grade I, and overall 5-year survival of 97% for Grade I, 100% for Grade II, and 50% for Grade III. Similarly, of the 33% of patients noted to recur in one series, 80% had either NF or radiation-induced tumors.[155,156,158-160]

## Neurofibromatosis

### *Pathophysiology*

Both NF1 or Von Recklinghausen neurofibromatosis and NF2 are autosomal dominant diseases.[163] NF1 occurs with an incidence of 1:4000 and is sporadic in ~50% of cases. It is characterized by a mutation at 7q11.2 leading to a loss of function of the neurofibromin gene, the protein product of which acts as a tumor suppressor implicated in P21RAS and mTOR signaling pathways.[164-166]

The NF2 occurs less frequently with an incidence of 1:40,000 and is characterized by a mutation at 22q12.2. This leads to a loss of function of the NF2 gene, which encodes the tumor suppressor protein Merlin or Schwannomin; dysregulation leads to an overproduction of Schwann cells.[167-169]

### *Presentation and Diagnosis*

The NF1 and NF2 are diagnosed on the basis of the criteria established by the National Institutes of Health.

For diagnosis of NF1, two or more of the following are required: cafe' au lait spots (≥ 5 mm in prepubertal patients ≥ 15 mm in postpubertal patients); ≥ two neurofibromas or 1 plexiform neurofibroma; axillary or inguinal freckling; optic pathway glioma; ≥ 2 Lisch nodules; osseous lesions; sphenoid wing dysplasia or cortical thinning of long bones +/– pseudoarthroses; first-degree relative with NF1.[170]

The NF2 is associated with multiple meningiomas, bilateral vestibular schwannomas, cranial nerve tumors—CN VIII most commonly followed by V, III, and VII—spinal tumors, and ocular abnormalities. Approximately, 50% of patients present with schwannoma and meningioma, and 90% have spinal tumors in addition to extraspinal schwannomas. Spinal lesions are typically extramedullary schwannomas or meningiomas, although less commonly may be intramedullary ependymoma, astrocytoma, or schwannomas.[171,172]

The NF2 diagnosis can be made based on the presence of bilateral vestibular schwannomas, or a unilateral vestibular schwannoma in a patient <30 years old with a first-degree relative with NF2, or unilateral vesti bular schwannoma and at least two of the following: meningioma, glioma, schwannoma, or juvenile posterior subcapsular lenticular opacity/juvenile cortical cataract.[170]

Pediatric patients with NF2 are typically diagnosed in their late teens with an average age of diagnosis of 25 years; there is no gender difference.[173]

At time of NF diagnosis patients undergo cranial and spinal screening imaging with MRI thin cuts through the internal auditory canal (IAC) to assess for schwannomas with repeat imaging at 6 months to assess stability. Patients subsequently undergo annual intracranial imaging to follow tumors and spinal imaging every 3 years to follow small spinal tumors. In the absence of spinal tumors, there is no need for serial imaging unless patients are symptomatic. Additional baseline screening includes a neuro-ophthalmologic examination.

### *Pathology*

The NF1 gene mutation predisposes to intracranial tumors, most commonly benign pilocytic astrocytomas of the optic apparatus and brain stem as well as cerebellum.[174] Seventy percent of optic pathway gliomas are associated with NF1 and up to15% of children with NF1 have asymptomatic gliomas, although symptoms may include visual changes and hypothalamic dysfunction.[175]

One in 10 pediatric cerebellar gliomas is associated with NF1, most commonly pilocytic astrocytoma followed by anaplastic astrocytomas, gangliogliomas, and pleomorphic xanthoastrocytomas less commonly. Typically, tumors associated with NF1 are located in the subependymoma of the fourth ventricle as compared with vermian or hemispheric location of non-NF1 posterior fossa lesions.[176]

Brainstem gliomas in NF1, most commonly located in the medulla, can be confused with UBOs (unidentified bright objects); however, they cause symptoms in 60–80% of patients including headache, cranial nerve dysfunction, or hydrocephalus. Rates of progression—both radiographic and clinical—range from 30% to 42% in the literature with 20–50%, requiring intervention (biopsy, resection, radiation, chemotherapy, or shunt placement).[177,178]

Sphenoid wing dysplasia occurs in 3–7% of NF1 patients.[179] The osseous lesion involves a defect in greater wing of sphenoid, compensatory changes in the lesser

wing, and sellar and ipsilateral orbital deformities, which requires both orbital and transcranial operative revision.[180]

Malignant peripheral nerve sheath tumors, multiple sclerosis, and moyamoya all have higher incidences in the NF1 population as well.[176]

### *Treatment*

The majority of neurofibromatous lesions are managed nonoperatively in the pediatric population. A 20-year case series out of MD Anderson noted that for 249 patients with NF, only 50 patients ultimately required operative intervention, and of those 23% of the interventions were intracranial for tumor resection, biopsy, or shunt.[181]

Optic pathway gliomas are marked by indolent growth and often spontaneous regression, which allows for conservative management with cautious observation, annual ophthalmological and endocrine evaluations.[175]

Surgical resection may be indicated if patients become symptomatic or if there is evidence of obstructive hydrocephalus; otherwise, surgical debulking is typically reserved for patients with ipsilateral visual loss and eye-threatening proptosis or eye pain refractory to chemotherapy. Radiation is controversial given higher incidence of radiation-induced secondary malignancies with no evidence of improved survival or visual symptoms.[182]

Varying chemotherapy regimens have been trialed including dactinomycin, vincristine; carboplatin; cisplatin, etoposide, vinblastine; carboplatin and vincristine; other multiagent regimens include 6-thioguanine, procarbazine, dibromodulcitol, lomustine, and vincristine. The current standard regimen for treatment of optic pathway glioma is carboplatin/vincristine. In a clinical trial with 58 patients treated with carboplatin/vincristine, 15 of whom had NF1, 58% of patients had tumor regression and 70% experienced PFS at 3 years.[183]

In NF2, the majority of the lesions—vestibular schwannomas, meningiomas, and spinal tumors—eventually require operative intervention. In the pediatric population, particular care is taken to maintain vision and hearing. In the case of acoustic schwannomas, schwannomas usually arise from superior vestibular nerve and can cause hearing loss, vestibular symptoms, and brainstem compression. Small tumors can be observed as can lesions where there is no potential for hearing preservation. In such cases, the role of surgery is to palliate symptoms of brainstem compression and to relieve hydrocephalus. In cases where lesions can safely be resected and the goal for hearing preservation is attainable, middle fossa resection is preferred. In a 12-year study out of the House Institute, 55% of patients who underwent middle fossa approach retained 70 dB or less pure tone average post-operatively.[184] Translabyrinthine and retrosigmoid approaches are appropriate when there is no chance for hearing preservation. In such patients, auditory brainstem implants (ABIs) may be utilized. In patients aged > 12 years old, ABIs can be placed in the lateral recess of brainstem against dorsal cochlear nucleus. Alternatively, cochlear implants can be trialed with an intact cochlear nerve.[185]

As with NF1, radiation carries risk of secondary malignancy; however, vascular endothelial growth factor inhibitors have a promising role in delaying need for surgery as well as treating inoperable lesions. A clinical trial of bevacizumab at Massachusetts General Hospital was performed on 10 patients aged 16–53 years (average 25 years). Of the 10 patients treated, nine patients had decrease in size of their tumors with 60% rate of imaging response, and hearing was improved in four out of seven patients with eligible hearing. The same response has not yet been shown in NF2 meningiomas.[93]

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CHAPTER

# 57 Pediatric Head and Neck Malignancies

*Matthew T Brigger, Michael J Cunningham*

## INTRODUCTION

Pediatric head and neck malignancies represent a wide range of diagnoses and prognoses that rank second only to trauma as a cause of mortality in children 1–14 years of age.[1] These disorders are distinctly different than those encountered in the adult population. Although the majority of pediatric head and neck masses are benign processes of inflammatory or congenital origin, a high level of suspicion is necessary given that over 10% of all biopsied masses are reported to be malignant.[2] A working knowledge of the diagnostic possibilities is requisite, as is recognition of the potential short- and long-term implications for the child and the family so afflicted. This chapter presents an overview of pediatric head and neck cancer with a focus on surgical therapy. Adjuvant therapies are covered in detail in Chapter 59.

## EPIDEMIOLOGY

The incidence of pediatric head and neck malignancies appears to be increasing, congruent with the overall rate of childhood cancer, based upon the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) tumor data.[3] Estimates of the number of pediatric primary malignancies arising in the head and neck vary from 5% to 12% depending upon whether or not retinoblastoma is included.[3–5] One of every four malignancies in the pediatric age group eventually involves the head and neck region.[6]

Reviews of childhood head and neck malignancies have demonstrated several histopathologic trends.[3,6] Across all reviews, lymphomas are the predominant neoplasms of the head and neck region. Soft tissue sarcomas, specifically rhabdomyosarcoma (RMS), are the next most common, whereas skeletal sarcomas are comparatively rare. Thyroid carcinomas and salivary gland malignancies are less frequently reported, with papillary carcinoma and mucoepidermoid carcinoma being the most prevalent in each gland, respectively. Neurogenic and germ cell neoplasms may occur as either primary or metastatic cervicofacial lesions. A summary of pathologic diagnoses of pediatric cervicofacial neoplasms between 1973 and 2010 as recorded by the SEER Tumor Registry of the National Cancer Institute is provided in Table 57.1. Table 57.2 presents the frequency and histologic diagnosis of various head and neck malignancies from a single large institution 20-year review based on site of presentation.

Pediatric head and neck cancer incidence rates vary significantly according to age, gender, race, ethnicity, and geography.[3] Malignant teratomas are primarily congenital lesions. Neuroblastomas likewise tend to occur in infancy. Hodgkin lymphoma (HL) usually occurs in early adolescence and rarely in children younger than 5 years of age. Sarcomatous neoplasms span the entire pediatric age range, with the majority of RMSs occurring in the preschool years. The non-Hodgkin lymphomas (NHLs) similarly demonstrate a broad age range, predominantly appearing later in childhood during the school-age years. Thyroid carcinoma, nasopharyngeal carcinoma, and salivary gland neoplasms occur predominantly as children reach adolescence. A summary of age-specific presentation patterns is listed in Table 57.3.

**Table 57.1:** Pediatric head and neck malignancies. National cancer institute seer tumor database (1973–2010)

| *Pathologic diagnosis* | *Number of malignancies* | | |
|---|---|---|---|
| | *Total* | *Male* | *Female* |
| Acinar cell carcinoma | 133 | 45 | 88 |
| Adenocarcinoma | 39 | 21 | 18 |
| Adenoid cystic | 37 | 12 | 25 |
| Germ cell | 58 | 25 | 33 |
| Lymphoma | 2239 | 1395 | 844 |
| Hodgkin lymphoma | 1399 | 800 | 599 |
| Non-Hodgkin lymphoma | 840 | 595 | 245 |
| Melanoma | 581 | 316 | 265 |
| Mucoepidermoid | 276 | 120 | 156 |
| Neural malignancies | 3277 | 1739 | 1538 |
| Neuroblastoma | 1447 | 810 | 637 |
| Retinoblastoma | 1533 | 794 | 739 |
| Other neural malignancies | 297 | 135 | 162 |
| Skeletal sarcoma | 256 | 150 | 106 |
| Osteosarcoma | 98 | 58 | 40 |
| Chondrosarcoma | 50 | 32 | 18 |
| Ewing sarcoma | 77 | 41 | 36 |
| Other skeletal sarcomas | 31 | 19 | 12 |
| Soft tissue sarcoma | 1030 | 536 | 494 |
| Rhabdomyosarcoma (RMS) | 755 | 395 | 360 |
| Non-RMS Soft tissue sarcomas | 275 | 141 | 134 |
| Squamous cell carcinoma | 149 | 95 | 54 |
| Thyroid carcinoma | 2763 | 541 | 2222 |
| Follicular | 250 | 43 | 207 |
| Medullary | 132 | 55 | 77 |
| Papillary | 2381 | 443 | 1938 |
| Total | 10838 | 4995 | 5843 |

## EVALUATION

The evaluation of a child with a suspected head and neck malignancy requires a thorough diagnostic approach often requiring multiple modalities. A comprehensive history should establish the presentation, progression, and associated symptoms of the lesion. Attention should be directed toward local site-specific symptoms as well as systemic manifestations. The history often delineates between infectious, congenital, and neoplastic processes. Malignancies are rarely noted at birth, typically have progressive growth, and are infrequently associated with localized tenderness or other inflammatory skin changes. However, the most common presentation of a cervicofacial malignancy is simply an asymptomatic mass. Special note is made of the child's past history of risk factors such as prior radiation therapy, exposure to carcinogenic or immunosuppressive drugs, a previous primary malignancy, and a family history of childhood cancer or systemic cancer predisposition.[7–9]

All children with a suspected malignancy require a complete otolaryngologic and systemic examination, generally including an endoscopic assessment of the upper aerodigestive tract. Additional attention during the physical examination should be directed at the abdominal, axillary, and inguinal areas owing to the frequency with which head and neck malignancy may be related to a process involving these regions.

Imaging is an important adjunct in the evaluation of suspected malignancies. The primary goals of imaging are to more precisely define the principal lesion and detect additional primary or metastatic sites of disease for accurate clinical staging. The imaging modality chosen is directed by the location and character of the mass, the age of the patient, the presence of hardware such as orthodontics, and medical conditions such as renal insufficiency or potential airway obstruction with sedation.

Ultrasonography provides an initial modality that is readily available and not associated with the risks of radiation, contrast administration, or sedation. Ultrasound allows determination of mass location and consistency as well as vascular flow characteristics. The real-time nature of this modality is ideal for guiding fine-needle aspiration (FNA) biopsies.

The comparatively improved anatomic detail provided by computed tomography (CT) or magnetic resonance imaging (MRI) is often required for both diagnostic and therapeutic decision making. CT has traditionally been the imaging modality of choice for many otolaryngologists given the ease of acquisition combined with an excellent ability to assess the degree of tumor extension within and across anatomic planes, provide differentiation between solid and cystic masses, and evaluate osseous erosion (Fig. 57.1). Concerns about diagnostic radiation exposure in children, however, have significantly increased interest

**Table 57.2:** Anatomic location at presentation of pediatric head and neck malignancies

| *Site* | *Pathologic diagnosis* | *Subtotal* | *No. of children* | *Percentage of total* |
|---|---|---|---|---|
| Neck | | | 286 | 70.0 |
| | Hodgkin lymphoma | 131 | | |
| | Non-Hodgkin lymphoma | 78 | | |
| | Thyroid carcinoma | 38 | | |
| | Neuroblastoma | 20* | | |
| | Rhabdomyosarcoma | 5 | | |
| | Other sarcomas | 10 | | |
| | Teratoma | 3 | | |
| | Parathyroid adenoma | 1 | | |
| Oronasopharynx | | | 71 | 17.0 |
| | Non-Hodgkin lymphoma | 33 | | |
| | Nasopharyngeal carcinoma | 18 | | |
| | Rhabdomyosarcoma | 18 | | |
| | Fibrohistiocytoma | 2 | | |
| Orbit/paranasal sinuses | | | 21 | 5.0 |
| | Rhabdomyosarcoma | 19 | | |
| | Chondrosarcoma | 2 | | |
| Parotid | | | 14 | 3.0 |
| | Mucoepidermoid carcinoma | 5 | | |
| | Non-Hodgkin lymphoma | 5 | | |
| | Adenocarcinoma | 2 | | |
| | Rhabdomyosarcoma | 2 | | |
| Facial region | | | 10 | 2.5 |
| | Rhabdomyosarcoma | 3 | | |
| | Synovial sarcoma | 2 | | |
| | Osteogenic sarcoma | 2 | | |
| | Chondrosarcoma | 2 | | |
| | Non-Hodgkin lymphoma | 1 | | |
| Ear/temporal bone | | | 6 | 1.5 |
| | Rhabdomyosarcoma | 5 | | |
| | Squamous cell carcinoma | 1 | | |
| Tongue | | | 3 | 1.0 |
| | Mucoepidermoid carcinoma | 2 | | |
| | Adenocarcinoma | 1 | | |
| Totals | | | 411 | 100 |

*Fifteen neuroblastomas were likely cervical metastases from the abdomen.
Adapted from Cunningham et al.[6]

in the alternative use of MRI. MRI offers additional advantages in comparison to CT including better contrast of tissues of similar densities, better delineation of neoplasms from surrounding soft tissue structures, and the avoidance of ionizing radiation or intravenous-iodinated contrast material (Figs. 57.2A and B). Disadvantages of MRI include prolonged imaging times with the need to keep children restrained and often sedated, high sensitivity to motion artifact, poor distinction of bone, and altered image quality in the setting of metallic foreign bodies or implants.

Positron emission tomography (PET) with 18-F-fluoro-2-deoxy-D-glucose (FDG) has supplanted most other radionuclide scans in the assessment of systemic metastases. PET can additionally be used to evaluate both primary and metastatic tumor response to treatment, as well as to screen for neoplastic disease recurrence (Fig. 57.3).[10,11]

**Table 57.3:** Age distribution at presentation of children with head and neck malignancies

| | *Average age (years)* | *Age range (years)* |
|---|---|---|
| Malignant teratoma | – | NB* |
| Neuroblastoma | 1.9 | NB–5 |
| Rhabdomyosarcoma | 6.4 | NB–17 |
| Non-Hodgkin lymphoma | 8.0 | 2–18 |
| Other sarcomas | 8.1 | NB–18 |
| Hodgkin lymphoma | 11.8 | 4–19 |
| Thyroid carcinoma | 12.4 | 6–18 |
| Nasopharyngeal carcinoma | 14.4 | 9–18 |
| Salivary gland malignancies | 15.2 | 7–8 |

*NB: Newborn.
Adapted from Cunningham et al.[6]

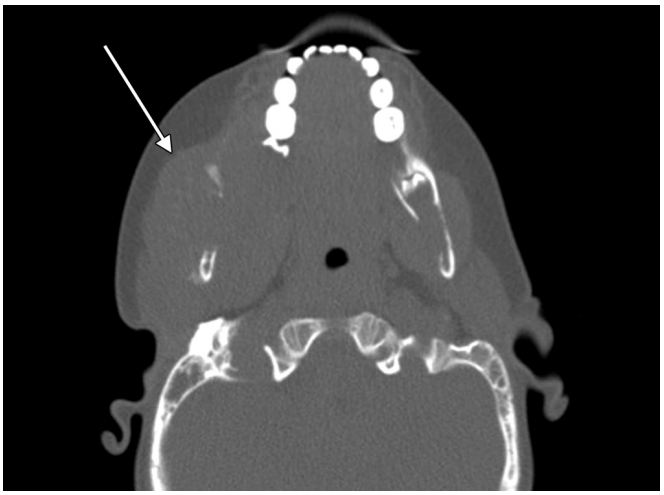
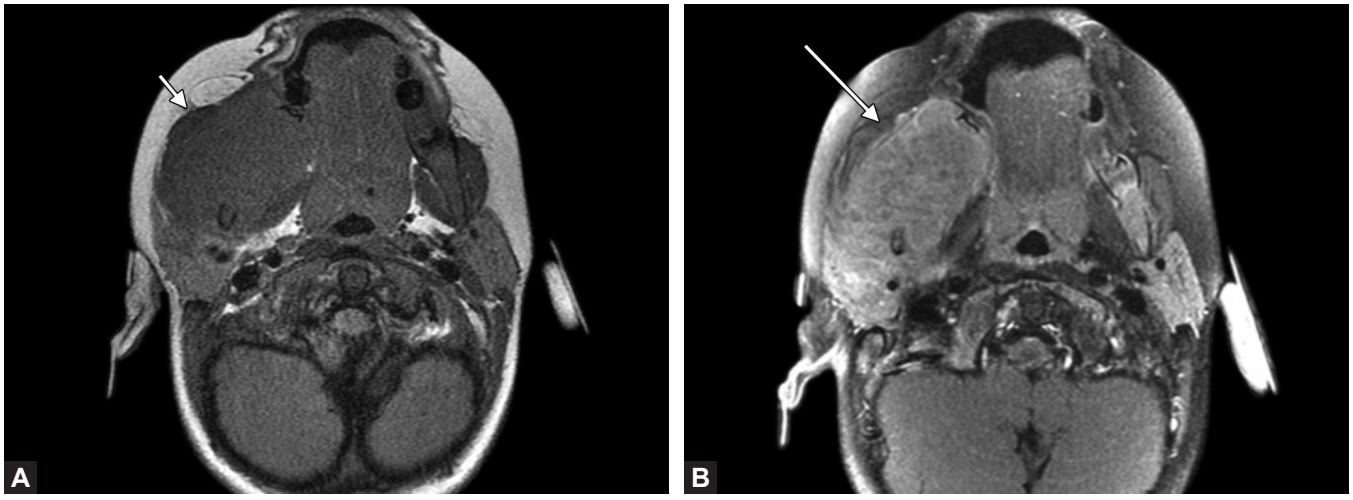


**Fig. 57.1:** Axial computed tomography (CT) without contrast, demonstrating a destructive lesion of the mandible (arrow).




**Figs. 57.2A and B:** Axial T1 MRI of same lesion (arrow) in Figure 57.1. (A) Prior to gadolinium enhancement; (B) Postgadolinium enhancement.

FNA biopsy has found widespread application in the evaluation of adult head and neck malignancies. FNA is particularly useful in the assessment of thyroid and salivary gland lesions, as well as in select additional neck masses.[12-14] The reliability of a FNA biopsy diagnosis is highly dependent on the expertise of the cytopathologist. The use of both monoclonal antibody techniques and DNA amplification with polymerase chain reaction have improved FNA biopsy sensitivity and specificity.[14,15]

An examination under general anesthesia may complement other elements of the diagnostic workup in defining the extent of the primary tumor and allowing for adequate tissue sampling. This is particularly true when there is a high index of suspicion and FNA techniques are not applicable or nondiagnostic. Preoperative communication between the surgeon and the pathologist regarding the clinical presentation can often enhance the likelihood of establishing the correct diagnosis.[16]

The open biopsy of a head and neck mass is performed in either excisional or incisional fashion depending on the size, location, and differential diagnosis of the lesion in question (Fig. 57.4). In certain circumstances, an excisional biopsy may be therapeutic as well as diagnostic. When planning excisional or incisional biopsy approaches,

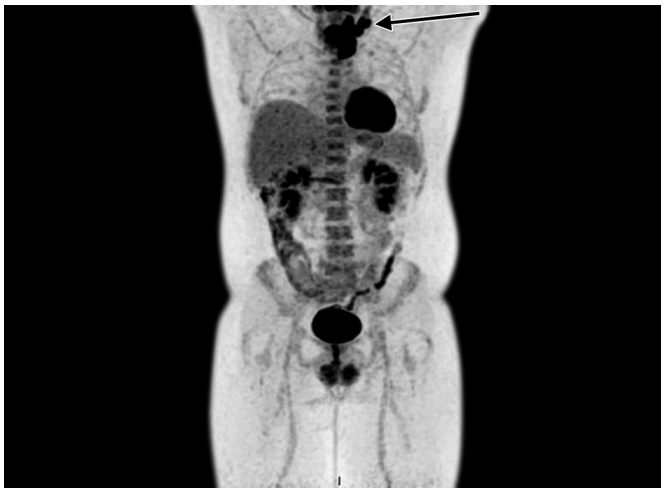


**Fig. 57.3:** Positron emission tomography (PET) with 18-F-fluoro-2-deoxy-D-glucose (FDG), demonstrating increased uptake in region of primary tumor in the neck (black arrow), but no distant FDG uptake other than in the expected stomach, kidney, and bladder sites.

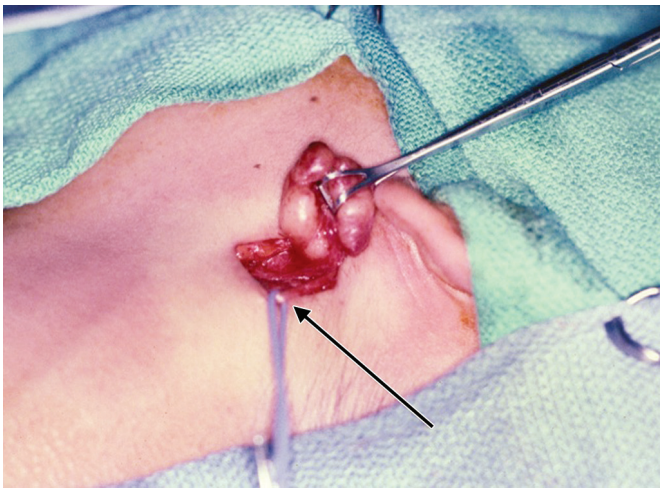


**Fig. 57.4:** A child undergoing excisional biopsy of a neck mass. Black arrow denotes retracted nerve.

potential implications with respect to future definitive resection from both a therapeutic and cosmetic standpoint require consideration.

Childhood head and neck malignancies typically require a multidisciplinary team to provide treatment. In addition to otolaryngologists, the team often includes pediatricians, medical oncologists, radiation oncologists, diagnostic and interventional radiologists, pediatric surgeons and additional pediatric surgical specialists. Supportive services including speech language pathologists, nutritionists, child psychologists, social workers, and child life specialists are also necessary. Most institutions that treat children with head and neck cancer do so in the setting of a multidisciplinary tumor board to coordinate their necessary comprehensive therapy.

## LYMPHATIC MALIGNANCY

There are numerous infectious and inflammatory causes of cervical lymphadenopathy in children. Although the vast majority of these etiologies are benign, neoplasms of the lymphatic system must be kept in mind as part of the differential diagnosis. The confirmation of a lymphatic malignancy is typically made by lymph node biopsy, most commonly performed in excisional fashion, preferably with the capsule intact. The immunogenic evaluation and classification of suspected lymphomas requires specialized laboratory methods. As such, the postoperative handling of lymphatic specimens is of critical importance. Most institutions have specific "lymphoma protocols" requiring the tissue to be sent directly to pathology as a fresh specimen without fixative to allow immediate processing for flow cytometry and specific immunogenic staining techniques.

### Hodgkin Lymphoma

HL is a malignant neoplasm of the lymphatic system with a bimodal age distribution, one peak occurring during adolescence and young adulthood, and another peak over the age of 50 years. HL is uncommon in preadolescent children and rarely occurs in children younger than 5 years of age.[17]

Although no definitive causal factors are known, there is an association between Epstein-Barr virus (EBV) infection and HL. Increased titers of EBV-induced antibodies have been documented in HL patients, and there is an epidemiologically confirmed increased risk of developing HL following a confirmed bout of infectious mononucleosis.[18,19]

HL is distinguished histopathologically by the diagnostic presence of Reed-Sternberg (RS) cells, which are multinucleated cells with large nucleoli and a halo or clear zone around the nucleolus (Fig. 57.5). Much debate and investigation has centered on the biologic basis and cellular origin of the RS cell as these cells represent the common malignant component of the diverse histologic subtypes of HL. Generally speaking, the RS cell appears to be most commonly of germinal center B-cell origin, but cases of T-cell origin have been described.[20,21]

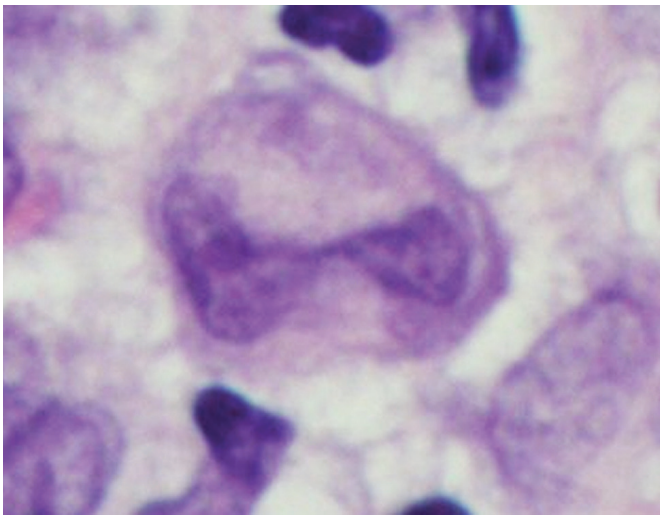


**Fig. 57.5:** Hematoxylin and eosin photomicrograph of a Reed Sternberg cell. Note bilobed nature of nucleoli.

The Rye classification system has historically been the most commonly employed method to designate the various types of HL. The Rye classification system recognizes four HL subtypes based upon the cellular background: lymphocyte predominant, lymphocyte depletion, nodular sclerosis, and mixed cellularity. Adolescent and young adult HL patients are more likely to have nodular sclerosis disease at the time of presentation; lymphocyte predominant and mixed cellularity disease are relatively more common in children age 10 years or younger; the mixed cellularity HL subtype has been particularly associated with human immunodeficiency virus (HIV) infection.[22,23]

Advances in immunophenotypic analysis have shown heterogenous antigenic profiles on RS cells with no convincing evidence of RS cell-specific antigens.[24] A combination of several markers including activation antigens, HLA-related molecules, T and B cell-associated antigens, and leukocyte common antigen is currently employed for the immunologic diagnosis of HL in routine pathology practice.[25] Recognition that nodular lymphocyte predominant HL (NLPHL) differs both morphologically and immunophenotypically from the other classical subtypes of HL led to an alternative pathologic classification, called the Revised European-American Lymphoma (REAL) classification system. This schema divides HL into two broad categories: classical HL and NLPHL.[26,27] Further rationale for this classification system is documentation that NLPHL has different virologic features and is clinically less aggressive than classic HL.[22] Ultimately the REAL classification was adopted into the WHO classification, the latter currently serving as the most widely accepted means to describe hematopoetic and lymphoid neoplasms (Table 57.4).[28]

HL arises within lymph nodes in > 90% of childhood, adolescent, and young adult cases.[29,30] The typical patient with HL has asymmetric lymphadenopathy that is firm, rubbery, and nontender. The cervical, supraclavicular, and mediastinal lymph nodes are the most frequent sites of presentation. Mediastinal node involvement has been particularly associated with right supraclavicular nodal disease. Obstruction of the superior vena cava or tracheobronchial tree may occur as a complication of mediastinal lymphadenopathy. Axillary, inguinal, and generalized lymphadenopathy are uncommon. Extranodal primary sites, such as within Waldeyer ring, are rare. Extranodal involvement does occur with disease progression; the spleen, liver, lung, bone, and bone marrow being the common organ systems affected. At presentation, children with HL have nonspecific systemic symptoms, termed B-symptoms, in 25–30% of cases; such B-symptoms include unexplained fever, night sweats, weight loss, weakness, anorexia, and pruritus.[19]

Once the diagnosis of HL is established, it is essential to define the full extent of disease in each patient before treatment. The Ann Arbor staging system (Table 57.5) is used to stratify risk for HL patients. This staging system is based on the premise that HL potentially progresses from a unifocal lymph node site, spreads via lymphatics to contiguous lymph node groups, and then involves extralymphatic sites, including the spleen, principally by hematogenous dissemination.[31] The system recognizes that localized extralymphatic spread may occur, and that such patients do as well as comparable patients of the same stage without local extralymphoidal disease. Such involvement is denoted by the letter E after the stage designation. Constitutional symptoms are also considered significant in the staging of the disease and are designated A when absent and B when present as previously defined.

The staging of HL has historically consisted of a combination of clinical and surgical staging with a laparotomy to assess for intra-abdominal disease and differentiate between Ann Arbor stage II and III disease.[32] However, the current quality of imaging techniques including the routine use of PET, as well as the expanding role of systemic chemotherapy in early stage disease, has obviated the need for surgical staging. Bone marrow aspirate and biopsy remains necessary for patients with clinical stage III or IV disease and for patients of any stage with B-symptoms.[19]

**Table 57.4:** World Health Organization classification of lymphoid neoplasms

| |
|---|
| *Mature B-cell neoplasms* |
| Chronic lymphocytic leukemia/small lymphocytic lymphoma |
| B-cell prolymphocytic leukemia |
| Splenic marginal zone lymphoma |
| Hairy cell leukemia |
| Splenic lymphoma/leukemia, unclassifiable<br>Splenic diffuse red pulp small B-cell lymphoma<br>Hairy cell leukemia variant |
| Lymphoplasmacytic lymphoma<br>Waldenström macroglobulinemia |
| Heavy chain diseases<br>α Heavy chain disease<br>γ Heavy chain disease<br>μ Heavy chain disease |
| Plasma cell myeloma |
| Solitary plasmacytoma of bone |
| Extraosseous plasmacytoma |
| Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) |
| Nodal marginal zone lymphoma<br>Pediatric nodal marginal zone lymphoma |
| Follicular lymphoma<br>Pediatric follicular lymphoma |
| Primary cutaneous follicle center lymphoma |
| Mantle cell lymphoma |
| Diffuse large B-cell lymphoma (DLBCL), NOS<br>T-cell/histiocyte rich large B-cell lymphoma<br>Primary DLBCL of the CNS<br>Primary cutaneous DLBCL, leg type<br>EBV-positive DLBCL of the elderly |
| DLBCL associated with chronic inflammation |
| Lymphomatoid granulomatosis |
| Primary mediastinal (thymic) large B-cell lymphoma |
| Intravascular large B-cell lymphoma |
| ALK-positive large B-cell lymphoma |
| Plasmablastic lymphoma |
| Large B-cell lymphoma arising in HHV8-associated multicentric castleman disease |
| Primary effusion lymphoma |
| Burkitt lymphoma |
| B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma |
| B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphoma |
| *Mature T-cell and NK-cell neoplasms* |
| T-cell prolymphocytic leukemia |
| T-cell large granular lymphocytic leukemia |
| Chronic lymphoproliferative disorder of NK cells |
| Aggressive NK-cell leukemia |
| Systemic EBV-positive T-cell lymphoproliferative disease of childhood |
| Hydroa vacciniforme-like lymphoma |
| Adult T-cell leukemia/lymphoma |
| Extranodal NK/T-cell lymphoma, nasal type |
| Enteropathy-associated T-cell lymphoma |
| Hepatosplenic T-cell lymphoma |
| Subcutaneous panniculitis-like T-cell lymphoma |
| Mycosis fungoides |
| Sézary syndrome |
| Primary cutaneous CD30+ T-cell lymphoproliferative disorders<br>Lymphomatoid papulosis<br>Primary cutaneous anaplastic large cell lymphoma |
| Primary cutaneous γδ T-cell lymphoma |
| Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma |
| Primary cutaneous CD4+ small/medium T-cell lymphoma |
| Peripheral T-cell lymphoma, NOS |
| Angioimmunoblastic T-cell lymphoma |
| Anaplastic large cell lymphoma, ALK-positive |
| Anaplastic large cell lymphoma, ALK-negative |
| *Hodgkin lymphoma* |
| Nodular lymphocyte predominant Hodgkin lymphoma |
| Classical Hodgkin lymphoma |
| Nodular sclerosis classical Hodgkin lymphoma |
| Lymphocyte-rich classical Hodgkin lymphoma |
| Mixed cellularity classical Hodgkin lymphoma |
| Lymphocyte-depleted classical Hodgkin lymphoma |
| *Histiocytic and dendritic cell neoplasms* |
| Histiocytic sarcoma |
| Langerhans cell histiocytosis |
| Langerhans cell sarcoma |
| Interdigitating dendritic cell sarcoma |
| Follicular dendritic cell sarcoma |
| Fibroblastic reticular cell tumor |
| Intermediate dendritic cell tumor |
| Disseminated juvenile xanthogranuloma |
| *Post-transplantation lymphoproliferative disorders (PTLDs)* |
| Early lesions<br>Plasmacytic hyperplasia<br>Infectious mononucleosis-like PTLD |
| Polymorphic PTLD |
| Monomorphic PTLD (B- and T/NK-cell types) |
| Classical Hodgkin lymphoma type PTLD |

*Contd...*

*Contd...*

Adapted from Campo et al.[28]

**Table 57.5:** Ann Arbor staging classification of Hodgkin lymphoma

| *Stage** | *Definition* |
|---|---|
| I | Involvement of a single lymph node region (I) or of a single extralymphatic organ or site ($I_E$) |
| II | Involvement of 2 or more lymph node regions on the same side of the diaphragm (II) or localized involvement of extralymphatic organ or site and of 1 or more lymph node regions on the same side of the diaphragm ($II_E$). An optional recommendation is that the numbers of node regions involved be indicated by a subscript (e.g. $II_3$) |
| III | Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of extralymphatic organ or site ($III_E$) or by involvement of the spleen ($III_S$), or both ($III_{SE}$). |
| IV | Diffuse or disseminated involvement of 1 or more extralymphatic organs or tissues with or without associated lymph node enlargement. The reason for classifying the patient as Stage IV should be identified further by defining site by symbols. |

*Each stage is subdivided into A and B categories indicating the absence or presence, respectively, of documented unexplained fever, night sweats, or weight loss (> 10% of body weight in the prior 6 months).

The treatment of HL varies according to stage. Surgery plays little role beyond initial diagnosis. Multimodal chemotherapy and radiation therapy serves to reduce the morbidity and mortality associated with the higher doses of chemotherapy or radiation therapy required for single modality therapy. Age specific management algorithms have been developed in an attempt to limit the high doses and extended fields of radiation therapy that cause considerable long-term morbidity for children and young adolescents. Similarly, chemotherapeutic regimens have been changed to reduce the risks of sterility, pulmonary toxicity and secondary malignancies.[19,33] HL patients who relapse may be candidates for autologous stem cell transplantation.[34]

With current therapeutic regimens, > 90% of all HL patients, regardless of stage, initially achieve a complete remission. Prolonged remission and cure is achieved in approximately 90% of patients with early stage I and II disease and in 35–60% of patients with advanced stage III and IV disease.[19,23] Histopathologic findings also have prognostic implications. Patients with lymphocyte predominant lesions have the most favorable survival statistics, followed in prognostic order by the nodular sclerosis, mixed cellularity, and unfavorable lymphocyte depletion subtypes.[23]

## Non-Hodgkin Lymphoma

NHL designates a heterogeneous group of solid primary neoplasms of the lymphatic system. In children, NHL most commonly occurs between the ages of 2 and 12 years and, as in HL, demonstrates a male predilection.[35,36] Both congenital and acquired immunodeficiency disorders predispose to the development of NHL.

The classification of the NHLs has been in evolution. In the 1950s, Rappaport and associates unified older classification systems by recognizing the resemblance of malignant lymphoma cells to their benign lymphocytic or histiocytic counterparts; clinicopathologic studies demonstrated this Rappaport classification system to be useful in the management and prognosis of NHL.[37,38] However, subsequent advances in the development of immunologic markers for lymphocytic subtypes led to further changes in NHL classification. Immunophenotyping allowed separation of NHL into categories of B-cell, T-cell, and true histiocytic origins, and the B- and T-cell lymphomas were further subdivided based on their morphologic appearance and degree of lymphocytic transformation.[39] In 2001, with an update in 2008, the World Health Organization developed an evidence-based classification system utilizing a combination of tumor morphology, immunophenotyping, genetic, molecular, and clinical features for all neoplasms of lymphatic origin. The neoplasms are stratified according to their cell lineage as well as derivation from precursor or mature lymphoid cells.[28] The WHO system has now emerged as the most robust and widely used classification scheme for all lymphomas (*see* Table 57.4).

The clinical features of NHL reflect the site of origin of the primary tumor and the extent of local and systemic disease. Asymptomatic lymphadenopathy is the most common initial presentation, with approximately 45% of patients found to have head and neck involvement at diagnosis.[40,41] Inguinal, axillary, and generalized nodal presentations are comparatively less frequent. Nodal growth may be rapid, but insidious presentations more often occur.

Atypical presentations of NHL result from extranodal involvement; this is more common in children than adults.[36,42] Extranodal sites in the head and neck include

Waldeyer ring of the oropharynx and nasopharynx, the nose and paranasal sinuses, the orbit, and the maxilla and mandible. The signs and symptoms attributable to extranodal cervicofacial NHL are quite variable and site specific. Such symptoms may include facial swelling, epistaxis, nasal blockage and other manifestations of upper airway obstruction, rhinorrhea, dysphagia, facial pain and other neurologic findings including cranial nerve deficits or central nervous system (CNS) symptoms.[40,41] Nasal, paranasal, and nasopharyngeal primary sites account for between 60% and 90% of extranodal head and neck NHL, and appear to be at greater risk for secondary CNS involvement.[43] Furthermore, the early detection of NHL involving Waldeyer ring may be difficult because it may mimic benign adenotonsillar hypertrophy. A biopsy via adenoidectomy or tonsillectomy may be warranted if there is asymmetry, discoloration, or evidence of systemic symptoms.[44]

Childhood NHL additionally differs from that in adults in that it has a greater likelihood of being composed of prognostically unfavorable cell types, a tendency toward both leukemic transformation and hematogenous dissemination, and an increase in CNS involvement.[36,42] Constitutional signs and symptoms that correlate with advanced disease include fever, weight loss, malaise, pancytopenia resulting from bone marrow infiltration, and neurologic manifestations.

The Ann Arbor staging classification for HL (*see* Table 57.5) is often still applied to patients with NHL. Alternatively the St. Jude's classification system (Table 57.6), first described in 1980, is commonly used.[45] The St. Jude's classification system attempts to account for the characteristic extranodal presentations and tendency toward hematogenous dissemination, bone metastases, and CNS involvement in childhood NHL.[42,45,46] The staging of NHL of the head and neck requires a comprehensive history and physical examination, serologic testing such as a complete blood count and lactate dehydrogenase level, chest radiograph, bone marrow biopsy, and cerebrospinal fluid analysis in addition to appropriate head and neck imaging by means of typically CT and often MRI.[47] More recently, PET has demonstrated utility for disease staging and for following disease progression during treatment. [48] When coupled with CT, PET imaging has demonstrated an improved ability to identify metastatic lesions.[49]

Stage I NHL is infrequently diagnosed in the pediatric age group. Approximately 80% of children with NHL have advanced stage II, III, or IV disease.[45,46] As in HL, surgery plays little role in NHL management beyond diagnostic biopsy and occasional surgical debulking in the setting of aerodigestive tract compression.[50] Stage I follicular lymphoma may be amenable to complete surgical excision alone.[51]

**Table 57.6:** St. Jude's non-Hodgkin lymphoma classification system

| *Stage* | *Criteria for extent of disease* |
|---|---|
| I | A single tumor (extranodal) or single anatomic area (nodal), with the exclusion of mediastinum or abdomen |
| II | A single tumor (extranodal) with regional node involvement.<br>Two or more nodal areas on the same side of the diaphragm.<br>Two single (extranodal) tumors with or without regional node involvement on the same side of the diaphragm.<br>A primary gastrointestinal tract tumor, usually in the ileocecal area, with or without involvement of associated mesenteric nodes only. |
| III | Two single tumors (extranodal) on opposite sides of the diaphragm.<br>Two or more nodal areas above and below the diaphragm.<br>All the primary intra thoracic tumors (mediastinal, pleural, thymic).<br>All extensive primary intra-abdominal disease.<br>All paraspinal or epidural tumors, regardless of other tumor site(s). |
| IV | Any of the above with initial CNS and/or bone marrow involvement |

Adapted from Murphy et al.[42]

The principal treatment for nearly all stages of pediatric head and neck NHL is systemic chemotherapy; the rapid doubling time of high-grade NHL makes it highly chemoresponsive.[40,41] Radiation therapy has a limited role in the treatment of NHL. CNS prophylaxis in children with high-grade NHL can be achieved with intrathecally administered chemotherapy alone. Treatment for relapse consists of high-dose chemotherapy; bone marrow transplantation may be considered.[36]

Prognosis is principally associated with disease stage and response to initial therapy. The overall 5-year disease-free survival rate for NHL of the head and neck approximates 70–76%.[40,41] The event-free survival rate for NHL

irrespective of site of origin is 85–95% for stage I and II disease and 50–85% for stage III and IV disease, depending on the histological type.[36] The potential role of immunotherapy, given the observation that most childhood NHL is characterized by T- or B-cell differentiation, continues to evolve.

## Burkitt Lymphoma

Burkitt lymphoma (BL) deserves special note due to its predilection for children. BL is a non-Hodgkin B-cell lymphoma that has distinct epidemiologic and clinical features.[52,53] Epidemiologic differences separate BL into an endemic and a sporadic type. Endemic BL is generally limited to equatorial Africa; its limited geographic distribution suggests an infectious etiology. Serologic evidence supports a role for the EBV. Almost all endemic BL patients demonstrate high antibody titers to EBV determinant antigens, and 80–90% of their tumor cells contain copies of the EBV DNA genome; in contrast, only 15–20% of patients with the sporadic form of BL demonstrate this serologic and histopathologic EBV association.[54]

BL is a disease almost exclusively afflicting children with a predilection for males.[52,53] The clinical presentation characteristics of endemic BL, however, differ greatly from that of the sporadic form. Endemic BL is diagnosed at an average age of 9 years and characteristically occurs as a facial mass originating from the jaw.[55,56] The maxilla is more frequently involved than the mandible. Loose dentition, facial distortion, trismus, and proptosis are common manifestations. Abdominal masses, when present, are typically of renal or gonadal origin. Splenic and lymph node involvement is rare.

Sporadic BL, in contrast, is associated with slightly older children (average age 12 years) and usually presents in the abdomen.[57] Approximately one quarter of sporadic BL cases involve the head and neck. Asymptomatic cervical lymph node enlargement is the most common presentation; jaw involvement as seen in endemic BL is comparatively rare. Waldeyer ring origin with nasopharyngeal, oropharyngeal, and parapharyngeal mass presentations has also been reported.[58–60] Bone marrow involvement is more common in sporadic BL, and CNS involvement may potentially occur with comparative equal frequency in both endemic and sporadic forms.[55,56]

BL has rapid proliferative potential and tumors may reach a large size quickly. Rapid diagnosis, staging, and treatment are advocated. Staging workup is similar to that used in other NHLs. PET scans and lactate dehydrogenase levels are useful to quantitate tumor burden and to follow patients serially.[11,53,55]

The primary treatment modality for both endemic and sporadic BL is multidrug chemotherapy. Because of the high proliferative rate of BL and the abundance of cells in various stages of the cell cycle, successive chemotherapy cycles result in greater cytotoxicity than do traditional fixed dose regimens.[61] Surgery has a limited role, principally for diagnostic biopsy purposes, in the management of BL. In endemic abdominal BL disease, however, the surgical reduction of tumor bulk has been shown to improve survival.[56,62] A similar role for tumor debulking or resection of head and neck BL has not been defined.

Three- and five-year event-free survival rates for both endemic and sporadic BL are 85–95% for limited disease and 75–85% for advanced disease; relapse rates are lower and survival rates significantly higher in patients with a smaller tumor burden at presentation.[63] For localized disease limited to the head and neck, a 90% long-term survival is reported.[64] Children younger than 12 years of age do significantly better than older patients, and high anti-EBV antigen titers in sporadic BL patients appear to be associated with a more favorable prognosis.[57,63]

# SOFT TISSUE AND SKELETAL MALIGNANCY

Soft tissue malignancies of mesenchymal origin present significant diagnostic and therapeutic dilemmas. These tumors are classified by the tissue of origin and have various degrees of aggressiveness.

## Rhabdomyosarcoma

RMS is the most common soft tissue malignancy in the pediatric age group, accounting for 50–70% of all childhood sarcomas.[65–67] The incidence of RMS diagnosis is 4.5 cases per million children per year.[68] According to the Intergroup Rhabdomyosarcoma Studies (IRS), 35% of pediatric RMS present in the head and neck. Approximately 70% of these children manifest their disease before 12 years of age, and 43% present at age younger than 5 years. There is no apparent sex predilection. RMS is four times more common in white children than in any other racial group.[69]

Though most cases of RMS are sporadic, there appear to be both environmental and genetic risk factors. Implicated environmental exposures of variable relevance

include parental smoking, in utero radiation exposure, advanced maternal age or a maternal history of prior spontaneous abortions, and recreational drug use by the mother.[70–73] Several familial syndromes including Li-Fraumeni syndrome, Beckwith–Weidemann syndrome, and Costello syndrome have been associated with an increased risk for pediatric RMS.[74-76] A higher incidence of congenital malformations has also been reported in children with RMS (32%) in comparison to the general population (3%).[77]

RMS has a spectrum of histopathologic subtypes. These include in order of relative frequency, embryonal (54%), alveolar (18.5%), undifferentiated (6.5%), and botryoid (4.5%) (Fig. 57.6).[78] In the head and neck, RMS is anatomically categorized as orbital, parameningeal, and nonparameningeal.[79,80] Parameningeal sites include the nasopharynx, paranasal sinuses, middle ear, and infratemporal fossa. All other cervicofacial sites are considered nonparameningeal.[81] In the head and neck region, the most common sites of origin, in descending order of frequency, are the orbit, nasopharynx, middle ear-mastoid region, and sinonasal cavities.[82] Presenting symptoms are based on tumor location and can be occult. Unexplained ptosis, refractory sinusitis symptoms, and unilateral otorrhea unresponsive to therapy should raise concern of RMS. Multiple cranial nerve palsies suggest extension of disease to the skull base or CNS.[83]

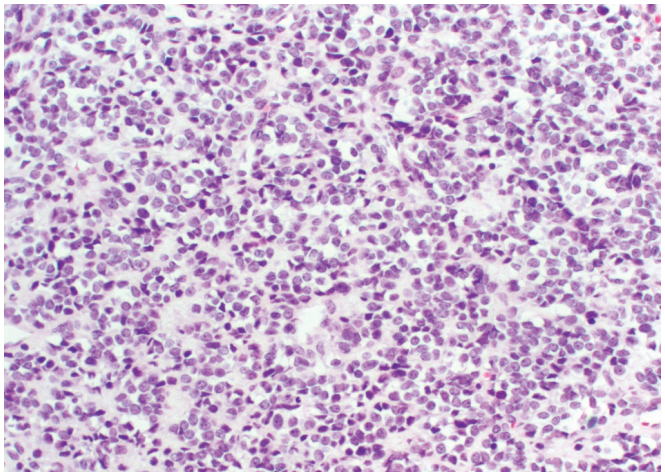


**Fig. 57.6:** Hematoxylin and eosin photomicrograph of alveolar rhabdomyosarcoma. Alveolar histologic findings include uniform loosely dispersed cells with a high nuclear to cytoplasmic ratio.

Metastatic spread of RMS occurs by lymphatic and hematogenous routes, both being notably rare with orbital RMS.[67,84] The incidence of cervical lymph node metastases otherwise varies with the primary site. The most common sites of hematogenous metastatic disease are the lung, bone, and bone marrow. About 13% of patients with RMS of the head and neck present with distant metastases.[85]

All RMS arising in the head and neck require detailed anatomic imaging. Parameningeal sites require both CT and MRI radiologic evaluation, as well as lumbar puncture with cerebrospinal fluid cytology, to assess for skull base erosion or CNS involvement.[86] Skeletal survey, bone scan, and bone marrow aspirate are necessary for complete systemic evaluation.

Staging of RMS is based on a combination of factors. These factors include histologic subtype, tumor node metastasis (TNM) grade based on location and size, and clinicopathologic grouping determined by resectability of local and regional disease.[87–89] Staging allows stratification into low-risk, moderate-risk and high-risk groups. A TNM-based staging system modified by the IRS accounts for size, location, regional, and metastatic disease (Table 57.7).

**Table 57.7:** TNM classification of rhabdomyosarcoma modified by the Intergroup Rhabdomyosarcoma Study Group

| *Stage* | *Site* | *T* | *Size* | *N* | *M* |
|---|---|---|---|---|---|
| I | Orbit, head, and neck, excluding parameningeal sites, genitourinary but not bladder or prostate | T1 or T2 | A or B | Any N | M0 |
| II | Bladder, prostate, T1 or T2 extremity, cranial parameningeal sites, other | T1 or T2 | A | N0 or Nx | M0 |
| III | Bladder, prostate, T1 or T2 extremity, cranial parameningeal sites, other | T1 or T2 | A<br>B | N1<br>Any N | M0 |
| IV | All | T1 or T2 | A or B | N0 or N1 | M1 |

Where TNM and the size of the tumor are defined as: T1 is confined to the site of origin; T2 has extension or fixation to surrounding structures; A is a tumor $\leq$ 5 cm; B is a tumor > 5 cm; N0 is clinically involved lymph nodes; N1 is regionally involved lymph nodes; Nx is clinical status of lymph nodes unknown; M0 is no distant metastasis; M1 is metastasis present; TNM: tumor, nodes, metastasis. Adapted from Pappo et al.[90]

Treatment guidelines established by the IRS emphasize the superiority of multimodality therapy. Before the IRS, the 5-year survival rate for RMS of the head and neck, all sites considered, ranged from 8% to 20%. Using multimodality treatment principles, the 3-year relapse-free survival rates have increased to 91% for orbital primary disease, 46% for parameningeal primary disease, and 75% for other head and neck sites.[85]

Surgical extirpation of the primary tumor is indicated when such removal imposes no major functional disability and when excision of the primary tumor permits either the elimination of postoperative radiation therapy or a reduction in radiation dose. This is true of many nonorbital and nonparameningeal head and neck sites.[91] When only partial tumor resection is possible, as is often true of parameningeal sites, solely surgical biopsy may be indicated. Some institutions do advocate complete resection of parameningeal tumors if surgically feasible, for example in the occipital and infratemporal fossa regions, in order to obviate the need for radiotherapy. Possible complications of such surgical management include cranial nerve injury, cosmetic deformity, and trismus.[79] Comparison of the role of surgical biopsy versus debulking in patients with IRS stage III RMS showed no difference in outcome; therefore, biopsy alone is warranted in extensive disease.[92]

Because the anatomic location in the head and neck often precludes complete resection, radiation therapy is commonly recommended. Recent advances in proton therapy techniques have allowed more precise dosing delivery and sparing of uninvolved critical structures. Additionally, almost all patients with head and neck RMS, regardless of resectability, receive systemic chemotherapy. Chemotherapy is typically administered postoperatively to patients with small resectable lesions. Preoperative chemotherapy may be administered to children with larger lesions to decrease tumor volume prior to excision. Completely excised lesions with a clinically negative neck generally require no treatment beyond chemotherapy and observation. Children with a clinically positive neck benefit from neck dissection with additional radiotherapy.[87] Radiation therapy is also indicated for any incompletely excised tumors.

The primary site is an important prognostic indicator for several reasons. The anatomic location of the primary tumor determines the signs and symptoms that lead to diagnosis or delay thereof. Furthermore, the likelihood of lymphatic spread and hematogenous dissemination varies with primary site and the location has implications with respect to the functional and cosmetic outcome of resection.[93]

The histopathologic subtype is also an important variable as embryonal histology has a more favorable prognosis than other histologic subtypes. A number of chromosomal abnormalities in RMS have been identified and are being investigated to determine their significance as prognostic indicators as well.[94]

Overall, children with localized disease receiving combination therapy have a 5-year survival rate of 70%. Such rates, however, are highly individual specific based on the multiple prognostic factors outlined above. After 5 years, relapses become uncommon.

## Nonrhabdomyosarcoma Sarcomas

Soft tissue sarcomas other than RMS account for 3–5% of all malignant neoplasms in children.[67,95] A bimodal age distribution curve with incidence peaks in children younger than 5 years of age and in adolescence is characteristic of almost all these lesions.[96] The soft tissue sarcomas of infants and young children primarily occur in the head and neck region, whereas lesions in adolescents predominantly arise in the trunk and extremities. Non-RMS sarcomas are considered separate from RMS because of the variety of different tumor types and variable response to standard RMS treatment protocols.

Because of their relative rarity, understanding the natural history of these neoplasms and the development of effective treatment regimens requires multi-institution collaboration. In general, with the exception of fibrosarcoma, soft tissue sarcomas demonstrate a tendency toward both local recurrence and metastatic hematogenous spread. This behavior dictates a multimodality therapeutic approach similar to that used in RMS patients.[97-100]

In general, complete surgical excision with a 1 cm margin is the treatment of choice. Radiation and chemotherapy are typically reserved for cases of incomplete resection or unresectable disease.[101,102]

## Fibrosarcoma

Fibrosarcoma is the most common sarcoma histology after RMS, accounting for 11% of all soft tissue sarcomas of childhood.[67,103] Although fibrosarcoma is primarily a malignancy of the extremities in adolescents, approximately 15–20% of fibrosarcomas occur in the head and neck region, predominantly in infants and young children.[96] The most common time of presentation in childhood is within the first 6 months of life.[104] Fibrosarcoma may also arise in older children as a secondary neoplasm following radiation therapy.[105]

Histopathologically, fibrosarcomas consist of malignant fibroblasts associated with variable collagen or reticulin production. Local infiltration distinguishes well-differentiated fibrosarcoma from nonmalignant juvenile fibromatosis. This distinction, however, can sometimes be difficult.[106] Fibrosarcoma of infancy histologically appears the same as in older patients but is less aggressive and has even clinically been mistaken for a hemangioma.[104,107]

Fibrosarcoma is unique among the soft tissue sarcoma as metastatic disease in infants and young children is infrequent. Lymph node metastases occur in < 10% of patients. The incidence of hematogenous metastasis to lung and bone is reported to be < 10% for children younger than 10 years of age, whereas rates approach 50% in patients older than 15 years.[108,109]

Therapy is primarily directed at local disease control. Complete surgical excision, when possible, is advocated. Maintenance of function at the expense of inadequate margins or incompletely resected disease is often necessary in childhood head and neck cases. In such situations, gross tumor resection is followed by local radiation therapy or chemotherapy.[107] Preoperative chemotherapy may also be used to decrease the size of the tumor in an attempt to make it completely resectable.[104] The incidence of local recurrence varies greatly with reported rates between 17% and 43%.[104] The 5-year survival rate of infants and young children with fibrosarcoma is between 80% and 90%.

## Synovial Sarcoma

Synovial sarcomas account for approximately 5% of all pediatric soft tissue sarcomas. Synovial sarcoma is primarily a malignancy of the extremities with fewer than 50 cases reported in the head and neck.[110,111] There is a slight female predominance.[110] Synovial sarcoma is thought to arise from synovioblastic differentiation of mesenchymal stem cells; this derivation accounts for the presence of synovial sarcomas in head and neck sites without normal synovial structures.[112]

Cervicofacial synovial sarcomas have been reported in the larynx, pharynx, tongue, tonsil, and facial soft tissues. The most common location is the neck, where they present as firm, gradually enlarging, parapharyngeal or retropharyngeal masses that become symptomatic by compromising contiguous structures. Delayed diagnosis is common.[110]

Treatment of local disease consists of the widest possible surgical excision followed by radiation therapy; chemotherapy is used in advanced stage lesions.[113] Five-year survival rates following combined surgical and radiation treatment regimens approximate 50%; children with small, localized lesions have the best outcome.[67]

## Malignant Peripheral Nerve Sheath Tumors

Malignant peripheral nerve sheath tumors (MPNSTs), also known as neurofibrosarcoma or malignant schwannoma, are tumors of neural sheath origin accounting for approximately 3–10% of all soft tissue sarcomas of childhood.[103,114] This malignant counterpart of a neurofibroma is the most common malignancy arising within peripheral nerves.[115] Children with neurofibromatosis type I (von Recklinghausen disease) are at increased risk for the development of this lesion; MPNST develops in approximately 3–16% of these children.[116,117] Patients who have neurofibromatosis type 2 are also at increased risk, and any NF child with a rapidly expanding mass or neurologic deficits should be evaluated for a possible malignancy.[117] Children who have undergone radiation therapy are also at increased risk for MPNSTs.[118–121]

Approximately 10% of all MPNSTs occur in the cervicofacial region, most commonly arising from the cranial nerves, cervical plexus, or sympathetic chain.[122] An enlarging cervical mass is the common presentation. Associated symptoms may include pain, paresthesias, or muscle weakness. Other symptoms reflecting nerve involvement or mass effect include dysphonia, dysphagia, facial nerve paresis, and muscle fasciculations.[123]

Surgical excision with a 2 cm margin has been advocated. This may not be possible without causing significant morbidity including cranial nerve deficits.[117,123] Local recurrence and hematogenous pulmonary metastases are common. As is the case for many non-RMS soft tissue sarcomas, MPNST is relatively insensitive to chemotherapy.[117] Patients with extensive local disease or distant metastases do poorly despite aggressive multimodality therapy, while cure rates are highest in patients with completely resectable local disease.[87,124] MPNST occurring in patients with NF1 tend to be particularly aggressive. The 5-year survival rate for this group of patients is 15–30% compared with 27–75% for patients with MPNST not associated with this syndrome.[122]

## Kaposi Sarcoma

Kaposi sarcoma is a rare neoplasm that histologically demonstrates a variable mixture of vascular and sarcomatous components.[125] Kaposi sarcoma is a neoplasm of endothelial cell origin caused by human herpesvirus-8.

This disease is rare in children without acquired immune deficiency syndrome (AIDS). The incidence in children with AIDS of documented minimum two years duration is 97 per 100,000 person years.[126] In children without AIDS, a variation termed classic Kaposi sarcoma is distinguishable. Most children with classic Kaposi sarcoma have been of African descent.[127] Classic Kaposi sarcoma is characterized by generalized lymphadenopathy with a predilection for head and neck glandular sites. The lacrimal, parotid, and submandibular glands are commonly involved, and skin lesions are sparse.

Most cases of Kaposi sarcoma in the pediatric age group in the United States occur in infants with AIDS born to mothers with established or suspected HIV infection.[128–130] Such congenitally HIV-infected children with Kaposi sarcoma are rare.[131,132] These infants clinically demonstrate a disseminated lymphadenopathy form of Kaposi sarcoma. They differ from their African counterparts in several respects including demonstrable failure to thrive with developmental delay as well as highly susceptibility to opportunistic infections such as *Pneumocystis carinii* pneumonia, mucocutaneous candidiasis, and disseminated herpes-virus infection. They have profound lymphocyte depletion and a reversed T4/T8 lymphocyte ratio.[133] In a group of children with AIDS and Kaposi sarcoma studied in South Africa, the most common presenting sites were the oropharynx and the inguinal/scrotal region.[128] The gastrointestinal tract has also been found to be involved with subsequent mucosal hemorrhage and intestinal obstruction in 30–50% of affected children.[134,135] Given this frequency, surveillance of the gastrointestinal tract should be considered.

In contrast to congenitally infected infants with Kaposi sarcoma, children and adolescents who acquire AIDS later in life present with the cutaneous form of Kaposi sarcoma in a fashion similar to that of adults.[125,136] Skin lesions, most frequently on the arms, face, and neck, and oropharyngeal mucosal lesions are prominent. The lesions appear purple, red, or brown with an oval appearance and a distinct border.[125] Multiple lesions are the rule, and generalized lymphadenopathy and visceral involvement are also common.

Surgical excision and radiation therapy have been the traditional treatments of choice of localized Kaposi sarcoma. Immunotherapy and systemic chemotherapy have been used to treat disseminated disease.[136] Both classic Kaposi sarcoma and that associated with AIDS in childhood are aggressive, invariably fatal diseases.[137] Experience with the treatment of Kaposi sarcoma in childhood is limited because of its rarity.

## Extraskeletal Ewing Sarcoma

Extraskeletal Ewing sarcoma (EES), also called primitive neuroectodermal tumor, is a malignant soft tissue tumor identical in histological appearance to Ewing sarcoma of bone. The specific cell of origin of EES is suspected to be a primitive mesenchymal stem cell.[138] Diagnostic criteria include the following: an absence of bone involvement on CT, no increased uptake on a bone scan or the periosteum near the tumor, histology demonstrating small round tumor cells, and conformational immunohistochemistry and/or electron microscopy with presence of glycogen within the cell.[139] Most individuals with EES are younger than 30 years of age at the time of diagnosis with an average age at presentation of 15 years.[140]

In the head and neck, EES typically arises within soft tissues adjacent to the cervical spine and present with pain, tenderness, and neurologic disturbances related to spinal cord compression.[141] Cases of EES of the scalp, neck and paraspinal muscles in the pediatric population have been reported.[140,142]

Treatment of EES generally consists of surgical excision alone or in combination with radiotherapy or chemotherapy. Mortality is high, due both to local recurrence as well as pulmonary and osseous metastases. The multimodality IRS protocols used in the treatment of RMS have been applied to both adults and children with EES.[140] In two retrospective evaluations of patients with EES, positive prognostic factors for disease free survival include age < 16 years, complete wide resection, higher hemoglobin and lower lactate dehydrogenase levels, and aggressive use of multiagent chemotherapy followed by either surgical resection or radiation therapy.[140,143]

## Hemangiopericytoma

Hemangiopericytomas account for 3% of the total number of childhood soft tissue sarcomas.[67] Approximately 5–15% of hemangiopericytomas are seen in the pediatric age group.[124,144] Two types of childhood hemangiopericytomas have been described. Congenital or infantile hemangiopericytomas occur within the first year of life and invariably follow a benign course despite malignant histopathologic characteristics.[144,145] Hemangiopericytomas in children older than 1 year behave in a clinical fashion similar to that observed in adults; approximately 20–35% prove to be malignant.[146] Most lesions are solitary, but multiple congenital hemangiopericytomas have been reported in the head and neck. Hemangiopericytoma has been diagnosed in utero on ultrasonography, which allows for interdisciplinary planning regarding potential airway compromise at birth.[147]

Hemangiopericytomas arise from the pericytes of Zimmermann, cells that lie external to the reticulin sheath of capillaries. Microscopically, the cells consist of uniform round or spindle-shaped cells intimately associated with a vascular background. Special stains reveal a characteristic histopathologic reticulin pattern, which distinguishes hemangiopericytomas from hemangiosarcomas and other richly vascular soft tissue tumors.[82] Infantile hemangiopericytomas may differentiate and mature into a benign tumor.[145] Findings suggestive of malignancy include increased mitotic index, hemorrhage, calcification, and necrosis.[144]

The nasal cavity and paranasal sinuses are the most common head and neck location of hemangiopericytomas; less frequent sites include the orbital region, parotid gland, and neck.[82] Sinonasal hemangiopericytomas frequently occur as a polypoid mass causing nasal obstruction and epistaxis. A slowly enlarging, painless mass of firm, fibrous consistency is the characteristic presentation in other locations. When hemangiopericytomas occur in the oral cavity, the most common location is the tongue.[148]

Surgical excision with as wide margins as possible is the cornerstone of therapy.[144,149] Surgery alone is sufficient for infantile hemangiopericytoma because of its benign clinical characteristics. In the rare case of an unresectable infantile hemangiopericytoma, the tumor has shown excellent response to high-dose chemotherapy.[150] In older children, adjuvant chemotherapy should be considered if there is gross residual tumor or metastatic disease. Radiation therapy, in combination with chemotherapy, is also used in cases of unresectable or incompletely resectable local disease.

A high incidence of both local recurrence and lung metastases characterizes noninfantile hemangiopericytoma of all sites including the head and neck.[124,151] The small number of cases reported in children does not allow for age-specific survival figures, although infantile hemangiopericytoma has a better prognosis. The overall survival rate at 5 years in adult series varies between 50% and 70%.[151] Patients with unresectable local disease or metastatic disease at the time of presentation do particularly poorly.

### Additional Soft Tissue Sarcomas

Additional soft tissue sarcomatous neoplasms of the head and neck region in children include malignant hemangioendothelioma, leiomyosarcoma, liposarcoma, alveolar soft sarcoma, and malignant fibrous histiocytoma.[67,152] The use of surgery and radiation therapy to control local disease, with the adjuvant administration of systemic chemotherapy to prevent metastases, appears applicable to these rare lesions as well.

### Osteosarcoma

Osteosarcoma is the most common primary malignancy in bone and is most frequently seen in the long bones.[153] Most cases involving the head and neck occur in adults as secondary lesions attributed to prior radiation therapy for another malignancy.[154–157] The largest series to date focusing on primary head and neck lesions in children documented 22 cases evaluated by the Armed Forces Institute of Pathology (AFIP) between 1970 and 1997. Based on the AFIP experience, the mandible is the most commonly involved bone and affected children ranged from 1 to 18 years old with a mean age of 12.2 years. All patients underwent surgical excision. Of 19 patients with suitable follow-up, 9 children underwent adjuvant treatment with chemotherapy, radiation or a combination. The raw 5-year survival was reported to be 63.2% despite seven children undergoing therapy for local recurrence. A recent review from the MD Anderson Cancer Center demonstrated similar findings in 16 patients diagnosed between 1983 and 2008.[158] Given the overall lack of data, similar treatment strategies to long bone disease based on surgical excision with adjuvant chemotherapy with or without radiation based on tumor grade appear warranted.

### Chondrosarcoma

Similar to osteosarcoma, primary pediatric head and neck chondrosarcoma is exceedingly rare. The AFIP experience between 1970 and 1997 revealed only 14 affected children.[159] Eight of the 14 cases involved the nasal cavity and paranasal sinuses. All children were treated with surgical excision. Of the 11 patients with adequate follow-up, 7 received adjuvant therapy. All patients were alive at 5 years and only one had recurrent disease. Ultimately, treatment of head and neck chondrosarcoma should likely follow conventional therapy based upon surgical excision with a limited role for adjuvant chemotherapy or radiation.

## SALIVARY GLAND MALIGNANCY

Salivary malignancies are quite rare in the pediatric population. An AFIP review of 10,000 salivary gland lesions revealed only 54 malignancies in the pediatric

age group, and a review of the SEER database from 1973 to 2006 revealed only 253 cases of salivary neoplasms (0.5% of all cancers).[160,161] Other major oncologic institutions have likewise compiled individual totals of only 10–25 malignant salivary gland cases in young patients.[161,162] An estimated 3% of salivary gland neoplasms, benign or malignant, occur in patients 16 years of age or younger.[163] The WHO classifies 14 types of benign neoplasms and 24 malignancies arising in the salivary glands (Table 57.8).

Malignant neoplasms of the salivary glands represent up to 50% of all salivary neoplasms.[165,166] The majority of such salivary gland neoplasms occur in older children and adolescents; cases involving infants and young children are rare. More than 90% of pediatric malignant tumors of salivary gland origin arise in the parotid gland.[167]

Although rare, the histopathologic findings in malignant salivary gland neoplasms in children are similar to those in the adult population; the relative frequency of occurrence of the various histological types, however, does vary. Mucoepidermoid carcinoma is by far the most common in children, accounting for at least half of all pediatric salivary malignancies. There is some disagreement between institutional reviews and SEER data regarding the relative frequency of acinic cell carcinoma, adenoid cystic carcinoma, and adenocarcinoma. However, these four entities clearly make up the vast majority malignancies in the pediatric population.[160] Carcinoma ex pleomorphic adenoma (1%) and squamous cell carcinomas (0%) are comparatively rare. Sarcomas, particularly RMS, and lymphoid malignancies can also present within the salivary glands in children.[168,169]

The most common presentation of a salivary gland neoplasm is an asymptomatic, firm mass in the lateral cervicofacial region or in the submandibular compartment of the neck. Rapid growth and pain raise concern of malignancy, as do ipsilateral cervicofacial lymphadenopathy or facial nerve weakness.

The initial evaluation of a suspected salivary gland neoplasm typically involves anatomic imaging. Contrast-enhanced MRI is ideal for determining the soft tissue boundaries of the mass and its probable site of origin. CT is particularly useful if there is a concern of osseous involvement or tumor entry into neural foramina.[170]

The relatively high risk of malignancy dictates a histopathologic examination of all firm salivary gland masses in children. FNA with cytologic diagnosis is used routinely in adults for this purpose.[171] FNA of salivary gland lesions is performed less frequently in the pediatric population, due in part to the need for sedation or general anesthesia. Although FNA clearly has potential benefits, its role as the basis for determining management decisions in the pediatric population remains controversial.[172] Under most circumstances, excisional biopsy via superficial parotidectomy with facial nerve identification, or total excision of the submandibular gland, is preferred.[173] Incisional biopsy of parotid masses is generally limited to masses involving the tail of the parotid region, and in clinically unresectable lesions for which diagnostic biopsy alone is needed.

The mainstay of treatment of salivary gland neoplasms in children, as in adults, is surgical excision. Submandibular gland lesions are treated with complete gland excision.

**Table 57.8:** World Health Organization classification of salivary neoplasms

| *Malignant epithelial neoplasms* | *Benign epithelial neoplasms* |
|---|---|
| Acinar cell carcinoma | Pleomorphic adenoma |
| Mucoepidermoid carcinoma | Myoepithelioma |
| Adenoid cystic carcinoma | Basal cell adenoma |
| Polymorphous low grade adenocarcinoma | Warthin tumor |
| Epithelial-myoepithelial carcinoma | Oncocytoma |
| Clear cell adenocarcinoma, NOS | Canalicular adenoma |
| Basal cell adenocarcinoma | Sebaceous adenoma |
| Sebaceous carcinoma | Lymphadenoma |
| Sebaceous lymphadenocarcinoma | Sebaceous |
| Cystadenocarcinoma | Nonsebaceous |
| Low-grade cribriform cystadenocarcinoma | Ductal papillomas |
| Mucinous adenocarcinoma | Inverted ductal papilloma |
| Oncocytic carcinoma | Intraductal papilloma |
| Salivary duct carcinoma | Sialadenoma papilliferum |
| Adenocarcinoma, NOS | Cystadenoma |
| Malignant myoepithelioma | |
| Carcinoma ex pleomorphic adenoma | *Soft tissue tumors* |
| Carcinosarcoma | Hemangioma |
| Squamous cell carcinoma, NOS | |
| Small cell carcinoma | *Hematolymphoid tumors* |
| Large cell carcinoma | Hodgkin lymphoma |
| Lymphoepithelial carcinoma | Diffuse large B-cell lymphoma |
| Sialoblastoma | Extranodal marginal zone B-cell lymphoma |
| | *Secondary Tumors* |

Adapted from Eveson JW et al.[164]

For parotid lesions, superficial or subtotal parotidectomy is adequate when the lesion in question is localized to the superficial parotid lobe and subsequent histopathologic examination reveals a benign or low-grade malignancy. Deep lobe parotid lesions and suspected or confirmed high-grade malignancies require total parotidectomy (Fig. 57.7). Resection of the facial nerve or its branches is recommended only when there is gross anatomic or histopathologic evidence of neural invasion at the time of surgery; resection is not performed simply based on tumor type or grade. When resection of the nerve is necessary, immediate repair by means of primary anastomosis or free nerve graft is advocated.

In the absence of confirmed cervical lymph node metastases, most centers limit neck dissection to patients with known high-grade malignancies, or advocate periglandular node dissection at the time of initial superficial parotidectomy or submandibular gland excision, proceeding with a more formal modified neck dissection if there is intraoperative frozen section confirmation of periglandular metastases.[174] Factors that increase the risk of lymph node metastases include facial nerve involvement, high-grade histopathology, perilymphatic invasion, and extraglandular extension.[175]

As the biological behavior of parotid malignancies in children appears to be similar to that in adults, the indications for radiotherapy are likewise similar. However, the potential for radiation-induced secondary malignancies and altered facial growth must be balanced against the likelihood of improved local and regional control. Positive margins following primary surgical excision increase the incidence of local recurrence, requiring either additional resection if anatomically feasible or postoperative radiotherapy.[176] Perineural invasion, extraglandular extension of tumor, or cervical metastases are additional histopathologic indications for postoperative radiotherapy at some centers, as are highly aggressive histological features as seen with high-grade mucoepidermoid carcinoma, poorly differentiated adenocarcinoma, adenoid cystic carcinoma, carcinoma ex pleomorphic adenoma, squamous cell carcinoma, and undifferentiated carcinoma.[174,175] Palliative radiation therapy may be the sole treatment of undifferentiated salivary gland malignancies that are unresectable at the time of presentation.

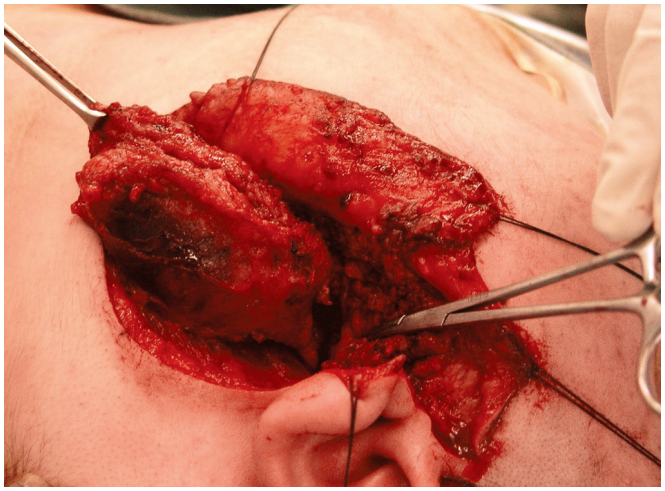


**Fig. 57.7:** A child undergoing excision of a parotid mass.

Chemotherapy has been investigated for use as adjuvant therapy in the treatment of high-grade salivary gland malignancies, and is more commonly reserved for use as palliative therapy in patients with metastatic or local/regional disease refractory to resection and radiation.

The survival of children with salivary gland malignancies is primarily determined by histopathology.[177] Children with low-grade malignancies such as grade I and grade II mucoepidermoid carcinoma, well-differentiated adenocarcinoma and acinic cell carcinoma tend to do well.[178,179] Those with high-grade malignancies such as grade III mucoepidermoid carcinoma, poorly differentiated adenocarcinoma and undifferentiated tumors do poorly. The long-term follow-up of adenoid cystic lesions makes survival assessment of this group of patients difficult.[180] The overall 5 and 10 year survival for children diagnosed with salivary malignancy was recently reported to be 95% and 94%, respectively.[160]

In addition to the described lesions, a uniquely pediatric lesion known as a sialoblastoma of infancy has been described. Less than 100 cases of this rare epithelial salivary tumor have been reported. Sialoblastomas most commonly present at birth or on antenatal ultrasound, but have been reported in children up to 5 years of age and are most commonly seen in the parotid gland with a male predominance.[181–183] These lesions have an aggressive histopathologic appearance reflective of its embryonic development, and are generally managed surgically with a goal of tumor free margins. Large or highly aggressive tumors have been successfully treated with adjuvant radiation brachytherapy and chemotherapy for metastatic disease.[183,184–186] Local recurrence is commonly reported and has been successfully managed with a combination of additional surgery and chemoradiation.[182,185,187]

## Neuroendocrine Malignancy

Neurogenic tumors of the head and neck include benign and malignant lesions, both of which generally present as lateral neck masses. Excluding CNS neoplasms, tumors originating from neural crest cells represent the most important neural etiology of head and neck malignancies. Neurogenic tumors derived from neural crest cells are typically associated with the sympathetic chain and may present with associated sympathetic nervous system manifestations.

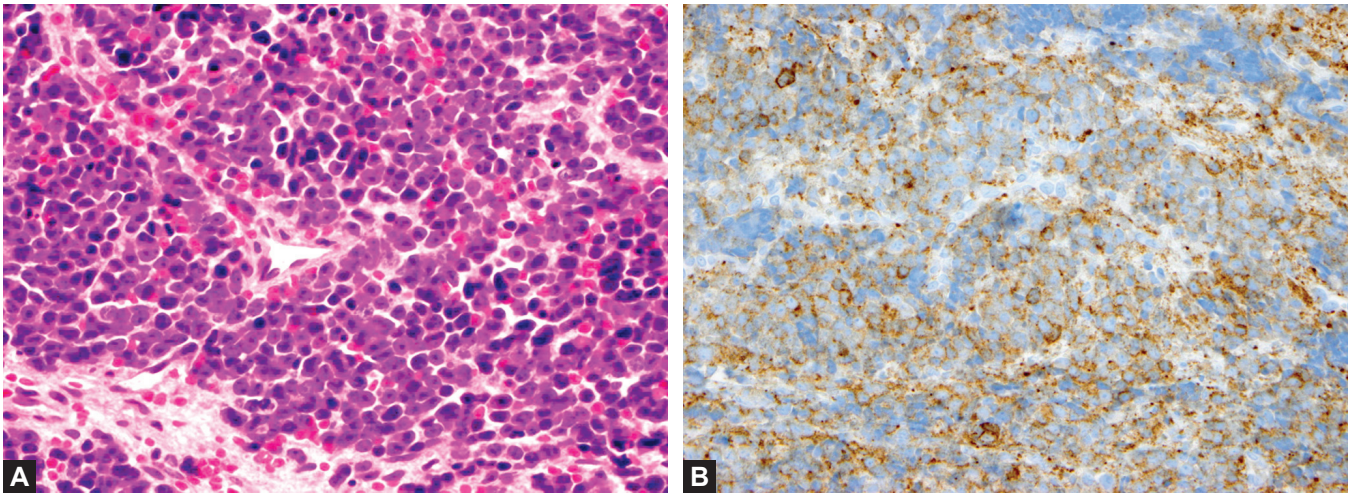
## Neuroblastoma

Neuroblastoma is the third most common pediatric malignancy and is the most common extracranial solid tumor malignancy in children under 5 years of age; 40% of neuroblastoma cases are diagnosed in children < 1 year of age.[188] Neuroblastoma is the most common histological subtype of the neuroblastic tumors, a category which also includes ganglioneuroblastomas and ganglioneuromas (Figs. 57.8A and B). These three histological subtypes represent different developmental stages of the same disease process ranging from the least differentiated (neuroblastoma) to most differentiated (ganglioneuroma).[189] The tumors exhibit a decreasing metastatic potential based on increasing degree of differentiation. The majority of cervical neuroblastoma lesions are metastasic from sites below the diaphragm; additional potential head and neck metastatic sites include the skull, orbit, maxilla, and mandible.[190] Neuroblastomas originate from neural crest cells of the sympathetic chain and as such can manifest a wide variety of symptoms. Findings of ipsilateral ptosis and anisocoria (Horner syndrome) or iridis heterochromia have been described.[191] Respiratory distress and feeding difficulties may occur due to direct tracheal or esophageal compression or may reflect involvement of cranial nerve IX, X, XI, or XII.

Neuroblastomas secrete a measurable increase in catecholamine levels in 70–90% of patients. High catecholamine levels have been correlated with immature histology, large primary tumors, and advanced disease; elevated LDH levels are an additional unfavorable laboratory finding.[192] Further evaluation for metastatic lesions includes bone scan, bone marrow biopsy, and meta-iodobenzylguanidine scintigraphy.[193]

The examination of biopsy specimens by molecular genetic techniques including proto-oncogene N-myc amplification, DNA ploidy, deletion of chromosome 1p, and expression of the TRK gene appears to have prognostic significance, allowing stratification of patients into low-, intermediate-, or high-risk groups.[194–196] Some patients have an inherited predisposition to the development of neuroblastoma, and current investigations are aimed at determining this genetic basis.[197]

The International Neuroblastoma Staging System (Table 57.9) is based on extent of disease and degree of resection. The choice of single-modality or multimodality therapy depends on the risk stratification of the patient. Surgical biopsy is initially necessary to establish the diagnosis and to help stage the disease from a molecular genetics screening standpoint as outlined above. In patients without N-myc amplification, complete tumor excision obviating the need for adjuvant chemotherapy is possible




**Figs. 57.8A and B:** Neuroblastoma histologic findings. (A) Dense population of hyperchromatic cells with scant cytoplasm with hematoxylin and eosin stain; (B) Chromogranin A stain demonstrates positivity consistent with neuroendocrine function.

**Table 57.9:** International neuroblastoma staging system (INSS) classification

| | |
|---|---|
| Stage I | Localized tumor with complete gross excision, with or without microscopic residual disease; representative ipsilateral lymph nodes negative for tumor microscopically (nodes attached to and removed with the primary tumor may be positive) |
| Stage IIA | Localized tumor with incomplete gross excision; representative ipsilateral nonadherent lymph nodes negative for tumor microscopically |
| Stage IIB | Localized tumor with or without complete gross excision, with ipsilateral nonadherent lymph nodes positive for tumor. Enlarged contralateral lymph nodes must be negative microscopically |
| Stage III | Unresectable unilateral tumor infiltrating across the midline, with or without regional lymph node involvement; or localized unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral extension by infiltration (unresectable) or by lymph node involvement |
| Stage IV | Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin and/or other organs (except as defined for stage IV-S) |
| Stage IV-S | Localized primary tumor (as defined for stages I, IIA or IIB), with dissemination limited to skin, liver, and/or bone marrow (limited to infants < 1 year of age) |

Adapted from Brodeur et al.[193]

in approximately 70% of primary cervical neuroblastoma cases. There is evidence in such patients that near complete resection with residual microscopic or even macroscopic disease may not adversely affect survival.[198] However, multiagent chemotherapy is generally indicated in patients after incomplete resection of primary cervical neuroblastoma, patients with metastatic disease to the head and neck from other primary sites, and in patients with resectable disease but positive N-myc amplification.

The prognosis appears to be influenced principally by age, stage and tumor N-myc amplification status.[192,196] Infants fare better than older children; this may simply be due to a greater proportion of favorably staged cases in the younger age group or to a higher incidence of unfavorable molecular characteristics in older children. Primary neuroblastoma of the head and neck has a better prognosis than thoracic and abdominal sites, principally attributable to greater likelihood of complete or near complete resection.[198] Overall 3-year event-free survival rates for INSS stage I, II, and IV-S disease range from 75% to 90%; in infants, rates for stage III and IV disease are 80–90% and 60–75%, respectively; for children older than 1 year, the rates are 50% and 15% for stage III and IV disease, respectively.[191,194]

## OTHER CONSIDERATIONS

The marked success of pediatric head and neck oncologic intervention and the resultant long-term survival of successfully treated children have revealed the potential deleterious aspects of treatment. The survivors of childhood head and neck cancer have a demonstrable increase in growth arrest, hypothyroidism, sterility, and pulmonary fibrosis.[19,33] Those treated in multimodality fashion are particularly at risk for the development of second malignancies involving the lung, gastrointestinal tract, breast, and thyroid, as well as both acute lymphoblastic leukemia and NHL.[18,19,22]

## CONCLUSION

Advances in both diagnostic and therapeutic regimens over the past 30 years have resulted in great strides in the treatment of childhood cervicofacial malignancies. The evolution of classification systems accounting for not only histology but also molecular genetics has redefined treatment algorithms. The coupling of functional imaging modalities such as PET with anatomic imaging has resulted in earlier diagnosis and more accurate staging. Advances in endoscopic surgical and free flap reconstruction techniques have expanded the definition of surgical resectability. Targeted chemotherapy with less toxic dosing regimens, and the increased precision of proton beam radiotherapy, has both significantly decreased the untoward side effects of cancer therapy.

*Disclaimer*: The views expressed in this chapter are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, nor the U.S. Government.

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CHAPTER

58

# Pediatric Thyroid Malignancy

***E Ashlie Darr, Michael J Cunningham, Gregory W Randolph***

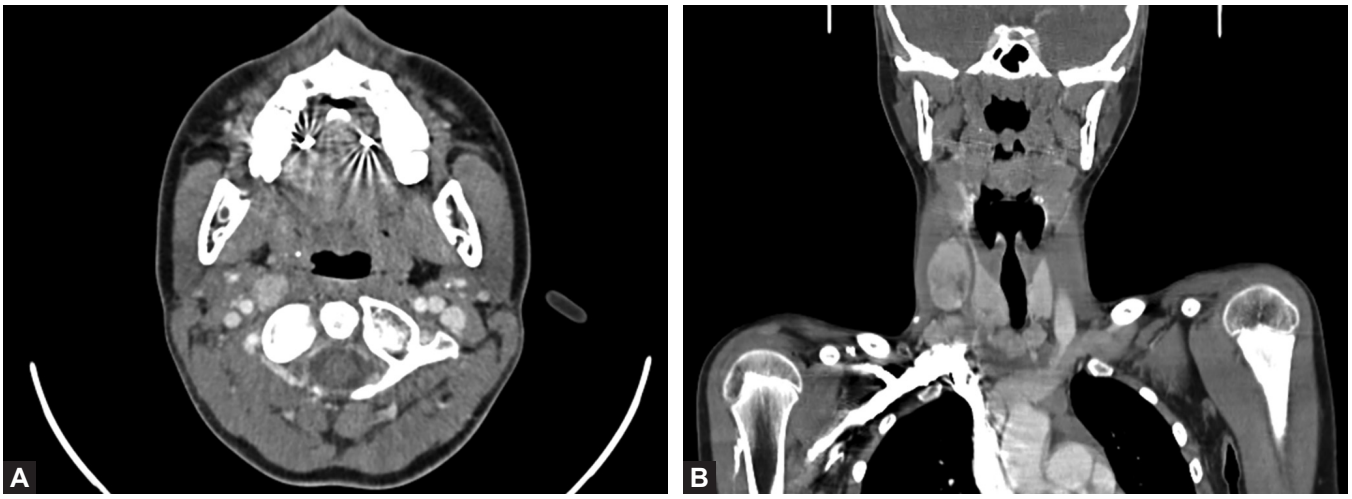
Thyroid carcinoma in children is a rare disease. In the United States, five cases of thyroid cancer are diagnosed in children aged 19 and younger per million per year,[1] and only 5% of all thyroid malignancies occur in children.[2] Thyroid cancer is responsible for 1.5% of all tumors in children <15 years of age and 7% of all childhood head and neck tumors.[3] In a study of 1753 patients aged 18 and younger between 1973 to 2004, the incidence of thyroid carcinoma increased by 1.1% per year, although 2.4% of these patients had been treated previously with radiation.[4] The incidence of thyroid cancer in children appears to increase during puberty, particularly in females. Thyroid carcinoma is diagnosed at comparable rates between male and female children under the age of 15 years; however, the male:female ratio from age 15–20 years increases to 3:1.[5] This suggests a role for female sex hormones in the pathogenesis of thyroid carcinoma, although this role has yet to be defined.

Thyroid nodules are encountered in 0.2–2% of children, compared with 5–35% of adults.[6,7] The risk that a thyroid nodule identified in a child is malignant is significantly higher than that in an adult, with an estimated malignancy rate of 26.4% in children versus only 5% in adults.[8] Solitary nodules in children are malignant in 10–25% of cases compared with only 1–7% of multinodular goiters.[9] Nodules that are identified in children under the age of 10 years have an even higher likelihood of malignancy,[10] and children in this age group are more likely to develop recurrent disease.[11]

The most salient risk factor for thyroid cancer development in children is exposure to radiation. Prior to the 1970s, radiation was used to treat benign conditions such as tonsillar hypertrophy and acne, and most children who developed thyroid cancer in that era had a history of such radiation therapy.[12,13] However, most of our understanding about the influence of radiation exposure on thyroid carcinogenesis was acquired through the aftermath of the Chernobyl disaster in 1986. The average radiation exposure in children in the surrounding area was 2.1–4.7 Gy.[14] In the Gomel region, which was the most contaminated area in Belarus, the incidence of pediatric thyroid cancer increased by 96-fold between the years of 1991 and 1994.[15] The youngest children appear to be most susceptible to radiation-induced thyroid cancer, and the minimal latent period from exposure to cancer development is 4 years[16] with a median time to diagnosis of 13 years.[17] Children treated with radiation have a 20% increased risk of having thyroid nodules by age 20 compared with adults who were not exposed to radiation.[18] It is recommended that children who were treated with radiation therapy to the head, neck, or thorax have serial ultrasounds for the first 5 years after treatment, followed by ultrasonographic and clinical surveillance every 3 years thereafter.[19] Despite the increased incidence of multicentricity of radiation-induced thyroid cancers, recurrence and mortality rates are similar to those of patients who have not been exposed.[20]

Additional risk factors for thyroid carcinoma include autonomous nodules, endemic goiter, Graves' and Hashimoto's disease, Hodgkin's lymphoma, $^{131}$I treatment, and increasingly, the use of chemotherapeutic drugs, such as alkylating agents in the treatment of other childhood malignancies.[21-23]

Thyroid cancer in children typically presents with an asymptomatic, firm neck mass, which may be related to the primary thyroid tumor or lateral neck metastatic




**Figs. 58.1A and B:** Contrast-enhanced computed tomographic scan of a 13-year-old male patient with papillary thyroid cancer with bulky lymphadenopathy.

lymphadenopathy (Figs. 58.1A and B). Signs and symptoms concerning for malignancy include voice changes, swallowing difficulty, a rapid change in size, or fixation of the mass to contiguous structures. Lateral neck nodes are palpable on presentation in about 45–75% of cases and are increased with radiation exposure.[20,24,25] Pulmonary metastatic disease is present upon initial evaluation in 15% of patients and metastasis to bone in 5%.[26] Despite having more aggressive disease, however, the prognosis of thyroid cancer in children is superior to that of similarly staged adults. For instance, cause-specific mortality rates for children with metastatic disease in the lungs were shown to be significantly lower than those of adults >45 years of age.[27]

## PATHOLOGY

Greater than 90% of thyroid carcinomas diagnosed in children are papillary or its follicular variant.[28] Much rarer in childhood are other thyroid cancers, including medullary thyroid carcinoma (MTC) (5%), follicular thyroid carcinoma (3–5%), Hurthle cell tumors (<1%), anaplastic carcinoma (<1%), sarcomas (<1%), and lymphoma (<1%). The histologic appearance of papillary thyroid carcioma (PTC) in children is identical to that of adults, although the tumors more frequently extend extracapsularly (Fig. 58.2). Intraglandular spread via lymphatics leads to multifocality in 30–80%.[29]

Approximately 20–25% of PTCs diagnosed in children are of the follicular variant, which tend to be encapsulated.[30] The diffuse sclerosing variant of PTC, a more aggressive form that tends to infiltrate and enlarge the gland, frequently affects children and young adults.

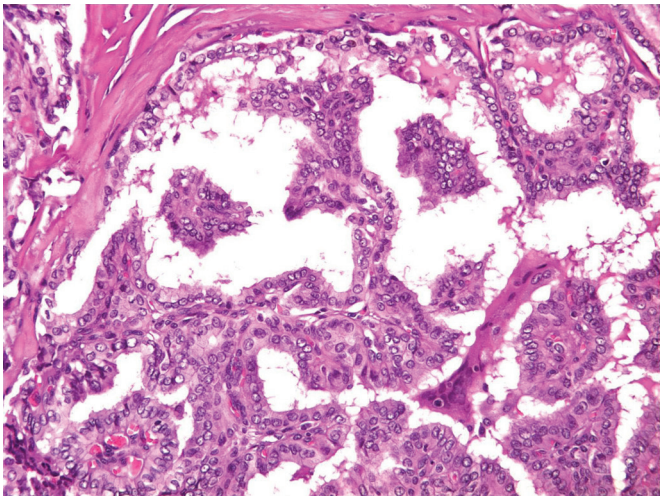


**Fig. 58.2:** Low-power view of classical type papillary thyroid carcinoma.

The diffuse sclerosing subtype is typically associated with increased rates of nodal metastasis and increased recurrence rates.[31] Poorly differentiated (solid), columnar, and tall cell variants are less common forms of PTC affecting children.

Follicular carcinomas are uncommon in children but are increased with radiation exposure.[32] They are well-differentiated tumors that rarely spread to lymph nodes and generally carry low mortality and recurrence rates. Diagnosis of the minimally invasive subtype depends on evidence of capsular or vascular microinvasion, whereas widely invasive tumors are apparent based on gross inspection. The latter are responsible for greater distant metastatic spread.

MTC is derived from calcitonin-secreting parafollicular 'C' cells, which are of neural crest origin. MTC may be found in association with a familial or hereditary syndrome in 25–30% of cases.[33]

# MANAGEMENT

## Diagnostic Evaluation

The workup of a thyroid nodule in the pediatric population is similar to that in adults and should include a thorough history, clinical examination, laboratory evaluation, thyroid and neck ultrasound, and a fine-needle aspiration biopsy (FNAB) when appropriate. An assessment of laboratory values for thyroxine (T4), triiodothyronine (T3), and thyroid-stimulating hormone (TSH) should be performed, which is typically normal.

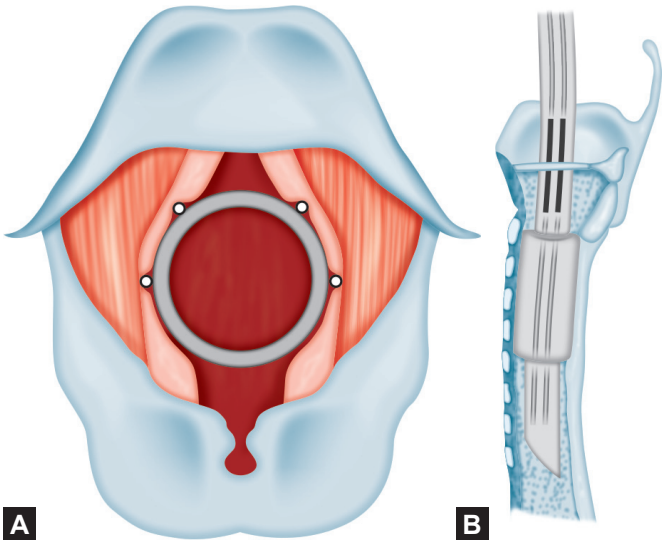
Calcitonin and carcinoembryonic antigen (CEA) levels should be checked in the case of medullary carcinoma. Positive antimicrosomal and antithyroid antibody titers, when present, do not exclude malignancy. A thyroid ultrasound should be obtained, which informs as to the nodular characteristics and the presence or absence of lymphadenopathy. Ultrasound carries the benefits of being noninvasive, with no associated risks of radiation exposure, and is readily obtainable in a cooperative child. A chest X-ray should also be acquired. Consideration may be given to further imaging using magnetic resonance imaging or computed tomography to further characterize the extent of disease, particularly if there is concern based on physical examination or ultrasound for local invasion of the tumor. There is little data regarding the use of positron emission tomography in the evaluation of pediatric thyroid cancer.

Ultrasound-guided FNAB in children carries a 94% sensitivity and 81% specificity rate,[34] with false-negative rates of 2–3%.[35,36] The nondiagnostic FNAB calls for a repeat biopsy or surgical removal. Decision making in this scenario should take into account high-risk data such as the presence of suspicious features on ultrasound, a positive family history, and previous radiation exposure. If the repeat biopsy is again inconclusive, surgery should be performed. Diagnostic lobectomy is advised by some clinicians even with a benign FNAB in light of the high rates of malignancy in the pediatric population, particularly in patients <10 years of age. Alternatively, benign nodules may be surveyed with serial examinations and ultrasounds. Technetium and iodine-123 thyroid scans have fallen out of favor as part of the workup algorithm for thyroid nodules in the absence of a suppressed TSH concentration, as their diagnostic contribution is limited.

## Thyroid-Specific Surgical Management

Recommendations on the surgical management of pediatric cancer are derived from little data due to the rarity of the disease. One of the largest series on PTC in childhood studied the long-term outcomes of 215 patients aged 3–20 years who were treated between 1940 and 2008 and followed over a median period of 29 years.[37] They found that approximately one third of patients developed recurrent disease after complete surgical resection by 40 years, but that only two patients died from their disease. At 30–50 years after surgery the number of deaths was significantly higher than predicted, but notably, 68% (15 of 22) of those deaths were attributable to second primary malignancies. The authors speculate that this increase in second cancers may have been related to postoperative treatments, including radioactive iodine (RAI), external beam radiation, and radium implants.

The goals of surgery for pediatric thyroid cancer are to remove the primary lesion and any associated cervical pathologic nodes in a manner that minimizes morbidity and recurrence rates while allowing for optimal long-term surveillance. Controversy exists as to whether a partial or total thyroidectomy should be performed, with some surgeons citing no improvement in survival rates with complete versus partial surgery despite incurring increased surgical risks. Others assert that total thyroidectomy should be performed due to the increased risk for multifocality with PTC, the improved ability to use thyroglobulin (Tg) levels in surveillance, and the optimization of RAI use. Multifocality of PTC in children is common, which may be related to RET/PTC mutations or intraglandular spread via lymphatics.[38] Several studies have demonstrated increased recurrence rates when partial rather than total thyroidectomy is performed for PTC in children.[39-42] With regard to surgical technique, intraoperative monitoring of the recurrent laryngeal nerve may be used in children as well as in adults (Figs. 58.3A and B).[43] Children with congenital vascular anomalies of the aortic arch, namely, a right aberrant, retroesophageal subclavian artery, should be assumed to have a right nonrecurrent laryngeal nerve (Fig. 58.4). Thyroid hormone supplementation must be administered after total thyroidectomy to maintain a euthyroid state. This promotes maximal suppression of TSH, which drives glandular proliferation.




**Figs. 58.3A and B:** (A) Endoscopic view of monitoring endotracheal tube in correct position. (B) Side cutaway view of the larynx and trachea showing endotracheal tube in place. Cuff is in the subglottis; blackened lines on the side of the tube represent the exposed segment of electrodes that come into contact with the luminal surface of the vocal cord.

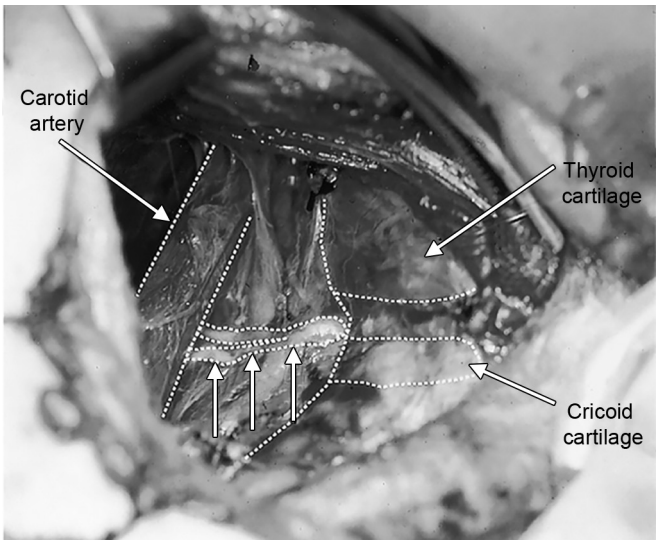



**Fig. 58.4:** Right lateral thyroid bed showing the nonrecurrent right laryngeal nerve. Three small white arrows point to bifid nonrecurrent right RLN emerging from behind the carotid artery (laterally, outlined in white dots) and extending to the larynx. The thyroid and cricoid cartilages and trachea (medially) are outlined in white dots.

The potential for postoperative hypoparathyroidism and hypothyroidism after total thyroidectomy in children creates challenges associated with the need for long-term medication compliance and repetitive laboratory evaluations. Morris et al. reviewed the incidence of postoperative complications in a series of 74 pediatric patients undergoing total thyroidectomy and found rates of temporary and permanent hypoparathyroidism of 30% and 8%, respectively, which doubled the number of laboratory assessments obtained over the first postoperative year.[44] Greater than 40% of these patients had at least one period of thyroid hormone replacement medication noncompliance leading to TSH levels out of the normal range, and this was not related to age at surgery. The reasons for noncompliance included financial issues, patient refusal, forgetting to take the medication or taking it at the wrong time, and family-related problems (e.g. dual households). Three patients abandoned the use of thyroid hormone at the age of 18 years due to insurance-related issues.

Papillary microcarcinomas (<1 cm) may be treated with hemithyroidectomy with isthmusectomy as long as there is no family history of thyroid cancer, no history of radiation, the opposite lobe is anodular, and there is no local or distant metastasis.[29] Follicular carcinomas <2 cm may be treated similarly as long as extracapsular invasion is minimal, as these are associated with very low recurrence rates. Follicular carcinoma is staged and treated similarly to papillary carcinoma and is sensitive to thyroid hormone suppressive therapy as well as RAI. Follicular lesions diagnosed by fine-needle aspiration warrant lobectomy. Frozen section may be performed intraoperatively to aid decision making as to the opposite lobe, although this is often nondiagnostic. In the event of an indeterminate diagnosis, final pathology must be awaited and a completion thyroidectomy is performed if indicated.

Postoperative follow-up should include annual physical examination, assessment of Tg serum levels and periodic neck imaging by ultrasound or $^{131}$I. A multidisciplinary approach to include the child's endocrinologist and pediatrician in addition to the surgeon is advised.

## Lymph Node Dissection

Elective lymph node dissection without evidence of regional nodal metastasis by clinical examination or ultrasound is not warranted.[45,46] Radical neck dissection in a child with PTC is also never required, as it only increases surgical morbidity without affecting mortality or recurrence rates.[32] When a central compartment dissection is undertaken, prelaryngeal (Delphian) nodes, pretracheal nodes, nodes along the recurrent laryngeal nerve (RLN), and nodes in the paratracheal region should be carefully assessed and removed, taking care to preserve

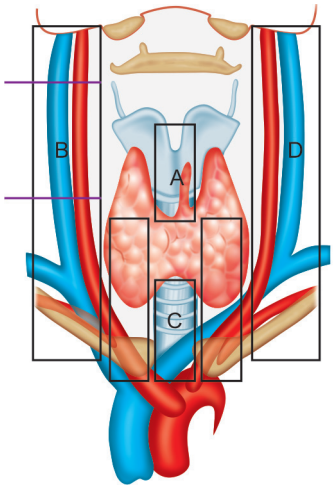



**Fig. 58.5:** The four major nodal-bearing areas within the central neck include the prelaryngeal (Delphian) (A), pretracheal (C), and bilateral paratracheal (B and D) regions.

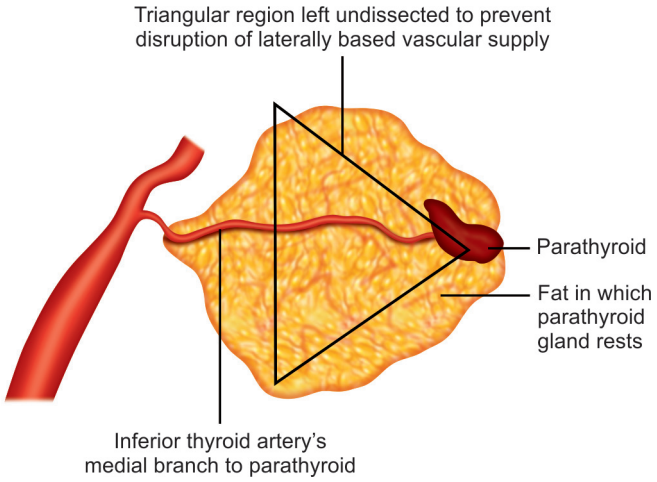



**Fig. 58.6:** Preserving parathyroid gland vascular supply. If the parathyroid has not been dissected from adjacent fat and if a triangular region is left undissected lateral to the parathyroid to prevent disrupting the laterally based vascular supply, then the parathyroid should be judged well vascularized.

the viability of parathyroid glandular tissue and the RLN (Fig. 58.5). The parathyroid glands in children contain less stromal fat than those of adults and thus differ in appearance. They are gray and translucent in infancy and become more reddish brown during adolescence. Great care must be taken to ensure preservation of the small parathyroid gland's delicate blood supply (Fig. 58.6). When a parathyroid gland is deemed to be devascularized, it should be morselized and autotransplanted into the sternocleidomastoid muscle as per standard techniques. Persistent lymphadenopathy after neck dissection may respond to RAI, but responsiveness to RAI may decline over time.[29]

## Radioactive Iodine Therapy

Radioactive iodine ablation using iodine 131 ($^{131}$I) is frequently employed in children after thyroidectomy. The aim of treatment is to obliterate any remaining normal thyroid remnant and any possible metastatic lymphadenopathy that has not been surgically treated. Optimal treatments lead to achievement of a negative whole body scan, low or negative Tg serum levels, and a negative ultrasound for optimal monitoring for disease recurrence. In addition, future metastatic lymphadenopathy that may develop may not be adequately treated with RAI when a thyroid remnant remains.[28] When RAI is administered, it should be done 6 weeks after surgery, preceded by a period of induced hypothyroidism. Children are placed on a low-iodine diet and L-triiodothyronine for 4 weeks, which is then withdrawn for 2 weeks with the aim of achieving a TSH level of >25 μU/mL. A diagnostic whole body scan is obtained one day before treatment. The dose required for ablation is related to the size of the remaining thyroid remnant.[47]

Children are thought to be significantly more vulnerable to the effects of radiation than adults[48] and thus are more susceptible to the development of second primary malignancies, predominantly leukemia, over their lifetimes. Other side effects of RAI include the development of pulmonary fibrosis in the presence of lung metastases, sialadenitis, nausea, vomiting, transient bone marrow suppression, and reversible damage to spermatogenesis.[49-51] The use of RAI in the treatment of pediatric thyroid cancer has been historically common; however, recent studies have observed no improvement in long-term recurrence rates when RAI is used versus surgery alone.[37]

# MEDULLARY THYROID CARCINOMA

Medullary thyroid carcinoma is responsible for approximately 10% of cases of pediatric thyroid cancer.[52] In addition to its sporadic form, MTC can be found in association with multiple endocrine neoplasia (MEN) syndromes 2A and 2B, as well as in familial MTC. One third of all cases of MTC are derived from hereditary disorders, which are associated with an autosomal dominant inheritance pattern. The sporadic form, however, typically presents

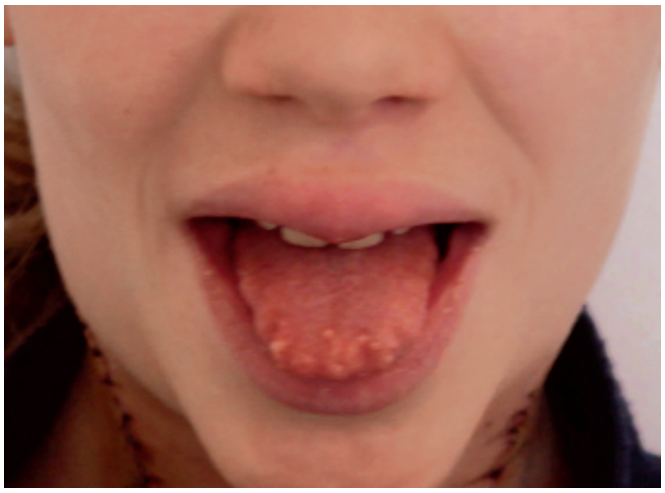


**Fig. 58.7:** Lip and tongue neuromas associated with multiple endocrine neoplasia 2B in a 12-year-old girl.

after age 30 and thus is uncommon in children.[53] Diagnosis is made most commonly as a result of screening in children with family members with MEN syndrome. MEN 2B is associated with oral stigmata that may elicit further diagnostic workup (Fig. 58.7). Serum calcitonin levels are sensitive markers of disease and can be used to monitor postoperatively for recurrence.

Gain-of-function mutations in the RET proto-oncogene, a tyrosine kinase receptor protein that is involved in cell signaling, lead to the development of MEN 2, whereas loss-of-function mutations lead to Hirschsprung's disease. RET genetic analysis is used in children with MEN 2 to predict the risk of acquiring MTC. All patients with a confirmed RET germline mutation should be treated with prophylactic thyroidectomy, even in the presence of normal calcitonin levels. This is due to the nearly 100% penetrance of MTC in MEN 2 syndrome.[52,54] The American Thyroid Association has established recommendations regarding the timing of surgery, which relate to the specific mutation found in the RET gene.[55] Codons C634 in MEN 2A and M918T in MEN 2B lead to more aggressive disease, thus prophylactic thyroidectomy as early as 12 months of age should be performed. For mutations associated with moderate risk, surgery should be performed before the age of 5 years, and for mild risk, surgery may be delayed until after 5 years.[55] MTC associated with MEN 2B syndrome as compared with MEN 2A is typically more aggressive and carries a worse prognosis. Nodal metastatic disease is common at the time of diagnosis of MEN 2B, and disease is often advanced at presentation.

Lymph node dissection is indicated with elevated calcitonin levels, invasive disease or imaging or clinical evidence of pathologic nodes. Prophylactic central neck dissection is considered in the presence of high risk mutations. Some surgeons advocate the use of intraoperative frozen section of nodes sampled for micrometastasis to guide the decision as to whether or not to perform a lateral neck dissection in the absence of clinically apparent disease. Preoperative laboratory assessment should include serum calcitonin, CEA, and calcium levels in addition to RET proto-oncogene analysis. Children with MEN 2B must be screened for pheochromocytoma by means of plasma or urine metanephrine assessment or high-resolution adrenal imaging. If a pheochromocytoma is detected, pharmacologic blockade and adrenalectomy are required prior to thyroid surgery.

## THYROGLOSSAL DUCT CYST CARCINOMA

The incidence of carcinoma arising in a thyroglossal duct cyst is 1%, and the median age at presentation is 40.[56] Less than 40 cases of thyroglossal duct cyst carcinoma (TGDCC) in patients aged 20 and younger have been reported in the literature. The majority of TGDCC lesions are classical papillary carcinomas, with follicular, mixed papillary–follicular, and squamous cell carcinomas much less common.[57-60] TGDCC is typically not suspected preoperatively, but is found only on final pathologic analysis after surgical excision. In the event of a preoperative FNAB diagnosis of PTC, en bloc resection of the cyst via the Sistrunk procedure is recommended. The need for thyroidectomy in this setting is controversial. If the focus of carcinoma is microscopic, with no evidence of cyst wall invasion without thyroid nodules or lymphadenopathy on ultrasound, further surgery may be avoided. A review of 21 cases of TGDCC in children showed a mean age-of-onset of 12 years for males and 13 years for females, capsular invasion in 10/21 (45%), and local invasive disease in 5/21 (23%).[61] Despite these features, in the 12 patients in whom thyroidectomy was performed, none revealed carcinoma in the gland.

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CHAPTER

# Adjuvant Therapy for Pediatric Head and Neck Malignancies

59

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## INTRODUCTION

Combined modality therapy is essential in the management of most of the common pediatric malignancies involving the head and neck region, and for nearly all of the high-grade malignancies. Most of the centers that treat childhood cancer in the United States are part of the Children's Oncology Group (COG), an organization supported by the National Cancer Institute that is dedicated to improving the outcomes of childhood cancer through cooperative clinical research trials. Through this group and through other organized, similar groups internationally, great strides have been made over the past three to four decades in childhood cancer treatment and outcomes. Given the complexity and the relative rarity of all pediatric malignancies, we would advocate for a multidisciplinary team approach to treatment at a specialized childhood cancer center and for participation in a clinical research trial whenever possible. There are usually active clinical trials ongoing for the more common pediatric head and neck malignancies, including the sarcomas, lymphomas, neuroblastoma, and nasopharyngeal carcinoma. Many of these trials also include pathologic review and biology studies, with a goal of gaining further knowledge into the cellular and molecular abnormalities that will guide the development of new treatment approaches.

## SOFT TISSUE SARCOMAS

Soft tissue sarcomas in childhood are generally divided into rhabdomyosarcoma (RMS) and nonrhabdomyosarcoma soft tissue sarcomas (NRSTS). As a group, they comprise about 6% of all childhood cancer, with half of those being RMS, and the other half a very heterogeneous collection of tumor histologies. We will separate the discussion into RMS and NRSTS as the role of chemotherapy and radiotherapy are somewhat different.

### Rhabdomyosarcoma

RMS represents the most common pediatric soft tissue sarcoma, with approximately 350 new cases per year within the United States.[1] The majority of these tumors arise in the head and neck (35%), and most are not readily resectable.[2] Within the head and neck, RMS is categorized into three groups: parameningeal (16%), nonparameningeal (10%), and orbital (9%). For treatment, RMS patients further are stratified into low, intermediate and high-risk groups based on site of origin, size, histology, lymph node involvement, metastatic spread, and extent of surgical resection.[3] Chemotherapy is the cornerstone of treatment for all RMS, including those of the head and neck, with local control consisting of radiation therapy, surgery (much less commonly), or a combination of surgery and radiation. The Intergroup Rhabdomyosarcoma Study Group (IRSG) was for many years the major North American-based cooperative group defining optimal treatment of RMS, until the COG formed through the merger of several cooperative groups, including the IRSG. This collaborative group approach has resulted in a steady improvement in long-term survival rate, with the most recent trials achieving 5-year survival rates of 70% for patients with nonmetastatic disease and of 39% for patients with metastatic disease. Relapses are uncommon after 5 years of disease-free survival.

The combination of vincristine, actinomycin-D, and cyclophosphamide has evolved as the gold standard chemotherapy regimen for most patients, though novel treatments are clearly needed for high-risk patients with metastatic disease whose outcome remains relatively poor. The duration of treatment ranges from 6 to 12 months, with a general approach of an initial 3 months of neoadjuvant chemotherapy, local control (usually in the form of radiation treatment that is given concurrently with chemotherapy), and then additional chemotherapy following local control. For patients with RMS of the head and neck region, it is unusual to be able to completely resect disease without significant morbidity at the time of diagnosis if in the parameningeal or orbital region, but in other head and neck sites, up front resection at the time of diagnosis or later may be possible. Therefore, radiation treatment is typically needed. The rare exception is in the case of a tumor with embryonal histology that is able to be completely resected with negative margins at the time of diagnosis. All patients with alveolar histology require radiation therapy regardless of the extent of resection. Therefore, the general surgical approach is to perform an initial biopsy for the purposes of establishing a tissue diagnosis, and only to perform a resection if this is felt to be likely to achieve at least a gross total resection without major compromise of cosmetic appearance or function.

Patients who have had an initial gross total resection with positive margins are treated with 36 Gy, those with resected positive nodes receive 41.4 Gy to the nodal bed and those with gross residual disease typically receive 50.4 Gy. Patients with a delayed primary resection receive RT regardless of surgical margin status and dose depends on margin status, nodal status and whether gross disease remains. The current dose for orbital tumors, which have a favorable prognosis, is 45–50.4 Gy.

Parameningeal patients make up the most common head and neck subsite, representing roughly 50% of all head and neck RMS.[4] Parameningeal tumors are classified as an unfavorable site and have a poorer prognosis than other head and neck sites. From a subgroup analysis of the IRS trials (II–IV), Michalski et al. found a 5-year overall survival (OS) and event-free survival (EFS) of 73% and 69%, respectively.[4] Due to location and the propensity for diffuse infiltration into soft tissue and bone, a biopsy alone is typically performed and local control relies heavily on radiation and chemotherapy. The parameningeal tumors are those around the base of skull that abut the meninges and have the potential to invade into the central nervous system, and include tumors in the middle ear/mastoid, nasopharynx/nasal cavity, parapharyngeal space, paranasal sinuses (ethmoid, maxillary, sphenoid), and the pterygopalatine/infratemporal fossa region.

While the timing of radiotherapy for parameningeal tumors has changed with the different cooperative group protocols, from immediate, to week 4 or week 12, it appears that timing of RT on reanalysis does not affect outcome (Spalding, IJROBP, 2013) and the next cooperative group study will likely put radiation at week 12 to allow for a response to induction chemotherapy and a shrinking radiation field technique. Radiation is delivered concurrently with vincristine and cyclophosphamide, but actinomycin is omitted due to radiosensitization, which can dramatically increase acute side effects such as mucositis and dermatitis and lead to an interruption in radiation treatment. The vast majority of these tumors (> 95%) are group III and therefore a radiation dose of 50.4 Gy is given, although European protocols give 55.8 Gy in patients with a poor response to chemotherapy. The treatment volume includes the prechemotherapy and extent of the tumor (based on pretreatment CT, MRI, and PET) plus a small margin, typically a centimeter, to account for microscopic tumor extension that is too small to be seen with imaging.

Lymph node involvement at presentation is relatively rare, ranging from 10% to 20% in most modern series, and nodal failure is also uncommon.[1–4] Therefore, regional lymph node beds are not typically irradiated unless clinically or pathologically involved lymph nodes are present. Grossly involved lymph nodes are treated to 50.4 Gy and resected nodes are treated to 41.4 Gy to the resection bed and involved lymph node region. Despite adequate tumor coverage, the majority of parameningeal tumors fail locally within the radiation field. Again from reports of IRS II–IV, the parameningeal patients had a local failure 13% and a distant failure rate of 8%.[4] On multivariate analysis, predictors of failure from the IRS series included age > 9 years, paranasal sinus or pterygopalatine fossa location, or cranial nerve palsy, cranial base erosion, or intracranial extension.

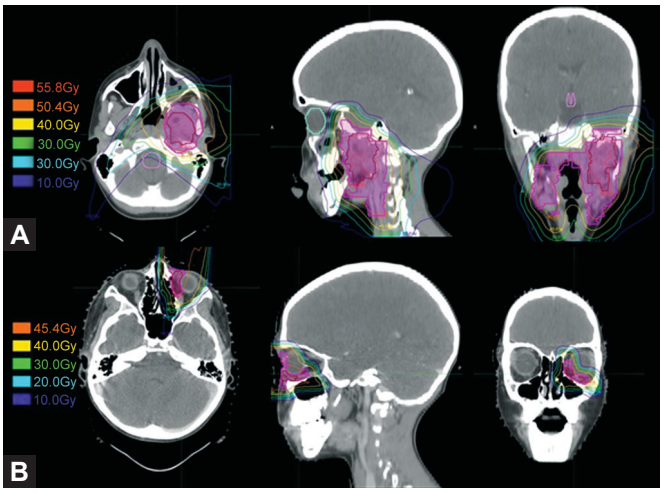
In contrast to the parameningeal sites, nonparameningeal head and neck tumors are classified as a favorable location, likely attributable to the increased resectability and predominance of embryonal histology in these sites. Sites of origin include the larynx, oropharynx, oral cavity, neck, parotid, and scalp and make up approximately

10% of all RMS cases. Prognosis is somewhat better in these tumors with a 5-year OS and EFS of 83% and 76% in IRS III–IV.[2] A slightly higher risk of lymph node involvement is seen, on the order of 20%. With a more surgically accessible origin, the majority of these tumors (63%) are classified as group I or II and radiation can be omitted in cases of complete resection with an embryonal histology (stage I, group I). All others receive radiation using the same techniques and doses as for their parameningeal counterparts but with radiation starting later in treatment at week 13. Like parameningeal tumors, failure is typically local and from IRS III and IV the 15-year cumulative incidence of tumor recurrence was local in 19%, regional in 5%, and distant in 9% of the patients.[6]

Primary tumors of the orbit characteristically do not extend to the adjacent meninges and are classified separately (although rarely in advanced cases, meningeal involvement can occur via bony erosion of the superior orbital fissure). Unlike their head and neck counterparts, orbital primaries have a very favorable prognosis and 5 year OS and EFS of 96% and 86% from the recent Intergroup D9602 study.[3] While most are embryonal in histology (> 80%), alveolar primaries are not infrequent and survival drops to 74% in these patients.[4] Orbital exenteration generally represents the only option for an oncologic complete resection and with the excellent disease control rates seen with radiation and chemotherapy alone, surgery is generally reserved for relapsed disease. Further, within the orbit, radiation dose does not change regardless of whether gross tumor or microscopic residual is left behind, and therefore surgical debulking is typically discouraged. Thus, most orbital tumors are stage 1 group III and are treated with doses between 45 and 50.4 Gy.

An example of a proton radiotherapy treatment plan for an orbital and parameningeal radiation plan is given in Figures 59.1A and B.

Local control is excellent in these tumors, and therefore a reduction in treatment intensity has been explored. An international workshop attempted to use chemotherapy alone in the treatment of orbital RMS but found that local failure was 44% compared to 8% in patients who received radiation.[5,6] The IRS has also attempted de-escalation of therapy with mixed results. Local control in IRS III was 84% at 5 years with VA chemotherapy and 45–50.4 Gy of radiation. This increased to 96% in IRS IV with the addition of cyclophosphamide and increased radiation doses to 50.4–59.4 Gy. In an effort to reduce toxicity, the subsequent




**Figs. 59.1A and B:** Proton plans for (A) a patient with node positive left infratemporal fossa embryonal parameningeal rhabdomyosarcoma (RMS) and (B) a patient with a near total resection of a left embryonal orbital RMS.

Intergroup D9602 trial reduced the radiation dose to 45 Gy and omitted cyclophosphamide, but local control dropped to 86%. Currently, the COG ARST 0331 has used the 45 Gy radiation dose, but added back cyclophosphamide at a lower dose. Therefore, the optimum combination of chemotherapy and radiation dose is yet to be determined. Loco-regional or distant failure is very uncommon in orbital tumors and most failures occur within the primary tumor volume. In the case of relapse, surgical salvage with orbital exenteration followed by chemotherapy is often curative with salvage rates of 75–82%, but with significant morbidity and disfigurement.[6,7]

For all three RMS sites in the head and neck, tumors arise in close proximity to critical structures in developing children, and toxicity from radiation can be significant. From the existing long-term photon studies, late toxicity for head and neck patients commonly includes hearing loss (17–20%), learning disabilities (10–49%), facial/orbital hypoplasia (34–36%), visual problems (17–30%), decreased height velocity due to hypothalamic and pituitary dysfunction (30–61%), and poor dentition or delayed eruption (23–29%).[8,9] Orbital patients frequently develop cataracts and mild to moderate facial hypoplasia from radiation. Dry eye, keratoconjuntivitis, and corneal abrasions are also seen and, less frequently, retinopathy and vision loss can occur. Rates of late toxicity with conventional radiation in orbital tumors were extremely high in the early IRS trials where large radiation volumes were

delivered.[10] With the adoption of intensity-modulated radiation therapy (IMRT), arc therapy, brachytherapy and proton therapy for these tumors, late toxicity appears to be much improved in single institution studies and mature data from the large trials is accruing.[8,11,12]

### Nonrhabdomyosarcoma Soft Tissue Sarcomas

NRSTS comprise about 3% of childhood malignancies and affect approximately 500 children under the age of 20 years in the United States each year.[6] The estimated 5-year survival of children and adolescents with nonmetastatic NRSTS is roughly 80%.[13,14] The heterogeneity and relative rarity of this group of tumors has made it very challenging to conduct prospective clinical trials, though there are currently efforts underway through COG to develop a systematic approach. The chance of cure is largely affected by surgical resectability, as children with grossly resected nonmetastatic tumors have a 5-year estimated survival of 89%, compared with 56% for initially unresected tumors.[15]

Radiation as an adjuvant is typically given to unresectable tumors, high-grade tumors <5 cm with involved surgical margins, or high-grade tumors >5 cm regardless of margin status, and can be used preoperatively with chemotherapy for delayed surgery in initially unresected disease. The doses of radiation used in the recently closed COG study for nonrhabdomyosarcomas ARST 0332 ranged from 45 Gy preoperatively to 55.8 Gy for microscopic residual and 64.8 Gy for gross disease. Anthracycline based chemotherapy can be given for large, high-grade tumors or metastatic disease. A pooled analysis of the European and US experience with pediatric NRSTS from 1980 to 2005 demonstrated a significant survival advantage to adjuvant radiation after incomplete resection.[16] In the study published by Ferrari et al., the 5-year OS was 35% for those that did not receive radiation compared to 69% for those that did receive radiation, and this significance was retained on multivariate analysis.

The role of chemotherapy for other NRSTS of the head and neck region in children is less well defined. Collaborations with medical oncologists with expertise in the management of sarcoma in the adult population may be fruitful in this respect, and much of the approach in pediatric patients has been modeled after the approach to adult patients given the lack of pediatric-specific data. Some histologies, such as synovial sarcoma are responsive to chemotherapy, with ifosfamide and doxorubicin considered to be the most standard chemotherapy regimen used in North America. Local control in the form of surgery and/or radiation treatment is the cornerstone of treatment for NRSTS, and again we would advocate for a multidisciplinary approach at an academic center with pediatric expertise.

## NASOPHARYNGEAL CARCINOMA

Nasopharyngeal carcinoma is relatively rare in childhood, representing < 1% of all childhood cancer. However, it accounts for about one-third of all cancers of the upper airway in children.[17,18] OS has improved steadily over the past four decades, with current 5-year survival rates above 80% with multimodality therapy.[19] The role of surgery of the primary tumor is generally limited to biopsy for tissue diagnosis, although there may be some role for surgery in the treatment of recurrent or resistant neck disease. Historically, the mainstay of treatment was high-dose radiation therapy to both the primary tumor and the neck, as the incidence of regional nodal disease in the neck is very high. However, studies have shown that the most effective therapy is combined-modality treatment using both chemotherapy and radiation.[20]

Nasopharyngeal carcinoma is a very chemosensitive tumor, and trials in children using methotrexate, cisplatin, 5-fluorouracil (5-FU), and interferon-beta have shown response rates over 90%.[21-24] The addition of chemotherapy prior to and during radiation has been found to reduce both locoregional and distant recurrences, though it does contribute to short- and long-term toxicities of treatment. A standard approach in the United States has been to administer neoadjuvant (preirradiation) chemotherapy with 5-FU and cisplatin, and then cisplatin concurrently with radiation treatment.

With escalation of radiation dose made possible by the widespread adoption of conformal radiation therapy, long-term survival of patients with nasopharyngeal carcinoma has improved significantly over the past four decades,[19] but there is still no consensus on the most appropriate radiation dose. While local control can be achieved with some success with lower doses of radiation, most modern series support the use of doses ranging from 60 to 72 Gy for gross disease and 45 to 54 Gy for at-risk nodal volumes.[17,20,25–27] At these doses, loco-regional control is 88–93%.[20,28] In very young patients, typically < 10 years old, some centers decrease the radiation dose by 5–10% to attempt to reduce treatment related toxicity.[29]

More than 90% of pediatric nasopharyngeal carcinoma cases present with locally advanced disease and lymph node involvement and therefore radiation fields are typically large. The primary target volume includes the gross disease plus a 1–2 cm margin and any involved nodal disease, and these volumes receive full radiation dose. Coverage for direct extension of microscopic disease includes the entire nasopharynx, posterior one-third of the nasal cavity and maxillary sinus, inferior one-third of the sphenoid sinus, bilateral pterygopalatine fossae and parapharyngeal space, and the anterior one-half to two-thirds of the clivus, foramen rotundum, foramen ovale, and foramen lacerum. For T3 or T4 disease, the entire sphenoid sinus and cavernous sinus are included. A dose of 60 Gy is typically given for areas at risk for microscopic disease. At-risk nodal volumes are always treated bilaterally and 45–54 Gy is typically given for subclinical lymph node spread. In node negative patients, the retropharyngeal nodes as well as levels II–IV are included in the radiation coverage. In node positive patients, level IB, level V, and the supraclavicular nodes are also covered.

Classically, large laterally opposed fields were used to treat nasopharyngeal patients with very little tissue sparing in the oropharynx, oral cavity, larynx, and neck. Subsequently, nearly all children treated in the era developed late effects such as xerostomia (45–100%), dental carries (15–30%), neck fibrosis and atrophy (10–64%), trismus and swallowing problems, osteoradionecrosis (5%), and pituitary dysfunction (73%).[20,27–29] With the widespread adoption of IMRT and the increasing availability of proton therapy, late effects have decreased significantly for these patients.[20] Still, a significant portion of patients will develop late toxicity and therefore pretreatment evaluation with baseline endocrine, audiology, and dental evaluations are recommended for all patients and long-term follow-up in a multidisciplinary oncology clinic is needed.

## ESTHESIONEUROBLASTOMA

Esthesioneuroblastoma, also referred to as olfactory neuroblastoma, is a rare tumor that arises from neural crest in the olfactory epithelium of the superior nasal cavity, near the cribriform plate. Despite its rarity, it is the most common cancer of the nasal cavity in pediatric patients, accounting for 28% of all cases.[13] Most patients present with advanced disease, with extension into the paranasal sinuses or beyond. Bony destruction and intracranial extension of tumor are common. Cervical lymph node metastases are present in 5% of cases, and their presence is a significant adverse prognostic feature.[14]

Surgery and radiation have been the mainstays of treatment, with the addition of radiotherapy decreasing the risk of local recurrence. Definitive radiation alone has typically yielded lower rates of disease control than surgery alone. A meta-analysis by Duguerov et al. of 386 patients from 37 trial between 1990 and 2000, showed the 5-year OS to be 37% for RT alone, 48% for surgery alone, and 65% for surgery and radiation combined.[14] More recently, a second meta-analysis including all published esthesioneuroblastoma series meeting criteria found no benefit to combined therapy, with a 5-year OS of 52% for radiation alone, 78% for surgery alone, and 73% for surgery and radiation.[15] This issue is complicated by the fact that patients are often referred for radiation only when margins are involved or the margin status is not clear. Therefore, direct comparison by Kadish stage without analysis of margins, histology and disease extension, as done in the meta-analysis, may obscure the benefit of radiation. Further, in a review of the University College London experience with esthesioneuroblastoma, all 42 patients were treated with craniofacial resection and 24 of these patients received radiation. The authors found that local recurrence was 28% for surgery alone and 4% for radiation and surgery combined, despite the use of an open procedure and the fact that those receiving radiation had more extensive disease at presentation.[16] At present, adjuvant radiation is strongly recommended for lymph node involvement, locally advanced tumors, and tumors where a wide local excision is not achieved.

When discussing the timing of radiation, there again is no consensus on the optimal sequence of treatment. At present, there are no convincing data demonstrating a benefit to preoperative over postoperative radiation, yet experience in other disease sites allows for recommendations to be made. In cases of large, locally advanced tumors where widely clear margins will not be possible, preoperative radiation is generally preferred, although it is used by many centers in all esthesioneuroblastoma cases.[30,31] Preoperative radiation has several advantages including more accurate target volume delineation as the gross tumor can be identified and targeted, reduced treatment volumes and normal structure sparing since sites at risk for surgical contamination are not present, and a lower total radiation dose from the absence of postsurgical bed hypoxia. Postoperative radiation is most useful in patients where a gross total resection with widely clear margins was attempted but not achieved.

Radiation dose for esthesioneuroblastoma ranges from 55 to 60 Gy for gross disease and 50 Gy for microscopic disease. Radiation dose can be reduced slightly in the

setting of neoadjuvant or concurrent chemotherapy. Elective coverage of the neck in N0 patients is typically not done unless there is high clinical suspicion, as the risk of occult nodal metastases is low.[14] In N+ patients, coverage of the involved nodal disease ( or nodal bed if given postoperatively) plus the adjacent at risk lymph node levels is done, with no coverage of the contralateral neck unless there is extensive unilateral disease or retropharyngeal nodal involvement. Radiation dose to the neck is typically 50 Gy, the dose for microscopic disease.

The role of chemotherapy is less clear, though reports of the use of neoadjuvant or adjuvant chemotherapy in advanced stage disease are promising, with some experts recommending the addition of chemotherapy for patients with Kadish group C disease and higher grade tumors, particularly those with unresectable disease at diagnosis.[32,33] There are no randomized trials but retrospective studies of small numbers of patients suggest a benefit of including all three treatment modalities (surgery, radiation, and chemotherapy) in high-risk patients.

## OSTEOSARCOMA

Osteosarcoma is a malignant neoplasm of bone that accounts for 2.4% of all childhood cancer.[34] It most commonly occurs in adolescents and young adults at the ends of long bones, in the extremities. However, it can occur in the axial skeleton, and about 8% are in the craniofacial region, including the skull and the jaw. Interestingly, patients with mandibular and maxillary lesions have a significantly better prognosis than patients with extragnathic, craniofacial tumors[35] and patients with craniofacial tumors fare better with surgery alone than patients with tumors in the appendicular skeleton. There appears to be a lower incidence of distant metastases with craniofacial osteosarcoma, perhaps due to generally lower grade histology within these lesions. Complete surgical resection with negative margins is a critical component of successful therapy of craniofacial osteosarcoma.[36,37] The role of chemotherapy for craniofacial osteosarcoma is less clear than it is for osteosarcoma in other sites, though meta-analyses and a retrospective analysis suggest a benefit from the addition of chemotherapy for high-grade tumors.[38] Cisplatin, doxorubicin, and methotrexate are the most commonly used chemotherapy agents, and a typical approach is administration of neoadjuvant chemotherapy over 10–12 weeks, followed by surgery, and then additional chemotherapy. Radiation treatment can play a role if there is a questionable or positive margin.

Traditionally, osteosarcoma has been viewed as a radioresistant tumor[39] and radiation has been used most successfully in the adjuvant and palliative setting.[40] A role for postoperative radiation in osteosarcoma of the head and neck, where gross total resection is frequently unattainable, was demonstrated by Guadagnolo et al. in their review of 119 adult and pediatric patients treated at MD Anderson Cancer Center (MDACC) with photon RT.[41] In the study, 92 (77%) patients underwent surgery alone, and 27 (23%) were treated with surgery and radiation (mean dose = 60 Gy). Compared to surgery alone, RT improved 5-year OS (80% vs. 31%), DSS (80% vs. 35%), and LC (75% vs. 24%) for patients with positive or uncertain resection margins. Despite improvements with adjuvant RT, local control still remains a significant problem and survival after local failure is typically as poor as with metastatic disease. Therefore, there exists great interest in using modalities such as charged particle therapy (i.e. proton or carbon ion radiotherapy) to escalate dose to residual tumor and/or resection bed.

The largest experience with protons and osteosarcoma comes from a retrospective series of 55 patients treated at Massachusetts General Hospital (MGH) between 1983 and 2009 with proton therapy or mixed photon–proton radiotherapy.[42] This cohort included pediatric and adult patients with a median age of 29 years (range, 2–76 years) with osteosarcoma of the pelvis, spine, ribs, skull, and facial bones. Most patients had positive surgical margins (49.1%) following surgery and the remainder had biopsy only or minor a resection with residual gross tumor. Radiation dose ranged from 50.4 to 80 Gy; 40% patients received a dose between 60 and 70 Gy and 50.1% received a total dose of ≥70 Gy. Preoperative RT was used in 13% of cases with a dose of 19.8 Gy. MGH often utilizes a low dose preoperative regimen with the goal of reducing intraoperative tumor seeding while protecting postoperative wound healing. All patients received neoadjuvant anthracycline-based chemotherapy.

Clinical outcomes were excellent with 3- and 5-year local control rates of 82% and 72%, respectively. Of those that recurred locally, 67% were tumors arising from bones of the skull and on multivariate analysis, skull primaries were associated with a hazard ratio of 2.6. At 5 years, DFS was 65% and OS rate was 67%. Further, a dosimetric analysis done by the authors showed that as doses reached 70 Gy or higher, the benefit of surgical resection prior to RT lost significance. With limited data available, the careful weighing of potential surgical morbidity against the potential late effects of high-dose RT should be done before treatment decisions are made.

## EWING SARCOMA

Ewing sarcoma is the second most common primary bone tumor of childhood, after osteosarcoma, comprising 1.4% of childhood cancer.[34] The cell of origin is a primordial-bone marrow derived mesenchymal stem cell. Ewing sarcoma can occur in any bony site, or with a primary site in the soft tissue (in which case, it is sometimes referred to as primitive neuroectodermal tumor, or PNET). Two percent of bony tumors arise in the skull, while 18% of extraosseous tumors arise in sites in the head and neck.[43] The prognosis for tumors that arise from the head and neck appears to be slightly improved compared to other sites.[44] Ewing sarcoma is treated with both multiagent chemotherapy and either surgery or radiation for the primary site. In contrast to osteosarcoma, Ewing sarcoma is more sensitive to radiation and thus surgery to resect the tumor is not essential to control the tumor locally. As with rhabdomyosarcoma, the decision for how best to achieve local control should be made in consultation with a multidisciplinary team, taking into account cosmetic and functional outcome, as well as the risks of long-term toxicities associated with the therapeutic modality used. The standard approach to Ewing sarcoma in North America is to administer neoadjuvant chemotherapy over roughly 12 weeks with alternating cycles of vincristine, cyclophosphamide, doxorubicin, and ifosfamide, etoposide. Surgery or radiation is then delivered, and chemotherapy is continued for a total of about 9 months of therapy. A randomized trial conducted through the COG for patients without overt metastatic disease compared the disease-free survival of patients who received their chemotherapy cycles every 2 weeks to those receiving it on the more traditional 3 week schedule, and there was a significant survival advantage with the intensified schedule (73% vs. 65% 5-year EFS).[45] Thus, the current standard is to administer the chemotherapy every 2 weeks, shortening the overall duration of treatment.

Radiation is used in conjunction with chemotherapy in 60% of all Ewing's cases,[46,47] but in the head and neck region where a gross total resection is often difficult and highly morbid, it is used more frequently. Radiation is given for lesions that are initially unresectable and/or show a poor response to chemotherapy. Typically, a dose of 55.8 Gy is used for gross disease and 50.4 Gy for microscopic residual. The treatment volume includes the prechemotherapy soft tissue and bone extension of the tumor with a volume reduction after 45 Gy to focus on the remaining postchemotherapy disease. Historically, surgery has been felt to provide superior local control when compared with radiation, with local control ranging from 86% to 100% for surgery alone and 53% to 86% with radiation alone.[46,48,49] Definitive radiation is used more frequently in pelvic lesions and in large unresectable tumors, both of which portend a worse prognosis, and therefore this direct comparison is somewhat unbalanced. In head and neck lesions, we would advocate for definitive radiation when surgical resection would be incomplete or come with significant morbidity.

## NEUROBLASTOMA

Neuroblastoma is the most common solid tumor of childhood outside of the central nervous system, accounting for about 7% of childhood cancer. Neuroblastoma arises in neural crest cells, either in the adrenal gland or in paraspinal locations anywhere along the sympathetic ganglion chain, including the neck, chest, abdomen, and pelvis. The majority of tumors occur in the abdomen, but it can present in the neck in the stellate ganglion as a cervical mass or with Horner syndrome. Children with Horner syndrome without apparent cause should be evaluated for neuroblastoma and other tumors.[50] However, the most common presentation of neuroblastoma that involves the head and neck region is from metastatic disease, as neuroblastoma is frequently widely metastatic at the time of initial diagnosis, with metastases to both bone and bone marrow. In addition to metastases to the skull and jaw, there is a propensity for retrobulbar metastases to the orbit, resulting in the clinical presentation of unilateral or bilateral proptosis and periorbital ecchymosis, sometimes referred to as "raccoon eyes", or raising initial concern for nonaccidental trauma. Neuroblastoma has an extremely heterogeneous prognosis, ranging from a generally benign course in infants (including even some infants with widely disseminated disease who may have spontaneous regression of their tumor) to a much more aggressive course in older children with disseminated disease. The age of the patient, tumor stage, and biologic features of the tumor (including histology, cytogenetic features, and the presence of amplification of the *MYCN* oncogene) are used to stratify patients into risk groups and guide therapy. Multiagent chemotherapy is the cornerstone of treatment for high-risk patients, often including high-dose alkylating agent-based chemotherapy with autologous hematopoietic stem cell transplantation, *cis*-retinoic acid, and immunotherapy. On the other hand, surgery alone can be effective treatment for lower risk patients. Patients with biologically favorable disease can become long-term

survivors even with incomplete resections, and decision-making regarding how to best address a seemingly localized tumor should always be made in consultation with a pediatric oncologist, as aggressive surgery may not be necessary or warranted.[51] Radiation is used in high-risk patients as part of multimodality therapy to treat the primary site after resection and any metastatic lesions with incomplete resolution after initial chemotherapy. It can be used as quick and effective palliation in cases where cord compression, airway obstruction, or organ compromise are seen at presentation. In these cases, doses of 9–20 Gy can be used effectively with response rates of 73–100% depending on site and dose used.[52,53]

## LYMPHOMA

Both Hodgkin lymphomas and non-Hodgkin lymphomas occur in children, with each form comprising about 6% of all childhood cancers. Hodgkin lymphoma is relatively rare in children under 10 years of age, and has a first incidence peak during adolescence and early adulthood. The vast majority of non-Hodgkin lymphomas that occur in children are high-grade neoplasms, in contrast to the adult population where there is a higher frequency of low-grade, relatively indolent lymphomas. The most common presentation of childhood lymphomas involving the head and neck region is that of cervical or supraclavicular lymphadenopathy. However, lymphomas can also present in the lymphoid tissues of the tonsils, Waldeyer's ring, nasopharynx, and oropharynx. Multiagent chemotherapy is the cornerstone of treatment for all high-grade childhood lymphomas, most of which have an exquisite sensitivity to chemotherapy and an excellent prognosis, even in the setting of advanced disease. The usual role of surgery for childhood lymphomas is biopsy to provide a definitive tissue diagnosis, with excisional biopsies that procure adequate sample for a thorough lymphoma workup greatly preferred over needle techniques.

In the case of Hodgkin lymphoma, there may be few, scattered malignant cells in a background of normal appearing lymphocytes within a lymph node, and fine needle aspirate is not sufficient to exclude a lymphoma diagnosis. There is generally no indication or role for surgical resection of childhood lymphomas, as they need to be treated systemically with chemotherapy, and for Hodgkin lymphoma, usually with the addition of low-dose radiation treatment depending on histology, stage, and response to chemotherapy. The specific chemotherapy regimen used depends on the type of lymphoma, and treatment can range in duration from as short as 3 months for localized forms of lymphoma to as long as 2 years for lymphoblastic lymphoma, which is treated similarly to acute lymphoblastic leukemia.

## LANGERHANS CELL HISTIOCYTOSIS

Although not considered to be a true malignancy, Langerhans cell histiocytosis (LCH) can sometimes behave like a malignancy with an aggressive course that involves multiple organ systems or multiple bony sites, commonly including sites in the skull, ear and mastoid region, sinuses, and jaw. Asymptomatic bone lesions with radiographic evidence of sclerotic margins often resolve spontaneously. Curettage or excision can be effective treatment for a single bony site of disease that is nonhealing or painful, with control rates of 70–90%, and there is no evidence that radiation following resection adds to disease or local control.[54–57] Postoperative radiation can be used when an absence of healing or lesion progression is seen after surgery. Radiation alone as definitive treatment is used in symptomatic sites where resection is not possible or significant morbidity would be incurred. There is no evidence of dose response for LCH, nor is there consensus on optimal dose. Low radiation doses of 5–10 Gy in young children and 15–20 Gy in older children are used with local control rates ranging from 82% to 96%.[58–60]

Chemotherapy is the treatment of choice for multifocal disease and a pediatric oncologist should be consulted to guide the evaluation and treatment of a child who is diagnosed with histiocytosis. The most commonly used chemotherapy regimen incorporates weekly vinblastine and daily prednisone over a 6-week induction phase, followed by vinblastine and 5-day prednisone pulses every 3 weeks for a total duration of about 1 year. There may be a role for the addition of other chemotherapy agents, such as 6-mercaptopurine and methotrexate, or for more intensive therapy for those unusual patients with refractory or recurrent disease.

## CHORDOMA AND CHONDROSARCOMA

Chordomas and chondrosarcomas most commonly arise in adults, with a peak incidence in the fourth and fifth decade.[61,62] Fewer than 5% of these tumors are diagnosed in patients under 20 years of age. In children, chordomas arise more commonly in the spheno-occipital region, rather than the sacral predominance seen in adults, but can

be found throughout the spine and sacrum.[63] Chordomas in the pediatric population can behave more aggressively than in adults, presenting with a shorter history of symptoms, a shorter interval to progression after surgery, and a higher rate of metastatic disease, especially in those under 5 years of age.[64,65] Whereas chordomas arise from notochord remnants within the axial skeleton, chondrosarcomas originate from cartilaginous elements within bone and are seen most often in the pelvis and femur but can occur in any number of locations, including the base of skull. The rates of long-term local control following treatment with surgery and radiation are significantly higher with chondrosarcoma than chordoma, ranging from 85% to 100%, and systemic therapy can be used in select situations.[63,66,67]

Management of chordoma and chondrosarcoma relies heavily upon surgery as primary treatment. Despite advances in microscopic and image-guided neurosurgical procedures, complete resection in these tumors is achieved in only 50–70% of cases, depending on location. Even with complete surgical resection, local recurrence ranges from 40% to 60%.[68–70] Following surgery, RT is indicated for the presence of gross or microscopic residual disease, or in cases where violation of the tumor capsule has occurred and there is concern for contamination. Radiation combined with surgery has been shown to reduce local recurrence rates and high doses of radiation, ranging from 70 to 78 Gy for chordoma and 64 to 70 Gy for chondrosarcoma are needed.[71,72] For this reason, proton RT has repeatedly demonstrated the ability to safely treat adult skull base patients and achieve higher local control than photon RT due to its ability to reduce exit dose and allow for sparing of critical CNS structures at high doses. In a systematic review of all the major published chordoma series, the benefit of proton RT was demonstrated with an overall 5-year LC/OS of 36%/54% for photons vs. 64%/80% for protons.[72] This benefit of RT has also been demonstrated in pediatric photon series and there is some data to suggest children have improved responses to radiation compared to their adult counterparts.[61] With the combination of surgery and proton RT, the OS for chondrosarcomas and chordoma ranges from 90% to 100% and 64% to 81%, respectively.[71,73,74]

## JUVENILE NASOPHARYNGEAL ANGIOFIBROMAS

Juvenile nasopharyngeal angiofibromas (JNAs) are highly vascular but benign tumors of the nasopharynx, typically occurring in the young male population. Management is typically with surgery alone, but these tumors can extend into areas around the skull base that make gross total resection impossible without undue morbidity. Radiotherapy is typically used in these circumstances and is generally well tolerated. All gross tumor is targeted with fractionated radiation therapy and typically doses 30–46 Gy are used. Outcomes with 36 Gy or more yield an 80–91% local control rate. There is some evidence that doses below 36 Gy are associated with an increased risk of local failure. Stereotactic radiosurgery has been used for small amounts of residual disease after surgery, but there is much less experience with this technique. Following radiotherapy, JNAs tend to regress slowly and response may occur over a period of years.[75–80]

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CHAPTER

# 60 Pediatric Salivary Gland Disorders

***Charles Parker, Charles M Myer III***

## INTRODUCTION

Salivary gland lesions are not an uncommon complaint among the pediatric population. Of the wide possible disease entities (Tables 60.1 and 60.2), inflammatory processes outnumber neoplastic lesions, both benign and malignant.[1] Establishing a definitive diagnosis may be challenging and often requires multiple diagnostic modalities.

## HISTORY AND PHYSICAL EXAMINATION

As in any disease process a thorough history and physical examination is key in being able to narrow the differential diagnosis in the pediatric patient with a salivary lesion. However, the possibility of a malignancy should always be considered in the child with a salivary mass. Questioning should enable the clinician to delineate between an inflammatory, congenital, or neoplastic process.

Age at presentation may suggest an underlying pathology. Common neonatal lesions include hemangiomas and neonatal sialadenitis. In patients younger than 10 years of age, inflammatory lesions far outnumber neoplastic processes, whereas in children older than age ten, neoplastic lesions become more frequent.[2] Key points that should be elicited during the interview include the onset, duration, location and severity of symptoms. Acute swelling or pain is frequently secondary to an inflammatory lesion. Chronic pain or swelling is often a diagnostic challenge as it can

**Table 60.1:** Differential diagnosis of pediatric salivary gland disorders

| *Inflammatory* | *Cystic* | *Developmental* | *Neoplastic* |
|---|---|---|---|
| *Acute sialadenitis*<br>• Viral—mumps, HIV, others<br>• Bacterial—acute suppurative sialadenitis, neonatal sialadenitis | Dermoid<br>Branchial cleft cyst<br>Mucous extravasation/retention cyst | Salivary agenesis and heterotopia<br>Salivary duct anomalies<br>Polycystic dysgenetic disease | Benign neoplasm—hemangioma, lymphatic malformations, Pleomorphic adenoma<br>Malignant neoplasm—mucoepidermoid carcinoma, acinic cell carcinoma, Rhabdomyosarcoma |
| *Chronic sialadenitis*<br>• Obstructive—sialolithiasis, ductal stenosis<br>• Autoimmune—juvenile recurrent parotitis, Sjögren's syndrome, sarcoidosis<br>• Infectious—nontypical mycobacteria, tuberculosis, *Bartonella henselae*, Actinomycosis | | | |

**Table 60.2:** Common salivary disorders based on location

| *Parotid gland* | *Submandibular gland* | *Sublingual and minor salivary glands* |
|---|---|---|
| Mumps<br>Acute suppurative sialadenitis<br>Juvenile recurrent parotitis<br>Sjögren's syndrome<br>Neoplasm<br>Extraglandular disorders—lymphadenitis, lymphadenopathy, pilomatrixoma, branchial cleft anomaly | Sialolithiasis<br>Neoplasm<br>Extraglandular—lymphadenitis, lymphadenopathy, branchial cleft anomaly | Mucocele—ranula<br>Necrotizing sialometaplasia<br>Neoplasm |

represent an inflammatory or neoplastic process. Slow painless enlargement is the most common symptom in patients with a benign neoplasm. Rapid painless growth is more concerning for malignancy. Bilateral salivary gland involvement often suggests an underlying systemic condition.[3] The presence of other symptoms is often helpful in determining the underlying process. Fever suggests an underlying infection. Pain or swelling with eating suggests an obstructive process such as sialolithiasis or ductal stenosis. Other important points to elicit are medication history, immunization status, recent trauma, recent surgeries, animal exposure, and sick contacts.

Physical examination includes bimanual palpation of the gland, inspection of the ductal orifice and saliva, palpation for associated adenopathy and examination of cranial nerves. Diffuse glandular enlargement suggests an inflammatory process, whereas an isolated mass is suspicious for neoplasm. It may be difficult to determine if a mass is cystic, solid, intraglandular or periglandular on physical examination alone. Inspection of the ductal orifice should be performed along with "milking" the gland to determine the quality of saliva produced. An erythematous duct with purulent drainage is pathognomonic for bacterial sialadenitis. Oropharyngeal bulging suggests deep lobe parotid involvement. Nerve paralysis is more likely associated with malignancies. Overlying violaceous skin changes is often seen in infections, in particular nontuberculous mycobacterial infections.

## LABORATORY STUDIES

Laboratory studies have a role in confirming certain diagnoses and in determining the adequacy of therapy in others. Inflammatory markers such as C-reactive protein can be used to determine effectiveness of treatment in infectious processes. Failure to fall or resolve after 48 h may indicate inadequate treatment or the development of an abscess. Culture of purulent fluid should be performed in suppurative infections to guide antibiotic therapy. Bilateral involvement often suggests a systemic process and may warrant further autoimmune testing. Common autoimmune studies include antinuclear antibody (ANA), rheumatoid factor, antineutrophil cytoplasmic antibody, SS-A, and SS-B. Other tests include HIV and tuberculin skin testing.

## IMAGING

While radiographic imaging is not necessary in the management of most patients with salivary gland pathology, it does play a key role in the diagnosis and preoperative planning of some. In the past, plain films and sialography were the main modalities obtained; however, these have been replaced largely by ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). The type of imaging obtained should be guided by the clinical picture, but the role of imaging is to localize the lesion, characterize its appearance, and determine the extent of involvement.

Conventional radiography has been used in the past to detect salivary stones and adjacent dental or mandibular lesions. On plain film, 60% of parotid and 80% of submandibular stones are radiopaque, which leaves a large percentage not visualized. US and CT scanning largely have replaced plain films in the diagnosis of sialolithiasis.[4]

Sialography involves retrograde injection of contrast into the salivary duct to visualize ductal anatomy and patency. It was used commonly in the workup of chronic sialadenitis, but now has largely been replaced by serology and advances in CT, MRI, and sialoendoscopy. Sialography should be avoided in acute sialadenitis as it can exacerbate the disease.

US is finding a larger role in the diagnostic workup of pediatric head and neck lesions. Some advocate US as the initial imaging study in patients with salivary gland pathology as it provides a quick, inexpensive, and noninvasive

assessment. US can identify intraglandular from extraglandular lesions, cystic versus solid masses, assess vascularity, the integrity of adjacent structures and provide a guide for fine-needle aspiration. US is used commonly in the evaluation of inflammatory lesions. It provides a quick imaging tool to rule out a suspected abscess or sialolithiasis. When a solid mass is detected further cross-sectional imaging is often obtained. Disadvantages of US are that it is operator dependent and displays the deep parotid lobe poorly.[5]

Cross-sectional imaging with CT or MRI have nearly identical sensitivities, close to 100%, in identifying salivary tumors. Advantages of CT imaging are that it can be obtained quickly and often without sedation that offers favorability in its use in children. Most mass lesions should undergo CT imaging initially. MRI should be employed if a neoplastic process is highly suspected. MRI offers better anatomic detail of the facial nerve, ductal anatomy, and possible tumor spread. However, the disadvantages of MRI are the cost, time required to perform the test and possible need for sedation. Imaging may suggest a benign vs. malignant process, but histologic diagnosis is needed for confirmation. Common findings on cross-sectional imaging for benign tumors include smooth, distinct borders, whereas high-grade malignant lesions have irregular, infiltrating, and indistinct margins.[4,6]

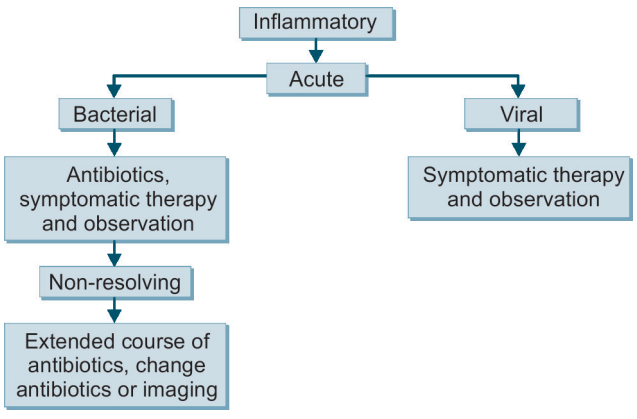
## BIOPSY

Fine needle aspiration (FNA) plays a large role in the diagnostic workup of salivary lesions among adults. Its role in the pediatric patient is less defined. FNA provides a safe way to differentiate between neoplastic and nonneoplastic lesions preoperatively.[7] Its use in pediatrics has been limited by the need for sedation in most young children to obtain a specimen and the lack of well-trained pediatric cytopathologists for reading the aspirate. Despite this, most children older than 10 years of age are cooperative enough where an FNA can be obtained. If an FNA cannot be obtained in a child with a lesion suspicious for malignancy, then an intraoperative frozen specimen can be obtained. This generally means a superficial parotidectomy or submandibular gland excision is performed as opposed to an incisional biopsy. The main objections in performing an incisional biopsy of the parotid are the risk of tumor spillage and increased risk of facial nerve injury should the patient require a second surgery. However, incisional biopsy is an acceptable alternative to a superficial parotidectomy in the workup of lymphoproliferative diseases and the suspected Sjögren or autoimmune process.[8,9] An incisional biopsy may be obtained by a small infra-lobular incision down to the parotid capsule with removal of a small amount of superficial parotid. Alternatively, a lip biopsy may be utilized to obtain these diagnoses.

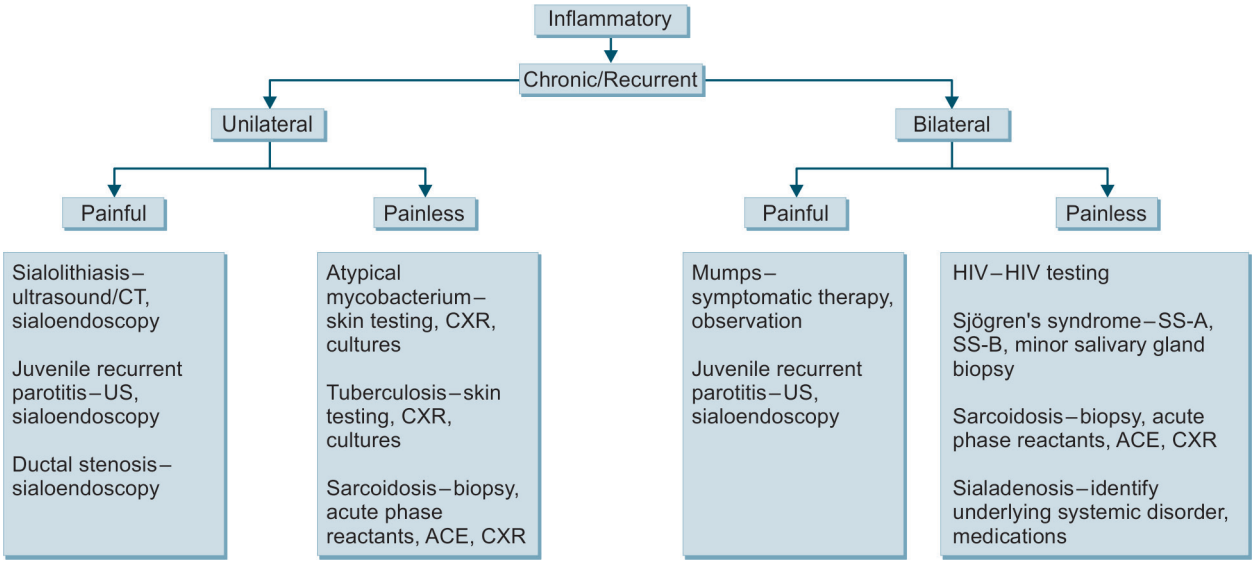
## DIAGNOSTIC ALGORITHM

The first step in evaluating a pediatric salivary disorder is to determine if the lesion is inflammatory or noninflammatory in nature (Flowcharts. 60.1 to 60.3). Due to the large proportion of salivary disorders that are inflammatory in etiology and, of those malignancies seen, most are considered low grade, some advocate a trial of antibiotics prior to further diagnostic workup.[10] Acute inflammatory lesions should undergo a trial of antibiotics, symptomatic therapy and observation. If the lesion fails to resolve after an appropriate course of therapy and observation then either an extended course of antibiotics is employed or further workup with an ultrasound can help determine if an abscess has developed or if another process should be suspected. In chronic or recurrent inflammatory salivary disorders, these can be categorized as unilateral or bilateral and painful or painless. Laboratory evaluation for autoimmune disorders plays a larger role in the workup of bilateral parotid disorders. Noninflammatory lesions often raise the question of a possible malignancy; a CT scan is often the initial step in management for these lesions. FNA should be performed if the patient is cooperative. If not, then a planned superficial parotidectomy with intraoperative frozen section will help guide the extent of excision.

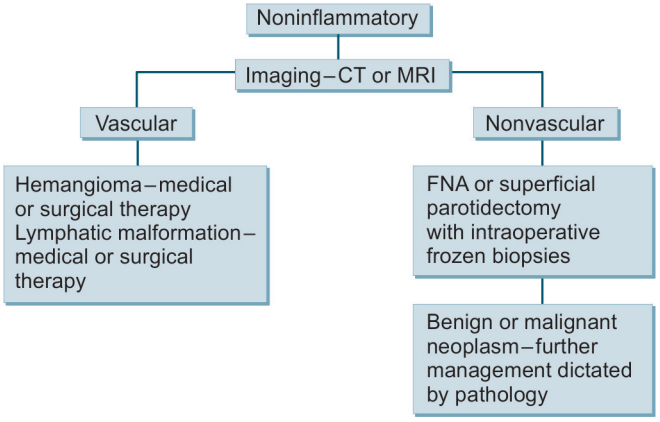
**Flowchart 60.1:** Algorithm for acute inflammatory salivary disorders.



**Flowchart 60.2:** Algorithm for chronic inflammatory salivary disorders.




**Flowchart 60.3:** Algorithm noninflammatory salivary disorders.




## INFLAMMATORY CONDITIONS

Inflammatory diseases of the salivary glands are the most common cause of salivary gland enlargement (SGE).[2] Inflammatory salivary diseases can be categorized as either an acute or chronic process.

### Acute Sialadenitis

#### *Viral Sialadenitis*

Viral parotitis secondary to mumps was once the most common cause of parotid swelling in children but its incidence has now decreased with the widespread vaccination against the paramyxovirus.[11] Clues to suspect viral sialadenitis include a prodrome of fever and malaise prior to the onset of salivary swelling. Bilateral enlargement is more common than in bacterial sialadenitis. Examination will often reveal clear saliva on bimanual examination and an erythematous ductal papilla. Mumps-like illness is most often due to other viruses, the most common isolated pathogen being Epstein-Barr virus.[12] Others include parainfluenza, adenovirus, enterovirus, and herpes virus. Most patients with suspected viral sialadenitis do not undergo etiologic testing and the disease process resolves with conservative management.

#### *Mumps*

The classic presentation is bilateral swelling and fever in a young child. With near universal vaccination against mumps since 1982, its presentation is becoming rare. Due to its low incidence, other causes of salivary swelling should be suspected in young children with a mumps-like illness that fails to resolve spontaneously or worsens clinically over time.

The paramyxovirus is a RNA virus with a predilection for the glandular epithelium of the parotid gland. Viral replication within the ductal epithelium results in local inflammation and edema and the resulting clinical findings of swelling and tenderness. Transmission occurs with direct contact or by droplets. The median incubation period is 19 days. Patients may remain contagious from several days prior to the onset of symptoms to several days after the resolution of symptoms. Most patients present with a history of fever, malaise, and anorexia for several

days before the onset of parotid swelling. Bilateral parotid swelling is present in ~90% of symptomatic patients. However, 10% may present with isolated submandibular swelling. Examination will demonstrate an enlarged tender and swollen parotid gland and a swollen and erythematous Stenson's papilla with clear salivary flow. Symptoms typically last up to 1 week. Other manifestations of Mumps infection are less common than parotitis and include orchitis, meningoencephalitis, pancreatitis, and sensorineural hearing loss. The diagnosis is made clinically from the findings of parotid swelling > 2 days without any other apparent cause, but it may be supported by elevated serum amylase levels, normal to slightly elevated white blood cell counts, viral serology and lymphocytosis in the CSF of patient with meningoencephalitis. Immunization status should be obtained. The vaccine is not 100% effective and receivers of the vaccine may still be susceptible to mumps infection. Outbreaks of mumps have not been uncommon in vaccinated regions, with most outbreaks occurring in young adults on college campuses. The treatment of parotitis is supportive due to the self-resolving nature of disease.[11]

### *Human Immunodeficiency Virus*

Human immunodeficiency virus salivary gland disease (HIV-SGD) may be present in nearly 50% of pediatric HIV patients and at times may be the initial manifestation of HIV. HIV-SGD may present as xerostomia, SGE, or a combination of both. Other salivary conditions seen in non-HIV patients may still occur in HIV patients and should also be considered.

Xerostomia is the most common manifestation of HIV-SGD. Causes are often multifactorial in nature and may be due the destructive process of lymphocytic infiltration in the salivary glands, ductal obstruction secondary to lymphoproliferation, and glandular enlargement or a side effect of antiretroviral therapy. Xerostomia has been linked to an increased incidence of oral candidiasis and dental caries among HIV patients. Management is supportive with sialagogues, aggressive oral hygiene, and frequent dental visits.[13,14]

SGE has been reported in up to 10% of pediatric HIV patients. This has decreased with use of antiretroviral therapy.[15] SGE typically manifests as slowly progressive and painless bilateral parotid enlargement. However, isolated submandibular or a combination of parotid and submandibular gland enlargement has been reported. HIV associated SGE is usually secondary to a lymphoproliferative process of the intra or periglandular lymph nodes and/or salivary parenchyma. Dave et al. classify HIV-associated SGE into three categories based on histologic findings and clinical presentation: benign lymphoepithelial cyst (BLEC), persistent generalized lymphadenopathy, and benign lymphoepithelial lesion (BLEL). Histologic findings associated with HIV-SGD are characteristic but not specific to HIV infection and are often seen in autoimmune processes and other chronic inflammatory states.[16]

BLEC in combination with persistent generalized lymphadenopathy is the most common classification of HIV SGE. Clinically, this presents as bilateral slowly enlarging parotid glands with cervical lymphadenopathy. Bilateral involvement is seen in 80% of patients and is typically painless. Of those with bilateral disease, 90% will have multiple palpable cysts and cervical lymphadenopathy on examination. Parotid enlargement typically presents early in the course of HIV infection and may manifest as the initial sign of HIV infection. Less common is diffuse solid enlargement of the parotid gland, as seen in BLEL. Patients with BLEL carry a higher risk of malignant transformation and should be monitored carefully. Evaluation for parotid enlargement in the HIV patient includes diagnostic imaging to characterize the nature of swelling, i.e., solid, cystic, or mixed. Ultrasound may be the preferred method of evaluation due to the noninvasive nature, reproducibility, potential for needle biopsy, and lack of radiation exposure. US findings include a wide spectrum from purely cystic to solid or mixed nodules. Most glands, however, demonstrate multiple small cystic areas with mixed internal echogenicity. CT and MRI will demonstrate multiple cystic structures within an enlarged inflamed gland (Fig. 60.1).

All patients with a finding of multiple parotid cysts should undergo HIV testing if the infection has not already been diagnosed. Further pathologic diagnosis of BLEC by FNA is recommended to rule out the possibility of other benign or malignant processes. Those patients with solid enlargement on imaging or with evolving cysts or nodules on follow-up should also have biopsies to rule out malignancy.

Most patients can be treated effectively with antiretroviral therapy and close observation to rule out malignant transformation. In patients with symptomatic enlargement that fails to improve after medical therapy, repeat aspiration, sclerotherapy, or total parotidectomy may be necessary.[15,16]

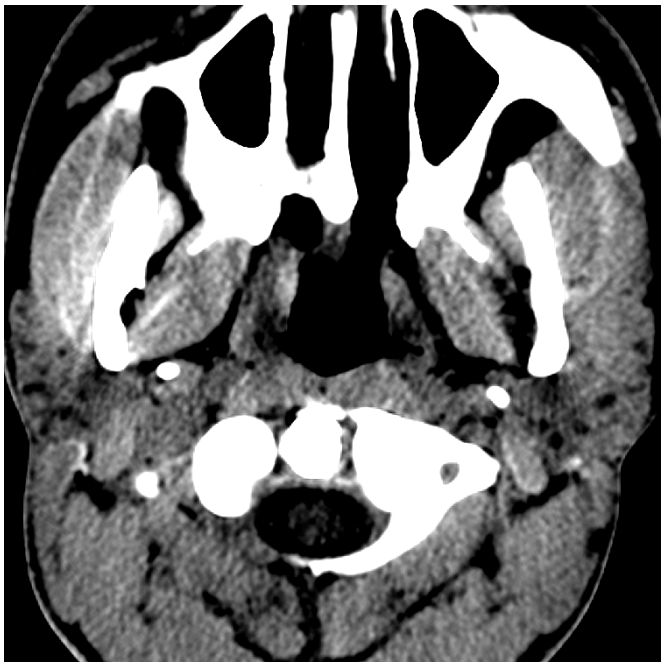


**Fig. 60.1:** Axial postcontrast CT in a child with HIV infection secondary to blood transfusions demonstrates multiple, bilateral low attenuation cysts throughout both parotid glands, typical of lymphoepithelial lesions in HIV-positive patients.

One must consider the possibility of opportunistic infections in those with advanced AIDS as a cause of parotitis. Possible pathogens include mycobacteria, histoplasmosis, candida, cryptococcus, and CMV. These organisms should be suspected in the HIV/AIDS patient that fails to respond to traditional antibiotic therapies.

## Bacterial Sialadenitis

### *Acute Suppurative Sialadenitis*

In contrast to viral etiologies, patients with acute suppurative sialadenitis often present with unilateral gland involvement, high fever, and pain. Pathognomonic for suppurative sialadenitis is the expression of purulence from the ductal system. The etiology of acute suppurative sialadenitis in children often can be suspected by identifying the involved gland. Acute suppurative parotitis commonly develops as a result of an underlying systemic factor. The most common scenario is the development of parotitis in a child following a bout of dehydration from a recent viral illness. Other predisposing factors include immunosuppression, comorbid medical conditions, trauma, or following surgery. In contrast, acute submandibular sialadenitis is typically secondary to stone formation and ductal obstruction.

The diagnosis of acute suppurative sialadenitis is usually made clinically based on the findings of unilateral painful swelling, fevers and purulence from the involved salivary duct. Other findings include overlying skin erythema and cervical lymphadenopathy. Imaging, ultrasound or CT, is often unnecessary but may be obtained if an abscess or mass is suspected on presentation or if the patient fails to respond to a trial of appropriate antibiotics (Figs. 60.2 and 60.3). Cultures of purulent fluid should be obtained prior to the initiation of empiric antibiotics. The most common pathogens include *Staphylococcus aureus* and *Streptococcus viridans*, but other bacteria are *Haemophilus influenzae*, *Escherichia coli*, and anaerobes. Other therapies include hydration, sialogogues, warm compresses, and gland massage to promote possible stone expulsion. Indications for admission for intravenous antibiotics include dehydration, high fever, leukocytosis, and additional comorbidity. A clinical response should be seen within 48 h after initiation of appropriate antibiotics. If the patient continues to progress, re-evaluation for possible abscess formation, ductal stone, or atypical infection such as tuberculosis should be pursued. Several complications of acute suppurative sialadenitis have been reported. Abscess formation should be suspected on presentation in the child with a fluctuant mass or in the gland that fails to improve after 48 h of antibiotic therapy. Abscess development is more frequent following acute suppurative parotitis. Treatment requires drainage by a parotidectomy-type skin incision, elevation of skin flaps to expose the fascia overlying the parotid, and blunt dissection parallel to the facial nerve into the abscess. Some advocate ultrasound guided needle drainage as the initial procedure; however, there is a nearly 50% recurrence rate, leading to eventual incision and drainage. Other complications include spread to deep neck spaces, facial nerve paralysis, and necrotizing fasciitis. The inflammatory response of a single episode of acute suppurative sialadenitis may lead to ductal stenosis, predisposing one to possible salivary stasis and recurrent or chronic sialadenitis.[17-19]

### *Neonatal Suppurative Sialadenitis*

Neonatal suppurative sialadenitis is a rare infection of the salivary glands in neonates. This process occurs more commonly in the parotid than submandibular gland. It has a higher incidence in premature infants and boys. Risk factors include low birth weight, oral trauma and immune suppression. It is suspected to arise in the newborn due to their increased risk of dehydration that leads

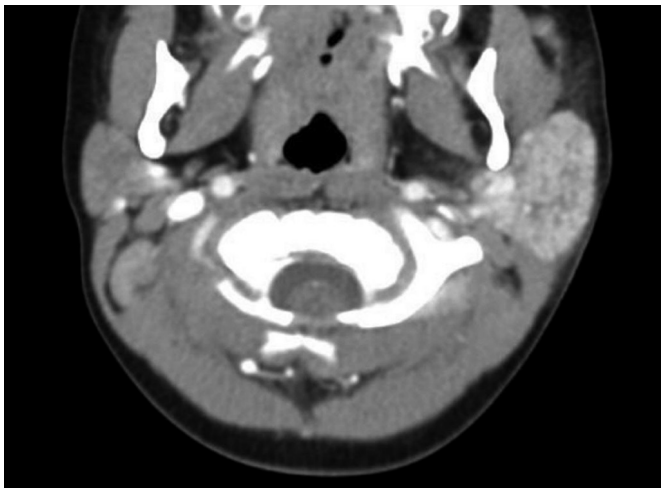


**Fig. 60.2:** Axial contrast-enhanced CT demonstrates diffuse enhancement and enlargement of the left parotid gland in a child with acute parotitis.

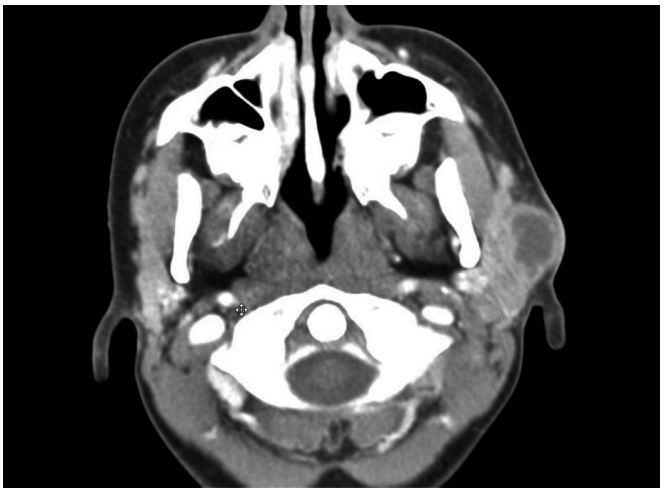


**Fig. 60.3:** Axial contrast-enhanced CT demonstrates an ill-defined low attenuation collection in the left parotid gland in a 6-year-old child with parotid abscess. Notice also that the left parotid gland is also diffusely enlarged, there is edema in the adjacent subcutaneous fat and there is thickening of the overlying skin.

to salivary stasis and ascending bacterial infection through Stensen's duct. Neonatal suppurative sialadenitis should be suspected in the neonate with salivary gland swelling and purulent drainage from the duct. Ultrasound may aid in the diagnosis of intraglandular abscess. The most common pathogen isolated is *S. aureus*, but others include gram-negative bacilli and anaerobes. Treatment includes empiric antimicrobial coverage for 7–10 days against staphylococcal species, gram-negative organisms and anaerobes.[20,21]

## Chronic Sialadenitis

Chronic sialadenitis describes a persistent or recurrent inflammatory state of the salivary gland. The potential etiology of this persistent inflammatory state in a child is often multifactorial in nature. A key finding in these patients, however, is a state of decreased salivary flow and salivary stasis leading to a gland that is more susceptible to repeated infections and inflammatory damage. Potential causes of chronic sialadenitis in the pediatric patient may be categorized as obstructive, infectious, or immune-related. Obstruction of the outflow duct may be due to intraductal or extraductal blockage. Infectious etiologies include multiple granulomatous diseases. Immune-related etiologies include juvenile recurrent parotitis (JRP) and autoimmune diseases.

Patients present with chronic pain or swelling of the affected gland. Most patients report several episodes of salivary pain and/or swelling in the past followed by periods of remission. The pain is milder in nature and ductal purulence is often not seen as compared with acute suppurative sialadenitis. A low-grade fever, malaise and other systemic symptoms may be present. Chronic inflammation ultimately may lead to gland atrophy and/or formation of a fibrotic mass suspicious for a neoplasm. A through history and physical examination are important in detecting a possible etiology. Patients may report a prior episode of acute sialadenitis that may have led to ductal stenosis. A history of gritty sand-like particles in the oral cavity is suspicious for sialolithiasis. Dental appliances, malocclusion or prior trauma are potential causes of ductal damage. Other comorbidities and medications should be elicited as these are potential culprits. A travel history and any recent animal exposure should also be obtained to rule out less common granulomatous infections. The diagnostic evaluation is tailored to the suspected etiology. Blood work may be obtained for autoimmune or infectious processes. Imaging often is necessary to rule out a possible neoplastic process as the cause of persistent swelling. Sialoendoscopy is often the procedure of choice in the child with persistent inflammation of unknown etiology as it may be both diagnostic and therapeutic.[22]

### *Obstructive*

Pediatric sialolithiasis occurs in <5% of all sialolithiasis cases. Over 90% of salivary stones are found in the submandibular gland. This predilection is thought to be due to the mucinous nature of submandibular saliva and the

curvature of Wharton's duct. The mean age at presentation is 12 years, with rare reports in children under 10 years of age. Most children complain of swelling and/or pain during or after eating. Recurring symptoms are present in 80% of patients and often are present for a year prior to diagnosis. Bimanual examination of the floor of mouth often reveals a palpable stone along the distal duct in greater than two-thirds of patients and is typically < 1 cm in size. A proximal duct or parenchymal stone is seen more frequently in older children. Only 20% of patients will have more than one stone. Ultrasound imaging often is obtained initially if examination findings are inconclusive, while CT is reserved for those with questionable ultrasound findings. Due to the distal location of most pediatric salivary stones, intraoral duct opening and stone removal is often successful. A proximal or intraglandular stone may require gland excision; however, there is a potential role of endoscopic removal of sialoliths in pediatric patients.

Intraductal stenosis can be secondary to an inflammatory process resulting in ductal fibrosis and narrowing or congenital ductal aplasia. Extraductal compression from a mass or aberrant ductal course may also lead to decreased salivary flow. Radiographic imaging reveals no salivary stone. Sialography can often demonstrate the narrowed ductal portion; however, sialoendoscopy can provide direct visualization of the ductal lumen and an option for therapeutic dilation.[22,23]

### *Autoimmune*

*Juvenile recurrent parotitis*: **JRP is the second most common** salivary disease in children following viral sialadenitis. JRP describes a nonsuppurative and nonobstructive parotitis in children. There are multiple suspected etiologies including chronic bacterial infection, allergy, ductal anomalies, immunologic dysfunction, and genetic factors. However, it is most likely multifactorial in etiology. JRP presents as recurring episodes of unilateral swelling, pain, and erythema. One-third of patients may have bilateral symptoms. The frequency of attacks can vary but most commonly occur every 3–4 months. A history of recurring attacks for over a year prior to diagnosis is seen in 70% of patients. The length of attacks varies individually but average 3 days and range from 2 to 7. Systemic symptoms of fever and malaise are frequently present. There is a male predominance with a peak presentation at 4–6 years of age. Resolution by puberty is most often the case, with one study reporting only 4% of patients with symptoms still by the age of 22 years. However, in selected patients, attacks may persist into adulthood and may require more aggressive management at that time. Examination will often reveal a tender and mildly erythematous parotid gland. There is a lack of purulence at the salivary duct as in acute suppurative sialadenitis but often the orifice to Stensen's duct may appear widened and yellow plaques may be expressed. Diagnosis by sialography was the mainstay prior to US and sialoendoscopy. The sialographic findings include scattered sialectasis with a combination of ductal strictures and dilations. US findings include scattered hypoechoic areas consistent with the scattered punctate sialectasis on sialography; this can also be seen on CT (Figs. 60.4 to 60.6). Sialoendoscopy findings include a white, bloodless ductal surface with both dilated and stenotic portions.

The goal of therapy is to provide relief in acute attacks and prevent future attacks with minimal morbidity. Due to the self-limiting nature of the condition, conservative therapy should be employed. Symptomatic therapy for acute episodes includes warm compresses, massage, hydration, anti-inflammatories and sialagogic agents. Antibiotics are typically reserved when a secondary bacterial infection is suspected on examination but are ineffective for prophylactic control. Prior aggressive management, which has included Stenson's duct ligation, total parotidectomy and tympanic neurectomy has mostly been abandoned. Recent studies show that sialoendoscopy with saline or balloon dilation is a highly successful intervention in reducing recurrent attacks until resolution by puberty.[24–26]

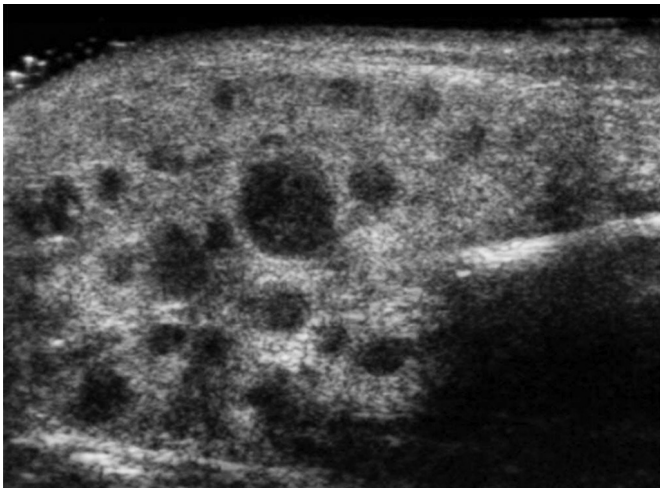


**Fig. 60.4:** Longitudinal ultrasound image shows multiple well-defined hypoechoic foci within the right parotid gland. The larger lesions likely represent small intraparotid lymph nodes and the smaller lesions are most likely microabscesses or dilated acini.

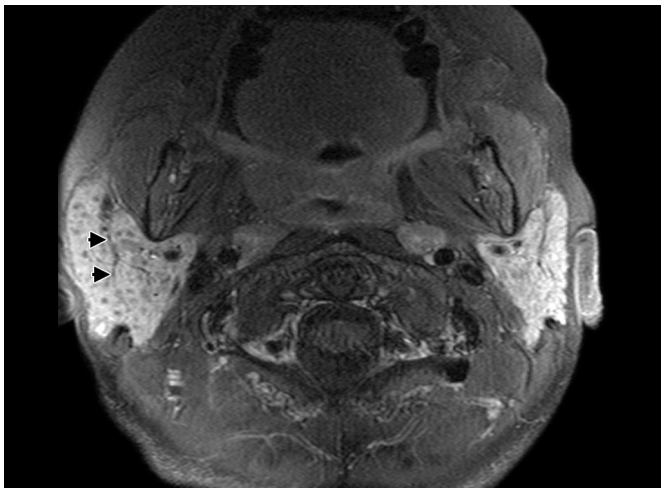


**Fig. 60.5:** Axial contrast-enhanced T1-weighted MRI with fat-suppression shows diffuse enlargement of the right parotid gland consistent with acute parotitis. There is dilatation of the intraglandular ducts (arrowheads) and multiple, round foci of decreased enhancement scattered throughout the parotid gland, which may represent small microabscesses or dilated acini secondary to chronic/recurrent inflammation/infection.

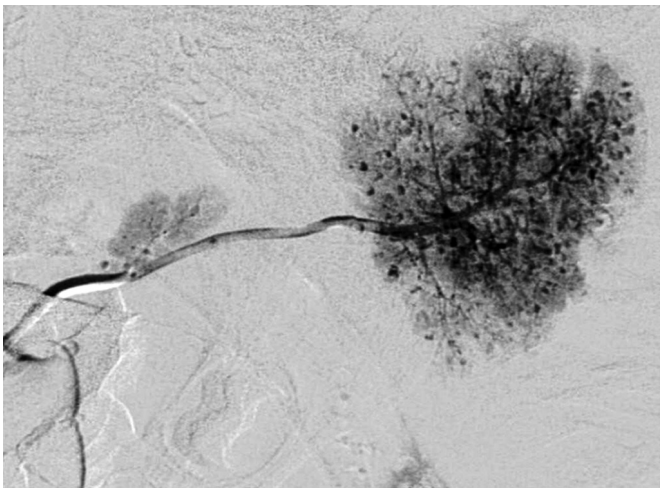


**Fig. 60.6:** Lateral sialogram in a patient with chronic parotitis shows normal caliber parotid duct and diffuse abnormal puddles of contrast throughout the parotid gland. Also noted is mild involvement of the small accessory parotid gland.

*Sjögren's syndrome*: Sjögren's syndrome (SS) is an autoimmune disease characterized by lymphocytic infiltration of the salivary and lacrimal glands, which leads to eventual destruction and manifestation of sicca symptoms, xerostomia, and xerophthalmia. SS is a rare disease among children that may be a primary disorder or secondary to other autoimmune diseases like systemic lupus erythematous or rheumatoid arthritis. Children with SS often present with bilateral parotid swelling without sicca symptoms. Pediatric SS is more common in females with a mean age of 10 years. Diagnosis should be suspected in the pediatric patient with recurrent bilateral parotitis. Criteria for the diagnosis of SS among adults have been established; however, many pediatric patients would not fulfill these criteria. The diagnosis of SS among pediatric patients is based on exclusion of other disease processes that can present with parotid swelling and supporting laboratory and biopsy findings. Laboratory studies to support the diagnosis of SS include positive ANA, SS-A/Ro and SS-B/La antibodies, rheumatoid factor, hypergammaglobulinemia and elevated acute phase reactants. Biopsy of minor salivary glands or the parotid to demonstrate lymphocytic infiltration and destruction may be necessary for diagnosis. Management of sicca symptoms may be all that is necessary; however, systemic inflammation may be treated with corticosteroids or immunomodulating agents.[27,28]

*Sarcoidosis*: Sarcoidosis is a multisystem granulomatous disease of unknown etiology that is relatively rare among the pediatric population. The classic presentation among adults is that of hilar lymphadenopathy, pulmonary infiltration, and ocular and cutaneous lesions. Children may present with what is termed early or late onset sarcoidosis. Late onset sarcoidosis is the most common presentation; it occurs at 13-15 years of age with a similar presentation as in adults. Early onset sarcoidosis is seen in children < 5 years of age and presents with a triad of rash, uveitis, and arthritis. Parotid involvement may be seen in both early and late onset childhood sarcoidosis, but overall is a rare manifestation of the disease with an incidence of only 6% among adult patients. Bilateral or unilateral diffuse swelling may be seen. Heerfordt syndrome, or uveoparotid fever, is defined as bilateral parotid enlargement, uveitis and cranial neuropathy, commonly the facial nerve. Diagnosis is made by clinical findings and supported by further studies. There is no definitive laboratory diagnosis; definitive diagnosis requires histologic findings of noncaseating granulomas of the affected organ. Biopsy may be obtained by FNA or excisional biopsy of minor salivary glands or enlarged lymph nodes. At times incisional biopsy of the parotid gland may be utilized. Other laboratory findings include elevated acute phase reactants, hypercalcemia and elevated angiotensin converting enzyme levels. A chest X-ray should be obtained to identify pulmonary involvement or hilar lymphadenopathy. For asymptomatic patients, no therapy is needed as the disease may run a self-limited course.

