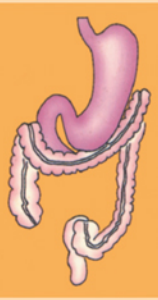
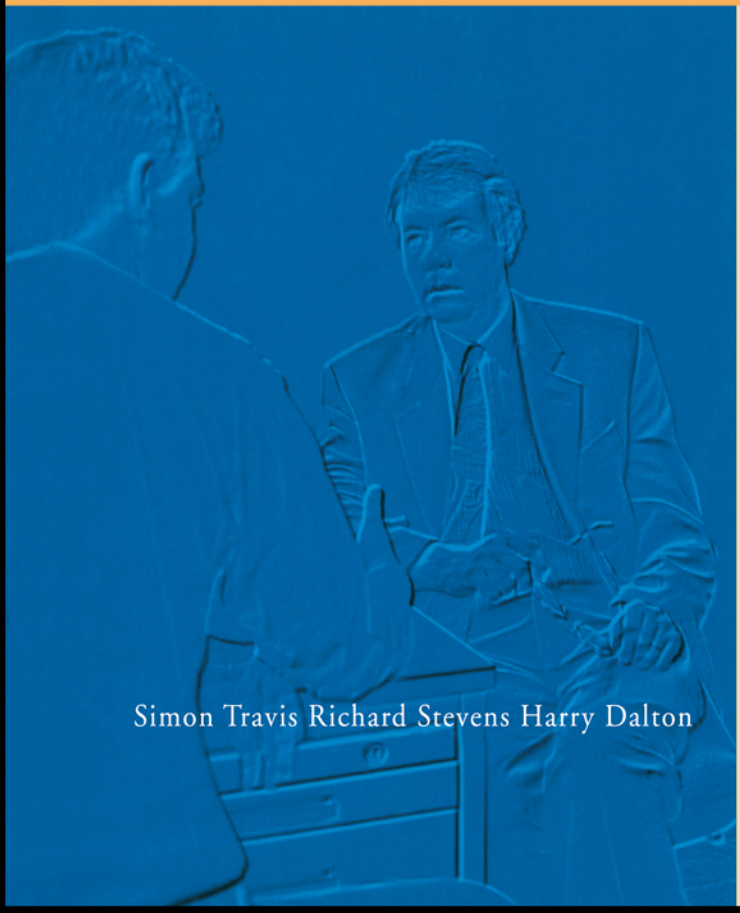
Shared Care in Gastroenterology

Family practitioners and hospital specialists working together to improve patient care





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Preface

This book is largely for family doctors but it is hoped that gastroenterologists will also want to read it, when considering how to improve the continuity of care for their patients. Its purpose is to act as a starting point for discussion between doctors in primary and specialist care about the recognition, follow-up and continuing management of patients with chronic gastrointestinal disorders. As such, it presents management options rather than prescriptive protocols, although in areas where data from controlled trials are sparse these options no doubt reflect the prejudice, practice and preference of the authors! We recognize that circumstances and opinions differ, so we will be content to have stimulated discussion even if this has arisen out of disagreement. In the introduction to the first chapter, we use a maritime analogy to construe the role of the gastroenterologist as navigator during the management of chronic disease, at hand for a light touch on the tiller when necessary. We hope this concept encapsulates the complementary nature of primary and specialist care, which are too readily divided either by organizational reforms or by neglect of the need to make shared care succeed.

We would particularly like to acknowledge the contribution of Professor Roger Jones to the whole study of gastrointestinal disease in primary care and its relationship to specialist practice. We are also grateful to the people who have helped us, especially Julian Grover and the team of Isis Medical Media Limited, Miss Jane Youle and the many clinical colleagues who have acted—often unawares—as sounding boards for our opinions. Above all, our thanks go to our families for their tolerance, forbearance and support.

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Chapter 1
Principles of sharing care in gastroenterology

Diseases of the gut, liver and pancreas are common. Some abdominal symptoms are so frequently experienced that they are regarded as normal, whereas similar symptoms can also represent serious disease. The challenge for all doctors in primary and specialist care is to sift the symptom pattern and manage each patient appropriately. The aim of this book is to suggest appropriate ways of using investigations, specialist clinics and drugs (or 'resources' in the current jargon) for patients with gastroenterological conditions in both primary and specialist care. The authors present the options that they consider to represent best management for common disorders, but are conscious that opinions and circumstances differ. Consequently these options (as opposed to rigid 'protocols') may simply act as a starting point for dialogue between doctors in primary care and specialist gastroenterology. To use a maritime analogy, for many gastroenterological disorders the specialist should be at hand for a light touch on the tiller, rather than acting as captain, first officer and bosun rolled into one. Indeed, the specialist's main role is often as a navigator, trying to plot the best course in the management of chronic relapsing disorders.

Historical perspective

The traditional general practitioner/specialist referral system central to British medical care occurred by accident rather than design. In the mid-19th century, increasing competition for patients between physicians (consultants) and apothecaries (family doctors) came to a head. Philanthropic endowment led to a rapid growth in the number of hospitals staffed by physicians who, in urban areas with outpatient departments, took patients away from apothecaries. However, in return for their hospital role, physicians conceded the principle of hospital referral by the general practitioner or family doctor, who thereby determined the patient's access to hospital and retained control of the patient's care. The introduction of the National Health Service (NHS) in 1948 endorsed the current distinction between the hospital role of the physician and the community role of the family doctor. The fundamental principle is that the responsibility for coordinating the care of the patient rests with the family doctor. The patient is returned to the care of the family doctor following specialist advice or treatment. This has the considerable advantage that a single medical record, held by the family doctor, contains all medical events relating to a patient including hospital treatment; however, it also restricts access to specialist care.

By contrast, in North America and some parts of Europe, the distinction between family doctors and specialists is less precise. To some extent, most American specialists tend to offer some primary as well as specialist care, and most family doctors practise in hospitals as well as in the community. Patients have direct access to specialist care, but

lack the benefits of the continuing and coordinated care provided by a single family doctor. With increasing recognition that primary care presents an opportunity to influence the health of the population through prevention or 'anticipatory medicine', the division between primary and specialist medicine in America may become more defined. Insurance companies increasingly see a referral system as a way of containing the escalating costs of specialist care. In countries without a traditional infrastructure of family doctors, however, an increasing distinction between primary and specialist medicine should not lose sight of the principle of sharing care.

Managed care

All health care systems operate in a changing environment. These changes principally occur as a result of demographic shifts, or the advent of new technologies or new drugs. They take place amid increasing expectations of patients and their relatives, who have greater access to information about their illness.

In the developed world, the major demographic change is that of an ageing population with chronic rather than acute diseases, often affecting more than one system. In other parts of the world, abandoning traditional diets and increasing urbanization has led to an increase in 'Western' diseases. The epidemiology of disease is also changing within populations: peptic ulcer disease, for instance, is declining in prevalence, while there is a concomitant increase in the morbidity from gastro-oesophageal reflux disease.

New technology is constantly being applied for the more accurate diagnosis and effective treatment of conditions, usually with increased cost implications. With therapeutic advances there has been a tendency for specialists to operate independently of primary care. Technological advances should, however, enhance rather than diminish the central role of family doctors. Clinical trials over the last 30 years offer an unprecedented opportunity to establish therapeutic guidelines for referring and managing disease. Gastrointestinal disease presents good examples of the enormous changes that have occurred in the last 20 years. Fibre-optic endoscopy is now widely available and potent acid-suppressing drugs are amongst the most prescribed drugs in primary care. Therapeutic endoscopy and minimally invasive surgical techniques are also increasingly used. The exciting result of understanding the pathogenesis of disease has been the prospect of curing chronic disease, rather than controlling symptoms alone. The eradication of *Helicobacter pylori* in duodenal ulcer disease is a clear example of avoidance of the appreciable morbidity and complications of chronic disease. The prospects of a vaccine to prevent *H. pylori* infection, or understanding of the immunogenetics of inflammatory bowel disease to predict patterns of illness, are examples of how technology will change the pattern of chronic disease in the next 20 years.

In many societies, patients have become more knowledgeable about medicine, the consequences of disease and its treatment. This rise in consumerism in medicine has been encouraged by doctors as well as the media and has been a principal reason why health care systems have become more patient-centred. Patients expect more information about their condition and have greater access to sources of information. Self-help groups exist for many conditions, both gastroenterological and non-gastroenterological. This increased

awareness should assist rather than threaten the fundamental partnership between patient and doctor in the management of chronic conditions.

In the face of these changes, combined with the pressure for cost-effectiveness and the vogue for evidence-based medicine, there is a shift to *managed care* in almost all health systems. This means agreeing selection and treatment criteria for patients with specific conditions. To be successful, the criteria must be based on interventions of established value and must be both practical and flexible, but above all they must be agreed by all parties involved. In formulating management protocols, non-clinicians sometimes fail to grasp the variable pattern of clinical medicine and the unpredictability of disease. This unpredictability, of course, makes clinical medicine endlessly fascinating, but it means that rigid protocols have limited value. This does not mean that it is pointless to try to agree on patterns of best management, but there must be a clear understanding that there are options in any given circumstance to allow for the unpredictability of clinical medicine. Ownership of management options by the parties involved is the single most important predictor of their successful implementation, with education and—very importantly—continuing education, necessary for their success.

The concept of shared care

In a number of gastroenterological disorders, the course is recurring or chronic. In these cases, *shared care* between the family doctor and specialist is appropriate. This should mean more than the ad hoc joint management that commonly exists between primary and specialist care, where each doctor functions largely independent of the other by reacting to events. It implies following a management strategy with the following aims:

- treating symptoms
- modifying the course of the condition
- identifying complications at an early stage
- minimizing the impact on work, family and social life
- improving the quality of life.

For this to work, the management options and responsibilities need to be agreed between family doctors and specialists, bearing in mind local needs, expertise and other resources. Discussing these options should provide mutual education and support, so that care can be properly shared in the interests of the patient.

Why share care?

Gastrointestinal symptoms are too common in the community for all people to be seen by their family doctor, let alone by a gastroenterologist. Neither is this necessary, since most people with symptoms will have no serious pathology. Family doctors, however, can make people aware of when it is appropriate to seek medical attention (such as new-onset dyspepsia over the age of 50) and play a central role in recognizing symptoms that justify further investigation. If resources are to be available for the minority of patients who need specialist investigation, family doctors should actively contribute to continuing care

of chronic or relapsing disorders that have previously been the province of a hospital clinic. Of course, this already happens to a greater or lesser degree, but in many areas of gastroenterology this cooperation could be improved by active discussion between doctors in primary and specialist care. Such discussion should lead to locally agreed criteria for referral and arrangements for follow-up, in the interests of protecting patients from inappropriate investigation or unnecessary treatment. It also seems to be the logical way of using limited resources in an attempt to detect serious disease at a more treatable stage (Tables 1.1, 1.2).

The ultimate goal

There is an ideal in health care that can probably only ever be a vision, but towards which we should strive because every step represents an improvement in care. In this ideal, patients would be informed and aware of the significance of gastroenterological symptoms. Information through informal sources such as the medical columns of newspapers and advice from patient groups would be available and accessible. Pharmacists or liaison nurses, whose role in the management of gastroenterological disorders is already

Table 1.1 Why a shared-care approach is needed

- In the UK, 30–53% of adults will have had dyspepsia in the previous 6 months. (Figure 1.1)
- 10% of all general practice consultations are for gastroenterological conditions
- Over 50% of patients attending gastroenterology clinics have functional bowel disorders
- Acid-suppressing drugs cost the NHS £400 million annually
- 60% of all endoscopies show no, or only minor, abnormalities
- The median time taken from first presentation to diagnosis in cases of gastric cancer is 7 months and has not changed since the advent of open access endoscopy
- Only 4–7% of gastric cancers are histologically early (5-year survival about 90%); the remainder have penetrated the muscle layer (overall 5-year survival about 15%)

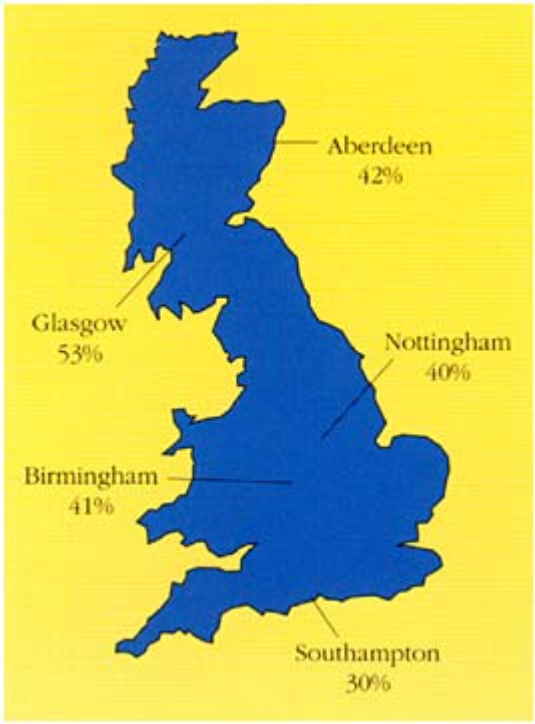

Figure 1.1 *Regional prevalence of dyspepsia in the UK, based on a random sample (n=7420) from the lists of family doctors in these areas. The prevalence of dyspepsia in the community is broadly similar throughout the UK.*

considerable, would give appropriate advice and medications for conditions that do not require medical attention. Patients would consult their family doctor at an early stage about potentially significant conditions. The family doctor would have ready access to diagnostic facilities and knowledge about their appropriate use. A wider range of conditions could then be managed in the community. Local specialists would provide support in the form of education, information and prompt access to specialist clinics. Appropriate management and follow-up would then be arranged, avoiding unnecessary hospital visits.

If sharing care is to produce the expected benefits, then communication is paramount. This must involve patients as well as family doctors, specialists and other professionals. This need not require high technology, although computer links between hospital and

health centre should expedite the transfer of results, letters and discharge summaries. Patient-held records in conditions such as

Table 1.2 Potential advantages of a shared-care approach for gastroenterrological disease

Patients	■ Greater continuity of treatment and follow-up
	■ Easier access to local medical advice
	■ Reduced hospital visits
	■ Shorter waiting times
	■ Greater contact with a doctor who is more aware of their social and family circumstances
Family doctors	■ Patients may be more open with doctors with whom they are familiar
	■ Opportunity to provide better patient care
	■ Deveolopment of new skills and broader knowledge in gastroenterology
	■ Stronger relations with specialists
	■ Reduced costs from more selective referral and follow-up
Specialists	■ Encourages referrals appropriate for specialist care
	■ Reduced clinic size owing to fewer follow-ups
	■ More time available for patients requiring specialist management
	■ Opportunity to provide better patient care
	■ Stronger relations with family doctors
	■ Reduced costs by more selective follow-up

inflammatory bowel disease (Figure 7.7, p. 134) can be developed to the advantage of everyone, since they can include a synopsis of management guidelines or referral criteria. Free communication between primary and secondary care not only helps the care of individuals but also disseminates new knowledge and assists management of local resources. Regular meetings for updating and auditing practice provide a formal setting for exchanging information and ideas.