Patients with multisystem involvement commonly require prolonged corticosteroid or immunosuppressive therapy.[29,30]

### *Infectious*

Chronic granulomatous diseases are not an infrequent cause of cervical lymphadenitis in the pediatric population. Involvement of periglandular or intraglandular lymph nodes is a potential cause of chronic salivary inflammation, whereas direct infection of salivary parenchyma is not as common. Potential pathogens include *Mycobacterium tuberculosis (TB)*, nontuberculous mycobacterium (NTM), Actinomycosis, and *Bartonella henselae*.

NTM species are becoming a common cause of head and neck infections among developed nations. These organisms are commonly found within soil, animals, and food products. Spread is through direct entry by oral or ocular mucosa. Children 1–3 years of age are commonly affected due to hand to mouth habits. Patients present with a painless, fluctuant mass with a violaceous color change to the overlying skin. This is sometimes referred to as a "cold abscess". Sinus formation may occur with time secondary to thinning of the overlying skin or from a prior incision and drainage procedure. Systemic symptoms are less common then in TB infections. Diagnosis is often made by the clinical picture alone; however, a positive purified protein derivative (PPD) of > 5 mm in a child with no prior TB exposure provides a high PPV (98%) of a NTM diagnosis. A positive PPD is often seen in NTM due to cross-reactivity among mycobacterial species. A chest X-ray is obtained and is frequently negative. Definitive diagnosis requires a positive culture for NTM. This may be obtained by FNA or during surgical excision. Often these patients experience an average of > 8 weeks of inappropriate antibiotic therapy and misdiagnosis before definitive therapy is initiated. Culture results often take > 6 weeks that delay treatment even further. Management requires surgical excision of the affected gland, involved lymph nodes and skin. A superficial or total parotidectomy should be performed when the parotid gland or intraparotid lymph node is infected. Several reports describe the management of parotid and cervical NTM infections by antibiotic therapy (clarithromycin and rifabutin) alone; however, a recent randomized controlled trial demonstrated that cure rates were higher in those who underwent surgical excision as compared to antibiotic therapy (96% vs. 66%, respectively). Due to the intimate involvement of the facial nerve, some advocate 3–6 weeks of antibiotic therapy prior to surgical excision to decrease inflammation and facilitate facial nerve dissection. Facial nerve paralysis may be seen, often involving the inferior branch, and is typically temporary.[31–34]

*B henselae* is the causative agent of cat-scratch disease. Most infections present as cervicofacial lymphadenopathy; however, parotid gland involvement is not uncommon. Clinical findings include red-brown tender papules at the scratch site, regional lymphadenopathy, and minor systemic symptoms. Intraparotid lymph node swelling can mimic a neoplastic process. Diagnosis can be made by the history of recent cat exposure and positive serologic detection for antibodies to *Bartonella henselae*. Antibiotic therapy is often not necessary in the immunocompetent host and the infection typically resolves within 1–3 months despite antibiotic therapy. Patients with associated systemic involvement or suppurative lymph nodes may benefit from a 5- to 10-day course of azithromycin. Surgical drainage may be performed in individualized patients with tender suppurative lymph nodes; however, there is the risk of a chronic sinus developing.[35,36]

Actinomycosis is an infection caused by an oral gram-positive anaerobe. Infections usually develop after oral mucosa or dental trauma. Cervicofacial involvement is common with extension of sinus tracts to surrounding soft tissues. Parotid involvement may masquerade as a neoplasm due to the slow growing nature of this process. Diagnosis requires demonstration of classic sulfur granules on histology. Therapy includes abscess drainage and a long course, up to 6 months, of penicillin.[37]

Involvement of the head and neck by TB is usually a result of secondary spread from a primary pulmonary infection. Primary TB of the salivary glands is uncommon and a difficult diagnosis to establish. Most patients with cervicofacial manifestations of TB are immunocompetent and report no prior history of pulmonary TB or contact of infected persons. TB of the salivary gland is more common in the parotid than submandibular glands. It usually presents as a unilateral, slow growing mass that is often misdiagnosed as a neoplasm. Diagnosis requires a high clinical suspicion complemented by further studies. A chest X-ray should always be performed, as evidence of active or resolved pulmonary TB will increase the suspicion of parotid TB. Tuberculosis skin-testing should also be performed; however, a negative result cannot rule out the disease. Radiologic evaluation may show a mass-like lesion, an abscess or necrotic lymph nodes. FNA of the lesion should be performed and specimens sent for cytology and culture. Culture demonstration of TB is the gold standard and provides a means for drug susceptibility

testing. Despite the availability of multiple diagnostic tests, extrapulmonary TB is often still diagnosed by histologic examination, demonstrating caseating granulomas. A superficial parotidectomy may still be performed if the clinical picture remains unclear and the concern for a neoplasm is still present. An incisional biopsy should be avoided as this may lead to the formation of a chronic draining sinus. The treatment of parotid TB is medical therapy with antituberculosis regimens.[38–40]

## Developmental Disorders

These are rare disorders that include heterotopic salivary glands, polycystic disease, accessory salivary glands, aplastic glands, and ductal anomalies. Vascular malformations, which include lymphatic malformations, are disorders that arise due to errors in vascular or lymphatic morphogenesis. Despite these being developmental in nature, most reports include these lesions under neoplastic processes. Heterotopic salivary tissue is most commonly found within periparotid lymph nodes but has been located in the middle ear, near the sternoclavicular joint and many other head and neck and distant sites. They may present as a mass or draining sinus, but most often are discovered incidentally during the workup for a different process. These lesions often undergo biopsy, which is both diagnostic and therapeutic. Accessory salivary tissue is most commonly seen with the parotid gland and may be present in up to 56% of patients based on autopsy reports. These accessory lobes often lie just anterior to the masseter muscle and are connected to Stensen's duct by a single accessory duct. This accessory salivary tissue is susceptible to the same pathologic processes as the main gland. Polycystic dysgenetic disease is a rare abnormality of the salivary duct that results in obstructed flow and diffusely cystic parotid lobes. It most commonly presents in females as recurrent painless swelling. Imaging often shows a diffusely cystic gland as opposed to an isolated cystic lesion that is more typical of a neoplasm. A superficial parotidectomy may be performed if needed for biopsy or cosmesis; however, most lesions are conservatively managed. Aplasia of the salivary glands may be complete, partial, unilateral, or bilateral (Fig. 60.7). Patients are usually asymptomatic. Some may present with xerostomia, early dental caries or compensatory unilateral salivary hypertrophy. Examination often reveals the lack of a salivary duct orifice associated with the affected gland. A familial form is associated with lacrimal gland aplasia and the lack of a lacrimal puncta. Technetium scans

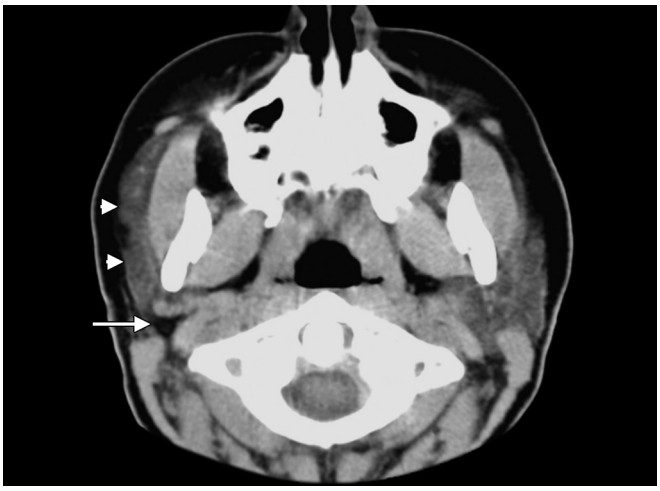


**Fig. 60.7:** Axial contrast-enhanced CT image shows absence of the right parotid gland in the normal location (arrow), with accessory parotid along the course of the right parotid duct (arrowheads).

can demonstrate the loss of uptake in the region of the major salivary gland. Management is symptomatic with increased oral hydration and hygiene with close dental follow-up. Ductal anomalies can include imperforate and duplicated ducts. Imperforate ducts may result in salivary gland swelling and ductal swelling with examination revealing no ductal opening and no expression of fluid with salivary palpation. Marsupialization of the cyst and ductoplasty is often curative.[41]

## Cystic

Cystic lesions of the minor salivary glands are an extremely common finding but those of the major salivary glands are often rare. When cystic lesions do occur in the major salivary glands, they are more frequent in the parotid and may be secondary to inflammation or neoplasm. Nonneoplastic or inflammatory cystic lesions of the parotid include first branchial cleft cysts, dermoids and salivary duct cysts. Minor gland cysts include mucous extravasation and mucous retention cysts.

Dermoid cysts of the parotid are uncommon, with only a few case reports describing their occurrence. Only 7% of dermoid cysts occur in the head and neck region, with most of these occurring along the orbit or submandibular area. Intraparotid dermoid cysts may present similarly to a neoplasm, requiring imaging and possible FNA. Superficial parotidectomy is often both diagnostic and therapeutic.[42,43]

Branchial cleft anomalies are one of the most common congenital head and neck lesion in children. Most of these

are of second branchial origin; however, first branchial cleft anomalies can account for 10–20% of branchial lesions. First branchial cleft anomalies have been classified based on histologic, anatomic, and clinical findings. The Work classification is based on histological findings. A Work type 1 is a cyst of ectodermal origin. A Work type 2 can be a cyst, sinus, or fistula that contains both ectodermal and mesodermal elements. Olsen classified first branchial cleft anomalies on anatomic findings as a cyst, sinus, or fistula. Triglia classified these lesions based on clinical presentation into three types. Cervical lesions may present with an abscess or fistula along level one of the neck, often near the angle of the mandible. Parotid lesions may present as a preauricular mass that may become secondarily infected. Auricular lesions may present as chronic otorrhea with otoscopy revealing a fistula along the floor of the external auditory canal. Most patients will have an associated parotid cyst that is initially diagnosed as a parotid tumor prior to further workup. Radiographic imaging should be obtained to define the extent of involvement. An MRI is often useful to delineate the location of the cyst or tract in relation to the facial nerve. Fifty percent of patients will have had a prior incision and drainage or incomplete surgical excision that often leads to a delay from onset to formal removal by a mean of 3–4 years. Surgical removal with a superficial parotidectomy allows for visualization of the facial nerve and its relation to the cyst or tract. Facial nerve paralysis has been reported in up to 15% of cases, with most of these being temporary and involving the inferior branch.[44,45]

Mucous extravasation cysts, or mucoceles, are pseudocysts that develop secondary to ductal trauma and the release of mucous into the surrounding soft tissue. These cysts can develop anywhere minor glands are present but most commonly are found on the lower lip. Rarely, mucoceles can develop along the ventral tongue involving the glands of Blandin-Nuhn.[46] These lesions present as a painless, fluctuant swelling of the oral cavity. They may appear translucent or bluish, depending on the depth of mucous extravasation. Treatment includes excision of the cyst and surrounding minor salivary glands. One study reported up to 43% of these lesions resolved by three months of observation, most likely by spontaneous rupture.[47] Larger lesions that if excised would lead to greater harm should be marsupialized and with a repeat procedure if necessary. Ranulas are mucoceles that develop along the floor of mouth, often involving the sublingual gland. These may remain intraoral or, at times, may extend beyond the mylohyoid and present as cervical swelling. These are termed plunging ranulas. Simple marsupialization of ranulas often leads to recurrences; thus, the proposed method of treatment is removal of the cyst along with the involved sublingual gland. Other nonsurgical therapies, such as sclerotherapy, have shown variable success in the management of these lesions.[48]

Mucous retention cysts are true cysts that are far less common than mucous extravasation cysts. These lesions develop as a consequence of ductal obstruction, often of unknown cause. A history of recent trauma is not seen as it is with a mucous extravasation cyst. These cysts may also develop within the parotid gland and are called a salivary duct cyst. Treatment is complete but conservative excision.[48]

## Neoplasm

Neoplasia of salivary origin is a rare occurrence accounting for < 10% of all pediatric head and neck tumors. Salivary malignancies compromise 2.5% of malignant tumors of the head and neck.[49] Tumors of the salivary gland can be vascular or nonvascular in origin. Studies that include both vascular and nonvascular tumors of the salivary gland show that approximately 80% of these masses are vascular in origin and, of these, hemangiomas outnumber lymphatic malformations. Pleomorphic adenoma is the most common nonvascular benign tumor of salivary origin, and mucoepidermoid is the most common malignant tumor. Reports demonstrate that up to 60% of nonvascular salivary tumors may be malignant in nature.[50] Of these malignant masses, 88.5% arise in the parotid, 7.7% in the submandibular gland, and 3.8% in the sublingual and minor salivary glands.[51] Despite a higher prevalence of malignancy within the parotid, a mass found with the submandibular gland or minor salivary glands has a higher incidence of being malignant. The mean age at presentation for a salivary tumor is 13 years old for both benign and malignant tumors, and only approximately 20% of salivary malignancies will present in children < 10 years of age. Most patients present with an asymptomatic mass. On examination, these masses are generally firm, mobile, and nontender. Findings suggestive of malignancy are rapid growth, pain, facial paralysis, and palpable lymph nodes.[52] If a neoplastic lesion is suspected, cross-sectional imaging should be obtained with either CT or MRI (Figs. 60.8 and 60.9). Preoperative biopsy by FNA is often useful in surgical planning. If a FNA cannot be obtained, a frozen section specimen at the time of surgery should be performed.

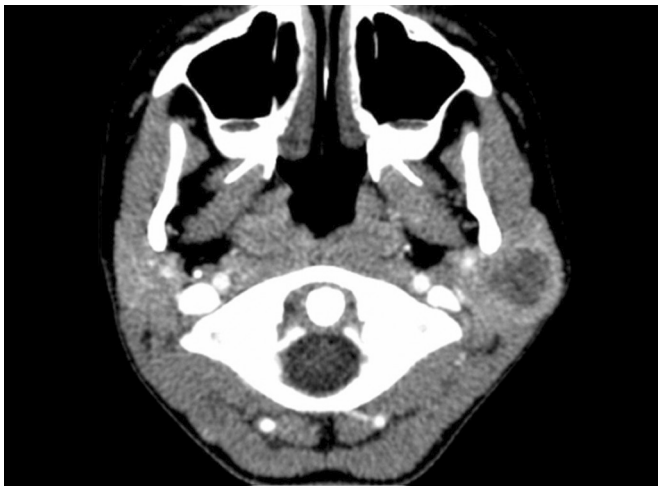


**Fig. 60.8:** Axial contrast-enhanced CT in a 13-year-old child with a palpable left cheek mass shows a well-defined low attenuation mass in the left parotid gland, without overlying inflammatory changes. This mass histologically proved to be a pleomorphic adenoma.

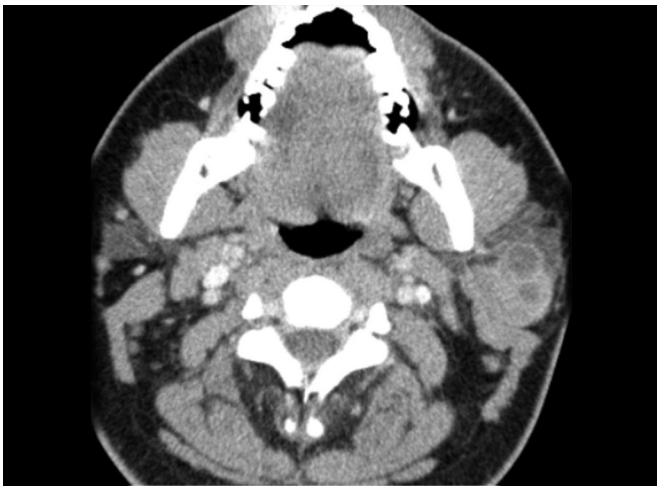


**Fig. 60.9:** Axial contrast-enhanced CT demonstrates a lobulated, mixed attenuation mass within the left parotid gland that histologically was a mucoepidermoid carcinoma.

Surgical vs. medical management of these tumors depends on the histologic type and extent of disease. Fortunately, most malignancies are histologically considered low grade and have a favorable long-term outcome.

## Miscellaneous

Salivary enlargement may be seen in several systemic conditions such as malnutrition, anorexia nervosa, bulimia, diabetes, hypothyroidism, acromegaly, cystic fibrosis, and liver disease. Medications that have been shown to cause SGE include iodine compounds, heavy metals, phenytoin, thiourea, methimazole and phenothiazine. Sialadenosis is a noninflammatory and nonneoplastic process of SGE, associated with an underlying systemic disorder. Bilateral parotid enlargement is most common. It can be associated with any of the above systemic conditions or medications.[41]

Pneumoparotitis is a condition where air flows through Stenson's duct to the parotid gland. It can present as recurrent episodes of acute pain and swelling similar to infectious parotitis. This condition can be seen in musicians who play wind instruments, glassblowers, dental cleaning, coughing during emergence from anesthesia, or in adolescents with psychosocial issues. On examination the parotid may be tender with overlying erythema, fever is not present and palpation may reveal crepitus. Diagnosis requires the finding of air within the parotid on CT scan. Management is with conservative therapy and avoiding the offending agent.[53]

Necrotizing sialometaplasia is a self-limited inflammatory process that mimics a destructive malignancy. Inflammation of palatal minor salivary glands leads to the development of a painless ulcerated nodule. Most lesions will resolve in 3–12 weeks. Due its destructive nature and resemblance to malignancy, most lesions undergo biopsy for definitive diagnosis.[40]

Blunt or penetrating trauma to salivary tissues can result in an acute inflammatory state, sialocele or hematoma formation or ductal injury resulting in chronic inflammatory episodes.

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CHAPTER

61

# Pediatric Sialendoscopy

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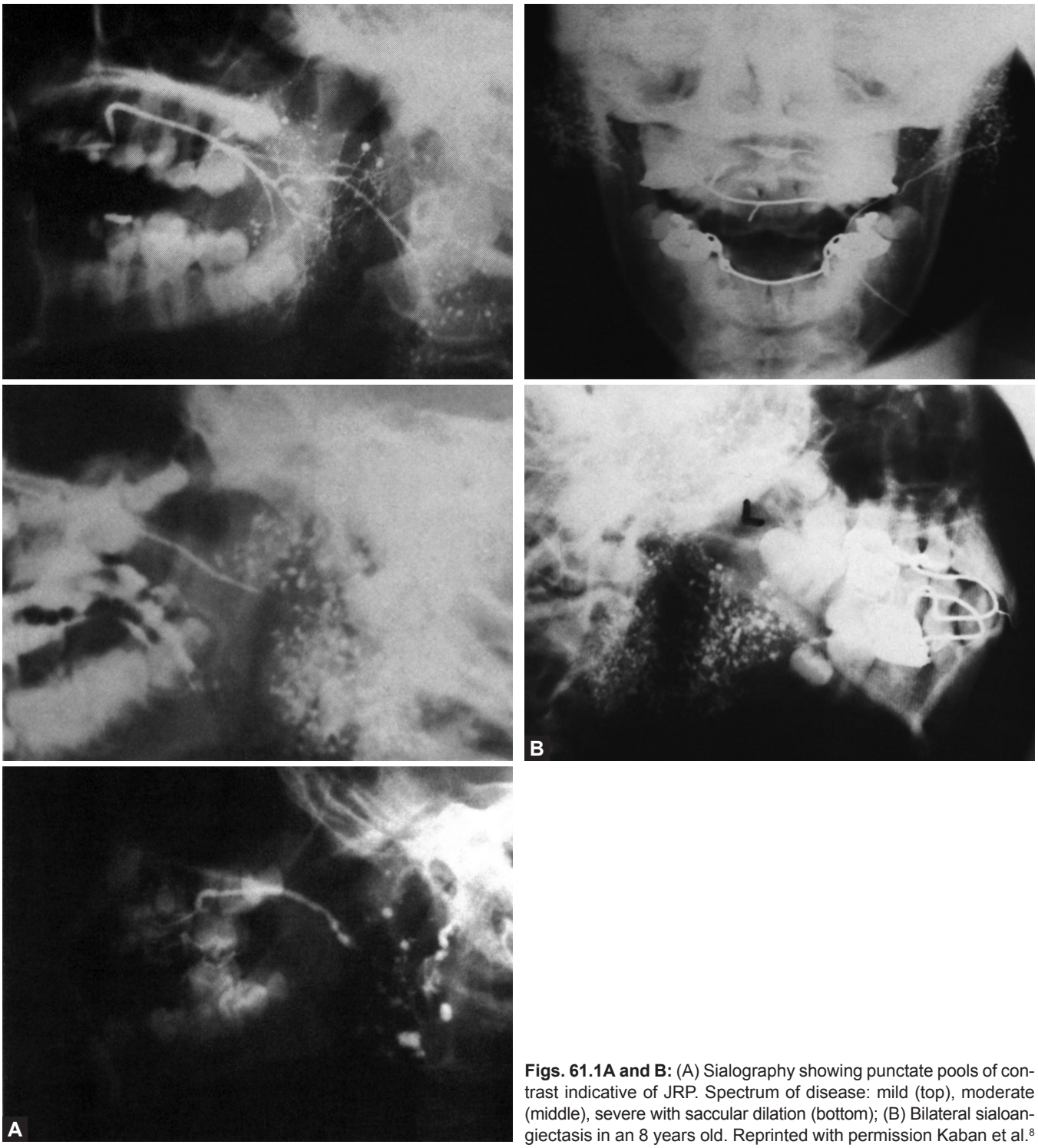
## INTRODUCTION

Sialendoscopy was introduced in the early 1990s as a minimally invasive alternative to standard methods for diagnosis and treatment of inflammatory and obstructive salivary gland disorders.[1] The technique was pioneered in adults; however, advances in instrumentation have allowed this to be adapted to the smaller ductal anatomy found in the pediatric population. Salivary gland disease is overall less common in children than adults, comprising approximately 10% of all cases, but is nonetheless a significant source of morbidity in those affected. Mumps and juvenile recurrent parotitis (JRP), respectively, are the two most common etiologies of salivary gland disease in childhood.[2] Other immunologic or inflammatory conditions, such as Sjögren syndrome and sarcoid, do occur but are rare. The differential diagnosis of recurrent sialadenitis in children also includes HIV associated lymphoepithelial lesions, neoplastic, infectious, and obstructive disorders.[3] Sialolithiasis is seen much less frequently than in adults, accounting for approximately 3–5% of all cases. As with adults, stones in the pediatric population occur most often in the submandibular gland. The vast majority of patients of all ages present with single rather than multiple stones.[4,5]

Prior to the introduction of endoscopy, treatment of salivary gland disease was limited to either conservative methods: antibiotics, sialagogues, massage, warm compresses, maintenance of hydration; or more aggressive surgical procedures: duct ligation, tympanic neurectomy, intraoral duct lithotomy, external adenectomy, all of which are associated with a variety of drawbacks and risks.[6] Endoscopy allows direct visualization of the ductal system for more accurate identification and localization of pathology such as stones, strictures, mucous plugs, kinks, and other anatomic or physiologic abnormalities. Therapeutic intervention is also now possible in many cases by means of stone extraction, dilatation of stenotic segments, ductal lavage with irrigation of debris, and instillation of anti-inflammatory medications.[7]

## JUVENILE RECURRENT PAROTITIS

JRP is a recurrent nonsuppurative inflammatory condition affecting one or both parotid glands, with overall male predominance and peak incidence between ages 3–6 years. There is often associated pain, fever, and malaise. Diagnosis is based primarily on the clinical presentation of recurrent acute gland swelling occurring before age 16, with severity defined by frequency of episodes. Occurrence of episodes is notoriously quite variable. Sialography was commonly used in the past to support the diagnosis, with characteristic 1–2 mm punctuate pools of contrast reflecting sialectasis of the peripheral ducts (Figs. 61.1A and B). These findings are often bilateral even in setting of unilateral symptoms.[6,9-12,38,39] Nozaki[13] evaluated the use of ultrasound as an alternative diagnostic modality in six children, with concurrent sialography performed in two cases. Small round hypoechoic areas measuring 2–4 mm were noted sonographically in 10 out of 12 glands studied; these were present in all clinically enlarged glands and corresponded to ectasia seen on sialography.[13] From a histologic perspective, it is known that affected glands in JRP exhibit sialectasis with periductal lymphocytic infiltration, and these authors speculated that ultrasound




**Figs. 61.1A and B:** (A) Sialography showing punctate pools of contrast indicative of JRP. Spectrum of disease: mild (top), moderate (middle), severe with saccular dilation (bottom); (B) Bilateral sialoangiectasis in an 8 years old. Reprinted with permission Kaban et al.[8]

features reflected areas of ductal ectasia with adjacent lymphocytic cuffing. Shimizu[14] looked at ultrasound findings in comparison with sialography in a larger group of JRP patients (21 glands in 14 patients) who were all examined with both ultrasound and sialography. Their findings also showed that hypoechoic areas in affected glands were uniformly larger than the corresponding sialographic opacities, indicating areas of ductal dilation with associated

lymphocytic infiltration. Their study included a control group of 26 normal volunteers who received ultrasound examination only, and distinctive hypoechoic areas were not observed in these individuals as seen in the JRP group. They concluded that sonography was useful and reliable in the diagnosis of JRP and preferred over sialography.[14] To date, ultrasound remains the favored radiographic modality for this condition. MRI and MR sialography are emerging as potential new diagnostic tools, however, have not shown superiority to date over ultrasound and pose some limitations for use in the pediatric population.[15]

The natural history of JRP follows a self-limiting course with symptoms generally resolving in the majority of cases near puberty, although Nahlieli has suggested that some patients may continue to experience inflammatory symptoms into adulthood.[11] The pathogenesis remains uncertain; however, various theories have included congenital malformations, hereditary genetic factors, viral or bacterial infection, allergy, and local manifestation of an autoimmune process. Ericson et al. proposed that congenital ductal malformation, exacerbated by dehydration, promoted retrograde infection.[16] Chitre et al. concurred, speculating that the parotid gland was preferentially affected due to a lower rate of secretion relative to the submandibular gland.[17] Marchal suggested that there is an imbalance between salivary secretion and clearance in symptomatic glands, with symptom onset occurring in association with increased secretory activity.[18] Capaccio et al.[19] supported an immunologic etiology, possibly related to a mucosa-associated lymphoid tissue (MALT) disorder. They further postulated that adenotonsillectomy may promote an increase in lymphocytic follicular hyperplasia in the salivary glands of susceptible children and that spontaneous resolution of symptoms at puberty may reflect maturation of the MALT immune system.[19] In a retrospective study of 133 patients, Kolho et al.[20] noted that onset of the first episode at an earlier age increased the likelihood of recurrent symptoms. They speculated that symptoms might be related to production of proteolytic enzymes in immature salivary glands, resulting in release of bioactive peptides causing gland swelling and inflammation.[20]

Use of sialendoscopy has aided both the diagnosis and treatment of JRP.[9,18,21,22] Endoscopic findings are very characteristic of the disease and include ductal strictures, mucus plugs, and a white avascular appearance of the duct lumen with lack of normal blood vessel pattern.[2] Treatment has traditionally embraced conservative measures given the self-limited nature of the disease. Use of antibiotics and analgesics in the acute phase has been advocated to ameliorate symptoms and prevent potential damage to the gland itself, even though an infectious cause has not been definitively identified. This is often followed by lower dose prophylactic antibiotics in an attempt to prevent recurrent attacks. Saarinen et al. evaluated 41 patients in a prospective fashion in an attempt to characterize the features of juvenile parotitis and concluded that antibiotics were not indicated.[23] Aggressive interventions including tympanic nerve section, duct ligation, injection of sclerosing agents, parotidectomy, and low-dose radiotherapy were previously reserved for severe cases and are no longer recommended. Galili et al.[24] described substantial therapeutic benefit following sialography in a group of 22 children and 26 glands, with marked decrease in frequency and intensity of episodes in most of the patients. They suggested at that time that the mechanical force exerted during injection of the medium helped to flush and dilate the duct, and that the medium itself might also contribute an antiseptic effect.[24] Katz reported a large series of 840 patients treated with sialography over a 7-year period with very high success rate.[12] Although sialography is now widely accepted as having potentially curative effects in patients with JRP, the use of ionizing radiation and risk of adverse reaction to contrast make this undesirable as a primary therapeutic modality.

Nahlieli et al. was the first to report results of sialendoscopy in JRP patients, demonstrating a high rate of symptom resolution: 92% in a series of 26 cases followed for 36 months.[2] Multiple subsequent studies have also shown clinical improvement following endoscopy. Quenin reported a success rate of 89% in 10 patients and 17 operated glands followed for 11 months.[18] Shacham et al. reported a large series of 70 children in which 93% of patients experienced resolution of symptoms after one procedure.[11] Jabbour et al. had no complications in five glands.[6] Gary et al. reported a series of 3 patients with success in all cases.[25] Konstantinidis et al. reported complete success in four out of seven children, with two children experiencing one recurrence within the first postoperative year and one child requiring repeat endoscopy.[10] Capaccio et al.[19] reported a series of 14 children and 20 glands studied preoperatively with ultrasound and color Doppler. They achieved a successful result in all patients, as defined by reduction in the number of acute episodes. Interestingly, they noted hypovascularization during the inactive phase of the disease using Doppler and hypervascularization during the acute phase, as well as presence of reactive intraparenchymal lymph nodes.[19]

Therapeutic benefit derived from endoscopy is thought to be related to hydrostatic pressure-mediated ductal dilation, lavage of debris under direct visualization, and instillation of anti-inflammatory medications. The goal of endoscopic treatment is to provide symptomatic relief as well as prevent recurrent swelling that may lead to irreversible changes and damage to the gland. Indications for the procedure include at least two clinically characteristic episodes within a 6-month period. Risks specific to this procedure for JRP involve swelling of deep parotid lobe with pharyngeal obstruction secondary to the volume of irrigation instilled, particularly if the procedure is performed bilaterally.

## Obstructive Sialadenitis

Management of obstructive sialadenitis due to lithiasis and ductal stenosis has been enhanced by the introduction of endoscopy.[22,26] Direct visualization of the duct lumen facilitates diagnosis, with ability to define the nature of the obstruction and distinguish entities such as stones, stenoses, ductal kinking, foreign bodies, and mucous plugs. This is of great benefit, as no other single method allows such distinctions to be made. Diagnosis of stones in children can be challenging, as their size tends to be smaller than in adults. Although the clinical presentation is similar, there is concern that missed or delayed diagnosis of obstructive disease may occur in children due to the relative rarity of the condition and lead to more serious sequelae.[27] Chung et al.[28] studied characteristics of adult versus pediatric sialolithiasis. They presented a series of 210 patients, including 29 children, in which they determined that pediatric stones were overall smaller, more distally located in the ducts, and presented with shorter duration of symptoms.[28] Very small stones measuring 2 mm or less may cause obstructive symptoms in a child but remain under the size limit of radiologic or sonographic detection. Martins-Carvalho et al. reported a series of 38 children, in which 6 out of 10 lithiasis cases were missed sonographically due to small stone size.[29]

Treatment for obstructive sialadenitis prior to development of endoscopic techniques largely necessitated open intraoral lithotomy or external gland excision.[8] Such procedures are associated with a variety of risks, including nerve injury, cosmetic deformity, postoperative infection and wound healing problems, inadequate residual salivary production, and duct stenosis. Less invasive nonendoscopic methods, including basket retrieval of stones guided by ultrasound or sialography, have been reported in children.[30] Endoscopic treatment can be rendered at the time of diagnosis by means of endoluminal stone retrieval or dilatation of stenoses with gland preservation, however should not be performed in setting of active bacterial infection due to increased risk for duct perforation. Given the relative rarity of sialolithiasis in childhood, there are few published studies of endoscopic stone retrieval in this population; however, the results are largely positive. Nahlieli et al.[26] reported a case series of 15 children treated endoscopically for stone removal from parotid and submandibular glands without complications or recurrence. Nine patients were treated under general anesthesia, and the remainder under local anesthesia.[26] Faure et al. reported a series of eight pediatric patients with obstruction caused by stones in six cases and ductal stenosis in two cases.[22] Hackett et al. reported a case series of 18 children treated endoscopically for salivary gland disease that included four cases of stones, three of which were detected preoperatively; unfortunately, two patients ultimately required gland excision.[9]

Endoscopic stone retrieval is achieved using an expandable wire basket passed through the working channel; however, this is limited by size of the stone: approximately 3–4 mm in greatest dimension for parotid cases and 4–7 mm in the submandibular gland. Larger stones can be fragmented within the duct lumen using a laser fiber or manual microdrill passed through the working channel, or with lithotripsy. A variety of lasers have been used for this application, including holmium, thulium, erbium, and pulsed dye. This technique is somewhat limited by difficulty in fragmenting the stones and potential thermal damage to the surrounding tissues. External lithotripsy is not currently approved by the FDA for use in the United States, however is seeing popular support elsewhere in the world. Ottaviani et al.[31] in Italy reported a series of seven pediatric patients successfully treated nonendoscopically with extracorporeal shock wave lithotripsy (ESWL) for both intraductal and intraparenchymal stones in parotid and submandibular glands. Complications were minimal, consisting of mild pain, reactive gland swelling, and ductal bleeding. Spontaneous elimination of stone fragments in this study was monitored over time using serial postoperative sonography.[31] Most practitioners, however, now couple ESWL with sialendoscopy to remove intraluminal stone fragments using wire baskets or microforceps passed through the working channel and have achieved similar excellent results. Large stones can also be removed using a combined endoscopic and open approach, utilizing the endoscope to localize the stone and facilitate a targeted lithotomy. Stenoses can

be dilated with inflatable balloons deployed through the working channel, center-hole bougies passed blindly over a guidewire, hydrostatic pressure from the irrigant, and using the tip of the endoscopy itself.[5,7,22,30,37]

## SIALENDOSCOPIC TECHNIQUE

The surgical approach and technical considerations in pediatric patients with nonneoplastic salivary gland disorders are similar to those in adults. The two main indications for sialendoscopy are mechanical obstruction, including lithiasis, mucus plugging, and stenosis due to recurrent inflammatory disease, and unremitting glandular pathology that may benefit from an endoscopic approach, such as sialadenitis related to JRP or Sjögren syndrome. Preoperative considerations include a standard medical work up that would usually be required for anesthesia. Most pediatric patients require general anesthesia; however, local anesthesia or a combination of local anesthesia with monitored sedation is a consideration. This decision should be tailored to the needs of the patient and based on patient comfort, parental input, level of surgical risk, and surgeon preference. The advantages and drawbacks of general anesthesia versus local anesthesia and sedation must be carefully considered prior to surgical intervention. Preoperative counseling and consent should include discussion regarding the possibility of a staged procedure based on findings at diagnostic endoscopy.

Preoperative diagnostic imaging should include salivary gland ultrasound or CT scan of the neck with and without contrast. Surgeons may wish to perform their own sonograms if access to equipment is available. Ultrasonography has the advantage of being more dynamic and repeatable, less invasive, less costly, and useful intraoperatively for stone localization. However, it is highly operator dependent and provides only a focused view of the target structure. Computerized tomography has the advantage of providing a broader view, which can help with orientation and localization of pathology. This is useful, for example, for pinpointing stones within the gland parenchyma versus hilar or ductal stones. The size and shape of a stone can also be more easily determined. Contrast should be used with imaging when a neoplastic process is suspected.

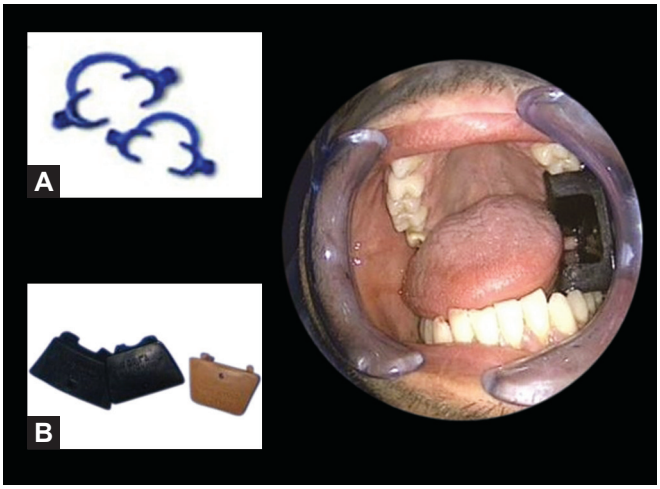
Access to the oral cavity is a very important aspect of successful surgical intervention, and the preferred type of intubation should be discussed with the anesthesia team preoperatively. Nasal intubation is generally recommended, especially for patients who may require a combined approach technique for the submandibular gland or in patients where multiple gland endoscopies are necessary. In other cases, oral intubation with the tube secured to the side opposite the surgical site can provide adequate access. There are a variety of devices available that can be used as mouth retractors or props and enhance access to the oral cavity (Figs. 61.2A and B). Additional considerations to discuss with the anesthesia team include avoiding anticholinergic medications, such as glycopyrrolate (Robinul), to help maintain salivary flow and aid in identification of the papilla.

Surgical technique can be stratified into the following steps:

1. Identification and dilation of the papilla
2. Diagnostic endoscopy
3. Endoscopic interventions
   a. JRP
   b. Salivary stones and strictures
      i. Endoscopic techniques
      ii. Combined approach techniques
4. Stents

### Identification and Dilation of the Papilla

Preoperative identification of the duct opening, with documentation in the patient's medical record, aids intraoperative localization of the duct orifice. Use of magnification, such as with surgical loupes, is also helpful. Massage of the salivary gland externally may express saliva from the duct orifice and facilitate localization. Leurs et al. described the use of methylene blue to identify the papilla, which can be useful in difficult settings.[32] Once the papilla has been identified, the surrounding area may be infiltrated with




**Figs. 61.2A and B:** Disposable cheek retractors (A) aid retraction of the buccal mucosa. Mouth props (B) enhance exposure to the oral cavity by providing stable mouth opening.

local anesthetic, which splints the pliable floor of mouth and can aid the initial dilation process by straightening the distal most portion of the salivary duct. However, this is optional and not necessary in the majority of cases.

After identification of the duct orifice, the next step is serial dilation of the papilla. This can be performed with either metal dilators of progressively increasing diameter or a Seldinger's technique using a guide wire and bougies. There are two metal dilator systems currently available. The Marchal system is sized from No. 0000 (smallest) to No. 8 (largest). Usually, dilation up to a size No. 4 probe allows introduction of a 1.1 or 1.3 mm sialendoscope and dilation to No. 6 allows introduction of a 1.6 mm sialendoscope (Fig. 61.3). The Schaitkin dilator system features fluted metal dilators sized from No. 1 to 5 (Fig. 61.4). The Seldinger's technique involves insertion of a guidewire through the duct orifice followed by serial dilation over the wire using center-hole bougies of increasing diameter (Karl Storz, Tuttlingen, Germany, Fig. 61.5). A system developed by Cook Inc., USA, uses disposable bougies. In this system, an indwelling access sheath replaces the dilator after initial dilation and serves as a surgical port to permit repeated introduction of the endoscope, thereby minimizing trauma to the papilla and duct (Figs. 61.6A to C).

In concept, all techniques involve dilating the first 1–2 cm of the papilla and duct. Once this has been achieved, assessment of the remaining portion of the duct can be performed endoscopically. Introduction of dilators or bougies blindly into the duct should be avoided, as this risks displacing stones more proximally or causing ductal perforations and false passages. In cases where the duct cannot be identified or easily dilated, options include papillotomy or formal duct exploration with marsupialization of the distal duct prior to endoscopy. This usually needs to be followed by stent placement. The type of stents and discussion on stents will be described in following sections.

## Diagnostic Endoscopy

Diagnostic endoscopy is performed following dilation of the papilla. Endoscopes are semirigid and typically range in size from 0.8 mm to 1.6 mm in external diameter. "All-in-one" endoscopes are designed with separate internal channels for irrigation, transmission of fiberoptic elements, and insertion of interventional instruments (Fig. 61.7). Continuous irrigation is necessary during the

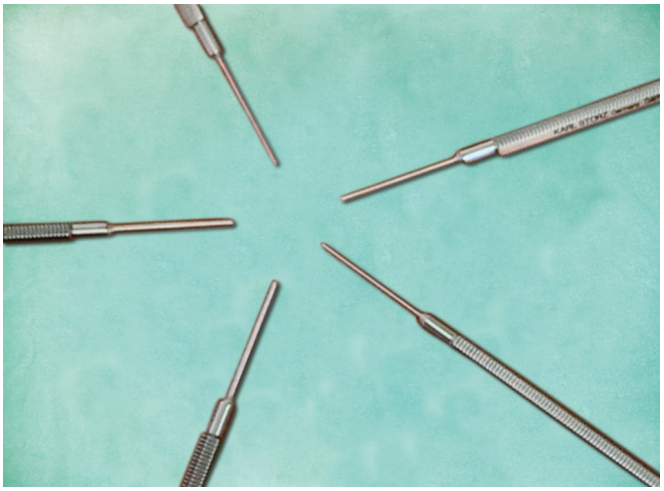


**Fig. 61.4:** The Schaitkin dilators system consists of fluted tip dilators ranging from No.1 to 5.

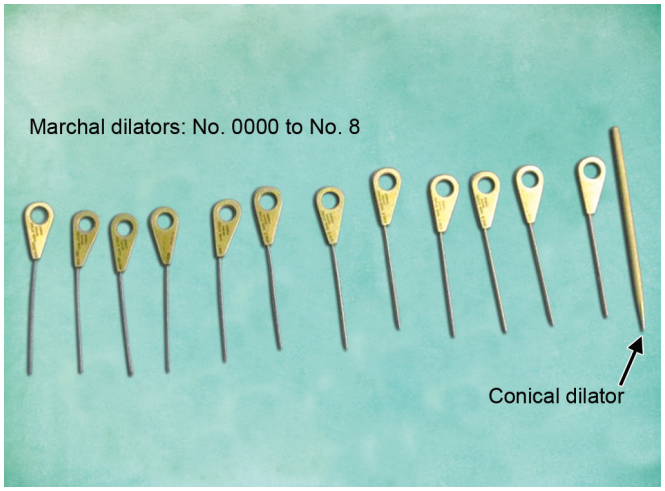



**Fig. 61.3:** The Marchal dilator system consists of metal dilators of increasing diameter from No. 0000 to No. 8. The conical dilator helps to transition between two dilators sizes.

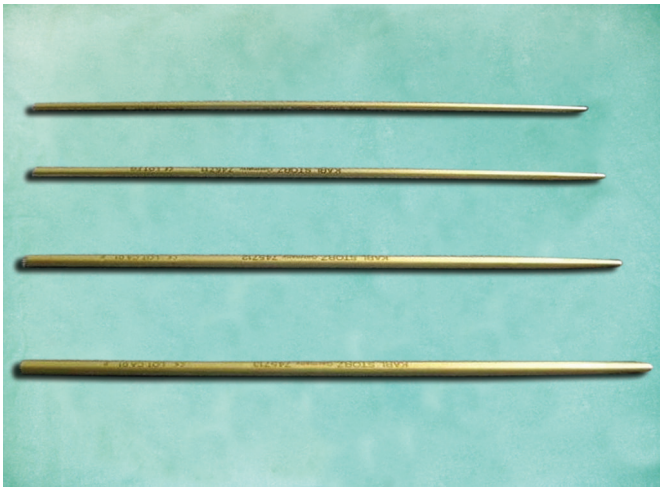
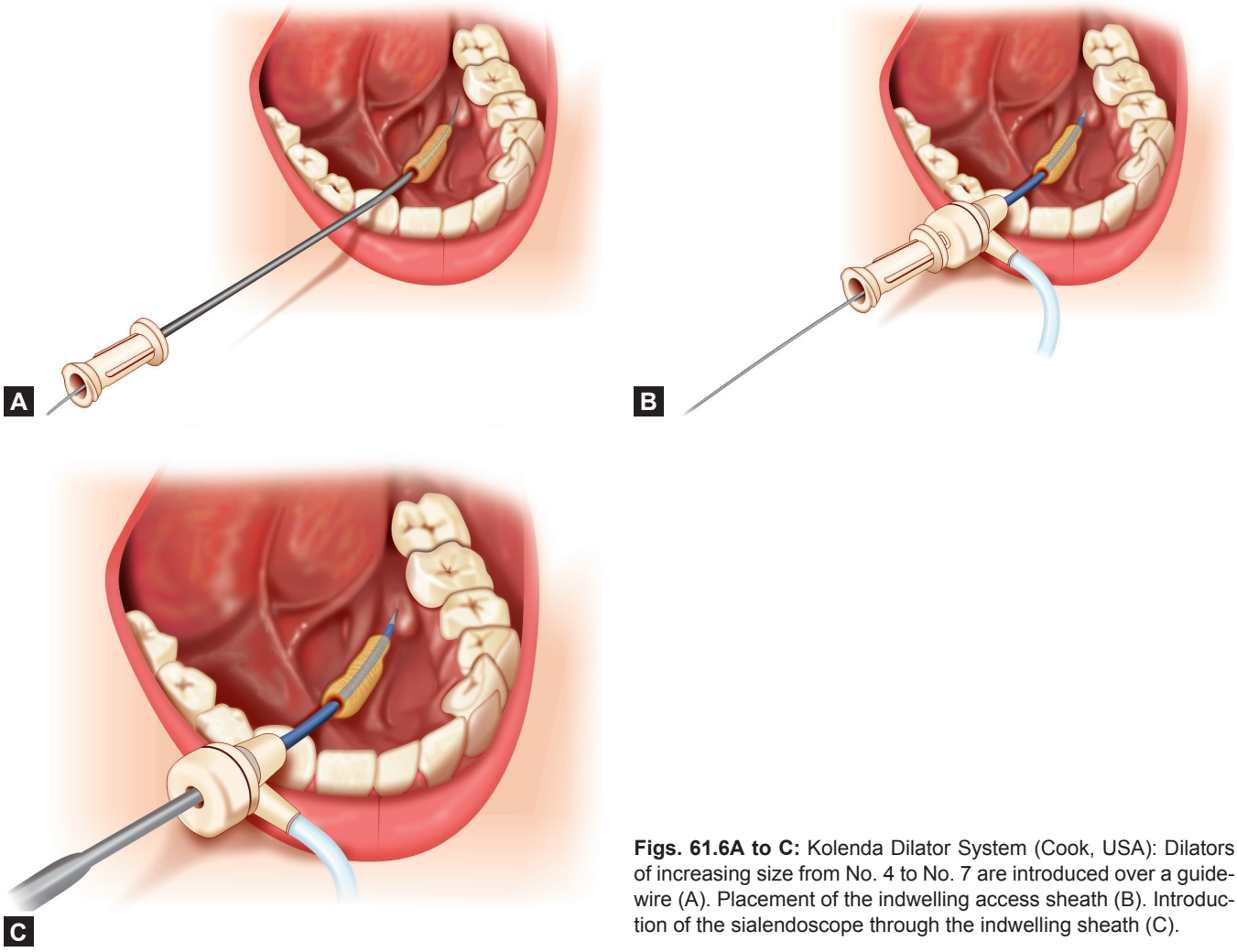


**Fig. 61.5:** Metal bougies of increasing size threaded over a 0.4 mm or 0.6 mm guidewire facilitate dilation of the papilla by Seldinger technique.




**Figs. 61.6A to C:** Kolenda Dilator System (Cook, USA): Dilators of increasing size from No. 4 to No. 7 are introduced over a guidewire (A). Placement of the indwelling access sheath (B). Introduction of the sialendoscope through the indwelling sheath (C).

procedure in order to maintain adequate duct patency for visualization. In the pediatric population, the 0.8 mm diagnostic endoscope is essential for navigating smaller ducts and tertiary branching systems; however, it does not contain an internal working channel through which instruments can be passed. It does allow intervention in JRP patients by means of irrigation of the ductal system and instillation of medications. The interventional capabilities of each endoscope vary but in general, the 1.1 and 1.3 mm sialendoscopes are capable of accommodating 0.4 mm wire baskets for stone removal, hand held micro-burs for manual stone fragmentation, and holmium laser fibers for stone fulguration. They are not large enough to allow introduction of balloon dilators or cup forceps, however such instruments can be introduced through the 1.6 mm sialendoscope. The 1.6 mm endoscope permits use of a larger 0.6 mm, wire basket as well as the Cook indwelling port.

In general, the submandibular ductal system is easier to navigate but more difficult to enter compared to the parotid. One feature exclusive to the parotid duct is the bend it makes over the anterolateral border of the masseter muscle before it penetrates the buccinator and enters the oral cavity. This "masseteric bend" can be manipulated into better alignment to facilitate introduction of the scope by pulling the cheek forward. The submandibular duct bends around the posterior edge of the mylohyoid muscle proximally and can pose a challenge in reaching the hilum of the gland given limited flexibility of the endoscope. Excessive pressure on the scope will result in disruption of the fiberoptic elements. In general, the main salivary ducts branch near the hilum into two or more secondary ductal systems that further branch into tertiary and quaternary ducts; however, the anatomy can vary and the surgeon should be attentive to branch points and accessory openings. When performing diagnostic endoscopy,

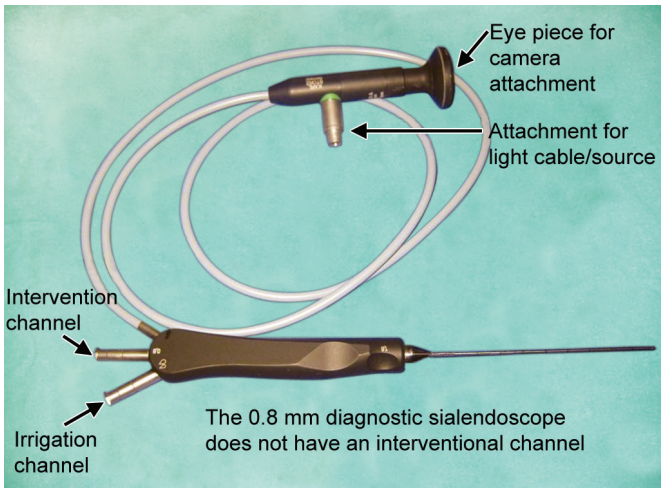
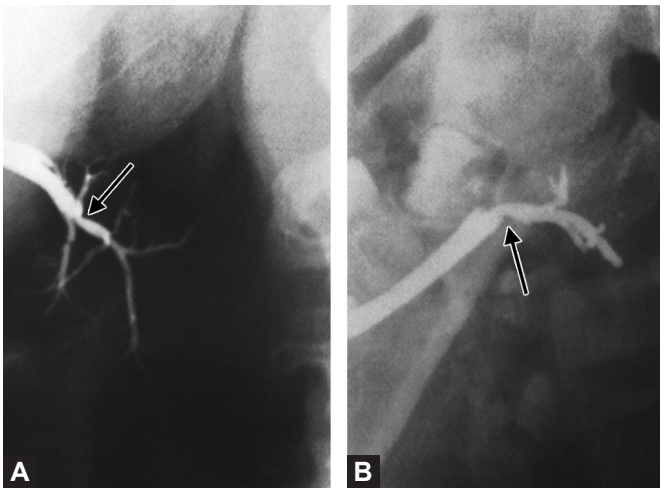



**Fig. 61.7:** All-in-one salivary endoscope with irrigation and interventional channels. 1.1 and 1.3 mm sialendoscopes are most useful in the pediatric population. The 0.8 mm diagnostic endoscope is extremely valuable for diagnostic endoscopy but does not have an interventional channel.




**Figs. 61.8A and B:** Sialogram depicting focal submandibular duct stricture at presumed site of previous obstructing calculus (arrow indicates stricture). Reprinted with permission Kaban et al.[8]

attention should also be paid to the caliber of the ducts, the color of the lumen, and presence of vascular markings versus blanching in the duct wall. In the case of a sialolith, endoscopic evaluation should include assessment of stone size, location within the ductal system, mobility, whether it is partially or completely visible, and associated stenosis. All of these factors influence the success of endoscopic removal. In the event of stenosis, endoscopic findings must be documented and correlated with preoperative imaging to determine whether it represents a localized versus more extensive stenosis before initiating intervention (Figs. 61.8A and B).

## Endoscopic Interventions

### *JRP*

In patients with JRP, treatment involves performing a thorough endoscopy with exploration and irrigation of debris from all negotiable ductal channels (Fig. 61.9). In addition, any obstructing mucus plugs should be removed with endoscopic basket retrieval or grasping forceps. Stenoses can be dilated with the endoscope itself or using the opening/closing action of the wire baskets. In cases where a larger diameter salivary endoscope can be guided to the stenosis, endoscopic balloon dilation may be performed. Blind dilation using bougies over a guide wire risks potential damage to the duct. The extent of irrigation required is gauged by monitoring inflation of the gland externally (Fig. 61.10). The gland may be infused with an anti-inflammatory agent, such as 40 units of Kenalog

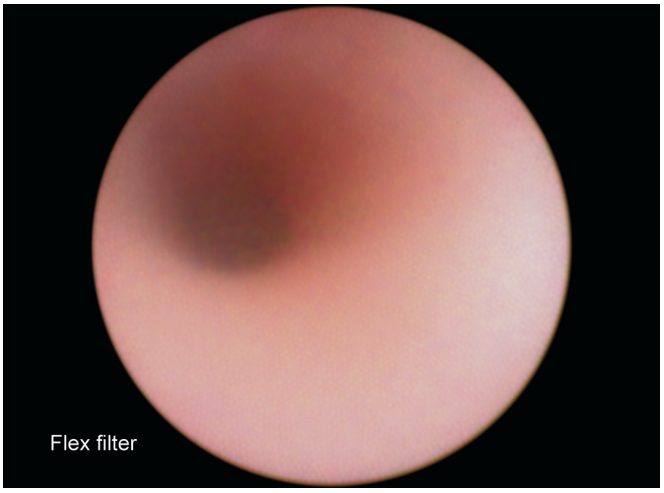



**Fig. 61.9:** Endoscopic view of parotid duct in a patient with JRP demonstrating lack of vascular markings, blanched appearance, and narrow lumen.

(triamcinolone acetate) diluted in 5 mL of saline, which is instilled into the lumen. If papillotomy is required in order to introduce the endoscope or dilation of stenosis is performed, then placement of a stent should be considered. Postoperative gland swelling is generally minor and usually resolves in 2–3 days; however, cases of airway obstruction have been reported due to pharyngeal swelling of the deep parotid lobes bilaterally. Recommendations for postoperative antibiotics and steroid medications are divided across the literature and tend to be surgeon specific, although there is general agreement for use following stent placement.

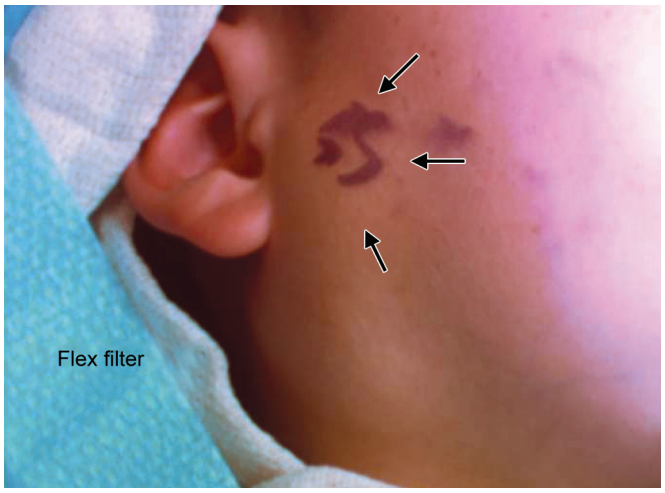



**Fig. 61.10:** Right parotid gland swelling (arrows) in a patient with JRP post sialendoscopy related to irrigation.

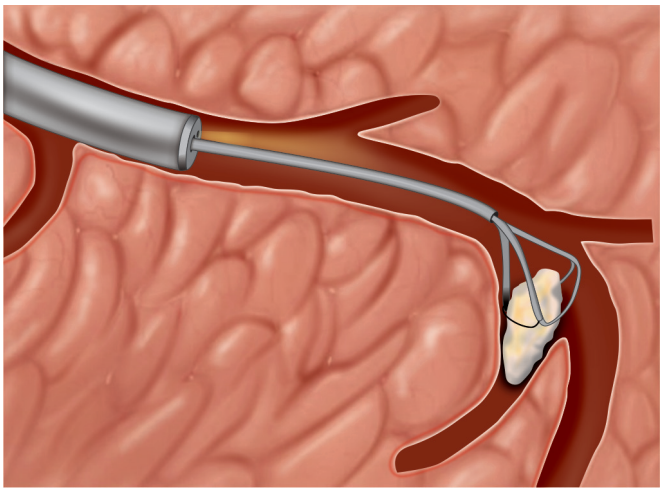


**Fig. 61.11:** Illustration of endoscopic stone retrieval using a forward opening NGage wire basket (Cook, USA).

### *Salivary Stones*

Options for endoscopic stone management include endoluminal removal using wire baskets or retrieval with grasping (alligator or cup) forceps if the stones are free floating or mobile. The criteria for primary endoscopic removal as described above include 3–4 mm stones in the parotid system and 4–7 mm stones in the submandibular system (Fig. 61.11; 61.1). Shape is also a factor, with higher success predicted for retrieval of smooth/spherical and long/thin stones versus irregularly shaped or rough surfaced stones.[33] For intermediate-sized stones, laser fulguration is an option; however, this often requires adjunctive endoscopic removal of stone fragments that would otherwise not pass spontaneously. Another important consideration is stent placement to prevent stenosis from laser-induced ductal trauma. As mentioned, lithotripsy in combination with sialendoscopy is being used outside the United States, with overall positive results reported.[34]

For larger or impacted/immobile stones, hybrid approaches incorporating endoscopic stone localization combined with either transoral or external lithotomy can be applied. With hybrid approaches to submandibular stones, it is important to be familiar with floor of mouth anatomy and the relationship of the lingual nerve to the Wharton's duct. The lingual nerve lies lateral to the duct in the posterior floor mouth but crosses under the duct as it traverses anteromedially. Following stone removal, the ductotomy may be left open to heal, plicated to the overlying mucosa, or reapproximated using microsutures in an interrupted fashion. Similarly, the mucosal incision can be left open or reapproximated with 3-0 interrupted resorbable sutures. Opinion varies as to whether placement of a stent is necessary. Combined approach techniques in the posterior floor of mouth can be technically challenging and newer methods utilizing robotic assistance to facilitate access are currently being evaluated. Results to date have proven to be quite promising, with improved surgical access and visualization as well as excellent outcomes and reproducibility.[35]

Hybrid approaches to parotid stones entail localization with sialendoscopy followed by external excision. Transfacial needle localization using intraoperative ultrasound can also be used. Ultrasound localization of the stone can complement or replace the endoscope when endoscopic stone localization proves difficult.[36] The surgical area is prepared in a sterile fashion to allow for a standard or modified parotidectomy incision with elevation of skin flaps and creation of a separate SMAS flap over the site of the stone. The parotid gland is dissected down to the level of the stone with use of facial nerve monitoring. The stone is identified endoscopically via transillumination, a ductotomy is made, and the stone is delivered through the wound. The duct can then be repaired with 7-0 nylon suture using microsurgical technique. The potential for development of postoperative sialoceles and salivary fistulae adds significant morbidity to the recovery and therefore stenting is recommended. Local injection of 60–100 units of botulinum toxin into the parotid gland and around the site of repair may also be performed. The indwelling endoscope can further be used to flush the duct and check the integrity of the anastomosis. The duct should also be examined for additional stones. Wound closure is performed in a standard fashion using absorbable sutures with an additional layer of closure of the SMAS. Closed suction drainage is recommended; otherwise a pressure dressing should be maintained for 72 h after surgery.

## Stents

Stenting is generally recommended in cases where formal papillotomy or duct marsupialization is necessary to allow endoscopic access, following dilation of stenosis, or after ductotomy and repair performed for stone removal using a combined approach technique. Stents are usually left in place for 2–4 weeks with concomitant broad-spectrum antibiotic coverage. A variety of materials can be utilized, including infant feeding tubes or angiocatheters. Commercial stents are also available in sizes 0.6, 1, 1.5, and 2.0 mm (Hood Laboratories, Pembroke, MA) (Fig. 61.12). The 0.6 and 1 mm sizes are most conducive to the pediatric ductal anatomy and are secured in place with a single anchoring loop stitch that is very helpful for stent retention.

## COMPLICATIONS

In general, sialendoscopy is a safe and effective procedure in the pediatric age group; however, there are several recognized complications that must be borne in mind. Table 61.1 lists the common complications associated with sialendoscopy and their recommended treatment.

The indications and capabilities of endoscopic salivary gland management are evolving rapidly, with emergence of ever newer technology and innovations as well as data on long-term effects of treatment. The advantages and limitations of the procedure must be borne in mind prior to intervention, and patients and parents must be counseled accordingly in order to optimize results and meet their expectations.

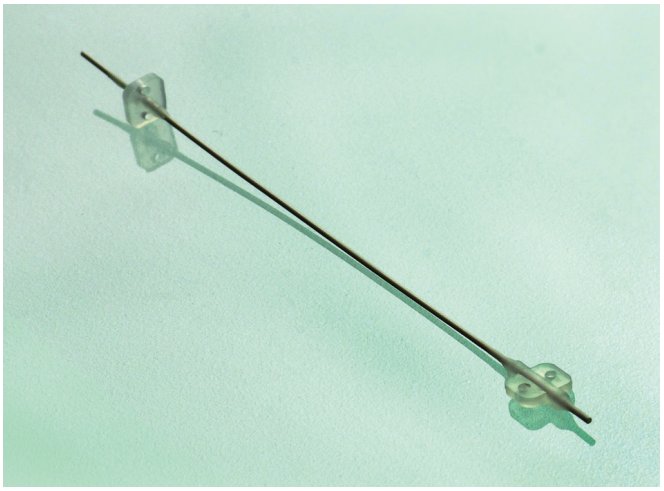


**Fig. 61.12:** Walvekar Salivary Stent (0.6 and 1 mm) double-headed design. The parotid and submandibular flanges facilitate ergonomic placement (Hood Laboratories, Pembroke, MA).

**Table 61.1:** Complications associated with sialendoscopy

| *Complication* | *Treatment* |
|---|---|
| Minor ductal tear | Stop procedure; initiate conservative therapy with antibiotics and anti-inflammatory medications. Anticipate spontaneous resolution without additional intervention |
| Major ductal injury or duct avulsion | Submandibular: duct repair if possible or reanchor duct to the floor mouth. Alternatively ductotomy and marsupialization of the duct to the floor mouth. If not possible then will require salvage via gland excision<br>Parotid: External approach with duct repair or salvage parotidectomy |
| Lingual nerve paresis | Occurs with combined approach for submandibular stones; spontaneous recovery in 2–4 weeks anticipated for neuropraxia |
| Floor mouth edema or parapharyngeal space edema | Related to over inflation of the gland or extravasation of irrigant during endoscopy. Stop procedure. Decompression with a floor of mouth incision and release of fluid collection may be necessary. In severe cases, the patient may need to remain intubated to avoid airway compromise |
| Facial nerve paresis | Not reported to date but remains a risk with external combined approach for parotid stones. Spontaneous recovery expected within 4–6 weeks if facial nerve integrity is maintained |
| Sialocele or salivary fistula | Associated with external parotid stone removal. Aspiration and compression dressings, antisialagogues (Robinul), Botox injection, reexploration and duct repair, salvage parotidectomy, and radiation therapy are consideration depending upon response to treatment or persistent of salivary fistula |
| Nonretrieval of stone or stone fragments | Observation, if symptoms resolve, can be considered. In most cases, a salvage procedure is necessary for stone removal using a combined or hybrid approach versus gland excision |
| Recurrent symptoms despite relief of mechanical obstruction or in JRP patients | Repeat sialendoscopy can be considered if feasible or if previous endoscopy had been beneficial. Alternatively, gland sacrificing procedures may have to be considered |

## VIDEO LEGEND

**Video 61.1:** Endoscopic stone removal using NGage forward grasping stone basket.

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CHAPTER

# 62 Pediatric Sialorrhea: Medical and Surgical Options

***Sam J Daniel***

## INTRODUCTION

Sialorrhea or drooling is the unintentional loss of saliva from the mouth. It is part of a child's normal development and improves gradually as progress is made in oral-motor skills and sensory function. Sialorrhea is considered pathological if it persists after the age of 4 years.[1–3] It is more common among neurologically disabled patients and is typically caused by an inability to swallow saliva frequently or efficiently rather than by an excessive production of saliva (hypersalivation).[1] Sialorrhea can be classified as anterior or posterior. Patients with anterior sialorrhea have visible leakage of saliva into the lower lip and chin areas. Patients with posterior sialorrhea have salivary spillage over the posterior tongue into the laryngeal area, which may manifest as a wet voice, congested breathing, coughing, gagging, and at times, penetration into the airway.[4] The subsequent aspiration pneumonia can be life-threatening.[5]

Drooling affects the quality of life of patients and their caregivers often secondary to psychological and physical factors. Medical complications include skin chapping and perioral infection, choking, aspiration, pneumonia, dehydration, feeding and speech issues, as well as damage to books and communication devices.[6] Drooling can also cause loss of self-esteem, social isolation, and in certain cases, it can interfere with the patient's daily care and rehabilitation therapies.

Sialorrhea can vary in frequency (occasional, frequent, or constant) and in severity (from mild to profuse). There are several measurement tools to quantify the extent of drooling and its impact on the patient and the caregiver. These include weighing cotton pledgets placed in the mouth, counting or weighing bibs, the Teacher's Drooling Scale, the Drooling Frequency and Severity Scale, the Visual Analogue Scale, and the Drooling Impact Scale[7–10] (Table 62.1).

The drooling quotient is calculated by determining, for every interval of 15 s, the presence or absence of drooling over a 10-min period. Drooling is defined as a drip of new saliva present on the lip margin or a string of saliva dropping from the area of the mouth. The drooling

**Table 62.1:** Examples of scales to assess drooling severity and frequency

| | | *Drooling severity and frequency scale* | | | |
|---|---|---|---|---|---|
| *Teacher drool scale* | | *Severity* | | *Frequency* | |
| *Grade* | *Finding* | *Grade* | *Finding* | *Grade* | *Finding* |
| 1 | No drooling | 1 | Dry | 1 | Dry |
| 2 | Infrequent drooling, small amount | 2 | Mild (wet lips) | 2 | Occasional drooling |
| 3 | Occasional drooling, on and off all day | 3 | Moderate (wet lips and chin) | 3 | Frequent drooling—every day |
| 4 | Frequent drooling, but not profuse | 4 | Severe (clothing wet) | 4 | Constant drooling—all day |
| 5 | Constant drooling, always wet | 5 | Profuse (wets environment) | 5 | Constant drooling—wet pillow |

quotient is expressed as a percentage of observed drooling episodes over the total number of intervals. A recent study has found the Drooling Quotient calculated over a 5-min period to be equivalent to the 10-min score as an accurate representative measure of anterior drooling. This modification saves time without affecting the accuracy of this objective drooling measurement.[10]

Several treatment options are available to manage children with sialorrhea. These include rehabilitative therapies such as oral motor and behavior therapy. Pharmacotherapy can be useful; however, it can cause many side effects. Other options include botulinum toxin injection into the salivary glands, radiotherapy, custom-made orthotic devices, and surgery. The plethora of possibilities is a testament to the lack of a single, universally accepted effective treatment.

## ANATOMY AND PHYSIOLOGY OF THE SALIVARY GLANDS

Between 0.5 and 1.5 L of saliva is secreted daily, depending on the size of the child.[11] These are produced by three pairs of major salivary glands: the parotid, the submandibular, and the sublingual glands, as well as hundreds of minor salivary glands. Each salivary gland is an aggregate of secretory units made of acini and ducts. Saliva produced by the secretory cells of the acini, passes through intercalated, intralobular, and excretory ducts, before ending in the main excretory duct of the gland.

The parotid gland consists of predominately serous acini secreting a watery fluid that makes about 25% of the total saliva produced at rest. This production increases significantly in response to eating and drinking. The submandibular gland is composed of a mixture of serous and mucinous acini, whereas the sublingual gland and minor salivary glands contain predominantly mucinous acini secreting thick mucinous fluid. About 70% of the saliva produced at rest is a high-viscosity fluid produced at a constant rate by the submandibular and the sublingual glands. The other minor glands produce 5% of the saliva.

Salivary flow is controlled via the autonomic nervous system. The secretomotor innervation of the parotid gland originates from parasympathetic preganglionic fibers that arise in the inferior salivatory nucleus of the medulla. These fibers travel with the ninth cranial nerve, leave the glossopharyngeal nerve as Jacobson's nerve and pass through the middle ear over the cochlear promontory before exiting the temporal bone as the lesser petrosal nerve. The latter exits the middle cranial through the foramen ovale, and the preganglionic fibers synapse in the otic ganglion. The postganglionic fibers travel with the auriculotemporal nerve to supply the parotid gland. The submandibular, sublingual, and minor salivary glands receive parasympathetic secretomotor innervation from preganglionic fibers originating in the superior salivatory nucleus of the pons. The latter leave the brainstem as the nervus intermedius to join with the facial nerve. They then leave the facial nerve with the chorda tympani in the mastoid segment, passing through the middle ear, and petrotympanic fissure into the infratemporal fossa. The presynaptic fibers are carried by the lingual nerve before they synapse in the submandibular ganglion. Postganglionic fibers innervate the submandibular and sublingual glands. All the parasympathetic postganglionic nerves release acetylcholine. Sympathetic innervation of the salivary glands takes place via preganglionic nerves in the thoracic segments T1-T3, which synapse in the superior cervical ganglion. Postganglionic sympathetic innervation is through the external carotid plexus, with postganglionic neurons releasing norepinephrine, which is received by β-adrenergic receptors on the acinar and ductal cells of the salivary glands. Parasympathetic stimulation is responsible for the secretion of large amounts of a low-protein, serous saliva. Sympathetic stimulation leads to the secretion of a small and variable amount of thicker saliva.

Saliva is composed mainly of water (99%), electrolytes, proteins, and enzymes. Its high content in bicarbonate is responsible for its relative alkaline pH of 7.4. Saliva plays a role in maintaining moisture within the oral cavity, food lubrication, and bacterial inhibition due to its lysozyme and immunoglobulin content. Saliva also helps to protect the teeth from decay and to prevent gingivitis, and salivary enzymes initiate carbohydrate digestion.[12]

The smaller the salivary gland, the more mucinous is its salivary output. Parotid gland secretions are mostly serous with high water and relatively lower mucin content. In contrast, the submandibular and sublingual gland secretions are more viscous with mixed mucous and serous saliva. Resting salivary secretions are produced predominantly by the submandibular glands. The parotid is the main contributor to stimulated saliva, with salivary flow increasing with the thought, sight, smell, and taste of food.

## COMMON ETIOLOGIES OF SIALORRHEA

Sialorrhea can be caused by a number of factors. This includes reduced neuromuscular control of the tongue, oral, and oropharyngeal structures. Also decreased swallowing or poor efficiency of the swallowing mechanism can be major contributors. Other factors include general hypotonia, altered concentration, inability to maintain an upright position of the head and trunk, orthodontic and occlusion issues, macroglossia, decreased orofacial sensory perception and feedback and obstructed nasal passages. Common causes of sialorrhea in pediatric patients include cerebral palsy (CP), developmental delay, mental retardation, and neuromuscular disorders. Over half of CP patients attending special schools have been found to drool and a third suffer from severe drooling.[13] Factors contributing to sialorrhea in this group include the integrity of oral structures, oropharyngeal motor function, rate of salivary secretion, and sensory and cognitive awareness of drooling.[14] Occasionally sialorrhea can be the result of increased saliva productions. This can be caused by oral inflammation or irritation (gingivitis, infection, oral ulcers, trauma, and appliances), gastroesophageal reflux disease, and medication side effects. Drugs that can lead to cholinergic stimulation and increased secretions include antipsychotics—especially clozapine and risperidone, certain anticonvulsants, bethanechol, and nitrazepam.

## APPROACH TO THE PATIENT WITH SIALORRHEA

All patients should be examined for perioral skin erythema, irritation, or maceration. A complete assessment of the nasal airway should be performed to detect narrowing or blockage. The oral cavity should be examined for ulcers, gingivitis, oral hygiene, dental caries, macroglossia, tongue thrusting, malocclusion, and orthodontic problems. The head and body posture should also be assessed as well as the efficiency of the swallowing mechanism, and the chest should be auscultated. A thorough evaluation of the severity and frequency of drooling should be performed and its impact on the patient's health as well as its psychosocial impact on the patient and the caregivers should be measured. Knowledge of the underlying etiology and its natural progression is essential. In most referred cases of anterior drooling under the age of 4 years, a conservative approach is in order as most will improve over time. Also, for many patients with underlying neurological conditions, a delay in oral motor function can persist up to 6 years of age, which should be taken into consideration before offering patients a surgical option.

In view of the multifactorial etiologies of sialorrhea and the proven benefits of treatment with multiple modalities, evaluation by a multidisciplinary team is optimal.[1] Team members may include a pediatric otolaryngologist, a pediatrician, an occupational therapist, a speech and language pathologist, a dentist, a neurologist and a social worker; the goal being to offer each patient a number of rehabilitative, medical, and surgical options, based on a consensus recommendation of the team in partnership with the patient and the caregivers.[1] In the author's multidisciplinary saliva management clinic, all patients are seen separately by the rehabilitation team, the medical team and the social worker. Each team makes its individualized assessment, analyzes factors that contribute to the drooling, and identifies strategies to address these factors. Subsequently, all team members meet as a group with the family and recommend a consensus approach that best suits the child's needs and setting. Medical and rehabilitative options are initiated on the very same day and treatable underlying contributing factors are addressed immediately. The latter can include nasal obstruction from adenoid hypertrophy or allergic rhinitis, gastroesophageal reflux disease, gum disease or caries. The patient's medications are scrutinized and those with hypersalivation side-effects are eliminated or substituted if possible. Patients who are not candidates for medical or rehabilitation options or who failed these treatment modalities are scheduled for surgery. Follow-up visits are preset in order to assess the progress of the child.

## TREATMENT OPTIONS FOR SIALORRHEA

### Conservative Measures

Different compensatory strategies can be used in cases of mild drooling. For example, a slant-board desk can be used to facilitate proper head alignment. Protective plastic film can be placed on book covers and keyboards. A picture can be placed on a child's desk at school as a visual reminder to close his/her mouth or to swallow. If a child is able to wipe his mouth, a terry cloth wristband may be more socially acceptable than bibs. Also a gentle dab across the mouth and chin instead of a wiping movement leads to less local stimulation to the salivary glands.[15] The child can also wear scarves, or dark turtle necks on which the saliva is less visible.

## Rehabilitation Options

Rehabilitation treatment options include exercises to improve head and trunk posture and control, oral-motor therapy (OMT) to improve oral control, sensory therapy to improve oral sensitivity and behavior therapy. All of these programs are noninvasive and safe.

OMT relies on a number of activities and exercises in order to improve the strength of the oral, buccal, and facial muscles.[16,17] The goal is to improve lip and tongue mobility, lip closure, jaw stability, oro-motor coordination, and swallowing of saliva. Active exercises used in OMT include active range of motion, stretching, and strength training. These exercises are used to increase endurance, and strength through the recruitment of additional motor units as muscle fibers are enlarged.[18,19] Passive exercises used include massage, vibration, and passive range of motion with the goal of reducing abnormal oral reflexes, improving muscle tone, and desensitizing the oro-buccal area. While a limited number of studies describe the various techniques, there is paucity of data in the literature on the long-term effectiveness of oral motor therapy.[20–22] Our experience at the multidisciplinary saliva management clinic is that OMT is more effective in younger children with mild to moderate oral dysfunction. Also the benefits seem limited in children with severe disabilities, it takes several months before an improvement is appreciated, and it requires time and energy commitment from the caregivers as the child will require significant long-term encouragement and support. Finally, we have found that OMT increases the success of other treatment modalities when used concurrently.

Oral-sensory therapies utilize the application of heat, cold, electrical stimulation, high-frequency vibration, or other agents to muscle tissues. This is to enhance sensory awareness and ultimately improve the swallow response.

The goal of behavior therapy for drooling is to increase targeted behaviors, such as swallowing, closing the mouth, wiping the chin, controlling the head and self-monitoring. Behavioral approaches may be divided into five main categories. The first four were detailed in a review from Van der Burg,[23] the last type was recently adapted and validated for the treatment of drooling by our group. These techniques are described in Table 62.2. While proven effective for many candidates, behavioral therapy cannot be used in patients with severe mental retardation and requires a significant time commitment from the patient and the caregiver. Also in our experience a number of patients can relapse on long-term follow-up, particularly if they have new stressors in their life (change of school setting, parental divorce).

## Medical Treatment

### *Pharmacotherapy*

Drug therapy consists mainly of agents that block the cholinergic muscarinic parasympathetic receptors in the

**Table 62.2:** Behavior therapies used in the treatment of drooling

| | *Type of behavior therapy* | *Detail and impact of the strategy used* |
|---|---|---|
| 1 | Instruction, prompting, and positive reinforcement | The patient is instructed or prompted to accomplish a specific action, e.g. swallowing his saliva. Following a successful performance, the patient is given a reinforcing stimulus, such as a positive remark, or a token[24] |
| 2 | Negative social reinforcement and declarative procedures | The patient is given an aversive stimulus (verbal reprimand) or a punishment through overcorrection when drooling (e.g. to wipe the chin 10 times after each drool).[25] This technique is never used by our group due to the aversive nature of this approach |
| 3 | Cueing techniques | The patient is presented with an auditory, visual, or tactile signal with the goal of providing reminders in order to increase the frequency of swallowing and/or wiping.[26–28] The long-term target is for the response to become automatic without the requirement for the cue |
| 4 | Self-management procedures | The patient is taught to develop independent internal control of drooling by self-monitoring and self-evaluating his physical appearance, in order to self-initiate an appropriate response, and to self-reinforce both the response and the physical appearance[29,30] |
| 5 | Cognitive Orientation to Daily Occupational Performance (CO-OP) | The patient is taught a structure toward skill acquisition: starting with identifying an objective or skill to be learned; identifying strategies to achieve that goal; carrying out the plan; checking that the plan was effective. This approach was developed by Polatajko for patients with motor impairment,[31,32] and was adapted for the first time for the treatment of drooling by our group, with great success in children presenting with a motor impairment while having intact cognitive abilities[33] |

salivary glands. While successful at decreasing salivary secretion, they do not address the swallowing dysfunction and they lack selectivity resulting in widespread and undesirable side effects. The latter include behavioral changes (restlessness, irritability), constipation, xerostomia, drowsiness, blurry vision, and urinary retention.[34] Several agents have been proven effective (Table 62.3) with the most studied being glycopyrrolate. One advantage of the latter over scopolamine and benzhexol is its inability to cross the blood–brain barrier, thus minimizing central adverse effects such as sedation, restlessness, and dysphoria.[37] Contraindications include glaucoma, gastrointestinal obstruction, and obstructive uropathy. A recent prospective, randomized, double-blind, crossover, placebo-controlled clinical trial demonstrated scopolamine efficacy in controlling drooling in severely disabled patients.[36] In another trial, all children tolerating glycopyrrolate demonstrated marked improvement in drooling.[34] Adverse effects including behavioral problems, constipation, xerostomia, and urinary retention, lead 20% of the patients to discontinue their medication.[34] Over half suffered these side effects while they were still receiving the lowest dosage level of 0.04 mg/kg.

Table 62.3 lists commonly used medication for sialorrhea in children. Dosing of these agents has to be done carefully and patients monitored long-term for potential side effects. Our approach is to start with the lowest possible dose and gradually increase it over the following weeks. We also find that most patients can skip the evening dose as drooling is not a major issue for them at night.

### *Botulinum Toxin*

Botulinum toxin injection to the salivary glands is an emerging safe and effective treatment option for sialorrhea.[1] Our group was among the first to perform this treatment as an outpatient procedure, without the need for general anesthesia in pediatric patients. We also pioneered the use of botulinum toxin injections in newborns with chronic and severe aspiration, with the ultimate goal of preventing a tracheostomy.[5] While seven antigenically distinct botulinum neurotoxins designated type A through G have been identified, botulinum toxin A (BoNT-A) is the most commonly used. Botulinum toxin works by preventing the presynaptic release of acetylcholine from the secretory parasympathetic nerve terminals through inactivation of SNAP-25. The latter is a 25-kDa synaptosome-associated protein essential for the fusion and release of acetylcholine-containing vesicles at the cell membrane. Botulinum toxin induced parasympathetic denervation of the gland occurs 2–3 days after the injection and lasts for approximately 3–9 months depending on the dosage, the injection technique and the patient's response. When reading the literature, it is extremely important to be vigilant as to the manufacturer and the dosing utilized, as for the same type of botulinum toxin (e.g. type A) various commercial preparations differ in terms of molecular structure and/or manufacturing processes. For example, the two distinct serotype A botulinum toxin products, onabotulinumtoxin A (Botox) and abobotulinumtoxin A (Dysport), and the serotype B botulinum toxin product rimabotulinumtoxin B (Myobloc) have all been used for the treatment of drooling and their doses are noninterchangeable.

In April 2009, the FDA updated A Boxed Warning for all approved botulinum toxin products highlighting the possibility of experiencing potentially life-threatening distant spread of toxin effect from the injection site. This can lead to dysphagia, aspiration pneumonia, muscle weakness, and death. Despite these potential side effects,

**Table 62.3:** Medication used in the treatment of sialorrhea

| *Medication* | *Dosage* | *Side effects* |
|---|---|---|
| Glycopyrrolate | Start with doses of 0.04 mg/kg/dose 3 times a day with gradual increases occurring no more frequently than once a week to reach a maximum dose of 2.4 mg for children weighing < 30 kg, and 3.0 mg for children weighing > 30 kg[34] | Xerostomia, blurred vision, irritability, behavioral changes, urinary retention, and constipation |
| Benztropine | Initial dose 0.5–1 mg per day<br>Dose gradually increased to a mean dose of dose 3.8 mg per day[9] | Xerostomia, blurred vision, tachycardia, urinary retention, constipation, irritability, listlessness, Insomnia |
| Trihexyphenidyl Benzhexol hydrochloride | 2–3 mg given twice per day[35] | Dizziness, blurred vision, and urinary retention |
| Scopolamine | 1.5 mg skin patch applied on the mastoid process for 72 h[36] | Xerostomia, blurred vision, irritability, somnolence, urinary retention, constipation, rash at site of application, temporary psychosis |

botulinum toxin injection has been shown by our group to be a safe and effective treatment for sialorrhea when done using a guided technique such as ultrasound. A review of our experience consisting of 1,200 injections revealed no deaths and no major morbidities related to onabotulinum toxin A injection in our clinic.[1] In a recent retrospective cohort reported by another group, few patients developed aspiration pneumonia, loss of motor control of the head, and severe dysphagia resulting in five hospitalizations and two nasogastric tube insertions.[38] However, the latter study used a dosage that is more than double of the dosage we utilize. This highlights the importance of future studies on dosing, dilution, and injection techniques to improve the safety of this intervention.

Despite the fact that Botulinum toxin is a clinically effective therapy that improves drooling severity in patients with sialorrhea, data are still lacking as to the best technique and dose required to achieve optimal outcomes.[39] In our experience, 10% of patients did not respond, regardless of the dosage used.[1] Also, performing the injection under guidance is extremely helpful due to the variability in anatomy, including occasional aplasia of one or more salivary glands.[40]

### *Radiotherapy*

Radiotherapy can be effective because serous acinar cells are sensitive to ionizing radiation. Andersen[41,42] published his successful treatment of severe drooling in patients with amyotrophic lateral sclerosis patients and a life expectancy under 2 years. He performed irradiation of the larger part of the parotid glands and the posterior part of the submandibular glands with 7.0–7.5 Gy in a single fraction. This reduced drooling significantly and led to permanent xerostomia in only one patient. Radiation use remains controversial because of its serious side effects of mucositis and osteonecrosis, as well as the long-term risk of malignancies.

## Surgical Treatment

Surgery is generally considered in patients who fail conservative, rehabilitative, and medical interventions; patients with severe to profuse anterior drooling that are older than 6 years; patients with posterior drooling causing choking or aspiration; and patients requiring chronic and frequent care to manage secretions.

Surgical treatment may include options other than salivary surgery such as adenoidectomy +/- tonsillectomy, turbinate reduction, tongue reduction (in cases of severe macroglossia preventing adequate mouth closure), and craniofacial or orthodontic surgery.

Surgical options for drooling can be classified as procedures to divert saliva such as duct relocation and procedures to reduce the amount of saliva such as duct ligation or submandibular gland ablation. Pros and cons of common interventions are listed in Table 62.4. It is very difficult to compare the success rates of different types of surgery due to the variability across studies in sample sizes, factors contributing to drooling and tools for outcome measurement.[43] Our approach is to discuss these procedures with the family and decide jointly on the best option for the child. It is crucial to organize a dental examination and follow-up due to the potentially increased postoperative risk of dental caries.[44]

**Table 62.4:** Surgical treatment options for sialorrhea

| *Type* | *Procedure* | *Pros* | *Cons* |
|---|---|---|---|
| Salivary diversion | Submandibular duct rerouting | No facial scar, decreases anterior spillage of saliva, most secretions at rest originate from the submandibular gland, less risk of xerostomia | Ranula if sublingual gland is not excised, risk of torsion & obstruction of duct, increased risk of aspiration, longer hospitalization |
| | Parotid duct rerouting | No facial scar, decreases anterior pooling of saliva | Obstructive duct and sialocele, risk of chronic parotitis |
| Salivary reduction | Gland excision | Reliably decreased amount of saliva, excellent choice in cases of severe aspiration | Xerostomia, risk of injury to lingual, facial, and hypoglossal nerves |
| | Ductal ligation | No facial scar, decreased surgical time, less surgical dissection | Sialocele or sialoliths, risk of fistulization, risk of xerostomia |
| | Tympanic neurectomy | No facial scar, easy to perform, low morbidity | Sialorrhea frequently returns to preoperative level within 6 months |

### *Submandibular Duct Relocation with Sublingual Gland Excision*

This procedure has been popularized by Crysdale.[2,45] It starts by raising an island of mucosa encompassing both submandibular papillae. The underlying ducts are dissected free all the way posteriorly until the level of their entry into the submandibular gland. The sublingual gland is excised using blunt dissection in order to separate it from the inner aspect of the mandible and from its mucosal and muscle attachments. Care is taken to avoid injuring to the lingual nerve. A tunnel is created from the anterior face of the submandibular gland to the tonsillar fossa bilaterally. The ducts are then pulled through this submucosal tunnel and sutured to the posterior surface of the anterior tonsillar pillar.

The addition of sublingual gland excision to the submandibular duct relocation (SDR) procedure has decreased the rates of complications requiring secondary surgery. In a large study of 475 patients that compared both groups no ranulas occurred in the SDRSGE (submandibular duct relocation with sublingual gland excision) group as opposed to an almost 9% incidence of ranulas in the SDR group. Also the secondary surgery rate for persistent drooling was fivefolds higher in the SDR group (10% for SDR compared to 1.9% for SDRSGE group).[45]

Interestingly, in the same study, 6 out of 11 patients who completed a salivary gland nuclear scan post-SDR had no function in either one or both submandibular glands.[45] This raises the possibility that some of the efficacy in decreasing sialorrhea post-SDR might be in fact attributed to a ductal blockage due to rotation or kinking during the repositioning into the tonsillar fossa.

### *Duct Ligation*

Salivary duct ligation is a well-established treatment modality for the management of sialorrhea. Options include ligation of Wharton and/or Stenson's ducts. Parotid duct ligation begins by cannulation of the duct with a probe. A small elliptical incision is made 5 mm anterior to the papilla (Fig. 62.1). After dissection and identification of the duct close to the duct orifice, a clamp is inserted around the duct, the probe is removed, and surgical clips are placed (Fig. 62.2). The buccal mucosa is closed.

Submandibular duct ligation begins with a small mucosal incision 1 cm behind the papillae. The ducts are identified and dissected from surrounding tissue (Fig. 62.3). A clamp is placed around the duct and clips are applied (Fig. 62.4). The mucosa is closed with simple interrupted absorbable sutures.

Several authors have reported their series post ductal ligation. Surgical options include ligation of both parotid ducts, ligation of both submandibular ducts, ligation of one parotid and two submandibular ducts, and ligation of all four ducts (both submandibular and both parotid ducts).[46–49] Multiple studies have documented a good success, including a highly significant reduction in

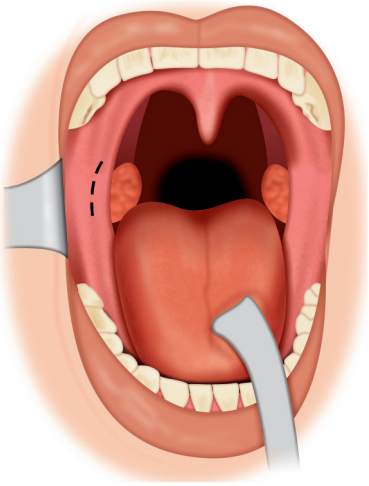

**Fig. 62.1:** Schematic diagram showing the location of incision anterior to the parotid duct orifice.

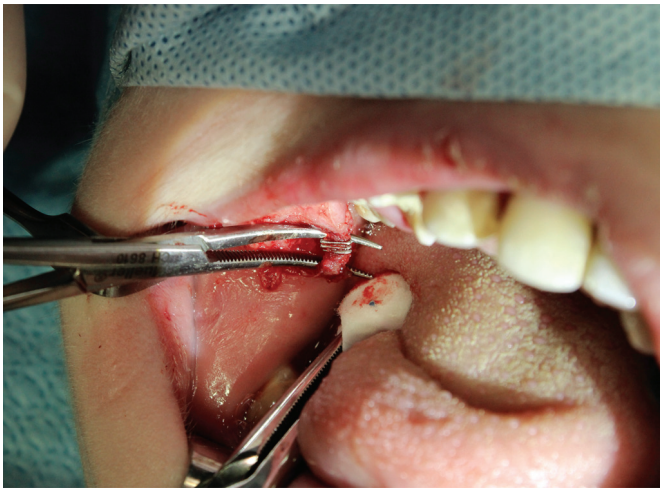

**Fig. 62.2:** Clamp passed around Stenson's duct and surgical clips applied.

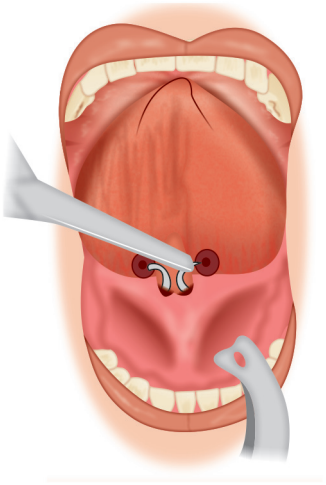

**Fig. 62.3:** Schematic diagram showing the location of incision posterior to the papillae and both submandibular ducts exposed and freed from surrounding tissue. Notice the tongue sutured to the palate in order to maximize the exposure.

anterior drooling, as measured by the drooling quotient and a caregiver visual analog score.[50] However, long-term results have been less optimal.[46] Postoperatively, there is usually a transient swelling that usually subsides over the following 2 weeks. Complications include increased salivary viscosity, buccal abscess, salivary collection, ranula, transient tongue edema, and fistula formation.[49,51]

### *Bilateral Submandibular Gland Excision and Parotid Duct Ligation*

Bilateral submandibular gland excision with parotid duct ligation has been shown to be safe and consistently effective for the treatment of chronic sialorrhea in children.[52–54] A recent study with a mean follow-up of 3 years reported a success rate of 87%.[52] The largest series to date with a follow-up interval ranging between 1 and 10 years reported no further drooling or significant improvement in 87% of patients while < 8% reported xerostomia and only 2 out of 93 reported an increase in dental caries.[53] In another study of children with CP who underwent submandibular glands excision and parotid ducts ligation, there was a reduction in the frequency of lower respiratory tract infections, rate of hospitalization for pneumonias, and the need for suctioning of upper airway secretion (mean 11 times/day in preoperative period and 3.1 times/day in the postoperative period).[52]

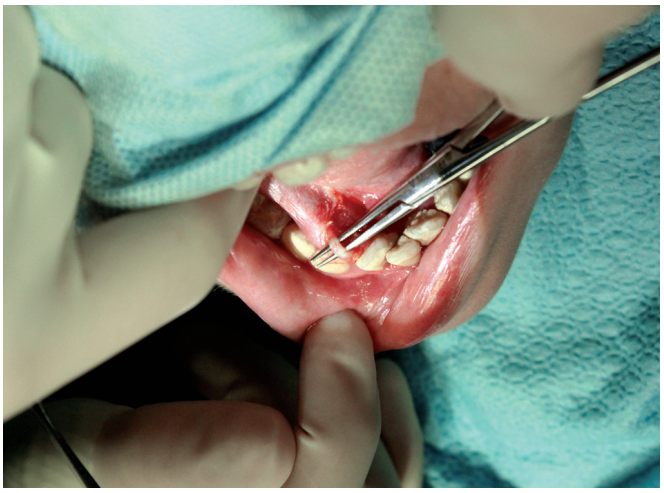

**Fig. 62.4:** Clamp passed around Wharton's duct.

### *Tympanic Neurectomy*

Tympanic neurectomy with or without chorda tympani section has been used in the treatment of drooling.[55] An endomeatal flap is raised and the tympanic plexus located just anterior to the round window niche is interrupted with a Rosen needle. In some cases, the chorda tympani (carrying the parasympathetic secretomotor fibers to the submandibular gland) is sectioned. While the surgical approach is simple, it has had inconsistent reported success rates, ranging from 25% to 87%.[56–59] In addition, it carries the risk of taste disturbance and is found to recur in many cases on long-term follow-up.

## CONCLUSION

There are several options available for the treatment of sialorrhea. These include rehabilitative strategies such as oral motor and behavior therapy, pharmacotherapy with several choices of anticholinergics, botulinum toxin injection into the salivary glands, radiotherapy, and surgery. The latter includes techniques to divert the saliva such as duct relocation and others to reduce the amount of saliva such as duct ligation or submandibular gland excision. Sialorrhea is a complex problem that needs to be approached in a multidisciplinary fashion. This ensures that patients have access to all the specialists that can input into a comprehensive assessment of their drooling condition and its bio-psycho-social impact, therefore allowing them to provide the most optimal treatment plan for the child.

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# SECTION 5

# Pediatric Sleep Medicine

CHAPTER

63

# Physiology of Pediatric Sleep

***Kenneth C Sassower***

## PHYSIOLOGY OF NEONATAL SLEEP

Brain maturation in the developing infant is reflected in the abundant changes of EEG activity that occur from the markedly preterm infant (28 weeks' gestation) through post-term infancy (up to 48 weeks' gestational age).

There are several unique features in the newborn EEG pattern that directly reflect brain maturation and development. From 28 weeks' gestation to 48 weeks' post-term gestational life, the EEG changes from an essentially flat recording to a continuous diffuse rich admixture of frequencies and classic EEG features that will serve as the template for brain wave activity throughout the life cycle of the individual.

There are two important distinguishing features of the newborn EEG. One is the presence of transient waveforms and sharp activity. As opposed to sharp waves found in EEGs of older infants, which may represent potential areas of epileptic dysfunction, sharp waves in the newborn need not connote pathology and are often expected features in an otherwise normal infant. The other unique feature of the newborn EEG is that the brainwave patterns of newborn infants during active or pre-REM sleep are virtually indistinguishable from that of wakefulness. As a result, we have to rely on extra-EEG monitoring (such as cardiorespiratory monitoring and the presence of body and eye movements) to help us determine the behavioral state of the infant. For example, an EEG devoid of excessive body movements is more likely to represent active sleep rather than wakefulness.

Prior to 28 weeks' gestation, the EEG background is markedly suppressed and essentially flat. There is no clear delineation between sleep and wakefulness. At 28 weeks, the first inkling of EEG activity is represented by "ripples of prematurity", which are really nothing more than sharply contoured theta rhythms occurring independently in both temporal regions. The likely reason why these waveforms are even discussed in the newborn EEG literature is because these rhythms represent the first bursts of EEG activity cast against an otherwise flat background.

Between 28 and 32 weeks' gestational age, two distinct neonatal sleep states emerge, "quiet sleep" and "active sleep".

Quiet sleep is considered to be an EEG precursor of "slow wave sleep" in childhood. Quiet sleep is first represented by the "discontinuous tracing", or "trace discontinue", starting around 32 weeks' gestation. This is characterized by an alternating pattern of brief intermittent bursts of moderate to high amplitude, sharply contoured, mixed delta and slow theta activity, lasting up to several seconds in duration, alternating with more prolonged stretches of similar attenuated activity.

The discontinuous EEG tracing merges over the next 6–8 weeks of preterm life into the more common "trace alternant", which is structurally similar to the "trace discontinue" but the interburst intervals are less flat, with a gradual emergence of more populated EEG activity. This results in a more continuous EEG tracing as the infant reaches full-term status.

Active sleep is believed to be a precursor of stage REM sleep. This is characterized by continuous diffuse mixed frequencies, and is virtually indistinct from preterm EEG wakefulness, save for the relative paucity of body movements.

At approximately 32 weeks' gestational age, there is the first evidence of "delta brushes". As the name implies, these bursts are characterized by moderate-to-high amplitude slow waves along with superimposed attenuated faster frequencies, which resemble bristles from a hairbrush. These "delta brushes" change location over the course of the preterm infant's life cycle, adopting a more central predominance at 32 weeks of age and occupying a more occipital localization at 36–38 weeks' gestation.

"Encoches frontales" refers to the presence of frontal sharp waves, usually between 32 and 36 weeks' gestation, and are often accompanied by brief runs of independent or bisynchronous bifrontal delta slow waves, known as "anterior slow dysrhythmias".[1]

It is not uncommon for sharp waves to dominate the preterm neonatal EEG. Frequent independent bitemporal sharp activity, more so than bicentral sharp activity, occurs between 32 and 38 weeks' gestation. Insofar as these sharp waves usually become less evident over the ensuing 2–3 months of newborn life, these waveforms are designated as "sharp transients", and usually dissipate by 48 weeks' post-term newborn life.

"Synchrony" refers to the relatively symmetric presence of bursts between both hemispheres and occupies about 50% of the EEG during early preterm neonatal life. By 40 weeks full-term gestation, synchrony should approach 100% of the EEG.

After full-term birth, characteristic EEG patterns become evident. There should become a decided attenuation of sharp transient EEG activity until approximately 48 weeks' post-term gestation, when such EEG sharp activity should no longer be present. In addition, the relative discontinuity of quiet sleep should progress into a more continuous sleep EEG background and the presence of stereotyped sleep EEG features such as sleep spindles become evident at approximately 2 months of post-term life.

Sleep stage architecture in newborns is characterized by an immediate sleep onset-to-REM latency, which is virtually unheard of in any other clinical setting other than in cases of narcolepsy or severe REM sleep deprivation in older individuals. It is said that approximately 50% of newborn sleep is composed of some version of pre-REM or stage REM sleep. On the other hand, quiet or slow-wave sleep occupies up to one-third of a newborn's sleep, and gradually diminishes in percentages across the childhood life cycle.

## PHYSIOLOGY OF INFANT SLEEP

Infant sleep represents a bridge between the transient EEG patterns of newborn life and the more classic and stereotyped features of childhood sleep. At 2 months of life, sleep spindles become evident over the fronto-central regions of the brain and typically last several seconds in duration or longer. At no other time in human brain development do sleep spindles last longer than one second in duration. Initially sleep spindles are independently evident over both fronto-central regions, and later become the classic EEG signature of non-REM stage II sleep. The other classic sleep feature of light sleep in the infant is the presence of vertex waves, which are sharply contoured bursts of delta slow wave activity which typically localize to the fronto-central regions in the first year of infant life, and occupy a more fixed and central location thereafter.

Over the course of the first year of life, there is also a gradual transition from a relatively indistinct amorphous and relatively undifferentiated EEG background to the presence of a distinct anterior–posterior gradient. This gradient is characterized by the presence of higher amplitude slower frequencies posteriorly and more lower amplitude faster frequencies bi-anteriorly. This anterior-posterior gradient is best evident when the infant awakens. The EEG develops a well-modulated, well-sustained symmetric posterior dominant rhythm, by the end of the first year of life. This posterior dominant rhythm is unique in that it is reactive to eye maneuvers; i.e. it becomes manifest when the eyes are closed and it becomes attenuated when the eyes are opened. The posterior dominant rhythm is best evident during a state of relaxed wakefulness. Thus, children who are anxious during EEG testing may often obscure their otherwise normal wakeful rhythm.

## PHYSIOLOGY OF CHILDHOOD SLEEP

In contrast to their adults, the sleep EEG in childhood is dominated by the presence of relatively slower frequencies and higher amplitudes during the pretoddler era.

In the latter half of the first year of life, there is distinct evidence of four stages of non-REM sleep, one stage of REM sleep, and one stage of wakefulness.

The first stage of non-REM sleep is that of light non-REM stage I sleep, or simply, drowsiness. Initially, the EEG background during early drowsiness is first characterized by the relative fragmentation of the preexisting posterior dominant rhythm of wakefulness, and then evolves into the presence of slow-rolling eye movements and subsequent presence of diffuse monomorphic slowing and central vertex waves. Body movements during drowsiness may be present, but are usually less prominent than during wakefulness.

Common clinical conditions that occur during drowsiness include so-called periodic limb movements of sleep, and many interictal EEG discharges of the more benign epileptic syndromes of childhood.

Non-REM stage II sleep is typified by the presence of generalized slowing and central sleep spindles, which range between 12.0 and 15.5 Hz and usually last no more than 0.5–1.0 s in duration. The EEG background during stage II sleep is characterized by a diffuse mixture of delta and slow theta frequencies, and is often punctuated by the presence of independent biposterior delta slow waves, particularly during the ages of 3–5 years.

Non-REM stages III and IV have now become conjoined by the American Academy of Sleep Medicine (or AASM) into one stage, N3 sleep.[2] The hallmark features of N3 or "slow wave" sleep are the dominant presence of moderate to high amplitude delta wave forms of 75 uV or greater, occupying > 20% of the sleep background.[3] Slow wave sleep is the time of deepest restorative sleep and highest arousal threshold.

Common clinical conditions that occur out of "slow wave" sleep are the classic non-REM arousal disorders of children, including sleepwalking, night terrors, and confusional arousals. By virtue of their high arousal threshold, these non-REM arousal disorders are usually accompanied by total or partial memory loss for the event.

Stage REM sleep is often described as "paradoxical sleep" as there is a deep restorative quality to this stage of sleep but also a relatively lower arousal threshold when compared to "slow wave" sleep. Stage REM sleep is often subdivided into phasic and tonic elements. Phasic elements of stage REM sleep include the presence of rapid eye movements as well as phasic submental EMG bursts, while tonic elements of stage REM sleep include lower amplitude mixed EEG waveforms that encompass theta, alpha, and sometimes beta frequencies. An additional classic tonic feature of stage REM sleep is the prominent attenuation of submental EMG tone.

There are two common clinical concerns that occur out of stage REM sleep. The first is narcolepsy, a REM sleep-wake boundary disorder. The second is sleep-disordered breathing, which is often activated in REM supine sleep and is often associated with a plummeting of oxygen saturations.[4]

## PHYSIOLOGY OF ADOLESCENT SLEEP

The sleep stages and sleep structure in adolescence is relatively similar to that of younger children. However, in adolescence, there is an increased amount of faster frequencies and accompanying lower amplitudes. Thus, when a 3-year-old child awakens, the typical posterior-dominant rhythm is expected to approximate 8 Hz, and 50–100 uV amplitude. In adolescence, the more common posterior-dominant rhythm is that of 9–11 Hz frequencies and lower amplitudes usually ranging between 25 and 50 uV. Similar increase in frequencies may also be seen in stage II sleep spindles, which can consist of frequencies as high as 14–15.5 Hz in adolescents.

During adolescent and early adult years, sleep stage architecture is dominated by relatively constant percentages of stage REM sleep, which occupy 20–25% of sleep and remains constant throughout the early and middle adult years. In contrast, slow wave sleep diminishes in a gradual fashion from late adolescence to senescence, where slow wave sleep is virtually absent in the elderly.[5]

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CHAPTER

# Evaluation of Pediatric Sleep Disorders: From the Clinic to the Sleep Laboratory

64

***Blake Kimbrell, Cristina M Baldassari***

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder that is characterized by intermittent episodes of upper airway collapse and disruption of airflow during sleep. OSA is the severest extent of a spectrum of sleep-disordered breathing that includes primary snoring and upper airway resistance syndrome. OSA affects 2–3% of preschool age children and has now replaced chronic tonsillitis as the most common indication for adenotonsillectomy. Thus, this disorder is a common cause for otolaryngology consultation. The evaluation of children presenting with snoring and tonsillar hypertrophy can be challenging. Through assessments such as clinical evaluation, radiographic imaging, and polysomnography, providers must determine which children have OSA and require further treatment.

## CLINICAL EVALUATION

Full-night polysomnogram (PSG) is considered the gold standard for the diagnosis of OSA in children. However, PSG is expensive and is not readily available in many parts of the United States. Thus, providers frequently must rely on other instruments to assess children with suspected OSA. Elements of clinical evaluation for pediatric OSA include history and physical examination, screening questionnaires, and home sleep recordings.

### History and Physical Examination

A focused sleep history should be obtained in children presenting to the otolaryngology clinic for evaluation of sleep-disordered breathing. The provider should determine the onset, duration, and frequency of snoring. Parents may also report labored breathing during their child's sleep including gasping, snorting, choking, or pausing. Restless sleep, frequent nighttime awakenings, night terrors, and enuresis are other symptoms that may be associated with OSA. Additionally, it is important to inquire about behaviors that impact a child's sleep hygiene including use of electronic equipment before bedtime, daily caffeine intake, and sleeping environment. OSA often has a significant impact on daytime functioning in children. Parents report problems with excessive daytime sleepiness, poor school performance, hyperactivity with difficulty concentrating, and irritability. Table 64.1 adapted from the American Academy of Pediatrics (AAP) guideline for "Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome" lists common signs and symptoms of this disease.[1] Detailed medical and family histories are also important to identify comorbidities that increase the risk of OSA. Such conditions include asthma, obesity, prematurity, craniofacial anomalies, Trisomy 21, and Chiari malformation. Children with neurological disorders such as hypotonia, cerebral palsy, Prader-Willi, and muscular dystrophy also have a higher incidence of OSA.

A thorough physical examination is an essential part of the evaluation of a child with OSA. An accurate height and weight should be obtained to calculate the child's body mass index (BMI). The Center for Disease Control recommends that the BMI percentile, which can be obtained by plotting the individual BMI on the BMI-for-age growth charts, be utilized to determine the child's weight status category.[2] Children that are less than the 5th BMI percentile are classified as underweight and children that are greater than the 95th percentile are considered obese. OSA has been associated with both failure to thrive and obesity in children.

**Table 64.1:** Signs and symptoms of OSA

| |
|---|
| *History* |
| Frequent snoring (> 3 nights/week) |
| Labored breathing during sleep |
| Episodes of apnea |
| Enuresis |
| Cyanosis |
| Morning headaches |
| Daytime sleepiness |
| Hyperactivity |
| Learning problems |
| *Physical Examination* |
| Underweight or obese |
| Tonsillar hypertrophy |
| Adenoid facies |
| Micrognathia/retrognathia |
| Hypertension |
| Hypotonia |

Adenotonsillar hypertrophy is the most common cause of upper airway obstruction in children. Tonsillar size should be assessed while the child has the mouth open with the tongue at rest in the oral cavity. The Brodsky grading scale, which is based on the ratio of tonsil size to the anterior tonsillar pillar, is the most common classification system used to describe tonsillar hypertrophy. According to Brodsky's scale, tonsils can be reliably graded from 0 (no tonsil tissue present) to 4 (tonsils that are touching in the midline) with good intra- and interobserver reproducibility.[3] Generally, children with grade 3 or 4 tonsils are considered to have tonsillar hypertrophy. Despite the fact that adenotonsillar hypertrophy is the most common cause of OSA in children, there is not a significant correlation between adenotonsillar size and sleep apnea severity.[4]

Signs of adenoid hypertrophy include hyponasal voice and adenoid facies (elongated face, allergic shiners, open mouth breathing, and a high arched palate). There are two ways to assess for adenoid hypertrophy: fiberoptic nasopharyngoscopy or a lateral neck soft tissue roentgenogram (X-ray). Fiberoptic nasopharyngoscopy has several advantages over lateral neck X-ray including direct visualization of the amount of obstruction caused by adenoid hypertrophy and no radiation exposure. In addition, fiberoptic examination enables the provider to identify other potential causes of upper airway obstruction including lingual tonsillar hypertrophy and supraglottic collapse.

While widely utilized in adults, the Mallampati score is not typically included in the evaluation of pediatric OSA. The Mallampati classification, which was derived from the anesthesia literature, involves scoring the ease of visualization of the oral cavity. Studies in adults that have utilized the Mallampati score to predict OSA have been equivocal. However, there is data to suggest that patients with the worst score of 4 (only the hard palate is visible when the patient opens his/her mouth and protrudes the tongue) have an increased incidence of OSA.[5] The Friedman score is an example of another grading system that has been used to describe oral cavity anatomy. The Friedman score is based on palate position, tonsillar size, and BMI. It has been utilized to stratify adult patients with OSA and determine which patients may benefit from surgical intervention.[6]

Providers should attempt to identify any other possible causes of upper airway obstruction during physical examination. Obese adolescents may have redundant soft palate tissue and a large base of tongue. Retrognathia and glossoptosis can cause significant obstruction, especially in children with Pierre Robin sequence. Poor muscle tone is another risk factor for OSA. In adolescents and adults, Muller's maneuver, which involves bearing down during awake, in-office fiberoptic nasopharyngoscopy, has been utilized to evaluate the site of obstruction. However, this technique often fails to accurately determine the location of upper airway collapse.[7] Sleep endoscopy, performed under sedation, can more accurately identify the site of obstruction in OSA patients.

Numerous publications, including at least two meta-analyses, have demonstrated that clinical diagnosis of OSA in children based on history and physical examination alone is inaccurate. Clinical evaluation yields a 30–80% success rate in predicting which children will have OSA.[8] The diagnostic accuracy of typical clinical symptoms and examination findings in children with suspected OSA is highly variable. For example, a recent meta-analysis showed that tonsillar hypertrophy had a relatively high sensitivity (range 48–82%), but had a low specificity (range 43–84% ).[9] Alternatively, caregiver reporting of observed apneas and daytime sleepiness had a high specificity, but a low sensitivity.

## OSA Questionnaires

In an attempt to improve the clinical accuracy of the diagnosis of OSA in children, numerous questionnaires have been developed. The Sleep-Related Breathing Disorder section of the Pediatric Sleep Questionnaire is one such instrument.[10] This is a 22-item survey that is completed by the parent. However, this instrument demonstrated a sensitivity of only 78% and a specificity of 72% when compared

to PSG, the current gold standard.[11] Other researchers have attempted to improve clinical detection of OSA by using composite scores that include both parent-reported symptoms and clinician examination findings. Goldstein et al. described one such clinical assessment score that featured 15 different items, including the presence of snoring, gasping for air, hyponasal voice, and tonsillar hypertrophy. Unfortunately, the composite score predicted a positive PSG for OSA in only 72% of children studied.[9]

There is a growing body of literature demonstrating the negative impact of OSA on quality of life (QoL) and cognitive function in children. Pediatric OSA has been associated with behavior problems, hyperactivity, cognitive deficits, and poor school performance. Disease-specific QoL instruments should not be used to make the diagnosis of OSA in children. However, such surveys can be extremely useful in determining the impact of OSA on a child's daytime functioning. The OSA-18 is one such survey that is widely utilized. This validated instrument has 18 questions and is completed by the caregiver.[12] In a recent meta-analysis, children with OSA had poor QoL as assessed by the OSA-18, but scores significantly improved following adenotonsillectomy.[13] Thus, this instrument can also be useful in assessing the impact of treatment modalities in pediatric patients with OSA.

### Sleep Tapes

With technology advances, including widespread dissemination of cellular phones with recording capabilities, many parents now present to clinic with audio and video recordings of their child's sleep. These recordings can provide more detailed information regarding the child's sleep. However, even when combined with history and physical examination, such recordings have not improved the diagnostic accuracy of clinical evaluation in pediatric OSA.[14,15]

## RADIOGRAPHIC EVALUATION

The gold standard for the diagnosis of OSA in children is PSG. Although PSG reliably measures the presence and severity of OSA, this study does not aid providers in identifying the site of airway obstruction. Imaging studies can be a useful addition to physical examination in determining the levels of obstruction in children with OSA. The most common imaging modalities used in the evaluation of pediatric OSA include lateral neck radiographs and cine MRI. Other modalities mentioned have been assessed for diagnostic accuracy, but are less commonly used.

### Lateral Neck Radiographs

Lateral neck X-rays are commonly obtained to assess for adenoid hypertrophy in pediatric patients with suspected OSA. Different measurements have been proposed for assessing adenoid size on lateral neck X-ray, including the adenoid-nasopharynx ratio (A/N ratio), the adenoid thickness (distance along a perpendicular line from the basiocciput to the adenoid convexity), and the linear distance between the antrum and adenoid tissue. The A/N ratio, the most commonly used measurement, is defined as the ratio of the measurement of the adenoid thickness and the nasopharyngeal aperture (the distance between the basiocciput and the posterior edge of the hard palate). There have been numerous papers published that have focused on the utility of the A/N ratio in diagnosing adenoid hypertrophy. However, a recent systematic review reported conflicting data on the accuracy of the A/N ratio.[16]

While lateral neck X-rays have the advantage of being noninvasive and quickly accessible in the clinical setting, these films are static in nature and are a two-dimensional representation of a three-dimensional space. Other limitations include radiation exposure and the impact of patient respiration and phonation on the interpretability of the results. For example, mouth breathing, crying, or swallowing during the examination may cause soft palate elevation and thus reduce the size of the nasopharyngeal cavity. To optimize image quality, lateral neck X-rays should be performed at the end of inspiration with the neck in slight extension. Due to the limitations of lateral neck films, flexible fiberoptic nasal endoscopy is frequently used in the clinic setting to evaluate for adenoid hypertrophy. Lateral neck film is reserved for children that need an objective assessment of their adenoid size but are unable to cooperate with endoscopic evaluation.

Cephalometric radiographs are another imaging study utilized to evaluate patients with suspected OSA. These skull films include a full lateral view of the mandible and are used to make cranial measurements. Examples of common cephalometric measurements obtained from these radiographs include posterior airway space, facial height, angle from the mandible to the sella, nasion, and supramentale (SNB), and hyoid position. Certain cephalometric features have been found to correlate with the presence of OSA in children. For example, when compared to controls, children with OSA have a smaller SNB angle and a lower hyoid position.[17] Despite these findings, no "formula" has been identified that allows for a combination of cephalometric measurements to reliably predict the presence and severity of OSA in children.

## Dynamic Radiography

A major limitation of lateral neck radiographs is their static nature. Thus, dynamic radiographic studies have been utilized in the evaluation of patients with OSA in an attempt to better identify the location of airway collapse. Examples of such dynamic studies include somnofluoroscopy and cine magnetic resonance imaging (MRI). Somnofluoroscopy is airway fluoroscopy that is performed while the patient is sleeping. Somnofluoroscopy can be combined with PSG to allow for determination of the site of obstruction during a recorded respiratory event. This imaging modality has not been extensively used in children due, in part, to concerns regarding radiation exposure. In contrast, cine MRI is a dynamic study that provides excellent soft tissue evaluation in multiple planes without radiation exposure. Rapid, real-time images can be captured during active snoring or desaturations. Cine MRI is particularly useful in the evaluation of patient populations with a propensity for complex or multilevel obstruction including children with Trisomy 21 and craniofacial anomalies.[18]

# POLYSOMNOGRAPHY

Full-night, in-laboratory PSG is the gold standard for diagnosis of OSA in children. PSG reliably measures the presence of OSA and provides an objective scale for OSA severity. In addition to reporting respiratory events, PSG also provides important information regarding other sleep parameters including sleep architecture, neurologic and cardiac events, and limb movements. Furthermore, there is no clinically significant night-to-night variability in pediatric PSG.[19] Both the American Academy of Sleep Medicine (AASM) and the AAP recommend PSG, when available, be performed in children with suspected OSA. This recommendation stems from data pointing to the lack of accuracy of clinical assessment.

Despite these recommendations, only 10% of patients undergoing adenotonsillectomy for suspected OSA have had PSG.[20] Several factors have contributed to the lack of extensive utilization of PSG in children including high cost, inconvenience for both parents and child spending the night in the laboratory, and the relative scarcity of laboratories with expertise in pediatric sleep disorders. Due to these issues, many children referred for PSG experience an extended waiting period before testing is completed. This can lead to a delay in treatment. Failure to quantify the impact of OSA on a child's general well-being, including emotional and behavioral health, is another limitation of PSG. QoL scores in children do not correlate with the severity of OSA as defined by the apnea hypopnea index (AHI).[21] Even with these limitations, PSG remains the most objective and accurate test currently available for the diagnosis of OSA.

## Indications for PSG

Which children should be evaluated with PSG? Recent guidelines have been developed to help providers answer this question. The AAP, the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS), and the AASM have all published recommendations regarding indications for PSG in children.[1,22–24]

The reported prevalence of OSA ranges from 1% to 3%.[25,26] Thus, the AAP has recommended routine screening for OSA by questioning about snoring during well child visits. In children with habitual snoring, a more focused history and physical examination should be completed. The AAP Guidelines on the Diagnosis and Management of OSA in Children recommend that children with regular snoring and additional signs of OSA such as labored breathing during sleep, enuresis, hyperactivity, or tonsillar hypertrophy, undergo PSG.[1] The AASM Practice Parameters for Respiratory Indications for Polysomnography in Children make a similar recommendation.[23] AAO-HNS Clinical Practice Guidelines for PSG endorse the utilization of PSG prior to surgical therapy in children with complex medical conditions.[22] Examples of such conditions include obesity, Trisomy 21, craniofacial anomalies, neuromuscular disorders, sickle cell disease, and mucopolysaccharidoses. PSG is also indicated prior to surgical intervention when there is discordance between tonsil size on physical examination and the reported severity of OSA.

## Components of PSG

Parents should discuss with their children what to expect during the PSG. A tour of the sleep laboratory prior to the study can help familiarize children with the equipment that will be used. This may be especially useful in special needs children and those who express anxiety about the testing. Ideally, the site of the PSG should be a child-friendly environment with an additional bed for a parent. The test should be performed by a sleep technician experienced in working with children and should begin around the child's regular bedtime. Prescription sleep aids should be avoided if possible.[27]

Parameters measured during pediatric PSG are similar to those recorded in adults. According to the AASM Manual for the Scoring of Sleep and Associated Events, the following parameters should be measured during PSG: electroencephalogram (EEG), electrocardiogram (ECG), chin and leg electromyogram (EMG), electrooculogram (EOG), body position, airflow signals, respiratory effort signals, snoring, and oxygen saturation.[28] In addition, $CO_2$ monitoring in children is recommended during PSG. Monitoring $CO_2$ levels enables identification of pediatric patients with hypoventilation.

PSG provides information regarding sleep architecture. Sleep stages, including Stage 1 (N1), Stage 2 (N2), Stage 3 (N3), and rapid eye movement (REM), are scored in 30-s intervals known as epochs. EEG, chin EMG, and EOG tracings can be utilized to determine the sleep stage. Typically, eight electrodes are placed to record EEG tracings from the frontal, central, and occipital regions. If there is concern for seizures, additional EEG leads should be added to the montage to detect any nocturnal neurologic events. Eye movements are recorded using EOG tracings from two electrodes placed just above the right outer canthus and just below the left outer canthus. Three electrodes are placed on the chin to record EMG. A discussion of the specific rules used to score sleep stages in children is outside the scope of this chapter. A detailed description of these rules can be found in the AASM Manual.[28]

PSG provides data regarding respiratory events including respiratory effort, airflow limitation, oxygen desaturation, and $CO_2$ retention. Respiratory effort is most commonly measured by respiratory inductance plethysmography. Inductance plethysmography uses an alternating current in belts fastened around the chest and abdomen to generate a signal based on changes in the inductance of belts during breathing. During obstructive respiratory events, chest and abdominal tracings may be out of phase. Less commonly, respiratory effort is measured by esophageal manometry. An oronasal thermal sensor is utilized to monitor airflow and detect apnea, while a nasal pressure transducer is used to identify hypopneas. Apneas can be classified as obstructive, mixed, or central events. Table 64.2 lists the AASM definitions for apneas, hypopneas, and respiratory effort-related arousals (RERAs).[28] During PSG, pulse oximetry is used to monitor oxygen saturation. The pulse oximeter should have a short sampling time of 2–3 s so that brief desaturations can be captured. $CO_2$ levels can be measured by either transcutaneous or end-tidal $CO_2$ monitors. If gas exchange abnormalities are suspected, an arterial blood gas can be used to confirm abnormalities in $CO_2$ levels.[27] Snoring is detected by a snore microphone paced on the anterior neck, technician observation, and audio recording.

**Table 64.2:** Definitions of pediatric respiratory events

*Obstructive apnea*
- Drop in peak signal of oronasal thermal sensor by ≥ 90% of pre-event baseline
- Duration of event lasts for at least 2 breaths
- Respiratory effort persists during the apneic event

*Central apnea*
- Drop in peak signal of oronasal thermal sensor by ≥ 90% of pre-event baseline
- Duration of event: (a) lasts for at least two breaths and is associated with an arousal or a ≥ 3% arterial oxygen desaturation OR (b) lasts for ≥ 20 s
- Respiratory effort is absent throughout the apneic event

*Mixed apnea*
- Drop in peak signal of oronasal thermal sensor by ≥ 90% of pre-event baseline
- Duration of event lasts for at least two breaths
- Respiratory effort present during a portion of the apneic event but absent for another portion

*Hypopnea*
- The nasal pressure signal drops by ≥ 30% of pre-event baseline
- The duration of the signal drop is at least two breaths
- The event is associated with a ≥ 3% oxygen saturation or an arousal

*Respiratory effort-related arousals (RERAs)*
- Event last > 2 breaths
- Event characterized by one of the following:
  - Increased respiratory effort
  - Flattening of the inspiratory nasal pressure waveform
  - An elevation of $CO_2$ leading to an arousal

Cardiac events and limb movements are also recorded during PSG. ECG monitors heart rate and rhythm through two leads placed on the torso. This allows for detection of cardiac pathology such as bradycardia and irregular ventricular rhythm. To score limb movements, the AASM recommends that an electrode be placed on the anterior tibialis of the right and left legs and that the EMG be recorded via two separate channels. Digital video is used to document patient positioning and any unusual sleep behaviors such as parasomnias.

## PSG Interpretation

The AASM Manual for the Scoring of Sleep and Associated Events is a comprehensive resource that provides rules for scoring sleep stages, arousals, cardiac events, leg movements, and respiratory events. Since the performance of

PSG has become more common in children, pediatric normative data for many of these parameters is now available. Providers treating children with sleep-disordered breathing should be able to interpret a PSG report to make the diagnosis of OSA and also identify other comorbid sleep disorders.

### *Sleep Architecture*

Ideally, PSGs should have a sleep efficiency (ratio of total sleep time to total time in bed) of 85% or better. A hypnogram provides an excellent graphic summary of the different stages of sleep that the patient exhibits during PSG. Figure 64.1 depicts a typical pediatric hypnogram. The amount of time spent in each sleep stage varies according to age, with younger children exhibiting more deep sleep. The nightly average percentiles for each of the sleep stages are as follows: N1 – 5 to 8%; N2 – 45 to 55%; N3 – 5 to 20%; REM – 20 to 25%. N3 sleep is usually concentrated in the first part of the night, while there is an increased amount of REM sleep in the second part of the night (Fig. 64.1). A PSG that features a decreased amount of REM sleep may underestimate the severity of OSA owing to the fact that obstructive respiratory events are more common during REM sleep.

### *Respiratory Events*

The obstructive AHI is the most widely utilized PSG parameter to determine the severity of OSA. This value is calculated by adding the total number of obstructive and mixed apneas and hypopneas and dividing this sum by the total sleep time in hours. The REM AHI is also commonly included in PSG reports. However, conclusive data linking the REM AHI to outcomes and QoL data in either children or adults is lacking.[29] PSG reports may also contain the Respiratory Disturbance Index (RDI). In addition to obstructive and mixed apneas and hypopneas, the RDI also includes RERAS. The central apnea index is the total number of central apneas divided by the total sleep time. The mean and nadir oxygen saturation should also be included in the PSG report. Finally, pediatric

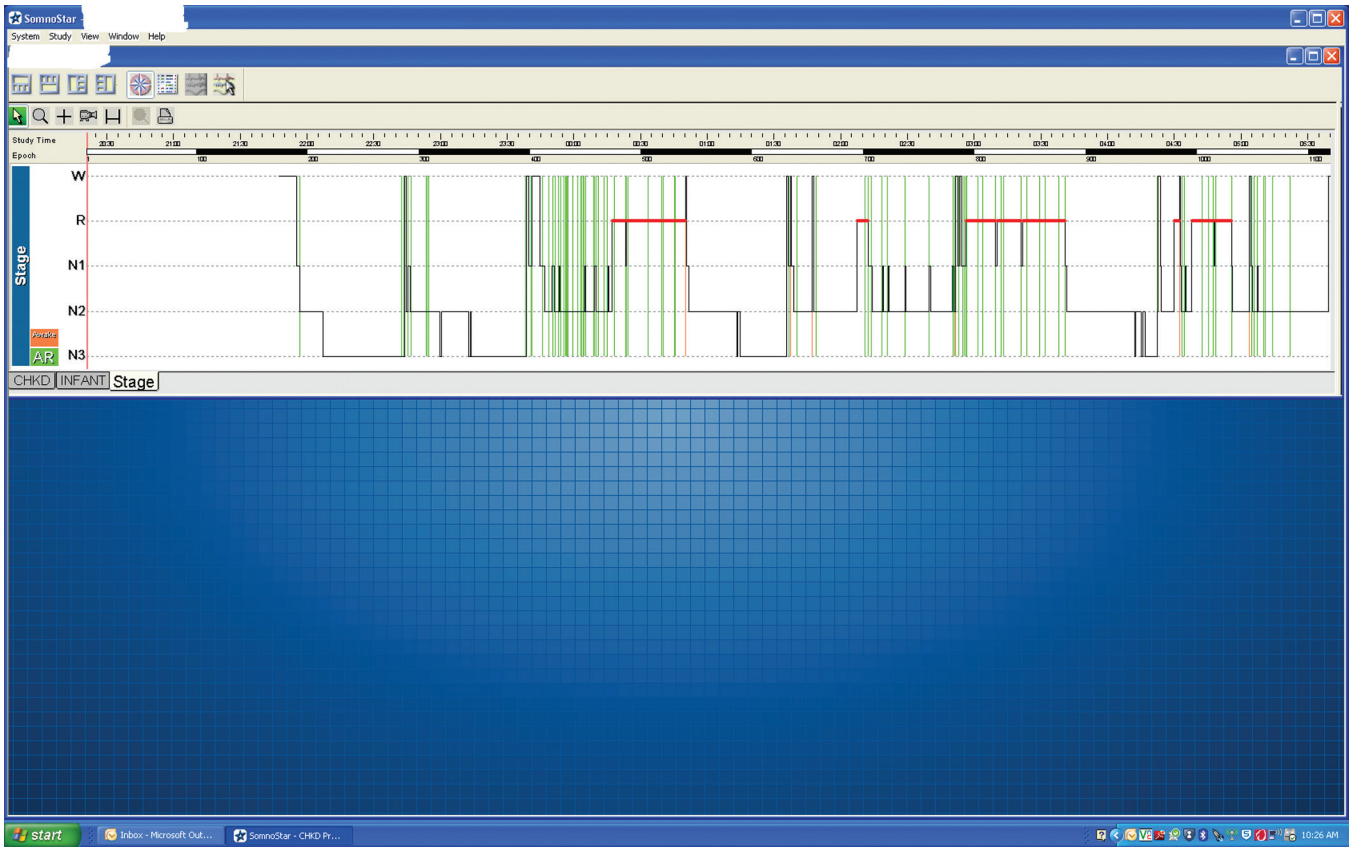


**Fig. 64.1:** Typical pediatric hypnogram showing the distribution of sleep stages, including N1, N2, deep sleep (N3), and REM sleep, during full-night polysomnogram. Deep sleep is concentrated in the first half of the night, while most REM sleep (denoted by red horizontal lines) occurs in the second half. The majority of obstructive respiratory events in pediatric patients occur during REM sleep.

PSGs will typically include $CO_2$ measurements. $CO_2$ levels above 50 for > 25% of the PSG are concerning for alveolar hypoventilation.

The classification system for OSA in children continues to be debated and has yet to be standardized. For example, the diagnostic criteria for pediatric OSA differ between sleep centers. Some providers diagnose OSA in children with an AHI > 1, while others consider an AHI of > 5 to be clinically significant. A conservative definition for pediatric OSA proposed by Katz and Marcus[30] is as follows:

- AHI < 1 = normal
- AHI 1–5.0 = mild
- AHI 5.1–9.9 = moderate
- AHI >10 = severe.

Large observational studies of healthy children have been conducted in an attempt to define reference values for respiratory parameters during sleep.[31,32] Interestingly, however, reference values for common PSG parameters such as AHI do not follow a normal distribution. This may be one explanation why both QoL and outcomes measures correlate poorly with AHI.

### *Arousals*

An arousal is defined as an abrupt change in the EEG tracing lasting at least 3 s with at least 10 s of stable sleep preceding the change. Arousals may be associated with respiratory events or leg movements or may occur spontaneously. The arousal index is the number of arousals divided by the total sleep time. This value can provide information regarding sleep fragmentation and sleep disturbance. The normal arousal index for children is < 10.

### *Leg Movements*

PSG reports typically contain mention of periodic limb movements. Most commonly, sleep providers will report the Periodic Limb Movement Index (PLMI), which is the number of PLM series divided by the total sleep time. Normal PLMI in children is < 5. Elevated PLMI can be associated with anemia, periodic limb movement disorder, and attention deficit hyperactivity disorder. In children with ferritin levels < 50 mg/L, ferrous sulfate supplementation for 3 months improves the PLMI.[33]

## PSG Alternatives

Due to full-night, in-laboratory PSG shortcomings such as expense and the weak correlation between AHI and outcomes, alternative testing modalities for pediatric OSA are being developed. Such alternatives include unattended home-based overnight oximetry studies, home-based multichannel studies, and nap (abbreviated) polysomnography. However, these modalities have not been widely utilized due to several significant limitations. Overnight oximetry studies can detect children with severe sleep apnea. However, children with milder forms of the disease in whom marked oxygen desaturation does not occur are not identified. Home-based multichannel studies are being performed more frequently in adults, but high-quality studies regarding their utility in children are lacking. In the Practice Parameters published by the AASM, nap polysomnography is not recommended for the evaluation of OSA in children. This statement is based on data from several studies that demonstrated that nap polysomnography underestimates the prevalence and severity of OSA.[23]

## BIOMARKERS

Researchers are working to develop novel diagnostic tests for pediatric OSA with improved specificity and sensitivity. Ideally, such modalities would be inexpensive, convenient, and correlate with QoL and treatment outcomes. Recent advances in the arena of biomarkers are promising. Simply defined, biomarkers are measurable factors that reflect the presence or absence of disease. Researchers theorize that OSA will lead to specific signatures in the expression of biomarkers such as genes or proteins. Transcriptomics and proteomics are being utilized to try to identify these biomarkers in readily available samples such as blood, urine, and exhaled condensates. For example, Gozal recently identified 16 unique proteins that were differentially expressed in the urine of children with OSA compared to controls.[34] If reliable biomarkers can be identified to diagnose OSA in children, the field would be revolutionized. This technology would expand screening and significantly reduce the health burden of pediatric OSA.

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CHAPTER

# 65 Sleep-Disordered Breathing and Obstructive Sleep Apnea

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## INTRODUCTION

Sleep-disordered breathing (SDB) refers to a broad number of sleep-related respiratory disorders that include primary snoring, obstructive sleep apnea (OSA), obstructive hypoventilation, and upper airway resistance syndrome (UARS). Within this spectrum of disorders the most frequently considered is OSA. OSA refers to a pattern of breathing during sleep characterized by upper airway obstruction resulting in partial or complete limitation of airflow through the mouth and/or nose that disrupts sleep.[1] OSA is typically diagnosed with a sleep study, and it is not possible to differentiate between OSA and other obstructive SDB without polysomnography (PSG).

Sleep-disordered breathing is a common presenting complaint for pediatric otolaryngologists comprising 10–50% of the typical practice.[2] The prevalence of snoring ranges from 1% to 15% with most estimates of habitual snoring averaging 5%.[3-11] OSA, as documented by PSG, suggests a prevalence of 1–4% but is significantly higher in certain high-risk populations.[12,13]

Multiple studies have shown the deleterious effects of SDB, especially when there is a clear diagnosis of OSA. Effects range from the physiologic to the neurocognitive. Hypertension, glucose intolerance, cor pulmonale, failure to thrive, and enuresis have all been associated with OSA.[14-17] School performance, attention and behavioral problems, and even IQ have been linked to OSA.[18] Although the data are not as robust, recent studies suggest similar associations with primary snoring.[7]

Understanding the diagnosis and management of pediatric SDB is essential to the otolaryngologist, given the prevalence of the disorder in otolaryngology practice as well as the potential morbidity associated with untreated SDB.

## CLASSIFICATION AND EPIDEMIOLOGY

SDB is best understood as a continuum of related conditions, of which OSA is most severe. However, even the less severe manifestations of SDB may cause considerable morbidity and merit the attention of the otolaryngologist (Fig. 65.1).

### Primary Snoring

Primary snoring is defined as snoring without accompanying respiratory abnormalities (e.g. hypoxia, apneas/hypopneas, hypercapnia) or arousals. The prevalence of primary snoring has been estimated at 6.1%.[7] Left untreated, 25.7% of pediatric cases resolve spontaneously after several years, 31.4% remain classified as primary snoring, and 37% progress to OSA. Excessive weight and persistent snoring both predict progression from primary snoring to OSA.[12] Although patients with primary snoring lack the major respiratory abnormalities associated with OSA, they still show evidence of increased respiratory effort, which in turn may be associated with significant sequelae (which will be detailed later).

### Obstructive Hypoventilation

Obstructive hypoventilation refers to snoring and increased respiratory effort with hypercapnia but without apneas/hypopneas or respiratory arousals. Diagnos-

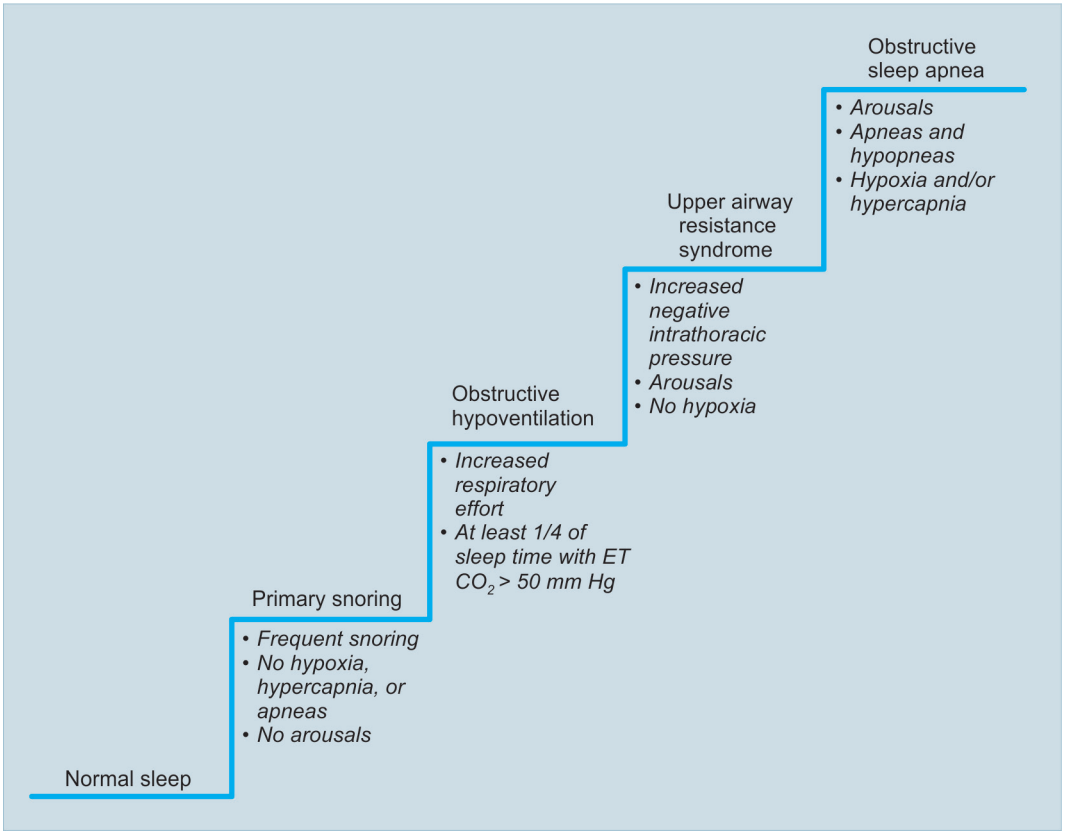


**Fig. 65.1:** Escalating symptoms of sleep-disordered breathing.

tic thresholds for hypercapnia vary, but the American Academy of Sleep Medicine recommends diagnosing obstructive hypoventilation when >25% of sleep time is spent with end-tidal $CO_2$ > 50 mm Hg.[19]

## Upper Airway Resistance Syndrome

Upper airway resistance syndrome is a pattern of increased respiratory effort with arousals but without significant decreases in airflow. Snoring and increased negative intrathoracic pressure (as measured by balloon esophageal manometry or paradoxical inward rib movements) provide evidence of increased respiratory effort.[20] Like OSA, UARS causes night-time arousals that lead to daytime sleepiness.[21] But unlike OSA, UARS is not associated with apneas/hypopneas or abnormal gas exchange. Because increased respiratory effort is difficult to measure without invasive esophageal pressure monitoring, many cases of pediatric UARS are misdiagnosed.[22] The prevalence of UARS in children is not known but may be more common than OSA.[22]

## Obstructive Sleep Apnea

OSA is the best-known, most severe end of the SDB spectrum. In OSA, airway obstruction and arousals are accompanied by apneic pauses as well as hypoxia and/or hypercapnia.

The etiology and risk factors of pediatric OSA differ from those seen in adults. Obstructive hypoventilation (specifically hypercapnia) is more common in children than in adults. Children with OSA are also less likely to be obese and more likely to have hypertrophic tonsils and adenoids than adults with OSA. Both genders are equally affected by pediatric OSA. Pediatric OSA is also less associated with daytime sleepiness than adult OSA. These differences are particularly true among younger children, who tend to present with failure to thrive rather than obesity.[23,24] However, rising obesity rates have led to the emergence of a childhood OSA variant that closely resembles the adult disorder. This has led to proposals to classify tonsil-/adenoid-related OSA and obesity-related childhood OSA as distinct disorders.[25]

Most studies report that OSA has an overall prevalence between 1% and 4%. Among snoring children, however, 18–25% may have OSA.[11,13,24-29]

## CONSEQUENCES OF SDB IN CHILDREN

Daytime sleepiness and neurocognitive disorders secondary to OSA are well documented and widely known.[30] A growing body of evidence shows that even the less severe forms of SDB also predispose children to widespread metabolic, cardiovascular, and developmental abnormalities. Childhood OSA increases children's all-cause mortality by a factor of 6.58 and nearly doubles their health-care utilization.[31-34] Although complications of SDB can harm a child's health in the long term, they are largely reversible with treatment. Thus, they underscore the need for otolaryngologists to diagnose and treat SDB in a timely manner.

### Neurobehavioral

Since observations of Hill on the "stupid-lazy child" in 1889,[35] clinicians have long appreciated the effects of SDB on children's academic performance and behavioral control. Impulsive behavior, externalizing behavior, and restlessness have all shown such strong relationships with SDB that the sleep disorder may be considered causal. Deficits in memory, intelligence, and executive function have also been linked to SDB, somewhat less robustly.[14,21,36-40] Although poor academic performance is clearly associated with SDB,[37,38,41-43] it may be more causally related to behavioral problems than to cognitive deficits.[30] OSA appears to exacerbate seizure frequency in predisposed children, again in a manner that is responsive to treatment.[55,56]

It is unclear whether neurobehavioral complications are mediated by sleep fragmentation, intermittent hypoxia, or inflammatory responses due to SDB; all three mechanisms are probably involved to some degree.[30,44-50] Many of these sequelae are at least partially responsive to treatment, particularly adenotonsillectomy.[51,52] But delays in treatment are widespread and may exacerbate the "learning debt" that persistently hinders school performance even after SDB treatment.[30,31,43,53,54]

SDB also has a role in many other sleep disorders. Children with SDB show a higher rate of parasomnias (e.g. night terrors, sleepwalking), perhaps triggered by apneic partial arousals.[57,58] Behavioral sleep disorders, particularly bedtime resistance, are associated with SDB and should be screened for in children presenting with SDB symptoms.[59] Enuresis has also been associated with OSA in children,[60-63] reversible with OSA treatment.[59,64-66]

### Cardiopulmonary

The SDB is also associated with a broad range of cardiovascular and pulmonary sequelae. Intermittent hypoxia induces pulmonary vasoconstriction and increases pulmonary artery pressure, which in turn may lead to pulmonary hypertension and cor pulmonale.[67] Studies have shown significant echocardiographic abnormalities in 7.7–45% of children with OSA, including reduced ejection fraction, wall motion abnormality, and left ventricular hypertrophy.[67-70] Perhaps most notably, cardiac structural abnormalities show a dose–dependent relationship with OSA severity.[68,71] SDB is additionally associated with increased asthma severity in children.[72,73] And it has shown correlations with sudden infant death syndrome (SIDS) and SIDS near-misses.[74-76]

The OSA is also associated with systemic hypertension, in a pattern well demonstrated in adults and increasingly apparent in children. Physiologically, intermittent arousals, hypoxemia, and increases in cardiac after load during apneic pauses are hypothesized to increase children's sympathetic tone and raise blood pressure even during the daytime.[77-80] A recent study showed increased urinary catecholamine levels in children with OSA, supporting the sympathetic overactivation hypothesis.[50] Endothelial dysfunction may also play a role in hypertension secondary to OSA.[14,81] Since childhood hypertension predisposes to hypertension in adulthood, the cardiovascular rationale for treating childhood SDB is quite clear.[82] Most cardiopulmonary derangements are responsive to treatment for OSA, including adenotonsillectomy.[52,58,83] But it remains unclear whether adenotonsillectomy in children improves cardiovascular mortality into adulthood.[82]

### Metabolic

Metabolic changes, most notably inflammation, may underlie many of the complications of childhood SDB. Elevated inflammatory markers, including C-reactive protein (CRP), have been found in children with SDB in a severity-dependent pattern responsive to adenotonsillectomy.[84-88] CRP is a well-studied predictor of atherogenesis, insulin resistance, and future cardiovascular morbidity.[89,90] SDB has also shown direct effects on lipid homeostasis and insulin resistance, even in nonobese children.[81,91] The metabolic and inflammatory sequelae of SDB are significantly more severe, however, in children with obesity.[91]

### Developmental

Sluggish growth and failure to thrive have long been observed in children with OSA.[60,92] They appear to be the result of increased caloric expenditure during breathing,[93] as well as decreases in growth hormone secretion and IGF-1[94] and dysphagia due to adenotonsillar hypertrophy.[25] However, the incidence of growth delay secondary to OSA has decreased substantially with earlier diagnosis and treatment. "Catch-up growth" after adenotonsillectomy has been well documented in both nonobese and obese children.[25,94]

### Morbidity with Primary Snoring

Otolaryngologists are quite familiar with the complications of childhood OSA. A considerable body of evidence is developing, however, on the sequelae of primary snoring—previously considered a benign condition, but increasingly understood as cause for concern in its own right. Like childhood OSA, primary snoring has been linked to academic and behavioral problems. Even in the absence of hypoxia and apneic pauses, snoring children have increased rates of hyperactivity, inattentive behavior, and learning difficulty.[7,40-43,95-98] It is also associated with echocardiographic and blood pressure abnormalities.[68,99] Thus, there is an emerging hypothesis that "benign" snoring does not in fact exist in children.[100]

Moreover, in 37% of children, primary snoring progresses to full-blown OSA.[101] Primary snoring is often the result of a constricted maxilla or chronic nasal obstruction. These can lead to further impairments in craniofacial and maxillomandibular development, increasing the likelihood of OSA in the future.[100,102] Perhaps most relevant to the otolaryngologist, though, is that primary snoring cannot be distinguished from OSA on the basis of history and physical examination alone.[103] Thus, patients presenting with habitual snoring should be assessed for the full spectrum of SDB.

## RISK FACTORS AND ETIOLOGY

Sleep-disordered breathing and OSA are the result of anatomic or functional narrowing in the upper airway. The primary risk factor for SDB in children is, of course, adenotonsillar hypertrophy. However, tonsillar size does not always predict the degree of obstruction, especially in older children.[5] A variety of conditions affect the patency of the upper airway and may increase a child's risk of SDB.

### Obesity

Obesity is the cardinal risk factor for OSA in adults, but it is becoming increasingly prevalent in childhood SDB as well—older children in particular. Waist circumference and body mass index (BMI) have been repeatedly established as risk factors for pediatric SDB.[5,9,104,105] For every increase of 1 kg/m$^2$ (BMI units) above the mean, a child's risk of developing OSA increases by 12%.[106]

Several mechanisms may explain this association. Adiposity in the neck, pharynx, thorax, and abdomen can increase airway resistance and decrease chest compliance.[107,108] Severe or syndromic (e.g. Prader–Willi) obesity is also associated with decreased central ventilatory drive.[109-113] Finally, a metabolic, inflammatory mechanism may be involved, since obesity exacerbates many of the inflammatory findings in children with SDB. A population-based study found that waist circumference was an independent risk factor for OSA, whereas neck circumference was not, supporting the metabolic hypothesis.[5] Similarly, a study of fat distribution found that visceral fat was independently predictive of apnea–hypopnea index (AHI), whereas BMI was not.[105]

As mentioned earlier, OSA in obese children is in many ways distinct from OSA in nonobese children. In obese children with SDB, adenotonsillar hypertrophy is less etiologically important, and adenotonsillectomy alone is less likely to lead to long-term cure (although it still improves quality-of-life).[114-118] Obese children with SDB may still be candidates for adenotonsillectomy, but they should be thoroughly assessed postoperatively to ensure the resolution of symptoms.[119]

### Superimposed Airway Inflammation

Adenotonsillar hypertrophy is one of the several causes of inflammatory airway obstruction in children. Many other common complaints in the otolaryngology clinic also contribute to SDB; in some cases, treating these inflammatory problems may address SDB without adenotonsillectomy. The importance of localized airway inflammation has been demonstrated at the molecular level; exhaled nitric oxide, an inflammatory marker, is higher in children with OSA and habitual snoring.[86]

Nasal obstruction, including septal deviation and turbinate hypertrophy, contributes to SDB; some cases of OSA can be corrected by nasal surgery alone.[120-122] Nasal anatomy is a more significant contributor in milder cases of SDB than in severe OSA.[5] Allergic rhinitis contributes

to nasal obstruction, adenotonsillar hypertrophy, and an elongated face, all of which predispose to OSA.[123] Treating allergies using conventional methods often alleviates SDB nonsurgically.[124-126] History of sinusitis is also an independent risk factor for childhood OSA.[106] Asthma may have a role, but some research suggests its effects are mediated by atopy and/or nasal obstruction.[72,106,127] Seasonal variations in SDB severity suggest both viral and allergic influences.[128] In addition, gastroesophageal reflux disease predisposes to SDB by inducing pharyngeal edema and contributing to adenoid hyperplasia.[123,129-131] Laryngomalacia, including subglottic stenosis, is also a risk factor for childhood SDB.[132-135]

Acute-onset OSA can also result from viral infections, most commonly infectious mononucleosis due to Epstein–Barr virus. Infectious mononucleosis can cause rapid, dangerous lymphoid hyperplasia in the pharynx. These patients may be treated with a nasopharyngeal airway and steroids until airway obstruction resolves.[136,137]

### Syndromic, Craniofacial, and Neuromuscular Abnormalities

Syndromic abnormalities can affect the craniofacial anatomy of children and their upper airway collapsibility, thus contributing significantly to their risk of SDB. Many congenital syndromes lead to maxillomandibular hypoplasia or displacement, including achondroplasia, Pierre Robin sequence, Treacher–Collins syndrome, Apert syndrome, Crouzon syndrome, and Pfeiffer syndrome. Anatomically, many children with these syndromes have retrognathia, micrognathia, steep mandibular plane, elevated hard palate, and elongated tongue and soft palate contributing to their upper airway obstruction.[22,28,138,139] Children with mucopolysaccharidoses (Hunter and Hurler syndromes) have anatomic derangements and copious secretions in the airway exacerbating SDB. As many as 89% of patients with mucopolysaccharidoses have OSA; airway obstruction is frequently their cause of death.[140-143] Pharyngeal flap surgery for velopharyngeal insufficiency also increases the risk of OSA postoperatively.[144-146]

Low muscle tone in the upper airway also contributes to the pathogenesis of SDB and occurs in several neuromuscular syndromes seen in children, such as cerebral palsy and Duchenne muscular dystrophy.[147-151] Pharyngeal hypotonia secondary to hypothyroidism also increases the risk of SDB.[152-154] Finally, Down syndrome combines many of the predisposing factors for SDB: craniofacial abnormalities, generalized hypotonia, and obesity are all common in this population, which has a 54–79% incidence of SDB.[155-158] In fact, some authors advocate that all children with Down syndrome undergo PSG (even those asymptomatic for SDB).[158] In patients with syndromic abnormalities, adenotonsillectomy is a useful first step in the treatment of SDB, but continued surveillance and more aggressive therapy are often needed.

### Demographics and Environment

Certain demographic and environmental characteristics have shown association with SDB in children. Black race increases the risk of SDB fourfold to sixfold, and the risk of recurrence after adenotonsillectomy approximately 15-fold.[106,114,159-161] Family history,[160,162] sibling risk,[163] and preterm birth[10] show significant associations with SDB, as do "neighborhood disadvantage",[164] second-hand smoke,[145,150] and socioeconomic status[4,163]—attesting to the multifactorial causes of the SDB spectrum.

## CLINICAL PRESENTATION

A common theme in the presentation of pediatric SDB is that chief complaints differ widely from adult SDB, relating more to night-time symptoms than to daytime issues. The most common presenting complaints in children with SDB are habitual snoring (76–99% of children with OSA), noisy breathing, or difficulty breathing during sleep.[165-167] Many parents report being frightened by their child's night-time breathing. At night-time, children may exhibit restless sleep, paradoxical respiratory movements, and sweating during sleep. Patients may also complain of morning headaches, dry mouth, frequent infections (e.g. sinusitis, otitis media), chronic nasal congestion and rhinorrhea, dysphagia, and poor appetite. Daytime sleepiness is a less common complaint in children than in adults, but it occurs in 10–19% of cases.[161] Academic and behavioral problems, potentially secondary to OSA, may not be volunteered unless specifically elicited by the clinician. History may also be positive for other comorbid sleep problems or other risk factors listed earlier in this chapter. In older children and adolescents, the presentation of OSA more closely resembles the adult disorder in risk factors (e.g. obesity) and symptoms (e.g. daytime sleepiness).[25,87]

On physical examination, children with SDB often exhibit mouth breathing, "adenoid facies", hyponasal speech, and adenotonsillar hypertrophy. Craniofacial abnormalities, obesity, poor growth, or a neuromuscular syndrome

should also raise the index of suspicion for SDB.[165] Despite these well-known diagnostic factors, though, many studies have shown that OSA cannot be distinguished from primary snoring on the basis of history and physical examination alone.[103,165,167,168] Although primary snoring is indeed worthy of the otolaryngologist's attention, PSG is necessary to diagnose OSA (as opposed to SDB, which can be diagnosed clinically). However, the indications for PSG and the treatment of SDB are the subject of considerable debate.

## DIAGNOSTIC CRITERIA AND INDICATIONS FOR TREATMENT

The risks of SDB, from primary snoring to OSA, are increasingly understood and widely accepted. Likewise, adenotonsillectomy is accepted as the first-line treatment for OSA in children. However, treatment comes with risks and expenses of its own, and there is still no consensus on the indications for treating SDB in children. Because of the cost, inaccessibility, and inconvenience associated with pediatric PSG—the gold standard for evaluating the severity of SDB—indications for PSG are also controversial.

On the grounds that PSG does not always reflect the impact of SDB on quality of life, the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) does not require PSG in every child with SDB (Table 65.1).[169] In children with demonstrated SDB and tonsillar hypertrophy, the AAO-HNS recommends using the presence of significant SDB sequelae (e.g. growth delay, academic difficulties, etc.) as the basis for surgical treatment. The AAO-HNS recommends PSG specifically for patients with certain comorbidities (e.g. obesity, syndromic disorders, etc.) that may predict surgical complications or persistent OSA after surgery. The AAO-HNS also recommends PSG in children for whom the need for surgery is uncertain, including those with tonsillar hypertrophy or symptoms of SDB but not both.[170] In children with SDB and tonsillar hypertrophy with abnormal PSG, the AAO-HNS recommends offering tonsillectomy as an option.

The American Academy of Pediatrics (AAP) and the American Academy of Sleep Medicine (AASM) endorse a more universal approach to PSG. The AAP recommends that all children be screened for snoring because of its strong association with OSA.[171] Both groups recommend that all children with suspected OSA undergo PSG to establish diagnosis before adenotonsillectomy, given the unreliability of clinical examination.[119,171] This is in contrast with the AAO-HNS guidelines, which recommend PSG when the case for surgery is unclear or when the patient is at high risk for complications and/or persistent OSA.[170] In essence, the AAP and AASM prioritize definitive diagnosis of OSA for all patients; the AAO-HNS prioritizes prompt surgical intervention in when the morbidities of SDB are clearly apparent and patients are otherwise healthy. However, all specialty societies agree on PSG for patients who may be at elevated risk for operative complications. They also recommend postoperative PSG in complex patients whose cases may not resolve after adenotonsillectomy.

Even once patients have undergone PSG, there are no validated guidelines explaining how severe OSA cases must be to warrant treatment. The AHI is the metric most commonly used by sleep laboratories to quantify the extent of obstruction, and many clinicians classify AHI of at least 10 as severe sleep apnea because of those patients' elevated postoperative risk.[172,173] The AAO-HNS also considers any case with an oxygen saturation nadir below 80% as severe OSA.[170] But the criteria for diagnosing and treating mild OSA are much less definitive, particularly in children with an AHI between 1 and 5. Katz and Marcus have proposed the following diagnostic cutoffs, which they suggest should be modified by gas exchange parameters (i.e. pulse oximetry and end-tidal $CO_2$) as needed[174]:

- AHI < 1 = normal
- 1 ≤ AHI ≤ 4 = mild OSA
- 5 ≤ AHI ≤ 10 = moderate OSA
- AHI > 10 = severe OSA

Again, the exact AHI warranting surgery is the subject of considerable debate. The obstructive AHI may prove to be a better guideline for determining the need for surgery. The AAO-HNS and others emphasizing clinical history over PSG diagnosis base their arguments on the morbidity associated with primary snoring and other less-severe manifestations of SDB, outlined earlier in this chapter. Several studies show that clinical history factors (e.g. snoring, time in bed) better predict neurocognitive delays than AHI alone.[175,176] In other words, AHI may be an imperfect surrogate endpoint for "true" clinical outcomes such as neurocognitive and cardiovascular morbidity.[177] And some evidence indicates those "true" outcomes are responsive to adenotonsillectomy even when the PSG is normal.[178,179] This line of argument may or may not justify the large proportion of otolaryngologists who tend not to request PSG preoperatively.[2] But it certainly supports broadening our concern from OSA to the full spectrum of SDB disorders in children.

**Table 65.1:** Select Specialty Society Guidelines for sleep-disordered breathing in children

| | *American Academy of Otolaryngology–Head and Neck Surgery*[169,170] | *American Academy of Pediatrics*[171] | *American Academy of Sleep Medicine*[119] |
|---|---|---|---|
| Indications for polysomnography (PSG) | • Before determining the need for tonsillectomy, refer children with sleep-disordered breathing for PSG if they exhibit certain complex medical conditions such as obesity, Down syndrome, craniofacial abnormalities, neuromuscular disorders, sickle cell disease, or mucopolysaccharidoses<br>• Advocate for PSG prior to tonsillectomy for sleep-disordered breathing in children without any of the comorbidities listed above for whom the need for surgery is uncertain or when there is discordance between tonsillar size on physical examination and the reported severity of sleep-disordered breathing<br>• In children for whom PSG is indicated to assess sleep-disordered breathing prior to tonsillectomy, obtain laboratory-based PSG, when available | • All children/adolescents should be screened for snoring<br>• PSG should be performed in children/adolescents with snoring and symptoms/signs of OSAS; if PSG is not available, then alternative diagnostic tests or referral to a specialist for more extensive evaluation may be considered | • PSG is indicated when the clinical assessment suggests the diagnosis of obstructive sleep apnea syndrome (OSAS) in children<br>• PSG is indicated in children being considered for adenotonsillectomy to treat OSAS |
| Indications for tonsillectomy | • Counsel caregivers about tonsillectomy as a means to improve health in children with abnormal PSG who also have tonsil hypertrophy and sleep-disordered breathing<br>• Ask caregivers of children with sleep-disordered breathing and tonsil hypertrophy about comorbid conditions that might improve after tonsillectomy, including growth retardation, poor school performance, enuresis, and behavioral problems | • Adenotonsillectomy is recommended as the first-line treatment of patients with adenotonsillar hypertrophy | n/a |
| Indications for overnight postoperative admission | • Admit children with obstructive sleep apnea documented on PSG for inpatient, overnight monitoring after tonsillectomy if they are < 3 years of age or have severe obstructive sleep apnea (apnea-hypopnea index of 10 or more obstructive events/hour, oxygen saturation nadir <80%, or both) | • High-risk patients should be monitored as inpatients postoperatively | |

*Contd...*

*Contd...*

| | *American Academy of Otolaryngology–Head and Neck Surgery*[169,170] | *American Academy of Pediatrics*[171] | *American Academy of Sleep Medicine*[119] |
|---|---|---|---|
| Residual symptoms; indications for postoperative PSG | • Counsel caregivers that sleep-disordered breathing may persist or recur after tonsillectomy and may require further management | • Patients should be re-evaluated postoperatively to determine whether further treatment is required. Objective testing should be performed in patients who are high risk or have persistent symptoms/signs of OSAS after therapy | • Children with mild OSAS preoperatively should have clinical evaluation after adenotonsillectomy to assess for residual symptoms. If there are residual symptoms of OSAS, PSG should be performed<br>• PSG is indicated after adenotonsillectomy to assess for residual OSAS in children with preoperative evidence for moderate to severe OSAS, obesity, craniofacial anomalies that obstruct the upper airway, and neurologic disorders (e.g. Down syndrome, Prader–Willi syndrome, and myelomeningocele) |
| Other guidelines | • Communicate PSG results to the anesthesiologist prior to the induction of anesthesia for tonsillectomy in a child with sleep-disordered breathing | • Continuous positive airway pressure is recommended as treatment if adenotonsillectomy is not performed or if OSAS persists postoperatively<br>• Weight loss is recommended in addition to other therapy in patients who are overweight or obese<br>• Intranasal corticosteroids are an option for children with mild OSAS in whom adenotonsillectomy is contraindicated or for mild postoperative OSAS | • PSG is indicated for positive airway pressure titration in children with OSAS |

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CHAPTER

# Evaluation of Airway Obstruction that Persists after T&A: Endoscopic and Drug-Induced Sleep Endoscopy versus Sleep Cine MRI

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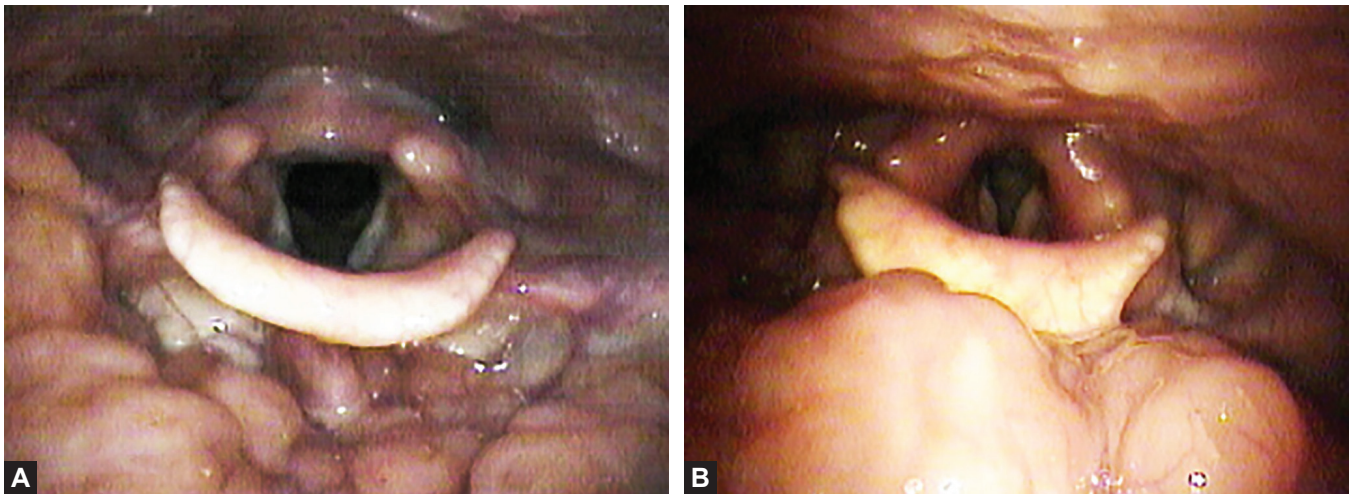
It has become apparent that although removal of the tonsils and adenoids improves upper airway obstruction in children, it is does not always fully cure the obstruction. Multiple studies have shown that persistent obstructive sleep apnea (OSA) occurs in children after tonsillectomy and adenoidectomy (T&A).[1-5] A large meta-analysis of 1079 patients showed that although nearly all patients improved after T&A, 33.7% continued to have OSA after T&A.[6] In one large multicenter study of >500 children, 70% of the children continued to have persistent OSA after T&A of which 20% had at least moderate OSA after T&A. Risk factors in this group of "typical" children with no underlying genetic or craniofacial problems included obesity, age >7 years, underlying asthma in the nonobese children, and more severe preoperative obstruction as documented by polysomnography (PSG).[1] Children with underlying craniofacial anomalies, chromosomal abnormalities, and neuromuscular syndromes are at even higher risks of persistent OSA after T&A.

When airway obstruction persists after removal of the tonsils and adenoids, further plans for treatment should be based on the knowledge of the site, or sites of residual obstruction. It is stressed that although this discussion reviews the advantages and disadvantages of the various evaluation techniques, these modalities to evaluate the residual airway obstruction do not provide objective data regarding the clinical significance and degree of obstruction that may still be present. It is therefore important to first have objective data about the patient's airway obstruction. This is provided by a PSG or sleep study. Knowledge of an abnormal obstructive apnea/hypopnea index with associated hypoxemia and/or hypercarbia confirms that the airway obstruction seen in the evaluation is actually clinically significant.

## ENDOSCOPIC EVALUATION OF THE AIRWAY

### Office Flexible Endoscopy

Flexible endoscopy of the airway in the office, with the patient awake, can be useful for evaluation of nasal obstruction from a deviated nasal septum or from enlarged nasal turbinates. It is also useful for evaluation of possible adenoid regrowth. Office endoscopy also provides a good view of the base of the tongue to rule out lingual tonsil hypertrophy as well as any base of tongue or vallecular masses, such as vallecular cysts or lingual thyroglossal ducts cysts (Figs. 66.1A and B). Laryngomalacia, although most common in the very young infants, can also be seen in older patients and flexible endoscopy in the office can be helpful, but may miss "occult" laryngomalacia (*see* below). Base of tongue obstruction is evaluated by the relationship of the tongue base, the vallecular visualization, and the amount of epiglottis that is seen. Base of tongue may be more obvious if the patient is placed in a supine position.[7] The examination seen in the office, however, may greatly differ from what is actually occurring when the patient is sleeping and may differ from your examination when the patient is under light anesthesia. Muscle tone, airway reflexes, body position, head and neck position, and lung volume all affect collapsibility of the airway differently in the awake and sleeping patient.




**Figs. 66.1A and B:** Enlarged lingual tonsils as seen on an office endoscopy with obliteration of the vallecula.

Proponents of both sleep cine magnetic resonance imaging (MRI) and drug-induced sleep endoscopy (DISE) point to poor surgical outcomes for the treatment of complex OSA where surgical decisions were made from only office examinations and stress that these evaluations better identify site or sites of obstruction compared with office examinations. Eichler et al. evaluated drug-induced surgical endoscopy (DISE) compared with a clinical office examination regarding identification of correct level of obstruction. This study showed significant differences in treatment recommendations when the patients were evaluated by both clinical office examination and DISE. Although similar recommendations were made regarding the need for tonsillectomy with both examination techniques, the DISE examination more often identified the site of obstruction at the level of the soft palate, the epiglottis and also identified potential success with a mandibular advancement splints. The clinical office examination more often identified the base of the tongue as the major site of obstruction. The authors postulated that the DISE examination held potential for increased success rates of noncontinuous positive airway pressure (CPAP) treatments for OSA.[8]

## Drug-Induced Surgical Endoscopy

Sleep endoscopy, nasendoscopy, airway flexible endoscopy, and DISE all refer to an endoscopic evaluation of the upper airway with the patient asleep, usually under a light anesthesia. This includes an endoscopic evaluation of the nasal passages, the nasopharynx, the posterior oropharnyx and velum, the hypopharynx, the supraglottic airway, the glottis and can also include an evaluation of the subglottis and tracheal airway. It was introduced by Croft and Pringle in 1991.[9] The three key features of DISE include: (1) the use of pharmacologic agents to provide sedation, (2) the goal of reproducing upper airway behavior similar to what is seen in natural sleep, and (3) endoscopic upper airway evaluation.[10] Despite being practiced in Europe for many decades, only recently have there been studies looking at the efficacy of DISE in treatment assessment and outcomes.

### *Technique*

A sleep study or PSG should be done prior to DISE. In the operating room, the patient is examined in a supine position, but it is also reasonable to evaluate the airway in a position similar to the patient's sleeping habits at home, e.g. with or without pillows, with or without dental appliances, braces, or dentures. It may be useful to examine the patient in a variety of positions. The nose is decongested with oxymetazoline prior to passing the flexible endoscope. Anesthetic agents commonly used include propofol and/or midazolam. Propofol is an ultrashort acting hypnotic but with a narrow therapeutic range. Its functional half-life is 4.6 minutes, with elimination half-life of 55 minutes. It enables a greater control of depth of sedation compared with midazolam but has depression on the central breathing. Studies have reported that while propofol does not change respiratory patterns or effect AHI levels, it does interfere with sleep architecture, with a reduction in rapid-eye-movement (REM) sleep.[11] It has also been shown that propofol decreases genioglossus

neuromuscular activity and may contribute to more tongue base collapse than what occurs in true sleep.[12,13] A combination of propofol and fentanyl has also been described in pediatric patients.[14]

Midazolam, a benzodiazepine, has a larger therapeutic range with active metabolites, such that accumulation of the drug is more common than for propofol where there are no metabolite products. Midazolam's functional half-life is 45–60 minutes, and elimination half-life is 150 minutes. It causes more muscle relaxation than propofol, which can affect true sleep findings. This includes causing a slight increase in the apnea index and changes in length of apneic events and REM sleep.[11,15]

One of the newer anesthetic agents being used for DISE as well as for cine MRI evaluations of the airway is dexmedetomidine (DEX).[16] An anesthetic "cocktail" of both DEX and ketamine has also been described.[14] DEX does not depress the respiratory drive and may mimic natural sleep better than other anesthetic agents due to less associated muscular relaxation and more normal respiratory effort.

Along with these anesthetic agents, oxygen is provided to the patient, using a variety of delivery techniques such as by nasal cannulas, anesthetic face mask, or endotracheal tube sitting in the posterior oropharynx.

Anesthetic depth is of key importance. The target depth of anesthesia has been reported to be at "loss of response to verbal stimulation",[10] but more realistically, it should also include loss of response to instrumentation of the airway passages. The target depth of sedation has also been described as the transition from consciousness to unconsciousness, and since patients have different responses to the anesthetic agents, a slow stepwise sedation technique is suggested. Oversedation could provide inaccurate information because deeper levels of sedation cause a decrease in upper airway dilator muscle tone and neuromuscular reflex activation, both of which increase airway collapsiblity.[10]

Once the desired level of anesthesia is achieved, the flexible endoscope, preferably with a digital video camera attachment or camera chip in the scope, is inserted into the nose with examination of the nasal passages, the nasopharynx, the velum, tongue base, supraglottis, and larynx. At the level of the nasopharynx, the position of the palate and uvula in relation to the posterior pharyngeal wall is assessed. At the level of the oropharynx, lateral wall movement is evaluated, particularly looking for lateral wall collapse. At the level of the hypopharynx, as the base of tongue comes into view, its position in relationship to the vallecula and the epiglottis as well as the posterior pharyngeal wall is noted. The examination can also then continue into the trachea to evaluate the subglottis and trachea. Edema and erythema of airway tissues should also be noted.

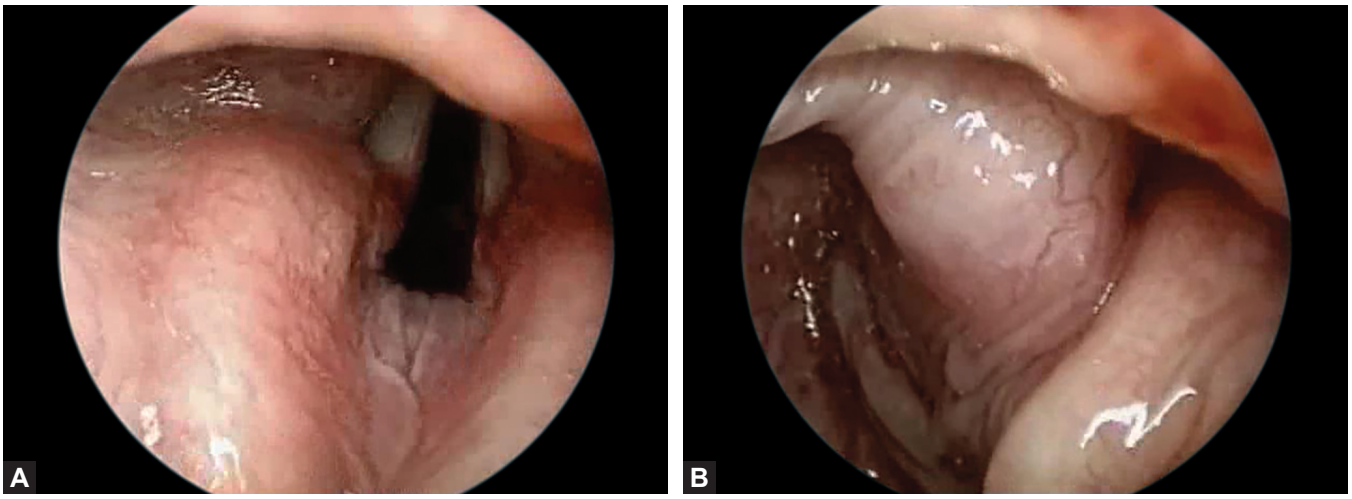
### *What Is Normal and Abnormal Anatomy?*

As described by Truong et al., the level of the nasopharyx, the airway opening should be horizontally oval and remain open throughout respirations.[14] Adenoid hypertrophy or regrowth of adenoids despite previous adenoidectomy can cause obstruction. In children with hypotonia or midface hypoplasia, the palate may collapse against any residual adenoids or onto the nasopharyngeal wall and cause obstruction. Partial obstruction can present with a fluttering of the leading edge of the palate and uvula.

At the level of the oropharynx, a normal examination would show mild lateral wall indentations, but a patent airway throughout the examination. Obstruction could show lateral wall collapse with obstruction, anterior–posterior (AP) collapse or circumferential collapse. If this examination is being done due to the patient having small tonsils that were not felt to be the source of obstruction, DISE may show an unexpected contribution of 1+ or 2+ tonsils to oropharyngeal crowding and airway obstruction during sleep.[17]

At the level of the tongue base, there may be a small amount of lingual tonsil tissue, but the vallecula should be visible at some point during the respiratory cycle. The epiglottis and aryepiglottis folds should be visible. There may be some mild retroflexion of the epiglottis toward the posterior pharyngeal wall. With enlarged lingual tonsils or in cases of glossoptosis, the tongue or tonsillar tissue fill the vallecular area and can cause either retroflexion of the epiglottis such that the epiglottis is only partially visible or totally obscured. In addition to this AP direction of obstruction, there can also be lateral wall collapse with more of a circumferential pattern of collapse. This circumferential pattern of collapse may be more common in patients with hypotonia, craniofacial anomalies, or more severe OSA.

At the level of the larynx, the supraglottic tissues remain open during respiration with full visualization of the vocal cords. Obstruction at this level could be from the epiglottis prolapsing over the glottis opening, or from arytenoid prolapse. "Occult" laryngomalacia occurs




**Figs. 66.2A and B:** Occult laryngomalacia with prolapse of left arytenoid during respirations during drug-induced surgical endoscopy.

when there is prolapse of the one or both of the arytenoid mucosa during respirations that was not appreciated in the awake endoscopy (Figs. 66.2A and B). Supraglottiplasty has been shown to be effective for older children who were found to have occult laryngomalacia on DISE.[18,19]

During the evaluation, maneuvers can be done to assess how changes in the mandible position affect base of tongue collapse. This includes the chin lift, where there is manual closure of the mouth (Fig. 66.3) and the jaw thrust or Esmarch maneuver, where the mandible is advanced 5 mm (Fig. 66.4). The jaw thrust is used to evaluate for base of tongue obstruction. When the base of tongue is displacing the epiglottis such that the larynx is not able to be visualized, the jaw thrust may provide better visualization of the larynx and thus suggests that base of tongue obstruction is a major source of obstruction. For older children and adults, the jaw thrust can be used to determine if a mandibular advancement prosthesis would be effective.[10] On the other hand, study of Vroegop et al. suggested that the use of simulation bite block placed at the time of DISE was a better predictor of efficacy of this nonsurgical treatment modality.[20]

### *Validity of DISE*

Several studies have explored the validity and reliability of DISE in adults, specifically looking at site of obstruction, degree of obstruction, and configuration of the obstruction.[11,15,21-24] Similar to the MRI studies on patients with PSG-confirmed OSA compared to those with no history of obstruction, DISE evaluations on patients with OSA have been shown to be significantly different compared to those without sleep-disordered breathing. More severe levels of OSA have been associated with more severe obstruction seen on DISE.[21] Inter-rater reliability has been shown to be "moderate to substantial" in one study of DISE done on adults.[22]

As DISE has started to be used more often in children, similar studies evaluating the validity of sleep endoscopy in the pediatric populations have been done.[14,17,25] Similar to what is seen in adults, the obstruction is primarily seen at multiple sites. However, in pediatric studies, published papers thus far have identified differing sites of obstruction as the most common for children. Ulualp and Szmuk found that in more severe OSA, multilevel obstruction was more common, with a combination of oropharyngeal lateral wall collapse along with obstruction at the level of the soft palate.[17] Base of tongue collapse was also frequently seen. Single-site obstruction was seen more often in the children with mild OSA. In children with 1+ or 2+ tonsils, lateral wall obstruction from even these small tonsils has been reported. More severe OSA in children has also been correlated with more severe multilevel obstruction on DISE.[17] In a study of 13 patients by Durr et al., the most common sites of obstruction when using DISE to evaluate residual obstruction after T&A were at the tongue base (85%), from adenoid regrowth (69%), and/or inferior turbinate hypertrophy (54%).[25] Truong et al. evaluated 151 children with persistent OSA after T&A reported sleep endoscopy to be most helpful for identification of regrowth of adenoids, differentiating enlarged lingual tonsils from tongue base collapse alone, and in diagnosing occult laryngomalacia.[14]

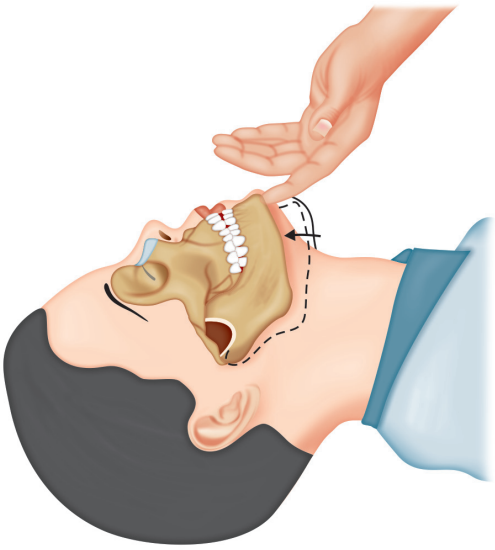


**Fig. 66.3:** The chin lift, providing manual closure of the mouth during drug-induced surgical endoscopy.

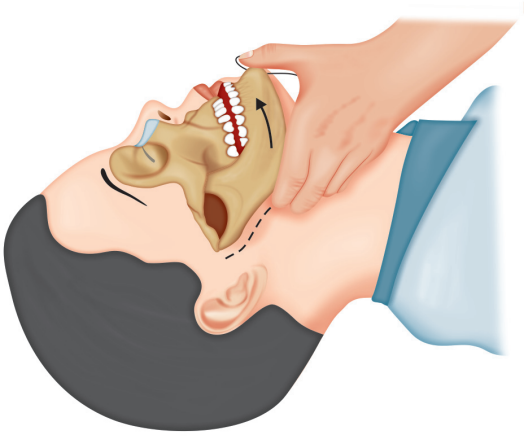


**Fig. 66.4:** The jaw thrust or Esmarch maneuver, advancing the mandible up to 5 mm.

There have been a few studies evaluating the ability for DISE to affect surgical plans.[26,27] Most have focused on selecting appropriate patients for uvulopalatopharyngoplasty, and results are mixed. Further studies are needed.

### *Classification System for DISE*

To date, there is not a standard classification system to characterize the endoscopic findings seen on DISE. This prevents comparison between evaluations performed at different institutions, between different patients, and for an individual patient before or after a therapeutic intervention. Two proposed systems include the VOTE classification system developed in adults with sleep-disordered breathing and the grading system described by Yellon for epiglottic and base-of-tongue prolapse in children.[10,28]

Hohenhorst et al. developed the VOTE classification system based on 7500 adult DISE examinations, in which they observed the structures involved in airway obstruction, the degree of obstruction, and the direction of collapse.[10] DISE was performed with the patient in supine position with basic cardiorespiratory monitoring and with the ability to administer supplemental oxygen. Atropine, or another anticholinergic medication, was given 20 minutes before the procedure to decrease salivation and prevent aspiration. A topical anesthetic was used in the bilateral nares, taking care not to overly anesthetize the posterior pharynx. Propofol and/or midazolam was used for sedation until the patient's transition from consciousness to unconsciousness was reached. Once the correct depth of anesthesia was reached, a flexible endoscope was placed in the nares and advanced to identify the level of obstruction and evaluate the upper airway. At that time, a jaw thrust and/or a chin lift could be performed to change the dynamics of the airway and evaluate improvement. The endoscopic examination was performed in the operating room or clinic, depending on physician's preference, degree of patient sleep disturbance, and patient health.

The VOTE acronym refers to the most common anatomical sites of obstruction seen on endoscopy, specifically: (V) Velum, (O) Oropharynx, (T) Tongue base, (E) Epiglottis. In addition to the level of obstruction, the classification system describes the direction of collapse including AP, lateral, or concentric. Obstruction is then qualitatively assessed as either (0) none, which is <50% narrowing compared with the nonapneic state; (1) partial, 50–75% narrowing; (2) complete, >75% narrowing with no associated airflow; or (X) not visualized. Partial obstruction can also be identified by vibration of the involved structure.

Velum (V) obstruction is found at the level of the soft palate, uvula, or lateral pharyngeal wall at the level of the velopharynx. Collapse is described as AP or concentric, rarely lateral. Oropharyngeal (O) obstruction includes the tonsils and lateral pharyngeal wall tissue, and lateral or concentric collapse is seen. Obstruction at the level of the Tongue base (T) is demonstrated by an AP collapse.

Epiglottic (E) obstruction is described as AP or lateral, but not concentric. Other levels of obstruction can be seen and described, but they are noted separately.

Another proposed classification system for the upper airway obstruction was devised by Yellon in a prospective study of 14 children (mean age 6.8 years) with epiglottic and base-of-tongue prolapsed.[28] Flexible nasopharyngoscopy during spontaneous respiration in the supine position was performed on patients who were lightly sedated with meperidine and nitrous oxide. Oxymetazoline was administered to the bilateral nares, without the use of topical anesthetic. Patterns were seen in this study population, and a grading system to assess severity and anatomic site of obstruction in the pharyngeal and supraglottic airway of pediatric patients was proposed. Grade 0 is normal. Grade 1 is a prolapsed epiglottis against the pharyngeal walls, with normal tongue position, which occurred in 50% of patients. Grade 2 is prolapse of the epiglottis and base of tongue, where only the tip of the epiglottis is visible (29%). Grade 3 is glossoptosis, where no portion of the epiglottis is visible (21%). In grades 1–3, the endolarynx is not visible without a jaw thrust or anterior retraction of the tongue.

The aim of both proposed grading systems is to establish a standardized approach to the assessment of upper airway obstruction in patients with sleep disorders. The VOTE classification includes the velopharynx and oropharynx, whereas the Yellon classification specifically looks at the epiglottis and base of tongue. In addition, the VOTE classification evaluates both the degree of obstruction and the specific type of narrowing, whereas the Yellon classification does not address the direction of collapse. It should also be noted that the VOTE classification was observed in adults, whereas the Yellon classification was described in pediatric patients. Regardless, the goal is to adopt a system of classification that can be used to compare pre- and postintervention results in a single patient, to compare findings in different patients, and to compare results among surgeons. This will allow treatment planning based on the type of obstruction and provide a guide for effective interventions based on the classification of obstruction seen in a particular patient.

Limitations of DISE include a lack of uniform anesthetic techniques with associated variations in the alterations and side effects of these medications on airway collapse. There is also a need for more standardized techniques for the endoscopy itself. For instance, there are differences in the airway obstruction if the examination is done with the patient's mouth open or closed. It has been shown that the position of the mouth greatly affects the patency and dynamics of the airway.[29,30] Should all the endoscopies be done in a similar mouth position, or should the examination be done in the patient's more common mouth position during sleep? In addition, there is still a lack of consensus regarding DISE classification systems. A standard classification system would increase our abilities to truly evaluate outcomes from the DISE evaluation of airway obstruction in OSA. The currently used grading systems also do not include inferior turbinate enlargement, adenoid regrowth, and laryngomalacia in its analysis, all common sites of obstruction.

## SLEEP CINE MRI EVALUATION OF THE AIRWAY

Sleep cine MRI provides a complete evaluation of the upper airway without the encumbrance of scopes and tubes; albeit, with artificial unconsciousness induced by general anesthesia (GA) or sedation. By taking multiple consecutive MRI images of the airway over a short period of time, these images can then be displayed in a "cine" or movie format.

Sleep cine MRI allows a dynamic evaluation of the airway. There are several advantages to sleep MRI compared with endoscopy. First, there is the absence of direct instrumentation of the airway, which can itself influence the dynamics of airway flow and collapse or arouse the patient. Second, there is the visualization of multiple levels of the dynamic airway motion on a single midline sagittal cine image, which can provide insight into the sequence of collapse.[31] Third, the anatomy of the airway is very well delineated as to the depth and thickness of tissues such as recurrent adenoids or lingual tonsils, and the relative size of the tongue and facial structures, which can contribute greatly to the collapse of the airway. Fourth, the dynamic motion of the airway can be observed and characterized in both the midline sagittal midline plane and transverse plane at areas of collapse or narrowing, mainly the retroglossal airway and nasopharyngeal airway. Overall, a thorough evaluation of the airway anatomy and physiology during unconsciousness is obtained and documented for debate and objectification and quantifiable analysis.

### Common Findings on Sleep Cine MRIs of the Airway

The usefulness of dynamic sleep MRI to evaluate the upper airway stems from the ability to see more than just

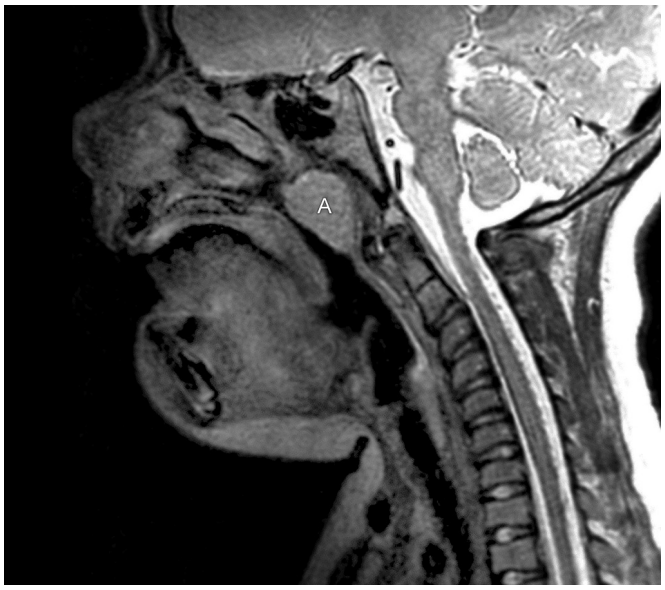



**Fig. 66.5:** Midline sagittal proton density weighted magnetic resonance imaging showing recurrent hypertrophy of the adenoidal tonsils (A) which contribute to this patient's sleep apnea.

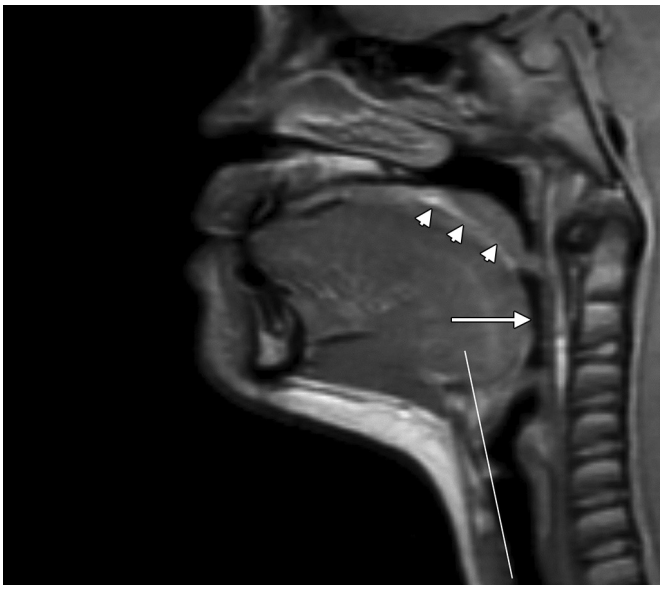


**Fig. 66.6:** Midline sagittal proton density weighted MRI shows macroglossia. The tongue fills the oral cavity, pushes the soft palate posteriorly and superiorly (arrowheads) narrowing the nasal pharyngeal airway, and projects posteriorly (arrow) to the anterior tracheal line (white line) nearly touching the posterior wall of the pharynx.

the superficial surface of internal structures. Both static and dynamic images can be useful in the evaluation to determine site or sites of obstruction. In addition, the airway can be visualized along its entire length with midline sagittal imaging. At the level of the nasopharynx, a common contributor to OSA is the hypertrophy of the adenoid tonsils (Fig. 66.5). Adenoid hypertrophy due to recurrent adenoid tonsil tissue growth, despite previous T&A was seen in 63% of a group of children with Down syndrome who continued to have OSA despite previous T&A.[31,32] Typically, adenoids are considered enlarged if they are >12-mm thick.[31,33] In addition, the dynamic images may show a greater than expected narrowing of the nasopharyngeal airway in cases of adenoids < 12 mm due to concomitant nasopharyngeal collapse and airway hypotonicity and elucidate a significant contribution of residual adenoids to the patient's airway obstruction and OSA.[31] Arens et al. evaluated children with OSA using MRI and showed that children with OSA had not only larger adenoids and but also larger soft palates than what was seen in controls.[34] The relative length of the soft palate and its contribution to the OSA can be qualitatively observed on the sagittal images.

The tongue and retroglossal airway are important areas to evaluate when studying OSA with sleep MRI. Both static and cine images provide a good evaluation of this area and the size of the tongue. Studies specifically looking at macroglossia, including studies using volumetric studies from MRI evaluations, have documented the importance of macroglossia as an etiologic factor in OSA.[35-37]These studies have shown that OSA can be associated with both "relative" macroglossia and true macroglossia. The relative macroglossia is more commonly seen in the midface hypoplasia associated with Down syndrome and in children with craniofacial deformities. However, OSA is also seen in cases of true macroglossia where the facial structures are normal.

If one looks at imaging studies of normal patients, the tongue does not typically fill the oral cavity when the mouth is closed. In the normal airway, if the mouth is open, the tongue does not push the soft palate superiorly and posteriorly, and it does not project beyond the dental confines anteriorly or laterally. In addition, the posterior tongue often projects substantially posterior of the anterior tracheal line in patients with OSA (Fig. 66.6), but only mildly in normal patients.

Persistent OSA after T&A can be caused also by enlarged lingual tonsils.[32,38] Although these are easily evaluated by endoscopy, the MRI provides a better picture of the extent and depth of the lingual tonsil tissue and can be more helpful in surgical planning (Fig. 66.7).

The dynamic, cine sequences of the sleep MRI are a key to evaluating the collapsing motion of the retroglossal airway. It has been shown that in patients with normal PSGs, the nasopharynx, the oropharyngeal, and the hypopharyngeal airway size should not have a diameter change >5 mm. Movement > 5 mm at the levels of the airway are associated with OSA.[39,40] By examining both sagittal and axial views of the airway, a better understanding of the complexity of the airway collapse is possible. For instance, the motion of the tongue on the midline sagittal cine provides assessment in the anterior and posterior plane. Significant, >5 mm of movement, is suggestive of glossoptosis. However, evaluating the retroglossal airway in cross-sectional axial views of the cine MRI can identify concomitant collapse of the lateral airway soft tissues resulting in hypopharyngeal collapse[40] (Figs. 66.8A and B). Although AP motion of the tongue is usually present in both hypopharyngeal collapse and glossoptosis, many believe that the description of glossoptosis should be reserved for cases in which the AP diameter change is greater than the transverse or lateral diameter change as is illustrated in Figures 66.9A to C.

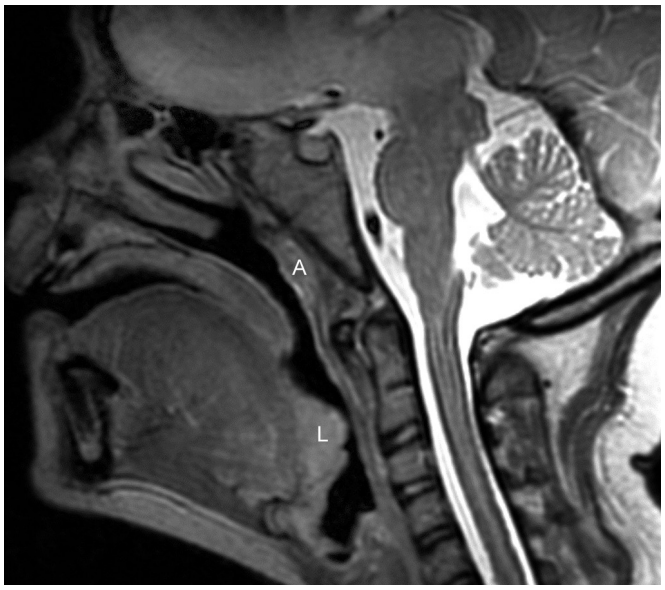
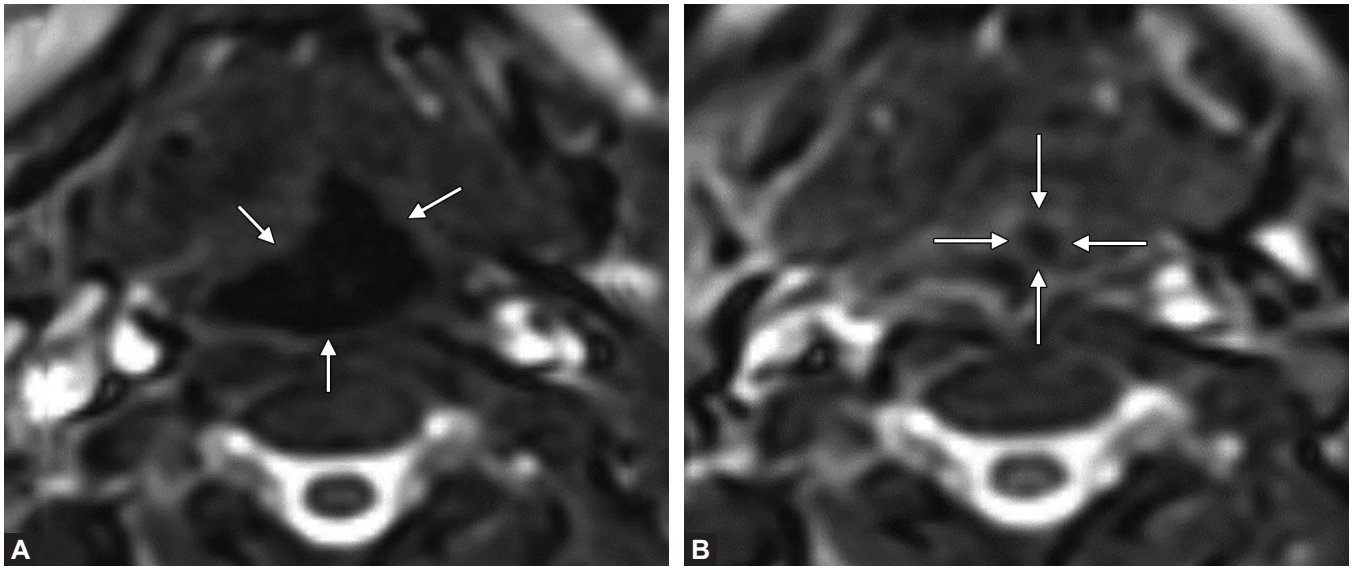
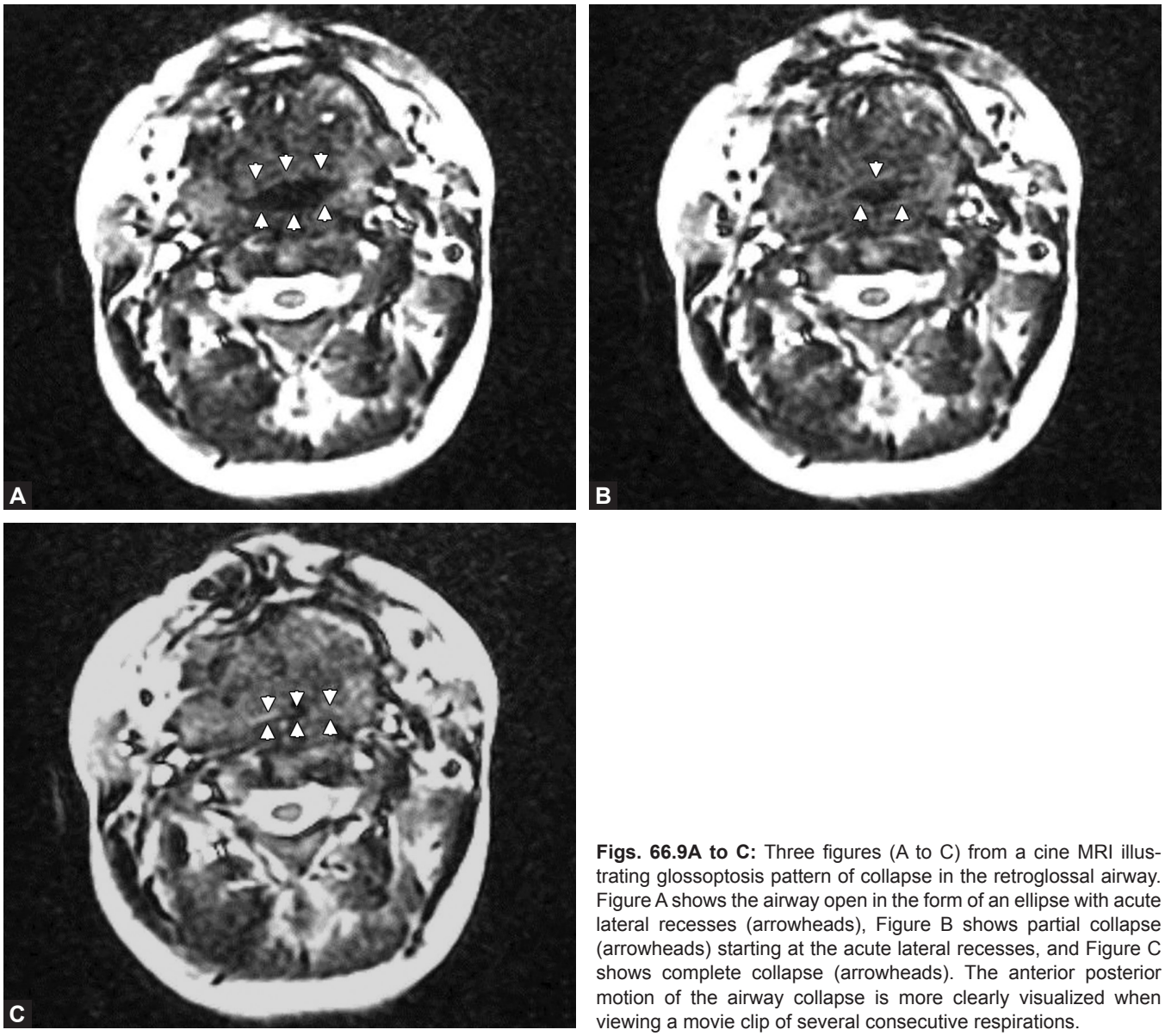



**Fig. 66.7:** Midline sagittal proton density weighted magnetic resonance imaging shows markedly enlarged lingual tonsils (L) which contribute to this patient's recurrent obstructive sleep apnea. Also note that the adenoid tonsils are not enlarged (A).

The cine MRI also allows for identification of primary and secondary sites of obstruction. On the midline sagittal cine MRIs, motion of the retroglossal airway can be secondary to obstruction of the nasopharyngeal airway level, and in some cases there is a clear collapse of the nasopharyngeal airway first and then the retroglossal airway secondarily, resulting in multilevel obstruction.[31] The vertical motion of the larynx associated with upper airway obstruction has been observed to be exaggerated in nasopharyngeal collapse.[39] Determination of primary and secondary sites of obstruction can be helpful in surgical treatment planning.




**Figs. 66.8A and B:** Two frames (A and B) from a cine MRI illustrating hypopharyngeal collapse in the retroglossal airway. Frame A shows the airway (arrows) widely patent with a triangular configuration, and frame B shows the airway collapsed centrally in a pattern of hypopharyngeal collapse (arrows).




**Figs. 66.9A to C:** Three figures (A to C) from a cine MRI illustrating glossoptosis pattern of collapse in the retroglossal airway. Figure A shows the airway open in the form of an ellipse with acute lateral recesses (arrowheads), Figure B shows partial collapse (arrowheads) starting at the acute lateral recesses, and Figure C shows complete collapse (arrowheads). The anterior posterior motion of the airway collapse is more clearly visualized when viewing a movie clip of several consecutive respirations.

Cine MRI has also shown that the retroglossal cross-sectional area is more variable in patients with OSA compared with normal control patients.[41] The result is a larger average airway over time despite the intermittent collapse. It has been hypothesized that this may be due to proximal anatomic narrowing at the nasopharynx or due to decreased tone and increased compliance in the airways of patients with OSA.[41] However, patients with severe OSA have also been observed to thrust their tongue and jaw while under GA to keep the airway open, which may also be an explanation for this observation. Currently, the tone and compliance of the soft tissues are beyond the scope of clinical practice of MRI, but techniques are being developed to estimate these characteristics during sleep cine MRI.

## Sleep Cine MRI Technique: General Considerations

Before using sleep cine MRI to evaluate the airway, there are some general considerations that should be addressed. Prior to the MRI, the patient should have a PSG to document the degree of obstructive versus central sleep apnea, which increases the appropriateness and

usefulness of the sleep MRI for management decisions. In addition, the patient should be screened for contraindications to MRI such as electronic devices (pacemakers, implanted defibrillators, vagal nerve stimulators, or other electronic devices), cranial aneurysm clips, or oral metal appliances such as braces or permanent retainers. Oral metal appliances can make it impossible to obtain adequate imaging of the airway due to artifact from the appliance. However, the amount of artifact depends on the iron content of the appliance. If the child is cooperative, test imaging can be performed immediately prior to sedation to determine if the artifact is too great for adequate imaging. If the degree of artifact interferes with evaluation, the referring physician can determine if the evaluation is clinically essential and have the braces removed.

Most children will require some degree of sedation for the MRI procedure. Many pediatric patients with OSA are complex with genetic disorders like Down syndrome and Pierre Robin sequence that contribute to their obstruction. Most will not be cooperative enough to fall asleep in an MRI scanner without the aid of medications. However, in older populations and in patients without developmental delay, natural sleep may be possible, especially after periods of sleep deprivation. One of the problematic issues is the noise of the scanner waking patients during the imaging, but new MRI scanners have modes of operation that can allow a substantial decrease in the degree of acoustic noise.

Since most patients require anesthesia or sedation to obtain a sleep-like state it is important to discuss some general principles regarding sedation in OSA. One of the more important points to remember is that upper airway collapsibility is markedly increased in both sleeping and anesthetized children.[29,30] Anesthetic agents impair the ability of the upper airway muscles to overcome the negative pressures during inspiration, resulting in increased upper airway resistance and predisposing the patient to obstructive events, especially in the retropalatal region resulting in oxygen desaturation under anesthesia. Anesthetic agents have variable effect on the suppression of the upper airway dilator muscles. Propofol sedation has a profound effect on the collapsibility of the upper airway and has been shown to reduce the cross-sectional area of the airway in a dose-dependent fashion.[42-44] Mahmoud et al. have compared the effect of propofol to DEX and found that artificial airway support to prevent oxygen desaturation during MRI sleep study is significantly less with DEX.[16,45] DEX has properties that result in a sedated state that parallels natural, non-REM sleep and is our preferred choice for GA in the sleep MRI studies. Previously, prior to anesthesia providing sedation services for radiology, patient were sedated with pentobarbital as part of a structured sedation program with sedation nurses and respiratory therapist monitoring the patient during MRI.[40] Pentobarbital, along with isoflurane and ketamine, causes a dose-dependent augmentation of genioglossus activity with increasing depth of anesthesia.[46-50]

Our current preferred anesthetic agent is DEX, but occasionally DEX is insufficient and propofol is used with the awareness that the airway may be more difficult to manage and result in desaturations during MRI. Oxygen desaturation can be managed with the application of CPAP nasally or by facemask, or with a nasal trumpet. CPAP can worsen the narrowing of the retroglossal airway in the presence of open mouth breathing. The CPAP pressure can push the tongue posteriorly, resulting in inaccurate retroglossal obstruction.[51] Therefore, it is important to remove these supports during image capture. CPAP is preferred since it does not distort the anatomy and is easily removed during the short periods of imaging by turning the CPAP support pressure to 0 cm of water. Removal of the nasal trumpet for subsequent repeat cine imaging (see technique) can result in arousal of the patient.

### *Sleep Cine MRI—Technique*

Patients are positioned supine in a head and neck vascular coil with the head and neck in neutral position, and anesthesia induction is performed. Placement of a face/nasal mask strap prior to induction can be helpful if CPAP is needed to maintain oxygen saturation. No attempt is made to open or close the mouth, but if an oral airway was placed temporarily during induction, it is removed before the subject is transferred to the MRI scanner. Supplemental oxygen by nasal cannula is provided while in the MRI scanner. Airway adjuncts are avoided unless subjects meet a predefined criteria: oxygen saturation below 90% in subject with mild OSA and below 85% for subjects with moderate to severe OSA.[16] Supplemental airway support with nasal CPAP is preferred when required. Nasal trumpet can also be used, but is less desired due to distortion of the nasopharyngeal airway and the potential of arousing the patient when it is removed for additional imaging.

The MRI protocol consists of a three-plane scout for localization, a respiratory triggered three-dimensional (3D) isotropic fast spin-echo (FSE) sequence for anatomy,

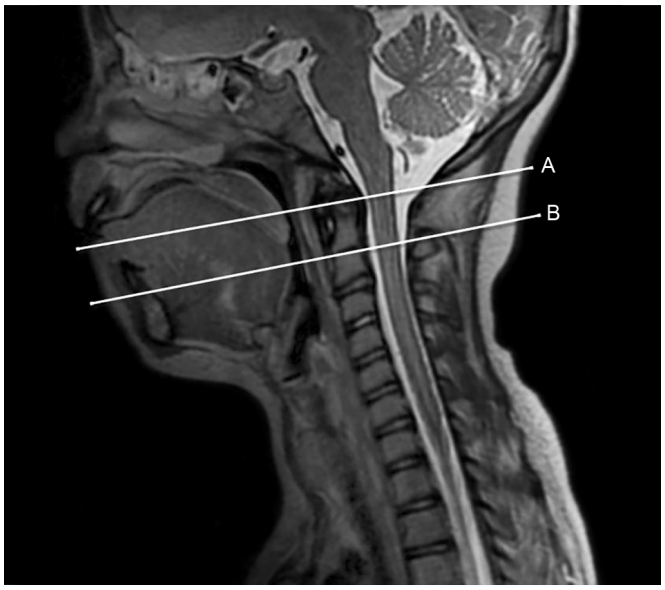



**Fig. 66.10:** Midline sagittal proton density images showing the positioning for the nasopharyngeal dynamic cine imaging (A) and the retroglossal dynamic cine imaging (B).

and cine gradient echo (GRE) sequence at the midline sagittal plane, transverse plane at the narrowest point of the retroglossal airway, and at the narrowest point of the nasopharyngeal airway (Fig. 66.10). Additional axial FSE T2 with fat saturation and sagittal FSE inversion recovery imaging is performed. Superiorly, the field of view (FOV) extends from the bony plate of the anterior cranial fossa to the subglottic trachea inferiorly, but this can often include a substantial portion of the trachea in smaller patients. The AP FOV includes the tip of the nose and chin, anteriorly, and the occipital skull posteriorly.

The use of a respiratory triggered 3D isotropic sequence provides a high-resolution dataset that can be viewed in any plane and even used to reconstruct detailed 3D images of the airway for modeling. Typical resolution for this type of sequence ranges from 0.6 to 1.0 mm depending on FOV, scanner, and coil used. All major MRI vendors have 3D isotropic FSE-based sequence available; CUBE (GE), VISTA (Phillips), and SPACE (Siemens), which can be used with respiratory triggering to alleviate motion artifact. Respiratory triggering occurs at end inspiration, because the airway is open and relatively static during this phase of respiration. The triggering is typically obtained from an abdominal bellows or band, which is standard respiratory triggering on most MRI scanners. However, more robust triggering can be obtained from airflow detected by a nasal cannula and can alleviated problems when paradoxical motion of the abdomen is present during obstructive episodes.[52] Specific parameters for a 3D FSE with proton density weighting are as follows: TR = 3156; TE = 35.022; flip angle = modulated; echo-train length 64; FOV = 240 mm; matrix = 256 by 256; slice thickness = 1.60 mm; slice interval = 0.80 mm. This sequence uses a modulated flip angle to decrease blurring and parallel imaging to reduce time resulting in a real 0.8-mm isotropic resolution with minimal blurring due to respiratory motion and is approximately a 5-minute acquisition depending on triggering efficiency.

The sequences for dynamic cine imaging include steady-state free precession and fast GRE. A single slice is obtained repetitively as fast as the MRI scanner can perform the sequence. Parallel image is method of accelerating the acquisition of the images and is available on nearly all current scanners over the past few years. The typical temporal resolution that can be obtained is 200 to 500 ms per image. That is a sample of 4 to 10 images per 2-second respiratory cycle if the patient is breathing at 30 times per minute. The spatial resolution is 1.5 to 2.0 mm and the slice thickness is 5 mm. The sagittal midline images provide a movie loop of the entire airway, including the nasopharyngeal airway, the retroglossal airway, and the oral airway, which can provide a wealth of information regarding areas of obstruction and the timing of airway collapse. It also elaborates on the motion of the tongue, mandible, and soft palate during these obstructive events. Since the sagittal midline view only shows motion in the AP direction and result overestimation of airway collapse due to the inherent volume averaging in a 5-mm-thick slice, this midline sagittal dynamic movie needs to be supplemented with axial dynamic cine images. These are performed perpendicular to the narrowest part of the retroglossal airway, which is usually just above the epiglottis and perpendicular to the narrowest point of the nasopharyngeal airway (Fig. 66.10). These images will show the true degree of motion and collapse of the airway, which is discussed above.

### *Sleep Cine MRI—Pros and Cons*

Like anything else in medicine, sleep MRI is not without controversy with regard to methods, safety, or usefulness compared with other methods for obtaining similar information. As with DISE, several controversies surround the use of sleep cine MRI for diagnosis and management of OSA. The most obvious controversy is that the drug-induced sleep does not accurately reproduce upper airway behavior seen in natural sleep. However, experience in DISE

and prior use of drug-induced sleep during fluoroscopy would argue against a substantial difference. It can be argued that although drug-induced sleep occurs in cine MRI, the amount of medication is much less than what is needed for patients to tolerate instrumentation as occurs in endoscopy. More recently, we have measured the critical closing pressure of the airway in a group of patients under DEX anesthesia and showed a high correlation with the obstructive index during sleep studies (unpublished data).

Another controversy regards the safety of sleep MRI while under sedation, but this is largely obviated by a team approach with good communication between the radiologist, anesthesiologist, and ordering physician, which manages the risk of GA in patients with OSA. Prior to adopting an institutional policy of anesthesiology presence for all sedations done in the radiology department, we performed sedation under a structured sedation program with a nurse and respiratory therapists in attendance at these studies with no adverse outcomes.

A lesser controversy is one of positioning. The position of the patient in the MRI may be different than how the patient actually sleeps. However, the position in which the patient sleeps is often a function of the underlying obstruction and supine positioning with the head and neck in neutral position could be considered a "stress test" for OSA. In addition, similar to the issue seen in DISE, but this is something that could be standardized in sleep MRI.

## AIRWAY ENDOSCOPY VERSUS SLEEP CINE MRI—IS THERE A "BEST" APPROACH?

Airway endoscopy, or DISE, provides a full examination of the airway from the nose through the trachea. It includes areas that the sleep cine MRI does not evaluate. However, only one level of the airway can be evaluated at a time and one is not able to stratify multilevel obstruction in terms of primary and secondary levels of obstruction. In cases of multiple sites of obstruction it is difficult with DISE to prioritize which surgery to do first if multiple interventions are needed. In cases of multiple sites of obstruction in children, there is unfortunately a higher incidence of oropharyngeal stenosis from multilevel surgery, over 8%, compared with doing the same surgeries at the same time in adults. Therefore, stratifying the primary and secondary sites of obstruction is more critical in the younger populations.[53] In addition, there is the concern of the need for more anesthesia in order for the "sleeping" patient to tolerate airway instrumentation, in addition to the lack of a standard anesthetic drug that is routinely used. Many have advocating doing the DISE evaluation and then proceeding with surgery at the same time. However, this may not an ideal plan in cases where several options of treatment are possible, and risks and benefits of the surgeries versus medical options need to be discussed with family members.

Sleep cine MRI allows full evaluation of the upper airway at the same time, and primary and secondary obstruction sites can be identified. In cases of adenoid and lingual tonsil hypertrophy, the depth of the tissue better appreciated on the MRI images. In addition, because there is no instrumentation of the airway, lesser amounts of anesthesia are needed for this procedure so the evaluation may more closely represents natural sleep. Both static and dynamic images are obtained in both axial and sagittal views and can be reviewed multiple times. The main limitation is that this technique does not include an evaluation of the nasal airway, the larynx and the trachea. This technique is available on all MR scanners but is still new to many locations.

Ideally, in cases of persistent OSA after T&A as documented by PSG, it would perhaps be best to get a sleep cine MRI first and then to consider a DISE procedure in the rare cases where the site(s) of obstruction are not identified by the sleep cine MRI.

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CHAPTER

# Surgical Management of Pediatric Obstructive Sleep Apnea

67

*Derek J Lam, Stacey L Ishman*

## INTRODUCTION

Pediatric obstructive sleep apnea (OSA) was first described in 1976 and since then has been recognized as a cause of significant neurobehavioral and cardiovascular morbidity in children. Unlike in adult OSA where continuous positive airway pressure (CPAP) is first-line treatment, surgical management is recommended as primary therapy for pediatric OSA by both the American Academy of Pediatrics[1] and the American Academy of Otolaryngology—Head and Neck Surgery.[2] Initial surgical management usually consists of adenoidectomy or adenotonsillectomy (TA). Because hypertrophy of the adenoids and tonsils is common in children with OSA and removal is often an effective treatment, we also review the effectiveness and impact of adenotonsillectomy on children with OSA.[1,2] When children have persistent OSA after TA or adenoidectomy, additional surgical procedures may be considered. Here, we present information on nasal surgery, especially turbinate reduction, palatal procedures, and surgery for the base of the tongue. Lastly, we present information on the role of supraglottoplasty and tracheotomy.

## ADENOTONSILLECTOMY

Each year >530,000 tonsillectomies are performed in the United States, and 77% of these are performed for OSA.[3,4]

### Polysomnography Impact

TA has been shown to be very effective in treating pediatric OSA as assessed by polysomnography in multiple studies.[5-8] Studies looking at changes in OSA severity usually report changes in the Apnea Hypopnea Index (AHI), although the Respiratory Disturbance Index (RDI) is also sometimes used. A 2006 meta-analysis by Brietzke and Gallagher reviewed the results of 14 studies published between 1980 and 2004. This systematic review demonstrated a mean improvement in AHI of 13.92 (95% confidence interval 10.05–17.79, $p < 0.001$) and successful normalization of sleep study parameters after TA in 83% of patients across 14 studies.[5] This was based on variable definitions of normalization with significant heterogeneity among the individual studies. A later meta-analysis reported by Friedman et al. was based on 23 studies published between 1995 and 2008. They found a lower rate of normalization (66.3%) based on the definitions of the individual studies included, and when cure was defined as an AHI < 1, the rate of treatment success was even lower (59.8%).[6] They also noted a significantly higher cure rate among uncomplicated patients compared with those with significant comorbidities (73.8% vs 38.7%, $p < 0.0001$), primarily obesity, severe OSA, or age < 3 years. In a multicenter retrospective study, Bhattacharjee et al. found a lower rate of cure (27.2%) among 578 children, but approximately 50% were obese. In multivariate analysis, they found that obesity and age >7 years were associated with residual OSA after TA.[7] Other reports comparing obese to normal weight children found significant improvements in polysomnography, quality-of-life (QOL), and behavior outcomes in both groups after adenotonsillectomy, but obese children were generally found to have higher rates of residual OSA with poorer QOL after TA.[9,10]

Although these and other studies have provided compelling observational data of the effectiveness of TA in treating OSA, to date only one randomized trial comparing tonsillectomy to watchful waiting has been published. In 2013, Marcus et al. reported the results of the Childhood Adenotonsillectomy Trial (CHAT) study.[11] In this study, 464 children aged 5–9 years old with OSA were randomized to either TA or watchful waiting with assessment of outcomes after 7 months. Although not the primary outcome, this study demonstrated a significantly higher rate of normalization on polysomnography in the TA group compared with watchful waiting (79% vs 46%, $p < 0.001$). This rate of normalization in the treatment group is higher than in previous observational studies. It is worth noting that the baseline AHI in this study was relatively mild (4.5 in the watchful waiting group and 4.8 in the TA group), so there may have been a proportion of subjects in both groups with borderline OSA who were misclassified at the initial evaluation and subsequently normalized due to regression to the mean. Subgroup analysis demonstrated worse cure rates among black and obese children and those with baseline AHI above the median. Secondary outcomes including validated caregiver and teacher ratings of behavior and executive function as well as generic and sleep apnea-specific QOL demonstrated significantly greater improvement in the TA arm compared with watchful waiting.

## Neurobehavioral and Cognitive Impact

Multiple studies have demonstrated improvement in behavioral and neurocognitive outcomes after TA.[11-15] Gozal studied a group of first-grade students whose school performance was in the 10th percentile of their class. Based on a detailed symptom screen followed by overnight pulse oximetry and transcutaneous $pCO_2$ monitoring, 54 children were identified with significant sleep-disordered breathing (SDB). Of these, 24 children then underwent TA while parents of the remaining 30 children declined surgery. The following school year, the children who underwent TA showed significant improvement in school performance with no significant change in the children who did not have surgery.[13] Chervin et al. compared validated measures of hyperactivity, cognition and attention, and sleepiness, in addition to AHI, in 78 patients undergoing adenotonsillectomy to 27 controls who either had unrelated surgery or did not have surgery at all. After 1 year, they demonstrated significant improvement in all measures among TA patients with no changes in the control subjects. Interestingly, the degree of improvement from baseline was similar even in patients for whom the clinical indication was not primarily for SDB.[14] Most recently, the CHAT study comparing TA to watchful waiting demonstrated no significant difference between study groups after 7 months in the primary outcome of attention and executive function testing. However, as noted above, there were significantly better secondary outcomes in the TA group including validated caregiver and teacher measures of behavior, cognition, and QOL.[11]

## Quality-of-Life Impact

TA has been shown to improve QOL in children with OSA as assessed using both generic QOL instruments and disease-specific instruments.[16-21] Compared to baseline, Goldstein et al. demonstrated improvement at 3 months post-tonsillectomy in both the generic Child Behavior Checklist instrument and the OSA-18 sleep-related QOL instrument with fair to good correlation between change scores in these two measures.[17] In a follow-up study, the improvement in QOL after TA was shown to be significantly greater than in a control population undergoing unrelated surgery.[22] Mitchell et al. further demonstrated long-term improvements on the OSA-18 survey at 6 months and between 9 and 24 months after TA.[19] A meta-analysis of 10 studies including both generic and disease-specific QOL measures before and after TA demonstrated worse baseline general QOL in patients with OSA compared with healthy children, similar to the QOL of patients with juvenile rheumatoid arthritis.[18] In addition, after TA there were significant improvements in disease-specific QOL as measured by the OSA-18 both in the short-term (< 6 months) and in the long term (6–16 months).

## Cardiovascular and Inflammatory Impact

Although the impact of treatment for OSA on cardiovascular morbidity has been well documented in adults, there have been far fewer studies assessing the impact of TA on cardiovascular outcomes in children. A recent systematic review reported on the results of 14 articles encompassing 418 study subjects.[23] Cardiovascular outcomes included blood pressure, heart rate, mean pulmonary artery pressure, and cardiac morphology and function. This descriptive review found that most cardiovascular parameters improve with improvement in OSA after TA. However, all included studies were observational with varied outcomes, and only three included polysomnography data before and after TA, thus no pooled analysis of outcomes was possible.

## Surgical Technique

Many techniques for performing tonsillectomy have been described, and they continue to evolve as new technologies are developed. The most commonly reported techniques involve "cold steel" (i.e. a combination of sharp and blunt dissection using a scalpel, scissors, Fisher knife, guillotine, or tonsil snare), electrocautery (either monopolar or bipolar), or radiofrequency ablation (coblation, bipolar radiofrequency ablation).[24-26] Other reported techniques include the use of harmonic scalpel,[27,28] microdebrider,[29,30] $CO_2$ laser,[31] and several different vessel sealing systems.[32] Many studies have been reported comparing the advantages and disadvantages of these different techniques with outcomes including operating time, intraoperative hemorrhage, primary and secondary postoperative hemorrhage, postoperative pain, duration of return to normal diet, and postoperative respiratory complications. Although individual studies may suggest superior outcomes with one technique or another, several meta-analyses have shown no significant differences in outcome with respect to cold techniques, electrocautery, and radiofrequency ablation.[32-34] There is a suggestion that electrocautery techniques may result in a slightly more painful postoperative recovery than cold steel or radiofrequency ablation, but with overall no difference in complication rate. Such systematic reviews are limited by the heterogeneity of the studies included, thus it is difficult to draw conclusions based on even systematic reviews. As a result, there is currently no consensus regarding the optimal tonsillectomy technique with respect to perioperative complication rate or surgical outcome. However, two recent meta-analyses comparing intracapsular tonsillectomy (aka partial tonsillectomy or tonsillotomy) to total (subcapsular or traditional) tonsillectomy found decreased postoperative pain, faster return to normal diet, and decreased rate of secondary hemorrhage in the intracapsular group, regardless of specific technique used.[35,36] As noted in the meta-analysis reported by Acevedo et al., the rate of tonsillar regrowth and need for completion surgery with intracapsular tonsillectomy remain unclear. Studies reporting the rate of revision tonsillectomy due to regrowth range from 0.5% to 11.9% with varying follow-up durations.[37-39]

## Perioperative Complications

Intraoperative complications of tonsillectomy include dental trauma, intubation trauma, airway fire, aspiration, intraoperative hemorrhage, and cardiac arrest.[2] Early postoperative adverse outcomes include nausea, vomiting, respiratory distress, and primary post-tonsillectomy hemorrhage (PTH). Late complications occurring after the first 24 hours include poor pain control with resultant dehydration due to poor oral intake of fluids and secondary PTH. Secondary PTH is defined as any bleed that occurs after the first 24 hours postoperatively but typically between 5 and 10 days after surgery. Primary hemorrhage occurs in 0.2–2.2% of patients, whereas secondary hemorrhage occurs in 0.1–3% of patients.[2,40] As noted above, several meta-analyses comparing different techniques of tonsillectomy have not found consistent differences in rate of postoperative hemorrhage with the exception of intracapsular tonsillectomy techniques, which have been found to have slightly lower rates of secondary hemorrhage.

Although PTH is a relatively rare occurrence and difficult to predict on an individual basis, there is evidence for a higher rate of potential respiratory complications in the perioperative period among patients undergoing TA for OSA.[41-45] Among studies specifically examining patients with polysomnography-proven OSA, the rates of postoperative respiratory complications ranged from 11.2% to 23%, depending on the definition of a respiratory complication. This rate was significantly higher in obese children. One case–control study found that obese children had an odds ratio of 6.03 for having a major perioperative event compared with normal weight controls with significantly longer hospital stays as well.[46] Other studies have identified age <3 years, severe baseline OSA, Down syndrome, craniofacial anomalies, neuromuscular disorders, and asthma as other potential risk factors for perioperative complications of TA.[41,43,45,47,48]

# ADENOIDECTOMY

Although less commonly performed as a solo procedure, adenoidectomy alone has been demonstrated to have some success in treating symptoms of OSA, especially in young children. In a study of 206 patients followed for 3–5 years postoperatively, Joshua et al. demonstrated that adenoidectomy resulted in improvement in specific preoperative symptoms (most commonly nasal obstruction, snoring, and chronic rhinorrhea) in 74–87% of patients. The rate of adenoid regrowth was relatively low with 81% of patients found to have no or minimal adenoid tissue at follow-up. Other authors have reported success rates after adenoidectomy varying from 80% to

100% though with variable definitions of success and specific outcomes evaluated.[49,50] Brietzke et al. found that among patients who had obstructive indications for adenoidectomy, 38% required subsequent adenoid or tonsillar surgery, and these children were three times more likely to require a second surgery than children who underwent adenoidectomy for nonobstructive disease.[51] In general, the effectiveness of adenoidectomy in treating obstructive symptoms is difficult to ascertain due to the variability in patient selection, indications for surgery, and frequent combination with other procedures like tonsillectomy. Thus, although the available evidence suggests that adenoidectomy alone may be effective for some patients, it remains unclear who is most likely to benefit.

## NASAL SURGERY

Although nasal obstruction is rarely a primary cause of OSA, several studies have reported that nasal obstruction can worsen or cause apnea in children.[52,53] Moreover, these reports have demonstrated that persistent pediatric OSA is more common after TA in children who have turbinate hypertrophy. A randomized, controlled trial of adults with OSA evaluated the effect of radiofrequency inferior turbinate reduction on nasal obstruction and found that treatment of the turbinates reduces nasal obstruction and improves nasal CPAP compliance.[54] A case–control study of septoplasty with turbinate reduction that compared surgery to a sham surgery in adults ($N = 49$) reported that AHI was not significantly improved in either group, although four patients had an improved AHI and one had complete response.[55] Another prospective case series found that 18 patients undergoing septoplasty had improved nasal obstruction scores and were able to increase CPAP use from 0.5 to 5.0 hours/night after surgery ($p < 0.05$).[56]

The proper management of enlarged turbinates is debated as some authors suggest that for those children already undergoing adenotonsillectomy, nasal turbinate reduction should be considered at the time of TA.[52,54] In contrast, other authors have suggested that turbinate hypertrophy improves after adenoidectomy without specific intervention to the turbinates, and they argue that these children should undergo adenoid removal or TA alone.[57] A 2012 study of 51 children with severe persistent allergic rhinitis and nasal obstruction underwent TA ($N = 28$) versus TA combined with microdebrider inferior turbinoplasty (TAMIT, $N = 23$).[58] They reported that the AHI improvement was significantly greater in the TAMIT group (15.6 to 0.8 events/hour) than in the TA group (15.0 to 3.5 events/hour, $p < 0.01$). In addition, nasal cross-sectional area and OSA-specific QOL were significantly better in the TAMIT group. However, there are no data on treatment of nasal obstruction as a primary for treatment of SDB.

## UVULOPALATOPHARYNGOPLASTY

There have been a few studies reporting the outcomes of adjunct surgical procedures beyond adenotonsillectomy in children. However, unlike in adults, these procedures are not widely practiced in part due to the high rate of success traditionally attributed to adenotonsillectomy alone. Guilleminault et al. reported their surgical outcomes for SDB in 400 children treated with a variety of medical and surgical treatments, including TA and TA with pharyngoplasty (suturing of the anterior and posterior tonsillar pillars together).[59] The results of this study are somewhat ambiguous due to inconsistencies in describing which patients underwent which surgery; however, the authors did advocate the use of this pharyngoplasty technique as an adjunct to TA in patients with a pharyngeal redundancy and a long soft palate. Building on this idea, Friedman et al. reported the results of a randomized trial comparing standard TA to a modified procedure composed of a TA with pharyngoplasty (closure of the tonsillar pillars) with 30 patients in each treatment arm.[60] In this study, they found no difference in cure rate (60% for standard TA, 56.6% for TA with pharyngoplasty, $p = 0.79$), defined as a postoperative AHI < 5, and a score of < 60 on the OSA-18 QOL questionnaire. However, this study was limited by loss to follow-up, resulting in only 19 patients in the TA with pharyngoplasty arm and 25 patients in the TA arm who completed the study protocol, thus limiting the power to detect any difference in outcome in an intention-to-treat analysis. Comparison of only those patients who completed the study protocol found a higher rate of cure in the TA with pharyngoplasty group (89.5% vs 72%, $p = 0.16$), although this difference was still not statistically significant.

## BASE OF TONGUE PROCEDURES

As in adults with OSA, children with residual OSA after TA frequently have obstruction in the retrolingual airway due to either enlarged lingual tonsils or glossoptosis or both. Procedures that have been investigated for the treatment of base of tongue obstruction in children include the

lingual tonsillectomy, midline posterior glossectomy,[61,62] tongue suspension suture, radiofrequency base of tongue reduction,[63] and less frequent procedures such as hyoid suspension and genioglossal suspension. Mandibular distraction osteogenesis is also employed for children with micro- and retrognathia, but this will not be covered in this chapter.[64-66]

## Lingual Tonsillectomy

While treatment of primary OSA rarely includes lingual tonsillectomy, increasing evidence suggests lingual tonsil hypertrophy is more commonly seen in children with Down syndrome and obesity.[67] There are no studies looking at treatment of primary OSA with lingual tonsillectomy; however, there are case reports and small case series, which report its utility in children with OSA after TA.[68,69] In 2009, Lin and Koltai reported the results of lingual tonsillectomy using endoscopic-assisted radiofrequency ablation in 26 patients (age range 3–20 years) who had previously undergone TA.[70] They found that RDI decreased from 14.7 to 8.2 events/hour ($p$ = 0.02), although two patients developed adhesions between the epiglottis and tongue base. A 2011 study by Abdel-Aziz et al. ($N$ = 16) looked at lingual tonsillectomy in a group with an AHI of 10.5 event/hour after TA and reported complete resolution of OSA in 14 children and residual mild OSA in the remaining two children. In this series, there were no reports of oropharyngeal scarring.[71]

Based on this evidence, it is reasonable to evaluate children with persistent OSA after TA, especially those with Down syndrome or obesity, with nasopharyngoscopy to screen for hypertrophy of the lingual tonsils. Techniques for lingual tonsillectomy include removal with electrocautery, microdebrider, robotic surgery, and radiofrequency ablation. Recent reports have recommended the use of radiofrequency ablation for lingual tonsillectomy as it is predominantly a bloodless technique that allows for easy cauterization.[72] However, caution is recommended before considering concomitant performance of TA with lingual tonsillectomy as oropharyngeal scarring has been reported.[70,73]

## Partial Midline Glossectomy

Partial midline glossectomy is intended to excise posterior tongue tissue and usually limits resection to within 1 cm on each side of the midline of the tongue. It can be performed using multiple techniques including electrocautery, microdebrider, laser, robotics, and radiofrequency ablation. Advocates recommend that laryngoscopes and/or endoscopes be used to facilitate optimal visualization. In addition, a minimally invasive technique, called submucosal minimally invasive lingual excision (SMILE), has been reported in at least three adult series that utilized radiofrequency ablation.[74-76] These evaluations of the SMILE technique in adults compared with base of tongue radiofrequency showed it to have a higher success rate at 65% versus 42% but resulted in more complications including hypoglossal paresis/paralysis, tongue edema, and increased pain.[76] Another study reported that the SMILE technique resulted in a significant reduction in AHI (17.7 ± 7.8 to 8.3 ± 4.1 events/hour) and the comparison group undergoing radiofrequency had a reduction in AHI (22.7 ± 12.3 to 10.4 ± 10.6 events/hour) that was not considered significant. In children, only pediatric cadaver studies with ultrasound guidance have been published.[61]

## Tongue Suspension/Radiofrequency to the Base of the Tongue

Tongue suspension and radiofrequency to the base of tongue are not widely evaluated in children. One early report found a decrease in RDI from 42 to 22 events/hour in a 16-month-old child with Simpson–Golabi–Behmel syndrome and associated craniofacial abnormalities, macroglossia, and base of tongue hypertrophy.[77] A trial of 31 children, 61% with Down syndrome, reported on children treated with both tongue suspension and radiofrequency ablation to the tongue base.[63] This investigation demonstrated a change in mean AHI from 14.1 to 6.4 events/hour ($p$ < 0.001) with an overall success rate of 61%. Success was defined as a reduction in AHI to ≤ 5 events/hour with minimum oxygen saturation ≥ 90%, and end tidal $CO_2$ > 50 mm Hg for < 10% of total sleep time.

## Additional Base of Tongue Procedures: Hyoid Suspension, Genioglossal Advancement

There is limited information on hyoid suspension and genioglossal advancement in children. A number of studies have evaluated hyoid suspension in adults with previous palatal surgery and found that 17–78% had a surgical cure.[78] In the pediatric arena, there is one case report describing hyoid suspension in a child with Down syndrome child, which did not demonstrate any improvement after surgery.[79]

There have only been a few case reports describing pediatric genial or genioglossal advancement (GGA); however, there have been no systematic studies in children. Adult studies have shown that GGA can result in reductions in RDI up to 70%; however, many of these GGA procedures were performed with additional adjunctive procedures.[80] Moreover, GGA cannot be considered in children until they have adult teeth and there are multiple potential comorbidities to consider including possible permanent injury to the tooth roots, mental nerve paresis or paralysis, tooth and chin numbness, hematoma, and cosmetic change.

## ADDITIONAL PROCEDURES

### Supraglottoplasty

In the last 10 years, there has been a greater appreciation that sleep-state dependent laryngomalacia can be a primary or secondary contributor to pediatric OSA, and congenital laryngomalacia has been recognized as a primary cause of OSA in infants < 1 year of age.[81-86] In a study of 126 infants 0–12 months of age diagnosed with OSA by polysomnography, Leonardis et al. identified laryngomalacia in 28.6%.[86] OSA identified in infants and treated with supraglottoplasty has been shown to be highly effective. Several authors have reported significant improvements in AHI and lowest oxygen level after supraglottoplasty.[87-89]

Late-onset or occult laryngomalacia contributing to OSA has also been reported in older children. In 1997, Amin and Isaacson coined the term state-dependent laryngomalacia in reference to children with normal breathing while awake and stridor and increased work of breathing during sleep.[90] Thevasagayam et al. reported an overall prevalence of laryngomalacia of 3.9% among 358 children with a median age of 5 years who presented with SDB and underwent sleep nasopharyngoscopy.[91] However, this study included only patients who were diagnosed with SDB based exclusively on reported symptoms and who underwent sleep nasopharyngoscopy as part of their workup, thus limiting its generalizability. In a cohort of children with a mean age of 25 months, Goldberg et al. identified laryngomalacia as a contributor to OSA in 44% of patients undergoing sleep endoscopy for evaluation of upper airway obstruction.[91a] Richter et al. presented a series of children age 2 and older who underwent supraglottoplasty for laryngomalacia.[91b] All of those with state-dependent laryngomalacia ($n = 7$, mean age 6.3 years), had resolution of symptoms after supraglottoplasty. Digoy et al. reported on 43 patients diagnosed with state-dependent laryngomalacia on sleep endoscopy who underwent supraglottoplasty.[91c] Median age at surgery was 56 months and 32 had undergone previous adenotonsillectomy. Thirty-six children underwent postoperative polysomnography and had significant improvements in obstructive AHI, and lowest oxygen saturation; 91% of caregivers noted subjective improvement in sleep symptoms. Chan et al. reported on 22 children (mean age 7.4 years) who underwent supraglottoplasty and had significant improvements in mean AHI (15.4 to 5.4 events/hour) with 14 of 22 (64%) having mild or no residual OSA after surgery.[91d]

In summary, supraglottoplasty appears to be highly effective in improving OSA in children diagnosed with laryngomalacia whether congenital or late onset. Consideration of the possibility of state-dependent laryngomalacia should be given to any patient who has residual OSA after adenotonsillectomy or who is suspected of having multilevel obstruction based on clinical examination. However, it remains unclear who should undergo sleep endoscopy to identify such patients. Conversely, the role of polysomnography in the workup for congenital laryngomalacia remains unclear, and further research is needed to better elucidate the clinical indications for polysomnography and its role in the decision to proceed with supraglottoplasty in OSA patients.

### Tracheotomy

Tracheotomy is a traditional and definitive surgical procedure for the treatment of OSA that is refractory to other treatments. This has generally been considered an intervention of last resort due to the associated cost and burden of tracheotomy maintenance, high-rate of complications (19–56%), and risk of mortality related to accidental decannulation or cannula obstruction (1–3.6%).[92-94] Indications for tracheotomy are highly varied, but they can be roughly categorized as (1) poor pulmonary toilet in chronic aspirators, (2) chronic ventilator dependence, and (3) severe airway obstruction. Potential causes of airway obstruction include craniofacial anomalies, severe laryngomalacia refractory to supraglottoplasty, vocal fold paralysis, subglottic or tracheal stenosis, tumors of the head and neck, and tracheomalacia.

Because of the wide spectrum of indications for tracheotomy that frequently exist in combination, there have not been any large epidemiologic studies that have examined the use of tracheotomy in the treatment of OSA in children.

However, in a study analyzing hospital discharge data in the Kids' Inpatient Database, Lewis et al. reported that the overall incidence of pediatric tracheotomy in the United States in 1997 was 6.6 per 100,0000 child-years with highest incidence in infants < 1 year of age at 41.5 per 100,000 child-years.[95]

Several large case series have reported on the outcomes of pediatric tracheotomy. Upper airway obstruction represented the primary indication in 40–72% of tracheotomy patients.[92,94,96-98] Carron et al. reported that among their series of 204 pediatric tracheotomies, indications for tracheotomy included craniofacial anomalies (13%), upper airway obstruction (19%), prolonged intubation (26%), neurologic impairment (27%), trauma (7%), and vocal fold paralysis (7%).[94] However, they included patients with pharyngeal collapse or severe OSA among those with neurologic impairment. In this same cohort, more than half the patients were less than 1 year of age at the time of tracheotomy. In most series, patients < 1 year of age represented the largest age subgroup with craniofacial anomalies, upper airway obstruction, and prolonged intubation as the most common indications for tracheotomy in this age group.

Although generally considered a failure of the initial treatments for laryngomalacia[88,99,100] and micrognathia,[101] tracheotomy has been reported as a primary treatment option for airway obstruction in patients with bilateral vocal fold paralysis (57–68%)[102-104] and severe micrognathia or Pierre Robin sequence.[105,106] Micrognathic patients requiring tracheotomy typically had multilevel obstruction or associated syndromes such as Goldenhar or Treacher Collins syndrome precluding more targeted procedures such as mandibular distraction.

## CONCLUSION

Adenotonsillectomy is the first-line treatment for pediatric OSA and remains highly effective for the majority of patients. By improving sleep quality, adenotonsillectomy can lead to improved neurobehavioral and cognitive outcomes, cardiovascular outcomes, and QOL. However, studies have demonstrated that a substantial proportion of patients will have residual OSA after adenotonsillectomy, and for these patients, additional surgical procedures are frequently needed to achieve an optimal outcome. Although further research is needed to clarify the indications and optimal implementation of these procedures, initial studies have shown promise for surgery beyond adenotonsillectomy in the treatment of pediatric OSA.

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CHAPTER

# Nonsurgical Management of Pediatric Obstructive Sleep Apnea

68

*Craig Canapari, Anna Labowsky Cook*

Obstructive sleep apnea (OSA) is a sleep disorder characterized by recurrent prolonged episodes of partial or complete upper airway obstruction resulting in disrupted sleep and gas exchange abnormalities.[1] The estimated prevalence of childhood OSA is 2–3%, usually occurring in children between 2 and 8 years of age.[2] The incidence of OSA in children has increased in the context of the obesity epidemic.[3] Untreated OSA is associated with poor growth and significant neurocognitive, behavioral, and cardiovascular morbidities.[2]

Since OSA results from increased upper airway resistance and collapsibility, any condition that narrows the upper airway is associated with an increased risk of OSA. Adenotonsillar hypertrophy is one of the more common pathophysiologic mechanisms of OSA in children between 2 and 8 years of age. Surgical removal of these tissues is therefore considered first-line therapy in most children.[2] However, adenotonsillectomy may not be curative in all patients. In a meta-analysis of the literature,[4] adenotonsillectomy had a cumulative cure rate of 80%. However, a more recent multicenter study of 578 children showed a cure rate [Apnea Hypopnea Index (AHI) <1 event/hour] only occurred in 27.2% of patients.[5] In this study, risk factors for residual disease include age <7 years, obesity, moderate to severe OSA (AHI >5), and asthma. In children with other comorbidities, causing increasing airway collapsibility, such as cerebral palsy, Down syndrome, craniofacial disorders, hypotonia, or neuromuscular disorders, persistent sleep-disordered breathing after surgery is common (Table 68.1).[6] These patients will frequently require a multimodal approach to treatment including adenotonsillectomy, craniofacial surgery, and/or medical therapies as described below.

**Table 68.1:** Risk factors for residual disease after adenotonsillectomy

| |
|---|
| Age >7 years |
| Moderate to severe OSA with AHI >5 |
| Obesity |
| Neuromuscular disorders |
| Craniofacial abnormalities |
| Down syndrome |
| Nasal septum deviation |
| Allergic rhinitis |

(AHI: Apnea Hypopnea Index; OSA: Obstructive sleep apnea).

For high-risk patients or patients with residual symptoms (e.g. snoring, sleep disruption, or daytime problems), polysomnography (PSG) is indicated, usually 6 to 8 weeks postsurgery, to identify residual disease in these cases.[5] There is also a subset of patients in whom surgery is contraindicated, including those with submucous clefts. Surgery in this particular group may result in worsening velopharyngeal dysfunction and changes in speech.[7] Moreover, adenotonsillectomy may be risky in patients with cochlear implants due to the need to avoid electrocautery. Finally, there is a subgroup of patients with borderline or mild disease where the indication of surgery is unclear (e.g. with an AHI between 1 and 5).[8] For all these children, nonsurgical interventions may be necessary to effectively treat their OSA. Similar to adenotonsillectomy, nonsurgical interventions improve airway patency and reduce collapsibility (Table 68.2).

**Table 68.2:** Potential nonsurgical interventions for children with obstructive sleep apnea

| *Intervention* | *Mechanism of action* | *Advantages* | *Disadvantages* |
|---|---|---|---|
| Continuous positive airway pressure (CPAP) | Delivers constant pressure throughout respiratory cycle to stent open airways | • Symptomatic relief<br>• Improvement in neurobehavioral function<br>• Improvement in polysomnography indices | • Poor adherence<br>• Suboptimal mask fit<br>• Not a cure |
| Bilevel positive airway pressure | Applies higher pressure during inspiration than expiration | • Useful in hypoventilation or central apnea<br>• Useful in children on high CPAP pressures >15 | • As above |
| Rapid maxillary expansion | Orthodontic device that opens sagittal sutures of hard palate | • Good for maxillary crowding | • Useful in only subset of patients<br>• Inability to anchor device to primary teeth<br>• Long-term consequences on myofascial functioning and orthodontia |
| Intranasal steroids | Act on glucocorticoid receptors on adenotonsillar tissue | • Improvement in AHI and oxygenation<br>• Safe, well tolerated<br>• Potentially useful in atopic children | • Duration of therapy and long-term benefits unclear |
| Leukotriene modifiers | Act on leukotriene receptors on adenotonsillar tissue | • Reduced size of adenotonsillar tissue<br>• Reduced severity of nocturnal symptoms<br>• Safe, well tolerated | • Duration of therapy and long-term benefits unclear |

## CONTINUOUS POSITIVE AIRWAY PRESSURE

Continuous positive airway pressure (CPAP) is a nonsurgical therapy for children with OSA who have significant residual disease after treatment or who are poor surgical candidates.[1] CPAP administers positive airway pressure via a nasal or oronasal mask at a constant level throughout the respiratory cycle. After the need for CPAP is determined, the pressure needed to treat a child's OSA is initially determined by titration during PSG in a sleep lab. During a CPAP titration, an entire night is needed to obtain a proper diagnostic study and to do an adequate titration. A split-night study, in which the first 2 hours are used to diagnose OSA, and the remainder of the night is used for CPAP titration if the first half demonstrates significant obstruction, is generally not recommended for children. Although sparing an extra night in the sleep lab is appealing, split-night studies may result in inadequate diagnostic and therapeutic information, as many children will have significant difficulty going back to sleep after starting CPAP. Split-night studies are generally reserved for older children (>12 years) without significant developmental delay or anxiety, or children who have previously used CPAP. Autotitrating CPAP (auto-CPAP) is a newer technology commonly used in adult patients that delivers a range of pressures based upon patient airflow. Auto-CPAP automatically adjusts pressures to keep the airway open and precludes the need for CPAP titration in a sleep lab. It can be provided quickly if there is a prolonged wait for in-lab CPAP titration.[9]

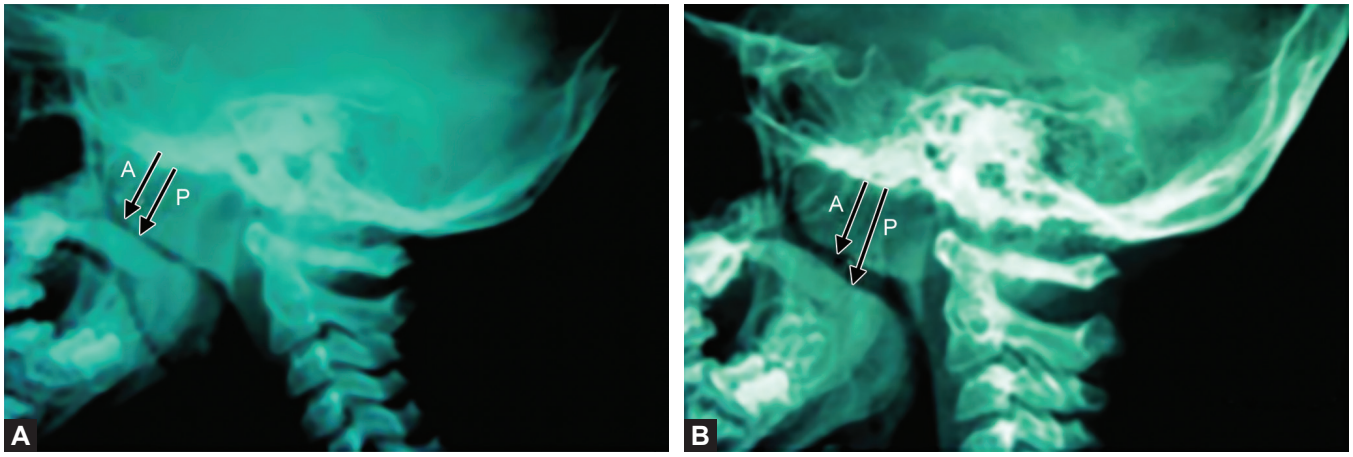
CPAP is an effective therapy for both the treatment of symptoms and polysomnographic indices of OSA, and it can lead to significant improvement in neurobehavioral function.[10] However, compliance with CPAP is often challenging, and studies have reported a 65% to 70% adherence.[1] Moreover, CPAP is a treatment and not a cure, unlike some other surgical and nonsurgical modalities. CPAP treatment is more likely to be successful if behavioral modalities such as habituation, modeling, and parent training are used, and appropriate mask fit is ensured.[11] Suboptimal mask fit may cause eye irritation,

nasal dryness, facial dermatitis, and skin ulceration. To improve compliance with CPAP, additional device features are more commonly being used. "C-flex" is a program on certain CPAP machines that may be helpful in patients who complain of not being able to fully exhale against CPAP. "C-flex" provides pressure relief during expiration but returns to therapeutic pressure just prior to inhalation. However, there are little data to support the benefit of this in improving compliance. Bilevel positive airway pressure (BiPAP or bilevel) applies a higher airway pressure during inspiration than expiration. It is used for children with OSA who also hypoventilate or have central apnea. It may also be useful for children on higher CPAP pressures (>15 cm $H_2O$), but it is not associated with improved compliance in children with OSA.[12] Predictors of improved compliance include use of nasal (vs full face) mask; higher level of maternal education; age between 6 and 12 years; higher reported quality of life; and lower body mass index.[13] Behavioral interventions may be helpful. Compliance remains a challenging issue in the use of PAP therapy in children and adults.

For those with a limited ability to tolerate CPAP, orthodontics may be used to treat OSA in a select pediatric population.[6] Rapid maxillary expansion (RME) is an orthodontic procedure that widens the sagittal suture of the hard palate and nasal orifices by means of a fixed appliance with an expansion screw anchored on selected teeth.[11] This treatment is specifically used in patients with maxillary crowding and residual disease after adenotonsillectomy.[14] For patients with maxillary restriction and adenotonsillar hypertrophy, treatment with both RME and adenotonsillectomy may be necessary. These devices seem to provide persistent benefits 36 months after initiation.[15]

For adults, there are a growing number of oral appliances designed to protrude the mandible forward or hold the tongue anteriorly to maintain the patency of the upper airway. There are only a few small studies documenting the efficacy of these oral appliances in children, and they seem potentially useful in teenagers.[16] However, the inability to anchor devices to primary teeth and unknown long-term effects on the functioning of fascial muscles and orthodontia are significant potential downsides. Typically, insurance will not cover these devices until the patient has had a trial of CPAP.

Intranasal corticosteroids and leukotriene modifiers are pharmacologic alternatives for treating mild OSA and can be considered when surgery or CPAP is not a viable option. Tonsillar and adenoidal tissues in the upper airway of children express an abundance of glucocorticoid receptors. Several studies have demonstrated that treatment with intranasal corticosteroids can lead to significant improvement in AHI and oxygenation, and the benefits often persist for 8 weeks after cessation of therapy.[2] However, there are no clear guidelines for the duration of therapy or the long-term benefits.[1] Leukotriene receptors are mediators in the inflammatory pathway, and their expression is also elevated in the tonsillar tissues of children with OSA. In a recent study, an oral leukotriene receptor antagonist given over a several month period decreased the severity of nocturnal respiratory symptoms and reduced the size of adenoidal tissue (Figs. 68.1A and B).[8]




**Figs. 68.1A and B:** Lateral neck soft X-ray in a 6-year-old patient with mild sleep-disordered breathing before and after 16-week course of montelukast. Increased upper airway diameter and recession of adenoid tissue are apparent in the post-treatment radiograph. (Arrows—A: Adenoid; P: Pharynx).

Notably, the drug was safe and well tolerated.[8] These improvements were also observed when leukotriene antagonists were used in conjunction with intranasal steroids.[1] In atopic children, allergy testing to determine the need for environmental controls may guide further treatment, including avoidance of specific allergens or immunotherapy.

Supplemental oxygen may be used short term in patients with severe nocturnal hypoxemia as a bridge to more definitive therapy. It is also reserved for patients who cannot tolerate CPAP or who are poor surgical candidates. Supplemental oxygen will blunt night-time oxygen desaturations, but it will not correct the underlying airway obstruction or fragmented sleep.[17]

Finally, weight loss may be recommended as adjunctive therapy in obese children with OSA based on studies conducted in adults. Obesity is thought to increase upper airway resistance. For an overview of obesity treatments in children, please refer to this recent Cochrane Review article.[18] However, there have been few studies on the effects of weight loss on OSA in children, perhaps because of the difficulty in obtaining persistent weight loss in obese children.

## FUTURE DIRECTIONS

For certain children, adenotonsillectomy and other surgical procedures may not be curative or feasible options. Many of the newer nonsurgical therapies for OSA are being developed for adults. Nasal expiratory positive airway pressure devices are small valves inserted into the nares, which have been shown to be effective in adults, and are commercially available but have not yet been studied in children. Stimulation of the hypoglossal nerve or directly to the genioglossus muscle may also prove to be an effective modality.[19] The use of hypnotics may improve sleep continuity and reduce the burden of disrupted sleep.[20] Clearly, further research to develop different modalities to treat OSA is warranted.

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CHAPTER

# 69 Central Apnea in Children: Diagnosis and Management

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Apnea describes the cessation of breathing. Obstructive apneas are the most common events observed in normal children and are associated with normal or increased breathing effort but the absence of flow due to a partial or completely obstructed airway. Central apneas occur in the absence of respiratory effort when the central nervous system does not trigger breathing. Occasional central apneas are common in the infants and children. However, frequent or severe events may be cause for concern. Thus, a sleep study is invaluable in describing and quantifying these events. On polysomnography, central apnea is defined as a respiratory pause lasting 20 s or greater, or respiratory pause spanning at least two missed breaths that is associated with an arousal or desaturation of at least 3%.[1] In newborns, guidelines further specify central apneic events as being pathologic if they are associated with bradycardia.[2] Understanding the etiology of central apnea is critical to determining appropriate treatment.

Central apnea is a rare clinical entity compared with obstructive sleep apnea (OSA). In the practice of otolaryngology, central apnea is typically encountered in a few different contexts. One common scenario includes incidentally finding documented central apneic events in the course of routine polysomnography. Another common context in which central apnea is considered is during the assessment of breathing problems in infants, or children with genetic syndromes. The goal of this chapter is to provide an overview of the assessment and significance of central apnea in children, as may be encountered in the practice of otolaryngology.

## DEFINITION OF CENTRAL APNEA

Central apneas are defined polysomnographically by a ≥ 90% drop in oronasal airflow coupled with the absence of respiratory effort (measured by chest and abdominal belts) as well as one of the following criteria:

1. The event lasts ≥ 20 s
2. The event lasts at least the duration of two breaths during baseline breathing and is associated with an arousal or a ≥ 3% arterial oxygen desaturation
3. The event is associated with a decrease in heart rate to < 50 beats per minute for at least 5 s or < 60 beats per minute for 15 s (infants under 1 year of age only).[3]

Note that in adults, central events > 10 seconds' duration are scored as central apneas. These criteria are applied after age 18 but may be selectively applied after age 13.

## PHYSIOLOGY OF CENTRAL APNEAS

Central apneas are due to variation in control of breathing. Normal respiratory control pathways carefully monitor arterial carbon dioxide (primarily) and oxygen (secondarily) and adjust ventilatory response to keep these levels within a physiologic range. Arterial levels of carbon dioxide and oxygen are monitored by peripheral chemoreceptors located in the upper airways and lungs, at the bifurcation of the common carotid artery and on the aortic arch. Central pH is measured within cerebrospinal fluid by chemoreceptors on the ventral surface of the medulla. These inputs are transmitted to the pre-Botzinger complex, located on the ventrolateral medulla, which in turn controls the pattern of breathing. Afferent signals from the pre-Botzinger

complex travel down respiratory pathways in the nucleus tractus solitarius and medulla, ending via nerve pathways at the hypoglossal and phrenic nerves.

Multiple physiologic ventilatory changes occur at the onset of sleep. Loss of voluntary breathing and behavioral inputs stabilize the respiratory rate. There is reduced metabolic rate resulting in reduced minute ventilation. Furthermore, there is decreased ventilatory responsiveness to $CO_2$ and $O_2$; $CO_2$ may, in fact, rises 3–7 torr during sleep.[4] Ventilatory patterns are also specific to phase of sleep (REM, NREM). In NREM sleep, the breathing pattern is regular and corresponds to regulation of carbon dioxide. In REM sleep, however, breathing is highly irregular and is influenced by central REM processes and less by carbon dioxide levels.

Respiratory pauses during sleep may be considered normal. Isolated respiratory pauses >10 s but <20 s are common but rarely are associated with impairment of gas exchange.[5] Nearly two-thirds of children will have pauses lasting 15–19 s during sleep.[6] In healthy children, however, true central apneic events lasting >20 s occur less than once/hour.[7,8] Most of these true apneic events occur in REM sleep[7] and those occurring in non-REM sleep tend to be associated with sighs or movement.[5] In our laboratory, central apneas warrant further investigation if events are (1) prolonged (>20 s), particularly if they occur during NREM sleep, (2) associated with significant oxyhemoglobin desaturations (e.g. <88%), or (3) occur more frequently than five times an hour.

## EVALUATION OF CENTRAL APNEAS

The evaluation of central apnea typically begins with a polysomnogram, allowing quantification of frequency and duration of events. In infants, a pneumogram is often the first-line study that is obtained due to its portability and ease of use in these small infants. These studies, however, are limited by the lack of EEG to define sleep vs. awake, and lack of observation by a skilled technician to correct artifacts as they arise. Thus, a pneumogram is a reasonable screening test but a polysomnogram is indicated if concerns arise. Once central apneas have been defined, evaluation to elicit the etiology may include brain imaging, $CO_2$ response curves, brainstem testing, genetic testing for syndromes such as central congenital hypoventilation syndrome, or EEG to evaluate for seizures.

### Treatment Overview

Treatments for central apnea are generally specific to its etiology. Oxygen may be used to prevent desaturations in affected children if there is no concern about hypoventilation (e.g. no observed elevations in carbon dioxide, history of neuromuscular disease, or unexplained elevation in serum bicarbonate). If hypoventilation is present, ventilatory support (either noninvasively or via tracheostomy) is the first-line treatment. Anatomic causes (such as a Chiari malformation) may warrant surgical correction; however, there remains a risk of unresolved postsurgical central apnea. In children with concomitant obstructive sleep apnea, treatment of the OSA via adenotonsillectomy or by other means will improve sleep physiology and in some cases may resolve the issue. Caffeine may be used, although typically only for apnea of prematurity or infancy.

### Specific Causes of Central Apnea

Central apnea is seen in two major categories of disease: diseases associated with decreased respiratory reserve and diseases of disordered control of breathing. Diseases of decreased reserve include parenchymal lung disease, low lung volumes due to restrictive processes (small chest wall, obesity) or neuromuscular weakness. Central apneic events may be scored more frequently in these disease states because they are more likely to have a desaturation with shorter duration of pause in respiration. Diseases of disordered control of breathing includes periodic breathing, apnea of prematurity, apnea of infancy, diseases related to abnormalities within the neurologic control of breathing, and genetic or syndromic causes. These disease processes are further described below.

### Disordered Control of Breathing

#### *Periodic Breathing*

Periodic breathing is typically a nonpathologic state, which may be seen in both REM and NREM sleep when a patient has three or more respiratory pauses lasting 3 S or longer, separated by no more than 20 s of normal breathing.[9] These events are infrequent in the immediate newborn period but increase over the first weeks of life, peaking by the second-fourth week of life, then taper off completely by 4–6 months of age.[10,11] Preterm infants are more likely to exhibit periodic breathing: 100% of preterm infants weighing < 1000 g at birth will have episodes of periodic breathing, whereas 30–80% term infants will have periodic breathing during sleep.[12,13] Periodic breathing occurs due to immaturity of the normal respiratory feedback loop. During the ventilatory cycle, $CO_2$ decreases below the apneic threshold, resulting in a respiratory pause. During this pause, $CO_2$ increases and $O_2$ decreases, triggering hyperventilation. This in turn leads to a drop in $CO_2$ below the apneic threshold, perpetuating the cycle.

Because of the low respiratory reserve in infant lungs, particularly premature infants, oxygen desaturations may also occur, given low lung volumes/reserve. Treatment is rarely warranted by may include supplemental $O_2$,[14] positioning,[15] CPAP,[16] and caffeine.[17]

### *Apnea of Prematurity*

Apnea of prematurity, on the other hand, is considered pathologic and is defined as apneic events lasting > 20 s with associated desaturation or bradycardia occurring in infants born < 37 weeks' gestation.[18] This entity is generally clinically diagnosed in the newborn intensive care unit or special care nursery, where these infants are followed for issues related to prematurity. The risk of apnea of prematurity is inversely correlated with gestational age and birth weight. Nearly 100% of all infants born < 29 weeks' gestation or weighing < 1000 g will have apnea of prematurity.[12,13] Apnea of prematurity improves over time, typically resolving by 44 weeks' postconceptual age.[19] Typically, apneic events do not occur in full-term infants, although they may rarely suffer from a similar entity called apnea of infancy (see below). The mainstay of treatment is caffeine, starting at 20 mg/kg loading dose, followed by 5–10 mg/kg/day. Caffeine improves diaphragmatic function and increases respiratory drive,[20] reduces duration of CPAP and $O_2$ therapy, decreases rate of bronchopulmonary dysplasia (BPD), and lowers incidence of cerebral palsy and cognitive defects.[21,22] Side effects may include increased irritability, sleep difficulties, or worsening of acid reflux. Caffeine therapy can generally be discontinued by 36 weeks' corrected gestational age,[23] although slowing weaning off caffeine with periodic monitoring for persistent apnea may be warranted. Other treatment modalities include CPAP[24] and positioning. Positioning, however, rarely resolves these apneic events,[25] and furthermore cannot be used as home treatment.

The goal of treatment for apnea of prematurity is to improve oxygenation, thereby affecting neurodevelopmental outcomes, and to prevent extreme apneic events, which may result in sudden infant death syndrome (SIDS). However, although premature infants have an increased incidence of SIDS,[26] it is not clear that apnea of prematurity is the cause for this increased risk. Furthermore, the risk of significant apneic events in preterm infants equals that of full-term infants by 43 weeks' postmenstrual age.[27] Premature infants with apnea of prematurity are often sent home on apnea monitors, although home monitors do not prevent SIDS.[28] For further guidelines on the use of home monitoring, please refer to the American Academy of Pediatrics published guidelines.[29]

### *Apnea of Infancy*

A subset of full-term infants will suffer from apnea of infancy, which is analogous to apnea of prematurity. These infants typically present in the immediate newborn period with witnessed episodes of color change or pause in breathing. Such events may represent an exaggeration of normal physiologic apneas. In a large cross-sectional study of infants 34–91 weeks' postconceptual age, frequent central apneas were observed. However, the duration of the central apnea was 7.5 and 6.2 seconds in NREM and REM sleep, respectively. The frequency of central events decreased with increasing postconceptual age and there were no events lasting > 20 s.[30] Therefore, prolonged apneic events in infants born after 34 weeks' gestation age should warrant further workup.

## Genetic/Syndromes

Several genetic diseases are associated with central apnea, most classically congenital central hypoventilation syndrome (CCHS). Several other syndromes may have features of central or mixed apnea, including Prader Willi, Down syndrome, mitochondrial disease, rapid-onset obesity with hypothalamic dysfunction, hypoventilation and autonomic dysregulation (ROHHAD), Rett syndrome, and Joubert syndrome.

### *Congenital Central Hypoventilation Syndrome*

CCHS, primarily caused by polyalanine repeats within the paired-like homeobox 2B (PHOX2B) gene, results in familial central apnea.[31] PHOX2B encodes a transcription factor for neural crest development and mutations within this gene lead to a multisystemic syndrome associated with abnormal neural crest migration and organ development.

Typically, CCHS presents in the newborn period with central apnea. Other findings include breath holding, temperature instability, or sporadic diffuse diaphoresis. CCHS patients have a characteristic phenotype with features that include a short, flat face, including nasal tip protrusion, decreased nasolabial angle and decreased upper lip height.[32] Additional findings include strabismus, papillary abnormalities, subtle neurocognitive delays, Hirschsprung's disease or constipation, and prolonged R–R interval with decreased heart rate variability.[33,34] CCHS patients carry an increased risk of sudden cardiac death due to arrhythmia[35] or due to complete heart block following certain anesthetics, such as propofol.[36] Patients with CCHS should undergo yearly ECG or echo, and pacemaker placement is recommended if R–R interval > 3 s is observed.[35] There is

also an increased risk of developing neural crest tumors, including ganglioneuroma, neuroblastoma and ganglioneuroblastoma. Certain patients may require yearly tumor surveillance with MRI.[33]

Nocturnal mechanical ventilation is the mainstay of treatment for CCHS, ranging from nocturnal ventilation, ventilation with exercise, or continuous ventilatory support. Children < 6 years of age generally require tracheostomy while older children and adults may be managed with noninvasive positive pressure ventilation or, less commonly, diaphragmatic pacing. Ventilatory support should be closely monitored twice yearly with polysomnography, with target end tidal $CO_2$ 35–40 mm Hg. The ventilator should be placed on the patient before the patient falls asleep and oximeter and end tidal carbon dioxide monitors should be in place with alarms set at 85% and 55 torr for oxygen and carbon dioxide, respectively. Patients require a back up power source in the event of a power outage.[33]

Importantly, patients with CCHS require counseling regarding their increased risk of respiratory failure. There is an increased risk of drowning due to lack of perceived apnea, and an increased risk of cardiorespiratory failure following anesthesia, viral respiratory illnesses, or use of sedative medications including cough suppressants, illicit drugs and alcohol.[33]

### *Rapid-onset Obesity with Hypothalamic Dysfunction, Hypoventilation and Autonomic Dysregulation*

ROHHAD is a disease affecting the pituitary/hypothalamic axis and central control of ventilation, associated with obesity. Patients with ROHHAD grow and develop normally until early childhood years (generally onset occurs at 1.5–7 years). These patients then exhibit rapid weight gain followed by associated features of ROHHAD over a 4- to 6-month period.[37,38] Features include water balance abnormalities, hyperprolactinemia, hypothyroidism, growth hormone deficiency, adrenal insufficiency, abnormal development of puberty. Strabismus, pupillary abnormalities, GI dysmotility, temp instability, decreased pain sensation, irregular heart rate. Scoliosis and neurocognitive delays may ensue.[38,39] Furthermore, they develop central apnea and may require up to 24 hours a day of continuous ventilatory support, depending on severity of the disease. Many of the symptoms related to autonomic dysfunction are similar to those in CCHS; however, there is no genetic mutation currently known to be associated with ROHHAD.

### *Prader-Willi Syndrome*

Prader-Willi syndrome (PWS) is caused by a deletion of paternally derived chromosome 15q and is associated with low tone, short stature, cognitive delays and extreme hyperphagia and obesity. Not all patients with PWS have sleep apnea, but those who do may have either obstructive events, likely related to obesity, narrow airways or hypertrophy of tonsils and adenoids, or central events. Some patients with PWS may have a blunted hypercapnic ventilatory response compared to the general population, which suggests abnormal peripheral chemoreceptor function.[40,41] OSA is a more concerning finding in these children, especially in the context of growth hormone therapy, as OSA frequently worsens after growth hormone therapy and has been associated in rare cases with sudden death.[42,43]

### *Down Syndrome*

Although Down syndrome is predominantly associated with obstructive sleep apnea related to midfacial and mandibular hypoplasia, macroglossia and glossoptosis, tonsillar and adenoidal encroachment, obesity, hypothyroidism and generalized hypotonia, 4–10% of patients with Down syndrome have been reported to have central apnea.[44,45] Although the cause of central apnea in Down syndrome is unclear, it has been hypothesized that it is related to diffuse abnormalities of the central nervous system, including excitability involving the brainstem.[46]

### *Rett Syndrome*

Rett syndrome is a disease affecting infant girls and causes clinical regression of developmental achievements by 6–18 months of age. Rett syndrome is caused by a mutation in the MECP2 gene on the X chromosome. Interestingly, disordered ventilatory events are seen in patients with Rett syndrome while awake, whereas sleep patterns tend to be normal with sleep. During wakefulness, two-thirds of patients with Rett syndrome will have periods of hyperventilation followed by central apnea and desaturation.[47]

### *Joubert Syndrome*

Joubert syndrome is disease characterized by the absence or under-development of the cerebellar vermis, visualized on MRI as the pathognomonic "molar tooth sign", and presents in the newborn period with hyperpnea, hypotonia, ataxia, oculomotor apraxia and developmental delays. Joubert syndrome may be transmitted in an autosomal recessive manner, or it may arise sporadically. Typically, patients with Joubert syndrome have short episodes of

tachypnea followed by apnea. This abnormal breathing pattern is seen in roughly half of the patients with Joubert syndrome (44–71%)[48] and it is thought to be related to underlying brainstem involvement.[49]

## Anatomic Lesions

Anatomic lesions within the central respiratory centers can also cause central apnea. These anatomic lesions are generally the result of compression of the respiratory centers in the brainstem, or infiltration into brainstem parenchyma. Compression of the brainstem may be caused either by herniation of cerebellar tissue through the foramen magnum, as is seen in Chiari malformations, or by cervicomedullar narrowing, as can be seen in achondroplasia.[50] Tissue compression is typically caused by brainstem tumors through infiltration of the local brain parenchyma.

### *Chiari Malformation*

Chiari malformations may be associated with sleep apnea. The more severe forms of Chiari malformations, type 2, which has are cerebellar herniation accompanied by a myelomeningocele, or type 3, with occipital encephalocele, syringomyelia, tethered cord and hydrocephalus may frequently have sleep apnea related to compression of the respiratory centers.[51] Type 1 Chiari malformation, which is defined as isolated caudal herniation of the cerebellar tonsils through the foramen magnum, although typically asymptomatic, may present with headaches, ataxia, numbness of the hands and feet, difficulty with swallowing, speaking or double vision. Some are identified incidentally on brain scans. Children with Chiari type 1 malformations may have subtle symptoms suggestive of sleep apnea with central apneic events on polysomnography. Furthermore, central events and sleep quality resolved following posterior fossa decompression, although in some cases central apneas may persist.[52,53]

## Other Causes

Other causes of central apnea may be secondary to medications that decrease respiratory drive, infections, metabolic derangements or seizures. Cheyne Stokes breathing is a pattern characterized by oscillations between hyperpnea and apnea that is often a sign of critical illness. This breathing pattern may be seen in heart failure, traumatic brain injury, or following a cerebrovascular event. Generalized processes like hypoxic-ischemic encephalopathy or encephalitis can also lead to central apnea.

Gastroesophageal reflux is often considered when infants present with an apneic, apparent life-threatening event (ALTE). However, the correlation between reflex and ALTE is unclear. Although 20–62% of infants presenting with ALTE will have reflux,[54–56] the temporal association of these events are varied, without a clear cause and effect relationship.[57,58]

Breath holding is also a common finding, which may develop in infancy. There is an increased prevalence of iron deficiency in patients with breath-holding spells, with reduction in episodes upon replacement with iron. Therefore, iron supplementation may be considered in children with breath-holding attacks, particularly if there is evidence of iron deficiency.[59]

## SUMMARY

Central apneas occur commonly in normal children, especially in infancy. However, they may be pathological in some infants and children when associated with significant desaturation, disordered control of breathing or hypercarbia. The finding of frequent or severe central apneas should prompt an evaluation as indicated by the clinical presentation.

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CHAPTER

# Circadian Rhythm and Sleep Movement Disorders in Pediatric Otolaryngology

70

*Donald G Keamy Jr, Karan R Chhabra*

## CIRCADIAN RHYTHM SLEEP DISORDERS

### Introduction

According to the International Classification of Sleep Disorders (ICSDs), circadian rhythm sleep disorders (CRSDs) are characterized by "a persistent or recurrent pattern of sleep disturbance caused primarily by alterations in the circadian timekeeping rhythm or a misalignment between the endogenous circadian rhythm and exogenous factors that affect the timing or duration of sleep".[1]

The definition of a circadian rhythm disorder hinges on misalignment between the patient's intrinsic sleep rhythms and the rhythms demanded of the patient. Thus, an unusual sleep schedule does not necessarily equate to a circadian rhythm disorder, if the schedule is in step with the patient's natural rhythms and does not cause the patient any impairment. Likewise, insomnia at all hours is not a circadian rhythm disorder.[1]

The CRSDs are intertwined with many disorders common in the pediatric population. Circadian dysfunction has been implicated in multiple mood disorders, including bipolar disorder, premenstrual dysphoric disorder, seasonal affective disorder, schizophrenia, and depression.[2-7] The intensive care environment has been shown to disrupt circadian rhythms in critically ill patients.[8-10] Mild traumatic brain injury is also highly associated with sleep disturbance, even if postconcussive syndrome is not present.[11-13] Finally, many neurological disorders alter the circadian system. Smith–Magenis syndrome and Rett syndrome both cause direct sleep cycle derangements.[14] Other disorders interfere with the child's ability to integrate environmental cues into normal sleep rhythms. For example, cerebral palsy, autism, mental retardation, depression, and central nervous system disease are all associated with melatonin or circadian rhythm disorders in children.[15,16] Because of these correlations and comorbidities, an appreciation of CRSDs can benefit the pediatric otolaryngologist.

According to the American Academy of Sleep Medicine, sleep logs are the indicated assessment method for suspected CRSDs. Actigraphy may provide useful supplementary information, although its benefit varies with the CRSD. There is insufficient evidence to support the use of polysomnography (PSG) to diagnose CRSDs in children, except to rule out another primary sleep disorder. There is insufficient evidence to support use of the Morningness-Eveningness Questionnaire (MEQ) to diagnose CRSDs.[17,18]

### Classification and Diagnosis of Circadian Rhythm Sleep Disorders

Six CRSDs are recognized by the ICSDs.[1] What follows is a discussion of the presentation, etiology, epidemiology, and diagnostic considerations associated with each. A schematic summarizing the CSRDs can be found in Figure 70.1. Treatment options will be presented later in this chapter.

#### *Delayed Sleep Phase Disorder*

Delayed sleep phase disorder, or DSPD, is the most common CRSD in children. Patients present with a stable sleep schedule set several hours later than the desired time, accompanied by an inability to fall asleep and

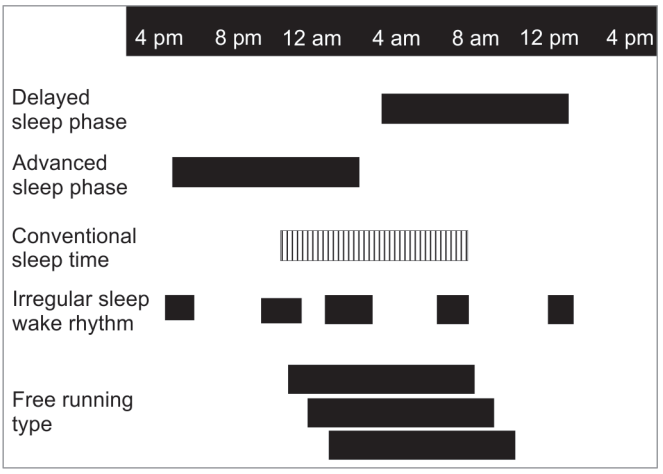


**Fig. 70.1:** Schematic representation of the major CRSD. Black bars represent sleep periods of the circadian disorders; striped bar represent conventional sleep time. Adapted from Lu et al.[40]

wake up at the desired time.[1,19,20] The diagnostic criteria require that patients would exhibit normal sleep quality and duration if allowed their delayed sleep schedule. They also require that sleep assessment of at least 7 days demonstrates a consistent delay in sleep phase and that the sleep disturbance cannot be explained by other medical or mental disorders (including sleep disorders).[1] Important differential diagnoses include primary insomnia, a delayed sleep schedule without adverse effects, and primary school avoidance (due to motivational and affective problems).[21-23] The actual times of sleep onset and arousal vary among patients, but adolescents with DSPD typically present with difficulties falling asleep before midnight and waking up before 10 am.[21,23]

The etiology of DSPD is unclear, but it appears to be reinforced by common patterns of light exposure. Evening light exposure promotes phase delay, and "sleeping in" prevents morning light exposure that would advance sleep phase.[19] Patients with DSPD show increased melatonin suppression in response to light, which may explain their sensitivity to evening light.[24] Mutations in the gene *PER3* may cause DSPD in some patients, although evidence is inconclusive.[25-28] Mutations in arylalkylamine *N*-acetyltransferase (AA-NAT), an enzyme in the biosynthesis of melatonin, have also been associated with DSPD.[29] The specific mechanisms of melatonin secretion and sleep cycle formation will be discussed later in this chapter.

Epidemiologically, DSPD is most common among adolescents; about 10% of adolescents have clinical DSPD.[1,22,23] The shift to eveningness begins at about 13 years of age, occurring even in children without DSPD.[30] Multiple studies have shown that males are more likely to exhibit evening preference, and females more likely to exhibit morning preference, although these effects are influenced significantly (and perhaps more strongly) by age.[30-32] (The effects of age on sleep will be discussed in detail later in the chapter.) Among ethnic groups, Hispanic children may have the least pronounced shift toward eveningness, African American children change most, and the shifts of Asian and Caucasian children are in the middle.[30] Delayed sleep phase often explains chronic idiopathic sleep-onset insomnia in children with attention deficit hyperactivity disorder (ADHD).[33] Family history is present in about 40% of patients with DSPD.[23,34]

Diagnostically, sleep logs are recommended to assess all CRSDs including DSPD, although there are no widely accepted, standardized sleep logs currently available. Actigraphy is also indicated (Table 70.1). The MEQ has not been validated as a test for DSPD. Although PSG and circadian phase markers may be valid assessments, they are less practical clinically.[19,35,36]

### *Advanced Sleep Phase Disorder*

Advanced sleep phase disorder (ASPD) mirrors DSPD, except that sleep phase is undesirably early rather than late. Patients present with a stable sleep schedule of normal quality and quantity set several hours than the desired time.[19] The differential diagnosis includes other causes of sleep maintenance insomnia, like depression.[1,19]

The etiology of ASPD is also unclear. However, ASPD was the first sleep disorder with a characterized genetic basis (although all cases do not have this etiology). FASPD, or familial ASPD, is an autosomal dominant trait; patients have sleep cycles several hours earlier in phase than the general population, but with normal sleep quality and quantity.[37] FASPD has been linked to mutations in the *hPER2* and *CKI*δ genes.[27,38,39]

As with DSPD, PSG is not currently required to diagnose ASPD; since many nights of data are required to establish a pattern, actigraphy or sleep logs are more practical. The MEQ alone is not sufficiently reliable to diagnose ASPD.[1,19]

### *Free-Running Disorder*

Free-running disorder (FRD) is also known as non-24-hour sleep–wake syndrome and hypernychthemeral syndrome. Patients with FRD present with periods of excessive insomnia and/or daytime sleepiness alternating with short asymptomatic periods, reflective of a circadian period somewhat > 24 hours.[40]

**Table 70.1:** Assessment and treatment guidelines for circadian rhythm sleep disorders

| *Disorder* | *Recommended evaluation tools* | *Recommended therapies* |
|---|---|---|
| Delayed sleep phase disorder | Sleep log; actigraphy | Prescribed sleep–wake scheduling; timed light exposure; timed melatonin administration |
| Advanced sleep phase disorder | Sleep log; actigraphy | Prescribed sleep–wake scheduling; timed light exposure; timed melatonin administration |
| Free-running disorder | Sleep log; actigraphy; circadian phase markers (optional) | Prescribed sleep–wake scheduling; timed light exposure; timed melatonin administration (if blind) |
| Irregular sleep–wake rhythm | Sleep log; actigraphy | Mixed-modality treatment (bright light, physical activity, sleep hygiene); melatonin administration |

Adapted from AASM Practice Parameters for the Clinical Evaluation of CRSD.[18]

The etiology of FRD is related to the natural human circadian period. Since the intrinsic circadian period is usually >24 hours (elaborated later), in research settings without time cues, free-running rhythms develop in normal subjects. However, natural phase setting in response to light makes this very rare in sighted individuals.[19]

Patients least able to process time cues are most susceptible to FRD. The condition is present in about 50% of blind people, often leading to recurrent insomnia and daytime sleepiness. The onset occurs with the loss of sight.[19,41] Although FRD is rare in sighted individuals, cases have been documented. Of sighted individuals with FRD, many (about 25%) have psychiatric disorders that may underlie the sleep syndrome. Most are male. The onset in sighted individuals typically occurs in the teens or twenties, and rarely after 30.[19,42] FRD has also been documented in cases of traumatic brain injury.[11,43]

Diagnostically, sleep logs are useful for documenting FRD. Circadian markers, specifically dim-light melatonin onset, may be useful for distinguishing FRD from other sleep phase abnormalities in blind patients. Circadian phase should be measured at least three times, at intervals of at least 1 week. PSG and the MEQ have not been tested as assessment tools for FRD.[19]

### *Irregular Sleep–Wake Rhythm*

Irregular sleep–wake rhythm (ISWR) is characterized by a lack of any discernible sleep-wake rhythm.[40] Patients present with insomnia, sleepiness, and randomly fragmented sleep; the longest sleep interval tends to last from 2 to 6 am.[19,44] The differential diagnosis includes poor sleep hygiene.[19,44]

The ISWR is most commonly associated with broader neurologic defects that in turn affect the circadian system. It is thought to be caused by defects of the suprachiasmatic nucleus (SCN), entrainment pathways, and/or a lack of environmental cycle-setting stimuli.[40] It is ascribed primarily to defects in the amplitude of circadian cycles (as opposed to circadian phase, which is implicated in DSPD, ASPD, and FRD).[19]

Epidemiologically, ISWR is more common among patients with neurologic disorders, such as mental retardation.[44-46]

For patients with ISWR secondary to accompanying mental defects, self-reported sleep logs may be infeasible, especially for those not in institutionalized settings. Actigraphy for at least three consecutive 24-hour periods is recommended as a more practical assessment for non-institutionalized patients. As with other CRSDs, PSG is not clinically necessary (Fig. 70.1).[19]

### *Other Circadian Rhythm Sleep Disorders*

Shift work disorder and jet lag disorder are the remaining two CRSDs recognized by the ICSD, and they are prevalent in the adult population. However, they are infrequently encountered in pediatrics and thus will not be emphasized in this chapter.

## Normal Circadian Rhythm Physiology

Influences on circadian rhythms are known as zeitgebers (literally, "time-givers"). The process of setting a normal, desirable circadian rhythm is known as entrainment. As mentioned earlier, the natural circadian rhythm in most humans is slightly >24 hours, which makes zeitgebers crucial to the maintenance of a 24-hour rhythm.[47] The majority of humans rely on zeitgebers to entrain a slight phase advance each day.[48] In CRSDs, the disparity between one's circadian rhythm and desired sleep cycle is quantified as the phase angle between both rhythms.

Light input, the most potent zeitgeber, is relayed by recently discovered non-rod, non-cone photoreceptors in the retinal ganglion that are most sensitive to blue light.[49] Relative to light input, one's customary sleep schedule has a relatively weak influence on circadian rhythms.[50] Light is conveyed to the SCN primarily via the retinohypothalamic tract, which transmits input from classical rod/cone photoreceptors as well as the specialized photoreceptors in the retinal ganglion.[51-53] This pathway has been shown to be intact in some blind patients.[54] However, light's effects are not constant throughout the day. It has the strongest effects at dawn and dusk, and the weakest in the middle of the circadian day.[55] Other hypothesized zeitgebers include the timing of meals (according to early animal research),[56-59] exercise (according to experiments with adults),[60,61] and "social rhythms" of interaction.[62,63]

The SCN, located in the hypothalamus, is where light and other zeitgebers are translated into circadian rhythms.[50] These signals are relayed to the pineal gland via the spinal cord and superior cervical ganglia.[64] In pinealocytes of the pineal gland, tryptophan is converted to serotonin, which is converted to N-acetylserotonin, then to melatonin. The enzymes AA-NAT and hydroxyindole-*O*-methyltransferase are largely responsible for the day-to-day melatonin rhythm, and their activity is modulated by the SCN via the spinal cord and superior cervical ganglia. (Mutations in AA-NAT are associated with DSPD).[29]

Melatonin is a lipid-soluble hormone with a half-life of 30–53 minutes, metabolized by the liver and excreted in the urine.[16,65] The pineal gland typically begins producing melatonin in the evening, with plasma levels peaking at 3 am, declining until the morning and insignificant throughout the day.[16] One to two hours before sleep, melatonin concentration physiologically increases 10- to 15-fold.[66,67] The mechanisms of melatonin's sleep-inducing effects have not been fully elucidated but may include peripheral skin vasodilation and core body temperature reduction.[68-70] Melatonin may also interact with gamma-aminobutyric acid (GABA) receptors, monoamine neurotransmitters, and glutamate, although these pathways are less well understood.[71]

"Circadian phase markers" can be used to measure patients' natural circadian rhythms. Core body temperature (CBT) is one popular phase marker, but it can be masked by activity, diet and sleep—making it somewhat impractical clinically. Thus, measurements of melatonin levels are gaining favor as a reliable circadian phase marker.[72] Melatonin levels are readily measured in plasma, saliva, or as the metabolite 6-sulfatoxy melatonin (aMT6s) in urine.[73] However, melatonin rhythm is not without its flaws: it can be masked by light exposure, certain drugs (e.g. beta-blockers, nonsteroidal anti-inflammatory drugs, and caffeine) and posture.[74-79] Clinically, the timing of the increase between day and night-time melatonin levels in dim lighting [known as the dim light melatonin onset, (DLMO)] is a reliable indicator of circadian phase and is commonly measured in sleep laboratories via serial saliva sampling.[80] CBT and DLMO are often used jointly, with strong levels of correlation, though of the two, DLMO seems most accurate.[49,81] Clinically, circadian phase markers are only indicated to determine circadian phase and to confirm diagnosis of FRD; there is insufficient evidence to recommend their routine use in other CRSDs.[18]

A second process, the homeostatic sleep–wake system, is thought to influence sleep timing relatively independently of circadian timing. In this model, "sleep pressure" (measured by electroencephalographic slow wave activity) accumulates with sleep deprivation and declines exponentially with the onset of sleep.[82,83]

The "two-process model" describes how circadian rhythms and homeostatic process additively influence sleep–wake activity. In this model, the circadian component is referred to as Process C, and the homeostatic component, Process S.[82-84] Process S oscillates regularly, increasing while awake and decreasing while asleep. Process C sets the "thresholds" for falling asleep and waking, also oscillating, under the influence of external zeitgebers. When Process S rises (due to time spent awake) above the threshold set by Process C, one will fall asleep, and when Process S has declined (due to sleep) below the threshold set by Process C, one wakes up.[22,82,83] Deficiencies in Process S have been hypothesized to play a role in depression (Fig. 70.2).[85]

## Circadian Rhythms Across Child Development

As most parents have doubtless observed, at birth, there is almost no circadian rhythm. Newborns' sleep patterns are highly fragmented and erratic.[56] At 2 weeks of age, the longest sleep period is typically 4 hours. Early rhythms begin to emerge around week 4 of life. Observable day-night rhythms in activity and hormone production appear at 12 weeks of age, with 70% of children showing at least a 5-hour night-time sleep period, and corresponding rhythms in cortisol and melatonin.[55,56,86-92]

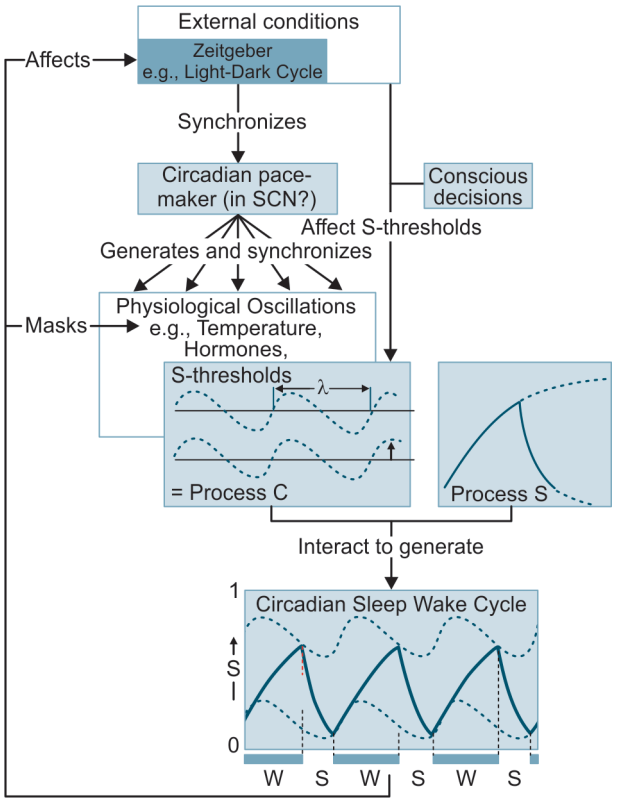


**Fig. 70.2:** Schematic representation of the two-process model of sleep-wake activity. Process C is the circadian cycle, and Process S is homeostatic sleep drive. W represents time spent awake; S represents time spent asleep. Adapted from Daan et al.[83]

Between 3 and 6 months, infants develop a "multimodal" sleep pattern consisting of nocturnal sleep and one nap in the midmorning and one nap in the afternoon. By 5 months of age, the longest sleep period is typically 7 hours. This remains constant till about 12 months. In general, across the first year of life, sleep periods lengthen, but total sleep duration decreases (attributable primarily to a decrease in daytime sleep).[93] By 18 months, toddlers outgrow the midmorning nap and shift to a "bimodal" pattern.

Between 1 and 5 years of age, total sleep duration normally decreases perceptibly. At 12 months, children typically sleep about 11 hours per night, falling asleep around 8 pm, and rising around 7 am. From 18 months to 5 years of age, children fall asleep later, between 9 and 9:30 pm, but continue to wake up at about 7 am. Night wakings are common during this period, but children's ability to return to sleep without parental involvement is important in preventing night wakings from progressing into a sleep disorder.[93]

By 6 years of age, most children give up the daytime nap altogether. Preschool-aged children who continue to nap sleep less at night than those who do not nap, although their total sleep time remains comparable.[56,93,94] Most school-aged children (ages 6–12 years) sleep approximately 8–10 hours each night and wake up spontaneously, with older children sleeping less than younger children, and girls sleeping more than boys.[93]

Adolescence brings the next major shift in sleep patterns, as children's time of day preference shifts to evening at about 13 years of age.[30] Despite less total sleep time than prepubescent children, adolescents may actually need more sleep than them. Although they are often expected to wake up earlier, their bedtimes shift later. Simultaneously, their circadian sleep period appears to elongate from a normal 24.5 to 25 hours. Process S (homeostatic sleep regulation) also changes, with sleep pressure accumulating more slowly in adolescents (Tanner 5) than younger children (Tanner 1–2), further delaying sleep onset.[22,9] Together, these factors produce a strong predisposition toward delayed sleep phase syndrome and daytime sleepiness.[96-98]

The physiologic changes in adolescents are exacerbated by caffeine, alcohol, lengthy afternoon naps, part-time work, and "sleeping in" on weekends and holidays.[21,23,99] "Sleeping in" is a particularly important part of teenage sleep habits. A comprehensive meta-analysis showed total sleep time declining from childhood to adolescence only when recordings were made on school days. On nonschool days, total sleep time remains constant from childhood to the end of adolescence.[100] For this reason, incorporating weekend and vacation sleep patterns in addition to school-day patterns is important for a comprehensive clinical history in children and adolescents.[22] All things considered, teenagers' predisposition to DSPD may be both physiological (due to a hormone-induced lengthening of their circadian rhythm) and environmental (due to peer-influenced patterns of staying up late and sleeping in)[1]. However, the physiological component appears to have a stronger correlation to circadian phase delay.[98] And the health effects of phase delay in adolescents are not trivial: sleep deprivation in adolescents has been connected to automobile accidents, academic underperformance, behavior disruption, and obesity.[101]

College is a time of minimal parental supervision, erratic schedules, demanding coursework, and relatively easy access to over-the-counter (OTC), prescription, and

recreational drugs. Thus, as expected, this population displays chronically restricted, erratic, and poor quality sleep tendencies.[102] Only about 30% of college students report adequate sleep. Bedtimes and rise times are significantly delayed (about 80 minutes) on weekends. In addition, they report long sleep latencies, frequent disturbances (often due to stress, noise, or sleeping with a partner), and frequent daytime sleepiness.[102]

The use of alcohol, OTC, and prescription drugs is positively correlated with poor sleep quality. However, among college students, stress appears to be the most potent predictor of poor sleep quality.[102] Social activity rhythms also influence sleep rhythms in college students, both negatively and positively. Students with highly variable social activity schedules tend to have poorer sleep quality. Consistent social rhythms are correlated with better sleep quality.[103] Although delayed sleep–wake schedules are preferred by many college students, good college-aged sleepers tend to rise, drink their morning beverage, go outside, and eventually sleep earlier than poor sleepers.[103] In college students, although a good understanding of sleep hygiene is weakly related to good sleep hygiene practices, it is not directly related to good overall sleep quality, suggesting that interventions need not only to increase knowledge about sleep hygiene but to ensure its uptake.[104]

## Nonpharmacologic Treatment Options for Circadian Rhythm Sleep Disorders

### *Behavioral Therapy*

Behavioral therapies are nonpharmacologic approaches based on the psychological concepts of classical and operant conditioning and social cognitive theory.[105] Clinically, they involve modifying the patient's behavior either to accommodate their physiology or to alter the pathophysiology of his/her disorder. For CRSDs, behavioral therapy is often focused on promoting circadian phase shifts that align with the desired sleep–wake cycle.

Ensuring proper sleep hygiene is the first-line approach for sleep disorders in all children. Sleep hygiene includes night-time environment, sleep schedule regularity, bedtime routine, and physiologic factors (caffeine, exercise, meal timing, etc.). Successfully instituting sleep hygiene is more difficult to achieve in children with neurodevelopmental disabilities.[106] For example, night lights are not recommended in children with cortical visual impairment because of their tendency to stare into light sources for self-stimulation.[107] Similarly, colorful objects around the sleep space may overexcite children with thalamocortical dissection and related inabilities to "gate" sensory stimuli. Parents should consider what is most calming when developing bedtime routines, especially for the child with neurodevelopmental disorders; certain activities like bathing and storytelling may overstimulate some children.[106,108,109]

Chronotherapy is a second-line behavioral therapeutic option for CRSDs. For DSPD, chronotherapy entails successively delaying bedtime and wake time by 3 hours each day, until the child reaches the desired sleep schedule. Once this schedule is reached, he or she must adhere to it strictly. Although this is a rational therapy, it is not yet supported by high-quality clinical trials.[19] It may be because it is often impractical and difficult to ensure adherence.[105] An alternate chronotherapy approach for DSPD is to advance sleep phase in small increments by progressively sleeping and waking a small amount earlier each day. Although this also appears logical, evidence supporting its effectiveness is inconclusive.

The FRD can be treated behaviorally by prescribing a sleep schedule that follows the patient's free-running rhythms. This entails using circadian phase markers to quantify a patient's circadian rhythm, then to prescribe sleep and wake times that follow the patient's unique non-24-hour cycle.

This has proven successful in one case study of a blind patient with FRD, but it may be impractical in other cases.[41]

Timed exercise may also help address several CRSDs. In experiments with adults, exercise has shown the ability to advance and to delay the circadian cycle. Nighttime exercise appears to delay the circadian pacemaker, which could have value in ASPD.[61] Daytime exercise may advance the circadian pacemaker, which would be more therapeutically valuable for patients with delayed sleep phase syndrome (the more common disorder).[110,111]

### *Cognitive Behavior Therapy*

Cognitive behavior therapy (CBT) for CRSDs consists of sleep education (for the parents if child is young); promoting sleep hygiene; mindfulness strategies for eliminating stress and sleep-inhibiting thoughts.[112-114] Its efficacy is well studied in children with primary insomnias but less so for CRSDs.[113-115] CBT in conjunction with bright light therapy has shown benefit in two studies of adolescents with DSPD, but these studies were not designed to discern whether CBT or light therapy was responsible for the treatment effects.[116,117] One randomized controlled

trial (RCT) in autistic children with primary insomnias showed that CBT boosted the benefits of melatonin to sleep latency, but this may not have had independent benefits to other parameters.[112]

### *Timed Light Administration*

Given light's potency as a zeitgeber, it should come as no surprise that it is considered a rational therapeutic approach for CRSDs. Quite simply, treatment consists of administering bright light during desired waking time and restricting light exposure during late afternoon, evening, and night time.[105] Bright light significantly suppresses melatonin secretion and shifts circadian phase, according to several studies.[118-121] These effects are dose dependent, with brighter light and longer exposure causing more substantial phase shifts.[122] Individuals acclimated to dim light appear to be more responsive to light of modest intensity.[123-126] In all cases, limiting night-time light exposure is an important adjunct to administering bright light, but compliance with this portion may be difficult to achieve clinically.[19]

Light therapy can be achieved with a high-intensity lamp. Generally, light intensities of at least 1000 lux appear necessary for treating CRSDs in most patients.[48] Light incorporating UV wavelengths is unnecessary for phase shifting and may damage the lens and retina.[127] Intermittent exposure to bright light may be nearly as effective as continuous exposure.[128]

Timed light administration is well studied for a variety of CRSDs. A bright-light mask that turns on 4 hours before desired waking appears to advance sleep phase in patients with DSPD.[129] For ASPD, most available evidence supports several hours of evening light therapy >2000 lux.[19] A regimen of 2500–3000 lux for 2 hours each morning has shown benefit in adult patients with ISWR.[130,131] In a small study of mentally retarded children with ISWR refractory to hypnotics and behavioral therapy, several responded to bright light therapy (4000 lux for 45 minutes each morning).[132] In sighted individuals with FRD, morning bright light exposure has been shown to successfully entrain circadian rhythms in several case reports.[19] Based on the discovery of dedicated sensory tracts toward the SCN,[51-53] the effects of light on clinically blind patients are under investigation. One study documents three blind patients lacking pupillary light reflex who nonetheless showed suppression of melatonin secretion in response to bright light. Perhaps as a result, those three responsive patients had no history of insomnia.[54] Building on early animal research,[133] therapeutic light cycling has been studied with premature infants. Light cycling does indeed appear to entrain preterm infants, but without apparent benefits in weight gain and head circumference.[134]

## Pharmacologic Treatment Options for Circadian Rhythm Sleep Disorders

### *Melatonin*

Melatonin is widely available OTC and has enjoyed considerable popularity due to its low cost and perceived safety. Although it is very well studied, ideal dosages in adults and children are as yet unclear. Melatonin is considered a supplement, and thus is not regulated for safety, purity, or efficacy by the Food and Drug Administration (FDA).[67,135] Mechanistically, melatonin may generate circadian phase shifts that help entrain patients with CRSDs. It may also induce daytime naps in patients with accumulated sleep debt.[135] To advance circadian phase, melatonin should be administered 4–8 hours before DLMO (DLMO typically occurs 1–2 hours before sleep).[67,135]

Small doses of 0.1–0.3 mg can generate physiologic nocturnal blood levels in adults.[67] Doses above 0.5 mg produce pharmacologic blood levels of melatonin in adults. Typical formulations available OTC contain 3 mg, which produces spikes that can exceed physiologic levels 50-fold. Pharmacologic doses may use a different mechanism (possibly involving GABA inhibitory neurons) from endogenously produced melatonin. Unfortunately, optimal dosing in children is not clear.[50,135] Melatonin should be considered with caution in patients with immune or lymphoproliferative disorders and in those taking corticosteroids or immunosuppressants, since melatonin can enhance immune function.[67]

Considerable evidence supports melatonin's efficacy in children with CRSDs. For DSPD in children, a meta-analysis of 4 RCTs showed that exogenous melatonin administration (doses 3–6 mg) advanced sleep onset by 38 minutes and prolonged total sleep time by 28 minutes. It also advanced wake-up time by a statistically insignificant amount.[136] Melatonin has also shown long-term efficacy and safety in developmentally disabled children with CRSDs resistant to nonpharmacologic treatment.[137] Melatonin is widely used for sleep disorders in visually impaired children, but a 2011 Cochrane review concluded that there are no high-quality data to support or refuse its use in this context.[138] However, in blind adults with FRD, several studies have shown that melatonin can entrain circadian rhythms. Treatment must be sustained for

weeks or months for successful entrainment, and patients may relapse if treatment ends.[19,139-141] Low, physiologic doses (0.5 mg) appear equally or more effective than pharmacologic doses (5–10 mg).[19,139,142] Some studies have shown benefit in developmentally disabled children with ISWR, but the evidence is mixed and of poor quality.[143-146] Light and melatonin are often used jointly but can offset each other's effects unless timed to produce the same results (i.e. limiting light exposure while administering melatonin).[50,60,147]

### *Vitamin B12 (Methylcobalamin)*

Vitamin B12, or methylcobalamin, has been shown in several adolescents to ameliorate circadian rhythm disorders.[148,149] Its mechanism is unclear, but it may potentiate the effects of light and melatonin on circadian rhythm.[149,150] However, the only available controlled trial on the effects of vitamin B12 in patients with DSPD showed no significant effects.[151] Thus, B12 is not currently recommended by the American Academy of Sleep Medicine.[19]

### *Prescription-Only Drugs*

Several prescription drugs are available for treating CRSDs, but most were developed for adults and thus must be prescribed off-label for use in children.[67] Pharmacologic approaches involving triazolam, zolpidem, or trazodone have been studied in adolescents with DSPD, but without sufficient sample size or placebo-control.[117,152,153] Zaleplon, a nonbenzodiazepine hypnotic, may theoretically have benefit in adolescents with DSPD. Its fast onset and short half-life should minimize next-day sedation and rebound insomnia. Ramelteon, a selective melatonin receptor agonist, may also have theoretical benefit in the same population.[67]

Although approved for insomnia in adults, hypnotics are not FDA-approved for use in children.[106] In addition, they are not recommended by the NIH State-of-the-Science Consensus Conference on Insomnia because of adverse effects.[106,154] Stimulants (during waking times) are not recommended by the American Academy of Sleep Medicine, because they have not been studied for safety and efficacy.[19]

## MOVEMENT DISORDERS

### Introduction

Sleep-related movement disorders, particularly restless legs syndrome (RLS) and periodic limb movement disorder (PLMD) are widely under-recognized, underdiagnosed, and undertreated. An 11.6-year lag has been demonstrated between the onset of symptoms and the diagnosis of definite RLS[155]; only 11% of definite RLS cases in children are diagnosed.[156] In fact, 44% of pediatric patients seeking consultation for definite RLS are told their symptoms are part of normal development.[156] When treated pharmacologically, the vast majority of children (97.5%) are given inappropriate treatment.[156] Yet most cases are easily and safely treatable.

RLS and periodic limb movements of sleep (PLMS) are related but defined as distinct in the ICSD.[1] PLMS refers just to a characteristic pattern of limb movements. When those movements lead to sleep disturbance, they are referred to as PLMD. RLS essentially consists of PLMS plus certain characteristic sensations; whereas PLMS is an essential factor for RLS in children, every case of PLMS is not necessarily RLS.

Movement disorders apart from RLS and PLMS do affect sleep in children. Children with cerebral palsy are at high risk for sleep disturbances affecting the child and the family, including sleep anxiety, night wakings, parasomnias, and sleep-disordered breathing.[157-160] Tourette syndrome is also accompanied by sleep disturbances in 62% of cases,[161] including rhythmic periodic movements, rapid-eye-movement (REM) sleep behavior disorder, and parasomnias.[162-164] Sleep disturbances, including RLS, are also noted in essential tremor.[165-167] However, the sleep disorders in these populations may be addressed by treating the primary disorder, and a detailed treatment of those sleep problems is beyond the scope of this text.

### Restless Legs Syndrome

#### *Diagnosis*

The RLS has four essential diagnostic criteria plus several additional characteristics:

1. Uncomfortable sensation, or otherwise unexplainable urge to move legs (may involve other body parts)
2. Increasing symptoms with rest or inactivity
3. Alleviation of symptoms with movement
4. Worsening of symptoms in the evening/night time.[168,169]

These symptoms can occur when the patient is awake or asleep. In children, definitive diagnosis requires all four above criteria AND a description from the child of leg discomfort (words like "wiggly", "tickle", "bugs", or "shaky" may be used), OR two of three "supportive criteria": (1) sleep disturbance for age, (2) a biologic parent or sibling with definite RLS, (3) PLMS index ≥ 5 on PSG.[156,170]

PSG is not necessary, but PLMS ≥ 5/hour supports the diagnosis in children. Immobilization tests are used to elicit neurologic findings in the clinic. In one such test, the Suggested Immobilization Test, the patient sits in a bed with legs outstretched while the anterior tibialis muscles are electromyographically monitored. This test has a sensitivity and specificity of 81%.[171,172]

The clinical history, in the child's own words, is an essential part of the diagnosis. It is important to avoid leading questions, allowing the child to express symptoms in his or her own words.[169,173,174] Patient complaints typically describe secondary effects of RLS (e.g. difficulty falling asleep) rather than primary sensations of RLS. Symptoms may also present as parasomnias, sleep-related movement disorders (e.g. rhythmical movement disorders), or other primary sleep disorders.[156,169] Because the diagnostic criteria rely on a description from the child, verbal fluency can present a barrier to diagnosis.[156,170] A recently developed questionnaire may help, but it is only considered valid for children 9 and up.[175] For these reasons, RLS is unlikely to be diagnosed prior to 5–6 years of age.[155] However, lack of awareness, rather than stringent diagnostic criteria, appears to be the primary reason for the low diagnosis rates of pediatric RLS.[156]

Distinguishing RLS from mimics and comorbid disorders and diagnosing it accurately is the most important aspect of treating RLS in children.[169] RLS is often misdiagnosed as growing pains, ADHD, insomnia, bedtime resistance, or limit setting-type behaviors.[14,173] When distinguishing between hyperactivity due to ADHD versus RLS, it is important to be aware that hyperactivity in ADHD is the result of external reactions to the environment, whereas the hyperactivity of RLS is related to an internal sensory discomfort.[169] Many patients with growing pains fulfill criteria for RLS, and the prevalence of growing pains may be as high as 37%.[176,177] If a child presents with growing pains and has a family history of RLS, the possibility of RLS in the child should be investigated.[169] The differential diagnosis of RLS also includes nocturnal cramps, peripheral neuropathy, dermatitis, Osgood-Schlatter disease, akathisia, and positional discomfort.[174]

### *Etiology*

The RLS is strongly associated with brain iron deficiency, particularly in the substantia nigra.[178-181] Serum iron measurements (total iron, hemoglobin, hematocrit) are usually within normal limits, but serum ferritin is almost always low in patients with RLS.[169] According to one study, 96% of children with PLMS have low ferritin.[182] RLS is also related to defective dopamine metabolism. This defect may be in a diencephalon-spinal pathway originating from A11 dopaminergic neurons.[178-180] The hypothesis linking both etiologies is that iron deficiency limits dopamine synthesis, since iron is a cofactor in dopamine's biosynthetic pathway (for the enzyme tyrosine hydroxylase).[173]

The symptoms of RLS are thought to result from sympathetic overactivation, which may predispose children to later cardiovascular and neurovascular complications.[183,184] Rises in nocturnal blood pressure with RLS/PLMD are well documented.[185,186] Symptoms also appear to have a circadian component, beginning in late evening and night and resolving between 12 and 2 am in typical cases.[187,188] Iron and dopamine metabolism follow a similar pattern, perhaps explaining RLS symptoms' rhythmicity.[173]

The RLS and ADHD are both etiologically and epidemiologically related. Both are defects in dopamine pathways that often present with symptoms of daytime hyperactivity, inattentiveness, impulsivity, and decreased school performance.[189] Both RLS and ADHD are associated with low ferritin levels.[190-192] Epidemiologically, there is considerable overlap. Of patients with ADHD, 10.5–44% have RLS. Of patients with RLS, 18–26% have ADHD.[192]

### *Epidemiology*

RLS is a common disease, despite being undiagnosed so frequently. A large study found an incidence of approximately 2% in US and UK children. Symptoms were moderate-to-severe in 0.5% of 8–11 years old, and 1% of 12–17 years old.[156] It is significantly more common in Caucasian children than in African American children.[193] RLS and PLMS are also common in children with chronic kidney disease, both dialysis dependent and nondialysis dependent.[194,195]

The disease has a strong familial component[196]; twin studies suggest heritability of about 54%.[197] Childhood-onset RLS appears to be primarily genetic, with multiple loci implicated.[169,173] Variation in the gene BTBD9 explains 50% of the genetic component of RLS and PLMD.[198]

## Periodic Limb Movement Disorder

Like RLS, PLMD is related to iron levels, responsive to dopaminergic medications, and follows a similar genetic and epidemiologic pattern.[169]

### *Diagnosis*

PLMS is a PSG finding, not necessarily pathologic on its own. When PLMS is associated with sleep disturbance or

daytime functioning symptoms, then it is referred to as PLMD.[173] PLMD has three diagnostic criteria:

1. PLMS > 5/hour in children documented by PSG
2. Clinical sleep disturbance or daytime dysfunction
3. Absence of another primary sleep disorder, including RLS, that would better explain symptoms.[1]

The repetitive movements in PLMS have certain characteristics in common. Typical movements involve extension of the big toe and dorsiflexion of the foot, with toe dorsiflexion spanning 25% of the full range of motion. They typically occur in stage N2 sleep, decrease in N3, and are much less frequent in REM. They last 0.5–5 seconds in duration, in a sequence of 4 movements or greater. These sequences are separated by an interval of 5–90 seconds.[1,173] As mentioned in the diagnostic criteria, PSGs are required for a diagnosis of PLMD. Since symptoms vary night-to-night, more than one PSG may be necessary to determine this diagnosis.[199]

### *Etiology and Epidemiology*

Like RLS, PLMD has been linked to a mutation in the gene *BTBD9*, although this locus does not explain every case.[198] PLMD also occurs secondary to narcolepsy, sleep deprivation, Parkinson's, Tourette syndrome, obstructive sleep apnea (OSA), continuous positive airway pressure for OSA, and certain medications [selective serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressants (TCAs)]. Thus PLMD should be in the differential diagnosis for sleep disturbances in patients with the above comorbidities or treatments.[169,200-202]

PLMD is a common condition, present in 8.4–11.9% of children.[203] It is also associated with nocturnal hypertension,[186] sickle cell disease,[204] migraine, seizure, ASDs, and narcolepsy.[182]

## Treating Sleep Movement Disorders in Children

First-line therapy for movement disorders, as for other sleep disorders, is to institute adequate sleep hygiene. This includes establishing a regular bedtime routine; avoiding excitement, food/drink, caffeine, and light exposure around bedtime; and removing activators of RLS (sleep deprivation and drugs including caffeine, SSRIs, TCAs, antiemetics, and antihistamines).[169] Although the effectiveness of sleep hygiene interventions on RLS/PLMD has not been explicitly studied, such interventions limit the level of sleep deprivation, which is known to exacerbate RLS/PLMD symptoms.[173]

As soon as RLS or PLMD are suspected, serum ferritin should be tested (total iron-binding capacities, transferrin, and soluble TfR can also be checked). If ferritin is below 50 ng/mL in children with RLS symptoms, iron supplementation is indicated until ferritin levels reach 80–100 ng/mL.[169] In the highest-quality trial to date, iron supplementation that successfully increased ferritin alleviated RLS/PLMS symptoms in 19 of 25 patients (76%).[205] Supplements should be taken on an empty stomach with vitamin C but without calcium-containing food or drink.[169,181] Serum ferritin levels should be assessed during treatment to avoid iron overload.[173] Intravenous iron supplementation has demonstrated effectiveness in adults with severe iron deficiency or malabsorption, but it has not fully been tested in children.[169]

Some RLS patients, of course, are not iron deficient. Iron supplementation also takes time to increase ferritin levels and does not eliminate RLS in every case. Thus, pharmacologic approaches are sometimes useful. There are no FDA-approved medical interventions for children with RLS, but several medications are frequently prescribed off-label.

L-dopa has been shown to be effective for RLS/PLMD in children.[206] But its half-life is short (1.5–2 hours), and it commonly causes RLS augmentation in patients, making symptoms appear earlier, more intensely, and in other body parts. Augmentation occurs in 70–80% of patients taking L-dopa, and tolerance and/or early-morning rebound effects may also occur.[207-209] Lower ferritin levels predict L-dopa-induced augmentation in adults.[210] Thus, the first response to augmentation should be to measure serum ferritin levels and supplement if needed. L-dopa is rarely used in children or adults.

Because of longer half-lives, dopamine receptor agonists are preferred for RLS prophylaxis in adults. These include ropinirole and pramipexole. Augmentation is less common with dopamine agonists, occurring in 15–40% of cases.[174,207] However, their developmental effects are not yet known.[169] Clonidine, the most commonly used pediatric sleep aid, has also been shown to treat RLS in adults without significant side effects.[211] Its antiadrenergic properties may interfere with the sympathetic dysfunction of RLS. It appears appropriate for as-needed use in children, but it may lead to tolerance, sedation, and hypotension.[169] Finally, gabapentin is frequently prescribed for children with RLS. Both gabapentin and gabapentin enacarbil (a prodrug) have shown benefit for RLS-related symptoms and are well tolerated in children.[169,212,213]

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CHAPTER

# Pediatric Sleep Disorders: Insomnia, Parasomnia, and Hypersomnia

71

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## INTRODUCTION

Sleep disorders comprise a wide spectrum of conditions that affect both children and adults. The objective of our chapter is to present a brief but comprehensive overview of three of the eight sleep disorder categories specified in the International Classification of Sleep Disorders (ICSD-2)[1]—insomnia, parasomnia, and hypersomnia. Our discussion will focus on the presentation and management of these conditions in children and briefly touch upon these topics in adults.

## INSOMNIA

Insomnia is defined as difficulty with sleep initiation, maintenance, or quality that occurs despite adequate time and opportunity for sleep. In children, this may present either as the resistance to bedtime or the inability to go to sleep or remain asleep without caregiver intervention. These problems arise in as many as 20–30% of preschoolers and have a significantly higher prevalence in children with neurodevelopmental or psychiatric comorbidities. The formal diagnosis of insomnia requires the presence of at least one symptom of daytime impairment, which is often reported by the caregiver; hallmark symptoms include fatigue, poor attention, decreased school performance, or daytime sleepiness.

The classification of insomnia (Table 71.1)[1] is based on duration of symptoms, the timing of symptoms (i.e., difficulty falling asleep versus difficulty staying asleep), and etiology. A diagnosis of acute insomnia requires symptoms to be present for less than 1 month, whereas chronic insomnia requires the presence of symptoms for 1 month or more. Sleep-onset difficulties are characterized by difficulty falling asleep, while difficulty maintaining sleep is referred to as sleep-maintenance insomnia. Regarding etiology, primary insomnia is idiopathic and secondary insomnia is diagnosed when sleep difficulty is related to other medical, psychiatric, or sleep disorders or the side effects of medications.

**Table 71.1:** Insomnia disorders

| |
|---|
| Behavioral insomnia of childhood |
| Adjustment (acute) insomnia |
| Idiopathic insomnia |
| Inadequate sleep hygiene |
| Psychophysiological insomnia |
| Paradoxical insomnia |
| Insomnia due to mental disorder |
| Insomnia due to drug or substance |
| Insomnia due to medical condition |
| Insomnia not due to substance or known physiological condition, unspecified |
| Physiological (organic) insomnia, unspecified |

Adapted from American Academy of Sleep Medicine.[1]

### Classification

#### *Behavioral Insomnia of Childhood*

Behavioral insomnia of childhood is characterized by difficulty falling asleep or staying asleep as a consequence of inappropriate sleep associations or inadequate setting of

**Table 71.2:** Diagnostic criteria for behavioral insomnia of childhood

| | |
|---|---|
| A. | A child's symptoms meet the criteria for insomnia based on parent or caregiver report. |
| B. | The child shows a pattern consistent with either the sleep-onset association or limit-setting type of insomnia described below. |
| | i. Sleep-onset association type: |
| | 1. Falling asleep is an extended process that requires special conditions. |
| | 2. Sleep-onset associations are highly problematic or demanding. |
| | 3. In the absence of the associated conditions, sleep onset is significantly delayed or sleep is otherwise disrupted. |
| | 4. Nighttime awakenings require caregiver intervention for the child to return to sleep. |
| | ii. Limit-setting type: |
| | 1. The individual has difficulty initiating or maintaining sleep. |
| | 2. The individual stalls or refuses to go to bed at an appropriate time or refuses to return to bed following a nighttime awakening. |
| | 3. The caregiver demonstrates insufficient or inappropriate limit setting to establish appropriate sleeping behavior in the child. |
| C. | The sleep disturbance is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, or medication use. |

Adapted from American Academy of Sleep Medicine.[1]

limits by the parents or caregivers. Three subtypes exist: (1) sleep-onset association, (2) limit setting, and (3) combined, which encompasses elements of both the sleep-onset and limit-setting subtypes. Each of these subtypes reportedly occurs in 10–30% of children, with no gender predilection. The etiology is multifactorial, involving a complex interplay between circadian, developmental, and environmental factors. Diagnostic criteria for behavioral insomnia of childhood are listed in Table 71.2.

Although sleep-onset associations are common in young children and may be a reassuring part of the bedtime routine, they are considered pathologic when the association is highly problematic or if caregiver intervention is required to initiate or resume sleep. Children with sleep-onset association have difficulty falling asleep in the absence of certain desired conditions; this typically occurs between 6 months and 3 years of age. These children develop a dependency on a specific stimulation (e.g., rocking), an object (e.g., bottle or pacifier), or setting (e.g., parents' bed or couch). In the absence of the specific condition, the child is unable to initiate sleep and sleep onset is significantly delayed. Unable to recreate these sleep associations during normal nighttime arousals, these children frequently need parental intervention to return to sleep. Nighttime sleep disturbance may result in neurocognitive dysfunction in children and poor parental sleep with subsequent daytime impairment.

Children with limit-setting behavioral insomnia are characterized by their refusal to go to sleep. This insomnia subtype typically presents after 2 years of age, when children are moved from a crib into a bed and have developed limited verbal communication. These children frequently have difficulty initiating and maintaining sleep and may use stalling techniques such as multiple trips to the bathroom, demand for drinks, or requests for additional stories, in an attempt to delay bedtime. In addition, they often refuse to return to bed following nighttime awakenings. Given that sleep usually comes naturally and quickly when a parent is able to effectively set and enforce limits, this refusal is generally a consequence of the caregiver's failure to consistently set and enforce bedtime limits.

### *Adjustment Insomnia*

Adjustment insomnia is characterized by an acute onset of sleep disturbance that is attributed to an identifiable stressor (e.g., death of a family member, divorce, or relocating to a new home). The sleep disturbance should be present for 3 months or less and may manifest as difficulty initiating or maintaining sleep, short duration, or poor-quality sleep. Adults will typically complain of daytime symptoms, including anxiety, rumination, or depression. Adjustment insomnia is expected to improve with resolution of or adaption to the stressor. Individuals with symptoms that persist beyond 3 months should be evaluated for chronic insomnia conditions such as idiopathic or psychophysiologic insomnia.

### *Idiopathic Insomnia*

Idiopathic insomnia is a lifelong chronic sleep disturbance that begins in infancy or early childhood. It is estimated to occur in 0.7% of adolescents and 1% of young adults.

Affected children present with lifelong sleep problems, which include difficulty falling asleep, repeated awakenings, and short overall sleep duration. There are no identifiable predisposing factors associated with the onset of this disorder and there are no sustained remission periods. As with other types of insomnia, the sleep disturbance results in significant distress and impairment in daytime function.

### *Inadequate Sleep Hygiene*

Inadequate sleep hygiene is a chronic condition in which the habits or behaviors of the child are not compatible with initiating or maintaining sleep for at least 1 month. It is reported in 1–2% of adolescents and young adults and may be either a primary or secondary diagnosis in 30–50% of children who present to a sleep clinic. Diagnosis requires the presence of at least one of the following five improper sleep practices: (1) improper sleep scheduling (e.g., frequent naps, variable bed and wake times, or excessive time in bed); (2) routine use of alcohol or stimulants such as nicotine or caffeine; (3) participation in strenuous physical or mental activity prior to bedtime; (4) frequent use of the bed for non-sleep-related activities (e.g., watching television or studying); and (5) failure to create a comfortable environment for sleeping. These children and their parents often lack insight regarding the deleterious effects of these sleep-related habits on sleep quality. Because inadequate sleep hygiene often coexists with other sleep disorders, sleep hygiene education is often provided as an adjunct to treatment for most sleep-related conditions.

### *Psychophysiological Insomnia*

Psychophysiological insomnia is characterized by conditioned difficulty with sleep or heightened arousal while in bed for at least 1 month. This condition rarely occurs in young children, but is seen in 1–2% of adolescents and adults. Diagnosis requires the presence of at least one of the following five symptoms: (1) excessive anxiety or focus on sleep; (2) difficulty falling asleep at planned times, with the capacity to fall asleep at monotonous times when sleep is not planned; (3) improved sleep when sleeping outside the home (e.g., at a hotel or a sleepover); (4) increased bedtime arousal from intrusive thoughts or the perception that mental activity cannot be ceased voluntarily; and (5) elevated tension in bed due to the perception that the body cannot be relaxed to allow for sleep. Affected patients worry excessively about their inability to sleep, resulting in increasing difficulty with sleep onset and conditioned arousal.

### *Paradoxical Insomnia*

Paradoxical insomnia is a chronic condition in which there is a mismatch between the perception of sleep and objective measures of sleep duration. This condition is uncommon in children and adolescents and usually presents in young and middle-aged adults; however, it is diagnosed in <5% of patients treated for insomnia. Patients complain of severe insomnia with little or no sleep during most nights; however, they have no need for daytime napping. They also report near constant awareness of nighttime environmental stimuli or conscious thoughts throughout the night, overestimate the time to sleep onset (known as sleep latency), and underestimate total sleep time. Nonetheless, objective measures of sleepiness, actigraphy, or overnight polysomnography (PSG) show significantly more sleep than is perceived by those affected.

## Diagnostic Evaluation

The diagnosis of insomnia is based upon clinical symptoms and requires the presence of significant daytime impairment. The initial evaluation therefore begins with a thorough history and physical examination that includes a detailed sleep history, including specific sleep complaints, sleep–wake patterns, and sleep hygiene (Table 71.3), as well as documentation of daytime impairment. A complete evaluation should also include information on medication, psychiatric conditions, medication, family history, and social history. Common comorbid medical and psychiatric conditions in children include attention deficit hyperactivity disorder (ADHD), asthma, autism, anxiety, migraines, and developmental delay. Information that is helpful includes caregiver questionnaires, symptom checklists, and sleep logs, and diaries.

The routine use of PSG and multiple sleep latency testing (MSLT) in the evaluation of primary insomnia is unwarranted. The MSLT is a test of the tendency to fall asleep in a darkened, quiet room during the day. It is the primary test for daytime sleepiness and is considered valid only if there have been at least 6 hours of polysomnographically characterized sleep before initiation and 2 hours between the nap opportunities. The time to sleep onset and the occurrence of sleep onset REM periods (SOREMPs) is recorded for four or five naps during the day.[2] The MSLT has not been normalized in children younger than 8 years of age, making diagnosis challenging.

**Table 71.3:** Key sleep history components

| |
|---|
| Primary sleep complaint: |
| Onset |
| Duration |
| Frequency |
| Severity |
| Perpetuating factors |
| Past and current treatments and responses |
| Sleep conditions: |
| Pre-bedtime activities including bedtime routine |
| Bedroom environment |
| Sleep–wake schedule: |
| Bedtime |
| Time to fall asleep |
| Awakenings |
| Total sleep duration |
| Nocturnal symptoms: |
| Snoring |
| Restless sleep |
| Limb movements |
| Night terrors or nightmares |
| Bedwetting |
| Daytime activities and function: |
| Nap duration |
| Exercise |
| Caffeine Intake |
| Daytime sleepiness |
| Hyperactivity |
| Poor school performance |

Adapted from Schutte-Rodin et al.[3]

In children, PSG is indicated when a comorbid sleep disorder such as obstructive sleep apnea (OSA) is suspected. When PSG is carried out, patients with insomnia and no comorbid sleep conditions often have a sleep latency >30 minutes and sleep efficiency <85%; decreased non-rapid eye movement (NREM) stage 3 sleep, decreased total sleep time, and increased wake time after sleep onset may also be seen.[3] A normal PSG does not, however, exclude insomnia. MSLT results are usually normal, suggesting an adequate level of daytime alertness. Actigraphy may be indicated if there suspicion of paradoxical insomnia or a comorbid circadian rhythm disturbance.

## Management

Longitudinal studies have shown that acute sleep disturbance presenting in infancy and early childhood can become chronic if not treated.[4] Insomnia can also be associated with decreased cognitive development, daytime behavioral problems, and decreased school performance. In addition, childhood insomnia can have a significant impact on families and contribute to decreased parental sleep, with resultant chronic sleep deprivation, maternal depression, and marital discord. Management strategies include behavioral therapy with parental education and pharmacotherapy, both of which are designed to improve sleep quality and daytime impairment.

### *Behavioral Therapy*

Based on a large systematic review of behavioral interventions that showed clinically significant improvements in bedtime resistance and nighttime awakenings in 94% (49 of 52) of the included studies,[4] the American Academy of Sleep Medicine (AASM) recommends behavioral therapy as initial treatment for all children with insomnia. Behavioral techniques include extinction (unmodified, modified, and graduated), positive routines, faded bedtime with response cost, and scheduled awakenings.

Extinction is a behavioral treatment aimed at eliminating inappropriate sleep habits. In unmodified extinction, frequently referred to as the "cry-it-out" method, parents are instructed to put the child to bed at a designated time and monitor for signs of illness or injury, but otherwise not respond to crying or tantrums. The greatest obstacle to the success of this method is lack of parental consistency caused by parental stress. Alternatively, in modified extinction, the parent remains in the child's room at bedtime but does not engage the child or acknowledge crying or other maladaptive sleep behaviors. In graduated extinction, commonly referred to as "sleep training", parents do not to respond to bedtime crying but may go in to briefly comfort their child at progressively longer time intervals. The duration between check-in times can be tailored based on the age of the child and parent preference. The comforting intervals can be incrementally increased within the same night or across successive nights.

Although extinction therapy is focused on the elimination of undesirable sleep behaviors, positive routines, and faded bedtime with response cost are designed to reinforce appropriate sleep habits. The positive routines

technique is based upon the establishment of a consistent, enjoyable bedtime routine. The faded bedtime with response cost is designed to reduce arousal at bedtime. This is accomplished by removing the child from the bed when he or she does not readily fall asleep, repeating the bedtime routine, and putting the child back to bed. The bedtime is also delayed to ensure timely sleep onset. Once the child consistently falls asleep after the nighttime routine is completed, the bedtime can be progressively moved to an earlier time by 10- to 15-minute increments until the desired bedtime is achieved.

Scheduled awakening is intended to improve sleep duration and consolidate nighttime sleep in children with frequent awakenings. With this technique, parents are instructed to awaken and comfort their child 15 minutes before a spontaneous arousal would typically occur. Time intervals between scheduled awakenings are then progressively increased until they are eliminated.

Although optimization of sleep hygiene alone does not cure insomnia, it is an essential part of treatment. Instruction to parents often includes information pertaining to the optimal sleep environment (e.g., the bedroom should be cool, comfortable, and dark). Patients should also be educated on the importance of maintaining a consistent sleep–wake cycle and avoidance of caffeine, long daytime naps, heavy meals, or use of electronic devices such as the television and computer within 1 hour of desired sleep onset.

### *Pharmacotherapy*

To date, no medications for the treatment of difficulty initiating or maintaining sleep in children have been approved by the Food and Drug Administration (FDA). Nevertheless, pharmacotherapy may be considered for the treatment of insomnia when any of the following conditions are met: (1) the child fails to respond to behavioral interventions; (2) there are short-term acute stressors such as a death in the family; and (3) insomnia occurs in the context of medical illness. Despite the AASM recommendation that behavioral therapy should be the first-line therapy for insomnia in children, a recent survey of community-based pediatricians showed that 75% recommended medication for sleep disturbance in the 6 months prior to the survey. The medications prescribed most commonly for children with insomnia are shown in Table 71.4.[5] Antihistamines were the most commonly recommended nonprescription medications, while α-receptor agonists such as clonidine were the most commonly recommended prescription medications. Also noteworthy, several small randomized controlled trials have demonstrated the efficacy of melatonin in treating insomnia in children with comorbid autism and ADHD.[6] In addition, herbal supplements such as valerian, chamomile, lavender, and kava have been used for the treatment of insomnia. Unfortunately, studies pertaining to the safety and efficacy of pharmacologic treatment for

**Table 71.4:** Medications used to treat pediatric insomnia

| *Drug* | *Medication class* | *Onset of action* | *Half-life* | *Metabolism* | *Side effects* | *Effect on sleep architecture* |
|---|---|---|---|---|---|---|
| Diphenhydramine | Antihistamine | 30 min | 4–6 h | Hepatic | Anticholinergic effects, daytime sedation | Decrease sleep latency |
| Clonidine | Alpha-agonist | 60 min | 6–24 h | 50% excreted unchanged in urine | Anticholinergic effects, rebound hypertension | REM suppression, decrease sleep latency |
| Melatonin | Hormone analogue | 30–50 min | 1 h | Hepatic | Lower seizure threshold, proinflammatory properties | Decrease sleep latency |
| Zolpidem (Ambien) | Benzodiazepine receptor agonist | 30 min | 2–4 h | Hepatic | Dizziness, complex sleep-related behaviors | Decrease sleep latency |
| Clonazepam | Benzodiazepine | 20–60 min | 19–60 h | Hepatic | Risk of addiction and withdrawal | Suppress slow wave sleep; decrease arousals |
| Trazadone | Atypical antidepressant | 30 min | 10–36 h | Hepatic | Priapism | REM suppression, decrease sleep latency |

Adapted from Owens et al.[5]

childhood sleep problems are scant. Moreover, limited information regarding appropriate dosing and duration of drug therapy make evidence-based recommendations extremely difficult.

## PARASOMNIA

Parasomnia is defined as unusual or undesirable physical events that occur during sleep or in the transition to and from wakefulness. These events are a result of the activation of skeletal muscles or the autonomic nervous system during sleep and are performed without volition or awareness. There are 15 parasomnia subtypes and the lifetime prevalence of parasomnias varies by subtype; however, up to 85% of children and adults have a parasomnia at least once in their lifetime and those with more than one parasomnia are described as having parasomnia overlap disorder. The 15 subtypes are grouped into three major classifications: (1) disorders of arousal, (2) parasomnias usually associated with rapid eye movement (REM) sleep, and (3) other parasomnias (Table 71.5).[1] Each classification involves distinct, complex, purposeful motor activities. These activities differ from sleep-related movement disorders, which are characterized by repetitive, simple movements.

### Classification

#### *Disorders of Arousal*

In disorders of arousal, motor activity is restored without full consciousness present, resulting in confusional arousals, sleepwalking, or sleep terrors. These events occur during NREM sleep, most commonly during stage 3 of NREM sleep, and decrease in frequency with increasing age. Because these events occur predominantly during stage 3 sleep, they usually occur in the first half of the night. All three major classifications of parasomnia are more common in children than in adults. Predisposing factors include stress, alcohol, and irregular sleep–wake cycles. Affected patients often have a strong family history of similar parasomnias.

*Confusional arousals*: Confusional arousals are characterized by episodes of confusion following spontaneous or forced arousal from sleep. The episodes are usually 5–15 minutes in duration but can last up to 1 hour. During a confusional arousal, children appear to be awake, but have impaired cognitive function and amnesia related to the event. Decreased vigilance, disorientation, and a blunted response to external stimuli are also common. Some children may even exhibit bizarre or violent or aggressive behavior. Confusional arousals are reported in 17% of children between 3 and 13 years of age. Two variants have been identified in adolescents and adults: (1) severe morning sleep inertia and (2) sleep-related abnormal sexual behaviors. While PSG is not required for diagnosis, common PSG findings during the events include repeated microsleeps and a diffuse alpha rhythm. Most patients can be managed without medication and with optimization of sleep hygiene. In patients with violent behavior, psychotherapy or off-label use of tricyclic antidepressants may be considered.

*Sleepwalking*: Sleepwalking (also referred to as somnambulism) involves walking while in an altered state of consciousness, often with open eyes. Affected children are difficult to arouse, lack awareness of their environment, and, if awakened, are confused and have no memory of the episode. The prevalence of sleepwalking peaks between 8 and 12 years of age and is reported in up to 20% of children in this age range. A positive family history is common, and the likelihood of sleepwalking increases to 60% if both parents have a positive history. The disorder may also be accompanied by other inappropriate, complex behaviors such as eating during sleep. Late-onset sleepwalking has been described in adolescents and adults with no childhood history of an

**Table 71.5:** Parasomnia disorders

| |
|---|
| NREM sleep parasomnias (disorders of arousal) |
| Confusional arousals |
| Sleepwalking |
| Sleep terrors |
| REM sleep parasomnias |
| REM sleep behavior disorder |
| Recurrent isolated sleep paralysis |
| Nightmare disorder |
| Other parasomnias |
| Sleep-related dissociative disorders |
| Sleep enuresis |
| Sleep-related groaning (Catatherinia) |
| Exploding head syndrome |
| Sleep-related hallucinations |
| Sleep-related eating disorder |
| Parasomnia, unspecified |
| Parasomnia due to drug or substance |
| Parasomnia due to medical condition |

Adapted from American Academy of Sleep Medicine.[1]

arousal disorder. The prognosis for spontaneous resolution is good, and most children become asymptomatic by adolescence.

*Sleep terrors*: Sleep terrors are episodes of crying or screaming that are associated with autonomic nervous system activation and behavioral manifestations of terror. Autonomic activation often manifests as tachycardia, flushing, diaphoresis, mydriasis, or tachypnea. These events occur in up to 6% of children, with the onset of events typically seen from 4 to 12 years of age. Diagnosis requires at least one of the following features to be present: (1) difficulty arousing the individual; (2) mental confusion or disorientation if awakened during an event; (3) inability to recall the event; and (4) dangerous or injurious behaviors during the episode. As with sleepwalking, a positive family history is common. Although there is no association between night terrors and psychiatric disease in children, adults with night terrors are more likely to suffer from anxiety, depression, or bipolar disorder. Most affected children do not require treatment, as even without it, the frequency of episodes diminishes significantly during adolescence.

### Management of Disorders of Arousal

Although most patients with disorders of arousal do not require treatment, therapy should be considered in patients with significant distress, sleep disturbance, or daytime impairment. Patients should be counseled to avoid substances such as alcohol and diphenhydramine and circumstances such as excessive night-time temperatures and sleep deprivation, all of which can trigger parasomnias. It is also important to discuss techniques to improve safety, such as door alarms for children with a history of sleepwalking. Nighttime awakenings scheduled for 15 minutes before the typical time of onset can be effective in treating sleep terrors. Coexistent sleep disorders such as OSA and periodic limb movement disorder can also exacerbate these parasomnias, and treatment may lead to a decrease in episodes or resolution of episodes.

### Parasomnias Usually Associated with REM Sleep

*REM sleep behavior disorder*: The hallmark signs of REM sleep behavior disorder (RBD) are abnormal movement or behavior during REM sleep that disrupt sleep or cause injury to those affected or their sleep partners. This disorder is estimated to occur in < 0.5% of the population and usually presents in men older than 50 years. Adults with RBD describe unpleasant, violent dreams from which they awaken quickly with immediate alertness. PSG findings include excessive, sustained, or intermittent submental or limb electromyography tone or twitching. Diagnosis requires a report of injury during sleep or behavior during sleep that can lead to injury or documentation of movement during REM on PSG. Prior to definitive diagnosis, nocturnal seizures should be ruled out. The presence of RBD is often a marker of the future development of neurologic disease, particularly Parkinson's disease, Lewy body dementia, stroke, or narcolepsy.

*Recurrent isolated sleep paralysis*: Recurrent isolated sleep paralysis is characterized by brief periods of paralysis at sleep onset or just after wake during which one is unable to move or speak despite the absence of narcolepsy. Although this usually resolves within seconds to minutes, it can be both frightening and anxiety producing. Estimates suggest that this parasomnia occurs in 15–40% of students younger than 30 years of age; however, the population prevalence likely approximates 5–6%. The onset of recurrent isolated sleep paralysis is usually between 14 and 17 years of age. Sleep deprivation is a significant predisposing factor. PSG usually shows the child to be in a dissociated state, which includes elements of both REM sleep and wakefulness. Management primarily consists of reassurance that the condition carries no significant physical consequences or risks.

*Nightmare disorder*: Nightmare disorder is characterized by recurrent disturbed dreams that elicit negative emotions, causing awakening from sleep. Upon awakening, affected children are fully alert and show no significant confusion or disorientation. This disorder is common in young children and up to 50% between 3 and 5 years have nightmares that cause them to awaken their parents. Typical onset is between 3 and 6 years of age, with peak prevalence between 6 and 10 years. Frequency and intensity generally decrease gradually after 10 years of age; however, the incidence of recurrent nightmares ranges from 2% to 8% overall. The prevalence of nightmares is especially elevated in children and adults with comorbidities such as post-traumatic stress disorder (PTSD); it is reported in up to 50% of these patients. Diagnosis requires either a delay in falling back to sleep or an occurrence in the last half of the typical sleep period. Medications affecting the dopamine, serotonin, and norepinephrine neurotransmitters may be associated with increased incidence.

## Management

The AASM best practice guideline on the treatment of RBD recommends both pharmacologic and environmental intervention.[7] Modification of the sleep environment is recommended to assure the safety of the affected individual as well as the sleep partner. In addition, surveillance for subsequent development of neurologic disease is warranted, as 40–65% of these patients will develop a synucleinopathy over the next 10–30 years. Pharmacologic therapy may include a benzodiazepine or melatonin. A number of other medications with weaker evidence have been studied and are summarized in the above-mentioned guideline.

Because recurrent sleep paralysis is not reported to have any sequelae apart from anxiety, reassurance and optimal sleep hygiene are recommended. Nightmare disorder may be addressed by reassurance if dreams occur only occasionally. If they occur more frequently, behavioral methods such as relaxation training or image rehearsal therapy may be used; in the latter, the nightmare is recounted and the dream is re-scripted.[8] This may be especially useful for patients who suffer from nightmare disorder associated with PTSD.

### *Other Parasomnias*

The AASM classifies nine parasomnias in the category of other parasomnias. With the exception of sleep enuresis, which commonly occurs in children, these conditions typically present in early or late adulthood. Because of the diversity of these conditions, information pertaining to diagnosis and management is included in each subsection.

*Sleep enuresis*: Sleep enuresis refers to recurrent involuntary bedwetting during sleep in children older than 5 years of age. It is estimated to occur in 10% of all 6-year-olds, decreasing to 5% by age 10. Diagnosis requires symptoms to occur at least twice per week for at least 3 months. This condition is further classified as primary or secondary. In primary enuresis, the child has never been consistently dry during sleep. In contrast, children with secondary enuresis begin having nocturnal enuresis after a period of at least 6 months of being consistently dry all night. Primary enuresis is more common than secondary enuresis and is more common in boys. It also occurs more frequently in children with ADHD or disorganized families. The spontaneous resolution rate is estimated to be 15% per year. Secondary enuresis is linked to a variety of factors including diabetes mellitus, diuretic use, psychosocial stressors, urinary tract pathology, and OSA.

For both primary and secondary enuresis, the pathophysiology is thought to involve a mismatch between bladder capacity, the amount of urine produced, and failure to arouse to a full bladder sensation.[9] It has also been suggested that these children may not experience the increase in vasopressin that is normally seen during sleep, which can lead to increased urine production that exceeds bladder capacity. Evaluation with laboratory and urologic studies is usually reserved for refractory cases or those in which the history or physical exam is suggestive of organic pathology. Behavioral therapy is the mainstay of treatment and includes limiting fluid intake after dinner and voiding prior to going to bed. Enuresis alarms are also effective for long-term control of primary enuresis. Medications such as vasopressin and tricyclic antidepressants (imipramine) have also been used. In some cases, psychiatric evaluation may also be advisable.

*Sleep-related dissociative disorders*: Sleep-related dissociative disorders are characterized by a disruption of the usually integrated functions of consciousness, memory, identity, or perception of the environment.[10] The prevalence of these disorders is unknown and disease onset ranges from childhood to middle age. Episodes may result in a multitude of behaviors, including self-mutilation, violence, or running. They usually occur before transition into sleep or just after awakening from stage 1 or 2 sleep. PSG is useful for diagnosis and often demonstrates an episode that occurs during wakefulness or in transition between sleep stages, allowing for differentiation from REM sleep behavior disorder. Patients often have a history of physical and sexual abuse and have corresponding daytime dissociative disorders.

*Sleep-related groaning (catathrenia)*: Sleep-related groaning, referred to as catathrenia, is characterized by expiratory groaning that occurs predominantly during REM sleep and is not associated with motor activity. Although the true prevalence of catathrenia is unknown, it is seen in <0.5% of sleep clinic patients. The mean age of onset is 19 years. Patients are unaware of the episodes, which typically occur several times per night. Physical examination, including upper airway endoscopy, is typically normal. PSG is not required, but if carried out, shows flat respiratory signals during a prolonged expiratory phase of bradypnea during the groaning. Oxygen desaturations

are not present, and sleep architecture is normal. Given that patients are asymptomatic, management primarily consists of reassurance that the condition carries no significant physical consequences or risks.

*Exploding head syndrome*: Exploding head syndrome is a rare disorder characterized by the perception of a loud noise or an explosion upon falling asleep or waking up that is imagined. The mean age of onset is 58 years, although cases have been reported in children younger than age 10. These children describe hearing a loud bang or explosion that may be accompanied by a flash of light or a myoclonic jerk. The episodes appear to diminish in frequency over years and there is no associated neurologic or psychiatric pathology. Management consists of reassurance that the frequency of episodes will diminish over time and that episodes have no significant effect on overall health.

*Sleep-related hallucinations*: Sleep-related hallucinations may be hypnagogic (i.e., occurring at sleep onset) or hypnopompic (i.e., occurring at upon awakening from sleep). Episodes occur most frequently during adolescence and young adulthood and then typically diminish with age. Hallucinations are usually visual, taking the form of complex vivid images of people, animals, or objects. They may also be associated with episodes of sleep paralysis or other parasomnias. Although sleep hallucinations are frequently associated with narcolepsy (see below), these hallucinations have also been reported in 25–37% of healthy individuals. Episodes are managed with optimization of sleep hygiene and reassurance that there are no serious physical consequences of this problem. However, patients in whom hallucinations are causing sleep disruption or anxiety are advised to undergo further evaluation for OSA or narcolepsy.

*Sleep-related eating disorder*: Sleep-related eating disorder is characterized by recurrent involuntary episodes of eating or drinking during sleep. The prevalence is estimated to be ≤5%, but is higher in children treated for eating disorders. Onset is in early adulthood, and females are most commonly affected. The episodes usually occur during partial arousals from sleep, with incomplete recall of the episodes upon awakening. The involuntary nature of this disorder distinguishes it from nocturnal eating syndrome in which there is full awareness during acts of compulsive eating. Eighty percent of these patients also have a coexistent primary sleep disorder, sleepwalking and confusional arousals being the most common. Sleep-related eating disorder tends to be chronic and unremitting, with nightly episodes. Management consists of pharmacotherapy, including the off-label use of benzodiazepines or tricyclic antidepressants.

### *Diagnostic Evaluation*

For the most part, parasomnias are diagnosed based upon history and physical examination. Therefore, detailed sleep, medical, social, and family histories are essential. The differential for parasomnias often includes seizures, panic attacks, and sleep-related movement disorders such as restless leg syndrome. Seizures from the frontal and temporal lobe are often associated with complex activities and behaviors. REM sleep behavior disorder is the only parasomnia that requires PSG for definitive diagnosis. PSG is also indicated if other comorbid sleep disorders such as OSA are suspected or if the child has an unusual or atypical presentation, if events occur greater than three times per week, or if there are potentially injurious behaviors. However, a single normal PSG does not exclude the diagnosis of parasomnias. In addition, additional EEG leads should be used during PSG for patients in whom suspicion for potential seizure-related activity is high. When carried out, PSG often demonstrates precipitous arousals from slow wave sleep preceding an episode of sleep walking or sleep terrors.

## HYPERSOMNIA

Hypersomnia is a term usually applied to disorders of excessive daytime sleepiness (EDS) that are not due to circadian rhythm disorders, sleep-related breathing disorders, or other causes of disturbed nocturnal sleep. EDS is best characterized as difficulty remaining awake or maintaining alertness, which results in unintentional daytime sleep or sleepiness. Establishing a definitive diagnosis requires ruling out or effectively treating coexisting sleep disorders. In addition, the symptoms must persist for at least 3 months after concurrent conditions are treated. As shown in Table 71.6, there are 12 distinct hypersomnic conditions. Our discussion will be limited to narcolepsy, recurrent hypersomnias, idiopathic hypersomnia, and behaviorally insufficient sleep syndrome.

### Classification

#### *Narcolepsy*

There are four primary narcolepsy subtypes: narcolepsy with and without cataplexy, narcolepsy due to a medical condition, and unspecified narcolepsy. Each of these

**Table 71.6:** Hypersomnia of central origin

| |
|---|
| Narcolepsy with cataplexy |
| Narcolepsy without cataplexy |
| Narcolepsy due to medical condition |
| Narcolepsy, unspecified |
| Recurrent hypersomnia |
| Kleine-Levin syndrome |
| Menstrual-related hypersomnia |
| Idiopathic hypersomnia with long sleep time |
| Idiopathic hypersomnia without long sleep time |
| Hypersomnia due to medical condition |
| Hypersomnia due to drug or substance |
| Hypersomnia not due to substance or known physiologic condition (nonorganic hypersomnia, NOS) |
| Physiologic (organic) hypersomnia, unspecified |

subtypes is characterized by EDS with associated symptoms, including sleep paralysis, hypnagogic hallucinations, and sleep fragmentation. When present, cataplexy is pathognomonic for narcolepsy and is defined as a sudden loss of muscle tone in response to a strong emotional stimulus. This loss is bilateral, transient (less than 2 minutes), and usually secondary to a strong positive emotion such as laughter or surprise. Negative emotions can also trigger cataplexy in some patients.

EDS is usually the first presenting symptom for both children and adults with narcolepsy, and must occur almost daily for at least 3 months. It is often disabling and characterized by repeated inadvertent naps that occur throughout the day. These sleep lapses tend to occur during monotonous, nonengaging situations; although rare, they can also occur during active situations. This may manifest as a recurrence of daytime napping in children who had previously discontinued such naps. Fifty percent of narcoleptics have an onset of symptoms before age 20, and onset prior to age 5 is rare. Cataplexy often follows the onset of EDS within a year; however, it may take many years to occur or may never manifest. Naps are often refreshing for affected children. Other significant causes of EDS such as sleep apnea, inadequate sleep duration, or periodic limb movement disorder should be ruled out or treated prior to considering a diagnosis of narcolepsy unless cataplexy is present.

Sleep paralysis occurs in 50% of narcolepsy patients; however, it is often difficult for small children to describe. Although the paralysis is associated with sleep deprivation; an isolated episode should not be interpreted as an indicator of narcolepsy, especially when seen in the setting of sleep deprivation. Hypnagogic or hypnopompic hallucinations are also associated with narcolepsy in 50% of those affected. Sleep–wake period transition experiences must occur regularly to be considered significant.

Narcolepsy without cataplexy occurs in 10–50% of narcoleptics. In adolescents presenting with new-onset narcolepsy, cataplexy also may present later in the disease course, leading to re-categorization of the disease subtype.

Narcolepsy due to a medical condition may be caused by insults to the hypothalamus from tumors, sarcoidosis, or plaques from multiple sclerosis. In addition, conditions such as head trauma, myotonic dystrophy, Prader-Willi syndrome, Neiman-Pick type C disease, Parkinson's disease and multiple system atrophy have all been associated with secondary narcolepsy. Genetic or neurologic disorders should also be considered, particularly with the onset of narcolepsy in children younger than 5 years of age.

### *Recurrent Hypersomnias*

There are two recurrent hypersomnias: Kleine–Levin syndrome and menstrual-related hypersomnia. Both are characterized by recurrent periods of hypersomnia that last from 2 to 28 days and occur at least once a year. These conditions are rare, with only a few hundred cases reported in the literature. Onset is usually during early adolescence, but may be slightly later for girls. Between episodes, patients are usually asymptomatic, with normal behavior, alertness, and cognition. Documentation of normal sleep and behavior between episodes is required for diagnosis. Sleep periods are often excessive and may last 16–18 hours a day, with patients arising only to eat or urinate. Attempts to arouse these patients during sleep often require strong stimuli, and the response is usually aggressive. If a verbal response is obtained, it is typically unclear.

*Kleine-Levin syndrome*: Kleine–Levin syndrome is characterized by episodes of severe sleepiness that lasts days to several weeks. This syndrome occurs four times more often in boys than in girls, and onset is usually during late adolescence. A single longitudinal study of these children showed that disease severity improved within a few years of onset (median, 4 years).[11] However, episodes have also reportedly persisted for up to 20 years.[1] This diagnosis is reserved for episodes of hypersomnia associated with behavioral abnormalities such as hypersexuality, binge eating, cognitive issues including confusion and hallucinations, and odd, irritable, or aggressive behavior.

Morbidity is primarily related to the social and occupational impairment experienced during these episodes.

*Menstrual-related hypersomnia*: Menstrual-related hypersomnia is characterized by recurrent hypersomnia associated with the menstrual cycle. The prevalence is rare, with fewer than 50 cases reported in the literature. Onset is usually within a few months of first menses, and duration is typically a week with rapid resolution at the end of menses. It is hypothesized that hormonal imbalance is the inciting event. Treatment with oral contraceptives usually results in remission.

### *Idiopathic Hypersomnia*

Idiopathic hypersomnia is characterized by constant and severe EDS, often associated with unintentional naps that are unrefreshing, despite the fact that they may last for 3 or 4 hours. Onset is primarily during young adulthood and is rarely seen prior to adolescence. Patients with idiopathic hypersomnia are further classified by the duration of their major sleep period as those with long sleep time (>10 hours) or those without long sleep time. These patients awaken feeling tired. They have difficulty waking up and often experience confusion upon awakening (referred to as sleep drunkenness). They are often so tired that they are not even awakened by an alarm clock.

Although there are a few reports of remission, this condition is usually persistent, and severity is stable over time. Because idiopathic hypersomnia is a diagnosis of exclusion, history and physical are critical. Sleep time can be documented by an interview, sleep log, or actigraphy. PSG is useful in these patients only to rule out other sleep disorders. MSLT is usually carried out along with PSG to evaluate for narcolepsy; it demonstrates reduced sleep latency, with a mean of 6.3 ± 3.0 minutes.[1] For those with long sleep time, the PSG should show a major sleep period of at least 10 hours duration in addition to short sleep latency. For those without long sleep time, the major sleep period should be between 6 and 10 hours in duration. Diagnosis also requires EDS to be present for at least 3 months on an almost daily basis. Additional testing may be warranted if brain lesions or other pathology are suggested by the history or physical exam.

### *Behaviorally Induced Insufficient Sleep Syndrome*

Behaviorally induced insufficient sleep syndrome is characterized by complaints of EDS or behavioral issues suggestive of sleepiness in young children that are present on an almost daily basis for at least 3 months. When the individual's sleep pattern is evaluated, it is shorter than that recommended by age-adjusted normative data or is shorter than the patient requires, which is particularly pertinent for those with long sleep time (>10 hours). Often, the sleep duration on holidays or weekends is significantly extended from the weekday schedule. Affected individuals do not have difficulty in initiating or maintaining sleep and they do not recognize the disparity between the actual and necessary sleep duration.

Because of the unintentional chronic sleep deprivation in these patients, sleep paralysis and hypnagogic hallucinations may occur. This can make the differentiation of this condition from narcolepsy confusing. Unlike the situation in children with narcolepsy, however, extension of the major sleep period in these patients is usually adequate to reverse the EDS or daytime behavioral issues. PSG is not necessary if patients respond positively to prolongation of the major sleep period. If PSG is performed, it typically shows a sleep latency less than10 minutes and sleep efficiency >90%. The MSLT is also not required if there is response to prolonged sleep duration, but when performed usually shows mean sleep latency less than 8 minutes and may or may not be associated with multiple SOREMPs.

## Diagnostic Evaluation

Sleepiness is most commonly measured by the MSLT after a documented night without significant sleep-disordered breathing.[12] The Epworth Sleepiness Scale may also be used to screen for sleepiness in this population.[13]

The diagnosis of narcolepsy, with or without cataplexy, is confirmed by a normal PSG followed by short mean sleep latency, less than 8 minutes, and at least 2 SOREMPs. However, this alone is not specific enough to definitively diagnose narcolepsy, as 30% of the normal population have sleep latency less than 8 minutes. Establishing the diagnosis in peri-adolescent children can be problematic, as shortened sleep latencies with multiple SOREMPs on MSLT are also commonly seen in patients with chronic sleep deprivation or delayed sleep phase syndrome, both of which are common in this age group. Treatment of these coexisting conditions is often necessary to confirm the diagnosis.

Narcolepsy can also be diagnosed by the use of a test for hypocretin-1 levels in thecerebrospinal fluid. In most (90%) patients who have narcolepsy with cataplexy, hypocretin-1 levels are usually <110 pg/mL. In children who have narcolepsy without cataplexy, only 20% have

hypocretin levels below this threshold. This cutoff is one-third that of the normal level, and it is rarely seen in patients with other pathology or in otherwise healthy patients. Nonetheless, since cataplexy is pathognomic for narcolepsy, hypocretin-1 levels are rarely required to confirm the diagnosis. Because narcolepsy with cataplexy is also closely associated with human leukocyte antigen subtypes DR2/DRB1*1501 and DQB1*0602, testing is commonly carried out.

## Management

The management strategy for all hypersomnic conditions primarily consists of optimization of sleep hygiene and extension of sleep duration. This is especially pertinent for behaviorally induced insufficient sleep syndrome, in which extended sleep time alone is usually curative.

Behavioral treatment strategies may include scheduled 20- to 30-minute naps. These naps may need to be scheduled during school lunch, recess times, study halls, or after school but prior to participating in extracurricular activities or doing homework. When naps are unfeasible or are inadequate, pharmacotherapy is often recommended.

The most commonly used pharmaceutical therapies for narcolepsy include modafinil, stimulant medication, and sodium oxybate. Modafinil is a nonamphetamine medication that promotes wakefulness and is recommended for effective treatment of EDS.[14] This agent is approved by the FDA for individuals 17 years of age and older, although clinical trials have also shown its effectiveness in younger children. In the initial company-sponsored pediatric trial, one patient had Stevens–Johnson syndrome (a severe skin reaction), which has not been seen again in subsequent clinical practice. Traditional stimulants, including amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are also recognized as effective and recommended for treatment of EDS associated with narcolepsy. Sodium oxybate is a rapid onset sedative-hypnotic medication that is recommended for treatment of EDS in addition to the cataplexy and disrupted sleep associated with narcolepsy; it is FDA approved for individuals 16 years of age and older. Sodium oxybate may also be an effective preventative agent for hypnagogic hallucinations and sleep paralysis. In view of safety concerns, however, this is not a first-line therapy. These concerns include the inability to awaken on one's own while under its influence, the need to re-dose in the middle of the night, and the potential for abuse.

Modafinil is also recommended for patients with EDS secondary to idiopathic hypersomnia. Moreover, strong expert consensus suggests that modafinil, amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are all reasonable options for the management of patients with other hypersomnias of central origin. Data on the use of these medications in children is scant, and for the most part, it comes from case series and non-controlled nonrandomized trials.

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CHAPTER

# Pediatric Sleep Disordered Breathing and Evidence-Based Practice

72

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## INTRODUCTION

Pediatric sleep disordered breathing (SDB) is among the most common presenting complaint to the pediatric provider. Furthermore, current trends suggest that SDB is still on the rise as diagnostic awareness and the underlying epidemic of pediatric obesity continue to grow to dangerous levels, increasing the public health impact of this problem even further.[1] This is particularly notable for the otolaryngologist as tonsillectomy and adenoidectomy (T/A) is the preferred first-line approach for pediatric SDB management and is consequently one of the most common surgical procedures in the world.[2] Despite these unquestionable facts, the evidence basis for the clinical decision making in the diagnosis and management of pediatric SDB is still quite limited in many areas. Therefore, it is very important that the pediatric provider with an interest in an evidence-based practice is thoroughly familiar with the key clinical evidence that is available regarding the diagnosis and management of pediatric SDB. The areas that currently have the most useful data to guide the clinician include epidemiology, the clinical diagnosis of SDB, and the effectiveness of T/A. These areas will be the primary focus of this chapter.

## EPIDEMIOLOGY

There are many studies in the literature reporting on the prevalence of pediatric SDB throughout the world. It is instructive for the provider who evaluates children for SDB to be familiar with these general epidemiologic trends. For the purposes of examining these studies, it should be noted that pediatric SDB is generally comprised of two subcategories: primary snoring and obstructive sleep apnea/hypopnea syndrome (OSAHS). Primary snoring is loosely defined as either a parental report of habitual (loosely defined as multiple nights per week) snoring or objective measures of snoring in the absence of a formal, objective diagnosis of OSAHS. OSAHS is formally diagnosed with an attended overnight sleep testing during which apneas and/or hypopneas are measured with resultant neurocognitive arousals and/or gas exchange abnormalities, specifically hypoxia and/or hypercapnia.

Several studies have been published reporting the prevalence of primary snoring and OSAHS in different populations[3–10] (Table 72.1). As would be expected, there is considerable variability in these reports based on the population being sampled and the specific criteria of how pediatric SDB is defined. In a general, unselected population the prevalence of objectively measured OSAHS is clustered in the range of 1–5%.[11] This is surprisingly consistent despite varying populations and diagnostic criteria. Of significant clinical interest, there is a clear pattern that a larger proportion of children habitually snore. Specifically upon closer study, although the exact numbers differ somewhat, the general trend is that the rate of reported primary snoring is approximately three to five times more common as objectively measured OSAHS (Table 72.1). While the morbidity implications of snoring and mild SDB are still unclear, this is still very useful clinical information for the pediatric provider to consider when evaluating pediatric SDB complaints in an unselected population and contemplating various diagnostic modalities.

**Table 72.1:** Selection of studies reporting prevalence of pediatric habitual snoring and objective obstructive sleep apnea hypopnea syndrome

| *Study* | *Country* | *n* | *Objective OSAS criteria* | *Prevalence of OSAHS (%)* | *Subjective snoring criteria* | *Prevalence snoring (%)* |
|---|---|---|---|---|---|---|
| Sanchez-Armengol et al. 2001[3] | Spain | 100 | AHI > 10 | 2.0 | "Often" | 14.8 |
| O'Brien et al.[4] | United States | 5728 | AHI > 5 | 5.7 | "At least 3 times/week" | 11.7 |
| Rosen et al.[5] | United States | 850 | AHI > 5 | 2.5 | "At least once per week" | 17.0 |
| Kaditis et al.[6] | Greece | 3680 | AHI > 5 | 4.3 | "Always" | 4.2 |
| Brunetti et al.[7] | Italy | 895 | AHI > 5 | 1.0 | "Always" | 4.9 |
| Sogut et al.[8] | Turkey | 1198 | AHI > 3 | 0.9 | "At least 3 times/week" | 3.3 |
| Anuntaseree et al.[9] | Thailand | 1008 | AHI > 1 | 1.3 | "Most nights" | 8.5 |
| Ng et al.[10] | Hong Kong | 200 | AHI > 1 | 0.1 | "At least every other night" | 14.5 |

(AHI: Apnea hypopnea index (events/hour); OSAHS: Obstructive sleep apnea hypopnea syndrome).

There are a few identifiable risk factors that have been conclusively shown to increase the prevalence of pediatric SDB with which providers evaluating children with SDB should be familiar. None of these associations is unanticipated but it is comforting to see that the evidence confirms these familiar associations. Chief among these is childhood obesity. Pediatric obesity is well known to be on the rise in the developed world and has been unquestionably shown to increase the prevalence of OSAHS with a reported prevalence range of 13–59%.[12] This is a striking increase from the prevalence rates reported within the general population (Table 72.1) discussed earlier. It is important to note that even though this prevalence is remarkably high, it is still not close to 100%. Therefore, the pediatric provider must understand that while obese children are undoubtedly at an increased risk of SDB, they still require a thoughtful diagnostic approach to reach the appropriate diagnosis and avoid misdiagnosis that can lead to a trend of overdiagnosis.[13] Other patient factors that are well established with evidence to increase the prevalence of pediatric OSAHS are various craniofacial syndromes that have 38 times increased odds of having OSAHS [Odds ratio (OR) = 38; 95% confidence interval (CI) = 24–60] compared to nonsyndromic controls. Trisomy 21 (OR = 51; 95% CI = 20–128) and orofacial clefts (OR = 40; 95% CI = 17–94) were specifically shown to have significantly increased odds of OSAHS.[14]

Unfortunately, more conventional patient factors such as age, sex, and race remain unclear predictors of pediatric SDB. There is currently little to no evidence to suggest there is a meaningful, clinically useful association between age and SDB severity.[11] Despite being a recognized predictor of SDB in adult patients, male sex continues to be an unclear factor for pediatric OSAHS. Essentially equal number of studies over the last two decades show either a valid association with male sex having an increased prevalence of SDB or no association based on sex and therefore, the overall truth remains unclear. Yet recently, higher quality evidence increasingly suggests there indeed may be a trend of an increased prevalence of SDB in pediatric males.[11] Hopefully, the truth will soon be known conclusively even though the magnitude of this association may be too limited to be useful clinically. Regarding race, there is little solid evidence on which to draw helpful clinical conclusions. Overall during the last two decades there was little association with race reported, but again more recent, higher quality data seem to support an association between African American race and an increased prevalence of SDB.[15]

## DIAGNOSIS

The accurate and efficient diagnosis of pediatric SDB presents a large challenge to the pediatric provider for several reasons. First, SDB is a very common problem yet the symptoms and signs of SDB occur at nighttime and therefore, the diagnosing provider is left with only indirect evidence from the history and physical examination during a routine clinic visit on which to base a diagnosis. Second, the objective testing that is available to complement the clinical diagnosis is cumbersome for pediatric patients and caregivers, costly, and limited in availability in many areas. Third, even when objective testing is available the objective diagnostic standards for pediatric OSAHS are somewhat variable and are not conclusively correlated to measures of morbidity in children, particularly for mild

disease. Fourth, the threshold for clinically significant pediatric SBD is evolving and may or may not include primary snoring or mild OSAHS. Important prospective studies are being reported and are ongoing in this area that may contribute largely to changes in practice and recommended management. Specifically, a high-quality prospective, randomized, controlled study on children undergoing adenotonsillectomy (CHAT Study) was recently completed that has clouded the clinical implications of mild SDB as a large portion of children in the control arm of the study with mild OSAHS were found to have no disease on repeat PSG later in the study.[16] It is unclear whether this is simply regression to the mean or a favorable outcome for the natural history of mild OSAHS as children grow. Further study in this area will be imperative to establish evidence-based treatment algorithms for mild OSAHS.

It is crucial for the pediatric provider to thoroughly understand the known limitations in making a clinical diagnosis of pediatric SDB. As the diagnosing clinician considers these limitations in the utility of clinical information, they must then carefully consider how objective testing can be effectively and efficiently used in their practice environment to complement their clinical evaluation. It is expected that crucial data will continue to be reported in this area in the next few years and thus a provider with a goal of evidence practice should remain current on emerging studies examining the diagnosis and morbidity of pediatric SDB. For the purpose of the detailed discussion to follow, the diagnosis of pediatric SDB will be broken down into its subsequent parts of the history, the physical examination, and objective testing.

## HISTORY

The initial step in the evaluation of pediatric patient for SDB is invariably the parental history. The clinical history is limited but still provides very useful data to guide the evaluating provider toward a potential diagnosis of SDB. Generally speaking, the clinical history will either support the diagnosis of SDB with reports of nightly snoring, gasping, witnessed apneas, restless sleep, etc., i.e. a "positive" history is elicited, or it will not, i.e. a "negative" history is elicited with the absence of these observations. To have an appropriate understanding of the limitations of the clinical history, each instance must be meticulously examined. Based on published meta-analysis data, the clinic history generally has a relatively high sensitivity (probability that the clinical history is "positive" when SDB is truly present) and a lower specificity (probability the clinical history is "negative" when pediatric SDB is truly absent).[17] What are the implications of this observation? In the case of a "positive" history, the clinician can be relatively confident that this indicates SDB is actually present. The meta-analysis data suggest that the sensitivity of various components of the history is likely well above 50%.[17] This is a comforting and encouraging observation that indicates the clinician will be correct well over half the time when using the "positive" clinical history as the basis for establishing a diagnosis of pediatric SDB.

Conversely, the "negative" clinical history is far more problematic. The "negative" clinical history is less instructive with a specificity of approximately 50% at best.[17] Of course, this presumes that the quality of the "negative" history is sufficient on which to make a diagnosis. In many cases it is not. The first and foremost step the evaluating clinician should take when encountering a "negative" clinical history is to ascertain the quality of this information by questioning the caregiver as to how often and at what times of the night they actually observe their child. This can vary substantially and in many instances the "negative" clinical history may in fact be a lack of general observation as opposed to a lack of observed symptoms. This is a crucial distinction to make in order to maintain diagnostic accuracy. To have an appropriate sample, it is recommended that the caregiver observes the child over an extended period (multiple nights) to include both early nighttime and late nighttime (early morning hour) observation. Early morning hour observation is of course generally more difficult for the caregiver, as it is more likely to interrupt their own sleeping pattern, but it is far more likely to display symptoms in the typical child. The reason for this is that rapid eye movement (REM) sleep occurs more frequently in the early morning hours and SDB is more likely to occur during REM sleep periods, as airway resistance and therefore airway collapse (apneas) are typically higher in REM periods.[18] Once the clinician is confident that the "negative" history is of sufficient quality, the diagnostic challenges unfortunately do not end there. The observed low specificity of the "negative" history means that the evidence indicates that the clinician will generally be unable to consistently and accurately exclude pediatric SDB on historical features alone. This is a troubling limitation that must be recognized and addressed. To maintain a high level of accuracy the clinician must look to other diagnostic clues (e.g. physical examination, although it too is limited) or objective testing.

## Physical Examination

As with the clinical history, the physical examination only provides the evaluating clinician with indirect clues to establish a diagnosis of SDB. With obesity being a strong predictor of OSAHS, body mass index (BMI) may be the most reliable physical examination component to establish a diagnosis. As discussed previously, obesity has been strongly associated with increased prevalence of OSAHS, but this relationship is not 100% pure, and further diagnostic evaluation may be required if obvious historical features and/or physical examination clues are not present.[13]

Tonsil size is widely embraced as perhaps the most objective component of the physical examination that can be used to make a diagnosis of OSAHS and select patients for management with T/A. However as may be unrecognized by many clinicians, the evidence regarding using tonsil size for the diagnosis of OSAHS is actually quite weak.[19] This is further complicated by the flaws of the commonly utilized Brodsky 0–4+ tonsil size scale. The Brodsky rating scale is universally recognized and rates the "size" of the tonsil using a 0 (no tonsil tissue visible) to 4+ (tonsils touching in the midline) scale.[20] The scale is universally embraced, as it is simplistic and adds a comforting "pseudo-objective" aspect to the physical examination. Aside from being plagued by obvious subjectivity, the scale is essentially only a one-dimensional assessment of the tonsils and is really more an assessment of tonsil position rather than true size. As any experienced tonsillectomy surgeon will certainly agree, tonsils can either be endophytic (positioned deeply in the tonsillar fossa) or exophytic (be positioned mostly outside of the tonsillar fossa). Thus, a 1+ tonsil can actually be quite large and a 4+ tonsil be smaller than estimated using the typical 0–4+ scale.

So is tonsil size or position more important in the diagnosis of pediatric OSAHS? The anatomy of the upper airway and the pathophysiology of airway collapse during sleep is unquestionably complex. The current evidence regarding tonsil "size" with the 0–4+ scale suggests that it is a weak predictor of OSAHS severity at best. A recent meta-analysis of this question established that several published studies report that there is an association between the 0–4+ scale and objective OSAHS severity and that several studies report no true association. However, a robust quality assessment of all the published studies indicated that the studies showing a lack of association between 0–4+ tonsil size and objective OSAHS severity were of a generally higher quality and were less likely to contain bias or error than the studies that reported no association.[18] Only two studies have assessed the true three-dimensional size of the tonsils either via a direct quantitative volumetric assessment[21] or using MRI,[22] and each demonstrated a positive correlation between the true three-dimensional size of the tonsil and objective SDB severity.

How can the clinician appropriately assess tonsil size taking into account the best available evidence? Unfortunately, there are no direct answers here but there are a couple of general principles that are useful to consider. First, a complete view of the tonsils is essential. This sounds obvious, but in the reluctant pediatric patient this often requires depressing the tongue fully and inducing an uncomfortable gag. Second, when considering the tonsils, evaluate them three dimensionally and assess their size and position separately. For example, even though the position is only 2+ is the bulk still significant? Conversely, the position may be 3+ but the bulk may not be that significant. Clearly this process, although more rooted in accordance with the current evidence, is still less than ideal. Development of a simple, useful tonsil size scale that incorporates both size and position that is predictive of objective OSAHS severity would be a significant advancement and should be a research priority.

The importance of adenoid hypertrophy in the pathogenesis of SDB and the clinical assessment of adenoid size are poorly studied and understood. Because of their less assessable location and the subsequent need for either an imaging study or nasal endoscopy to fully assess their size, there is far less evidence evaluating the contribution of the adenoid to SDB severity. It is generally accepted that nasal endoscopy is a superior means to assess adenoid size and its potential obstruction of the upper airway. Moreover, nasal endoscopy does not require exposure of the child's head to radiation such as is required in a lateral skull plain X-ray film.[22] On the other hand, nasal endoscopy is generally not well tolerated in pediatric patients and therefore poses its own problems. It would be expected that after a full discussion of the options, most parents (perhaps not the children though!) would prefer the momentary discomfort of nasal endoscopy over the unpredictable effects of ionizing radiation to their child's skull and brain. Studies evaluating adenoid size in association with tonsil size with MRI have demonstrated some association with SDB severity.[23] A more complete understanding of the role of adenoid hypertrophy is needed.

Drug-induced sleep endoscopy (DISE) is an emerging diagnostic modality for pediatric OSAHS and deserves brief mention. Substantial evidence supporting DISE exists for adult sleep apnea evaluation. However, it is important to distinguish that surgery is not the primary treatment modality in adult sleep apnea management, as it is in pediatric SDB. DISE is, therefore, used in adults as a discriminating diagnostic technique to select anatomical structures for modification with multilevel sleep surgery. In pediatric patients, there is much less experience and published data. DISE has been shown to have sufficient inter-rater reliability in pediatric patients to be considered reliable.[24] Additionally, there are some early case series using DISE to evaluate the upper airway in children where T/A has already been completed and OSAHS remains or where the tonsils appeared small and unlikely to be contributing to OSAHS. In all these cases the "small" tonsils were still found to be significant contributors to airway obstruction.[25] The optimal role of DISE in the evaluation of pediatric SDB has yet to be determined.

## OBJECTIVE TESTING

The clear limitations of the clinical history and physical examination have been well-established. Thus, it would be ideal if objective testing for pediatric SDB was simple, inexpensive, and readily available to complement the clinical evaluation. Yet, this is clearly not the case. The gold standard objective test of attended overnight polysomnogram (PSG) is inconvenient, expensive, and its availability is limited in many areas. Because pediatric PSG is a limited resource, multiple detailed guidelines have been established by various organizations to guide clinicians in the use of PSG in pediatric patients. These guidelines have been developed by different groups with different audiences in mind and therefore have conflicting recommendations[26–29] (Table 72.2). There are no easy solutions to this problem and with many diverse stakeholders involved there will likely not be a consensus on the use of pediatric PSG anytime soon. Consequently, each clinician will have to assess their own current practice environment, available access to pediatric PSG, and the diagnostic challenges of their own patient population to establish an appropriate algorithm to include the use of PSG to complement their clinical diagnostic tools.

Significant interest has arisen in the use of home sleep testing and screening tests to fill the gap between the clinical evaluation and PSG. A simple inexpensive screening test that could accurately assess pediatric SDB would be very useful. Many attempts to provide a simple solution to include the use of home pulse oximetry,[30] parent obtained videos,[31] and parent obtained audio taping[32] have been

**Table 72.2:** Selected Recommendations from various clinical practice guidelines (CPG) addressing use of polysomnography (PSG) to diagnose pediatric obstructive sleep apnea hypopnea syndrome (OSAHS)

| *Clinical area* | *Otolaryngology CPG*[26] | *Pediatrics CPG*[27] | *Sleep medicine CPG*[28] |
|---|---|---|---|
| Limitations of the history and physical examination | "Caregiver reports of snoring, witnessed apnea or other nocturnal symptoms may be unreliable if the caregiver does not directly observe the child while sleeping or only observes the child early in the evening" | "The sensitivity and specificity of the history and physical examination are poor" | "Snoring and other nocturnal symptoms … showed inconsistent correlations with respiratory parameters of PSG" |
| Indications for PSG in a "healthy" pediatric patient | "The clinician should advocate for PSG prior to tonsillectomy for SDB in children …. for whom the need for surgery is uncertain or when there is discordance between tonsillar size on physical examination and the reported severity of SDB" | "Clinicians should either:<br>(1) obtain a PSG OR<br>(2) refer the patient to a sleep specialist or otolaryngologist for a more extensive evaluation" | "Polysomnography is indicated in children being considered for adenotonsillectomy to treat obstructive sleep apnea syndrome" |
| Use of portable monitoring (PM) home sleep testing in children | "Laboratory-based PSG remains the gold standard for the diagnosis of OSA in children…. recommends against the routine use of PM over in laboratory PSG" | "If PSG is not available, then clinicians may order alternative diagnostic test such as nocturnal video recording, nocturnal oximetry, daytime nap PSG, or ambulatory PSG" | "Nap (abbreviated) PSG is not recommended for the evaluation of OSAS"<br>Separate statement paper recommends against use of portable monitors[29] |

**Table 72.3:** Important meta-analyses of pediatric adenotonsillectomy (T/A)

| *Authors* | *Specific topic investigated* | *Study conclusions* |
|---|---|---|
| Brietzke and Gallagher[33] | Overall efficacy of T/A in treating OSAHS | The summary success rate of T/A in "normalizing" PSG on an individual study basis was 82.9% (random effects model 95% CI = 76.2–89.5%, p < 0.001) |
| Freidman et al.[34] | Overall efficacy of T/A in treating OSAHS | When "cure" was defined as an AHI < 1 random-effects model estimate for OSAHS treatment success with T/A was 59.8% (95% CI = 43.6–74.0%) |
| Baldassari et al.[35] | Quality-of-life (QOL) changes after T/A | OSA-18 score and each domain score improved ($p < 0.0001$) after T/A. At long-term follow-up, QOL scores remained significantly improved |
| Brigger and Brietzke[36] | Complication rates of outpatient T/A | T/A complication rate estimate of 8.8% (95% CI = 5.5–12.1%, $p < 0.001$). Children under age 4 have a higher rate of early complications and unplanned admissions |
| Acevedo et al.[37] | Complication rates of tonsillotomy vs. tonsillectomy* | Differences in hemorrhage and dehydration were not evident in high-quality studies. Data regarding tonsil regrowth rates and efficacy in treating SDB are not yet sufficient for formal analysis |
| Costa and Mitchell[38] | Overall efficacy of T/A in treating OSAHS in obese children | T/A improves but does not resolve OSA in the majority of obese children. Overall T/A success rates were 49% (success criteria = AHI < 5), 25% (AHI < 2), and 12% (AHI < 1) |

*Included some adult patients but the overall grand mean age was 7.1 years.
(AHI: Apnea hypopnea index; OSAHS: Obstructive sleep apnea hypopnea syndrome; T/A: Tonsillectomy and adenoidectomy).

attempted. However, complicating factors including variable data quality, poor compliance in the unattended setting, and poor specificity have precluded their widespread use. The development of ambulatory technology to develop an effective screening test for pediatric SDB for children of all ages would be a significant advancement in the diagnosis of pediatric SDB.