A variety of specialties have already developed shared care in the form of outreach clinics, including diabetes, asthma, elderly care, maternity, psychiatry and paediatrics. Simply shifting a clinic from hospital to the community has little value unless the primary health care team is closely involved. Liaison attachments, where the specialist and the family doctor are involved in assessment of new cases, or group discussion about cases, have an important potential for mutual professional education. The main disadvantage is the commitment of scarce specialist resources to one practice at a time. This reflects the paucity of specialists in the UK, where there may be one gastroenterologist for 225,000 population, compared with one per 25,000 in parts of the USA and Japan. With the new appointment of specialists, however, it is appropriate to consider a community

commitment and the simultaneous appointment of specialist liaison nurses to facilitate follow-up of patients with chronic conditions. Regular combined consultations are appropriate only for a minority of gastroenterological conditions.

The development of shared care needs to be properly planned and offers the opportunity to alter the balance between primary and secondary care in the interests of patients. Implementation needs locally agreed options about the initial management and use of resources such as endoscopy, as well as referral criteria and conditions for follow-up. This can be facilitated by local management, but must be driven by clinicians actively involved in patient care. It is not necessarily a cheaper option than the current system, but should reduce unnecessary referrals, limit return visits to hospitals and use the skills of physicians in primary and specialist care more appropriately. Greater use might be made of specialist or liaison nurses, especially for follow-up of some patients with inflammatory bowel disease, coeliac disease or gastro-oesophageal reflux.

Pursuing the concept of 'a light touch on the tiller', patients might be seen once in, for example, a dyspepsia clinic. Patients could be referred, have a specialist consultation and appropriate investigations (such as endoscopy or ultrasound), so that a diagnosis and treatment plan would be drawn up at this single visit. The patient's continuing care would then be managed by the family doctor, with no outpatient follow-up. The resource consequence of this approach is that fewer patients could be seen in any individual clinic or endoscopy session, although the total hospital time for assessment, investigation and follow-up would be reduced. This sort of approach has already been taken in some parts of the UK where gastroenterologists (rather than clinical assistants) perform open-access endoscopy. Advice is given in the endoscopy report, which saves patients the waiting times for the initial outpatient appointment and subsequent follow-up clinic visit. This makes sense to patients and seems to be what most family doctors want.

Key points

- Shared care between specialists and famiky doctors is needed to provide better continuity of care for patients with chornic or relapsing disorders, to avoid unnecessary Follow-up in hospital clinics and to encourage optimum use of hospital resources.
- Clinical trials in the last 30 years offer an opportunity to establish therapeutic options for referrong and managing gastrointestinal disease.
- Family doctors and gastroenterologists need to agree referral criteria, therapeutic options (rather than 'guidelines' or 'protocols') and arrangements for follow-up, at a local level. This can be facilitated by local management, but must be driven by clinicians actively involved in partient care.
- The development of shared care must be properly planned and is not necessarily cheaper than the current system.

Further reading

British Society of Gastroenterology. *Guidelines in Gastroenterology 1996.* Contact BSG Sectretariat, 4 St Andrews Place, London NW1 4LB. Separate guidelines cover dyspepsia,

antibiotic prophylaxis in gastrointestinal endoscopy, oesophageal manometry and pH monitoring, inflammatory bowel disease, coeliac disease, artificial nutritional support and tests for malabsorption.

Jones RH. *Gastrointestinal Problems in General Practice.* Oxford: Oxford University Press, 1993.

Orton P. Shared care. *Lancet* 1994; **344:**1413–15.

Chapter 2
Clinical skills

As many readers will have years of clinical experience, the topic of clinical skills is approached here with caution. Some simple truths, however, bear repeating. For instance, a history of nocturnal diarrhoea very frequently indicates organic disease, whereas constant abdominal pain and bloating without weight loss very rarely indicate pathology. Gastrointestinal diseases frequently occur in the absence of symptoms, but the converse also applies.

The initial consultation needs to elicit a differential diagnosis, determine the underlying anxieties and assess the degree of impairment caused by the symptoms. It can be difficult to achieve a rapport with patients who are embarrassed by their gastrointestinal symptoms. A minute or two spent talking about a subject familiar to the patient before starting to take the history can pay dividends. Confidence is established by expressing an interest in the patient's own activities and the potential impact of the disorder on the patient's work can be assessed. It also allows general observation about the level of anxiety and how best to approach subsequent explanations of diagnosis and treatment.

The major gastroenterological complaints in approximate order of frequency are abdominal pain, diarrhoea, constipation, gastrointestinal bleeding, vomiting, weight loss and dysphagia. Symptoms are usually best addressed in chronological order, first evaluating individual symptoms, then establishing any relationship between symptoms. The purpose of this chapter is to draw attention to features that help discriminate between an organic and a functional origin of symptoms, since this is a common clinical dilemma. Some guidance is also given on initial investigations and management, where these are not covered in other sections.

Consultation and referral behaviour

Symptoms are more common in the community than in medical practice, and the factors that influence a person to seek medical care do not relate to the severity of the symptoms. In a survey of 2000 people in the south of England, 38% admitted to suffering from dyspepsia in the previous 6 months and only 26% of those who currently had dyspepsia had consulted their family doctor (Figure 2.1).

Enquiry into the reported frequency and severity of dyspeptic symptoms revealed little difference between the group of patients who sought medical help and those who did not (Figure 2.2). Associated symptoms of nausea, vomiting, heartburn and abdominal distension were also unrelated to whether a patient sought medical

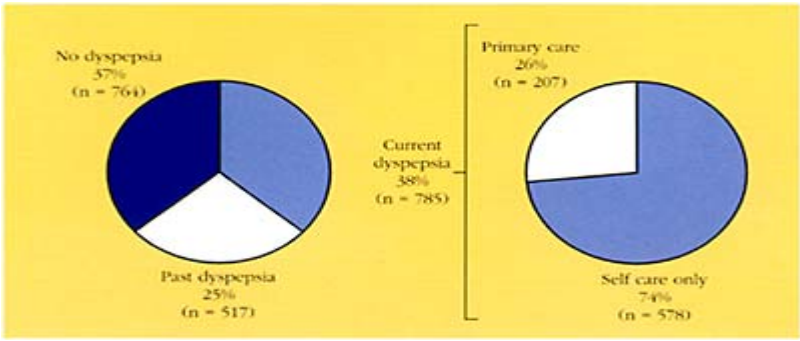

Figure 2.1 *Prevalence of dyspepsia in the general population. Only a minority will seek medical attention for their symptoms.*

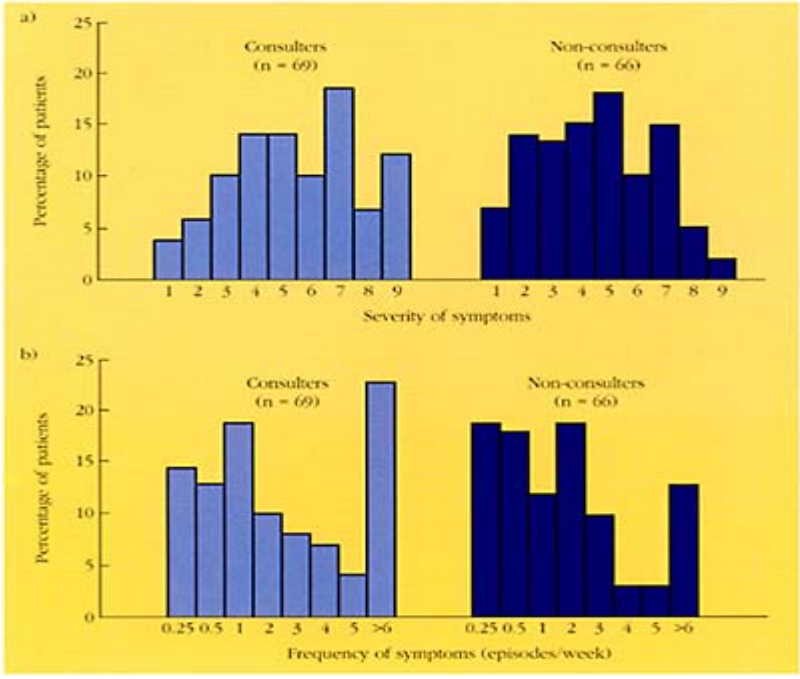

Figure 2.2 *(a) Severity and (b) frequency of symptoms in people with dyspepsia. Severity was scored by patients on a scale from 1 (none or minimal symptoms) to 9 (severe*

symptoms interfering with daily activity). Neither the severity nor the frequency of symptoms is related to the decision to consult a doctor.

attention. However, when health concerns were examined, anxiety that symptoms might represent a serious or fatal condition, worries about cancer in general or a family history of abdominal cancer and a fear about heart disease were all significantly related to the decision to seek medical advice.

The message is clear: the basis of good care starts with a careful history in general practice. People entering the health care system do not necessarily represent those with the most severe symptoms and patients' concerns may be as important to treat as their symptoms. Those who fear unnecessarily that they may have cancer are in need of reassurance, which may not best be provided by making a referral or ordering an investigation. This is not to say that referrals or investigation should be avoided, merely that exploring and dealing with a patient's health concerns is sometimes a better approach.

Referral to specialists also varies enormously in primary care. In a study of 179 family doctors in the UK, the number of referrals made in a 12-month period varied from less than 5 to more than 95, after correction for workload. With agreed criteria for referral and guidelines for management in a shared-care system, referral rates may become more standardized and appropriate.

Assessing the impact of symptoms

In establishing the impact of symptoms on a patient's job or social life, questions should be as objective as possible. For instance, some patients with Crohn's disease may say they feel well if they do not have pain, but will not volunteer symptoms of persistent diarrhoea or even of faecal incontinence unless asked. One patient when reviewed said that 'everything was fine', but on closer questioning admitted to driving with a caravan in tow for any distance of over 20 miles, in order to have a lavatory immediately available! Consequently, the frequency of bowel actions per day and at night, the number of 'accidents', and ability to travel on public transport, are all important indicators of the impact of symptoms. The amount of time taken off work or education should be mentioned in any referral letter, to help the specialist assess the priority in allocating outpatient appointments.

Abdominal pain

Classically, the history should identify the site, timing, intensity and character of abdominal pain, with aggravating and relieving factors. The presence of associated symptoms such as bowel disturbance, vomiting, and urinary or gynaecological symptoms

must also be elicited. Chronic or recurrent abdominal pain, as opposed to acute abdominal pain, is the main issue for shared care.

The *site* of chronic pain is of limited value in determining the cause, because the viscera receive afferents from both sides of the spinal cord, leading to poor localization. Over half the patients reporting recent dyspepsia from whatever cause have experienced both upper abdominal and retrosternal discomfort (Figure 2.3). The *timing* or *pattern* is more informative: intermittent pain more frequently suggests an organic cause than continuous pain in the absence of associated features. Pain immediately on eating is rarely pathological if food is not painful to swallow (odynophagia is characteristic of oesophagitis), except in the rare instances of mesenteric ischaemia, when the patient becomes afraid to eat. Postprandial pain, occurring 20–60 minutes after a meal, more often suggests disease. Specific questioning about the *character* of pain is helpful, since colicky pain (coming in waves, bearing some similarity to contractions and readily recognized by women) indicates biliary or small intestinal obstruction. Sharp stabbing pain is less likely to have an organic origin, but the possibility of referred pain from the back, or non-visceral abdominal pain (p. 88) must be considered. *Aggravating* or *relieving* factors can be indicative: pain that persists despite effective acid suppression (with H2-receptor antagonists or proton-pump inhibitors) is highly unlikely to be due to an acid-related disorder such as a peptic ulcer. Pancreatic or retroperitoneal pain is often made better by curling up and is aggravated by lying flat.

Clinical examination often does little other than determine the site of tenderness in the region of maximum pain. The importance of careful inspection, however, should be emphasized: cheilitis, glossitis, or visible peristalsis are otherwise overlooked. Rectal examination, including inspection of the perineum, is essential because this may show features of Crohn's disease, confirms the stool consistency and can identify local pelvic tenderness.

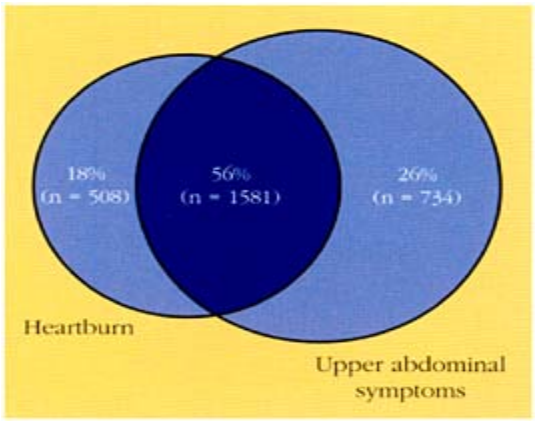

Figure 2.3 *The site of pain is not necessarily a useful pointer to the couse. In dyspepsia, more than 50% of patients will describe both retrosternal*

and upper abdominal pain, whatever the cause.

As the symptom complexes of many diseases overlap (gastric or duodenal ulcer, gastric cancer, pancreatic disease, gall stones, or irritable bowel syndrome), further *investigation* is often needed to achieve a diagnosis. For a substantial proportion of patients in primary care, however, it is reasonable to make a clinical diagnosis in the first instance and to review the patient after addressing underlying concerns or a trial of treatment. How long this approach continues before initiating investigation depends on the ill-defined term 'clinical judgement'. Although over-investigation of abdominal pain should be discouraged since it is frequently attributable to a motility disorder, there may be a perceived benefit from a normal test result.

It is inappropriate to list all the methods of investigating abdominal pain, but some general points are worth making. For instance, serology tests for *Helicobacter pylori* in patients under 45 years will help to select those needing endoscopy, because negative serology effectively excludes a peptic ulcer (chapter 4, p. 53). Similarly, a normal full blood count and normal inflammatory markers [erythrocyte sedimentation rate (ESR), C-reactive protein, or plasma viscosity] in a young person with chronic abdominal pain and bloating will be consistent with an irritable bowel (chapter 5, p. 77) and are often sufficient to exclude other pathology without further investigation. Examination of the urine for microscopic haematuria should not be overlooked at any age, to rule out renal pathology.

An abdominal ultrasound examination is a good non-invasive method of identifying hepatobiliary or pancreatic pathology, but may depend on the operator for reliable identification of conditions other than gall stones. Abdominal CT scanning often provides better definition than ultrasound for fat patients, since sound waves have limited penetration and fat planes assist resolution of the image in CT scanning. It is also particularly helpful in frail or elderly patients, because it can obtain good views of the colon and may thus avoid the need for a barium enema. An abdominal CT scan, however, exposes the patient to a radiation dose about a thousand times greater than that from a chest radiograph. When investigating lower abdominal pain, a barium enema is rarely helpful unless there is an associated change in bowel pattern.