## MANAGEMENT

The management of pediatric SDB includes both medical and surgical approaches. Although some controversy exists as to the preferred management of SDB, surgery with adenotonsillectomy (T/A) is generally considered the first step in management of pediatric OSAHS for uncomplicated patients with no surgical contraindications. This is in stark contrast to adult SDB management in which medical therapies are generally considered first line. Like in adults, medical management strategies in children can also be effective but are overtly plagued by poor compliance and unclear treatment endpoints. Both surgical and medical management strategies will each be considered below with a brief discussion of the available supporting evidence.

### Surgical Management

Surgical management with tonsillectomy and adenoidectomy is widely considered the first-line management step for most uncomplicated cases of pediatric SDB.[26–28] Multiple studies and subsequent meta-analyses have demonstrated the subjective and objective efficacy of T/A in the management of OSAHS (Table 72.3). The success rate of T/A in curing OSAHS is understandably dependent on the definition of "success" that is utilized. Two meta-analyses of the success of T/A have been performed to date, each with a slightly different approach of how "success" was defined. Using a range of definitions for treatment "success" that were individually employed in each distinct study yielded an overall "success" rate of T/A for the management pediatric OSAHS of approximately 83% (95% CI = 76.2–89.5%).[33] Whereas, if a strict definition of a postoperative apnea hypopnea index (AHI) of less than or equal to one event per hour is used as the definition of "success", the overall "success" rate drops to approximately 60% (95% CI = 43.6–74.0%).[34] Since the threshold where SDB becomes harmful to the pediatric patient is not entirely known, each approach has merit and the true "success" rate of T/A is specifically known. A subsequent meta-analysis focused on quality of life outcomes with T/A and demonstrated that the sleep-related quality-of-life gains from T/A were substantial and persisted over long term (range = 6–16 months) follow-up.[35]

Complications of T/A are statistically uncommon on an individual basis, but given the widespread performance of T/A, they do occur at a population level. A meta-analysis of T/A complications concluded that

outpatient performance of T/A is reasonable for the great majority of cases and that age <4 was the only risk factor that was supported by the data to be associated with T/A complications with an odds ratio 1.64 (95% CI = 1.16–2.31).[36] Unfortunately, insufficient data were available to fully assess the role of SDB diagnosis in T/A complications. This is an area where a new systemic review and meta-analysis could be attempted that would be useful to the otolaryngologist who is continually faced with pressure to perform surgical procedures in outpatient and ambulatory settings for cost reasons.

The partial tonsillectomy ("tonsillotomy") was reintroduced in the late 1990s as an alternative to tonsillectomy that would be potentially less morbid and result in reduced recovery time. The term "reintroduced" is appropriate as a partial tonsillectomy approach was first described and extensively utilized in the preanesthetic era.[39] A subsequent meta-analysis of tonsillectomy versus tonsillotomy concluded that the majority of the evidence showed that tonsillotomy was indeed less morbid with lower bleeding rates and postoperative dehydration rates. However, on more detailed evaluation, a subgroup of higher quality studies (randomized, blinded, etc.) within the analysis suggested this difference was not significant.[37] Most importantly, the meta-analysis concluded that the key questions of tonsil regrowth rates following tonsillotomy and efficacy of tonsillotomy in the management of pediatric SDB could not be addressed due to insufficient evidence. These critical issues should be appropriately addressed before tonsillotomy is embraced as a true alternative to traditional tonsillectomy.

Adenoidectomy alone is infrequently used as the solitary surgical procedure for the management of pediatric OSAHS. This is most commonly encountered when younger patients (<2 years) present with OSAHS symptoms but are felt to be at too high a risk to undergo tonsillectomy. Thus, the key questions that inevitably follow are "how many patients who undergo adenoidectomy alone for SDB will ultimately need to undergo a tonsillectomy in the future for persistent/recurrent SDB symptoms?" and "what clinical factors are predictive of this event?" Selected studies have addressed these relevant questions and have shown similar results.[40–42] Perhaps surprisingly, each study showed only a minority of pediatric patients who undergo adenoidectomy alone for SDB are found to return for tonsillectomy for persistent obstruction. The study designs were not robust enough to assess the potential role of loss to follow-up as the main contribution to this observation. Not surprisingly, younger age at the time of adenoidectomy and larger tonsil size at the time of adenoidectomy were each associated with increasing odds of future tonsillectomy. These trends indicate that adenoidectomy alone can be a viable surgical treatment for younger patients with SDB in which tonsillectomy is not appropriate, although specified risk factors should be assessed and possible future tonsillectomy should be included in the informed consent process.

Turbinoplasty is a minimally invasive procedure that is often performed in conjunction with T/A for management of obstructive symptoms. The procedure is attractive, as it is simple, concise, and has low morbidity. One study has objectively examined the effectiveness of turbinoplasty used in conjunction with T/A for the management of SDB.[43] In this nonrandomized study, the turbinoplasty group was shown to have superior quality-of-life improvement as well as a significantly decreased postoperative apneahypopnea index compared to the T/A only group (0.8–3.5 events per hour, $p < 0.01$). These results are encouraging but further study with a randomized study and further investigation into optimal patient selection are urgently needed.

As reported above, the overall success rate of T/A for pediatric OSAHS is high but it is not 100%. Therefore, some patients undergoing T/A will have residual SDB. In these cases, medical therapy may (and perhaps should) be considered as the next option. However, medical therapies for pediatric SDB are often plagued by poor compliance and ill-defined treatment endpoints. Therefore, in selected cases surgical procedures beyond T/A may be attempted including uvulopalatopharyngoplasty (UPPP), tongue reduction procedures, and lingual tonsillectomy. The otolaryngologist is cautioned that there is very little evidence available to describe the success of these types of procedures in children. What data are available are typically primarily in the context of treating patients with severe OSAHS with obesity and/or craniofacial syndromes such as trisomy 21.[44,45] Outcome data from these case series are likely not directly applicable to a general pediatric population. Moreover, the complications rates with these procedures are measurably higher than T/A. More study is clearly required to ascertain the optimal role of these procedures in children with residual SDB as well as how much residual SDB after T/A actually requires treatment. At this time in the absence of guiding data, pediatric patients with residual OSAHS following T/A should be evaluated on an individual basis, ideally in the context of a multidisciplinary team including

otolaryngology, pulmonology, sleep medicine, oral surgery, and other specialties where all available treatment modalities can be equally explored and presented.

Medical therapy is generally considered second line behind T/A for the management of uncomplicated pediatric OSAHS. Yet, medical therapy is commonly employed for treatment of residual moderate to severe OSAHS following T/A, in complex patients who are not candidates for T/A, or by parental preference over T/A. Continuous positive airway pressure (CPAP) is first-line therapy in adult OSAS (obstructive sleep apnea syndrome) and has also been reported for use in children, although there are far less pediatric CPAP data available. As with adults, CPAP is highly effective in the management of SDB but suffers from very poor compliance.[46,47] Successful use of CPAP in children requires an intensive support from the sleep laboratory as well as complete "buy in" from the parents.[48] Even then, long-term success rates can be suboptimal.

With the prominence of pediatric obesity weight loss is also a common nonsurgical management approach in the management of SDB. The etiology of the pediatric obesity epidemic is multifaceted and involves many complex factors including genetics, parenting style, socioeconomic issues, and the impact of society's modern lifestyles that value convenience and entertainment over healthy habits such as exercise and sleep. Thus, it should be expected that effective solutions for childhood obesity will consequently need to be complex and inclusive. Comprehensive treatment approaches have been developed that include nutrition, physical training, parent coaching, and psychological support.[49,50] Unfortunately, even this type of comprehensive approach has produced only limited success with only 25–30% of patients demonstrating significant improvement in their BMI after extended periods of treatment. Effectiveness of weight loss programs specifically targeting the treatment of pediatric OSAHS have not yet been investigated with high-quality studies. Unquestionably, this area will require future high-level studies to determine the optimal role of weight loss strategies in the management of pediatric SDB.

Lastly, pharmacotherapy can also be utilized for treatment of pediatric OSAHS. High-level randomized, blinded, placebo-controlled studies have been completed that show both nasal steroids and oral montelukast are effective in treating pediatric OSAHS, albeit with relatively small sample sizes. Topical nasal steroid therapy was shown to successfully treat 54% (26 of 48) of pediatric patients with mild OSAHS after 6 weeks of therapy.[51] Oral montelukast (Singulair, Merck, Inc) was also shown to be effective with a minimum 50% reduction in AHI being demonstrated in 65% (15 of 23) of patients after 12 weeks of therapy.[52] The two agents were subsequently combined and studied in pediatric patients with mild residual OSAHS following T/A with demonstration of a significant reduction in the mean AHI (0.3 vs. 4.7 events per hour, $p < 0.04$) after 12 weeks of therapy.[53] There are important results that establish pharmacotherapy as a viable treatment option specifically for mild to moderate OSAHS. However, there are unanswered questions including effectiveness for patients with moderate to severe OSAHS, the possibility of long-term side effects, and the uncertainty of treatment endpoints that will need to be addressed.

## CONCLUSION

There is considerable evidence available to guide the pediatric provider in the diagnosis and management of pediatric SDB. Epidemiologic data are available that inform the provider on the general trends of general SDB and specifically OSAHS that are useful in determining baseline risk. The efficient and accurate diagnosis of pediatric OSAHS remains somewhat elusive but plentiful data exist that describe the limitations of the history and physical examination that are essential for the provider to understand and consider in daily practice. Surgical management of pediatric SDB predominates but has important limitations and unanswered questions of which the otolaryngologist must be aware. Medical treatments are also available for patients who fail surgical therapy, which appears to be an increasing problem. The various medical therapies including CPAP and pharmacotherapy can be effective but also have limitations that should be acknowledged. Overall, the evidence basis regarding the treatment of pediatric SDB is substantial but is still in need of development in several select, key areas.

*Mandatory Disclaimer:* The views herein are the private views of the author and do not represent official views of the Department of Defense or the Department of the Army.

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# SECTION 6

# Pediatric Voice

CHAPTER

73

# Anatomy of the Pediatric Larynx

***Joshua B Silverman***

## INTRODUCTION

The larynx is essential for a newborn's ability to breath, feed, and cry. As such, it is vital for the otolaryngologist to understand the anatomy of the pediatric larynx. As children grow older, predictable changes occur to the laryngeal structures, and knowledge of these changes allows recognition of anatomical anomalies at the time of endoscopy. In this chapter, we examine the anatomy and physiology of the pediatric larynx and compare its structures to those of the mature larynx.

## LARYNGEAL DEVELOPMENT

Due to the complex functions of the larynx, specific embryologic growth patterns must be followed to allow development of two independent tracts for breathing and swallowing. Errors in development interfere with these vital functions, most commonly manifested as either stenosis or atresia. Most of laryngeal development occurs during the embryonic period (first 8 weeks of gestation), though important maturation occurs during the subsequent 32-week fetal period.[1] The widely used Carnegie Staging System divides the embryonic period into 23 developmental steps. Laryngeal development predictably occurs from Carnegie Stage 11 to 23. Holinger and Henick[2] have divided this time period into 8 phases, each corresponding to key points in laryngeal development (Fig. 73.1). The first seven phases occur during the embryonic period, while the eighth stage occurs during the fetal period.

At Carnegie stage 11, the respiratory primordium is represented by an epithelial thickening along the ventral aspect of the foregut.[3] This represents Phase I in the Holinger-Henick system.[2] Phase II occurs as the respiratory primordium expands, and a ventral outpouching forms to become a respiratory diverticulum. This diverticulum gives rise to bilateral bronchopulmonary buds that eventually develop into the lower respiratory tract. In Phase III, the upper foregut and respiratory diverticulum separate from the bronchopulmonary buds, which migrate caudally and inferiorly, and the two main bronchi and carina are formed. The tract between the respiratory diverticulum and carina becomes the trachea.[4]

In Phase IV, obliteration of the ventral lumen of the foregut region representing the primitive laryngopharynx gives rise to the epithelial lamina. Eventually, the primitive laryngopharynx gives rise to the supraglottic larynx.[5] The epithelial lamina is thought to be a key region for recanalization to allow communication between the upper and lower airways later in development. Arytenoid and epiglottic swellings first appear during Phase IV as well. During the next two Phases, V and VI, the laryngeal cecum appears and slowly descends from the level of the arytenoid swellings to the future glottis along the ventral aspect of the epithelial lamina. Recanalization of the epithelial lamina begins in Phase VII. The last portion of the primitive laryngopharynx to recanalize is at the glottic level, and when finished, a complete communication is established between the supraglottis and infraglottis, apparent in Phase VIII. Incomplete recanalization can

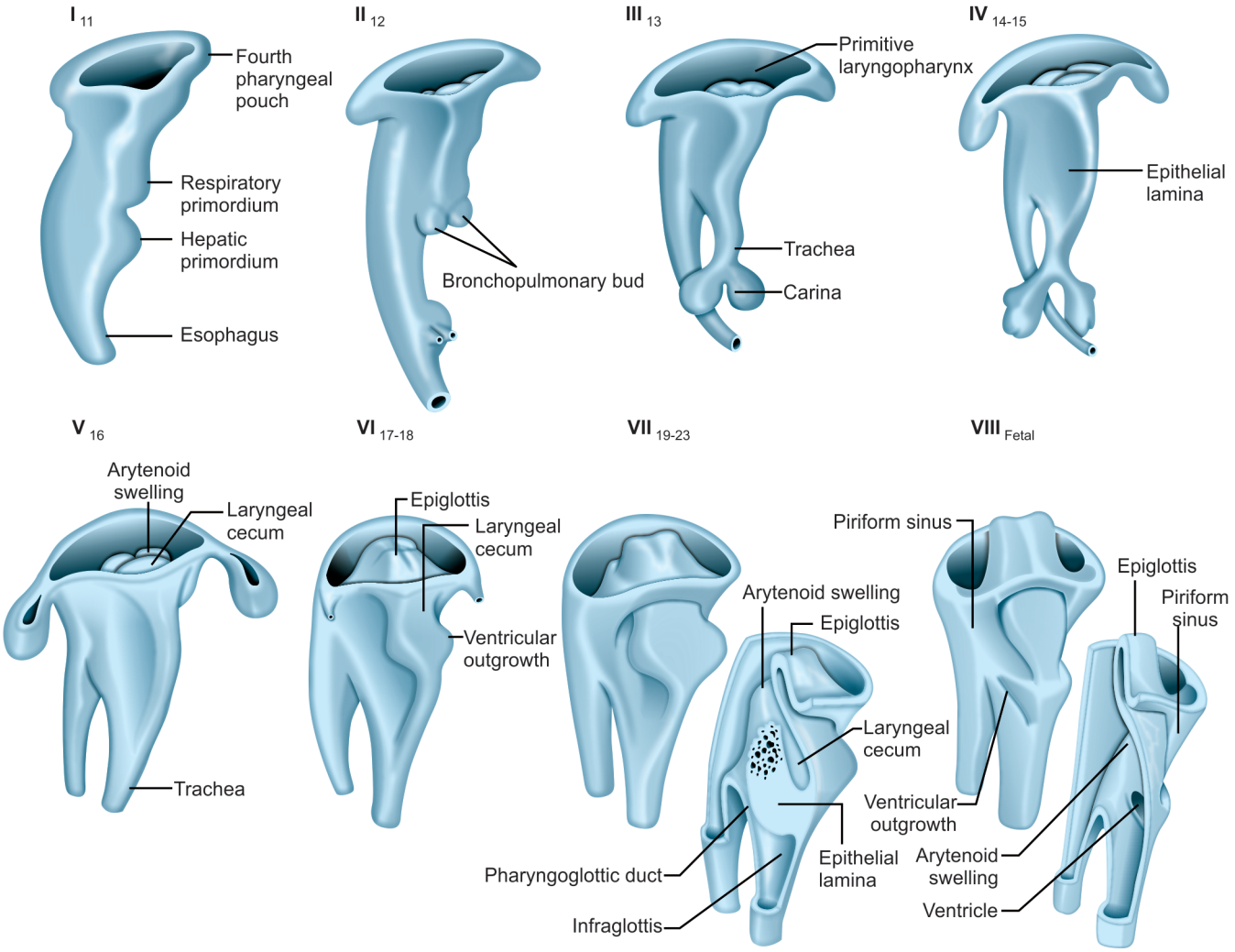



**Fig. 73.1:** Eight phases of laryngeal development. Adapted from Kakodkar.[4]

result in webbing or atresia of the supraglottis or glottis. Phase VIII also describes the development of the laryngeal ventricles, which arise from lateral outgrowths of the laryngeal cecum.[2]

In 1990, Sanudo and Domenech-Mateu[3] described two areas of continued controversy regarding laryngeal development: (1) the level of the respiratory primordium from which the larynx develops and (2) the importance of the epithelial lamina in creation of the laryngeal cavity. In studies on human embryos, they suggested that there are multiple levels of the respiratory primordium that give rise to various laryngeal structures. They also observed two separate epithelial structures named epithelial septum and epithelial lamina, which contribute to formation of the laryngeal cavity.[3] This theory contrasted with those previously proposed in which only the epithelial lamina is primarily responsible for development of the laryngeal cavity, first put forth by Walander in 1950, and later supported by Henick.[6]

While the larynx initially forms as an outpouching of the pharynx in the third week of development, the laryngeal cartilages and intrinsic muscles of the larynx develop from the 4th and 6th branchial arches. Arytenoid swellings form in the region of the 6th arch and begin to chondrify to form the arytenoid cartilages in the 7th week. While chondrification of the thyroid, cricoid, cuneiform, and corniculate cartilages begins around the same time as the arytenoids, epiglottal cartilage does not appear until the 5th month, leading to debate as to the initial progenitor cells of the epiglottic swelling.[1] Also in the 5th month, squamous epithelium becomes present on the vocal fold with respiratory epithelium present in the posterior glottis.[5]

## LARYNGEAL ANATOMY AND PHYSIOLOGY

### Cartilaginous Structures (Fig. 73.2)

Motion of the arytenoid cartilage rotationally over the cricoid cartilage is the key to vocal fold adduction. The vocal process is one of two pointed ends of the faceted arytenoid cartilage. It is the attachment site for the vocal ligament and the end of the vocal fold. The arytenoid rotates to bring two pliable surfaces in close apposition. It is the column of air being expelled from the distal airways up the trachea that powers the vibratory system. The arytenoid cartilage also tilts, as there is interplay between the thyroid and the cricoid cartilages and the thyroid and arytenoid cartilages. Changes in the vocal fold length lead to modulation of pitch of the voice.

The small corniculate cartilages sit atop the arytenoids. The cuneiform cartilages rest within the aryepiglottic folds, and do not directly articulate with the arytenoids.[7] The cricoid cartilage is a complete ring at the top of the trachea that is much taller posteriorly than anteriorly. This posteriorly based cephalad slope in the cricoid raises the arytenoid to the midportion of the thyroid cartilage. The thyroid cartilage is composed of two alae forming a three-directional shield that protects the vocal folds. The anterior commissure, where the vocal folds blend anteriorly against the posterior surface of the thyroid cartilage, is located approximately halfway from the inferior border of the thyroid cartilage.

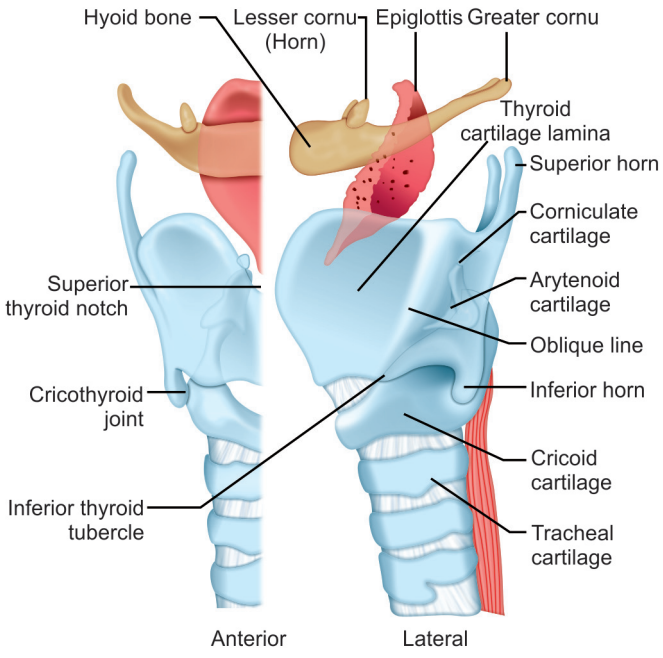


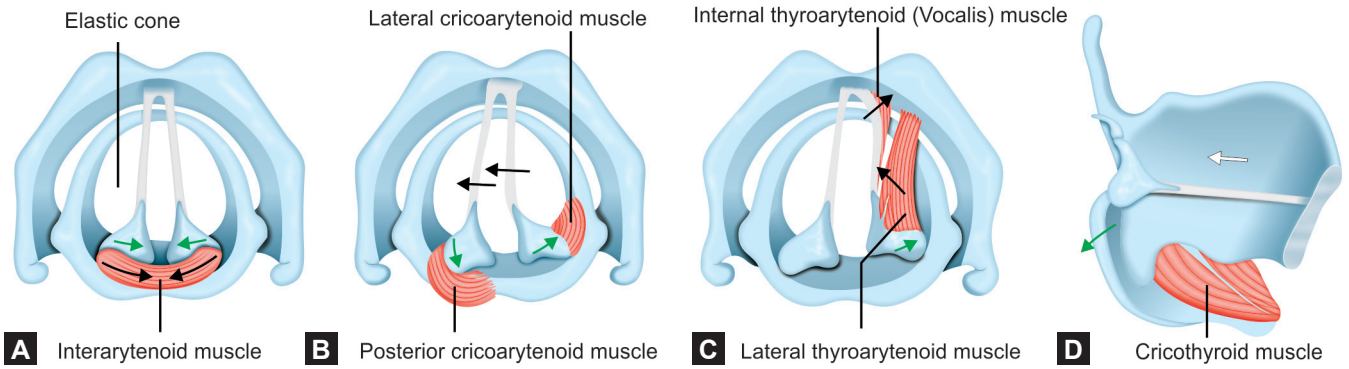

**Fig. 73.2:** External framework of the laryngeal complex. Adapted from Janfaza et al.[7]

The hyoid bone is the only bony component of the laryngeal complex. The bone has numerous attachments that anchor it to the mandible and skull base, as well as link it to the larynx. These attachments allow for elevation and depression of the entire laryngeal complex. During swallowing, the relationship between the hyoid bone and the larynx changes, such that the bone is elevated and displaced anteriorly. This leads to a change in epiglottis position. Due to its ligamentous connections, including the centrally located hyoepiglottic ligament, the epiglottis folds posteriorly down over the laryngeal vestibule, helping to protect against aspiration.

### Muscles of the Larynx

The muscles of the larynx are either extrinsic or intrinsic, divided by their ability to move the whole larynx or individual components, respectively. Extrinsic muscles either depress the larynx or elevate it. Depressors include the omohyoid, sternohyoid, and sternothyroid muscles, while the digastric, stylohyoid, and mylohyoid elevate the larynx. The surrounding pharyngeal muscles change the pharyngeal inlet and thus modify the shape of the air passage.[5] These include the stylopharyngeus, palatopharyngeus, and middle and inferior pharyngeal constrictor muscles.

The intrinsic muscles are the posterior cricoarytenoid (PCA), lateral cricoarytenoid (LCA), cricothyroid, thyroarytenoid, interarytenoid, and vocalis. Only the PCA muscle abducts the vocal folds by displacing the muscular process of the arytenoid cartilage medially, posteriorly, and inferiorly. Contraction of the remaining intrinsic muscles narrows the glottic opening by adduction of the arytenoids. The LCA displaces the muscular process of the arytenoid forward and laterally, thus opposing the action of the PCA and causing vocal fold adduction. The interarytenoid muscle approximates the two arytenoid cartilages, helping to close the posterior glottis. The vocalis muscle runs parallel to the vocal ligament and unopposed action can shorten the vocal fold by moving the arytenoid cartilage anteriorly. The vocalis is opposed by the cricothyroid muscle, though, and thus helps to further adduct the vocal folds (Figs. 73.3A to D).[7] The cricothyroid muscle closes the anterior gap between the thyroid and cricoid cartilages and increases the distance between the posterior cricoid and anterior commissure, which results in lengthening and tensing of the vocal folds.[8]




**Figs. 73.3A to D:** Actions of intrinsic musculature of the larynx. Adapted from Janfaza et al.[7]

## Vasculature and Innervation

The larynx receives its blood supply from the superior and inferior laryngeal arteries. The superior laryngeal artery arises from the superior thyroid artery and pierces the thyrohyoid membrane to penetrate into the submucosal tissues of the piriform sinus, supplying the intrinsic laryngeal muscles and laryngeal mucosa. The superior laryngeal artery runs with the internal branch of the superior laryngeal nerve. The inferior laryngeal artery arises from the inferior thyroid artery and enters the larynx below the inferior constrictor muscle to anastomose with the superior laryngeal artery and also feed the intrinsic structures of the larynx.[9] The cricothyroid artery also originates from the superior thyroid artery and traverses the cricothyroid membrane. The superior and inferior laryngeal veins parallel the arteries and drain into the superior and inferior thyroid veins, respectively. Note should be made that lymphatic drainage is separate from the supraglottic and infraglottic regions, and no direct connection exists between these groups of nodes.[7]

Innervation of the larynx arises from branches of the vagus nerve. The superior and inferior laryngeal nerves enter the larynx differently and hold different functions. The superior laryngeal nerve can be found medial to the bifurcated carotid arteries, where it divides into an external and internal branch. The external branch supplies motor function to the cricothyroid muscle. Bilateral injury to the external branches changes voice, as high tones can no longer be produced. The internal branch travels with the superior laryngeal artery to pierce the thyrohyoid membrane and carries sensation from the valleculae, base of tongue, epiglottis, piriform sinuses, ventricles, and posterior laryngeal and anterior pharyngeal walls at the level of the cricoid cartilage (Fig. 73.4).[7]

The inferior or recurrent laryngeal nerve runs superiorly near or in the tracheoesophageal groove with the

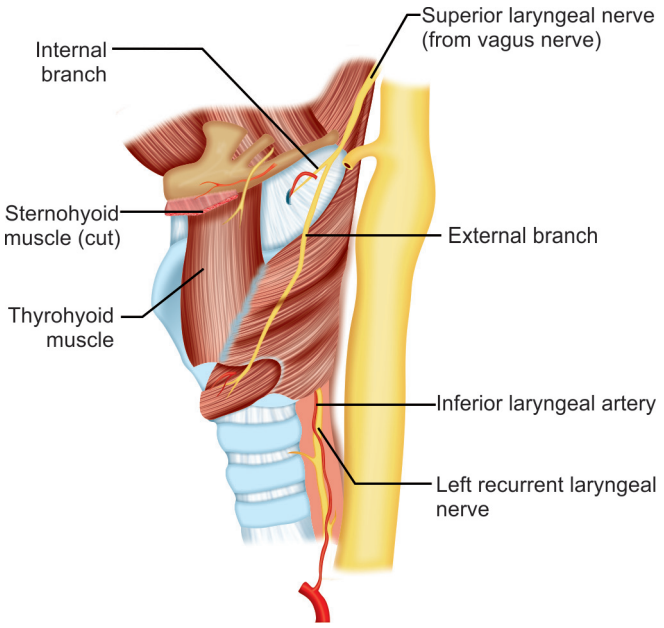



**Fig. 73.4:** Innervation of the larynx, lateral view. Adapted from Janfaza et al.[7]

inferior thyroid artery to enter the larynx behind the cricothyroid articulation (Fig. 73.4). The recurrent laryngeal nerve divides into anterior and posterior branches either before or after its entrance into the larynx. The anterior or adductor branch travels on the lateral aspect of the LCA and thyroarytenoid muscles to innervate these structures in addition to the vocalis and aryepiglottic muscles.[7] The posterior or abductor branch innervates the PCA muscle. Injury to the recurrent laryngeal nerve may result in vocal fold immobility. Permanent bilateral injury usually produces dyspnea, and frequently requires surgical intervention to establish an adequate airway. Finally, abundant sensory receptors supply the larynx and respond to airway pressure, airflow, vocal fold motion, and chemical stimuli, particularly in the mucosa of the supraglottis and posterior glottis.[8]

## Respiration and Phonation

The posterior glottis is the inferior portion of an air funnel that forces air past the posterior edge of the vocal folds. The rigid nature of the completely ringed cricoid cartilage controls airflow and forces expiration past the glottis. Importantly, it is the supraglottic interarytenoid tissue that collapses to close off the airway posteriorly, not the glottis. The posterior supraglottis collapses medially and also anteriorly towards the epiglottis, as these two structures connect through the aryepiglottic folds. Therefore, the two regions of the glottis perform different functions, with the posterior glottis important primarily for respiration and the anterior glottis for phonation.[4]

The sphincter function of the larynx protects the distal airways from aspiration. This occurs at three levels: glottis closure, adduction of the false vocal folds, and closure of the epiglottis to touch the posterior supraglottic structures.[7] These processes can be seen during coughing, swallowing, and laryngospasm. The cough reflex with the glottis functioning as a valve allows the forceful expulsion of air and provides ability to clear the lower respiratory tree. In a child with a laryngeal cleft, there can be incomplete closure of the larynx during swallowing or coughing, and aspiration can lead to recurrent pneumonias. Surgical repair is necessary if aspiration occurs secondary to the cleft.

The airflow from the trachea up through the larynx produces a wave within the pliable vocal folds that vibrates the vocal instrument. The wave moves from inferior to superior as the superficial lamina propria slides over the vocal ligament. Phonation is preceded by adduction of the vocal folds and an increase in activity of the intrinsic muscles. Changes in the vocalis muscles are likely responsible for variations in pitch.[7]

## Differences between Infant and Adult Larynges with Clinical Implications

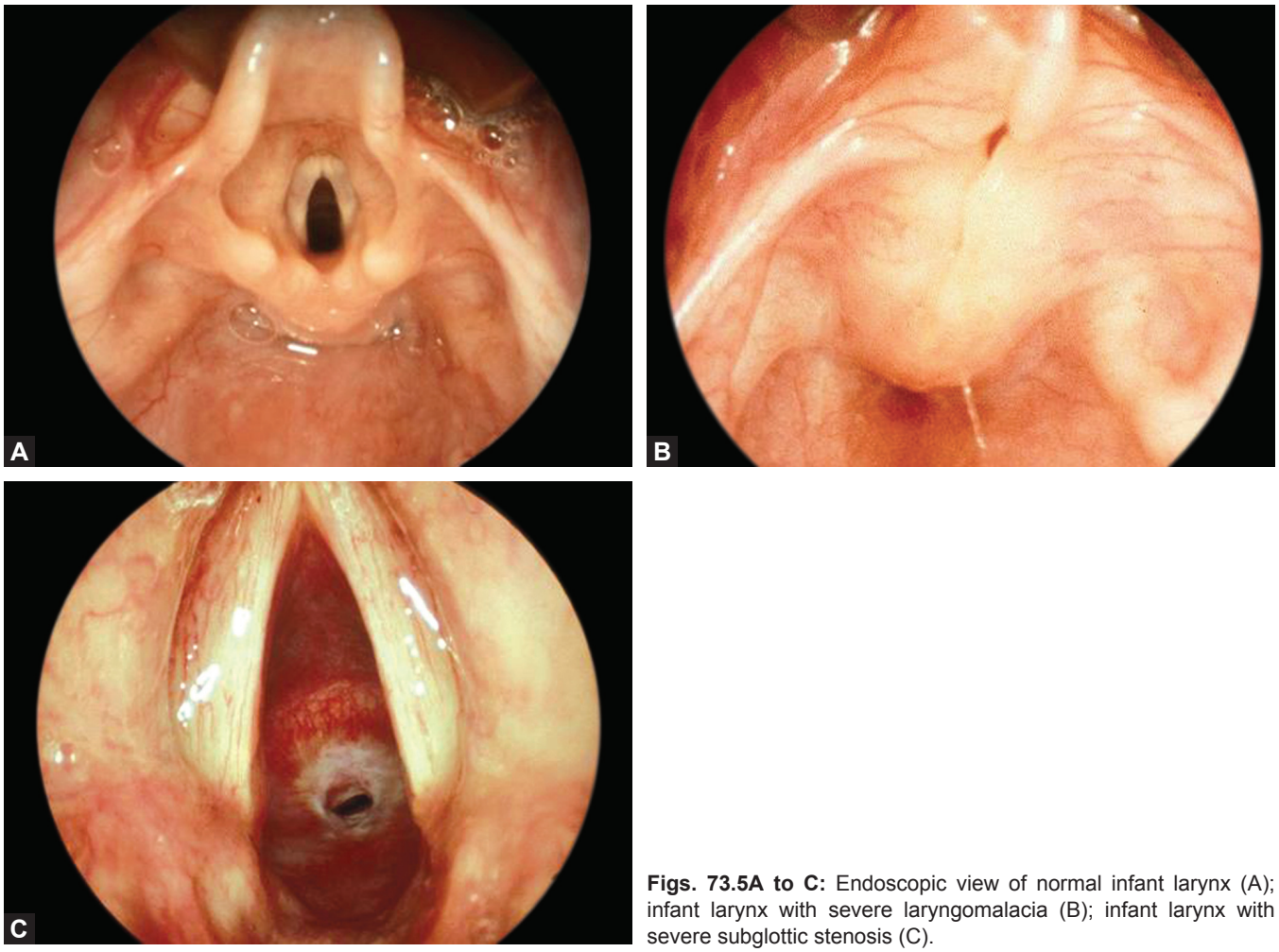
The infant larynx is located cephalad compared to its eventual descended position in the adult. The distance between the hyoid bone and thyroid cartilage significantly increases as this descent occurs, but during infancy, the epiglottis is near the soft palate, allowing for simultaneous sucking and breathing. This positioning decreases aspiration risk but also forces obligate nasal breathing. The infant cricoid is located at the fourth cervical vertebra (C4) and descends to C7 by adulthood.[2]

During puberty, changes occur in male larynges that differ from female larynges. At this time, the male larynx increases in size, and the thyroid cartilages project anteromedially. The anteroposterior diameter of the neck nearly doubles in size as well.[7] In a recent study of age-related changes, Seo et al. found that gender differences in the laryngeal volume become apparent after 14 years of age, and differences in tracheal volume occur earlier in the 8–13 age range.[10] For both sexes, there was significant laryngeal growth from ages 3 to 13.

Overall, the infant larynx is approximately one-third the size of the adult larynx. The membranous vocal folds are short, reaching 6–8 mm in length, whereas adult membranous vocal folds range in length from 12 to 18 mm. The vocal folds of the infant also differ from the adult in their ratio of membranous and cartilaginous portions. The infant vocal fold is one-half membranous and one-half cartilaginous, while the adult vocal fold is two-thirds membranous and one-third cartilaginous.[7] The infant epiglottis is omega-shaped compared to the more flattened appearance of the adult. This difference in the epiglottis combined with the increased pliability of the infant submucosal tissues leads to a greater decrease in airway caliber during inflammatory conditions and can explain the pathophysiology of supraglottic narrowing observed in laryngomalacia (Figs. 73.5A to C).[2]

The cricoid ring also enlarges relative to the glottis, leading to changes in airflow patterns. The infant subglottic larynx has a diameter of 5–7 mm, thus explaining how even a 1-mm decrease in diameter can cause significant subglottic stenosis and resultant respiratory distress. In comparison, the adult subglottic diameter is 25 mm in male adults and 18 mm in female adults.[7]

The small caliber of the infant subglottis makes this portion the narrowest area of the infant airway. In contrast, the glottic opening is the smallest area of the adult larynx. Therefore, the pediatric laryngeal airway is funnel shaped as it narrows inferiorly through the vocal folds into the subglottis, while the adult shape is more cylindrical due to the larger subglottic area.[5] A recent study has suggested a change in this classic description based on sizing the airways of anesthetized, paralyzed children. Dalal et al. measured the diameters at the glottic opening and the superior aspect of the cricoid and found that the glottis is the narrower point from infancy to adolescence.[11] The authors suggested that the pediatric laryngeal airway is more cylindrical than funnel-shaped, when the larynx is paralyzed. However, the vocal folds are distensible and mobile, and the findings do not appear applicable to spontaneously breathing children. The findings are relevant, though, to endotracheal tube sizing for intubation, as a tube that fits through the cricoid may still potentially cause trauma to the vocal folds.




**Figs. 73.5A to C:** Endoscopic view of normal infant larynx (A); infant larynx with severe laryngomalacia (B); infant larynx with severe subglottic stenosis (C).

## CONCLUSION

The primary functions of the larynx are respiration, feeding, and phonation. The larynx must allow airflow to the lungs while preventing aspiration, since there is no sphincter distal to the larynx in the tracheobronchial tree. Additionally, the larynx produces phonation through muscular modulation of the sound wave. Most of the laryngeal muscles contract to close the sphincter. It is the motion of the arytenoid cartilages that primarily change vocal fold position to allow creation of phonation. A thorough understanding of laryngeal embryology and anatomy allows for recognition and treatment of common pathologies, such as laryngomalacia and laryngeal stenosis.

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CHAPTER

# 74

# Development of the Human True Vocal Fold

***Derek J Rogers, Christopher J Hartnick***

## INTRODUCTION

Speech remains one of the most important factors resulting in our complexity as human beings. Human civilization and its advances depend on speech for communication and the verbal exchange of ideas. When we are born, our speech needs are quite limited; simply crying alerts our caregivers to our basic needs. As we age, our brain continues to develop, and we require more complex ways of communicating ideas. It makes sense that the human true vocal fold begins with a monolayered lamina propria and gradually develops three layers as we reach adolescence. The microanatomic structure mirrors its functional requirements.

The structure and function of the human larynx have been studied for millennia. As early as the fifth century BC, a clear understanding existed regarding the relationship between airflow and speech. Aristotle (circa 384-322) noted that the character of voice production relied on a mechanical interaction between the airstream and the structures enclosing the airstream. Using animal dissections of the airway, Galen (circa 131-201 AD) described the "membranous lips" of the vocal folds and the recurrent laryngeal nerve. He realized that a voice cannot be produced without a narrowing of the glottal passage.[1]

Of all the contributions over the past centuries providing meaningful insights in the structure and function of the human true vocal fold, French anatomist Ferrein (1693–1796) provided the most exhaustive work on the principles of voice production using both animal and human larynges.[2] He described the vocal fold as a vibrating string composed of several layers, and he was perhaps the first to delineate the layered structure of the vocal folds. Fournie, a French physician, wrote that the voice was a sound produced by a particular reed having modifiable walls under the influence of muscular action, with an overlying vibrating mucous fold. Fournie realized that the frequency varied depending on the stiffness of the folds.[3] Although great strides were made by these pioneers in understanding the structure and function of the true vocal folds, they lacked knowledge of how the microanatomy of the folds changes in response to external stresses.

## ADULT TRUE VOCAL FOLD COMPOSITION: COVER AND BODY DEFINITIONS

Hirano's seminal work in 1975 characterized the growth of the human vocal fold with time by examining developing larynges (Table 74.1).[4,5] Hirano focused on the histologic structure of the human vocal fold and described the laminar structure in detail. He divided the layers into a surface epithelial layer followed by a trilaminar lamina propria: superficial lamina propria (SLP), middle lamina propria (MLP), and deep lamina propria (DLP).[4,6,7] He described a "cover" consisting of the surface epithelium and SLP and a "body" composed of the DLP and vocalis muscle, with the MLP representing the "transition zone" (Fig. 74.1). One must remember that this characterization was merely an anatomic description and not based on functional considerations.

Multiple definitions of the cover and body concept have been subsequently developed (Table 74.2). Hammond et al. defined the cover as consisting of epithelium, the SLP, and most of the MLP.[8] The body is represented by the remainder of the MLP, the DLP, and the vocalis muscle.

**Table 74.1:** Hirano's characterization of the development of the human vocal fold in terms of length of the membranous fold (M), cartilaginous fold (C), and ratio of the two (M/C)

| *Age* | *Overall length of vocal fold (mm)* | *Membranous vocal fold (mm)* | *Cartilaginous vocal fold (mm)* | *M/C* |
|---|---|---|---|---|
| Newborn | 2.5–3.0 | 1.3–2.0 | 1.0–1.4 | 1.1–1.8 |
| Adult males | 17–21 | 14.5–18 | 2.5–3.5 | 4.7–6.2 |
| Adult females | 11–15 | 8.5–12 | 2.0–3.0 | 3.3–4.5 |

**Table 74.2:** Different definitions of the cover/body of the vocal fold lamina propria

| | *Cover* | *Body* | *Transition* |
|---|---|---|---|
| Hirano | Epithelium, SLP | Vocalis muscle | MLP, DLP |
| Titze | Epithelium, SLP, MLP | DLP, Vocalis muscle | |
| Hammond | Epithelium, SLP, MLP | MLP, DLP, Vocalis muscle | |
| Dikkers | Epithelium, SLP | Conus elasticus, Vocalis muscle | |

(SLP: Superficial layer of lamina propria; MLP: Middle layer of lamina propria; DLP: Deep layer of lamina propria).

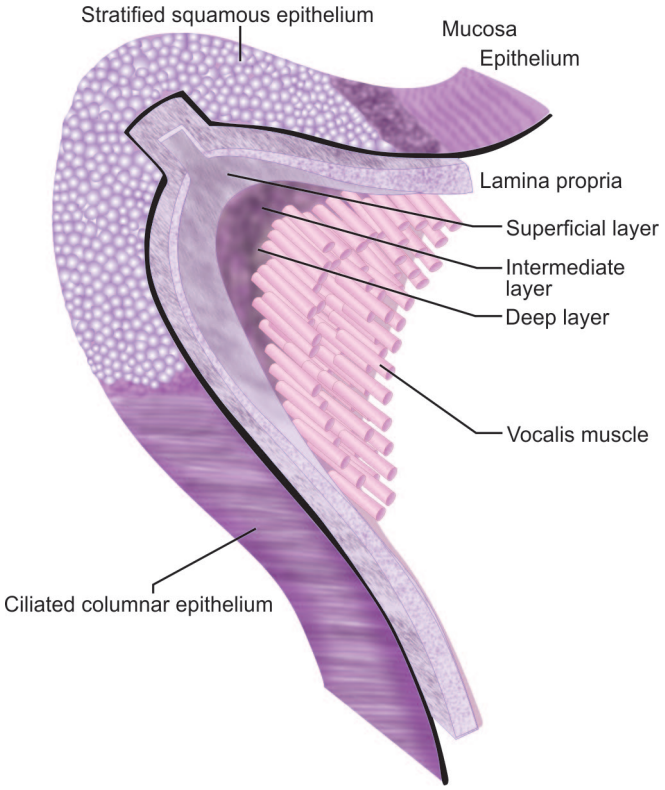



**Fig. 74.1:** Diagram of Hirano's layered structure of the human true vocal fold.
*Source:* Reproduced with permission from Hirano.[4]

Dikkers described the cover as the epithelium and the SLP and the body as the vocalis muscle and conus elasticus. He defined the conus elasticus as collagen, elastin fibers, the DLP, and the MLP.[9] Titze developed both a two-layered and three-layered system. In the three-layered system, the epithelium and the SLP comprise the mucosal layer, the MLP and DLP the ligament, and the thyroarytenoid the muscular layer. In the two-layered system, the body is defined as the DLP and vocalis muscle, and the cover is the epithelium, the SLP, and the MLP.[10] A lack of consensus regarding the definition of the cover and body of the human true vocal fold obviously still exists.

## PEDIATRIC TRUE VOCAL FOLD COMPOSITION

If the controversy regarding the layers of the adult true vocal fold were not enough, even less is understood about the microanatomy of pediatric true vocal folds. The true vocal fold begins with a single-layered lamina propria and begins to develop into an immature, multilayered system by about 7 years of age.[11,12] Although three layers are present in the preadolescent years, the mature, adult three-layered structure with elastin in the middle layer and collagen in the deep layer does not align parallel to the vocalis muscle until the teenage years. Exactly how this occurs and at what age each layer develops remain to be fully elucidated. Sato et al. hypothesized that maculae flavae located at both ends of the human true vocal fold mucosa are involved in the metabolism of extracellular matrices in the vocal fold mucosa and form the characteristic layered structure of the human vocal fold mucosa.[13] They also discovered an interstitial cell with a stellate appearance in the human maculae flavae located at both ends of the vocal fold mucosa, which constantly synthesized extracellular matrices essential for the vocal fold mucosa.[14–20] Sato et al. hypothesized that tensions caused by phonation after birth stimulate the stellate cells in the maculae flavae to accelerate production of extracellular matrices and form the vocal ligament, Reinke's space, and the layered structure.[21,22] The mucosae of young adult unphonated true vocal folds were found to be hypoplastic and

rudimentary with no vocal ligament or Reinke's space. A monolayered lamina propria with degenerated stellate cells demonstrating decreased production of extracellular matrices was seen.[13] Future studies will attempt to better characterize the composition of the different layers and quantify fibroblasts, myofibroblasts, histiocytes, and density of blood vessels.

## Fetal or Newborn True Vocal Fold

The epithelium of newborn true vocal folds appears to be similar to that of adults. Tucker et al. although noted that distinct ciliary patterns change over time.[23] When looking at the lamina propria itself, studies have shown a monolayered lamina propria with no vocal ligament (Fig. 74.2).[5,12,22] The regions at the anterior and posterior ends of the membranous vocal folds (maculae flavae) are believed to be involved in the production of hyaluronic acid and development of the vocal ligament.[21,24] The maculae flavae are composed of unique stellate cells, fibroblasts, ground substance, elastin fibers, reticular fibers, and collagen fibers.

## Infant True Vocal Fold

Cellular differentiation and movement toward a bilaminar lamina propria occurs by 2 months of age (Fig. 74.3).[12] The superficial layer is hypocellular, and the more cellular deeper layer contains plumper cells that those seen in the first few days of life. No traceable mucin is found in the superficial layer but mucin is seen in the deeper layer. The amount of mucin in this deeper layer is less than that found in the newborn true vocal folds. A three-layered structure began to appear by 11 months of age in 20% of the specimens in one study.[12] Immediately beneath the epithelium exists a superficial hypocellular layer followed by a deeper, more cellular layer. Also, a deeper, less cellular layer above the vocalis muscle appears.

## Child True Vocal Fold

An immature, multilayered lamina propria structure develops by about 7 years of age (Fig. 74.4).[12] The superficial layer remains hypocellular. The middle layer becomes denser with almost two distinct regions: a superficial layer exists with greater cellularity and a deeper layer with greater collagen and elastin deposition. The deep layer of the lamina propria is less cellular. Of note, the vocal ligament itself has not developed by this age. The size of the SLP begins to approximate that of the adult SLP by 7 years of age.[11]

## Adolescent True Vocal Fold

By early adolescence, or approximately 11–12 years of age, maturation has likely occurred with fiber deposition (Fig. 74.5).[12] The classic pattern of a hypocellular superficial layer followed by a middle layer of mostly elastin fibers and a deeper layer of mostly collagen fibers develops. The deep fibrillar structure is oriented so that the fibers are parallel to the direction of the deeper vocalis muscle fibers. This pattern continues through at least 17 years of age and possibly remains through adulthood. Ishii et al. also confirmed a three-layered lamina propria by 17 years of age by performing electron microscopy on pediatric cadaveric larynges.[25]

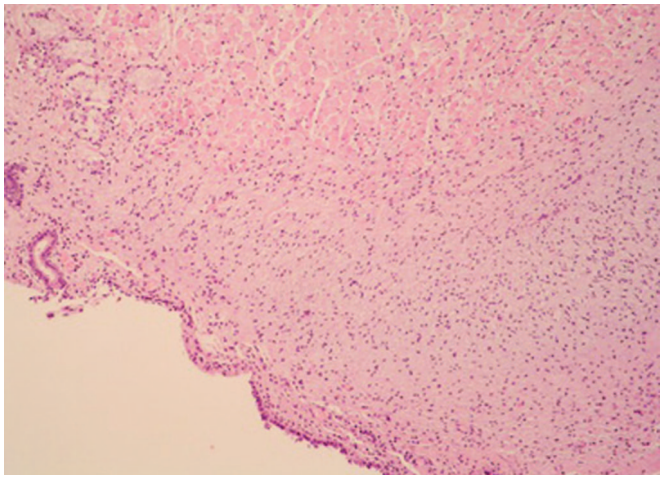


**Fig. 74.2:** Hematoxylin and eosin stain of a true vocal fold from a 2-day-old neonate showing a cellular monolayer with no vocal ligament.
*Source:* Reproduced with permission from Hartnick et al.[12]

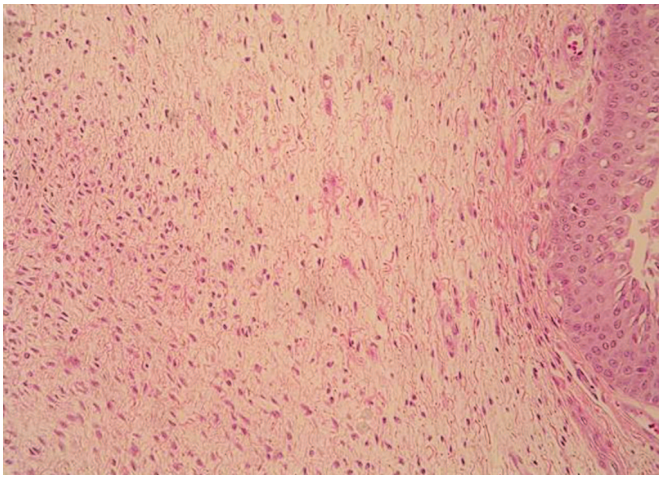


**Fig. 74.3:** Hematoxylin and eosin stain of a true vocal fold from a 2-month-old infant showing a bilaminar structure with two cell densities.

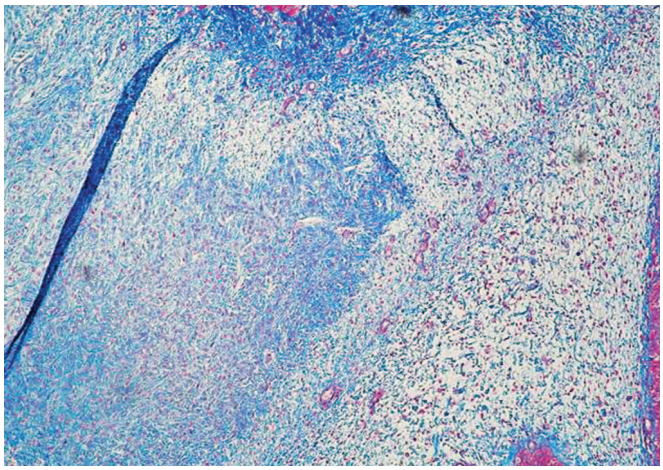


**Fig. 74.4:** Alcian blue stain of a true vocal fold from a 7-year-old child showing an immature, trilaminar structure.

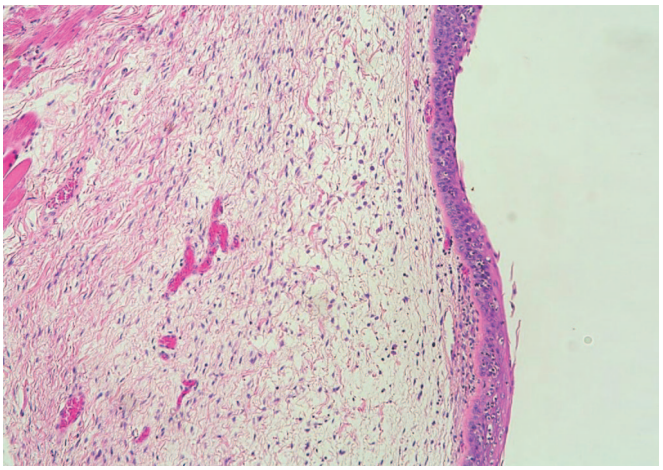


**Fig. 74.5:** Hematoxylin-eosin stain of a true vocal fold from a 13-year-old adolescent showing a fully trilaminar structure with dual fiber composition of collagen and elastin.
*Source:* Reproduced with permission from Hartnick et al.[12]

## STRESS THEORY

The process by which the lamina propria becomes layered is not well understood. Cell signaling and selective apoptosis likely convert the monolayered lamina into three layers as the mechanical tasks required of the true vocal folds increase in complexity over time. This process of development was described according to what was seen in the lamina propria of adult true vocal folds.[4,6] Perhaps the stellate cells discovered in the maculae flavae by Sato et al. serve an important role.[16,20] The characteristics required to distinguish between the various layers included elastin and collagen fiber deposition and direction with respect to the direction of the vocalis muscle fibers. Elastin stains have thus been used to distinguish between the MLP and DLP.

The vascular surgery literature delineates how different mechanical properties (stress/strain patterns) of elastin and collagen allow for appropriate functioning within a given environment.[26,27] Several studies have investigated these stress/strain patterns according to protein fiber concentration to explain how the mechanical functions of the true vocal fold can be explained histologically.[26–28] Collagen fibers have been shown to align their orientation to withstand longitudinal stress from vocal fold oscillation.[22,29] The maximum bending stresses occur at the maculae flavae, where the stellate cells reside.[30] The vascular surgery literature explains how vascular flow causes physical structures to adapt by producing varying mechanical forces. The mechanical dynamics of airflow through the glottis may be similar to the vascular model. In the lamina propria, perhaps mechanical stress patterns triggered by environmental stimuli produce regions of selective apoptosis similar to vascular smooth muscle cells.[31]

Describing the development of the pediatric true vocal fold in terms of a layered cellular composition rather than a fiber makes it more difficult to define when the vocal ligament and mature cover/body develop. If the vocal ligament is defined by the adult definition consisting of a combination of middle and deep layers with an organized distribution and orientation of elastin and collagen fiber deposition[4], then this full maturation is not seen until adolescence. Even in adolescents both elastin and collagen fibers can be seen interspersed throughout both the middle and deep layers. However, when looking at cell population and density, a clear demarcation exists between the MLP and DLP by 7 years of age. Ideally, biomolecular markers of proliferation and apoptosis could be used to better quantify this description of cellular distribution. Perhaps a more functional description of the layered structure of the human vocal fold correlating to the histologic structures and changes in mechanical properties seen will arise as the functional demands of the developing larynx are better understood.

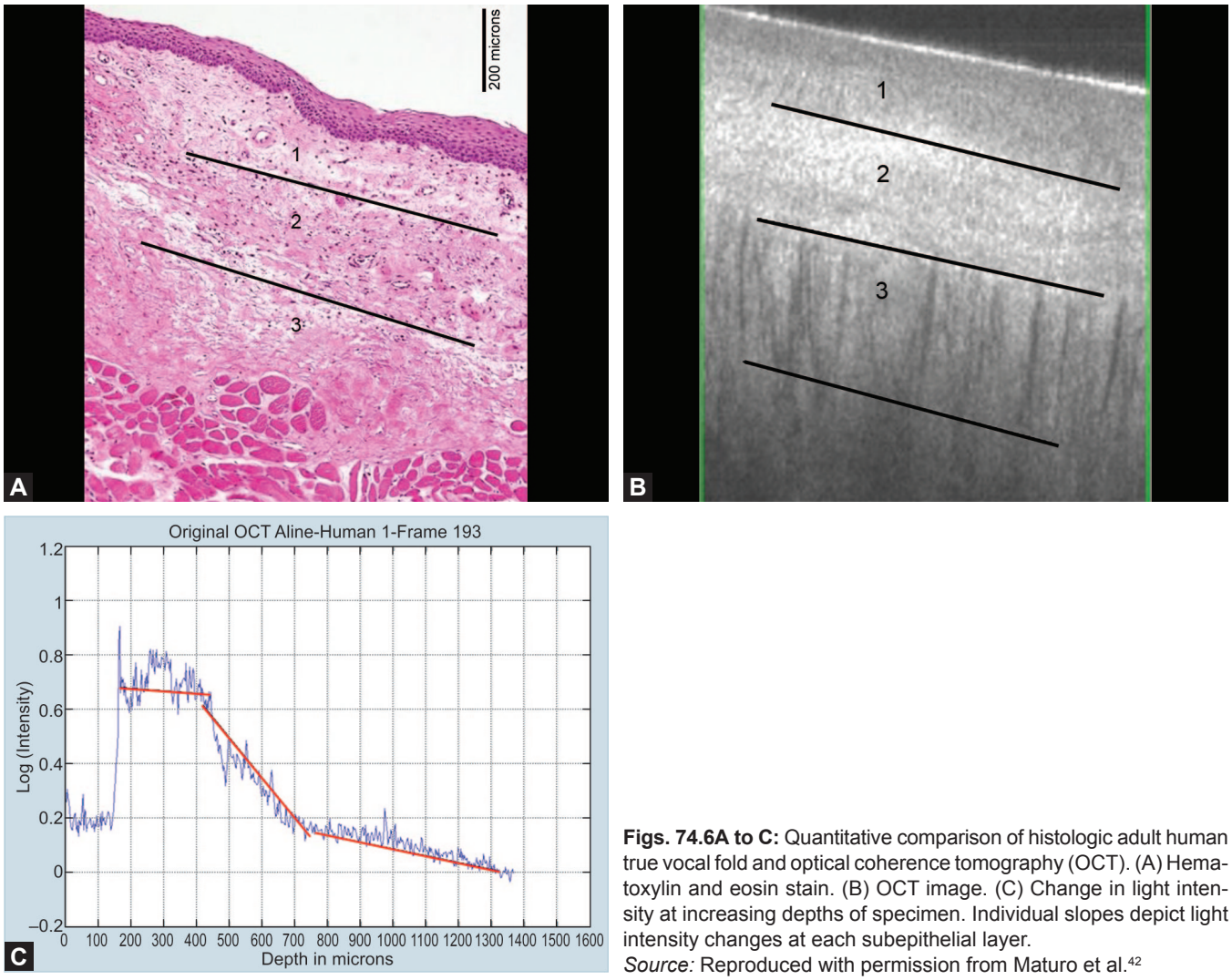
## BIOCHEMICAL EVIDENCE

Some preliminary work has been done to investigate endocrine involvement in the true vocal folds. Newman et al. found that different amounts of progesterone receptors are seen in the nucleus and cytoplasm of cells in the vocal fold depending on age and gender.[32] In contrast to this study, Voelter et al. noted no progesterone receptors in the human vocal fold and instead found mostly androgen receptors concentrated in the basal and intermediate layer of the stratified epithelium and the lamina propria.[33]

Scheider et al. could not definitively identify any steroid hormone receptors in the true vocal folds they studied.[34] Others have looked at the role that growth factors such as hepatocyte growth factor, transforming growth factor B1, epidermal growth factor, and basic fibroblast growth factor play in wound healing and development of scar within the lamina propria.[35,36] Future studies are needed to determine how hormones and growth factors influence the earlier process of development and maturation.

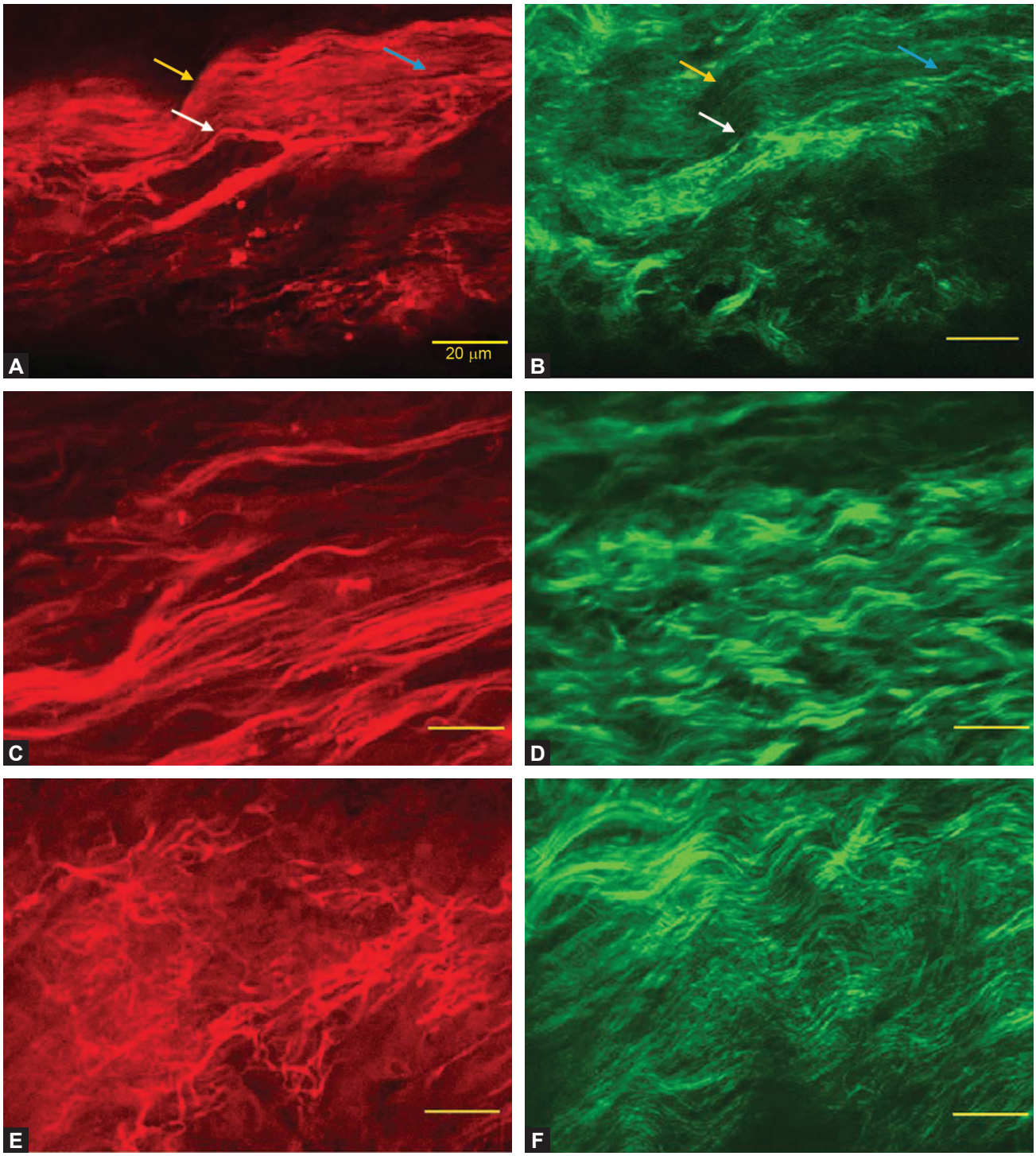
## EMERGING TECHNOLOGIES

To enable a better understanding of pediatric voice development and the microanatomy of the vocal fold, several noninvasive microscopic imaging techniques are being investigated.[37] A few of the optical microscopy technologies that have been developed for in vivo use include optical coherence tomography (OCT), such as optical frequency domain imaging, full-field optical coherence microscopy, and endoscopic spectrally encoded confocal microscopy. Optical coherence tomography uses interferometric technology to provide cross-sectional images of backscattered light[38] and has been implemented in ophthalmology, gastroenterology, cardiology, and dermatology. Each modality has its own imaging capabilities regarding field of view, depth of penetration, image acquisition, speed, and resolution. Optical coherence tomography is capable of obtaining high-resolution microanatomy images of pediatric airway in vivo tissue[39] and may distinguish benign from malignant lesions in vivo without biopsy.[40,41] Maturo et al. demonstrated the ability of OCT to distinguish separate layers of the lamina propria ex vivo by presenting a quantitative comparison of OCT and histologic findings (Figs. 74.6A to C).[42] The next step is to implement a quantitatively proven OCT probe for in vivo use to image pediatric true vocal folds.




**Figs. 74.6A to C:** Quantitative comparison of histologic adult human true vocal fold and optical coherence tomography (OCT). (A) Hematoxylin and eosin stain. (B) OCT image. (C) Change in light intensity at increasing depths of specimen. Individual slopes depict light intensity changes at each subepithelial layer.
*Source:* Reproduced with permission from Maturo et al.[42]

Two other potential imaging modalities for true vocal folds include nonlinear laser scanning microscopy (NLSM) and ultrasound with B-mode and Nakagami imaging. Miri et al. showed the capability of NLSM to image the extracellular macromolecules in human vocal fold lamina propria (Figs. 74.7A to F).[43] The NLSM images depicted the




**Figs. 74.7A to F:** Typical images of the human true vocal fold lamina propria using nonlinear laser scanning microscopy (NLSM). The left (red) images correspond to two-photon fluorescence (TPF) and the right (green) second harmonic generation (SHG). The bright arrows depict where the elastin fibers are colocalized within the collagen network.
*Source:* Reproduced with permission from Miri et al.[43]

helical shape of the collagen network and the basket-like structure of the elastin network. Ultrasound with B-mode imaging is gaining popularity to identify masses, lesions, nodules, and even paralysis of the true vocal folds. Tsui et al. combined B-mode imaging with Nakagami imaging, a new parametric imaging method, and were able to visualize relative concentrations of collagen and elastic fibers in the lamina propria.[44] An advantage of ultrasound is that it may be easily used while the patient is awake by placing the probe directly on the neck.

## FUTURE DIRECTIONS

A larger library of pediatric cadaveric larynges taking into account various ethnicities and linguistic backgrounds is needed to further characterize the development of the human true vocal fold. Continued study of molecular pathways will hopefully uncover the cell signaling that promotes this cellular differentiation and maturation. Once quantitative methods of describing this maturation process are developed, these methods can be used to better delineate the adult vocal fold. Pediatric laryngology depends on the understanding of adult vocal fold structure. We still do not know whether there are two or three layers biologically and functionally. Once this is known, mathematical models will be established to describe mechanical function using the histologic and molecular data available. Most surgeries of the true vocal fold rely on the presence of the SLP to dissect with minimal scar formation; it is still unknown exactly when this layer develops. If the maturation process of the pediatric vocal fold is better understood, diagnostic and therapeutic modalities should improve.

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CHAPTER

# Voice Evaluation from the Otolaryngologist's Perspective

75

***Paolo Campisi***

## INTRODUCTION

Children commonly present with voice complaints to otolaryngologists in both community and academic health centers. In fact, the prevalence of voice disorders in children is significant, ranging from 6% to 9%.[1] The spectrum of voice pathologies in children is wide, and the otolaryngologist should anticipate a wide variety of diagnoses that are less common than vocal fold nodules. In academic centers with active cardiac surgery services, for example, unilateral vocal fold insufficiency is frequently encountered.

Otolaryngologists interested in developing a pediatric laryngology practice will need to enhance their knowledge of laryngeal physiology and pathology in children, acquire equipment and technical skills that facilitate the examination of young patients, and assemble a team of individuals that has a similar strong interest in pediatric voice disorders. These requirements are essential as the assessment of a child is more challenging than in adults. Children may be more apprehensive and have a very limited tolerance of laryngeal imaging with endoscopy.

It is strongly recommended, therefore, that the otolaryngologist develop and use a standardized assessment protocol that is multidimensional, child appropriate, and time efficient. The protocol must include a thorough intake history, a general head and neck examination, subjective and objective assessments of voice quality and impact of the voice disorder, and laryngeal imaging with endoscopy. Furthermore, the assessment measures should be reproducible and obtained with tools that are widely accepted by colleagues. This will allow for meaningful clinical outcomes research and multicenter collaborations that will ultimately translate into improved, evidence-based clinical care.

## THE CLINIC

The pediatric voice clinic should be spacious to accommodate a proper examination chair, endoscopy tower, computer(s) for subjective and objective voice analyses, and cabinetry to secure endoscopy equipment, supplies, and charts. It is also recommended that anatomical and pathological illustrations be displayed on the wall that are helpful with explanations during the patient and family debrief at the end of the clinic visit. A poster describing the clinic protocol is also helpful if it includes photos of children participating in the various steps of the protocol. An example of a voice clinic layout is demonstrated in Figures 75.1 and 75.2.

## BUILDING A TEAM

The modern day pediatric voice clinic requires an otolaryngologist with a strong interest in pediatric laryngology, who serves as the clinical lead in the clinic and is responsible for establishing a diagnosis and prescribing treatment. The otolaryngologist collaborates with one or more Speech-Language Pathologists. This is clearly the most important interprofessional relationship in the voice clinic. In some centers, the Speech-Language Pathologist may be performing the flexible and rigid endoscopies in children

**Fig. 75.1:** Voice clinic layout showing the examination chair, laryngostroboscopy unit, and anatomical and pathology illustrations on the back wall.

**Fig. 75.2:** Voice clinic layout showing the laryngostroboscopy unit and Computerized Speech Laboratory unit (KayPentax Inc., Lincoln Park, NJ). A poster outlining the assessment protocol is prominently displayed on the back wall.

for review with the otolaryngologist at a later time. Clinic nurses with experience in pediatric endoscopy are also essential.

The voice clinic team must maintain their training and knowledge of new technologies by attending and participating in conferences and continuing medical education courses. It is the responsibility of the otolaryngologist to support and encourage the team to improve their skills to enhance the experience of patients and families attending the voice clinic.

In addition to the core members of the voice clinic, a network of community Speech-Language Pathologists should be developed to distribute the voice therapy workload and, more importantly, to ensure a high level of care provided in those outpatient environments. On occasion, patients may also require consultation with other medical disciplines, such as neurology, neurosurgery, cardiology, gastroenterology, psychiatry, and others. Communication and coordination of these medical consultations are the responsibility of the attending otolaryngologist.

## TIME MANAGEMENT

The thorough assessment of a child with a voice disorder may require a minimum of 30–60 min, depending on the age of the child and the nature of the presenting voice problem. The majority of the appointment time is invested in building patient rapport and the completion of the subjective and objective voice analyses by the attending Speech-Language Pathologist. In most instances, the otolaryngologist does not need to be present for this component of the assessment. During this time, the otolaryngologist may attend to an adjacent general pediatric otolaryngology clinic to optimize time management and overall clinic efficiency. Once the initial assessment is complete, the otolaryngologist will have the necessary data to review the history and characteristics of the voice disorder with the patient and Speech-Language Pathologist efficiently and determine the laryngeal imaging modality best suited for the patient. Once the laryngeal images are obtained, the salient features of the recording may be reviewed with the patient, caregiver, and Speech-Language Pathologist to develop a management plan. If the most appropriate treatment is voice therapy, the otolaryngologist may excuse himself or herself from the full length of the debrief between patient and Speech-Language Pathologist and attend to other patients in the adjacent general pediatric otolaryngology clinic.

## ASSESSMENT PROTOCOL

Although there are no established pediatric-specific assessment protocols, most centers with pediatric voice clinics apply protocols that are derived from guidelines developed for adult patient care. For example, the voice clinic of the Royal Hospital for Sick Children in Glasgow, United Kingdom, has suggested that the recommendations of the European Laryngological Society be adopted for children.[2,3] In addition to a voice history and otolaryngological examination, the following assessments should be routinely obtained: "perceptual evaluation of voice, videostroboscopic imaging of vocal fold movement, acoustic

analysis of specific voicing aspects, aerodynamic support for voicing, and a subjective rating of voice impact". Similar suggestions have been made in North America.[4,5]

The protocol described below is consistent with the above suggestions and is currently employed at the Centre for Paediatric Voice and Laryngeal Function at the Hospital for Sick Children, University of Toronto.

## History

A thorough history will provide the otolaryngologist with valuable insight regarding factors that predispose and contribute to the child's voice disorder and the degree to which the symptoms impact the child. Obtaining a systematic and detailed history is very time consuming, potentially onerous, and may be limited by the caregiver's recall if requested at the time of the initial visit. To avoid this problem, the parents of referred patients are mailed a detailed questionnaire for completion prior to the scheduled clinic appointment. The questionnaire (*see* Appendix A) is organized in sections that include demographics, family history, education and social history, history of the voice problem, voice use history, medical history, and developmental history with an emphasis on speech and language development. This approach allows for the efficient gathering of a large amount of information and provides the caregiver ample opportunity to reflect on the voice problem and recall accurate historical data.

Prior to the clinic appointment, the completed questionnaire is reviewed by the Speech-Language Pathologist to ensure that the referral is appropriate for the voice clinic. The aim is to identify and redirect referrals for dysphagia, hyponasality due to adenotonsillar hypertrophy, hypernasality due to velopharyngeal insufficiency, and speech/language problems to the appropriate clinic. The identification of inappropriate referrals saves valuable clinic time and avoids frustration for caregivers.

## Physical Examination

A directed physical examination of the head and neck is an essential component of the otolaryngologist's assessment of children with voice disorders. There are several physical findings that may have a direct or indirect effect on voice production. The presence of bilateral middle ear effusions with longstanding conductive hearing loss or sensorineural hearing loss, for example, disrupts auditory feedback that is essential for control of pitch and loudness of voice. Palate abnormalities, such as a submucous cleft palate or palatal weakness due to a brainstem lesion, will result in hypernasality. In contrast, adenotonsillar hypertrophy or nasal obstruction will result is hyponasality. The abnormal resonance may be perceived by the patient or caregiver as a voice disorder. Neck masses, especially thyroid tumors, may impinge or invade the recurrent laryngeal nerve resulting in vocal fold insufficiency. Dysfunction of multiple cranial nerves is a worrisome finding as it suggests the presence of a primary neurological disorder or a brainstem lesion. Finally, facial dysmorphisms may be indicative of an underlying genetic syndrome associated with laryngeal abnormalities.

## Perceptual and Objective Voice Assessments

With experience, an otolaryngologist may acquire the skill to distinguish voice disorders from speech disorders, such as problems with resonance, articulation, fluency and oro-motor control. Once a voice disorder is identified, the otolaryngologist should also be able to further perceive the difference between a problem with pitch, loudness, and quality of phonation. Although the formal perceptual assessment of voice is performed by the Speech-Language Pathologist, a basic knowledge of the types of voice and speech disorders affecting children should be understood by the attending otolaryngologist. The otolaryngologist must also be familiar with commonly used perceptual rating scales such as the GRBAS (grade, roughness, breathiness, asthenia, strain) and CAPE-V (consensus auditory-perceptual evaluation of voice) assessment tools.

Objective voice assessments are derived from commercially available computerized hardware and software packages. They are useful to monitor specific voicing parameters such as fundamental frequency, frequency and amplitude control, and noise to signal ratio. The acoustic assessments are based on sustained phonations and can be used to monitor changes in voice over time or following treatment. At the Centre for Paediatric Voice and Laryngeal Function, objective voice assessments are performed with the Computerized Speech Laboratory and Multi-Dimensional Voice Program (KayPentax Inc., Lincoln Park, New Jersey). There are several other commercially available systems.

The perceptual and objective assessment tools must be clinically relevant, have high inter- and intrarater reliability, and be easy to use with young children. Although there is considerable variability of tools used, pediatric

voice clinics must strive for standardization of measures across academic centers as this is required for meaningful assessment of voice outcomes after treatment and clinical research. More detailed information regarding voice assessments is available in the chapter "Voice Evaluation from the Speech and Language Pathologist's Perspective".

## Endoscopy in Children

There are several challenges encountered when performing endoscopy in children. Children are commonly apprehensive and may be outright uncooperative. They have a strong gag reflex and usually do not tolerate long periods of examination. However, an unrushed and gentle approach improves the probability of obtaining a useful examination of the larynx in the voice clinic. Investing the time to explain the process, demystifying the equipment and rehearse the procedure will further alleviate any apprehension. Nonetheless, there will be instances where examination of the larynx is not possible in the clinic and examination under anesthesia is required.

It has been demonstrated in the literature that pediatric endoscopy can be successfully performed in the majority of children assessed in a voice clinic setting. In 2005, Hartnick and Zeitels successfully examined 25 children aged 19 months to 13 years with trans-nasal flexible laryngostroboscopy.[6] In the same year, Wolf and colleagues successfully performed rigid laryngostroboscopy in 31 of 42 children.[7] Seven of the children were under 10 years of age. A short phonation time and strong gag reflex were the most common causes of failure to complete the rigid laryngostroboscopy. In 2010, Mortensen and colleagues retrospectively reviewed their experience with 80 pediatric patients aged 3–17 years.[8] Successful examinations were performed in 50 patients with rigid laryngostroboscopy and in a further 28 patients with flexible laryngostroboscopy. The remaining 2 patients did not tolerate either procedure. In general, older patients were more likely to tolerate rigid endoscopy. Mackiewicz-Nartowicz and colleagues reported their experience with laryngostroboscopy in 150 consecutively examined children.[9] All children aged 2.5–6 years and some children aged 6–10 years were premedicated with 3.5 mg of midazolam prior to rigid laryngostroboscopy. All but one child was successfully examined. However, the duration of the examinations was very short in the younger patients limiting the utility of the examination to the exclusion of organic lesions only. In these instances, assessment of vocal fold vibration was not possible, which questions the value of stroboscopy in very young children.

## Endoscopy Equipment

Advances in the quality of fiberoptic endoscopes and the development of very small diameter flexible videoscopes ("chip on the tip") have greatly improved the quality of laryngostroboscopic assessments in very young patients who do not tolerate rigid endoscopic procedures. Further improvements in lighting sources and high definition cameras has rendered stroboscopy useful in almost all patients. It should be noted that videoscopes require the use of digital processors that are very costly.

Small rigid endoscopes with excellent optics are also available for use in children ranging in size from 4 to 9 mm in diameter. The smaller diameter rigid endoscopes provide excellent resolution and are surprisingly well tolerated by young children. The smaller size minimizes contact with the tonsils and palate, and this is helpful in children with strong gag reflexes. The technical specifications of flexible and rigid endoscopes appropriately sized for children and commercially available are listed in Table 75.1.

An endoscopy tower with a software package designed to acquire and archive endoscopic assessments is an absolute requirement. In children, many of the recordings are brief and the ability to pause and review in slow motion or "frame by frame" is indispensable. The ability to rapidly recall previous recordings is helpful to monitor patient progress and for providing explanations to the patient and caregiver.

# CONCLUSION

Pediatric laryngology has evolved over time into a bona fide subspecialty of pediatric otolaryngology. The assessment and management of children with voice disorders requires a team of individuals dedicated to improving their technical skills and the development of standardized assessment protocols that are widely accepted by otolaryngologists, Speech-Language Pathologists, and patients. As consensus is achieved with respect to clinical outcome measures, clinical research and multisite collaborations will be facilitated, resulting in more effective treatments that are based on evidence.

**Table 75.1:** Technical specifications of flexible and rigid laryngoscopes appropriately sized for use in children

| *Product* | *Manufacturer* | *Imaging modality* | *Distal end diameter* | *Field of View* | *Angulation range* |
|---|---|---|---|---|---|
| *Flexible endoscopes* | | | | | |
| ENF-XP | Olympus | Fiberscope | 2.2 mm | 75° | 130° ↑↓ |
| ENF-V2[†] | Olympus | Videoscope | 3.2 mm | 90° | 130° ↑↓ |
| FNL-7RP3 | KAYPENTAX | Fiberscope | 2.4 mm | 75° | 130° ↑↑ |
| VNL-1070STK[‡] | KAYPENTAX | Videoscope | 3.1 mm | 85° | 130° ↑↓ |
| *Rigid endoscopes* | | | | | |
| 8700 CKA[*] | Karl Storz | Hopkins telescope | 5.8 mm | 50° | 70° |
| 9108 | KAYPENTAX | Hopkins telescope | 6 mm | 35° | 70° |

[†]Requires video processor EVIS EXERA II, VISERA or OTV-SI.
[‡]Requires video processor EPK-1000.
[*]Suggest using with locking handle model 8700H.

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# APPENDIX A

THE HOSPITAL
FOR SICK CHILDREN

Departments of Otolaryngology and Communication Disorders
Voice Clinic
Room 6171, 6th Floor, Elm Street Wing
555 University Avenue
Toronto, ON M5G 1X8
Tel: (416) 813-2192
Fax: (416) 813-5036

**PARENT QUESTIONNAIRE**

***Dear Parent: Please complete this form to your best knowledge. The information you provide will assist us with our voice evaluation. Bring the completed form to your clinic appointment.***

**Date:** _____

**Completed By:** _____

***Section A: Patient Information***

Name: _____ Date of Birth: _____ Sex: ☐ Male ☐ Female Height ___ Weight: ___

Address: _____ Telephone: _____

Language(s) spoken in the home: ☐ English ☐ Other _____

Pediatrician: _____ Referred by: _____

***Section B : Family History***

Does you child have any siblings? ☐ No ☐ Yes ☐

If Yes, are they brothers? ☐ No ☐ Yes Are they older or younger? ☐ Older ☐ Younger

Do they have any Health or Speech/Language Difficulties ☐ No ☐ Yes Describe:_____

Does your child have any sisters? ☐ No ☐ Yes Are they older or younger? ☐ Older ☐ Younger

Do they have any Health or Speech/Language Difficulties ☐ No ☐ Yes Describe: _____

Is there a history of speech, language, or voice problems in your family (including parents, aunts, uncles, etc). ☐ No ☐ Yes

Describe: _____

Does your child's voice sound like anyone else's in you family? ☐ No ☐ Yes Describe: _____

***Section C: Education and Social History***

**Preschool Child**

Where does your child spend most of the day? ☐ At home ☐ daycare/ nursery ☐ babysitter/nanny ☐ Other _____

**School-Aged Child**

Name of School: _____ Grade: _____

Address: _____ Teacher: _____

What type of program is your child in?

☐ Half-day program ☐ Full-day program ☐ Regular class placement ☐ Special class placement

☐ Receiving any remedial help ☐ Other (Describe:)_____

Describe your child's school performance: ☐ Excellent ☐ Good ☐ Fair ☐ Poor

Is your child teased because of his/her voice difficulties? No ☐ Yes ☐

***Section D: History Of The Voice Problem***

1. Describe your child's voice problem. (Fill in all that apply.)
   - ☐ Hoarseness
   - ☐ Breathiness
   - ☐ Poor volume
   - ☐ Loss of voice
   - ☐ Voice breaks or cracks
   - ☐ Other _____

2. Does your child have any of the following problems? (Fill in all that apply)
   - ☐ Throat pain
   - ☐ Throat dryness
   - ☐ Shortness of breath
   - ☐ Swallowing
   - ☐ Choking
   - ☐ Noisy breathing

3. Did your child's voice problem begin during or after any of the following events? (Fill in all which may apply.)
   - ☐ Birth
   - ☐ Voice strain or abuse
   - ☐ Illness
   - ☐ Intubation
   - ☐ Exercise
   - ☐ Stressful Event
   - ☐ Surgery
   - ☐ Hospitalization
   - ☐ Puberty
   - ☐ Accident/Injury
   - ☐ Tracheotomy
   - ☐ Exposure to toxins/smoke
   - ☐ Other _____

4. Describe your child's voice problem.
   (a) How did your child's voice problem begin? ☐ suddenly ☐ gradually
   (b) How is it changing? ☐ Better ☐ Worse ☐ Staying the same
   (c) Is your child's problem constant or does it vary? ☐ Constant ☐ Varies
   (d) If it varies, what is it dependent on? ☐ Time of day ☐ Season ☐ Activity ☐ Health status

5. Has your child been previously evaluated or treated by any of the following?
   (a) Ear, Nose and Throat Physician ☐ No ☐ Yes, describe _____
   (b) Speech-Language Pathologist ☐ No ☐ Yes, describe _____

6. Has your child ever received formal voice training (e.g. singing/vocal lessons) ☐ No ☐ Yes, describe _____

***Section E: Voice Use History***

***Below is a list of behaviors that sometimes influence voice quality. Please check how often you observe these behaviors in your child.***

| | Occasionally | Frequently | Most/all of the time | | Occasionally | Frequently | Most/all of the time |
|---|---|---|---|---|---|---|---|
| Coughing, croup | ☐ | ☐ | ☐ | Throat clearing | ☐ | ☐ | ☐ |
| Crying | ☐ | ☐ | ☐ | Whistling | ☐ | ☐ | ☐ |
| "Funny voices", impersonations | ☐ | ☐ | ☐ | Yelling, shouting | ☐ | ☐ | ☐ |
| Loud talking | ☐ | ☐ | ☐ | Caffeine consumption | ☐ | ☐ | ☐ |
| "Non-stop" talking | ☐ | ☐ | ☐ | Use of inhalers | ☐ | ☐ | ☐ |
| Singing | ☐ | ☐ | ☐ | Mouth breathing | ☐ | ☐ | ☐ |
| Acting, performances | ☐ | ☐ | ☐ | Smoking | ☐ | ☐ | ☐ |

***Section F : Medical History***

1. Has your child ever had any of the following? (Fill in all that apply.)

☐ Asthma
☐ Sinusitis
☐ Postnasal drip
☐ Frequent colds or throat infections
☐ Dry/sore throat
☐ Respiratory problems (e.g., wheezing)
☐ Neurological problems
☐ Head injuries
☐ Seizures
☐ Nasal Regurgitation
☐ Reflux/"heartburn"
☐ Weight loss
☐ Anorexia and/or bulimia
☐ Vomiting
☐ Heart problems
☐ Endocrine problems
☐ Exposure to toxins, chemicals
☐ Exposure to cigarette smoke
☐ Pain in ear
☐ Jaw joint problems
☐ Thyroid problems
☐ Tics/involuntary movements
☐ Feelings of depression/sadness
☐ Lethargy or fatigue
☐ Stress-related problems
☐ Other _____
_____

2. Has your child ever had surgery? (Fill in all those that apply.)

☐ Cardiac surgery
☐ Brain surgery
☐ Bronchoscopy
☐ Tracheostomy
☐ Other head and neck surgery
☐ Thyroid surgery
☐ Laryngoscopy
☐ Esophageal surgery
☐ Adenoidectomy

3. Has your child ever had any of the following tests?
   (a) Hearing test? ☐ No ☐ Yes If yes, describe _____
   (b) Swallowing assessment? ☐ No ☐ Yes If yes, describe_____
   (c) Gastrointestinal evaluation? ☐ No ☐ Yes If yes, describe_____
   (d) Allergy test? ☐ No ☐ Yes If yes, describe_____
   (e) Neurological examination? ☐ No ☐ Yes If yes, describe_____
   (f) Psychological or psychoeducational assessment? ☐ No ☐ Yes If yes, describe_____
   (g) Genetics test? ☐ No ☐ Yes If yes, describe_____
4. Does your child have any of the following?
   (a) Drug allergies ☐ No ☐ Yes If yes, describe_____
   (b) Environmental allergies ☐ No ☐ Yes If yes, describe_____
   (c) Food allergies ☐ No ☐ Yes If yes, describe_____
5. Does your child take any medications? ☐ No ☐ Yes If yes, describe_____
6. Does your child require prophylactic antibiotics prior to medical procedures (e.g. dental )? No ☐ Yes ☐ If yes, describe_____

***Section G: Developmental History and Speech/Language Information***

1. Describe your child's speech and language skills. Please fill in any items that are a concern to you or your child:

☐ Late to talk
☐ Difficulty "pronouncing" sounds
☐ Hard to understand his/her speech
☐ Sounds "stuffy" as if he/she has a cold
☐ Sounds as if he/she is talking through the nose
☐ Stuttering or getting stuck while talking
☐ Talking too fast
☐ Difficulty expressing ideas, sequencing events
☐ Difficulty understanding directions
☐ Difficulty hearing sounds or words
☐ Other _____
_____

2. Please fill in any items that are currently a concern to you:
   - ☐ Difficulty paying attention
   - ☐ Always needing to be on the move
   - ☐ Difficulty with fine motor tasks (e.g., coloring, cutting)
   - ☐ Difficulty with gross motor tasks (e.g., running, riding a bike)
   - ☐ Other _____

***Section H: Additional Comments***

If there is any additional information which you feel would be helpful to us, please describe below. Attach additional sheets or reports.

CHAPTER

# Evaluation and Treatment of Paradoxical Vocal Fold Motion: A Speech-Pathologist's Perspective

76

***Catherine L Ballif***

## INTRODUCTION

Paradoxical vocal fold motion (PVFM) has been defined as the abnormal closing of the vocal folds during inspiration. This is often interpreted to mean a complete adduction of the vocal folds, resulting in an occlusion of the upper airway and preventing the normal passage of air into the lower airway. However, clinical practice has documented PVFM symptoms, including restricted breathing, throat tightness, and stridor, in the absence of visualized complete vocal fold adduction and airway occlusion. In these cases, other behaviors including partial or incomplete adduction of the vocal folds, arytenoid hooding, anteroposterior compression of the epiglottis, and posterior pharyngeal wall constriction are often observed endoscopically. Indeed, any degree of constriction of the airway at the level of the larynx, pharynx, and/or anterior neck can result in the perception of restricted breathing, even in the absence of complete vocal fold adduction.

Paradoxical vocal fold motion has been referred to by a variety of other names including vocal cord dysfunction (VCD), episodic laryngospasm, episodic laryngeal dyskinesia, psychosomatic stridor, emotional laryngeal asthma, irritable larynx, Munchausen's stridor, and many others.[1-3] A meta-analysis of 288 articles on PVFM involving more than 1,000 patients described prevalent symptoms of dyspnea (73%), "wheezing" (36%), perceivable stridor (28%), cough (25%), chest tightness (25%), throat tightness (22%), and voice change (12%).[4]

The National Heart, Lung, and Blood Institute estimates that nearly 40% of the 22 million patients (8.8 million) diagnosed with asthma may in fact have PVFM.[5] Paradoxical vocal fold motion is often misdiagnosed as asthma, among other diagnoses, with studies showing that 10–40% of patients diagnosed with severe refractory asthma actually suffer from PVFM.[6,7] Similarly, more than 5% of children between 10 and 18 years of age in the United States are estimated to have PVFM.[8] The 2012 U.S. Census reports 18 million children in this age range,[9] which implies that over 916,000 children are afflicted with PVFM today.

Given the variety of prevalent symptoms known, a variety of medical disciplines and treatment approaches may be involved. In addition to treatment with asthma medications, other approaches include treating reflux with antireflux medications and lifestyle modifications, addressing underlying psychiatric disorders with psychotherapy, progressive relaxation, hypnosis, and psychiatric medications, and using Botox injections for refractory cases.[1] The most common first-line therapeutic approach remains voice therapy. Voice therapy is therapeutic training and application of techniques developed through a specialized area of speech-language pathology focusing on restoring and/or rehabilitating the complex functions of the larynx and voicing. In fact, studies assessing the effectiveness of treating PVFM with respiratory retraining and other approaches through voice therapy report success rates of 63–80%.[1,10-12]

## VOICE THERAPY APPROACH

The voice therapy approach to treat PVFM can be viewed as addressing nine potential target areas (Table 76.1). In brief, these target areas are as follows: description of PVFM (related to the patient), endoscopic visualization of PVFM behaviors, biofeedback to laryngeal control postures, laryngeal health and hygiene, training of the

**Table 76.1:** Outline of voice therapy approach for treating PVFM

| *Voice therapy target* | *Method* | *When addressed* |
|---|---|---|
| Description of PVFM | Speech pathologist provides education using pictures, diagrams, and other educational materials and resources identifying specifics to the patient | At evaluation; continues during the course of therapy as needed |
| Endoscopic visualization of PVFM behaviors | Obtain endoscopic views of the larynx prior to and after inducing PVFM symptoms when possible | At evaluation but could be done during course of therapy if needed |
| Biofeedback of laryngeal control postures | With transnasal endoscope in place, obtain images of the larynx and pharynx during application of various laryngeal control postures | At evaluation but could be done during course of therapy if needed |
| Laryngeal health and hygiene | Speech pathologist provides education regarding hydration, laryngopharyngeal reflux, allergy, GI management as applicable, and behavioral modification of phonotraumatic behaviors | Either at evaluation or during the course of therapy as time and circumstance permit |
| Training of rescue breathing technique | Speech pathologist begins initial training of the rescue breathing technique for the patient to apply during the next acute PVFM episode | At evaluation; continues during the course of voice therapy as needed. This represents Level 1 of voice therapy |
| Therapy trials | Under the supervision and modification of the speech pathologist, the patient systematically explores and applies various laryngeal control exercises in applicable physical activities to determine the exercise best fit for the patient | During voice therapy sessions. This represents Level 2 of voice therapy |
| Outside practice | Patient continues the process of exploring and applying techniques trained in voice therapy in "real-life" context gradually becoming independent in application of knowledge and skills | During and after course of voice therapy. This represents Levels 2 and 3 of voice therapy |
| Laryngeal massage | Speech pathologist initially applies laryngeal massage and digital manipulation techniques to manually release musculoskeletal tension in the laryngeal and neck muscles. The patient is also trained in self-application methods to continue independently. Where desired, family members, teammates, coaches, etc. can also be trained | During the course of voice therapy as needed |
| Clinical medical hypnosis | Patient is guided through clinical medical hypnosis to achieve better control of the laryngeal response during future PVFM episodes by a trained practitioner, either a speech pathologist or appropriate mental health professional | During the course of voice therapy if administered by a speech pathologist or during the course of treatment by a mental health professional |

rescue breathing technique, therapy trials, outside practice, laryngeal massage, and clinical medical hypnosis. Application of target areas is based on the individual patient's needs and circumstances. This means that a patient may not target all nine areas if a target is not needed, nor are all targets addressed to the same degree for every patient.

Target areas are addressed during both the evaluation and subsequent therapy visits. Some targets may be completed during the evaluation, such as endoscopic visualization of PVFM behaviors and biofeedback of laryngeal control postures. Others are initially addressed during the evaluation visit and continue to be expounded upon during subsequent therapy visits, as needed. These include providing a description of PVFM, training the rescue breathing technique, and discussing laryngeal health and hygiene. Others are addressed during subsequent therapy sessions, including therapy trials, outside practice, laryngeal massage, and clinical medical hypnosis.

Mastery of voice therapy techniques is demonstrated through completion of three levels described later in this chapter. Completion of each level is based on patient report supported by clinical observation. The overarching goal of the voice therapy approach is to empower the

patients with knowledge, strategies, and skills, enabling them to feel more in control of the larynx within the context of breathing.

## EVALUATION

The voice therapy evaluation consists of a case history intake (including a description of symptoms from the patient and the caregiver, where applicable), pertinent medical history, laryngeal endoscopy including assessment of laryngeal control postures and observance of laryngeal behavior at rest and during an induced episode when possible, preliminary patient/caregiver education, and initial training of a rescue breathing technique. Patient/caregiver education and training in laryngeal control exercises will be further addressed in therapy but should begin during the evaluation, whenever possible. Acoustic and laryngeal function testing can also support the finding of PVFM but are not an integral part of the evaluation process.

Though endoscopic visualization of PVFM during an acute episode helps provide a definitive diagnosis, it is not always possible during an evaluation due to lack of endoscopic equipment, restrictions in time allotted for the evaluation, or inability to feasibly trigger an episode based on the individual's personal triggers (i.e., "It only happens during wrestling tournaments", "I can run 15 minutes before it starts", "It only happens with swimming", etc.). To date, the most widely accepted practice of diagnosing PVFM is based on case history through patient's report of symptoms and triggers.

A series of differential diagnosis questions (Table 76.2) based on the work by Mathers-Schmidt in 2001[13] may aid in distinguishing PVFM behavior from sports-induced asthma (SIA). The answers to these questions will help guide the clinician to identify and quantify the extent of a possible laryngeal component to the patient's breathing difficulties. However, caution should be taken in interpreting answers as absolute determiners or exclusion criteria.

The popularity of the SIA diagnosis has been known to influence a patient's memory of symptoms when removed from context. Clinical experience has documented patients, initially diagnosed with SIA, recalling symptoms of chest tightness and wheezing during athletic activity from memory, reporting throat tightness and stridor later during an induced episode in the clinic. Even a subtle laryngeal component may still be present in the absence of typical verbal responses to differential diagnostic questions. Paradoxical vocal fold motion behaviors will respond to laryngeal control exercises and other voice therapy techniques.

Other factors to consider during the case history are as follows: when episodes take place, how long it takes for symptoms to start, and what intensity of physical activity induces symptoms. Consider if symptoms are present during practices versus games versus tournaments (indicating a possible competitive component), in hot, humid, or cold weather or in poor air quality (indicating a possible environmental sensitivity), at night upon lying down or waking up in the night (indicating a possible reflux component), with physical activity only or at rest (indicating a possible psychoemotional component). The individual should also report how long it takes for symptoms to exacerbate (immediately on engaging in physical activity versus after 20 minutes versus after 5 miles versus not until after activity has stopped). In some cases, patients report that onset of symptoms is directly related to intensity of activity (i.e., "It only happens with *strenuous* activity" or "when I push myself").

**Table 76.2:** Differential diagnosis questions for distinguishing SIA symptoms from those of PVFM symptoms[13]

| *Question* | *Answers typical of SIA* | *Answers typical of PVFM* |
|---|---|---|
| Is it harder to breathe in or out? | Out | In |
| Is there tightness in the chest or throat? | Chest | Throat/Both |
| Does the person make a sound when breathing? If yes, when breathing in or out? | Out (wheeze) | In (stridor) |
| Do symptoms respond to use of an inhaler? | Yes | No/Sometimes |
| What were the blood oxygen levels during an acute episode (if known)? | Drop below 90% | Stay above 90% |
| How long does it for breathing to recover upon activity cessation? | > 10 minutes several hours more than a day | Upon activity cessation/Within minutes of cessation |

Quality of life measures, pulmonary function testing results, and acoustic analysis can also support the patient's report of PVFM symptoms. The Dyspnea Index[14] specifically addresses the patient's perception of PVFM symptoms on his or her quality of life. This instrument has recently been validated for use with the adult population with upper respiratory symptoms. Preliminary validation data from work by Hartnick et al. suggest that this tool may also be appropriate for adolescent self reporting (personal communication). Pulmonary function testing demonstrating an upper airway obstruction instead of a lower airway obstruction can also support the diagnosis of PVFM in the absence of endoscopic visualization. Regardless of diagnostic results, the real determiner is whether the symptoms will respond to behavioral therapy techniques covered in voice therapy.

Endoscopic examination of the larynx in cases where an acute episode cannot be readily induced may still prove beneficial in the treatment of PVFM. Observing the larynx at rest may provide some insight into the patient's baseline laryngeal status prior to initiating formal voice therapy. Clinical experience has documented behaviors during quiet breathing at rest, such as a narrower glottis, brief adduction of the vocal folds, and arytenoid hooding during quiet inspiration. These behaviors are often observed though the patient has reported no breathing difficulties at the time. Endoscopy can also provide patients with visual biofeedback through application of specific strategies, which will be targeted in voice therapy to ascertain which strategies will be most effective in helping them gain control over laryngeal/pharyngeal constriction.

## TREATMENT

Treatment for PVFM involves the following: (1) Education regarding the normal function of the larynx and the nature of PVFM. (2) Ongoing identification and control of environmental, physical, and emotional factors potentially contributing to PVFM behavior. (3) Empowering the patient with strategies to control and/or reduce laryngeal, pharyngeal, and anterior neck muscles. Voice therapy strategies focus on controlling the *laryngeal response,* not necessarily the etiology triggering the response. Education begins during the voice therapy evaluation. It involves providing information regarding normal function of the larynx, the nature of PVFM, possible contributing factors, general vocal/laryngeal hygiene, and initial training in laryngeal control exercises.

The primary function of the larynx in the human body is to protect the lower airway—especially the lungs—from foreign bodies and to secure an open airway for proper breathing. It accomplishes this by closing the airway at the level of the glottis in times of need and protection. Protective laryngeal closure is observed in such activities as coughing, throat clearing, gagging, swallowing, and in extreme cases, laryngospasm. It is also present in activities, such as vomiting, sneezing, valsalva, gasping, hiccupping, and the "knot in the throat" sensation.

Laryngeal closure can occur with the threat of an actual penetration of the lower airway (aspiration of liquid or exposure to inhalants), as part of an infection (upper respiratory infection), or as a result of physical or emotional distraction away from the vulnerable and otherwise open airway. If an individual is distracted by physical or emotional circumstances, the larynx can respond with a closure pattern to prevent any possible chance of accidental penetration. This is readily recognized in the case of nervousness (stage fright and performance anxiety) or just before crying when the throat muscles tighten, causing the "knot/lump in the throat" sensation. The individual's attention is distracted emotionally away from the open airway, which is still exposed to the elements and the potential threat of penetration and aspiration into the lungs. This can similarly be observed in the athlete who is "in the zone" or highly competitive/driven during athletic activity, also demonstrating emotional/mental distraction of attention. Ironically, the natural panic and anxiety associated with not being able to breathe can also result in exacerbation of the already occurring PVFM behavior. Understanding the nature of the laryngeal response (to close) and the individual's capacity to control a laryngeal response can often take the mystery out of the episode ("I can't breathe! What if I die?") and provide the patient enough insight and empowerment to spontaneously resolve future occurrences of the response. In other cases, identification and control of contributing factors as well as training in voice therapy techniques and laryngeal control exercises may also be needed.

Contributing factors and triggers resulting in laryngeal closure can be environmental, physical, and/or emotional in nature. Environmental factors typically pose a direct threat to the airway and include aspiration/penetration of liquid, food, saliva, mucous (postnasal drip) and inhalation of fumes, scents, noxious inhalants, smoke, pollution, "thick" air typical of a gym or basketball court, allergens,

and even particles in a rescue inhaler used for SIA. Other environmental triggers involve exposure to temperature extremes.

Aspiration risks in the category of physical factors include reflux contents (including vomit) and secretions (saliva, mucous, postnasal drip), most likely from allergies. Other physical factors can include asthma, upper respiratory or other infections, physical/athletic exertion, hormone levels (including menstrual cycles in females), pain, and inadequate hydration, nutrition, and/or sleep. Most physical factors are a result of distracting the individual's attention away from the airway, triggering the laryngeal response to close preventatively. Another physical factor contributing to PVFM response may involve tightness of the laryngeal and/or anterior neck musculature. Many patients clinically respond to the manual release of muscle tension through laryngeal massage, myofascial release, and other approaches.

It is well known that the laryngeal mechanism is connected to the limbic system and emotions. We have already cited the example of the knot/lump in the throat sensation associated with being upset, nervous, or mad. In the early days of treating PVFM or VCD, it was commonly believed in the medical field that breathing difficulties in the absence of a positive asthma test indicated a psychogenic condition. The individual was often seen as seeking some sort of secondary gain and was often told "It's all in your head". Indeed, shortness of breath, stridor, hyperventilation, and throat tightness are certainly known symptoms of a panic attack. However, all laryngeal responses cannot be solely linked to high psychoemotional states. In a retrospective study of adolescents treated for PVFM symptoms by Maturo et al.,[1] the majority of participants reported resolution of PVFM symptoms with voice therapy strategies alone, dispelling the common belief that PVFM is a purely psychogenic or psychoemotional condition.

Laryngeal responses to emotions are not limited to negative emotions. Competitive drive is a successful and effective motivating force for many athletes, whether the athletes are in competition with other competitors, teammates, or themselves. "Being in the zone" for the athlete and other states of focused attention, such as "zoning out", are examples of productive focused mental states that can distract the individual's attentions away from protecting the airway. The degree of mental/emotional distraction, however, may trigger a laryngeal response to protect preventatively. Inspiratory stridor can also be observed in an individual celebrating a joyous occasion, as manifested through gasping. Moreover, clinical experience has documented episodic laryngospasms and/or loss of consciousness in individuals as a result of having "laughed too hard".

We have identified many potential contributors to PVFM behavior existing more certainly. However, PVFM behavior may not be the result of only one factor alone. It is possible that laryngeal closure occurs due to a cumulative result of various factors and intensities. Voice therapy identifies specific contributors and provides strategies and education on how to control what can be controlled to keep the cumulative result down, and thus, hopefully avoid a PVFM response.

In addition to environmental, physical, and emotional contributors, brain functions must be considered. Generally, the brain tends to program frequently occurring muscle patterns. This explains why one can walk through his or her house in the dark and still find the light switch, or why one can turn off his or her alarm clock while still in a state of half consciousness. Learning through repetitive practice builds muscle memory, whether practice is intentional (shooting basketballs from the foul line) or unintentional (turning off the alarm clock). The laryngeal response ( to close) involves muscular action, making it susceptible to muscle memory programming. Furthermore, the brain prefers to draw associations, as seen with Pavlov's experiments with the salivating dog. An athlete who may have initially experienced a PVFM response during athletics from any of the aforementioned environmental, physical, and/or emotional factors—or combination of factors—legitimately triggering the muscular action for laryngeal closure, may subsequently experience similar closure patterns as a result of the brain associating laryngeal closure with athletic/physical activity. This association is reinforced each time the individual engages in physical activity and experiences laryngeal closure, creating a strong association the longer it continues without treatment.

Regardless of the contributing factors, triggers, or documented extent of vocal fold adduction, any degree of constriction to the airway at the level of the larynx, pharynx, and/or anterior neck can be perceived by an individual as a narrowing or constriction of the airway, resulting in the sensation of restricted breathing. This perceived restriction to breathing can in turn trigger a natural sense of panic and anxiety of not being able to breathe when one considers the potential consequences.

Again, during an acute episode of PVFM, when the larynx is presumably closing off and effecting the individual's ability to breathe, the natural panic and anxiety associated with not being able to breathe can result in increased laryngeal closure behavior exacerbating the overall episode.

Education continues with basic vocal health and hygiene. This may be addressed either during the evaluation visit or during a therapy visit, as deemed appropriate. Target areas of vocal health and hygiene may differ between individuals as specific factors for the individual are identified. Vocal health and hygiene education includes discussion of proper hydration levels, effects of phonotraumatic behaviors such as yelling and throat clearing/coughing on the larynx, and proper management of physical conditions that have an impact on the larynx such as asthma, allergies, and acid reflux. Often, these conditions may require medications that may have an effect on the upper airway mucosa.

Initial training in a basic laryngeal control exercise typically concludes the evaluation visit. The most commonly used laryngeal control exercise involves nasal inhalation with exhalation through a semioccluded oral cavity, either through pursed lips or sustained /s/ sound production. The patient is often encouraged to practice a version of rescue breathing, when not engaged in athletics, to build muscle memory and skill in order to prepare for application the next time PVFM symptoms are experienced. In some cases, the understanding of what is happening in PVFM and knowing that it can be controlled is sufficient to resolve PVFM symptoms. With this knowledge, they are able—sometimes spontaneously—to control the laryngeal response without formal training through a course of voice therapy. For others, however, additional education, practical application of laryngeal control exercises, and even laryngeal massage are needed to help gain control and build confidence in ability.

Voice therapy for PVFM involves completion of three levels. Time in each phase varies between patients. Formal voice therapy consists of up to six (1 hour) sessions. The frequency of sessions depends on the individual's specific situation and athletic seasons. Sessions typically occur every 1–4 weeks, allowing time for practical application in real-life situations outside the clinical setting. Ideally, therapy should span an athlete's sporting season to ensure successful application and carryover. It is important for the patient to be able to control PVFM symptoms during an athletic season when the elements of competition and best performance, which are difficult to duplicate in the therapy setting, are naturally occurring. Many athletic seasons only occur once a calendar year, especially if they are school athletics. However, there is also benefit in addressing the training and practice of techniques withdrawn from the additional stressors of performance and competition. Therapy sessions review education and the ongoing identification and control of possible contributing factors as well as address the three levels of training and mastery of laryngeal control exercises.

Level 1 involves applying laryngeal control exercises to stop an already escalated laryngeal response. It is typically first addressed during the evaluation with the training of a rescue breathing technique. Completion of Level 1 is achieved when the patient feels able to successfully and confidently apply basic laryngeal control exercises, including rescue breathing techniques and laryngeal control postures, during acute episodes of PVFM and restore normal breathing pattern at the level of the larynx/throat quicker than without application of laryngeal control exercises. Although this level is typically initiated during the evaluation visit, completion of this level may occur during the course of formal voice therapy.

Level 2 of voice therapy entails the systematic application and practice of laryngeal control exercises in various athletic activities and intensities to enable the patient to control PVFM symptoms from escalating during the athletic activity. Athletic activities specific to the individual should be addressed as much as possible. Depending on the individual, it may not be possible to completely eliminate all PVFM symptoms. However, the individual may be able to control throat tightness and shortness of breath within reasonable and tolerable levels and continue in the activity.

The individual should identify and practice the application of laryngeal control exercises within a voice therapy session to increase understanding of how to practice and apply these skills outside the clinical setting. Far too often, an athlete returns for an additional course of voice therapy, claiming that the laryngeal control exercises from the previous course(s) do not work. Further investigation of previous experience often reveals that the patient was trained in effective laryngeal control exercises via education, discussion, and practice at rest in the therapy room, but was never observed in a practical application exercise where modification and personal tailoring of the techniques could take place. When observed within an athletic context, it is often discovered that the application

of the rescue breathing technique, as understood by the patient, is not what the original treating clinician had intended for application during training in the therapy room. After a little retraining and modification to application, the patient indeed benefits from the techniques addressed in previous therapy courses.

Many successful variations of laryngeal control exercises are used to treat PVFM in the clinical setting. These include such techniques such as abdominal breathing, sniff–shush technique, nasal inhalation with exhalation through pursed lips, and exhaling through a semioccluded vocal tract. However, since PVFM is defined as the abnormal adduction of the vocal folds on inspiration, it reasonable to focus on retraining of inhalation behaviors rather than exhalation.

In its pure form, the rescue breathing technique of breathing in through the nose and out through the pursed lips will be effective for the vast majority. However, rescue breathing for PVFM is not as much about getting a deep breath as it is about opening the airway to allow for breathing. It is possible to sniff or inhale through the nose and constrict the laryngeal, pharyngeal, and anterior neck musculature. Focus should be placed on relaxing the laryngeal and pharyngeal muscles and allowing for a *wide* breath, not necessarily a *deep* breath. Deep breaths will become possible as the airway opens at the level of the larynx and pharynx. In some individuals, the traditional nasal inhalation technique does not achieve sufficient laryngeal/pharyngeal opening. Some respond better to inhalation and exhalation, transorally with a puckered lip posture.

As stated earlier, the purpose of laryngeal control exercises is to allow the individual to control the laryngeal and pharyngeal structures from narrowing the upper airway, resulting in the sensation of restricted breathing. If traditional rescue breathing strategies prove less effective in accomplishing this, the individual may benefit from application of various laryngeal control postures. Laryngeal control postures are actions that result in a widening or opening of the larynx and/or pharynx, though this is not necessarily their primary purpose. These include yawning or yawn posture, swallowing, popping ones ears through a deliberate jaw movement, thrusting the jaw forward briefly, stifling a laugh or laugh posture, and moving the tongue to the posterior lower teeth (as if cleaning out food). These activities and other activities can result in the widening of the larynx and pharynx, as observed endoscopically. Laryngeal control postures also prove effective for the athlete whose sport does not allow for traditional rescue breathing techniques such as swimming. Many laryngeal control postures can be executed without actively breathing. Similar adaptations made be needed for other sports.

The purpose of voice therapy is to find which laryngeal control exercises work best for the individual patient in various situations and contexts. The more naturally the strategy can be executed within athletic context and in the presence of perceived throat tightness or restricted breathing, the more successful the individual will be at controlling PVFM symptoms from escalating. When exploring application of laryngeal control exercises in the therapy setting, the patient is instructed to wear proper athletic attire for the given activity and have any applicable asthma medication, including a rescue inhaler, with him/her during therapy. For therapeutic trials, an athletic activity is chosen in which distance, speed, and athletic intensity are controlled as best as possible, leaving the application of various laryngeal control exercises as the determining factor in management and improvement of symptoms. The patient explores and applies various patterns of rescue breathing and/or laryngeal control postures, assessing his or her ability to control PVFM symptoms during trials. The patient then has to apply this same process to various athletic activities of various intensities outside the clinical setting until the next therapy session.

Therapy progresses in Level 2 as the patient learns to apply his or her particular laryngeal control strategies early with the first detectable signs of PVFM symptoms, rather than waiting until symptoms have escalated to the point they can no longer be controlled. Level 2 is primarily focused on empowerment and building the confidence of the patient to control throat tightness and other PVFM symptoms during athletic activity. Therapy at this level may also include laryngeal massage and adjustment maneuvers. Application of laryngeal massage and adjustment maneuvers can manually relieve any muscle tension in the laryngeal and neck areas possibly contributing to PVFM symptoms. The patient and, where appropriate, trusted family members are also trained in application.

Clinical medical hypnosis has also been used clinically to treat PVFM symptoms. According to guidelines established by the American Society of Clinical Hypnosis (ASCH), trained clinicians may use hypnosis to treat conditions they normally would treat using other conventional

methods. Hence, speech pathologists can be trained to use hypnosis to treat PVFM. Hypnosis, as described by ASCH, is a state of inner absorption, concentration, and focused attention.[15] We are able to use our minds more powerfully when in a concentrated and focused state. Application of clinical medical hypnosis in voice therapy sessions can aid the patient, while in a focused concentrated state, to better address and manage body function and emotional factors contributing to PVFM symptoms. Patients are able to formulate an internal plan of addressing PVFM symptoms, while blocking out unnecessary factors that may only complicate and distract their attention away from successfully controlling PVFM behaviors. Typically, 1–3 sessions of hypnosis are needed in PVFM therapy. If not responsive or if more support is needed, the patient may be referred to child mental health services for additional treatment, including additional hypnosis sessions.

Level 2 is achieved when the patient successfully and confidently feels he or she is able to control PVFM symptoms from escalating out of control through successful application of rescue breathing techniques, laryngeal control postures, and/or laryngeal massage techniques. The important part at Level 2 is that the patient feels he or she is controlling the intensity of symptoms, rather than feeling that symptoms have stopped occurring as frequently and spontaneously.

Level 3 of therapy is achieved when the patients report natural or effortless application of laryngeal control strategies. They no longer feel burdened with worrying about their breathing or consciously trying to control it. This may be either because application comes naturally to them without much conscious effort or thought, or because the need to apply the strategies has been reduced/eliminated. Most importantly, they report feeling confident in their ability to control PVFM symptoms, should they occur again in the future. Carryover is demonstrated once Level 3 has been attained and the patient consistently demonstrates ability to apply therapy techniques to applicable athletic activities of various intensities.

Training in laryngeal control exercises and strategies should typically not take longer than six therapy sessions. Exceptions may occur, such as in cases where muscle memory patterns may prove quite strong and resistant to behavioral retraining, when timing of the athletic seasons plays a role in assessing successful carryover, or if discovery of other contributing factors is not identified until later in the therapy process. One such situation may be the determination that the patient would benefit from clinical medical hypnosis after a few sessions of behavioral retraining. In general, response to voice therapy techniques should be demonstrated within the first few sessions, even if additional sessions are needed to master the application of techniques.

Should PVFM symptoms not respond sufficiently to voice therapy within six sessions, it is possible that the factors contributing to PVFM behavior are more than behavior retraining can successfully address. These may be medical, physical, or psychological in nature. Referrals to appropriate medical professionals, athletic trainers, and mental health professionals should be considered. The multidisciplinary team approach is the most effective in treating PVFM involving pediatric cardiopulmonology, otolaryngology, gastroenterology, child mental health services, and voice therapy with additional support from sports medicine, sports psychology, and personal trainers, as applicable. Maturo et al. noted that the single, most determining factor for evaluation and consultation with child mental health services was the presence of symptoms, especially stridor, occurring at rest. Although these patients may have shown some improvement with voice therapy techniques, sufficient resolution of symptoms was achieved with help from child mental health services.

## SUMMARY

In the past, PVFM behavior in the absence of asthma was commonly viewed as primarily a psychogenic or conversion disorder. While PVFM behaviors can be part of psychological conditions, they do not occur exclusively in this context alone. In fact, PVFM is a laryngeal response to multiple contributory factors (environmental, physical, and emotional in nature), possibly coupled with brain functions such as association and muscle memory encoding.

Prior to understanding the nature and presentation of PVFM and laryngeal responses, patients can feel out of control and helpless. The natural anxiety of not being able to breathe and the looming implication of what could happen if they are not able to regain control of their breathing can exacerbate the overall laryngeal response. However, PVFM behavior can be controlled through practice and application of voice therapy strategies in context. Empowering patients with strategies enables them to feel in control again and reduce the anxiety of not being able to breathe. A multidisciplinary approach addressing possible contributing factors, coupled with

voice therapy, to empower the patient to regain control of the laryngeal response is the best practice for treating PVFM. Voice therapy targeting training and application of laryngeal control exercises, laryngeal desensitization strategies, laryngeal massage techniques, abdominal and laryngeal breathing techniques, proper laryngeal hygiene, relaxation methods, and, where warranted, clinical medical hypnosis, is effective in helping the individual regain control of PVFM behaviors. The key is to guide the patient in applying strategies effectively in context whenever possible to better facilitate successful carryover outside the clinical setting.

Laryngeal responses, including PVFM behaviors, respond to voice therapy techniques. If limited progress in voice therapy is experienced, the contributing factors triggering the laryngeal response may need to be further addressed and controlled before success with voice therapy strategies can be achieved. The contributing factor itself may inhibit benefit from voice therapy techniques and limit progress in therapy. In these cases, techniques should be applied to address the laryngeal response as much as possible in the context of an uncontrolled contributing factor.

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CHAPTER

# Neurolaryngological Disorders and Pediatric Laryngeal Electromyography

77

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## INTRODUCTION

The subspecialty of pediatric voice has advanced immensely in recent years. The widespread, simplistic view of the pediatric hoarse voice as something to outgrow is no longer true, and it has acted as a disservice to the patients and their families. Voice disorders in children are increasingly being noted as a barrier to success in the school environment in terms of academic achievement and socialization.[1] Significant advances in pediatric voice over the past decade in evaluation, diagnosis, and management of pediatric voice disorders have improved both short-term and long-term outcomes for the dysphonic child.

Voice disorders in the pediatric population are as varied as they are in the adult population. There is a wide spectrum of "normal" voice in the pediatric population, which varies by age, sex, and pubertal development. It is important to note that different adults [parents, teachers, speech language pathologists (SPL), and pediatricians] interacting with the child may perceive the child's voice differently and may not be in agreement as to whether the child is dysphonic and the degree of dysphonia. This range of opinion provides a complicating factor in discerning the presence of a voice disorder and how to manage it appropriately. The prevalence of pediatric dysphonia in the literature is generally 6–9%, with one study noting dysphonia as high as 38%.[2-4] In studies of school-aged children, an incidence of hoarseness of 18–23% had been noted,[5-9] with males more frequent than females. Interestingly, there is no difference in incidence in school-aged children identified as "child singers".[10] Parent questionnaires have been shown to score lower incidence than SPL or clinic evaluation,[11] most likely leading to underdiagnosis of voice disorders in children in general. Past advice for the dysphonic children was to "let them outgrow it", which was poor advice. While some children may resolve their dysphonia with time, a longitudinal study of 203 dysphonic children showed 35% continued to be dysphonic at one year and 9% continued to be so four years after diagnosis.[12]

There is a wide ranging differential in pediatric dysphonia, including but not limited to glottic web, glottic or subglottic stenosis, postsurgical changes, infectious/inflammatory, functional, and neurogenic causes. Neurogenic voice disorders include vocal fold paralysis/paresis and neuromuscular disorders of the larynx. This subset of dysphonia is challenging to diagnose and even more challenging to treat. Vocal fold paralysis or paresis is a more common cause of neurogenic dysphonia than movement disorders in both the adult and pediatric population.

## ANATOMY OF VOCAL FOLD INNERVATION

The larynx is innervated by branches of the vagus nerve which contain motor, sensory, and parasympathetic fibers. The two major nerves that innervate the laryngeal musculature and sensory component are the superior laryngeal nerve and the recurrent laryngeal nerve (inferior-laryngeal nerve). The superior laryngeal nerve descends toward the larynx medial to the carotid artery and divides into the internal branch and external branch. The internal branch enters the larynx through the thyrohyoid membrane to innervate the sensory and parasympathetic components

of the mucosa of the supraglottis. The external branch of the superior laryngeal nerve innervates the cricothyroid muscle on the outside of the laryngeal complex.

The recurrent laryngeal nerve takes two separate courses in the body depending on the side. The left recurrent laryngeal nerve courses to the left of the aortic arch and around the ligamentum arteriosum. It then ascends in a course next to the tracheoesophageal groove and enters the larynx just posterior to the cricoarytenoid joint. The right recurrent laryngeal nerve courses inferiorly to the right subclavian artery, winds around the artery, then ascends similarly to the left recurrent laryngeal nerve, and enters the larynx just posterior to the cricoarytenoid joint. As the recurrent laryngeal nerve enters the larynx, it divides into an anterior and posterior branch bilaterally.[13] The anterior branch innervates the lateral cricoarytenoid, thyroarytenoid, and vocalis muscles. The posterior branch innervates the posterior cricoarytenoid (the only true abductor muscle of the larynx) and the interarytenoid muscles. Sensory and parasympathetic innervation of the infraglottis is supplied by bilateral recurrent laryngeal nerves.

## EVALUATION OF DYSPHONIA

Evaluation of the dysphonic child is best done with a multidisciplinary team comprised of an otolaryngologist, an SPL, the child's pediatrician, the child's parents, and possibly, further specialized care (gastroenterologist, pulmonologist, neurologist, allergist) in voice clinic setting with appropriate office-based equipment. Children are initially oriented to the entire voice clinic team and then are evaluated with a thorough history and physical with the airway nurse or team. A pediatric voice history, including the onset and progression of symptoms, voice variability, developmental history, typical voice activities, and psychosocial environment, is completed. Particular attention is made to their functional, structural, and neurological basis. The parents also fill out a quality of life study to determine how disabled their child is from their dysphonia. One of these quality of life studies is the Pediatric Voice Handicap Index (pVHI), a recent adaptation of the adult voice handicap index. It is a 23-question validated tool, created in 2005 for the dysphonic child to evaluate the functional, emotional, and physical impact of a voice disorder on their daily activities.[14] It is a useful tool to follow their dysphonia through medical, surgical, and behavioral modifications. Other quality of life surveys in use include the Pediatric Voice Outcomes Survey[15] and the Pediatric Voice-Related Quality of Life questionnaire.[16]

An experienced SPL then performs subjective and objective evaluations of the voice, including an acoustic and perceptual evaluation. Objective assessments of a child's voice include measurements of fundamental frequency (pitch), range, sound pressure (loudness), intensity perturbation (shimmer), and frequency perturbation (jitter). Voice recordings are noninvasive and generally well tolerated by the patients. An electroglottography uses surface electrodes to measure the glottic cycle and assess basic objective measures such as pitch and jitter. It also measures vocal hyperfunction in the case of incomplete glottic closure. Further aerodynamic measurements can provide a more detailed understanding of the glottic air flows and subglottic pressures. Currently, both PAS® and KayPentax® have aerodynamics equipment in use for adults but still in the evaluation phase for children. The aerodynamic measurements combined with the objective and subjective voice data gives a useful picture of the nature of the voice pathology.

Once the SPL completes his or her evaluation, the otolaryngologist then performs a thorough history and physical, including a videostroboscopy to best evaluate vocal fold pathology (Fig. 77.1). Children more commonly have limitations in tolerating rigid stroboscopy than adults, although rigid stroboscopy can typically be done in children as young as 4 years of age. Both rigid videostroboscopy and flexible videostroboscopy provide valuable information. Rigid videostroboscopy allows for a

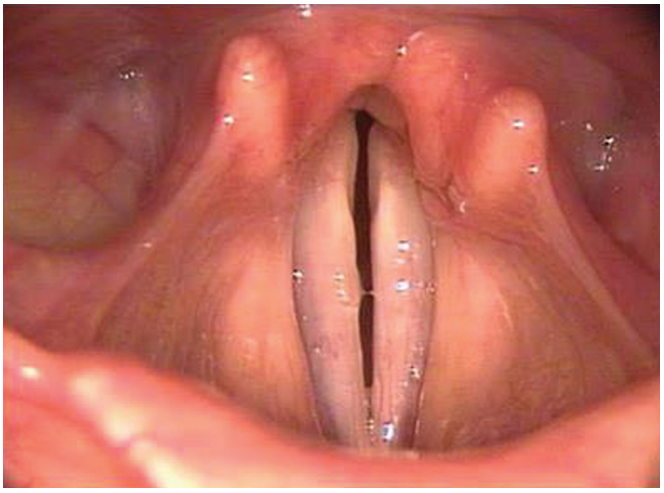


**Fig. 77.1:** Bilateral vocal fold paresis seen with rigid stroboscopy.

very clear picture with a narrow depth of field but does lead to a higher gagging rate due to the need to pull out the tongue during the examination. Flexible video stroboscopy causes less gagging of the patient and allows for better visualization of connected speech. In the past, images from the flexible laryngoscopes were poorer in quality than the rigid ones. However, with the recent advent of chip-in-tip technology, flexible videostroboscopy has similar image quality in the flexible laryngoscopes compared to that of rigid scopes.[17,18] Both flexible and rigid stroboscopy are important tools in the evaluation of a dysphonic child. Specific tasks have been designed by the SPL to accommodate children's shorter attention span, while providing quick and accurate information of assessing their dysphonia. Oral-motor assessment of facial motion, including range of motion, strength, speed, and coordination, helps to assess neurologic involvement of the presenting voice disorder.

Specific laryngeal functions noted on videostroboscopy include vocal fold motion, glottis closure, mucosal wave abnormalities, vocal fold irregularities, phase symmetry of the vocal fold motion, arytenoids movement, supraglottic compression or compensation, presence of erythema and/or edema, and the presence of pooling of secretions adversely affecting the voice. In considering a possible neurolaryngological disorder, particular aspects of the videostroboscopy that are telling include asymmetric vocal fold motion, spasmodic motion of the vocal fold, asymmetric vibratory phase patterns of the mucosal wave, and the ability to effectively adjust pitch. Particular tasks, such as maximum phonation time, are very helpful in measuring a child's efficiency of speech and breath support. Pitch and volume measurements can help to map out the flexibility of the child's voice.

## VOCAL FOLD PARESIS/PARALYSIS

Vocal fold paresis/paralysis can be congenital or acquired in nature and can be due to birth trauma, cardiovascular, iatrogenic, neurogenic, infectious, or idiopathic causes. Birth trauma-related vocal fold paresis is typically associated with a forceps delivery, which places a traction injury on the recurrent laryngeal nerve. Up to 21% of bilateral vocal fold pareses have been attributed to birth trauma.[19]

As described above, the path of laryngeal innervation can be disrupted at several points along its course. Given the complicated and lengthy course of the innervation of the larynx via the laryngeal nerves, the right recurrent laryngeal nerve traveling around the right subclavian and the left recurrent laryngeal nerve traveling around the aorta make the nerves particularly vulnerable to surgical stretch, trauma-related stretch injury, and vascular abnormalities.

Cardiac and vascular abnormalities, such as vascular rings, ventricular septal defects, and patent ductus arteriosus, have been associated with concomitant vocal fold palsies,[20] while it is most common to see an iatrogenic vocal fold paresis after the repair is completed. Thirty-five percent of children undergoing cardiac surgery have been noted to have a unilateral vocal fold paresis postoperatively.[21] Furthermore, vocal fold paresis can occur simply with excess pressure along the cricoarytenoid joint from intubation trauma, an oversized endotracheal tube, or an overinflated cuff on the endotracheal tube.

Central neurogenic causes include structural abnormality, such as Arnold–Chiari malformation, cerebral palsy, tumors, or leukodystrophies. In the case of Arnold–Chiari malformation, patients frequently present with bilateral vocal fold paresis due to the typical inferior cerebellar tonsil displacement and vagal rootlet traction, although unilateral paresis has also been reported.[22] Other causes of vocal fold paresis include infectious causes[23] (tuberculosis, West Nile virus, Lyme, poliomyelitis, pneumococcus, other viral infections), intubation,[24] foreign bodies, and chemotherapy.[25] Congenital bilateral voice fold paresis has been shown to have a genetic component in an X-linked and autosomal dominant fashion with incomplete penetrance.[26] Idiopathic causes of unilateral vocal fold paresis in children range from 7% to 41% depending on the study.[27,28]

Evaluation of vocal fold paresis/paralysis involves a detailed birth, family, and surgical history. Examination should note the nature of the stridor and its correlation with respiration (inspiratory stridor versus expiratory stridor), the presence of suprasternal or substernal retractions, and the presence of any craniofacial abnormalities, masses, or surgical scars. A thorough neurological evaluation, particularly the cranial nerve examination, is essential in picking up more subtle findings. Flexible fiberoptic laryngoscopy allows excellent visualization of the vocal folds and helps to assess vocal fold motion, asymmetric vibratory phase patterns of the mucosal wave, and whether there is any decreased sensation in the supraglottic airway. It can also assess other concomitant issues, such as laryngomalacia or the presence of a mass. If a flexible fiberoptic laryngoscopy is not tolerated in

the office, a rigid examination in the operating room yields excellent visualization and allows the surgeon to rule out vocal fold fixation, by palpating the cricoarytenoid joint. A swallowing evaluation with videofluoroscopic visualization should be performed if there is any history of feeding issues as well. Imaging should be considered if there is no clear iatrogenic etiology of the vocal fold paresis, along the entire course of the laryngeal nerve pathway.

## LARYNGEAL ELECTROMYOGRAPHY

Laryngeal electromyography (LEMG) is another extremely useful tool in distinguishing vocal fold fixation from neurogenic paresis. This is easily done in the awake, cooperative adult, but relies on percutaneous placement of EMG needles for monitoring. Typically these are monopolar leads, but they can be fine wire electrodes or hook wire electrodes depending on the available equipment and the sophistication of the examination. In children, it is rare for such cooperation, and general anesthesia or sedation is more commonly used if an EMG is deemed necessary. In these cases under anesthesia, a direct laryngoscopy and placement of monopolar hook wire electrodes is typically the choice for an accurate measurement. As sedation does play a specific role in volitional movement of the laryngeal musculature, sedated examinations typically attempt to measure LEMG data as the patient wakes up and the anesthetic is minimum.

A standard LEMG tests two groups of muscles bilaterally, typically the thyroarytenoid and/or cricothyroid muscles. For more in-depth LEMG analyses, multiple muscle groups are tested and may include thyroarytenoid, cricothyroid, posterior cricoarytenoid, and/or lateral cricoarytenoid muscles.

Techniques and normative values of LEMG were established in the 1950s.[29] Weddel et al.[30] were the first to suggest that LEMG may have prognostic value for VFP, and others have subsequently suggested the same.[31-35] There is no well-established natural history of VFP, as there is in facial palsy.[36] Clearly, the potential for spontaneous improvement varies from clinical scenario to clinical scenario, but simplified, "all-or-none" concepts of paralysis and paralytic dysphonia do not reflect the clinical reality of heterogeneous recovery.[37]

Laryngeal electromyography is able to identify normal innervation, absence of innervation, reinnervation and even synkinesis by characteristic electrical signals. However, LEMG has often been dismissed as being subjective. While this is true in certain aspects, particularly judgments regarding degree of impairment, most electromyography findings such as fibrillation potentials, normal and polyphasic motor unit potentials, and positive sharp waves are clear, both in appearance and significance. Volitional activity by the patient allows the muscles to contract to observe these complex muscle patterns. Complete relaxation of the muscle is rare as there is always a background respiratory pattern that causes a background of voluntary motor units to contract. Normal motor unit potentials have a reproducible distinct pattern. Fibrillation potentials, described as sounding like light rain on a tin roof, and positive sharp waves are believed to be similar electrical activities measured from different distances. This abnormal spontaneous activity is representative of muscle membrane instability that develops in the setting of loss of neural input and denervation. Polyphasic motor units are the other side of the coin, when a single muscle's fibers are not well synchronized. This occurs most often in the case of reinnervation. Close observation of these motor unit patterns can guide one to judge whether a nerve is in a state of normal function, denervation, or reinnervation.

While there is an ever-growing number of studies that use LEMG as a tool to judge vocal fold motion and recovery, the specific diagnostic criteria for recovery and nonrecovery remain inconsistent but in general agreement.[38] Studies particularly involving children noted safety in the use of LEMG and that LEMG recordings were helpful in differentiating vocal fold paralysis from arytenoid dislocation or fixation.[39,40] Standard nerve monitoring equipment, while not as sophisticated and quantitative as typical LEMG equipment, has been noted to be useful in intraoperative LEMG.[41] Timing of use of LEMG is important for its usefulness. Spontaneous fibrillation activity indicating axonal degeneration does not appear until 10–14 days after the initial injury,[34] which probably means that LEMG performed before that time may not be fully reflective of the extent of injury. Similarly, LEMG performed later than 6 months after the onset of symptoms yields little useful results as few patients recovered after that interval.[42,43]

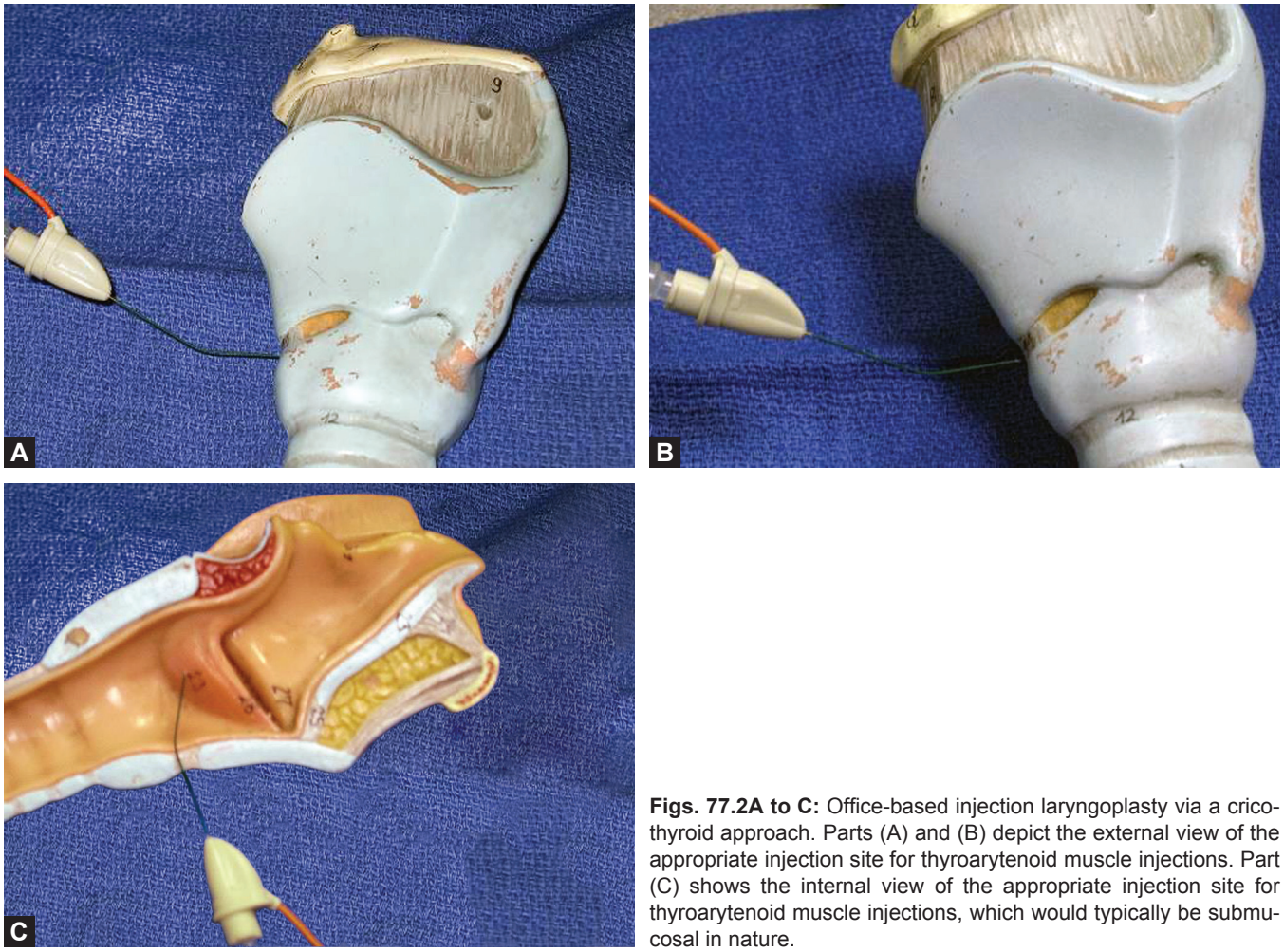
Meta-analysis notes that those with poor prognosis on initial LEMG have a high likelihood of remaining with a vocal fold palsy after the standard recovery period has passed.[35,37] Laryngeal electromyography has been shown to be a good predictor of poor recovery, but an indifferent predictor of recovery due to the admixture of adductor and abductor fibers within the recurrent nerve trunk,[38] potentially leading to either full recovery, poor recovery, or synkinetic nerve recovery in which there is reinnervation

but poor motion. This studied conclusion can be helpful as LEMG can be used to select patients with predicted poor recovery for early definitive intervention, eliminating a several-month wait for a vocal-disabled person, or the need for one or more temporary interventions when a definitive one is likely to be ultimately necessary.

## TREATMENT FOR VOCAL FOLD PARESIS/PARALYSIS

Treatment of vocal fold paresis depends on the etiology of the paresis. Many mild cases only need observation, while the majority of more severe cases need surgical intervention. An honest, open discussion of the potential interventions as well as the need for voice therapy and postoperative care is important to the success of the intervention. Injection laryngoplasty, thyroplasty, and nerve reinnervation can be performed in pediatric patients with good outcomes and an acceptable safety profile.[44]

Injection laryngoplasty, in which a "filler" material is injected into the paraglottic space, helps medialize the immobile vocal fold (Figs. 77.2A to C). This allows for better closure and better voicing, but does narrow the airway. Materials for injection include autogenous fat, several formulations of hydroxylapatite, and absorbable gelatin foam. Teflon was a material used in the past, but is rarely being used currently due to the risk of granulation formation.[45] Medialization thyroplasty (type I) is a more permanent solution to medializing the vocal fold by directly placing a permanent implant in the paraglottic space through an open procedure done under mild sedation. Implant materials include cartilage, silastic, and Gore-Tex. In children, it is important to note that the vocal folds lie more inferior within the thyroid cartilage relative to an adult. This procedure can be combined with an arytenoid adduction if deemed necessary by the anatomy. Medialization thyroplasty has been done successfully in children[46] with good results, due its ability to precisely




**Figs. 77.2A to C:** Office-based injection laryngoplasty via a cricothyroid approach. Parts (A) and (B) depict the external view of the appropriate injection site for thyroarytenoid muscle injections. Part (C) shows the internal view of the appropriate injection site for thyroarytenoid muscle injections, which would typically be submucosal in nature.

place the implant. Laryngeal reinnervation surgery through a primary neurorraphy can help to provide tone and subsequent bulk to the denervated laryngeal musculature. Multiple nerves have been brought to anastomose with the recurrent laryngeal nerve, including the ansa cervicalis or phrenic, as a bare nerve neurorraphy or with a muscle pedicle. Ansa cervicalis is the typical nerve of choice and it is identified just deep to the omohyoid muscle in the neck and anastomosed with the recurrent laryngeal nerve proximal to the larynx. This anastomosis provides neurogenic signals to the laryngeal musculature, providing tone and bulk, but not specific motion. This in combination with an injection laryngoplasty provides immediate relief followed by decreased rate of atrophy over time. Studies have shown improvement in voice outcomes and better approximation of the vocal folds over time.[47] A multicenter randomized clinical trial noted effective surgical outcomes from both medialization and reinnervation, with recommendation to consider both laryngeal reinnervation and/or medialization in younger adult patients and children.[48]

For patients with bilateral vocal fold paresis, many have a tracheotomy due to their airway compromise. There are several surgical interventions that can be implemented to provide a larger airway, sacrificing some voicing in the hopes of possible decannulation. Endoscopic resection, such as laser posterior cordectomy or arytenoidectomy (typically using the $CO_2$ laser), allows for a more appropriate airway while preserving the anterior margin of the true vocal fold for vibration and formation of reasonable voice. External lateralization and expansion laryngotracheoplasty can also be used to allow a more adequate airway. Both provide a larger airway by lateralizing the vocal fold (one directly, one indirectly by placement of a midline graft), sacrificing quality of voice in the process.

## NEUROMUSCULAR AND MOVEMENT DISORDERS

Neurogenic causes of dysphonia secondary to neuromuscular and movement disorders can be limited to laryngeal manifestations. Frequently, however, there can be associated extralaryngeal neurological manifestations. Neuromuscular diseases that lead to weakness or paralysis of the laryngeal muscles include disorders of the neuromuscular junction, peripheral nerve, and motor neuron disease. Myasthesia gravis, botulism, Lambert–Eaton myasthenic syndrome, and medications that affect the neuromuscular junction can all cause direct paralysis of the laryngeal musculature. Bulbar amyotrophic lateral sclerosis (ALS), poliomyelitis, syringomyelia, spinal bulbar atrophy, stroke, and brainstem encephalitis can all contribute to laryngeal dysfunction. While movement disorders can adversely affect the larynx, it is rare that a primary muscle disorder affects the larynx. Movement disorders include Parkinson's disease (PD) and dystonias, including focal dystonias, segmental dystonias, multisegmental dystonias, and generalized dystonias.

Evaluation of a patient with a suspected neuromuscular weakness, thorough assessment of the history and physical is paramount. Examination of the neck and mediastinum for recent surgery, trauma, or mass is needed as well as a thorough neurological examination to assess language, cranial nerve function, muscle strength, sensation, and cerebellar function. A standard videostroboscopy to examination can determine any vocal fold weakness, sensation detriments, or swallowing difficulties. An LEMG is a secondary essential component of the examination to ensure that this is truly neurologic in origin and vocal fold fixation has been ruled out. Details of LEMG examination findings and conclusions are noted above. Any observed abnormalities in the LEMG allow one to conclude whether there is normal anatomy, vocal fold weakness, vocal fold paralysis, or vocal fold recovery from previous weakness.

Many of the neuromuscular diseases occur in adulthood, including central nervous system disorders, such as ALS and spinal bulbar atrophy. However, there are several central nervous system disorders that can present in childhood. While rare, these disorders typically present with vocal fold weakness and can be progressive. They include spinal muscle atrophy[49] (type 1 is the most progressive), poliomyelitis,[50] post-polio syndrome, syringomyelia,[51] Arnold–Chiari malformations (typically presents with bilateral vocal fold dysfunction),[52] and stroke (rare in children). Peripheral nervous system disorders include lesions compressing the vagus (meningioma, trauma), glomus vagale,[53] hereditary conditions (such as Charcot-Marie-Tooth, Shy-Drager, spinocerebellar ataxia, and multiple system atrophy), and autoimmune neurological disorders (Guillain-Barre, chronic motor axonal neuropathy). Treatment for these varied disorders is dependent on the cause and frequently involves pharmacotherapy directed by the neurologist and interventional therapy directed by the multidisciplinary team. As some of the above disorders are progressive, early intervention may be critical to optimizing voice and airway, and in certain case may prevent a life-threatening situation.

Patients with movement disorders are either classified as idiopathic or symptomatic. As the genetics have partly been uncovered, many "idiopathic" cases have become symptomatic cases. There remains a great deal to discover to understand the full genetics of movement disorders, and research is ongoing.

Parkinson's disease manifests with tremor at rest, rigidity, and bradykinesia with loss of postural reflexes. Idiopathic PD is the most common subtype and is progressive in nature. While this is by and large an adult disease, juvenile parkinsonism should lead one to do further investigation into possible Wilson's disease or Huntington's disease as a possible cause. Voice production is weakened due to hypokinetic movement and decreased airflow due to weakness in the respiratory system. Voice typically presents with hypophonia of a monopitch and monoloudness. On examination, vocal folds typically bow with a mild glottic gap (Fig. 77.3). Vocal fold tremor is frequently associated with vocal fold movement. Treatment is multidimensional and includes pharmacotherapy, speech therapy, and neurosurgical ablative or stimulation procedures.

Dystonia is a wide-ranging syndrome which in its most basic form causes sustained muscle contractions. Dystonia can involve any voluntary musculature and is frequently misdiagnosed. Dystonia can be focal, segmental, multisegmental, and generalized and can rarely begin early in life, as early as an infant. There is a noted bimodal peak in prevalence of dystonia at ages of 8 and 42 years. The earlier in life the neurological disorder is noted, the more likely there are more global symptoms and signs. Therefore, proportionally more adults present with limited neurolaryngologic issues secondary to a movement disorder, while more pediatric patients present with more global symptoms associated with their presenting neurolaryngological issues secondary to a movement disorder.

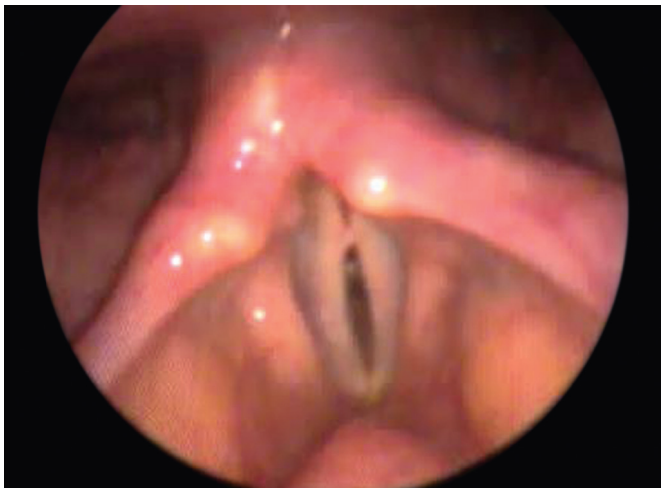


**Fig. 77.3:** Vocal fold bowing secondary to Parkinson's disease.

Spasmodic dysphonia (SD) is considered a focal laryngeal dystonia in which a patient experiences excessive laryngeal muscular contractions during speech, adversely affecting speech production. The most common form, adductor SD, produces a strained and strangled speaking pattern. Abductor SD is less common and results in a breathy or whispering speaking pattern. Although the task specificity for focal laryngeal dystonia has been observed mostly for speech, there is a low incidence of adductor breathing dystonia that may produce inspiratory stridor and singing dystonias. The etiology of laryngeal dystonia falls into the same categories as forms affecting other areas of the body. Traube first described SD in 1871 within a treatise detailing the effects of typhus on the larynx:

The spastic type of nervous (neurologic) hoarseness was observed by Professor Traube in a hysterical young girl. The very hoarse, almost aphonic patient could, with great strain, only produce very high, whistle-like sound.[54,55]

The diagnosis of SD relies on history and physical examination, including a videostroboscopy. Laryngeal electromyography is an essential adjunct to diagnosis and to guide chemodenervation of affected musculature.

Vocal characteristics vary depending on the type of SD. Patients with adductor SD have a characteristic strangled, effortful speech with vocal breaks and frequency shifts. There is often a reduction in loudness and prosody. These individuals have spasms of the vocal fold closing musculature, primarily the thyroarytenoid and lateral cricoarytenoid muscles cutting off airflow and vocalization. These spasms are most prominent with voiced sounds such as vowels, and counting from 80 to 90 will be difficult. Patients with abductor SD have a breathy, though still effortful, voice quality with aphonic whispered segments. These individuals have spasms of the vocal fold opening musculature, the posterior cricoarytenoid muscle, causing the vocal folds to remain open. Abductor breaks are particularly marked when attempting to phonate a vowel after a voiceless consonant such as p, f, t, s, d, k, or h. Abductor SD patients have hyperabduction and have trouble overcoming this opening spasm to bring the folds together to create a voiced vowel sound. These individuals have particular difficulty with "Harry's happy hat" and "the puppy bit the tape".

Patients experiencing spasms in both adductor and abductor groups are occasionally seen. These individuals are challenging, as appropriate treatment may only be determined after treatment of the individual muscle groups has failed. Laryngeal electromyography can confirm abnormal laryngeal muscle spasms diagnostically and can guide treatment to the more involved muscle groups if it is an atypical presentation.

The gold standard of treatment for SD dystonia is via electromyography-guided transcutaneous injection of botulinum toxin. Results are typically excellent and will temporarily restore voice back to one's baseline. The specific adductor or abductor muscle groups are targeted and the dose of botulinum toxin is titrated to produce just enough weakness to relieve spasm in target muscles without causing unnecessary weakness in neighboring muscles resulting in dysphagia, prolonged breathiness (adductor), or airway compromise (abductor). Dosing must be individualized to provide adequate relief from varied severities of the disease. As the severity of the dystonia can vary over time, dosing may need to adjust to accommodate the dystonia's symptoms. Typical starting doses are around 0.5–1 unit of botulinum toxin injected bilaterally. The thyroarytenoid or lateral cricoarytenoid are usually targeted for adductor SD, and the posterior cricoarytenoid muscle is targeted for abductor SD. Successful treatment of SD lasts around 3–4 months with need for further injections typically needed, but the timeframe for further treatment depends on the return of the dystonic symptoms. Pharmacological treatment is recommended in patients with severe spasmodic dystonia unsuccessfully controlled with botulinum toxin or in patients with more global dystonia (cranial/axial, multisegmental generalized) that need more global treatment. Routine collaboration with a neurologist provides these patients with the best treatment options and highest likelihood for successful long-term treatment.

## CONCLUSIONS

Pediatric voice disorders remain a varied and challenging evolving field. As the evaluation of pediatric dysphonia, particularly neurolaryngological disorders, is becoming more sophisticated and targeted, the potential treatment therapies are as well. Comprehensive voice evaluation in children with subjective markers (voice history questionnaires, QOL studies) and objective markers (acoustic and perceptual evaluation, videostroboscopy, laryngoscopy, and LEMG) is essential in properly assessing pediatric dysphonia. While treatment for voice disorders has improved both short-term and long-term outcomes for the dysphonic child, there is still significant room for improvement. Further outcomes studies are needed to demonstrate the efficacy of the current and future comprehensive regimens (surgical, nonsurgical, and combined) in the treatment of this new and evolving field of pediatric dysphonia.

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55. Translation from German courtesy of A.F. Jahn, M.D.

CHAPTER

# 78

# Paradoxical Vocal Fold Motion

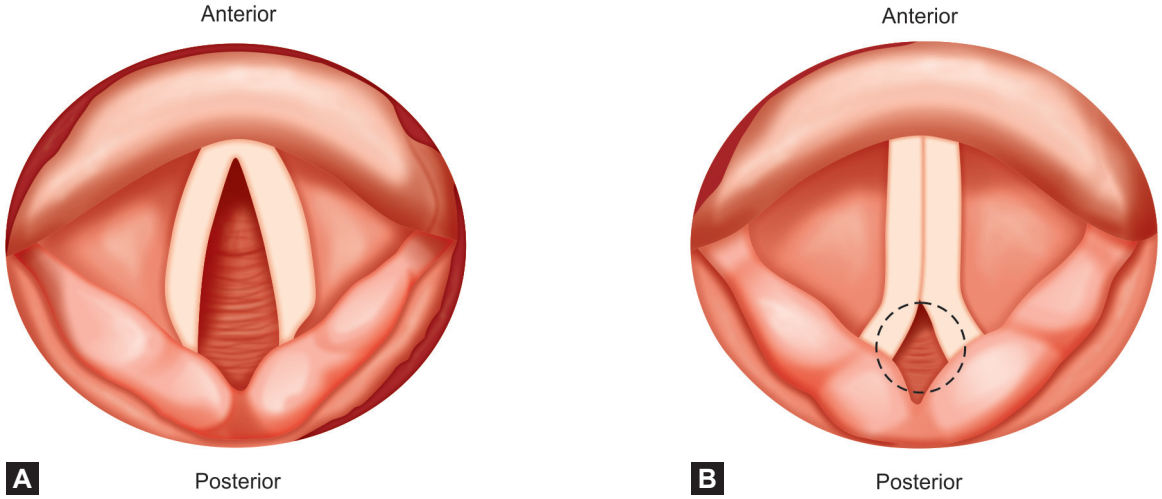
***Karissa A Brazauskas, Mary Shannon Fracchia***

Paradoxical vocal fold motion (PVFM), also known as vocal cord dysfunction (VCD), is a common problem not commonly diagnosed (Figs. 78.1A and B). Technically speaking, it is the inappropriate adduction of the vocal cords primarily during inspiration.[1-3] This results in glottic obstruction with subsequent shortness of breath and noisy breathing (including both stridor and wheeze). Paradoxical vocal fold motion is often misdiagnosed as asthma because of the similar presenting symptoms, and most patients are subjected to unnecessary tests and medications before the problem is diagnosed. It has dramatically increased in incidence and is now an important respiratory condition in children.

## DEFINING PARADOXICAL VOCAL FOLD MOTION

### Anatomic Findings

The larynx contains the glottis, which is composed of the vocal folds and the rim glottides, or the space between the vocal folds. The movement of the vocal folds determines the width of the rim glottides, and therefore the airflow into and out of the lungs. The posterior and lateral cricoarytenoid muscles, innervated by the recurrent laryngeal nerve, are responsible for vocal fold motion. The posterior cricoarytenoid muscle contracts during normal




**Figs. 78.1A and B:** The vocal cords during normal inspiration (A) and during inspiration in a patient with vocal cord dysfunction with the posterior chink highlighted by the dashed circle (B). Adapted from Patterson DL, O'Connell EJ.[5]

inspiration, resulting in vocal fold abduction and opening of the rim glottides (Fig. 78.2). During normal expiration, the lateral cricoarytenoid muscle contracts, resulting in adduction of the vocal folds and narrowing of the rim glottides. However, in PVFM there is abnormal adduction of the vocal folds during inspiration. Classically, there is adduction of the anterior two-thirds of the vocal cords with a posterior "chink", or diamond-shaped gap at the posterior aspect of the vocal folds.[4]

## Epidemiology

The prevalence of PVFM is not clearly defined. A 2.8% prevalence of PVFM was reported in a study of 1,025 patients with dyspnea.[6] However, other studies suggest that PVFM may be a common problem that is not commonly diagnosed, especially among specific subgroups of patients. A study by Morris et al. found a prevalence of 12% among a cohort of active duty military patients with shortness of breath on exertion.[7] Similarly, Abu-Hasan et al. reported an almost 10% incidence of PVFM in children with exercise-induced dyspnea.[8] Among a cohort of patients with refractory asthma, a 1995 study by the National Jewish Centre for Immunology and Respiratory Medicine found that up to 10% of patients in fact had PVFM, and another 30% of patients had both paradoxical vocal cord motion disorder (PVCM) and asthma.[9] More studies are necessary to gain a better understanding of the true incidence and prevalence of PVFM.

Among patients diagnosed with PVFM, a 2006 review found about one third of patients with PVFM reported in the literature were under the age of 18.[4] Among pediatric patients, PVCM is primarily seen among teenagers.[10] There is a 2:1 female predominance.[4]

## Etiology

Historically, PVFM was thought to be primarily a psychological phenomenon present in young women with psychiatric disorders. However, further investigation has shown that PVFM is more complex.

To date, little remains known regarding the specific pathophysiology of PVFM. There have been several proposed classification schemes,[1,11] highlighting the fact that there is not a single cause of PVFM. Christopher and Morris proposed three categories in which to classify PVFM by etiology: (1) psychogenic, (2) exertional, and (3) irritant.[12]

### *Psychogenic*

In many early reports, PVFM was attributed to a purely psychogenic cause. Terms such as "Munchausen's stridor", "psychosomatic stridor", "hysteric croup", and "emotional laryngeal wheezing" can be found throughout the literature. There is a clear association between PVFM and psychiatric diagnoses, including anxiety disorder, depression, conversion and factious disorders, personality disorders, and post-traumatic stress disorder. The rate of psychopathology among patients with PVFM ranges between studies from 30.5 to 73% of patients with PVFM.[2,9] Additionally, a history of family conflict and abuse, especially sexual abuse, is often identified among patients with PVFM.[10]

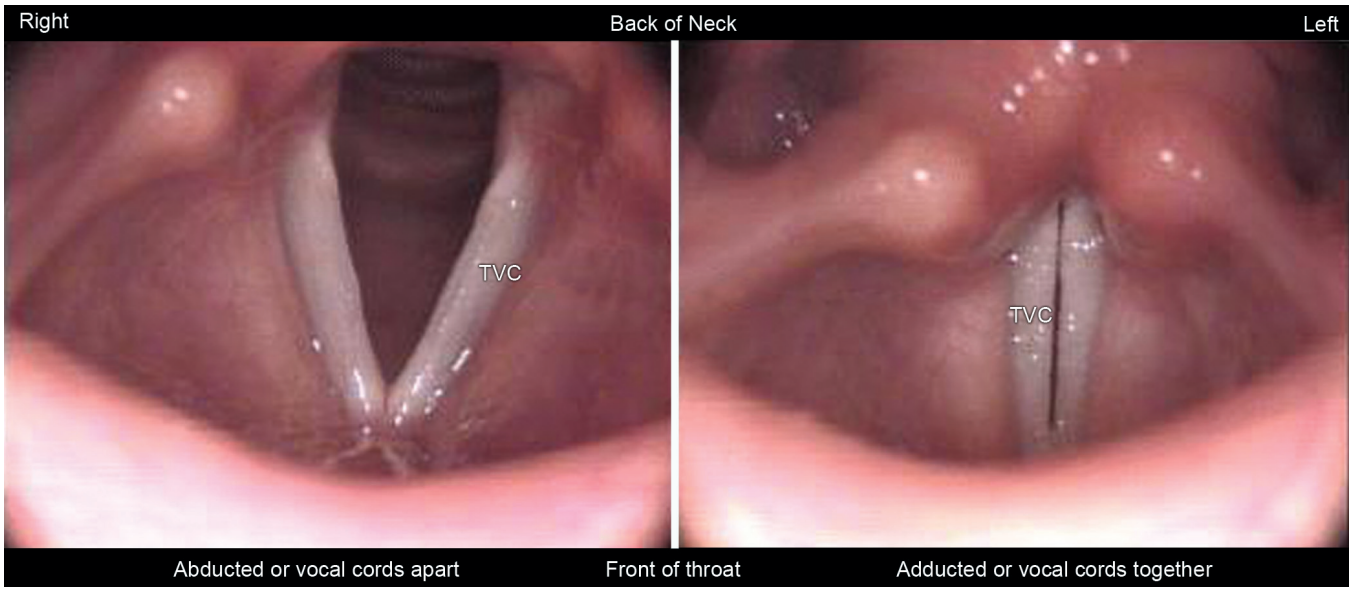



**Fig. 78.2:** Fiberoptic examination of true vocal folds during abduction and adduction. (TVC: True vocal cord).

Importantly, it is now recognized that although psychogenic factors play a definite role in the course and management of PVFM, the disorder cannot be attributed to such origins alone. Recognition of the impact of comorbid psychopathology when diagnosing and treating PVFM is an important step to successful management. Maturo and colleagues found that psychiatric treatment was especially successful in two subgroups of patients with PVFM, those who: (1) failed to improve with speech therapy and (2) experienced symptoms at rest.[2]

### *Exertional*

Approximately 18% of patients identify exercise as the trigger for PVFM.[4] Patients with exertional PVFM may be misdiagnosed with exercise-induced asthma.[7,8] However, in contrast to patients with exercise-induced asthma, patients with PVFM will not respond to bronchodilators. Patients with PVFM are often competitive athletes.[1] While prior studies have suggested that underlying psychopathology contributes to the presentation, a recent study by Tilles and colleagues found that psychiatric conditions were not more common among patients with exercise-induced PVFM.[13] The specific pathophysiology of how exercise precipitates PVFM remains unknown.

### *Irritant-Associated*

There are both intrinsic and extrinsic irritants that precipitate PVFM. Intrinsic irritants include gastroesophageal reflux, laryngopharyngeal reflux, sinusitis, and rhinitis. Extrinsic irritants include chemicals (chlorine, ammonia, cleaning supplies), foods, smoke, or other sensory irritants such as perfumes.[1] The proposed pathophysiology is that the irritant induces exaggeration of the glottic closure reflex, potentially as a protective response.[1]

When considering irritant-associated PVFM in the pediatric population, the strongest association is identified with gastroesophageal reflux disease (GERD) among infants. In a study of nine infants with documented inspiratory vocal cord adduction, eight had a history of GERD and improved with treatment.[14] For all patients with PVFM, a review of the literature found that 18% also carried the diagnosis of GERD.[4] Given this association, it is important to consider the treatment of symptomatic reflux in a patient with PVFM.

## DEFINING THE DIAGNOSIS

The diagnosis of PVFM can be established by clinical presentation and laryngoscopic evidence of vocal fold adduction. Pulmonary function testing can aid in establishing the diagnosis; however, this is not independently diagnostic. An algorithm for the evaluation and treatment of children presenting with symptoms of PVFM is shown in Flowchart 78.1.

## Symptoms/Signs

Classically, a patient with PVFM will present with shortness of breath and inspiratory stridor associated with intense emotion or during exercise. A literature review found dyspnea to be the most common symptom (73%), followed by wheeze (36%), stridor (28%), cough (25%), chest tightness (25%), throat tightness (22%), and change in voice (12%).[1] On physical examination, auscultation will reveal a high-pitched inspiratory sound localized over the trachea. Symptoms often develop rapidly and can be quite dramatic. Patients often have a history of recurrent emergency department visits and/or hospitalizations. PVFM is often misdiagnosed as asthma although patients frequently have a history of failure to respond to multiple asthma medications. Diagnosis is typically delayed, leading to unnecessary morbidity.

## Investigations

Laryngoscopy is the diagnostic studies of choice for PVFM. Pulmonary function tests are also useful in establishing the diagnosis. There is no confirmatory radiographic or laboratory study.

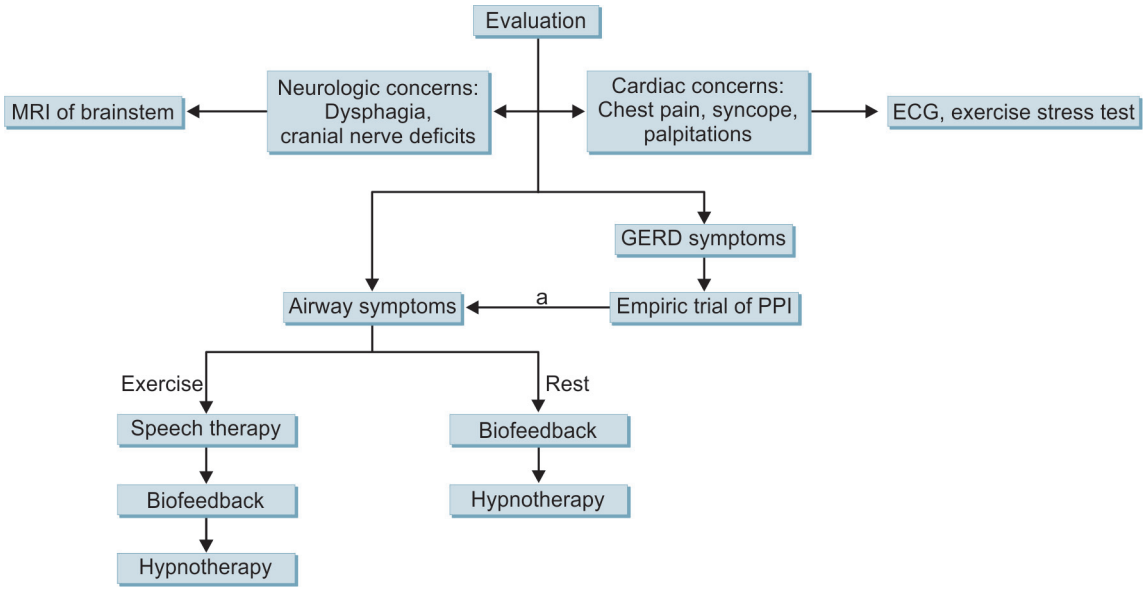
### *Otolaryngologic Findings*

In PVFM, visualization by laryngoscopy reveals adduction of the anterior two-thirds of the vocal cords on inspiration. A posterior chink is the classic finding; however, it presents in the minority of cases.[15] However, laryngoscopy will appear normal in asymptomatic patients. There are several methods that can be used to induce symptoms. These include irritants such as methacholine and histamine, exercise, and breathing maneuvers (including panting, sniffling, deep breathing, phonating, and coughing). However, despite such maneuvers classic findings cannot always be elicited among patients with PVFM.[9] Therefore, some clinicians and researchers do not consider this the gold standard for diagnosis.[2]

### *Pulmonary Function Tests*

In the symptomatic patient, spirometry will classically reveal flattening and truncation of the inspiratory

**Flowchart 78.1:** Proposed algorithm for treating children with paradoxical vocal fold motion.




(MRI: Magnetic resonance imaging; PPI: Proton pump inhibitor; GERD: Gastroesophageal reflux disease; ECG: Electrocardiogram).

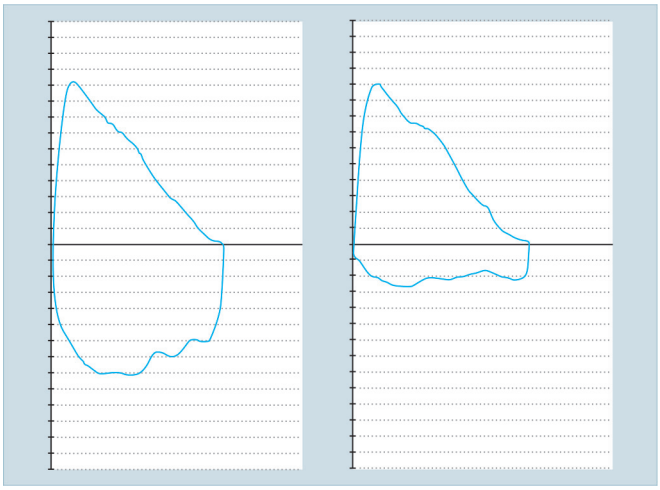


**Fig. 78.3:** Picture on the left reveals normal spirometry, while the picture on the right reveals a flattened inspiratory loop suggestive of paradoxical vocal fold motion. Adapted from Benninger C et al.[17]

flow-volume loop (Fig. 78.3). The mid-expiratory to mid-inspiratory flow ratio is elevated. The FEV1 and FVC can be reduced. Typically the FEV1/FVC ratio is normal; however, the expiratory-flow loop can have a concave appearance. It is important to recognize that this can occur even in patients without co-occurring asthma.[12] Furthermore, it is important to recognize that spirometry will be normal in the asymptomatic patient. Therefore, while spirometry is helpful in the symptomatic patient, it cannot be relied upon alone for diagnosis.

The utility of exercise testing and methacholine challenge testing (MCT) in diagnosing PVCM is unclear. One study found that patients with PVFM induced by exercise were more likely to have an elevated FEF50/FIF50 ratio following exercise in comparison to patients with exercise-induced asthma.[16] A study by Morris et al. found that 60% of patients with PVFM had inspiratory loop truncation after MCT.[7] However, other studies have found that such changes are not diagnostic of PVFM.[15] Importantly, a negative MCT is useful in suggesting that asthma is unlikely the diagnosis.

## MANAGEMENT

The first line of managing a patient with PVFM is reassurance. Although PVFM is an extremely frightening phenomenon to experience, it is relatively harmless and simple to treat. Initial treatment for PVFM is speech therapy.[17] In particular, speech therapists use laryngeal control maneuvers to control, reduce, and eliminate symptoms. These maneuvers include but are not limited to panting, pursed-lip breathing, breathing through a nose or straw, and exhaling with a hissing sound.[18] Maturo et al. looked at 59 pediatric patients in our aerodigestive clinic and revealed an overall 68% success rate in those patients

receiving speech therapy.[2] In particular, these patients had PVFM with exercise. The more common activities associated with PVFM were running, soccer, and swimming. The success rate for patients with PVFM at rest was lower, i.e., 56%. When speech therapy is not successful, psychiatric therapy is indicated. Psychiatric therapy for patients with symptoms at rest was 100% successful in our cohort.[2] Patients who received psychiatric care were more likely to have inappropriate vocal cord adduction while sitting comfortably than children who did no receive psychiatric care. The psychiatric therapies used to treat PVFM included biofeedback, hypnosis, psychotherapy, and antianxiolytics. Proton pump inhibitors were not successful in treating PVFM alone.

In conclusion, PVFM is a common entity present in children with a complaint of shortness of breath and noisy breathing. Recognizing signs and symptoms of PVFM could save a child from a lot of unnecessary tests and medications used to treat asthma. Although not foolproof, some indications that a child has PVFM and not asthma is the absence of cough, normal expiratory time, normal spirometry, or blunted inspiratory loop on pulmonary function test, and a lack of response to asthma medication. Speech therapy and possible psychiatric treatment are the main therapeutic interventions used to treat PVFM.

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CHAPTER

79

# Vocal Fold Paralysis in Children

***Marshall E Smith***

Vocal fold paralysis (VFP) is recognized as a major cause of stridor, hoarseness, and dysphagia in infants and children. It affects any or all of the normal laryngeal functions of swallowing protection, respiration, and voice production. The manifestations of VFP vary greatly with age, however. This chapter describes the various etiologies for VFP, an approach to evaluation of the child with VFP, and suggested management strategies. Unilateral and bilateral VFP are both discussed with emphasis on their differing presentations, evaluation, and treatment decisions in the pediatric patient.

The entity of VFP may be more descriptively termed as "impaired vocal fold mobility".[1] Sometimes the terms "adductor paralysis" or "abductor paralysis" have been used to describe impaired glottal movement. The term "paresis" is also used to describe reduced mobility, without complete immobility. There is a spectrum of vocal fold motion impairment. The term "paralysis" implies a complete lower motor neuron dysfunction, but in practice there is often motion impairment without complete flaccidity or denervation.[2] Some adductor movement may be seen even though abductor movement is impaired. Dysfunctional innervation of the immobile "paralyzed" vocal fold, rather than complete denervation, is likely responsible for the spectrum of observations regarding laryngeal movement in VFP.[3]

## EPIDEMIOLOGY

Over five hundred cases of pediatric VFP have been tabulated in many reports.[4–17] Several patterns emerge from these cases. Bilateral VFP is more commonly seen in neonates, whereas unilateral VFP is seen more commonly in older children.

VFP, unilateral or bilateral, accounts for approximately 10% of all congenital laryngeal lesions.[5] It is second in frequency only to laryngomalacia as a cause of neonatal stridor.[7] Due to difficulties in making the diagnosis, the previously reported incidence of VFP in the literature may not represent the true number of children with it. Now, flexible laryngoscopy and improved anesthetic techniques allow otolaryngologists to make this diagnosis more accurately. With these technical advances and improved infant survival rates, the actual incidence of VFP may need to be re-examined. VFP manifests early in life and is without gender predilection.[7,11,13] In 1953, Clerf reviewed a series of 293 patients with unilateral VFP; in 10% the onset of the condition was congenital.[18] Goff analyzed 229 cases of VFP in 1979. He was the first to divide the etiology of VFP into congenital and acquired.[12] The majority of VFP is recognized before the age of 2.[7] Cohen et al. reported 100 children with VFP, 58% of whom presented within the first 12 h of birth.[11]

In the newborn or infant age group, unilateral or bilateral VFP can be only one manifestation of a multisystem anomaly. Although most frequently associated with central nervous system (CNS) malformations, VFP can be seen in conjunction with other congenital anomalies such as cardiovascular or pulmonary malformations.[19] A higher incidence of other associated laryngeal malformations, such as clefts or stenosis, also has been reported.[5,7,20] At an individual center, the volume of pediatric cardiothoracic surgery will affect the frequency of unilateral VFP, while the occurrence of bilateral VFP should be fairly consistent.

## ETIOLOGY

It is important to recognize that VFP is a sign or physical finding, not a diagnosis. A thorough search for the underlying cause is essential in each case. Children are subject to some of the same causes of VFP as adults, namely, surgical trauma and neoplasms. However, these are not necessarily the most common causes in children. An idiopathic or a neurologic etiology remains the most common factor in children.[13] Traditionally, VFP in children has been divided into two broad categories: congenital and acquired. Each group accounts for approximately one half of the cases.[13,19,20] Table 79.1 summarizes the etiologies of VFP.

### Central Nervous System

CNS anomalies are implicated in pediatric VFP in 25–35% of cases.[13,14,21] CNS involvement is almost always the result of brainstem pathology. Supranuclear etiologies are rare causes of VFP because of the extensive interhemispheric connections of the laryngeal efferent neural pathways.

The most common CNS congenital anomaly that is implicated in VFP is the Arnold-Chiari malformation (ACM). Typically, it is associated with bilateral VFP. Some physicians feel that any infant born with an ACM and high-pitch, inspiratory stridor has bilateral VFP until proven otherwise.[21]

There are two forms of ACM. *Type 1 ACM* involves an isolated caudal displacement of the cerebellum without an associated meningomyelocele. *Type 2 ACM,* which often is associated with a meningomyelocele, manifests caudal displacement of the cerebellum and brainstem. Although both types are associated with VFP, type 2 is implicated more commonly.[22–24] The pathogenesis of bilateral VFP in ACM patients is thought to be secondary to traction on the vagus nerve by caudal displacement of the cerebellum and/or brainstem (although many physicians indicate that this is an oversimplification of what is probably a complex, multifactorial process).[4,25–27] The complex nature of the respiratory problems in ACM patients cannot be overemphasized. These children often have concomitant central respiratory dysfunction and may continue to experience respiratory difficulties even after tracheotomy is performed.[13]

Less frequent CNS causes of VFP include leukodystrophy, encephalocele, hydrocephalus, and cerebral or nuclear dysgenesis.[4,14,27–30] Central neural degenerative diseases, such as syringomyelia or syringobulbia, can be associated with bilateral VFP.[29,30] Amyotrophic lateral sclerosis (ALS), occasionally presenting in the second decade

**Table 79.1:** Etiologies of laryngeal paralysis in infants and children

- I. Congenital
  - A. Central nervous system
    - a. Cerebral agenesis
    - b. Hydrocephalus
    - c. Encephalocele
    - d. Meningomyelocele
    - e. Meningocele
    - f. Arnold-Chiari malformation
    - g. Nucleus ambiguous dysgenesis
  - B. Peripheral nervous system
    - a. Congenital myasthenia gravis
    - b. Skull base platybasia
  - C. Cardiovascular anomalies
    - a. Cardiomegaly
      - i. Interventricular septal defect
      - ii. Tetralogy of Fallot
    - b. Abnormal great vessels
      - i. Vascular ring
      - ii. Dilated aorta
      - iii. Double aortic arch
      - iv. Patent ductus arteriosus
      - v. Transposition of the great vessels
  - D. Associated with other congenital anomalies
    - a. Bronchogenic cyst
    - b. Esophageal cyst, duplication, atresia
    - c. Cricopharyngeal stenosis
- II. Inherited
  - A. Genetic
    - a. Autosomal dominant
    - b. Autosomal recessive
    - c. X-linked
    - d. Isolated mutation
  - B. Associated neurologic disease
    - a. Charcot-Marie-Tooth disease
- III. Acquired
  - A. Trauma
    - a. Birth injury
    - b. Postsurgical correction of cardiovascular or esophageal abnormalities
    - c. Vagal nerve stimulator
    - d. Foreign body ingestion
  - B. Infections
    - a. Pertussis encephalitis
    - b. Polyneuritis
    - c. Polioencephalitis
    - d. Diphtheria
    - e. Rabies
    - f. Syphilis
    - g. Tetanus
    - h. Botulism
    - i. Tuberculosis
    - j. Guillain–Barré syndrome
  - C. Neurotoxicity
    - a. Vincristine

of life, also may manifest as unilateral or bilateral vocal fold involvement.[20] Neural injury secondary to perinatal hypoxia also must be considered as a cause of VFP. Rarely, bilateral VFP has been attributed to a cortical stroke.[31]

## Peripheral Nervous System

Peripheral neuropathic and progressive neurologic disorders also may affect vocal fold function in children. Myasthenia gravis, although usually a disorder of young adults, can affect infants and children and cause stridor or dysphonia.[32,33] Vocal fold involvement can be a rare manifestation of myasthenia gravis. However, when this occurs, there is usually bilateral vocal fold immobility.[20,34] Myotonic dystrophy, Werdnig-Hoffman disease (i.e. infantile muscular atrophy), benign congenital hypotonia, facioscapulohumeral dystrophy, spinal muscular atrophy, and Charcot-Marie-Tooth (CMT) disease all have been implicated in pediatric VFP.[7,20,34] CMT disease (or hereditary motor and sensory neuropathy) is an inherited condition and is the most commonly described disorder.[35–38] The onset can occur in infancy or later childhood. There are several subtypes based on the spectrum of involved symptoms. Though CMT type 2, especially CMT-2C is particularly associated with laryngeal paralysis, it is also seen in type 1.[35,39] Several genetic mutations have been recently identified in both CMT 1 and CMT-2C.[40,41] This condition persists into adulthood.

## Trauma

Direct or surgical trauma to the vagus or recurrent laryngeal nerve (RLN) is a common cause of VFP in children. Surgical trauma involving the vagus nerve and its branches is most common after thoracic surgical procedures that involve the heart or great vessels.[4,9] Zbar and Smith reported a frequency of 8.8% of left VFP after patent ductus arteriosus ligation.[19] Recent series indicate that this percentage is much higher in small infants. A large case series where all PDA-ligated newborns underwent screening flexible laryngoscopy found a 25% incidence of VFP in infants who weighed 1150 gm or less at the time of PDA ligation.[42] Any surgical procedure that comes in proximity to the vagus or RLNs may cause VFP. Traumatic VFP is usually unilateral, although unilateral and bilateral VFP may occur following tracheoesophageal fistula repair.[11] Central venous catheter or ECMO catheter placement may also cause VFP. Posterior fossa trauma, as well as closed head injuries, also are known causes of bilateral VFP.[43,44] VFP after vagal nerve stimulator implant,[45] esophageal foreign body ingestion,[46] and cricopharyngeal stenosis[47] have been reported.

Trauma from instrumentation of the larynx and hypopharynx can cause transient or permanent VFP. Unilateral and bilateral VFP is a well-documented complication of endotracheal intubation; it usually is associated with cuffed endotracheal tubes in adults.[48–50] In a large series of over 31,000 patients who underwent intubation for surgery, no patient under 20 years of age developed VFP, and only 4 of the 24 patients were under 50 years of age.[51] Transient bilateral VFP after laryngeal mask airway (LMA) insertion has been reported.[52]

Birth trauma, which is often associated with unilateral paralysis, may be a potential source of injury. A history of difficult delivery, forced traction, or neck torsion during delivery have been implicated in VFP.[7,11] Abnormal cervical traction due to unusual intrauterine positioning is another possible etiologic factor.

## Neoplasia

Tumors and congenital neoplasms of the skull base, neck, or mediastinum are a less common source of VFP in children. Unilateral VFP is more common when a neoplasm is the underlying cause, although bilateral VFP also has been reported.[7] In these situations, the VFP is a slow, progressive process that initially affects one side. Thyroid malignancy and benign thyroid hyperplasia can affect vocal fold function, but these are rare in children.[53]

## Inflammatory Causes

Viral, bacterial, and granulomatous conditions have been implicated in pediatric VFP. Various encephalopathies (e.g. Reye's syndrome), poliomyelitis, diphtheria, rabies, tetanus, syphilis, and botulism have been reported as causing VFP in children.[5,7,17,54,55] Fortunately, many of these diseases are rare today because of the use of antibiotics and immunization programs. Guillain–Barré syndrome continues to be associated with pediatric VFP. This demyelinating neuropathy rarely affects laryngeal function, but may involve both vocal folds.[56]

## Cardiovascular Anomalies

Congenital anomalies of the cardiovascular system frequently are associated with VFP. Left VFP is more common than right VFP. Because of its longer course and closer

proximity to the heart, the left recurrent nerve is more vulnerable than the right in cases of congenital heart disease or cardiac surgery. Ventricular septal defect, tetralogy of Fallot, and cardiomegaly have been associated with VFP. Abnormalities of the great vessels including vascular rings, double aortic arch, and patent ductus arteriosus all have been implicated in laryngeal paralysis.[5,7] It is also termed the cardiovocal or "Ortner" syndrome of infancy.[57–60] Dilation of the pulmonary artery with compression against the RLN from pulmonary hypertension has been implicated as the cause of this condition.

### Metabolic and Toxic Causes

Unilateral and bilateral VFP have been reported in association with hypokalemia and organophosphate poisoning.[61,62] Vincristine-induced VFP has been well documented. The paralysis is dose-related and resolves slowly over a 4- to 8-week period after discontinuing the medication.[63–65]

### Genetic Causes

Although rare, a familial pattern of VFP can occur. In the first report by Plott in 1964, congenital laryngeal abductor paralysis was found in three brothers, who also had mental retardation.[66] Inheritance was found to be X-linked recessive. Subsequent reports have substantiated this observation but with different variations. An article by Raza et al. summarized 21 reports of familial VFP.[67] Though there is a spectrum of associated findings, several themes are present. It usually presents with stridor or respiratory distress after birth or in childhood and is usually described as an abductor paralysis, though it has also been reported as adductor paralysis[68] or to have onset in adulthood.[69] There may be associated neurological delays.[66,70–73] The inheritance of this condition has most frequently been found to be autosomal dominant.[68,74–76] Gene linkage analysis of one family with this disorder localized to chromosome 6q16.[77] Autosomal dominant mode of inheritance in three generations was observed in the family of a patient cared for by the author (personal observation). In the 21 reports summarized by Raza et al., 9 were autosomal dominant, 2 were X-linked recessive[66,70], 3 were X-linked or autosomal dominant[75,78,79], 3 were autosomal recessive[67,78,80], 1 was a single mutant gene, and 4 were unknown. Though the condition is unusual, study of these cases may further elucidate the neural development of the larynx.[71] Congenital bilateral adductor VFP has been reported to occur with Robinow or 22q11 deletion syndromes.[81] These cases are managed along the same lines as patients with VFP due to other causes. Because there is a tendency toward spontaneous improvement in laryngeal function, a conservative approach is advised.[67]

### Idiopathic Causes

In many studies, idiopathic paralysis ranks as the first or second most common cause of VFP in children, accounting for 36–47% of the cases in a variety of series.[9,11,14] Idiopathic VFP may represent a viral neuropathy similar to Bell's palsy or sudden sensorineural hearing loss (SNHL); however, such a link remains difficult to prove.

## SIGNS AND SYMPTOMS

Any or all of the normal laryngeal functions (i.e. voice, respiration, or deglutition) may be abnormal in the pediatric patient with VFP. The signs and symptoms may be subtle, going unnoticed for months or being attributed to recurrent croup or asthma.[82] The most common manifestation of unilateral or bilateral VFP in children is stridor.[7,11,13,14,19] Ineffective cough, aspiration, recurrent pneumonia, reactive airway disease, and feeding difficulties can be associated with unilateral or bilateral VFP. Respiratory distress is more severe in cases of bilateral VFP. Consistent stridor, cyanosis, and apnea are frequent findings in these cases. Voice and cry may, in fact, be fairly normal in children with bilateral VFP. Children with unilateral VFP frequently have changes in phonation, with hoarseness in speaking voice, a soft voice with reduced volume, inability to yell or scream loudly, or an abnormal cry.[13]

## DIAGNOSTIC EVALUATION

The evaluation of a child with suspected VFP begins with a thorough history and physical examination. This examination includes a description of the quality of the voice or cry, the presence and severity of the stridor, and any associated feeding difficulties. A weak cough or a history of aspiration or recurrent pneumonia, or coughing during feedings can be additional clues that point toward the larynx as a source of the child's problems. Any history of surgical or accidental trauma, including birth and surgical procedures involving the posterior fossa, thorax, or neck, must be elicited. Associated medical conditions or congenital anomalies, such as neurologic disorders or congenital heart disease, must be investigated. The initial physical examination centers on a survey of the stigmata of associated congenital anomalies. Associated findings

pertinent to the severity or degree of the respiratory compromise, such as intercostal retractions and respiratory rate, should be documented.

Various methods have been used and reported in the literature to document VFP. Methods such as cinefluoroscopic examination, ultrasound, pulmonary function tests, and direct laryngoscopy under general anesthesia were frequently used to evaluate laryngeal function in children.[5,7,13,21,71,80,82–84] For a variety of reasons, these methods have proven unsatisfactory, though laryngeal ultrasound has the most appeal as an adjunctive measure.[85] During visualization of the vocal folds, rigid laryngoscopy may result in distortion of the larynx due to poor placement of the metal blade. This technique may lead to a misdiagnosis of VFP.[13,21,84] The depth of anesthesia also affects vocal fold mobility, so this may also confound the diagnosis.

Vocal fold mobility is optimally assessed in the awake patient. With the introduction and wide availability of flexible endoscopic equipment, flexible laryngoscopy in the awake patient has become the standard procedure for diagnosis of pediatric VFP. The vast majority of children with VFP are diagnosed accurately using this technique alone.[13] Nevertheless, flexible laryngoscopy can be challenging in the very young child with copious secretions, rapid respiration, narrowed epiglottis, or anterior-appearing larynx. In such cases, there may be a role for some of the previously mentioned techniques. When a child is taken to the operating room for a comprehensive airway examination, flexible laryngoscopy can be performed first with the child awake, before the anesthesia is administered. These findings can then be compared with observations under anesthesia.

Flexible laryngoscopy has several advantages over other methods of laryngeal evaluation in the pediatric patient. Flexible nasopharyngoscopy provides a dynamic view of the upper respiratory tract with minimal distortion. Other advantages of flexible laryngoscopy include the fact that it is a relatively safe and well tolerated in all age groups. Flexible nasopharyngoscopy also can be performed at the bedside or in the office setting and does not require a general anesthetic. Flexible laryngoscopes may not always pass easily through the nose, and so the examination can be done via the peroral route, if needed.[86]

The clinical findings of VFP obligate the otolaryngologist to search for an underlying cause. In neonates, infants, and young children with suspected VFP, the focus and workup differs from that required for adults. The focus of anatomic etiologies in children is on the brainstem and mediastinum as well as any potential etiologic factors elicited in the initial history and physical examination.[21] For cases in which the etiology is not apparent, the entire course of the vagus and RLNs should be imaged. Computerized tomography (CT) is preferable for imaging the neck and chest/mediastinum. Magnetic resonance imaging (MRI) is preferred for the brain, brainstem, and skull base. These imaging studies may demonstrate congenital anomalies of the brainstem, such as ACM, or of the mediastinum.

Swallow function studies and cinefluoroscopy remain important components in the evaluation of children with VFP. These studies are important for two reasons: first, swallow function studies can provide evidence of subtle neurologic disorders that are associated with an abnormal swallowing mechanism and that also may be related to abnormal vocal fold function[21]; and second, a barium swallow may provide valuable information about the afferent laryngeal nerve input, revealing evidence of laryngeal penetration of barium or aspiration. Additionally, a barium swallow may identify an associated mediastinal anomaly, such as a vascular ring. Swallowing studies may also be performed with the flexible laryngoscope, called the functional endoscopic evaluation of swallow (FEES). Advantages include the lack of exposure to radiation, ability to perform a longer examination with multiple food consistencies, and a test of laryngeal sensation by palpation with the tip of the fiberscope or air pressure testing.

Although flexible laryngoscopy has become invaluable in the diagnosis of pediatric VFP, rigid laryngoscopy and bronchoscopy in the operating room continue to play a significant role in the identification of associated airway anomalies and unknown etiologies of VFP after noninvasive workup has been completed. The diagnosis of idiopathic VFP requires the exclusion of underlying systematic conditions, occult neoplasm, or associated anomalies. This is usually done with imaging studies. An uncomplicated (no serious airway obstruction symptoms) case of clearly diagnosed unilateral VFP by flexible laryngoscopy does not generally require a subsequent examination under general anesthesia. Bilateral VFP, or complicated cases when other airway pathology is suspected, requires an evaluation of the airway in the operating room. This includes palpation of the arytenoid to rule out cricoarytenoid fixation. Direct laryngoscopy is critical in cases involving endolaryngeal trauma or endotracheal intubation. It is necessary to rule

out cricoarytenoid fixation or posterior glottic stenosis, both of which can mimic VFP. Direct laryngoscopy allows close visual inspection and palpation of the arytenoid cartilage and the posterior glottis. This examination can best be performed under general anesthesia with spontaneous ventilation.[13,21,84] Appropriate anesthetic technique is critical in order to allow complete assessment of the child's airway.

In difficult cases, confirmation of unilateral or bilateral VFP may require laryngeal electromyography (EMG). In contrast to adults, this diagnostic procedure in children usually is performed under a general anesthetic at the time of the endoscopy (Fig. 79.1). There are several reports of laryngeal EMG in children.[87–94] While it does not appear to have much utility in prognostic assessment of congenital VFP,[91,92] it has been helpful in selected cases of new onset paralysis, tumors affecting laryngeal nerves, or decannulation decisions.[92] Combining laryngeal EMG with simultaneous recording of chest wall excursion and intercostal muscle EMG to synchronize with respiration is suggested for bilateral VFP paralysis cases.[87] It has also been used in intraoperative monitoring during thyroidectomy or other neck procedures in children[95] or videothoracoscopic patent ductus arteriosus ligation.[96]

## MANAGEMENT

Factors that must be considered in management decisions include etiology of the paralysis, prognosis for recovery, unilateral or bilateral involvement, and the severity of symptoms or associated conditions. These factors must be evaluated in conjunction with the goals of any intervention. Treatment goals in children with VFP include (1) establishing and maintaining a safe and stable airway; (2) obtaining or preserving intelligible speech; and (3) swallowing without aspiration.

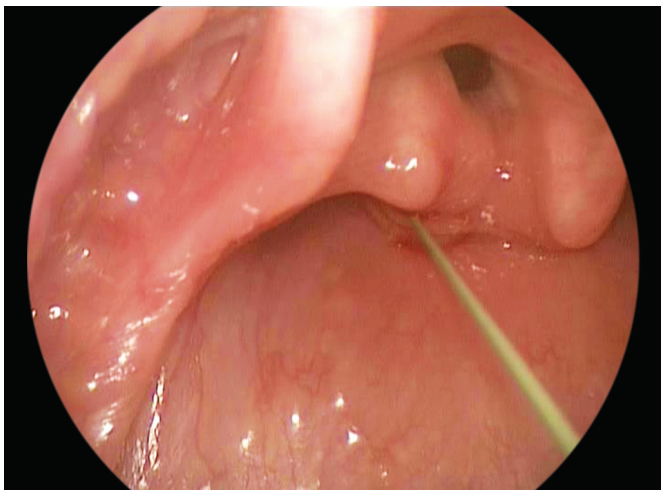

**Fig. 79.1:** Laryngeal electromyography during microlaryngoscopy with insertion of needle electrode in the left posterior cricoarytenoid muscle.

Management strategies vary depending on the child's underlying condition. A global assessment of the child is essential. For example, a child with a progressive neuromuscular disease has little potential for recovery from the paralysis. In other cases with a treatable condition, the VFP is potentially reversible. A well-known example is the timely treatment of ACM or the decompression of hydrocephalus.[5,7,9,21] Many authors suggest that children with a meningomyelocele, ACM, and bilateral VFP not undergo an invasive airway procedure, such as tracheotomy, until a ventriculoperitoneal shunt or posterior fossa decompression procedure is performed.[11,19,21,97] Grundfast and Harley stress that for cases with favorable potential for airway improvement and recovery of vocal fold movement, the airway should be secured and supported for at least 4 weeks prior to considering tracheostomy.[21]

The reported rate of recovery of unilateral VFP or bilateral VFP varies within the literature from 16% to 64%.[7,11,13,14,19] Recovery has been noted from 6 weeks to 5 years after the initial diagnosis.[7,11,13,14,19] In the management of children, observation for at least one year, and probably longer, is prudent before any decision is made concerning irreversible laryngeal procedures. It is important to recognize that recovery of neuromotor function (vocal fold movement) does not always correlate with recovery of laryngeal function (phonation, airway, swallowing).[98] Patients accommodate to VFP and can recover voice, maintain airway and swallowing protection to a remarkable degree. Partial reinnervation, synkinetic reinnervation, compensatory cross-innervation, or other individual factors may be responsible. Attention is paid to each patient and how they manage each function in which the larynx plays a role.

### Bilateral VFP

The skill and judgment of the pediatric otolaryngologist is crucial in management of an infant with bilateral VFP. The airway can be markedly compromised, usually resulting in stridor and respiratory distress. The main issue involves the decision regarding tracheostomy placement. Table 79.2 reveals that in earlier studies the practice was to perform a tracheostomy in most cases of bilateral VFP. However, many infants with bilateral VFP have been managed without a

**Table 79.2:** Frequency of tracheostomy in several published case series of infant vocal fold paralysis

| *Authors* | *Bilateral* | *Unilateral* |
|---|---|---|
| Holinger and Brown[10] | 36/56 | 3/28 |
| Cohen et al.[11] | 45/62 | 0/38 |
| Swift and Rogers[6] | 7/13 | |
| Rosin et al.[13] | 19/29 | 8/22 |
| Murty et al.[8] | 0/11 | |
| Zbar and Smith[9] | 0/4 | 0/13 |
| de Gaudemar et al.[14] | 10/52 | 0/61 |
| Daya et al.[15] | 28/49 | 7/53 |
| Average | 145/276 (53%) | 18/215 (8%) |

tracheostomy. This includes a surprising 11 of 11 patients reported by Murry et al.[8] and 4 of 4 patients reported by Zbar and Smith.[9] In these studies, all patients had eventual recovery of vocal fold movement at 5–26 months. Improvements in neonatal care, the assessment and monitoring of apnea, and use of nasal CPAP or high-flow air by nasal cannula to "buy time" may be responsible for this. In order to make the decision regarding tracheostomy, the otolaryngologist needs to fully evaluate the cause of the VFP, assess the infant for sleep apnea, lung disease of prematurity, gastroesophageal reflux, neurologic status, and swallowing function, as well as the severity of airway obstruction and work of breathing. All these factors influence the airway management decisions. For example, the bilateral VFP patient found to have hydrocephalus and Chiari malformation who receives a ventriculoperitoneal shunt may be observed to see if the relief of brainstem compression improves laryngeal nerve function and vocal fold mobility.[26] Bilateral VFP patients from traumatic forceps delivery with neck stretching may also be observed as this neuropraxic injury often recovers. Infants with more profound central neurologic injury may be less likely to recover quickly. However, long-term recovery has been described in these patients, even up to 11 years after diagnosis.[15]

The evaluation of these cases usually involves sleep apnea studies, neurological assessment and imaging studies, tests for gastroesophageal reflux, and swallowing studies (by radiography or videoendoscopy). Swallowing studies are especially important in the assessment of the infant with bilateral VFP. The act of swallowing becomes an additional stress on the airway in infants who share the pharynx for both functions. For some infants, oxygen desaturation and obstruction may become symptomatic with oral feedings. Nasogastric to gastrostomy tube feedings are necessary for a period of time while observing for clinical improvement in vocal fold mobility and stridor symptoms.

Tracheostomy remains a safe surgical management step for the treatment of pediatric bilateral VFP. It is a potentially reversible procedure, allowing time for possible spontaneous laryngeal recovery. It also maintains a stable airway that affords an unobstructed view of the larynx for sequential re-evaluation of vocal fold function. Once a tracheostomy is performed, repeat examinations are necessary to detect spontaneous return of laryngeal function or to plan further intervention. Serial endoscopic examination of these patients should be performed to detect return of laryngeal function. Because of the various factors involved (including the variable time interval for spontaneous recovery) the length of follow-up required before further surgical intervention is considered in children is difficult to determine. Approximately 50% of children that need a tracheostomy for VFP require it to be in place for > 3 years.[7,8] Most physicians recommend waiting several years before an irreversible lateralization procedure is attempted.[11,13] A recent report argued for an even longer interval. In Berkowitz' report of three patients with bilateral VFP and tracheostomy, with time and growth two were decannulated without other procedures after 5 years of age, and the third patient was 4 years old and had minimal vocal fold abduction.[99] Even without vocal fold abduction, growth of the larynx may increase glottic dimensions sufficient to allow the child to have an adequate airway after the first 5 years of life, though some exertional dyspnea may persist.

Children with bilateral VFP and a tracheostomy have several options for surgical procedures to facilitate decannulation. There is no consensus regarding the age at which to pursue these. Because of reports of long-term (> 3 years) recovery of vocal fold movement in some patients,[15,99] the argument to wait is compelling, especially if the etiology of the VFP is central neurologic injury. However, this is not true for unrecovered peripheral nerve injuries from trauma or surgery. Daya et al. reported that iatrogenic VFP had the lowest rate of spontaneous recovery (46%).[15] The child with a tracheostomy from bilateral VFP can usually acquire speech by means of a speaking valve or by covering the tracheotomy tube with their chin. Removal of the tracheostomy is often desirable before children start attending school. Some parents, however, may choose to keep the tracheostomy to not impair vocal function.

As the parent understands the trade-offs involved with potential to sacrifice of the child's voice and possibly swallowing function for an improved airway, there are a many surgical options to increase airway patency and facilitate decannulation. They may be divided into "static" procedures and "dynamic" procedures. Static procedures involve *tissue removal* (e.g. posterior cordotomy,[100] arytenoidectomy[16]) and *laryngeal framework modification* to enlarge the airway (e.g. lateralization,[101] posterior cricoid graft[1,102,103]). Dynamic procedures include *laryngeal reanimation procedures* (e.g. reinnervation by nerve-muscle pedicle (NMP), neurorrhaphy, direct nerve implant), and *functional electrical stimulation*.

## Static Procedures

*Static procedures* improve airway patency by enlarging the glottic aperture. This can be accomplished either by excising laryngeal tissue (vocal fold and/or the arytenoid cartilage) or by fixation techniques that rely on mechanical lateralization of the vocal fold. Static techniques often employ both tissue removal and mechanical lateralization methods simultaneously, as in the Woodman procedure.[104] Surgical widening of the glottis to increase airway patency must necessarily impair glottal closure to create some degree of breathy dysphonia and possible aspiration. The parents must be made fully aware of this trade-off prior to consenting their child for surgery. In adults, cordectomy or arytenoidectomy may be performed through various external approaches, including a lateral cervical approach, translaryngeal approach, or laryngofissure.[104–108] The *Woodman procedure,* first introduced in 1946, was the culmination of the extralaryngeal approach to bilateral VFP.[104] A modification of the King technique,[109] it included removal of a portion of the arytenoid with suture anchorage of the posterior vocal fold to the inferior cornu of the thyroid cartilage.[55] By the 1950s, the Woodman procedure had become the most common operation for bilateral VFP in adults and was performed occasionally in children.[110,111] The external approach in children or adults is technically more difficult, but similar to arytenoid adduction laryngoplasty. It requires precise suture placement and can be complicated by excessive scar tissue formation. A variation of this approach that stays extramucosal, called arytenoid abduction laryngoplasty, has also been recently described by Woodson.[112] Scar tissue formation can be a significant concern in the pediatric airway because of the smaller glottic dimensions. The studies that advocate endoscopic laser techniques report that external lateralization techniques are associated with a 20–40% decannulation failure rate.[113–115]

The carbon dioxide ($CO_2$) laser was introduced for the endolaryngeal management of bilateral VFP by Eskew and Bailey in 1983.[113] Using a canine model, they found that the laser provided an easy and safe method of enlarging the glottic lumen. Ossoff et al. were the first to report the clinical application of this technique.[116] Successful decannulation was reported in 10 of 11 adult patients with bilateral VFP. Objective documentation of voice outcomes in these reports is generally lacking. A more recent approach to the endoscopic restoration of an adequate airway is *endolaryngeal laser partial cordectomy with or without arytenoidectomy*. Various methods have been described with results similar to that accomplished with laser arytenoidectomy.[117–119] Eckel et al. prospectively compared 18 adults undergoing laser subtotal cordectomy to 10 adults undergoing laser arytenoidectomy, and comparison of decannulation rate, phonation, and respiratory function between these groups showed that both methods were equally effective and reliable.[119] The arytenoidectomy group had more problems with aspiration. Voice outcomes were variable between the groups.

The results are less clear when this method is used in children.[14,21,120] One major problem is the size constraint of the pediatric larynx relative to the adult larynx. It can be difficult to determine the proper balance between airway patency and voice issues in children. Ossoff et al. noted a higher rate of late failures in children compared to adults because of scar tissue formation and the smaller glottic diameter in children.[114]

Modifications of this the endoscopic approach with less tissue excision involve *endolaryngeal vocal process resection and posterior cordotomy.* First described in children by Bigenzahn and Hoefler,[120] the vocal process of the arytenoid cartilage is vaporized, creating a posterior-glottic triangular defect and separation of the vocal fold from the arytenoid cartilage. After wound healing, the glottic airway becomes enlarged. Bilateral procedures also can be performed. This procedure or variations of it have been reported in several pediatric case series.[121]

Bilateral VFP has also been treated with posterior cricoid cartilage graft placement. Also termed "arytenoid separation", this widens the posterior glottis to increase the airway. It is felt to be preferable when there is some adductor vocal fold movement observed but no abductor movement, and the child has no aspiration symptoms.[1,103,122]

The potential for detrimental phonatory effects on swallowing and phonation of posterior graft laryngoplasty are being more extensively documented.[123]

Some comparative studies on outcomes of the above static procedures have been reported. Bower et al. reviewed the surgical treatment results of 30 children with bilateral VFP.[124] Nineteen children underwent open arytenoidectomy via laryngofissure, 12 children had laser arytenoidectomy, and 1 child underwent a Woodman procedure. Decannulation was successful in 84% of the children after an open laryngeal approach compared with 56% of those undergoing laser arytenoidectomy. No significant difference in voice quality was noted between groups and aspiration was not encountered. Brigger and Hartnick reviewed the results of several studies including 55 children treated with various endoscopic and open procedures described above for bilateral VFP. They concluded that a combination of anterior laryngofissure, arytenoidopexy and vocal fold suture lateralization was the most reliably successful.[125] All these studies use tracheostomy decannulation as a standard outcome measure. No reports have specifically addressed the effects of these procedures on the voice in a rigorous manner, in children or adults.[126] However, they have an expected effect on vocal function: creating a larger glottal airway necessarily creates a degree of glottal insufficiency for phonation, with consequent reduction in volume and a breathy voice quality.

## *Laryngeal Reinnervation*

*Reanimation techniques for bilateral VFP*: Extralaryngeal and endolaryngeal approaches have established success rates in decannulation, albeit at the expense of swallowing and phonation, whose outcomes have not been adequately studied. Laryngeal reinnervation has been considered the ideal form of rehabilitation for bilateral VFP to reanimate the vocal folds. Specifically, the goal is restoration of both abductory movement of the vocal folds to create a patent airway during inspiration and adductory movement to protect the airway for swallowing and facilitate phonation. Because there are no mucosal incisions or disruption of the laryngeal framework, the risk of scarring is reduced, which should improve swallowing and voice outcomes. Methods that have been described include phrenic nerve to RLN anastomosis, phrenic nerve to posterior cricoarytenoid muscle, and omohyoid NMPs.[127,128] Tucker studied laryngeal reinnervation by ansa cervicalis NMP transfer to the posterior cricoarytenoid muscle. He reported a 50% decannulation rate in children with this procedure in 9 of 18 tracheotomized children under 5 years of age.[129] A recent study at another institution of six children with bilateral VFP treated with this procedure also reported a 50% decannulation rate.[130] Two of the three failures were felt in retrospect to have impaired cricoarytenoid mobility that would have been a contraindication for the procedure. In the future, laryngeal pacing may add to the options for these patients.[131] Based on comparative studies, NMP is felt to be the least effective technique of reinnervation.[132] Other techniques include selective reinnervation of the adductor or abductor branches of the RLN, or direct implantation of nerve graft to the target muscles. Reinnervation techniques continue to be studied in treatment of bilateral VFP in children. J.P. Marie has pioneered laryngeal reinnervation for abductor laryngeal paralysis using the following technique: an upper phrenic nerve root via an interposition graft of the greater auricular nerve (GAN) is implanted directly into the PCA muscles bilaterally. Additionally, the adductor laryngeal branch is anastomosed to the nerve of the thyrohyoid muscle (branch along the hypoglossal nerve) bilaterally via GAN interposition grafts.[133] Results in three children were recently described: two under 3 years of age with congenital bilateral VFP and a 17 years old with postsurgical bilateral VFP from lymphangioma excision. The adolescent recovered bilateral inspiratory laryngeal abduction, was decannulated, had an excellent voice, and was able to play rugby 3 days a week. One younger child's results are also reported. The airway markedly improved but residual stridor was present with intensive exertion.

## *Laryngeal Chemodenervation*

We have treated 10 bilateral VFP pediatric patients at our institution over 10 years with vocal fold botulinum toxin A injections to avoid tracheostomy, facilitate tracheostomy decannulation, or maintain tracheostomy decannulation.[134] Although 4 of the 10 required a tracheostomy or could not be decannulated, the procedure had clinical benefit in the others. Five of the patients continued to receive injections every 6–12 months as stridor recurred. This idea is not new; Cohen et al. in the late 1980s reported canine experiments on augmentation of the airway through chemodenervation, targeting the cricothyroid muscles.[135,136] Our experience has found thyroarytenoid muscle injections to be more effective than cricothyroid for airway augmentation. Favorable candidates include those with marginal airways attempting decannulation, or

those with exertional stridor after decannulation. The disadvantage of this approach is the temporary effect of botulinum toxin, which requires retreatment.

## Unilateral VFP

While pediatric otolaryngologists generally believe that infants adjust well to persistent, unilateral VFP with little sequelae, there is limited data to support this assertion. Unilateral VFP usually results in a weakened cry, but generally it is assumed that these children are able to maintain an adequate airway and safe swallowing. Additional stresses such as prematurity, trauma, vigorous activity, or an upper respiratory infection may not be as well tolerated. An example population includes newborns that undergo patent ductus arteriosum (PDA) ligation resulting in left VFP. It is not uncommon for these patients to have problems with aspiration and require intervention for airway, feeding, or voice.[137] We reviewed a group of 120 infants at our institution that underwent PDA ligation. Nearly all those who had left VFP were under 1150 g, with an incidence of 34%. Compared with newborns of comparable weight that did not have VFP, the length of hospital stay for infants with left VFP was 25% longer (132 days vs. 106 days). Comparing feeding status at discharge, 58% of the infants with left VFP had nasogastric feedings, compared with 13% of those without left VFP (unpublished study). Long-term complications in premature infants with left VFP after PDA ligation have been recently reported.[138] Compared with comparable infants who did not have VFP, they found an increased incidence of bronchopulmonary dysplasia (82% vs. 39%), reactive airway disease (86% vs. 33%), and need for gastrostomy tube (63% vs. 6%). The mechanism of long-term pulmonary injury in these patients may be chronic microaspiration combined with pulmonary hypertension.[139] An interesting recent study examined 13 adults who had PDA ligation as a premature infant, and 7 patients (54%) had left VFP.[140] They were found to frequently have voice-related complaints and exertional dyspnea. These symptoms due to an undiagnosed VFP can be mistaken for other problems. Office laryngoscopy is advised in any patient who had a prior PDA ligation in infancy.

Several large reviews have reported that the natural history of laryngeal paralysis in children tends toward spontaneous "recovery". "Recovery" is not well defined, and objective or patient-based outcome measures of voice and swallowing are generally lacking. Cohen et al. described 38 children with unilateral VFP: although 14 were lost to follow-up, 13 recovered completely.[11] Emery and Fearon reported 30 cases of unilateral VFP in children.[141] Peripheral nerve injuries usually recovered (60% of cases). In laryngeal paralysis, it is important to distinguish between neuromotor (return of vocal fold movement) and phonatory (improvement in voice) recovery, since they are not always the same.[98] The infrequent reports of surgical management of dysphonia in children from laryngeal paralysis may reflect (1) a trend toward natural improvement in voice through compensatory means, with or without recovery of vocal fold movement, (2) parental and social accommodation to the child with mild or moderate degrees of dysphonia and the lack of "disability" that dysphonia is to a young child, and (3) reluctance to surgically manage this problem on the part of pediatric otolaryngologists. Patient or surrogate-based validated metrics that accurately reflect vocal dysfunction in children are needed.[142] Historically, there has been a paucity of surgical procedures available to restore lifelong vocal function for children with unilateral VFP. While speech therapy is advocated as the first-line treatment for unilateral VFP in children,[21,129] reports documenting its efficacy are limited. In adults with unilateral VFP, positive outcome with speech therapy has been reported.[143,144] However, adults in these studies have usually had an acute onset of paralysis after surgery, trauma, or stroke, in which peripheral or central nerve injuries may be evolving. In children, the paralysis may be longstanding from infancy. Also, it is difficult to compare compliance with therapy techniques between adults and children.

Surgical management of glottal insufficiency and laryngeal paralysis has received much attention. Beginning in the early 1960s, Teflon paste injection of the vocal fold was commonly performed in adults until other techniques replaced it in the 1980s. There are reports of Teflon injection in three children.[141,145] It has several disadvantages in children, including irreversibility and unpredictable long-term effects.[129] However, the principle of vocal fold injection for medialization to treat glottal incompetence has merit and much reported experience. Other materials for injection, including Gelfoam, collagen, and carboxymethylcellulose gel (Radiesse Voice Gel), are available as a temporary treatment of glottal incompetence, and have been successfully used in a few children.[129,145–147] We have had favorable results with Cymetra collagen injection for temporary medialization in adolescents with unilateral VFP, as have other centers.[148,149] Autologous fat injection is also an option.[150] Calcium hydroxylapatite (CaHA, brand

name Radiesse Voice) is an injection material available for about 12 years. Regarding use in children, two reports of vocal fold injection with CaHA have been published. Sipp et al. reported a 13-year-old child who underwent CaHA injection and was followed for 4 months.[149] Cohen et al. reported on three pediatric patients who received CaHA injection.[147] Two patients had only one injection, one of them went on to thyroplasty. One patient had nine total injections which each lasted about 7 months. This material is expected to gradually resorb, as this gradually occurs in adults followed up to 12 months.[151] A recent study suggests the average benefit of CaHA injection laryngoplasty in adults is 18.6 months.[152] Though it resorbs more slowly than other injectables, it is still not long lasting or permanent. It also has unfavorable viscoelastic properties that adversely affect phonation if placed medially into the lamina propria.[153] Complications of CaHA injection laryngoplasty related to intense inflammatory reaction, migration, and compromised vocal function have been reported.[154] This author recommends against its use in children.

A variety of phonosurgical techniques have been popularized as alternatives to vocal fold injection.[155,156] These laryngeal framework procedures have had some limited application in children.[157–159] Twenty-four cases of thyroplasty in pediatric patients have been reported in the medical literature.[147,149] In the largest series, Link et al. reported on eight patients with unilateral VFP treated with type 1 medialization thyroplasty for dysphonia or aspiration symptoms.[158] The arytenoid adduction procedure,[160] while appropriate in theory for closure of posterior glottic defects, has technical problems that preclude its use in young children.[157] The arytenoid muscular process is not as well-defined and easily palpable in the pediatric larynx as it is in adults. The arytenoid and thyroid ala cartilage is softer and does not hold the suture as well. Even with adduction of the arytenoid, the larger posterior pediatric glottis (relative to the anterior half of the glottis) still remains partially open during phonation, resulting in a more breathy voice. It has been successfully used in adolescents with large posterior glottal gap.[161]

Development of exertional dyspnea may also be a concern with arytenoid adduction, though it has not been a problem in our limited experience. This procedure may be appropriate in adolescents with unilateral VFP and large glottal gap and concomitant aspiration symptoms. Though our experience has been positive, a review of three studies on the topic found that arytenoid adduction yielded no benefit over medialization laryngoplasty alone.[162] This finding was contradicted by a recent study which did document the additional benefit of arytenoid adduction over medialization alone.[163] These laryngoplasty procedures can be done under local anesthesia in adults. This is not possible in most children. The use of LMA and intraoperative fiberoptic laryngoscopy to adjust implant location has been reported in two children.[159]

Reinnervation of the paralyzed larynx is an attractive surgical option for dysphonia from unilateral VFP.[164,165] The procedure is permanent and expected to last throughout the child's life, does not involve a foreign body implant, and is technically straightforward to perform with the consistent outcomes. Two variations of this approach have been investigated: ansa hypoglossi to RLN anastomosis[166] and NMP implantation into adductor laryngeal muscles (lateral cricoarytenoid or thyroarytenoid).[167] Both of these techniques aim to reinnervate laryngeal muscle to prevent atrophy, increase tone, and improve glottal adduction and voice. Direct neurorrhaphy is now largely preferred over NMP. Large series of adults with unilateral VFP who underwent ansa-RLN reinnervation are now available that document its efficacy.[168,169]A prospective surgical trial of 24 adult patients with unilateral VFP randomized to thyroplasty vs. ansa-RLN reinnervation found that reinnervation had superior voice results in those < 52 years of age, and thyroplasty tended to have better voice results in older patients.[170]

In older pre-teens and adolescents with unilateral VFP, in selected cases we have utilized the technique of combining arytenoid adduction with ansa hypoglossi reinnervation.[148,171] This combines the benefits of framework surgery to close the posterior glottis and reinnervation. Regarding outcomes of ansa-RLN reinnervation for unilateral VFP in children there are several recent reports.[149,161,172–174] In a case series of six adolescents who underwent ansa-RLN reinnervation for unilateral VFP, the average voice quality self-rating was 82% of normal.[161] Average blinded listener perceptual ratings of overall voice quality on visual analogue scale found improvement from 50 mm preoperatively to 82 mm postoperatively. Improvements in dynamic range (pitch and loudness) were also observed. A case report with favorable outcomes in two children 3 and 6 years of age was recently published.[174] We recently reported on 13 children under 10 years of age with unilateral VFP after PDA ligation or coarctation repair who underwent ansa-RLN reinnervation who had improved voice and swallowing outcomes and no complications.[172] To date, we have experience with 40 laryngeal reinnervation cases in children, and find it a very useful option for management of severe dysphonia from unilateral VFP.

The ansa-RLN reinnervation for unilateral VFP has significant advantages for children.[165] The procedure is conducted under general anesthesia, avoiding the intraoperative adjustments required for thyroplasty, or guesswork of injection laryngoplasty. The procedure is done the same way each time, so comparable results can be expected from each procedure. There is no foreign body implant with risk of injection or rejection. The procedure is expected to provide muscle tone to the vocal fold and maintain voice quality, pitch, and loudness for the child's entire life.

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CHAPTER

# 80

# Benign and Malignant Vocal Fold Lesions

***Jason A Brant, Karen B Zur***

## INTRODUCTION

Voice disorders are common in children and should be assumed to be organic in nature until proven otherwise.[1] Although the vast majority of laryngeal lesions in children are benign, many are treatable and should be evaluated thoroughly. A high index of suspicion must be maintained, however as early identification of malignant lesions may potentially allow for more treatment options and higher long-term functionality. A careful history and physical examination including indirect laryngoscopy using a flexible endoscope can provide a diagnosis in most cases; however, there are several conditions that require direct laryngoscopy in the operating room to fully evaluate the larynx and airway. Lesions of the true vocal cords can cause dysphonia by several mechanisms. The alteration of the structure of the lamina propria can lead to changes in the mucosal wave, mass effect from the lesion can cause glottic insufficiency or alter the gross motion of the cord, and large lesions can alter the airflow through the glottis.

Benign lesions of the pediatric larynx are often related to voice abuse and voice therapy remains a mainstay of treatment.[2] Lesions that do not respond to voice therapy and medical management of contributing factors such as laryngopharyngeal reflux, or are large enough to cause airway obstruction, may require operative intervention. Malignant lesions may also lead to dysphonia in children and need to be recognized and addressed appropriately to ensure and safe airway, minimization of permanent damage if possible, and improved voice and swallowing outcomes.

## NODULES

Vocal fold nodules (VFN) (Fig. 80.1) are the most common cause of dysphonia in children. They form at the junction of the middle and anterior thirds of the vocal folds are often symmetric. Their effect on voice seems to be due to changing the mass of the vocal fold and prevention of normal apposition without affecting the mucosal wave.[3] The resulting glottic gap leads to a breathy, strained voice. VFN are frequently the result of chronic voice abuse.[2,4] Frictional trauma of the vocal cords causes edema and submucous hemorrhage that develops into an immature nodule, which then matures with continued abuse. Immature nodules are red and gelatinous and are more

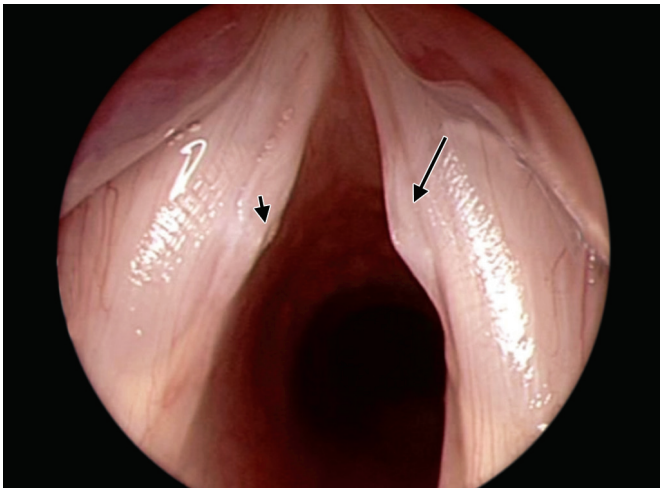

**Fig. 80.1:** Vocal fold nodule of the right vocal cord (long arrow) with reactive inflammation of the left vocal fold (short arrow).

common in children, while mature nodules are firm and white.[5] There is a 17% incidence of nodules in school aged children, with a two to one male predominance.[5] The incidence of nodules decreases in males during puberty, but increases in females, with the highest prevalence in post-pubescent girls and young women.[6]

Vocal hygiene and therapy is the primary treatment; however, nodules persist in 30% of patients, and only 44% will have normal vocal folds after puberty. [6] The remaining patients show residual effects including mild mucosal changes or incomplete vocal fold closure. Changes are highly sex dependent with persistent nodules in 47% of females and only 7% of males. Surgery is reserved for patients in whom associated medical conditions have been optimized, speech therapy has been tried for at least 6 months, and vocal nodules continue to be evident on endoscopy. This is likely more relevant in the professional voice user. It is rarely required for VFN, especially in children.[7] Depending on the age of the child and the severity of dysphonia, observing the child over time with intermittent voice therapy sessions for reinforcement can help avoid the need for surgery. If needed, the procedure involves incision through the mucosa overlying the lesion with careful blunt dissection to free it from the surrounding tissue. Often a plane can be developed and the nodule will "shell out" without significant disruption of the surrounding structures. Postoperative voice hygiene is essential to long-term remission.

## POLYP

Vocal fold polyps are uncommon in children and adolescents (Fig. 80.2). They are benign lesions with edematous connective tissue and multiple vascular channels, but normal overlying mucosa and underlying muscle.[1] Some have argued that they represent a more chronic outcome of the changes seen in VFN.[8] They are exophytic, appear translucent or hemorrhagic on laryngoscopy, and often appear at the junction of the anterior and middle thirds of the free edge of the vocal fold.[9] They may be pedunculated or sessile, and are most often unilateral. Similar to nodules, stroboscopy is generally minimally affected in vocal fold polyps.[10] The underlying pathogenesis is thought to involve rupture of the blood vessels of the superficial layer of the lamina propria secondary to vocal abuse. The resulting inflammation leads to deposition of new matrix that limits the apposition of the true vocal folds. This causes hoarseness and increased vocal effort. The resulting increased subglottic pressures and hyperfunction of the adductor muscles of the larynx leads to increased inflammation, perpetuating the cycle and leading to more polyp formation.[9]

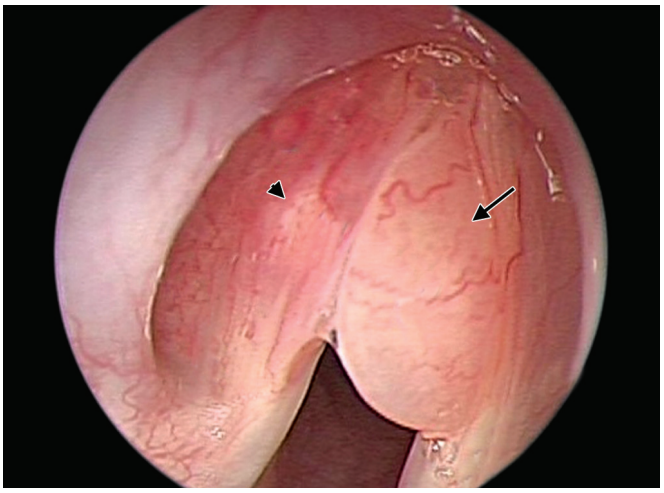

**Fig. 80.2:** Polyp of the right vocal fold (arrow), and possible intracordal cyst of the left vocal fold (arrow head).

Treatment for vocal fold polyps has traditionally been surgical excision. More recently, several studies have shown that many polyps will resolve with conservative treatment including voice therapy. Attributes that make conservative therapy more effective include smaller polyps, shorter duration of symptoms, and female gender.[9] Another group found that translucent polyps, patients with muscle tension dysphonia, and complete vocal fold closure are more likely to respond to voice therapy.[11] Even in patients who undergo surgical excision, pre- and postoperative voice therapy is recommended to prevent recurrence. Surgical excision using either microsurgical instruments or $CO_2$ laser is indicated for patients who have failed conservative therapy. Recently, office-based procedures for removal of polyps using flexible fiberoptic endoscopes have been proposed,[12,13] but are not likely to be feasible in children.

## CYSTS

Vocal fold cysts (Fig. 80.3) are the second most common cause of dysphonia in children.[2] Although most commonly located at the glottis, cysts can appear on any part of the larynx, and the symptoms are dependent on their location and size, ranging from asymptomatic, to mild dysphonia, to stridor and airway obstruction.[14] They are classified as either epidermal or mucous-retention types. Epidermal cysts can be caused by epithelium trapped in the lamina propria during embryonic development, or secondary to

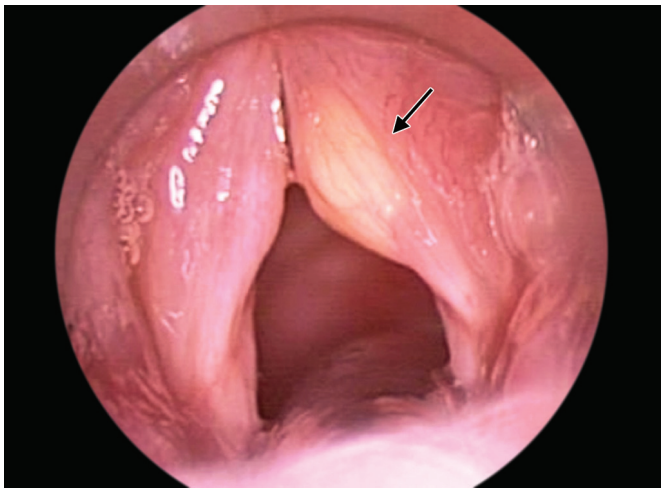

**Fig. 80.3:** Right vocal fold cyst (arrow).

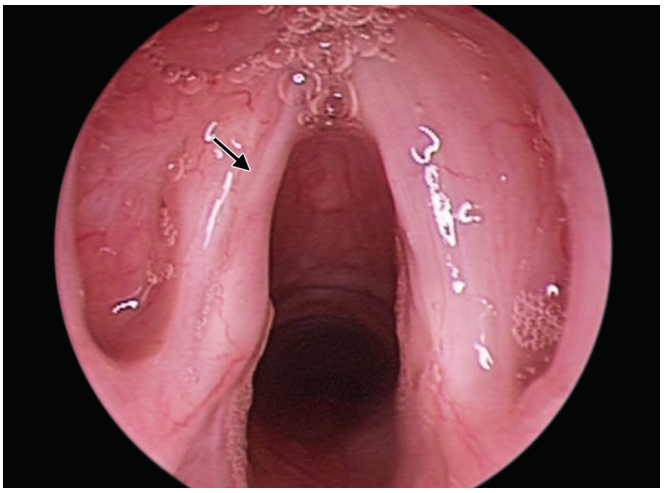

**Fig. 80.4:** Sulcus vocalis of the left vocal cord (arrow).

voice abuse. Mucous-retention cysts develop secondary to obstruction of a glandular duct.[15] In children, cysts are most commonly epidermal and diagnosis is based on the presence of a pearly lesion with overlying dilated blood vessels. Differentiation from VFN may be difficult, especially in cases of a contralateral reactive nodule or bilateral cysts. Videostroboscopic evaluation can be helpful as the mucosal wave is reduced or even absent over vocal fold cysts.[15] The sex distribution is similar to that of VFN, higher in males before puberty and females following puberty.[15]

Unlike nodules, vocal fold cysts will not involute with conservative methods. Medical optimization and voice hygiene continue to be important as they can reduce reactive damage to the contralateral vocal fold, and may help to prevent future lesions by minimizing compensatory behaviors. Management for laryngeal cysts is complete surgical excision. Under direct laryngoscopy with an operating microscope, a medial microflap is developed and carried to the cyst capsule.[16] The cyst itself is then dissected from the surrounding tissue with care to avoid cyst rupture or damage to surrounding mucosa. If the cyst does rupture during excision, the operative site must be inspected carefully to ensure no portion of the capsule is left behind.

## SULCUS VOCALIS

Sulcus vocalis refers to a longitudinal groove along the free edge of the vocal fold (Fig. 80.4). Debate remains as to the etiology of sulcus vocalis: congenital or acquired. It is likely that for some patients the underlying cause may be a congenital weakness in the regulation of collagen and elastin in the vocal fold, while others are acquired secondary to infection, inflammation, or vocal fold cyst rupture.[17] Although the etiology is not well understood, the histological appearance is of an absent lamina propria resulting in direct adherence of the epithelium to the vocalis ligament. A classification schema was developed by Ford et al. Type 1 refers to cases in which the sulcus is composed of an epithelial invagination into the lamina propria that does not cause a vibratory disturbance. Type 2 indicates sulcus vergeture, which is characterized by epithelial invagination down the vocal ligament that results in vibratory disturbances. Type 3 refers to true sulcus vocalis and indicates an epithelial invagination that completely penetrates the vocal ligament and causes severe dysphonia.[18] Dysphonia results from inhibition of closure of the vocal folds with glottic leakage and stiffness of the mucosa preventing normal propagation of the mucosal wave. Acoustically, the voice becomes strained and the patient experiences vocal fatigue. There are high pitch disturbances that are more pronounced in men, decreased voice adaptability, and an inability to speak loudly without fatigue. There may also be periods of aphonia.[17] Diagnosis may be difficult, as the vocal folds may appear normal under flexible laryngoscopy. Indirect signs such as a spindle-shaped glottis, compensatory hypertonia, or dilated veins on the vocal fold may be apparent.[17]

The rate of sulcus vocalis in children is low. One study found no cases in children under the age of 15, while another found that 5% of dysphonia in children was a result of sulcus vocalis.[19] Studies are conflicting on the percentage of patients with sulcus vocalis who had dysphonia during

childhood.[20] This suggests that the underlying defect may have been congenital, but diagnosis was not made until later in life.

The treatment for sulcus vocalis is not straightforward. A surgical option includes excision of the mucosa overlying the sulcus and creating a mucosal flap to cover the defect. Fascia, fat, and collagen have been proposed as fillers to eliminate the defect of the sulcus and to eliminate scarring of the mucosal flap to the underlying tissues. Additionally, medialization has been used to close the glottic gap created by the sulcus. Some have argued that bilateral lesions should have staged repairs; however, others have performed simultaneous repairs without complications.[20] Another option for management of such a scar is the injection of synthetic fillers such as semipermanent injectables. Others have advocated for a steroid injection to soften the scar. Results are variable and depend on the etiology that led to the development of the sulcus. A persistent challenge in this area is that no single treatment modality is successful for the majority of patients, and there is no evidence-based decision algorithm for matching a given treatment to a given patient.[21] Voice therapy may help to reverse, or prevent unhealthy vocal habits that result from the presence of the sulcus vocalis, or its treatment.[17]

## WEBS

Failure of recanalization of the larynx during the tenth week of embryonic development can lead to congenital laryngeal webs (Fig. 80.5). Most commonly, the web represents fibrous tissue bridging the anterior third of the vocal folds, but can extend posteriorly or into the subglottis. Rare instances of webs bridging other areas of the larynx have also been described. Symptoms depend on the degree of obstruction and can range from dysphonia or weak cry to respiratory distress and stridor. Congenital webs are considered a form of laryngeal malformation and should prompt a workup for other congenital anomolies.[22] Specifically, submucous cleft and bifid uvula should be noted, as these can be signs of velo-cardio-facial syndrome.[23] The classic triad of velo-cardio-facial syndrome is found in a significant number of children with webs: laryngeal web, cardiovascular disease, and chromosome 22q11 deletion.[24] Acquired laryngeal webs can be secondary to intubation trauma, surgical procedures, reflux, or infection. Complete workup for a laryngeal web includes fluorescent in situ hybridization (FISH) testing for 22Q deletion and microlaryngoscopy under general anesthesia to define the extent and thickness of the web. The posterior glottis should also be palpated for a laryngeal cleft.

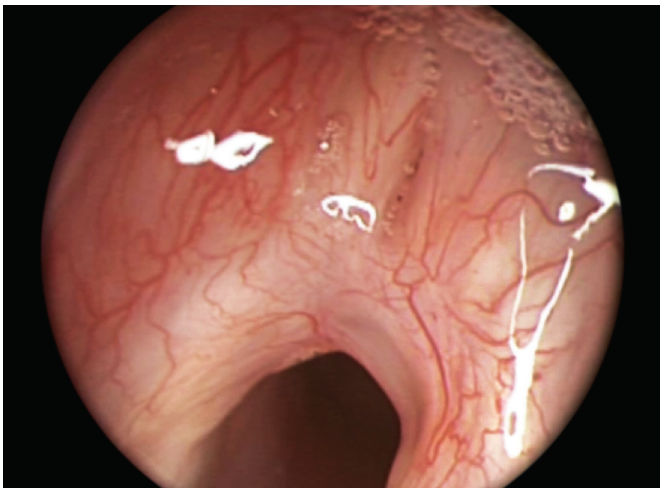

**Fig. 80.5:** Anterior glottic web in an infant.

The treatment goal for a laryngeal web is primarily security of the airway, and secondarily improvement of voice outcomes. Webs that are asymptomatic may be observed. Endoscopic approaches may be used for small but symptomatic webs. Some surgeons prefer to develop a "micro-trapdoor" flap that will cover one side of the surgical bed and prevent recurrent scarring.[25] Others advocate dilation with laryngeal dilators or balloons. Postoperative application of mitomycin C has been reported to help in the prevention of scarring as well,[26] and some advocate its use as an adjunct to a dilation/incision procedure. The results with mitomycin C are mixed. Another option to prevent scarring is the placement of a keel. Thick webs, or those associated with subglottic stenosis, may require open repair. The technique will vary depending on the associated abnormalities, but may involve anterior or posterior cartilage grafts, or both.[22] Caution should be undertaken in patients with 22Q deletion and long-term placement of a keel/stent.[27]

## JUVENILE RECURRENT RESPIRATORY PAPILLOMATOSIS

Juvenile recurrent respiratory papillomatosis (JRRP) represents a rare but dramatic cause of dysphonia and airway obstruction in children (Figs. 80.6 and 80.7). It presents with progressive hoarseness and stridor and there is often a prolonged interval between onset of symptoms and diagnosis.[28,29] It is characterized by exophytic, wart-like lesions that may be present anywhere along the airway, but most commonly involve the larynx. There is a predilection for areas of squamo-ciliary transition: limen vestibuli, nasal soft palate, laryngeal epiglottis, margins

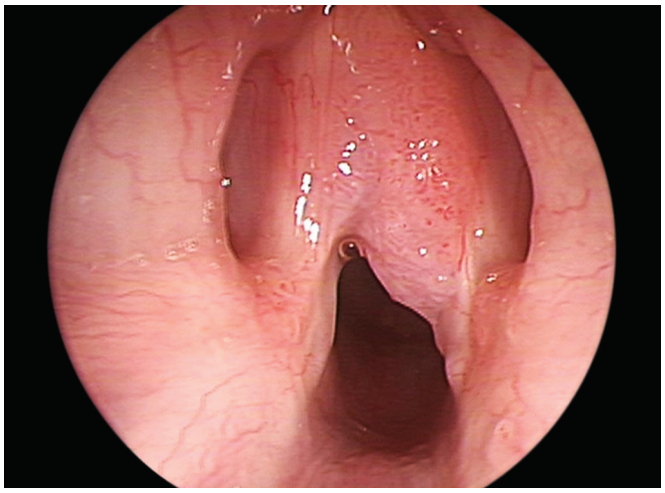

**Fig. 80.6:** Papilloma of the right vocal fold.

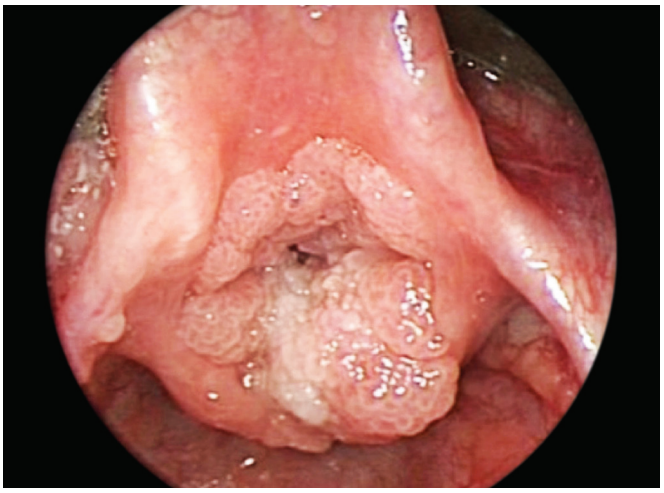

**Fig. 80.7:** Juvenile recurrent respiratory papillomatosis nearly completely obstructing the airway of a child.

of the vestibule, undersurface of the vocal folds, carina, and bronchial spurs.[30] JRRP is the most common benign laryngeal tumor in children with an incidence between 1 and 4 per 100,000 children in the United States.[31,32] Sex distribution is equal and most diagnoses are made between 2 and 3 years of age, with over 75% of diagnoses before age 5 years.[33,34] Patients diagnosed before the age of 3 have a more aggressive course. They require more frequent surgical intervention and are more likely to have two or more anatomical sites affected.[33] Papillomas are the result of human papilloma virus (HPV) infection, with types 6 and 11 being the most prevalent. Although there is some contradictory data, it is thought that HPV type 11 portends a more aggressive course.[29] Transmission is thought to be vertical from infected mothers to infants; however, the exact mechanism is unclear.[29] The classic case is a vaginally-born, first child of a white mother of low socioeconomic status and a history of genital warts.[32] The vocal manifestations of JRRP are due not only to the disease itself, but also the treatment. The lesions replace the normal mucosa of the vocal folds, abolishing the normal mucosal wave. Treatment involves surgical excision, which can lead to permanent scarring and vocal dysfunction even after the disease itself has "burned out". Mortality from JRRP is uncommon and is the result of airway obstruction or pulmonary involvement.[28]

The standard of care for JRRP is complete surgical excision of the papillomas with preservation of the normal structures.[35] Several techniques have been described including various types of lasers ($CO_2$, pulsed dye, or pulsed KTP) or a microdebrider. All of the lasers have the potential for thermal injury beyond the pathologic areas, but are more precise in sensitive anatomical areas such as the anterior commisure.[36] The disease tends to recur and patients need repeat procedures. On average, patients need over four procedures per year, with those diagnosed at younger ages needing more frequent procedures.[33,37] The interval between surgeries can be highly variable even in the same patient.[38] Over half of patients will require >10 procedures during their lifetime, and 7% will require over 100.[28,32] Often, the decision regarding timing of the procedures is based on the rate of recurrence of dysphonia. Patients who require multiple procedures who do not have an associated airway compromise will return for a procedure when they notice a change in their vocal quality, indicating worsening/recurring disease.

Local medical adjuvants including interferon, ribavirin, acyclovir, and cidofovir have been utilized with varying degrees of success in preventing recurrence. There have also been attempts to improve voice outcomes by preserving the extracellular matrix of the vocal folds through injectables such as hyaluronic acid hydrogels.[39] The recent development of the HPV vaccine and its widespread utilization may help to decrease the incidence of JRRP in the future.

## GRANULOMA

Vocal process granulomas (VPG) are benign inflammatory lesions of the vocal process of the arytenoid cartilages and are associated with injury or irritation of the posterior glottis (Fig. 80.8). Clinically they present with hoarse voice, odynophagia, frequent throat clearing, globus, and otalgia.[40] On laryngoscopy they commonly appear as an ulceration of the mucosa overlying the vocal process, or

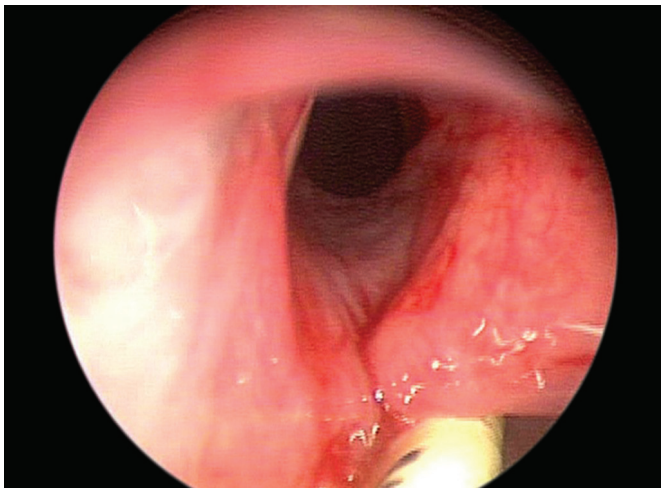

**Fig. 80.8:** Early granuloma formation on the right vocal process of an adolescent after a prolonged intubation.

a reddish or gray mass. Common causes include laryngopharyngeal reflux, intubation trauma, or voice abuse.[41] These do not account for all cases however, and a clear cause is not found in a large portion of these patients. Another proposed mechanism is glottic insufficiency leading to increased pressure and inflammation of the posterior glottis while attempting to appose the vocal folds.[41] VCG is more common in men than in women, except for those associated with intubation, and often appears in middle age.[42] There is little data on VCG in children, however the size of the pediatric larynx presumably increases the risk of VCG secondary to intubation trauma.

Treatment of vocal cord granuloma should focus on both the underlying cause and any exacerbating factors. Treatment often includes the use of acid suppressing medications and voice therapy.[43] In cases caused by intubation this is often sufficient for rapid resolution.[41] Inhaled and systemic steroids have been advocated to attempt to control the inflammatory component, and antibiotics to treat an underlying or exacerbating infection, but are less frequently used. Botulinum toxin injection has been evaluated for difficult to treat granulomas with the goal to reduce the force of adduction of the posterior glottis and to allow the mucosa to heal. This has proven effective in several series.[40,44] Surgical excision may be considered in patients with symptomatic lesions that have failed conservative measures for and extended amount of time;[45] however, this technique has a failure rate as high as 90% which is likely due to the underlying cause not being addressed.[41] Multiple other techniques have been employed to attempt to remove the lesion including zinc sulfate, and low-dose radiotherapy.[41] Ultimately the prognosis tends to be dependent on the cause. VCG secondary to intubation has a very good prognosis with almost all cases resolving with conservative treatment. Similarly, those caused by vocal abuse or reflux carry recurrence rates under 25%, while idiopathic cases may not be cured in up to 50% of patients.[44]

## MALIGNANCIES

Malignant lesions of the larynx in children are exceedingly rare. In a recent review of laryngeal cancer from the National Cancer Institute's surveillance, epidemiology, and end results database only 99 cases of laryngeal cancer in patients under 30 years of age were found, only 10% of which were under 19 years of age.[46] A review covering the literature from 1980 to 1999 discovered 47 reported cases of laryngeal cancer in children under the age of 18. The most common forms were rhabdomyosarcoma (42.5%) and squamous cell carcinoma (27.6%). Other malignancies included other sarcomas, malignant fibrous histiocytoma, lymphoma, malignant schwannoma, and mucoepidermoid carcinoma.[47] Most cases of squamous cell carcinoma (SCCa) of the larynx in children are degeneration from JRRP; however, this remains a rare occurrence.[48] Reports have noted that all cases of JRRP that have degenerated to SCCa have been HPV-11 related; however, one more recent case has not followed this pattern.[48,49] Although rare, the principal risk factor for carcinoma of the larynx in children is radiation of juvenile papillomas; however, many of these carcinomas do not present until after 16 years of age.[50]

Given the rarity of the disease, there are no well-established guidelines for the treatment of laryngeal malignancies in children. Multimodality therapy with surgery, chemotherapy, and radiation therapy should be considered. The long-term effects of radiation therapy on the pediatric larynx should be considered, as there can be significant effects of scarring, and a longer latency period for induced malignancies.[50] A high index of suspicion is required and biopsy is necessary as benign and malignant lesions cannot be reliably differentiated on clinical examination.[47]

## CONCLUSION

The workup and diagnosis of a child with dysphonia should be thorough. Although unlikely to represent a neoplasm, many of the lesions that lead to hoarseness in children are generally treatable and can improve voice

outcomes and quality of life. Initiation of voice therapy, and management of contributing medical conditions may improve the communication ability of the child, resolve the underlying lesion, and prevent worsening or irreversible changes to the vocal folds. The diagnosis and treatment of these lesions is a team approach that involves the primary care physician, otolaryngologist, speech therapist, and especially the patient and their caregiver.

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CHAPTER

# 81 Evaluation and Management of Pediatric Dysphonia

***Derek J Rogers, Catherine L Ballif***

Awareness of dysphonia in the pediatric population continues to grow as more otolaryngologists and speech-language pathologists receive specialized pediatric voice training. The prevalence of voice disorders in children is likely much higher than previously thought. Pediatric dysphonia often remains untreated because children and their parents do not perceive it as a reason to seek medical attention. Children may suffer from dysphonia due to either acquired or congenital pathology. Acquired pathology is similar in children and adults, and includes use-related trauma, intubation, and surgery. Congenital pathology consists of such entities as glottic webs, vocal fold paralysis, sulcus vocalis, papillomatosis, and subglottic stenosis.[1] Dysphonia secondary to papillomatosis is discussed in a separate chapter. Regardless of the cause, the evaluation and management of pediatric dysphonia deserve special focus and will be covered in this chapter.

## EVALUATION OF PEDIATRIC DYSPHONIA

Voice evaluations may occur in a variety of locations, including an otolaryngology office, voice clinic, hospital, or school. A speech-language pathologist with training in voice therapy should be closely involved in the care of any pediatric patient with dysphonia. Speech-language pathologists are uniquely qualified to address the nonmedical aspects of dysphonia due to their holistic understanding of the communication process. They are a valuable resource in providing education to medical providers concerning the effects of dysphonia on the child's communicative, interpersonal, and socioemotional development as well as the benefits of speech therapy in establishing a functional voice in children without a structurally normal voicing mechanism.[1]

### Initiation of Referral

Referrals of children with dysphonia may originate from physicians, teachers, parents, or school-based speech-language pathologists. Once a voice evaluation is requested, the children are usually first referred to their pediatrician. The pediatrician then refers the children to an otolaryngologist. The otolaryngologist decides which children warrant a formal voice evaluation from a speech-language pathologist and determines if additional subspecialty referrals are needed.[1]

### Multidisciplinary Care

A multidisciplinary team remains best suited to evaluate a child with dysphonia. The team typically includes the child's otolaryngologist, speech-language pathologist, pediatrician, and parents; however, a pulmonologist, gastroenterologist, neurologist, allergist, and school teacher may be involved as well. The speech-language pathologist gathers and correlates information from the various specialties and relays this information to the parents and school.[1]

### Pediatric Voice History

A thorough voice history is paramount to identify and further characterize the dysphonia. Pertinent details of the dysphonia include its onset, progression, and variability.

It is important to obtain the perspectives of both the child and the caregiver regarding voice quality. Children with early onset of dysphonia may not perceive a problem with their voice if this is the only voice quality they have ever known. They may perceive their current voice quality as their "normal voice". A dysphonic voice quality may be a concern for parents, physicians, and teachers, but may be viewed as "normal" to the child. Regardless of the child's awareness level, vocal hygiene should be addressed, such as hydration, vocal abuse, exposure to second-hand smoke and other environmental irritants, and reflux. Medications, past medical and surgical history, and social history, including family size and dynamics, extracurricular activities, and special interests, should be obtained. Developmental history is particularly important in the pediatric population to determine physical, cognitive, social, and communication parameters as well as to assess the impact of the dysphonia on the child's development within these parameters. Communication history should focus on articulation, vocabulary development, receptive language, and fluency. Assessing these other aspects of verbal communication is important as they interface with voice production in overall speech intelligibility. However, reduced speech intelligibility, as a result of a voice disorder (i.e., unclear voicing signal, soft volume, unstable voicing, and insufficient glottic closure), should be distinguished from reduced speech intelligibility as a result of articulation disorders, phonological disorders, apraxia, velopharyngeal insufficiency, and other communication disorders *in the presence of normal voice production*. One should also realize that cultural factors may impact the manner in which evaluation tasks are completed.[1] Special consideration should also be exercised when assessing children for whom English is a second or concurrent language. In many households, the child is the most proficient in English. Therapy delivery may be beneficial in one language in clinic, but carryover activities may be facilitated at home in another language.

## Assuring Child Participation

Obtaining an adequate voice evaluation demands application of age-appropriate activities and interactions to facilitate participation from the children. The provider may begin casually interacting with the parent first, allowing the shy child to adjust to the new environment. Asking the parents to bring a favorite toy or book may help facilitate easier interactions with the provider and provide material for obtaining a spontaneous voice sample. Tasks may first be acted out with the toy or puppet to help the child feel more comfortable. If a child is less responsive to direct interactions with the provider initially, modeling and parallel play by the provider may spark interest in the child from which the provider can eventually make transition to more interactive play and more readily engage the child in a less threatening interaction. Incorporating the parents or siblings into interactions with the provider may also create a less threatening environment for the child being assessed. Vocal tasks should be observed multiple times during the assessment, as performance may vary.[1]

## Specific Assessments

### *Oral Motor*

The oral–facial mechanism should be assessed for strength, speed, coordination, and range of motion of the articulatory structures, which could be contributing to the child's vocal symptoms. The oral-motor assessment evaluates motor speech disorders, such as developmental speech apraxia or dysarthria. Oral structure, oral movement skills, and motor speech function (single-word articulation, age-appropriate connected speech, and diadochokinesis) should be assessed. Fluency and articulation disorders may coincide with voice disorders.[2] One should evaluate articulation skills to see that they are age appropriate and that no delayed phonological patterns exist. A cranial nerve exam is also performed to determine if a more extensive neurological condition is responsible for the dysphonia.[1]

### *Perceptual*

A speech sample is obtained and a perceptual assessment is completed to investigate the child's vocal characteristics, learning style, temperament, motivation, and social interaction with the caregiver.[3] The child's vocal quality can be rated using a standardized tool such as the grade, roughness, breathiness, asthenia, strain (GRBAS) scale (Appendix 81.1) or the consensus auditory perceptual evaluation voice (CAPE-V) (Appendix 81.2). The child's alertness, attention, muscle tone, and emotional stability should be observed during this conversational task.[3]

Obtaining a spontaneous speech sample representative of the child can be achieved either through direct interaction or observation. One can observe the parent–child interaction during free play. If the child is too uncomfortable to participate in free play, book reading may engage the child. The child can be asked to describe

the story you have just read or asked open-ended questions to elicit longer utterances. The rate of speech should be calculated from the speech sample in syllables per minute.[1]

### *Respiratory*

Speech patterns, such as choppy sentences or breathlessness at the end of phrases, may result from respiratory incoordination. Typical uncoordinated respiratory patterns include clavicular breathing, inadequate breath replenishment, resulting in the child speaking too long in one breath or in shorter phrases and excessive use of strap muscles during inhalation. To conduct the respiratory assessment, the child should be asked to count or say the alphabet while syllables per breath are measured. Parents should also be asked whether their child works hard to phonate by the end of the day.[1]

### *Pitch and Volume*

Vocal flexibility can be characterized using pitch and volume measures. Vocal inflexibility can negatively impact intelligibility and how natural speech sounds because spoken inflection depends on pitch and volume. Volume discrepancies may indicate a structural problem in the glottis.[1] Some children struggle to produce soft voice and use increased volume to compensate for poor glottal valving.[4]

Pitch flexibility may be assessed using visual aids such as Visi-Pitch™, where the child uses his or her voice to draw a hill on the screen. The child could also trace his or her finger up and down a hill on a piece of paper while phonating. Volume flexibility can be documented using animal metaphors; large animals would elicit a louder voice and small animals a softer one. The child can also be asked to use his or her "outdoor voice" versus "indoor voice". Inflection should be evaluated during collection of the speech sample.[1]

### *Maximum Phonation Time*

The efficiency of coordination between the respiratory and phonatory systems is assessed using the maximum phonation time. This parameter may be difficult to obtain depending on the cognitive level of the child. The child could be asked to phonate until a toy moves from one place to the next, across the floor, to help suggest prolongation to him or her. Multiple trials are usually needed to improve accuracy.[1]

### *Stimulability*

Stimulability tasks serve to decrease muscular tension and improve airflow and/or vocal quality. The child's ability to participate in direct therapy can be determined based on his or her response to stimulability tasks.[1] These tasks may involve decreasing or increasing rate, increasing attention to resonance, exaggerating articulation, implementing negative practice, or imitating the therapist.[4]

### *Quality-of-Life*

Validated rating scales have been developed to help delineate the functional and social impacts of the child's dysphonia. The three most commonly employed quality-of-life assessments include the pediatric Voice Handicap Index (pVHI), Pediatric Voice Outcomes survey (PVOS), and Pediatric Voice-Related Quality-of-Life survey (PVRQOL). The Pediatric Voice Handicap Index is a modified version of the adult VHI in content and language to eliminate questions unrelated to children, resulting in a 23-item parental proxy product.[5] The PVOS was designed for the caregiver to complete and consists of only four multiple-choice questions used to identify voice concerns.[6] Some children, such as those who have undergone airway reconstruction, present with severe vocal impairments with the potential of additional social, educational, and functional concerns. In these cases, the PVOS may not be sensitive enough to provide adequate information regarding the impact of the dysphonia.[7] The PVRQOL is a 10-item instrument adapted from the adult VRQOL survey designed to function as a parental proxy for children under the age of 12 years rather than a self-administered questionnaire (Appendix 81.3).[8] The PVRQOL raw scores are converted to a scale of 0–100, with subdomain scores reflecting both social–emotional and physical–functional effects.

## Acoustic and Aerodynamic Recording Methods

Acoustic parameters typically measured include fundamental frequency, frequency range, maximum phonation time, average intensity and range, S/Z ratio, harmonics-to-noise ratio, jitter, and shimmer. A computer-based system, such as Voice Evaluation Suite™, Computerized Speech Lab (CSL™), or Visi-Pitch™, is most commonly used for ease and convenience. However, most acoustic parameters can be assessed without sophisticated equipment if unavailable or if the child is unable to participate.

Proper assessment of jitter, shimmer, and harmonics-to-noise ratio does require the use of computer software. Some children may be unable to provide adequate voicing samples for acoustic analysis by computer-based systems, either due to a highly dysphonic voice quality or because of noncompliance. Analysis of a short recorded speech sample at a later time with help of a stopwatch, piano keyboard, and sound pressure level (SPL) meter can provide most necessary acoustic data, but the process can be laborious.

Another parameter of objective voice outcomes data is aerodynamic evaluation or the measurement of laryngeal airflow and pressure changes during phonation. The Phonatory Aerodynamic System (PAS) or Aerophone by KayPENTAX® is capable of recording aerodynamic parameters in children. Particularly useful aerodynamic measures include mean SPL, mean peak (subglottic) air pressure, and mean airflow during voicing. Phonation threshold pressure may also be measured, but no normative data exist for children. High subglottic pressure is associated with increased respiratory effort needed for phonation in the presence of compromised glottic closure from vocal fold pathology and/or as a result of laryngeal hyperfunction. Subglottic pressure measures along with average airflow rate help quantify the valving efficiency of the laryngeal system. For example, a hyperfunctional voice may result in decreased airflow rate and increased subglottic pressure, whereas increased airflow and subglottic pressure may result with a vocal fold lesion compromising glottic closure.

## Physical Examination

An awake, transnasal fiberoptic laryngoscopy or transoral, rigid laryngoscopy with stroboscopy, when possible, should be performed to evaluate the laryngeal and supraglottic structures as well as to assess gross vocal fold mobility and symmetry. The choice of transnasal or transoral technique is guided by the patient's age, the position of the larynx (i.e., if the epiglottis is clearly visualized when a child opens his or her mouth, a transoral technique may be more easily accomplished), and patient compliance. Stroboscopy, which requires patient compliance with the necessary task functions, may be difficult for some children to tolerate; the key is proper visualization of vocal folds during phonation to assess for mobility patterns, glottal aperture defects, and regions of scarring or decreased pliability. Any compensatory mechanisms, such as alternative vibratory sources within the larynx, should be noted. Supraglottic compression and arytenoid prolapse are common in children after airway reconstruction and may obscure the view of the true vocal folds. In fact, often the false vocal folds function as the primary vibratory source through supraglottic compression. Voice therapy techniques (covered later in this chapter) that reduce supraglottic compression may be initiated, allowing better visualization for the clinician and effective biofeedback for the child.[7] The theoretic concern is that if the supraglottic phonation developed as an adaptive strategy to achieve a voice in face of a scarred and damaged larynx, then therapy to reduce compensatory supraglottic compression may actually diminish the overall phonatory output, resulting in a weaker voice.

## Parental Discussion

Good communication with the parent is mandatory and begins with the interview and continues through the treatment plan. The speech-language pathologist should discuss potential interventions and answer any questions. The interventions should be worked into the family's daily schedule to ensure maximal participation. Proper vocal hygiene and any harmful vocal behaviors should be covered at the conclusion of the evaluation.[1]

It is important to obtain perspectives from both the parents as well as the child. The child may not recognize any problem in his or her voice, especially if the dysphonia has been present since early in life. Parents may have concerns beyond merely good voice production. They may be concerned with their child's ability to interact with peers, participate in educational opportunities, and even communicate danger or pain in times of emergency.

Parents, like many adult voice patients, are often seeking resolution of dysphonia through voice therapy. Their primary goal is often clearer voice production. While improvement to voice quality is most desirable, this may not always be possible in the pediatric dysphonia case. The primary goals of pediatric voice therapy are to (1) increase the child's awareness of vocal hyperfunction and phonotraumatic behaviors; (2) reduce hyperfunction, strain, and phonotrauma through behavior modification; and (3) replace less effective compensatory phonatory patterns with the most effective patterns possible, given the child's vocal mechanism. Improved voice quality may not be noted during the course of therapy or immediately following, but rather over time with application

of effective phonation patterns as the vocal mechanism continues to grow and mature. Increasing awareness of phonotrauma and establishing effective phonation behaviors will prevent the perpetuation of phonotraumatic behaviors and ineffective compensatory phonation patterns on the growing larynx.

## MANAGEMENT OF PEDIATRIC DYSPHONIA

### Voice Therapy

The speech-language pathologist's management of dysphonia focuses on voice therapy, which minimizes inappropriate voice use and restores normal phonatory function. The multifactorial nature of pediatric dysphonia requires a comprehensive combination of indirect and direct treatment techniques.[9,10] Voice therapy programs for children progress through several distinct phases. The first phase involves general awareness of voice production and vocal behavior, the second phase more specific awareness of the vocal behaviors requiring change, the third phase direct voice therapy or vocal exercises, and the last phase generalization or carryover activities.[11,12]

It is commonly believed that young children are not appropriate for voice therapy, as they lack the cognitive insight and skills of meta-analysis to participate in behavior modification therapy. However, the key to successful voice therapy with any child is to apply the various techniques in an age-appropriate manner and in a way that engages the child's individual interest. Children as young as 2 years of age can participate in play-based voice therapy. Play and imagination are the media through which most young children learn. Linguistically, young children are still in the phoneme acquisition phase, which means their ability to distinguish between small changes in vocal production is keen, perhaps more than in adults. Young children are capable of following the speech pathologist's models of resonant voice production without lengthy explanations or instructions. Through modeling and shaping, the speech pathologist can provide contrast of the target resonant voice from hyperfuntional or phonotraumatic productions, thus increasing the child's awareness in his or her own productions. The older the children are, the more appropriate they are for structured behavior therapy with proper age-appropriate reinforcements and encouragement. Younger children typically want to please adults including parents, teachers, and speech pathologist. The adolescent can often tolerate application of therapy approaches typical to adults. However, it is important to note that the adolescent may be more responsive to voice therapy if the speech pathologist is seen more as a guide than as an authoritative figure.

Unlike adults who typically acquire dysphonia later in life, many children do not perceive the dysphonia if the current voice quality is the only voice they have known. Participation in therapy may be difficult for them if they do not perceive a problem. The speech therapist might need to take the approach of showing them "another way" to produce voice and see which way they like better, rather than approaching from the standpoint of "fixing their voice". For many children, the way their voice sounds is part of their identity. Changing the voice may be seen as changing who they are or how they perceive themselves. By introducing voice therapy as a way to do something differently, the option to return to their "typical" way remains, and participation in voice therapy becomes less threatening.

#### *Indirect Therapy Techniques*

Indirect therapy techniques consist of patient/family education and vocal hygiene. The educational component should cover vocal fold anatomy and physiology, normal and disordered voice production, and patient awareness to the voice disorder. Age-appropriate delivery of education in various activities, interactive models, and computer programs to facilitate understanding and increase motivation can be utilized. The child's caregiver should be involved in the educational sessions to ensure appropriate understanding of voice production during the child's daily activities. Supplemental reading materials should be provided to the family.[13]

Vocal hygiene addresses vocal behaviors that may be affecting the child's voice production. The goal is to eliminate potentially harmful voice patterns and promote a healthy voice through proper hydration for the larynx, reduction of irritant exposure (cigarette smoke), elimination of frequent throat clearing and coughing, and reduction of abusive voice patterns. A voice checklist and log of voice behaviors have traditionally been used and may or may not be effective for the individual child and family situation. Children should be taught alternative actions, such as a dry swallow or forced yawn instead of throat clearing.[13]

### *Direct Therapy Techniques*

Direct therapy techniques include resonant voice techniques, vocal function exercises (VFEs), voice-facilitating techniques, confidential voice, manual circumlaryngeal therapy, biofeedback, relaxation techniques, and training in voice projection techniques with minimal laryngeal impact. The goals of direct therapy techniques are to optimize the balance of voice production and laryngeal mechanism, improve breathing during voice production, and achieve appropriate quality, pitch, and loudness with minimal laryngeal effort.[13] Many of these techniques can be implemented in children by using unique approaches. For instance, small-group therapy sessions, peer monitoring, and multimodality cues can be used to address posture and shoulder and neck tension.[14]

*Resonant therapy*: Resonant voice therapy aims to achieve the strongest possible voice with the least amount of effort and least impact on the vocal folds.[15,16] These techniques are based on motor learning principles and they establish a new motor pattern, optimizing phonation efficiency and minimizing vibratory impact stress and/or vocal fold injury.[17,18] The vocal folds are barely adducted during resonant voicing. This approach stresses the role of processing sensory and kinesthetic information to monitor the "feel" of voicing and to concentrate on the auditory feedback. Resonant techniques require mastery of a basic voice-training gesture, daily practice to facilitate a new motor pattern, and gradual progression to more complex tasks within a voice-task hierarchy.[19] The basic training gesture includes the vowel /i/, the semivowel "y" (ybuzz), and humming (/m/).[13]

*Vocal function exercises*: Vocal function exercises are another common direct voice therapy approach. These exercises are based on the theory that the laryngeal mechanism is a muscular system that may become strained and imbalanced.[15,16] Vocal function exercises use a neuromuscular training approach to balance the subsystems of voice (airflow, laryngeal musculature, and tone) and to restore balance, strength, and ease of phonation.[13] Four exercises are practiced at home for 6–8 weeks. The exercises involve maximum vowel prolongation and pitch glides using specific pitch and phonetic contexts.[19] They are effective in optimizing vocal fold vibratory function secondary to a vocal fold mass or compensatory muscle tension.[20] Vocal function exercises are easily modified to be age appropriate and incorporate the child's individual interests. Children 9 years of age and older are often appropriate to follow the adult protocol without much modification or adaptation.

*Voice-facilitating techniques*: Several techniques are used to target specific voice symptoms. Voice-facilitating techniques attempt to eliminate functional voice misuse and facilitate the patient to produce improved phonation through direct symptom modification.[15,16,21] The original 20 voice-facilitating techniques are listed in Table 81.1.[12,21] The facilitating techniques frequently used in children are altered tongue position, elimination of hard glottal attacks, yawn–sigh approach, open-mouth exercises, change of loudness and pitch, and voice rest.[13] Elimination of hard glottal attacks and promotion of easy voice onset are useful to teach easy coordination of airflow and phonation and to reduce laryngeal tension.[21] Hard glottal attacks are eliminated by having the child insert the phoneme "h" in front of an initial vowel or voiced consonant, such as "hhhegg" for "egg".[13] The yawn–sigh technique is accomplished by having the child pretend to yawn and end with a sigh, slowly shaping this posture into real sounds or words. The goal is to lower the larynx to reduce laryngeal tension and foster easy airflow and phonation.[15,21]

**Table 81.1:** Voice-facilitating techniques

| | |
|---|---|
| 1. | Altering tongue position |
| 2. | Changing loudness |
| 3. | Chewing exercises |
| 4. | Digital manipulation |
| 5. | Ear training |
| 6. | Elimination of vocal abuses |
| 7. | Elimination of hard glottal attacks |
| 8. | Establishing new pitch |
| 9. | Explanation of the problem |
| 10. | Feedback |
| 11. | Open-mouth exercises |
| 12. | Pitch inflections |
| 13. | Pushing approach |
| 14. | Relaxation |
| 15. | Respiration training |
| 16 | Target voice models |
| 17. | Voice rest |
| 18. | Yawn–sigh approach |
| 19. | Negative practice |
| 20. | Hierarchy analysis |

Adapted from Andrews[12] and Colton et al.[21]

*Confidential voice therapy*: Confidential voice therapy, or breathy phonation, is used less often with young children and is essentially a voiced whisper. Children are instructed to use a soft voice with reduced volume, with the vocal folds still vibrating, unlike a voiceless whisper.[21] Confidential voice therapy should be used as an interim therapy to allow mucosal repair following traumatic laryngeal pathologies, hyperfunctional voice use, or surgery.[13] Therapy should then shift toward increased voicing and long-term techniques after short-term use of confidential voice techniques.[21]

*Manual circumlaryngeal therapy*: Manual circumlaryngeal therapy, or laryngeal reposturing techniques, involves direct palpation of the larynx and is often used to reduce musculoskeletal tension in hyperfunctional voice disorders. The hyoid and thyroid cartilages are palpated while the voicing of the patient (hum or prolonged vowel), with gradual removal of tactile cues during the voicing.[22,23] These techniques are difficult to perform in young children and more appropriate for school-aged children and older. Vocal gains with manual circumlaryngeal therapy are usually made quickly and maintained long term.[13]

*Biofeedback*: Biofeedback uses auditory or visual feedback to enhance progress in voice therapy. Most forms of biofeedback should be reserved for school-aged children or older. Children younger than 6 years of age may not be able to assess vocal production retrospectively, as they are too far removed from the production. Studies have shown surface electromyography to be effective in facilitating motor relearning in patients with vocal hyperfunction.[24,25] Patients receive direct feedback during their voice therapy to help them relax their laryngeal musculature. Acoustic and aerodynamic feedbacks can also be used for voice therapy. Yamaguchi et al. demonstrated the effectiveness of visual feedback of airflow and acoustic data on a phonolaryngograph in patients with vocal nodules.[26] Visual biofeedback is usually accomplished using videostroboscopy, but ultrasound is occasionally used as well. Videostroboscopy may reduce the amount of time needed to successfully manage voice disorders, such as muscle tension dysphonia.[27] Furthermore, computer programs have been designed to provide visual feedback during voice therapy.[28]

*Relaxation techniques*: Many children with voice disorders present with inappropriate muscle tension, usually within the jaw, neck, or shoulder region. Relaxation techniques aim to eliminate this compensatory muscle tension and extraneous muscular effort during voice production.[20,29] Using visual cues, such as a mirror, picture, or adult model, helps children distinguish between inappropriate and appropriate muscle tension. Stretching and relaxation exercises can be used to directly address the tense areas.[13]

*Training in voice projection techniques with minimal laryngeal impact*: Traditionally, children with dysphonia have been trained not to yell as part of their vocal hygiene. They are often asked to track their yelling on the voice checklist or log and are trained in alternative methods, such as using a whistle, clapping their hands, or some other way of making noise to get attention that does not involve the vocal folds. However, this has proven to be ineffective at best and unrealistic. Voice projection is part of both the pediatric and adult lives. Young children are often on the playground, older children are participating in organized sports, and all children have the need to express frustration, anger, pain, and fear. Children with dysphonia have a greater need to learn strategies to yell using phonation patterns focusing on resonant placement, reduced laryngeal effort and strain, proper breath support, and anchoring techniques to minimize the overall impact on their laryngeal mechanism. By increasing their awareness of pressed laryngeal effort level, the child can be trained to reduce laryngeal strain and improve resonant placement during voice projection. While it is true that there is no safe way to yell, through voice therapy, a child can and should be equipped with strategies to learn "safer shouting".

## Surgery

Though the focus of this chapter is the evaluation and management of pediatric dysphonia from the speech-language pathologist's perspective, some pediatric voice disorders may require surgery. However, voice therapy remains paramount both preoperatively and postoperatively in any voice disorder. Postoperative voice therapy can help the child transition from the use of compensatory phonation patterns, used out of necessity preoperatively, to the establishment of effective phonation patterns with the new laryngeal mechanism postoperatively. Without postoperative voice therapy, there is a potential for the child to perpetuate old phonation patterns or establish new ineffective and potentially phonotraumatic phonation patterns. Surgical management of pediatric dysphonia is covered in separate chapters within the Pediatric Voice Section of this text.

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## APPENDIX 81.1

**GRBAS Scale**

Protocol number:_____ Voice number:_____ Date: ___ / ___ / ___

G _____ R _____ B _____ A _____ S _____

## APPENDIX 81.2

**Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V)**

Name:_____ Date: _____

The following parameters of voice quality will be rated upon completion of the following tasks:

1. Sustained vowels, /a/ and /i/ for 3–5 seconds duration each.
2. Sentence production:
   a. The blue spot is on the key again.
   b. How hard did he hit him?.
   c. We were away a year ago.
   d. We eat eggs every Easter.
   e. My mama makes lemon muffins.
   f. Peter will keep at the peak.
3. Spontaneous speech in response to: "Tell me about your voice problem." or "Tell me how your voice is functioning."

| Legend: | C | = Consistent | I = Intermittent |
|---|---|---|---|
| | MI | = Mildly Deviant | |
| | MO | = Moderately Deviant | |
| | SE | = Severely Deviant | |

SCORE

Overall Severity _____ C I /100
MI MO SE

Roughness _____ C I /100
MI MO SE

Breathiness _____ C I /100
MI MO SE

Strain _____ C I /100
MI MO SE

Pitch (Indicate the nature of the abnormality): ____
_____ C I /100
MI MO SE

Loudness (Indicate the nature of the abnormality): ____
_____ C I /100
MI MO SE

_____ _____ C I /100
MI MO SE

_____ _____ C I /100
MI MO SE

COMMENTS ABOUT RESONANCE: NORMAL
OTHER (Provide description): _____
_____

ADDITIONAL FEATURES (for example, diplophonia, fry, falsetto, asthenia, aphonia, pitch instability, tremor, wet/gurgly, or other relevant terms):

Clinician: _____

## APPENDIX 81.3

### Pediatric Voice Related Quality-of-Life Survey

Please answer these questions based upon what your child's voice (your own voice if you are the teenage respondent) has been like over the past 2 weeks. Considering both how severe the problem is when you get, and how frequently it happens, please rate each item below on how "bad" it is (that is, the amount of each problem that you have). Use the following rating scale:

| | |
|---|---|
| 1 = None, not a problem | (10) |
| 2 = A small amount | (7.5) |
| 3 = A moderate amount | (5) |
| 4 = A lot | (2.5) |
| 5 = Problem is "as bad as it can be" | (0) |

| Because of my voice | How much of a problem is this? |
|---|---|
| 1. My child has trouble speaking loudly or being heard in noisy situations | 1 2 3 4 5 |
| 2. My child runs out of air and needs to take frequent breaths when talking | 1 2 3 4 5 |
| 3. My child sometimes does not know what will come out when she/he begins speaking | 1 2 3 4 5 |
| 4. My child is sometimes anxious or frustrated (because of his or her voice) | 1 2 3 4 5 |
| 5. My child sometimes gets depressed (because of his or her voice) | 1 2 3 4 5 |
| 6. My child has trouble using the telephone or speaking with friends in person (because of his or her voice) | 1 2 3 4 5 |
| 7. My child has trouble doing his or job schoolwork (because of his or her voice) | 1 2 3 4 5 |
| 8. My child avoids going out socially (because of his or her voice) | 1 2 3 4 5 |
| 9. My child has to repeat himself/herself to be understood | 1 2 3 4 5 |
| 10. My child has become less outgoing (because of his or her voice) | 1 2 3 4 5 |

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CHAPTER

# 82

# Treatment of Functional Voice Disorders

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## OVERVIEW

The primary focus of this chapter is to identify common behavioral and vocal characteristics of patients diagnosed with functional voice disorders and discuss practical treatment approaches that have been successful in restoring voice in these patients. The chapter is written in a "How I do it" approach but is certainly not intended to be a comprehensive review of all techniques that can be implemented with these patients. These are specific therapeutic guidelines that are offered for the treatment of voice disorders that often present with a wide range of signs and symptoms.

## TERMINOLOGY AND CLASSIFICATION ISSUES

Koufman describes functional dysphonia as the presence of a voice disorder in the absence of identifiable neurologic or structural pathology.[1] Aronson used the term *psychogenic voice disorder* to refer to a voice disorder, which is "a manifestation of one or more types of psychological disequilibrium, such as anxiety, depression, conversion reaction, or personality disorder".[2] According to Aronson, a conversion voice disorder exists despite normal structure and function of the vocal folds, is created by anxiety, stress, depression, or interpersonal conflict, has symbolic significance for that conflict, and enables the patient to avoid facing the interpersonal conflict directly and extricates the person from the uncomfortable situation. The work of Roy et al. in 2000 revealed that functional dysphonia may be related to anxiety, inhibitory laryngeal motor behavior, and elevated tension states that can lead to maladaptive posturing of both the intrinsic and extrinsic laryngeal muscles.[3] Emotional stress has been widely accepted as a major underlying cause of psychogenic voice disorders. For some, these terms and many others are used interchangeably, often referring to the same disorder. However, the absence of organic pathology, such as vocal fold lesions or neurological impairment of the vocal folds, does not confirm the presence of a psychogenic voice disorder. For example, many patients successfully treated for functional aphonia describe the onset as occurring during an upper respiratory infection (URI) and included significant hoarseness that became so severe that they found it "easier" to purposely whisper rather than continue to speak in the severely dysphonic voice. However, once the URI and acute laryngitis resolved, they were unable to extract their voice from the whisper phonation pattern and subsequently were "locked" into the aphonic voice. The precipitating event that led to the voice problem, the URI, is not what maintained the problem. The new "muscle memory" pattern, established by means of the whisper phonation, became the patient's "default voice" once it was habitualized. As with most patients with this type of functional voice problem, nonspeech phonation, in the form of a cough, throat clear, laugh, cry, and gargle, was preserved. Additionally, the use of terms such as conversion voice disorder, psychogenic voice disorder, hysterical aphonia, and conversion hysteria should be restricted to use by the appropriately trained medical professionals. Brodnitz stated the term conversion hysteria should not be used in the "presence of the patient because of the social stigma attached to it".[4] The presence of stress,

anxiety, and/or depression in these patients often comes about in response to the impact of attempting to communicate with a severe voice disorder rather than the initial presence of these behaviors.

Laryngeal muscle tension can be primary or secondary in nature and is present in many disordered voices. Patients are often relieved to hear that a problem does indeed exist (muscle tension dysphonia or aphonia), thus confirming that the problem "is not all in your head". Validation is extremely helpful in comforting patients' fears of their problem and allows them to move forward in treatment. For some, it provides an "out" for their medical condition, regardless of whether or not there may be a psychogenic component present.

## CLINICIAN-BASED FACTORS

### Establishing the Clinical Bond: Trust, Empowerment, and Responsibility

Effective voice therapy begins with a thorough understanding of the patient's voice problem and the establishment of a patient–clinician relationship that fosters trust and confidence. By the time patients with voice disorders are seen for their initial voice therapy session, many have already been evaluated by more than one specialist and been given several, often conflicting, etiologies and medical diagnoses for their voice problem. A workup by a gastroenterologist may reveal the presence of reflux followed by a strict treatment regimen of medication, dietary restrictions, and other behavioral interventions. A sinus specialist may diagnose postnasal drip and treatment the patient with nasal sprays. A pulmonary specialist may diagnose a variant of asthma and treat the patient with various inhalers. An allergist may perform a comprehensive allergy workup revealing several environmental or food allergies, which are then treated via injections. A psychotherapy consult may reveal that medication and psychotherapy may be beneficial for the patient with stress, anxiety, or anger management. Patients often follow the various treatment recommendations only to find that there is little change in their vocal signs and symptoms. After months of treatment by several specialists without significant improvement, patients may be skeptical that voice therapy will help improve or eliminate their problem. An important first step in securing the patient's confidence is to acknowledge that they most likely were accurately diagnosed; that is, they may have reflux, allergies, and/or postnasal drip, but these particular conditions may not be responsible for his or her voice disorder. Some patients indicate during their initial therapy session that they have been informed by a medical professional that "there are no lesions on the vocal folds (there is nothing wrong)" and that the "problem is all in your head". The foundation of successful voice therapy begins with acquiring the patient's *trust* in the clinician's abilities, which is reflected by the confidence the speech pathologist has in their own skills and how this is portrayed to the patient.

Once the patient understands that the muscle tension problem exists, the initiation of treatment can focus on the patient understanding that this is a "curable" condition that they, the patient, can actually learn (re-learn) to take control over (again). Patients may interpret this as "blame" and become defensive; thus, it is important to inform them at this point that the voice problem is not something they are doing purposely and that if they could have "fixed" the problem when it first began they would have done so. Most patients do not understand that the imbalance in muscle tension is under their control, and the successful clinician focuses on *empowering* the patient to improve the problem. The patient comment "some days *it* does this and some days *it* does that and most days *it* does whatever it wants to do" is quite common and reflects the patient's feeling that the voice disorder can be variable but in no way is under their control. This is indicative of a lack of control, which often leads the patient to lack confidence not only in their voice but their everyday life. The process of empowering patients to improve their voice begins by explaining that there is no "it" controlling the voice, and they have more control over their voice than they realize. The use of negative practice is a simple way of initiating this empowerment process (Table 82.1).

### The Use of Negative Practice: Taking Responsibility

Since the focus of treatment at this point is on convincing patients they have control over their voice, the use of negative practice can be used to illustrate this point. Negative practice involves having the patient purposely produce the voice with *increased* muscle tension beyond the baseline level he or she experience during conversational voice. This may seem counterintuitive to have the patient increase laryngeal muscle tension to produce a tighter, more strained vocal quality. However, once this is achieved, the patient is asked to assess what *he or she* did to achieve that voice. Often they will note the increased laryngeal muscle tension, or the "holding" of

**Table 82.1:** Treatment of muscle tension dysphonia/aphonia : Clinician-based factors

| |
|---|
| *Describe the problem: laryngeal muscle tension!* |
| Provide patient with an "out" |
| "It's not all in your head" |
| "If you could have fixed your voice on your own you would have...you are not to blame for this problem" |
| "You have a *physical problem*...muscle tension!" |
| "If you were told there is nothing wrong with your larynx they were wrong! You have muscle tension dysphonia/aphonia!" |
| "BUT this particular muscle tension problem can be readily fixed" |
| Explain negative practice. |
| Don't spend a lot of time figuring out "why"... |
| Why ask Why? Just Do It! |
| *Lay ground rules to be enforced during progression!* |
| You must set aside everything that everyone else has told you! "My previous therapist told me not to clear my throat!" |
| Do exactly what I tell you to do! |
| No side talk! |
| I'm not here to be your friend...I'm here to fix your voice! |
| You will be in complete control of your voice |
| You will be able to flip back & forth between the good voice and the bad voice (negative practice) |
| Maintain strict criterion of what is acceptable voice |

**Table 82.2:** Methods to elicit normal voice : Technique-based factors

| |
|---|
| Cough |
| Laryngeal massage |
| Head up |
| Throat clear |
| Laryngeal manipulation |
| Head down |
| Laugh |
| Masking |
| Inhalation phonation |
| Cry |
| Delayed auditory feedback |
| Sigh |
| Pulling the tongue |
| Vocal fry |
| Humming |
| Rigid endoscopy |
| Phonation on exertion |
| Singing |
| Fiberoptic endoscopy |
| Forward focus; kazoo |
| Lip trills |
| Gargle |
| Tongue trills |
| Role playing/recreating conversation when voice "was lost" |
| Talking about emotional impact of voice loss |

breath, or the locking of the upper chest in order to achieve the strained vocal quality. Once the patient has the ability to increase the tension consciously, he or she is instructed to *reduce* the muscle tension and "don't allow that to happen". This leads to further control of laryngeal and respiratory muscle tension, with appropriate coordination of respiration and phonation, as the patient begins to take *responsibility* for the manner in which his or her voice is produced.

## Success Involves Detailed Treatment Guidelines

Numerous voice therapy techniques exist that can be implemented to treat functional dysphonia/aphonia (Table 82.2). Although each approach is known to be successful, strict adherence to specific treatment guidelines or "clinician-based factors" is required to obtain the best clinical results. Voice clinicians are often frustrated and dismayed when treatment of patients with muscle tension aphonia/dysphonia is unsuccessful even though they have attended a course and learned a particular therapy technique such as laryngeal manipulation. The successful return to normal voice in one therapy session is achieved by a combination of technique-based factors, such as gargling, coughing, throat clearing, and laryngeal manipulation, but more importantly the successful implementation of clinician-based factors such as the use of "no side talk", the use of nonlinguistic utterances, and the manner in which transitions toward successful voicing occur. The ability to empower the patient to take control of his or her voice production has been detailed above. The importance of the patient developing trust in the clinician cannot be overstated. Clinicians who lack confidence in their own clinical abilities will have difficulty in establishing the trust of the patient. Clinician confidence breeds patient confidence. One of the most important clinician-based factors that should be implemented during the transition back to normal voice production is the use no "side talk" by the patient, as described by Kadar (A. Kadar, Personal Correspondence, 1998). This involves instructing the patient *not* to phonate unless instructed by the clinician. This is

important because although normal voice may be elicited when producing a nonspeech utterance, the improvement in voice may be lost if the transition to linguistic productions occurs too early in the transition. Nonspeech utterances include a cough, throat clear, gargle, laugh, or cry to name a few. Although many speech pathologists have been trained to shy away from eliciting potentially phonotraumatic utterances, the use of a cough or exaggerated throat clear can be very successful in eliciting normal phonatory patterns. These are used for short term to assist in resetting vocal fold closure patterns, especially when increased muscle tension interferes with vocal fold closure, a condition described as muscle tension pattern I by Morrison et al.[5,6] Once normal phonation is achieved, the rate of transition from nonspeech utterances to meaningful linguistic units is determined by the clinician's insight and experience relative to the patient's level of success. The process of motor relearning or the re-establishing of muscle memory is quite variable from one patient to the next, and thus the use of strict treatment criteria is essential to the success of the treatment. Sound productions that are not entirely clear and free of perceived muscle tension cannot be accepted as normal. At this point, the patient clinician relationship must be one of support but strict at the same time. Often, the extended use of single and multisyllabic "nonsense" (nonlinguistic) utterances is necessary to re-establish and maintain the normal voice. Progressing too rapidly at this time can lead to relapse. However, once established, it is not necessary to follow the traditional hierarchy of sound, word, and phrase production. Transitioning to normal conversational voice occurs quickly once single word production is mastered. As success is achieved with return of normal phonatory patterns, the level of patient responsibility is accelerated as they now begin to understand that *they* are in control of their voice. The use of negative practice is once again demonstrated so that the patient is able to produce one sentence of a reading passage or conversational voice in the "disordered voice" and the next in "normal voice" demonstrating complete control and confidence. The use of "resets" is discussed with the patients so they understand what they need to do to re-establish normal voice should the problem reoccur in the future. The patient understands that "resets" are not "crutches" but simply quick ways to re-establish normal voice. Resets might include the exaggerated throat clear into sustained phonation, a phonatory interjection such as "hum" or "ah", or an internal reduction of muscle tension or *internal self-correction* that leads to improvement in the coordination of respiration and phonation. Patients are instructed that it may take a few days before their "vocal defaults" are reset, meaning that the old, muscle tension voice may be spontaneously produced if the patient does not monitor their voice production. A helpful analogy is to explain that the change from normal to disordered voice is much like disrupting of the defaults on their home computer in that their customary normal voice "defaults" have been replaced by muscle tension "defaults", which may creep back into their conversational voice if not monitored and corrected immediately. Another explanation describes the presence of two sets of parallel "vocal train tracks" and that for most of their life their voice has been normal, one set of tracks. Then something happened that changed the voice, possibly an URI that led to the development of a strained vocal pattern, phonating in a whispered voice, which then represents the other parallel set of tracks. The disordered voice "tracks" are well embedded (muscle memory) and become the primary voice pattern (the "default"). The fact that the other parallel set of tracks representing the normal voice still exists but is no longer "embedded" like the muscle tension tracks. However, the patient should understand that the transition from one voice to the other often occurs quite rapidly. At this time it is also important to stress that the original cause of the voice change, possibly the URI, is not what is maintaining the voice problem and the role of muscle memory plays in the process. The "setup", that is, the explanation of the problem, what to expect as the normal voice is elicited, and why normal voice can be achieved often takes longer than the actual "fix" and return of normal voice.

During the process of eliciting and re-establishing normal voice production, the clinician should be aware that the patient may experience an emotional release as evidenced by sobbing or crying. This behavior should be encouraged for several reasons. Often the patient has been frustrated and angered by the impairment of their voice. One adolescent expressed the embarrassment he felt because of the high pitch of his voice, a condition known as puberphonia. This led to significant depression and other behavioral issues. "My entire life has changed because of my voice problem". The act of crying, while beneficial in releasing emotion, is also helpful in physically lowering laryngeal positioning in the neck that reinforces the better voice.

## Indications for Psychiatric Referral

Personality-related issues and other psychological disorders may restrict the progress made in re-establishing normal voice. A combination of psychological, social, and physiological factors can impact normal voice production. Several clinical signs have been identified, which were considered indications for psychiatric referral. These include reduced patient motivation, inappropriate patient response to demonstrated voice improvement, recurrence of dysphonia following initial recovery, and persistent signs of anxiety, depression, or psychological conflict.[7] Secondary gain should also be explored as a reason for maintaining a functional voice disorder and the lack of progress in voice therapy. However, the lack of organic lesions on the vocal folds should not automatically result in the voice problem being labeled "psychogenic" in nature. The presence of puberphonia that occurs in the absence of laryngeal pathology does not necessarily indicate that the patient has a voice disorder of psychogenic origin. The vast majority of the patients with "functional dysphonia/aphonia" treated by this clinician over a 35-year period have not been viewed as having a psychogenic component to their voice disorder.

# SPECIAL CONSIDERATIONS: TREATMENT OF PUBERPHONIA

Puberphonia refers to the persistence of a high-pitched voice beyond the age at which voice change is expected to have occurred. Although primarily a male problem, the persistence of a high habitual pitch in a woman can also occur; however, as Colton and Casper noted, the problem is typically more pronounced in males because the laryngeal growth results in a more significant drop in fundamental frequency in males (one octave) than in females (three to four semitones).[8] Boone describes puberphonia as "the high-pitched voice in a young man who has already completed puberty", and that the "typical puberphonic patient is obviously 'thrilled' with hearing his lower pitched speaking voice".[9] While this positive reaction to their new found voice may be true for many puberphonic patients, some will state they are not pleased with the sound of the lower pitched voice and may decide they are not ready to use the new voice in everyday communication.

The initial presentation of puberphonia can vary from use of a consistently high-pitched conversational voice to persistent diplophonia, with the vocal pitch varying from falsetto to chest voice with frequent pitch breaks. One patient was readily able to demonstrate his "other voice" and readily spoke in a lower pitched, age-appropriate voice but stated he was indifferent about using the lower pitched voice at the present time. Still others have been quite pleased with the elicitation of the lower pitched voice, often achieved within minutes of implementing specific vocal techniques aimed at lowering laryngeal positioning. Although bullying has been tolerated much less in recent years, most puberphonic boys are quite aware of the difference in the sound of their voice. However, in a couple of instances, the referral for evaluation was requested by the parents when in fact their son did not feel his voice was a problem. The presence of psychosocial factors should be explored in individuals where male identity issues may be of concern, the transition to adulthood is difficult, or the pressure to succeed in school is an issue. Two clinical cases below illustrate these issues.

## Clinical Case 1: Jose, a 14-Year-Old Eighth Grader

"*The new voice is not my voice…it is not me!*"

Jose was accompanied to the voice evaluation by his mother, who previously was being treated by an otolaryngologist for ear pain when he noted her son's high-pitch voice. During stimulability testing, a normal, lower pitched voice was elicited using digital laryngeal reposturing and vegetative vocalizations including cough. The reaction of the individual to the dramatic change in voice should always be noted. Typically the reaction involves surprise, joy, and happiness. In Jose's case, he became very quiet and subdued for several minutes and eventually began to cry. When prodded, Jose stated that "the new voice is not my voice…it is not me". After a long discussion with Jose and his mother, it was apparent that he was not ready to accept his "new voice", and the emotional reaction of hearing the lower pitched voice was extremely traumatic for him at that time in his life. The decision was made to offer Jose a follow-up appointment in 4–6 months if he so desired with the option of returning at any time if he wanted to be seen sooner. The option of counseling was mentioned to Jose's mother if she felt he would benefit from further exploration of his feelings about his voice.

The concern of how friends and family would receive the individual's lower pitched voice is quite common in this clinician's experience. For some, the suggestion that they wait until a school vacation or other break before implementing the voice change has been well received. Puberphonia patients are typically males who have recently gone through puberty. However, several patients have been older, one in particular being age 45; when asked why he was pursuing voice therapy to change the pitch of his voice, he stated his fiancée had asked him to consider treatment. Once the lower pitch was established, he decided to wait until he went on an extended vacation before permanently implementing the voice change.

## Clinical Case 2: Sally, a 16-Year-Old High School Student

"*I only lose my voice when I have to give a speech…but I like doing it!*"

Sally presented with a 12-month history of frequent voice loss and high-pitched (falsetto) voice whenever she became extremely nervous and especially when she had to do an oral presentation at school. She denied any fears of public speaking and stated she actually enjoyed giving speeches in front of her class. She stated that her voice would often return to normal several weeks after becoming breathy and high pitched. "Sometimes it just goes up and I lose it for no reason!"

The importance of undergoing a complete workup with an otolaryngologist including endoscopic examination of the larynx with all voice patients must be stressed. Once the presence of organic pathology has been ruled out and the patient has been diagnosed with muscle tension dysphonia/aphonia or what some clinicians refer to as a "functional voice disorder", the speech pathologist can further assess the perceptual characteristics of the voice as well as obtaining acoustic and aerodynamic data that should complement the endoscopic/stroboscopic examination findings. For example, many patients who have severe laryngeal muscle tension and breathy, whisper-like vocal quality often present with vocal folds that are not completely adducted the entire length, yet are extremely stiff. This is a condition sometimes referred to as "nonadducted vocal hyperfunction" or a whisper configuration pattern of glottal closure in which there is severe isometric muscle tension in the intrinsic laryngeal muscles (muscle tension aphonia). When the patient is instructed to cough, phonation is essentially normal indicating that "the system" is capable of producing normal voice in terms of pitch, loudness, and quality. Although many speech-language pathologists and voice specialists have been appropriately instructed that coughing, throat clearing, laughing, and other aggressive phonatory maneuvers can be detrimental to the larynx and if maintained, can lead to phonotraumatic changes to the vocal folds; these tasks can be extremely successful in eliciting normal voice when used appropriately for short term by the skilled clinician. The elicitation of normal voice during a cough also helps to rule out the presence of other pathology such as vocal fold restriction or fixation, which can also present as breathy vocal quality and confirms the diagnosis of muscle tension dysphonia/aphonia.

The therapeutic approach used to elicit normal voice with Sally involved the use of laryngeal manipulation to lower the laryngeal positioning in conjunction with coughing, which was extended into a brief period of aggressive throat clearing that was eventually shaped into the /a/ vowel followed by the addition of numbers. The transition from the throat clear to the extended /a/ vowel and number was completed without interruption of the breath or phonation. All phonation was completed on one continuous breath. The importance of not allowing Sally to use "side talk" during this therapeutic maneuver was critical to the successful transition from phonation on the throat clear to the production of linguistic units. As with most patients, it was not necessary for Sally to follow a complete traditional hierarchy of speech production during this transitional period. For example, once automatic speech has been achieved the patient can be instructed to read a standard passage or transition to conversational voice. On occasion, patients may experience difficulty transitioning from the vowel to counting and may require production of nonsense (nonlinguistic) syllables, which are achieved by adding consonants to the initial vowel before reintroducing linguistic units.

In Sally's case, she never sought additional voice therapy after regaining her voice in the initial voice therapy session. Whether she continued to experience voice loss prior to oral presentations is unknown. However, patients who experience numerous bouts of voice loss and return for additional voice therapy on several occasions usually demonstrate a lack of control over their voice and may be considered to have a psychogenic component to their voice problem.

**Table 82.3:** Laryngeal manipulation to open the thyrohyoid space

- Palpate thyroid cartilage
- Slide superiorly into thyrohyoid space
- Palpate hyoid bone superiorly
- Provide deep rotary massage of area
  - 8–10 revolutions forward/downward
  - 8–10 revolutions backward/upward
  - 8–10 seconds pull down and hold
- Palpate thyrohyoid space during spontaneous laugh

## LARYNGEAL MANIPULATION: HOW I DO IT

There are many successful techniques that can be used to unload laryngeal muscle tension and return the patient's voice to normal (Table 82.3). The use of circumlaryngeal massage first described by Aronson,[10,11] later made popular by Roy,[12,13] and adapted by many to include laryngeal manipulation and manual therapy techniques[14,15] has been extremely successful in repositioning the laryngeal musculature and eliciting normal voice. The implementation of effective laryngeal manipulation techniques requires thorough knowledge of laryngeal anatomy, familiarity with palpation of normal and disordered laryngeal musculature, caution when manipulating laryngeal structures, and most importantly, common sense. Although the biomechanics of the larynx continue to be poorly understood, at a basic level it is known that increased musculoskeletal tension in the larynx rarely involves a single muscle group. Moreover, laryngeal muscles work together synergistically as well as antagonistically to produce an overall muscle "balance" during vocal fold vibration and normal voice production. It is an imbalance in the functioning of these muscle groups that can lead to vocal symptoms and, in many instances, vocal fold pathology.

The range of symptoms related to excessive musculoskeletal tension in the larynx is broad and can include odynophonia (pain on phonation) and/or pain at rest, ranging from sharp, stabbing pain to dull, aching pain, odynophagia (pain on swallowing), dysphagia, generalized laryngeal discomfort, increased throat clearing, fatigue of voice, globus sensation in the throat, restricted pitch and/or loudness and/or flexibility range, as well as any number of vocal quality issues including vocal fry, creak, hoarseness, harshness, and breathiness. The physical symptoms, such as pain, may be unilateral or bilateral

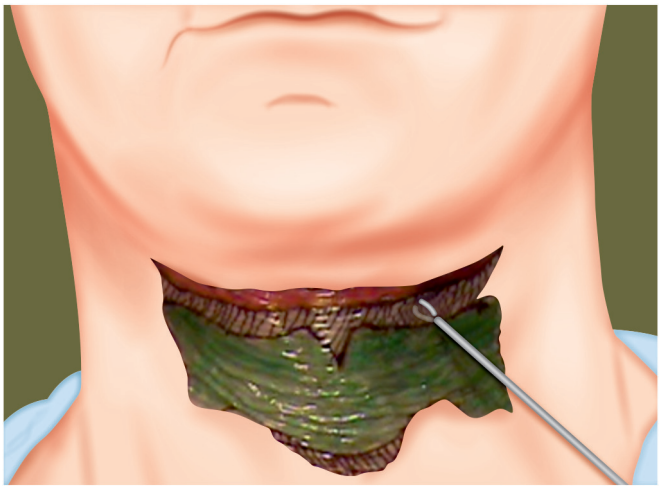
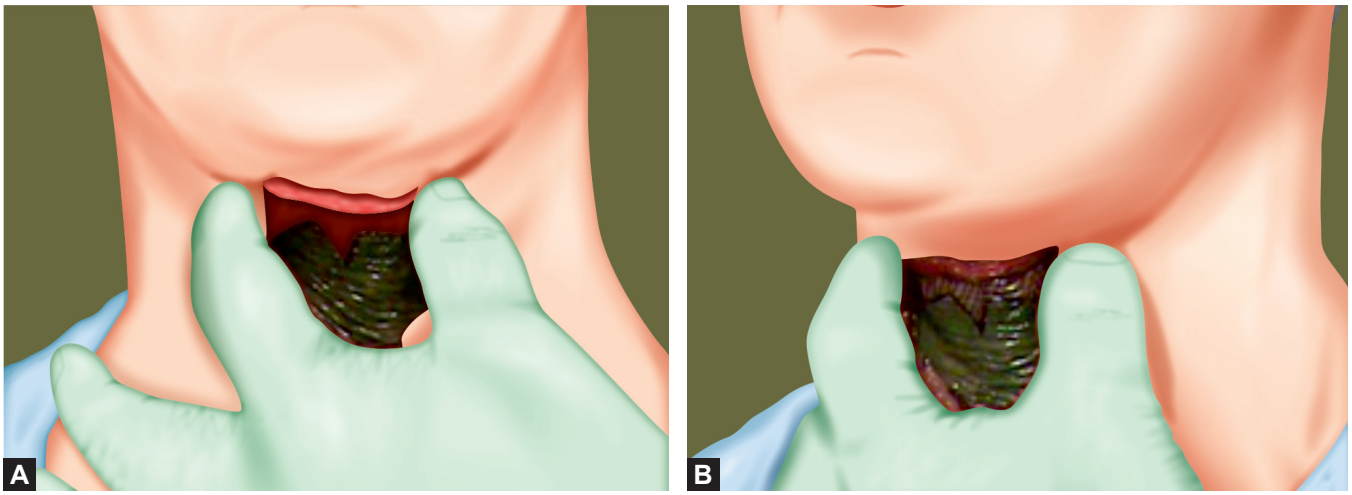


**Fig. 82.1:** Template depicting the laryngeal structures. Pointer indicates the thyrohyoid space.

and may be symmetric or asymmetric in nature. An extensive, detailed history taken by the clinician before implementing the manipulation work is imperative to fully understand the extent of the patient's symptoms. Likewise, the clinician must remain focused on "reading" the patient during the manipulation work so that areas of discomfort can be properly assessed and treated. The clinician's ability to properly palpate the laryngeal musculature is crucial to the overall success of the techniques used.

There are many different areas of the larynx that can be digitally manipulated using several different manual techniques. Many of the patients with muscle tension dysphonia, musculoskeletal tension dysphonia, or nonadducted vocal hyperfunction present with high laryngeal positioning in the neck. The larynx is elevated as evidenced by decreased space between the thyroid cartilage and the hyoid bone, and pain on palpation of the area. Tightness in the base of tongue is often reported, and overall restricted inferior and/or lateral movement of the thyroid cartilage is noted on palpation.

Two techniques that can be used involve repetitive manipulation and stretching. After appropriate palpation of the entire laryngeal area has been completed, the manipulation begins by placing the thumb and index fingers on either side of the thyroid cartilage at the level of the thyroid lamina. The fingers are slid upward into the thyrohyoid space, the space between the superior aspect of the thyroid cartilage and the inferior aspect of the hyoid bone (Fig. 82.1). If there is no space palpated between the thyroid cartilage and the hyoid bone, the manipulation/massage begins where the two structures meet. Short,




**Figs. 82.2A and B:** Illustrations showing thyrohyoid manipulation.

elliptical-shaped movements with the thumb and index finger are made within the space in an anterior-posterior motion that is relatively deep yet tolerated by the patient (Figs. 82.2A and B). Eight to 10 rotary elliptical motions are made (repetitive manipulation) followed by a pull down motion (stretch) that is held for 8–10 seconds. The patient is then instructed to swallow and the entire manipulation is repeated. Typically, the exercise is continued for a period of 8–10 minutes making sure that proper placement is maintained and that there is no migration of the manipulation laterally, which could place pressure on the carotid arteries. If at any time during the exercise a carotid pulse is palpated, the manipulation is stopped, and the thumb and index finger are repositioned toward the midline of the thyroid cartilage. The depth and strength used during the manipulation/massage is influenced by what the patient is able to tolerate. Often, the level of discomfort subsides as the manipulation progresses.

## ASSOCIATED PROBLEMS: RESPIRATION, PHONATION, ARTICULATION, AND RESONANCE

### Clinical Case 3: Franklin, a 15-Year-Old Acting Student

"*My voice and my breathing are both tight; it's hard to get the words out*"

Occasionally, patients present with impairment of multiple systems, some of which are directly related to one another, others completely independent of the other. Franklin presented with a 3-month history of gradual onset (over a three day period) of strained, strangled voice quality, shortness of breath, and changes in resonance and speech. Palpation of his laryngeal musculature revealed elevated laryngeal positioning with absence of the thyrohyoid space in the presence of severe pain in the hyoid and cricothyroid region. His speech was characterized by moderate hypernasality with prolongation and distortion of several phonemes, particularly initial position sibilants.

Treatment focused on reducing laryngeal musculoskeletal tension through gargling and laryngeal manipulation. Following aggressive manipulation, normal voice was re-established and treatment focused on reducing hypernasality and the dysfluent speech pattern. Before implementing specific treatment strategies, the suggestion was made to the patient that the resonance and speech difficulties were the result of increased muscle tension, which had become habitualized but could readily be improved. The idea that Franklin had the ability to control the tension in his speech was reinforced ("don't allow this to happen…") and through the use of modeling and negative practice, he was able to eliminate the hypernasality and the dysfluent speech. The terms "functional stuttering" and "functional hypernasality" were appropriate terms to describe the disordered behaviors since all system impairments were resolved within the initial extended voice therapy session. Once again, the process of empowering the patient was successful beyond the realm of voice therapy, as both resonance and fluency improved dramatically, too. It was important to convince the patient that the problem with the fluency of his speech and the resonance of his voice was under his control and could be readily improved.

## DOCUMENTING THE EFFICACY OF TREATMENT

As the demands for accountability of efficient, successful treatment continue to be stressed in healthcare, clinicians are being called upon to objectively document this progress. Progress made in the treatment of muscle tension aphonia/dysphonia can be monitored not only via acoustic and aerodynamic assessment, but more importantly through quality of life measures. The use of pediatric voice-related quality of life with pediatric voice patients and the voice handicap index (VHI) with adults and children can dramatically help document patient progress. Patients often begin voice therapy with scores that indicate that the voice disorder is significantly impacting their life and within one therapy session readministration of the VHI, for example, reveals a significant drop in scores to well within the normal range. These measures help to illustrate the importance of the treatment being provided.

## SUMMARY

Some of the most satisfying work by a voice therapist can occur in the treatment of patients with functional voice disorders. Dramatic changes that result in the return of normal voice often within the initial treatment session is extremely satisfying for both the patient as well as the clinician. Mastery of these clinical techniques is essential in the overall success achieved with these patients. Critical listening and learning to "read the patient" must be incorporated into these therapy sessions. However, the clinician must also know when to take control of the therapeutic interaction, providing strong rationales for the techniques being implemented. Patients respond best when they are informed that they do indeed have a problem and a reason for their voice disorder (muscle tension) and that the problem is "not all in their head". Once the transition is made from "you are not to blame for your voice problem" (if you could have fixed it months ago you wouldn't be here now) to "you are now empowered…you now control your own voice" (there is no "it"), the focus of responsibility shifts to the patient as does the reward for the improvement in voice. The patient has now gained confidence not only in his or her voice but in his or her life as well.

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CHAPTER

# 83

# Surgical Treatment of Benign Vocal Fold Masses

***Melissa M Statham***

When maximal behavioral and medical interventions do not achieve satisfactory improvements in voice production, surgical treatment may be considered for amenable lesions. Basic science and clinical research performed over the last two decades has yielded an improved understanding of benign laryngeal lesions in adult patients. Further study in the developing vocal fold mucosa in children has contributed to theories regarding phonotrauma mechanisms in the pediatric patient, and histological characteristics of vocal folds in the developing child are covered elsewhere in this text. Advancements in understanding microanatomic characteristics of developing vocal fold mucosa, histopathological characteristics of phonotraumatic lesions, improvements in diagnosis, and phonomicrosurgical techniques have all contributed to improvements in surgical care of vocal fold lesions.

## EMPHASIS ON ACCURATE DIAGNOSIS

Although novel methods of assessing vocal fold oscillation, such as high-speed photography, videokymography and photoglottography, have emerged over the last two decades, laryngeal videostroboscopy remains the most practical and clinically useful tool in assessing vocal fold vibratory characteristics and glottal configuration. As advancements in endoscopic imaging modalities have improved and endoscopes have gotten smaller, ease of performing highly magnified, videostroboscopic examinations in children during a clinical visit has also improved. As such, vibratory information over a range of phonatory tasks, and vocal intensities can be easily obtained.

A recent report highlights the importance of videostroboscopic evaluation of children with dysphonia when compared with flexible laryngoscopy. Mortensen et al. reported on a cohort of 80 children who had previously been examined with flexible laryngoscopy and treated with voice therapy for the presumed diagnosis of vocal fold nodules.[1] After performing videostroboscopy in all of these patients, only 51% of these children were noted to have nodules. With videostroboscopic examination, many other laryngeal pathologies were able to be diagnosed in this cohort, and treatment was further guided in a substantial proportion to involve surgical intervention in 20% of patients as well as larger group being treated with other medical interventions. More accurate diagnosis changes expectations of voice therapy and may more appropriately guide surgical candidacy in children with mid-membranous vocal fold pathology.

## PEDIATRIC PATIENTS

### Unique Considerations for Phonotrauma

Vocal fold oscillation during phonation leads to impact stress during repeated contact, and Titze has analyzed these stress forces such that the maximum impact stress occurs in the mid-membranous vocal fold.[2] Further studies investigating the rheological characteristics of vocal folds during phonation as well as models investigating characteristics of vocal fold scar have demonstrated that repeated trauma leads to fibrovascular changes in the mid-membranous vocal fold. These models of vibratory forces are also based on a more adult configuration of a

mature vocal fold with the membranous vocal fold being two-thirds the length of the vocal fold. Young children have a proportionally larger respiratory glottis such that the rheological characteristics of the vocal folds during oscillation may differ in children until their vocal folds grow to more adult proportions.

The vocal folds are subjected to several forms of mechanical stress forces during phonatory tasks and other forceful adductory tasks, such as coughing, repeated retching, or vomiting. Repetitive vocal overuse, abuse, and/or misuse as well as the aforementioned presumably causes trauma from increased stress forces and the ensuing inflammatory responses in the vocal fold mucosa. The true incidence of congenital vocal fold lesions is unknown. Previous studies examining phonotrauma and the inflammatory markers involved in remodeling of the superficial lamina propria, and to a lesser extent the vocal fold epithelium, demonstrate that the pathological changes in vocal fold polyps, cysts, and nodules occur within the superficial layer of the lamina propria.[3-6] Histopathological studies examining phonotraumatic lesions in pediatric patients have not yet been performed. In addition, inflammatory mediators involved in phonotrauma continue to be elucidated, but studies are in models of more mature vocal fold mucosa,[7-8] and the mediators in pediatric phonotrauma in the developing lamina propria have not been characterized.

Children with vocal fold lesions may also have other confounding communication impairments such as motor speech abnormalities, apraxia, motor planning difficulties, or abnormal resonance, such as in the setting of velopharyngeal insufficiency. In these confounded clinical scenarios, prioritizing treatment of communication impairments and recommendations for surgical treatment of vocal pathology can be challenging. For instance, it remains unclear if phonotraumatic behaviors are adopted as a compensatory mechanism for another deficit, and the treatment of this deficit may make treatment of the vocal fold pathology more straightforward, i.e. treatment of velopharyngeal insufficiency prior to considering surgical excision of a vocal fold cyst.

## VOCAL FOLD PATHOLOGY

### Epithelial Lesions

Epithelial lesions of the vocal folds are causes by infectious etiologies (most commonly fungal), epithelial keratosis, papillomatosis lesions (covered elsewhere in this text), and malignant masses (covered elsewhere in this text). The main concern for keratosis of the vocal folds is the potential for malignant degeneration of keratotic lesions, which is extremely rare in children. Evaluation and treatment of keratotic lesions include a careful diagnostic evaluation including microlaryngoscopy with high-powered operative magnification and excisional biopsy performed with phonomicrosurgical microflap technique (see below).

### Subepithelial Lesions of the Lamina Propria

As outlined elsewhere in this text, the lamina propria is a vital structure to vocal fold oscillation, and as such, viscoelastic properties of the lamina propria effect vocal quality. Lesions arising in the lamina propria are most commonly caused by repeated trauma. The region of the vocal fold in which these lesions most commonly occur is in the mid-membranous vocal fold, in a region termed the "striking zone" as based on the conceptual modeling of maximal collision forces in this location.[9] Lesions in this location are typically bilateral. Nomenclature and description of these lesions are discussed elsewhere in the text.

## PHONOMICROSURGERY

### Introduction

When maximal behavioral and medical interventions do not achieve satisfactory improvements in voice production, surgical treatment may be considered. With refinements of microsurgical endoscopic techniques and instrumentation, reports in the literature have led to advancements in understanding optimal surgical approaches for mid-membranous vocal fold pathology. Phonomicrosurgery includes a broad category of surgical procedures with the goal of improving vocal quality. The surgical principles are based on the microanatomy of the vocal folds within the construct of minimal disruption and preservation of vibratory mucosa as based on its importance in vocal fold physiology. Techniques aim to limit dissection to as superficial of a plane as possible as to maximally preserve uninvolved vibratory mucosa (lamina propria and epithelium).

### Preoperative Considerations

Phonomicrosurgery is an elective procedure and is offered when less invasive behavioral and medical modalities have failed to adequately improve vocal quality. Realistic

and thorough evaluation of the patient's functional limitations and impairment from their vocal quality should be reviewed within the context of the underlying etiologies of the resultant phonotrauma as well as their other medical conditions. Preoperative voice therapy is performed as psychological and behavioral preparation for vocal rehabilitation postoperatively (see below). When timing the surgical intervention of vocal fold lesions, consideration should be paid to the patient's confounding vocal demands and potential for phonotrauma in the perioperative period. For instance, surgery should be planned at the conclusion of sports season or after a child is particularly symptomatic with seasonal allergies with concomitant coughing. Ideally, all children who are undergoing phonomicrosurgery for vocal fold lesions should undergo preoperative videostroboscopy, and this examination should be used to augment operative examination for incision site planning as well as degree of dissection and excision.

## Equipment and Surgical Exposure

In general, the largest laryngoscope that can be safely placed in the pediatric patient is preferred for phonomicrosurgery. This allows for improved operative exposure and access to the vocal fold lesion(s). Key instrumentation includes microlaryngeal knives, specialized blunt microdissectors, a variety of angled scissors, a variety of angled grasping forceps, and small suctions (3, 5, and 7-French). Special considerations in children include the need for shorter instrumentation such that the surgeon can be stably positioned and also closely positioned to the patient. Laryngoscope suspension apparatus include gallows suspension and rotational/fulcrum devices.

Multiple telescopes should be used to photo-document as well as to characterize the morphology and extent of lesions. Particularly, the diagnostic utility of the 70-degree telescope in the operative evaluation has been described.[10] This view allows clear visualization of the laryngeal ventricles, anterior commissure, and particularly the infraglottic vocal folds. Typical focal length on the operative microscope used for phonomicrosurgery should be 400 mm, as this allows adequate space for instrumentation to pass between the microscope and the proximal end of the laryngoscope. In children, a fine focused microscope with adjustable focal lengths can be advantageous as this allows the surgeon to position closer to the patient. Binocular vision at the highest powered level of magnification should be maintained throughout the procedure. The microscope and surgeon are positioned such that the view through the laryngoscope is coaxial with the longitudinal axis of the laryngoscope.

A distinct difference in pediatric phonomicrosurgery is the small size of the patient's vocal folds and glottis. Many times, placement of an endotracheal tube can greatly obscure the membranous vocal fold, and placement of even a relatively small endotracheal tube in children can make microdissection nearly impossible. As such, an anesthetic technique with spontaneous ventilation can be advantageous, but this must be performed in a very controlled setting as to minimize vocal fold movement during dissection. Jet ventilation can be performed, and transtracheal ventilation is preferred over supraglottic jet ventilation as the former avoids tissue vibration and desiccation of the vocal fold mucosa.

Patients are placed in a supine position on the operating table. Optimal head and neck position is having the neck flexed and the head extended in a "sniffing" position.[11] Placement of a shoulder roll places the patient in a suboptimal position for laryngoscope placement and obscures a coaxial microscopic view of the larynx, and as such, should not be used. Dental protection, with placement of a tooth guard device, should be performed before insertion of a laryngoscope.

The laryngoscope should be placed and positioned to be just proximal to the respective vocal fold lesion(s). Care should be undertaken such that the laryngoscope does not touch the vocal folds themselves as this can obscure the anatomic orientation and nature of the vocal fold and often distort the pathology as well. External compression on the anterior neck can aid in posteriorly displacing the vocal folds for better visualization of pathology, and this can be performed with the aid of Velcro straps or wide surgical tape application.

## Surgical Principles

The microflap approach to excision of vocal fold lesions is a key concept to phonomicrosurgical procedures. This technique involves making an incision immediately lateral to the epithelial or subepithelial pathology, and in doing so, minimal disruption to surrounding tissue is performed. Prior to planning an incision site, the lesion(s) should be palpated (Fig. 83.1). Subepithelial injection can be useful as a hemostatic measure as well as creating a plane of dissection beneath the epithelium and Reinke's space, thus elevating a mass in this plane. This injection can also result in tension on the epithelium that aids in blunt dissection from the superficial lamina propria.

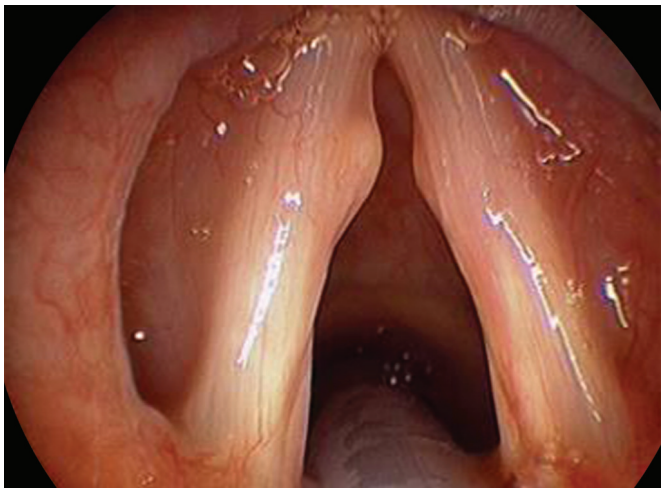

**Fig. 83.1:** Operative magnified microscopic view of left vocal fold cyst and right vocal fold reactive lesion.

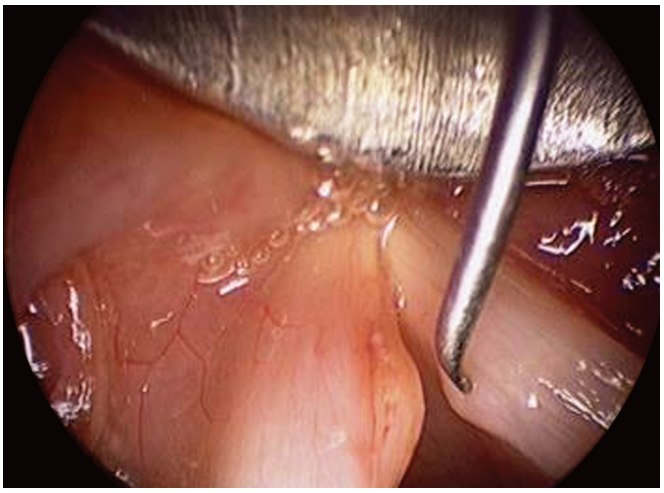

**Fig. 83.2:** Operative magnified microscopic view after epithelial microflap incision lateral to left vocal fold cyst and palpation of right vocal fold reactive lesion.

The incision is performed with sharp microlaryngeal scissors or a sharp microlaryngeal knife, as using less sharp instruments can tear the epithelium and injure involved tissues. Care should be undertaken to only penetrate the epithelium and not disrupt deeper structures (Fig. 83.2). A small curved blunt microdissection elevator can be used to start the elevation of the microflap medially. This plane has been well demonstrated in histologic studies. In a human cadaveric study, Grey et al.[12] found a consistent plane of dissection approximately 20–47% of the depth of the lamina propria when a blunt dissection technique is performed with semiblunt surgical microdissectors. This plane of dissection corresponds with the transition of the superficial layer of the lamina propria to the deep layer. Initiation of this dissection plane can often most easily be performed anterior and posterior to a particular vocal fold lesion. Careful blunt dissection with the elevator is performed around the lesion beneath the epithelium and creates the microflap.

Gentle retraction on the flap medially can be performed with a variety of forceps. Alternatively, the lesion can be retracted with gentle suction (Fig. 83.3). The surgeon should take great care to avoid fenestration of the microflap as this complicates the dissection of the epithelium from the subepithelial pathology as well as the ability to preserve the overlying microflap for primary wound healing. Preservation of the vocal fold cover is advantageous for optimal primary wound healing, and healing by secondary intention is avoided when circumstances allow. The value of this has been reported when lesions arise in the superficial layer of the lamina propria and when overlying epithelial cover has normal appearance at the time of microdissection, and reports have highlighted the importance of preserving vocal fold epithelium and superficial lamina propria when surgically treating pathologic lesions lying deep to the epithelium.[13] However, some vocal fold lesions, such as pedunculated polypoid lesions, have attenuated overlying epithelium, and as such, can be treated well with surgical truncation.

Some lesions are not in the immediate subepithelial space but are deeper in the lamina propria toward the vocal ligament, and in this setting, microflap elevation is more easily accomplished. However, dissecting the vocal pathology from the vocal ligament can be very difficult. Fibrous bands tend to adhere the pathology to the vocal ligament, and these should be carefully released from the ligament and in doing so, always erring on the side of the pathologic lesion. Particularly, management of large intracordal vocal fold cysts can be very challenging, as these lesions tend to lead to also atrophy or dehiscence of the deeper layers of the lamina propria. In these cases, maintenance of an intact cover particularly optimizes preservation of the vocal fold mucosa. However, reports have suggested that surgical marsupialization of intracordal vocal fold cysts is associated with substantial improvements in vocal quality and vocal fold oscillation.[14] Recurrence rates after marsupialization are unknown, and as such, this may complicate further surgical approaches.

At the conclusion of lesion removal, the microflap is redraped in the anatomic position (Fig. 83.4). After this is performed, palpation of the operative site should be performed to determine if any residual abnormality remains.

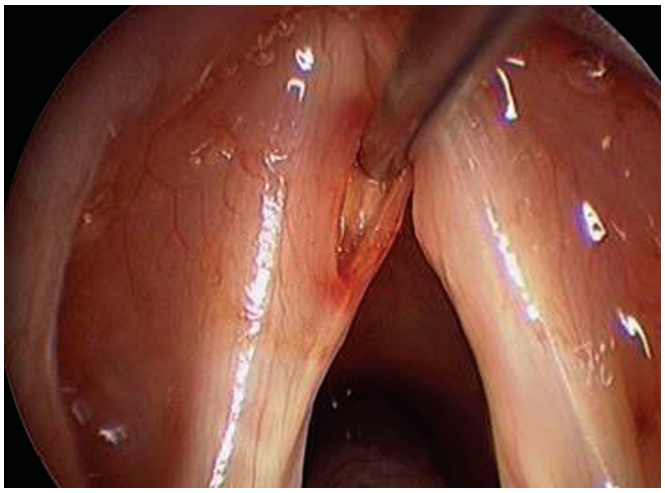

**Fig. 83.3:** Operative magnified microscopic view of left vocal fold cyst being retracted by suction during phonosurgical microdissection.

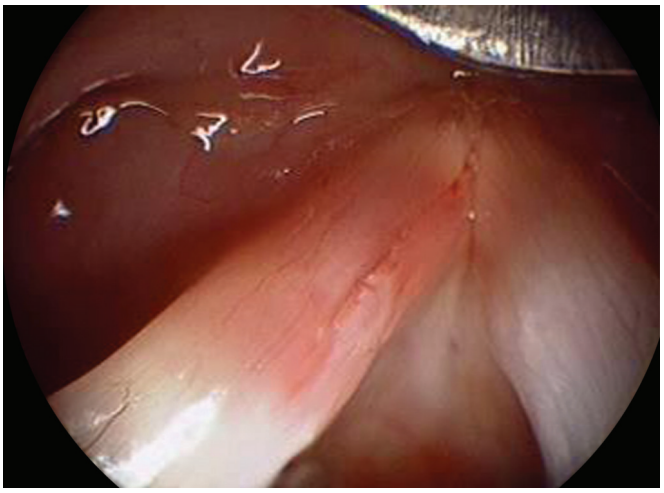

**Fig. 83.4:** Operative magnified microscopic view of left vocal fold cyst operative site after phonomicrosurgical excision.

If any pathology remains, this should be removed in the most complete and conservative fashion. Overly aggressive removal should be avoided, however, as over-removal of deeper vocal fold tissues can result in scar and permanent deformity of the free edge of the vocal fold. Ultimately, the free edge of the vocal fold should be straight after a lesion is removed.

Vocal fold microflap adhesion has been theorized as optimal for wound healing after phonomicrosurgery. In a canine model, Fleming et al. compared wound healing of vocal fold epithelial defects by secondary intention versus microflap suturing techniques.[15] In this model, a trend was identified toward improvement in scar with microsuturing of epithelial defects over secondary healing. Improved technical instrumentation for simplified endoscopic microsuturing and further study needs to be performed in this area prior to its use being more easily translated for pediatric patients.

With regard to techniques, few reports have been published comparing cold microsurgical techniques versus other technologies, such as the $CO_2$ laser. In a well-designed randomized prospective trial, Benninger compared cold microsurgical technique versus microspot $CO_2$ laser-assisted dissection for surgical treatment of benign vocal fold lesions.[16] Of the clinical outcomes measured, no difference was noted in the acoustic analysis, airflow rates, videostroboscopic features, or auditory-perceptual analysis of postoperative patients with either technique. This study highlights the importance of knowledge and skills needed by the surgeon in patient outcomes over the specific surgical tools used in phonomicrosurgery.

## OPTIMIZING RESULTS

### Role of Preoperative and Postoperative Voice Therapy

Though the role of voice therapy in the pediatric patient with a vocal fold lesion or lesions is covered elsewhere in this text (citation), many clinicians would argue that preoperative voice therapy in children can be very helpful to improve breath support with phonotory tasks. Preoperative voice therapy can provide better insight into healthier vocal hygiene and phonatory function, and as such, can promote improved compliance and potentially improved efficacy of postoperative voice therapy. This can also prepare children psychologically for the rehabilitation they will undertake after surgery. Postoperative voice therapy is very useful to rehabilitate the operated vocal fold(s) with maximized efficiency of the speaking and singing vocal mechanism to reduce vibratory trauma that led to the vocal fold lesion(s).

### Voice Rest

Considerations for postoperative voice rest are important when planning surgical intervention for a vocal fold lesion in the pediatric patient. With regard to postoperative care, authors have advocated for a period of 4–14 days of absolute voice rest following vocal fold microsurgery, but much of these previous recommendations are based on animal models of wound healing[17] and/or clinical practice styles. The true duration of needed voice rest

remains unknown. Practice styles vary in the United States with phonosurgeons prescribing variable durations of voice rest, but most prescribed courses range from 7 to 14 days.[18] Compliance with long periods of voice rest can be particularly challenging in children, and the surgeon should base timing of elective phonomicrosurgery on an individual child's ability to be compliant with prescribed absolute voice rest.

A recent study in an animal model demonstrated the phonation-related changes seen in the postmicroflap vocal fold and the relation to optimal type (relative vs. absolute) and length of time of postoperative voice rest.[19] Inflammatory markers were monitored in the lamina propria with phonation at different postoperative time points, and results indicated postsurgical inflammation was stabilized by postoperative day #3 and absent by postoperative day #7. These results suggest absolute voice rest may not be necessary, and relative voice rest allowing up to 30 min of conversational phonation may be safe as early as postoperative day #3. In addition, when high-speed laryngeal imaging was used to investigate the natural time course of postmicroflap adherence in the same animal model, results revealed restoration of physiologic vibratory properties by postmicroflap days 3 to 7, corresponding to the same inflammatory phase of vocal fold wound repair.[20] These data are particularly interesting in children, who may have substantial compliance challenges with voice rest depending on respective age and maturity.

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CHAPTER

# 84

# Voice Rehabilitation after Airway Reconstruction

***Derek J Rogers, Catherine L Ballif***

The early 1970s marked a period of tremendous advances in pediatric airway reconstruction. Robin Cotton, Philippe Monnier, and other pioneers adapted the techniques of adult airway surgeons, such as Fearon and Rethi, to meet the unique needs of children with laryngotracheal stenosis. Many children who required a tracheostomy for laryngotracheal stenosis were finally liberated from this encumbrance and allowed to experience a more normal childhood. Since the 1970s, airway surgeons have continued to advance both open and endoscopic techniques, which have led to improved rates of decannulation.[1]

As the surgical techniques and perioperative care continue to improve, focus has shifted from survival and decannulation outcomes to postoperative quality of life. Postoperative voice outcomes as well as swallowing function have become primary foci in determining quality of life after airway reconstruction. Most children who undergo airway reconstruction will survive and successfully achieve decannulation of their tracheostomy tubes. However, approximately 50% of children who undergo airway reconstruction for subglottic stenosis have a significant risk of developing voice disorders.[2]

Normal voice requires airflow across the subglottis and glottis; it also requires proper glottal closure patterns as well as the propagation of a mucosal wave.[3] Most children requiring airway reconstruction necessitate tracheostomy due to prolonged intubation and the development of subglottic stenosis. Such prolonged intubation, therefore, not only causes airway obstruction but also leads to scarring and stiffness of the vocal folds themselves and is also associated with vocal fold fixation and glottal aperture defects. Airway lesions as well as the presence of a tracheostomy tube alter transglottic airflow causes turbulent flow through the vocal folds or inability to achieve vocal fold vibration.[4] Airway surgery with rib grafting near or between the vocal folds and often with prolonged airway stenting causes further damage to the phonatory structures. The combination of the development of airway stenosis and the subsequent surgeries and stenting to achieve eventual decannulation together often results in significant postoperative dysphonia.

Initially, the focus of parents of a child with laryngotracheal stenosis is a safe airway and swallowing, successful decannulation, and some sort of functional voicing. Once a safe airway is established and the child begins to grow, parents become more concerned with the quality of voicing. This chapter describes the evaluation of pediatric dysphonia after airway reconstruction and provides a systematic approach to voice rehabilitation in these challenging scenarios.

## EVALUATION OF PEDIATRIC DYSPHONIA

The evaluation and management of children with dysphonia mandate a multidisciplinary team approach. The patient, his/her parents and caregivers, a speech language pathologist, and the otolaryngologist must work in close coordination.[5] A wide variety of voice disorders and laryngeal dysfunction may result after airway reconstruction. As a result, detailed documentation must be kept regarding communication ability and condition of the larynx. Of particular importance is the patient's potential for voicing before and after airway reconstruction.

Initial evaluation of a child with chronic laryngotracheal stenosis involves an assessment of the child's communication ability, potential for voicing, and alternative methods of communication.[4] If the child still has a tracheostomy, the smallest tracheostomy tube should be chosen not only to allow for a safe and stable airway, but also to allow for maximum phonation. If possible, the tracheostomy tube should either be capped or a speaking valve placed (if the child is old enough and if the airway above the tracheostomy is patent enough to allow for this). Passy-Muir speaking valves should be tested for elevated transtracheal pressure (> 10 cm $H_2O$) and if needed may be drilled to improve tolerance and limit the risk of carbon dioxide retention and pulmonary injury.[6,7] A formal preoperative voice assessment may be difficult in a prelingual child but one should note the strength of cry, whether the child babbles, and if stridor is present. Perceptual assessment may be performed by either the otolaryngologist or speech language pathologist. Commonly used here are the visual analog scale-based expert consensus auditory-perceptual evaluation of voice (CAPE-V) and the grade, roughness, breathiness, asthenia, strain (GRBAS) scoring systems. The CAPE-V rating system was developed following a consensus conference on perceptual voice quality measurement to enable clinicians to document more voice quality features than the GRBAS across more speech tasks, and it allows for supplemental feature scales and comment areas (*see* Chapter 81, Appendix 81.2).[8] The GRBAS is a widely used rating system but it only rates the five aspects of voice quality listed above (*see* Chapter 81, Appendix 81.1).[9] Although the validity of perceptual voice evaluation has been questioned,[10] the perceptual descriptors of voice quality determine patient, caregiver, and professional satisfaction. One should assess inter-rater reliability if using perceptual data in research.[11]

To provide effective guidance and treatment of pediatric dysphonia after airway reconstruction, one must understand the effect of the child's vocal quality on peer interactions and the child's ability to function appropriately in school and extracurricular activities.[4] School services may assist these children by providing specific classroom accommodations to ensure that the child is heard and understood in the class.[5] Validated rating scales have been developed to help delineate the functional and social impacts of the child's dysphonia. The three most commonly employed quality of life assessments include the pediatric Voice Handicap Index (pVHI), Pediatric Voice Outcomes Survey (PVOS), and Pediatric Voice-Related Quality-of-Life survey (PVRQOL). The pVHI is a modified version of the adult VHI in content and language to eliminate questions unrelated to children, resulting in a 23-item parental proxy product.[12] The PVOS was designed for the caregiver to complete and consists of only four multiple choice questions used to identify voice concerns.[13] Since children who have undergone airway reconstruction usually present with severe vocal impairments with the potential of additional social, educational, and functional concerns, the PVOS may not provide adequate information.[5] The PVRQOL is a 10-item instrument adapted from the adult VRQOL survey, designed to function as a parental proxy for children under the age of 12 years, rather than a self-administered questionnaire (*see* Chapter 81, Appendix 81.3).[14] The PVRQOL raw scores are converted to a scale of 0–100, with subdomain scores reflecting both social–emotional and physical–functional effects.

An awake, transnasal fiberoptic laryngoscopy or transoral, rigid laryngoscopy with stroboscopy, when possible, should be performed to evaluate the supraglottis and to assess the glottis for mobile vocal folds and any scarring. The choice of transnasal or transoral technique is guided by the patient's age, the position of the larynx (i.e., if the epiglottis is clearly visualized when a child opens his or her mouth, a transoral technique may be more easily accomplished), and patient compliance. Stroboscopy requires patient compliance with the necessary task functions, so it may be difficult; the key is proper visualization of vocal fold mobility patterns, glottal aperture defects, and regions of scarring or decreased pliability. Any compensatory mechanisms, such as alternative vibratory sources within the larynx, should be noted. Supraglottic compression and arytenoid prolapse are common in children after airway reconstruction and may obscure the view of the true vocal folds. In fact, due to supraglottic compression, often the false vocal folds function as the primary vibratory source. Voice therapy techniques that reduce supraglottic compression may be initiated, allowing better visualization for the clinician and effective biofeedback for the child.[5] The theoretic concern is that if the supraglottic phonation developed as an adaptive strategy to achieve a voice in face of a scarred and damaged larynx, then this form of therapy may actually diminish the phonatory source and produce a weakened voice. Careful pretherapeutic analysis and discussion are required.

The unique videolaryngostroboscopic findings and their diagnostic and treatment implications in patients who have undergone airway reconstruction have only recently been described.[15] Dohar et al. reported the following

findings: supraglottic lateral squeeze (plica ventricularis), supraglottic anteroposterior squeeze (arytenoid hooding), glottic muscle tension, and posterior cricoarytenoid bulge. The supraglottic findings likely represent compensation for laryngeal hypofunction. In their series, all cases with arytenoid hooding were asymmetric and the more hyperfunctional arytenoid contributed the most to glottic insufficiency (posterior glottic gap). They were not able to fully visualize the true vocal folds in any of the patients due to the obscuring supraglottic structures, and half of the patients demonstrated a "mucosal wave" propagating along their false vocal folds.

Acoustic evaluation represents one method of obtaining objective voice outcomes data in children who can provide speech samples before and after airway reconstruction.[5] Some children may be unable to provide adequate preoperative voicing samples to allow acoustic evaluation. A computer-based system, such as Voice Evaluation Suite, Computerized Speech Lab (CSL), or Visi-Pitch, is most commonly used for acoustic evaluation. Acoustic parameters, typically measured, include fundamental frequency, frequency range, maximum phonation time, average intensity and range, harmonics-to-noise ratio, S/Z ratio, jitter, and shimmer. Few studies exist in the literature that objectively measure voice outcomes after pediatric laryngotracheal reconstruction. Sell and MacCurtain studied 16 children who underwent laryngotracheal reconstruction and found most had low vocal pitch and rough, breathy voices.[16] Zalzal et al. analyzed voice outcomes in 16 patients after laryngotracheal reconstruction and reported that 15 patients had aberrant voice quality, characterized by low pitch, breathiness, and hoarseness.[17] Smith et al. found markedly decreased fundamental frequency, diminished frequency range, decreased vocal intensity, and shortened maximum phonation time in a study of five patients who underwent laryngotracheal reconstruction.[18] Krival et al. studied 16 patients who had undergone laryngotracheal reconstruction and noted all patients had some degree of voice disorder, but those who used primarily supraglottic/mixed phonation exhibited worse overall severity, roughness, and pitch deviance ratings than those who used primarily glottic phonation.[11] Periodic vibration was seen in 10 of the 16 patients, and analysis of these voices revealed low fundamental frequency in 3 of the 5 patients with supraglottic phonation and 2 of the 5 patients with glottic phonation. As shown in this study, children who use primarily supraglottic phonation tend to have lower fundamental frequencies. As they learn to use their true vocal folds more, the fundamental frequencies rise, which may be a good measure of improved laryngeal function. However, one must remember that the supraglottis may the only phonation source for some patients.

Aerodynamic evaluation by measuring airflow and pressure changes during phonation represents another method of collecting objective voice outcomes data. The Phonatory Aerodynamic System (PAS) or Aerophone by KayPENTAX is capable of recording aerodynamic parameters in children. Measures such as open quotient, speed quotient, and maximum flow declination rate for true vocal fold vibration will not be accurate if the child uses alternative sources for phonation.[5] Particularly useful aerodynamic measures in children after laryngotracheal reconstruction include mean sound pressure level during voicing, mean peak air pressure, and mean airflow during voicing. Phonation threshold pressure (PTP) may also be measured but no normative data exist for children. High estimated subglottic pressure measures are associated with increased respiratory effort needed for phonation and laryngeal hyperfunction. Subglottic pressure measures along with average airflow rate help quantify the valving efficiency of the laryngeal system. For example, a hyperfunctional voice may result in decreased airflow rate and increased subglottic pressure. Although their results failed to reach statistical significance, Weinrich et al. found higher airflow measures for children with glottic phonation and higher subglottic pressure measures for those with supraglottic voicing in 12 children who underwent laryngotracheal reconstruction.[19] Further studies are needed to determine the absolute utility of aerodynamic parameters in dysphonic children after airway reconstruction.

## CHRONIC TRACHEOSTOMY

Many children with laryngotracheal stenosis require a tracheostomy. Dysphonia may develop in these children or any child with chronic laryngotracheal stenosis due to extensive use of supraglottic laryngeal structures.[19] Supraglottic compression in these children may benefit from voice therapy.[20] Inspiratory phonation is another compensatory speech method used in children who have undergone tracheostomy.[18]

## SYSTEMATIC APPROACH TO VOICE REHABILITATION

Children may present with an array of extraordinarily complex causes of dysphonia after airway reconstruction.

Clinicians must remain organized and keep meticulous documentation regarding these patients' histories, physical exams, and interventions. Moreover, the patient and the caregiver should drive the treatment course because their perception of the patient's voice is of utmost importance.

One must remember that voice rehabilitation after airway reconstruction presents a balance between airway obstruction, voice, and swallowing. Some rehabilitative procedures may result in another tracheostomy, although this is usually temporary. Aspiration remains a serious risk with additional airway surgery. Airway surgeons must decide whether to stage procedures or attempt to correct multilevel sources of dysphonia simultaneously. The role for voice therapy and behavioral treatment by a qualified speech language pathologist cannot be over emphasized. Since dysphonia in patients after airway reconstruction may result from dysfunction in any part of the larynx or trachea, one effective method for voice rehabilitation is to take a top–down approach. The following is a discussion of potential sources of dysphonia from the supraglottis down to the trachea, realizing that these children may also have oral/oropharyngeal and/or pulmonary disorders impacting their phonation ability. An illustrative case is presented to demonstrate possible treatment strategies for a patient with multilevel sources of dysphonia after airway reconstruction.

## Supraglottis

A whole host of anatomic and functional abnormalities may occur in the supraglottis after airway reconstruction. Most severe subglottic stenoses require a posterior cricoid split, which sets the stage for many sources of dysphonia. If the interarytenoid muscle is not lysed during the posterior cricoid split, destabilization of the arytenoid could occur leading to arytenoid prolapse and supraglottic compression.[21] Petiole prolapse may also result from superior dissection into the pre-epiglottic region during the anterior laryngofissure. Placement of a posterior cricoid graft usually creates some degree of glottic insufficiency. Surgeons need to limit the width of the posterior cricoid graft to prevent over distracting this region. The natural compensatory mechanism in a child with glottic insufficiency is to form a supraglottic sphincter by compressing the arytenoids onto the epiglottis.[22] Supraglottic phonation produces a strained, harsher tone with a deeper phonatory quality and is associated with the development of laryngoceles in patients who have undergone airway reconstruction.[4,19] Kelchner et al. studied 21 children with supraglottic phonation after airway reconstruction and described 4 primary supraglottic compression patterns and 3 distinct sound sources.[23] Hyperfunctional phonation can negatively affect communication and social skills and classroom performance.[12]

Several options exist to treat the various supraglottic abnormalities described above. Because supraglottic compression may be the child's only source of phonation, it may be prudent to augment the supraglottic sphincter to improve supraglottic speech. One option is to inject the petiole with hydroxylapatite or autologous fat to improve supraglottic closure during phonation. A precarious situation arises when the arytenoids must be trimmed to enable adequate visualization of the true vocal folds. Surgeons must use caution here because this may disrupt the child's primary phonation source. Petiole prolapse may benefit from hyoepiglottopexy to both open the airway and limit compression. Furthermore, speech therapy can be used to either train the child to phonate more effectively with his/her supraglottic structures or to limit the use of these structures, depending on the status of the true vocal folds.

## Glottis

Airway reconstruction may cause glottic dysphonia through many mechanisms. While performing a laryngotracheal reconstruction, an anterior laryngofissure is often necessary to provide an excellent view of the entire larynx and facilitate full access to the posterior cricoid lamina. Anterior laryngofissure must be performed precisely to avoid direct vocal fold damage, and misapproximation of the anterior commissure may lead to asymmetric vocal fold height, inadequate vocal fold approximation, and subsequent dysphonia due to wave irregularities.[5] Common irregularities affecting the glottis found on fiberoptic laryngoscopy in children after laryngotracheal reconstruction include anterior commissure blunting and decreased movement of the arytenoids.[24] One study evaluated eight pediatric patients with voice disturbance after laryngotracheal reconstruction and found that two had glottal incompetence due to inadequate adduction, two arytenoid fixation, three anterior commissure blunting or widening, two vertical asymmetry of the vocal folds, and three vocal fold scarring.[18] Vertical mismatch of the true vocal folds occurs when the anterior commissure is

inappropriately reapproximated after anterior laryngofissure (Fig. 84.1). Scarring may occur within the substance of the true vocal folds, along their undersurface, or may present as webbing between the folds. One complication particularly detrimental to phonation is atrophy or scarring of the strike zone of the true vocal fold, resulting in an absence of lamina propria (Fig. 84.2). A sulcus vocalis could also occur due to trauma (Fig. 84.3). As mentioned previously, placement of a posterior cricoid graft displaces the true vocal folds, causing glottic insufficiency. Another possible cause of glottic dysphonia in children after airway reconstruction is an unsuspended true vocal fold (Fig. 84.4). The true vocal fold may become detached from Broyle's ligament at the anterior commissure during anterior laryngofissure or in rare cases may detach from the vocal process of the arytenoid. Vocal fold immobility may result from either scarring or denervation during airway reconstruction. Arytenoid prolapse and/or fixation remains a known complication from manipulating the lateral cricoarytenoid muscles and destabilizing the cricoarytenoid joint, which could prevent vocal fold motion.[25] In addition, recurrent laryngeal nerve injury rarely occurs during lateral tracheal dissection for a cricotracheal resection or tracheoplasty.

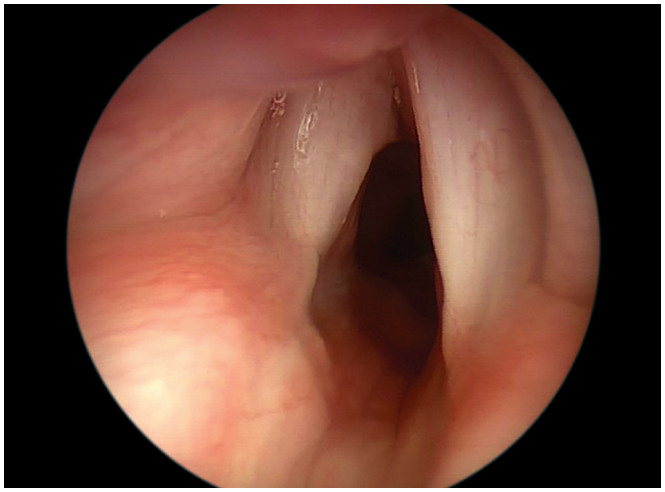


**Fig. 84.1:** Vertical mismatch of the true vocal folds caused be inaccurate reapproximation of the anterior commissure after laryngofissure.

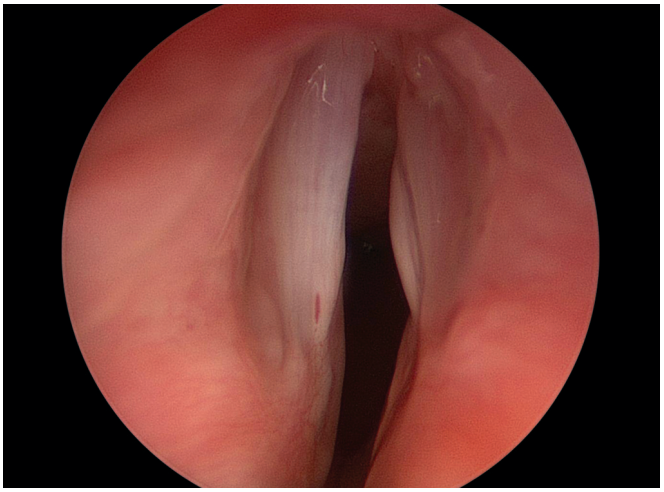


**Fig. 84.2:** Atrophy with resultant loss of superficial lamina propria at the strike zone of the right true vocal fold.

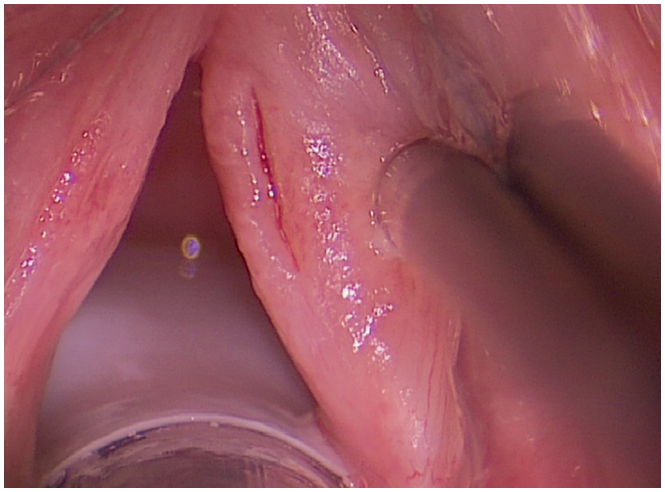


**Fig. 84.3:** Sulcus vocalis of the right true vocal fold.

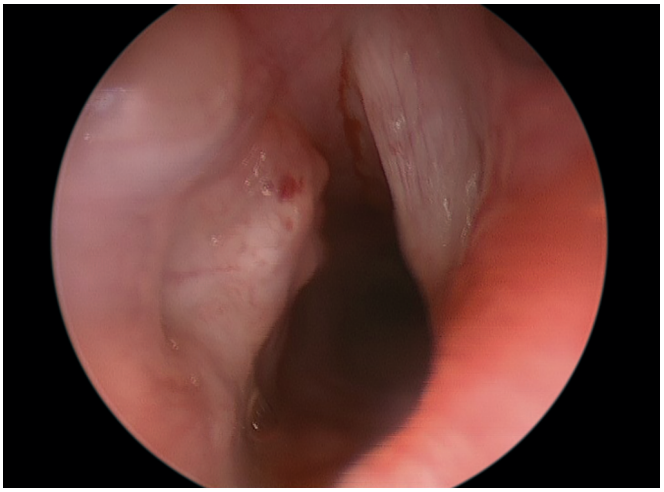


**Fig. 84.4:** Left true vocal fold unsuspended from anterior commissure.

Depending on the anatomic structure affected, many options are available to treat dysphonia originating in the glottis. Vertical mismatch of the true vocal folds is best treated by repeat laryngofissure. The anterior commissure can then be realigned to ensure proper orientation of the true vocal folds. Vocal fold scarring may be obvious or could be more subtle, discovered during stroboscopy. Atrophy of the lamina propria and shallow sulci can be treated with injections; autologous fat, micronized acellular dermis, hydroxylapatite, and gelatin foam are all options. Deeper scars or sulci may require a more formal procedure, such as Sataloff's endoscopic approach with buccal fat graft[26] or Gray's external minithyrotomy.[27] The treatment for an unsuspended true vocal fold depends on the site of detachment. The true vocal fold may be reattached to the anterior commissure during a repeat laryngofissure with the use of Monocryl suture. An endoscopic approach could be used to reattach the true vocal fold to the vocal process of the arytenoid also using Monocryl suture.

Vocal fold immobility represents another glottic source of dysphonia after airway reconstruction. Although the immobility may rarely be due to recurrent laryngeal nerve injury, it is more commonly a result of mechanical causes after airway reconstruction. If the source of vocal fold immobility remains in question, laryngeal electromyography should be performed to rule out neurological causes.[28] Possible mechanical causes include cricoarytenoid joint ankylosis, interarytenoid scarring, and posterior glottic stenosis. A temporary treatment for vocal fold immobility is injection medialization with autologous fat, micronized acellular dermis, hydroxylapatite, or gelatin foam. Favorable results have been shown in children.[29] Depending on the type of injected material, effects may last for 3 months or longer. A more permanent procedure is medialization thyroplasty, which has been performed in children as young as 2 years of age. Gore-Tex, silastic, or cartilage can be used in the paraglottic space through a window in the thyroid cartilage during an open approach.[29,30] Arytenoid fixation may be treated with endoscopic or open arytenoidectomy, arytenoid adduction,[31] or adduction arytenopexy.[32] These arytenoid procedures may be combined with a medialization thyroplasty. A posterior glottic scar may require an expansion laryngotracheoplasty (either endoscopic or open approach), which may increase the risk of aspiration. If the vocal fold immobility is due to recurrent laryngeal nerve injury, one may consider a laryngeal reinnervation procedure (usually ansa cervicalis anastomosed to stump of recurrent laryngeal nerve or directly to thyroarytenoid muscle).[33] Vocal fold tone and bulk typically improve but the fold will remain immobile.[34]

## Subglottis/Trachea

Anatomical changes in the subglottis and trachea could result in dysphonia after airway reconstruction. Persistent stenosis in this portion of the airway produces reduced and turbulent airflow, limiting the ability to vibrate the true vocal folds. An A-frame deformity or persistent tracheomalacia could produce the same effects. Since cricotracheal resection requires removal of the cricothyroid membrane and cricothyroid muscle, patients experience deeper phonation and loss of higher pitches.[4] Patients may require additional procedures to open the subglottis, such as endoscopic $CO_2$ laser division with balloon dilation or revision open laryngotracheal reconstruction. Tracheal deformities could necessitate tracheoplasty to open the trachea and prevent suprastomal collapse.

## ILLUSTRATIVE CASE

To demonstrate the inherent complexities involved with voice rehabilitation after airway reconstruction, a case is presented here. Clinicians must determine the best way to evaluate the dysphonia from these complex airway disorders. The following questions should be addressed while managing these patients. Should voice therapy be combined with surgery? When should surgery be avoided? What discussions are necessary to have with the patient and family?

A 13-year-old pleasant female presents with a chief complaint of hoarseness for many years. The patient is the primary historian, and few records are available for review. She is accompanied by her aunt, who is her legal guardian. Her aunt states that the patient has been hoarse since about 5 years of age. Her hoarseness started shortly after removal of her tracheostomy tube. The tracheostomy tube was presumably placed for respiratory failure, as the patient was born at about 24 weeks. She tolerates a regular diet and denies dysphagia or aspiration symptoms. However, upon further questioning, the patient remarks that she cannot climb a flight of stairs without becoming short of breath. The patient had a G-tube as a baby, which was removed several years ago. She underwent a laryngotracheal reconstruction "years ago" to remove her tracheostomy tube.

The first task is to establish why the patient presented at 13 years of age and not much earlier. In this case, she was becoming frustrated at school because she was progressively more difficult to understand. Also, her shortness of breath with exertion was gradually worsening.

After a thorough history, the evaluation continued with head and neck exams. Her neck demonstrated scarring consistent with prior tracheostomy and laryngotracheal reconstruction. She had no stridor or retractions at rest. Her voice was considerably hoarse and breathy, with a harsh quality (📻 84.1). Flexible fiberoptic laryngoscopy was performed, and a speech language pathologist completed a perceptual assessment while visualizing the larynx (📻 84.2). The laryngoscopy revealed left greater than right arytenoid prolapse and supraglottic phonation. The supraglottic obstruction was so severe that the true vocal folds could not be adequately visualized. The patient underwent an acoustic evaluation prior to surgery. Due to the degree of aperiodic and disordered voicing signal, her voice quality and sustained phonation preoperatively were insufficient for objective measures to be obtained or analyzed. However, her score on the PVRQOL was 24, suggesting a poor quality of life due to her voice. The decision was made to perform a direct laryngoscopy and bronchoscopy (DLB) in the operating room to fully evaluate the glottis, subglottis, and trachea (Figs. 84.5 to 84.8). The DLB revealed the following findings: left cricoarytenoid joint dislocation, left redundant false vocal fold, posterior glottal

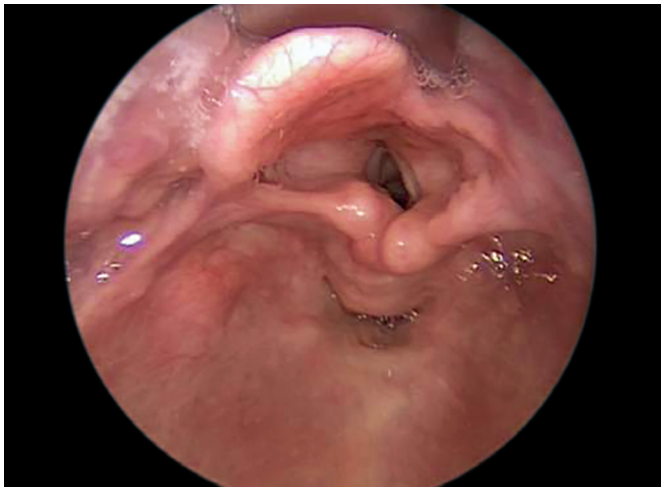


**Fig. 84.5:** Intraoperative photo showing left cricoarytenoid joint dislocation and left redundant false vocal fold.

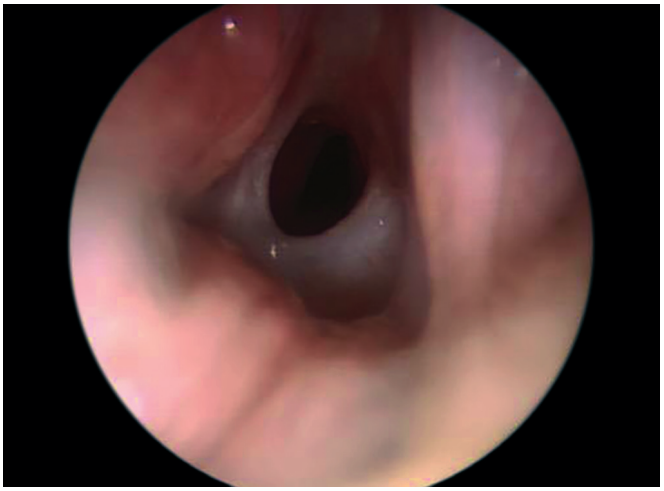


**Fig. 84.6:** A posterior glottal aperture defect, left unsuspended true vocal fold, vertical mismatch of the true vocal folds at the anterior commissure, and grade 2 subglottic stenosis by a web are evident.

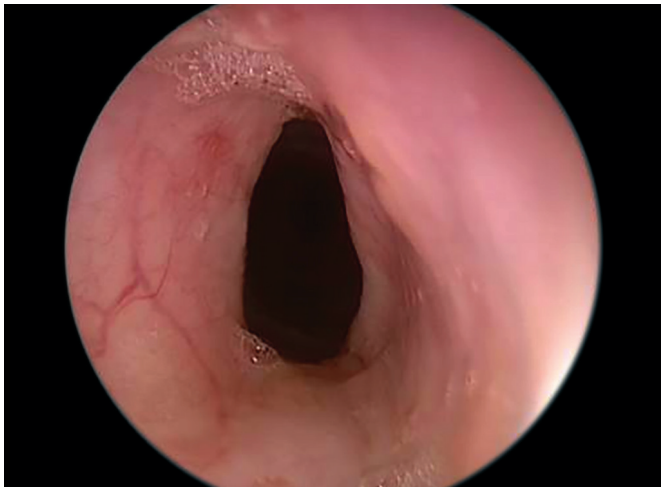


**Fig. 84.7:** A-frame deformity of the trachea.

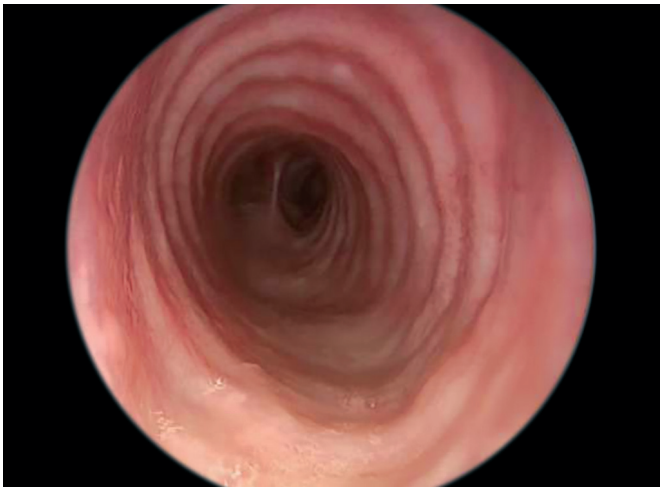


**Fig. 84.8:** Complete tracheal rings.

aperture defect, left unsuspended true vocal fold, vertical mismatch of the true vocal folds at the anterior commissure, grade 2 subglottic stenosis by a web, A-frame deformity of the trachea, and complete tracheal rings. During the DLB, a $CO_2$ laser was used to perform a left arytenoidectomy and to lyse the subglottic web before balloon dilation (Figs. 84.9 and 84.10). The left arytenoidectomy was needed to enhance visualization of the glottis, and the subglottic web was lysed to improve the patient's exercise tolerance, while hopefully providing more airflow to phonate more effectively. These procedures represented a good starting point for vocal rehabilitation because they did not necessitate a tracheostomy.

The patient then underwent voice therapy for several months with little improvement in her dysphonia. She was still quite frustrated with her voice. The next question to answer was: is it worth needing another tracheostomy in an effort to improve her dysphonia? The patient and her family were thoroughly counseled regarding this risk. All procedures have the risk of worsening the airway. Specific goals and expectations were delineated. We emphasized to the patient and her family that no cookbook approach existed to determine which procedure(s) might be best. Furthermore, one must decide whether to try to treat all potential sources of dysphonia in one setting or to perform a staged set of procedures with re-evaluation after each step. The patient and her family elected for the latter option.

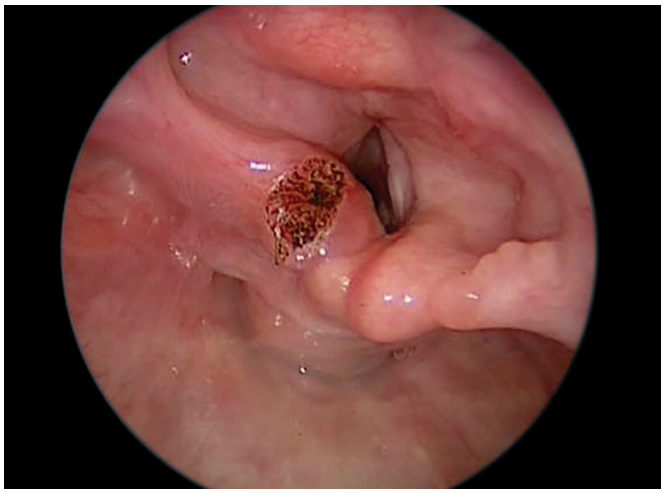


**Fig. 84.9:** $CO_2$ laser used to perform left arytenoidectomy.

The next surgical options were divided into endoscopic or open procedures. The endoscopic options included left true vocal fold injection medialization, petiole injection to improve supraglottic phonation, and/or excision of more supraglottic tissue. The open options involved thyroplasty, vocal fold reapproximation, and/or arytenoid repositioning. The first step consisted of a tracheostomy, laryngofissure with correction of the vertical true vocal fold mismatch, left arytenoid repositioning, and left true vocal fold resuspension (📹 84.3, Fig. 84.11). Unfortunately, the patient's dysphonia was grossly unchanged after surgery. Repeat flexible fiberoptic laryngoscopy revealed no marked change in arytenoid position and a persistent posterior glottal notch with glottal aperture defect.

The next step in her voice rehabilitation involved another surgical procedure approximately 2 weeks after her last surgery. The patient underwent suspension laryngoscopy with revision supraglottoplasty (Fig. 84.12). A $CO_2$

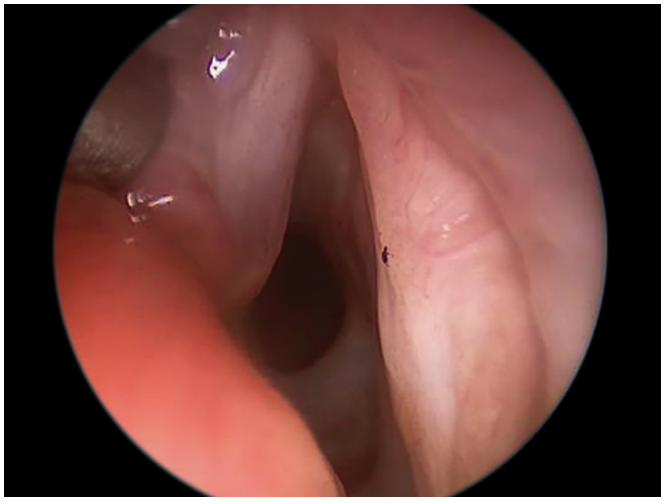


**Fig. 84.10:** View of subglottic web before lysis and balloon dilation.

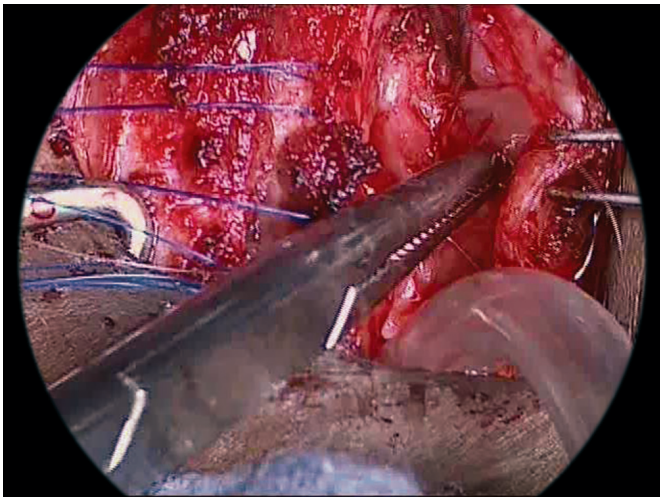


**Fig. 84.11:** Resuspension of left true vocal fold.

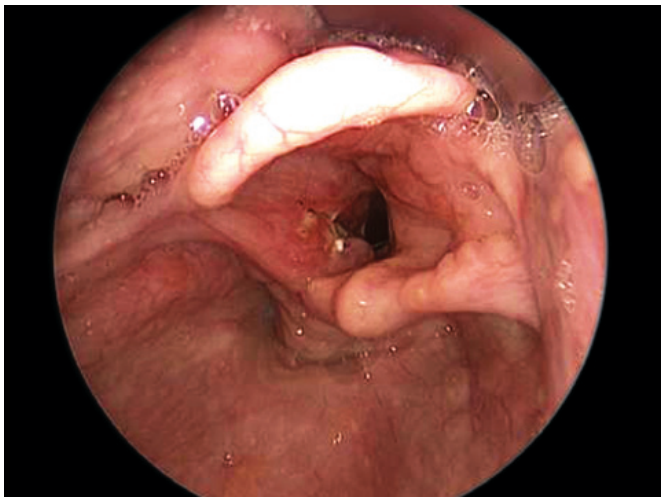


**Fig. 84.12:** DLB showing no marked change in arytenoid position and a persistent posterior glottal notch with glottal aperture defect.

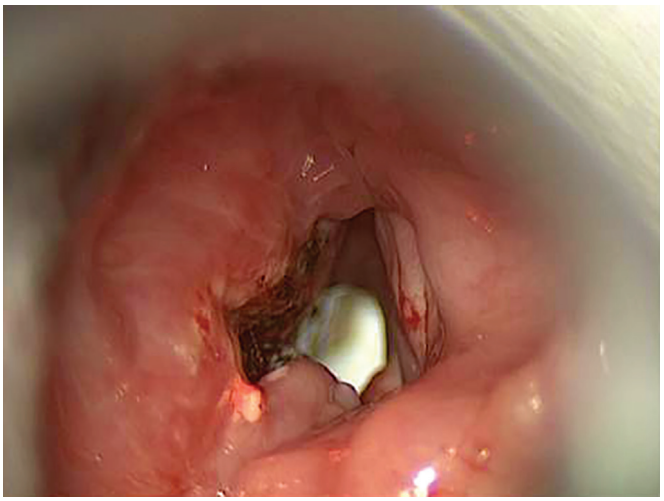
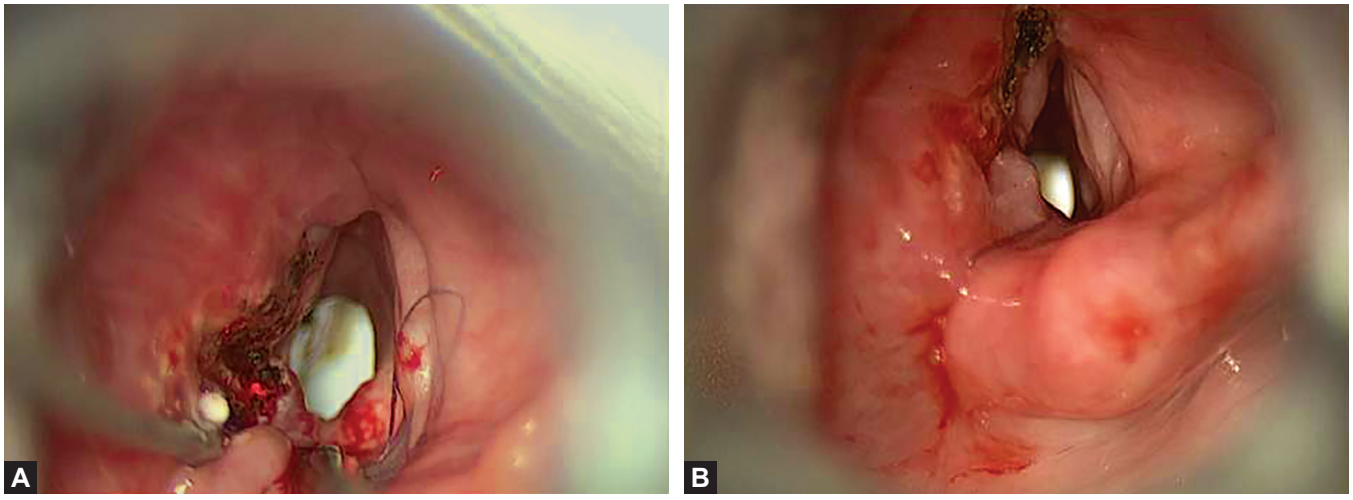


**Fig. 84.13:** $CO_2$ laser used to treat the prominent, redundant left false vocal fold.

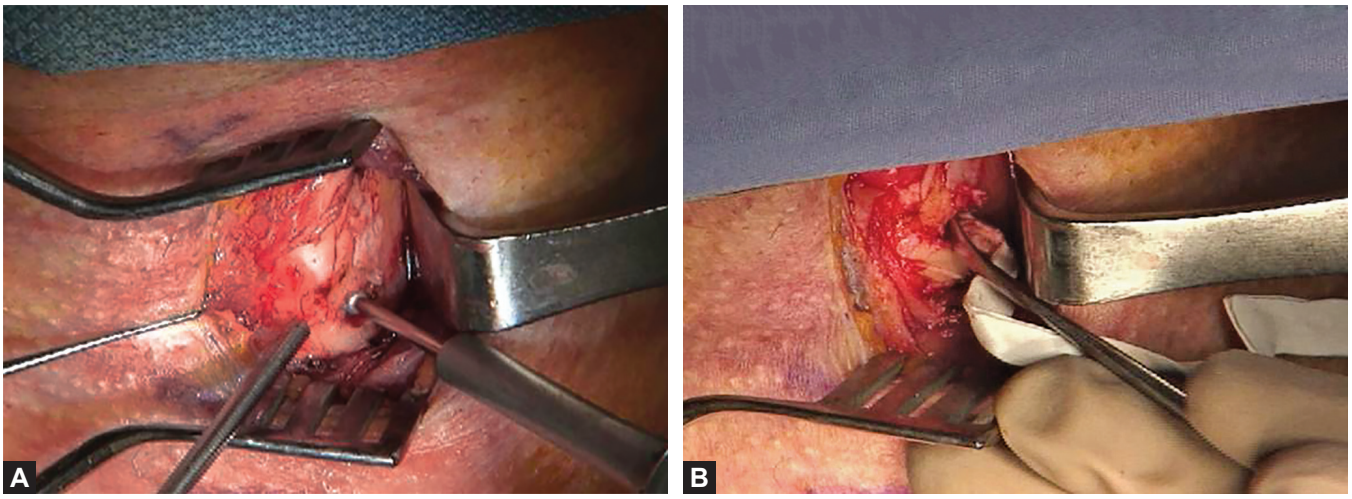



**Figs. 84.14A and B:** (A) Endoscopic suturing of left true vocal fold to vocal process of arytenoid, (B) Left true vocal fold reapproximated.

laser was used to treat the prominent, redundant left false vocal fold (Fig. 84.13). In addition, the left true vocal fold was reapproximated to the vocal process of the arytenoid (Figs. 84.14A and B). After surgery, the dysphonia again showed no marked change. She continued to have a glottal aperture defect; however, her airway was widely patent with a mobile contralateral true vocal fold.

Two weeks after this surgery, the last step in the patient's voice rehabilitation required one more surgery. She underwent left medialization thyroplasty using a cardiac Gore-Tex patch (Figs. 84.15A and B). The patient was subsequently capped and decannulated. Her airway status was markedly improved, with no shortness of breath during exertion. Flexible fiberoptic laryngoscopy revealed a widely patent airway with minimal supraglottic compression and arytenoid prolapse, and good apposition of the true vocal folds (84.4).

The patient's dysphonia had significantly improved, allowing her to be understood easily by her friends and family (84.5). Her voicing signal was sufficient to analyze using the PAS and Voice Evaluation Suite, demonstrating overall improvement of the voicing signal produced postoperatively. Average speaking frequency in connected speech was 202 Hz (within normal limits for her age), maximum phonation was 6.3 seconds (short for her age), average speaking intensity was 74.2 dB (slightly louder than normal for her age), jitter was 2.3% (high), shimmer was 4% (high), harmonics-to-noise ratio was 4.8




**Figs. 84.15A and B:** (A) Drill used to create window in left thyroid cartilage, (B) Gore-Tex patch placed in paraglottic space to medialize left true vocal fold.

(low), and the S/Z ratio was high, showing shorter duration with voice production (/z/). Aerodynamic readings postoperatively demonstrated mean peak air pressure at 10.5 cm $H_2O$ (high for her age), mean airflow during phonation at 0.05 (within normal limits for her age), and PTP of 5.0. Her PVRQOL score improved to 69.5 postoperatively, indicating a much higher quality of life.

## CONCLUSION

Voice rehabilitation after airway reconstruction presents many challenges. A thorough workup is required to determine the patient's voicing potential. Voice therapy by a qualified speech language pathologist throughout the management of these patients is imperative. Concrete goals and objectives must be established. Patients and family members must be thoroughly counseled regarding the risks inherent in any surgery to treat dysphonia, including the possible need of a tracheostomy. A staged approach with careful attention to anatomic and physiologic principles of voice production is most effective in treating these complex disorders.

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## VIDEO LEGENDS

**Video 84.1:** Face tape demonstrating harsh, breathy voice.
**Video 84.2:** Flexible fiberoptic laryngoscopy showing left greater than right arytenoid prolapse with supraglottic phonation.
**Video 84.3:** Endoscopic view of left arytenoid repositioning.
**Video 84.4:** Flexible fiberoptic laryngoscopy revealing a widely patent airway, minimal arytenoid prolapse and supraglottic compression, and good apposition of the true vocal folds.
**Video 84.5:** Face tape demonstrating significant improvement in dysphonia, allowing the patient to be easily understood.

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CHAPTER

# Juvenile Onset Recurrent Respiratory Papillomatosis and the Voice

85

***Seth M Pransky***

## INTRODUCTION

Juvenile recurrent respiratory papillomatosis (JRRP) is a benign neoplasm caused by infection by the human papilloma virus (HPV) and characterized by recurrent wart-like growths in the upper aerodigestive tract. It most commonly affects the larynx and typically presents as hoarseness in a young child. Treatment consists of multiple surgical debulking procedures and adjuvant therapies. In the past, vocal cord function and the voice were often compromised due to aggressive surgical excision, as the primary concern was prevention of airway obstruction, distal tracheobronchial spread and malignant transformation. Increased understanding of the disease process and improved laryngeal tissue sparing techniques has now allowed focus on voice preservation. With greater awareness of voice as a critical issue in papilloma management, earlier and more aggressive voice therapy can help improve communication in this often long-term disease process.

## EPIDEMIOLOGY

The incidence of JRRP is 4.3 per 100,000 children in the United States.[1] A more recent Canadian national pediatric database identified the incidence of juvenile disease to be 0.24 per 100,000 and the prevalence to be 1.11 per 100,000 children.[2] Infants born of young mothers from a lower socioeconomic status have an increased likelihood of being diagnosed with JRRP.[3] HPV infection has also been found to be more prevalent in women of lower poverty index, young maternal age, unmarried status, and less education,[4] epidemiologically correlating the association between JRRP and HPV.

On average, children undergo 19 lifetime procedures or 4 surgeries per year.[5] Patients requiring 50–100 procedures are not uncommon. More than 15,000 procedures are performed per year in the United States. In 2000, the estimated lifetime cost for one patient with JRRP ranges from $60,000 to $470,000.[1] Increased severity of disease, need for frequent surgical intervention and risk of progressive disease are associated with early age of diagnosis.[6]

## PATHOPHYSIOLOGY

HPV is a DNA virus from the family Papovaviridae that has a propensity to infect mucosal epithelial cells at the squamo-mucosal junction and integrate with native cell DNA. Its mechanism of action is thought to be due to viral proteins inhibiting the action of the tumor suppressor gene proteins, p53 and pRB.[7] HPV was first identified in JRRP pathological specimens in the early 1980s.[8,9] The subtypes 6 and 11 are associated with JRRP, with type 11 subtype thought to cause a more aggressive disease process.[10] HPV can remain dormant in normal appearing mucosal cells. What triggers the wart-like growths in some patients and not others is unclear; host immune dysfunction is thought to be a contributing factor.[7] The risk of malignant transformation is approximately 1–4%.[11]

It is thought that the virus is vertically transferred from the mother to fetus during birth. In one study, women with genital condylomata had a 231 odds ratio of having a child infected with JRRP compared to unaffected women. Prolonged labor increases an infant's risk of infection and hypothesized to be due to longer exposure to the virus during the birth process.[12] The incidence of JRRP in infants

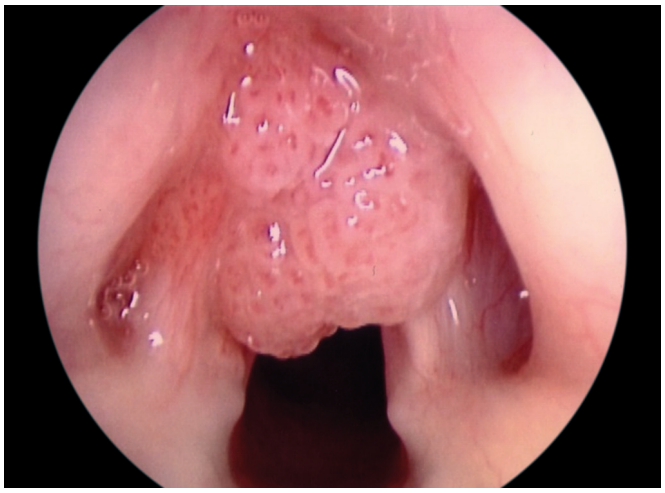

**Fig. 85.1:** Juvenile onset recurrent respiratory papillomatosis with large bulky papilloma obstructing the anterior half of the larynx.

born from women with active condylomata, however, is still small (1 in 400),[13] suggesting that other factors such as infant immunity or mucosal trauma play a role.[14] A cesarean section (C-section) has not been shown to fully protect against acquisition of the disease, and despite the association of cervical and vaginal papilloma with the development of JRRP, a C-section is still not recommended by the American College of Obstetrics and Gynecology for a woman known to be infected at the time of delivery.[15] Recent studies, however, do suggest that an intact amniotic sac prior to cesarean section decreases viral transmission to the fetus.[16]

Respiratory papilloma appears as exophytic cauliflower-like growths located at the junction of respiratory and squamous epithelium (Fig. 85.1). Histologically, papillomata have multiple projections consisting of a fibrovascular core covered by stratified squamous epithelium.[17] Common locations include the upper and lower ventricle margins, undersurface of the vocal cord, laryngeal surface of the epiglottis, carina, bronchial spurs, nasal limen vestibule, and the nasopharyngeal surface of the soft palate.[3] Tracheostomy can accelerate papilloma spread as the mucosal trauma creates a new junction of squamous and respiratory epithelium lower in the respiratory tract.[18,19]

## CLINICAL PRESENTATION

Seventy-five percent of patients with JRRP are diagnosed by the age of 5 years.[20] JRRP can manifest as various respiratory symptoms, the most common being hoarseness and dysphonia as the larynx is most often affected. Children are initially treated for more common ailments such as croup, asthma, allergies, or vocal cord nodules, resulting in a delay in diagnosis. The development of stridor indicates progression of disease and warrants a higher index of suspicion. Rarely do patients initially present with recurrent pneumonias, failure to thrive or acute airway obstruction.[7,18]

## EVALUATION/DIAGNOSIS

A thorough history must be obtained including onset of symptoms, history of airway trauma such as endotracheal intubation, and comorbidities. A maternal history of genital condylomata should be elicited. Physical examination includes flexible laryngoscopy in the office to evaluate the entire upper airway with a focus on the larynx and vocal cord movement. Signs and symptoms of airway distress require emergent operative evaluation and debulking the lesion to maintain the airway.

Definitive diagnosis consists of operative direct laryngoscopy and bronchoscopy with biopsy and histopathologic assessment. Photo and/or video documentation is recommended in order to communicate findings with other physicians and the family and provide comparison during treatment of the disease. Derkay and Coltrera have developed a commonly used staging system that incorporates subjective and objective findings. Part of staging includes an evaluation of voice quality.[21] Specific HPV typing is commercially available but is still not universally carried out due to cost and test availability. However, identifying HPV type may ultimately have a role in predicting future behavior of the infection. At a minimum, the papilloma should be categorized as high risk (type 16, 18) versus low risk (type 6, 11) for malignant transformation.

## SURGICAL TREATMENT

Treatment for respiratory papilloma is primarily surgical. Surgery consists of comprehensive airway assessment followed by laryngeal suspension and microscopic or endoscopic resection. The goal is to debulk papillomata while preserving the underlying laryngeal epithelium. Multiple techniques have been utilized including cold dissection, microdebrider resection, various lasers, and coblation. Spontaneous ventilation has become the anesthetic approach of choice in children and apneic techniques are generally not utilized any longer. The absence of an endotracheal tube allows optimal visualization of the larynx and ease of disease removal[22] but requires

experience by the anesthesiologist as well as effective communication between the anesthesiologist and the otolaryngologist. For obstructive disease, an endotracheal tube can be placed initially to secure the airway. If the patient is intubated and a laser is used, a laser safe endotracheal tube must be used. Jet ventilation can be utilized by those anesthesiologists comfortable with jet technology but should not be used in cases of significant laryngeal obstruction.

Cold dissection consists of using microlaryngeal instruments to gently remove exophytic islands of disease from the larynx. It was the primary surgical mode prior to the advent of the laser and the microdebrider. Its disadvantages include bleeding and lack of precision.