Diarrhoea

The *definition* of diarrhoea depends on a patient's normal bowel habit. Although a stool volume of more than 200 ml (200 g)/day provides a helpful definition for research purposes, it is rarely useful in clinical practice. Consequently, it should first be determined whether, by diarrhoea, the patient means an increase in stool frequency or a decrease in stool consistency. Both daytime and nocturnal *frequency* should be recorded in clinical notes. Early morning frequency is common in patients with an irritable bowel, but may occur with proctitis. Nocturnal diarrhoea is almost always pathological. When the *stool consistency* is explosive, frothy, malodorous or difficult to flush away, the possibilities of bacterial overgrowth, giardiasis or malabsorption are raised. Variable consistency (loose and watery, followed by faecal pellets like rabbit droppings) suggests

an irritable bowel, as does an erratic or unpredictable *pattern* (diarrhoea one day, constipation the next). Continuous diarrhoea for more than 3 weeks is an indication for referral (p. 123). *Associated features* such as bleeding and weight loss are powerful indicators of disease, and diarrhoea with weight loss despite a good appetite strongly suggests thyrotoxicosis. On the other hand, diarrhoea of long duration with a sensation of incomplete evacuation, abdominal bloating or abdominal pain, usually indicates an irritable bowel. Sympathetic inquiry about faecal incontinence ('accidents') is important, because this may not be volunteered and is often the patient's main concern. Indeed, the patient may use the term 'diarrhoea' as a less embarrassing way of complaining about incontinence.

Clinical examination should look for signs of nutritional deficiency (weight loss, glossitis, cheilitis) and an abdominal mass, and should include rectal examination. The pulse rate and temperature are simple objective signs that help determine the severity of inflammatory bowel disease (Table 7.3, p. 128), but are too frequently overlooked.

Investigation of diarrhoea should include a stool sample for culture and sensitivity, and a request for assay of *Clostridium difficile* toxin, as well as microscopy for cysts and parasites if the culture is negative. Three stool samples are needed for reliable detection of pathogens such as *Giardia lamblia,* and it is pointless to examine formed stool. Sigmoidoscopy *and* a rectal biopsy are mandatory if inflammatory bowel disease, microscopic, or collagenous colitis (p. 121) are to be diagnosed. A full blood count and tests for inflammatory markers, electrolytes and thyroid function should be performed at an early stage. Pathology is unlikely if these are all normal but, if malabsorption is being considered, the calcium, ferritin, red cell folate and B12 levels should also be checked.

As a general rule, a significant change in bowel habit in any patient over the age of 40 warrants a barium enema. A colonoscopy is more appropriate if there is a history of rectal bleeding or visible inflammation on rigid sigmoidoscopy, so that colonic biopsies can be taken. If iron deficiency anaemia is present with diarrhoea, then investigation of the small bowel by endoscopic biopsy to exclude coeliac disease and contrast radiology (barium follow-through or small bowel enema) to detect Crohn's disease is necessary.

Some patients continue to have diarrhoea despite normal results of investigations. For patients with *difficult, persistent diarrhoea* it is worth sending a urine sample for chromatography to identify laxatives. Alternatively, a small quantity of stool may be mixed with molar sodium hydroxide: if phenolphthalein is present, the stool turns pink. Finally, admission to hospital to measure stool weights may help. In many patients with an irritable bowel, the diarrhoea disappears on admission and the clue is a stool output less than 400 g/day when no other cause has emerged. Large-volume (>400 g/day) diarrhoea can be further separated into secretory and osmotic types by the response to a 48-hour fast: secretory diarrhoea (due to very rare peptide-secreting tumours) continues, whereas osmotic diarrhoea (usually due to disaccharidase deficiency) abates during a fast.

Constipation

There is no generally accepted definition, but constipation implies a decrease in stool frequency and increase in consistency or 'hardness' of the stools. The usual cause in

Western populations is insufficiency of dietary fibre, but anal disease and other causes need to be considered (Table 2.1).

The *frequency* of defaecation, *duration* of constipation and *associated features* should be recorded. Recent-onset constipation suggests a dietary, drug-induced, metabolic or colonic cause, whereas associated features such as perianal pain or bleeding point to anal pathology. Long-standing constipation may be dietary, but neurological causes and hypothyroidism should be excluded. Idiopathic slow-transit constipation should be considered when the bowel frequency has been less than once a week for a number of years. This is an idiopathic condition commonly affecting young women, which can be distinguished from constipation-predominant irritable bowel syndrome by transit studies.

Clinical examination should look for signs of hypothyroidism or an abdominal mass. Careful rectal examination is mandatory, including assessment of perineal sensation if there is a suspicion of

Table 2.1 Causes of constipation

- Dietary fibre insuffeciency (including anorexia).
- Motility disorder (irritable bowel syndrome, pseudo-obstruction, idiopathic slow-transit constipation)
- Drugs (analgesics, aluminium-constaning antacids, iron tricyclic antidepressants, verapamil)
- Anorectal disease (fissure, ractal mucosal prolapse, proctitis)
- Colonic disease (obstructing stricture)
- Metabolic disorders (hypothyroidism, diabetes, phaeochromocytoma)
- Endocrine disorders (hypothyroidism, diabetes, phaeochromocytoma)
- Neurological disease (paraplegia, parkinson's disease, cauda equina lesion, aganglionosis)

neurological disease. Asking the patient to strain while the perineum is inspected may reveal marked perineal descent or provoke rectal mucosal prolapse, which are causes of constipation that may otherwise be overlooked.

Investigation of constipation is not always necessary, as the history and rectal examination are often sufficient. Blood tests for thyroid function and calcium should be taken before referring a patient for investigation. A barium enema is usually appropriate when constipation occurs for the first time in a patient over the age of 40, once dietary causes have been excluded. Transit studies are rarely necessary, except when stools are very infrequent and slow transit constipation is suspected. In such a study, the patient swallows 20 radio-opaque markers, and plain abdominal X-rays are taken on days 3 and 5 after ingestion. If more than five markers remain visible after 5 days, then transit is said to be prolonged (Figure 2.4). Life-long osmotic laxatives, often in large doses, are then necessary.

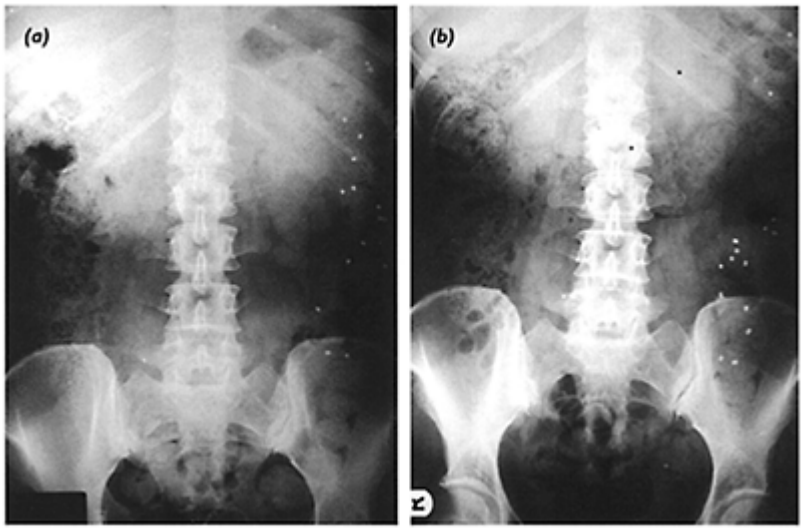

Figure 2.4 *Transit studies in idiopathic slow-transit constipation. (a) After 3 days, (b) after 5 days.*

Gastrointestinal bleeding

Since investigation and management of acute bleeding from the upper or lower gastrointestinal tract is the province of hospitals rather than shared care, only some general points are made here. Haematemesis and/or melaena indicate *upper gastrointestinal bleeding* and are almost always an indication for direct admission to hospital. Requests for outpatient endoscopy in patients with melaena but without haematemesis are illogical, since a larger volume of blood loss has usually occurred to cause melaena than that which provokes a 'coffee-ground vomit' or haematemesis from oesophagitis. Occasionally a patient will present with a good (ie., reliable) history of melaena having occurred some days previously. In these cases a clinical decision has to be made about the urgency of investigation, but a rectal examination to confirm the absence of melaena and a full blood count must be considered essential. If the patient is anaemic or unwell, then a telephone call to the local gastroenterologist or endoscopy unit would be more appropriate than out-patient referral.

A number of studies have shown that patients admitted to a hospital with a specialist GI bleeding unit have a lower mortality (about 5%) than when admitted to a hospital where no designated area for managing such patients exists (mortality around 15%). It is worth reflecting that the latter figure is similar to the in-hospital mortality rate (around 13%) of patients admitted with acute myocardial infarction. This emphasizes the importance of effective resuscitation, early recognition of continued or renewed bleeding and close cooperation between nursing staff, physicians and surgeons.

Acute lower gastrointestinal bleeding is more commonly a surgical than a medical problem, but a distinction must be drawn between rectal bleeding with a change in bowel habit (often indicating a colonic tumour) and bloody diarrhoea (often indicating colitis). As with all other symptoms, rectal bleeding is more prevalent in the community than among those presenting as patients. In a survey of industrial employees aged over 40 years, 11.8% of 916 people answering a questionnaire admitted to rectal bleeding within the previous 12 months. When 99 consecutive patients over the age of 40 presenting with rectal bleeding to 17 general practices in Newcastle upon Tyne were subjected to colonoscopy, 44% had serious pathology: eight had colorectal cancer, 25 had polyps and 11 had inflammatory bowel disease. This high rate may partly be explained by selection of patients by the practices concerned, but the message is that rectal bleeding of recent onset (<12 months) must always be investigated over the age of 40 years. Of interest is that blood mixed in with the stool, a change in bowel habit, or abdominal pain were significantly associated with serious pathology, but that the colour of blood (fresh or dark) was not.

Chronic or recurrent gastrointestinal bleeding of obscure origin can be one of the most vexing problems in gastroenterology, but the specialist investigation involved is beyond the scope of this chapter.

Vomiting

Vomiting is common and is a feature of functional, inflammatory or obstructive gastrointestinal disorders, as well as systemic infections, metabolic mayhem, migraine, drug toxicity and pregnancy.

The *timing* and *content* of the vomit should be determined, as well as *associated features*. Vomiting in the morning soon after waking is characteristic of pregnancy, alcohol abuse, raised intracranial pressure, or metabolic disturbance such as uraemia. Vomiting during or very soon after a meal is usually functional, especially when the history is prolonged or in the absence of weight loss. Pyloric canal ulcers, however, can provoke vomiting very soon after eating. Delayed vomiting, 1–2 hours after eating, usually indicates a peptic ulcer, gastric cancer or intestinal obstruction. An important clinical clue to gastric outflow tract or intestinal obstruction is the presence of a succussion splash: if the volume of the vomit is large and the content is of partially digested food, this too indicates obstruction. Completely undigested food in the vomit suggests regurgitation due to a motility disorder, achalasia or pharyngeal pouch. Chronic or recurrent vomiting due to psychological causes is not uncommon. There is often a long history of vomiting that is related to stressful events (for instance school examinations) that can usually be suppressed until the patient reaches the bathroom. There is often no weight loss—unless it is a feature of anorexia nervosa, when vomiting is provoked by inserting a finger into the pharynx. The diagnosis should be made quickly and extensive investigation avoided, although antiemetics are often of little value.

Consequently, *investigation* of vomiting should include tests of urine for glucose (or pregnancy if relevant), blood for electrolytes, creatinine and serum calcium, then a request for endoscopy. If all investigations are normal, then a barium follow-through to

exclude obstruction should be considered. In diabetic patients, isotope gastric-emptying studies to detect gastroparesis are occasionally necessary.

Weight loss

Weight loss in the presence of other symptoms usually indicates pathology. In contrast, on the occasions when it presents as an isolated complaint, a cause is frequently difficult to find. Unless there are associated gastrointestinal symptoms, the possibility of nongastrointestinal conditions must first be investigated, including tests of urine for glycosuria, thyroid function tests and a chest X-ray. One diagnosis that can trap the unwary is diffuse small intestinal Crohn's disease in teenagers: this can present as weight loss alone, often misattributed to anorexia, but can readily be distinguished by the presence of anaemia or raised inflammatory markers. A useful maxim is that anaemia associated with 'anorexia nervosa' is due to Crohn's disease until proved otherwise.

Dysphagia

It is usually possible to distinguish between oropharyngeal and oesophageal causes by a careful history. The interval between swallowing and dysphagia, the type of food provoking dysphagia, the pattern and any associated features are fundamental characteristics (Figure 2.5).

Acute or *progressive dysphagia* for solids needs urgent *investigation*. The radiologist or gastroenterologist should be telephoned to arrange a chest X-ray and barium swallow, followed by endoscopy. Confirmation by request form or letter can follow later. The chest X-ray may show a hilar tumour, mediastinal fluid level or absent gastric bubble (in achalasia), or right lower lobe consolidation from aspiration. An interval of 12–18 hours between the barium swallow and endoscopy will allow barium to clear, so that brushings, biopsies and dilatation can be performed.

Patients with *intermittent dysphagia* without weight loss, or those with symptoms indicating an oesophageal motility disorder can be investigated electively.

Dysphagia with a normal barium swallow is not uncommon. The usual cause is oesophageal dysmotility (p. 42), but oesophagitis,

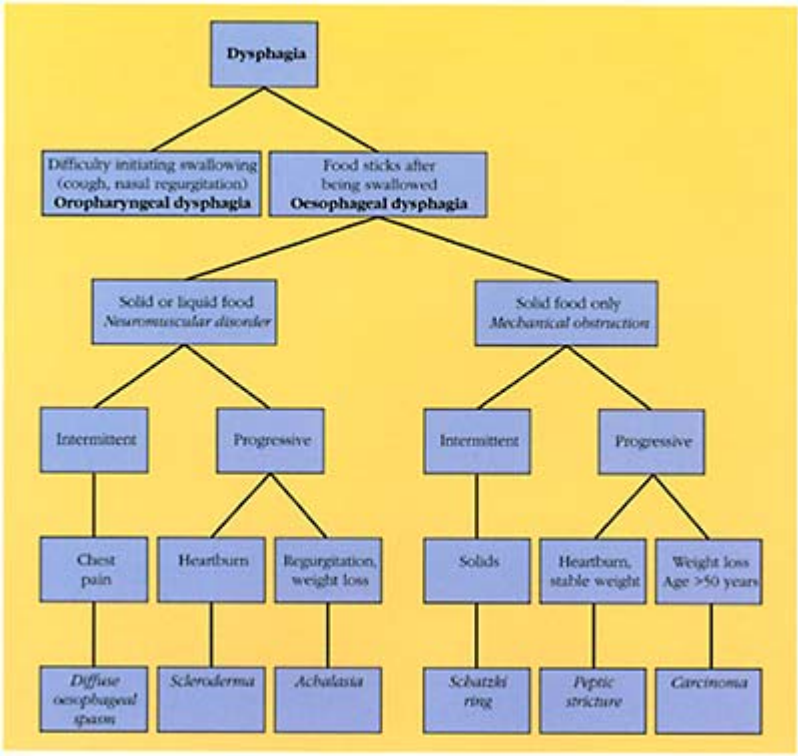

Figure 2.5 *Diagnosis of dysphagia.*

(Adapted from Castell DO, Donner MW. Evaluation of dysphagia. Dysphagia *1987;* ***2:****65–71.)*

achalasia and strictures may be overlooked. Globus hystericus is characterized by a constant sensation of a lump in the throat, in addition to difficulty in swallowing. The history should be retaken, especially asking whether dysphagia is for liquids *as well as* solids, which usually suggests dysmotility. Any weight loss should be documented and the films checked. A barium swallow should show all the oesophagus. If an organic lesion is still suspected, then endoscopy by an experienced endoscopist is appropriate. Referral for manometry (p. 40) is indicated for persistent symptoms, because obscure cases of diffuse spasm or achalasia may be detected.