The microdebrider is a powered instrument with an oscillating blade that allows removal of JRRP without thermal damage. It is excellent for bulky exophytic disease. However, it is less valuable for sessile disease especially along the true vocal folds and in the ventricles. Regardless of this restricted utility, voice outcomes are good as long as it is not used along the vibratory mucosa of the true vocal folds. A randomized control study comparing laser excision to the microdebrider showed that the microdebrider is less costly, requires less operative time, and has rapid improvement in voice outcomes.[23] A more recent study objectively evaluated voice outcomes and also concluded that the microdebrider results in better immediate and early postoperative voice compared to the $CO_2$ laser.[24] Much of this may depend on the surgeon and how aggressively the $CO_2$ laser is used and does not take into account use of more recent use of the angiolytic lasers.

For many years, the $CO_2$ laser had been the primary mode of surgical excision. Carbon dioxide's wavelength optimizes vaporization of papilloma in a precise manner. It is excellent for sessile disease, especially in hard to reach regions of the larynx, and now with the fiberoptic fiber and endoscopic techniques visualization is markedly improved improving precision. However, it is more costly than the microdebrider. At high-wattage settings, thermal damage to the underlying epithelium can occur and place the voice at risk. In some studies, anterior and posterior glottis scars can be as high as 36%.[26] This risk is reduced by great care in the extent and location of the $CO_2$ resection of the lesions.

The 585-nm pulse dyed laser and the 532-nm potassium-titanyl-phosphate pulsed laser have more recently been advocated over the $CO_2$ laser. The chromophore is oxyhemoglobin for both of these lasers, making them ideal for removal of vascular JRRP lesions while minimizing thermal damage to the overlying epithelium. There is thus less risk for scarring.[27,28] The pulse dyed and KTP lasers are particularly beneficial for disease at the anterior commissure, ventricle, and true vocal fold/infraglottic regions, demonstrating improved voice preservation.[29,30] Voice recovery, however, is longer compared to the microdebrider. Similar to the $CO_2$ laser, the KTP and pulse-dye laser are less effective for bulky disease.

Coblation has recently been used on papilloma with some success. Like the microdebrider, it is best on bulky disease. It works rapidly with excellent hemostasis and with improved laryngeal devices there is less concern for collateral damage.

The main challenge with any surgical intervention is removing diseased tissue as thoroughly as possible while preserving normal adjacent tissue. All current techniques depend upon gross visual inspection and even a magnified view does not clearly differentiate normal from pathologic tissue. The result is either incomplete removal of papilloma or injury to noninvolved mucosa. To help improve outcomes there are two new developing tools that may allow more precise identification of abnormal tissue that will translate into more precise excision and help reduce iatrogenic damage to the larynx. Narrow band imaging (NBI) is an in vivo optical enhancement technique that increases the visibility of blood vessels on mucosal surfaces. In a recent study, NBI significantly increased the sensitivity of detecting JRRP and consequently improved surgical removal of the lesions.[31] A second promising tool is optical coherence tomography (OCT). This is a noninvasive imaging modality that provides cross-sectional images without need for tissue penetration. Theoretically this will allow assessment of the subepithelial structure and help differentiate normal from abnormal tissue. As research progresses OCT may be applicable in JRRP to provide, in real time, information about the depth of the subepithelial lesions and allow more precise surgical excision.[32]

Given the tremendous variability in JRRP presentation and involvement of laryngeal tissues, it is incumbent upon the JRRP surgeon to be familiar with state of the art technology and utilize a combination of techniques and tools to achieve optimal results. Thus, bulky disease can be removed with one tool and a laser utilized for management of finer, sessile lesions, especially those located in difficult to reach and "more sensitive" locations. More refined identification of disease is developing and should help reduce postoperative scarring and adverse voice outcomes.

## ADJUVANT TREATMENT

Adjuvant systemic or intralesional therapies have been described for recalcitrant disease. Given the inherent variability and rarity of the disease process, it remains difficult to determine effectiveness of these treatments. More than four surgeries per year, aggressive disease and distal airway spread are typical criteria for consideration of adjuvant therapies.[18] The hope is to reduce frequency of surgical intervention and achieve remission thus prevent long-term damage to the vocal cords and the voice by repetitive surgery.

The most commonly used adjuvant agent today is intralesional injection of cidofovir. Cidofovir is an analog of cytosine that has been shown to halt DNA virus proliferation. Systemic treatment is currently FDA approved for the treatment of cytomegalovirus retinitis in patients with HIV and side effects include nephrotoxicity, neutropenia, and hepatotoxicity. For JRRP, cidofovir has been used off-label as an intralesional injection. While in animal studies cidofovir has shown carcinogenic potential, no clear cut malignant transformation with intralesional use has been reported in humans. Intralesional injection is thought to be safer since high local concentrations can be achieved without causing high plasma concentrations.[33] A recent retrospective review of 275 patients treated with intralesional injection of cidofovir from 11 countries predominantly throughout Europe found no evidence for long-term nephrotoxicity, neutropenia, or increase in laryngeal malignancy.[11] The literature on the effectiveness of cidofovir is based predominantly on case studies and a recent Cochrane review has called for an adequately powered and well-designed control study.[34] However, several uncontrolled studies have shown effectiveness in concentrations of 5–10 mg/mL, including a series with a mean follow-up of 51.6 months.[35] A recent review of the literature has shown an 80% partial or complete response with the use of cidofovir.[36]

Other adjuvant agents include systemic interferon alpha and indole-3-carbinol. Interferon-α is an endogenous human leukocyte protein that acts against various stages in the virus life cycle. The side effects of systemic interferon are significant including flu-like illness, neuropsychiatric disease, neutropenia, and thrombocytopenia. Effectiveness of systemic interferon administration on JRRP is mixed. Healy et al. compared surgery alone to surgery plus interferon and showed that disease growth rate decreased with adjuvant interferon within the first 6 months. This difference however disappeared after 6 months.[37] Leventhal et al. on the other hand did see a long-term effect and recommended disease re-evaluation after 6 months and interferon continued if there was a positive response.[38] Indole-3-carbinol is a nutritional supplement approved by the FDA that is effective against hormone-dependent tumors.[39] Some studies show indole-3-carbinol to be effective in adults with papilloma; no study to date has shown an effectiveness of indole-3-carbinol in children.

Recent attention has turned to bevacizumab (Avastin) as a new adjuvant agent for JRRP. Bevacizumab is a human monoclonal antibody that targets vascular endothelial growth factor (VEGF) isoforms, resulting in an antiangiogenic effect. It is FDA approved for the systemic use to treat metastatic colorectal cancer. An injectable form has been used to treat diabetic retinopathy and wet macular generation. Side effects include bleeding, blood clotting, hypertension, and hypothyroidism. The presence of VEGF receptors on papilloma specimens has sparked investigation of bevacizumab intralesional therapy. Preliminary studies under the direction of Steven Zeitels in adults are promising.[40] Maturo et al. have published a small case series showing some efficacy of the drug in pediatric patients.[41] Larger and long-term studies are currently underway.

## PREVENTION

Prevention of HPV infection would be the most effective treatment of JRRP. Gardasil (Merck) is a quadrivalent vaccine against the HPV subtypes 6, 11, 16, and 18. It became available in 2006 and is currently recommended for female aged 11–26 years and male aged 9–26 years to prevent the spread of HPV and decrease the risk of cervical cancer. It consists of three injections spread over 6 months. Because it is effective against the subtypes 6 and 11, the hope is that it will also reduce the incidence of JRRP.[42] At present it is still proving challenging in the United States to achieve universal or even acceptable vaccination rates and completion of the three injection protocol. However, in Australia in 2007, vaccination became a nationally funded program, and vaccination rates were 83% for the first dose, 80% for the second dose, and 73% for the third dose in 12- to 13-year-old girls in 2010. In a study of the impact of this vaccination program on genital warts (almost all caused by HPV types 6 and 11), there was a dramatic decline in genital warts in woman under 21 by almost 93% in 2011 to < 1% compared to 10.5% before the vaccination program started. In addition, herd immunity

was demonstrated by declining rates of genital warts in men despite men not being vaccinated at that time.[43] Although the effect of the vaccine on the incidence of JRRP is yet to be determined, this type of response to the vaccine on genital warts is quite promising. Furthermore, with the development of second-generation vaccines, there will be broader coverage of oncogenic HPV types, thus continuing to reduce the significant cancer burden for cervical, anal, penile, and oropharyngeal cancers.

## REFLUX

Gastroesophageal reflux disease (GERD) with secondary extraesophageal reflux can cause laryngeal mucosal damage and inflammation that is theorized to exacerbate papilloma proliferation. Antireflux medications have been shown in one study to place patients in remission. Another study advocates for antireflux medications in the prevention of laryngeal web formation.[44] It appears that antireflux medications are helpful in the control of JRRP and preservation of the voice.

## JRRP AND THE VOICE

Vocal function and voice quality are at risk with JRRP due to the recurrent nature of the disease, the primary area of involvement being the larynx and the iatrogenic damage that comes with multiple surgical interventions. The disease itself creates voice abnormalities such as hoarseness and dysphonia. The necessary surgical debulking and/or injections risk permanent damage to the laryngeal epithelium further jeopardizing voice function. Papillomata that affect the anterior commissure and true vocal folds are especially difficult to manage as scarring and webbing and impact to the vibratory mucosa in these areas have serious consequences to the voice. A recent study from Finland that compared the voice of adults with a history of JRRP to matched controls (age, gender, smoking, allergy, and gastroesophageal reflux disease history) showed that acoustic quality and perceptual quality was much worse. Fortunately, the patients did not report a significantly worse health-related quality of life or voice handicap.[45]

Previously, prevention of airway obstruction, distal tracheobronchial spread, and malignant transformation was the primary concern and treatment was carried out often at the expense of voice dysfunction. Now with more sophisticated understanding of the disease as well as improved surgical techniques, we have an opportunity to focus on voice preservation. The microdebrider, the 585-nm pulse dyed laser and the 532-nm KTP pulsed laser have all improved our ability to remove papilloma while preserving the laryngeal epithelium. The pulse dye and KTP laser are particularly beneficial for disease involving the anterior commissure and true vocal fold. Adjuvant therapies hopefully reduce the number of debulking procedures and thus the number of times the larynx is at risk for damage. Antireflux medications can potentially limit the extent of mucosal damage.

Given that there is no perfect tool for removal of laryngeal papilloma without concern for collateral damage to the vocal folds and development of dysphonia, especially in severe cases where chronic hoarseness is "inevitable", it is prudent to initiate voice therapy early in the course of the disease process. This serves to ensure focus on communication skills during the active disease maximizing voice production and also plays a role in anticipatory management and support of the psychosocial issues for the patient and family that arise with chronic voice difficulties. As the disease progresses the goals of voice therapy will be to establish the most optimal communication possible at each stage. It is critical to understand and manage the psychological impact of dysphonia on the school-aged child and adolescent who may be unable to participate in classroom activities or school functions or is confronted by his peer group with "what is wrong with your voice". Discussion of these issues with the family, involvement of the teachers at school and directed referral for counseling should be part of the management of these patients. During the intersurgical intervals true vocal fold phonation should be optimized and compensatory hyperfunction reduced. At times of severe disease or vocal fold damage augmentative and alternate communication strategies such as utilizing other vibratory sources (ventricular phonation, pharyngeal phonation, esophageal speech) or electronic devices (speech generation devices, tablet use) will be important. Fortunately, this is rare in the pediatric population. And finally speech therapy plays a role in long-term management of voice deficits, even after the disease has been controlled.

## CONCLUSION

Juvenile recurrent respiratory papillomatosis is a benign neoplasm caused by the HPV virus that affects the aerodigestive tract, particularly the larynx. The disease as well as the treatment have a long-term effect on voice quality and function. Timely diagnosis and careful treatment that minimizes laryngeal epithelial damage can control disease spread while preserving the voice. Of course, universal vaccination will help eliminate the disease entirely and obviate any need for surgical management.

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# SECTION 7

# Pediatric Velopharyngeal Insufficiency

CHAPTER

# 86

# The Anatomic Basis of Velopharyngeal Insufficiency

***David J Crockett, Christopher T Wootten***

## INTRODUCTION

Velopharyngeal insufficiency (VPI) is the term used to describe an anatomic or structural defect that prevents adequate velopharyngeal closure.[1] It is the most common type of velopharyngeal dysfunction (a condition where the velopharyngeal valve does not close appropriately during the production of oral sounds). The typical manifestations of VPI include hypernasal speech, increased nasal resonance, nasal regurgitation, and nasal emission during phonation.[2] VPI has many causes that require various approaches for proper management. This chapter will discuss the anatomy of the velopharynx, function of the velopharyngeal sphincter, and causes of VPI.

## EMBRYOLOGY (DEVELOPMENTAL ANATOMY)

Facial development begins during the fourth week of gestation. Neural crest cells migrate, combine with mesoderm, and subsequently begin forming the facial primordia. Maxillary prominences subsequently develop and are derived from the first branchial arch. During the sixth and seventh weeks of gestation, outgrowths of these bilateral maxillary prominences (palatal shelves) appear on both sides of the tongue, elevate, and fuse. The fusion of the palatal shelves forms the secondary palate (the palate posterior to the incisive foramen). The secondary palate growth begins at the incisive foramen and progresses posteriorly. The muscles of the soft palate are detailed below. These begin to migrate toward the midline from both sides of the posterior developing oropharynx during the fifth and sixth weeks of gestation. By the 10th week of development, these muscles have moved into a horizontal orientation, paralleling the palatine shelves. During the 10th to 12th weeks of development, the soft palate tissue fuses.

Any failure of the proper midline fusion will lead to clefting. This may be due to impairment of adequate tissue migration or from mechanical obstruction. For example, mechanical obstruction is known to occur with altered tongue position in patients with Pierre–Robin sequence. Varying severities are known to occur from submucous clefting to complete bilateral clefting.[3]

## ANATOMY AND FUNCTION

### Anatomy

A fundamental understanding of the anatomy and function of the velopharyngeal mechanism is required in order to be able to provide treatment to patients with VPI. The velopharyngeal sphincter is a muscular valve that extends from the posterior surface of the hard palate anteriorly to the posterior pharyngeal wall posteriorly. The lateral pharyngeal walls and the soft palate (or velum) compose the sphincter. Several muscles provide the functional component. These muscles include the muscles of the soft palate (levator veli palatini, tensor veli palatini, musculus uvulae, palatoglossus, and palatopharyngeus), superior pharyngeal constrictor muscle, and salpingopharyngeus.[4]

The primary velar elevator is the levator veli palatini muscle.[5,6] It arises from the petrous portion of the temporal bone (near the base of the styloid process) and from the adjacent cartilaginous eustachian tube. Passing

between the superior pharyngeal constrictor and the middle pharyngeal constrictor muscles it inserts onto the oral or upper surface of the palatine aponeurosis and into the median raphe of the palate. The fibers of this muscle interdigitate with other soft palate muscles.[7] As this muscle contracts, the midportion of the soft palate moves superiorly and posteriorly.[8] Contact with the posterior pharyngeal wall is achieved in this manner, with likely assistance from the superior pharyngeal constrictor, and provides closure of the velopharynx.[9]

The majority of the palatal aponeurosis is composed of the tensor veli palatini muscle. This muscle arises from the scaphoid fossa of the sphenoid bone and the lateral aspect of the medial pterygoid plate. A significant portion of the muscle is attached to the lateral hook of the eustachian tube cartilage.[10] It narrows to a tendon as it descends along the lateral wall of the nose and turns medially around the pterygoid hamulus. Afterward, it fans out to become the palatal aponeurosis. The principal function of this muscle is to enhance middle ear aeration through its effects on the eustachian tube orifice. The muscle is also able to tense the soft palate; however, its contribution to the closure of the velopharyngeal sphincter appears to be minimal.[8,10]

The musculus uvula is a paired, longitudinally oriented, midline muscle.[11] It extends between the aponeurosis anteriorly and the base of the uvulae posteriorly and lies directly above the levator palatini muscle. While the uvula itself is mainly composed of glandular and connective tissue, the musculus uvula contributes to midline bulk. On contraction it likely contributes to posterior velar thickening and extension, enhancing midline velopharyngeal contact with the posterior pharyngeal wall.[11] However, functional effect on speech with contraction of this muscle has been difficult to demonstrate.[12]

The palatoglossus muscle has been described as having a fan-shaped attachment in the soft palate that subsequently courses through the loose connective tissue of the anterior tonsillar pillar with a tapering termination in the tongue.[13] The palatopharyngeus muscle originates from the palatal aponeurosis and the posterior hard palate.[14] Vertical fibers comprise the posterior tonsillar pillar and insert on the thyroid cartilage, while horizontal fibers insert on the pharyngobasilar fascia and are frequently associated with the superior pharyngeal constrictors. The palatoglossus and palatopharyngeus muscles have been found to provide inferior pull on the velum and thus oppose the superior pull of the levator on contraction.[15]

The palatoglossus and palatopharyngeus have important speech functions, specifically aiding in position of the tongue and pharynx. The palatoglossus assists tongue elevation and the palatopharyngeus contracts to narrow the pharynx. Varying combination of contraction between these two muscles and the levator veli palatini can alter velar position during speech and swallow.[15]

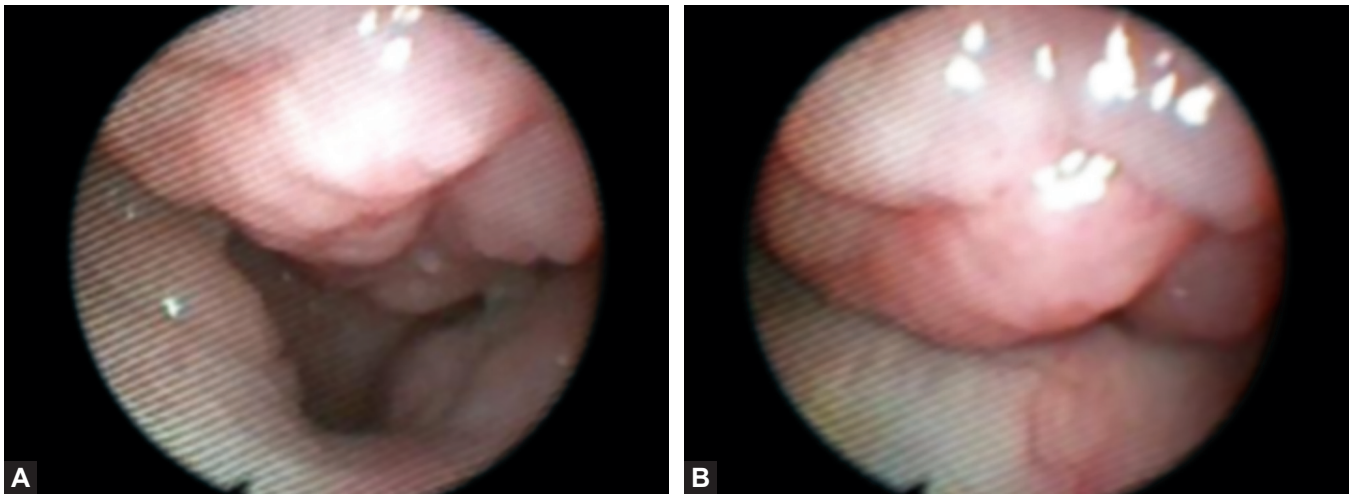
In general, the superior pharyngeal constrictor is a fan-shaped muscle with its fibers converging from posterior to anterior. From the midline raphe, the superior fibers extend inferiorly and anteriorly, the inferior fibers extend slightly superior and anterior, and the central fibers are horizontal.[10] The most superior fibers seem to insert on the velum in most individuals and may assist in drawing the velum posteriorly.[16] With contraction, the lateral pharyngeal wall may constrict, allowing for improved velopharyngeal closure. The velar fibers of this muscle also likely produce Passavant's ridge with potential contribution from the palatoglossus muscle in approximately a third of individuals.[17] This ridge may assist with velopharyngeal closure in some individuals.[18] Overall, the electromyographic data regarding the function of the superior pharyngeal constrictor muscle as pertaining to velopharyngeal competence are inconsistent.[15]

The muscle fibers of the salpingopharyngeus muscle arise from the palatopharyngeus muscle and attach to the torus tubarius. This muscle seems to have little, if any, functional velopharyngeal significance.[16]

Motor innervation to the muscles of the velopharynx is principally innervated by the pharyngeal plexus derived from the glossopharyngeal and vagus nerves. The tensor veli palatini muscle is innervated by the mandibular division of the trigeminal nerve.[19]

## Function

The main function of the velopharyngeal sphincter is to provide a tight seal between the velum and the pharyngeal wall, allowing separation of the oral and nasal cavities. The jaw, tongue, lips, pharynx, larynx, and velopharynx work together to produce the various sounds associated with speech.[20] The velopharynx assists with proper articulation and resonance associated with speech. The velopharyngeal port can adjust its state of being open or closed in order to balance nasal and oral airflow during speech production (Figs. 86.1A and B). Velopharyngeal competence is necessary to produce normal speech phonemes during vocalization. In the English language only /m/, /n/, and /ng/ are produced with an open velopharyngeal port (📻 86.1 and 86.2).[4] All other sounds are orally resonated.




**Figs. 86.1A and B:** (A) Endoscopic view of a normal open velopharyngeal port in a 6-year-old female. Notice the large adenoid tissue posteriorly; (B) Endoscopic view of a normal closed velopharyngeal port in a 6-year-old female.

When the velopharynx is not functioning properly, speech will be perceived as abnormal and velopharyngeal dysfunction will be the result. Any deficit in obtaining complete closure will lead to velopharyngeal incompetence. Hypernasality, nasal emission, and nasal turbulence are the result.[21] Hypernasality is an increase in nasal resonance with non-nasal phonemes. Nasal emission is the sound of air escaping through the nose. Nasal turbulence is the sound made when air is forced through nasal mucous. When an obstructive process is present, the nasal airflow may also be hyponasal. Careful evaluation for VPI should be performed with any of these findings.

## Closure Patterns

As mentioned previously, velopharyngeal closure is achieved through the combined coordination of the pharynx and the soft palate. Scholnick et al. described patterns of velopharyngeal closure based on the contribution of the components of the sphincter. Using lateral and base projection videofluoroscopic views, they observed four basic closure patterns: coronal, circular, circular closure with the Passavant ridge, and sagittal.[22]

The coronal pattern of closure occurs when the posterior surface of the soft palate approximates the posterior pharyngeal wall, which remains immobile. Little movement of the lateral pharyngeal walls occurs medially to approximate the lateral edges of the soft palate. The major component of closure occurs in the anteroposterior direction. Croft et al. found this closure pattern to occur in 55% of normal subjects and 45% of those with VPI.[23]

The sagittal pattern of closure is characterized by marked movement of the lateral pharyngeal walls toward the midline. Posterior movement of the soft palate is limited. This pattern of closure was found to be used in 16% of normal subjects and 11% of those with VPI.[23]

The circular pattern of closure occurs when there is an equal amount of movement in the soft palate and lateral pharyngeal walls. Increasing movement of the lateral pharyngeal walls diminishes broad contact between the soft palate and the posterior pharyngeal wall. There is virtually no movement of the posterior pharyngeal wall. This pattern of closure was identified in 10% of normal subjects and 20% of those with VPI.[23]

Circular closure with the Passavant ridge is similar to the circular pattern of closure, but there is anterior movement of the posterior pharyngeal wall resulting in a true sphincteric closure pattern. Of note, the Passavant ridge is not always located at the level where the valving occurs.[24] Therefore, the presence of a Passavant ridge does not always correlate with a circular closure pattern. Circular closure with the Passavant ridge is found in 19% of normal subjects and 24% of those with VPI.[23]

# CAUSES OF VELOPHARYNGEAL INSUFFICIENCY (ANATOMICAL AND NEUROLOGIC FAILURES)

VPI can be categorized according to the underlying pathologic mechanism. Any disruption to the proper function or the anatomy of the velopharynx may lead to velopharyngeal dysfunction. The causes of VPI can be classified

into neuromuscular abnormalities, structural abnormalities, and functional abnormalities. These causes can be further subdivided into acquired and congenital causes. In children, VPI is typically caused by structural, iatrogenic, or neuromuscular anomalies.[2]

## Structural Abnormalities

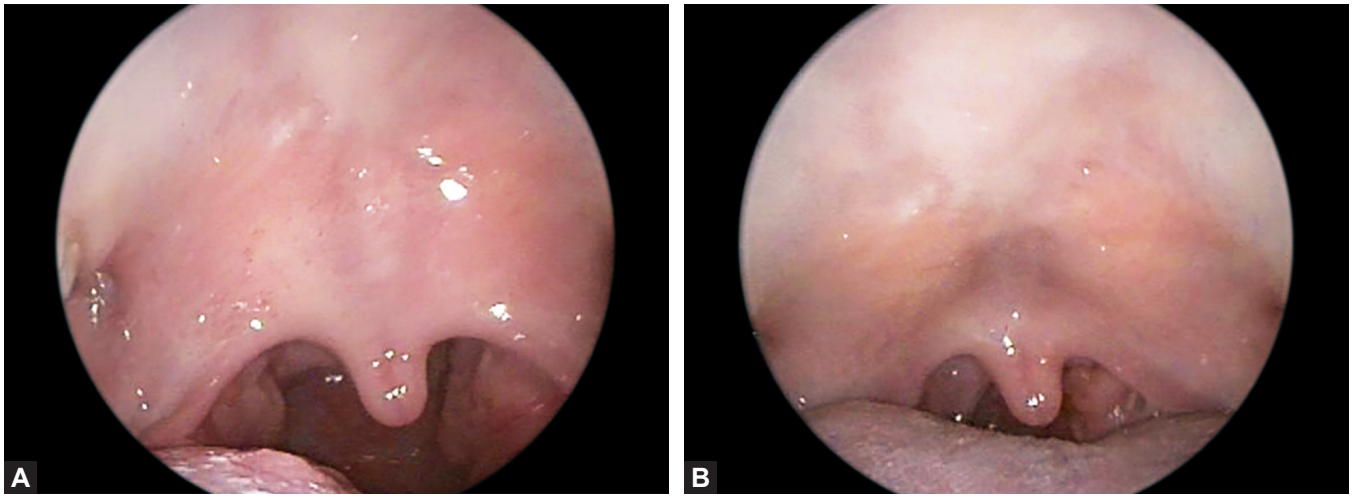
As mentioned, structural abnormalities can be further classified into congenital and acquired causes. Congenital causes include the presence of a cleft palate, submucous cleft, or an occult submucous cleft. Velopharyngeal dysfunction is common in patients with a repaired cleft palate or an unrepaired submucous cleft palate.[25-27] The overt cleft palate, both before and after repair, is the most common cause for VPI.[28] VPI should be suspected in any patient who has had a cleft palate, especially if there is any concern for abnormal resonance, language delay, or problem with intelligibility.[21]

Three essential differences in the anatomy of patients with cleft palates have been described, as compared to the normal anatomy discussed above.[29] First, the general orientation of the muscle fibers is anteroposterior rather than transverse. Second, the palatal aponeurosis is absent. Third, the anteroposteriorly directed fibers often terminate directly on the posterior bony edge of the hard palate. These findings are also found in those with isolated submucous clefting. The misorientation of the normal muscular anatomy results in improper elevation and elongation of the palate during speech. The goal of the cleft palate and velopharyngeal surgery is to restore normal anatomy or to modify existing anatomy to improve velopharyngeal closure.[30]

The majority of patients who present with VPI and do not have an overt cleft palate or prior surgery are likely to have a submucous cleft palate (Figs. 86.2A and B). The classic findings of a submucous cleft consist of a bifid uvula, palatal muscle diastasis, and a bony notch of the hard palate. An occult submucous cleft is diagnosed when a muscle defect is visible only on the nasal mucosal surface of the soft palate.[31] Lewin et al.[32] found that approximately 44% of patients assessed with VPI without an overt cleft palate had a classic submucous cleft palate and 22% had an occult submucous cleft palate.

Children with VPI may have other anatomical or structural abnormalities. A congenital short palate and/or large pharynx may also contribute to VPI. The tonsils have an intimate relationship with the velopharyngeal valve and subsequently can influence the velopharyngeal mechanism by hindering or assisting speech.[33] Hypertrophic tonsils can impede palatal closure and cause insufficiency.[34]

Structurally acquired causes are principally iatrogenic and include palatal scarring associate with palatal surgery, postadenoid complications, and posttonsillectomy complications. Hypernasality after adenotonsillectomy has been found to occur in approximately one in 1,500 procedures.[35] Rather than resulting from palatal scarring, however, the most common etiology of postadenoidectomy (or adenotonsillectomy) VPI appears to




**Figs. 86.2A and B:** (A) Transoral view of the palate of a 7-year-old male with a submucous cleft. (B) Transoral view of the palate of a 7-year-old male with a submucous cleft during phonation. Notice that he has adequate functional elevation of his soft palate.

be the removal of adenoid tissue that was structurally important to velopharyngeal closure. In these patients, bulky adenoid tissue was thought to be compensating for a short and/or poorly mobile palate.

## Neuromuscular Abnormalities

Multiple congenital and acquired neuromuscular abnormalities may contribute to VPI. As previously discussed, cranial nerves IX and X (with possible contributions from V, VII, XI, and XII) innervate the muscles of the velopharynx.[28] Any congenital or acquired neurologic insult to these nerves or the brainstem could potentially cause VPI. Common or well-known congenital causes include Mobius syndrome, Down syndrome, cerebral palsy, muscular dystrophies, velocardiofacial syndrome (22q11 deletion), and craniofacial microsomia. Acquired causes include neural disease (cerebrovascular incidents, encephalopathy, intracranial processes, palatal paralysis, progressive neurologic deterioration, amyotrophic lateral sclerosis, Parkinson's disease, myasthenia gravis, multiple sclerosis), muscular dystrophies, and head and neck tumor surgery.[2,17,20,28]

## Functional Abnormalities

Functional abnormalities that contribute to or exacerbate VPI include compensatory misarticulation and mislearned errors of articulation.[2] Children with a postsurgical reconstructed palate are prone to develop errors of articulation and faulty compensatory speech patterns, which exacerbate the hypernasality problem associated with VPI.[36,37] Rarely VPI may be associated with a learned behavior. A very small subset of children may exhibit persistent signs and symptoms of VPI as a result of overexposure to faulty speech models in their environment or due to an exaggerated regional dialect pattern. Formal speech therapy is helpful to correct the learned behavior when it interferes with conversational speech intelligibility.[37]

## CONCLUSION

In summary, velopharyngeal insufficiency is the term used to describe an anatomic or structural defect that prevents adequate velopharyngeal closure. The main function of the velopharyngeal sphincter is to provide a tight seal between the velum and the pharyngeal wall, allowing separation of the oral and nasal cavities. The velopharynx assists with proper articulation and resonance associated with speech. Any disruption to the proper anatomy and its function will lead to velopharyngeal dysfunction. A fundamental understanding of the anatomy and function of the velopharyngeal mechanism is required in order to provide treatment to patients with VPI.

## VIDEO LEGENDS

**Video 86.1:** Video endoscopy of a 6-year-old female with normal velopharyngeal function. Transoral view of the palate.

**Video 86.2:** Video endoscopy of a 6-year-old female with a normal velopharyngeal functional closure. Transnasal view of the velopharynx.

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CHAPTER

# The Role of the Otolaryngologist in Velopharyngeal Insufficiency Evaluation

87

***Matthew T Brigger***

## INTRODUCTION

The evaluation and management of velopharyngeal insufficiency (VPI) requires close coordination between a variety of disciplines, most notably between speech-language pathologists and otolaryngologists or other craniofacial surgeons. The success of the team, and ultimately, the child's outcome requires recognition of individual roles coupled with close communication among team members. In the context of a team-based multidisciplinary approach, the role of the surgeon is to understand, evaluate, and diagnose the specific anatomic abnormality resulting in VPI, allowing development and successful execution of a surgical plan.

The production of intelligible speech relies on complex neuromuscular interactions, resulting in the sphincteric interaction of the palate (velum) within the pharynx. Velopharyngeal insufficiency, or the inability to effectively seal the nasopharynx, results in loss of resonant control of speech and the ability to maintain requisite intraoral pressure to generate orally directed speech sounds. Given that the nasopharynx is effectively closed during the vast majority of speech, this can significantly impact speech intelligibility. This lack of speech intelligibility has a clear detrimental effect to affected children. However, even mild cases of VPI may alter an effective communication and result in a decrease in the child's overall well-being. The etiology of VPI varies from residual speech patterns after cleft palate repair to congenital anomalies of the soft palate (e.g. shortness and submucous cleft) as well as weakness or motor planning difficulties.[1] Subsequently, the approaches to assessment and intervention are variable and often need to be tailored to the individual child.

## SEMANTICS

Terminology used within the VPI literature is limited by redundancy and inconsistencies. In addition to VPI, commonly used terms include velopharyngeal dysfunction (VPD), velopharyngeal inadequacy, and velopharyngeal incompetence. These terms are frequently used interchangeably. When standardized terminology is used, variations of the classification introduced by Trost in 1981 seem to be the most common.[2] In the classification, an all-encompassing term velopharyngeal inadequacy is used to describe velopharyngeal mislearning (faulty learning of articulation patterns), velopharyngeal incompetence (neurologic dysfunction leading to impaired motor control of the palate) and VPI (an anatomic deficiency of insufficient tissue for closure). A similar, widely used all-encompassing term is VPD.[3] For the purposes of this chapter, VPI will be used to connote VPI.

## PERTINENT ANATOMY

While the anatomic components forming the velopharynx are well described in Chapter 86, there are several functional aspects of particular note. A specific distinction is made between the physiology involved in closing the nasopharynx during swallowing and speech exercises. A common situation is seen when children have evidence of severe VPI with speech, but exhibit no nasal regurgitation during swallowing. Shprintzen and colleagues classified differences in pneumatic (speech, blowing, and whistling) and nonpneumatic (gagging and swallowing) closure mechanisms based on videofluoroscopic findings.[4] Furthermore, an electromyographic study of levator function during speech, blowing, and swallowing suggests that

different muscle types are activated during swallowing exercises as compared to speech and blowing exercises.[5] Ultimately, the complex neuromuscular interaction and subspecialization of muscle fibers highlights the importance of approaching VPI as more than a simple anatomic deficit and realizing that the manifestations of VPI can result from a variety of insults.

## Closure Patterns

As stated above, a simplistic approach to understanding velopharyngeal anatomy and physiology fails to reveal the high degree of coordination, complexity, and variation involved. The sum motion is one in which the palate elevates posteriorly and contacts the pharyngeal wall circumferentially. On a lateral view, the palate appears to flex like a knee due to the bulge of the uvula maximizing contact with the posterior pharyngeal wall (Fig. 87.1).[6] However, in order to better understand the sum motion in three dimensions, Skolnick described four patterns of velopharyngeal closure presented as coronal, sagittal, and circular with or without posterior pharyngeal wall involvement.[7] Pragmatically speaking, of primary surgical planning concern is the ability to describe the presence or absence of significant lateral pharyngeal wall motion to identify the nature and location of velopharyngeal air escape. The choice of surgical procedure is generally predicated on dynamic anatomic considerations of lateral wall motion, particularly when the surgeon is contemplating pharyngeal flap surgery versus a sphincter pharyngoplasty.

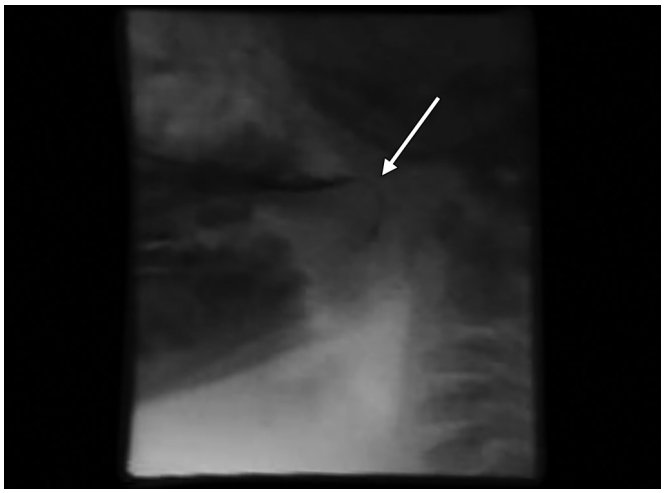
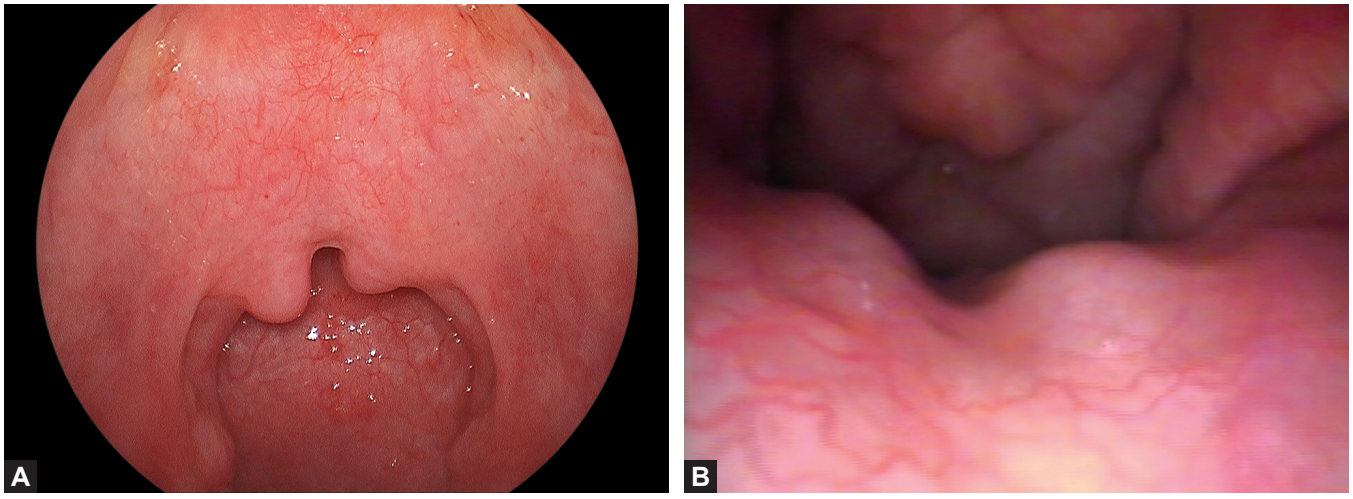


**Fig. 87.1:** Multiview fluoroscopy demonstrating palatal flexion and contact with the posterior pharyngeal wall.

## ETIOLOGY AND PATHOPHYSIOLOGY

The otolaryngologist serves a vital role in the diagnosis of VPI. In particular, the surgeon must be well versed in the myriad of syndromes, diseases, and congenital dysmorphisms associated with VPI. Velopharyngeal insufficiency is most commonly seen in children with associated craniofacial developmental anomalies of which cleft palate is the most common. Despite successful palatoplasty, postrepair prevalence of VPI has been reported to be 20–50%.[6,8] A special case is the submucosal (occult) cleft palate. In this situation, no overt cleft is seen, but a failure of the midline fusion of the velar muscles is present often manifesting as a bifid uvula, hard palate notch or a bluish line of a visible diastasis (Figs. 87.2A and B). Although a common cause of VPI, the majority of these children will have no speech deficits during their lifetime.[9]




**Figs. 87.2A and B:** Submucous cleft palate as viewed from the oral cavity (A) and nasal cavity (B).

## Associated Syndromes

Over 200 syndromes have been described where cleft palate is a reported manifestation. Any such syndrome can be associated with VPI. Of special note is velocardiofacial syndrome, which typically does not manifest an overt palatal cleft. The syndrome was first described in 1977 by Shprintzen and colleagues.[10] The syndrome has a wide spectrum of phenotypes including congenital cardiac anomalies, VPI, and characteristic facial dysmorphisms.[11] The prevalence in the United States is estimated to be 1:2,000.[11] The difficulty lies in the wide variability of presentations and propensity for misdiagnosis. Proper diagnosis is essential in that patients with velocardiofacial syndrome (VCFS) must be screened for potentially lethal cardiac anomalies. From a surgical standpoint, there have been a number of reports of carotid artery medialization that may possibly represent hazardous surgical anatomy (Fig. 87.3).[12,13] Additionally, surgical outcomes for VPI have been reported to be inferior to the results achieved in children without VCFS.[14]

## Postadenoidectomy

Velopharyngeal insufficiency manifesting after adenoidectomy is relatively rare and generally of short duration, with most cases resolving within 6 weeks. Given the bulk of adenoid tissue, many children produce velopharyngeal closure by approximating the velum to their adenoid pad. In most children, removal of the adenoid pad is of no consequence because their velum has adequate length to reach the posterior pharyngeal wall. However, in select children, the new dynamics of velopharyngeal closure do not allow adequate apposition. Permanent VPI after adenoidectomy requiring intervention is reported to occur in approximately 1:1,500 adenoidectomies.[15,16] In retrospect, many children have suggestions of marginal velopharyngeal competence including physical stigmata of a submucosal cleft, preoperative hypernasality or regurgitation. In a review of 23 children with VPI after adenoidectomy, 14 children were found to carry the VCFS genotype.[17] In situations where an adenoidectomy appears to be indicated in a child with features concerning for marginal velopharyngeal competence, a superior pole adenoidectomy can be performed in which the inferior aspect of the adenoid pad is maintained to prevent the development of VPI.

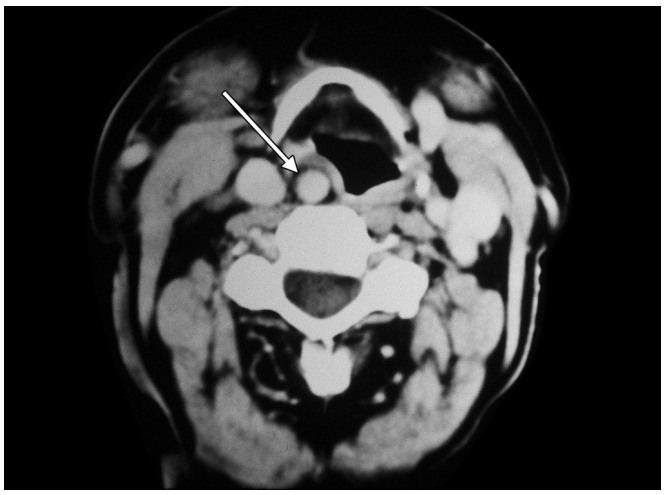


**Fig. 87.3:** Contrast enhanced CT scan demonstrating medialized right internal carotid artery (white arrow) in a child with velocardiofacial syndrome.

## Other Causes

Velopharyngeal insufficiency has been noted in a variety of other settings. Any surgery that involves orthognathic maxillary advancement (often performed in children with craniofacial abnormalities) places a child at risk for developing VPI. Hypertrophied tonsils have been associated with clinical VPI and resolution has been documented after tonsillectomy.[18] Additionally, neuromuscular disorders resulting in poor control of pharyngeal musculature can result in hypernasality and dysarthria.

# DIAGNOSTIC EVALUATION

## History

Evaluation of a child with suspected VPI starts with simply listening with a keen ear. Although children are often referred for grossly abnormal speech, a great deal can be learned by listening to the child speak. Using standard phrases weighted with sibilants and plosives will help to uncover the extent of VPI. A comprehensive medical, surgical, and family history is imperative for all children. Particular emphasis on any developmental anomalies, familial associations, past medical history, and past surgical history may yield clues to syndromes or other problems that can be seen in the setting of VPI. Eliciting any history of hearing loss or other anomalies that potentially increase the child's communication difficulties is essential. A developmental and psychological history is useful in determining the extent of disability imparted by the communication difficulties.

## Physical Examination

A comprehensive physical examination is requisite in all children with VPI. All children must be assessed for the presence of syndromic stigmata, craniofacial dysmorphisms, and the presence of cardiac abnormalities. A thorough head and neck examination includes an assessment of the middle-ear status. An oral examination is performed to identify the presence of a cleft and status of repair (Fig. 87.4). As described below, flexible nasopharyngoscopy has proven to be a well-tolerated and invaluable tool in examining and formulating a treatment plan for these children.

An expanded orofacial examination is often helpful in the initial evaluation. The complete evaluation consists of close intraoral examination with attention to oromotor skills, the occlusal and dental status as well as direct visualization and palpation of the velum. Facial examination during speech in relation to characteristic grimaces and gestures are often noted.

## Additional Evaluation

Several perceptual evaluation scales have been developed and validated. While speech and language pathologists most commonly administer these instruments, it is imperative that otolaryngologists understand the utility of placing quantitative values of the degree of dysfunction. One of the most commonly used is that of McWilliams and Phillips that is sometimes referred to as the Pittsburgh Weighted Speech Scale that rates five components of speech including nasal emission, facial grimace, nasality, phonation, and articulation.[19] Additionally, otolaryngologists need to be familiar with objective measures of nasal emission such as the nasalance score obtained by nasometry that measures the nasal acoustic energy within speech and provides a ratio to normative total acoustic energy.[20] Both perceptual evaluation and nasometry provide a potential means to track therapeutic outcomes.

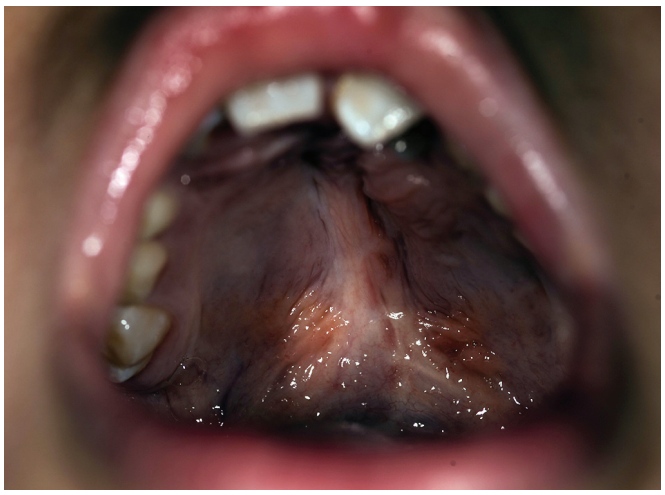


**Fig. 87.4:** Intraoral photograph of the palate in a child with velopharyngeal insufficiency who has previously undergone palatoplasty.

## Assessment of Velopharyngeal Closure

### *Flexible Nasopharyngoscopy*

Flexible nasopharyngoscopy has become indispensable in the evaluation of children with VPI. The development of high-quality, small-caliber flexible endoscopes permits excellent visualization in most children. The flexible endoscope is passed transnasally to a position in the posterior nasal cavity allowing a complete "bird's eye" view of the velum and nasopharynx during speech (📹 87.1). Children of all ages can be evaluated anatomically; however, it is generally around age six that children can cooperate and perform the comprehensive vocalizing tasks for a complete evaluation. Flexible nasopharyngoscopy provides an excellent view of the nasal surface of the palate and may provide the only sign of a submucous cleft palate as described above. Additionally, flexible nasopharyngoscopy allows an examination of the larynx, which may uncover additional pathologies associated with compensatory measures, such as vocal nodules, that may have developed in response to the VPI.

### *Multiview Fluoroscopy*

Multiview fluoroscopy, generally performed by speech and language pathologists, was for many years the primary means of assessing velopharyngeal closure. Three views to identify velopharyngeal closure patterns are traditionally used after instilling a small amount of high-density barium into the child's nose to coat the nasopharynx. Videofluoroscopy allows excellent visualization of the shape of the velum and angle of elevation in lateral view and may serve as a better tolerated alternative for children who are noncompliant with nasopharyngoscopy. The requirement of ionizing radiation in addition to potential difficulties in standard positioning with resultant child compliance issues are potential limitations of the study. An important concept is that often videofluoroscopy and nasopharyngoscopy provide complementary information.

### *Nasopharyngoscopy, Multiview Fluoroscopy, or Both?*

Over time, much has been written about the merits and disadvantages of both nasopharyngoscopy and multiview fluoroscopy. Both techniques accurately assess velopharyngeal anatomy to assist in developing a treatment plan, particularly surgical methods. Nasopharyngoscopy allows an excellent view of velopharyngeal closure patterns, but can be limited by optical distortion and tolerance by the child undergoing the examination. Multiview fluoroscopy allows an excellent view of lateral wall motion as well as closure patterns. The closure patterns of the velopharynx were initially described based on fluoroscopic studies. Difficulties arise in interpreting anatomic findings in the presence of multiple shadows. Additionally, post-surgical examination particularly in the setting of a pharyngeal flap is quite difficult with fluoroscopy, but is easily visualized directly with nasopharyngoscopy. A recent review suggests that both modalities provide complementary data, but that nasopharyngoscopy may provide a higher correlation with VPI severity.[21]

### *Grading and Standardization of Velopharyngeal Closure Measurements*

In 1990, an international working group of clinicians and researchers headed by Karen Golding-Kushner reported a standardized grading scale for reporting findings on nasopharyngoscopy and multiview fluoroscopy.[22] The scale serves to outline both quantitative and qualitative scoring to accurately describe and grade the anatomic defects associated with VPI.

## BASIC TENETS OF THERAPY PRIOR TO SURGERY

Prior to surgical repair of VPI, a speech language pathologist with specialized training can help guide parents to elicit sound play with their infant, expand consonant repertoires, and to minimize patterns of glottal stops.

As language and speech emerge for the toddler and preschool age child, it is important to discern if speech errors are developmental, obligatory, or compensatory. When children with cleft or noncleft velopharyngeal problems display articulation errors and resonance abnormalities, the developmentally appropriate articulation issues are addressed first. It is important to remediate developmental speech errors as well as establish accurate placement of the articulators and manner of production (e.g. fricative versus stop consonants), even when the anatomy prohibits the ability to achieve an orally produced sound. This is especially true for children under 4 years of age with a cleft palate who are often too young for consideration of a secondary surgery. However, speech therapy specifically addressing the VPI cannot work against atypical anatomy and if attempted may cause undue frustration to the child.

Perhaps the primary concern for every child, parent, and VPI surgeon is to avoid operating when a child has a functional speech abnormality that can be masking as what appears to be VPI secondary to anatomical deficit. A thorough evaluation by a speech and language pathologist is necessary to accurately diagnose such disorders preoperatively. Comprehensive therapy often involves much more than simply filling the anatomic defect.

## FUTURE DIRECTIONS

The management of VPI continues to be an evolving field. Recent advances in evaluation include the widespread use and acceptance of nasal endoscopy. Of recent note, the utility of magnetic resonance imaging (MRI) as an evaluation tool has emerged as stronger magnets and imaging algorithms have allowed the development of cine MRI sequences that provide high-resolution detailed velopharyngeal movement visualized without ionizing radiation.[23]

## CONCLUSION

Ultimately, the otolaryngologist must take a primary role in the evaluation of children with VPI. The heterogeneity of the problem leads to a wide variety of manifestations and therapies. The care of these children requires an individualized approach to each patient in a multidisciplinary fashion. Fortunately, given the opportunity, most children can achieve intelligible speech and experience minimal vocal disability long term.

*Disclaimer*: The views expressed in this chapter are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, nor the US Government.

## VIDEO LEGEND

**Video 87.1:** Flexible nasendoscopy demonstrating examples of children with velopharyngeal insufficiency who have good lateral wall motion and poor lateral wall motion.

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CHAPTER

# The Role of the Speech Pathologist in the VPI Evaluation

88

***Ann W Kummer***

## INTRODUCTION

Normal velopharyngeal function requires coordinated movement of the structures of the velopharyngeal valve—the velum, the lateral pharyngeal walls, and the posterior pharyngeal wall. During nasal breathing, the velopharyngeal valve is open. As such, the velum rests against the base of the tongue and the lateral walls are wide apart, thus providing a patent upper airway. During oral speech, however, the velum moves in a superior and posterior direction to close firmly against the posterior pharyngeal wall (or adenoids in young children). At the same time, the lateral pharyngeal walls move medially to close against the velum. Complete closure of the velopharyngeal valve is required for all speech phonemes (consonants and vowels), with the exception of nasal sounds (m, n, ng).

There are three components to normal velopharyngeal function: anatomy, neurophysiology, and learning.[1] Of course, velopharyngeal closure requires normal structure (anatomy) and normal movement (neurophysiology). What is often forgotten is that the velopharyngeal valve is an articulator, just like the tongue and the lips. As such, it has a learned component.

When the velopharyngeal valve does not close consistently or completely during the production of oral sounds, this is often called velopharyngeal dysfunction (VPD). VPD is typically used as a general term that encompasses disorders of any of the three basic components of velopharyngeal function (structure, function, or learning).[1,2] Other terms are used for more specificity as to the type and causation of VPD.[1–5] For example, velopharyngeal insufficiency (VPI) is most often used to describe a structural defect that prevents adequate velopharyngeal closure (Fig. 88.1). VPI is the most common type of VPD because it can be caused by a history of cleft palate or submucous cleft. It can also be caused by a deep pharynx (due to cervical spine or cranial base anomalies), or even irregular adenoids, which prevent a tight velopharyngeal seal. Acquired VPI can occur following adenoidectomy or maxillary advancement. In contrast, velopharyngeal incompetence (also abbreviated VPI) is used to refer to a neurophysiological disorder in which poor movement of the velopharyngeal structures results in incomplete velopharyngeal closure (Fig. 88.2).

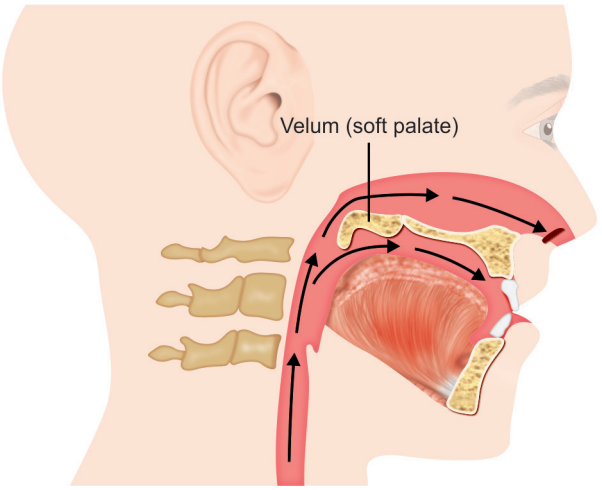



**Fig. 88.1:** Velopharyngeal insufficiency. Velopharyngeal insufficiency is due to a structural cause. In this drawing, the velum has normal movement, but is too short to achieve velopharyngeal closure. Adapted from Kummer AW. Cleft palate and craniofacial anomalies: The effects on speech and resonance. Clifton Park: Cengage Learning; 2014.

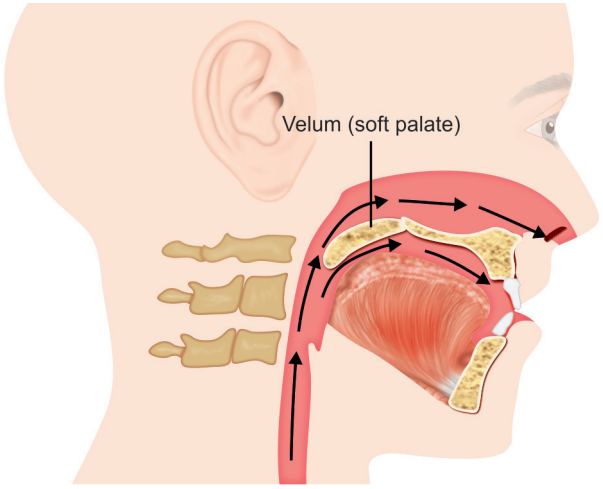



**Fig. 88.2:** Velopharyngeal incompetence. Velopharyngeal incompetence is due to a neuromotor disorder. In this drawing, the velum is normal in structure, but doesn't move well enough to achieve velopharyngeal closure. Adapted from Kummer AW. Cleft palate and craniofacial anomalies: The effects on speech and resonance. Clifton Park: Cengage Learning; 2014.

Neurological conditions that can cause velopharyngeal incompetence include cerebral palsy, myotonic dystrophy, myasthenia gravis, neurofibromatosis I, cerebral or brainstem tumors, traumatic brain injury, or cerebral vascular accident. Finally, velopharyngeal mislearning refers to an articulation disorder where speech sounds are inappropriately produced in the pharynx. As a result of this placement, the velopharyngeal valve is open, thus mimicking VPI during attempted production of certain speech sounds.

It is important to note that both types of VPI (velopharyngeal insufficiency or incompetence) require physical management for correction.[1] Physical management usually involves surgery, but may include prosthetic management if surgery is not an option. On the other hand, velopharyngeal mislearning requires speech therapy only. It is not uncommon for a patient to demonstrate both VPI and velopharyngeal mislearning. For example, children with velopharyngeal insufficiency often develop compensatory productions (a form of velopharyngeal mislearning). In these cases, surgical correction is required first in order to correct the VPI and "normalize" the structure. After structural correction, speech therapy is necessary to correct the faulty articulation productions in the pharynx that continue to result in "nasality".

The differential diagnosis of the type of VPD is of critical importance, as it forms the basis for determination of the appropriate treatment modality (surgery, prosthetic device, and/or speech therapy).[1,6,7] Making this diagnosis through perceptual and instrumental assessment is, therefore, the primary role of the speech pathologist in the speech evaluation. If surgical correction is needed, the speech pathologist can assist in determining the type of surgery that has the best chance of success for the patient, based on the size and location of the velopharyngeal gap. If a prosthetic device is indicated, the speech pathologist can assist in fitting the device for maximum benefit. Finally, if speech therapy is needed, the evaluation results are used for development of an individualize treatment plan and determination of therapy strategies.

A speech pathology evaluation to rule out VPI is indicated around the age of 3 for all children with a history of cleft palate.[1,2,7,8] It is also indicated both before and after secondary surgery for VPI. The following is an overview of the components of the speech pathology evaluation of velopharyngeal function, and how the results of the evaluation are used to make treatment decisions.

## PERCEPTUAL EVALUATION OF VELOPHARYNGEAL FUNCTION

The evaluation of velopharyngeal function begins with a perceptual evaluation of the patient's speech. During this evaluation, the examiner's ear is used to analyze the acoustic product of velopharyngeal function in order to make inferences about the function of the velopharyngeal valve. There are some standardized protocols for rating different parameters of speech and velopharyngeal function and reporting evaluation results.[9] From a thorough analysis of what is perceived, a determination can be made regarding the status of velopharyngeal function and its potential for change.

The perceptual evaluation typically includes an analysis of various components of speech, including resonance; presence of nasal emission; speech sound production; and phonation. These are further described in the following sections.

### Resonance

Resonance is typically evaluated by listening to connected speech. The speech pathologist must determine if the resonance is normal or abnormal. If resonance is abnormal, the speech pathologist determines the type of resonance (e.g. hypernasal, hyponasal, cul-de-sac, or mixed). This is of utmost importance because the type of resonance suggests causation, which determines appropriate treatment.[1,7,10,11]

Patients with VPI often (but not always) demonstrate hypernasal speech. Hypernasality is characterized by excess sound in the nasal cavity during the production of oral sounds. The speech is perceived as low in intensity, muffled, and unclear. Hypernasality is most perceptible on vowels, which are produced by altering oral resonance. There may also be nasalization of voiced consonants, so that oral phonemes sound more like their nasal cognates (e.g. m/b, n/d, ng/g). As a general rule, if nasal sounds are heard more frequently than normal, or if nasal sounds are substituted for oral sounds, the resonance is hypernasal. Although many patients with VPI demonstrate hypernasality, the absence of hypernasality does not rule out VPI. This is because hypernasality is only perceived when the velopharyngeal gap is about 5 mm in size or larger.

Because resonance disorders are not mutually exclusive, the speech pathologist will assess for other types of resonance deviations. For example, there may be hypernasality on oral sounds due to VPI, but also hyponasality on nasal sounds due to a blockage in the pharynx. Hypernasality due to VPI can also occur in combination with cul-de-sac resonance, which is the result of blockage at the exit of one of the resonating cavities (pharyngeal, oral cavity, or nasal cavity).

Although hypernasality is most commonly caused by VPI, it can also be due to other factors. If there is a submucous cleft, for example, hypernasality can be due to excess sound radiating through a thin velum. A large fistula can also cause hypernasality. Hypernasality can even be "phoneme-specific" due to misarticulation. For example, if the patient produces nasal sounds for oral sounds (i.e. ng/l or ng/r), this gives the impression of VPI, though this type of nasality is due to a functional articulation disorder. Even the habitual use of a high posterior tongue position can give the perception of hypernasality. Because some of these causes require physical management, while others require speech therapy alone, it is very important that the speech pathologist not only identify the type of resonance but also make a differential diagnosis as to the cause.

## Nasal Emission

When there is a suspicion of VPI, the speech pathologist will assess for the presence of audible nasal air emission. Nasal emission can occur with hypernasality, if the gap is fairly large, or it can occur without hypernasality, if the gap is relatively small.[1,10–12]

If nasal emission is present, the speech pathologist will determine whether it is low in intensity, which is usually the result of a larger velopharyngeal opening, or whether it is the "bubbly" nasal rustle (turbulence). A nasal rustle occurs when the air is forced through a small velopharyngeal opening, which increases its pressure. When it is released on top of the velopharyngeal valve, it results in loud bubbling of secretions.[12] The examiner will also note the occurrence of a nasal snort, which is produced most often with /s/ blends. A nasal grimace commonly accompanies nasal air emission. This is an important observation because it reflects the patient's extra effort in attempting to close the velopharyngeal port.

The consistency of the nasal air emission is also tested. Nasal emission that occurs during the production of all pressure-sensitive phonemes suggests a large velopharyngeal opening, particularly if it is associated with hypernasality. Nasal emission that occurs inconsistently suggests a smaller opening because the patient can close the gap with short utterances or with effort. In both cases, surgical intervention is needed for correction. On the other hand, nasal emission that occurs consistently on certain speech sounds, but not on all pressure-sensitive sounds, indicates that the cause is faulty articulation placement, rather than VPI. Therefore, speech therapy alone is indicated for correction.

## Speech Sound Production

In assessing articulation (speech sound production), the speech pathologist will record speech sound errors, including substitutions, omissions, and distortions. The potential cause of the errors is also identified (e.g. abnormal structure, possible apraxia, phonological disorder, delayed development, or normal developmental error). When there are structural anomalies, such as VPI, the speech pathologist will also determine whether there are any obligatory distortions or compensatory articulation errors.[1,11]

Obligatory distortions occur when the articulation placement (the function) is normal, but the abnormality of the structure causes distortion of speech. Obligatory distortions secondary to VPI include hypernasality, nasal emission, and nasalized consonants. Compensatory articulation errors occur when the placement of production is moved in response to the abnormal structure. When VPI causes inadequate oral airflow for consonant sounds, the patient may compensate by producing the sounds in the pharynx, where there is airflow.[11] Common compensatory productions for VPI, therefore, include glottal stops, pharyngeal plosives, pharyngeal fricatives, and posterior nasal fricatives. These productions can often be coarticulated with the correct oral sound, making the diagnosis a little challenging.

Hypernasality and nasal emission can occur due to either obligatory distortions or compensatory errors that are produced in the pharynx. A differential diagnosis between the two is of critical importance because obligatory distortions can only be corrected with physical correction, while compensatory productions require speech therapy (preferably after the abnormal structure has been corrected).[11]

### Phonation

Dysphonia due to vocal cord nodules is common in individuals with VPI, particularly those with a relatively small velopharyngeal opening. This may be due to strain in the entire vocal tract with attempts to achieve velopharyngeal closure. In addition, breathiness is sometimes used as a compensatory strategy to mask the hypernasality or to mitigate the nasal emission. Finally, patients with VPI secondary to a craniofacial syndrome are at higher risk for laryngeal anomalies. Therefore, an assessment of phonation is usually part of the evaluation of velopharyngeal function.

As part of the assessment, the speech pathologist listens for characteristics of dysphonia, including hoarseness, breathiness, roughness, glottal fry, hard glottal attack, strain, inappropriate pitch level, restricted pitch range, diplophonia, or inappropriate loudness. When present, these findings are often rated on a severity scale from mild to severe using the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V).[13] Nasopharyngoscopy and/or stroboscopy is then typically done to identify the cause of the dysphonia so that appropriate treatment can be implemented.

## INTRAORAL EVALUATION

Although velopharyngeal function cannot be determined through an intraoral examination, an oral examination has some importance in the evaluation of VPI and abnormal resonance.[2,14] If the patient has a history of cleft lip/palate, the speech pathologist will examine the palate for a fistula. If there is no history of cleft, the examiner will look for evidence of a submucous cleft, including a zona pellucida (thin area); a bifid or dysplastic uvula, and diastasis of the levator muscles, which are apparent as an upside down "V" shape during phonation.[2,14] In some cases, the palatal palpation will reveal a notch in the posterior border of the hard palate. A very thin velum is noteworthy as it can be the cause of hypernasality because more sound will be transmitted through thin tissue. During phonation, the position of the velar dimple and uvula are examined. If the velar dimple is skewed to one side or the uvula points to one side, the muscle function on the opposite side may be inadequate, causing a lateral velopharyngeal gap. This is commonly seen in patients with hemifacial microsomia. If the uvula is consistently deviated to the side of a large tonsil, this indicates that the tonsil is pushing against the posterior faucial pillar and probably extends into the oropharynx.

## INSTRUMENTAL EVALUATION OF VELOPHARYNGEAL FUNCTION

The speech pathologist will usually use instrumental procedures as part of the VPI evaluation. Instrumental procedures can provide valuable additional information to augment the perceptual evaluation results.[2,15–17] There are two basic categories of instrumental procedures for evaluation of velopharyngeal function—those that give indirect yet objective information, and those that give direct yet subjective information.

Indirect instrumental procedures include the use of nasometry and aerodynamic instrumentation. The advantage of these procedures is that they provide objective data regarding the results of velopharyngeal function, such as acoustic output or airflow and air pressure during speech. They are considered indirect measures because they do not allow visualization of the structures. In contrast, direct instrumental procedures include videofluoroscopy and nasopharyngoscopy. The advantage of these procedures is that they allow the examiner to directly visualize the structures of the velopharyngeal valve during speech. However, these procedures require interpretation of the examiner, and therefore, they are subjective.

### Nasometry

Nasometry is a method of measuring the acoustic correlates of resonance, audible nasal emission, and velopharyngeal function through a computer-based instrument (Fig. 88.3).[16,18] The nasometer captures data regarding acoustic energy from both the nasal cavity and the oral cavity during speech in real time. It then calculates the average ratio of nasal over total (nasal plus oral) acoustic energy and converts this to a percentage value called the nasalance score. This score gives the examiner information about the relative percentage of hypernasality in speech. Because nasometry measures both hypernasality and audible nasal emission, there is not a good correlation between velopharyngeal gap size and the nasalance score. However, with the knowledge of the speech characteristics,

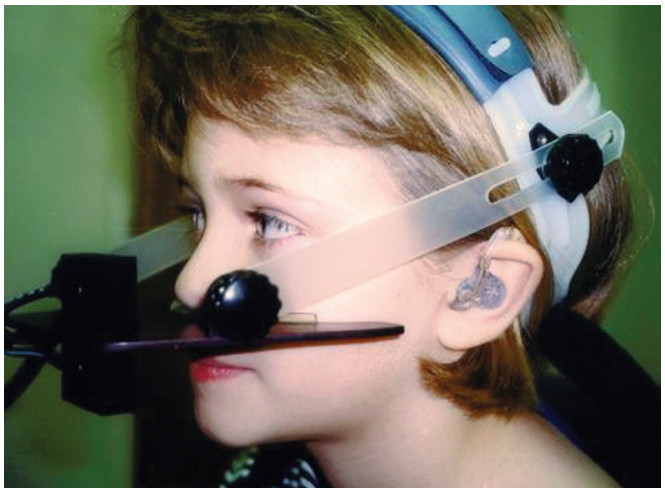


**Fig. 88.3:** This shows the nasometer headset in place. The nasometer collects acoustic data from the oral and nasal cavities during speech. From Kummer.[18] Reprinted with permission.

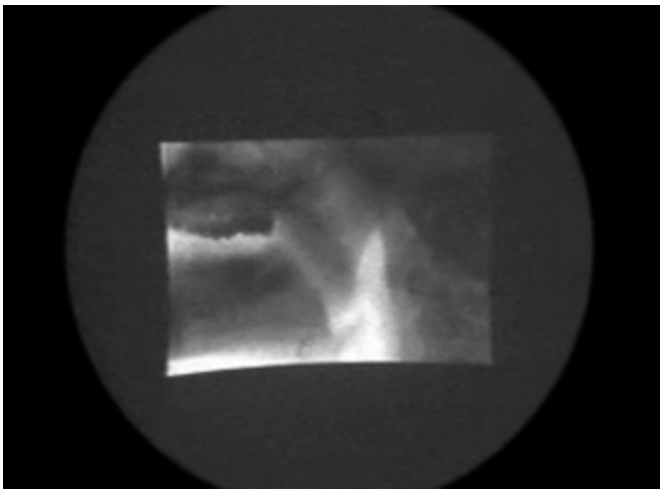


**Fig. 88.4:** This is a lateral view that shows the velum and posterior pharyngeal wall during speech. In this case, the velum is normal in structure, but has very poor movement. As a result, there is a large velopharyngeal gap due to velopharyngeal incompetence. From Kummer.[21] Reprinted with permission.

the speech pathologist can use the nasalance results to confirm clinical impressions, and to do pre- and postsurgical comparisons.

## Speech Aerodynamics

Speech aerodynamics is a procedure to measure the mechanical properties of airflow and air pressure during speech production.[16,19,20] The aerodynamic procedure involves the use of oral and nasal catheters, which are connected to pressure transducers, and a flow tube that is connected to a heated pneumotachograph. The transducers convert the detected air pressure or flow into electrical signals. The pneumotachograph determines the rate of airflow.

Aerodynamic instrumentation can be used by the speech pathologist to provide objective documentation of intraoral air pressure levels and the amount of nasal air emission. With this data, the examiner can calculate an estimate of velopharyngeal orifice size during consonant production. Aerodynamic instrumentation can also provide evidence of airway obstruction through measurements of nasal airway resistance.

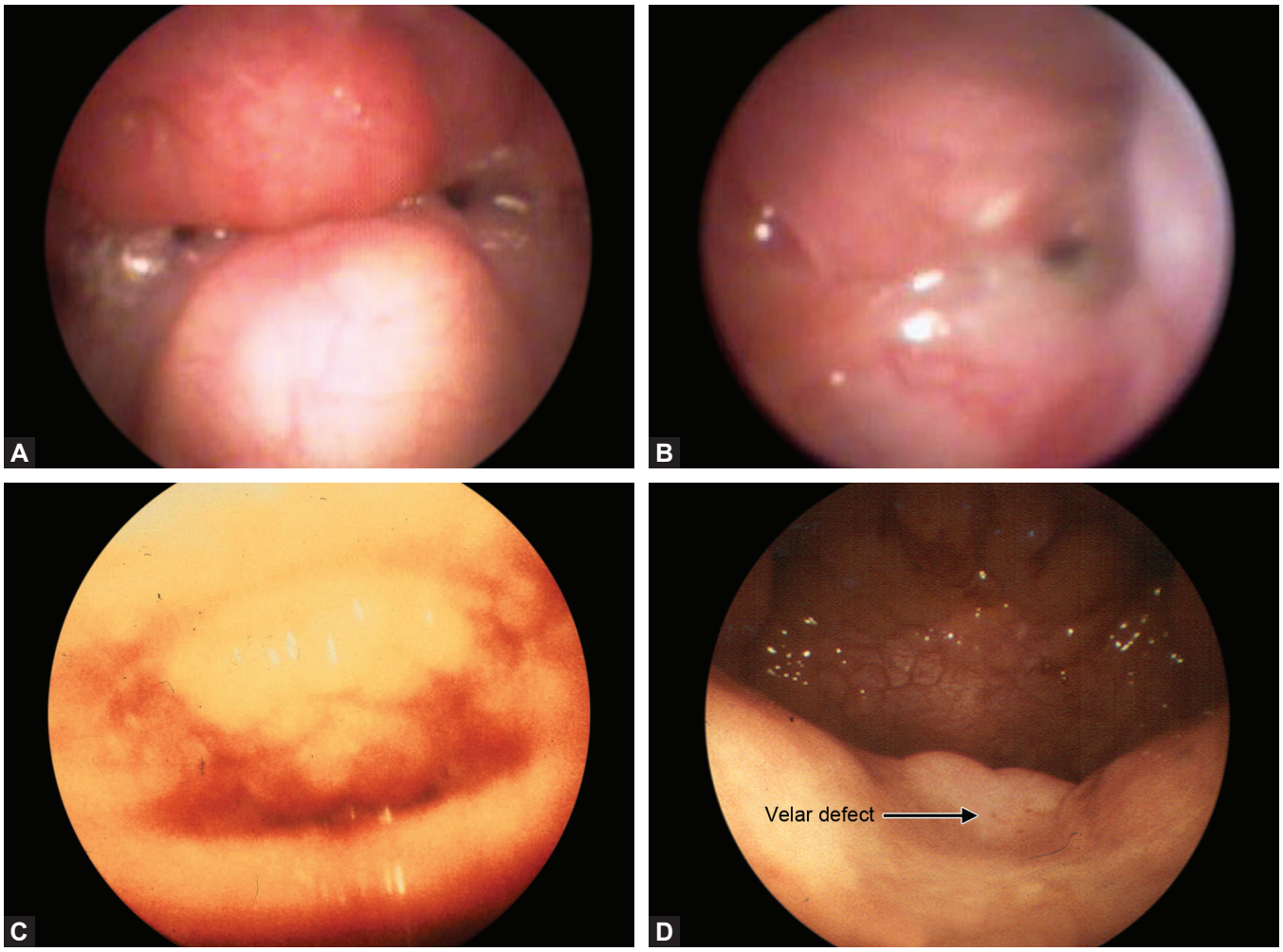
## Videofluoroscopic Speech Study

Once the diagnosis of VPI has been made by the speech pathologist, a *videofluoroscopic speech study* may be done to find the location of the opening for surgical planning.[15,16,21] Because videofluoroscopy involves two-dimensional imaging, a speech study requires several views in order to see all aspects of the velopharyngeal port (Fig. 88.4). The speech pathologist must select the speech sample, based on the results of the perceptual evaluation, and should always be involved in the interpretation of the results, based on knowledge of the speech characteristics and the probable cause.

## Nasopharyngoscopy

Nasopharyngoscopy (also called nasendoscopy or videonasendoscopy) allows direct visualization of the entire velopharyngeal mechanism during speech.[15,16,22] In many centers, nasopharyngoscopy is done in addition to or even instead of videofluoroscopy.[23] This is because nasopharyngoscopy has several advantages over videofluoroscopy. The bird's-eye view of nasopharyngoscopy has been found to have a stronger correlation with VPI severity than videofluoroscopy.[24] Nasopharyngoscopy is superior to videofluoroscopy in finding the location of a velopharyngeal gap and confirming the size of the opening (Fig. 88.5A). Even very small, pinhole sized openings can be seen through nasopharyngoscopy (Fig. 88.5B). The effect of the adenoids (positive or negative) on velopharyngeal function can be directly visualized (Fig. 88.5C). The nasal surface of the velum can be examined for evidence of an occult submucous cleft (Fig. 88.5D).[24] Finally, nasopharyngoscopy is very effective in the assessment of the results of surgery for VPI.

Passing the scope to perform this examination is within the scope of practice for speech pathologists. However, what is most important is that the speech pathologist is




**Figs. 88.5A to D:** (A) Nasopharyngoscopy shows "bowtie closure", with good closure in midline, but lateral gaps. This is important to know for surgical planning; (B) Nasopharyngoscopy shows a small opening, just to the (patient's) left of midline. Again, knowing the location of the opening is very important in order to determine the best surgical procedure for the patient; (C) In this case, nasopharyngoscopy shows a protrusive adenoid pad. This results in velopharyngeal closure in midline against the adenoid, but gaps on either side; (D) Nasopharyngoscopy allows visualization of the nasal surface of the velum. This is particularly helpful in identifying a submucous cleft. In this case, note the significant depression in midline. From Kummer.[22] Reprinted with permission.

at least present during the examination and is part of the interpretation of the results. As with videofluoroscopy, knowledge of the speech sample and speech characteristics is essential in interpretation of the results. This is because a velopharyngeal opening does not necessarily indicate VPI, which requires surgical intervention.

## SUMMARY

In summary, the speech pathologist plays a primary role in evaluation of velopharyngeal function for speech. Through the perceptual evaluation, the speech pathologist can diagnose abnormal resonance and determine the type and therefore, the probable cause (oronasal coupling or vocal tract obstruction). If there is hypernasality, the speech pathologist can determine if it is due to VPI (insufficiency or incompetence), a fistula, a thin velum, or misarticulation of pharyngeal or nasal sounds for oral sounds. If there is VPI, the speech pathologist can predict the approximate size of the velopharyngeal gap, based on the perceptual assessment of hypernasality and nasal emission. Through the use of instrumental procedures, the speech pathologist can obtain objective data relative to the function of the velopharyngeal valve, in order to make pre- and post-treatment comparisons. Through the use of videofluoroscopy and particularly with nasopharyngoscopy, the speech

pathologist can determine the location of the velopharyngeal opening and confirm the cause. Identification of the location and cause can lead to the determination of the best surgical procedure for the patient. If speech therapy is needed, the data from the speech assessment can form the basis of the treatment plan. Perhaps the most important role of the speech pathologist in the VPI evaluation is to make the appropriate diagnosis as to causality of speech characteristics so that patients receive the appropriate type of intervention.

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CHAPTER

# 89

# Noncleft Velopharyngeal Insufficiency

***Noel Jabbour, Steven L Goudy***

Noncleft velopharyngeal insufficiency (VPI) refers to speech that is characterized by hypernasality and nasal air emission without an overt cleft of the palate.

The velopharynx should close completely for all phonemes in the English language with the exception of /m/, /n/, and /ng/, which are nasal sounds.[1,2] Closure of the velopharynx is accomplished by the palatal muscles—the musculus uvulae, tensor veli palatini, and levator veli palatini—pulling the palate superiorly and posteriorly and the superior pharyngeal constrictor muscles narrowing the velopharyngeal port.[1,2] Incomplete closure results in nasal air escape and hypernasality. Secondary articulation errors, facial grimacing, and glottic stops may be present as compensatory mechanisms in patients with velopharyngeal insufficiency, especially if the hypernasality was present prior to the development of articulation.[1,3]

## ETIOLOGY AND PRESENTATION

Incomplete closure of the velopharyngeal port may be present with our without an obvious abnormality in the velum, such as a submucous cleft of the palate, which is characterized by a bifid uvula, zona pellucida, and V-shaped notch in the posterior hard palate. The prevalence of a submucous cleft palate is estimated as 1:1250 to 1:6000.[1] In the absence of an obvious anatomic abnormality, velopharyngeal incompetence may be due to neuromuscular weakness or discoordination or a combination of anatomic and neuromuscular abnormalities.[4] Additionally, VPI may develop or be unmasked following any procedure that changes the dynamics of velopharyngeal closure such as adenoidectomy, uvulo-palatal-pharyngoplasty, or Le-Fort advancement.

Historically, the terms velopharyngeal incompetence and velopharyngeal inadequacy have been used interchangeably with VPI. Some authors have attempted to subclassify the "insufficiency" into etiologic categories where *incompetence* may refer to neuromuscular dysfunction causing incomplete closure of the velopharyngeal port and *inadequacy* may refer to anatomic deficit of tissue causing incomplete closure.[5] However, recently, the term "insufficiency" has been favored, in part due to the negative connotation of the words incompetent and inadequate.

While noncleft VPI largely refers to nasal air escape during speech, there is a small subset of patients who may present with nasal air escape when playing musical instruments that require high oral pressures in order to generate sound, such as brass and woodwind instruments.[6] This "stress VPI" can potentially be career limiting for amateur and professional musicians.[7]

## GENETICS

The most common genetic abnormality in noncleft VPI involves a deletion on the long arm of chromosome 22. This deletion, 22q11.2, produces a classic pattern of varying degrees of VPI, conotruncal abnormalities, medialized carotid arteries, facial dysmorphic features, and behavioral or learning disabilities. The nomenclature for this syndrome can be confusing, as it is interchangeably referred to as velocardiofacial syndrome (VCF) or Shprintzen syndrome, for Robert Shprintzen who first described this phenotypic pattern in 1978.[8] There is also overlap with DiGeorge syndrome, which involves absent or dysfunctional thymus and varying degrees of immunodeficiency. Often both

VCF and DiGeorge are referred to collectively as 22q11 deletion syndrome or 22q11.2 deletion syndrome. The prevalence of 22q11 deletion syndrome is estimated as 1 in 4000; it may be inherited in an autosomal dominant fashion, though it is most often a novel deletion. VPI has also been described in an inherited fashion in families without a submucous cleft palate and with negative genetic testing for 22q11. Thus, it is likely that multiple other genes may be involved in noncleft VPI without a submucous cleft palate.[2] Associations with Turner syndrome, VATER syndrome, and neurofibromatosis have been shown.[9,10] However, it is most critical when non-cleft VPI is identified to offer screening for 22q11, as a positive screen may allow parents to anticipate, to monitor and to seek treatment for potential cognitive and neuropsychiatric disorders associated with VCFS.[11]

Patients with a submucous cleft palate share the same genetic and environmental risk factors as patients with overt cleft palate, as submucous cleft palate represents failure in the final stages of the anterior to posterior fusion of the paired palatal shelves during embryogenesis. Approximately 50% of cleft palate patients are considered to have nonsyndromic genetic causes. Syndromic causes include Van der Woude syndrome – lower lip pits and cleft lip and/or palate (IRF6 gene); Stickler syndrome – flattened facial appearance, eye abnormalities, cleft palate, hearing loss, and joint abnormalities (Col2A1 gene); and VCF, among others.

## IATROGENIC CAUSES

Many children exhibit veloadenoidal closure during speech. With increasing age and decreasing size of the adenoids, there is a gradual transition to velopharyngeal closure.[12] For children with veloadenoidal closure, adenoidectomy may result in VPI, which is most often transient. In patients with an underlying anatomic abnormality or neuromuscular dysfunction, adenoidectomy may unmask or increase a previously existing VPI. The incidence of VPI postadenoidectomy has been estimated to range from 1:1500 to 1:10,000 cases.[13] It is thus crucial during preoperative evaluations for otolaryngologists to recognize hypernasality and the signs of submucous cleft palate. If adenoidectomy is necessary in this setting, an adenoidectomy may be limited to the superior ½ of the adenoids, leaving the inferior ½ of the adenoid pad present to participate in velopharyngeal closure. Careful attention should be given to recognition of medialized carotid arteries.

It should be noted that in some patients with significant tonsillar hypertrophy, velopharyngeal closure may be prevented by a posterior and cephalad extension of the superior tonsillar pillars bilaterally, leaving a central gap during attempted closure. Tonsillectomy alone may resolve this cause of hypernasality. However, tonsillar hypertrophy may also mask a bifid uvula, and careful examination of the palate should be performed to distinguish these two entities and to rule out a submucous cleft palate.[14]

VPI may develop or be unmasked following uvulopalatopharyngoplasty due to shortening of the palate and scar formation limiting palatal elevation.[15] Similarly, orthognathic surgery may be another potential iatrogenic cause of VPI. In patients with severe malocclusion, orthognathic surgery has the potential to improve articulation by improving the maxillary mandibular relationship. However, there is also the potential to cause or unmask VPI, especially in patients with borderline VPI preoperatively.[16]

## EVALUATION OF VPI

Despite advances in diagnostic instrumentation to detect VPI, perceptual observation is still considered the gold standard for evaluation of VPI.[1] Detection of VPI requires careful attention to resonance, articulation, and nasal air emissions during spontaneous and provoked speech.[17] Various tactile and auditory tools and exercises may help the clinician in detecting nasal air emission.[17] Indirect quantitative measures of nasal air emission are available. The most commonly used of these is Nasometry, which measures nasalance, the ratio of nasal resonance to oral resonance. Video nasal endoscopy offers a direct view of the velopharynx from above in order to evaluate closure with phonation and the size and shape of gap if present. Multiple radiographic methods have been described to evaluate VPI, including fluoroscopy and Cine MRI.[18]

## TREATMENT

Speech therapy is the first-line treatment for noncleft VPI to identify and correct articulation errors. For patients who fail to improve substantially with speech therapy, surgical and non-surgical options exist to address structural or functional abnormalities. For patients with submucous

cleft palate, surgery is directed towards redirecting and reapproximating the abnormally oriented muscles of the palate and lengthening the palate. This is accomplished with a double-opposing Z-plasty, as described originally by Furlow.[19] A variety of other procedures have been described for the treatment of VPI in the absence of a submucous cleft or with persistence of VPI following double-opposing Z-plasty. The most common of these involve narrowing the velopharyngeal port with a sphincter pharyngoplasty or creating two smaller ports with a pharyngeal flap. Both sphincter pharyngoplasty and pharyngeal flap have the potential to decrease nasal airflow and as a result increase the risk of sleep apnea. There should be a low threshold for obtaining a sleep study following these procedures for any patients with sings or symptoms of sleep apnea.

In patients with known 22q11 deletions, the speech outcomes of surgical correction of velopharyngeal insufficiency may be inferior to the outcomes of patients without 22q11 syndrome and it may take significantly longer in therapy to attain the same speech results when they are achieved.[9,20,21] This is consistent with the etiology of the VPI as a neuromuscular dysfunction rather than a structural abnormality.

In recent years, there has been increased interest in fillers to augment the posterior pharyngeal wall. Teflon, one of the first fillers to be used, has largely been abandoned; however, a variety of other fillers have been described, including collagen, hyaluronic acid, calcium hydroxyapatite, or autologous fat.[22–25]

Nonsurgical intervention with creation of a velopharyngeal obturator or palatal lift prosthesis may be an option for patients who are not candidates for surgery, have large palatal defects, or have failed multiple surgeries.[26] Obturator molding may also be employed as a form of velopharyngeal therapy, whereby incremental improvement in velopharyngeal closure is encouraged by progressive decreases in the size of the obturator.[26,27]

## CONCLUSION

Otolaryngologist should be familiar with the signs and symptoms of noncleft VPI. The attentive otolaryngologist may play a key role in identification of VPI in patients and prevention of iatrogenic causes of VPI. Surgical treatment of noncleft VPI is a growing niche within otolaryngology.

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CHAPTER

# 90 Nonsurgical Management of VPI and Resonance Disorders

*Cheryl J Hersh, Marie J Rozeboom*

## INTRODUCTION

The role of the speech language pathologist (SLP) in nonsurgical management of velopharyngeal insufficiency (VPI) is multifaceted and continually changing across the developmental trajectory. Once VPI has been identified via comprehensive instrumental evaluation by the otolaryngologist (ORL) and speech pathology team, recommendations and treatment planning may include nonsurgical management options. Nonsurgical management in the form of speech and resonance intervention is a key component of treatment planning and is used for a variety of functions across the developmental trajectory. This chapter discusses the different functions of speech and resonance therapy in relation to development as well as in the setting of pre- and postsurgical management. The importance of exclusively providing nonsurgical management to children who present with VPI in the setting of oral motor planning difficulties and/or phoneme-specific nasal air emissions (PSNAEs) is also discussed.

## DEVELOPMENTAL TRAJECTORY OF NONSURGICAL MANAGEMENT

The role of the SLP is continuously changing across the developmental trajectory as the child matures and his or her therapeutic needs evolve. The framework below as seen in Figure 90.1 was developed to describe the focus of nonsurgical management at several points along the developmental progression. In the early developmental stages, the emphasis of treatment is stimulation and acquisition of early speech and language skills. As the child transitions to the preschool years, the emphasis shifts to articulation placement, exploration of oral versus nasal sound production, and remediation of compensatory speech errors if appropriate. Secondary surgical intervention is often considered during the late preschool years and early school age years to establish normalized velopharyngeal (VP) function. It is not uncommon for children to fluctuate between phases of therapeutic intervention during this time as remediation of compensatory errors is targeted in the pre- and postsurgical time frames. Once growth has slowed in the adolescent years, maxillary advancement, dental and orthodontic intervention may be indicated. Reinitiation of therapeutic intervention once the facial structure has been normalized if necessary.

It is important to note that children may require differing amounts of time in each of these progressions and that they may skip or repeat phases as clinically indicated. It is certainly important to always consider individual needs and variations as a team when determining the progression of nonsurgical management for each child.

### Facilitation of Early Speech and Language Skills

One of the earliest purposes of nonsurgical management includes initiation of speech language treatment as early as 9 months of age to promote early speech and language skills. Research suggests children with a history of cleft palate are at risk for delayed expressive language development.[1] Lengthy or repeated hospitalizations, psychosocial issues, frequent ear infections, and cognitive deficits are all potential factors contributing to risk of language delay.[1,2]

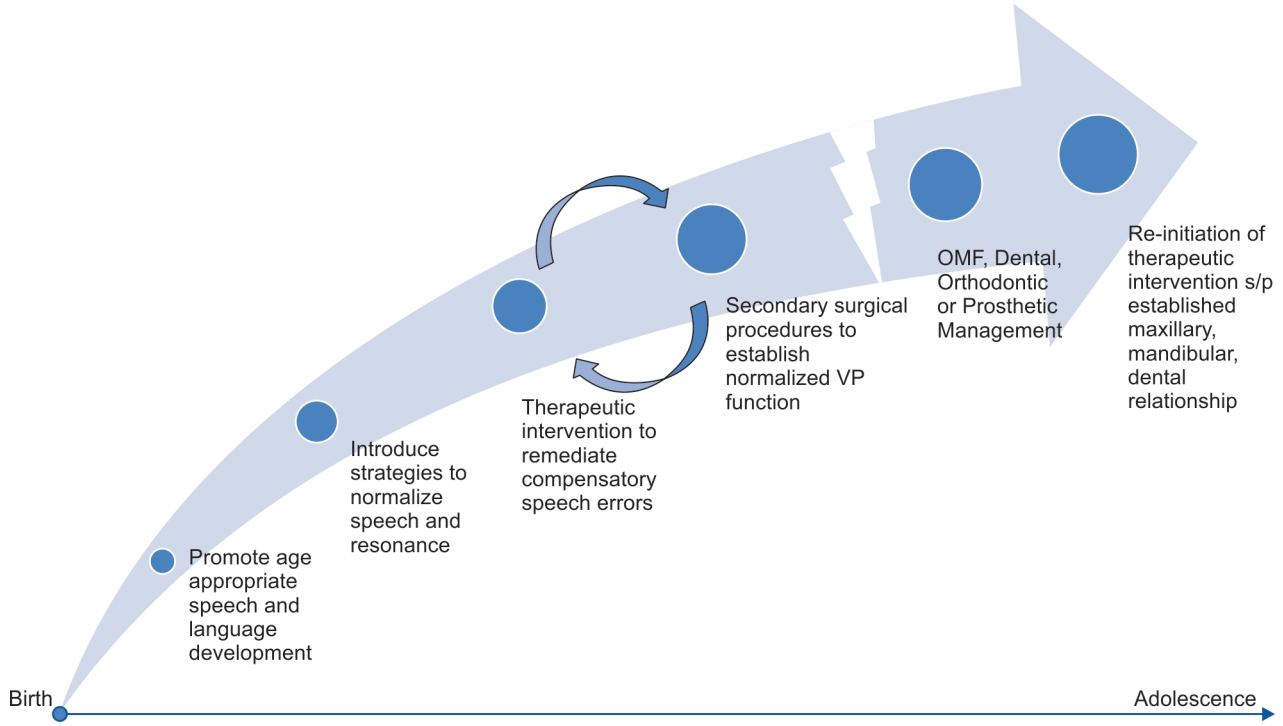


**Fig. 90.1:** Developmental progression of nonsurgical management.

It is important to note that children with a syndromic diagnosis are at a higher risk of language delay than children with an isolated cleft lip and/or palate. The need for speech and language services and secondary surgery increases as the severity of the cleft increases.[3] Research also suggests children with cleft palate and speech deficits are at higher risk for delays in development of early literacy skills, particularly children with persistent speech difficulties.[2]

Speech language intervention for children under three years of age focuses on language stimulation and quantity of language acquired.[4] Common goals of therapy include expansion of vocabulary, use of language for a variety of functions, and development of early speech sounds including /p,b,w,h m,n/. Early intervention is essential in assuring children with cleft palate have a functional means of communication to limit frustration and avoid acquisition of compensatory speech patterns in the face of anatomical limitations.[5,6] Speech language therapy is more effective when parents are involved and trained to carry-over therapeutic strategies in the home setting.[7] Although resonance balance is not a focus of early speech language intervention, awareness of oral and nasal airflow may be introduced by contrasting early oral sounds /p,b, w,h/ with nasal speech sounds /m,n/ through play based therapy approaches.

The experienced SLP establishes a different focus when a child is over 3 years of age. By this age, the preschool age child may have a variety of phonemes in his or her repertoire, and expressive communication consists primarily of sentences and conversational speech. Goals of speech and resonance therapy at this age include exploration of oral versus nasal sound production, modification of articulatory placement for compensatory speech errors, and stimulability testing for phonemes not yet developmentally acquired.[4,8,9] Multisensory experiences facilitate progress when the child is able to explore and define resonance with visual, tactile, auditory and multimedia feedback to differentiate between oral and nasal sound production. Initial goals include the identification of speech sound elements, and subsequently, the production of these speech sounds as a focus of therapeutic intervention. The SLP emphasizes articulatory placement (for phonemes not yet acquired and compensatory articulations), while awaiting decisions regarding a secondary surgery to restore adequate velopharyngeal function. Often, compensatory articulations have developed whereby the child creates the point of contact inferior to the velopharyngeal port (e.g. at the level of the vocal folds or between the base of tongue and posterior pharyngeal wall). Use of discrimination, biofeedback for airflow (described in subsequent sections of this chapter), facilitation of phonemes and

phoneme contrasts, nose-pinch techniques, increased volume, attention to oral articulators, and play based sound stimulation are documented therapeutic strategies for this developmental phase.[3,4,6]

## Remediation of Compensatory Speech Errors

An additional function of nonsurgical management across the developmental trajectory includes remediation of compensatory speech errors. A thorough evaluation completed by the SLP provides information regarding a child's compensatory speech sound productions, if any, prior to shifting the focus of treatment to remediation efforts. The SLP then works with the child to eliminate these nonfunctional, nonprimary language based speech sounds, as the child strives to obtain closure along the oral, pharyngeal, and nasal passages to communicate as effectively as possible.

Diagnostic therapeutic approaches are used to assess whether atypical resonance balance and/or deviant speech patterns are the result of VPI or velopharyngeal mislearning.[8] Diagnostic therapy techniques may include use of nasal occlusion during speech efforts (i.e. cul-de-sac test[10]), lowering the back of the tongue to decrease perception of hypernasality, and modification of articulatory placement to identify any changes in hypernasality or nasal air emissions (e.g. use of a prolonged /t/ sound in order to achieve /s/) in order to promote accurate articulatory placement and oral airflow.[4–6] If developmental errors or compensatory speech errors are noted, formal speech and resonance therapy may be recommended to promote accurate placement and oral airflow prior to pursuing secondary surgery.

There are two differing viewpoints in the field of speech language pathology when it comes to recommending speech and resonance treatment in the face of compensatory speech errors. Kummer[4] recommends pursuing secondary surgery as soon as VPI has been identified as it is faster, more cost effective, and less frustrating when the child no longer presents with anatomical limitations. She also argues the goal of surgery in preschool years is to take advantage of brain development to maximize speech language progress prior to entrance into the school setting. Other professionals in the field recommend remediation of compensatory errors prior to pursuing secondary surgery as it provides more reliable information regarding velopharyngeal closure. Generally, there is no closure of the velopharyngeal port when a child is engaging in compensatory speech errors; therefore, surgical planning may be based on faulty information.[11] When considering whether or not to recommend speech and resonance therapy for remediation of compensatory errors prior to surgical intervention, the evaluating SLP should consider the patient's cognitive status and ability to carryout therapeutic techniques. The family's access to a clinician trained in resonance disorders as well as their ability to promote generalization in the home environment should also be considered.[11]

It is also important for the SLP to take into consideration normal developmental acquisition of speech sounds. A child with or without cleft palate who presents with VPI may have many speech sound substitutions. It is critical to allow normal developmental patterns to evolve when the speech substitutions are within normal range for the child's age. In contrast, if the child is not producing typical substitutions, those atypical patterns may be appropriate for remediation. On occasion, when overall intelligibility is reduced, a child may be able to produce an accurate speech sound that may be beyond developmental expectations (e.g. /th/ in a 4 year old). The SLP may want to test stimulability for these sounds if this will improve overall intelligibility while waiting for oral/nasal resonance to be re-established. Figure 90.2 depicts the order of speech-sound acquisition in continuous speech as a reference point.

If surgical intervention is deferred to a later age due to airway concerns, medical stability, or other confounding variables, treatment strategies may work on establishing

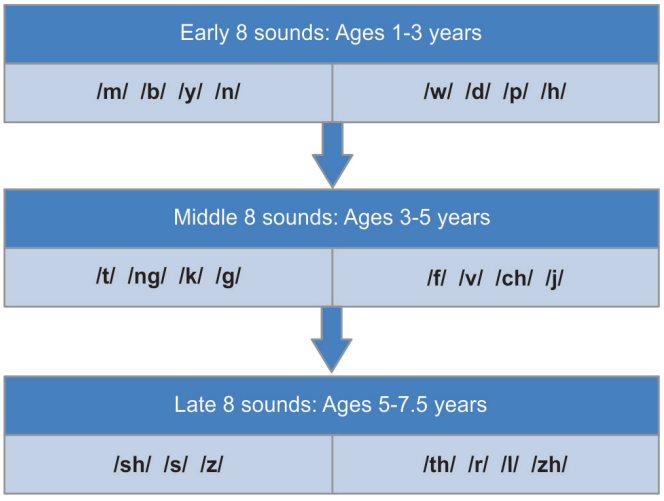


**Fig. 90.2:** Order of speech-sound acquisition in a continuous speech sample. Adapted from Shriberg.[28]

accurate placement for each speech sound. This promotes opportunities for adequate communication while waiting for the child's anatomy to mature. Once oral anatomy is normalized or corrected, speech and resonance treatment can be reinitiated.

### *Special Populations*

There are certain populations who are not appropriate for surgical intervention and therefore benefit exclusively from nonsurgical management plans. These populations include children with VPI characteristics secondary to oral motor planning difficulties and children who present with velopharyngeal mislearning, otherwise known as PSNAE.

In the setting of hypotonia, dysarthria and/or apraxia of speech, children often present with oral motor planning difficulties and speech imprecision. These characteristics may masquerade as VPI.[8,12] Apraxia of speech is a motor speech disorder that is characterized by disrupted speech motor control in the absence of muscle weakness or paralysis. The child's brain has difficulty coordinating and sequencing muscle movements to produce desired speech output. It is common for this population to present with inconsistent error patterns, vowel distortions, difficulty with production of multisyllabic words, and disturbances in prosody and speech intonation.[13,14] They may also present with characteristics of VPI including hypernasality and nasal air emissions secondary to difficulties coordinating the timing and closure of the velopharyngeal mechanism in the setting of the disrupted speech motor control.[8] If hypernasality, nasal air emissions, and/or compensatory errors are inconsistent or responsive to diagnostic treatment techniques (particularly in the absence of a cleft palate), the role of oral motor planning difficulties and speech imprecision should be considered as a contributing factor to VPI.

It is important to identify whether VPI is the result of an anatomical defect or oral motor planning difficulties as these cases should be managed nonsurgically with speech and resonance treatment. It is the experience of our center, that as a child's speech precision and oral motor planning abilities improve, the characteristics of VPI often improve as well. It should be noted that children with syndromic diagnoses such as 22q11 may present with VPI that is related to both structural limitations as well as oral motor planning difficulties. In these cases, collaboration between the SLP and the ORL is essential in identifying the primary source of VPI and the limitations as well as the potential of the VP mechanism.

An additional population that should be managed nonsurgically is children who present with velopharyngeal mislearning, or PSNAE. Phoneme-specific VPI is an abnormal articulation pattern that results in opening of the velopharyngeal port during production of nonnasal speech sounds. This results in nasal air emission with production of only certain phonemes (most frequently fricative sounds /s, z/) in the absence of velopharyngeal dysfunction. It is common for the child to continue to direct airflow into the nasal cavity during production of these sounds even when the nares are occluded, thereby suggesting a functional VPI. Children who present with this pattern are not surgical candidates and generally are successful remediating errors with speech and resonance treatment and techniques to achieve speech sound production via alternative methods (e.g. prolonging a /t/ sound to achieve /s/).[8,15]

Identification of surgical versus nonsurgical candidates is essential in determining which patients will benefit from secondary surgical management. 90.1 and 90.2 depict examples of oral motor planning issues resulting in VPI, whereas 90.3 depicts an example of PSNAE. These patient examples are not ideal surgical candidates, as the primary factors affecting intelligibility are not necessarily reduced VP closure resulting from impaired anatomy, but rather impaired coordination, apraxic patterns, or VP mislearning including sound-specific nasal air emission. Figure 91.3 provides a breakdown of appropriate candidates for surgical versus therapeutic intervention.

| Therapy candidates: Abnormal articulation | Surgery candidates: Abnormal structure |
|---|---|
| Developmental speech errors | Speech deficits related to incomplete closure of the velopharyngeal mechanism (e.g. short palate, stiff palate) |
| Inconsistent speech and/or resonance production due to motor planning difficulties (e.g. apraxia, hypotonia) | Deviant speech patterns (e.g. glottal stops) not amenable to diagnostic therapy techniques |
| Persistent VPI immediately following surgical correction | |
| Phoneme specific nasal air emissions | |
| Improvement in speech or resonance with diagnostic therapy techniques | |

**Fig. 90.3:** Appropriate candidates for therapeutic vs. surgical intervention.

## Maximizing the Benefits of Surgical Intervention

An additional function of nonsurgical management includes initiation of speech and resonance therapy to maximize the benefits of surgical intervention. It is critical for the medical team (including the ORL and SLP) as well the family to have a clear understanding of the expectations for speech changes following surgical intervention. Most frequently, a period of speech and resonance therapy is required following surgery to aide in the development of normal speech patterns. The goal of treatment is to attain normal speech, not just improved speech.[4]

Following improvement and/or normalization of the child's structure and velopharyngeal valving function, the SLP targets resolution of compensatory articulation patterns as the patient now receives feedback following each speech production attempt given restored VP function.[15] In addition, the speech pathologist may include developmentally appropriate speech sound production errors as a component of the therapeutic intervention. Two mechanisms are required for a child to achieve normal speech: motor learning and motor memory. Motor learning is dependent on following directions as well as trial and error and feedback (visual, verbal, and tactile). The result of adequate motor learning includes refined speech production, which is the goal of speech therapy with the SLP. The second mechanism required is motor memory. To establish carry over and ultimately motor memory, the child, family, and/or school is required to participate in home practice. Motor memory develops automaticity of the movement, which may ultimately translate to generalization in daily conversation.[15]

The ORL and speech language pathology team continue to work closely throughout this process. If obligatory errors persist following the surgical procedure, the child may be a candidate for a revision procedure to attempt to normalize the VP mechanism.

## Modifications Following Oral Maxillofacial, Dental and Orthodontic Intervention in Adolescence

An additional function of nonsurgical management, which is less frequent, includes direct speech and/or resonance therapy following oral maxillofacial, dental, and/or orthodontic modifications in adolescence. Midface hypoplasia, dental anomalies, and malocclusion are structural issues that may impact speech production and intelligibility. The SLP works closely with the oral maxillofacial team, and the dental and orthodontic team, to determine appropriate periods of time along the developmental trajectory where speech and resonance treatment is indicated. Timing of surgical, dental, and orthodontic intervention is child focused and typically appropriate once growth has slowed during the early adolescent years.[16]

The SLP determines if the child/adolescent's reduced speech intelligibility is due to obligatory errors or compensatory errors.[4] Obligatory errors are the result of anatomy or dentition and do not yield positive results in a speech therapy session. For example, an open bite may result in tongue protrusion upon production of the /s/ phoneme given the lack of physical boundaries. In contrast, a class III malocclusion, or under bite, may result in tongue protrusion upon alveolar sound production (e.g. /t, d, s, n/). In these cases, it may be beneficial to discontinue speech therapy when speech sound errors are the direct result of an anatomical deviation. Speech therapy should be suspended until the child's oral anatomy is normalized, to minimize frustration, cost, and unachievable speech goals. Once the occlusion pattern and maxillary structure are managed surgically to provide the child/adolescent with optimal structural relationships, speech therapy can be reinitiated to maximize surgical outcomes.

Children with cleft palate and/or craniofacial anomalies may be candidates for maxillary advancement via distraction osteogenesis or a Le Fort 1 procedure.[17] Risk factors associated with exacerbated VPI following midface advancement include only a short soft palate and large pharyngeal depth.[18] Although it is reasonable to expect that pre-surgical mild or intermittent VPI would be a risk factor for exacerbated VPI following midface advancement,[19] review of the current literature suggests contradicting and inconclusive evidence.[17,20] Inconclusive evidence is reported for a correlation of exacerbated VPI to factors including type of procedure (Le Fort 1 osteotomy vs. distraction osteogenesis), and/or distance of maxillary advancement (>10 mm).[17,18]

Articulation and overall speech intelligibility following maxillary advancement and normalized dental occlusion is also inconclusive in published research.[19,21]

Given the contradictions in the literature, the involvement of the SLP is critical to determine presurgical resonance and articulation patterns. In addition, the SLP may provide appropriate parent counseling to shape post-surgical expectations. Diagnostic therapy is beneficial to determine the extent of stimulability for both speech

sound production and for adjustments in resonance. Diagnostic speech therapy following maxillary advancement will also help to determine if resonance issues are obligatory, and therefore necessitate a secondary surgery, or if they are compensatory in nature and may be responsive to speech therapy.

## Modifications Following Prosthetic Treatment

There may be times when surgical intervention as a management strategy for VPI may be contraindicated. In these cases, prosthetic treatment including palatal lift appliances, palatal obturators and speech bulb obturators may be considered. These prostheses are individually designed appliances that are intended to promote improved velopharyngeal function, palatal anatomy, and speech production.[4] Palatal obturator prostheses restore the congenital or acquired defects of the soft palate and promote improved closure of the palatopharyngeal sphincter.[22] Goals of prosthetic treatment include both improvement of oral nasal resonance and reduction of nasopharyngeal regurgitation with oral intake.

Given advances in surgical procedures and improvements in understanding of craniofacial growth, pediatric outcomes have improved. Therefore, prosthetics are less commonly employed in the pediatric population.[23] Case reports from India, Turkey, and Europe[22,24] indicate successful placement of prostheses; however, in the United States, this is more infrequently used, only intermittently tolerated, and only occasionally covered by insurance management options. Young pediatric patients in particular tolerate the appliance with a low rate of success and/or interest. Often, it is the older child or the adolescent for whom this is a consideration. The literature refers to case studies of adolescents who may tolerate the device as a preference over nasoregurgitation of foods or liquids and or compromised speech clarity. The older child and young adolescent may be highly motivated to use the obturator, given social embarrassment with nasopharyngeal reflux of foods or liquids and improved communicative success with peers.

Similar to remediation to maximize the outcomes of a secondary surgical procedure, the SLP's role following prosthetic placement is to facilitate improved and normal speech production. Speech language therapy targeting compensatory patterns or mislearned articulation can be reinitiated following the placement and tolerance of the prosthetic devise.

## MAXIMIZING SUCCESS IN THE THERAPEUTIC SETTING

The use of biofeedback in speech and resonance therapy is highly beneficial when the child has the capability to achieve complete velopharyngeal closure.[4] *Visual* feedback methods include use of Nasometry and/or See-Scape device, while *auditory* feedback methods include use of a simple straw or listening tube.[5,6,25] Each method provides a child feedback regarding changes in hypernasality and/or resonance while reinforcing correct production. Biofeedback is particularly effective when a child is stimulable, but not consistent, in achieving accurate productions with diagnostic therapy techniques.

In contrast, nonspeech oral motor exercises (NSOME), primarily "blowing and sucking" exercises, have been discredited in the literature as a treatment strategy. Although "blowing and sucking" exercises[26] were once documented to promote "velopharyngeal strengthening", current literature suggests that they should be discontinued as a treatment strategy given lack of data supporting their benefit. Lof and Ruscello (in press) highlight four reasons NSOME such as blowing are not an appropriate strategy to promote velopharyngeal function. First, in respect to relevance, NSOME are not akin to the finely coordinated muscle activation and coordination required for speech production. Second, blowing tasks lack specificity. Nonspeech production results in different neurological and muscle activations than speech production. Muscle strengthening relies on the combination of multiple repetitions with appropriate resistance that cannot reliably be generated and/or extrapolated to speech production with blowing actions. Finally, oral awareness and feedback cannot be achieved via blowing if the child's anatomy and structure does not allow for adequate VP activation and closure. In addition, velopharyngeal closure patterns viewed via radiological imaging suggest velopharyngeal closure for speech activation is different than for nonspeech activation.[9,27]

## CONCLUSION

The SLP plays an essential role in managing the care of children with VPI. Nonsurgical management in the form of speech and resonance therapy is a key component of treatment planning and is used for a variety of functions across the developmental trajectory. Initially, speech language therapy is used to promote the development of age appropriate speech and language skills, as this population

is at risk for delays in expressive language. As the child matures and acquires a larger speech sound repertoire, therapy may be used to remediate compensatory speech errors the child has acquired in the face of anatomical limitations of the velopharyngeal mechanism. Nonsurgical management may also be used to maximize the benefits of surgical intervention (e.g. following placement of pharyngeal flap) or to assist with speech modifications following placement of prosthetic devices or intervention by oral maxillofacial surgery, orthodontics, or dentistry. Nonsurgical management is generally pursued for children who present with velopharyngeal mislearning and/or oral motor planning issues resulting in VPI.

The SLP and ORL work closely together throughout the developmental progression to determine whether surgical or nonsurgical management is indicated at varying time points. It is essential for the medical team (including the ORL and SLP) as well as the family to have clear expectations of speech outcomes following surgical intervention. Most frequently, a period of speech therapy is required following secondary surgery to aide in the development of normal speech patterns. The goal of treatment is to obtain normal speech, not just improved speech.[4] Biofeedback methods are used as therapeutic tools to provide feedback regarding changes in hypernasality and/or resonance while reinforcing correct speech production. In contrast, NSOME have been discredited in the literature as a treatment strategy. A paucity in the development of innovative technology and novel therapeutic resonance techniques documented in the literature remains an area in need of additional research.

## VIDEO LEGENDS

**Video 90.1:** Example of oral motor planning issues, apraxic patterns resulting in VPI.

**Video 90.2:** Example of oral motor planning issues, apraxic patterns resulting in VPI.

**Video 90.3:** Video of phoneme specific nasal air emission (PSNAE).

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CHAPTER

# 91 The Surgical Management of Velopharyngeal Insufficiency

***Ryan L Sload, Matthew T Brigger***

## INTRODUCTION

The surgical management of velopharyngeal insufficiency (VPI) relies on a functional understanding of the complex interactions required to effectively seal the nasopharynx in speech production. The ability to maintain this seal allows control of nasal resonance and maintains adequate pressure to deliver orally directed speech sounds. Failure to maintain oronasal separation results in poor speech intelligibility, particularly during connected speech. The lack of intelligibility of spoken speech has well-known profound effects on childhood development. Surgical approaches designed to improve childhood speech intelligibility are a cornerstone of the multidisciplinary care that such children require.

The velopharyngeal (VP) complex is a functional port between the oropharynx and the nasopharynx. The complex is anatomically limited by the soft palate as well as the lateral and posterior pharyngeal walls resulting in an essential role in deglutition, nasal breathing, and speech.[1] Velopharyngeal insufficiency is the inability to anatomically close the VP port during speech. This ineffective seal results in the leakage of air into the nasal cavity causing hypernasal resonance and nasal emissions (rhinolalia). The sphincteric interaction of the palate (velum) within the pharynx is critical to the production of intelligible speech.

In general terms, the VP port is a sphincter that regulates air flow through the nasopharynx. The degree of regulation manifests in the production (or lack thereof) of nasal resonance. Velopharyngeal insufficiency is most frequently seen as a congenital condition, most commonly associated with the cleft palate. Other causes include neuromuscular disorders, tonsillar hypertrophy, and iatrogenic causes from aggressive adenoidectomy.[1-4]

The VP sphincter is composed of six paired muscles intimately related to the soft palate that act in a concerted fashion to produce VP closure. These muscles include the levator veli palatini, tensor veli palatini, musculus uvulae, superior constrictor, palatopharyngeus, and palatoglossus muscles.[5] Motor control is primarily mediated through the branches of cranial nerve X except for the tensor veli palatini that is innervated by a motor branch of cranial nerve V. The paired levator veli palatini interdigitate in the midline to form a sling from its origin on the petrous portion of the temporal bone and medial lamina of the eustachian tube and provide the bulk of musculature for port closure. The tensor veli palatini serves to tense and stabilize the soft palate along with opening and closing the eustachian tube. The musculus uvulae are a paired muscle that arises from the tendinous palatal aponeurosis and function to shorten and add bulk for VP closure. The superior pharyngeal constrictor serves to provide lateral wall motion of the nasopharynx to close the VP port.[6] The superior pharyngeal constrictor produces anterior and medial displacement with contraction, allowing contact with the aforementioned muscles. Within the area of the VP isthmus, 20% of individuals may show development of a discrete transverse muscular ridge during superior constrictor contraction known as the Passavant ridge.[5]

## ETIOLOGY OF VPI

With regard to children, the cause of VPI is typically anatomic, iatrogenic, or neuromuscular. Nomenclature surrounding VP disorders is confusing, but intended to reflect the underlying pathological mechanism. Traditionally, the term VPI refers to a neurologically intact VP that is structurally or anatomically deficient in respect to position, size, or tissue volume. Examples of VPI include cleft palate, aggressive adenoidectomy, tonsillar hypertrophy, or short palate, all of which may or may not be a result of congenital syndrome.[5] VPI is a common characteristic of many pediatric syndromes whether it is a structural deficiency or neuromuscular hypotonia.

Cleft palate is the most common cause of VPI. After surgical repair of the cleft, VPI persists in 20% of patients, often due to palatal scarring and stiffness; short but functionally intact reconstructed soft palate; or adequately sized but nonfunctional palate.[5] A nonfunctional soft palate is often due to levator veli palatini musculature disorientation or palatal fistula complication. Long-term postpalatoplasty VPI is often attributed to the decreased stretch factor of the repaired soft palate tissue in the setting of age-related involution of adenoid tissue. This stretch phenomenon occurs in 57% of children who receive palatoplasty.[5]

Submucosal cleft palate is a rare etiology of VPI with an estimated prevalence of 1:1,250 to 1:6,000.[7] The classic findings indicative of submucosal cleft include a bifid uvula, with the absence of the posterior nasal spine, and the presence of a faint blue zona pellucida on the soft palate representing a separation of the levator veli palatini at the midline. This triad is present in 25–93% of children with submucosal cleft.[8] It is estimated that 17–55% of patients with VPI in the absence of an overt cleft palate have submucosal clefts and often present with chronic eustachian tube dysfunction.[8] Assessment for a submucosal cleft palate is often difficult, but essential prior to adenoidectomy as postadenoidectomy VPI is thought to commonly occur due to an occult submucosal cleft.

Postadenoidectomy VPI is an uncommon complication reported to occur in 1 in 1,500 to 1 in 10,000 adenoidectomies.[9] Large adenoids can compensate for a short or poorly mobile palate. After surgery, veloadenoidal closure is suddenly absent, thus causing VPI. Although more commonly seen in children with submucous cleft palates, this complication has been reported in patients without evidence of clefts. Despite the often transient nature, post-adenoidectomy VPI may require surgical management.

## VELOPHARYNGEAL CLOSURE PATTERNS

Velopharyngeal port closure is the summation of a complex coordination of multiple muscles in the velopharynx. The resultant motion is one in which the palate elevates posteriorly and contacts the pharyngeal wall circumferentially. On lateral view, the palate appears to flex creating a bulge of the uvula maximizing contact with the posterior pharyngeal wall.[4] Closure patterns allow preoperative classification of muscle function in relation to deficient VP closure. The pattern of VP closure depends on the degree of opposition of the velum, lateral pharyngeal wall, and posterior pharyngeal wall to form a sphincter. While closure patterns vary among patients, individuals will tend to have a constant closure pattern across varied consonant utterances.[10] In 1973, Skolnick introduced the use of videofluoroscopy to delineate four patterns of VP closure as described in previous chapters.[11] Pragmatically speaking, for many surgeons, selection of procedures is primarily dependent on the degree of lateral pharyngeal wall motion.

## PREOPERATIVE CONSIDERATIONS

Preoperative evaluation by both an otolaryngologist and a speech pathologist is requisite in the diagnosis and treatment of VPI. History and physical examination are essential to determine comorbid syndromes, cleft palate, and associated otologic or oropharyngeal pathology. The speech pathologist is an integral part of the team as perceptual speech assessment remains the gold standard for diagnosis of VPI. Further, speech therapy is useful to address compensatory misarticulations.[12] Direct assessment of the VP port may be achieved by either nasendoscopy or multiview videofluoroscopy (MVF). Whether used alone or in conjunction, nasendoscopy and MVF are critical to help determine the most appropriate surgical intervention.[12]

With velocardiofacial syndrome (VCFS) being a common diagnosis in patients requiring surgical correction of VPI, specific anatomic anomalies associated with this syndrome deserve mention. Anomalies of the internal carotid arteries in VCFS were first recognized in 1987

by Mackenzie.[13] He discovered the anomaly after observing prominent pulsations in the posterior pharyngeal wall, which were later confirmed by angiography, revealing medialization of the internal carotid arteries. The preoperative management of these patients prior to pharyngeal flap surgery has been controversial regarding the need for angiography.[14,15] In a series of patients by Sherard, 20% of patients with VCFS requiring pharyngeal flap surgery had carotid arteries in the donor site dissection and 100% had medialization of the internal carotid arteries to some degree.[16] Of these, 65% had pulsations visible on nasopharyngoscopy. It was found that observations of pulsations did not predict the medial deviation of the internal carotid arties, and that medial deviated arteries did not always result in visible pulsations.[17] The overall consensus recommends internal carotid artery imaging prior to pharyngeal flap surgery in patients with VCFS, due to the difficulty in predicting the location with endoscopy and the potential morbidity of carotid injury.[15-17] Modalities include MRI/MRA versus contrast enhanced CT.

Obstructive sleep apnea (OSA) is a common condition found in children with craniofacial abnormalities, notably cleft palate. It may result in daytime somnolence, feeding difficulties, behavioral and cognitive defects, failure to thrive, hypotonia, pulmonary hypertension, and cor Pulmonale in severe cases.[18] Further, corrective surgery for VPI, notably pharyngeal flap, and more recently sphincter pharyngoplasty have been associated with new-onset or worsening OSA postoperatively.[18-20] The OSA in this patient population is due to increased resistance in the upper airway in an attempt to improve hypernasal speech. Poiseuille's law illustrates this phenomenon showing that resistance is inversely proportional to the fourth power of the radius. Particularly in the relaxed state, the resultant narrowing of the nasopharynx after sphincter or posterior flap pharyngoplasty can greatly reduce the radius, thus causing OSA. The concern for OSA is greatest in the immediate postoperative period with rates of OSA quoted around 90% within days after surgery.[21] Resolution of OSA to preprocedure apnea–hypopnea indices, however, is the norm by 3 months postoperation. Larger studies have demonstrated an incidence of OSA after pharyngeal flap surgery from 2% to 10%[22-24] and 22% in a smaller series after sphincter pharyngoplasty.[18] Clinical screening for OSA in this patient population is imperative. Polysomnography should be considered preoperatively in patients with presumed OSA and surgery tailored to decrease likelihood of worsening obstruction. Newer staged approaches by performing tonsillectomy and adenoidectomy weeks prior to pharyngeal flap surgery—with short, high-based flaps with vertical advancement for closure of the donor site—have shown promise in reducing incidence of OSA.[19]

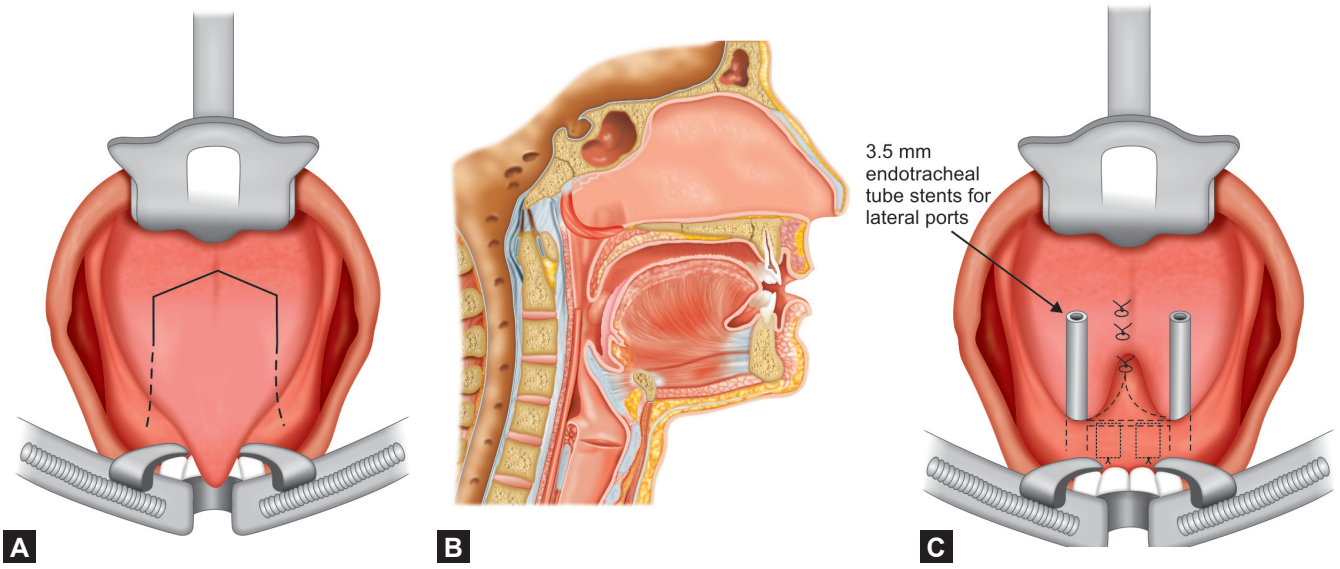
## SURGICAL PROCEDURES

Surgery is the foundation of effective treatment of patients with anatomic defects and, when used appropriately, has been shown to result in resolution of VPI in 62 to 98% of cases.[10,19,25-32] Selection of a surgical procedure relies largely on the anatomical deficit, comorbid conditions, and the surgeon's experience.

The goal of all approaches to surgically manage VPI is to decrease the degree of nasal air escape during the production of oral phonemes. Several strategies have been employed to this end, including functionally obturating the velopharynx in the midline, narrowing the velopharynx with or without a dynamic component, augmenting the posterior pharyngeal wall, or lengthening the palate. Each strategy employs different surgical techniques and procedure selection is based on the accurate diagnosis of the deficiency and the surgeon's experience.

### Posterior Pharyngeal Flap

Efforts to lessen the nasal emission of VPI were first described by Passavant in 1865 when he reported adhesion of the soft palate to the posterior pharyngeal wall.[33] This was subsequently followed in 1875 when Schoenborn described the inferiorly based posterior pharyngeal flap, followed by his introduction of a superior based flap 10 years later.[34] Hogan is accredited with describing the contemporary pharyngeal flap surgery, which is used as the basis of more modern modifications.[35] He describes a superiorly based posterior pharyngeal wall flap. The procedure has subsequently undergone numerous modifications, but the principle remains the same. The goal of a posterior pharyngeal flap is to effectively obturate the nasopharynx with a biologic obturator. The procedure involves elevating an inferiorly based flap of the posterior pharyngeal wall muscle and mucosa. An incision that is of similar width is placed on the nasal aspect of the soft palate and a back-elevated pocket to inset the flap is developed. The elevated inferior aspect is subsequently secured to the nasal surface of the soft palate with the nasal palate mucosa (Figs. 91.1A to C). This can




**Figs. 91.1A to C:** Illustration demonstrating superiorly based, posterior pharyngeal flap. (A) Incisions. (B) Flap inset. (C) Oral view after closure of the posterior pharyngeal wall.

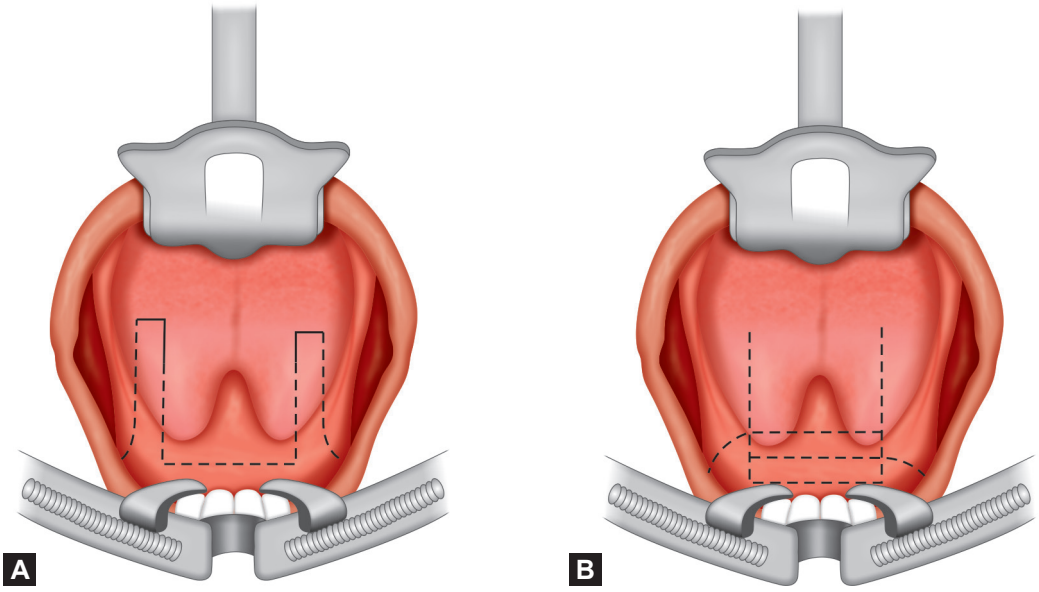
be accomplished either with or without splitting the soft palate. Once completed, the central region of the nasopharynx is obturated by the superiorly based flap, while lateral ports for air escape remain open to allow an attenuated degree of nasal transmission. As such, a prevailing concept is that children with adequate lateral pharyngeal wall motion tend to fare better with the approach.

Regarding flap design, the authors' preferred technique involves a nonpalate splitting approach, if possible (📻 91.1). In general, flap width is estimated to be the distance between the posterior tonsillar pillars. The inferior extent is approximately equivalent to the midpoint of the tonsillar fossa. The flap length can be estimated by measuring the distance of the free edge of the soft palate to the posterior pharyngeal wall. It is critical to avoid designing a flap that is too long. The proper plane of elevation is devoid of major vessels and superficial to deep neck vasculature, even in the case of medialized carotid arteries. Elevation proceeds to the level of natural VP closure and can be correlated with landmarks seen on preoperative nasendoscopy. Lateral ports are generally sized with 3.5 mm endotracheal tubes and care is taken to avoid tension. The lateral ports will ultimately allow for nasal air passage in an attenuated fashion.

Posterior pharyngeal flap surgery is an effective and safe procedure with success rates of resolution of VPI postoperatively quoted between 72 and 99%.[25,28,30,36-38] Despite its success, posterior pharyngeal flaps have been implicated in causing new-onset or worsening of OSA symptoms as discussed above. Current modifications of pharyngeal flap surgery are associated with a relatively rare iatrogenic OSA rate of 0–3.3%.[19,24,39] New emphasis placed on patient selection, increase in preoperative polysomnograms, and consideration of possible obstruction has provided improved insight into intraoperative decision making and postoperative care.[24]

## Sphincter Pharyngoplasty

Sphincter pharyngoplasty, first described in the 1950s by Hynes and later revised most notably by Ortichochea, is a procedure aimed at addressing the dissatisfactions with posterior pharyngeal flaps.[40] The initial report by Hynes described a two-stage approach. In the first operation the salpingopharyngeus muscles were transposed to the posterior pharyngeal wall and during the second procedure the palate defect was corrected and moved posteriorly.[41] Ortichochea describes the first "dynamic" pharyngoplasty using the palatopharyngeus muscles and creating a sphincter that can voluntarily open and close during speech to help produce the desired sounds. The sphincter pharyngoplasty has evolved into a single-stage surgery where two lateral superiorly based flaps from the region of the posterior tonsillar pillars are elevated.[42-44] A transverse incision is made in the posterior pharyngeal wall mucosa, and the flaps are rotated 90° and subsequently inset into the transverse incision, potentially placing the dynamic muscle (palatophayngeus) into an orientation to create a dynamic sphincteric




**Figs. 91.2A and B:** Illustration demonstrating the sphincter pharyngoplasty procedure. (A) Incisions and flap elevation; (B) Flap inset.

effect (Figs. 91.2A and B, 91.2). A study comparing pre- and postoperative videofluoroscopy suggested that there is some degree of dynamism after sphincter pharyngoplasty, which is difficult to quantify.[45] In distinction to the obturation by a pharyngeal flap, a sphincter pharyngoplasty is generally pursued in the settling of a child without dynamic lateral pharyngeal walls.

Contemporary procedures reflect the technological advancements in nasendoscopy and the ability to objectively assess the degree of insufficiency and the anatomical point at which the velum contacts the posterior pharynx. Sphincter pharyngoplasty is now tailored to each individual patient to address the specific incompetence to optimize outcome. The level in the nasopharynx where flap placement occurs is critical as placement below the level of contact likely contributes to poor outcomes. However, success rates of procedures aimed at higher, more anatomical placement of the posterior tonsillar pillar have been reported at 84–87%.[27,29,45,46]

The literature lacks many reports of airway problems after sphincter pharyngoplasty compared to pharyngeal flaps. A small set of data, however, suggests that sphincter pharyngoplasty can be associated with some degree of airway dysfunction. Witt et al. reported eight cases of perioperative overt airway dysfunction, all of which required positive airway pressure and most resolved within three days.[47] Ettigner reported an increase in CPAP use from 1.4% preoperatively to 22% postoperatively.[18] The most common complication of sphincter pharyngoplasty is reoperation. Indications for reoperation are most commonly for persistent hypernasality, flap dehiscence, and inferior flap position.[40,45,48]

## Furlow Double-Opposing Palatoplasty

First introduced in 1978, the Furlow double-opposing Z-plasty was designed to lengthen the soft palate and to restore the normal velar anatomic function resulting in improvement of VPI symptoms particularly in patients with a submucosal cleft or short velum. In concept, the goal is to reposition the palatal musculature, specifically the tensor levator aponeurosis, to restore function of the velar mechanism and opposition with the posterior pharynx as well as effectively lengthen the palate.

The initial design of the Furlow Z-plasty addresses the oral layer with Z-incisions at angles of approximately 60 to 70° (Fig. 91.3). The flaps are raised so one is purely mucosal and the opposite is a mucosal muscle flap. The flaps are then tagged and pulled laterally to reveal the underlying nasal layer. The nasal sides of the flaps are then incised in a reversed configuration from that of the oral flaps. These nasal flaps frequently require extensive dissection, laterally onto the palatopharyngeal surface, for adequate mobilization. Closure is done by transposing the nasal flaps in a typical Z-plasty manner. The left-sided nasal flap is transposed anteromedially and the opposite flap is transposed posterolaterally; in each the far corner is sutured using horizontal mattress. The

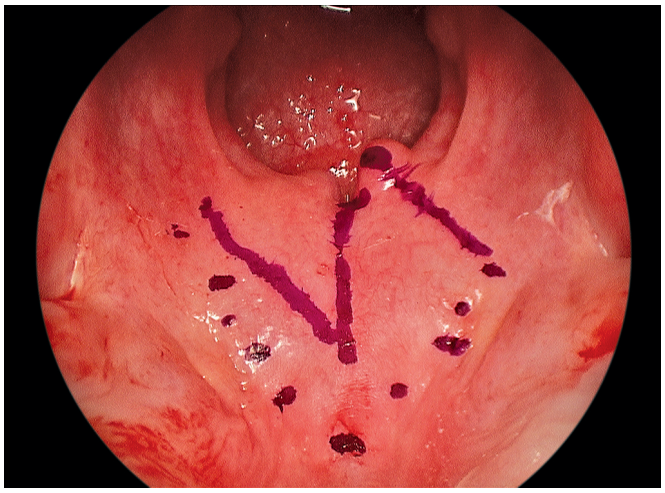


**Fig. 91.3:** Intraoperative photo of planned incisions for Furlow palatoplasty in a child with a submucous cleft palate.

remaining edges of the nasal flaps are then secured using interrupted 4-0 or 5-0 absorbable sutures. The oral flaps are then transposed with the right side anteromedially to the hard palate margin and the left side myomucosal flap is then transposed posterolaterally along the anterior oral flap (Figs. 91.4 and 91.5). By placing the nasal and oral Z-flaps in the manner, the horizontal tensor–levator aponeurosis muscle sling is oriented horizontally in the correct anatomic position.[49]

The advantages of the Furlow procedure allows correct orientation of the palatal musculature resulting in improved speech attributed to the realignment of the muscular sling. The palate is lengthened in the anterior–posterior plane at the expense of width based on the Z-plasty effect.[50] Further, fistula rates are decreased as the suture lines on the nasal and oral flaps are perpendicular to each other with minimal overlap.

The Furlow palatoplasty has been shown effective in addressing patients with minimal VPI due to a small central VP gap with good velar motion.[51] The Furlow procedure has traditionally been suggested for gaps <5 mm; however, data on success rates up to 10 mm are reported. Success rates in selected patients after careful preoperative examination are from 72 to 97% for both large- and small-gap VPI.[30,50,52-55]

## Posterior Pharyngeal Augmentation

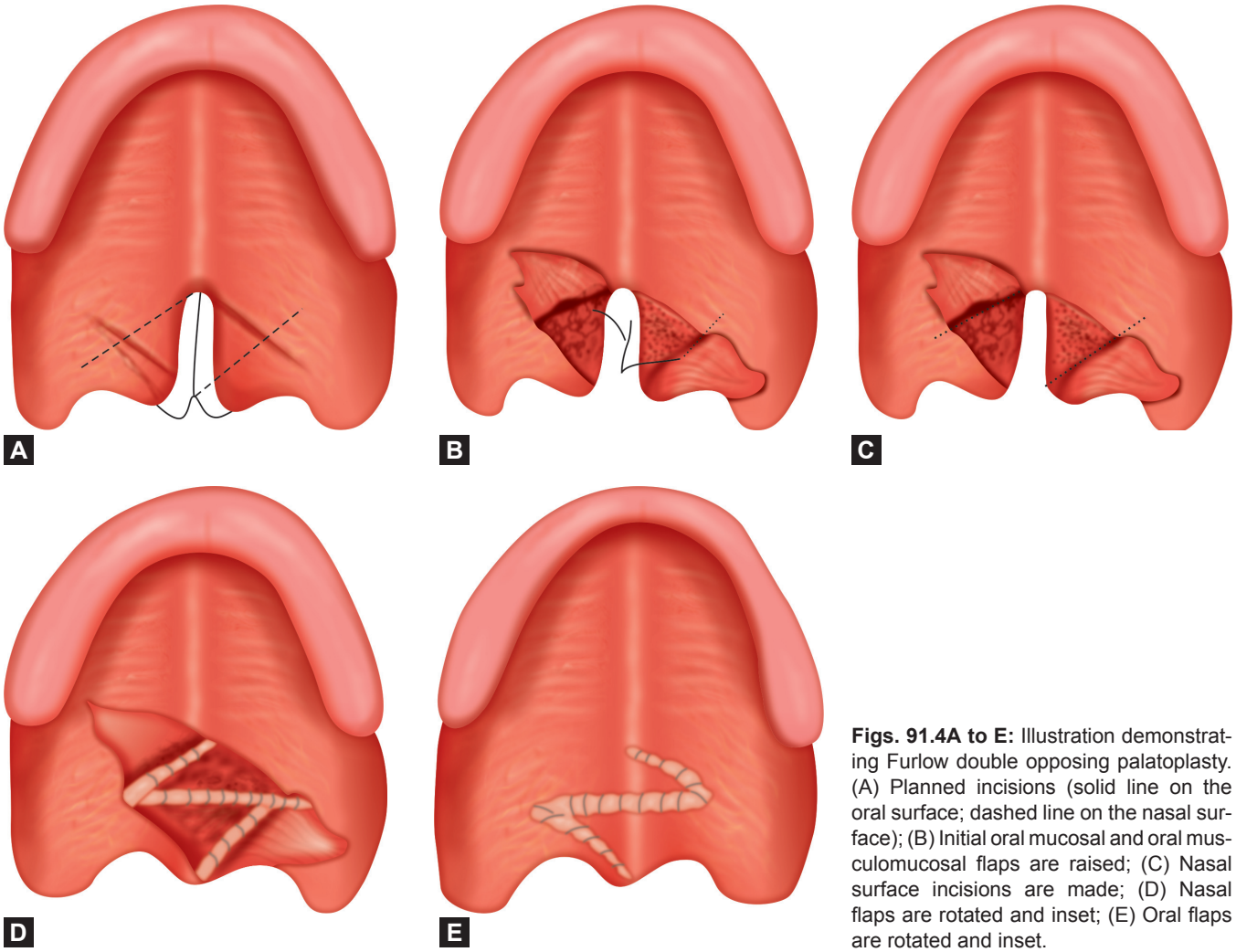
Posterior pharyngeal augmentation (PPA) offers an alternative approach to bridge the gap between incomplete VP closure. It was first introduced by Passavant using an inferiorly based posterior pharyngeal flap rolled or folded upon itself to create a bulk and augment the posterior pharyngeal wall.[33] Unfortunately, long-term results of such rolled flaps are compromised by the fact that the flaps ultimately shrink to a fraction of their original size. Outcomes demonstrated no significant benefit with regard to hypernasality, auditory nasal emission, or closure characteristics at 3 months postoperatively.[56]

However, alloplastic implants have emerged to combat the poor long-term outcomes of autogenous augmentation. A variety of implant materials have been published, including cartilage, fat, fascia, paraffin, silicone, acellular dermis, polytetrafluoroethylene, and calcium hydroxylapatite (CaHA).[57-64] Variable degrees of success have been reported and endoscopic examination is useful to determine the optimal site of implantation based on the level of the largest VP gap.

Solid material implantation is introduced into the posterior pharynx through a high vertical incision through the mucosa and superior pharyngeal constrictor to the level of the prevertebral fascia. A pocket is created to avoid placement of the implant directly behind the incision and adequate dissection is preformed to encompass the entire width of the posterior pharynx. Hemostasis is achieved with epinephrine-soaked cotton. The implant material is properly shaped and sized based on exam findings and placed above the superior limit of the incision. The incision is then closed in a layered fashion with the superior aspect of the deep sutures incorporating the prevetrebral fascia in the closure of the pharyngeal constrictor.[65]

Injection pharyngoplasty involves injecting alloplastic materials into the posterior pharyngeal wall under direct visualization. Generally, this is performed using a 120° endoscope with a soft palate retractor. The carotid arteries are palpated laterally to ensure that they do not lie in the injection site. A 25-gauge needle is inserted transnasally or transorally into the posterior pharyngeal wall until the bone is contacted and then withdrawn 2 mm to inject in the retropharyngeal space. Injection volumes range from 1 to 4 mL and depend on the severity of the defect.[66] The authors' preference is to use calcium hydroxyapatite as their injection material (Figs. 91.6A and B, 91.3).

Success rates of posterior pharyngeal wall augmentation using a variety of solid implant material have been reported from 69% to 74% with regard to complete resolution or great improvement in speech hypernasality.[57,61,62,65] Injection material success rates have been reported from 57% to 75%.[63,66] While solid implants do not resorb,




**Figs. 91.4A to E:** Illustration demonstrating Furlow double opposing palatoplasty. (A) Planned incisions (solid line on the oral surface; dashed line on the nasal surface); (B) Initial oral mucosal and oral musculomucosal flaps are raised; (C) Nasal surface incisions are made; (D) Nasal flaps are rotated and inset; (E) Oral flaps are rotated and inset.

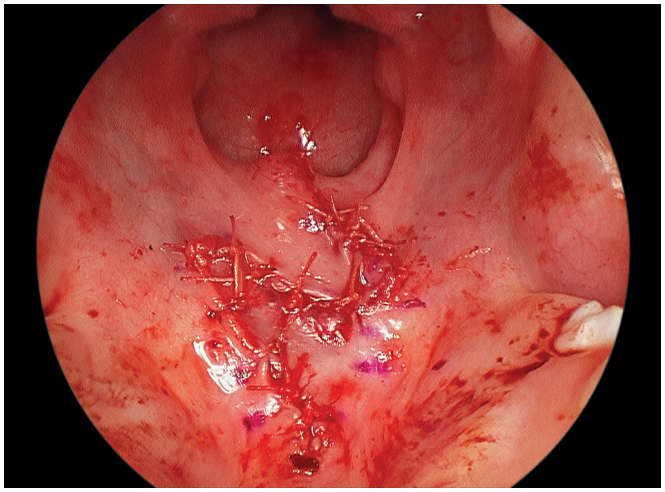
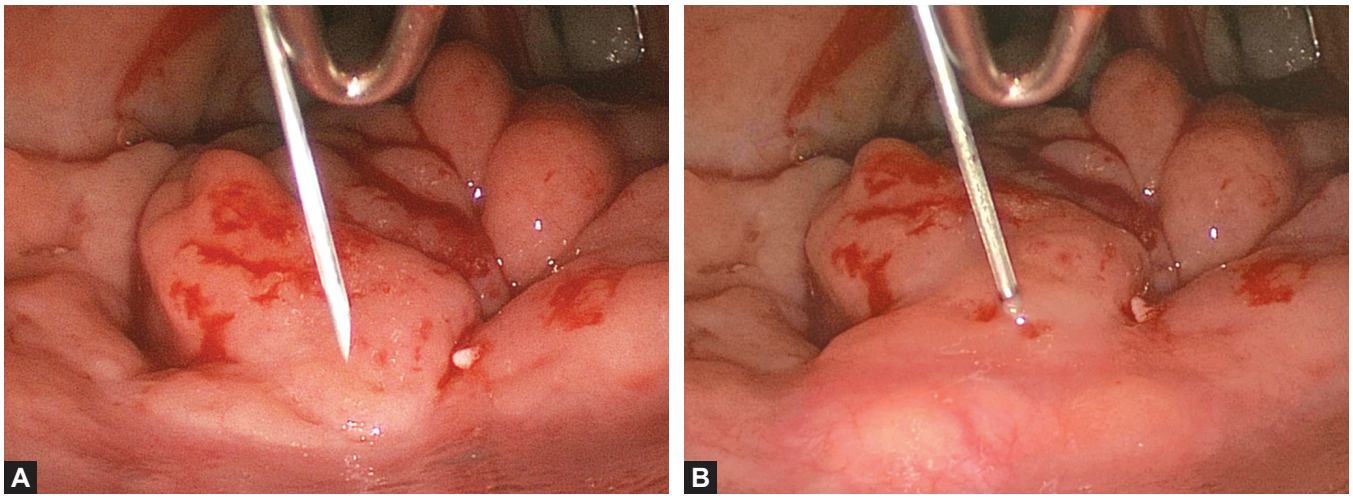


**Fig. 91.5:** Intraoperative photo of completed Furlow palatoplasty in a child with a submucous cleft palate.

extrusion is the major disadvantage. Witt reports a 10% extrusion rate using mostly a textured silicone pillow, gore tex block or rolled gore tex.[56] Of note, one third of rolled gore tex implants and one third of smooth silicone block implants are extruded, leading to their discontinued use by the authors of the review.[56] Infection is an uncommon complication and may lead to extrusion. Obstructive sleep apnea has been reported in 1–2.7% of patients after augmentation.[56,66]

## Tonsillectomy

A rarely described, but clinically important cause of VPI is obstructed velar closure secondary to tonsillar hypertrophy. Tonsillectomy can be curative in such children.[67] A careful endoscopic or fluoroscopic evaluation is required to determine the presence of the VP gap and to




**Figs. 91.6A and B:** Injection pharyngoplasty for mild velopharyngeal insufficiency in a child with a small central gap viewed through a 120° endoscope. (A) Posterior pharyngeal wall just prior to introduction of the needle; (B) Needle placed into the posterior pharyngeal wall injecting calcium hydroxyapatite inferior to the adenoid pad.

visualize the role that the tonsils play in contributing to the overall gap configuration and dimensions (Fig. 91.7). Additionally, a subset of children will present with sleep-disordered breathing secondary to tonsillar hypertrophy while undergoing evaluation for VPI and may benefit from tonsillectomy to relieve obstruction. There has been controversy over whether it is advisable to proceed with simultaneous or staged tonsillectomy with VP surgery.[68-70] Both avenues appear to be reasonable; however, it is the authors' experience that a staged approach with tonsillectomy approximately 6 weeks prior to VP surgery is associated with less postoperative complications (airway obstruction, flap dehiscence, problematic breathing) and may result in significant improvement of VPI once enlarged tonsils are removed.

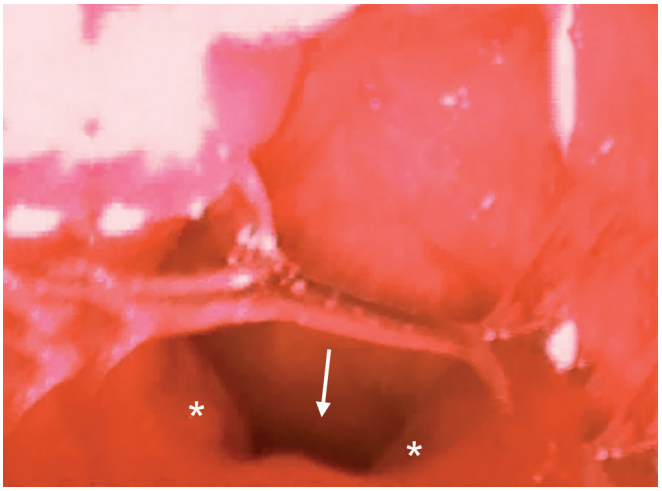



**Fig. 91.7:** Nasendoscopy demonstrating hypertrophic tonsils (denoted by asterisks) limiting palate movement resulting in a central velopharyngeal gap (white arrow).

## SELECTION OF PROCEDURE

As suggested above, success rates for surgical interventions for VPI are generally fairly high. The wide range in success rates is likely secondary to variability of degree of VPI improvement defined for a successful operation as well as integrity and quality of each procedure performed. Perhaps, the largest factor in the variability of surgical success lies in the selection of surgical intervention and the surgeon's experience. Proper surgical selection is dependent on a thorough history and physical examination, including a functional evaluation of the VP gap, speech evaluation, and in selected cases, imaging. While surgeon experience often dictates procedure selection, the performed procedure is often based on the VP closure pattern.

Historically, the pharyngeal flap procedure was the treatment of choice for VPI; however, more recently surgical technique selection has been tailored to the patient's particular pathophysiology. The sphincter pharyngoplasty procedure has gained popularity in some institutions due to the perceived decreased incidence of postoperative OSA and the potential dynamic nature of the procedure. Many surgeons base surgical decision making on VP closure patterns particularly focusing on lateral wall movement. In general, one would expect that patients with good lateral wall motion to have greater success with a pharyngeal flap, while those with poor lateral wall motion would derive more benefit from a sphincter

pharnygoplasty. However, both procedures have demonstrated adequate success in a variety of closure patterns. In comparison of pharyngeal flap and sphincter pharyngoplasty, patients with the coronal closure pattern are less frequently corrected with pharyngeal flaps than those with the noncoronal closure pattern.[71] Specifically, in patients with VCFS, prominent medialized and superficial carotid arteries are important to note. However, appropriate elevation of musculomucosal flaps should be in a plane superficial to the vessels.

The Furlow palatoplasty is an effective technique for patients with poor velar movement due to abnormal insertion of the levator aponeurosis and small velar gaps or submucosal clefts. The Furlow procedure is typically reserved for patients with gaps <5 mm, but has been described in gaps up to 10 mm. Further, the Furlow procedure is not commonly associated with obstructive airway symptoms. Overall, the Furlow procedure is ideal for patients with poor velar motion most commonly from the overt or submucosal cleft palate with minimal VPI.[51]

Posterior pharyngeal augmentation is an alternative technique to the more common pharyngoplasty procedure. The primary advantage is the ease and decreased morbidity and recovery time compared to more extensive procedures. The procedure is appropriate in cases of small central gaps or in cases where closure can occur, but the seal cannot be maintained. Patients with poor lateral closure are less likely to benefit from posterior augmentation.[66] Long-term efficacy of implants, most notably autologous tissue roll, cartilage or fat grafts, as well as alloplastic materials is of concern due to absorption or extrusion. Patient selection for posterior augmentation is debatable, but most agree that it provides reasonable results for small (<5 mm) central gaps with circular closure patterns.

## REVISION SURGERY

As noted above, the surgical management of VPI enjoys an overall high rate of success. However, many children will require revision surgery. Such procedures are generally individually tailored to specific deficits and often require a thoughtful approach using endoscopic assessment. The specific procedures can vary from simply modifying the lateral ports of a pharyngeal flap to essentially repeating the initial surgery. A prior history of a previous procedure does not preclude revision surgery. In particular, a previous pharyngeal flap does not preclude a sphincter pharyngoplasty or vice versa. Additionally, injection pharyngoplasty does not preclude more invasive pharyngeal or palatal procedures.

## CONCLUSION

Overall, the selection of surgical procedures to manage VPI is based on an individual patient's pathophysiological cause of VPI as well as the individual surgeon's experience. Most importantly, a surgical procedure should be offered to the patient who presents the highest likelihood of success and with lowest potential morbidity.

*Disclaimer*: The views expressed in this chapter are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, nor the U.S. Government.

## VIDEO LEGENDS

**Video 91.1:** Video depicting highlights of a superiorly based pharyngeal flap procedure

**Video 91.2:** Video depicting highlights of a sphincter pharyngoplasty procedure

**Video 91.3:** Video depicting highlights of an injection pharyngoplasty procedure

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CHAPTER

# 92

# The Origins and Operative Repair of Palatal Clefts

***Andrew R Scott***

## INTRODUCTION

Orofacial clefting, one of the most common birth defects affecting children worldwide, is a condition that is inherently complex and requires long-term treatment planning. Because facial clefts affect both form and function, a multidisciplinary approach to therapy, rehabilitation, and reconstruction is warranted. Interventions are required throughout early childhood and may continue until the late teens or early twenties in some patients.

The purpose of this chapter is to review the embryology, epidemiology, and genetics of orofacial clefting and to discuss the timing and methods of the various interventions that may be required throughout childhood for cleft palate in particular. A number of palatoplasty techniques will be discussed along with the controversy surrounding the optimal timing for surgical repair of soft and hard palate defects. Operative complications and potential deleterious downstream effects of surgery will also be discussed.

## EMBRYOLOGY OF THE MAXILLA AND PALATE

The musculoskeletal structures that form the head and neck region are ultimately derived from mesoderm, ectoderm, and neural crest cells. Neural crest cells migrate from the primitive central nervous system (rostrally into the facial region and ventrally into the pharyngeal arches) to form the midface and pharyngeal arch skeletal framework. Such neural crest cells are the source for nearly all structures in the palatal region including cartilage, bone, dentin, tendon, and glandular stroma among others.

In the fourth and fifth weeks of development, the pharyngeal (or branchial) arches appear. These are bars of mesenchymal tissue separated by deep clefts. As the external clefts become more defined, internal invaginations (branchial pouches) form along the lateral walls of the pharyngeal foregut. Each of the branchial arches is composed of a core of mesenchymal tissue with an external covering of surface ectoderm and an internal lining of endodermal epithelium. As noted above, this core of mesenchyme is derived from mesoderm, ectoderm, and neural crest cells, which migrate into the arches to contribute to the skeletal components of the face. For this reason, each branchial arch is characterized by its own muscular components, a specific cranial nerve, and a named artery. The first branchial arch is the focus of this chapter due to its role in maxillary development.

By the end of the fourth week, the center of the face is formed by the stomodeum, which is surrounded by the first pair of branchial arches. The first arch is bordered rostrally by the frontonasal process and caudally by the second branchial arch. The first arch forms two mesenchymal prominences, a dorsal portion (the maxillary process) and a ventral portion (the mandibular process). Mesenchyme of the maxillary process will go on to form the maxilla, zygoma, and temporal bone. The first arch is innervated by the trigeminal nerve and derives its blood supply from the maxillary artery.[1]

## EMBRYOLOGY OF THE FACE

The primitive face begins to form at the end of the fourth week. A proliferation of mesenchyme ventral to the brain

forms the frontonasal process, constituting the upper border of the stomodeum. The maxillary processes are situated lateral to the stomodeum and the mandibular processes caudal to the stomodeum. Nasal (olfactory) placodes form as thickenings of surface ectoderm on either side of the frontonasal process, and during the fifth week, these invaginate, creating nasal pits. As a result of this invagination, a circumferential mound of tissue is formed. The medial aspect of this mound is termed the medial nasal process and the lateral aspect the lateral nasal process. The anterior nasal septum arises from the medial nasal processes, and the fontal process gives rise to the posterior septum.

## EMBRYOLOGY OF THE PRIMARY AND SECONDARY PALATE

The two medial nasal processes merge to form the intermaxillary segment; fusion on the surface creates the philtrum and prolabium, and fusion internally creates the premaxilla or primary palate. This structure is referred to as the primary palate, as it appears chronologically earlier in development than the posterior palatal elements. The coalescence of the intermaxillary segment provides continuity of the upper jaw and lip, separating the nasal pits from the stomodeum. The intermaxillary segment of the upper jaw, the premaxilla, is the site in which the four upper incisor teeth will develop. Because the intermaxillary segment maintains its connection to the frontonasal process, the premaxilla is contiguous with the nasal septum and therefore supplied by the nasopalatine neurovascular bundle.

The secondary palate (named this because it forms after the appearance of the primary palate) is derived from two outgrowths of the maxillary processes that appear during the sixth week of development. The secondary palate receives its innervation and blood supply laterally from the greater and lesser palatine vessels.

There are three elements that make up the definitive palate: the two lateral palatal processes (shelves) of the secondary palate and the primary palate derived anteriorly from the frontonasal prominence. At first, these three elements are widely separated by the obstructing tongue that initially occupies most of the stomodeum. However, during the eighth week of development, the palatine shelves ultimately fuse with each other in an anterior-to-posterior direction, starting first with the primary palate. There is a sex difference in the timing of this closure, with shelf elevation and fusion taking place a few days earlier in male embryos than in female embryos.[2] This slight delay may account for the higher incidence of isolated cleft palates in females. The fetus must be freely floating within the amniotic sac to allow for spontaneous jaw opening and tongue withdrawal. In cases of oligohydramnios, the neck may remain flexed against the heart prominence, impeding jaw growth, jaw opening, and adequate tongue withdrawal. This chain of events has been implicated in certain forms of cleft palate with glossoptosis and micrognathia (Robin sequence).[3]

After palatal fusion has taken place, the trifurcation between the three elements of the primitive palate persists as the incisive foramen. Since the canine teeth and remaining dentition normally arise from the secondary palate, clefting between the primary and secondary palates most commonly occurs in the incisive fissure, separating the lateral incisors from the canine teeth. As the fusion proceeds posteriorly, the nasal septum grows down to merge with the cephalic aspect (maxillary crest) of the newly formed palate.

Ossification proceeds during postconception week 8 but does not occur in the most posterior aspect of the palate, giving rise to the soft palate. Myogenic mesenchymal tissue from the first and fourth branchial arches migrates into this region, giving rise to the various soft palate musculatures. The palate continues to grow in length, breadth, and height during the second and third trimesters. Between 7 and 18 weeks, there is a greater change in length, after which the width increases faster than the length.[4] This may explain the relative maxillary constriction seen in premature infants. At birth, the length and breadth of the palate are almost equal.

## EPIDEMIOLOGY, GENETICS, ENVIRONMENTAL AND NUTRITIONAL RISK FACTORS

Cleft palate may occur in isolation or in the context of cleft lip. Isolated palatal clefting is morphologically and genetically different from palatal clefting associated with cleft lip.

Isolated cleft palate occurs at a rate of 1:2,000 births and is equal across ethnicities. There is a 2:1 ratio of females to males. The most common form of palatal clefting is a bifid uvula, which is present in more than 2% of the population. Isolated cleft palate is associated with a syndromic diagnosis in nearly 50% of cases.

Cleft lip and palate, on the other hand, are more common in males than females and have rates that vary across ethnicities. Asians and Latinos have the highest rate (2:1,000–3:1,000 births) and African Americans the lowest (0.4:1,000 births). The rate of cleft lip and palate in Caucasians falls in the middle at approximately 1:1,000 births.[5] Syndromic diagnosis in cleft lip and palate occurs at a much lower rate than in cases of isolated cleft palate.

## Genetics

The majority of orofacial clefting appears to be inherited heterogeneously, as recurrence rates do not follow a Mendelian pattern of inheritance. There are some syndromic forms of clefting associated with single-gene defects (Van der Woude, Treacher Collins, velocardiofacial, and Stickler syndromes) that follow autosomal inheritance patterns; however, several candidate genes continue to be examined, including several that have been mapped to the 6p, 4q, and X loci.[6,7]

## Environmental and Nutritional Risk Factors

It is a widely held belief that the causes of oral clefts are multifactorial, with both genetic predisposition and environmental exposures contributing. Over the years, several potential risk factors have been identified including cigarette smoking, alcohol, corticosteroids, antidepressant medications, anticonvulsant medications, maternal infections, and nutritional deficiencies. The evidence for many of these factors will be briefly discussed below.

### *Tobacco Use*

There have been conflicting results between studies examining the rate of clefting in mothers who smoke as compared to those who do not. A meta-analysis of these studies concluded a weak association between maternal smoking and orofacial clefts, with an overall odds ratio of 1:32 for cleft palate.[8] Even with only a modest association, the public health impacts of maternal smoking may be significant, given the number of women who continue to smoke during the third trimester of pregnancy.

### *Excessive Alcohol Use*

There is a statistically significant increase in the risk of cleft lip and palate among mothers who consume five or more drinks per day on five or more drinking days (OR 3.0 (95% CI 1.1–8.5).[9] Due to inadequate power, it is not clear whether or not there is an increased rate of cleft palate alone in children of mothers who drink excessively during pregnancy.

### *Epilepsy*

Women with seizure disorders are at an increased risk for having a child with an oral cleft; however, it remains unclear as to whether or not this is related to certain drug therapies used to treat epilepsy or another unidentified factor. A high-powered study that would control these factors has not yet been conducted. Certain anticonvulsant medications are known folic acid antagonists, which may affect the developing fetus. Mothers undergoing polytherapy for epilepsy during pregnancy had a tenfold increase in having a child with an orofacial cleft in one study (OR 10.5, 95% CI 1.52-59.9), which represents the most convincing evidence linking anticonvulsant therapy to clefting to date.[10] Additional studies involving the use of benzodiazepines during pregnancy have been performed, and the effect of these drugs on orofacial development is less convincing.

### *Corticosteroid Use*

A potential connection between oral clefts and maternal steroid use during pregnancy has been proposed based on animal studies.[11] Subsequent case–control studies have suggested a threefold to ninefold increase in the rate of cleft lip and palate in the context of corticosteroid use during pregnancy.[12,13] A possible explanation for this effect is that steroids are acting directly on fetal tissues, disrupting fusion, and collagen synthesis.

### *Folic Acid Intake*

Folate deficiency has been implicated in oral clefting as well as in other malformations. Most notable, folic acid deficiency has been linked to neural tube defects and fetal death.[14] In one animal study, folate supplementation was successful in preventing oral clefts in a line of dogs with a genetic predisposition to this disorder.[15] There are no human experimental trials that have proven or disproven the link between folic acid deficiency and oral clefting, and such a study is not ethically feasible, given the standard of recommending folate supplementation in all pregnant women and the United States' practice of fortifying foods with folate as a basic public health measure.

## FUNCTIONAL ANATOMY AND CLASSIFICATION SCHEMA

The normal palate is composed of a bony portion, which is symmetric and may be divided into five elements: the alveolus and premaxilla anteriorly and the paired maxilla, palatine bones, and pterygoid plates posteriorly. The soft palate is situated posterior to the palatine bones. Pathology within the muscles and soft tissue of the palate has the greatest impact on velopharyngeal and eustachian tube function.

There are six muscles that control soft palatal function: the levator veli palatini, superior pharyngeal constrictor, uvular muscle, palatopharyngeus, palatoglossus, and tensor veli palatini. The three muscles with the greatest contribution to velopharyngeal function are the levator veli palatini, uvular muscle, and superior pharyngeal constrictor. The tensor veli palatini does not contribute to the movement of the soft palate but rather improves the ventilation and opening of the eustachian tube.

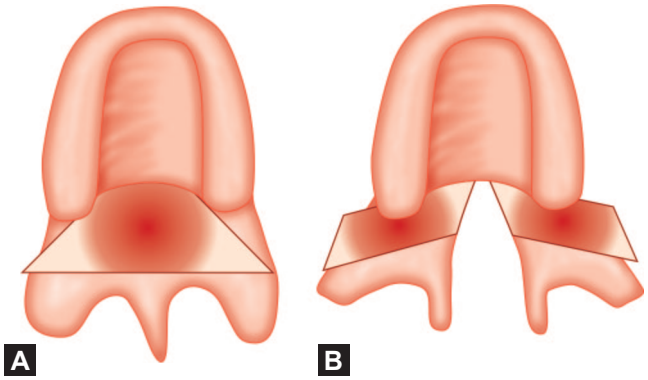
The relationship of the six soft palate muscles as well as their insertions is altered in the case of cleft palate. Normally, the aponeurosis of the tensor veli palatini serves as the common point of attachment for all of the soft palate muscles comprising the velum. In the scenario of cleft palate, however, the aponeurosis of the tensor veli palatini attaches more anteriorly along the medial margins of the bony cleft (Figs. 92.1A and B). This results in a shorter palate and impaired eustachian tube function, owing to the midline dehiscence of the tensor veli palatini musculature. Additionally, the levator veli palatini muscle sling is interrupted, leading to impaired elevation of the velum during speech and swallowing (Figs. 92.2A and B).

Several attempts have been made to standardize reporting of orofacial cleft deformities, as accurate reporting of these anomalies optimizes retrospective and prospective analysis of presentation and treatment outcomes and enables multicenter collaboration. The most basic classification scheme is the Veau classification, in which palatal clefts are divided into one of four groups. Group 1 clefts are posterior, involving only the soft palate structures. Group 2 clefts involve tissues of the hard and soft palate but are limited to clefts posterior to the incisive foramen. Group 3 clefts are those associated with cleft lip and palate, in which the cleft involves the primary palate and alveolus as well as the secondary palate. Group 4 clefts are the bilateral form of Group 3 clefts.

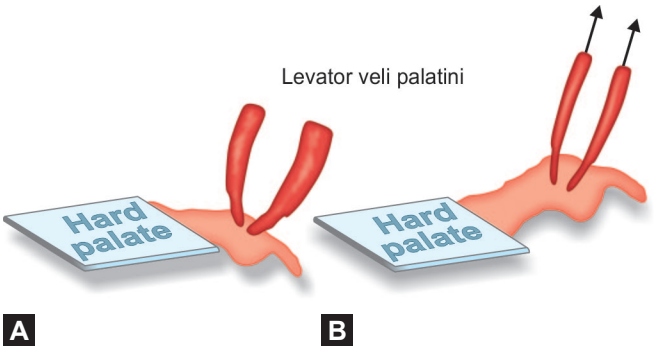
In 1971, Kernahan introduced a new classification scheme that was subsequently modified by Millard and others, allowing for computerized entry for all anatomic cleft variants. The scheme consists of a diagrammatic, Y-shaped symbol, with the incisive foramen represented at the trifurcation. The primary palate and prolabial elements are represented by the two arms of the Y, and the posterior, secondary palatal structures are represented by the central body of the Y (Fig. 92.3). Figures 92.4A to D provide a photographic summary of the spectrum of palatal clefts.

## PATHOPHYSIOLOGY

The presence of an unrepaired cleft palate usually leads to feeding difficulty, which may result in nutritional deficiency in infants and children. The connection between the mouth and nose impairs the normal sucking and swallowing mechanism of an otherwise healthy baby, and the impaired tensor veli palatini often causes eustachian




**Figs. 92.1A and B:** Muscular attachments of the levator veli palatini muscle in a normal individual (A) and in the case of cleft palate (B).




**Figs. 92.2A and B:** The action of the levator veli palatini muscles on the soft palate. (A) Relaxation; (B) Contraction.

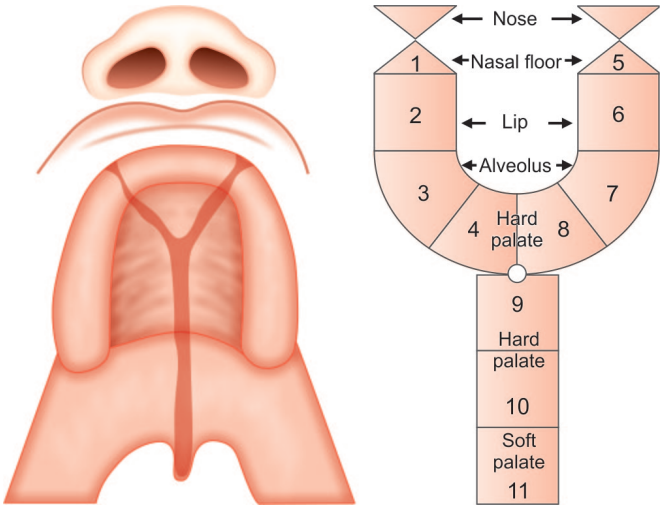



**Fig. 92.3:** Diagrammatic representation of the cleft lip and palate deformities; Millard's modification of Kernahan's 'Y' scheme; the circle at the trifurcation represents the incisive foramen.

tube dysfunction leading to chronic serous effusions, conductive hearing loss, and (over time) cholesteatoma formation. More consistently, however, the impaired velar function leads to characteristic speech disturbance, including hypernasality and associated maladaptive compensatory speech mechanisms.

There are three anatomic goals of cleft palate repair: separate the oral and nasal cavities, realign and reposition the soft palate musculature, and lengthen the palate. In achieving these anatomic goals, the surgeon hopes to ameliorate functional deficits, thereby improving speech while minimizing potential surgical complications such as maxillary growth restriction.

Surgical repair of the palate may negatively affect midface growth potential, especially when palate repair is carried out prior to 10 months of age. However, early repair of cleft palate (prior to 12 months of age) generally results in improved speech outcomes compared to those children who undergo late repair.

The evidence that cleft palate repair decreases the incidence of middle ear dysfunction is not consistent. For reasons that are not clear, children with cleft lip and palate have a higher rate of residual eustachian tube dysfunction and subsequent cholesteatoma formation than those children with isolated cleft palate. Proper repair of cleft palate has a positive effect on speech resonance and overall speech development; however, the timing of this intervention must be weighed against the potential for maxillary growth disturbance. Disagreement exists as to the optimal timing of surgery to minimize the harmful effects of scar formation and scar contracture in the areas of denuded palatal bone. In many European countries, a two-stage palatal closure is performed in which the soft palate is closed early and the hard palate repair delayed until several years later in an effort to minimize palatal growth disturbance.

## TIMELINE FOR INTERVENTION AND CONTROVERSY

In general, physicians agree that early palatal repair is associated with better speech results; however, earlier repair also tends to impart more severe dentofacial deformity. The author performs palatoplasty between 10 and 12 months of age, depending on the extent of the cleft and additional comorbidities. Soft palate clefts may be repaired earlier than 10 months, but the potential for improved speech outcomes must be balanced against the increased technical difficulty of performing palatoplasty in smaller infants. It is the author's opinion that cleft palate repair seems to have deleterious effects of maxillary growth, and that this effect is a risk of palatal surgery, regardless of whether the repair takes place during late infancy or when the patient is a toddler.[16]

## SURGICAL TECHNIQUES

In general, palatoplasty procedures for cleft palate employ a pedicled mucoperiosteal flap for repair of hard palate defects and may also utilize superiorly based vomer flaps to assist in closure of the nasal layer in wide, hard palate clefts. Procedures used to re-establish normal soft palate anatomy include intravelar veloplasty and double-opposing Z-plasty (Furlow) techniques. In either case, the aberrant palatal muscular attachments to the back of the hard palate are divided or mobilized and the muscle sling is retropositioned to recreate the levator sling and lengthen the soft palate.

The Furlow palatoplasty accomplishes three goals: it lengthens the soft palate, it radically retropositions and realigns the soft palate musculature, and it creates a nonlinear scar that does not risk shortening the palate with subsequent scar contracture. Pitfalls of Furlow palatoplasty include relying on robust soft tissues, a characteristic of healthy children that is not always the case in pediatric populations encountered on overseas missions. Additionally, the apex of the cleft palate repair,

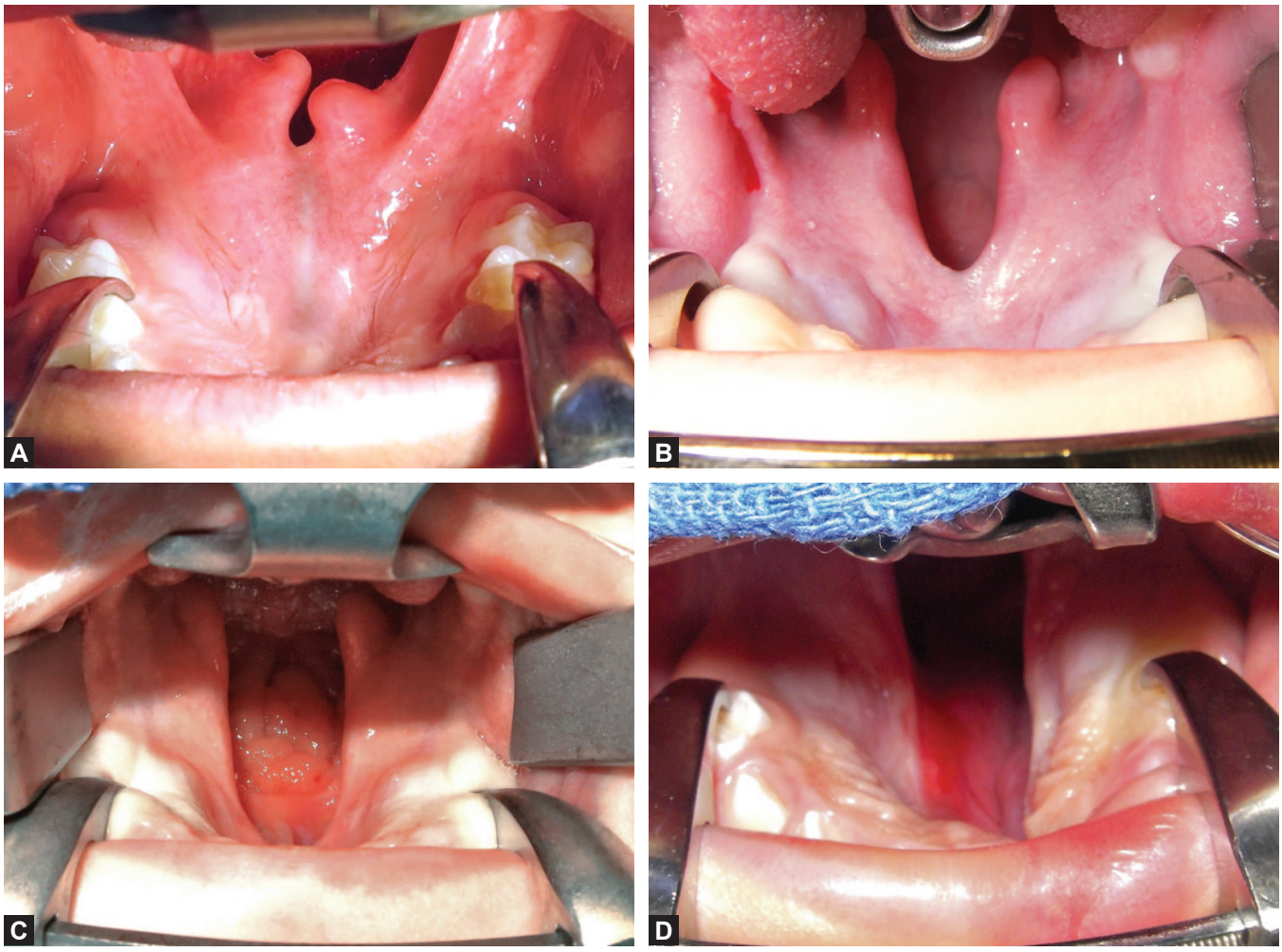



**Fig. 92.4A to D:** Various forms of cleft palate. (A) Submucous cleft palate (note central 'zona pellucida' caused by muscular dehiscence along the median raphe). (B) Cleft of the soft palate only. (C) Cleft of the soft and posterior hard palate (incomplete cleft palate, extending to incisive foramen). (D) Complete cleft palate (note fusion of septum to left maxillary shelf).

which is at the hard/soft palate junction, is susceptible to fistula formation, as there is less overlap of the nasal and oropharyngeal flaps at the apex of the repair. It is out of concern for this potential fistula formation that the author prefers to limit the opposing Z-plasty closure technique to submucous clefts and those clefts confined to the soft palate.

## PROCEDURES

The author's particular approach to the repair of palatal clefts is as follows: isolated submucous and soft palate clefts are repaired using the Furlow double-opposing Z-plasty technique. Incomplete clefts that involve both the hard and soft palate are repaired with a two-flap, V–Y pushback technique with intravelar veloplasty. Complete palatal clefts that extend to the alveolar ridges are repaired using a Bardach two-flap repair with intravelar veloplasty. In wide, hard palate clefts, vomer flaps are used, whenever possible, to minimize tension on the closure of the nasal layer. The details of the author's operative technique for each of these procedures will now be described.

### Operative Technique

General anesthesia is induced with mask ventilation and intravenous (IV) access is established. A dose of IV cephazolin or clindamycin is given. The trachea is intubated with an oral right-angle endotracheal tube and the bed is rotated 90°. A shoulder roll is placed and the child is belted securely to the OR table to allow for Trendelenburg positioning. The child is draped in the standard fashion and a Dingman mouth gag is inserted into the mouth and placed over the drapes. The child is gently suspended on

a roll of towels and the oral cavity is exposed. Approximately 4 mL of 1% lidocaine with 1:200,000 epinephrine is injected into the mucoperiosteum of the hard palate and the soft palate tissues, depending on the child's weight. Oxymetazoline-soaked cottonoids are placed into both nasal cavities as well. An adequate amount of time is allowed to pass to optimize vasoconstriction. During this time period, and for 30–60 second periods throughout the case, the Dingman mouth gag is taken down at 15–20 minute intervals to allow for reperfusion of the tongue.[17] It is the author's opinion that postoperative tongue edema is minimized with this practice and for this reason, a tongue stitch is not routinely placed at the end of the case.

## Furlow Double-Opposing Z-Plasty

For soft palate clefts, the medial margins of the cleft are incised from the tips of the uvular appendages to the anterior extent of the soft palate cleft. In the case of a submucous cleft palate, the zona pellucida is converted to a full-thickness soft palate cleft by incising the zona pellucida with a 15 blade and extending this cut anteriorly to, but not past, the hard/soft palate junction. A diagonal incision is planned on the right side, extending anterolaterally from the uvular base to the region of the hamulus at a 60° angle from the midline. A parallel incision is planned on the left side, extending from the apex of the cleft anteriorly to the region of the hamulus posterolaterally on the left side.

Reynolds scissors or Tenotomy scissors are used to develop an anteriorly based mucosal flap on the right side, with back elevation from the apex of the flap at the uvular base. The dissection plane is deep to the minor salivary glands but remains superficial to the soft palate musculature. As back elevation proceeds more anteriorly, the aberrant attachment of the muscle to the posterior aspect of the hard palate is encountered and transition is made to a supraperiosteal plane over the palatine bone. Next, the anterior apex of the left myomucosal flap is dissected and a posteriorly based triangular flap of muscle and oropharyngeal mucosa is raised, leaving only the nasal mucosal layer down. While the medial dissection plane is quite shallow, the lateral dissection courses deep and over the fascia of the medial pterygoid musculature laterally. Once these two flaps are raised, the apices are secured to the Dingman with 3-0 silk to improve exposure of the nasal layer.

Next, the scissors are used to make a cut through the deep tissues on the right side, extending from the apex of the cleft to the region of the eustachian tube orifice posterolaterally and deep. This cut travels parallel to the base of the oral mucosal flap and is placed slightly posteriorly to leave a small cuff of muscle attached to the posterior aspect of the hard palate to facilitate closure. This cut creates a posteriorly based triangular myomucosal flap made up of soft palate musculature and nasal mucosa. The cut is extended laterally until the Eustachian tube orifice can clearly be seen. On the contralateral side, a diagonal cut is made through the nasal mucosa-only flap, extending from the base of the left uvula medially to the region of the eustachian tube orifice anterolaterally and deep.

With the four triangular flaps created, attention is now turned to closure. The author performs the entire closure with interrupted sutures of 4-0 vicryl, using a TF needle for the nasal layer and a RB-1 needle for the oral closure. The closure takes place in an anterior-to-posterior direction, starting first with closure of the left sided, anteriorly based nasal mucosal flap to the remnant cuff of the right nasal myomucosal flap, which is still adherent to the right posterior hard palate. The plane of closure changes from horizontal medially to a more vertical orientation laterally, and this transition becomes apparent with careful approximation of the nasal mucosa. Next, the horizontal limb of the Z-plasty incision is closed with reapproximation of the right-sided, posteriorly based nasal myomucosal flap to the nasal mucosa-only flap, which is already attached to the posterior hard palate. Then the remaining limb of this myomucosal flap is approximated to the free edge of the posterior soft palate mucosa laterally. Again, this lateral closure is in more of a vertical plane, starting deep and lateral in the region of the left eustachian tube orifice. As the closure of this flap nears its base, the free mucosal edges of the uvular elements are encountered and reapproximated. As the suture line passes around the uvular apex, the closure makes a transition from the nasal surface to the oropharyngeal surface of the palate.

Closure of this oral surface starts posteriorly at the base of the uvula and the posteriorly based, right-sided oral myomucosal flap is inset into the left side with the oral mucosa-only flap rotated to the left, thereby completing the double-opposing Z-plasty closure (Fig. 92.5).

The mouth is irrigated and suctioned and the Dingman mouth gag is removed, completing the case.

## V–Y Pushback (Two–Flap Palatoplasty with Intravelar Veloplasty)

After injection of local anesthesia, an incision is made from the apices of each uvular process along the free margin of the soft palate. As the hard/soft palate junction is approached, the incision line cheats along the oral surface

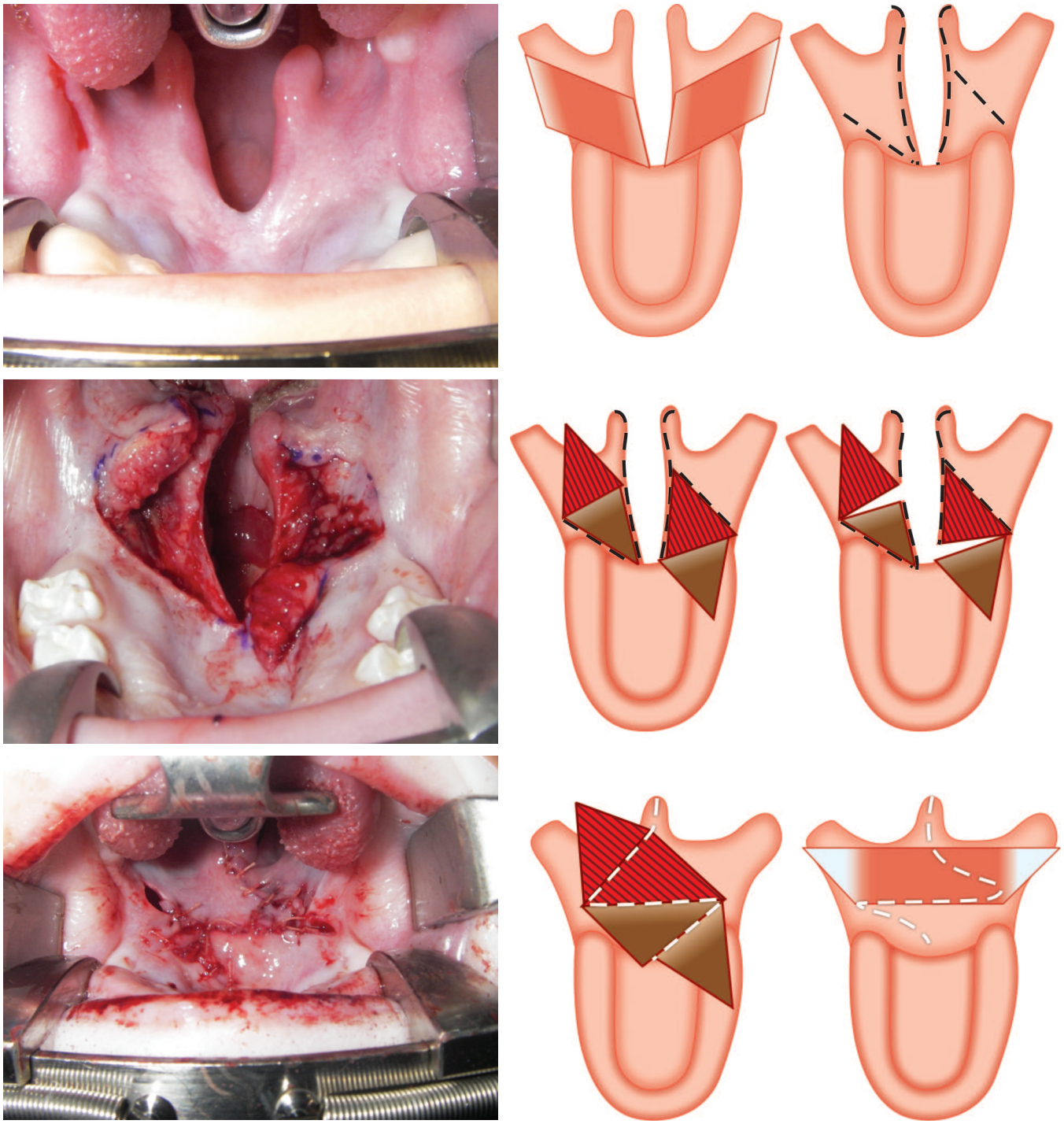


**Fig. 92.5:** Schematic representation of the steps of a Furlow double-opposing Z-plasty closure. Note how creation and closure of the Z-plasty incisions allows for realignment and radical posterior repositioning of the soft palate musculature. Photographs: a soft palate cleft amenable to Z-plasty closure; after elevation of the oral flaps; appearance following closure.

of the hard palate by approximately 3 mm and continues laterally and anteriorly to the hard palate cleft until the transition is made to the contralateral side. At this point, the author prefers to begin dissection of the soft palate by raising a plane between the nasal mucosa and the soft palate musculature on both sides. This plane is continued

posteriorly to the uvula to facilitate future closure of this structure. Next, a Cottle elevator is used to complete the hard palate incisions assuring that these cuts are through the periosteum and down to the bone.

Now, needle tip electrocautery on a setting of 15/15 is utilized. The location of the greater palatine neurovascular bundles is estimated by palpating for the hamulus and marking the location of this structure on each side. On cutting mode, an incision is made through the oral mucosa, starting from the lateral aspect of the soft palate posteriorly and coursing anteriorly to the maxillary tuberosity and cheating medially along the inner surface of the alveolar process. This incision is carried anteriorly until the approximate location of the lateral incisor teeth. Next, an incision is made from the apex of the marginal cleft incision to intersect with the alveolar process incision anteriorly. Mirror images of these incisions are then made on the contralateral side. The sharp end of a freer elevator is then used to establish a subperiosteal plane of dissection and the oral mucoperiosteal flaps are elevated in an anterior-to-posterior direction. As the vascular pedicle is approached, several small spicules of bone are encountered. Dissection is then carried medially and laterally to the location of the greater palatine vessels. Further elevation of the flap off the maxillary tuberosity is facilitated with electrocautery dissection, once the vascular pedicle can be seen and protected under direct vision. Elevation is carried posteriorly to the palatal bone at which a small right angle dissector may be used to communicate the medial and lateral planes of dissection behind the greater palatine vessels. Once this maneuver has been performed, further posterior elevation of the oral mucosa off of the underlying palatal musculature may take place safely. The proper plane of this dissection may be further delineated by dissecting the palatal mucosa off of the hamulus. The aberrant muscular attachments to the posterior hard palate may be exploited to provide counter tension, allowing for blunt separation of the oral mucosa from the levator sling and tensor veli palatini aponeurosis. Hemostasis may be obtained with fine bipolar cautery and needle tip electrocautery. An identical procedure is performed on the contralateral side.

At this point, the oral mucoperiosteal flaps have been raised and may be retracted by placement of a 3-0 silk suture attached to the Dingman. The only oral mucoperiosteum that remains adherent to the palate at this point is the "V" overlying the premaxilla.

Next, the nasal turn in flaps are elevated off of the oral surface of the hard palate using a Cottle elevator and further lateral dissection off of the nasal floor may be performed using a Woodson elevator. At this point, vomer flaps may be raised if necessary. To do this, the inferior edge of the vomer is incised with a 15 blade and mucoperiosteal flaps are elevated on each side. Small back-cuts are made posteriorly, allowing for lateral release of these flaps. Each side may then be approximated to the ipsilateral turn in flap to close the nasal surface of the hard palate under less tension.

Finally, attention is turned to the elevation and retropositioning of the soft palate musculature. The space of ernst is entered, allowing for lateral release and medial mobilization of the soft palate muscles. Next, the free edge of the nasal surface of the soft palate is grasped on one side by the assistant, and the surgeon meticulously separates the attachments of the soft palate muscles from the posterior hard palate and elevates the muscle from the delicate nasal mucosal layer. Prior separation of these layers, performed at the beginning of the case, facilitates this maneuver. As the palatal attachments are divided laterally in the region behind the vascular pedicle, there is release of the tensor aponeurosis and levator sling, allowing for retropositioning of this muscle complex. A similar procedure is performed on the contralateral side.

With dissection, complete attention is turned to closure. The author uses 4-0 vicryl on a TF needle and an RB-1 needle to close. Starting at the base of the uvula and continuing anteriorly, the nasal mucosal layer is closed in either a running or interrupted fashion. Vomer flaps are incorporated into the closure, if necessary. A small gap is left in the region of the hard/soft palate junction, if necessary, as the tension on the closure is highest in this area.

Next, an intravelar veloplasty is performed with placement of two horizontal mattress sutures of 4-0 vicryl through the retropositioned levator sling. Once this has been accomplished, the nasal and oral surfaces of the uvula are closed. Finally, the oral closure of the soft and posterior hard palate is completed using alternating simple and vertical mattress sutures, allowing for optimal tissue eversion. The apex of the approximated flaps is then affixed to the apex of the V-shaped adherent mucoperiosteum, thus completing the V-to-Y closure (Fig. 92.6).

The lateral slots are inspected for hemostasis. Some surgeons pack this area with Surgicel; however, the author has not raised concerns for potential aspiration hazard.

Irrigation and suctioning are then performed and the mouth gag removed, thereby completing the procedure.