Key points

- Gastrointestinal symptoms are very common in the community and only minority of people with symptoms such as dyspepsia will present to their family doctor and become ‘patients’.
- The frequency and serverity of symptoms are, unrelated to the to the decision to seek medical attention.
- Anxiety that symptoms might represent a serious condition such as heart disease or cancer, as well as a family history of abdominal cancer, are significantly related to the decision to consult.
- A careful history is the basis of good health care. The diagnostic featuers and preliminary investigations for common presenting dasrointestinal symptoms are summarized. In doing this, attention is drawn to features that help discriminate between an organic and a functional origin of symptoms, since this is often the principal clinical dilemma.

Further reading

British Society of Gastroenterology. *Guidelines in Gastroenterology 1996.* Contact BSG Sectretariat, 4 St Andrews Place, London NW1 4LB. Separate guidelines cover dyspepsia, antibiotic prophylaxis in gastrointestinal endoscopy, oesophageal manometry and pH monitoring, inflammatory bowel disease, coeliac disease, artificial nutritional support and tests for malabsorption.

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Chapter 3
Gastro-oesophageal reflux disease

Gastro-oesophageal reflux is very common, but does not always cause symptoms. Up to 15% of the population experience symptomatic reflux every month, but only a minority seek medical attention (Figure 3.1). When symptoms occur, they are often due to oesophagitis, or oesophageal dysmotility, but an important minority present with complications such as bleeding and stricture, or have columnar epithelial (Barrett's) transformation of the lower oesophageal mucosa that predisposes to adenocarcinoma.

Some reflux occurs in everybody, but it is more marked in people with symptoms of oesophagitis. When typical symptoms of heartburn and acid regurgitation are present, gastro-oesophageal reflux can reliably be assumed to be present. *It is common to get symptomatic reflux with no signs of oesophagitis at endoscopy.* Abnormal reflux is largely caused by dysfunction of the lower oesophageal sphincter. Damage to the oesophageal mucosal barrier is determined by the duration of acid exposure. Delayed clearance of refluxate prolongs mucosal exposure to a low pH (<4) and initiates oesophagitis. Gastric acid secretion is generally not increased, but gastric emptying is delayed in up to 40% of patients with reflux. In addition to acid, bile acids and pepsin also disrupt mucosal integrity, or provoke oesophageal dysmotility. *Helicobacter pylori* is unrelated to reflux oesophagitis.

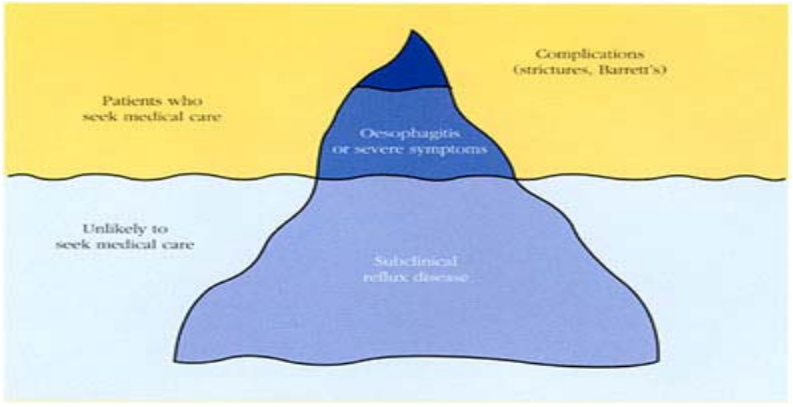


Figure 3.1 *The iceberg of reflux disease. Gastro-oesophageal reflux is the commonest couse of dyspepsia in the community. Only a minority of symptomatic people come to medical*

attention and a very small minority develop complications. (Modified from Castell DO et al., eds. Gastro-esophageal Reflux Disease. Mt Kisco, NY: Futura, 1985; 3–9.)

Presentation

Abnormal reflux is more reliably diagnosed clinically than by endoscopy or barium studies. Consequently, patients should initially be treated symptomatically and not investigated; however, as only a minority of people with symptomatic reflux seek medical advice, the family doctor must also find out the reason for consulting.

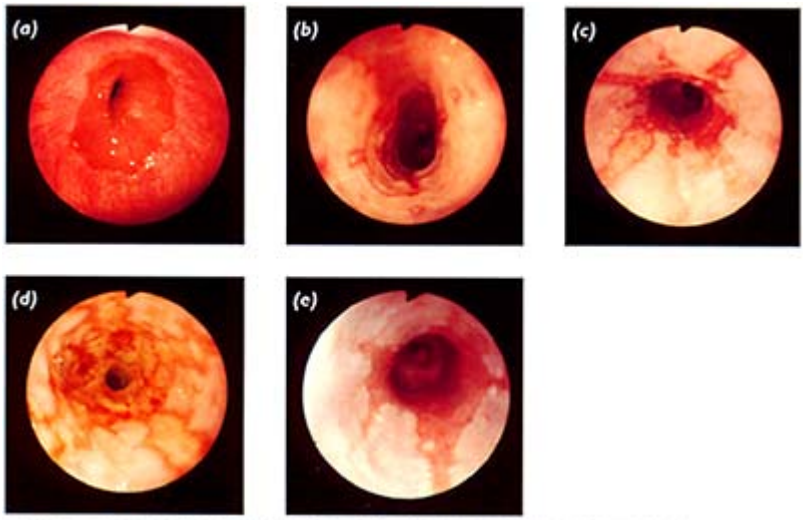
Establishing the diagnosis

History. The characteristic symptoms are heartburn and acid regurgitation. *Heartburn* is described as retrosternal burning or discomfort, often related to meals, lying down, stooping or straining and occasionally to exercise. *Acid regurgitation* or 'waterbrash' is the effortless return of gastric or oesophageal contents into the pharynx. Patients often have difficulty in describing the taste as bitter or sour. *Episodic dysphagia* may be due to peristaltic dysfunction. Persistent dysphagia for solids indicates a stricture and needs prompt investigation (p. 26). Pain during swallowing *(odynophagia)* is unusual unless there is severe oesophagitis.

Other symptoms include excess salivation during pain, and relief by antacids. Chest pain, related to posture or exercise (both of which increase intra-abdominal pressure), can sometimes be difficult to distinguish from angina (p. 42). Pain may occasionally radiate to the neck or back, or predominate in the left upper quadrant. Nocturnal asthma can also be the only symptom, especially in children, and may be relieved by treatment of reflux. Oesophagitis is sometimes asymptomatic and there is no clear relation between the severity of symptoms and the severity of oesophagitis at endoscopy.

Investigations. Typical symptoms of reflux that are relieved by alginates or occasional acid suppression should not be investigated. Endoscopy adds little to the routine management of younger patients. It can even be confusing in patients who have symptoms and a normal endoscopy, but this does *not* exclude reflux. *Endoscopy* is indicated for persistent symptoms in spite of empirical acid suppression, to identify the severity of oesophagitis (Figure 3.2), and is required in patients over the age of 45 or 50 who develop new symptoms or in those with dysphagia, bleeding or unintentional weight loss. It cannot, however, predict the risk of a complication developing, as the natural history of oesophagitis is unknown.

A *barium swallow* should be considered the first investigation in dysphagia and should precede endoscopy (p. 26). A *barium meal* is never indicated for investigating symptomatic reflux. Radiological reflux can be provoked in everybody if the radiologist tries hard enough by tipping a patient head-down on the X-ray table. A hiatus hernia is not a diagnosis (below).



(Reproduced with permission from Schiller K et al. A Colour Atlas of Gastrointestinal Endoscopy. Chapman & Hall.)

Figure 3.2 *Serverity of oesophagitis at endoscopy. Normal oesophagus (a). The Severity of oesophagitis is most usefully graded by the Savary-Miller dassification: grade 1, erythema and early erosive (c); grade 3, circumferential erosions; grade 4, chronic mucosal lesions such as ulcers (d) or Barrett's oesophagus (e).*

When to refer for endoscopy or to outpatients

The majority of patients with gastro-oesophageal reflux can be managed in primary care without referral or investigation. Referral for *open-access endoscopy* (if available) is usually appropriate for patients with persistent symptoms, new onset of symptoms in those aged over 45 years, or for those needing more than two prescriptions of a proton-pump inhibitor, although the threshold depends on the local accessibility of diagnostic endoscopy (see also Table 4.6, page 61). Associated symptoms such as dysphagia, unintentional weight loss or bleeding are clear indications for urgent investigation.

Referral to outpatients is indicated for those with refractory symptoms, or those with sinister features (weight loss, anorexia, epigastric mass or anaemia). However, with the appropriate use of open-access endoscopy and one-stop dyspepsia clinics, and recognition of dysmotility as a cause of persistent oesophageal symptoms in some patients who are otherwise well, outpatient referral for reflux should be limited.

Management

Explaining the diagnosis to the patient

There is little or no relationship between the common sliding hiatus hernia and symptoms of reflux: patients with a radiologically huge hiatus hernia may have no symptoms whatsoever and patients with normal anatomy may have very severe oesophagitis. It is a myth regrettably fixed in the minds of many patients and their doctors that symptoms are due to an hiatus hernia, rather than oesophagitis or oesophageal dysmotility provoked by reflux.

A diagram outlining the oesophagus and stomach, indicating acid production and subsequent reflux to provoke oesophagitis or dysmotility, aids explanation and takes a few seconds to draw. Approaches to treatment can be added during the discussion.

Treatment strategy

Patient expectations. Addressing patients' anxieties about the implications of their symptoms and general measures to reduce reflux are more important than drugs, in most patients (Table 3.1). Explanation and reassurance may be all that is necessary, but even in these patients it is often helpful to alleviate symptoms.

Medical treatment. If general measures alone are insufficient, drug treatment is indicated. There is controversy about the best approach, but proton-pump inhibitors (PPI) are unequivocally the most effective treatment and are best given in the morning. However, at the first presentation liquid alginates appear to be more cost-effective than acid suppression with H2-receptor antagonists, as up to 50% respond equally well to either. Consequently, a stepped-care approach is usually best tailored to the individual patient, beginning with the simplest and cheapest measures and adjusting the treatment according to response (Figure. 3.3).

Alginates (such as Gaviscon™ or Gastrocote™) often provide symptomatic relief. No further treatment is necessary in up to 50% of patients at a second consultation. Alginates are best taken after meals

Table 3.1 General measures to reduce reflux

- Reduce fat intake (fat promotes reflux)
- Weight reduction (redusing diet: p. 204)
- Raise the bedhead by 10 cm, using blocks (for nocturnal symptoms)
- Small, regular meals
- Check that dentures fit so that food can be properly chewed
- Allow 3 hours between last meal and retiring at night
- Avoid hot drinks or alcohol before bed
- Change or avoid drugs that provoke symptoms or alter oesophageal motility (NSAIDs, nitrates, tricyclic antidepressants, theophylline compounds)

- Avoid drugs that damage the oesophageal mucosa (slow-release potssium)
- Stop smoking (evidence unfortunately equivocal!)
- Use antacids or alginates (Gaviscon™, Gastrocote™) for symptomatic relief

and at bedtime; they work by forming a floating, viscous layer on top of gastric contents and present a physical barrier to reflux. Formation of this raft, however, requires a low pH, so combination with acid-suppressive measures is theoretically inappropriate.

Prokinetic drugs (such as cisapride 10–20 mg twice daily, metoclopramide or domperidone 10 mg three times daily) accelerate oesophageal clearance of acid and gastric emptying, as well as increasing lower oesophageal sphincter pressure. They are about as effective as modest doses of H2-receptor antagonists at relieving symptoms and healing mild oesophagitis.

Acid suppression is the mainstay of treatment for persistent symptoms. Virtually all trials have been conducted in patients with *endoscopic* oesophagitis, which represents a minority of those with gastro-oesophageal reflux. *H2-receptor antagonists* (such as cimetidine 800–1600 mg/day, or ranitidine 300–600 mg/day, famotidine or nizatidine, best given after supper rather than at night) are effective for minor degrees of oesophagitis. Response is inversely proportional to the severity of oesophagitis. Combination with prokinetic agents is better than either alone, but these are more expensive and less effective than *proton-pump inhibitors*. Lansoprazole 30 mg/day, omeprazole 20–40 mg/day or pantoprazole 40 mg/day provide symptomatic relief within days and heal 95% of erosive oesophagitis within 4 weeks. (Pantoprazole is limited in the UK to 8 weeks' continuous therapy.) Otherwise, there is no significant difference in the side-effect profile of the proton-pump inhibitors and in countries (including the UK and USA, many European countries and Australia) where lansoprazole or omeprazole have been granted a long-term product licence, the choice is largely dictated by cost.

Long-term treatment

Intermittent treatment of recurrent symptoms is often necessary. Symptomatic erosive oesophagitis represents a small proportion of patients with reflux, but relapses within 6 months in 80% on no treatment, 40% on ranitidine 300 mg or omeprazole 10 mg daily, and 15% on omeprazole 20 mg daily.

Continuous treatment may be considered for patients with mild oesophagitis and frequent, recurrent symptoms, with cisapride 10 mg twice daily, ranitidine 300 mg after supper, omeprazole 10 mg, or lansoprazole 15 mg in the morning. The idea that 'maintenance therapy' requires a lower dose than 'healing therapy' is probably illogical. Those patients whose oesophagitis remains in remission on 10 mg omeprazole daily almost certainly would have healed on this dose in the first place. Although it is reasonable to start with a dose known to heal about 95% of cases of oesophagitis and to tailor the dose later, the term 'continuous' rather than 'maintenance' treatment is preferable. Higher doses of omeprazole (20–40 mg daily) are indicated for patients with confluent oesophagitis, a peptic stricture or Barrett's oesophagus (p. 43). There are no

data on lansoprazole for these conditions, but there is no reason to suspect that it is any less effective than omeprazole.

Concerns about long-term sequelae of proton-pump inhibitors may well be unfounded, but post-marketing surveillance continues. Accelerated gastric fundal mucosal atrophy, or even metaplasia, in patients with *Helicobacter pylori* is a particular area of concern, and interference with vitamin B12 absorption, intestinal bacterial overgrowth, or hypergastrinaemia with G-cell hyperplasia are others. Eradication therapy before long-term treatment for those with *H. pylori,* or more careful tailoring of dose during long-term treatment, may be necessary.

Patients with bloating due to a co-existent irritable bowel, and those who are overweight and who smoke and drink, characteristically continue to have symptoms.

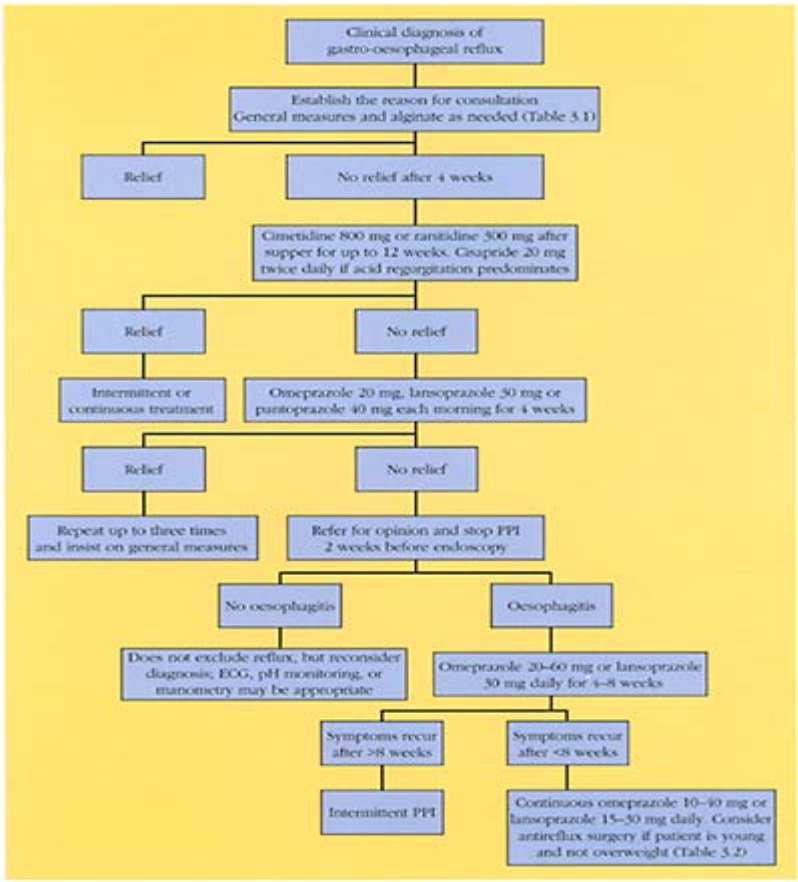


Figure 3.3 *Management plan for symptomatic gastro-oesophageal reflux.*

Continuing care by the family doctor

Frequency of review

Once the diagnosis is established, the only patients who need review are those requesting frequent repeat prescriptions of acid-suppressing medication (three or more per year) and those with a previous peptic stricture, or Barrett's oesophagus. These should probably be reviewed every 6 months.

Three *questions* provide a simple index of control, identify potential complications and assess the effect of general measures. These concern (1) the proportion of time that symptoms occur, (2) whether there is any dysphagia and (3) a review of the weight, which should be documented on each visit.

Other aspects

It is sensible to check the full blood count to exclude anaemia in patients with persistent symptoms. Anaemia should never be attributed to oesophagitis (or, worse still, to an 'hiatus hernia') without further investigation.

All family doctors are concerned about the impact of long-term proton-pump inhibitors or H2-receptor antagonists on their drug budget. Although the former are clinically indicated in patients with severe erosive oesophagitis, a previous peptic stricture, or Barrett's oesophagus, repeat prescriptions for other patients should be carefully scrutinized. The health services in some European countries require a repeat endoscopy before a second repeat prescription for a proton-pump inhibitor. General measures (Table 3.1) should be vigorously pursued if symptoms are disproportionate to the severity of oesophagitis. If abdominal bloating with eructation ('gas-bloat') is prominent, then treatment for an irritable bowel (p. 80) may be beneficial.

Hospital visits

Assessment

The duration and character of symptoms, any atypical features, or the presence of dysphagia should be recorded, together with the weight. Specific questions concerning symptom pattern, eating habits, alcohol intake and response to drug therapy may identify general measures that can be pursued, before reviewing results of previous investigations.

Further investigations

As there is poor correlation with symptoms, *endoscopy* is the only way of assessing the severity of oesophagitis or detecting Barrett's oesophagus, but there is currently no evidence that early diagnosis alters the prognosis (p. 44). Although a case can be made from published data not to subject to endoscopy any patients with uncomplicated symptomatic reflux, many patients are referred to outpatients with a view to endoscopy.

In patients describing reflux incidental to other medical conditions, it may help in management to have an objective assessment of the severity of oesophagitis.

A *chest X-ray* is necessary if a cough or weight loss is present, to look for evidence of aspiration or a bronchial malignancy. *Monitoring of pH* and *oesophageal manometry* should be performed if surgery is being considered, both to confirm that reflux is the cause of symptoms and to exclude a motility disorder that will impair the results of antireflux surgery. Occasionally, these investigations are necessary when it is difficult to distinguish symptomatic reflux from other causes of chest pain, but they are not part of routine management.

Frequency of review. Patients with uncomplicated reflux oesophagitis can be discharged to the care of their family doctor with advice on general measures and intermittent acid suppression to control symptoms. So, too, can patients with a peptic stricture after dilatation, with the advice to remain on a proton-pump inhibitor long term and to contact the endoscopy unit directly (give the patient the telephone number) if dysphagia recurs.

Patients in whom surgery may be an option should be reviewed (every 3–6 months) until a decision is reached. Those with Barrett's oesophagus should usually remain under endoscopic review (p. 43) and on long-term omeprazole 40 mg daily.

Indications for surgical referral. Surgery is rarely indicated. Laparoscopic antireflux surgery currently has risks similar to those with open procedures: these include lack of efficacy, postoperative stricture, vagal denervation, inability to belch, and splenic or oesophageal damage. Mortality is about 1%, which is a factor to be considered, but results are good in well-selected patients. With these caveats, surgery by an experienced surgeon should be considered if the criteria in Table 3.2 are met. Successful antireflux surgery leads to a significant reduction in the need for proton-pump inhibitors and may be cost-effective for young patients needing continuous treatment, although results of long-term follow-up are scanty.

Special situations and prognosis

Oesophageal stricture

The history and investigation of patients presenting with dysphagia is covered in chapter 2 (Figure 2.5, p. 27). A benign oesophageal stricture due to reflux may need to be dilated on more than one occasion, but maintenance omeprazole 20–40 mg daily reduces the

Table 3.2 Selection of patients for antireflux surgery

- Severe symptoms despite all medical treatments vigorously applied (especially if there is volume reflux, with acid regurgitation of waterbrush)
- 24 hr pH monitoring provides objective evidence of severe reflux
- Oesophageal dysmotility has been excluded by manometry
- Age <60 years

frequency, as well as being cost-effective. To save time, patients should be told to make appointments directly with the endoscopy unit if dysphagia recurs. Recurrence of symptoms less than a month after dilatation raises the possibility of a carcinoma.

Oesophageal dysmotility

Oesophageal dysmotility accounts for up to 50% of patients referred with oesophageal symptoms. The *presenting features* are chest pain or dysphagia for both liquids and solids; these symptoms are often intermittent or exacerbated by hot and cold liquids. Chest pain may mimic cardiac pain and be provoked by stress, but a persistent ache between severe episodes usually distinguishes it from angina. Abdominal bloating is common, and this should suggest oesophageal dysmotility as a cause of a patient's symptoms. Co-existent symptoms of an irritable bowel, anxiety or depression are also frequent, but weight loss is notably absent.

Symptoms are often disproportionate to the results of *investigations*. Endoscopy may be normal or show mild oesophagitis. A barium swallow is rarely helpful, as symptoms are episodic. It may show a corkscrew appearance in severe cases of oesophageal spasm and helps to exclude achalasia, but oesophageal manometry is better. High-amplitude aperistaltic contractions without a demonstrable organic lesion indicate diffuse oesophageal spasm, which is rare. More often, manometry is itself unremarkable or shows only minor evidence of disordered peristalsis. If the symptoms are characteristic, a diagnostic label of oesophageal dysmotility may help the patient.

Treatment is difficult. Reassurance that the pain is not cardiac is essential, also explaining that the drugs prescribed are often used for angina. A proton-pump inhibitor (lansoprazole 30 mg, omeprazole 20–40 mg, or pantoprazole 40 mg daily) should be tried first, since dysmotility may be provoked by acid reflux. Isosorbide dinitrate 5–10 mg sublingually four times daily or nifedipine 5–10 mg three times daily are adjunctive treatments, since they may relax oesophageal smooth muscle. Unfortunately, the response is unpredictable and sideeffects are common. Prokinetic agents can make symptoms worse, because they may exacerbate oesophageal spasm. Empirical treatment with amitriptyline in low dose (10–75 mg daily), imipramine (10–50 mg daily) or Motival (1–3 tabs daily) more frequently help, despite their adverse effect on oesophageal emptying.

Barrett's oesophagus

Barrett's oesophagus is a histological diagnosis, *defined* as the presence of columnar-lined epithelium with intestinal metaplasia proximal to the gastro-oesophageal junction. It is caused by gastrooesophageal reflux over many years, which has often caused surprisingly few symptoms. The significance is that oesophageal carcinoma develops in 2–5% and dysplasia in 10% over 5 years. The risk of carcinoma is broadly related to the length of Barrett's oesophagus, being more common when the length exceeds 5 cm. Multiple endoscopic oesophageal biopsies are needed to exclude dysplasia at diagnosis and subsequent follow-up.

The only *treatment* that has been shown to induce regression is omeprazole 40 mg daily, and long-term treatment is usually indicated. The current consensus is that endoscopy should be repeated to rebiopsy after 6–12 months' treatment in patients who

are candidates for surgical resection if dysplasia is identified. If foci of high grade dysplasia are found, oesophagectomy should be considered, because 60% will develop invasive adenocarcinoma.

Surveillance endoscopy, however, has not yet been shown to reduce mortality. Despite this, it seems reasonable to continue vigorous antisecretory therapy and repeat endoscopy every 6 months in patients with low-grade dysplasia, and every 24 months in other patients with Barrett's, for as long as they remain candidates for surgery. It must be recognized, however, that by far the commonest presentation of carcinoma complicating Barrett's oesophagus is in patients who present with symptoms from the carcinoma itself.

Prognosis

In a 10-year study conducted before effective acid suppression was available, 80% of patients without erosive oesophagitis responded to simple medical measures. For patients with erosive oesophagitis, most have symptoms for 1–3 years before seeking medical help, but then continue to have chronic relapsing symptoms. After oesophagitis has been healed with omeprazole, 80% of patients develop recurrent oesophagitis within 6 months (see above).

On the other hand, there is neglible mortality from reflux oesophagitis, which is why it is wise to have a high threshold for antireflux surgery at present. There are no reliable figures on the incidence of peptic strictures or Barrett's oesophagus, as only a minority of patients with reflux come to medical attention (Figure 3.1). Of those who are investigated, the prevalence of a peptic stricture or Barrett's oesophagus is about 10%.

Summary

General	Reflux is reliably diagnosed clinically in patients with heartburn and acid regurgitation. Symptoms are caused by oesophagitis or oesophageal dysmotility and not a hiatus hernia.	
Referral criteria	**Outpatients**	Reflux with dysphagia, anorexia, anaemia or weight loss (urgent). Refractory or atypical symptoms.
	Endoscopy	More than two prescriptions/yr for a proton-pump inhibitor. New symptoms at age >45-50 years.
Clinical	Heartburn: retrosternal burning or discomfort after meals, stooping or lying down Acid regurgitation: effortless return of contents into the pharynx Odynophagia: pain on swallowing, often indicates oesophagitis Dysphagia: difficulty in swallowing solids suggests a stricture, but for liquids indicates dysmotility.	
Treatment	**General measures**	**Drugs**
	Reduce fat intake. Weight reduction. Raise the bedhead for nocturnal	Alginates alone for up to 4 weeks; then cimetidine 800 mg/day or ranitidine 300 mg/day for up to 12 weeks. Cisapride 20 mg twice daily for regurgitation; if refractory, give lansoprazole 30 mg/day or omeprazole 20–40 mg/day for up to 12 weeks; then

	symptoms. Small, regular meals. Avoid hot drinks or alcohol before bed. Avoid drugs that adversely affect oesophageal motility. Antacids or alginates for symptomatic relief.	endoscopy if symptoms persist or recur.				

Continuing treatment

Give intermittent therapy if possible, except for peptic strictures orBarrett's oesophagus.

	No oesophagitis	**Oesophagitis**	**Peptic stricture or Barrett's**			
				General measures.Alginates as needed. Treat irritable bowel if present.	Cisapride 20–40 mg/day if mild, or cimetidine 400 mg after supper, or ranitidine 300 mg after supper or omeprazole 10–40 mg or lansoprazole 15–30 mg/day.	Omeprazole 40mg/day long term.
Indications for surgery		Severe symptoms despite all medical treatments vigorously applied. 24-hour pH monitoring provides objective evidence of severe reflux. Oesophageal dysmotility has been excluded by manometry.				

Key points

- Gastro-oesophageal teflux is the commonest cause of dyspepsia in the community and can be reliably diagnosed on the history.
- A normal endoscopy does not exclude the diagnosis of reflux, but indicates that there are no complications such as oesophagitis, stricture or Barrett's oesophagus.
- Symptomatic treatment with general measures to reduce reflux, alginates and acid suppression is appropriate for the majority of patients, without referral or

investigation.
- Patients with 'alarm' symptoms or signs (weight loss, dysphagia, anorexia, anaemia) should be referred directly to outpatients.

- Referral for open-access endoscopy (if available) is appropriate for patients requiring more than two prescriptions per year of a proton-pump inhibitor to control symptomatic reflux, or new-onset dyspepsia in patients over the age of 45–50 years.
- Patients with a privious peptic stricture or Barrett's oesophagus should remain on a proton-pump inhibitor (such as omeprazole or lansoprazole) long term.

Further reading

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Chapter 4
Helicobacter pylori and peptic ulceration

Upper gastrointestinal mucosal integrity has traditionally been considered to be a balance between acid/pepsin attack and mucosal defence factors (Figure 4.1). Over the last decade, the discovery that the organism *Helicobacter pylori* is pathogenic in humans has not only altered our understanding of the aetiopathogenesis of peptic ulceration but also has fundamentally altered the way in which this disease is diagnosed and treated.