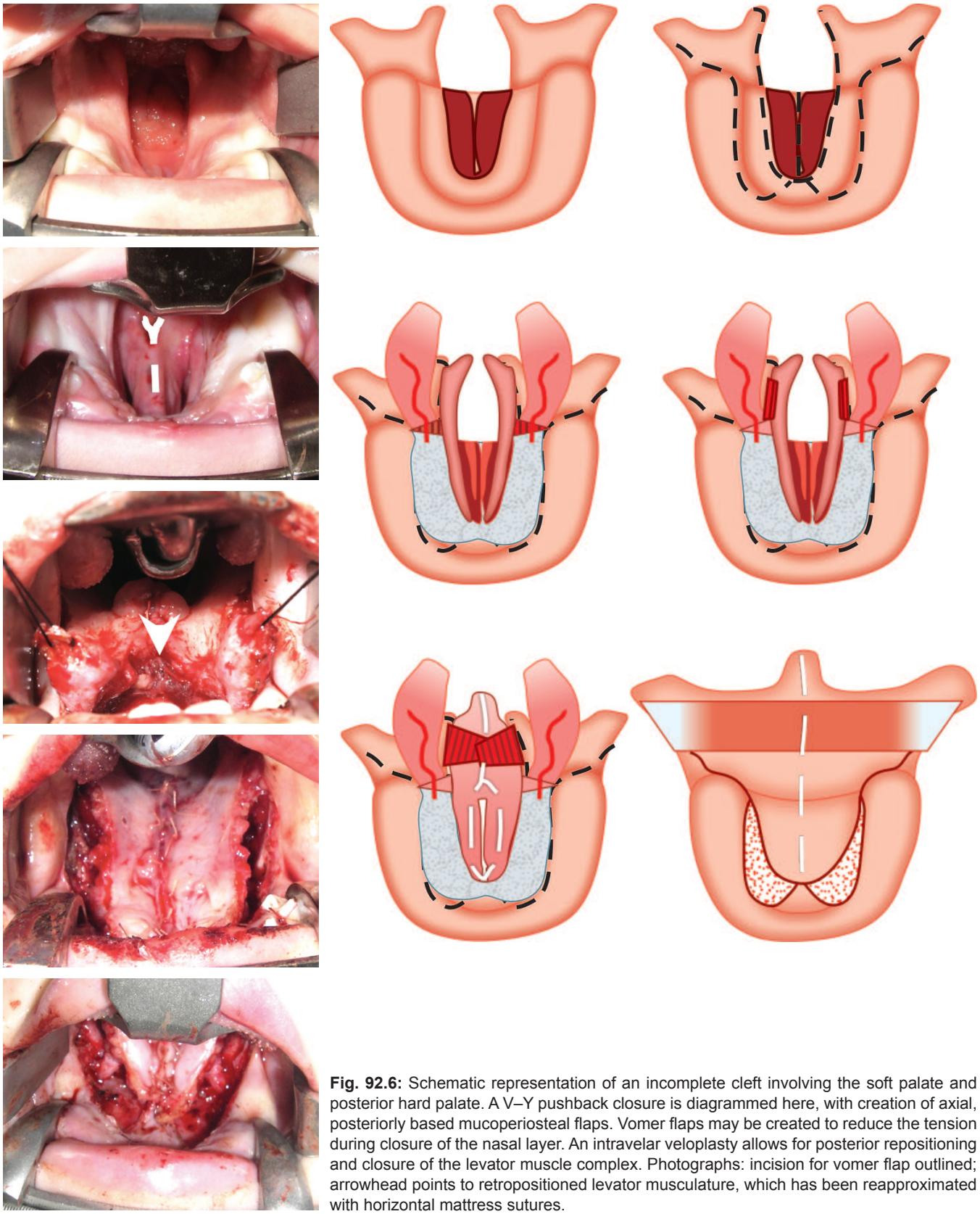


**Fig. 92.6:** Schematic representation of an incomplete cleft involving the soft palate and posterior hard palate. A V–Y pushback closure is diagrammed here, with creation of axial, posteriorly based mucoperiosteal flaps. Vomer flaps may be created to reduce the tension during closure of the nasal layer. An intravelar veloplasty allows for posterior repositioning and closure of the levator muscle complex. Photographs: incision for vomer flap outlined; arrowhead points to retropositioned levator musculature, which has been reapproximated with horizontal mattress sutures.

## Bardach Two-Flap Palatoplasty

Following injection of local anesthetic, incisions are made in a similar fashion to those described in the V–Y pushback technique. Incisions along the cleft margin are continued anteriorly to the posterior aspect of the alveolar cleft. It is the author's philosophy not to perform a gingivoperiosteoplasty at the time of initial cleft palate repair. In the case of a bilateral cleft palate, the free margins of the bony cleft are incised approximately 3 mm onto the oral surface of the cleft margin, and bilateral vomer flaps are frequently utilized. In cases of unilateral cleft lip and palate, the palate is fused to the septum on the contralateral side; however, an obvious raphe is often encountered and this landmark serves as a useful guide as where to place the medial oral cut on the noncleft side. The superiorly based septal flap is then utilized in a similar fashion to a vomer flap, allowing for a relatively tension-free closure of the nasal mucosal layer on the cleft side.

After the oral mucoperiosteal flaps have been raised and the soft palate musculature mobilized, closure takes place in a similar fashion to the V–Y pushback. In cases of complete cleft lip and palate, however, there is no residual adherent mucoperiosteum. Therefore, closure is limited to a simple reapproximation of the oral flaps and a meaningful palatal lengthening is not possible, given the fact that there is an anterior component to the palatal defect that requires coverage (Fig. 92.7). It is therefore noteworthy that there is a higher rate of palatal revision surgery in children with unilateral and bilateral complete cleft lip and palate as compared to those children with isolated cleft palate and incomplete palatal clefting alone.[18]

## Postoperative Care

For the reasons stated above, the author does not routinely use a tongue stitch postoperatively. Children are admitted for one or two nights following palatoplasty, with continuous pulse oximetry on a standard pediatric inpatient unit. Children with significant hypotonia and those with Pierre Robin sequence are usually admitted to the pediatric intensive care unit for the first postoperative night. Intravenous access is maintained until adequate oral intake is demonstrated. The author chooses to use arm restraints for the first 2 weeks in children with repaired hard palate defects in which there are anterior sutures, which could be disturbed by a wayward hand or object in the mouth. Restraints are used only for times in which the child is left unattended. The data supporting the use of arm restraints are of poor quality and multicenter studies examining the use of restraints are ongoing.

Intravenous morphine sulfate is transitioned to oral acetaminophen, ibuprofen, and tramadol, once the child is able to take oral medication. Typically, pain may be controlled with acetaminophen or ibuprofen alone by postoperative day number 2. Oral amoxicillin is given for 1 week, and a soft diet is maintained for 2 weeks.

The use of pacifier is discouraged; parental spoon-feeding and use of a valveless sippy cup are recommended. In those children who will only feed via bottle, use of a cleft feeder or high-flow nipple is permitted.

# COMPLICATIONS

Complications following cleft palate repair are relatively infrequent. However, immediate complications may include bleeding, infection, dehydration, wound dehiscence, and airway compromise. While use of a vomer flap allows for less tension on closure of the nasal layer, elevation and coaptation of the mucoperiosteal flaps from the nasal floor and septum create a midline dead space that decreases the cross-sectional area of the nasal airway.[19] Delayed complications may include fistula formation, persistent velopharyngeal insufficiency, scarring, and maxillary growth restriction. The incidence of fistula formation has been estimated from 0 to 34%, with an average around 4%.[20] Maxillary growth disturbance is significant enough to merit later orthognathic surgical intervention in nearly 25% of patients with complete cleft palate (cleft lip and palate).[21]

# OUTCOMES

The most important outcome measure in cleft palate repair is the establishment of normal speech. Nevertheless, approximately 15–20% of patients will develop speech production issues, regardless of the type of palatoplasty performed.[22]

Improved eustachian tube dysfunction is also a goal of palatoplasty; however, hearing outcomes are inconsistent even among the most experienced surgeons.

Regardless of the outcome of palatoplasty, all children with orofacial clefts should be followed by a multidisciplinary team throughout their childhood.

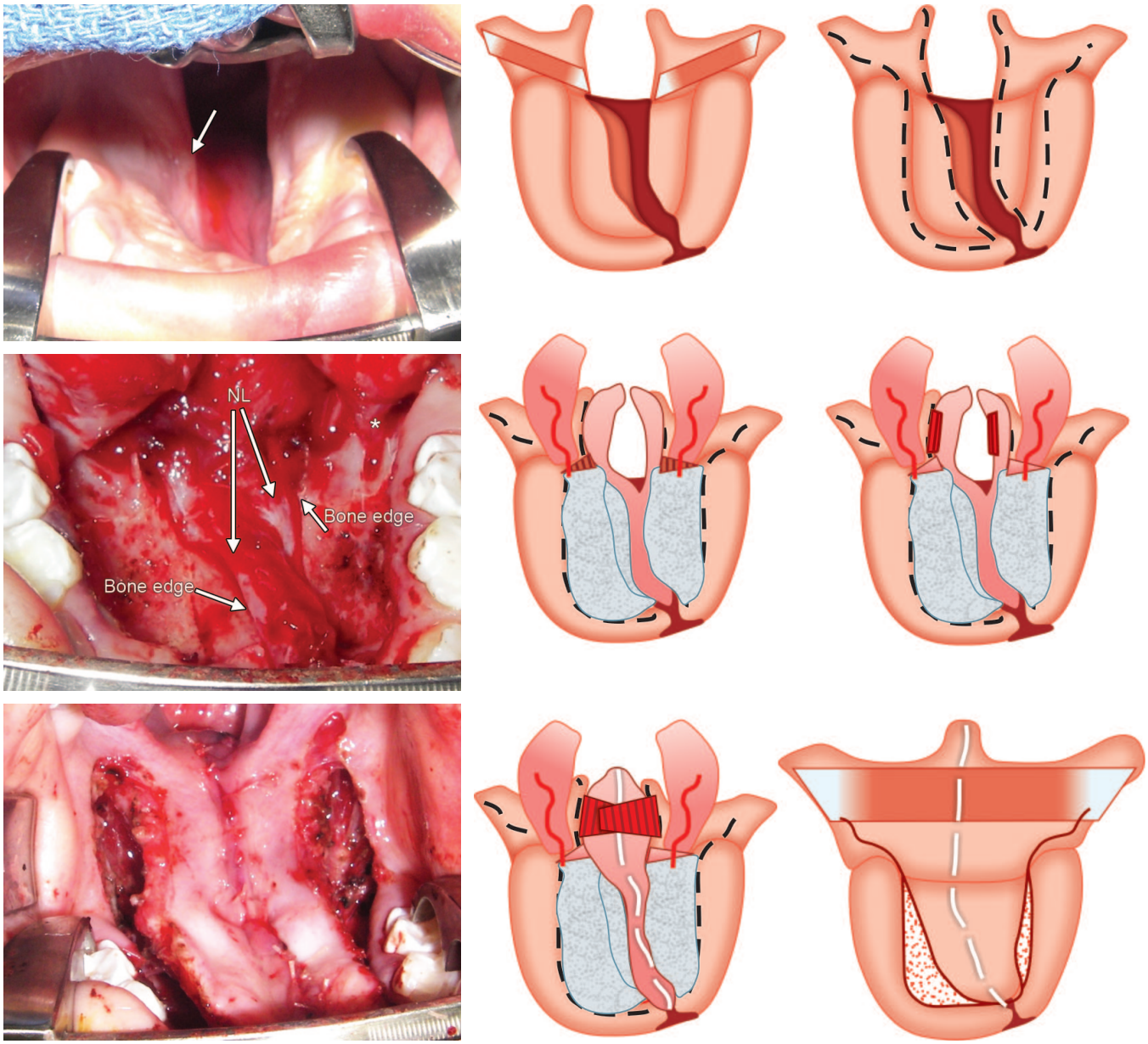



**Fig. 92.7:** Schematic representation of a complete cleft palate. Closure using a Bardach, two-flap technique is illustrated. Photographs: an arrow points to the raphe formed by the junction of the septal and hard palate mucosa. Asterisk marks vascular pedicle; NL, nasal layer after closure. Given the need for anterior tissue to close the primary palate, primary palatal lengthening may be less successful in these cases.

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CHAPTER

# 93 Evaluation and Management of the Cleft Lip

*Elias R Zgheib, Ghassan Abu Sitta, Dunia Abdul-Aziz, Derek J Rogers, Usama Hamdan*

## INTRODUCTION

Cleft lip and palate are the most common congenital craniofacial anomalies. Patients born with these anomalies face multiple problems related to the anatomic and physiologic malformations and the ensuing psychosocial issues. A multidisciplinary team approach is crucial for comprehensive cleft care. The ideal team consists of plastic surgeons, otolaryngologists, maxillofacial surgeons, orthodontists, pediatricians, speech therapists, nutritionists, child psychologists, social workers, and a team coordinator. With advancing knowledge of craniofacial disorders, including perioperative management, surgical repair, and postoperative rehabilitation, new techniques are being developed and old techniques refined to enhance outcomes.

This chapter discusses the history, embryology, etiology, anatomy, and surgical treatment of unilateral and bilateral cleft lip deformities and highlights the importance of a multidisciplinary approach in comprehensive cleft care. The goal is to achieve optimal restoration of form and function of the combined lip, maxillary, and nasal abnormality. In this endeavor, intervention from multiple medical specialties across many years may be necessary. To this end, there has not been a unified agreement on the optimal approach and timing of interventions. An overview of the historical underpinnings to currently used methods for surgical repair of the cleft lip is provided, as well as the author's approach to the correction of unilateral and bilateral clefts lip defects. The nuances of the techniques along with the consequences of inadequate repair are also reviewed.

## EMBRYOLOGY

The head and neck structures develop during the third and eighth weeks of gestation and are derived from the five paired branchial arches, the derivatives of vertebrate gills. This process, detailed below, relies on mesenchymal migration and fusion of the paired somite derived facial elements. Failure of fusion of different elements results in various forms of clefting. By the third week of gestation, the mesoderm involved in facial development (a separate kind of tissue of ectodermal origin) starts to differentiate. Simultaneously, the ectoderm of the neural plate folds on itself to form the neural tube. During the formation of the neural tube, neural crest cells differentiate from the ectoderm and separate the neuroectoderm from the cutaneous ectoderm. These neural crest cells have properties associated with both ectoderm and mesenchyme and are thus termed ectomesenchyme.[1]

The ectomesenchyme migrates between the planes of the mesoderm, ectoderm, and endoderm anteriorly into the regions that will eventually form the five facial processes (Fig. 93.1).[1] This migration pattern is controlled by mediators in the local tissue environment.[2] Failure and/or abnormal migration patterns are responsible for clefting of the lip, palate, and the face.

During the fourth week of gestation, a facial precursor forms from the five processes. First, the frontonasal process evolves and develops over and anterior to the growing brain. The paired maxillary and mandibular processes grow simultaneously and develop around the branchial arches and the stomodeum. The stomodeum is the primitive mouth and is formed cephalad by the

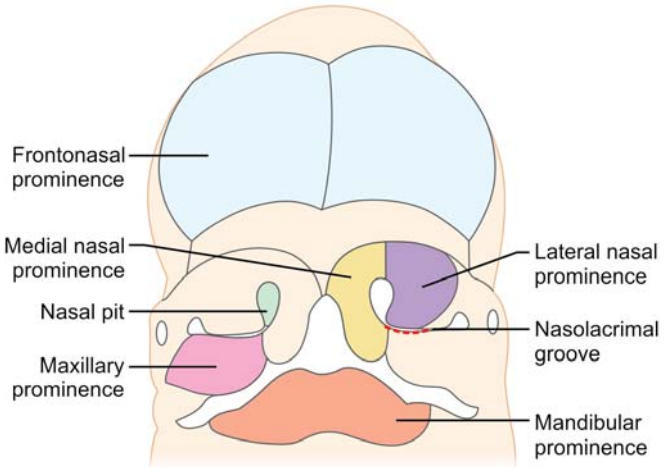



**Fig. 93.1:** Five facial processes.

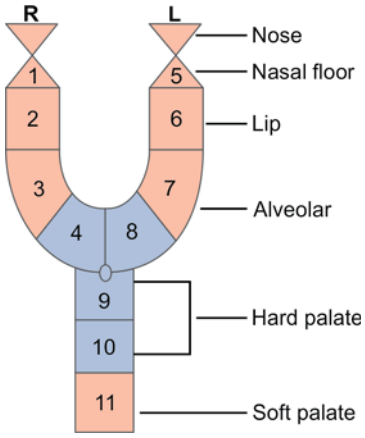



**Fig. 93.2:** Millard's modification to Kernahan's striped 'Y' classification (adapted from Millard, 1976).

frontonasal prominence, caudally by the paired mandibular prominences, and laterally by the paired maxillary prominences.[2]

During the fifth week of gestation, the frontonasal process develops prominences called nasal placodes. These placodes in turn form pits that are surrounded by medial and lateral nasal prominences. Once the embryo reaches the sixth week of gestation, the maxillary prominences grow medially and fuse with the formed medial nasal prominences. At the same time, these nasal prominences fuse to form the philtrum, premaxilla, and the primary palate. Simultaneously, the secondary palate is formed by the fusion of the maxillary prominences (Fig. 93.1).[2] Of note, the development of the primary palate (lip and palate anterior to the incisive foramen) differs from the secondary palate (palate posterior to the incisive foramen).

Failure of both the medial nasal and maxillary prominences to fuse and the degree of abnormal fusion leads to a range of clefting of the palate and lip.[2]

Two main theories have been proposed in the pathogenesis of clefting:

- *Classical theory* proposed by Durscy[3] and His[4] assumes closure of the processes in a similar manner to normal wound healing through direct fusion of the ectodermal and mesodermal elements. According to this theory, cleft lip results from abnormal or lack of fusion between the fused maxillary and lateral nasal prominences with the medial nasal prominence
- *Mesodermal penetration theory* proposed by Pohlmann,[5] modified by Veau,[6] and popularized by Stark[7] postulates that the upper lip consists of mesoderm that is sandwiched by two layers of ectoderm. The mesoderm migrates between the two layers of the ectoderm and reinforces the ectoderm at different points during its route. According to this theory, cleft lip results from the lack of mesodermal involvement and consequent epithelial breakdown and separation.

It is most likely that the classical theory explains the formation of the secondary palate, whereas the mesodermal penetration theory relates more to the formation of the primary palate. Nevertheless, neither theory is sufficient to completely explain the formation of different craniofacial clefts, such as the lateral oro-ocular clefts, that are present in an area where no embryologic facial groove exists.

## CLASSIFICATION

The first classification of cleft lip was published in 1962 by the Nomenclature Committee of the American Association of Cleft Palate Rehabilitation.[8] However, it was abandoned due to its complexity. At the time, Kernahan had suggested a simplistic 'Y' classification that he modified in 1971 and named the 'Striped Y.'[9] Kernahan's striped 'Y' classification provides a common framework in outlining the extent of the cleft.[9] This classification system was subsequently modified by Millard and others to address the extent of associated nasal deformities (Fig. 93.2).[10,11]

## EPIDEMIOLOGY

The incidence of cleft lip is variable across race, gender, socioeconomic status, and influenced by family history.

**Table 93.1:** Cleft epidemiology

| *Ethnicity* | *Incidence of CL+/- CLP per live births* |
|---|---|
| Overall | 1 in 1,000 |
| Asian | 1 in 500 |
| Caucasian | 1 in 750–1,500 |
| African | 1 in 2,000 |
| Cleft lip alone | 1 in 2,000 (constant among races) |

Modified from Fraser.[12]

**Fig. 93.3:** Family with bilateral clefts and pits.

*Race*: There appears to be a racial heterogeneity in the incidence of cleft lip and palate (CL and CLP) that is not present in cleft palate (CP) alone. Table 93.1 illustrates the incidence between people of different races.[12]

*Gender*: CLP is twice as common in females than in males (F:M = 2:1).[13]

*Socioeconomic status*: A higher incidence of clefts occurs in lower socioeconomic classes and is partly attributed to the mother's poor nutritional status and vitamin deficiency.[14]

*Occurrence of clefts*: The incidence of CLP is two times the incidence of isolated cleft lip (CLP:CL = 2:1). Cleft lip and palate consists of 46% of the cases, cleft palate 33%, and isolated cleft lip 21% (CLP > CP > CL). In addition, a left cleft is two times more frequent than a right cleft and six times more abundant than a bilateral cleft (L cleft > R cleft > bilateral = 6:3:1). Finally, 3% of CLP patients are syndromic.[15,16]

*Familial occurrence*: Once a child with a cleft is born, the likelihood of having a second child with a cleft increases. Table 93.2 illustrates the incidence that varies with the number of siblings having the defect (Fig. 93.3).

**Table 93.2:** Familial occurrence

| *Family members with CP* | *Probability of next child with CP (%)* | *Probability of next child with CLP (%)* |
|---|---|---|
| One sibling | 2 | 4 |
| One parent | 2–4 | 2–4 |
| One child and a positive family history | 7 | 7 |
| Two children and unaffected parents | 1 | 9 |
| One affected parent and one affected child | 15 | 14–17 |

## ETIOLOGY

The etiology of cleft lip deformity, with or without cleft palate, is multifactorial, with both genetic (primarily autosomal dominant, with some X-linked factors) and environmental elements.[17] More specifically, factors that affect the incidence are as follows:

- *Parental age*: A higher incidence of clefting is encountered in parents over the age of 30 years with the father's age being a more important factor[18]
- *Medications*: Several medications have been linked to an increased risk of CLP, such as phenytoin, methylprednisolone and other steroids, phenobarbital, diazepam, and isotretinoin[19,20]
- *Smoking*: Tobacco use and exposure have been linked to increased risk of clefts[21]
- *Maternal diabetes*: This is associated with an increased risk for clefts of the lip and palate[22]
- *Infections*: Perinatal infections, especially rubella and toxoplasmosis, are associated with an increased risk for cleft deformities[23]
- *Nutritional deficiencies*: dolic acid and vitamin B6 deficiencies are associated with an increased risk of cleft palate[24]
- *Syndromes*: Cleft deformities are associated with a large number of syndromes. The incidence of associated congenital deformities varies from 8% to 45%, with orthopedic, cardiac, and neurological being among the most frequent.[25] The incidence seems to be highest in bilateral CLP deformities and lowest in isolated cleft lip deformities.[25]

**Table 93.3:** Treatment timeline

| *Timing* | *Treatment timeline* |
|---|---|
| Prenatal | Diagnosis |
| Newborn | Multidisciplinary |
| 0–3 months | Presurgical infant orthopedics |
| 3–5 months | Cleft lip repair |
| 12 months | Cleft palate repair and myringotomy tubes |
| 1 year to school age | Speech rehabilitation, palate lengthening or pharyngoplasty, speech obturator |
| School age | Treatment of secondary cleft deformities |
| 7–9 years | Alveolar bone grafting |
| Postalveolar graft | Presurgical orthodontics |
| Puberty | Definitive rhinoplasty |
| Skeletal maturity | Orthognathic surgery |
| Birth-adulthood | Psychosocial (continuous patient and family support) |

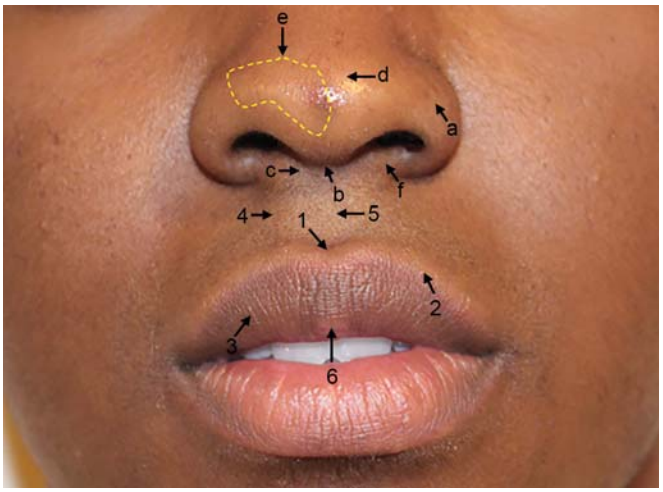



**Fig. 93.4:** Normal lip anatomy.

## MULTIDISCIPLINARY APPROACH TO CLEFT CARE

The approach to the treatment of patients with CLP requires specialized and coordinated efforts from multiple medical and surgical specialties to optimize treatment outcomes. The cleft patient faces many difficulties after birth, including feeding problems, speech difficulties, and orthodontic and craniofacial challenges. In addition, psychosocial challenges and pressures affect both the patients and their families.

Typical members of a cleft team include audiologists, dentists, nurses, dietitians, cleft surgeons, otolaryngologists, pediatricians, psychologists, speech pathologists, and social workers. The goals of the multidisciplinary team approach are to maximize the efficiency of the treatment and provide a supportive environment for the patient and the caregivers. Table 93.3 summarizes the multidisciplinary approach at different stages of cleft care.

## ANATOMY

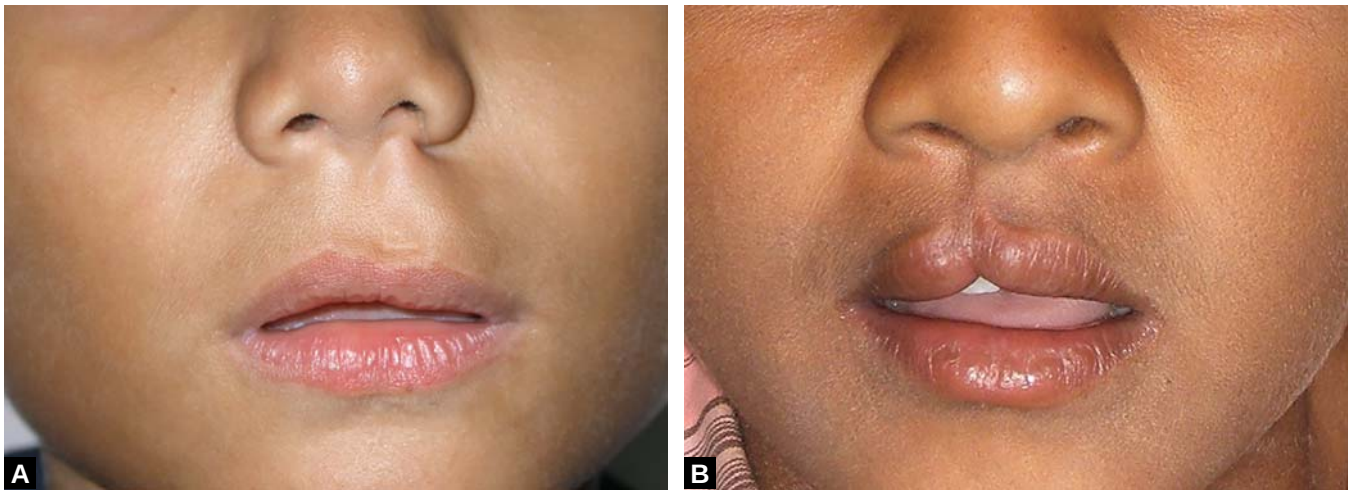
The main anatomical landmarks of the upper lip include (Fig. 93.4):

- *Cupid's bow*: With its two high points and one low point
- *Vermilion border*: The three-dimensional and well-demarcated line at the junction of the white and red part of the upper lip. It is devoid of any hair follicles
- *Vermilion*: The red part of the upper lip overlying the orbicularis oris muscle and consisting of a dry mucosa
- *Philtral ridges*: The two elevated structures originating from the base of the medial crural foot plates and ending at the respective high points
- *Philtral dimple*: The slight midline depression in the skin part of the upper lip between the two philtral ridges
- *Philtral tubercle*: The midline fullness of the vermilion part of the upper lip
- *Orbicularis oris muscle*: Divided into superficial and deep portions as described by Nicolau in 1983.[26] The deep component originates at the modiolus, lies close to the mucosal surface, works with the other muscles of the oropharynx, and captures food in a sphincteric motion. The superficial component works with the other facial muscles in relaying facial expressions.[26]

The main anatomical nasal landmarks include (Fig. 93.4):

- *Ala nasi*: Devoid of cartilage expect for minimal sesamoid pieces of cartilage in its most lateral aspect right over the alar valve area. The alar crease separates the alar lobule from the lateral crus of the lower lateral cartilage
- *Columella*
- *Columellar-labial angle*: The line separating the columella from the upper lip skin
- *Nasal tip*: Defined by the two domes of the lower lateral cartilages
- *Lower lateral cartilages*: Lateral crura, domes, transverse crura, medial crura, and medial crural footplates.
- *Nostril sill*: Junction of the medial crural footplate and the medial aspect of the alar lobule.

The blood supply to the upper lip arises from the superior labial artery that anastomoses with the anterior ethmoid, posterior septal, and greater palatine arteries. The motor innervation stems from the buccal and zygomatic branches of the facial nerve (CNVII), and sensation




**Figs. 93.5A and B:** (A) Microforme (very mild form): abnormal insertion of orbicularis oris muscle on left side and asymmetrical Cupid's Bow; (B) Microforme (more apparent orbicularis oris muscle deficiency).


**Figs. 93.6A and B:** (A) Incomplete cleft lip with some orbicularis oris muscle decussating along the upper border; (B) Incomplete cleft lip with Simonart's band and no muscle decussation.

is through the infraorbital branch (V2) of the trigeminal nerve (CNV). Sensory innervation to the nasal tip is through the infraorbital branch (V2) and external nasal branch of the ophthalmic nerve (V1).[27]

## UNILATERAL CLEFT LIP

### Classification

Cleft lip deformities are divided into the following:

- *Microform (forme fruste)*: Defect is predominantly limited to the lip, defined by a notched vermilion. The orbicularis oris muscle is partially intact. There is no involvement of the nasal sill or alveolus (Figs. 93.5A and B)
- *Incomplete*: More extensive defect in the vertical lip but with an intact nasal sill (Simonart band) and alveolus (primary palate). Associated nasal deformity is common secondary to the vertical lip deficiency (Figs. 93.6A and B)
- *Complete*: Defect of the lip that extends into the nasal sill. The cleft involves the lip, alveolus, and nose and often occurs in association with a secondary cleft palate (Fig. 93.7).

### Anatomy

The cleft lip and associated nasal deformities have a wide spectrum of anatomical disruptions, including the following (Figs. 93.8A and B):

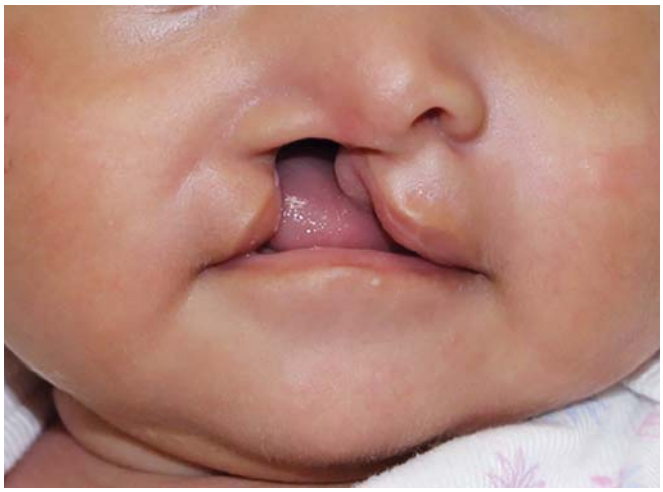
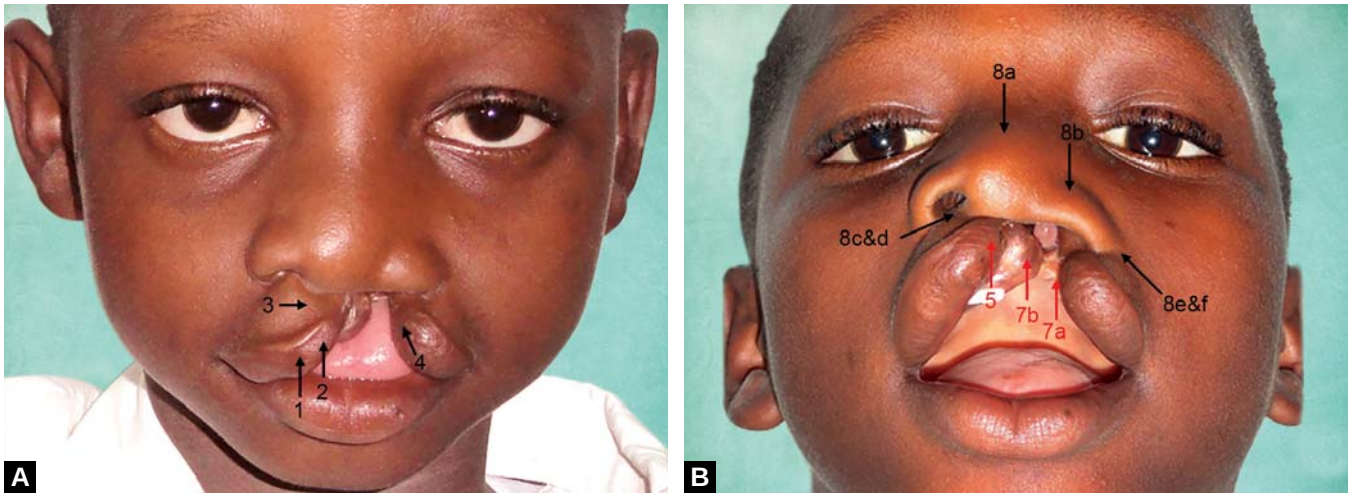


**Fig. 93.7:** Complete cleft lip.




**Figs. 93.8A and B:** Cleft lip-nasal anatomy.

- Asymmetric Cupid's bow with the high point on the cleft side being higher than the noncleft side
- The three-dimensional vermilion border on the cleft side is rotated superiorly and turns into a flat two-dimensional line as it courses into the alar base
- The philtral ridge on the cleft side is short and contracted
- Abnormal insertion of the orbicularis oris muscle into the alar base on the cleft side
- The orbicularis oris muscle on the noncleft side inserts into the base of columella and the nasal spine, with the abnormal insertion of some of the fibers extending onto the alar base laterally.

In some incomplete cleft lips where the cleft deformity is minimal, the superior fibers of the orbicularis oris muscle might decussate across the intact part of the upper lip (Fig. 93.6A). However, the deficiency in the orbicularis oris muscle is quite evident, more so in those incomplete clefts with only Simonart's band (Fig. 93.6B).

- In complete clefts:
  - A degree of maxillary hypoplasia is evident on the cleft side in the area of the piriform aperture
  - Anterior rotation of alveolar ridge and primary palate on the noncleft side and inward rotation on the cleft side.
- The associated cleft nasal deformity includes:
  - Poor tip definition
  - Lower lateral cartilage deformity on the cleft side, including the following:
    - Outstretched and thinned lateral crus on the cleft side

    - Short or absent outflaring on the medial crural footplate
    - Depressed dome.
  - Short columella that is rotated to the noncleft side with poor tip support
  - Septal deviation toward the noncleft side
  - Asymmetry of nasal axes
  - Laterally displaced alar lobule on the cleft side.

## Objectives

The building block of any successful cleft lip repair is the orbicularis oris muscle. Regardless of the type and degree of the cleft deformity, proper release, and alignment of muscle fibers are essential for restoring normal anatomic appearance and physiological function. Correct realignment of the orbicularis oris also enhances the outcome of nasal repair by minimizing the lateralizing forces on the alar lobule during the postoperative phase (Fig. 93.9).[28] Primary cleft lip rhinoplasty has become an integral part of the initial surgical repair, enhanced by better understanding of the nasal anatomy and improved surgical techniques. By restoring nasal symmetry and allowing a more natural growth of the nasal structures, the extent of the secondary rhinoplasty after puberty is minimized (*see* Fig. 93.37B). Meticulous repair should be directed toward achieving lip and nasal symmetry and function:

- *Lip symmetry*:
  - Cupid's bow symmetry both vertically and horizontally. The distance between the two high points and the low point should be matching as well as the distance between the high points and the nostril sills
  - Philtral ridge symmetry
  - Slight philtral dimple depression between the two philtral ridges
  - Philtral tubercle fullness
  - Smooth continuity and fullness of the orbicularis oris muscle, especially throughout its vermilion component without any deficiency at the repair line
  - Well aligned wet–dry vermilion line.
- *Lip function*: A well-repaired orbicularis oris muscle will enhance both the expressive and sphincter function of the lip.
- *Nasal symmetry*: This is achieved by the following:
  - Repositioning the lower lateral cartilage on the cleft side

**Fig. 93.9:** Pre- and postlip repair and primary rhinoplasty.

  - Enhancing nasal tip definition
  - Repositioning the alar base and maintaining matching lobule thickness and vertical heights
  - Enhancing columellar and domal tip support
  - Restoring nostril axes' symmetry and nostril width
  - Correcting any redundancy in the anterior soft tissue angle
  - Preserving integrity of the alar valve and nasal function.

## Preoperative Considerations

### *Indications*

Patients born with cleft lip with or without cleft palate are candidates for cleft lip repair once they have received full preoperative clearance for surgery and have met the appropriate age, weight, and hemoglobin level requirements.

### *Preoperative Workup*

Patients should undergo full preoperative evaluation by a pediatrician and pediatric anesthesiologist to ensure that there are no contraindications for general anesthesia.

### *Presurgical Infant Orthopedics*

The aim of presurgical infant orthopedics (PSIO) is to reduce the size and severity of the cleft prior to the first surgical lip repair. These techniques include lip taping, nasoalveolar molding (NAM), Latham appliance, and surgical lip adhesion. They can be implemented at birth or within the first few weeks of life.

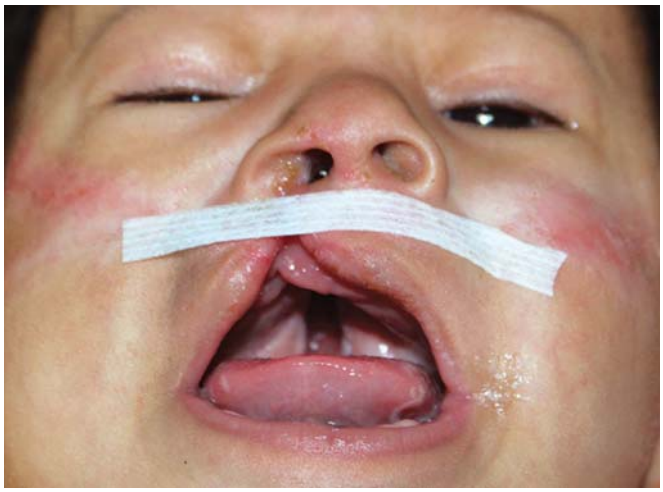


**Fig. 93.10:** Lip taping.

Lip taping and passive intraoral devices are easy techniques that are used in the absence of other more advanced methods. Lip taping entails taping both edges of the lip together under a certain degree of tension with the aim of narrowing the gap across the cleft (Fig. 93.10). On the other hand, passive intraoral appliances do not actively close the alveolar clefts; rather, they prevent the tongue forces from further displacing the palatine shelves laterally.

Other methods utilize active expansion of the palatine shelves and active closure of the alveolar cleft. Use of the Latham appliance entails the insertion of a pin retained device at an average age of 2 months for a period of 3 to 4 weeks prior to the lip repair. However, it does not address the nasal cartilage or the columellar deformity.[29]

Nasoalveolar molding is a more advanced method that utilizes an appliance that actively approximates the distant alveolar segments and molds the nasal cartilages, facilitating tension-free closure of the lip during the surgical repair (Figs. 93.11A to D). It can also help with centering and lengthening of the deviated columella. The first NAM impression is taken at 1 week of age, and NAM therapy is initiated during the second week. Although this technique is not available in most cleft centers, we recommend its use based on improved outcomes and experience where trained specialists (craniofacial pediatric dentists, orthodontists, and prosthodontists) can provide such care and close follow-up.[28,30–32]

Surgical lip adhesion entails the surgical approximation and suturing of the lip edges without any muscle repair. It is performed at 6–8 weeks of age to facilitate tissue approximation at the time of the definitive repair. It has fallen out of favor due to inconclusive evidence supporting its benefit but is still used by some surgeons to approximate the soft tissues in patients with wide clefts.[26]

### *Timing of Repair*

While optimal timing of repair is controversial, most surgeons perform unilateral lip repair at approximately age 10–12 weeks. The rule of 10's (hemoglobin 10 g/dL, weight 10 lbs, and 10 weeks of age), proposed by Wilhelmsen and Musgrave,[33] is used as a reference that considers the anesthetic complications of general anesthesia on infants and proposes the preferred time of repair when the benefits outweigh the risks. Although there are some reports of surgical repair within the first 1–9 weeks of life for very selective group of patients, the authors believe that attempts for surgical repair under 10–12 weeks of age is not advisable, especially due to potential short- and long-term higher risks for neonates undergoing general anesthesia and limited evidence of exceptional neonatal lip repair outcomes.[34–37]

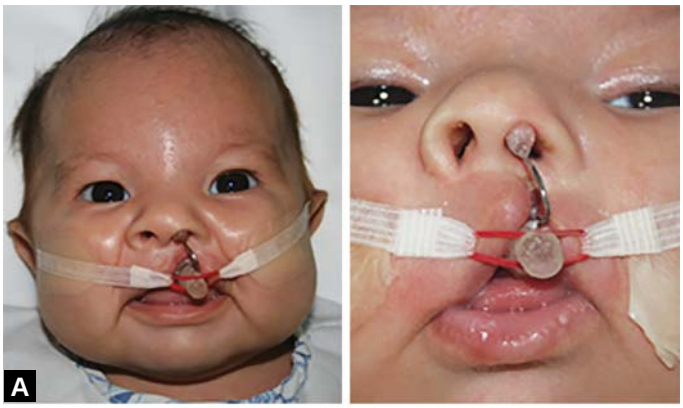
Table 93.4 summarizes the timing of the different interventions and patient follow-up.

## Surgical Repair

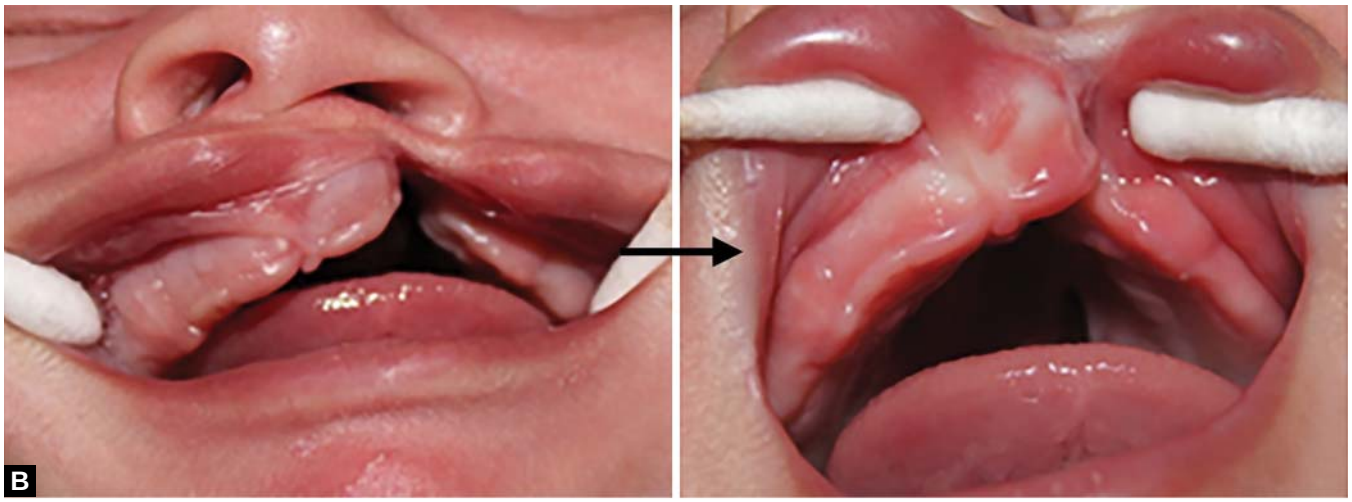
### *History and Background*

Historically, the repair of the cleft lip defect has evolved from straight-line closure to complex geometric rearrangements of tissue. Hippocrates and Galen are accredited with the first mention of "lagocheilos" (harelip). The first cleft lip closure was performed in China by an unidentified physician in 390 AD.[38] An illustration of the cleft deformity and potential repair via straight-line closure can be traced to Pare's writings about "Bec de Lievre" ("Hare Lip") in the 16th century. This technique was the basis for cleft lip repair until the 19th century.

The use of geometric tissue rearrangement in the repair of unilateral cleft lip was first introduced by Mirault in 1844, who described the insertion of a triangular flap from the lateral side into the medial side of the cleft to achieve lip lengthening.[39] The introduction of the lateral flap to fill the lip defect served as the basis for subsequent closure techniques. In 1848, Hagedorn applied the Z-plasty technique and used a rectangular flap, rather than a triangular flap, to lengthen the cleft lip. Tissue rearrangement has revolutionized the modern day management of cleft lip defects, and many modifications




NAM appliance in place with both components:
1. Nasal stent to help lift and shape the nose for symmetry and from
2. Intraoral component that helps close and reduce the alveolar cleft




Note the closure of the cleft with the alveolar segments in contact prior to surgery

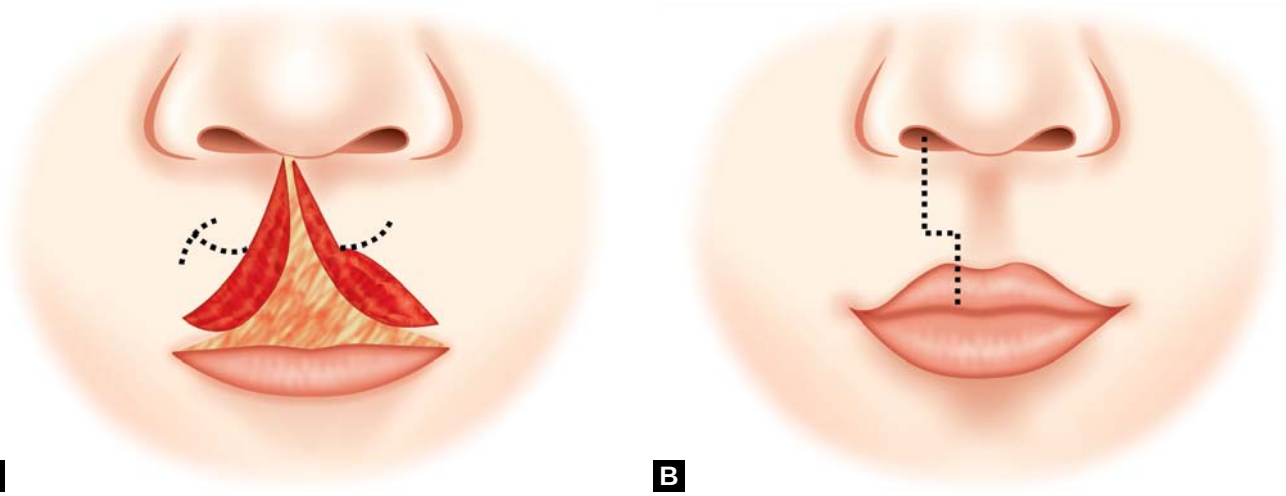

Note the change in the affected left side of the nose: Increased in height, shape and form to a more normal, symmetrical position

Before and 1 years after NAM therapy and cleft lip repair

**Figs. 93.11A to D:** (A) NAM appliance; (B) Pre- and post-NAM therapy. Note significant narrowing of alveolar defect; (C) Pre- and post-NAM therapy. Note columellar lengthening and improved tip definition; (D) Pre- and 1 year post-NAM therapy and lip repair.

**Table 93.4:** Timing of multidisciplinary care

| *Procedure* | *Age* |
|---|---|
| First appointment | Diagnosis made in utero or at birth |
| Presurgical orthopedics | 2–4 weeks |
| Primary unilateral lip and nasal repair<br>Primary bilateral lip and nasal repair | 10–12 weeks<br>3–5 months |
| Palate repair and myringotomy tubes (if needed) | 9–12 months |
| Speech assessment and therapy | Preoperative assessment and therapy initiated 6 weeks after palate repair (patient dependent) |
| VPI surgery | 5–8 years (if present) |
| Delayed orthodontics | Perialveolar bone grafting |
| Alveolar bone grafting | Starting 8 years |
| Secondary nasal repair | 5 years and older |
| Orthognathic surgery | Adolescence (16+ in females, 18+ in males) |
| Adult rhinoplasty and genioplasty | Adulthood |



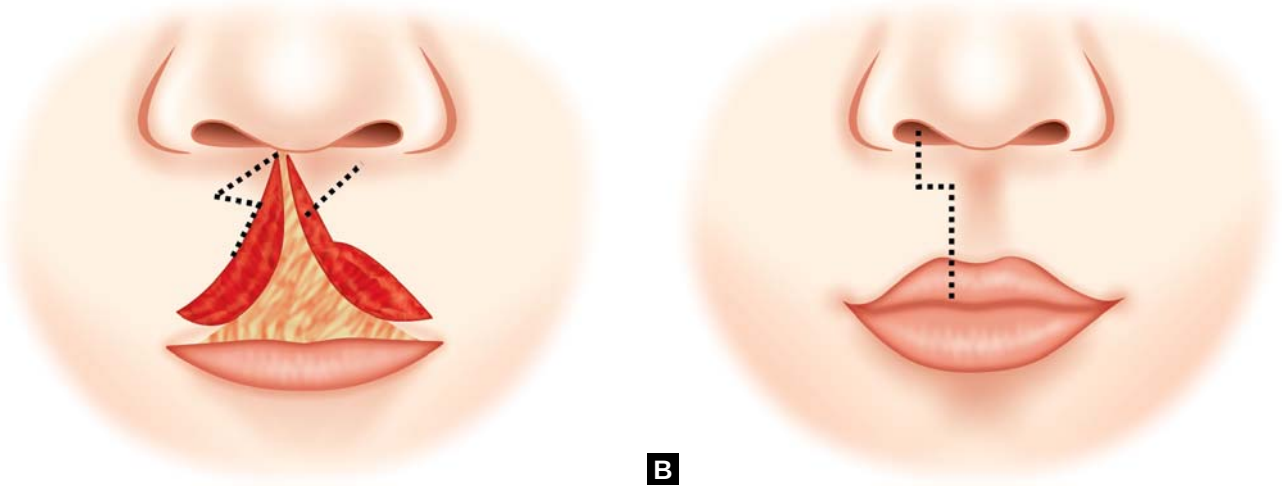

**Figs. 93.12A and B:** Le Mesurier technique.

have been proposed, including Arthur Baker, Le Mesurier's quadrilateral flap repair (Figs. 93.12A and B), Tennison's triangular flap (Figs. 93.13 A and B), and Millard's rotation advancement flap (Figs. 93.14A and B). All aim to bring in tissue to the deficient side and orient it to achieve lip lengthening.

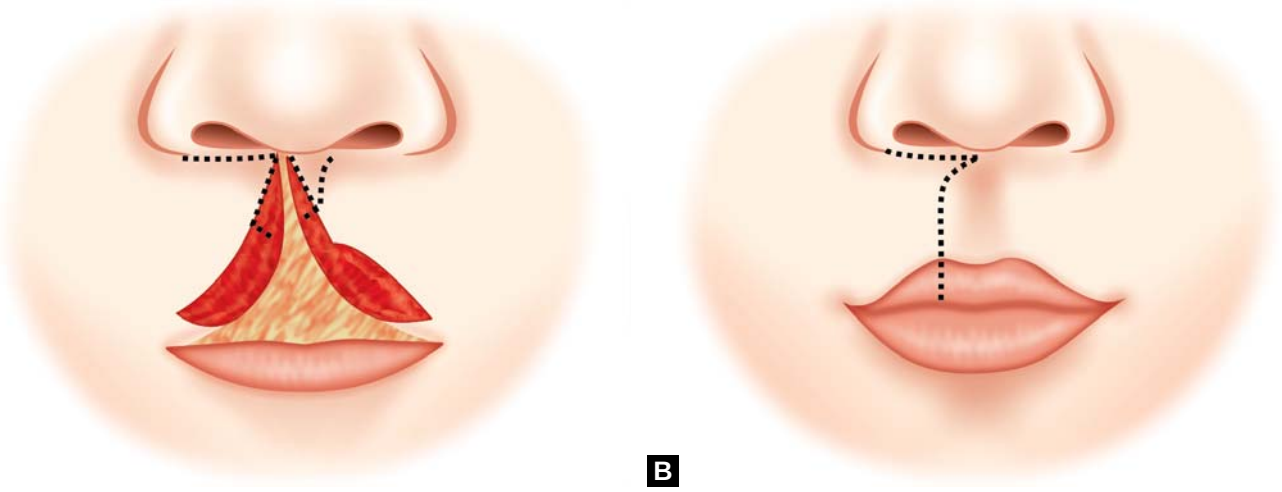
In 1955, Millard[40] presented his rotation-advancement technique for repair of unilateral cleft lip at the First International Congress of Plastic Surgery in Baltimore. Unlike previous techniques, Millard used an advanced lateral flap (cleft side), coupled with a rotation of the medial segment caudally. His technique preserved Cupid's bow and the philtral dimple, placed the tension of the closure under the alar base, transformed the incision from a straight line into a Z line, reduced alar flaring, and helped in the molding of the underlying alveolar process. Following Millard, several techniques were proposed by Davies,[41] Skoog (Fig. 93.15),[42] Wynn,[43] and Trauner.[44] These techniques involved the use of multiple triangular flaps. In spite of multiple proposed modifications, Millard's technique remained the most popular and the most widely used.

## *Surgical Techniques*

Unilateral cleft lip repair can be divided into straight-line repair, triangular flap repair, and rotation-advancement




**Figs. 93.13A and B:** Tennison's technique.




**Figs. 93.14A and B:** Millard's technique.

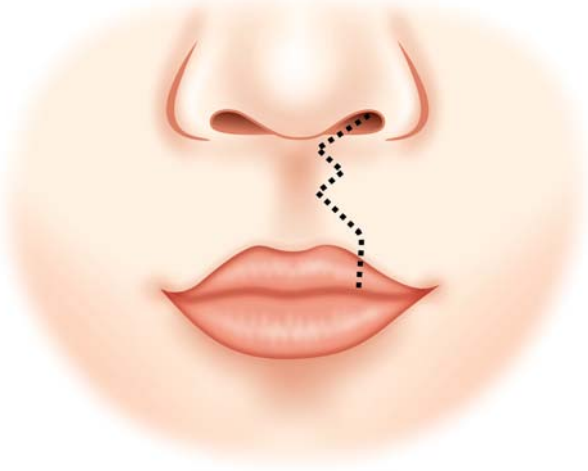


**Fig. 93.15:** Skoog's technique.

repair, with various modifications using the Z-plasty technique.[45] Few studies are available to compare the different types of repairs, but the Tennison-Randall and Millard techniques remain the most popular.

### *Straight-line repair*

Introduced by Thompson in 1912 this technique is currently used for minor residual vermilion border deficiencies (Fig. 93.16).[46]

### *Triangular flap repair (Tennison-Randall)*

Originally described by Tennison (Figs. 93.13A and B) and later modified by Randall[47] (Fig. 93.17) in 1959, the triangular flap repair remains a popular technique

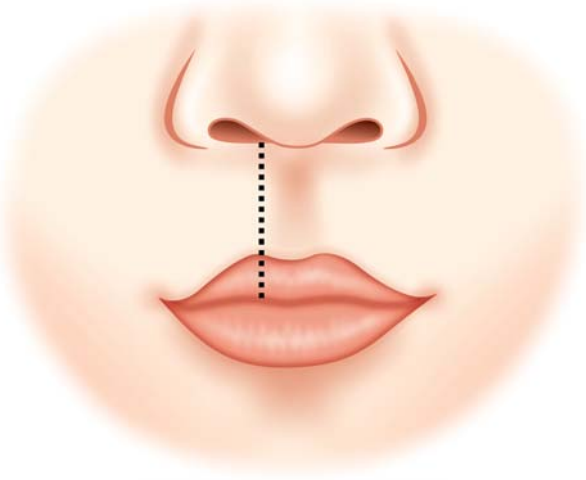


**Fig. 93.16:** Linear repair.

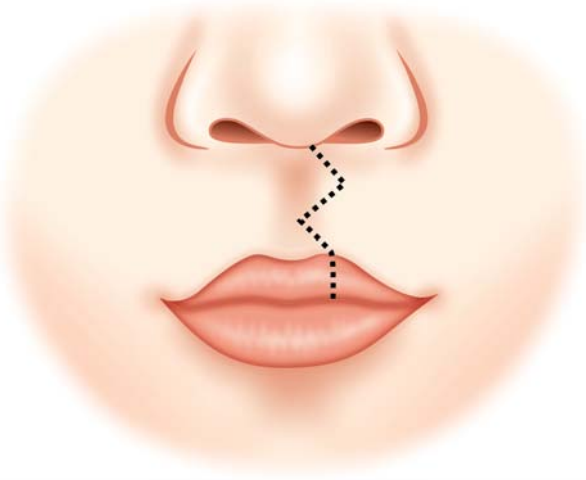


**Fig. 93.17:** Tennison-Randall technique.

**Table 93.5:** Comparison of Tennison, Millard, and Mohler techniques

| *Procedure* | *Indications* | *Advantages* | *Disadvantages* |
|---|---|---|---|
| Millard | Unilateral clefts | Minimal tissue discarded<br>Some incision lines hidden in nostril sill, alae, lower philtral column<br>Preserves Cupid's bow & philtral dimple<br>Addresses alar base repositioning | Lip short due to under rotation<br>Tension across repair of wide clefts<br>May have constricted nostril on side of repair |
| Tennison–Randall | Unilateral clefts, preferred for wide clefts | Adapts to wide and narrow clefts<br>Preserves Cupid's bow<br>Good lip length<br>Treats nasal deformity<br>Minimal soft tissue dissection<br>Easy to learn | Scar crosses the philtrum<br>Needs the incisions to be precise<br>Flattening of the philtral dimple<br>Late lengthening of the vertical lip component |
| Mohler | Unilateral clefts | Minimal tissue discarded<br>Incision lines hidden in columella minimizing alar base skin incisions | Does not transpose a lateral advancement flap to fill the defect created by the downward rotation of the medial lip element |
| | | Places the back cut used to rotate the medial lip element at the base of the columella instead of the upper lip<br>Addresses alar base repositioning | Lip width significantly increased with time<br>Lip width significantly smaller on the cleft side postoperatively |

currently utilized. A triangular skin incision is placed directly above the vermilion border with a goal of minimizing the possibility of a postoperative scar contracture resulting from a straight-line or curvilinear closure. Its advantages and disadvantages are compared to Millard's technique in Table 93.5.

### *Rotation-Advancement Repair (Millard)*

The rotation-advancement flap technique was described by Millard in 1968 (Figs. 93.14A and B) and is still one of the most commonly used methods for unilateral cleft lip repair with several ensuing modifications.[48] The noncleft side of the lip is rotated inferiorly and the laterally-based triangular flap is advanced medially. The resultant upper lip scar follows the natural contour of the philtral ridge with a medial curvature into the columellar-labial angle crease.

### *Mohler Technique*

In 1987, Mohler described a modification of the Millard technique, altering the marking of the medial lip segment in the uppermost portion to allow the use of tissue from

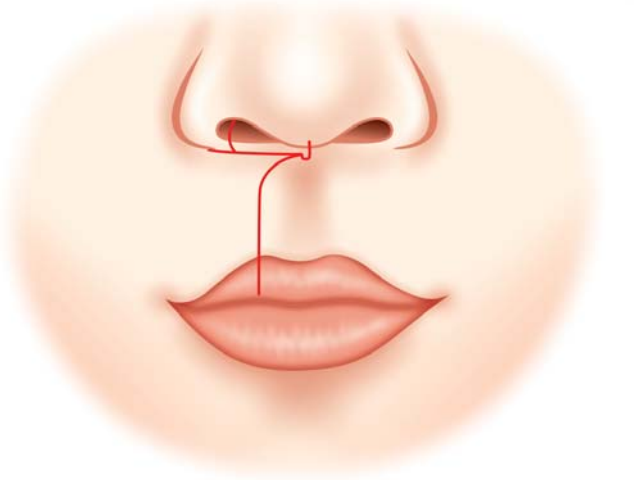
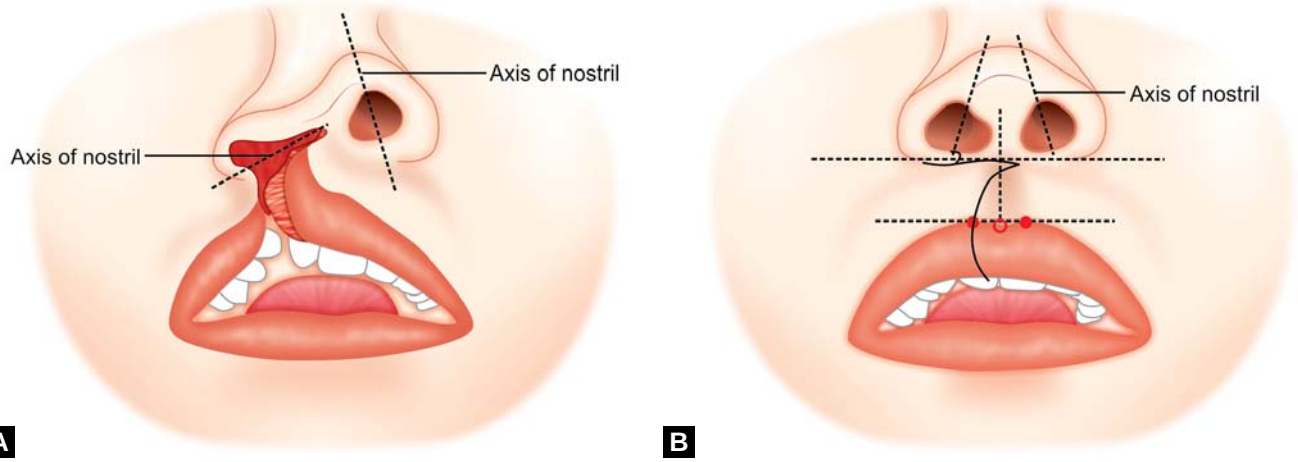


**Fig. 93.18:** Mohler's technique.




**Figs. 93.19A and B:** Goals of lip repair and primary rhinoplasty.

the columellar base (Fig. 93.18). This technique minimizes the alar base skin incisions and places the back cut used to rotate the medial lip element at the base of the columella instead of the upper lip. By placing the medial lip incision 1 mm up on the columella and three fifths along its width, it aims at positioning the upper lip scar in a direction parallel to the contralateral philtrum instead of curving across the philtral groove. It also creates a vertical scar that mirrors the noncleft philtral ridge and does not violate the philtral groove. In addition, as opposed to the Millard technique, Mohler does not transpose a lateral advancement flap to fill the defect created by the downward rotation of the medial lip element.[49]

### *Z-plasty Technique*

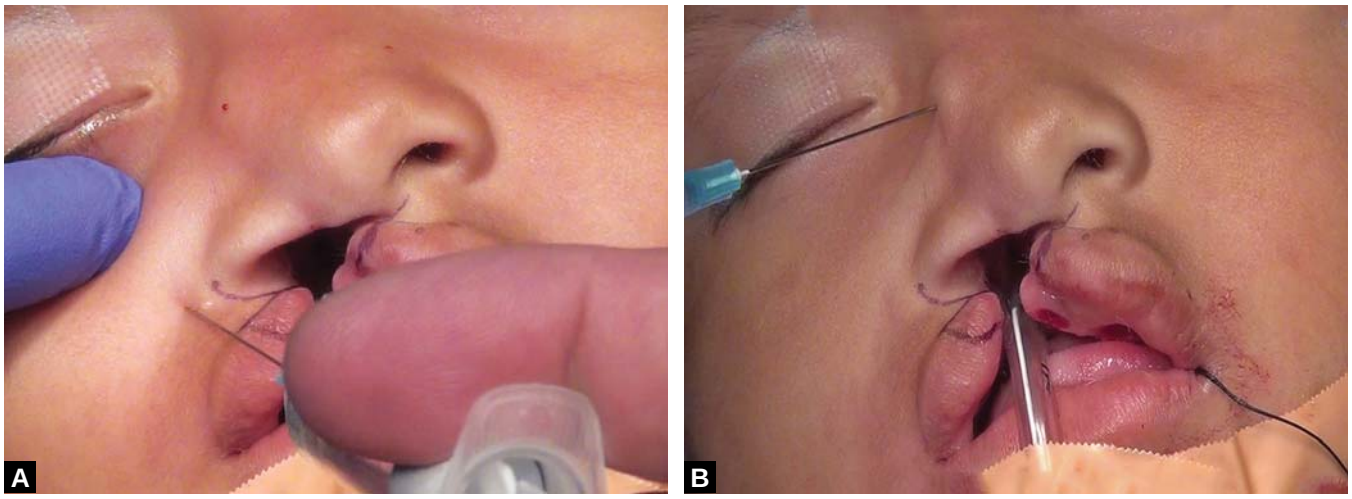
Many modifications of this technique are utilized in repairing microform cleft lips, residual lip deformities, and vermilion border and wet–dry mucosal asymmetries.

### *Hamdan Technique for Primary Repair of Unilateral Cleft Lip/Nasal Deformity*

Achieving lip and nasal symmetry and restoration of oral sphincter and nasal function are crucial for successful lip repair. The orbicularis oris muscle is the major scaffold of the lip. Residual cleft deformities will ensue if the muscle is deficient, poorly anastomosed, or not adequately freed from its abnormal insertions with potential negative implications on the outcome of lip/nasal repair. Presurgical infant orthopedics is beneficial for tension-free closure of the lip and for enhancing nasal repair.

Goals of a successful repair include (Figs. 93.19A and B):

- Nasal symmetry and adequate nasal function:
  - Symmetrical domes with adequate tip support
  - Symmetrical nostrils along their respective axes
  - Noncollapsed columella
  - Functional alar valves.




**Figs. 93.20A and B:** (A) Infraorbital nerve block; (B) External nasal nerve block.

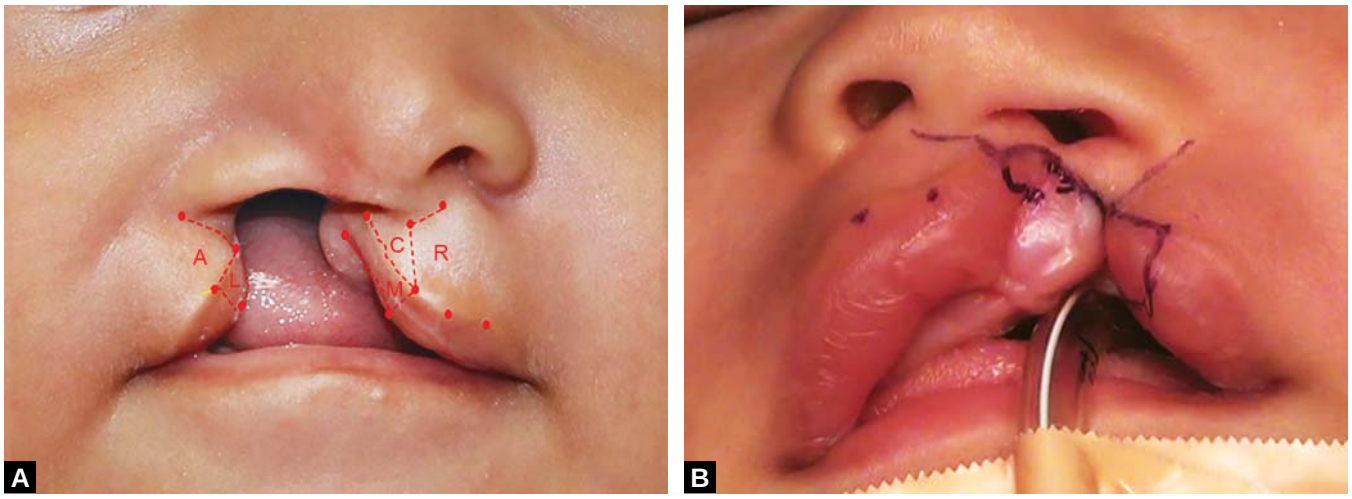
- Lip symmetry and height and fully functional orbicularis oris muscle:
  - Equidistant Cupid's bow
  - Symmetrical philtral ridges
  - Adequate philtral tubercle
  - No residual muscle deficiency along the repair line
  - No incision extending into the alar crease on cleft side.

The senior author's technique for repair of the unilateral cleft lip is a modified approach to Millard's rotation-advancement flap and utilizes the Hamdan sliding V-cheiloplasty for muscle repair and lip lengthening.[28] This technique also mobilizes the cleft side-alar base medially, thus minimizing the lateralizing vectors of healing on the ala. Careful anastomosis of the orbicularis oris muscle fibers is essential for reconstructing a fully functional muscle and also provides a natural and smooth flow of muscle fibers along the repair line.[28]

## Surgical Procedure

The same steps are followed for incomplete and complete cleft lip:

- Bilateral infraorbital and external nasal nerve blocks are performed at the beginning of the procedure to ensure adequate intraoperative and postoperative analgesia. The combination of lidocaine/epinephrine and bupivacaine/epinephrine provides analgesia up to 8 hours postoperatively, thus minimizing the need for postoperative opioids in the recovery room with their potential side effects
- Infraorbital and external nasal nerve blocks are performed (Figs. 93.20A and B). Anesthetic mixture for patients younger than 12 years of age: 1 cc/kg of 1:1 combination of 0.5% lidocaine in 1:200,000 epinephrine with 0.25% bupivacaine in 1:200,000 epinephrine
- Marking of the surgical site (Figs. 93.21 A and B): The senior author uses similar skin markings as described by Ralph Millard for rotation and advancement flaps.[11]
  - Cupid's bow low point is first marked, followed by the high point on the noncleft side. Distance between the two points is measured with a caliper and transposed to the opposite side to mark the high point on the cleft side, usually a distance of 2–2.5 mm between low and each high point
  - Rotation flap (R): marking starts at the junction of the columellar-labial angle with peak of philtral ridge on the noncleft side, follows the columellar-labial angle till its end, and then courses inferiorly toward the marked high point on the cleft side, mimicking the location of the philtral ridge
  - Columellar (C) flap is outlined by marking the skin-bearing side of the flat vermilion border as it courses from the cleft side high point towards the nose. Make sure to maximize the use of any usable skin for the (C) flap since it will be used to lengthen the columella and mimic the natural outflaring of the medial crural footplate
  - Medial (M) mucosal flap is outlined by drawing a perpendicular line in the vermilion from the cleft-side high point toward the wet–dry mucosal line. A line is then marked parallel to the lateral edge of




**Figs. 93.21A and B:** (A) Surgical markings—complete cleft lip; (B) Surgical markings—incomplete cleft lip.

the (C) flap and continues into the gingivobuccal sulcus with slight widening of the base of the flap right as it reaches the sulcus

- Advancement flap (A) is outlined. The three-dimensional vermilion fold abruptly turns into a flat two-dimensional line as it courses medially. That transformation junction coincides with the high point on the cleft side and is marked accordingly. The marking continues superomedially along the junction of white and red skin till the base of the nostril sill where it courses laterally along the nostril sill crease and terminates the base of the alar crease
- Lateral (L) mucosal flap is outlined similar to the (M) flap by drawing a perpendicular line in the vermilion from the cleft-side high point toward the wet–dry mucosal line. A line is then marked parallel to the lateral edge of the (A) flap and continues into the gingivobuccal sulcus with slight widening of the base of the flap right as it reaches the sulcus.

- Upper lip and nose are then infiltrated with the combination of local anesthetic and a 12-minute waiting period is employed to ensure the maximum vasoconstrictive effect of epinephrine.

## Complete Unilateral Cleft Lip/Nasal Repair (93.1 to 93.3)

- Using a #15 blade, a thick (C) flap is elevated (skin and subcutaneous layer) followed by scoring the markings of the mucosal (M) flap. Both skin and mucosal flaps are then raised with fine and sharp dissecting scissors
- Gingivobuccal sulcus releasing incisions are performed with a #15 blade with preservation of the maxillary periosteum and infraorbital nerve
- The orbicularis oris muscle is freed from the abnormal insertion into the alar base and dissected from overlying skin in a graduated fashion (Fig. 93.22), with dissection stopping at the vermilion border. The buccal mucosa is dissected for a distance of 1 mm from the underlying orbicularis oris muscle
- Primary cleft lip rhinoplasty: lower lateral cartilages are dissected away from the overlying nasal tip skin (Fig. 93.23). Access is through the columellar-labial angle. Alar crease and lower lateral cartilages are preserved
- The advancement (A) flap is then elevated following the original markings and ensuring that the flap is thick to include skin and subcutaneous layers. The (L) flap is scored. Both (A) and (L) flaps are then raised with sharp dissecting scissors
- Gingivobuccal sulcus releasing incisions are performed with a #15 blade with preservation of the maxillary periosteum and infraorbital nerve
- The orbicularis oris muscle is freed from the abnormal insertion into the alar base and dissected from overlying skin in a graduated fashion, with dissection stopping at the vermilion border
- The alar base flap is raised by placing the incision on the upper edge of the vibrissae, and stopping 2 mm behind the posterior edge of the lateral crus (Fig. 93.24). By maintaining an adequate cutaneous–mucosal layer, the integrity of the alar valve is preserved

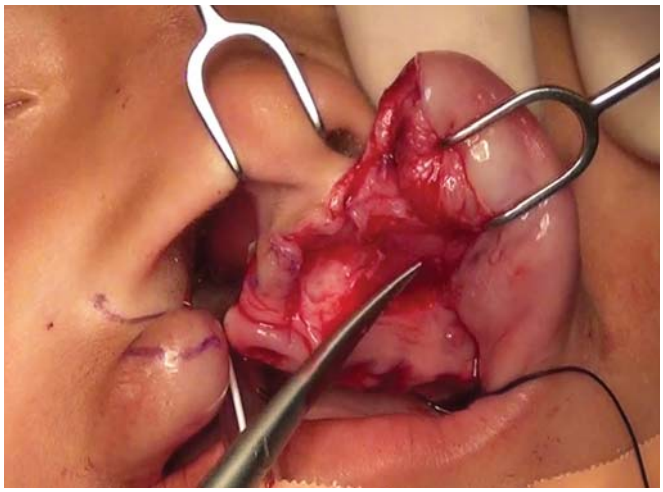


**Fig. 93.22:** Orbicularis oris muscle dissection.

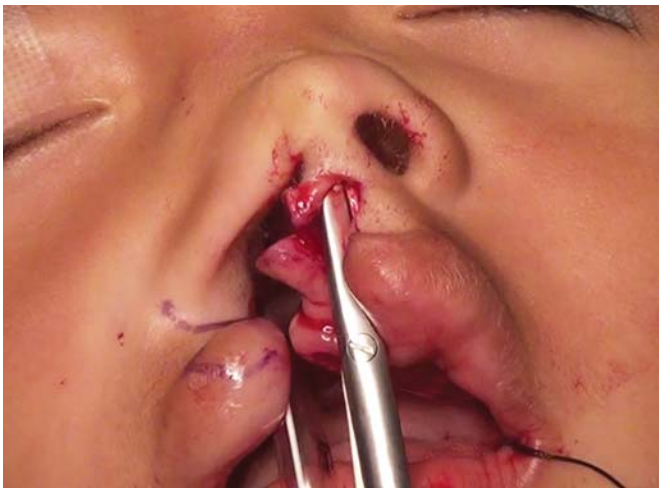


**Fig. 93.23:** Primary rhinoplasty dissection: skin separation from underlying lower lateral cartilage with preservation of alar crease.

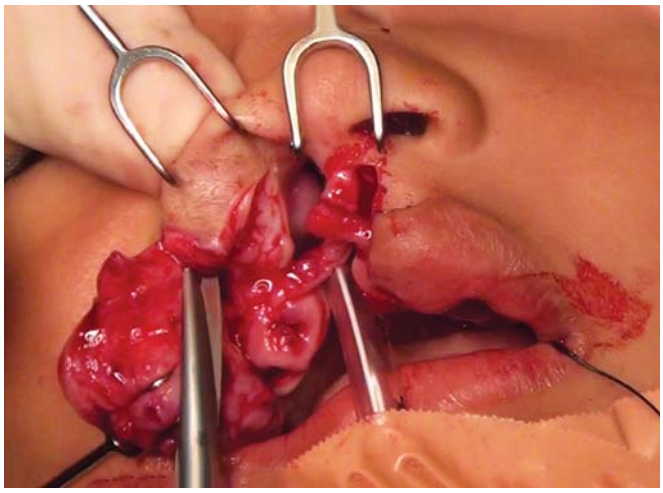


**Fig. 93.24:** Alar base flap being raised.

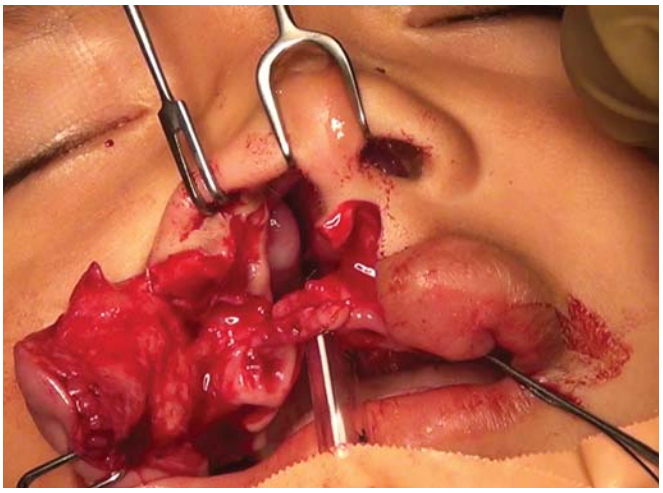
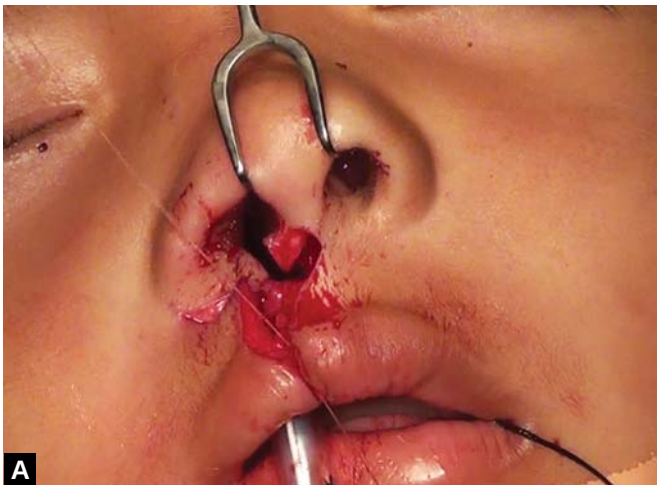
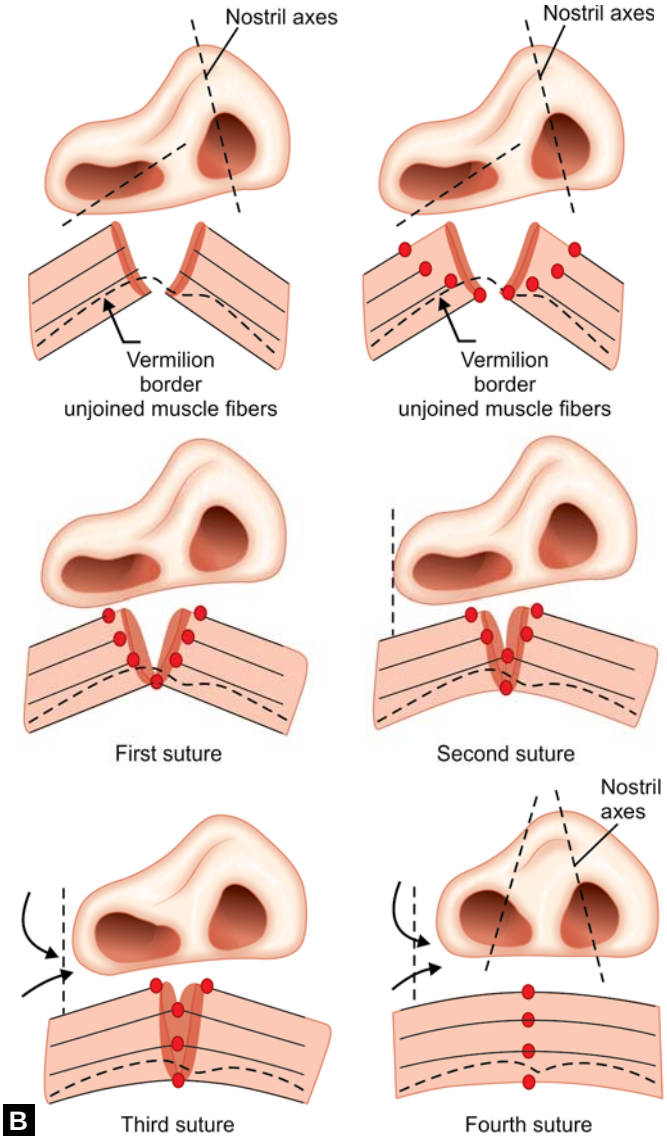
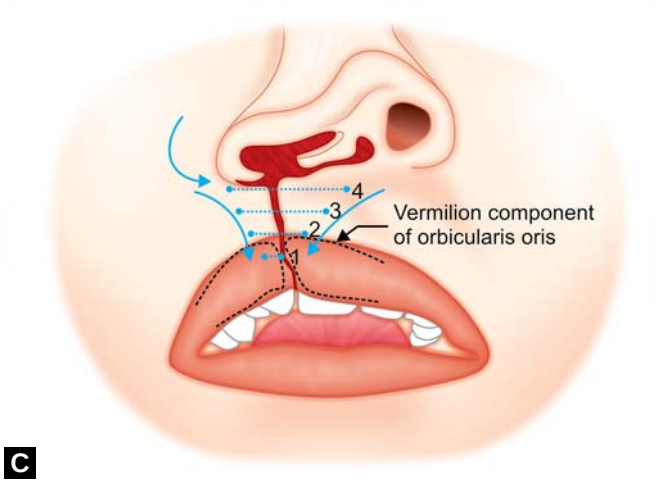


**Fig. 93.25:** M & L flaps crisscrossed and sutured.

- The (M) and (L) flaps are crisscrossed and sutures to opposite alveolar ridges with a 5-0 Vicryl™ suture on an RB-1 needle. A fine mid-flap suture is also applied to hold the two flaps together (Fig. 93.25)
- The buccal mucosal flaps are then carefully aligned and sutured with the 5-0 Vicryl™ suture ensuring that their heights are adequate by maintaining symmetry through the dry–wet vermilion line
- The orbicularis oris muscle is then repaired utilizing Hamdan sliding V-cheiloplasty techniques (Figs. 93.26A to C).[28] This allows lengthening of the upper lip and medial mobilization of the alar base on the cleft side. The 4-0 and 5-0 Vicryl™ sutures are used for muscle repair in the pediatric age group and the 3-0 and 4-0 Vicryl™ sutures in patients over 12 years of age
- The (C) flap is rotated medially to lengthen the columellar-labial angle and provide a natural contour for the medial crural footplate (Fig. 93.27)
- The alar base suspending suture is applied between the alar base and the opposing subcutaneous tip of the medial crural footplate. The suture is not tied till the (R) and (A) flaps are in position to ensure the symmetry of both nostrils and avoid nostril constriction (Figs. 93.28 A and B)[28]
- The advancement (A) flap is sutured in place by a subcutaneous transverse suture applied 2–3 mm behind the tip of the flap (Fig. 93.29)
- Two double dome sutures are applied utilizing 4-0 Monocryl™ on a PS-2 needle, with the knot placed on the noncleft side (Figs. 93.30A and B)




**Figs. 93.26A to C:** (A) Vermilion component muscle suture applied; (B) Hamdan sliding V-cheiloplasty technique; (C) Hamdan sliding V-cheiloplasty lengthens upper lip and medializes alar base.

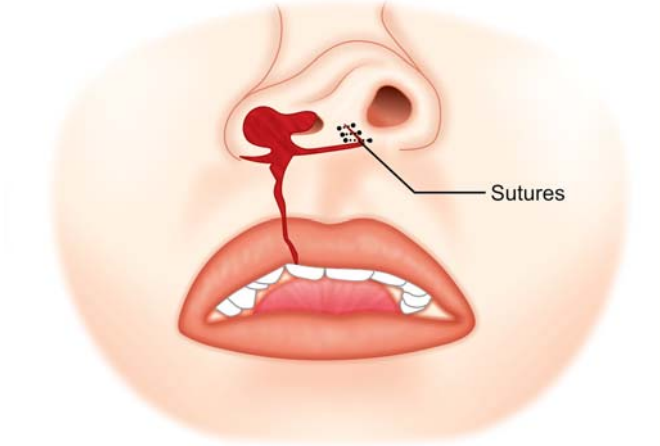
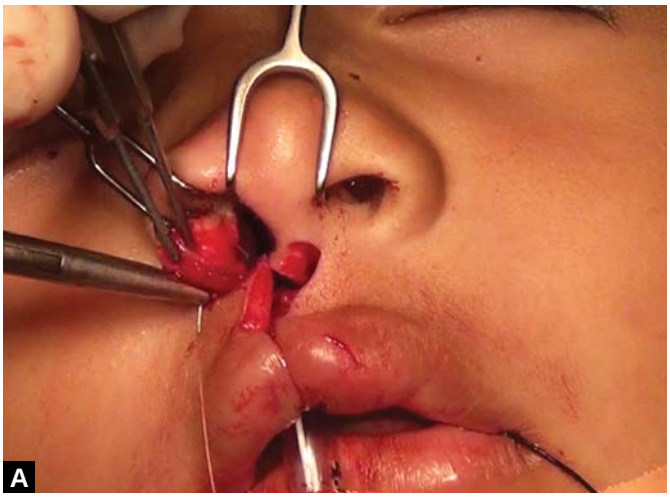
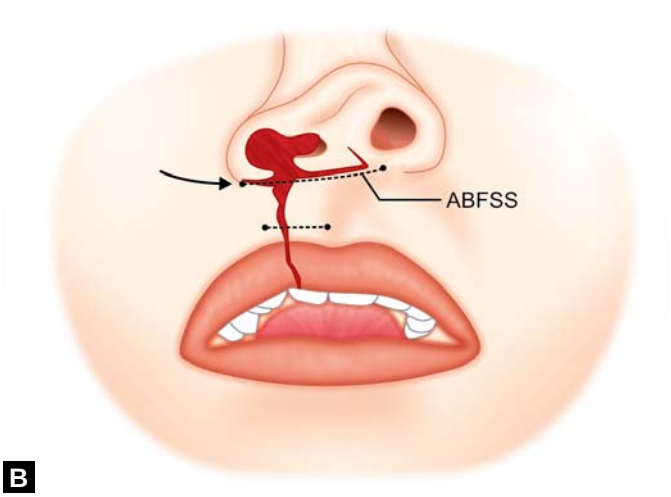



**Fig. 93.27:** C flap rotated and sutured.




**Figs. 93.28A and B:** Alar base suspending suture applied.

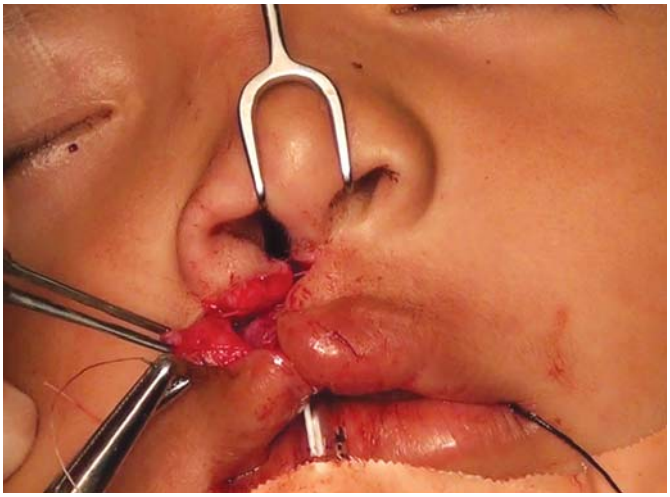
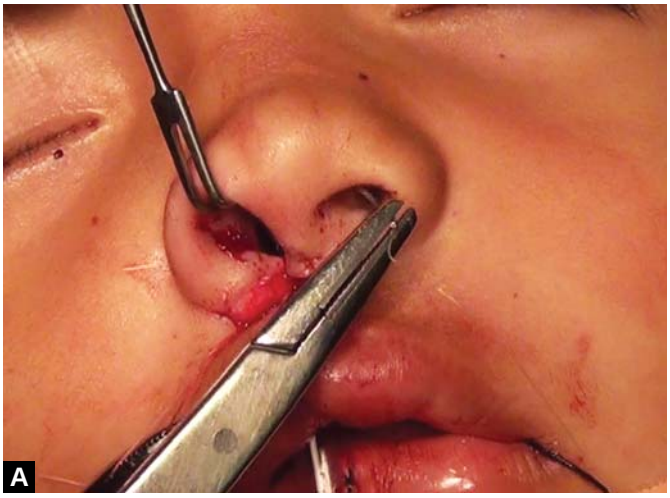
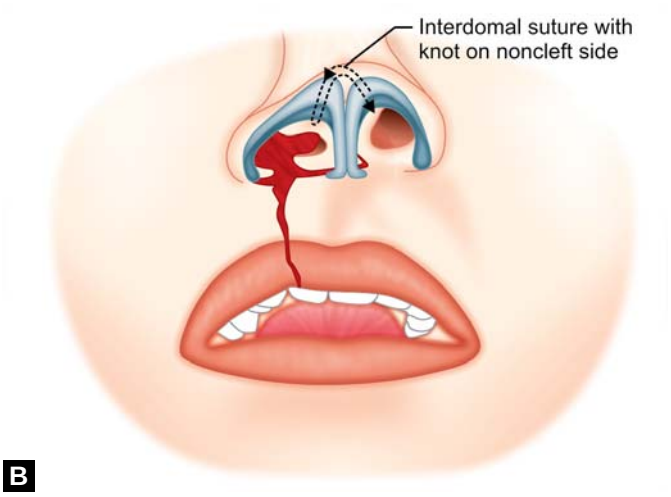


**Fig. 93.29:** Transverse suture applied 2–3 mm behind the tip of the (A) flap.




**Figs. 93.30A and B:** Double dome suspending suture applied.

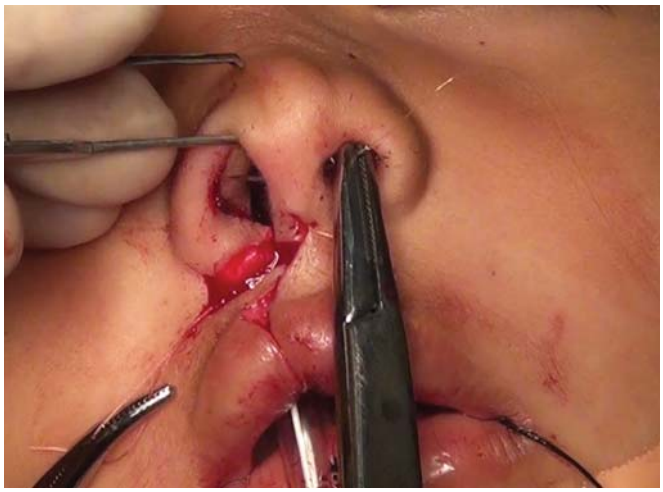


**Fig. 93.31:** Transverse crural transfixion suture.

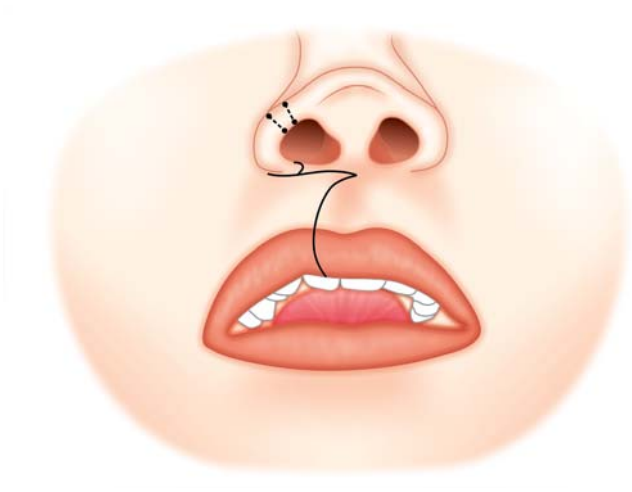


**Fig. 93.32:** Alar crease transfixion suture.

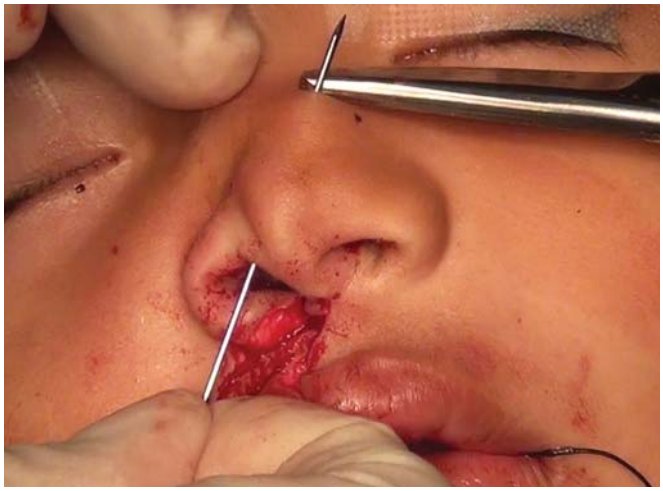


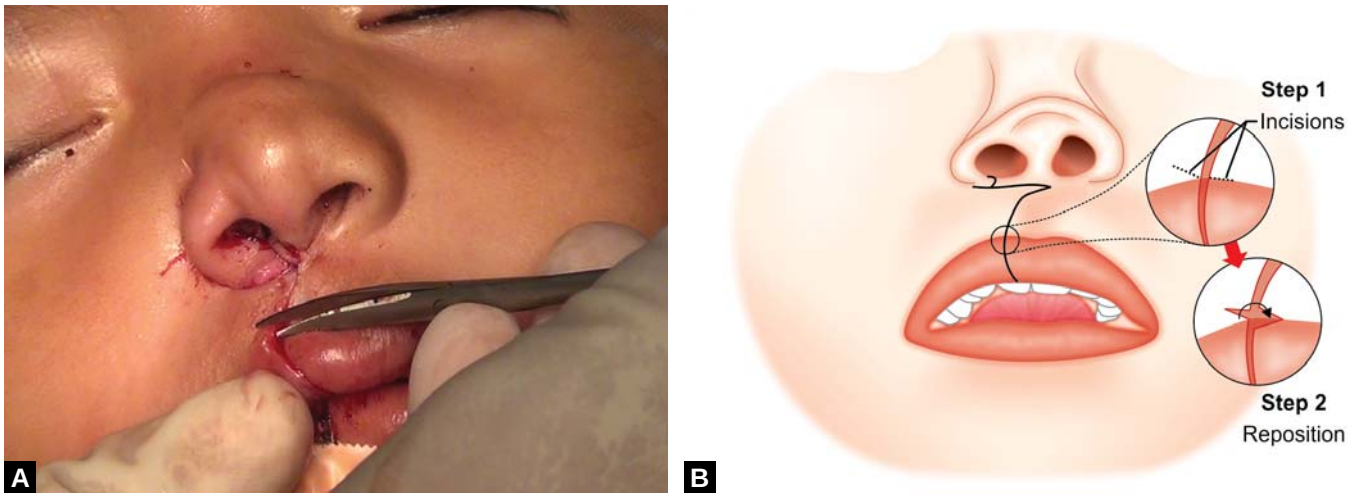
**Fig. 93.33:** Anterior soft tissue angle suspending suture.

- The transverse crural transfixion suture is gently applied with 4-0 Monocryl™ on a PS-2 needle (Fig. 93.31)
- One to two alar crease transfixion sutures are applied to prevent any potential dead space and thick scar formation in the alar lobule utilizing 5-0 or 6-0 Monocryl™ (Fig. 93.32)
- One to two anterior soft tissue angle suspending sutures are placed to minimize any tissue redundancy utilizing 4-0 Monocryl™ on a PS-2 needle or 3-0 Monocryl™ on a straight Keith needle (Fig. 93.33)
- A 0.75–1 mm lateral vermilion flap rotated medially and sutured to the cleft side high point utilizing 6-0 Monocryl™ on a P-1 needle or 6-0 Fast Absorbing Plain Gut™ on a PC-1 needle (Figs. 93.34A and B)
- Multiple transverse orbicularis oris muscle sutures are applied along the circumference of the vermilion component of the muscle to ensure smooth continuity and eliminate any potential residual deficiency (Figs. 93.35A and B)
- The skin of the lip is closed with 5-0 and 6-0 Monocryl™ or Vicryl™ subcutaneous sutures followed by absorbable skin sutures (5-0 or 6-0 Fast Absorbing Plain Gut™ on a PC-1 needle) (Figs. 93.36 and 93.37).

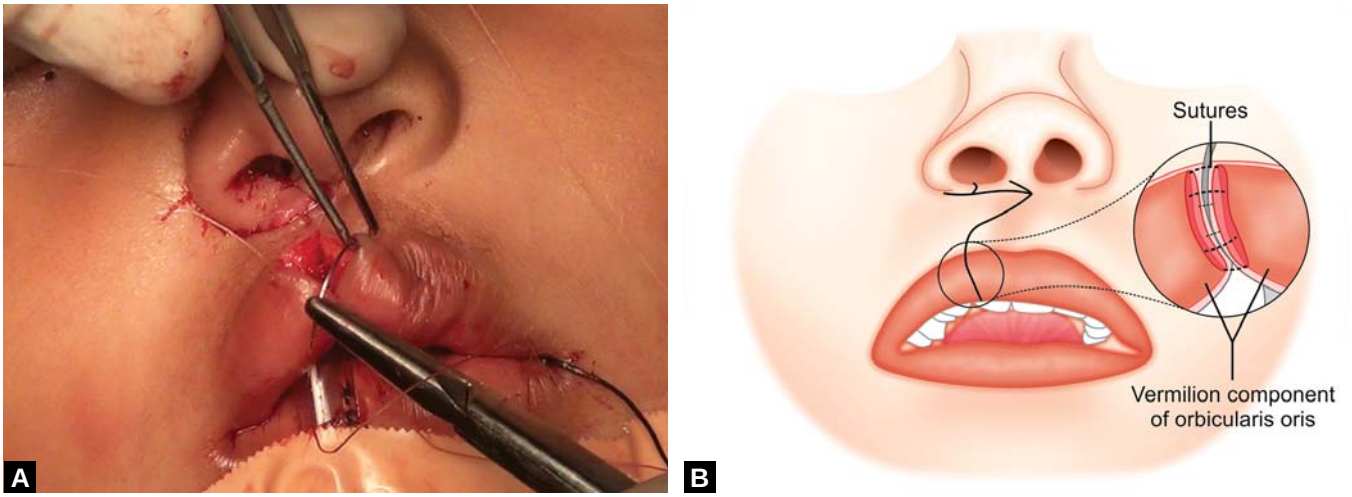
In the recovery room, Dermabond is lightly applied only on the upper skin part and after ensuring that the wound is dry. Avoid Dermabond application in the nostril.

## Cleft Lip Repair Under Local Anesthesia

- Patients over 12 years of age can undergo primary as well as revision cleft lip repair under local anesthesia with or without intravenous sedation and after thorough preoperative patient and family counseling
- Anesthetic mixture for patients older than 12 years of age: 0.5 cc/kg of 1:1 combination of 1% lidocaine in 1:100,000 epinephrine with 0.5% bupivacaine in 1:200,000 epinephrine
- Infraorbital and external nasal nerve blocks are performed with a 30-gauge 1-inch needle after application of topical anesthetic
- Local infiltration of the upper lip with same anesthetic mixture after a 15-minute waiting period to ensure nerve block effectiveness




**Figs. 93.34A and B:** (A) Vermilion border flap being raised; (B) Vermilion border flap.




**Figs. 93.35A and B:** Transverse sutures applied along the circumference of the vermilion part of muscle.

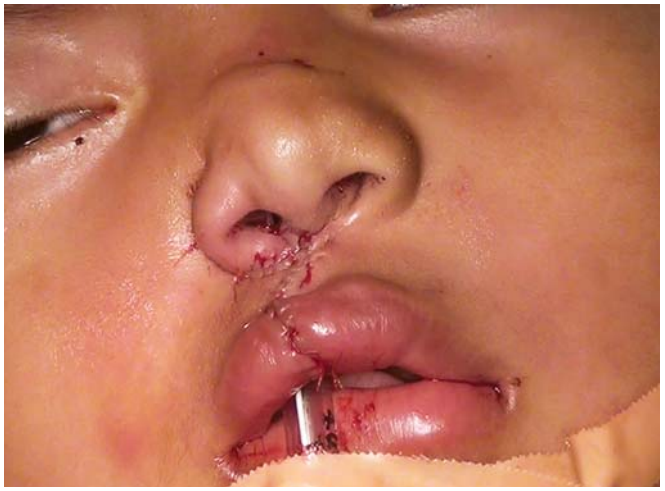
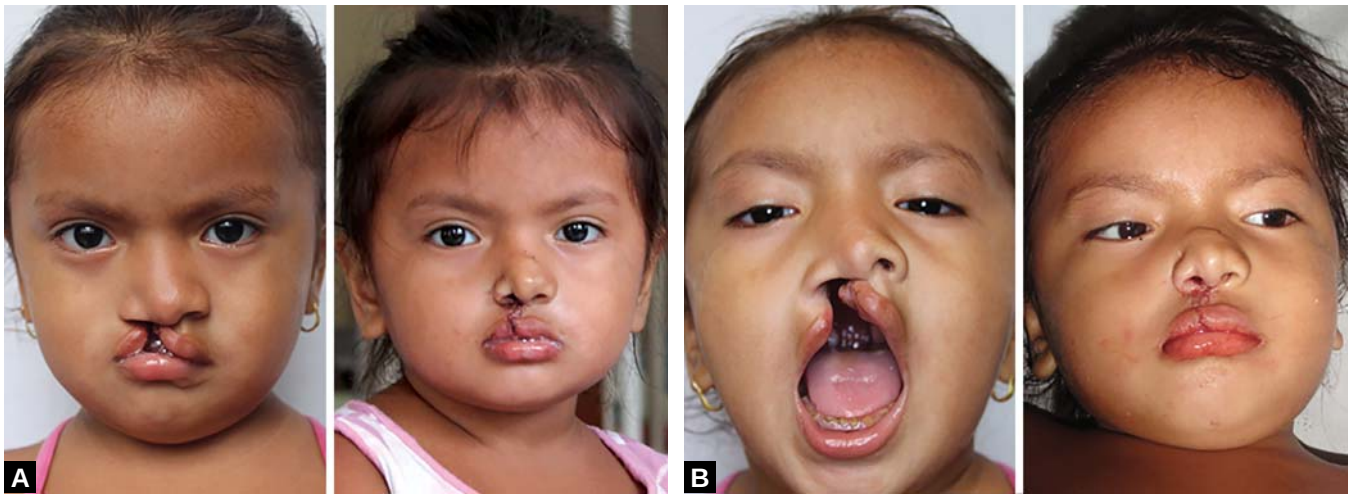


**Fig. 93.36:** Skin and subcutaneous closure with absorbable sutures.




**Figs. 93.37A and B:** Pre- and postcomplete cleft lip repair and primary rhinoplasty.

- Surgical steps are the same as those in cleft lip repair under general anesthesia (Figs. 93.38A to I).[27,28,50]

## BILATERAL CLEFT LIP

Unilateral and bilateral cleft lip deformities share a similar classification scheme, treatment approach, and timing of procedures. Bilateral cleft lip and nasal deformity presents the surgeon with the challenge of establishing normal form and function in the setting of a protruding premaxillary segment, prolabium that lacks muscle, normal attachment, and discontinuity of the orbicularis oris, lateralized alar bases, thinned and stretched lower lateral cartilages, and a shortened columella. Thanks to major advances in presurgical orthopedics and refinement of surgical techniques, the final esthetic outcomes have markedly improved.

### Classification

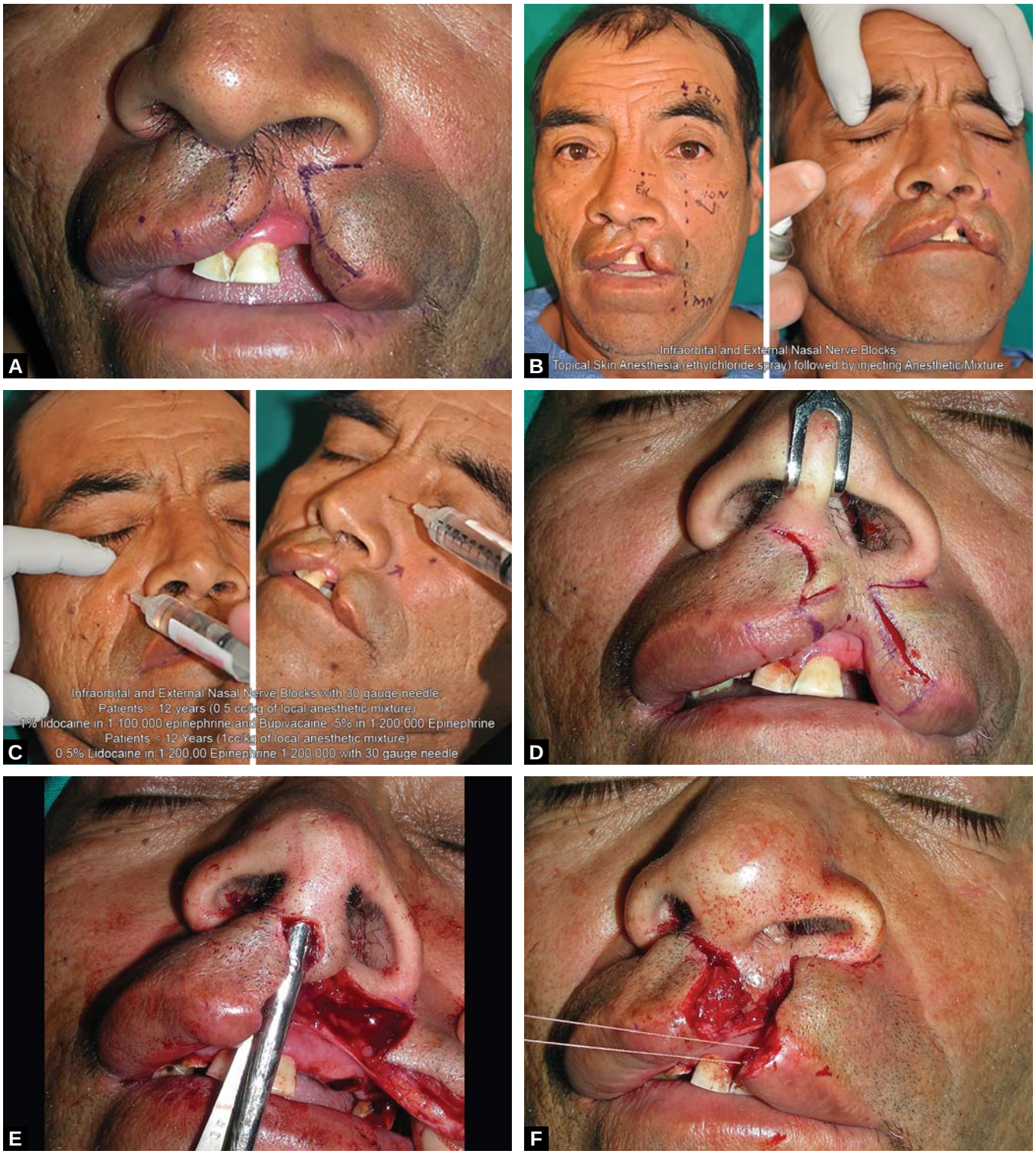
Bilateral cleft lip can have one of the following presentations:

- *Bilateral incomplete cleft lip*: Intact nasal floor and nostril sill. Rarely some upper orbicularis oris muscle fibers might extend into the lateral edge of the prolabium but they do not decussate over the midline (Fig. 93.39). The alveolus, in general, is intact
- *Incomplete and complete bilateral cleft lip*: Intact nasal floor and nostril sill on one side and complete CL with absent nasal floor and sill on the opposite side. Premaxilla is often rotated toward the incomplete cleft side (Figs. 93.40A and B)
- *Bilateral complete cleft lip*: Premaxilla is projected anteriorly with absent nasal floors bilaterally (Fig. 93.41).

### Anatomy

Anatomical abnormalities in bilateral cleft lip deformity can be divided into:

- Upper lip:
  - *Muscle*: The contracted orbicularis oris muscle fibers abnormally insert onto the alar bases with thickened medial edges
  - *Vermilion*: Lateral segment of the vermilion border is well defined as a three-dimensional fold that abruptly transforms into a two-dimensional flat line medially. The transition point references the high point of Cupid's bow on the lateral segment of cleft lip.
- Nose:
  - Wide and flattened nasal tip with poor tip support and definition
  - Wide and laterally stretched alae
  - Septum is usually midline
  - Short and mostly absent columella
  - Contracted transverse crura.
- Premaxilla and prolabium:
  - In most complete bilateral clefts, the premaxilla is projected anteriorly. When one side is incomplete, the alveolar ridge is rotated on the complete cleft side




**Figs. 93.38A to F:** (A) Surgical markings—incomplete cleft lip under local anesthesia; (B) Topical anesthesia applied prior to nerve blocks; (C) Infraorbital and external nasal nerve blocks; (D) Incisions made; (E) Primary cleft lip rhinoplasty dissection; (F) Vermilion component muscle suture applied.


**Figs. 93.38G to I:** (G) Hamdan sliding V-cheiloplasty sutures applied; (H) C and A flaps sutured; (I) Pre- and 1 month postlip repair and primary rhinoplasty.

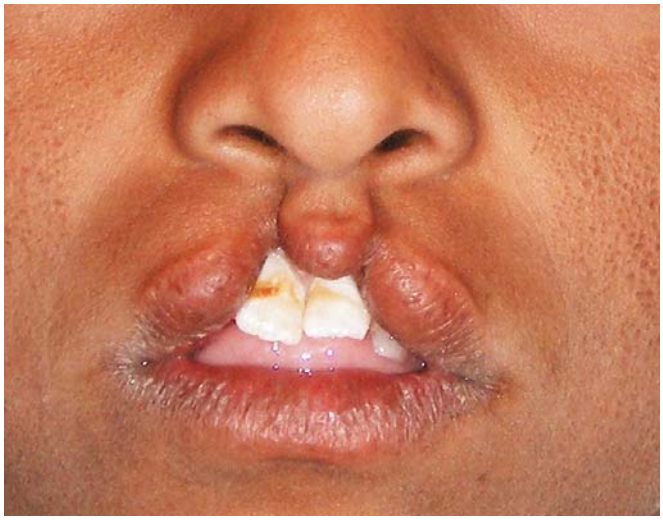
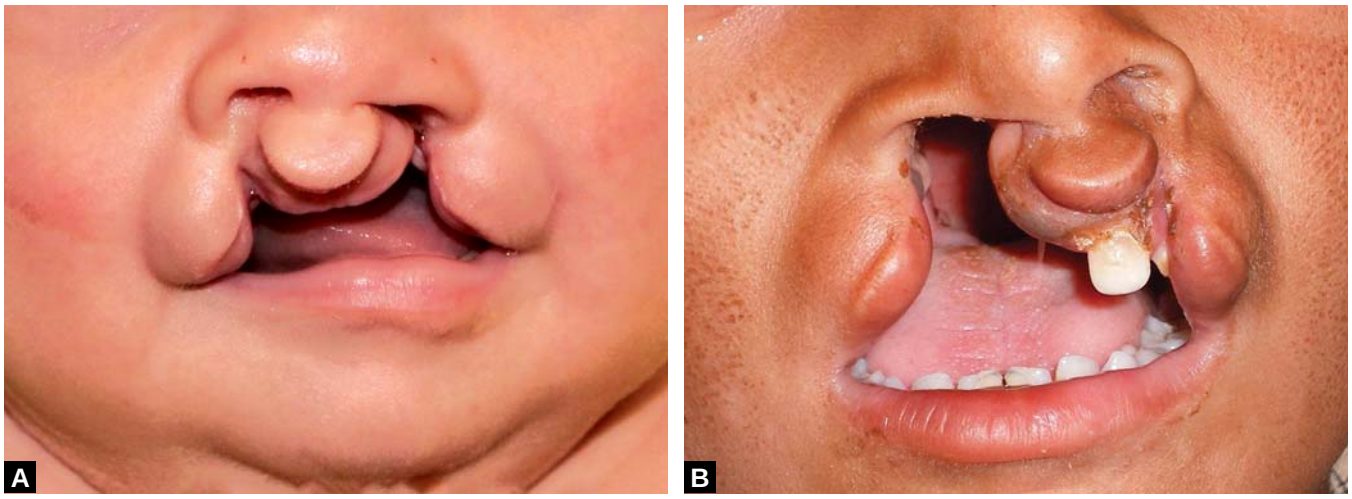


**Fig. 93.39:** Incomplete bilateral cleft lip.




**Figs. 93.40A and B:** Bilateral CL-incomplete left and complete right.

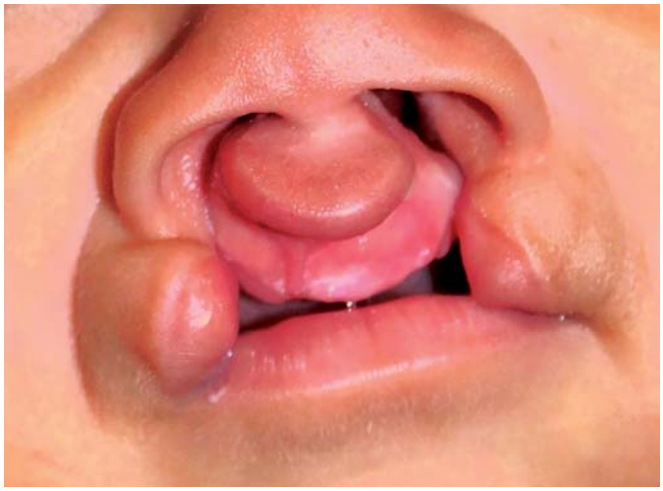


**Fig. 93.41:** Bilateral complete cleft lip.

- *Prolabium*: The prolabial skin can vary from being wide and abundant to short, contracted, and barely visible, depending on the extent of the cleft deformity
- *Muscle*: The orbicularis oris is absent from the prolabium. In incomplete clefts, few upper muscle fibers might extend into the lateral edge of the prolabium, but never decussate across the midline. Thus, restoration of muscle continuity during bilateral cleft lip repair necessitates draping of the muscle from the lateral segments across the premaxilla. The lateral segments of the orbicularis oris muscle are shortened and insert into the alar bases
- *Vermilion*: The prolabial vermilion is hypoplastic and lacks philtral columns and a central dimple. The white roll is diminished. Cupid's bow low point is identifiable at times, but in some patients it is not discernible
- The wet–dry mucosal junction is visible but typically the exposed mucosa is dried out due to the premaxillary projection and lack of continuity of the buccal mucosa and the gingivobuccal sulcus
- The philtral ridges and tubercle are absent or significantly diminished, with an absent philtral dimple.

- *Maxillary shelves*: The piriform apertures are hypoplastic with retropositioned maxillary shelves.

## Goals

The goals of repair are restoring symmetry and function of the upper lip, including the following:

- Reconstruction of Cupid's bow, philtral ridges, dimple, and tubercle
- Creation of continuity of the orbicularis oris muscle that flows smoothly across the upper lip without any deficiencies
- Creation of a gingivobuccal sulcus
- Achievement of nasal tip projection and adequate columellar length
- Reconstruction of a naturally flowing three-dimensional vermilion fold and avoiding asymmetry of Cupid's bow or distance between the oral commissures and the high points

**Fig. 93.42:** Lip taping for bilateral cleft.

- Alignment of the dry vermilion bilaterally to avoid any vermilion inversion or over-rotation.

## Presurgical Infant Orthopedics

The aim of PSIO is to align the alveolar segments, retract the premaxilla, and improve arch form prior to surgical repair. This facilitates a single-stage repair, especially in wide bilateral clefts. Techniques include from lip taping, lip adhesion, Latham appliance, and more recently NAM.

Lip taping is commonly used when other modalities are not readily available due to limited resources or family compliance (Fig. 93.42). The objective of lip taping is to approximate the alveolar segments, including the premaxilla in bilateral cases, to a more normal position to facilitate surgical closure. However, lip taping does not address the common challenge faced in bilateral deformity: the collapse of the posterior alveolar segments toward one another resulting in further retraction of the premaxilla segment. This compromised position can lead to complications during surgical repair and difficulty during orthodontic therapy later in life.

The Latham appliance utilizes the active expansion of the palatine shelves and active closure of the alveolar cleft.[29] However, it does not address the nasal cartilage deformity or the short columella.[29]

Nasoalveolar molding therapy places emphasis on reducing the severity of deformity in the soft tissue of the nose, the nasal cartilages, and the alveolar processes prior to the initial surgical repair. The objective of NAM is to achieve presurgical reduction in nasal cartilage deformity, reduce the size of the alveolar gap, approximate the lip segments at rest, increase the surface area of nasal mucosal lining, and nonsurgically elongate the columella. Nasoalveolar molding therapy consists of two components that are simultaneously working together to create this change:

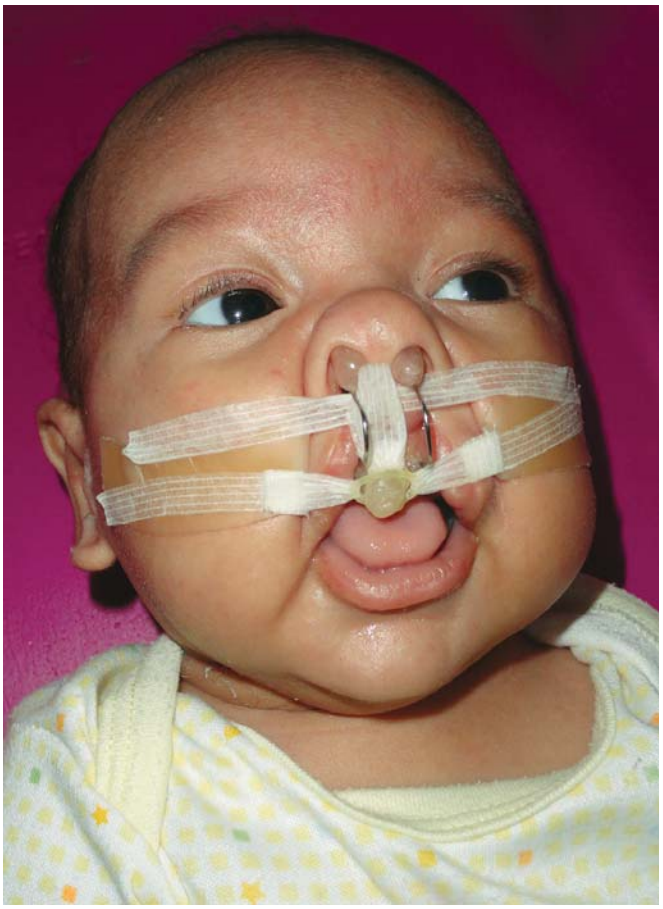


**Fig. 93.43:** NAM appliance for bilateral cleft lip.

- *Intraoral component*: Reduces alveolar gap by approximation of the alveolar segments and retraction of the projected premaxilla (Fig. 93.43)
- *Nasal component*: Provides an upward force to the nasal vestibule, resulting in cartilage molding, expansion of nasal mucosal lining, improved nasal tip projection, and columellar lengthening.

Nasoalveolar molding requires weekly visits to activate the appliance and adjust it for the growing infant.

The choice between the various PSIO options is controversial and is often dictated by the available resources and training. Nevertheless, NAM is the preferred option for the authors when available, due to the reported advantages in nasolabial appearance and symmetry.[51]

## Surgical Repair

### *History and Background*

Historically, the repair of the bilateral cleft lip has had to address not only the soft tissue defect, but also the protruding premaxilla and associated nasal deformity. Over time, procedures have been proposed that vary in the extent of prolabium dissection, soft tissue origin of the central vermilion, muscular continuity, methods for columellar lengthening, and nasal reconstruction. Until the mid-20th century, it was believed that the prolabium lacked the potential to grow and that the philtrum had to be elongated[52] through the use of rectangular or triangular flaps[47] cut from each edge of the lateral segment and fitted to the medial segment. These methods often resulted in asymmetric scars and long and tight lips.[39]

Whether to preserve the entire prolabial vermilion versus leaving a tiny strip in the center also became the subject of debate. Approximation of the orbicularis muscle was not addressed until the second half of the 20th century. The nasal deformity was initially neglected during the primary repair due to the fear of compromising the philtral blood supply. Bilateral cleft lip repair continued evolving until the late 20th century when columellar and nasal deformities started being addressed during the primary repair.[53] Finally, successful bilateral cleft lip repair has been significantly advanced by the use of preoperative orthodontic care, in particular NAM, which repositions and lengthens the nasal cartilage and aligns the maxillary and alveolar segments.

The current and most commonly used techniques for bilateral cleft lip repair aim to reconstruct an aesthetically acceptable Cupid's bow, produce a well-aligned orbicularis oris muscle, and correct any associated cleft nasal deformities.

### *Millard Repair (Fig. 93.44)*[54]

Millard's repair of the bilateral cleft lip has been widely used and modified by several surgeons including Mulliken[55] and Noordhoff.[56] It is based on restoring the orbicularis oris muscle continuity under the prolabium to avoid residual whistle deformity, as encountered in some of the earlier repairs. It also utilizes forked flaps derived from the prolabium to lengthen the columella. The advantage of this technique is its good results even when the prolabial white roll and the vermilion are deficient. Nevertheless, it yields an unnatural appearance to the nose with the use of the forked flaps, has a sharp columella-labial angle, laterally stretched nostrils and significantly short columella, and can result in a tight upper lip.[57]

### *Mulliken Repair (Fig. 93.45)*[55]

The Mulliken repair shares many similarities with Millard's technique but emphasizes the growth effect on the repaired lip. The newly reconstructed prolabium is smaller than would be expected, accounting for its future growth. In addition, the columella is derived from the repositioning of the alar cartilages rather than from the forked flaps used by Millard, using the principle that the columella should

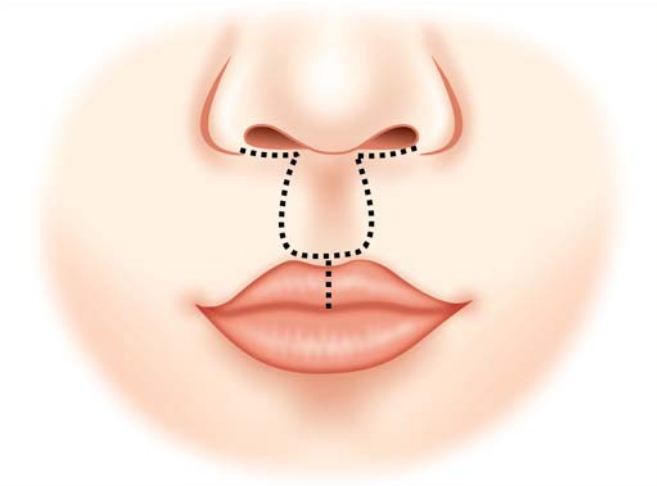


**Fig. 93.44:** Millard's bilateral cleft lip technique.

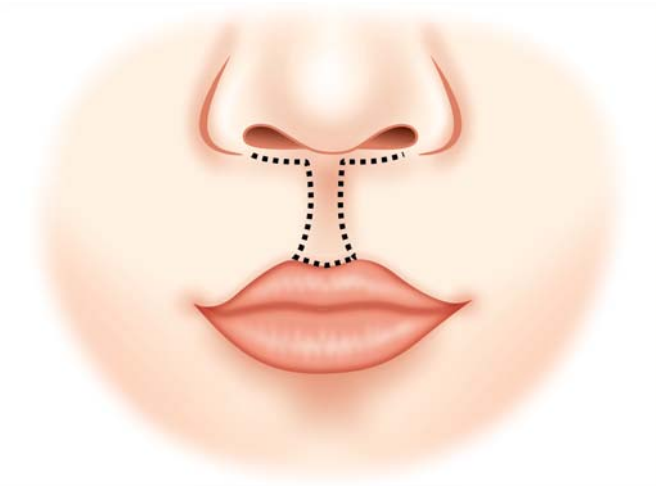


**Fig. 93.45:** Mulliken's bilateral cleft lip.

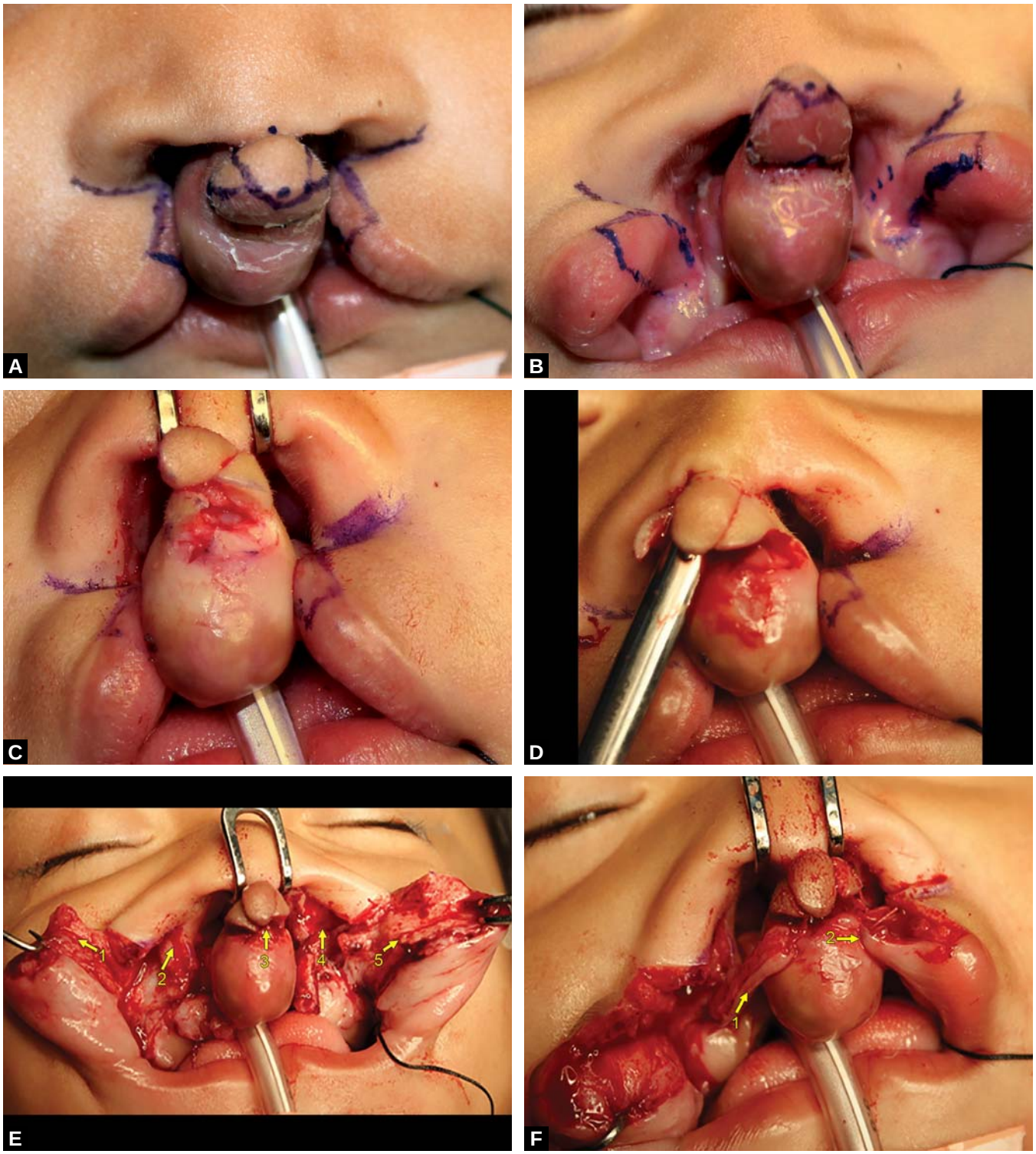
be derived from the nose. It also addresses the nasal deformity with satisfactory surgical results.[57]

### *Senior Author Technique for Primary Repair of Bilateral Cleft Lip/Nasal Deformity (93.4)*

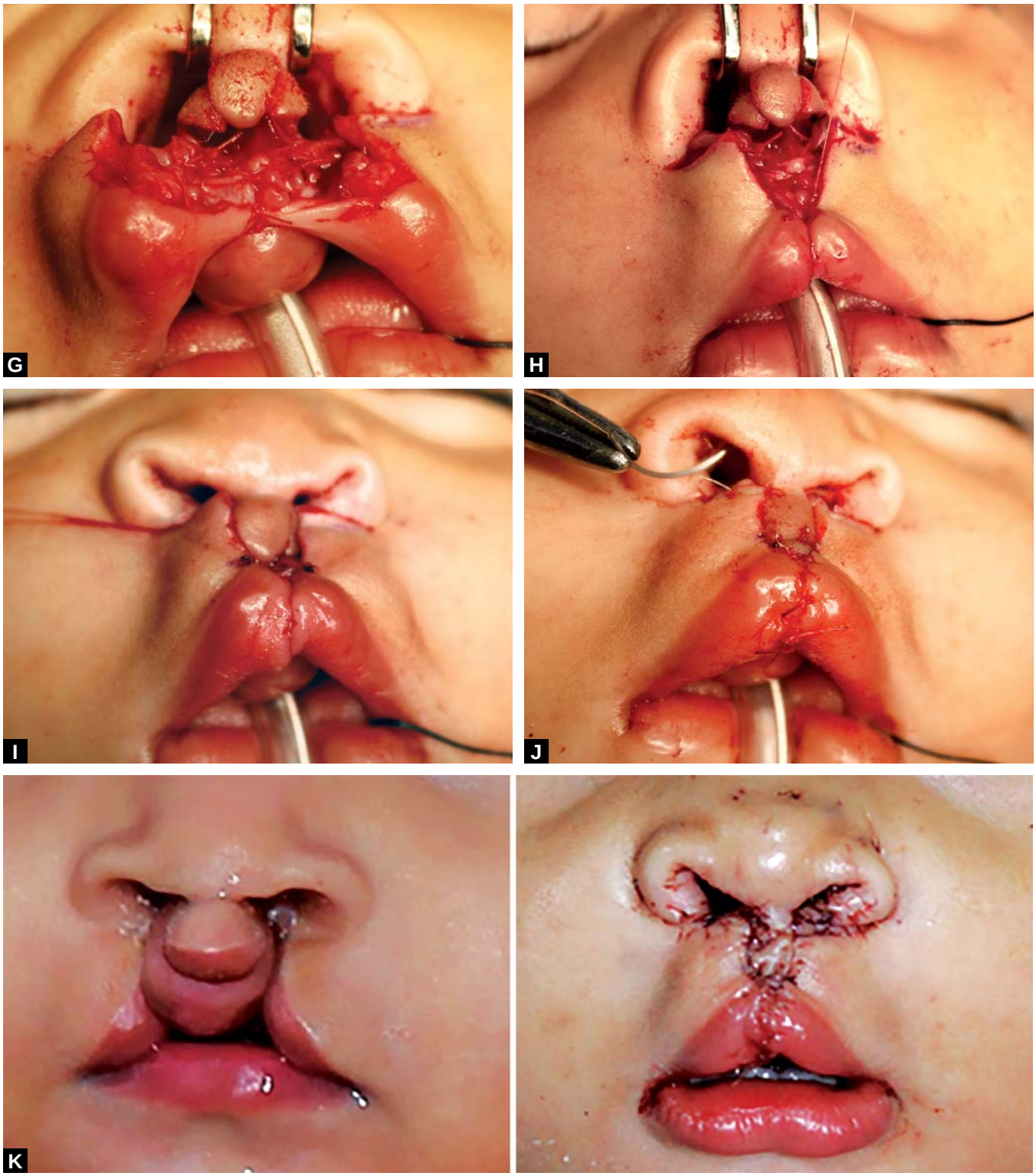
The senior author's technique for repair of bilateral cleft lip employs the same concepts of sliding V-cheiloplasty for orbicularis oris muscle repair as in the unilateral cleft lip. Nasal repair includes the alar base suspending suture, double dome sutures, transverse and alar crease transfixion sutures, and anterior soft tissue angle suspending sutures. Repair of bilateral cleft lip deformity is preferable at 4–5 months of age to maximize the benefits of PSIO.

Surgical procedure (Figs. 93.46A to K)

- *Surgical markings*: Repair is performed under general anesthesia for patients under 12 years of age. Patients older than 12 years can undergo repair under local anesthesia with standby intravenous sedation utilizing the infraorbital and external nasal nerve blocks and after thorough counseling of the patient and family.[27,50]
  - Low point of Cupid's bow is marked followed by the two high points (2–2.5 mm on each side). If the low point in not clearly visible, its location is discerned by dropping a perpendicular line from the mid-columella to the vermilion fold. The incision is marked 0.5 mm below level of actual Cupid's bow to preserve the natural contour of the vermilion fold
  - *Prolabial (P) flap*: Philtral ridges are marked by dropping two parallel lines from the lateral base of the columella to the respective high points
  - *Columellar (C) flaps*: V-shaped with the peak at the respective high points of Cupid's bow, the medial segment being the philtral line, and the lateral segment extends toward the nose along the skin-bearing area of the vermilion line
  - *Inverted V-shaped mucosal (M) flap*: A 2-mm midline mucosal flap is marked at the junction of the prolabial mucosa with the premaxilla, where a natural frenulum should be located
  - *Advancement (A) flaps*: High points on the cleft side are marked at the medial most aspect of the visible three-dimensional vermilion border as it abruptly changes to a two-dimensional flat line. Distances between the alar bases and the marked high points are measured with a caliper and should be symmetric. The (A) flap markings follow the flat vermilion line toward the nose and then acutely turns laterally along the medial aspect of the alar crease. It stops at a point corresponding to the base of the outer flare of the alar lobule. Care should be exercised not to carry the incision into the alar crease as this will cause visible postoperative scars
  - Vermilion (L) flaps are marked by a drawing a perpendicular line in the vermilion from the cleft-side high point toward the wet–dry mucosal line. A line is then marked parallel to the vermilion line and continues into the gingivobuccal sulcus with slight widening of the base of the flap right as it reaches the sulcus
  - Alar base flaps are outlined by marking the upper edge of the vibrissae and stopping 2 mm behind the posterior border of the lateral crura.
- Infraorbital and external nasal nerve blocks as well as local infiltration of upper lip with a combination mixture of lidocaine/bupivacaine with epinephrine are performed
- Prolabial, mucosal, and alar base flaps are raised
- The orbicularis oris muscle is dissected
- Buccal mucosal flaps are sutured to the inverted prolabial V-shaped mucosal flap. The same sutures are used in bilateral cleft lip repair as in unilateral cleft lip repair
- Nasal tip undermining is performed from a medial columellar approach, separating the lower lateral cartilages from overlying skin with preservation of alar creases
- Orbicularis oris muscle is repaired utilizing the Hamdan sliding V-cheiloplasty technique
- Vermilion border flaps on the lateral advancement flaps are raised, rotated inferomedially and sutured to corresponding high points on the prolabial flap
- Bilateral advancement flaps are sutured to corresponding lateral bases of the prolabial flap utilizing transverse subcutaneous sutures placed 2–3 mm behind the tips of the advancement flaps
- The columellar (C) flaps from the columella are trimmed and use to mimic outflaring of medial crural footplates.
- Primary rhinoplasty:
  - Alar base flap and suspending suture is applied between both alar bases and tightened enough to produce bilateral nostril symmetry
  - Two double dome sutures, passed through the upper and power aspect of the nasal dome, are applied to improve tip projection




**Figs. 93.46A to F:** (A) Markings for bilateral CL repair; (B) Markings for bilateral cleft lip repair; (C) Prolabial flap raised; (D) Primary rhinoplasty dissection; (E) Orbicularis oris muscle dissected (1), alar base (2) and prolabial (3) flaps raised; (F) (L) flap (1) and buccal mucosal flap (2) sutured.




**Figs. 93.46G to K:** (G) Bilateral buccal mucosal flaps sutured in midline; (H) Sliding V-cheiloplasty sutures placed; (I) Vermilion border flaps raised; (J) Double dome suture placed; (K) Pre- and postbilateral cleft lip repair.

  - Transverse crural transfixion sutures are lightly placed to prevent retrodisplacement of the lower lateral cartilages
  - Alar crease transfixion sutures are applied to prevent any hematoma buildup in a potential dead space and/or postoperatively thickened alar lobule due to scar formation
  - Anterior soft tissue angle suspending sutures are placed to address soft tissue triangle redundancy.
- *Lip closure*: Buccal mucosal flaps and skin are closed with absorbable sutures in a similar fashion as detailed with unilateral cleft lip repair
- Dermabond is gently applied over the skin sutures.

## POSTOPERATIVE MANAGEMENT

Prophylactic broad spectrum antibiotics (usually oral cephalosporins) are administered intraoperatively and postoperatively. Elbow restraints are used on infants and toddlers for 2 weeks to avoid accidental injury to the repaired lip. Families are counseled on supervised periodic removal of the elbow restraints throughout the day. Breast and bottle feeding are avoided for 2 weeks to allow lip healing. Teaspoon and dropper feeding is utilized for the infant and toddler age groups.

Since absorbable sutures are used for mucosal and skin closure, there is no need to bring the patient back into the operating room for suture removal. The skin sutures, covered with Dermabond, do not require wound care until the Dermabond falls off in 10–12 days. Any crust buildup around the mucosal sutures can be gently cleaned with a Q-tip dipped in saline.

Patients are seen weekly for the first 2–3 weeks to ensure adequate wound healing. Sun protection is recommended to avoid scar hyperpigmentation. Massaging the upper lip in initiated on the 4th to 5th week postoperatively, 4 to 5 times/day for 2–3 months, to prevent any potential thick scarring in the upper lip or skin retraction during the healing process.

## POSTOPERATIVE COMPLICATIONS

A wide variety of postoperative lip and nasal complications can occur following unilateral or bilateral cleft lip repair. In the immediate postoperative period, potential complications include infection, bleeding, hematoma, seroma, extensive crusting, lip dehiscence, and suture abscess. Potential postoperative complications beyond the 2–3 weeks result in residual (secondary) cleft lip and nasal deformities that will be discussed in the next section.

## SECONDARY DEFORMITIES

Secondary cleft lip deformities can involve defects in the muscle, skin, or mucosa singularly or in combination. Muscle deficiency can result from insufficient release during primary repair, inadequate suturing of all the fibers, infection during the postoperative phase, or postoperative trauma.

Residual skin deformities can be attributed to retraction due to short skin flaps, wide or hypertrophied scars, asymmetry of the lip elements, poor suturing techniques, infection, or trauma. Lack of fullness in the philtral tubercle can result from muscle or vermilion deficiencies or a combination of both. Inadequate release of the buccal mucosa can result in varying degrees of pull on the overlying muscle with secondary retraction or deficiency.

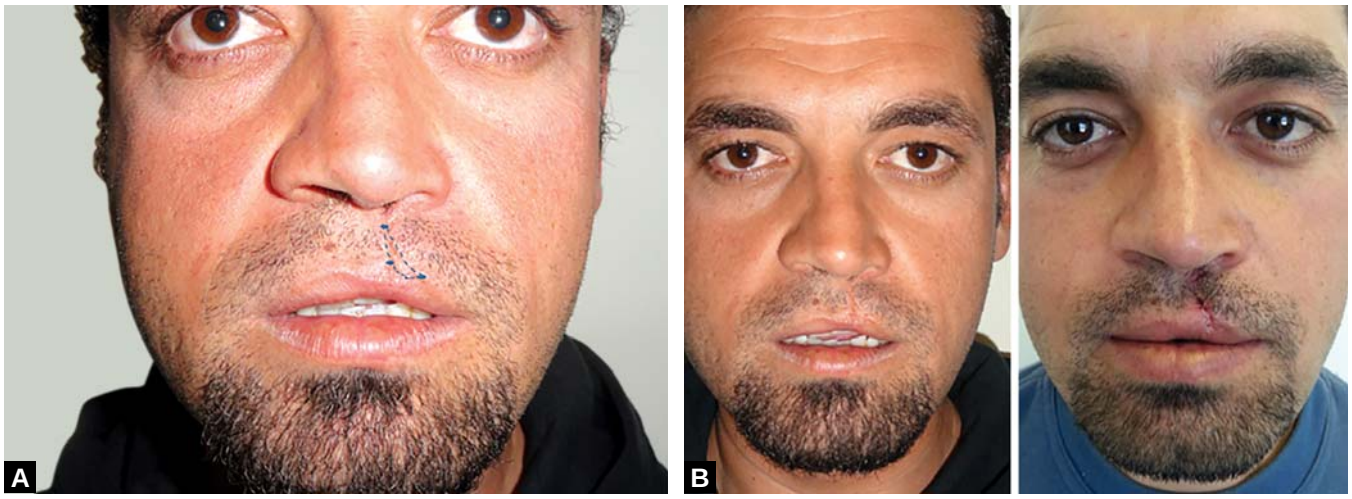
Secondary cleft nasal deformities are broad and may include:

- Nasal axes asymmetry with widened and lateralized nostril on the cleft side
- Nostril constriction on the cleft side
- Underprojected nasal tip
- Thickened alar lobule
- Obliteration of the alar crease due to attempt at laterally accessing the lower lateral cartilage through the alar lobule
- Alar valve constriction
- Alar rim buckling or notching
- Poor tip projection and/or shortened columella
- Residual redundancy along the anterior soft tissue angle.

The senior author has proposed a classification system for secondary deformities, based on the complexity of the surgical procedure needed for correction (Table 93.6).[28]

**Table 93.6:** Classification system for residual cleft lip and nasal deformities

| *Type* | *Deformity* |
|---|---|
| I | Minor revisions requiring skin and subcutaneous tissue mobilization: Z-plasty, V-Y closure, linear excision, etc. |
| II | Vermilion component orbicularis oris muscle deficiency: requiring mucosal and muscle repair without skin or nasal correction |
| III | Lip revision involving muscle, skin, and mucosal repair without nasal surgery |
| IV | Major lip revision requiring muscle, skin, mucosal, and nasal repair |




**Figs. 93.47A and B:** (A) Type I revision; (B) Pre- and post-type I revision.

**Fig. 93.48:** Type II bilateral cleft lip revision-philtral tubercle reconstruction.

## Type I Repair

It involves only skin and subcutaneous repair to correct asymmetries affecting Cupid's bow, vermilion fold, and upper lip contraction involving skin without need for muscle, nasal, or mucosal repair. Corrective procedures utilized can include Z-plasty for the correction of white roll deformity, V–Y flap, and straight-line closure (Figs. 93.47A and B).

The range of deformities requiring type I repair include:

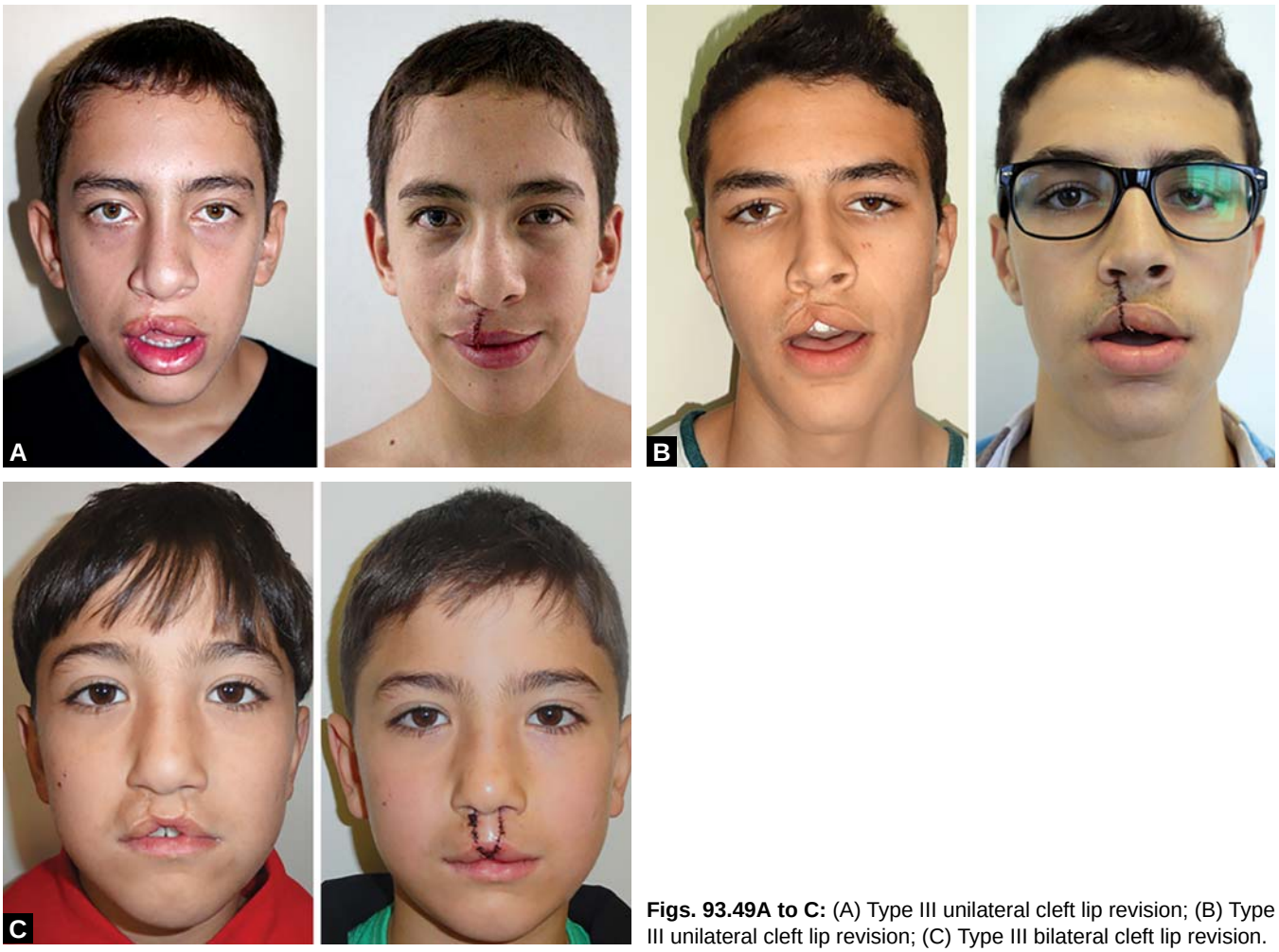
- Vermilion border asymmetry that can be corrected with a Z-plasty, V–Y flap, or straight-line repair
- *Short upper lip*: Treated with Z-plasty or diamond-shaped skin excision
- *Long upper lip*: Corrected by excising a horizontal strip of upper lip skin at its junction with the nostril sill crease with secondary shortening of the upper lip and elevation of the vermilion border to matching latitude with the noncleft vermilion border
- Philtral ridge defects include the absence of a philtral column or a wide philtrum with no muscle abnormality. V–Y advancement flaps, Z-plasty, or excision of the excess skin with straight-line repair are three possible treatment options
- *Deficient gingivobuccal sulcus*: Corrected via Z-plasty, local buccal advancement flaps, or buccal mucosal grafts.

## Type II Repair

It is employed for correction of orbicularis oris muscle and/or vermilion mucosal deficiencies without the need for skin or nasal repair and with a symmetric Cupid's bow. This defect is commonly seen when the vermilion component of the orbicularis oris muscle fibers is deficient along the repair line, both in unilateral and bilateral cleft deformities.

Repair involves raising a V-shaped mucosal flap with the two peaks of the V-incision stopping at the wet-dry vermilion border, excising the scar between the orbicularis oris muscle fibers and repairing the muscle with interrupted Vicryl sutures. The mucosal flap is then sutured in a Y-fashion to enhance the vermilion fullness along the repair line (Fig. 93.48).

As discussed at the beginning of this chapter, the building block of successful cleft lip repair or revision is




**Figs. 93.49A to C:** (A) Type III unilateral cleft lip revision; (B) Type III unilateral cleft lip revision; (C) Type III bilateral cleft lip revision.

the orbicularis oris muscle and its continuity along the upper lip. Attempts at correcting any muscle deficiency with dermal or fat grafts, Alloderm, or simple vermilion Z-plasty without simultaneous realignment of the deficient muscle fibers is not considered a functional repair. These procedures do not address the underlying structural defect involving the muscle; they might enhance the cosmetic appearance of the lip for a few months and until the edema subsidies postoperatively.

### Type III Repair

It involves muscle, mucosal, and skin repair without any associated nasal work. Rhinoplasty is not performed in Type III repair either because the residual deformity does not affect the nose or because the patient needs a final cleft lip rhinoplasty at a later stage (Figs. 93.49A to C).

### Type IV Repair

The surgical correction involves muscle, skin, mucosal, and nasal structures. This entails a complete lip/nasal revision much similar to all the steps employed in the primary repair. The procedure corrects deficiencies in the orbicularis oris muscle; contractures in the mucosa and skin; asymmetries of the nasal tip, alar lobule, and nostril axes; and irregularities of the vermilion border and Cupid's bow (Figs. 93.50A to C).

## CLEFT CARE IN THE OUTREACH SETTING

Managing cleft patients through a comprehensive team-based approach that is often available in major medical centers is challenging in itself. Trying to provide cleft care


**Figs. 93.50A to C:** (A) Type IV unilateral cleft lip revision: flaps outlined (left), anterior soft tissue angle suspending suture applied (right); (B) Pre- and post-type III unilateral cleft lip revision resulting in Cupid's Bow, philtral ridges, and nasal symmetry as well as repair of vermilion component orbicularis oris muscle deficiency; (C) Type IV bilateral cleft lip revision.

on a humanitarian basis and in an outreach setting has many added complexities, including the following:

- Inadequate medical supplies and resources
- Inadequate or lack of medical and nursing skills to handle complex cases, especially airway patients
- Lack of familiarization of the outreach team members with the hospital site, infrastructures, available equipment, and hospital policies
- Quality assurance and patient safety issues related to malnutrition, distances that patients and families must travel for care, associated congenital deformities, infections, and in many cases, inadequate perioperative care and long-term postoperative follow-up
- Well-intentioned but not always cohesive and adequately trained teams both in cleft care and outreach programs.

In spite of all these difficulties, outreach cleft missions have a positive impact on both patients and in-country health care providers. Thus, outreach teams must strive for the highest attainable quality in operative outcomes, patient safety, and comprehensive long-term cleft care in underserved areas in a manner congruent with ethical, legal, and medical standards present at the home base. When planning a medical mission, it is useful to divide it into pre-, peri-, and postoperative phases. Herein, we discuss the senior author's approach for providing comprehensive and multidisciplinary cleft care in outreach settings.

## Preoperative Stage

The preoperative stage is hallmarked by three goals:

- *Site selection*: Based on the actual need for an outreach mission, presence of a significant number of cleft patients, and lack of ability of local staff and resources to handle that patient load

- *Site visit*: Carried out 6–8 months prior to the scheduled mission, it is crucial to assess the location, facility, safety concerns, local team staffing and preparedness, cleft incidence and prevalence in the region, number of visiting teams to the same site, best timing for the mission, and selection of a local mission coordinator, local surgeon, and local nonprofit organization to coordinate the various logistical issues that are essential for a successful mission[28,58]
- Develop a comprehensive algorithm for the visiting team to follow and appoint a team leader to review the site and determine the needed equipment and resources to be acquired and transported for the mission.

## Perioperative Stage

A team member should arrive to the designated country a few days ahead of the team to facilitate the arrival of the team, meet with the local community, and prepare the settings for the easy incorporation of the team upon its arrival. Three months prior to the team's arrival, patient selection should be carried out by the local surgeon and PSIO initiated.

A comprehensive cleft team should include senior cleft surgeons who perform cleft procedures in their current home-based practice, pediatric anesthesiologists, OR- and PALS-certified and qualified pediatric PACU nurses, a pediatrician, a perioperative nurse, a speech therapist, a psychosocial professional, craniofacial pediatric dentists, and support staff.

Upon the arrival of the team, the presurgical period should include touring the facility and meeting the local staff, emergency preparedness, patient selection based on rigorous patient safety criteria, and setting the OR schedule. The following five operating days should concentrate on performing surgery on the younger patients at the beginning of the day, avoiding any airway cases beyond midafternoon, having an on-call team in case of an emergency, and ensuring that the team is healthy, well-rested, and not overworked. No airway cases should be performed if the hospital is not equipped and staffed to handle such cases, and no such procedures should be performed within 72 hours of team's departure. Extensive hands-on training and educational programs should be implemented for the on-site staff to ensure their empowerment and enhance the sustainability of these outreach programs.

## Postoperative Stage

The aim of the postoperative stage is to provide clear, concise, and understandable instructions to the patients and their families in a language that suits their understanding regarding the immediate and long-term postoperative care, follow-up visits, and any future treatment plans. All patients should be reassessed on the last day of the mission to evaluate the healing process and any potential complications. The on-site cleft surgeon should ensure proper follow-up of the patients for at least for the first 4–6 weeks postoperatively and their return for care when needed.

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## VIDEO LEGENDS

**Video 93.1:** *Incomplete cleft lip repair*: Video demonstrates step-by-step repair of an incomplete cleft lip deformity, including Hamdan sliding V-cheiloplasty for muscle repair, primary cleft lip rhinoplasty, including alar base suspending suture, interdomal, transverse crural and alar crease sutures as well as alignment of Cupid's bow to achieve lip and nasal symmetries.

**Video 93.2:** *Complete cleft lip repair*: Video demonstrates step-by-step repair of a complete cleft lip deformity, including Hamdan sliding V-cheiloplasty for muscle repair, primary cleft lip rhinoplasty including alar base suspending suture, interdomal, transverse crural, and alar crease sutures as well as alignment of Cupid's bow to achieve lip and nasal symmetries.

**Video 93.3:** *Incomplete cleft lip repair under local anesthesia*: Video demonstrates step-by-step repair of an incomplete cleft lip deformity on an adult patient under local anesthesia, including infraorbital and external nasal nerve blocks, Hamdan sliding V-cheiloplasty for muscle repair, primary cleft lip rhinoplasty including alar base suspending suture,

interdomal, transverse crural, and alar crease sutures as well as alignment of Cupid's bow to achieve lip and nasal symmetries.

**Video 93.4:** *Complete bilateral cleft lip repair*: Video demonstrates step-by-step repair of a complete bilateral cleft lip deformity, including Hamdan sliding V-cheiloplasty for muscle repair, primary cleft lip rhinoplasty including alar base suspending suture, interdomal, transverse crural, and alar crease sutures as well as alignment of Cupid's bow to achieve lip and nasal symmetries.

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CHAPTER

# Craniofacial Disorders: The Otolaryngologist's Perspective

94

***Gregory G Capra, Matthew T Brigger***

## INTRODUCTION

The Italian architecture that epitomized the Renaissance period was inspired by Vitruvius' principles of numeric proportions and geometric rhythms that he described in *De Architectura*. Rooted in those principles was the human form that was so eloquently displayed in Leonardo da Vinci's "Vitruvian Man" in the late 15th century.[1] Two-thousand years later, the same concepts of measured proportions are used to describe the human body, especially as it relates to the human face.[2] Although not always thought of in this way, the application of human proportions is relevant in the diagnosis and management of craniofacial anomalies. Understanding the underlying pathogenesis and how it relates to normal craniofacial architecture ultimately aids in the correct treatment planning for the patient. As expected, the patient's craniofacial function can be affected equally or more than the aesthetics outwardly displayed. Further, it has been shown that the impact on hearing, speech, appearance, and cognition has a profound influence on social integration and mental health.[3] Therefore, management of those with craniofacial anomalies is an endeavor that requires the cooperation of multidisciplinary teams that include craniofacial surgeons, oral surgeons, audiologists, speech therapists, pediatricians, geneticists, mental health professionals, and social workers to name a few.

## EMBRYOLOGY

The embryologic development of the craniofacial apparatus is a consequence of the evolutionary changes our species experienced. Possibly as a response to the development of larger brains, bipedalism, and the advent of cooking, anthropologists have documented the transition from the prognathism seen in our predecessors to the flat facies characteristic of humans today.[4] The complexity of the evolution of these structures is equal to that of the morphogenesis of craniofacial construction, which develops in an organized fashion through embryologic and fetal development. Understandably, any misstep along the way can lead to craniofacial anomalies. Therefore, the study of dysmorphology begins with the study of normal morphology, as understanding one gives insight to the other.

Normal development of the human face and its underlying structures begins at the point of conception and progresses as the embryo is formed. Ultimately, three primary germ layers are recognized: the ectoderm, mesoderm, and endoderm. The ectoderm differentiates into cutaneous and neural portions by day 20 of gestation, and they ultimately form the future epidermis and neural tube, respectively. Cells lying at the roof of the neural tube begin an epithelial-to-mesenchymal transformation as arrangement of the neural crest cells begins.[5,6]

Integral to craniofacial formation are the cephalically located cranial neural crest (CNC) cells that form the craniofacial mesenchyme. Described as a transient population of migratory stem cells, the CNC cells migrate and differentiate under the guidance of differential gene expression and signaling patterns, which determine the postmigratory identities of cells. Cranial neural crest cell migration is primarily directed dorsal and ventrolateral to the optic cup. The CNC eventually becomes the major source of connective tissue that differentiates into cranial

nerves, bones, muscles, and arteries. Additionally, the CNC aids in modeling neighboring ectodermal tissue.[5,7] An organized segregation, migration, and differentiation of CNC cells within the first 12 weeks of gestation are critical to craniofacial morphogenesis and without these processes, congenital defects would result.

The face takes shape from five facial prominences, the frontonasal process and the paired maxillary and mandibular processes that surround the future mouth (stomodeum). These prominences develop simultaneously during the fourth week of gestation and, except for the frontonasal process, arise from six mesodermal arches that are separated by corresponding ectodermally lined branchial clefts (grooves) and endodermally lined pharyngeal pouches. The frontonasal process, in contrast, originates from the fusion of the medial nasal processes and the intervening forebrain to form the future forehead and nasal dorsum. The lateral nasal folds separate the olfactory pits from the gradually developing eye region.[6]

Lateral to the stomodeum and the frontonasal prominence sits the dorsal portion of the first arch that becomes the maxillary prominence. Through membranous ossification, this gives rise to the maxilla, zygomatic bone, and a portion of the temporal bone. Caudal to the stomodeum is the mandibular prominence of the first arch, which undergoes membranous ossification of mesenchymal tissue surrounding Meckel's cartilage to form the mandible. Additionally, the first branchial arch gives rise to the muscles of mastication, the head of the malleus, the short crus and body of the incus, a portion of the auricle, the anterior two thirds of the tongue, and the mandibular branch of the trigeminal nerve.[6] At the end of the fifth gestational week, these two paired processes gain in size but have not fused. By the end of the following week, though, the jaw is formed.[5]

The second arch originates from the mesenchymal-derived Reichart's cartilage. By the sixth week, it overlaps and covers the third, fourth, and sixth arches. This arch leads to the formation of the styloid ligament, those portions of the malleus, incus, and stapes within the mesotympanum, and the lesser horn and body of the hyoid. Muscles involved in the second arch are all innervated by the facial nerve and include the muscles of facial expression, the stapedius, the stylohyoid, and the posterior belly of the digastrics muscle.[6] At the end of the eighth week, the human face is formed. The five prominences have met and fused in the midline and normally any grooves have long since disappeared.

## DYSMORPHOLOGY

With an understanding of human morphogenesis, a study of dysmorphology is possible. Abnormal morphology is in large part the study of abnormal growth and development of an organ or body parts. However, simply noting that something looks "different" is often not enough to define a child as dysmorphic in nature. Depending on the anomaly, though, a distinction between normal morphology and dysmorphology is often more subtle than the human eye can detect. Thus, the study of dysmorphology is reliant upon the objective classification of normalcy and comparing those features of an individual to the norms of a particular group. Also of great importance to the field of dysmorphology is the understanding that in many cases, anomalies do not occur in isolation. Rather, many have repeatable and identifiable patterns that are in clear association with other anomalies in the same patient. Knowledge of these patterns may provide insight into the underlying origin of the anomalies and provide diagnostic clues. Lastly, with more experience in this subject, one can more easily provide accurate information to a family regarding recurrence, expectations, and predictions of future growth and development of the child.[8]

Congenital anomalies can be classified based upon etiology, pathogenesis, and patterns. Most structural defects can be categorized into one of four etiologies: environmental (teratogenic), chromosomal, single-gene, and multifactorial. Within the subcategory of environmental anomalies, the four identifiable causes include exposure to radiation, infection, maternal idiosyncrasies, and chemicals.[5] In regard to chromosomal and single-gene defects, an ever growing number of craniofacial anomalies have an identifiable chromosomal aberration that has been isolated and structurally identified. Although these numbers have expanded over the years, these still only represent a fraction of total craniofacial anomalies. Further complicating the matter is the fact that many anomalies are due to complex polygenic interaction with environmental factors, i.e., multifactorial.[3]

An anomaly can be further classified as a malformation, disruption, deformation, or dysplasia. This classification approach is helpful in determining the different implications of the anomaly and clinical expectations. Two additional useful terms in describing this section are intrinsic and extrinsic. When describing an anomaly as intrinsic, the developmental potential of that organ was abnormal from fertilization. In other words, the organ never had a chance to be normal. In contrast, when an

anomaly is extrinsic, the organ had the developmental potential, but that potential was never realized because an extrinsic factor such as an infection or teratogen interfered with the development that then proceeded abnormally.[9]

Erroneously, many anomalies are thought to be malformations when in fact a specific subset of anomalies falls within this category. Spranger et al.[9] define a malformation as a morphologic defect arising from an intrinsically abnormal developmental process. This can affect an organ or body part, portion thereof, or a larger region of the body. Rarely is the anomaly a single defect but instead most are related to field defects. Morphogenetic fields are described as embryonic regions that develop in concert with one another to form complex anatomic structures. When an intrinsic disturbance, that is a malformation, occurs, the field defect results in adjacent anatomic anomalies. The earlier this occurs in gestation the more pronounced the defect.[9]

A disruption is a morphologic defect of an organ, part of an organ, or a larger region of the body resulting from an extrinsic breakdown of, or an interference with, an originally normal developmental process. Thus, the organ or body part had the developmental skills to promote normal morphology but because of an insult such as infection or a teratogen, morphogenesis was derailed and an anomaly resulted. Although inherited factors can contribute to disruptions, a disruption itself is not inherited. Further, distinguishing a disruption from a malformation may be difficult in the postnatal period.[9]

A deformation is a natural response to mechanical forces that create an abnormal form, shape, or position of a body part that would otherwise undergo normal morphogenesis. Unlike the previous two terms, deformations can be either extrinsic or intrinsic in nature. Respectively, two examples include intrauterine constraint and a nervous system defect that results in hypomobility in a fetus. This type of pathogenesis usually has a good prognosis once the offending mechanical force is removed because the organ itself is normal. The favorable prognosis is distinct from malformations that generally fare poorly because the organ is inherently defective. Upon release of the deforming force, one would expect normalization of the developmental process in the form of catch-up growth.[9]

Dysplasia is the fourth type of abnormal morphogenesis. It is defined as the process of dyshistiogenesis that leads to abnormal organization of cells into tissue. Although originally described as neoplastic tissue development, dysplasia applies to any form of abnormal histogenesis. The result is gross tissue defects at any site where the affected tissue element is present. Therefore, widespread involvement is possible and multiple organ systems may be affected. Localized forms of dysplasias are possible and an example of this is a vascular tumor that occupies a single organ.[9]

Micrognathia provides an example of how each of these processes can lead to one common craniofacial anomaly. Simply put, micrognathia is a result of mandibular undergrowth as a whole or in individual portions, but its origin may differ. In Treacher Collins syndrome (TCS), malformation of the mandible is due to a TREACLE protein abnormality that leads to impaired neural crest cell proliferation. It also results in field defects of the first and second branchial arches.[10] Stickler syndrome (ophthalmoarthropathy) represents dysplasia of the mandible, secondary to collagen defects, usually from a COL2A1 gene mutation. But like other dysplasias, its anomalies are not limited to one body part. Stickler syndrome also affects other organs and tissues, such as the vitreous fluid of the eye and joints, which utilizes that particular collagen type.[11] Radiation therapy, a well-known teratogen in pregnant females, has been shown to increase the incidence of micrognathia in newborns and represents disruption of a developing mandible.[12] Finally, oligohydramnios is an often cited form of an extrinsic mechanical force that can cause deformation of the mandible. This form may be mild or more severe in cases of nonsyndromic Robin sequences. Either way the prognosis is better than other forms of abnormal morphogenesis, as this type of micrognathia usually displays catch-up growth in the postnatal period.

## Patterns

As briefly mentioned above, micrognathia does not always appear in isolation. In fact, many newborns phenotypically express an undersized mandible in association with other anomalies. More commonly, some patients may express a collection of anomalies that are secondary repercussions of the original anomaly, micrognathia. Yet, in rare occasions, micrognathia may have a proven association with other anomalies only by statistics. Just as it is important to understand the etiologic and pathogenetic origins of specific anomalies, it is also valuable to understand the patterns associated with these anomalies. If etiology is the cause of an abnormal structure, form, or function and pathogenesis describes the mechanism(s) that lead(s)

to the anomaly, then patterns refer to the relationship between the pathogenesis of multiple anomalies. By understanding the patterns of morphologic defects, a team can better identify, treat, and predict the abnormal development of the whole dysmorphic child.

### *Sequences*

The first pattern, termed a sequence, is described as a series of defects occurring secondarily in a nonrandom fashion as a result of a primary inciting event, such as another anomaly or a mechanical factor.[8,9] Specifically, a sequence may arise from a malformation, disruption, dysplasia, or a deformation that began a cascade of abnormal development. The Robin sequence can be explained by each of these, with the end result being secondary to micrognathia that subsequently causes a glossoptosis and then airway distress, palatal clefting, or both. Similarly, the Potter sequence facies provides another example of a pattern of sequence. It is causally heterogeneous; it can be genetic or nongenetic in nature or it may be intrinsic to the fetus such as in renal agenesis or extrinsic to the fetus as in premature rupture of amniotic membranes. Whichever the cause, oligohydramnios is the inciting event and the abnormal facies that develop are a result of the sequences that follow.

### *Syndromes*

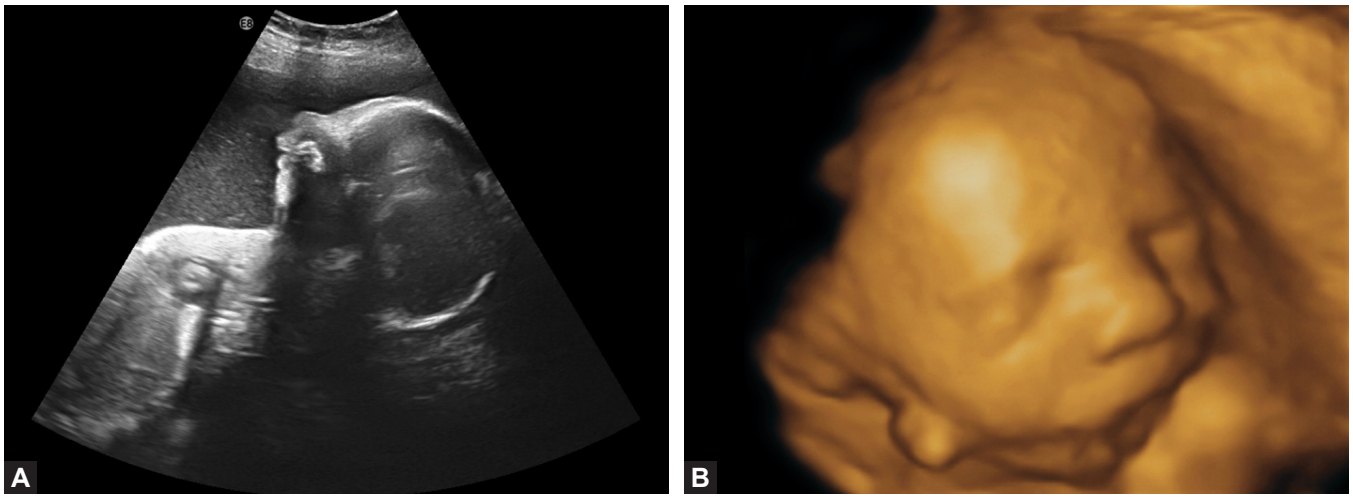
Similar to the misuse of malformations in the description of anomalies, the term syndrome often is generically applied to a group of anomalies in an erroneous fashion. A syndrome is a pattern of multiple anomalies that are pathogenetically related yet do not represent a single sequence. Similar to sequences, they result from a single cause and display multiple defects in one or more tissues. Achondroplasia describes a constellation of symptoms brought together by a common genetic mutation in the fibroblast growth factor receptor 3 (FGFR3) gene. Multiple developmental fields may be abnormal; the skull base, midface, proximal limbs, and spine are but a few anomalies. However, as Spranger et al.[9] described, the use of the term syndrome implies a lower level of understanding than sequence when describing pathogenic patterns. In sequences, the secondary effects are a known result of a cascade of events from a primary event. In a syndrome, the same level of understanding is not present. In fact, a syndrome may represent an, as of yet, unknown sequence, which describes the dysmorphology of two or more developmental fields. Therefore, further research into these patterns is warranted. On the other hand, a syndrome has a known relationship, for example a genetic mutation. This is another requirement of a syndrome, meaning two or more dysmorphic body parts occurring by a statistical association or a chance occurrence do not constitute a syndrome.

### *Associations*

To categorize these latter types of anomalies, a third term, association, is used in the patterning of anomalies. An association is a nonrandom presence of certain malformations that occur together in a frequency more common than would be expected by chance alone. Associations are not causally or pathogenetically related but are statistically related anomalies. Usually, the name of an association is derived from major component defects in the form of an acronym, such as the VACTERL association. In some cases, though, with improved research and understanding, an association may be reclassified as a syndrome or sequence.[9] An example of this is the formerly known CHARGE association, which is now considered a syndrome due to the identification of the CDH7 gene mutation as the likely cause.[8] Regardless of whether the origin is known or not, the power of an association classification is that with the presence of one anomaly, a clinician may be alerted to a second anomaly that is statistically related. With further knowledge of dysmorphology through research such as the Human Genome Project, more genetic mutations will be identified and more appropriate categorization will occur.

## ROLE OF IMAGING IN CRANIOFACIAL DISORDERS

Traditional roles of imaging in the prenatal period include fetal growth tracking, detection of developmental anomalies, and as a procedural aid. Along with earlier and more accurate identification of craniofacial anomalies, advances in radiography have also permitted more appropriate prenatal planning of neonatal care. In some cases, the successful management of a neonate requires an early knowledge of risk factors for postpartum complications. For example, a child with severe micrognathia, as seen in TCS, may require additional delivery support, ranging adjunctive airway support to an ex utero intrapartum therapy procedure with surgical airway management rather than normal vaginal delivery. In addition to guiding early




**Figs. 94.1A and B:** Prenatal ultrasound demonstrating sagittal view (A) and surface view (B) of a fetus with severe micrognathia.

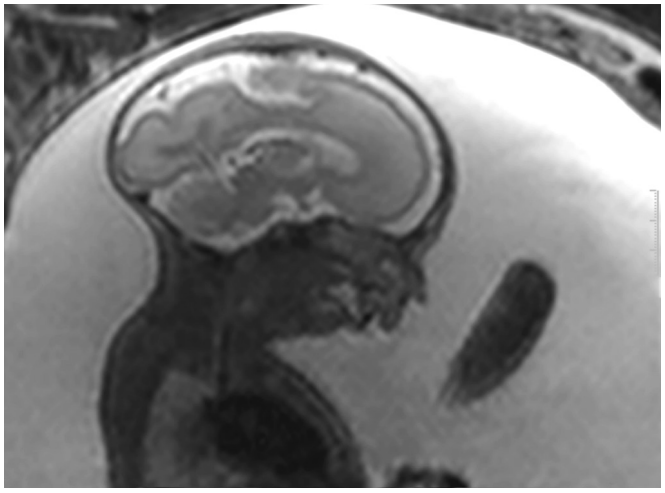


**Fig. 94.2:** T2 fetal MRI oriented to provide sagittal reconstruction of a fetus with severe micrognathia.

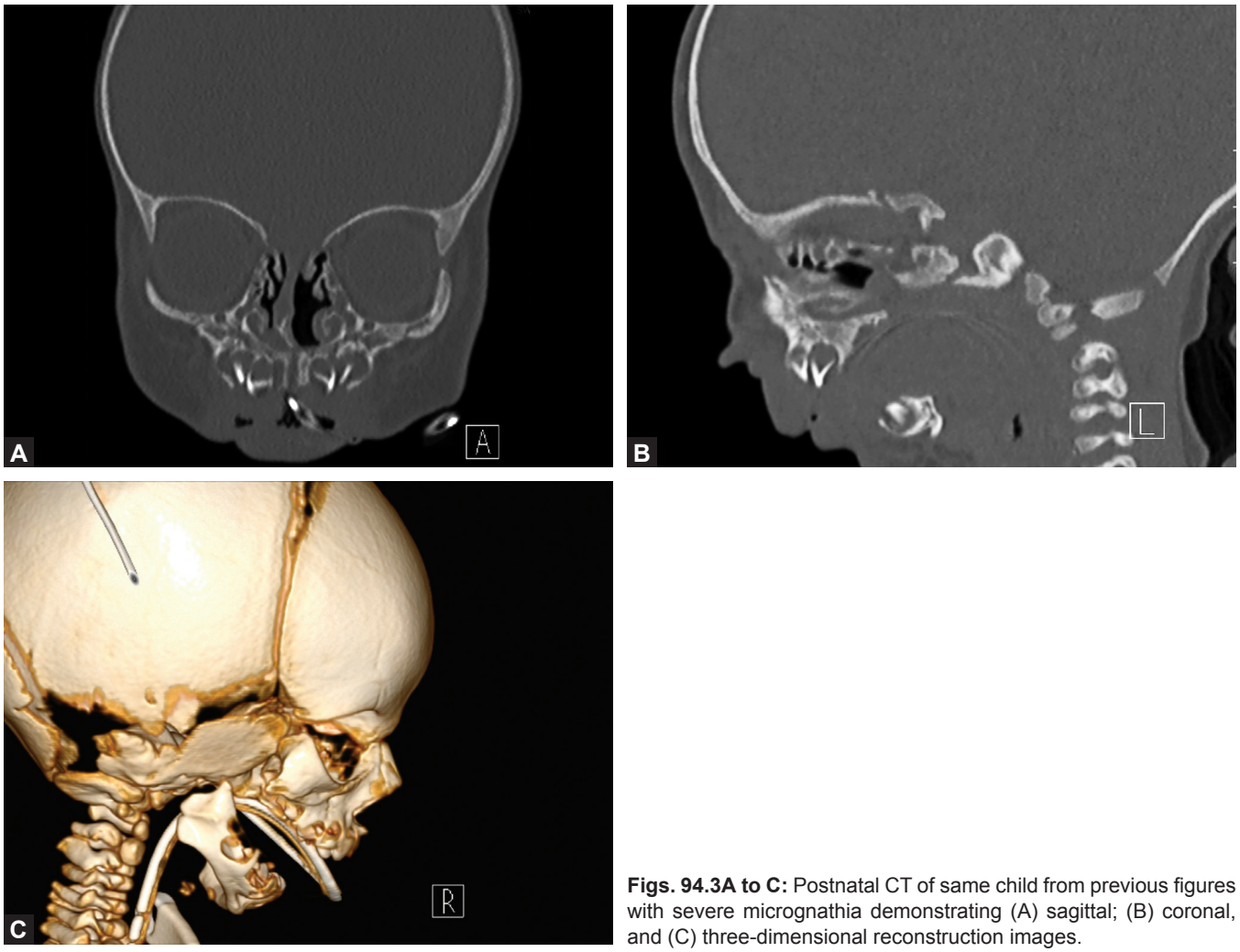
interventions, imaging may also permit the facilitation of multispecialty management of the neonate or transfer of care to tertiary hospitals. In other ways, radiography is beneficial long after birth in the surveillance and surgical management of craniofacial anomalies. Whether it is ultrasonography (US), magnetic resonance imaging (MRI), or computer tomography (CT), the modalities are complementary to one another.

## Ultrasound

The earliest tool to be used in the diagnosis of craniofacial anomalies is ultrasound. The age range for initial screening is between 18 and 20 gestational weeks. This permits early identification of defects, which allows ample time to permit further studies, yet not so early that the fetus is too small that it reduces the sensitivity of the study. Three-dimensional (3D) ultrasound images have advanced in recent years. Essentially, a two-dimensional image acquisition as a sweep or volume, 3D ultrasounds permit the clinician surface-rendered images as well as improved profile views of the face (Figs. 94.1A and B). When cinematic sequence is added to the image, the image is referred to as 4D technology.[13] However, there are drawbacks to this technology. Ossification of bone creates shadows that may obscure images, particularly later in gestation. Also, first trimester US may fail to detect craniofacial anomalies that are more apparent with gestational age.[14] In these instances, MRI may be of benefit.

## Magnetic Resonance Imaging

Magnetic resonance imaging is complementary to ultrasound and used when a complete evaluation of fetal or soft tissue anomalies is needed. The T2-weighted images are the primary format used to evaluate the fetus and contrast is avoided.[4] Depending on the view used, different fetal structures are optimally evaluated. The sagittal view inspects anomalies of the frontal and nasal bones, palate, mandible, and tongue (Fig. 94.2). Therefore, frontal bossing, nasal anomalies, palatal clefting, micrognathia, and macroglossia can be identified in this view. Coronal images also aid in examining cleft lips or palates. In addition, they are also beneficial in evaluating the eyes, nose, and ears. Axial images also assist in orbital evaluation and may be used with age-related norms to




**Figs. 94.3A to C:** Postnatal CT of same child from previous figures with severe micrognathia demonstrating (A) sagittal; (B) coronal, and (C) three-dimensional reconstruction images.

identify hypotelorism or hypertelorism. Anomalies of the nasal cavity, maxilla, mandible and ears are seen in this view. In addition to craniofacial anomalies, MRI is also used to detect associated anomalies of the heart, kidneys, extremities, and spine for instance, which may aid in identifying any dysmorphology patterns. Finally, fetal MRI can aid in surgical planning and delivery.[13,14]

## Computed Tomography

In contrast, CT imaging is not recommended prenatally because of the associated risks of radiation exposure.[13] However, it is invaluable in the management of craniofacial anomalies as the child grows. In particular, CT is the technique of choice when evaluating anomalies affecting skeletal development due to the improved resolution of osseous structures compared to MRI and ultrasound. High-resolution CT permits additional reconstruction in the form of 3D images (Figs. 94.3A to C). With such imaging, a global interpretation of anomalies is possible and may aid in the diagnostic and prognostic assessment of the patient. Further, 3D CT reconstruction can aid in surgical planning by using images to create life-sized models of the anomalies. Additionally, CT with intravenous contrast can be used to evaluate any vascular anomalies, as in the case of the aberrant course of the internal carotid artery sometimes associated with velocardiofacial syndrome (VCFS).[6]

# COMMON ANOMALIES

Recognition and description of the various anomalies are critical in the evaluation and diagnosis of children

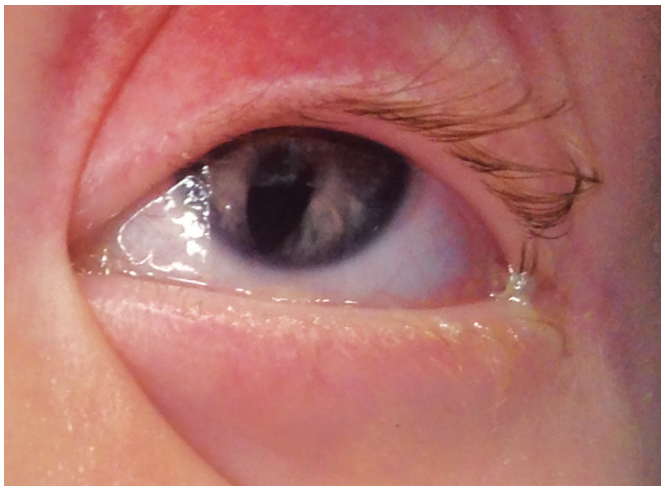


**Fig. 94.4:** Child with an inferior iris coloboma. Also note the associated epicanthal fold.

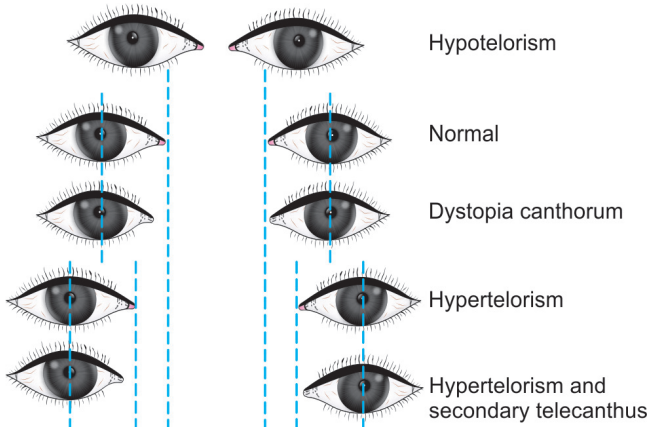



**Fig. 94.5:** Illustration of variable relationship between inner canthi and eyes.

with craniofacial dysmorphisms. A systematic approach in a multidisciplinary format is recommended. Specific, consistent nomenclature is requisite to ensure clear communication across disciplines.

## Eyes

### *Eyelid Coloboma*

Eyelid coloboma is a full-thickness cleft of the eyelid margin, either triangular or quadrilateral in shape. It more commonly occurs in the upper lid (e.g. Goldenhar syndrome) than the lower lid (e.g. TCS).

### *Uveal Coloboma*

Uveal coloboma (Fig. 94.4) is a cleft within the iris, choroid, and/or optic nerve as a result of failure of the choroid fissure to close by the seventh week of normal development.

### *Orbital Hypertelorism*

Orbital hypertelorism is present when interorbital distance between the medial orbital walls is greater than 2 standard deviations above the mean. The upper limit of normal in adults is 30 mm.

### *Ocular Hypertelorism*

Ocular hypertelorism is excess interpupillary distance in the presence of normal-sized eyes. Its existence can be assumed if the interorbital distance is greater than 2 standard deviations above the mean.

### *Orbital Hypotelorism*

Orbital hypotelorism is present when interorbital distance between the medial orbital walls and interpupillary measurement is decreased.

### *Telecanthus*

Telecanthus is an increased distance between the inner canthi due to lateral displacement of the lacrimal punctae and inner canthi. The eyes are otherwise normally spaced. The normal inner canthal-to-outer canthal distance ratio is 1:3 (Fig. 94.5).

### *Epicanthus*

Epicanthus is a fold of skin covering the inner canthus of the palpebral fissure (Fig. 94.6).

- Epicanthus supraciliaris—epicanthal folds arise from the region of the eyebrow toward the lacrimal sac.
- Epicanthus palpebralis—epicanthal folds arise above the tarsal fold in the upper lid and extend to the lower orbit margin.
- Epicanthus tarsalis—epicanthal fold arises laterally above the tarsal fold and ends adjacent to the inner canthus.
- Epicanthus inversus—epicanthal fold arises in the lower lid and extends upward to partially cover the inner canthus

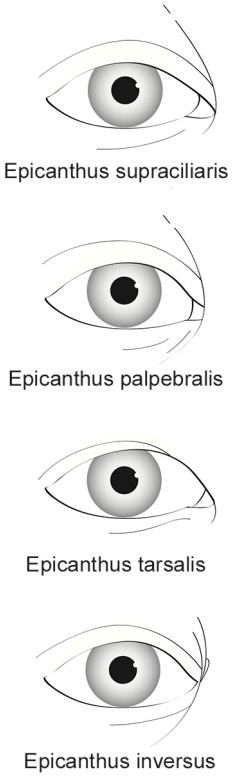



**Fig. 94.6:** Illustration of various types of epicanthal folds.

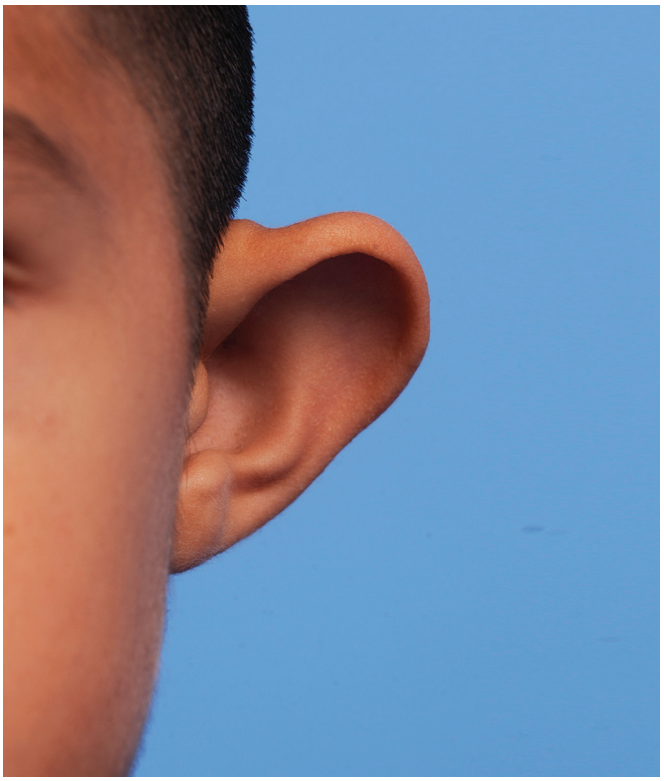


**Fig. 94.7:** A child with protruding ears due to the absence of an antihelical rim and enlarged conchal bowl.

## Ears

### *Cryptotia*

Cryptotia is the incomplete separation of the superior and posterior aspects of the helix from the scalp. It is also referred to as the "hidden ear deformity".

### *Lop/Cup Ear*

Lop/cup ears are the downward folding and deficiency of the superior aspect of the helix as a result of underdevelopment or hypoplasia of the superior one-third of the auricle. An overdevelopment of the concha is often associated with this anomaly.

### *Protruding Ears*

Protruding ear is a normal-sized ear with lateral prominence of the auricle at an angle from the head greater than 40°. It is considered a variation of the lop/cup ear (Fig. 94.7).

### *Posteriorly Rotated Ears*

Posteriorly rotated ears occur when the vertical axis of the ear is rotated posteriorly. It is often confused with low-set ears.

### *Low-Set Ears*

Low-set ears are present when the auricles and/or meatus are situated low on the lateral face. Ears are considered low set when a horizontal line passing from the inner to outer canthi lies above the root of the helix. Another definition suggests ears are low set when the highest point of the external meatus lies below the level of the upper edge of the nasal ala.

### *Microtia/Anotia*

Microtia refers to a congenital deformity of the pinna, which is underdeveloped (Fig. 94.8). Anotia occurs when a pinna is completely undeveloped.