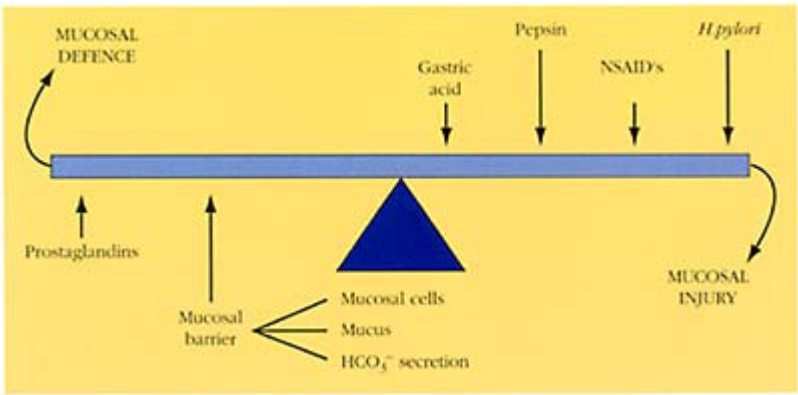

Figure 4.1 *The balance that maintains gastrointestinal mucosal integrity.*

Helicobacter pylori

Background

It has been known for decades that curved organisms that were difficult to stain with standard histological techniques were commonly found in the mucous layer of the human stomach. The perceived wisdom (possibly because of their very frequent occurrence) was that these organisms were 'commensals'. It was not until Barry Marshall first cultured *H. pylori* from human gastric biopsies and subsequently infected himself with these cultures (so fulfilling Koch's postulates) that this view was seriously challenged. We now know that *H. pylori* has a central role in the aetiopathogenesis of gastritis, of duodenal and gastric ulceration, and possibly of gastric cancer. The pathogenic mechanisms of *H. pylori* are still not fully understood.

In the developed world, *H. pylori* is found in approximately 50% of patients over the age of 50 years. The prevalence in younger people is much lower (Figure 4.2) and is unlikely to change. This is referred to as a cohort effect and is attributed to infection in childhood or adolescence, probably by the oro-faecal route. The major risk factor for infection is poor socioeconomic conditions in childhood: childhood bed-sharing is said to be a particularly strong risk factor. The relatively high prevalence of the infection in the older age-group

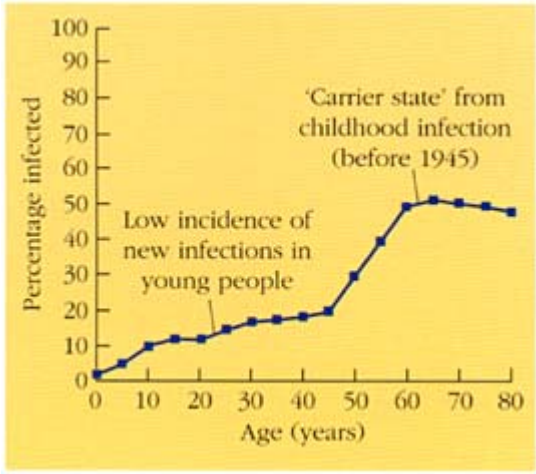

Figure 4.2 *Current prevalence of* H. pylori *infection in the USA related to age. As infection is acquired in childhood, the low prevalence at a young age is a feature of improving socioeconomic conditions in recent decades and is not expected to change (a 'cohort' effect).*

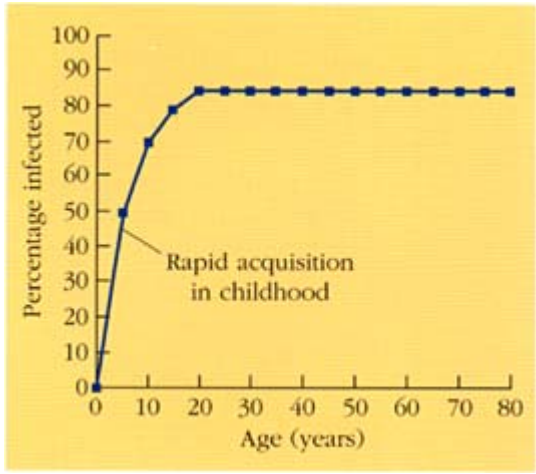

Figure 4.3 *Prevalence of* H. pylori *in developing countries. In many countries, over 85% of 20-year-olds are already infected.*

therefore reflects the socioeconomic conditions in the 1930s, 40s and 50s. Longitudinal studies on stored serum suggest that the prevalence of *H. pylori* has fallen over the last two decades in the developed world as living conditions have improved. It is notable that the incidence of peptic ulceration is also declining. In developing countries the prevalence of *H. pylori* is completely different: in many countries, over 85% of 20-year-olds are already infected (Figure 4.3).

Over 95% of patients with duodenal ulceration are infected with *H. pylori* (Figure 4.4). Eradicating the infection in such patients completely alters the natural history of duodenal ulcer disease. The yearly relapse rate in patients who have a persisting infection is around 80%, but less than 10% in those who have had *H. pylori* eradicated (Table 4.1). Gastric ulcers are also strongly associated with *H. pylori:* about 75% of patients with gastric ulcers are infected (Figure 4.4). Eradicating the organism in such patients also makes sense, and evidence is now emerging that adopting this approach alters the natural history of gastric ulcer disease in a similar manner to that of duodenal ulcer disease.

H. pylori has been classified by the US National Institutes of Health and the World Health Organization as a class 1 (definite) carcinogen. This is partly because it has definitely been implicated in rare, low-grade B-cell lymphomas of the stomach, but previous infection is also associated with a two- to five-fold increased risk of developing gastric cancer. This may

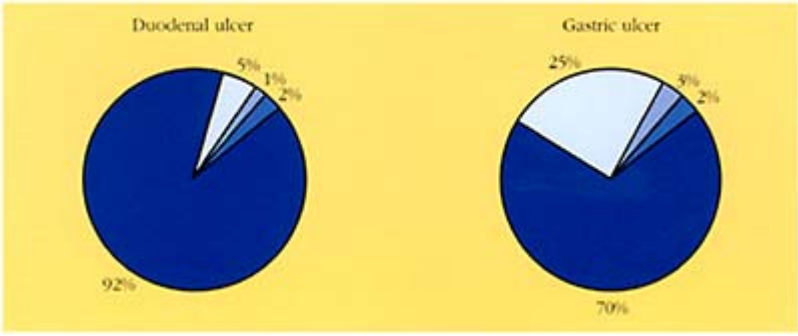

Figure 4.4 H. pylori ■ *in patients with duodenal or gastric ulceration.* H. pylori *infection is almost invariable in patients with a duodenal ulcer and is strongly associated with benign gastric ulceration.* □*, NSAID;* ■*, Cancer (Zollinger-Ellison syndrome);* ■*, other factors*.

be appreciable, but is an order of magnitude less than the association between smoking and lung cancer. It is not yet known whether eradicating *H. pylori* reduces the subsequent risk of gastric cancer.

Table 4.1 Duodenal ulcer relapse rates one year after after eradication of *H. pylori*

Study	**Relapse rate (%) in patients in whom *H. pylori* infection had been succesfully eradicated**	**Relapse rate (%) in patients with persistent *H. pylori* infection**
Rauws et al. (1990)	0	89
Graham et al. (1992)	12	95
Bayerdorffer et al. (1993)	9	64
Hentschel et al. (1993)	2	85

The vast majority of people, however, will ‘carry’ the organism throughout life without any discernible untoward effect. Why some will develop peptic ulceration

whereas most do not, is unknown. It could reflect different virulence in strains of *H. pylori,* or different genetic susceptibility in concert with other factors such as dietary nitrosamines. There is some evidence to support this view, because peptic ulceration is most strongly associated with a strain of *H. pylori* that produces a cytotoxin called cag A.

Diagnosis

The several ways of diagnosing *H. pylori* infection are shown in Table 4.2 on page 54.

Serology. Blood tests that measure serum immunoglobulin G (IgG) antibodies to *H. pylori* are not as widely available as they could be, at least in the UK. Out of 103 laboratories who responded to a postal survey, only 63% offered serum-antibody tests to family doctors. The tests are highly sensitive and specific in the young and middle-aged, but it must be realized that up to 20% false negatives occur in the over 65s, including some with gastric cancer. The sensitivity of desktop kit tests depends on how accurately the instructions are followed, but their main *advantages* are their simplicity, relatively non-invasive nature and cost (about £5). The *disadvantage* of any serological test is that it may take several years for antibodies to disappear after successful eradication therapy. This means that *H. pylori* serology has no role in monitoring the success of treatment.

H. pylori serology can aid clinical decision-making in two main ways:

- To help decide whether a patient who has had a previous peptic ulcer will benefit from eradication therapy.
- As a method for assessing whether younger patients with dyspepsia will benefit from an endoscopy. If patients aged <45–50 years are *H. pylori* negative, it is highly unlikely that endoscopy will reveal peptic ulceration as long as they are not taking non-steroidal anti-inflammatory drugs (NSAIDs). Such patients can safely be managed on clinical grounds alone.

Table 4.2 Diagnosis of *H. pylori* infection

Method		Indication
Endoscopy	■ *CLO test*	Rapid result during endoscopy; subject to sampling error.
	■ *Histology*	When biopsies taken to identify gastirtis or other pathology.
	■ *culture*	
serology		Patients with dyspepsia aged <45–50 years. Patients on long-term acid suppression. No use for confiming eradication.
Breath test		Most reliable means of identifying infection. Mainly used to confirm eradication after treatment. False negatives caused by proton-pump inhibitors.
Salivary antibodies stool culture Polymerase chain reaction		Research tools only

Endoscopy. Until serology testing became more widely available, endoscopy was a common way of obtaining a diagnosis of *H. pylori* infection. Gastric antral biopsies are obtained and *H. pylori* can be identified by a urease reaction (CLO test), histology or culture. The advantage is that endoscopy allows full evaluation of the upper gastrointestinal tract. A normal endoscopy may itself help in managing a patient. The main disadvantage, apart from the invasive nature, is that the small biopsy is subject to sampling error, so false negatives occur. Current therapy with ulcer-healing drugs also suppress *H. pylori,* which may also lead to false-negative results.

Breath tests. The most reliable non-endoscopic method for detecting *H. pylori* is the ^{13}C or ^{14}C breath test. This relies on the urease enzyme produced by *H. pylori*. Radiolabelled urea is given by mouth and if *H. pylori* is present in the stomach, ^{14}C is split from urea by the enzyme to release CO_2 and the amount of exhaled ^{14}C tracer is measured. The radiation dose from ^{14}C is less than that of a chest radiograph, while ^{13}C is a stable isotope that does not expose the patient to any radiation, but needs a spectrometric assay which is more expensive.

Breath testing is the best way of confirming eradication of the organism after therapy, although proton-pump inhibitors must have been stopped for the preceding 2–4 weeks, as they can cause a false-negative result. The test takes about 40 minutes and costs £25–£60, although the price is declining. Unfortunately, breath tests are not generally accessible to family doctors in the UK; only 8% of 103 laboratories offered an open-access service in 1995.

Treatment

Selection of patients (Table 4.3). All patients who have peptic ulcers documented by endoscopy or barium meal and who are *H. pylori* positive should receive eradication therapy. Patients who are on long-term 'maintenance' treatment with ulcer-healing drugs (such as H2-receptor antagonists) should have their *H. pylori* serology checked, and eradication therapy prescribed if this is positive, because it will often be possible to stop these drugs.

There is no relationship between gastro-oesophageal reflux and *H. pylori*. No symptomatic benefit can be expected in eradicating the organism in patients with reflux and the main consequence of treating such patients with eradication therapy is to give the treatment a bad name.

Table 4.3. *H. pylori* eradication: patient selection

Proven benefit	Uncertain value	No effect on symptoms
Duodenal ulcer	Non-ulcer dyspepsia	Gastro-oesophageal reflux
Gastric ulcer	Deceasing risk of gastric cancer Positive serology without symptos	

The jury is still out regarding the efficacy of eradication therapy for patients with non-ulcer dyspepsia who are *H. pylori* positive. There have been 16 double-blind trials on this

subject to date, eight of which showed eradication to be beneficial and eight of which did not. A large Medical Research Council trial is currently in progress in Glasgow, which should provide a definitive answer to this question in a couple of years.

The question of whether asymptomatic patients with *H. pylori* infection should receive eradication therapy remains open. There is some logic in prescribing a simple 1-week course of treatment for a potential pathogenic organism, but no scientific justification for a 'shoot on sight' policy. For instance, it is not known whether eradicating the organism in a patient who has harboured the organism for decades lessens the risk of gastric cancer and there are theoretical reasons why it may not. Furthermore, antibiotic therapy carries a small, but definite, risk in terms of side-effects. There have been several reports of pseudomembranous colitis following eradication therapy. In addition, indiscriminate use of eradication therapy will promote antibiotic-resistant strains of *H. pylori,* and metronidazole resistance is already common in some countries.

***H. pylori* eradication regimes.** Although *H. pylori* is sensitive *in vitro* to a range of antibacterials, including clarithromycin, amoxycillin, metronidazole and bismuth, single-agent therapy is not an effective way of clearing the organism. At least two or three antibiotics must be used concurrently to eradicate the organism *in vivo,* usually with powerful acid suppression.

A bewildering array of *H. pylori* eradication regimes are now available, many of which claim eradication rates of 80–90% in controlled trials. Clinical experience of many of these regimes, however, has been rather disappointing, with eradication rates nearer 50%. The reasons for this discrepancy probably relate to differences in antibiotic resistance between populations and to compliance. Some of the regimes have required 15–20 tablets to be taken 3–4 times daily for 2 weeks, and side-effects are common. This particularly relates to the bismuth/amoxycillin or tetracycline/metronidazole regimes, which are no longer recommended.

Dual therapies have been advocated as a way of addressing the problem of compliance. Examples include omeprazole 20 mg twice daily and amoxycillin or clarithromycin 500 mg three times daily for 2 weeks, or ranitidine bismuth citrate 400 mg twice daily with clarithromycin 500 mg twice daily for 2 weeks. The problem is that the eradication rate is variable (although around 95% in recent studies), despite improved compliance and side-effect profile.

More recently, *short-course triple therapy* has become generally accepted (Table 4.4). Examples include omeprazole 20 mg, clarithromycin 250 or 500 mg and metronidazole 400 mg, all twice daily for 1 week. Lansoprazole 30 mg twice daily can be substituted for omeprazole and tinidazole 500 mg twice daily for metronidazole without loss of efficacy. Another regime is omeprazole 20 mg (or lansoprazole 30 mg) twice daily, amoxycillin 500 mg and metronidazole 400 mg both three times daily for 7–10 days. Such regimes reliably clear the organism in 84–95% of patients in clinical practice. Compliance is excellent and side-effects few, apart from a metallic taste or nausea from metronidazole. Omeprazole 20 mg (or lansoprazole 30 mg), amoxycillin 500 mg and clarithromycin 500 mg all twice daily is a further alternative which avoids metronidazole.

Table 4.4 Short-Course triple-therapy eradication regime for *H. pylori*

Drug	Dose (mg)	Frequency	Duration
Omeprazole	20		
Clarithromycin	500	all twice daily	all for 1 week
Metronidazole	400		
Alternatives			
Lansoprazole	30	twice daily in place of omeprazole	
Amoxycillin	500	three times daily in place of clarithromycin or twice daily in place of metronidazole	
Tinidazole	500	twice daily in place of metronidazole	

Presentation

Establishing the diagnosis

In the UK, about 4% of all consultations with family doctors are for dyspepsia. Factors influencing the decision to consult are discussed in chapter 2 (p. 14). Although this represents a relatively small proportion of patients, it uses considerable resources. Ulcer-healing drugs are the most expensive of all categories in the primary care drug budget, leaving aside expenditure by individuals on over-the-counter medication and the impact of days lost from work.

Dyspepsia is a poorly defined term that can relate to any symptoms arising from the upper gastrointestinal tract. It usually refers to epigastric pain occurring after meals, but can include nausea, early satiety, bloating and heartburn. Although retrosternal burning pain and regurgitation of acid with a postural element have a high predictive value for gastro-oesophageal reflux disease (chapter 3), the traditional teaching that duodenal or gastric ulcers can be diagnosed from the history is no longer tenable. Symptoms are often a poor pointer to underlying pathology and the situation is further complicated by studies that show that up to 1% of a Norwegian population have an asymptomatic peptic ulcer.

The diagnosis of peptic ulceration is made by either endoscopy or barium meal (Table 4.5). There is no doubt that the sensitivity and specificity of endoscopy is superior to that of barium studies in making the diagnosis; furthermore, endoscopy provides an opportunity to take biopsies. Unfortunately, in the UK the choice of procedure may depend on local factors, such as the waiting time for endoscopy.

When to refer for endoscopy or to outpatients

There is very poor correlation between the dyspeptic history and subsequent endoscopic findings. For example, duodenal ulcer pain as classically described in textbooks (hunger pain, worse in the early hours of the morning) is actually fairly uncommon. Moreover, referral patterns are fundamentally affected by the availability and ease of access to diagnostic services. Only 10% of patients attending their family doctor with dyspepsia will be referred for hospital consultation of investigation, and universal investigation for dyspepsia is neither desirable nor affordable.

Table 4.5 Endoscopic diagnoses in dyspepsia for all age groups

Normal	30%
'Gastritis', 'duodenitis' or 'hiatus hernia' (see text)	30%
Oesophagitis	10–17%
Duodenal ulcer	10–15%
Gastric ulcer	5–10%
Gastric cancer	2%

It is therefore difficult to give hard and fast rules about who should be referred to endoscopy. There is general agreement that *dyspepsia in association with alarm symptoms or signs at any age* (unintentional weight loss, dysphagia, vomiting, previous gastric ulcer, NSAID use, previous gastric surgery), or any patient *over the age of 45–50 years with recent-onset dyspepsia,* should be referred for endoscopy. There is also general agreement that endoscopy is *inappropriate* in patients known to have a duodenal ulcer who have responded symptomatically to treatment, or who are less than 45–50 years old and are asymptomatic after a single episode of dyspepsia, or have recently undergone a satisfactory endoscopy for the same symptoms.

In patients under the age of 50 with uncomplicated dyspepsia, *H. pylori* serology can be helpful in selecting patients for endoscopy. If *H. pylori* serology is negative, it is exceedingly unlikely that an endoscopy will show a peptic ulcer or gastric cancer. Several centres around the UK are using serology testing in patients less than 45–50 years old to focus their endoscopic activity and this approach has been recommended in the management guidelines for dyspepsia by the British Society of Gastroenterology.

Endoscopy has been shown to reduce prescribing costs, decrease consultation rates and lead to management changes, even in patients in whom no significant disease is found. The assumption is that the procedure provides reassurance to patients and doctors, allowing more rational prescribing. As similar benefits have been reported following negative *H. pylori* serology without endoscopy in those in whom endoscopy would otherwise have been performed, the practice of *H. pylori* serology testing in dyspeptic patients under 45 before referring for endoscopy is to be encouraged. As yet, however, there is no evidence to support treatment of young dyspeptic people with positive *H.*

pylori serology without any further investigation, and this is not condoned. This is because less than 10% of dyspeptic patients with positive serology will have a duodenal or gastric ulcer.

Table 4.6 Indications for diagnostic endoscopy

Appropriate

1. Any dyspepic patient with alarm symptoms or signs:

   Unintentional weight loss

   Iron deficiency anaemia

   Dysphagia (after barium swallow) or odynophagia

   Persistent vomiting

   Previous gastric ulcer

   Previous gastric surgery

   NSAID therapy

   Epigastric mass

   Suspicious barium meal

   Epigastric pain severe enough to hospitalize patient

2. Any patient over the age of 45–50 with recent onset dyspepsia
3. Patient under age of 45–50 with troublesome dyspepsia who are positive for *Helicobacter pylori* on non-invasive testing (serology or breath test)

Inappropriate

1. Patients known to have duodenal ulcer who have responded symptomatically to treatment
2. Patients under 45–50 asymptomatic after a single episode of dyspepsia
3. Patients who have recently undergone a satisfactory endoscopy for the san for the symptoms

Management

Duodenal ulcer disease

Newly diagnosed duodenal ulcer (Figure 4.5). About 95% of patients with a newly diagnosed duodenal ulcer will have *H. pylori,* unless they are taking NSAIDs. This will usually have been confirmed by biopsy at endoscopy, but *H. pylori* serology can be checked if this has been omitted, or in those with a duodenal ulcer diagnosed by barium meal. It must be remembered, however, that there is a false-negative rate of up to 20% for *H. pylori* serology in the elderly and an argument can be made for assuming *H. pylori* infection in newly diagnosed duodenal ulcers in the absence of NSAIDs. Rare causes of duodenal ulceration (Crohn's disease, Zollinger-Ellison syndrome, lymphoma) tend to cause recurrent or post-bulbar ulcers.

Patients who are *H. pylori-positive* should receive a course of ulcer-healing therapy *and* a course of eradication therapy. Ulcer-healing therapy means an H2-receptor antagonist for 6 weeks (cimetidine 800 mg or ranitidine 300 mg as a single dose in the evening) or a proton-pump inhibitor for 4 weeks (omeprazole 20 mg, pantoprazole 40 mg or lansoprazole 30 mg once daily). The latter is usually more convenient, since proton-pump inhibitors are part of triple-therapy regimes for *H. pylori* eradication and may be more cost-effective than H2-receptor antagonists.

Current optimum regimes for *H. pylori* eradication are as follows: either omeprazole 20 mg, clarithromycin 250 mg (or 500 mg) and tinidazole 500 mg (or metronidazole 400 mg), all twice daily for 1 week, or omeprazole 20 mg twice daily, amoxycillin 500 mg three times daily and metronidazole three times daily, all for 1 week (Table 4.4, page 58). These regimes are well tolerated and side-effects (metallic taste in the mouth, nausea, diarrhoea, skin rash) are uncommon. Recent evidence suggests that lansoprazole can be substituted for omeprazole. Alcohol should be avoided because of the metronidazole (Antabuse-like effect) and smoking discouraged.

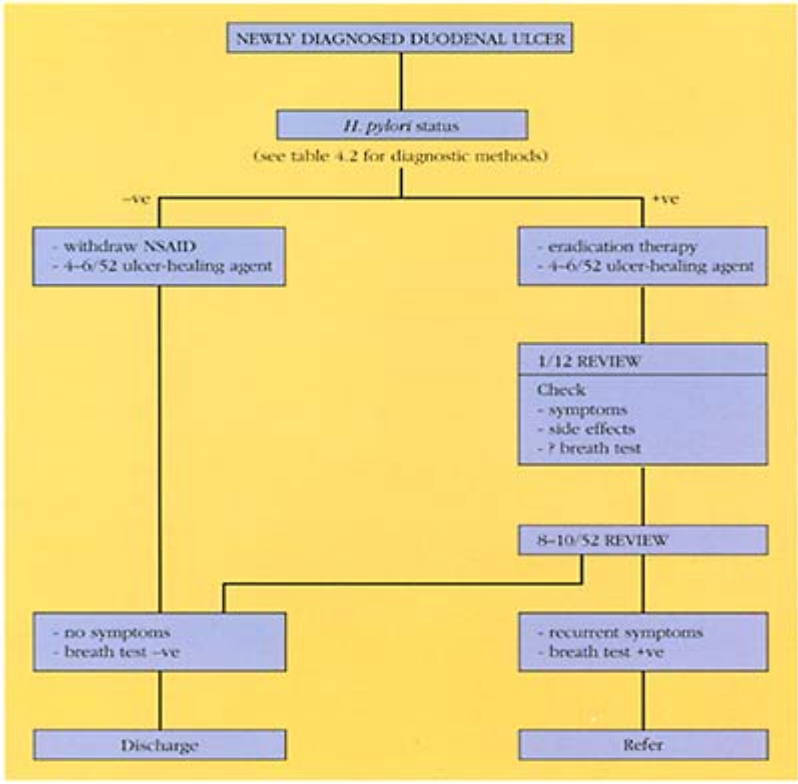

Figure 4.5 *Algorithm for the management of duodenal ulceration.*

Patients should be *reviewed by their family doctor at 1 month* to check on progress and side-effects and to decide whether the patient should have a breath test to confirm eradication. In an ideal world, all patients would have eradication confirmed, but in reality it is more practical to limit this to patients who have had a complication (such as haemorrhage) or who continue to have symptoms. Access to breath tests may be becoming more widely available, but is still usually restricted in the UK to patients under consultant follow-up. Breath tests should be performed at least 4 weeks after eradication therapy and not when patients are taking a proton-pump inhibitor, antibiotics, or bismuth compounds, which can all lead to a false-negative result because *H. pylori* may be suppressed rather than eradicated.

One *further review* a month later is sensible. At this time patients will have been off treatment for several weeks. Many will be asymptomatic and breath-test negative; these can be considered 'cured', because relapse or reinfection with *H. pylori* is very uncommon and such patients need no further follow-up. Some will have continuing symptoms or be breath-test positive, indicating continuing infection. Such patients are probably best referred to a gastroenterologist for further advice.

Patients who have *continuing infection despite triple therapy* are uncommon and may be difficult to treat. A further course of triple therapy, emphasizing the importance of compliance, is usually the first approach. Persistent infection in spite of this may need quadruple—or even quintuple—antibacterial and acid-suppressive therapy to clear the organism, sometimes after culture of antral biopsies to determine *in vitro* antibacterial sensitivities.

Patients who have continuing symptoms may have gastro-oesophageal reflux, irritable bowel syndrome, gall stones or pancreatic pain or, very rarely, persistent ulceration due to Zollinger-Ellison syndrome, Crohn's disease or lymphoma. These can be tricky issues to sort out and such patients are best referred to a gastroenterologist.

Recurrent symptoms from a previously diagnosed duodenal ulcer (Figure 4.6). There is a large cohort of patients who have had chronic duodenal ulcer disease before the importance of *H. pylori* was appreciated. Many have continued on 'maintenance' ulcer-healing agents. Such patients should have serology tests for *H. pylori* and should be given a course of eradication therapy if positive. Given the false-negative rate for *H. pylori* serology in older patients, it may make more sense to treat such patients without bothering to test for antibodies.

Following eradication therapy, acid-suppressive therapy can be stopped except in patients taking concomitant NSAIDs. A gratifying majority will come back for review saying that they have never felt better. This is the clearest indication that we have moved into a new pattern in the treatment of peptic ulcer disease: it is now possible to cure this chronic disease, rather than simply to suppress it with long-term ulcer-healing agents.

In common with patients with newly diagnosed duodenal ulcer disease, a proportion (about 20%) report recurrent or persistent symptoms at review, once acid-suppressive therapy has been stopped. Most will have reflux or an irritable bowel, but patients with recurrent symptoms are probably best referred for further evaluation by a gastroenterologist.

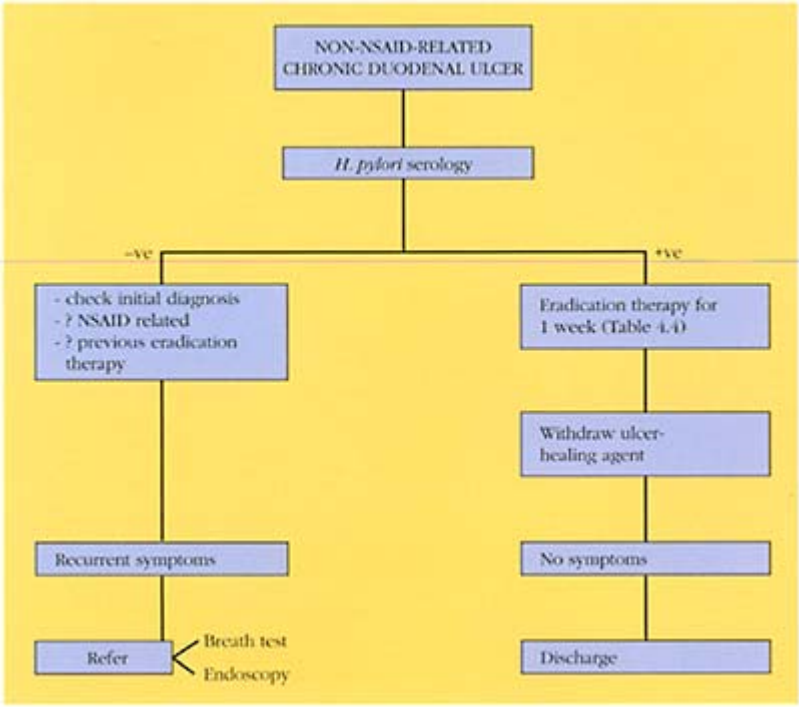

Figure 4.6 *Algorithm for the management of patients with symptoms from a previously documented duodenal ulcer.*

Gastric ulcer disease (Figure 4.7)

The *principles* of managing gastric ulcer disease are very similar to those of duodenal ulcer disease, with two important differences. First, a small proportion of patients will have a gastric cancer in what initially looks like a benign gastric ulcer. For this reason, all patients with a gastric ulcer must have a repeat endoscopy after 6–8 weeks of treatment to check healing and to take further biopsies to exclude carcinoma. Secondly, gastric ulcer is less strongly associated with *H. pylori* (70–80%) and a significant minority of patients will have NSAID-related ulcers. Such patients should have NSAIDs stopped if possible (see below, p. 68).

In terms of *shared care,* therefore, patients should be seen by their family doctor 1 month after initial endoscopy. The purpose of this visit is to ensure that patients are receiving an ulcer-healing agent (H2-receptor antagonist for 8 weeks or proton-pump inhibitor for 4 weeks) and have taken eradication therapy if they are *H. pylori* positive. Furthermore, the visit ensures that the follow-up endoscopy has been booked and that NSAIDs have been withdrawn, if possible.

The *follow-up endoscopy* checks ulcer healing and allows biopsies to be taken from the edge of an unhealed ulcer, as well as from the antrum to look for persistent *H. pylori* infection. If the ulcer has healed and antral biopsies confirm eradication, the patient can safely be discharged.