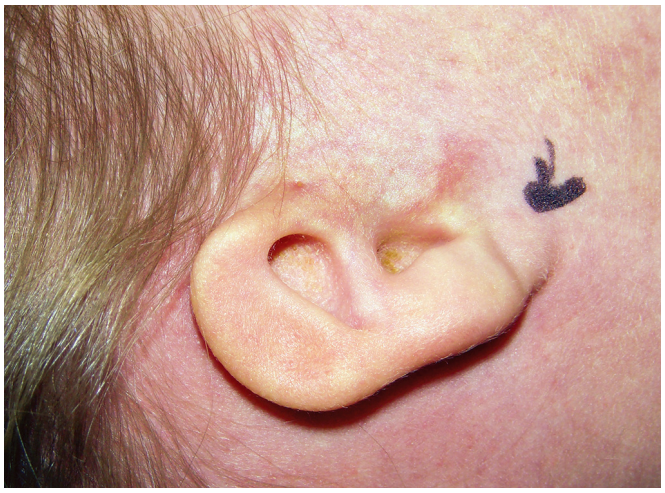


**Fig. 94.8:** A child with microtia demonstrating an underdeveloped pinna.

## Facial Skeleton

### *Congenital Asymmetry of the Facial Skeleton*

Congenital asymmetry of the facial skeleton is a quantitative size difference of either side of the face using the midsagittal plane as the midline.

### *Absence and Hypoplasia of the Zygoma*

Absence and hypoplasia of the zygoma are first branchial arch anomalies causing the underdevelopment of the zygomatic bone, which results in midface and orbital floor deficiency.

### *Midface Retrusion and Hypoplasia*

Midface retrusion and hypoplasia are the posterior positioning or impaired development of the midface that affects the orbits, nasal bones, and maxilla. This may result in a semilunar appearance of the face on profile and may be present in neural crest, cranial base, or branchial arch development.

### *Micrognathia*

Micrognathia is a reduction in size of one or all parts of the mandible.

### *Retrognathia*

Retrognathia is the posterior displacement of a normal-sized mandible or maxilla in relation to the skull base.

## Tongue

### *Macroglossia*

Macroglossia is the enlargement of the tongue. It may be classified as a true or relative enlargement. True macroglossia is further subdivided into congenital or acquired forms. Relative macroglossia refers to a normal-sized tongue that appears large also due to congenital or acquired causes.

### *Glossoptosis*

Glossoptosis is the downward or posterior displacement of the tongue into the pharynx.

# CLINICAL CONSIDERATIONS IN THE MANAGEMENT OF CHILDREN WITH CRANIOFACIAL ANOMALIES

## Airway Issues

Clinically, airway anomalies are relatively common in craniofacial disorders and in some studies are found in nearly two thirds of patients. It is generally assumed that the upper airway is the primary site of airway obstruction in these patients and ranges from mild nasal obstruction to severe respiratory distress. Some cases are so mild, that they may only become symptomatic in the presence of upper respiratory infections or poorly managed gastroesophageal reflux. In rare cases, airway obstruction can lead to cardiopulmonary arrest and even death. Realistically, craniofacial anomalies are often associated with other respiratory anomalies that exist below the level of the glottis. Known sequelae from either level of obstruction include failure to thrive and neurodevelopmental delay.[15]

The origin of airway obstruction is multifactorial in nature. Some cases are anatomic and static, others are physiologic and dynamic, but most are a combination of the two. Beginning with the nasal airway, alterations in the nasal dorsum or reduced pyriform aperture diameter can impair nasal respiration. Further, nasomaxillary hypoplasia, choanal atresia or stenosis, or a shortened cranial base can contribute to nasal or nasopharyngeal airway obstruction. Abnormal skull base anatomy may interfere with the remaining pharyngeal airway as well. Similarly, the effect of oral cavity anatomy may impact the

pharynx. Most notably, mandibular hypoplasia can result in glossoptosis manifested as airway distress. This may further be impaired as a result of adenotonsillar hypertrophy, which can present as airway distress or sleep apnea, in a child once deemed to have a safe airway.[16,17]

Laryngotracheal structures can be affected in craniofacial anomalies and may result in fixed or dynamic airway obstructions. Presentation may be recurrent croup, stridor, or poor exercise tolerance. Cartilage anomalies can affect the glottic structures presenting as laryngomalacia; laryngeal clefts may present as recurrent respiratory illnesses secondary to aspiration, and subglottic stenosis may be a result of congenital or iatrogenic causes. Tracheal and bronchus support may be deficient in some cases, leading to tracheobronchomalacia. If one were to limit the area of investigation to structures above the vocal cords then such findings may never be identified. Therefore, panendoscopies are warranted in the setting of airway difficulties, which can identify anomalies not otherwise identified by flexible laryngoscopy or imaging studies.[15] Similarly, without visualization of all levels of the airway, neurologic disorders, such as pharyngeal hypotonia or vocal cord dysfunction, may not be identified.

The need for airway management can present itself early in neonatal life or may be delayed until a child is much older. Determining the type of airway management that is needed and the timing at which it is done are often dependent upon the severity and prognosis of the anomaly, which in turn may be reliant upon the underlying syndrome, sequence, or association. One study suggested that certain syndromes are more likely to require definitive airway management. The highest rates were found amongst craniofacial synostosis and mandibulofacial dysostoses patients, whereas those with craniofacial microsomia (CFM) were amongst the lowest.[18]

Definitive airway management for children with craniofacial anomalies is a tracheotomy. Studies suggest that up to a third of all children with severe craniofacial anomalies will require a tracheotomy in their lifetimes.[15,18] Those that had multilevel airway obstruction, particularly nasal obstruction and midface retrusion in the setting of oropharyngeal obstruction, were among the highest rates. Further, those requiring ventriculoperitoneal shunts due to hydrocephalus also had high tracheotomy rates, likely because of acute skull base angles that impaired CSF outflow, reduced nasopharyngeal volume as well as the association with neurologic deficits. In contrast, children with cleft palate tend to have lower rates of tracheotomy, possibly owing to the increased nasopharyngeal volume due to the cleft providing a patent airway. Children treated with tracheotomies before age 4 often went years before decannulation, but those with tracheotomies after this age usually were decannulated within weeks.[18] Regardless of indication, children that did receive a tracheotomy have been shown to have improved growth and development. The utility of a tracheostomy must be balanced with the potential-associated morbidity. Most notably, the procedure requires complex nursing care for parents and can result in secondary laryngotracheal disorders such as subglottic stenosis or in rare cases death due to mucus plugs or accidental decannulation.[16]

While tracheotomy is the gold standard for complex airway management, many children with craniofacial anomalies do not require tracheotomies, but may require special considerations when undergoing anesthesia. A multidisciplinary approach to airway management between pediatric anesthesiologists and pediatric otolaryngologists is often critical. Advanced techniques for airway control including fiberoptic orotracheal or nasotracheal intubation, laryngeal mask airway stabilization, and video-assisted laryngoscopy are routinely used.

Based on the degree and acuity of symptoms ranging from subtle obstructive sleep apnea (OSA) to florid reflux, a variety of adjunctive diagnostic algorithms and therapeutic procedures may prove useful in these children. In particular, polysomnography should be utilized to evaluate children with symptoms consistent with OSA. Based on specific anomalies and degree of dysfunction, procedures such as noninvasive positive pressure ventilation, adenotonsillectomy, tongue base reduction or suspension, midface and mandibular advancement, and antireflux surgery have proven useful.[15,18]

## Feeding Issues

The risk of a feeding disorder is increased in the presence of craniofacial anomalies with or without cleft lip and palate. The normal feeding process of a newborn requires precise coordination of sucking, swallowing, and respiration that is reliant upon functional anatomy and intact neurologic and respiratory systems. Without such an environment, nutritional or respiratory compromise can occur. Nasal obstruction in the first 2–3 months of life, either from choanal stenosis or atresia, impairs respiration while the child is an obligate nasal breather. Clefting of the lip and/or palate disrupts the normal feeding-respiration

cycle, as well as impairment of sucking and squeezing required for adequate feeding. Midface and mandibular retrusion impairs the child's ability to feed in addition to obstructing the airway. Tongue movement restriction, motor dysfunction, and pharyngeal obstruction due to glossoptosis further complicate nutritional status. Cranial nerve palsies can lead to pharyngeal hypotonia, and in some cases, oral incompetence may be secondary to facial nerve weakness. Finally, laryngotracheal anomalies, such as laryngeal clefts or tracheoesophageal fistulas, may permit chronic aspiration and cause recurrent respiratory infections and impaired respiratory health.[19]

As is the case with airway management, a multidisciplinary approach to feeding disorders is necessary. Diagnosis often requires dedicated swallowing evaluations including videofluoroscopic swallowing studies or functional endoscopic evaluation of swallowing. Conservative measures such as upright positioning, assistive breast and nipple squeezing, imposed pauses, and thickening of liquids often will suffice. Occasionally, specialized nipples, palatal obturators, or temporary feeding tubes may be necessary. In more rare cases, surgical techniques, primarily those involving management of the airway, will be needed. Alternatively, gastrostomy tubes may be required. In many cases, appropriate management of the airway will often times permit adequate management of feeding disorders.[19] Significant effort is aimed at avoiding dependence on a gastrostomy tube due to the well-described development of oral aversions in such children. Therefore, if possible, craniofacial teams should focus on continuing to attempt oral feeding to prevent feeding difficulties in the future.

## Otologic Issues

As is the case with airway findings in craniofacial disorders, otologic anomalies may be multilevel, affecting the external, middle, or inner ear structures. In some cases, there are embryologic restrictions to what may be affected, for example TCS is limited to the structures of the first and second branchial arches lateral to the otic capsule, while in other cases, all three regions may be affected, as in CHARGE syndrome.[20] Further, abnormal otologic findings can result in anatomic, functional, or mixed anomalies depending on the underlying dysmorphology.

The clues to otologic anomalies may be subtle or overt on initial anatomic inspection. This is true for external ear anomalies, which may range from slightly abnormal to severely dysmorphic in appearance. In some cases, structures may even be absent depending on the underlying cause. Cup and lop ear deformities are common in some conditions, whereas in others, microtia and canal atresia may be present. In the middle ear, ossicles can be malformed or absent.[20] The ossicles may not be the only abnormality present as neighboring structures, such as the facial nerve, jugular bulb, or internal carotid artery can also suffer from abnormal embryogenesis. The inner ear can be affected variably as well. Some variations may be mild, such as an asymptomatic but abnormal appearing petrous bone. In others, the cochlea or vestibular system may be malformed, hypoplastic, or absent altogether.[20] Therefore, anatomical abnormalities may be the initial clue that a condition exists, but keep in mind, they do not necessarily reflect the degree of otologic dysfunction.

Given the prominence of the ears, dysmorphisms of the external ear can be associated with deleterious psychological effects in some children. Such considerations are made when decisions regarding surgical management are made. If possible, performing surgery for congenital ear deformities is often initiated at approximately age 4–6 years to decrease the associated stigmata as children begin their formative school years.

Dysfunction of the hearing not only impacts one's ability to experience the world, but may also impact one's ability to interact with others. Depending on a multitude of factors, children may experience conductive, sensorineural, or mixed hearing losses. Conductive hearing losses (CHL) are often secondary to Eustachian tube dysfunction, but it can also be due to ossicular abnormalities. Sensorineural hearing losses (SNHLs) are common and can be progressive with age. This requires clinicians to be vigilant in terms of otologic examinations among these patients. Further, it may help to identify those at risk for speech delays. This is particularly true in those children who are more likely to suffer from developmental delay with abnormal hearing and speech, such as in Down's syndrome.[17,20] Therefore, hearing testing should be routine for screening and follow-up including auditory brainstem response (ABR) testing at birth. Further follow-up should include speech as well as pure-tone audiometry. Otoscopy is useful in evaluating middle ear disease and can also be used to identify middle ear abnormalities, such as a high riding jugular bulb. Finally, objective otologic studies may be needed in those children who are either too young or uncooperative, and it may include ABR or otoacoustic emissions testing.[17]

Otologic dysfunction can be treated either medically or surgically. In most cases, CHL may improve upon placement of pressure equalization tubes. In others, ossiculoplasty or stapedectomy may be warranted. Hearing augmentation may also be useful in more severe cases. Available options include hearing aids, bone-anchored hearing aids, and in some cases cochlear implantation. Whichever method of treatment is used, speech therapy should also be considered as part of the treatment plan.[20]

## SPECIFIC CRANIOFACIAL DISORDERS

While otolaryngologists must be prepared to care for patients with the full spectrum of craniofacial dysmorphisms, several entities warrant specific consideration. In particular, entities commonly evaluated by otolaryngologists with associated airway and feeding issues are described below. Of note, many affected children have associated hearing issues.

### Robin Sequence

Pierre Robin initially described an association of upper airway breathing difficulty with micrognathia and glossoptosis in the 1920s. He later modified this description to include a cleft palate. Although termed Pierre Robin Syndrome in the 1960s, the eponym has had many name changes over the years. Since the observed anomalies arise secondarily from a primary anomaly (micrognathia), the term Pierre Robin sequence (PRS) best describes this condition. Nosologic confusion over the years persists due to a lack of agreement as to the defining characteristics of PRS. Breugem and Courtemanche[21] polled 73 teams of the American Cleft Palate-Craniofacial Association in order to better define PRS. Of those polled, 18% defined PRS as Robin's original description, while nearly half used his modified definition that included cleft palate. Due to the widespread confusion of PRS classification, a wide range of prevalence is reported. However, a general belief is that PRS occurs in approximately 1 in 8500 births. Further complicating an accurate prevalence rate is the differentiation of syndromic and isolated (nonsyndromic) classification. Shprintzen[22] earlier observed that 80% of cases were related to syndromes while more recent studies have found nonsyndromic PRS comprises 55–75% of cases.[3,7] In their observations, Stickler syndrome followed by VCFS, fetal alcohol syndrome, and Treacher Collins were the most commonly associated syndromes to PRS.[22-24]

Embryologically, the sequence begins prior to the ninth week in utero, whereby mandibular hypoplasia results in posterior and superior displacement of the tongue between the palatal shelves. It is this mechanical disruption, rather than a primary molecular or genetic factor, that prevents palatal fusion between the eighth and tenth week of gestation. Although unable to identify dysmorphology at a very early stage, advances in ultrasonography have made the diagnosis of micrognathia in utero more common. However, confirmation of glossoptosis and cleft palate is less reliable and diagnosis of PRS is commonly made at birth.[25]

Micrognathia is the hallmark of PRS, but retrognathia is also possible. The two may be difficult to distinguish until an appropriate amount of time for postnatal mandibular catch-up growth is observed.[21] Substantial catch-up may be seen with near normalization of the facial profile in some patients in the first decade. If malformational in origin, such as seen with syndromes like Treacher Collins, then the mandible will remain small through life and dysmorphic features may progress without surgical intervention. In contrast, if the mandible is intrinsically normal but was constricted in utero (deformational), then mandibular catch-up can be expected.[22,26]

Generally, mandibular length is shorter in all cases of PRS and retraction of the mandibular alveolus on average is 10–12 mm posterior to that of the maxillary alveolus. Specifically, the mandible has been shown to have a smaller body, shorter ramus, more obtuse gonial angle, altered cranial base angles, and a posteriorly displaced or diminutive mandibular condyle.[25,27,28] Mandibular dysmorphology, though, is variable and its degree is dependent on the underlying etiology. Rogers et al.[26] found that syndromic Robin patients had a shorter mean mandibular length than isolated PRS and Suri et al.[29] found that the greatest deficiency exists in the mandibular body. Key syndromic specific findings include a shortened ramus in Stickler syndrome, retrognathia secondary to altered cranial base angles in VCFS, and the greatest gonial angle, and foreshortening of mandibular length in TCS. Specific cephalometric measurements by Suri et al.[29] in nonsyndromic PRS patients found both a smaller mandibular body and ramus but a larger than normal ramus-to-body ratio. The maxilla tended to be retrognathic, leaving the perception that maxillomandibular dysplasia was less pronounced.

Physical exam reveals a posterior and superior positioning of the tongue that may lead to oropharyngeal

obstruction, but the tongue may also be within the palatal cleft particularly when the patient is supine.[25] Macroglossia and ankyloglossia are rare findings in PRS. During fetal development, the tongue position between palatal shelves is thought to contribute to the U-shaped cleft, often seen in Robin sequence, which spares the alveolus. In some cases, a V-shaped palatal defect is present, while in certain syndromes, such as VCFS, the defect may be incomplete such as a bifid uvula or a submucous cleft.

The two most important clinical issues for PRS patients are airway management and feeding. The spectrum of airway obstruction may range from mild positional to occult respiratory distress, and it may progress with age as the respiratory needs of the newborn increases.[24,25,30] Syndrome-specific contributions to the degree of airway obstruction include skull base anomalies in Treacher Collins and Stickler syndromes, pharyngeal hypotonia in VCFS, and central nervous impairment associated with VCFS and fetal alcohol syndrome.[22] Evans et al.[24] found that 56% of airways in PRS patients were safely managed without surgery and Meyer et al.[23] reported that two thirds of PRS patients were managed with prone positioning, nasopharyngeal airway, or endotracheal intubation.[23,24] The broad diversity of PRS patients inhibits a universal paradigm in airway management, but surgical indications generally include when nonsurgical methods fail or will likely fail.[23,30] Given that the level of obstruction is oropharyngeal or hypopharyngeal, acute interventions include nasopharyngeal airways and tracheal intubation. However, the degree of micrognathia and glossoptosis may complicate direct laryngoscopy. The patients most likely to require surgical intervention include syndromic patients because of associated infraglottic and nasal airway anomalies in conjunction with comorbid systemic diseases independent of glossoptosis.[25,30] The most commonly described airway management techniques include tongue–lip adhesion and mandibular distraction osteogenesis, which has gained in popularity in recent years. Tracheostomy is indicated when other procedures fail or are not recommended, and it is more likely in patients with associated neurocognitive disorders.[24,25]

Adequate feeding is also of major concern in PRS. Poor feeding may be a result of glossoptosis causing airway obstruction or inefficient suction and squeezing of the nipple, as seen in cleft palate patients. The micrognathic jaw may be associated with orbicularis oris incompetence further impairing suction. Lastly, pharyngeal hypotonia and dysmotility may also contribute to poor feeding in syndromic patients.[25,31] The consequences of poor feeding include oral aversion, nasogastric or gastric tube dependence, and failure to thrive.[22,24] As with airway management, feeding may be improved with positioning or other nonsurgical techniques. Shprintzen[22] argued that by relieving airway obstruction, improved feeding can be expected and Lidsky et al.[31] confirmed this and showed that early airway intervention further improved outcomes. In early life, airway management and feeding issues should be addressed appropriately and associated syndromes should be identified in order to plan for future medical or surgical interventions.

## Treacher Collins Syndrome (Mandibulofacial Dysostosis)

Treacher Collins syndrome (TCS) is a rare craniofacial malformation that lacks associated limb deformities. Initially described by Thomson and Toynbee in 1846–1847, much of the credit to its description has been given to Berry in 1889 and later Edward Treacher Collins in 1900. Franceschetti and Klein in 1949 labeled it as a mandibulofacial dysostosis. Treacher Collins syndrome is a first and second branchial arch, pouch, and groove disorder present in roughly 1/50,000 live births.[10,32,33] Primarily autosomal dominant in nature, TCS is most commonly associated with the heterozygous mutation of the TCOF1 gene (Treacher Collins–Franceschetti) (93%) in 5q32-q33.1 and the subsequent truncation of the TREACLE protein.[10] More recently, though, Dauwerse et al.[34] described POLR1D and POLR1C mutations in nonTCOF1 TCS patients. The subsequent abnormality from the TCS mutations is an error in ribosomal biogenesis with a high level of penetrance but variable expressivity. Sixty percent of the cases are spontaneous in nature.

Anthropometric analysis of TCS has identified the unique craniofacial features of these patients. The zygoma and its related processes have been shown to be the primary source of the midface hypoplasia that characterizes TCS. In general, patients have been shown to have significantly lower zygomatic bone volumes compared to controls.[32] The body of the zygoma is the least affected part of the bone. In contrast, Marsh et al.[35] found the most consistent site of skull dysplasia to be the zygomatic process of the temporal bone, which at times is aplastic (89%), creating an incomplete zygomatic arch or cleft. Likewise, the ventral portion of the arch was also deformed in most patients. The neighboring external auditory meati were absent in 43%

of cases but this finding did not necessarily correlate with other skull anomalies. Classically, the external auditory canal, middle ear space, and ossicles are malformed, while the inner ear is generally spared.[10]

As expected, the orbit in TCS has been shown to have dysplastic features. Marsh et al.[35] characterized the antimongoloid horizontal axis orientation in orbital deformities. In addition to the zygoma contributions to the deformities of the orbit, Posnick et al.[36] found a decreased interzygomatic arch distance that also contributed to the malar hypoplasia. They further noted globe protrusion to be a common characteristic in TCS that was secondary to foreshortened medial and lateral orbital wall lengths. However, unlike other studies, they did not find hypo- or hypertelorism to be a defining characteristic. Posnick[37] further characterized the abnormalities of the cranial base in TCS. Similar to Marsh et al.,[35] who noted it to be shortened in all directions with an acute angulation, Posnick et al.[36] documented a diminished intercoronal width that contributed to the abnormal shape of the anterior cranial vault in patients and the narrow upper face, forehead, and temporal regions.

Nasal constriction is common and resultant of the narrowed nares and hypoplastic alar cartilages. In rare cases, choanal atresia may be present. Externally, the nose appears large relative to the neighboring hypoplastic midface and nasal process of the frontal bone. The nasofrontal angle is excessively obtuse with a broad nasal bridge and mid-dorsal hump.[37]

The maxilla generally is not defective in isolation,[35] but maxillary lengths have been shown to be shorter than norms.[38] The retrognathic maxilla in conjunction with an expected mandibular deficiency presents with a shortened mandible and midface in the anteroposterior plane. The mandible, though, is considered one of the defining characteristics of TCS. Similar to other syndromes with PRS-like features, the mandible has variable dysmorphism from near normalcy to severe dysplasia. The gonial angle is excessively obtuse and Marsh found that in some cases it neared 180°.[35] The excessive angles may contribute to an underestimation of the micrognathia seen in these patients. Further key features of the TCS mandible include decreased vertical ramus height, mandibular body length, antegonial notch height, and chin prominence.[38] In combination, these dysmorphologies contribute to the obtuse mandible plane angle of TCS patients, which is not likely to experience catch-up growth seen in other forms of PRS. Clinically, it also contributes to open bite deformities and premature posterior dental contact. Underlying this convex facial profile, is a restricted nasal and oropharyngeal space.[38] Glossoptosis is common and the resultant cleft palate deformities that are seen in PRS are also present. As such, TCS patients face many of the same clinical airway and feeding difficulties as their PRS counterparts. Of note, syndromic-associated PRS typically has more significant clinical symptoms and requires more aggressive surgical management of their airways and feeding.[31]

In addition to the bony anomalies of TCS, soft tissue anomalies also exist and contribute to the abnormal facies and clinical difficulties of these patients. Orbital findings of the eyes are present but the eyes are characterized by downsloping palpebral fissures, outer third lower lid colobomas, and a lack of lid lashes medial to this defect. The midface has variable soft tissue deficiencies centered about the underlying skeletal anomalies, primarily affecting the jugal, zygomatic, orbital, and infraorbital regions. The prezygomatic and buccal fat pads are lacking in volume as is the temporal fossa all of which complicate future reconstruction.[39,40]

Auricular malformations are common and the ears may be low set near the angle of the mandible. In addition to the often stenotic or atretic external auditory canal is the hypoplastic middle ear space and ossicular abnormalities that largely contribute to the conductive hearing loss seen in TCS. Intelligence is grossly normal, but cases of mental retardation have been reported. It is suspected that these mental deficiencies may be secondary to the hearing loss.[10,37]

Management of TCS patients is often complicated and occurs throughout many stages of life. Much like other severe forms of PRS, airway and feeding difficulties are addressed shortly after birth and the cleft palate, if present, is managed early in life. Similarly, speech and hearing are aggressively treated and may include hearing aids or bone conduction hearing aids. Posnick[37] summarizes nicely the timing for surgeries in these patients. Zygomatic and orbital reconstruction should be performed between 5 and 7 years of age at a time when cranio-orbitozygomatic bony development is complete. Herlin et al.[32] argue for a time period of 7 to 12 years of age with soft tissue reconstruction carried out prior to skeletal reconstruction. Maxillomandibular reconstructive surgery, depending on its severity, may be done early in life to aid in airway management or may be performed later in life for esthetic purposes. Posnick[37] recommends ages 13–16 years for

orthognathic surgery in mild to moderately malformed patients. Rhinoplasty is often required and should be performed after orthognathic procedures. Lastly, microtia repair should be performed after 4–6 years of age and it should precede any atresia and middle ear reconstruction.

## Stickler Syndrome (Arthro-Ophthalmopathy)

Arthro-ophthalmopathy is a connective tissue disorder first described by Stickler et al.[41] in 1965, which includes ocular, skeletal, orofacial, auditory, and cardiac features. Traditionally labeled as autosomal dominant in nature, recent evidence has shown autorecessive inheritance in rare cases.[42,43] Stickler's initial description was of a five-generation family that showed progressive myopia early in life that later progressed to retinal detachment and blindness. The affected family members also showed premature degenerative joint disorders with abnormal epiphyseal development and hypermobility during childhood. Later, the syndrome was found to have variable expression of hearing loss, flat facies, and findings consistent with PRS. Approximately, 1 in 7,500–9,000 newborns are affected by this syndrome and depending on the mutation, chromosomes 1, 6, or 12 are involved.[43-45] Primarily a disorder of collagen synthesis, there are a variety of described mutations affecting collagen types II, XI, and IX.[42-44,46] Each of these collagen types is expressed in similar areas of the body to include "hyaline cartilage, the vitreous of the eye, intervertebral disk, and inner ear where they form a heteropolymeric fibril."[42] Mutant forms of these collagens predispose the patient to collagen-based multiple organ system disorders or anomalies.

Understandably, patients display variable degrees of expression depending on the type of mutation present, which may result in delayed or missed diagnosis in some cases. Midfacial hypoplasia is classically seen in these patients and associated with prominent eyes, epicanthal folds, decreased nasal projection, anteverted nares, broad nasal ridge, and micrognathia. With time, the flat facial characteristic appearance in childhood has the potential to improve to near-normal features by adulthood. An example of such is the catch-up growth of the mandible seen in some cases consistent with features of PRS, where patients are less likely to have persistent micrognathia.[26] Considered the most common syndromic form of PRS, Stickler syndrome is diagnosed in up to a third of these cases.[22-24,26] The mandible length is shortened as a result of decreased ramus height and body length. The degree of shortening in one study suggests it to be slightly worse than nonsyndromic forms of PRS and closer to normal values than other syndromes, such as Treacher Collins (TCS), in part due to relatively normal mandibular morphology.[26] As such, those affected with Stickler syndrome are less likely to have airway and feeding issues compared to other syndromic forms of PRS and were shown to have less frequent need for tracheostomy or other airway interventions.[24] It is suggested that distraction osteogenesis may result in mandibular prognathism after complete skeletal development.[26] Other craniofacial features of Stickler syndrome include a variable degree of midline palatal clefting that may involve the hard and soft palate as seen in PRS or only a bifid uvula.[45]

A survey by Stickler et al.[47] found that 95% of Stickler patients had ophthalmic issues, ranging from retinal detachment (60%), myopia (90%), and blindness (4%). Myopia is congenital and nonprogressive, as are cataracts in these patients, but presence in children <6 years of age along with other syndromic features suggests a Stickler diagnosis. Abnormal anterior chamber drainage may also predispose patients to glaucoma.[45] Various vitreous abnormalities are pathognomonic for several Stickler genotypes. Perhaps the greatest concern with regard to vision, though, lies in the risk of spontaneous retinal detachment. Giant retinal tears are common and have been associated with increased incidence in those <30 years of age and with a family history of retinal detachments. Despite improved ophthalmic techniques in the management of chorioretinal degeneration, sudden bilateral blindness as a result of retinal detachment remains a significant risk in in some Stickler genotypes.[47] In fact, Stickler et al.[47] reported that 60% of all patients had retinal detachment or cataracts in their lifetime.

The second most common feature is a variable degree of arthropathy (90%), although in most cases, symptoms are mild, age dependent, and only noted through radiographs.[47] When patients present with early onset myopia and associated joint hypermobility, however, the diagnosis of Stickler syndrome should be considered. Newborns and infants also display prominent joints and radiographically have enlarged epiphyses and metaphyses along with dumb bell-shaped long bones. In childhood, joint symptoms may mimic juvenile arthritis when severe. Spine changes are possible and manifest in the form of scoliosis and kyphosis. With increasing age, hypermobility reduces and gives way to degenerative arthropathy of variable severity, with osteoarthritis present by the third or fourth decade.

Some degree of hearing loss is also common (70%) and, like skeletal disease, is age dependent in origin.[47] With time, conductive or mixed hearing losses (CHL) seen in children may progress to normal hearing in the third decade that eventually develops into a high-frequency SNHL seen in 40% of older adults.[11,45] In children, the CHL is associated with chronic otitis media and its sequelae, which are exacerbated by the presence of palatal clefting.[47] Unlike the CHL seen at younger ages, the SNHL in older patients has an unknown origin and is variable in severity depending on which collagen mutation is present. Some theories of inner ear pathology include an underdeveloped organ of Corti or abnormal hair cell development. Vestibular symptoms are rare, and if present, are likely secondary to ocular or skeletal abnormalities.[11]

Other reported clinical findings in Stickler syndrome include normal intelligence and mitral valve prolapse (MVP) in 50% of patients. Snead and Yates,[45] however, found no echocardiographic evidence of MVP in any of their 100 patients surveyed. This variability in phenotypes illustrates the difficulty in developing diagnostic criteria for Stickler syndrome. Some advocate diagnostic suspicion in any patient with early onset ocular findings and joint changes consistent with the syndrome, whereas in some cases, nearly 25% of patients may be identified because of an initial PRS diagnosis alone.[47] Nonetheless, a Stickler syndrome diagnosis should be considered when two or more of the following are present: ophthalmologic, craniofacial, audiologic, or skeletal anomalies. Besides early identification, long-term surveillance and management of these disorders are needed. The patient will require regular ophthalmologic exams and possible treatment for refractory defects, cataracts, or signs of retinal detachment. Patients should be warned of impending signs of spontaneous retinal detachment, especially before the age of 30, and should refrain from activities such as contact sports that may cause a traumatic detachment. Regular audiologic exams are necessary and treatment for recurrent otitis media may be warranted. Hearing and visual impairments may also result in learning deficits therefore educational assessment and considerations are also vital. Craniofacial abnormalities are managed much in the same way as PRS patients but may also include other orthognathic procedures and nasal reconstruction. Mitral valve prolapse is possible and when present requires future prophylactic antibiotic therapy for certain surgeries. Lastly, genetic counseling for at-risk family members is necessary, as it has been established that Stickler syndrome has a high level of penetrance but a variable degree of phenotypic expression.

## 22q11 Deletion Syndrome

Previously thought of as separate entities, DiGeorge syndrome (DGS) and VCFS have been shown to arise from a common hemizygous microdeletion of chromosome 22 at the q11.2 band. Termed 22q11.2 Deletion Syndrome (DS), the wide phenotypic variation of this syndrome has created much nosocomial confusion surrounding its diagnosis. It has been said that 22q11.2 DS represents one clinical spectrum for which many previously independent syndromes fall under. Generally, hypertelorism, a broad nasal root with a prominent nasal tip, and abnormally angulated ears are present, but some cases may have little in common or present with few signs that an underlying disorder is present.[48] Due to the highly variable presentation, a true prevalence rate of 22q11.2 DS is difficult to ascertain. However, some studies have suggested that a number between 1 in 4,000–7,000 live births is accurate.[49,50] A population-based study found a higher prevalence among Hispanics than other races.[49] Perhaps with improved microarray technology in the future, a more accurate assessment is possible.

22q11.2 DS is a contiguous gene deletion that is inherited in an autosomal manner. In reality, over 90% of probands represent a de novo deletion of 3 million base pairs consisting of over 30 genes.[50,51] Although 95% of the deletions are shared between syndromes, the exact effect of particular deletions is debatable, as many genotypes that fall within this spectrum disorder have variability in their deletions, yet may express common phenotypic expression.[50,51]

Amongst the most common phenotypes expressed are DGS and VCFS. The first is an eponym described by Angelo DiGeorge in 1965 that has since been proven to carry the 22q11.2 deletion in 90% of cases. Described initially as a syndrome with a prominent third and fourth pharyngeal pouch field defect, it is well known for the associated conotruncal cardiac anomalies, hypocalcemia, and poor T-cell production that typically present in the neonatal period.[52,53] Velocardiofacial syndrome on the other hand tends to be recognized later in life in craniofacial centers when speech and learning disabilities are problematic. First described by Robert Shprintzen in 1978, VCFS has since been found to have the 22q11.2 deletion in 80% of cases. It presents with a combination of palatal anomalies, often velopharyngeal insufficiency (VPI), associated with

congenital heart anomalies and learning disabilities. Dysmorphic facial features are common amongst these two syndromes as they are with others that share the 22q11.2 deletion.[50,53]

The list of clinical features of 22q11.2 DS is broad and each is variably expressed. However, there are some common features to this syndrome of importance to otolaryngologists. First, the palate is abnormal in three quarters of patients and ranges from an overt cleft in some to a submucosal cleft in others. Velopharyngeal insufficiency was the most common palatal anomaly in one study, which showed that 27% of patients presented with this finding.[54] Palatal anomalies may be primary defects in some, whereas in others, they may be secondary to a Robin sequence due to the retrognathic mandible common to this syndrome. Much of the abnormal appearance of the face can be attributed to an obtuse angulation of the cranial base. In addition to the aforementioned retrognathia, the cranial base anomaly causes forward projection of the frontal bones and an appearance of midfacial hypoplasia. In reality, though, the malar bones are intrinsically normal, much like the mandible. A long facial appearance is common in these patients because of excessive vertical maxillary height, which may be secondary to facial musculature hypotonicity that also presents with asymmetric crying facies. Additionally, suborbital congestion secondary to vascular anomalies, not allergies or nasal congestion, in combination with a mouth-open posture gives the appearance of adenoid facies seen in these patients. Finally, a broad nasal root with a bulbous tip completes the characteristic appearance seen in 22q11.2 DS.[51]

Cardiovascular anomalies are of great interest in these patients and at times may be a presenting sign of the underlying disorder. In one study, 74% of patients with 22q11.2 DS were found to have cardiac anomalies. The most common anomaly was tetralogy of Fallot and then interrupted aortic arch, truncus arteriosus, vascular rings, and conoventricular septal defects. These findings, confirmed by other studies, suggest there may be an increased frequency of this syndrome in those patients with these anomalies and when present warrant an evaluation of 22q11.2 deletions.[49,54,55] Vascular anomalies are not limited to the chest but may be seen anywhere in the body. The great vessels of the neck, particularly the internal carotids, may be affected. Of concern to craniofacial surgeons, is an aberrant course of the carotids that results in medial displacement of the vessels in the posterior pharyngeal wall.[51]

Endocrine disorders may present in the neonate period. In particular, hypocalcemia has been shown to occur in nearly half of these patients due to a lack of parathyroid function. With time, calcium normalizes but issues have been known to occur in times of illness or puberty.[50,54] Growth hormone may also be deficient, which explains why one study found that 41% of patients were significantly below the fifth percentile in height for age-related norms.[54]

Immunologically, three quarters of 22q11.2 DS patients have mild or moderately diminished numbers of circulating T-cells but cell-mediated immunity remains intact. The underlying issue is thymic hypoplasia, and in rare cases aplasia, due to third branchial arch anomalies.[53] Within 1–2 years, though, thymic involution begins and even healthy children show signs of a decreasing T-cell population. In contrast, 22q11.2 DS patients' downtrend appears to be more blunted. Overall, one can expect these patients to have improved T-cell production with age. Humoral immunity is grossly intact and studies have shown normal mitogen responses in these patients. There are some occasions where IgA deficiency or specific antibody defects can occur. These children are also at risk for autoimmune disorders, with the most common being juvenile rheumatoid arthritis and hematologic autoimmune diseases.[52] It is rare for these children to experience opportunistic infections but when they do, it tends to be upper respiratory in nature. Finally, live viral vaccinations are not likely an issue except in those cases with very low T-cell counts or thymic aplasia.[53]

Due to abnormal craniofacial development, 22q11.2 DS can lead to aerodigestive complications early in life that most commonly mirror that of Robin sequence. One of the most significant issues, though, is VPI that occurs in 25% of this population.[54] In addition to clefting of the palate and pharyngeal hypotonia, these children are predisposed to VPI because of an increased depth of the pharynx secondary to platybasia, which displaces the pharyngeal wall posteriorly. These are also the reasons for an increased incidence of nasal regurgitation in infants.[52] Again, when treating VPI, surgeons should be aware of the possibility of medially displaced internal carotid arteries prior to performing any posterior pharyngeal wall procedures.

Lastly, 22q11.2 DS patients are at increased risk of neurocognitive disorders. Their overall mean IQ is below that of their peers, and expressive and receptive language development is often delayed. Despite this, patients

perform best in reading and spelling. In addition to learning disorders, psychosocial impairment is present. In children, 20% display signs of an autistic spectrum disorder and in adults, 25% present with psychological disorders, most commonly schizophrenia.[56] As is the case with other craniofacial disorders, 22q11.2 DS patients have a myriad of clinical issues that require a multiteam approach to management. Regular system-based surveillance is needed throughout their lifetime.

## Achondroplasia

Achondroplasia is the most common of the chondrodysplasias and presents between 1:10,000 and 1:30,000 live births.[57-60] Autosomal dominant in all cases, about 80% are due to de novo gene mutation. This occurs most commonly in association with advanced paternal age, from whom the gene is inherited, with a recurrence risk in sporadic mutations of <1%.[17,57,61] Genetically, the defect arises from an arginine–glycine substitution in the transmembrane domain encoding for FGFR3 that results in faulty endochondral ossification. As such, these patients are characteristically short in stature. Early endochondral ossification also affects craniofacial growth, particularly the maxilla, which causes the distinctive facies in this condition.[58,62] Other features include macrocephaly, disproportional limb length, normal trunk length, trident configuration of hands, genu varum, and exaggerated lumbar lordosis with age.[57,58,61,63,64] Due to achondroplasia's characteristic phenotype and 100% penetrance, clinical and radiographic evidence often restricts the need for genetic confirmation for diagnosis.

Head growth is rapid in the first 6 months of life and the characteristic facial appearance results from a short cranial base, early spheno-occipital closure, and resultant macrocephaly with frontal bossing. The foramen magnum is stenotic in up to 80% of patients and in those ultimately requiring surgery for decompression may be nearly 5 mm shorter in the transverse dimension.[62,65] Clinically, this can contribute to cervicomedullary compression and central apneas with or without hydrocephalus. Additionally, changes in the cervical spinal cord, focal neurological deficits or myelopathy, and impaired conscious state are all possible results of a narrowed foramen magnum. Hydrocephalus occurs in <5% of cases, is most common in the first 2 years of life, and thought to be secondary to increased intracranial venous pressure due to jugular foramen stenosis.

The greatest risk, though, of craniocervical junction complications is sudden death from compression of the brainstem and upper cervical cord. These findings were supported by Hecht et al.[63] and Wynn et al.[66] who showed a 7.5% risk of sudden death in the first year of life and was the source of half of all patient deaths by the age of 4, regardless of a confirmed diagnosis of stenotic foramen magnum. Hypotonia as well as direct compression to respiratory control centers have been implicated as a cause.[57,58] Between 5 and 24 years of age, sudden death was found to be related to central nervous and respiratory causes, but over 25 years, it was most likely from cardiovascular complications. Ultimately, these studies found a life expectancy 10 years shorter than the general population. Their findings were independent of gender and despite better health care showed no improvement in mortality rates in their follow-up study.[63,66]

The temporal bone is also affected in achondroplasia. Radiographic studies have shown poorly developed mastoid air cells, foreshortened carotid canals, distorted petrous bones, and abnormal rotation of the inner ear. The most concerning of the findings, though, is the evidence of jugular bulb dehiscence in this condition. This is clinically relevant because achondroplasia patients have high rates of otitis media and conductive hearing loss (40–68%), secondary to a shortened Eustachian tube and its dysfunction, and half of all patients will require some form of otologic surgery in their lifetime. There have been reports of brisk bleeding after myringotomy in some cases and a high riding jugular bulb has been implicated.[17,58]

The upper airway is also of clinical relevance to the otolaryngologist. Premature endochondral ossification results in the classic midface hypoplasia. A cephalometric study by Onodera et al.[60] showed the following craniofacial abnormalities compared to norms: decreased nasal floor length, maxillary and pogonion retrusion, and increased mandibular plane and gonial angles. Expectantly, upper airway stenosis ensues and may be complicated further by posterior cranial base growth failure. Also, midface hypoplasia, reduced facial height, and a depressed nasal bridge can contribute to nasal obstruction.[58,60]

Sleep-disordered breathing is common in achondroplasia. A combination of pharyngeal muscle hypotonia, pharyngeal airway narrowing, retrognathia, increased lower facial height, midface retrusion, and adenotonsillar hypertrophy are all thought to contribute to this finding. In 1 series, adenotonsillar hypertrophy was reported to occur in 41% of patients.[65] Other theories into the cause include

jugular foramen and hypoglossal canal stenosis, which may contribute to muscular upper-airway obstruction.[65] Although central apnea does occur, it has been shown to be less frequent than obstructive causes. Obstructive sleep apnea incidence ranges from a third to one half of all patients and has been shown to occur more frequently and severe in children <2 years of age. Further, the same study by Afsharpaiman et al[65] found that 28% of patients with OSA had hydrocephalus versus none in those without OSA. Ultimately, nearly 30% may require some form of airway surgery for sleep-disordered breathing.[65] Of note, other sources of respiratory complications include hypotonia, cor pulmonale, and restrictive lung disease due to decreased chest wall compliance.[58]

Trotter and Hall[61] provide an excellent source for health supervision of children with achondroplasia. From an otolaryngology perspective, the key issues remain early identification and treatment of middle ear disease and sleep-disordered breathing as well as their associated sequelae. Annual hearing exams and sleep apnea screening are recommended for all achondroplasia children. Although ventriculoperitoneal shunting for elevated intracranial pressure is less frequent than in years past, cervicomedullary decompression in the form of suboccipital craniectomy and C-1 laminectomy is needed in 15% of patients by adulthood.[58,67] Due to the elevated risk of cervicomedullary compression and sudden death, particularly in those under 5 years, any concern should be addressed promptly and a neurosurgical evaluation is recommended. Parents should also be given neck safety precautions, which include careful handling of the head and utilizing rear-facing car seats.[58,67] Obstructive sleep apnea should be managed primarily with adenotonsillectomy. Prior to surgery, assessment of the foramen magnum and possible cervicomedullary compression should be reviewed. Postoperative polysomnograph is warranted, as children with achondroplasia may be at risk for incomplete resolution of sleep apnea from adenotonsillectomy. Consideration is given for other treatments, such as CPAP, midface advancement, and rarely tracheostomy. Much is known about achondroplasia patients and the clinical challenge they pose. Vigilant surveillance is a must and multidisciplinary management is lifelong in nature.

## Craniofacial Microsomia

Asymmetric underdevelopment of the first and second branchial arches can lead to a diagnosis of CFM. Variable in severity, CFM may involve the ear, orbit, maxilla, mandible, underlying soft tissue of the face, and the facial nerve, which may impair the function of the craniofacial apparatus.[68,69] Literature suggests that 1 in 3,000 to 1 in 5,000 live births are affected by CFM. However, wide phenotypic variability leads to many undiagnosed cases. Further, a wide variety of names for this condition, such as hemifacial microsomia, Goldenhar syndrome, oculoauriculovertebral syndrome, may cause nosocomial confusion when identifying these patients. Thus, the actual incidence is likely higher than what is reported. The cause of the field defects seen in CFM may be environmental, heritable, or more likely multifactorial in nature. When inherited, there appears to be an autosomal dominant pattern, but most cases are usually sporadic and represent one proband within a family.[70]

Despite a wide variability in phenotypic expression, classification schemes have been developed to standardize descriptions of CFM. Some have used the mandible as a centerpiece to classify CFM, but these descriptions lack additional information for other associated craniofacial anomalies. One grading system, OMENS, does take into account other anomalies. The acronym scores the severity of defects to the orbit, mandible, eye, nerve, and soft tissue in a similar way that TNM staging is used to describe cancers.[68]

Anomalies primarily develop in the first and second branchial arches, but noncraniofacial anomalies may present. The face is asymmetric from variable amounts of midface or mandibular hypoplasia, either unilateral or bilateral in nature. Preauricular skin tags or pits may be present, as may be variable degrees of microtia with an associated aural atresia.[70] Hearing may be further affected and represent usually conductive hearing losses, although sensorineural or mixed hearing losses are possible. Because of abnormalities in temporal bone development, the facial nerve may aberrant in its course or it may be dysfunctional in part or as a whole. The hypoglossal and trigeminal nerves may also be affected.[2] Soft tissues may be hypoplastic or atrophic. For example, lateral facial clefting, often associated with Goldenhar syndrome, can occur, as can other orofacial and craniofacial clefts.[68,70] Noncraniofacial findings include those involving vertebral, gastrointestinal, cardiac, renal, radial limb, and central nervous system anomalies. The most well known of these patterns include VACTERL associations and CHARGE syndrome lending some to hypothesize that such patterns may represent an otherwise unknown spectrum of disorders associated with mesodermal dysplasia.[69,70]

The treatment goal of multidisciplinary teams is to improve form and function of the craniofacial anomalies, with due consideration of expected growth patterns and psychosocial factors. Each patient's treatment plan is individualized to account for the severity of anomalies. Some may require early mandibular distraction for airway and feeding difficulties, whereas others receive orthognathic treatments once full craniofacial growth has been achieved. In general, the team aims to ensure appropriate respiratory and feeding capabilities of the infant, speech and hearing therapy, optimal dental occlusion, and improvement of facial esthetics. Another special consideration is that of facial reanimation. Due to abnormal motor end plate development secondary to facial nerve anomalies, some patients require transposition muscle flaps for lateral oral movement or tarsorrhaphy or gold weights for ocular protection. Lastly, soft tissue defects are managed either with microscopic free tissue transfer or dermal fat grafts.[68] The course of CFM management is not unlike other craniofacial anomalies that a team encounters and the approach to management is as variable as the anomalies themselves.

## Craniosynostosis and Deformation Plagiocephaly

Similar to many terms in dysmorphology, craniosynostosis can be incorrectly applied to cases with any type of cranial deformation regardless of origin. In reality, many prenatal and postnatal causes of cranial deformation exist, and despite different mechanisms of deformation, they may result in similar-appearing outcomes. In this section, the focus will be on those cases that are due to premature fusion of cranial sutures (craniosynostosis) and deformational cranial flattening due to extrinsic forces (deformational plagiocephaly (DP)) (Fig. 94.9).

### *Craniosynostosis*

To achieve normal functional and esthetic outcomes, the cranial vault must expand rapidly in response to the tremendous growth of the brain during the first 2 years of life. Premature fusion of one or more of the cranial sutures can restrict growth and lead to abnormal outcomes. Specifically, when premature fusion does occur, termed craniosynostosis, growth restriction perpendicular to the fused suture line results. To permit continued, unrestricted intracranial growth, compensatory growth ensues in a predictable pattern along open suture lines as a normal response to the constraint. Thus, craniosynostosis is a

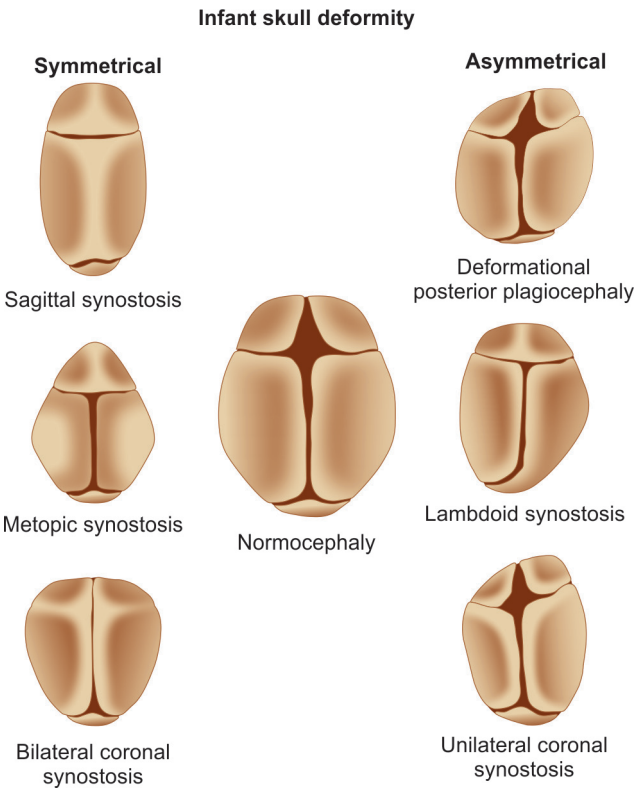



**Fig. 94.9:** Illustration of variable causes and appearances of abnormal head shape.

byproduct of normal physiologic response to an abnormal process. The majority of these cases are single suture, nonsyndromic in nature, and are estimated to occur in <1 in 5000 infants. However, some can be associated with syndromes. These cases are much less prevalent, between 1 in 25,000 and 1 and 100,000 infants and often involve the coronal ring made of the frontosphenoid, sphenoethmoidal, and paired coronal sutures.[71]

### *Scaphocephaly*

Scaphocephaly results in a saddle or football-shaped skull as a result of premature fusion of the sagittal suture. It is the most common of the craniosynostotic conditions. Premature fusion causes decreased growth in a transverse dimension resulting in compensatory anteroposterior growth of the calvarium. The child ultimately has decreased biparietal and bitemporal growth posterior to the anterior fontanelle along with decreased vertical height of the posterior cranium. This causes the characteristic long and narrow head. Frontal bossing is also present but facial asymmetry is rare. Finally, head circumference is usually in excess of the 90th percentile for age-related means.[72]

### *Trigonocephaly*

Trigonocephaly is a result of premature metopic or frontal suture fusion. The frontal suture lies between the two developing frontal bones and premature fusion results in a triangular forehead and deceased bifrontal diameter.[72] Described as keel shaped in appearance, it rarely has any functional consequences. Abnormal facial development is possible, particularly with regard to hypotelorism. At the fusion site in the midline forehead, a midsaggital ridge is palpable and in some cases may be the only presenting finding of this condition.

### *Brachycephaly*

Brachycephaly occurs due to bilateral coronal synostosis. In contrast to deformational brachycephaly, which involves symmetric occipital flattening, the synostic form has severe forehead retrusion. Growth is impaired in the anteroposterior direction, causing growth of the cranium laterally and superiorly. Turricephaly ("tall" head) or acrocephaly ("pointed" head) is present. Bilateral superior orbital rims are retruded behind the anterior surface of the globe giving the appearance of prominent eyes. The hairline is low and the usually well-defined glabellar depression is absent.[71,72]

### *Plagiocephaly*

*Plagiocephaly comes in two forms*: Synostotic or the more common deformational types. Regardless of etiology, the head is asymmetric and flattened in one or more regions. The synostotic forms are a result of unilateral, premature coronal (anterior) or lamboidal (posterior) synostosis. Whereas DP leads to a parallelogram-shaped head, synostic plagiocephaly presents with a quadrangular appearance when viewed from above. Both synostic forms are quite rare. As compared to the symmetric synostoses (sagittal and metopic), which show a male predominance, asymmetric synostoses are more common in females.[72]

Features of anterior synostosis include a flattened forehead on the affected side with an elevated and posteriorly displaced supraorbital rim. The cornea lies anterior to these structures when normally the opposite should be true. There is nasal root and midfacial angulation with the nasal root deviated toward the affected side. Contralaterally, forehead bossing is present; ipsilaterally, the auricle is anteriorly displaced; and posteriorly, the occiput is generally normal.[72]

Often confused with deformational plagiocephally, posterior synostosis is actually quite rare and results in occipital flatness on the affected side. There is asymmetric cranial height with a foreshortening on the affected side. This contrasts the deformational subtype and gives lamboidal synostosis a wind-swept appearance of the head. The forehead is generally spared but the ipsilateral auricle is posteriorly displaced. Lastly, there is ipsilateral mastoid bossing.[72]

### *Syndromic Craniosynostosis*

There are many forms of syndromic craniosynostosis that are a result of in utero suture fusion. Apert and Crouzon are among the two most common types. In addition to craniofacial abnormalities, these subtypes of craniosynostosis may have significant airway issues as a result of abnormal midface development and laryngeal or tracheal abnormalities.[72]

Apert syndrome is autosomal dominant, occurs in 1 in 100,000 neonates, and is related to FGFR2 mutations. It is characterized by brachycephaly and has associated midface retrusion with exorbitism. Other findings include complex acrocephalosyndactyly of the hands with occasional fusion of the thumb to the fingers and complex syndactyly of the feet with great toe fusion as well. Radiohumeral fusion is also present as is neurodevelopmental delay.[71]

Crouzon syndrome is similar to Apert syndrome in that brachycephaly is present. However, the entities are distinguished by normal hands and feet as well as a lack of neurodevelopmental delay in Crouzon syndrome. Occurring in 1 in 65,000 neonates, this syndrome is also a result of FGFR2 mutations that are transmitted in an autosomal-dominant pattern. There is wide phenotypic variability but common findings include exorbitism with hypertelorism and maxillary hypoplasia with relative mandibular prognathism.

### *Deformational Plagiocephaly*

Deformational plagiocephaly is a term used to describe asymmetric flattening on one side of the head. The greatest degree of deformation typically peaks at 4 months of age. The exact mechanism of this anomaly is debated. One theory suggests that there may be a hereditary predisposition while another suggests that the cranium of infants is more malleable. In reality, neither is likely the cause. Instead, Rogers[72] compares DP to the deformation of a pumpkin from constant external forces during its growth.

The portion of the cranium in constant contact with the counterforce has impaired growth in that particular direction. Despite this, intracranial volume continues to expand. Similar to synostosis, which describes an intrinsic resistance to growth, compensatory growth in DP is in the direction of least resistance. Further, research has shown that the severity of deformation is directly related to the rate of growth and the degree of force applied. This could explain why those with rapid head growth, such as in premature infants, and those with larger head sizes, as in males and large infants, show an increased frequency of DP. Other predisposing factors include those that may limit an infant's ability to change head position, as in developmental delay or congenital torticollis. More recently, though, some would argue that the application of the Back-to-Sleep Campaign has resulted in a higher frequency of DP, although this does not explain why the majority of these infants never show signs of DP.

The shape of the head is described as a parallelogram, although trapezoidal is likely more descriptive because the degree of ipsilateral frontal bossing is not equivalent to that of occipital flattening. The face of the patient is affected due to the anterior displacement of the ipsilateral zygoma. This causes a shortening of the lateral canthus leading to a shortened lateral-to-medial canthus distance. Tarsal plate tension therefore is reduced and the ipsilateral eye appears more open. This gives the perception of contralateral eyelid ptosis.[72] Another form of cranial deformation is deformational brachycephaly. This form describes symmetric occipital flattening with compensatory widening of biparietal dimensions. In reality, even these patients have some form of asymmetry present. Therefore, plagiocephaly is likely a more accurate term for these patients as well.[72]

## Facial Clefting

Craniofacial anomalies vary in frequency but arguably cleft lip/palate deformities are amongst the most common. Much less common are other types of craniofacial clefts. Despite an incidence of near 1 per 100,000 live births, these anomalies have been studied extensively for the past century. During this time, they were described independently by many authors in small reports, but the descriptions often were inaccurate or misleading. This classification paradigm changed when Paul Tessier's presented at the Second International Congress on Cleft Palate in Copenhagen in 1973 and published in 1976 his

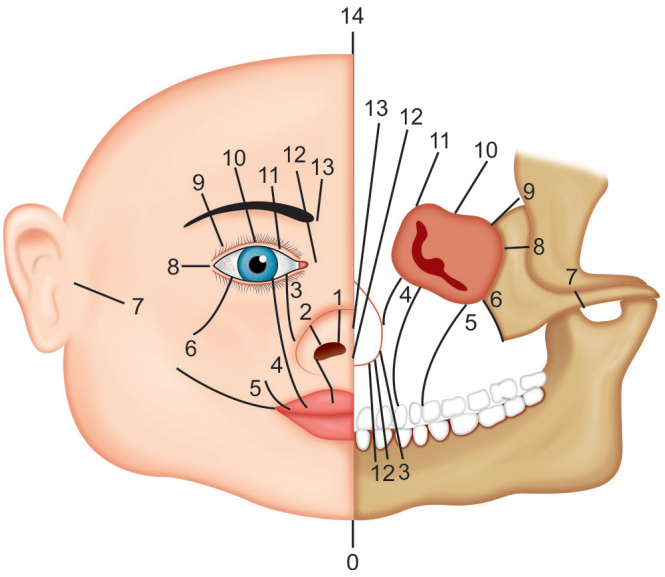



**Fig. 94.10:** Illustration demonstrating Tessier's schema for classifying facial clefts.

classification scheme of craniofacial clefts, one that is better suited to the study and treatment of these anomalies today[73,74] (Fig. 94.10).

The exact pathogenesis of such clefts is debatable. Some have argued for a mesodermal penetration theory, whereby failure of adequate mesenchymal migration and penetration of ectodermal elements cause subsequent failure of overlying epithelial tissue. The result is dehiscence of these epithelial elements and a cleft is produced. The extent of clefting is inversely proportional to the degree of mesodermal penetration in this theory. Another explanation that exists is described as the failure of fusion theory. This suggests that a failure of facial processes to contact their adjacent counterpart inhibits mesenchymal penetration and will result in a cleft. Although both theories seem plausible, they do not necessarily explain those cases where clefting occurs in nonpredictable embryological patterns, i.e., away from embryologic fusion planes. Perhaps other factors are at play and contribute to these patterns, such as environmental cleftogens that insult normal development after closure of facial ectoderm.[5,74]

When Tessier[73] described his classification scheme he based his findings on nearly a thousand surgical and pathological specimens. The foundations of his findings were built around ten key concepts. The first two regarded differentiating between clefts and hypoplasia, the latter of which is present on the edges of clefts but does not develop into a cleft itself. Further, he noted that clefting

occurs in syndromes when an interruption of soft tissue or its underlying skeleton is present. He found that bony and soft tissue clefting was variably involved to include more severe soft tissue defects medial to the infra-orbital foramen and predominantly bony defects laterally. Clefts occurred in predictable locations and did not involve corresponding vessels and nerves. He found they presented along well-defined craniocaudal axes except for those most lateral. Finally, Tessier found that craniofacial clefting was best described in relation to the orbit, which allowed differentiation between cranial and facial clefts.[73]

In his description, Tessier[73] developed a plan of craniofacial cleft mapping. Centered about the orbit, he described the face and cranium as analogous to a globe. Similar to a globe, there are hemispheres. There are left and right sides, much like western and eastern hemispheres, which are mirror images of one another and described independently. In the northern hemisphere, there exists the cranium, in the southern lies the facial component, and between the two is the orbit. Similar to the different time zones (axes) on the globe, there are different time zones within the craniofacial apparatus. There are northbound axes superior to the orbit and southbound axes inferiorly. There are a total of 15 zones in Tessier's classification. First, in the southbound midline axis is Tessier no 0. Similar to a clock face, the numbers increase ipsilaterally until number 14; the northbound no 0 is equivalent in the cranial midline. In total, there are 15 meridians to Tessier's classification. Numbers 0 through 6 lie southbound, 8 through 14 are northbound, and no 7 is considered a laterofacial cleft. The one exception to the rule is the Tessier 30 cleft, which is a caudal extension of the 0 cleft into the lip and mandible that may be associated with a bifid tongue.

Three of the fifteen meridians are of particular interest to known syndromes. These are Tessier clefts 6–8. In his research, Tessier found that TCS was involved in one, two, or all three of these clefts, which correspond to clefts of the maxillary (no 6), temporal (no 7), or frontal (no 8) processes of the zygomatic bone. This explains the variability of malar hypoplasia and zygomatic arch aplasia with mandibular ramus, condyle, and coronoid deformities in this syndrome. Further, Tessier found cleft no 7, the most lateral of clefts, is also related to hemifacial microsomia, while no 8 is seen in Goldenhar syndrome. Again, he noted that these more lateral clefts were predominately bony rather than soft tissue defects, thus making them less obvious. This may explain why earlier accounts of lateral clefts were so poorly described.[73]

Despite being well received, there are some deficiencies in Tessier's classification. Most notably, it does not adequately explain why some clefts occur at non-embryologic fusion sites. In an attempt to remedy this, Van der Meulen and Vaandrager[75] described a dysplasia classification based on embryology. They described four primary clefts to describe those types that are caused by failure of fusion of the following junctional processes; these include between the two medionasal processes in the midline, the lateronasal process, the maxillary process, and the mandibular process. They found that primary clefts occurred at an early developmental stage prior to a 17-mm crown-rump length. Clefts after this stage were termed secondary or pseudoclefts and occurred after differentiation had begun. These types are in areas of skeletal developmental arrest and form hour-glass deformities of the hairline, nose, maxilla, lips, and eyelids in a craniocaudal direction.[75] Despite giving more insight into why clefts occur at nonembryologic fusion planes, Tessier's classification remains the more popular of the two schemes amongst craniofacial surgeons.

Treatment of craniofacial clefts should be independently tailored to the individual. However, there do exist fundamental principles that are universally applicable. First, initial priorities include management of the airway and feeding, as well as corneal protection. One should also note that in most cases the growth potential of underlying bone is impaired in these patients, therefore the need to delay surgery until "growth is completed" is not warranted. Other areas of interest include functional correction of macrostomia, separation of oral, nasal, and orbital spaces, and finally cosmetic correction of deformities.[5,74,75]

## ONGOING RESEARCH AND PUBLIC DOMAIN RESOURCES

With the improvement of medical technology and the subsequent advancement of diagnoses in craniofacial anomalies, the medical literature is constantly evolving. An anomaly once considered independent of other anomalies may now be seen as part of a syndrome or sequence. Rather than specifically describing the multitude of less well-described craniofacial anomalies, the reader is directed to two excellent resources that exist through the National Institute of Health's public domain. The first resource is OMIM, the Online Mendelian Inheritance in Man, which can be accessed at the following website: http://www.ncbi.nlm.nih.gov/omim. Another resource is Gene Reviews accessed at http://www.ncbi.nlm.nih.gov/books/NBK1116/. Both may aid in one's ability to access

contemporary literature of particular genetic conditions, to include those less common craniofacial anomalies.

## CONCLUSION

Early dysmorphology was in many ways an unscientific endeavor that aimed at categorizing, or at least acknowledging, how congenital anomalies varied from the norm. It was a daunting task that often led to incorrect associations and improper conclusions about patients. The advancement of science has done much to overcome the hurdles that past clinicians faced. As the knowledge base and genomic technology have improved, significant strides have been attained, allowing the use of objective evidence to properly categorize anomalies and make accurate predictions of the future. What started as simply a picture described by Crick and Watson, has now become a subject of science unto itself. In fact much of the knowledge today about congenital anomalies can be attributed to the clinical application of genetic testing. With that said, though, attainment of a diagnosis is more than just analyzing a drop of blood for a myriad of different medical conditions. At this point in time, it is not practical nor is it economically feasible to screen for thousands of conditions. Rather, one needs a practical approach to diagnosis and treatment, which begins with a suspicion that a condition exists. In some cases, it is obvious, while in others, the clues are subtle. Either way, there is no substitution for the deductive spirit, which has and always will guide the clinician in the study of dysmorphology.

*Disclaimer*: The views expressed in this chapter are those of the authors and do not necessarily reflect the official policy of position of the Department of the Navy, the Department of Defense, or the US Government.

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CHAPTER

# Mandibular Distraction Osteogenesis for Airway and Feeding Concerns in Infancy

95

***Andrew R Scott***

## INTRODUCTION

Micrognathia is a craniofacial deformity characterized by a small and retrusive mandible in which the mandibular alveolus is significantly posterior to the maxillary alveolus. This mandibular hypoplasia may present in isolation or in the context of glossoptosis and a U-shaped, incomplete palatal cleft. This latter entity is referred to as Pierre Robin sequence (PRS). Both micrognathia and PRS may occur as isolated findings or as manifestations of an underlying syndromal diagnosis. It is important to understand, however, that PRS is not a syndrome in and of itself, but rather a sequence in which multiple secondary anomalies are derived from a single primary malformation. The exact cause of neonatal micrognathia remains unclear; however, the prevailing hypothesis implicates hypoplasia of the mandible (either from a primary growth disturbance or from intrauterine crowding causing hyperflexion of the neck) before 9 weeks in utero as the inciting factor. The small jaw positions the tongue posteriorly and superiorly where it lies between the lateral processes of the developing palate, physically preventing fusion of the palatal shelves, which normally occurs between the 8th and 10th weeks of gestation. It is this mechanical disruption of palatal closure and not a primary molecular or genetic factor that leads to the occurrence of incomplete cleft palate in the context of micrognathia (Fig. 95.1).

Symptoms of micrognathia that present during infancy are due primarily to glossoptosis or posterior displacement of the tongue. This tongue base obstruction leads to varying degrees of upper airway compromise that may complicate coordination of swallowing or adequate ventilation, even at rest. Initial management strategies may involve repositioning or use of an adjunctive airway device (nasal trumpet or custom oral appliance).[1] For those children who fail these interventions, surgical intervention is warranted. The timing of surgical intervention is driven by the degree of symptoms present. Nearly 40% of infants with micrognathia will come to merit surgical intervention for airway and feeding concerns, owing to their difficulty coordinating breathing and swallowing within the context of tongue-base obstruction and a cleft palate.[2]

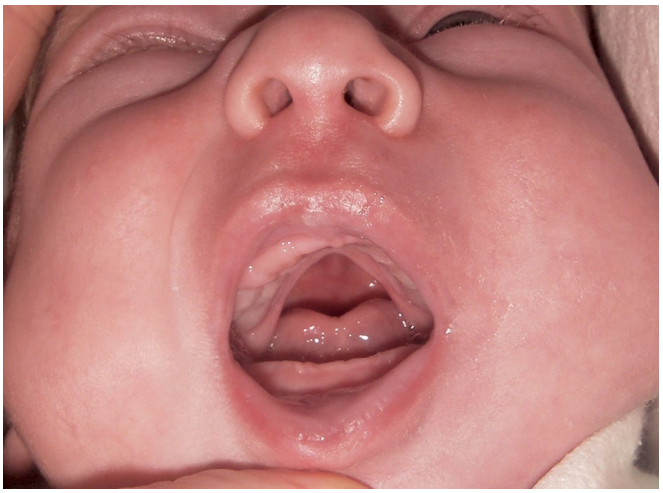
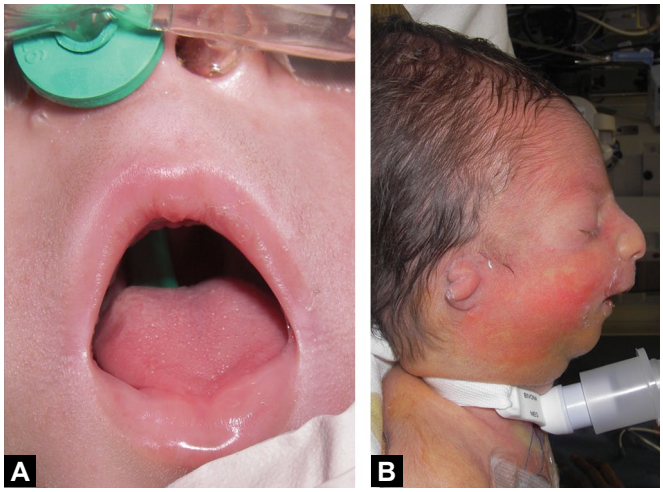


**Fig. 95.1:** Glossoptosis and cleft palate in the context of micrognathia (Robin sequence). Note the position of the tongue, lying between the lateral palatal shelves.

Surgical interventions for airway and feeding concerns related to micrognathia are aimed at addressing or bypassing tongue base obstruction. Glossopexy procedures such

as tongue–lip adhesion (TLA) may be performed to pull the tongue forward and open the airway. This operation, when successful, ameliorates glossoptosis but does so at the expense of tethering the anterior tongue to the lower lip (Fig. 95.2A). For this reason, surgical gastrostomy or months of gavage feeding via nasogastric tube are usually necessary to assure adequate nutritional intake.[3–5] Tracheotomy allows for complete bypass of upper airway obstruction (Fig. 95.2B), but concomitant surgical gastrostomy is usually necessary as these children remain unable to effectively coordinate breathing and swallowing in a manner consistent enough to maintain adequate oral nutrition.



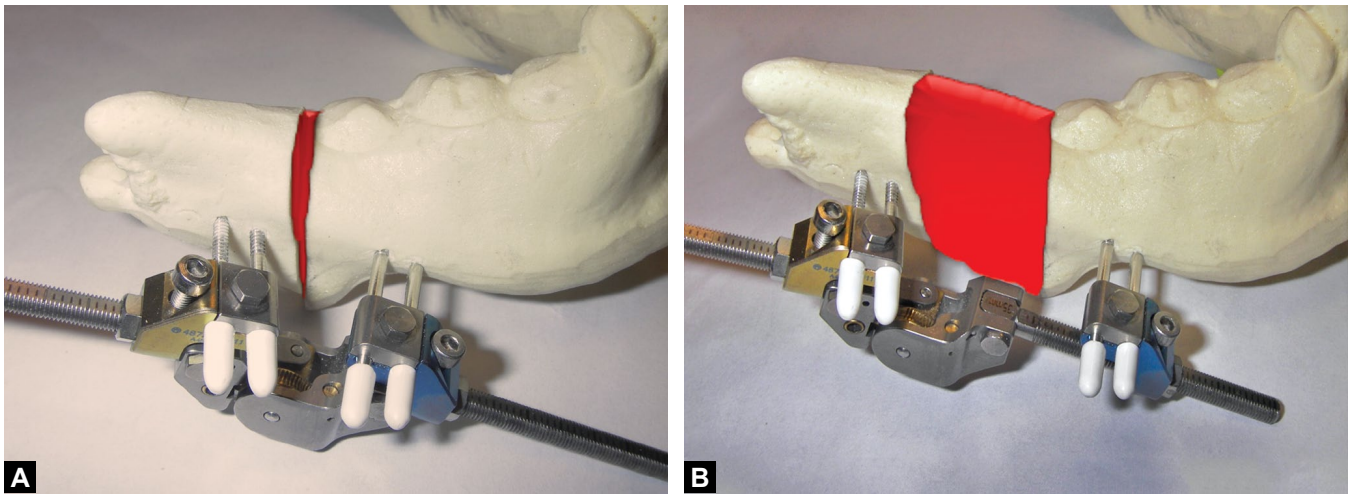

**Figs. 95.2A and B:** Alternative surgical airway interventions for tongue base obstruction associated with micrognathia. (A) Tongue lip adhesion. (B) Tracheotomy in a child with syndromic Robin sequence (Treacher Collins syndrome).

Another surgical option for management of airway obstruction secondary to mandibular hypoplasia in the neonatal period is mandibular distraction osteogenesis (MDO). Distraction osteogenesis is a technique in which a bone is gradually lengthened after an initial osteotomy. Following a short latency period, distraction begins at a slow, steady rate. During this phase (referred to as the activation phase), bone segments are separated by small increments and induction of new bone formation takes place within the gap. After the desired lengthening has been achieved, a consolidation period ensues in which the bone segments are held securely in their advanced position. The immature bone (referred to as "the regenerate") remodels and matures during this consolidation phase, after which the distraction hardware is removed (Figs. 95.3A and B and Flowchart 95.1). Since distraction proceeds at a slow pace, related muscles, blood vessels, nerves, skin, and mucosa are also elongated during the process. This concomitant soft tissue expansion is one of the main advantages of MDO.

This chapter seeks to outline the benefits and limitations of early MDO as a way of managing both airway obstruction and feeding difficulty in children with isolated micrognathia and PRS. The author's indications for the procedure, details of the operative technique, operative complications, and potential pitfalls will be discussed.

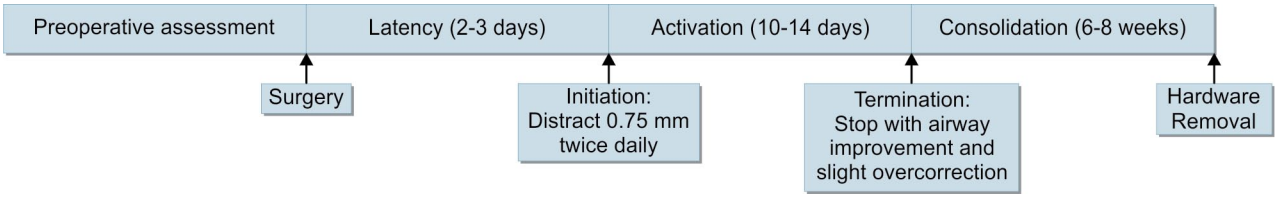
## EPIDEMIOLOGY

The birth prevalence of PRS varies by race and region. The National Birth Defects Prevention Study in 2009 estimated the birth prevalence of PRS to be between 0.5 and




**Figs. 95.3A and B:** The concept behind mandibular distraction osteogenesis. Medical model demonstration of how lengthening regenerate bone (red) results in improved mandibular projection over time. (A) Formation of regenerate following initial mandibulotomy. (B) Formation of regenerate bone following gradual linear distraction.

**Flowchart. 95.1:** Timeline of neonatal mandibular distraction osteogenesis favored by the author.




1.2:10,000 live births, and demonstrated that compared to non-Hispanic Whites, the birth prevalence of all cleft types was lower among non-Hispanic Blacks.[6] More recent data also supports this observation, suggesting that the highest rate of isolated PRS is in whites (2.1/10,000 live births) and the lowest rate in non-Hispanic Blacks (<0.5/10,000 live births). Isolated PRS is more common in the Midwest (2.2/10,000 live births) and less common in the Northeast (1.2/10,000 live births). The rate of syndromic PRS is less variable across races and regions and is approximately 1.4/10,000 live births.[7] Rates of surgical airway intervention may also vary across regions; however, most case series that have been reported demonstrate a consistent surgical airway intervention rate of approximately 40% in infants with PRS.[3,4,8]

## EMBRYOLOGY AND RELEVANT ANATOMY

The musculoskeletal structures that form the head and neck region are ultimately derived from mesoderm, ectoderm, and neural crest cells. These neural crest cells are the source of many structures in this region including cartilage, bone, dentin, tendon, dermis, pia and arachnoid, and glandular stroma.

In the fourth and fifth weeks of development, the pharyngeal (or branchial) arches appear. The center of the face is formed by the stomodeum, which is surrounded by the first pair of branchial arches. The first arch is bordered rostrally by the frontonasal process and caudally by the second branchial arch. The first arch forms two mesenchymal prominences, a dorsal portion (the maxillary process) and a ventral portion (the mandibular process). Mesenchyme of the maxillary process will go on to form the maxilla, zygoma, and temporal bone. The mandibular process contains Meckel's cartilage, which ultimately involutes leaving only two small portions at its dorsal end, which persist as the malleus and incus. During the process of involution, the mesenchymal tissue surrounding Meckel's cartilage undergoes membranous ossification, thereby forming the mandible.

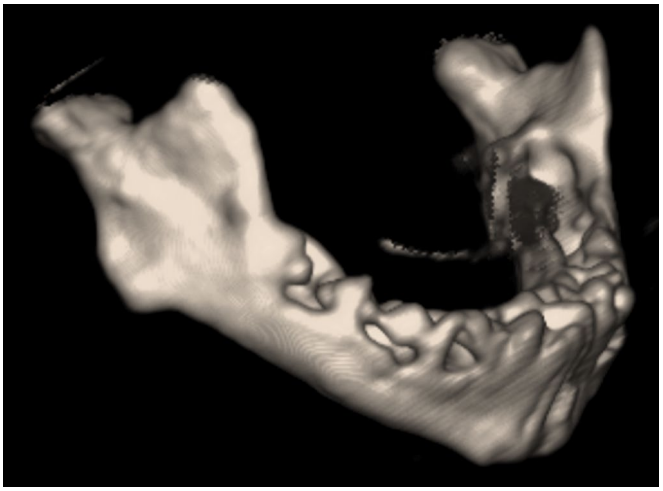


**Fig. 95.4:** Three-dimensional computed tomography reconstruction of the neonatal mandible in an infant with micrognathia. Note the obtuse mandibular angle and relatively short mandibular ramus.

The fetal mandible continues to develop and at the time of birth, several prominent landmarks are easily identifiable, however, there are still significant morphologic and compositional differences between the infant and adult mandible.

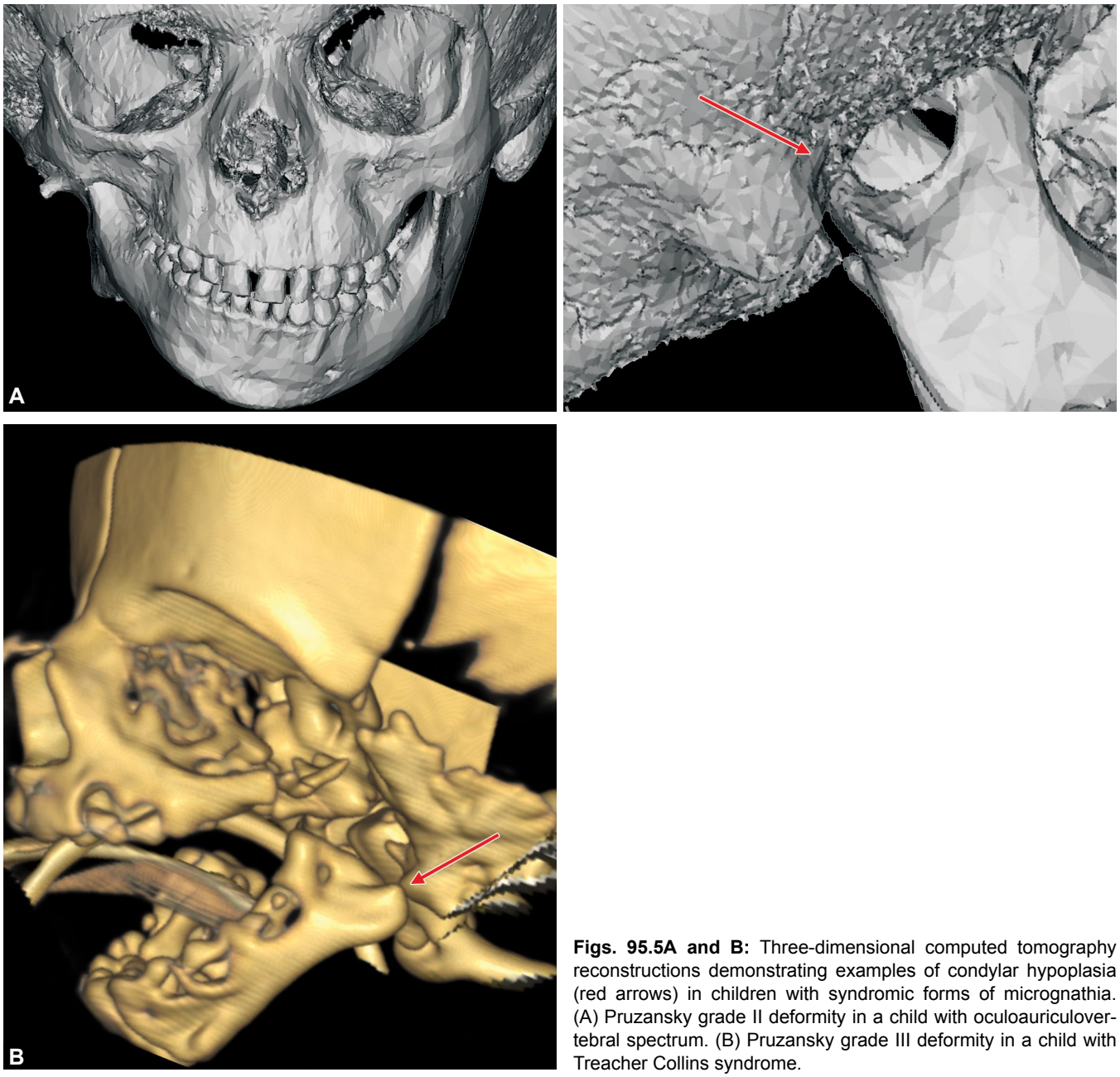
At birth, an infant's lower jaw is characterized by an obtuse mandibular angle and a relatively short ramus compared to adult mandibular morphology (Fig. 95.4). As a child ages the mandible's bony structure becomes more dense and key anatomical structures and surgical landmarks change in shape and position. Over time, a more acute gonial angle develops and concurrent enlargement of the ramus and body take place. Additionally, significant growth of the alveolar process is observed, as the deciduous and permanent dentition erupt throughout early childhood. As a result, the distance between the developing dentition and the inferior mandibular border increases over time. During this phase of alveolar process enlargement, the inferior alveolar nerve and canal undergo significant superior displacement, which positions the mental foramen more posteriorly as the child ages into adulthood.[9]

## Mandibular Hypoplasia

Congenital malformations of the mandible most commonly involve hypoplasia of the mandibular body, with or without associated abnormalities of the ramus, condyle, and temporomandibular joint. In 1969, Pruzansky reported a grading system for mandibular deficiency. He defined grade I as minimal hypoplasia of the mandible; grade II as a functional but deformed temporomandibular joint in which the condyle is displaced anteriorly and medially, and grade III as absence of the ramus and glenoid fossa (Figs. 95.5A and B).[10] Other classification schemes have been proposed; however, the Pruzansky classification has proved to be the most influential in regards to how these children are managed surgically.

## HISTORY OF MDO

The concept of distraction osteogenesis was introduced by Codvilla in 1905[11] and improved upon by Ilizarov in the




**Figs. 95.5A and B:** Three-dimensional computed tomography reconstructions demonstrating examples of condylar hypoplasia (red arrows) in children with syndromic forms of micrognathia. (A) Pruzansky grade II deformity in a child with oculoauriculovertebral spectrum. (B) Pruzansky grade III deformity in a child with Treacher Collins syndrome.

1950s, when the concept of bone lengthening was revisited in the context of treating leg length discrepancies.[12] The first reported use of mandibular distraction in children with micrognathia was in 1992, when McCarthy utilized the technique for gradual lengthening of the mandible in older children with mandibular deficiencies.[13] Additional reports soon followed, describing the use of bilateral MDO to treat obstructive sleep apnea in children with craniofacial anomalies. In 1998, successful use of the technique was reported in a child 14 weeks of age.[14] By 2001, multiple groups had published additional reports documenting the use of bilateral MDO for the primary purpose of relieving upper airway obstruction in infancy.[15,16] Many centers across the country and around the world now utilize the technique of bilateral MDO to improve airway obstruction and feeding difficulties in infants and newborns with Robin sequence. There is a growing body of literature pertaining to the positive long-term results of early bilateral MDO for relief of upper airway obstruction.[17,18–23] Feeding outcomes in general are more favorable than those observed with TLA, allowing children to avoid both a tracheotomy and a gastrostomy tube in most cases.[17,14–15,23,24]

## LIMITATIONS OF MDO

Caution is advised in children with absent mandibular condyles, absent coronoid processes, and/or poorly defined glenoid fossae (Pruzansky grade III), as such children are not ideal MDO candidates.[25] Many children with oculoauriculovertebral spectrum, Treacher Collins syndrome, or Nager's syndrome, for example, have an underlying disturbance in the growth center below the mandibular condyle that may limit, if not prevent, growth of the jaw. As part of this mandibular deformity, these infants lack a well-defined glenoid fossa on the affected side. Therefore, if mandibular distraction is performed, the posterior mandibular segment may not engage properly against the skull base. This lack of engagement allows seemingly infinite posterior movement of the posterior mandibular segment into the soft tissue of the mastoid area, thus preventing effective anterior advancement of the mandible with distraction of the mobile segments.

Costal cartilage grafting and creation of a pseudarthrosis at the temporomandibular joint site allows for a means of addressing Pruzansky III deformities (Figs. 95.6A to C).[26,27] Such procedures are not performed in infancy but rather later in childhood. Costal bone grafting, in which the normal growth center within the harvested rib is surgically affixed to the malformed mandible, allows for further growth, or even *overgrowth*, of the mandible. If inadequate growth is observed, the jaw may be advanced through distraction of the grafted rib segment. Alternatively, if overgrowth occurs, resection of excess bone may be necessary.

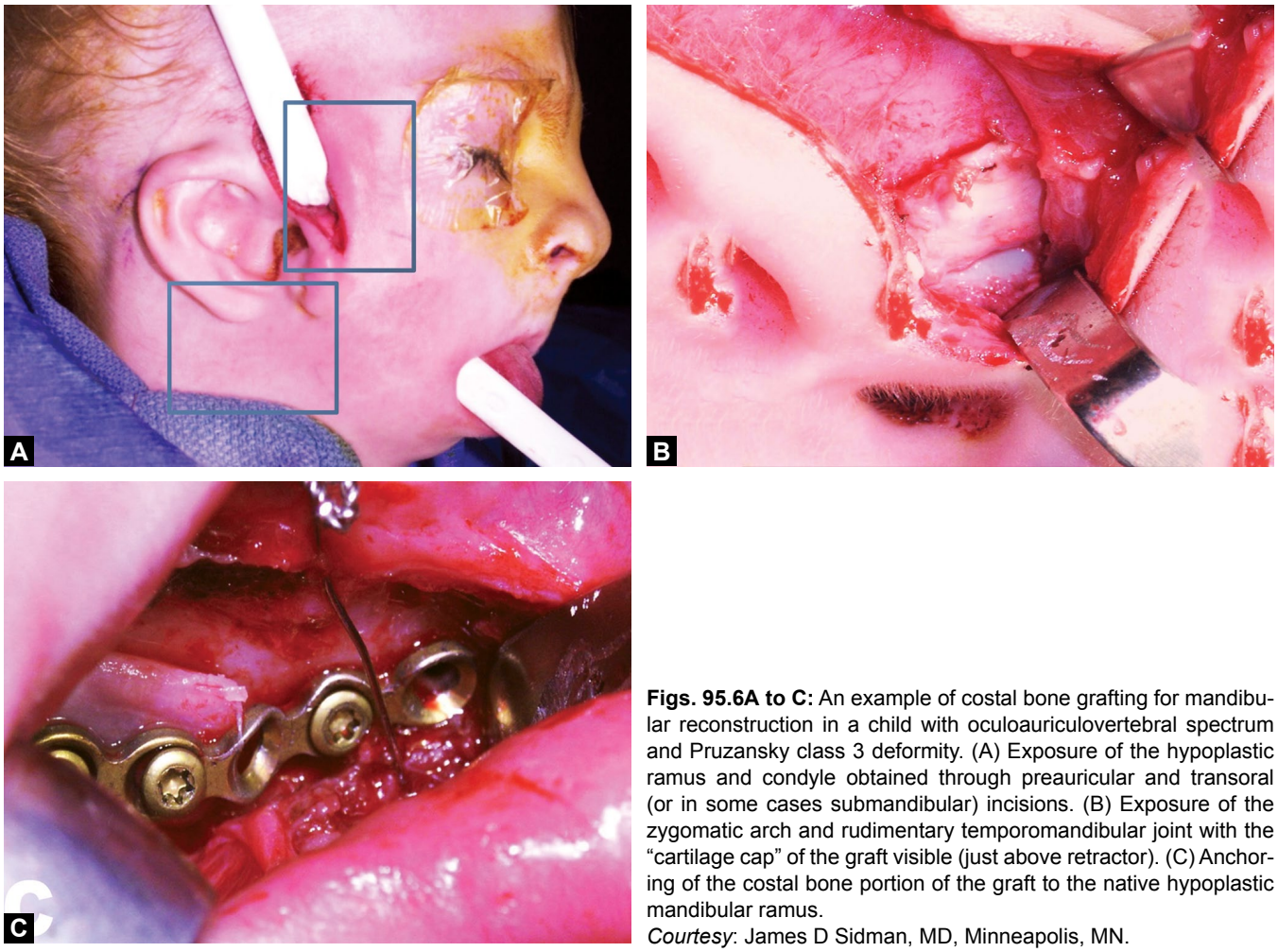
In children with unilateral mandibular hypoplasia, unilateral mandibular distraction is an option. The indications for this are based on malocclusion and facial asymmetry, so surgical intervention is typically deferred until later in childhood, even in cases when costal cartilage grafting is not necessary.

Free tissue transfer with a fibular free flap reconstruction provides the largest amount of available vascularized bone stock and is especially useful in cases of severe hypoplasia in which a free bone graft is neither practical nor advisable.

## PREOPERATIVE ASSESSMENT: EVALUATING VENTILATION AND FEEDING

If an infant with micrognathia demonstrates signs and symptoms of acute airway obstruction in the delivery room, the airway must be secured either with endotracheal intubation or emergent tracheotomy. The details of managing acute airway obstruction in a child with craniofacial differences are beyond the scope of this chapter. Recent data suggest that newborns with PRS who are in acute distress may be nasal fiberoptically intubated or temporized with a laryngeal mask airway (LMA) prior to tracheotomy, in cases in which nasal fiberoptic intubation is not possible.[28,29] However, it is the author's opinion that any child with airway obstruction significant enough to merit an invasive intervention within the first 24 hours of life will likely come to require a more definitive surgical airway intervention during his or her infancy.[29]

When an otherwise stable newborn with PRS displays signs of chronic upper airway obstruction it is most reasonable to begin with conservative measures first. Prior to intervention, the airway should be assessed with bedside flexible laryngoscopy to rule out a synchronous airway lesion. Such lesions may include choanal atresia (sometimes seen in Treacher Collins syndrome), laryngomalacia, laryngeal cleft (CHARGE association), or a glottic web with or without subglottic stenosis (velocardiofacial syndrome). The presence of an additional site of airway obstruction may suggest the need for intervention and may influence the choice of procedure for definitive surgical airway intervention. In instances of significant multilevel




**Figs. 95.6A to C:** An example of costal bone grafting for mandibular reconstruction in a child with oculoauriculovertebral spectrum and Pruzansky class 3 deformity. (A) Exposure of the hypoplastic ramus and condyle obtained through preauricular and transoral (or in some cases submandibular) incisions. (B) Exposure of the zygomatic arch and rudimentary temporomandibular joint with the "cartilage cap" of the graft visible (just above retractor). (C) Anchoring of the costal bone portion of the graft to the native hypoplastic mandibular ramus.
*Courtesy*: James D Sidman, MD, Minneapolis, MN.

airway obstruction it is most prudent to move forward with tracheotomy to definitively secure the airway until the additional sites of obstruction can be addressed sequentially.

In the most common scenario of mild-to-moderate or intermittent obstruction (episodic oxygen desaturations at rest or with feeds, signs of chronic respiratory acidosis on capillary blood gas, inability to take in an adequate volume of oral feeds), the author's philosophy is to start with side-lying and prone positioning. If this fails to improve ventilation, placement of a nasopharyngeal airway or nasal trumpet to bypass tongue-base obstruction and break the seal made between the oropharyngeal tongue and the posterior pharyngeal wall may prove more effective. A variety of custom oral appliances may be fashioned for the purpose of relieving obstruction.[30–32] Other authors have described success at simply customizing a nasoendotracheal tube to relieve obstruction.[33] Nonsurgical management of upper airway obstruction in children with PRS is always preferable. Most case series examining airway interventions in infants with PRS demonstrate that these children may be successfully managed nonoperatively upward of 60% of the time.[2–4,34–36] The decision to move forward with a surgical intervention remains controversial.

A number of objective criteria are available to aid in the assessment of the need for additional intervention. The author relies primarily on feeding trends, obstructive events, carbon dioxide retention, and weight gain to determine which infants merit a definitive surgical airway intervention.

## Feeding Interventions

The infant with PRS must overcome the inherent difficulty of feeding with a cleft palate as well as the added burden of a variable degree of airway obstruction from glossoptosis. General feeding strategies begin with the same principles

of any child with cleft palate – the absolute admonition to avoid attempts at direct breast-feeding, recommendations for pumping mother's breast milk for delivery by bottle, and the use of a special bottle/nipple to facilitate delivery of breast milk or formula without the need for an effective suckle (e.g. Haberman Feeder, Mead Johnson Cleft Palate Nurser, and Pigeon Nipple).

Failure to thrive in the PRS population is due to two mechanisms that are *not* mutually exclusive: caloric intake and work of breathing. Consultation with an experienced feeding therapist (occupational or speech therapist, or feeding nurse specialist) should be initiated for any newborn noted to be struggling with feeding. In some cases, members of the neonatal feeding team can successfully feed such infants, but may find that the rest of the nursing team has variable results. In these cases the family is rarely able to achieve similar feeding volumes as well. Common problems are failure to achieve adequate caloric intake in spite of supplementation with high calorie formula or prolonged feeding times leading to progressive fatigue and decreasing feeding efficiency. Sometimes, feeding difficulties are ameliorated with placement of a nasopharyngeal airway owing to relief of airway obstruction. Other times, feeding is negatively impacted by the presence of an airway device and this device needs to be removed during feeds. In the long run, failure to translate successful feeding strategies to the infant's direct caregivers will result in failure to thrive and may lead to surgical intervention. The need for direct professional-to-family education in feeding technique cannot be overstated.

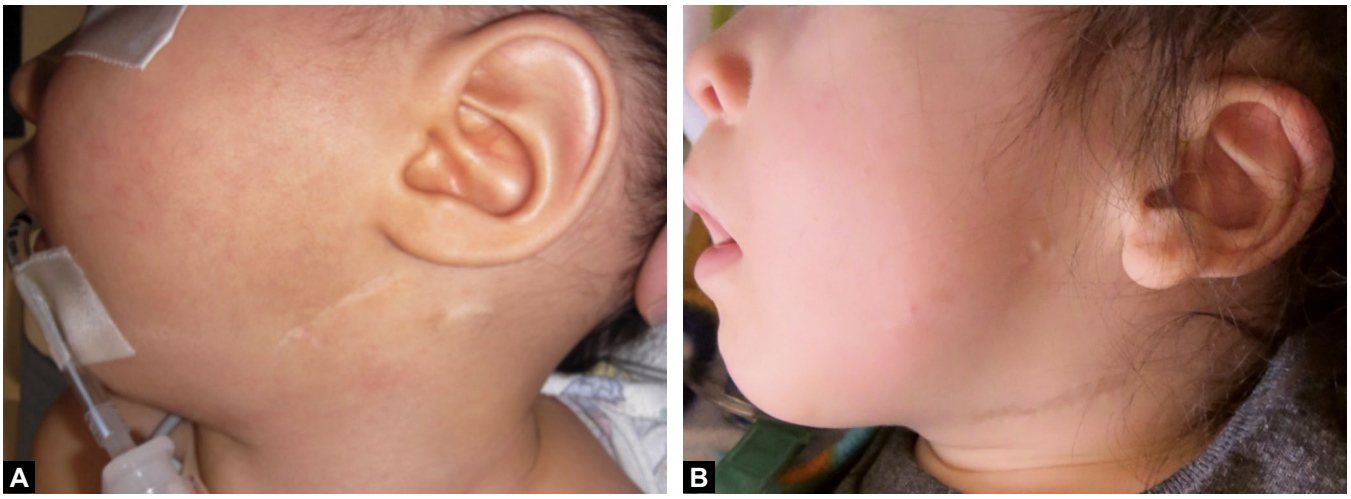
Even in cases in which adequate caloric intake is achieved, the infant may still demonstrate poor weight gain. In such cases, it becomes important to reassess the work of breathing to overcome upper airway obstruction, as this effort may result in increased caloric expenditure, which contributes to failure to thrive. While such a scenario may be temporarily addressed with fortification of breast milk or formula, a nutritional supplementation strategy merely addresses one symptom of the underlying problem—significant upper airway obstruction—and therefore is not a sustainable "solution" as the child grows.

The feeding performance of an infant with PRS may be highly variable, and an observation period of 7–14 days is recommended for any newborn in which feeding impairment is suspected. A formula-fed/supplemented child with a cleft palate is expected to regain his or her birth weight by 2 weeks of age. A high suspicion for chronic airway obstruction should be expected for any infant with PRS who is unable to take in regular volumes of oral feeds. Serial capillary blood gases (drawn in the morning and not after a prolonged period of stimulation, crying, or activity) should demonstrate $CO_2$ levels in the 40s. When levels increase into the 50s and the bicarbonate level rises (suggesting metabolic compensation of a chronic respiratory acidosis), a higher suspicion for chronic airway obstruction should exist. If the child is clinically faring poorly, these more objective measures may offer support for an intervention. Polysomnography may also be performed; however, neonatal polysomnography is difficult to interpret and not always reliable. For this reason, the author tends to use feeding trends, oxygen saturation readings, and serial capillary blood gases as objective measures for determining the degree of chronic upper airway obstruction that is present.

## THE MANDIBULAR DISTRACTION PROCEDURE

### Surgical Approaches and Device Selection

The pediatric mandible may be approached surgically through an external or intraoral approach. In neonates, the former is more common, owing to difficulty in transoral exposure in a newborn, which may also suffer from some degree of ankylosis and limited jaw opening in cases of micrognathia. The external approach results in a 2–3 cm scar in the submandibular area, which may be avoided through a transoral procedure (Figs. 95.7A and B). Infant mandibular distraction may be accomplished with use of either buried (subcutaneous) hardware attached to the bone with monocortical screws or external devices, which are affixed to the mandible though percutaneous, bicortical k-wires. In order to allow for activation of the device, a portion of hardware (the activation arm) is externalized through a separate incision when buried hardware is used. This incision may be external (most common) or intraoral. The advantages of using buried hardware are a secure and close approximation of the device to the mandible, use of monocortical screws that may limit damage to tooth buds, and avoidance of paramandibular scars from percutaneous k-wires. Disadvantages include an inability to perform multivector distraction, inability to access the device if troubleshooting of mechanical failure is required, and a more extensive operation for hardware removal with potential facial nerve injury during re-exploration. Advantages of external hardware include use of multidirectional devices which allow for immediate correction




**Figs. 95.7A and B:** Side-by-side comparison of the scarring associated with neonatal mandibular distraction osteogenesis. (A) External approach using a buried device, 2 years postoperatively. (B) External approach using a multivector external device, 2 years postoperatively.

of open bite deformities or mandibular asymmetries during the activation process, easy access to the device for any troubleshooting, and ease of subsequent hardware removal, a process that can be performed under minimal sedation or at the bedside. With the exception of certain syndromic forms of PRS, preoperative computed tomography is not necessary prior to mandibular distraction when external hardware is used. This saves a considerable amount of money and avoids exposing a newborn to radiation. Disadvantages of external hardware include injury to tooth buds during placement of bicortical k-wires, facial nerve injury during k-wire placement, potential for device loosening, infection of percutaneous k-wires, and presence of more conspicuous paramandibular scars.

## Risks of Surgery

Complications of MDO may occur, regardless of the approach used. Operative complications include facial nerve injury, injury to the inferior alveolar nerve, incomplete mandibulotomy leading to poor projection, damage to the molar tooth buds, intraoperative and/or postoperative bleeding requiring transfusion, and infection. The length of the latency phase may be too short (preventing ossification of the regenerate) or too long (premature consolidation). During the activation phase, mandibular deformities such as asymmetry or development of an open bite may occur. Infection of hardware through the exposed activation hardware or percutaneous k-wires may develop leading to a minor cellulitis or progressing to frank osteomyelitis. Stretch of the soft tissues during activation may lead to a facial nerve palsy, though this is usually transient. Even if an optimal result is obtained at the end of the activation phase, complications during the consolidation period may include mandibular regression with asymmetry or decreased projection with a relapse of airway and feeding symptoms; infection is also possible. Hardware removal of an external device is a simple process without complications; however, removal of buried hardware is a more extensive procedure. Scarring and repositioned anatomy within a previously operated field puts the facial nerve at risk, especially when accessing posterior screws in an infant, which requires retracting soft tissue over an underdeveloped mastoid tip.

Long-term complications following neonatal MDO include residual obstructive sleep apnea and/or recurrent dysphagia, facial scarring, mandibular asymmetry, deformed or absent second molars, dentigerous cyst formation, and need for further mandibular procedures.

In spite of the significant risk involved in neonatal mandibular distraction, this technique has gained wide acceptance among pediatric otolaryngologists and plastic craniofacial surgeons in the United States and beyond. Children who undergo MDO tend to do well clinically in regards to airway and feeding outcomes, when compared to those children who undergo alternative interventions such as TLA or neonatal tracheotomy.

## Description of Procedures

The author prefers to use an external approach, with placement of buried bidirectional devices in older children and

use of an external, multidirectional device in neonates, given the risk and benefit profiles for each procedure, which were detailed earlier.

## Neonatal Mandibular Distraction Osteogenesis

Intervention is deferred until the child reaches a minimum of 2.5 kg, given the low circulating blood volume of smaller newborns, the need for nasotracheal intubation with a practically sized tube (3.0–3.5) allowing for suctioning and adequate ventilation during a 5-day period of postoperative sedation, and the size mismatch of mandibular hardware to the neonatal mandible in children < 2.5 kg.

Optimal communication between pediatric anesthesia and pediatric otolaryngology providers is a must to assure safe management of a tenuous airway. It is the author's opinion that a team approach to anesthesia induction is indicated, with anesthesia providers focusing on access and titration of sedation while otolaryngology assumes complete control of the airway until endotracheal intubation has been secured. It is easy to underestimate the precariousness of the airway in an infant with PRS, and providers are best served with a healthy respect for how even a small amount of sedation can precipitate an airway emergency in these children.

Prior to the child entering the room, the following devices should be immediately available: a variety of oral airways and nasopharyngeal airways (nasal trumpets), a neonatal intubating flexible bronchoscope, size 2.0–4.0 uncuffed and microcuffed endotracheal tubes, a small allis clamp (for retracting the tongue anteriorly), a size 1 infant LMA and if available an infant intubating LMA, a pediatric glidescope, infant Parson's laryngoscopes (sizes 1 and 2), and a pediatric tracheotomy kit.

Following supine positioning, the airway is maintained with or without an oral or nasopharygeal airway as needed. IV access is assured and the child is lightly sedated while still allowing for spontaneous ventilation. A microdirect laryngoscopy and bronchoscopy is performed by an experienced otolaryngologist. It is during this assessment that the surgeon may determine if the child can be intubated transorally and if so the difficulty of this intubation can be graded. This information is useful for the neonatal intensivists who will care for the child postoperatively. Even if the child can be intubated transorally, the author prefers to perform a nasal intubation and usually accomplishes this over a flexible neonatal bronchoscope using a Seldinger technique. The fiberoptic intubation can be difficult owing to the disorienting lack of a nasal floor in a child with cleft palate, the presence of glossoptosis, and the superior positioning of the infant larynx. Tongue-based obstruction may be overcome during fiberoptic intubation by grasping the anterior tongue with a small allis clamp and pulling the tongue base forward, bringing the larynx into view. Even an experienced pediatric anesthetist can become disoriented by the aberrant anatomy, and navigating the airway while providing optimal anesthesia and assuring working access in a neonate is not a reasonable expectation for one provider.

Once nasotracheal intubation has been secured the pediatric anesthesia team may establish a central line if a peripheral intravenous central catheter has not already been placed. The bed can be left in a standard position and the circuit brought over the forehead, which is padded accordingly. However, the author prefers to have the bed turned 180° with the circuit traveling over the anterior chest and back to the anesthesia team. Positioning this way prevents pressure from the endotracheal tube on the soft triangle of the nose and also allows for easy access to the feet and groin if additional venous lines are necessary. A dose of IV cefazolin is given.

The child's eyes are padded with eye pads as it is easy to lean on these during retraction and precipitate an oculocardiac reflex. A shoulder roll is placed and the patient is then prepped with diluted Betadine solution and draped in a sterile fashion. For an external approach, a 2–3 cm incision is planned within a relaxed skin tension line of the neck, at least one finger-breadth below the mandible (Fig. 95.8). A minimal amount of local anesthetic with epinephrine is injected for hemostasis. Incision is made sharply and dissection carried down through the superficial layer of the deep cervical fascia. A subfascial flap is raised superiorly over the submandibular gland to protect the marginal mandibular branch of the facial nerve. The facial vessels are identified, and frequently the facial vein is sacrificed. Often the facial artery may be retracted posteriorly or anteriorly but at times this must be sacrificed as well. The mandibular periosteum is incised down to bone and elevation in a subperiosteal plane over the buccal surface of the mandible is performed using a dental instrument, severing the masseteric attachments to the ramus. Elevation is continued superiorly until the ramus is exposed. Caution should be noted here as excess elevation posteriorly and superiorly can expose the subcondylar area and provoke pterygoid bleeding, which is unnecessary. Anterior elevation is then performed identifying the retromolar trigone area superiorly and antegonial

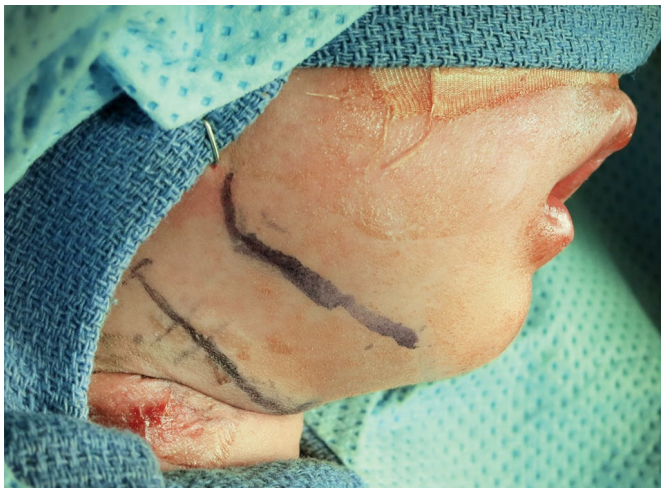


**Fig. 95.8:** Skin markings for planning neonatal mandibular distraction osteogenesis, external approach.

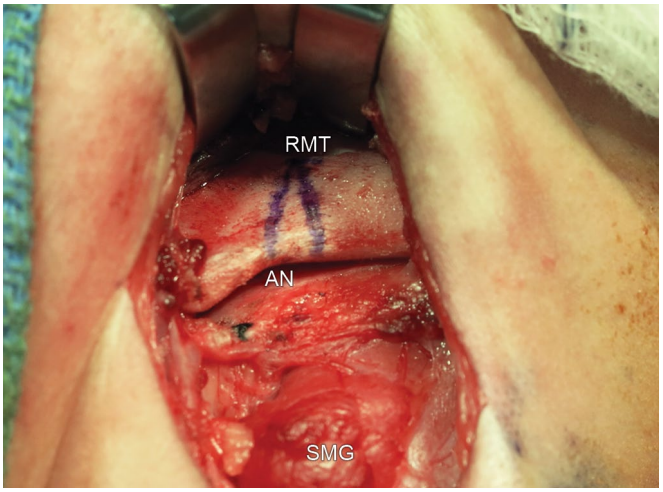



**Fig. 95.9:** Exposure of the right mandibular angle and planning of osteotomy. In this case the more anterior and vertical mandibulotomy was chosen. (RMT: Retromolar trigone; AN: Antegonial notch; SMG: Submandibular gland).

notch inferiorly. Further anterior dissection is carried out until just shy of the mental foramen. The subperiosteal elevation along the lingual surface of the mandible is then performed. This will precipitate some venous bleeding, which is usually self-limited.

Now the critical planning of a mandibulotomy is made. The osteotomy must be anterior or posterior to the mandibular angle in order to preserve this important esthetic landmark and optimize the vector of mandibular advancement. The author prefers a vertical mandibulotomy anterior to the angle in neonates. A nerve hook may be used to create a plumb line, which extends from the retromolar trigone area superiorly down to an area anterior or through the antegonial notch inferiorly. At this point, measurements should be taken to assure that there is adequate bone stock anterior and posterior to this planned mandibulotomy (Fig. 95.9). Careful attention here is made to assuring that the nerve hook is in the retromolar trigone and not the sigmoid notch, as the latter would result in a posteriorly positioned mandibulotomy that travels through the subcondylar growth center of the mandible and effectively amputates the condyle from the mandibular ramus.

Once markings have been made, a malleable retractor is placed deep to the lingual surface of the mandible to protect the deeper soft tissues, and an outer corticotomy is made using a 1.2-mm side cutting dental drill, which allows for a fine cut without excess loss of bone stock. Alternatively, a piezoelectric device may be used. Piezoelectric systems may limit trauma to the soft tissue structures within the mandible (dental follicles and inferior alveolar nerve), which may occur during the mandibulotomy. The mandibulotomy is not completed at this time.

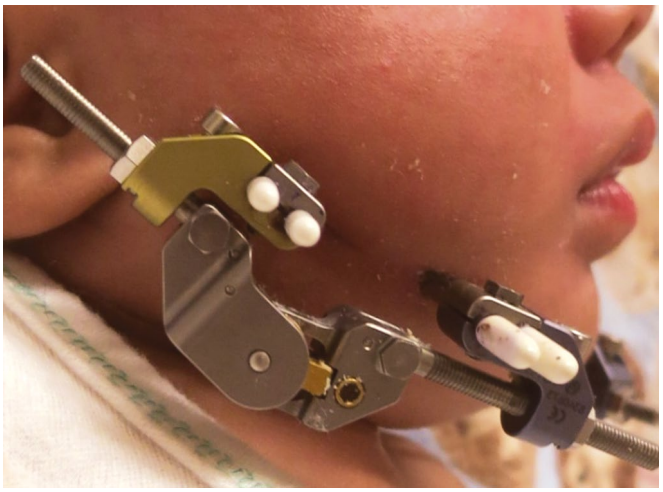


**Fig. 95.10:** Multivector external distraction device in place.

## External Hardware

Next, for the use of external distraction devices, the placement of percutaneous k-wires is planned. The author uses an external multidirection distraction device made by Synthes (no proprietary affiliation or conflict of interest). Distraction rods of varying length are available; the author uses a 20-mm distraction rod anteriorly and a 15-mm rod posteriorly (Fig. 95.10). The distraction bodies when set closest together position those k-wires closest

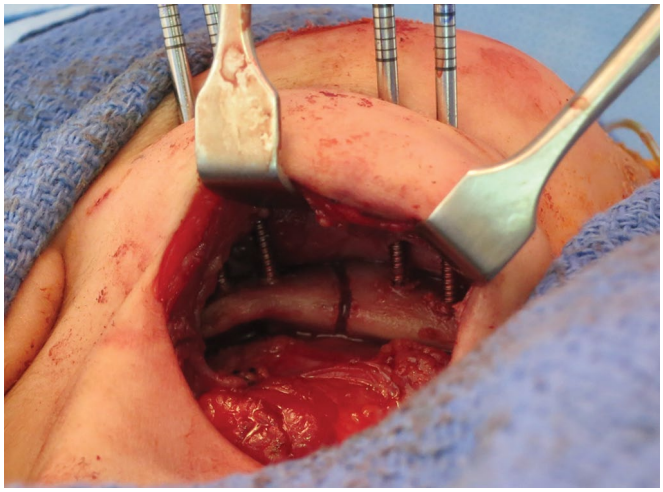


**Fig. 95.11:** Percutaneous k-wires placed on either side of the outer corticotomy prior to completion of the mandibulotomy.

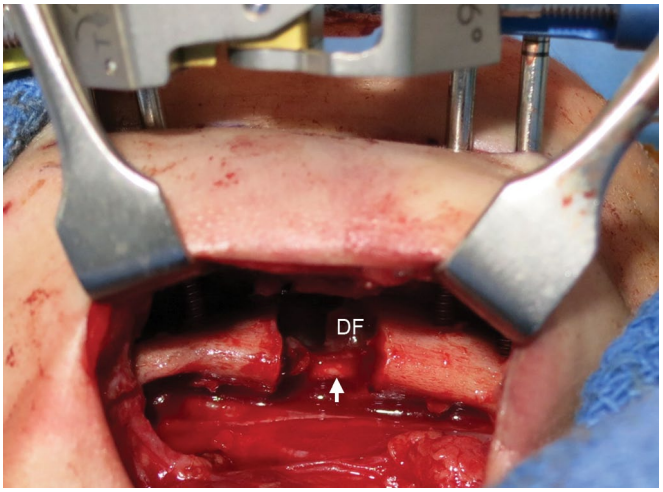



**Fig. 95.12:** Trial distraction performed to assure that the mandibulotomy is complete. DF: Dental follicle; arrow points to inferior alveolar nerve, which is on stretch.

to the mandibulotomy at 10 mm apart. For this reason, and to assure that the k-wires are secure and adequately spaced from the mandibulotomy, the most proximal k-wires must be 5–7 mm away from the outer corticotomy. Measurements are made with calipers. A 27-gauge needle is inserted through the soft tissues of the cheek to assure a straight trajectory through the soft tissues down to the inferior ramus and body of the mandible. The entry point of the needle is marked on the skin to plan the ideal surface location of the paramandibular stab incisions. A 10-mm incision is planned posteriorly and one anteriorly to accommodate the posterior and anterior k-wires. After local is injected through the soft tissues, the skin is sharply incised and blunt dissection performed through the parotid and buccal soft tissues using a hemostat, spreading in an anterior to posterior direction to limit traction on the branches of the facial nerve. A trochar is then placed through this tunnel and the k-wire insertions are planned, again assuring that the wires closest to the mandibulotomy are at least 5–7 mm away from the outer corticotomy.

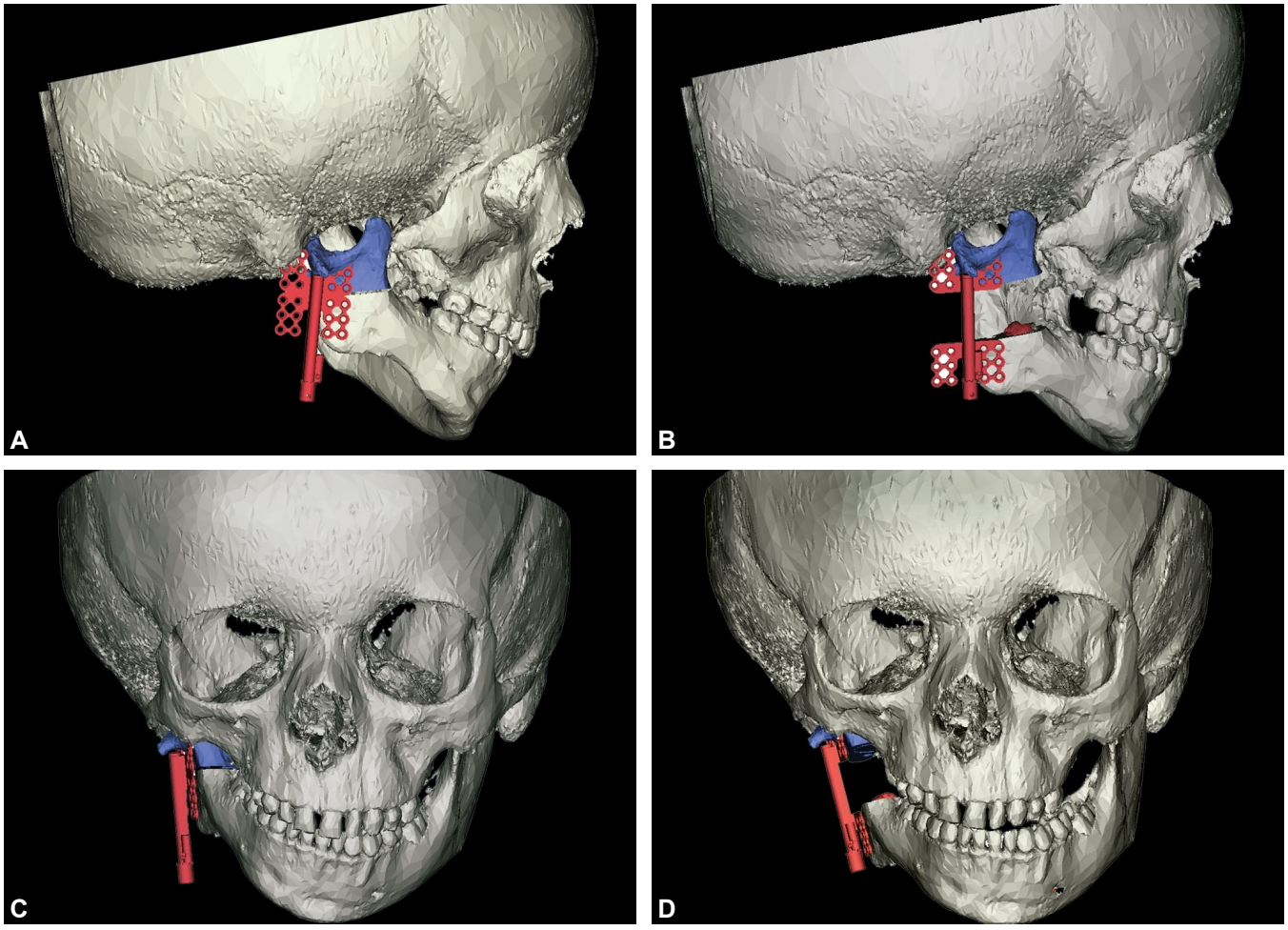
The neonatal mandible has the consistency of refrigerated butter and can be quite soft posteriorly. The author prefers to hand-drill these 2-0 k-wires to optimize control of their placement and assure adequate stability. The wires are inserted through the full thickness of the mandible until the tip of the wire can be palpated along the lingual surface of the mandible. The anterior of the two posterior k-wires (the one closest to the mandibulotomy) is placed first followed by the posterior k-wire. The wires are inserted at an angle that is perpendicular to the midsagittal plane and not necessarily perpendicular to the surface of the mandible. Next the anterior k-wires are placed, again with the posterior of these two wires no closer than 5–7 mm anterior to the outer corticotomy (Fig. 95.11). The assembled mandibular distraction device is then lowered over the k-wires and its optimal position marked on the k-wires. The device should be approximately 7 mm above the surface of the skin to allow for postoperative swelling. Once markings have been made, the distractors are slid off the k-wires without altering the orientation of the distractor. The outer corticotomy is then converted to a complete mandibulotomy, again using the side cutting drill burr. The region of the inferior alveolar canal is spared to avoid injury to the nerve. The mandibulotomy is then completed using a combination of angled and straight osteotomes.

The distractor is then placed back over the k-wires and tightened down at the height of the previous markings. It is easy to leave a small bridge of bone superiorly along the mandibular alveolus during the completion mandibulotomy. Therefore a trial of linear distraction is performed to assure a complete mandibulotomy and rule out green-sticking. If bridges of bone are appreciated, these are taken down with a small osteotome until it is clear that the mandibulotomy is complete and there is no resistance to linear distraction. With the soft tissue on stretch, the anatomic continuity of the inferior alveolar nerve may be confirmed (Fig. 95.12). The bone segments are then returned to their resting, anatomic position. Excess k-wires are cut and silicone caps applied over their sharp ends. The k-wires beneath the distractors are wrapped in strips of xeroform gauze, and a small kling dressing is wrapped around the entire distraction device.

## Buried Hardware

The author's buried distractor of choice is the KLS Martin Zurich distractor (no conflict of interest). A neonatal linear distractor with 15, 20, or 25 activation arms is available. For older children, a dual vector distractor is available. Buried curvilinear distractors (Smythes) are also available; these may be customized to each patient based on preoperative imaging. Following the deep scoring of the buccal cortex (outer corticotomy) the buried mandibular hardware is brought into the field. These are unidirectional devices in neonates and infants and may be positioned to allow for the activation arm to exit the skin anteriorly or posteriorly. Anterior location of the activation arm results in a slightly more conspicuous scar, but allows for easier access to the device during the activation phase. Most surgeons tend to site the activation arm posteriorly, exiting over the mastoid. In older infants, a posterior activation arm may contact the skin leading to irritation and edema and in infants with a lot of hair, the arm may become tangled. For unidirectional devices, planning the vector of distraction is critical for assuring mandibular symmetry and avoiding development of an open bite deformity. A more anteriorly placed osteotomy and a slight superior angulation of the hardware may limit this complication. Alternatively, children may undergo computed tomography scanning preoperatively followed by vector analysis with planning software (Figs. 95.13A to D). Commercial products are available through most device companies that allow for medical modeling, preoperative customization of hardware, and cutting templates to optimize surgical planning. This technology, while impressive, does significantly add to the expense of the procedure.

The buried hardware is optimally positioned, often based on preoperative planning software or use of a medical model. Monocortical screws are placed after any unnecessary plates are trimmed. The activation arm is attached and a small anterior or posterior stab incision




**Figs. 95.13A to D:** An example of computer-assisted virtual surgery for planning linear mandibular distraction.

is made to allow for externalization of this aspect of the device. Next that hardware is removed and the mandibulotomy completed with the 1.2-mm side cutting bur and a combination of small and large osteotomes. The hardware is replaced and a trial distraction performed to assure completion of the osteotomy as above. The device is then returned into resting position.

In older children, a bidirectional buried device may be used. In this case, a second activation arm is externalized inferiorly, allowing for angulation of the device if an open bite deformity develops later during the course of linear distraction. Alternatively, a customized curvilinear device will accomplish the same goal with the use of a single activation arm.

### Closure

The submandibular wound is checked for hemostasis, irrigated, and closed with 4-0 Vicryl fast-absorbing suture and skin glue. The k-wires or activation arm(s) serve as passive drains.

The head is then rotated to allow for access to the contralateral side and an identical procedure is performed. Following completion of the contralateral side, the child is turned over to the transport team and returned intubated and sedated back to the neonatal intensive care unit or pediatric intensive care unit.

## POSTOPERATIVE CARE

The author prefers to leave neonates and infants intubated and sedated for several days following this procedure. This is a painful operation, and given preoperative airway concerns coupled with postoperative edema and use of analgesics, the risk for airway compromise is high. In leaving the child intubated, analgesics can be given liberally without concern for respiratory depression. Given issues with premature self-extubation and prolonged withdrawal following deeper sedations, the author and colleagues developed a clinical pathway following neonatal and infant mandibular distraction. A combination of agents including morphine, midazolam, lorazepam, vecuronium, and dexmedetomidine may be utilized to assure a period of immobilization while limiting postoperative withdrawal symptoms. With use of this protocol, children are usually off all sedating medications by postoperative day 7.

### Latency Period

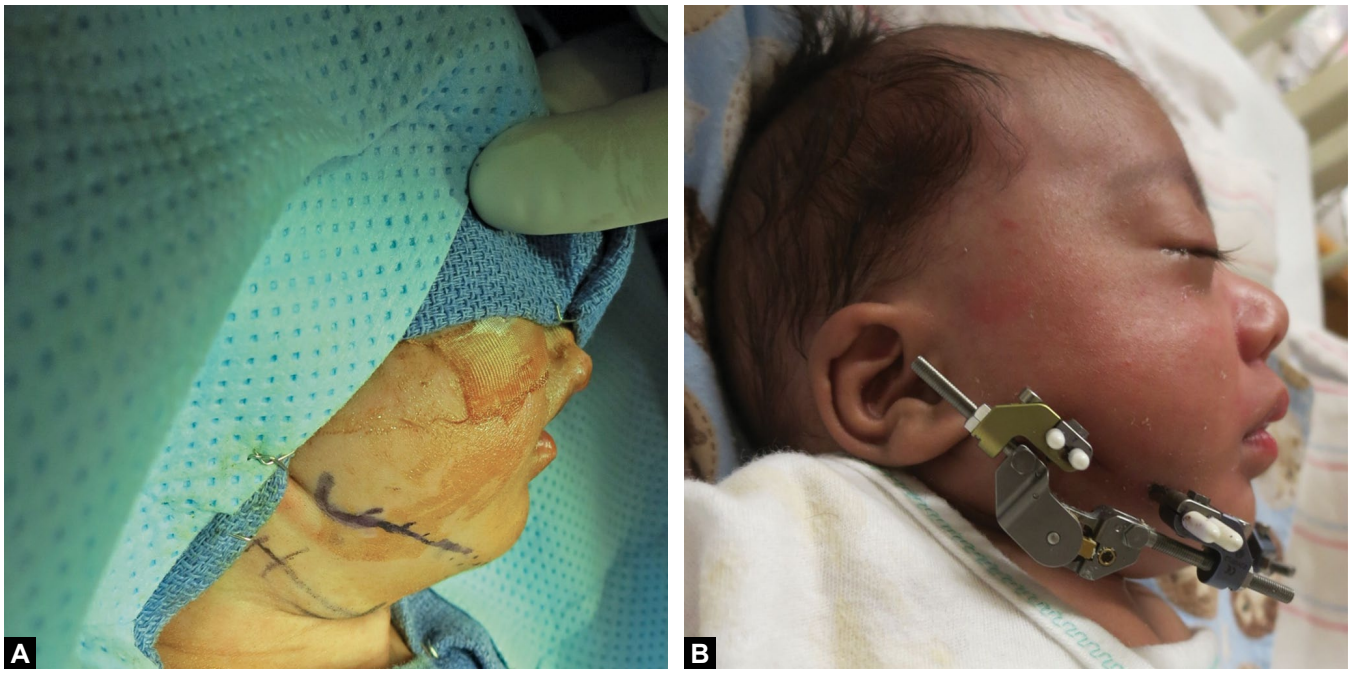
Variations exist in the length of latency for neonatal and infant mandibular distraction. The author uses a 48- to 60-hour time period for the latency phase. IV cefazolin is maintained throughout the latency and subsequent activation periods. A nasotracheal or orogastric feeding tube is placed and trophic feeds started and advanced once bowel sounds are detected.

### Activation Period

Controversy exists in regards to the optimal velocity of mandibular advancement in neonates, children, and adults following MDO. The author performs twice daily distractions, ideally close to 12 hours apart, with 0.75 mm advancement of the mandibular segments each time, amounting to a rate of 1.5 mm each day. Activation usually starts in the evening of postoperative day two. Prior to the first activation, the cling and xeroform dressings are removed and pin care is started with full-strength hydrogen peroxide. Pin care is continued three times daily for the length of admission. The same care is given to the exposed activation arms in cases in which buried devices are used. IV cefazolin is maintained and then transitioned to enteral cephalexin to maintain antibiotic prophylaxis throughout the activation period. The infant is left intubated and sedated until POD 5–6, at which point the mandible has been advanced 5 mm. A linear advancement of 5 mm has been shown to be enough to break the seal of the tongue base against the posterior pharyngeal wall.[14] Following extubation, a nasal trumpet may serve as a temporary bridge if necessary until further mandibular advancement has taken place.

Oral feeding is started once sedation has lightened and this is advanced as tolerated. Frequently gavage feeds may be completely discontinued prior to the completion of the activation period. Placement of a surgical gastrostomy tube is almost never indicated in a patient with isolated PRS and rarely necessary in a patient with syndromic PRS who is an appropriate candidate for neonatal MDO.[24]

The activation is continued until symptoms resolve and an appropriate degree of mandibular projection has been obtained. Frequently an open bite deformity will develop after 10–12 mm of linear distraction; this may be immediately corrected with angulation if a multidirectional distraction device is utilized. Any other mandibular asymmetries may be addressed with differential (asymmetric) distraction. In cases in which a multivector external device is used, varus or valgus distraction, and angular distraction may be performed as necessary. The goal should be to achieve slight overcorrection, bringing the infant into end-to-end occlusion based on the alveolar ridges (Figs. 95.14A and B). In female infants, distraction




**Figs. 95.14A and B:** Initial results of neonatal mandibular distraction osteogenesis. (A) Preoperative mandibular profile. (B) Mandibular profile at completion of activation phase (note the slight overprojection).

may cease just prior to end-on occlusion in order to avoid the masculine characteristic of prognathism. Once activation has ended, usually postoperative day 10–14, antibiotic prophylaxis is discontinued and discharge planning initiated.

## Consolidation Phase

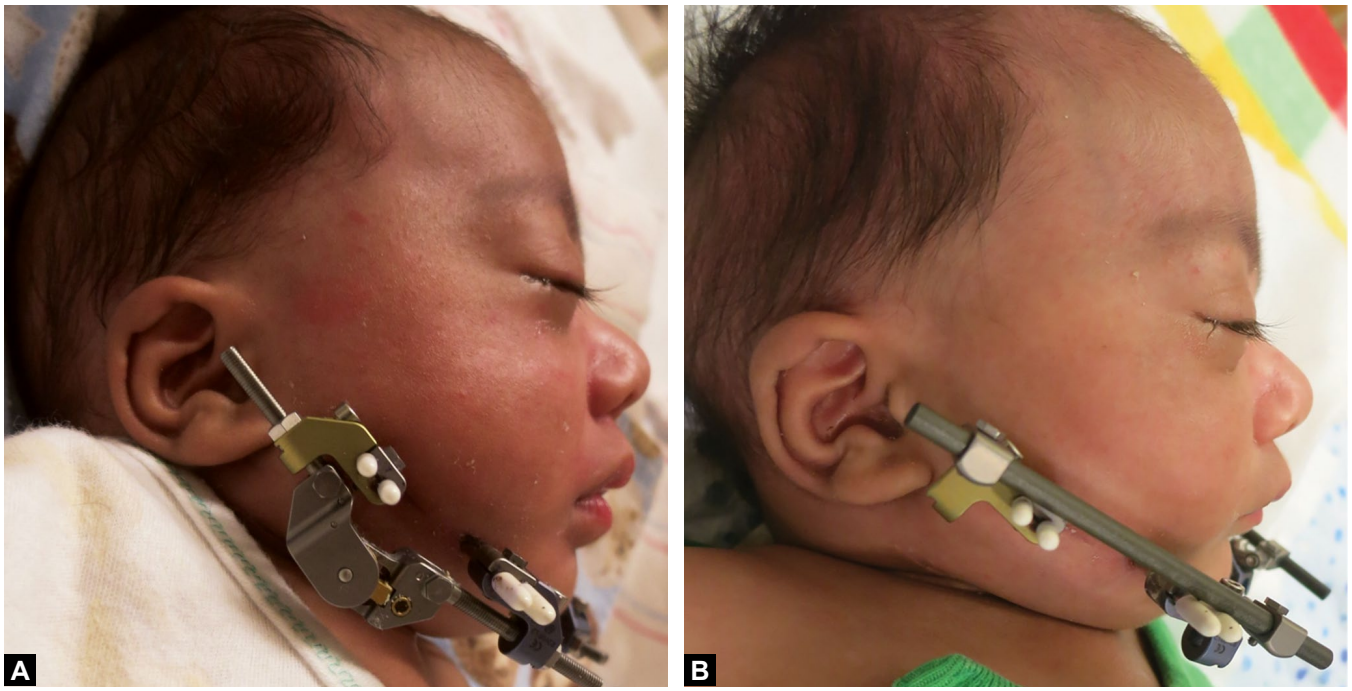
Outpatient services beyond weight checks are rarely needed following neonatal mandibular distraction. With correction of the airway, monitoring and tube feedings are usually no longer necessary. Parents are instructed on pin care. The surgeon may choose to lock down an external device or replace the distractor with lightweight, lower profile, graphite consolidation rods (Figs. 95.15A and B). With buried devices, the modular activation arms may be removed at the bedside. An outpatient visit is scheduled for the first 2 weeks after discharge. The author prefers a consolidation phase that is at least three times the length of the activation phase to assure optimal ossification of the regenerate.

For external devices, an outpatient procedure for hardware removal under a light anesthetic (mask or LMA airway) is planned for 6 weeks following completion of the activation phase (Figs. 95.16A and B). During this procedure, the consolidation rods are removed and the k-wires unscrewed using a needle driver. This is a percutaneous procedure that takes 2 or 3 minutes and results in minimal if any blood loss. The wounds are dressed with bacitracin and Band-Aids.

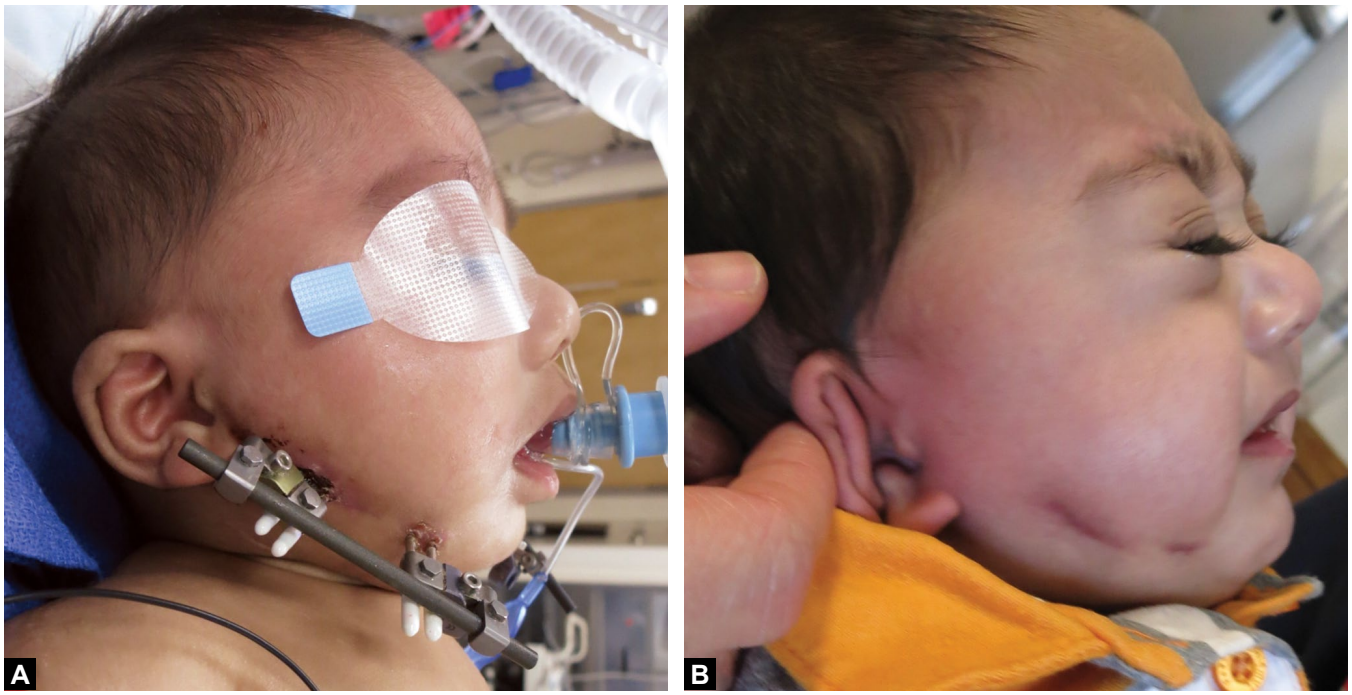
In cases with buried hardware, a more extensive operation is necessary. This takes place under general anesthesia. After the child is intubated, prepped, and draped the prior submandibular incision is used for access. The hardware is usually easily identified within an inflammatory capsule; however, the size of the hardware is now much larger following linear advancement. With careful traction, the anterior footplates may be exposed and the monocortical screws removed. Access to the posterior footplate must be undertaken with caution as the main trunk of the facial nerve is relatively lateral due to the underdeveloped neonatal mastoid tip. Once the hardware has been removed, the wound is irrigated and closed. A drain may be left in place. A similar procedure is performed on the opposite side and the child is usually admitted overnight and discharged the following day after removal of the drain.

## COMMON PITFALLS

- Obtain a computed tomography scan of the facial bones to confirm the presence of mandibular condyles in dysmorphic infants with PRS. In syndromic children with primary growth disturbances of the mandible,




**Figs. 95.15A and B:** Expected regression during the consolidation phase. (A) Mandibular profile at beginning of consolidation. (B) Profile following 6 week consolidation phase. Note the light-weight graphite consolidation rods in place.




**Figs. 95.16A and B:** Hardware removal and early scarring. (A) The k-wires and consolidation rods are removed as a 5-minute day surgery with a laryngeal mask airway in place. (B) Puckering and hyperpigmentation 2 weeks after removal of k-wires.

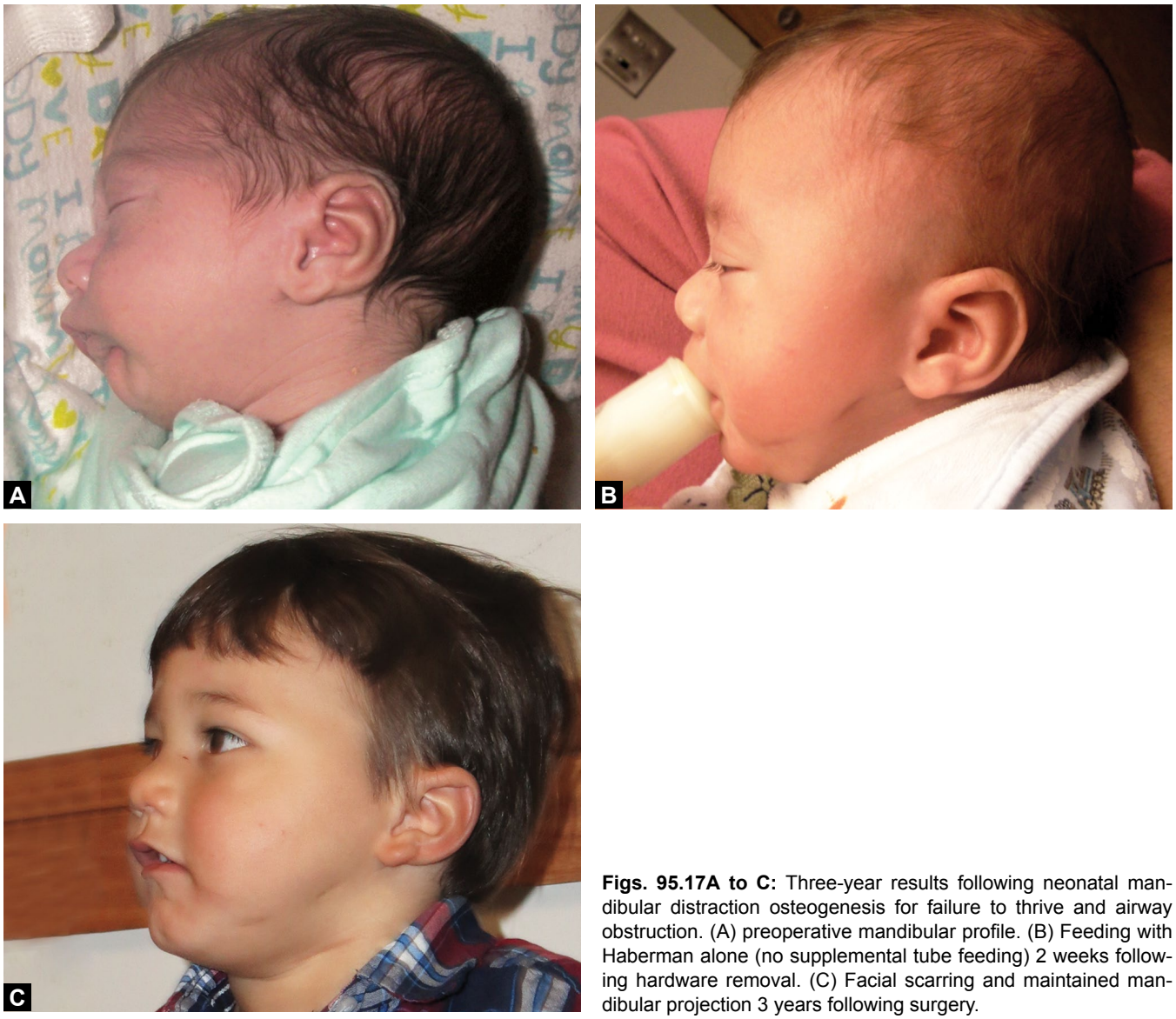
such as those with oculoauriculovertebral, Treacher Collins, or Nager syndrome, for example, there is an underlying disturbance in the growth center below the mandibular condyle, which may limit, if not prevent, growth of the jaw, even after a "head start" offered by early mandibular distraction. In addition, children

with absent mandibular condyles, absent coronoid process, and a poorly defined glenoid fossa (Pruzansky grade III)[10] are not ideally suited for early distraction (Fig. 95.7).[25] In these infants, the posterior mandibular segment may not engage properly against the skull base, allowing seemingly infinite posterior movement into the soft tissue of the mastoid area, thus preventing effective anterior advancement of the mandible with distraction of the mobile segments. The author choses to treat this subset of children with up-front tracheotomy followed by costal cartilage grafting and creation of a pseudarthrosis at the temporomandibular joint site later in childhood. Following these procedures, the jaw is advanced through distraction of the grafted rib segment if necessary.

- Confer with the neonatologist and geneticist prior to moving forward with mandibular distraction to assure that you are operating on a neurologically normal child. There is no sense putting a child through neonatal MDO if that baby will ultimately require a tracheostomy for aspiration and a feeding tube for dysphagia related to underlying neurological compromise. Several studies have sought to identify preoperative characteristics in infants with PRS that could be used to predict which patients will fail procedures other than tracheotomy. Two studies in 2011 described factors that were predictive of poor airway outcomes following TLA and MDO with eventual need for salvage tracheotomy:
  - Rogers and colleagues[5] developed the GILLS (gastroesophageal reflux, intubation preoperatively, late operation (older than age 2 weeks), low birth weight (<2,500 g), and syndromic diagnosis) score, which can be used to identify those patients with PRS who have a high likelihood of failing TLA. The acronym GILLS was created to serve as a 5-point scale, with GILLS scores of 3 or more suggestive of a failure rate above 40%.
  - A smaller study involving long-term follow-up of children with PRS who underwent early MDO (younger than 3 months) showed a trend toward poor outcomes (need for eventual tracheotomy and/or gastrostomy, among other unfavorable results) in syndromic PRS infants who also had neurologic impairment such as seizures, hypotonia, and chronic aspiration.[23]
  - The overarching theme of both of these studies suggests that nonsyndromic PRS children tend to have favorable airway outcomes following TLA or MDO, and that certain syndromic children without neurocognitive comorbidities (e.g. Stickler's syndrome) fare equally as well as their nonsyndromic peers.[4,5,23]
  - Many investigators have noted that children with PRS who are also neurologically impaired are at risk for airway compromise from factors that are independent of their glossoptosis.[4,5,23,34–36] For this reason, addressing tongue-base obstruction with glossopexy or distraction alone in this subset of patients with syndromic PRS is not appropriate, as these surgical interventions do not treat coexisting hypotonia, poor coordination, or chronic aspiration. For children with these comorbidities, tracheotomy and gastrostomy-tube placement allows for bypass of any and all sites of upper airway obstruction, improved pulmonary toilet, and maintenance of enteral nutrition. Treating neurologically impaired children with TLA or MDO incurs additional costs and avoidable surgical risks related to such operative interventions.
- Communication and collaboration between the pediatric anesthesia team and the otolaryngologist is essential. Obtaining vascular access and safely maintaining an optimal plane of anesthesia with spontaneous ventilation may prove challenging in a neonate with chronic airway obstruction. It is the author's opinion that a pediatric otolaryngologist should assume complete responsibility for the airway until successful endotracheal intubation has been confirmed.
- Assure adequate bone stock posteriorly prior to performing outer corticotomy as the ramus is awfully thin in neonates. If the wires or screws are not secure enough posteriorly, the distraction procedure will not work.
- Postoperatively, a size 1 LMA and nasal trumpets should be left at the bedside. If the baby self-extubates, reintubation in the setting of postoperative edema and a 3 piece mandible will be challenging. An LMA or nasal trumpet can be inserted until the otolaryngology team arrives. If reintubation is necessary, the author would recommend a nasal fiberoptic approach to minimize manipulation of the mandible.

## OUTCOMES

Multiple series have been published identifying the short-term and long-term complications of MDO in general. Overall, long-term outcomes of *neonatal* mandibular distraction are still in evolution; however, a 2011 study of




**Figs. 95.17A to C:** Three-year results following neonatal mandibular distraction osteogenesis for failure to thrive and airway obstruction. (A) preoperative mandibular profile. (B) Feeding with Haberman alone (no supplemental tube feeding) 2 weeks following hardware removal. (C) Facial scarring and maintained mandibular projection 3 years following surgery.

19 children who underwent neonatal mandibular distraction had an average length of follow-up of 5.6 years and suggested that this procedure allows for a sustained correction of airway and feeding difficulties that persists into early childhood (Figs. 95.17A to C).[23]

With potential long-term complications related to tooth malformation and mild malocclusion, the importance of multidisciplinary craniofacial follow-up after MDO is clear. All children with PRS require regular follow-up with pediatric dentistry, orthodontics, and oral surgery regardless of any history of surgical intervention, and children undergoing early mandibular distraction are no exception. The purpose of the MDO procedure is to avoid a tracheotomy and a feeding gastrostomy tube. Additional benefits, such as improved occlusion and mandibular profile, are only secondary goals of MDO. The primary aim of neonatal MDO is to ameliorate breathing and feeding difficulty in the neonatal period. Therefore, subsequent use of orthodontic appliances and secondary esthetic procedures such as sliding genioplasty may still be indicated in adolescence in these children.

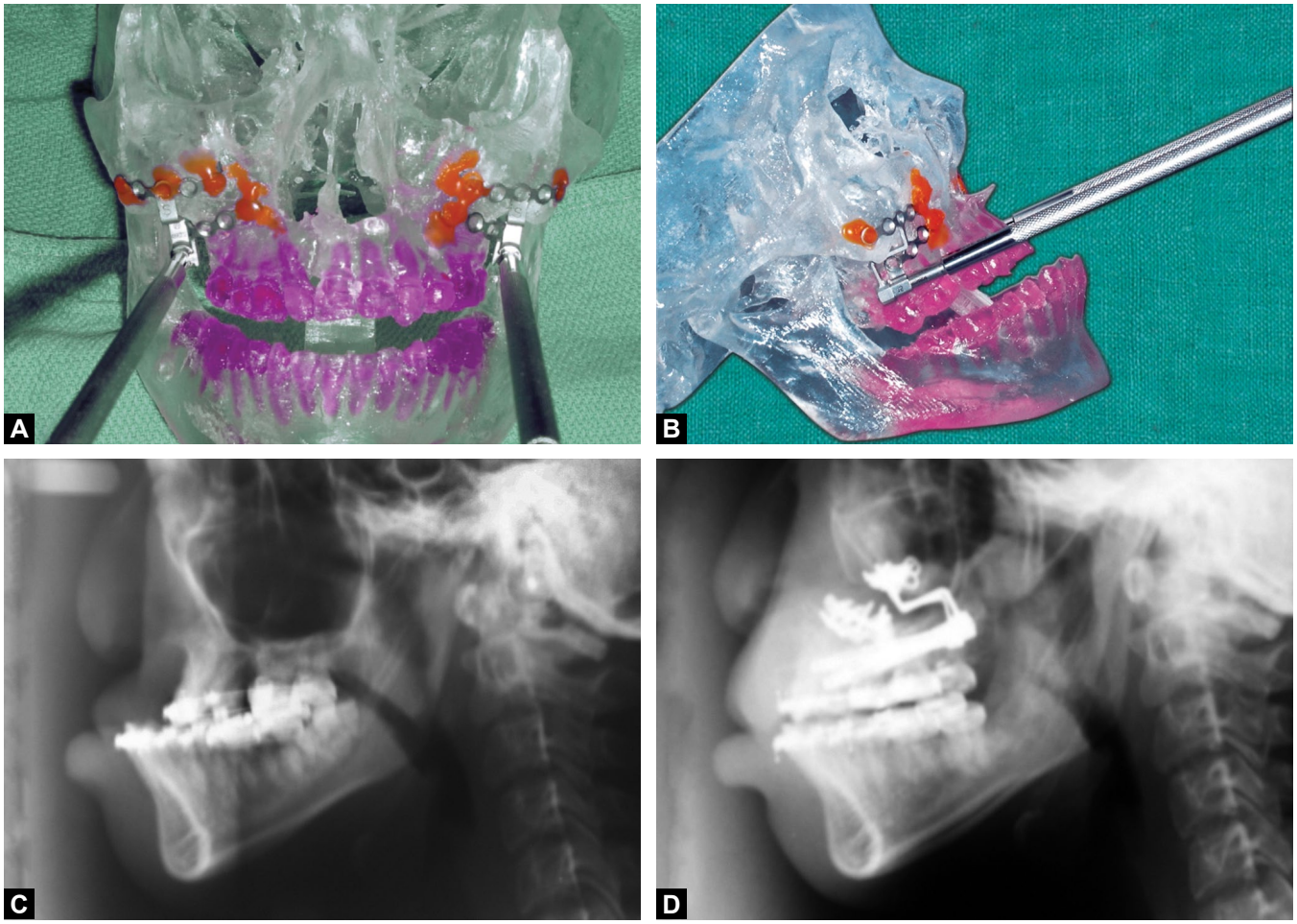
Short-term outcomes following early MDO have been more clearly delineated. Evidence supporting this intervention remains modest, however, with literature supporting early MDO limited to case series. Nevertheless, the benefits of early MDO on feeding and breathing are clear; most newborns who have previously undergone tracheotomy are able to be decannulated after MDO, with most babies avoiding tracheotomy altogether when MDO is used as a primary intervention. Benefits on feeding are

also clear, with early MDO allowing for early removal of gastrostomy tube or avoidance of surgical gastrostomy altogether, especially in those infants with isolated PRS.[24] The benefits of early MDO on feeding are especially meaningful, as this outcome is what distinguishes MDO from other surgical airway interventions for PRS, such as TLA and tracheotomy.[37,38] In a select patient population, TLA allows for avoidance of tracheotomy at a rate similar to that of MDO when TLA is performed by an experienced surgeon. However, the g-tube rate following TLA approaches 50% in this population, whereas the g-tube rate following neonatal MDO is closer to 5%.[5,23]

## MAXILLARY DISTRACTION

Congential and acquired maxillary hypoplasia manifest as a class III skeletal relationship with the mandible (underbite) with or without midface hypoplasia. Surgical correction of maxillary hypoplasia is usually deferred until the eruption of permanent dentition, when malocclusion becomes apparent. Because of concerns regarding interference with midface growth, the LeFort 1 procedure is typically deferred until the completion of facial growth, early or late in adolescence. Maxillary advancement is prone to problems with regression in the postoperative period, owing in part to limitations in stretching the overlying soft tissue envelope. This is especially problematic for children who have undergone prior cleft palate repair, as the vertical scar band in the palatal soft tissue opposes the vector of anterior maxillary advancement.

In cases of severe maxillary hypoplasia, midface distraction osteogenesis may be considered (Figs. 95.18A to D). In this technique, osteotomies are made at the optimal LeFort level following placement of pins or plates on either side of the planned bone cuts. After a brief latency




**Figs. 95.18A to D:** An example of maxillary distraction osteogenesis in a teenager with a history of cleft palate. (A) and (B): Medical model used for planning hardware placement and vector selection. (C) Preoperative occlusal relationship. (D) Occlusal relationship at the end of the activation phase.
*Courtesy*: Daniel E Sampson, DMD, Minneapolis, MN.

period, the anterior hardware is pulled forward with wires or pushed forward with buried devices at a pace of approximately 1 mm per day. This allows for maxillary advancement with concomitant expansion of the overlying soft tissues over the duration of the distraction period. With this technique, larger mandibular/maxillary discrepancies may be overcome.[39] Midface distraction osteogenesis is prone to relapse during the consolidation phase for the same reasons as traditional orthognathic surgery. However, unlike standard maxillary advancement, the distracted maxilla can be overcorrected to accommodate for this anticipated relapse during consolidation.[40] An additional concern of any form of maxillary advancement in children with cleft palate is unwanted expansion of the retropalatal space leading to postoperative velopharyngeal insufficiency.[41]

## LEVEL OF EVIDENCE

Virtually all of the literature supporting early MDO is retrospective and most studies are case studies and single-center findings. There is little evidence beyond expert opinion and single-center evaluation regarding diagnosis, treatment, and long-term outcomes of neonates with PRS.[42] Because of the relative rarity of PRS and the multiple variables that factor into the clinical decision to move forward with mandibular distraction (regional variations in the management of PRS, surgeon and parental influences on choice of intervention), it will be difficult to improve upon the existing level 4 evidence. A coordinated multicenter study with a standardized diagnostic and treatment algorithm has been recommended to develop evidence for the diagnosis and treatment of neonates with PRS.[42]

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CHAPTER

# Contemporary Workup of the Air-Bone Gap in the Pediatric Patient

96

*Yin Ren, Elliott D Kozin, Daniel J Lee*

## OVERVIEW

Similar to the assessment of the adult patient with a conductive hearing loss (CHL), evaluation of the pediatric otologic patient should proceed in a systematic fashion. Key steps to make an accurate diagnosis are a thorough history and physical examination, including a full head and neck examination. Special emphasis should be placed on understanding the child's birth history and developmental milestones. Office-based hearing tests, such as fork examinations, may provide initial information on the type of hearing loss in older children; however, a formal audiologic evaluation remains the cornerstone of diagnosis and provides pivotal information regarding the degree and quality of hearing loss. Once a preliminary differential diagnosis is established, additional studies such as imaging tests will help to solidify a diagnosis and guide the otologist to the proper treatment modality. In this chapter, we describe the contemporary evaluation and workup of CHL in the pediatric population.

## DIAGNOSTIC TOOLS

### History

Hearing loss is a frequent complaint in the pediatric population. A thorough history is the first and crucial step of the otologic workup. The process of history taking will provide an opportunity to observe the general health and behaviors of the child and to establish rapport with the patient and family. Similar to the history of adult patients, standard questions include onset, duration, quality, and severity of hearing loss, as well as any associated history of otalgia, otorrhea, tinnitus, vestibular complaints, or noise exposure. Past medical and surgical history, medications, allergies, and review of systems should be sought. A careful birth history that focuses on risk factors such as low birth weight, prematurity, neonatal jaundice, admission to a neonatal intensive care unit, and maternal illnesses during pregnancy, including infection, diabetes, or illicit substance use, should be reviewed. A family history of hearing loss, ossicular abnormalities, and other congenital syndromes should be documented. One should also consider the child's developmental history, including major motor milestones, speech development including age of first word, vocabulary, and comprehension.

Even though parents and family members are usually involved in the care of the pediatric patient and will provide much of the history, one should also attempt to direct questions to the child, if age appropriate, as the history may vary. Keep in mind that the child may be too young to recognize chronic or abnormal otologic symptoms. Medical records from pediatricians and geneticists may provide important ancillary information. Nevertheless, it is the ultimate duty of the otologist to synthesize information from different sources to make an accurate diagnosis.

### Physical Examination

A complete head and neck examination should be conducted as a part of the initial evaluation. Most components of the examination should not cause discomfort; nevertheless, it should be performed in a calm and reassuring manner to further build rapport between the otologist

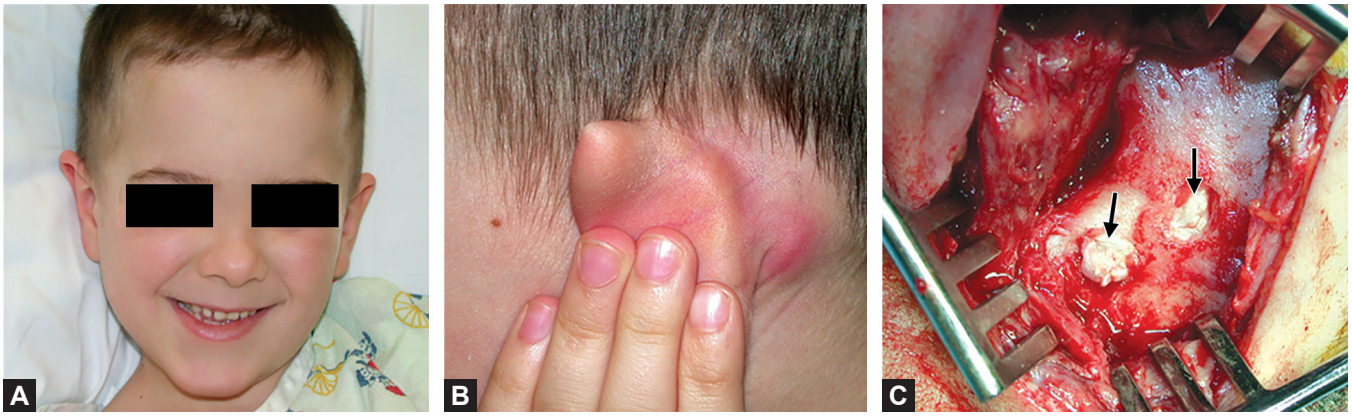
and the child. In particular to the evaluation of a CHL, the external ear, including the pinna and external auditory canal, should be examined for any evidence of congenital malformations, inflammation, edema, or debris. The mastoid area should be assessed for signs of erythema, tenderness, and swelling, as these may be the signs of mastoiditis in an otherwise well-appearing child (Figs. 96.1A to C). A thorough evaluation of the tympanic membrane (TM) should include assessment of its appearance, mobility, evidence of perforation, or middle ear effusion. While the otoscopic examination should not be painful, pneumatic otoscopy should be explained beforehand so the child will not be startled. Middle ear structures, such as ossicles or masses, should also be noted. Parents can play an active role by holding or distracting the child during either the examination or minor office procedures such as cerumen removal. Papoose boards or sedation is typically unnecessary, but may be indicated if the patient is unable to remain still or there is a chance of significant discomfort.

## Hearing Assessment

A number of tools are available to further assess auditory function in a child. Fork tests, such as the Rinne and Weber, are quick screening tests that may provide an initial indication of a conductive, sensorineural, or mixed hearing loss. The Rinne test compares air conduction (AC) to bone conduction (BC), and disease in the external or middle ear may produce a CHL, resulting in a negative Rinne (BC > AC) in cases with more than mild CHL. The Weber test localizes to the ear with a CHL or to the opposite ear if there is sensorineural hearing loss. However, both the Rinne and Weber tests require cooperation and active participation by the patient, which may be challenging in younger children.

Formal audiology testing remains the cornerstone of hearing assessment, and includes pure tone audiometry, speech audiometry, impedance audiometry, and electrophysiology testing. Pure tone audiometry measures the lowest dB threshold at which a sound at a given frequency can be detected by the child 50% of the time, plotted as hearing threshold as a function of frequency. If a child can participate in verbal communication, speech audiometry can be performed to measure the speech threshold and word discrimination score. Otherwise, hearing in children as young as 6 months of age may be assessed with visual reinforcement audiometry, where verbal cues are replaced with visual rewards based on specific behavioral responses.

In children with developmental delay, tuning fork testing and behavioral audiometry may be difficult to perform as they require subjective assessment by the patient. Objective studies, such as impedance testing, auditory brainstem responses (ABR), otoacoustic emissions (OAE), and acoustic reflexes, are excellent methods of hearing assessment that do not require cooperation from the child. Impedance tympanometry is a useful complementary tool to otoscopy for evaluating middle ear effusions




**Figs. 96.1A to C:** Four-year-old male patient with left otalgia and a CHL. (A) The child was nontoxic-appearing afebrile with a nonproptotic ear but had a bulging and intact TM on otoscopy without evidence of a retraction pocket (not shown). Preoperative audiogram demonstrated a maximum CHL with type B tympanometry (not shown). (B) Examination of the postauricular and mastoid area reveals focal erythema, fluctuance, and tenderness to palpation, suggesting acute mastoiditis. Imaging suggested complete opacification of the middle ear with mastoid coalescence and erosion of the incus and stapes (not shown). He underwent an uneventful canal wall down mastoidectomy and was found to have an extensive congenital cholesteatoma erupting from the mastoid cortex. (C) Black arrows point to cholesteatoma.

and thereby indirectly assessing the function of the Eustachian tube. Impedance tympanometry also measures middle ear pressure, TM mobility, and continuity and mobility of the ossicles. An ABR consists of a series of electrical potentials recorded from the scalp of a child under sedation as the auditory stimulus travels via the auditory nerve to the brainstem. A change from the potential's characteristic waveform may be indicative of abnormalities in the middle ear, cochlea, auditory nerve, or brainstem nucleus.[1] Otoacoustic emissions, a noninvasive test commonly performed in newborn hearing screening, measures acoustic emissions generated from the cochlea and are indicators of the health of outer hair cells.[1] Compared to ABR, OAE has the advantage of providing cochlea-specific information over a broad frequency range without the need for patient sedation. However, middle ear dysfunction, such as an effusion, can confound the results of OAE testing. Therefore, a negative OAE should be followed by tympanometry testing to assess the integrity of the middle ear. Finally, the acoustic reflex measures sound-evoked contraction of the stapedius muscle mediated by the facial nerve and, although in the past was helpful in evaluating retrocochlear pathology,[2] is now used primarily to assess the mobility of the ossicular chain.

## Imaging

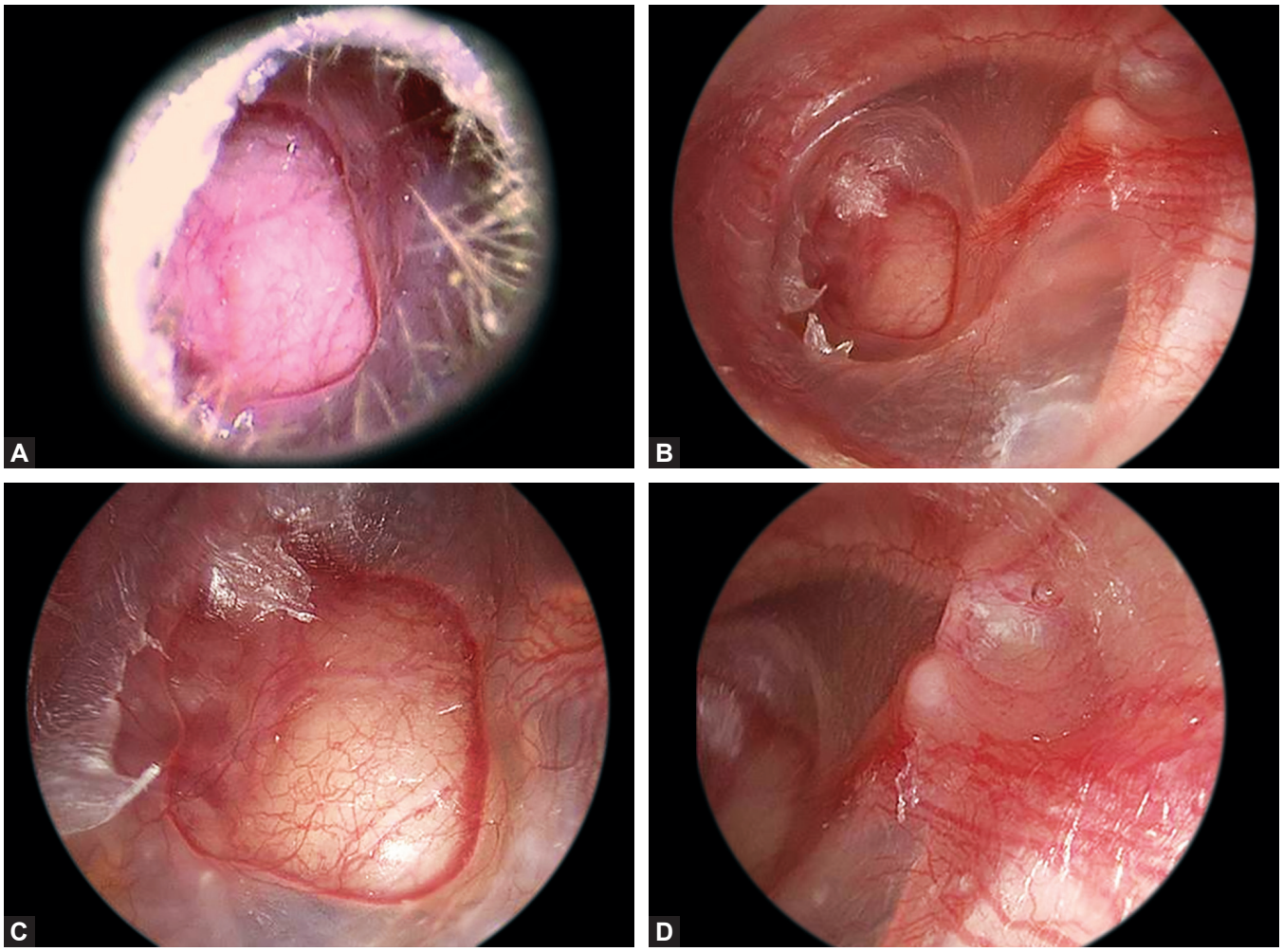
The two major forms of imaging in the evaluation of pediatric patients with CHL are computed tomography (CT) and magnetic resonance imaging (MRI). Computed tomography scanning uses ionizing radiation to generate images of tissue cross-sections based on differences in attenuation. Specialized acquisition techniques such as multislice scanning and cone-beam CT have been developed to minimize radiation dose while maintain adequate resolution.[3] At our institution, temporal bone CT imaging is performed that generally spares the orbits. High-resolution temporal bone CT scans should be acquired at < 1 mm thin sections in order to provide enough detail to assess for subtle findings of the middle and inner ears. Either direct coronal imaging or multiplane reformations are invaluable in detecting pathologies in the tegmen, cochleae, semicircular canals, and the skull base. While CT provides excellent evaluation of bony anatomy, MRI is widely used in the pediatric population as it does not involve ionizing radiation and provides excellent soft tissue detail. Heavily T2-weighted sequences such as constructive interference in the steady state and 3-T fast imaging employing steady-state acquisition are crucial to provide information on the anatomy of the fluid-filled inner ear. Oblique sagittal MRI is excellent at visualizing the cranial nerves within the internal auditory canal and detecting lesions at the cerebellopontine angle. As such, MRI is often employed to rule out CNS causes of sensorineural hearing loss with normal CT scans (especially in children with profound deafness and no detectable auditory thresholds to rule out auditory nerve hypoplasia or aplasia).

## Rigid Endoscopy of the Ear

Operative endoscopy for the ear was first performed over 20 years ago in exploratory surgery of the mastoid cavity, and is currently employed as an adjunct technique in the surgical management of cholesteatomas[4] and operations in the petrous apex.[5] Compared to the binocular microscope and ear speculum, endoscopy provides a wider field of view and enables superior visualization of the anatomy and potential pathology of the tympanic cavity in its entirety (Figs. 96.2A to D).[6,7] The small diameter of the endoscope (3 mm) allows one to examine ear canals that are narrow, such as in children with Down's syndrome or OE, as well as ear canals that are obstructed, such as in children with a prominent anterior canal wall bony overhang. The endoscope can also be readily converted into a hand-held portable diagnostic device for ear screening in resource-limited or emergency settings (Figs. 96.3A and B). Despite these advantages, the endoscope is yet to be widely adapted as a diagnostic tool for routine use in the office setting. The otomicroscope, unlike the endoscope, provides the otologist the freedom of bimanual manipulation of the ear for procedures such as cerumen disimpaction and retrieval of foreign bodies. Therefore, the endoscope and the otomicroscope may be considered as complementary diagnostic modalities for evaluating and treating ear problems in children.

# DIAGNOSTIC WORKUP

Conductive hearing loss is typically caused by an abnormality of the TM, middle ear space, or the ossicular chain. Conditions that lead to CHL include infections of the outer or middle ear, TM perforation, Eustachian tube dysfunction (ETD), middle ear effusions, ossicular abnormalities, and inner ear pathologies such as large vestibular aqueduct syndrome (LVAS) or superior canal dehiscence (SCD). Conductive hearing loss can be either



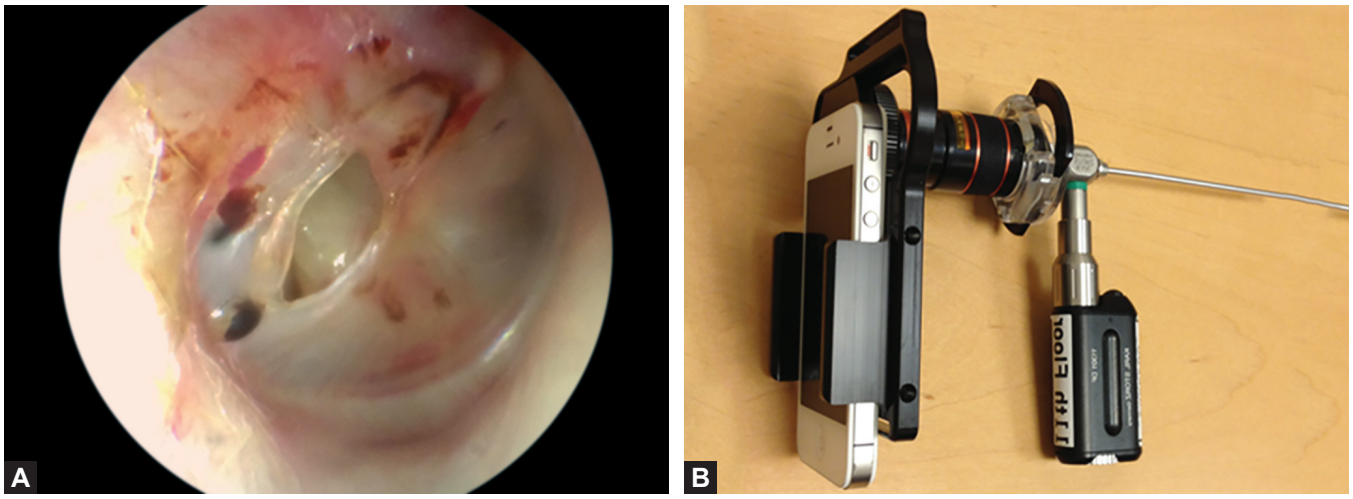

**Figs. 96.2A to D:** Six-year-old female patient with a history of chronic OM, tympanostomy tube placement in the past, and a mild left ear air-bone gap in the low to mid frequencies. (A) Digital image taken with 4-mm aural speculum under binocular microscopy with an HD camera showing a limited view of a deep TM retraction to the promontory of the cochlea. (B) Digital image captured with a 0°, 3-mm-diameter, 14-cm-long rigid endoscope paired with an HD camera reveals a wide angle view of the entire TM and the precise extent of the central retraction down to the promontory, with global dimeric changes evident. (C) Close-up endoscopic views of the primary retraction. (D) Close-up endoscopic view of a shallow attic retraction. The patient underwent uneventful cartilage graft tympanoplasty and T tube placement to address this disease process.

congenital or acquired. Although the majority of children with CHL do not have abnormal findings on physical examination, the otologist should assess the general appearance while paying special attention to other features of the head and neck examination that might be demonstrative of syndrome-associated features. Further, since up to 50% of children with severe to profound hearing loss have ocular pathologies, an ophthalmologic examination may be warranted if clinical suspicion is high.[8] In most scenarios, the child should be formally evaluated with an audiogram to characterize the degree of hearing loss, and subsequent imaging, laboratory, or genetic studies will be conducted based on audiogram findings.

## Evaluation of a Child with an Air-Bone Gap

A child with an AC threshold higher than BC threshold (air-bone gap) on audiogram has CHL. The initial diagnostic approach to CHL includes a basic otoscopic examination, impedance tympanometry, and acoustic reflex testing (Figs. 96.4A to D).

The majority of otologic conditions that result in CHL can be diagnosed with otoscopy alone. These include otitis media with effusion (OME), retraction pocket of the TM secondary to ETD, or progression of retraction with contact to and erosion of ossicles (Fig. 96.4A). Otitis media with effusion is the most common cause of acquired



**Figs. 96.3A and B:** Examination findings in a patient with a traumatic TM perforation and CHL of the right ear associated with the Boston Marathon bombing on April 15, 2013. (A) Digital image acquired using a camera application on a smartphone and a 0°, 2.7-mm, 10-cm Storz Hopkins II rigid endoscope revealing a central posterior TM perforation. Endoscopy allows for a more accurate assessment of perforation size and location than binocular microscopy as the entire TM can be seen in a single view without the anterior overhang obscuring the anterior sulcus. (B) Photograph showing the hand-held rigid endoscope adapter (Summit Medical, St. Paul, MN) with an encrypted, hospital-approved smartphone mounted.

CHL in children. Up to 60% of children in the first year of life may have asymptomatic OME and up to 30% of 3- to 6-year-old children suffer from effusions.[9] On otoscopic examination, the TM usually appears mildly inflamed, the handle and short process of the malleus are brought into relief due to TM retraction, and the TM may appear yellow or white due to the presence of effusion. The presence of effusion is readily confirmed by the lack of TM movement upon insufflation. When properly performed, pneumatic otoscopy has a high sensitivity of 94% and a specificity of 80% in diagnosing middle ear effusions.[10]

In the setting of chronic ear disease, pathologies that affect the ossicular chain may manifest as CHL that range from mild at the early stage to near-complete if left untreated and ossicular erosion occurs. Progression of a retraction pocket in the attic or posterosuperior quadrant of the TM may contact the ossicles and result in myringoincudopexy or myringoincudostapediopexy with or without bony erosion. Tympanosclerosis, characterized by deposition of calcium phosphate plaques within the TM in children with a history of OM, can lead to a CHL and in more advanced cases, ossicular fixation. A diagnosis can be made by visualizing ossicular defects on otomicroscopic examination. High-resolution temporal bone CT scan can help confirm the extent of disease affecting the middle ear structures, even if the bony defect is small.

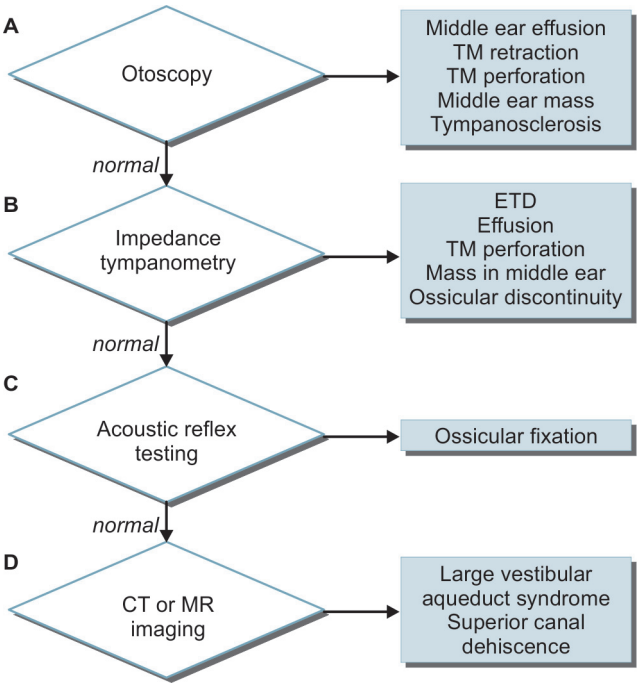
If no abnormalities are identified on otoscopy, additional workup including impedance tympanometry, acoustic stapedius reflex testing, and OAE are indicated to either confirm the presence of effusion or rule out OME in favor of other etiologies (Figs. 96.4B and C). A normal (type A) tympanogram has a sensitivity and specificity between 90% and 95% and can effectively rule out the presence of middle ear effusion. A normal acoustic stapedial reflex requires normal impedance in the middle ear; the presence of profound CHL will demonstrate an abnormal acoustic reflex. Similarly, OAE is another method that provides a highly sensitive measure of middle ear impedance; emissions from the cochlea require retrograde transmission of acoustic energy across an intact ossicular chain, middle ear, and TM to be detected. Therefore, if a child with a normal tympanogram has absent acoustic reflexes or OAE, the hearing defect may be secondary to a congenital anomaly of the ossicular chain. The most common of these congenital anomalies is fixation of the stapes, as well as fixation of the malleus, abnormality in the incus, or fixation of the incudomalleolar joint. While congenital anomalies are typically associated with external ear deformities, they can be difficult to assess in the awake patient. Diagnosis can be confirmed by either direct palpation under anesthesia or via exploratory tympanotomy.

A negative (type C) tympanogram is suggestive of a retracted TM secondary to ETD with a sensitivity approaching 95%. Two forms of ETD exist: either ET opening is impaired due to functional and mechanical obstruction, or ET is overly compliant and allows the reflux of nasopharyngeal contents into the middle ear space.

An abnormal flat (type B) tympanogram indicates an immobile eardrum, which can be a result of effusion or TM perforation. Most patients with a history of chronic ear disease, an abnormal tympanogram, and absent reflexes should also be examined for the presence of a middle ear mass, such as a cholesteatoma. High-resolution CT of the temporal bone can be helpful in identifying a soft tissue mass or the extent of bony erosion within the middle ear.

In a child with CHL but with normal otoscopy, impedance tympanometry, acoustic reflex testing, and otoacoustic emission, one should consider the "third window" phenomenon from etiologies such as LVAS and SCD (Fig. 96.4D). A large vestibular aqueduct has been theorized to shunt acoustic energy away from the cochlea and increases the AC threshold.[11] At the same time, there is a decrease in BC threshold due to increased impedance within the cochlear partition[11] (Fig. 96.5). Similarly, SCD is also felt to act as a third mobile window (in addition to the oval and round windows) for acoustic energy to dissipate, thereby elevating the threshold for air-conducted sounds and reducing the threshold of BC (Fig. 96.6). Although encephalocele and meningoencephalocele of the temporal bone have been associated with SCD and CHL in adults, such phenomena are rare in children.[12,13]

In summary, a diverse set of outer, middle, and inner pathologies may be associated with an air–bone gap on audiometry. A thorough, systematic investigation utilizing not only otoscopic examination but also ancillary testing is often indicated. Consideration of both infectious and structural etiologies (especially inner ear abnormalities in the setting of a normal examination and impedance testing) underlying CHL is merited to avoid unnecessary tympanostomy tube placement and negative middle ear explorations.[14]




**Figs. 96.4A to D:** Decision tree to guide the evaluation of the air-bone gap in the pediatric patient. (A) Otoscopy can diagnose the most common conditions involving the TM and middle ear associated with CHL. (B) Impedance tympanometry is useful when the examination is normal. Abnormal tympanometry can result from ETD, a middle ear effusion, or middle ear mass. (C) If both otoscopy and tympanometry are normal, acoustic reflexes can be assayed to measure the activity of the stapedius muscle. An absent acoustically evoked stapedial reflex suggests an ossicular abnormality, such as congenital fixation of stapes or malleus fixation. (D) If a malformed ossicular chain is suspected or if the examination and impedance testing are normal, then noncontrast temporal bone imaging should be performed to rule out an ossicular anomaly (CT) or a "third window" due to an enlarged vestibular aqueduct (CT or MR) or SCD (CT). Proper evaluation of an air-bone gap is essential to avoid unnecessary surgery, such as a myringotomy or middle ear exploration in a child with an otherwise normal examination and testing. A child with an air-bone gap and a SCD should undergo *cervical vestibular evoked myogenic potential (cVEMP)* testing if he or she is old enough if surgery is being considered to repair the defect. cVEMP responses are generally of larger amplitude and lower threshold in symptomatic SCD ears and can help confirm that the bony defect is contributing to the child's symptomatology preoperatively.

## Evaluation of a Child with Congenital CHL

Congenital defects of the external ear may result in mild to severe CHL. For example, mild CHL can be seen in grade II microtia due to the stenosed external ear canal. Further, the total absence of the auricle and stenosis of the external ear canal is associated with moderate-to-severe CHL. Numerous craniofacial abnormalities are associated with ear canal atresias with or without microtias. These craniofacial abnormalities include chromosome 18 deletions, Crouzon syndrome, Pierre-Robin sequence, hemifacial microsomia (Goldenhar syndrome), and Treacher Collins syndrome.[15] Similarly, CHL can be observed in pediatric patients with congenital abnormalities of the ossicular chain or may be associated with external canal atresia, microtia, or as a part of a generalized condition such as osteogenesis imperfecta.[16] Finally, Pendred syndrome is

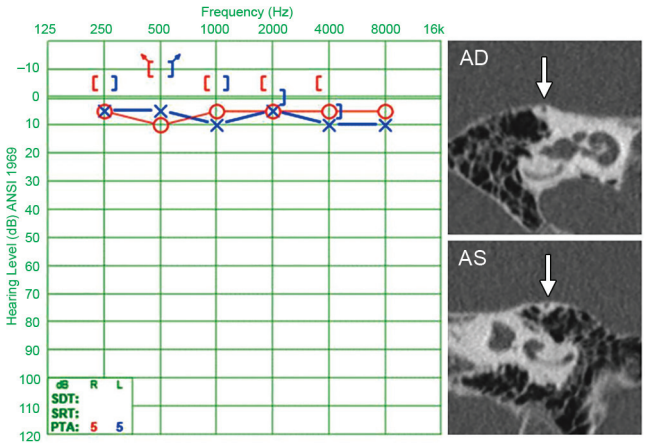



**Fig. 96.5:** Seven-year-old male with complaints of severe hyperacusis, aural fullness, and a bilateral CHL. He had normal otoscopy. Left: pure tone audiogram reveals bilateral low- to mid-frequency air-bone gaps, type A tympanometry, and present acoustic reflexes. Right: temporal bone CT, Stenver reconstruction, from the same patient. AD: right; AS: left. Arrows indicate very thin bone or a pinpoint defect of the arcuate eminence of the superior semicircular canal bilaterally.

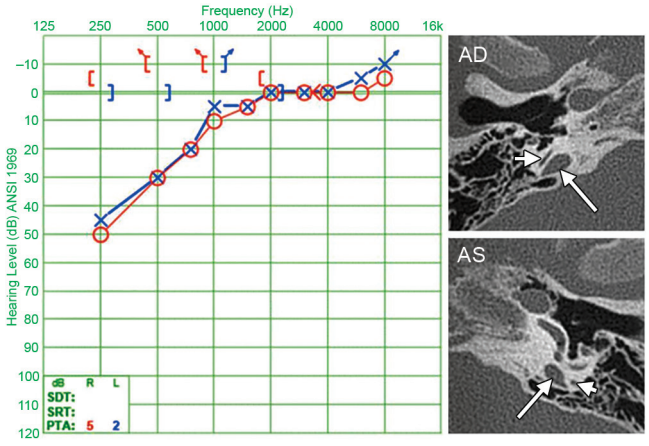



**Fig. 96.6:** Fourteen-year-old female with progressive hearing loss initially presented for consideration of tympanostomy tube placement. Left: pure tone audiogram revealed bilateral low-frequency air-bone gaps. She was found to have normal otoscopy, type A tympanometry, and intact acoustic reflexes in both ears. Right: axial CT scans from the same patient demonstrate a large vestibular aqueduct in both ears. AD: right; AS: left; Long arrow: Vestibular aqueduct; Short arrows: Posterior semicircular canal.

commonly associated with inner ear anomalies, such as enlargement of the vestibular aqueduct, and may lead to varying degrees of CHL.[17]

It is critical to identify and diagnose children with congenital defects associated with CHL early. If amplification is provided promptly and appropriately, these children have the potential for normal speech and language development.[18,19]

## Associated Symptoms

Although chronic hearing loss is typically painless, otalgia and otorrhea are complaints that can be associated with CHL in the acute setting. Therefore, the evaluation of pediatric patients who present with such symptoms should always include a hearing assessment. The evaluation of otalgia begins with a careful history and examination focusing on the characteristics of the pain. Keep in mind that a prelingual child may exhibit nonspecific symptoms, such as fussiness, irritability, and ear pulling.

The most common cause of otalgia that is also associated with possible hearing loss is acute otitis media (AOM) and otitis externa (OE). The underlying etiology of AOM is typically an upper respiratory infection that ascends via the Eustachian tube to the middle ear space. On examination, the TM can be bulging due to a suppurative infection and/or retracted due to mechanical obstruction of the ET. A child with AOM may have systemic signs, such as fever and tachycardia. If TM rupture occurs, bloody otorrhea may be seen in the ear canal. Symptoms of OE can vary from mild discomfort to severe pain that worsens with movement of the ear canal. Physical examination may reveal redness and tenderness in the external ear canal. Hearing loss may occur if the canal becomes significantly edematous. The most common organism associated with OE is *Pseudomonas aeruginosa*. Malignant otitis externa, characterized by extensive granulation tissue in the ear canal and involvement of the temporal bone, is an aggressive variant of OE that may occur in an immunocompromised host. Computed tomography imaging is indicated to delineate the extent of the infection and guide urgent surgical intervention.

Discharge from the ear is typically associated with an underlying infectious etiology, such as OE and chronic suppurative otitis media. Since these conditions can result in hearing loss if left untreated, prompt diagnosis and management is indicated. Diagnosis can be usually made with high certainty with otoscopic examination alone. In the absence of pain or other findings on physical examination, evaluation for the potential of cholesteatoma is usually warranted, including imaging workup by high-resolution CT. If a child has a history of trauma to the head and neck, fracture of the temporal bone, or surgery of the skull base, a cerebrospinal fluid (CSF) leak may present as otorrhea and can be diagnosed with imaging and laboratory studies testing for CSF.

## Speech Delay

One of the most important developmental milestones is the acquisition of language skills. Today, up to 15% of 2-year-old children have impairment in language development.[20] Speech delay can occur in isolation or in the setting of global developmental delay (such as autism spectrum disorders). It can be sequelae of singular medical, neurological, or genetic conditions and influenced by environmental and psychosocial risk factors.[21] While a majority of children with speech delay spontaneously "catch up" during preschool years, significant proportions remain as "late talkers". Once a child has been referred to the otolaryngologist, it is important to determine first whether the child has a disorder of language (impaired comprehension and/or use of language) or a disorder of speech (impaired articulation of sounds or fluency). All types of hearing loss, including a CHL, can potentially affect all aspects of speech articulation and fluency.

Age-appropriate language milestones can be used as a metric to determine the chronicity of the language delay. Signs that speech delay may be secondary to hearing impairment include difficulty with abstract words, difficulty with understanding or writing complex sentences, and inability to hear quiet speech sounds. If either unilateral or bilateral hearing impairment is identified, formal audiology evaluation should not be delayed so that interventions may be completed in a prompt fashion.[22] Significantly improved language and education development has been associated with early identification of hearing loss and early intervention.[19] Formal evaluations by a pediatric speech and language pathologist and a developmental psychologist are critical toward formulating a management plan.

## SUMMARY

Today, the pediatric otologist has an abundance of advanced diagnostic tools to call upon, including rigid endoscopy, specialized CT and MRI sequences, and genetic testing; however, the cornerstone of diagnosis remains to be history, physical examination and a comprehensive audiogram. One should keep in mind that the focus of the pediatric history differs slightly from that of the adult patient. Much of the history in the pediatric setting will derive from caregivers and medical specialists. New diagnostic approaches for CHL, including rigid endoscopy of the external ear, have tremendous potential, but it may still be necessary to perform a basic otologic examination or debridement under anesthesia in select pediatric patients to ensure comfort and safety. It is ultimately the responsibility of the otologist to synthesize information from a host of different sources to make determine the type and degree of hearing loss as well as the underlying pathology.

## KEY POINTS

- A thorough history and physical examination are integral first steps of the pediatric otologic evaluation.
- Specific elements of the pediatric otologic history include history of chronic ear infections, family history of hearing loss, complications during pregnancy, birth and vaccination history, as well as documentation of key developmental milestones.
- A comprehensive audiogram or, in the case of infants, ABR or OAE provide critical information on the type and degree of hearing loss and to pinpoint the site of the lesion in the external, middle, or inner ear, and will suggest retrocochlear pathologies if present.
- The rigid endoscope is being used increasingly in the pediatric otology clinic as a diagnostic tool, especially in cases of a small external auditory canal.
- Otologic examination under sedation may be necessary for select patient populations unable to undergo an office-based examination.
- In a pediatric patient with air-bone gap but normal otoscopy, tympanometry, otoacoustic emission, and acoustic stapedial reflex, further workup such as imaging is indicated to rule out pathologies in the inner ear such as LVAS or SCD.
- Modern imaging modalities that include high-resolution temporal bone CT and 3-T MRI with reformats are tools to better assess more complex middle and inner ear abnormalities not evident from the physical examination.

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