Patients with an *unhealed ulcer* should have their histological samples closely scrutinized. It may be necessary to increase the dose

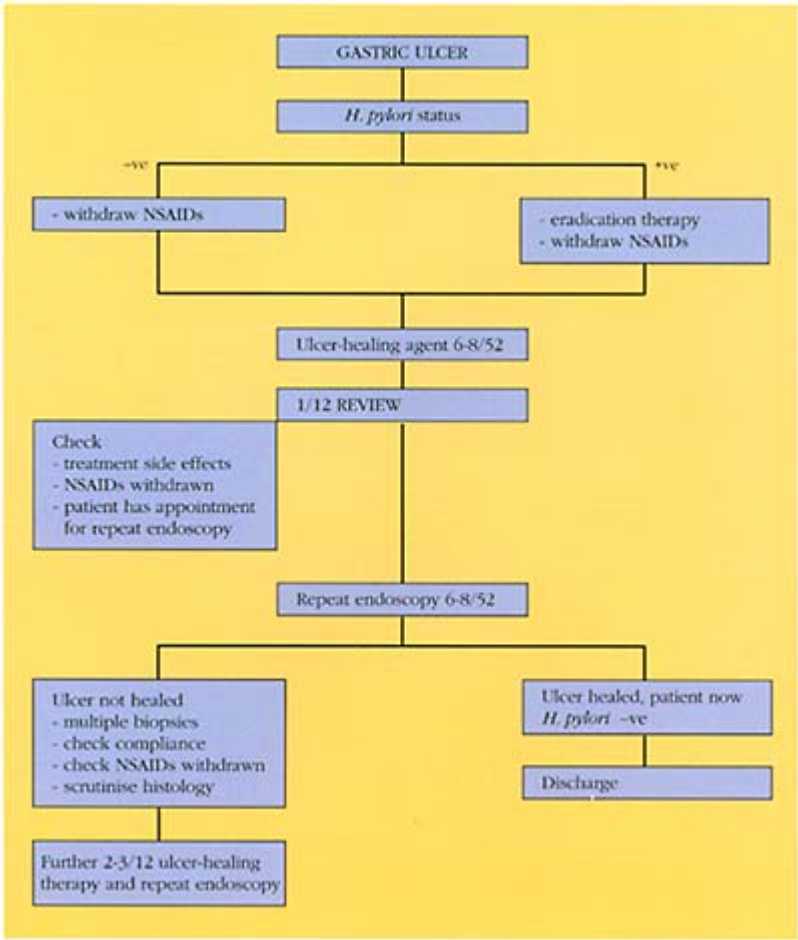

Figure 4.7 *Algorithm for the management of gastric ulceration.*

of ulcer-healing agent after checking compliance and that NSAIDs have been stopped. It may be necessary to give a further course of eradication therapy. Such patients inevitably need a further endoscopy and are best managed by a gastroenterologist.

NSAID-induced peptic ulceration

About 5% of duodenal ulcers and 20–25% of gastric ulcers are related to the ingestion of NSAIDs. All patients who have a documented peptic ulcer should have a careful drug history taken, including questions about over-the-counter medications. Different NSAIDs have differing ulcerogenic potential. Prophylactic aspirin therapy appears to increase the risk of peptic ulcer, but the risk is less than for other NSAIDs.

Following diagnosis, NSAIDs should be withdrawn, if possible, and a 4–6-week course of ulcer-healing medication (such as omeprazole 20 mg daily, or lansoprazole 30 mg daily) started. If the patient is also *H. pylori* positive, a course of eradication therapy should be given concomitantly. Patients with gastric ulcers should have a further endoscopy after 6–8 weeks in the standard way. For patients with a duodenal ulcer the decision to repeat endoscopy is more difficult, but it is often appropriate to do this if NSAIDs are needed long term. This may best be performed once NSAIDs have been reintroduced, because NSAID-related ulcers are frequently asymptomatic until bleeding occurs.

In a few patients (such as those with severe rheumatoid arthritis) it will not be possible to stop NSAIDs without an unacceptable increase in joint pain or limitation of mobility. Such patients should be monitored closely by a gastroenterologist and may require high doses of proton-pump inhibitors, which are superior to H2-receptor antagonists in this situation. Repeat endoscopy to confirm healing is usually advisable.

‘Gastritis’ and ‘duodenitis’

These terms frequently appear on endoscopy reports, but the correlation of endoscopic appearance with either symptoms or histological abnormality is poor. The endoscopist usually means that the mucosa looks a bit redder than normal—and it would be far better if this was stated rather than using quasi-diagnostic terms. When there is a visible break in the mucosal integrity (erosion or erosive duodenitis), however, it is reasonable to consider this as part of the spectrum of duodenal ulcer disease and to treat it accordingly.

Consequently, an endoscopic report of ‘gastritis’ or ‘duodenitis’ should be interpreted as unremarkable unless supported by histological evidence of inflammation. Even the presence of inflammation does not correlate with symptoms or predict a response to *H. pylori* eradication therapy. Symptomatic remedies can be tried until evidence suggests alternative specific treatments. Expensive antisecretory treatment cannot be justified if cheaper alternatives work. Other causes of symptoms (biliary, pancreatic, dysmotility) should be considered and investigated as appropriate.

Special situations

Dyspepsia with a normal endoscopy

This situation is sufficiently common to make it difficult to justify the epithet ‘special’, but it is convenient to consider the problem here. A ‘normal’ endoscopy includes those in which there is symptomatic reflux with no macroscopic mucosal abnormality, or an incidental finding of a hiatal hernia. The cause of symptoms in these patients is usually

unclear. There are likely to be multiple factors involved, including disordered motility, *H. pylori* infection and psychological problems. Treatment should be symptomatic, but is often disappointing.

The dyspepsia working party of the British Society of Gastroenterology has agreed a consensus approach to management. This includes:

- stopping NSAIDs if possible and considering other drugs as provoking agents;
- general reassurance, since this alone may be sufficient;
- assessing whether symptoms are acid-related by giving a 2 week course of a proton-pump inhibitor in adequate dose (omeprazole 40 mg or lansoprazole 30 mg daily), then titrating treatment to cheaper alternatives or considering cisapride if there is no response;
- investigating the biliary tree by ultrasound;
- repeating investigations if serious symptoms develop.

The working party specifically did not recommend eradication of *H. pylori* outside of clinical trials until more information is available. Many clinicians, however, would offer eradication therapy whilst explaining to the patient that infection may very likely be unrelated to their symptoms and the response is unpredictable.

Peptic prophylaxis in NSAID users

NSAIDs are commonly associated with gastroduodenal injury. Most patients taking NSAIDs will have endoscopic evidence of gastric erosions, even if asymptomatic. Of rheumatology patients taking NSAID therapy, 10–20% will have evidence of peptic ulceration and, every year, 1–2% of patients taking NSAIDs will have a complication such as bleeding or perforation. The risk of ulcer-related mortality in these patients is increased about fivefold. Consequently, the question of ulcer prophylaxis frequently arises. Misoprostol 200 μg twice daily reduces the incidence of both gastric and duodenal ulcers by 70–80% in patients taking NSAIDs. Furthermore, major complications of peptic ulcers are reduced by one-third. H2-receptor antagonists are probably less effective than misoprostol at preventing NSAID-induced peptic ulceration, whereas proton-pump inhibitors are probably more effective, although more data are needed.

The cost of co-prescribing misoprostol or an H2-receptor antagonist for every patient given an NSAID would be prohibitive. It has been estimated that the cost of preventing a single major gastrointestinal event by this approach would be several hundred thousand pounds. Selection is therefore necessary. Most NSAID-related gastrointestinal complications occur in the following:

- patients over 65 years of age
- those with a past history of peptic ulceration
- those with concomitant systemic disease (especially cardiovascular)
- those with concomitant use of a corticosteroid.

The risk of a major complication in patients with two or more of these risk factors is increased by about 10-fold and it seems sensible to target prophylaxis to patients who fall into this high-risk category.

Complicated peptic ulcer disease

The major complications of peptic ulceration are perforation and bleeding. Clearly these problems should be dealt with in hospital. Once the acute event has passed, however, the principles of management are similar to those for uncomplicated peptic ulcer disease.

Patients who present with *haematemesis or melaena* should be referred as an emergency. Such patients are ideally managed in a dedicated GI bleeding unit, with joint input from GI physicians and surgeons. Such units have significantly lower rates of mortality (5% vs. 15%). Initial therapy is directed at stabilizing the patient haemodynamically. Once this is achieved, and certainly within 12 hours, the patient should undergo upper gastrointestinal endoscopy. This allows accurate diagnosis and offers the opportunity for endoscopic intervention by injection or thermocoagulation of ulcers at high risk of re-bleeding. It is becoming less common for patients with bleeding ulcers to require surgical intervention as endoscopic treatment becomes more widespread.

When the patient is stabilized, treatment should be directed at healing the ulcer and keeping it healed. A full 4–6-week course of an ulcer-healing agent (proton-pump inhibitor or H2-receptor antagonist) is necessary, with eradication therapy for those who are *H. pylori* positive. Management after discharge from hospital is the same as for uncomplicated peptic ulcer (see above), but it is particularly important to check for successful eradication by breath test or endoscopic biopsy. This is because recurrent ulceration is common in those who have persistent infection. There is increasing evidence that it is safe to discontinue ulcer-healing agents in patients who have had a haemorrhage after the ulcer has healed and *H. pylori* has been eradicated. Some gastroenterologists, however, may still advise that patients who would be at very high risk if bleeding should recur (such as the elderly with cardiovascular disease) should continue to receive regular H2-receptor antagonists.

Zollinger-Ellison syndrome

This is a rare condition caused by a gastrin-secreting tumour. Symptoms are due to intractable peptic ulceration, which may also affect the jejunum and oesophagus, commonly associated with diarrhoea. There is, however, a spectrum of severity in the disease and the syndrome is probably underdiagnosed. Clinical clues include multiple peptic ulcers, ulcers resistant to ordinary therapy, and peptic ulceration with diarrhoea (due to acid inactivation of pancreatic lipase).

Diagnosis is established by elevated fasting gastrin concentrations and gastric acid secretion studies. If the primary tumour can be found, surgical resection may be possible. The tumours are often small and may be multiple but, even after metastatic spread has occurred, the growth rate is very slow. High doses of proton-pump inhibitors are very effective at relieving symptoms and some patients respond to octreotide.

Summary

H. pylori *diagnosis*	**Serology**	Patients on long-term ulcer-healing drugs. Patients aged <45–50 years presenting with dyspepsia. Note up to 20% false-negative rate in older patients.

	Breath test	To confirm successful eradication 4 weeks after treatment (note, no proton-pump inhibitors, antibiotics, or bismuth).
	Antral biopsy	At endoscopy to give a rapid result (CLO test).
Referral criteria for endoscopy		Dyspepsia with alarm features (vomiting, weight loss, anaemia, etc.). New-onset dyspepsia (age >45–50 years). Patients aged <45–50 years who have troublesome dyspepsia and have positive serology for *H. pylori.*
Referral criteria to outpatients		Persistent symptoms in patients with a documented ulcer, despite ulcer-healing treatment and eradication therapy. Persistent *H. pylori* infection despite triple therapy. Ulcers that are refractory to standard treatment.
Treatment	**Duodenal ulcer healing**	Omeprazole 20 mg or lansoprazole 30 mg daily for 4 weeks or cimetidine 800 mg or ranitidine 300 mg in the evening for 6 weeks.
In addition to:	***H. pylori* eradication**	Omeprazole 20 mg, clarithromycin 250 mg and metronidazole 400 mg, all twice daily for 1 week or omeprazole 20 mg twice daily, amoxycillin 500 mg three times daily and metronidazole 400 mg three times daily, all for 1 week.
	Gastric ulcer healing	As for duodenal ulcer, but if H2-receptor antagonists are used, continue treatment for 8 weeks. Give eradication therapy concomitantly if *H. pylori* positive. Always repeat the endoscopy after 6–8 weeks to confirm healing and to exclude malignancy.

Key points

- Recognition of the role of *Helicobacter pylori* has revolutionizsd the management of peptic ulcer disease, which in most cases can now be cured by eradication therapy. Provided that there is adequate access to endoscopy and *H. pylori* diagnostic testing, such patients can be largely managed in the community.
- A serological test for *H. pylori* antibodies is an appropriate initial investigation for patients less than 45–50 years old with dyspepsia.
- Dyspeptic with positive serology should have a diagnastic endoscopy before treatment, unless there has been a previously documented duodenal ulcer.

- Serology is unreliable in patients and cannot be used to confirm eradication.
- Short-course triple therapy (such as omeprazole 20 mg, clarithromycin 250 mg metronidazole 400 mg, all twice daily for 1 week) is currently the first choice for eradicating *H. pylori*.
- Breath tests are the best way of confirming eradication and are usually indicated for patients with a complicated peptic ulcer or if symptoms persist of eradication and healing therapy.
- Patients with a gastric ulcer should have a repeat endoscopy to confirm healing and to take further biopsies to excludemalignancy.

Further reading

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Chapter 5
Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a motility disorder recognized clinically as the co-existence of abdominal pain, abdominal bloating and altered bowel habit, in the absence of organic disease. It is the commonest reason for referral to gastroenterologists and is close to the common cold as a cause of absence from work. Although 15–20% of the population have symptoms that justify the diagnosis of IBS, only 20% of these seek medical attention. The reason that some seek medical attention (and become 'patients') whereas others with a similar severity of symptoms do not, remains unclear (chapter 2, p. 14). The prevalence of IBS in the population is similar between the sexes, but female outnumber male patients by 2:1.

It is helpful to distinguish between clinical patterns of IBS, as these influence investigation and management. The common patterns are *diarrhoea-predominant IBS, constipation-predominant IBS, pain-predominant IBS,* and *non-ulcer dyspepsia*. The evidence that these are motility disorders comes from studies that show high-amplitude colonic pressure waves 10 times more commonly in pain-predominant IBS than in controls, others that show post-prandial augmentation of colonic motility or altered motility during stressful interviews, and data demonstrating decreased tolerance to rectosigmoid balloon distension. There are, however, no consistent pathophysiological features.

Presentation

Establishing the diagnosis

The diagnosis of IBS can be made with confidence according to recognized criteria (Table 5.1), but it is essential to be alert to clinical features that may indicate organic disease (Table 5.2). If such indicators of organic disease are absent, few investigations should be undertaken. A full blood count and assessment of C-reactive protein (CRP) (or plasma viscosity or ESR) to exclude anaemia or inflammatory disorders, and a sigmoidoscopy should be sufficient. A barium enema is prudent if the patient develops new symptoms over the age of 40, or has risk factors for colorectal cancer, but other tests should be avoided in the absence of good clinical indications.

An early, confident diagnosis keeps tests to a minimum and reassures the patient. Such reassurance may be the doctor's most effective therapeutic weapon.

Table 5.1 Criteria for diagnosing IBS

At least 3 months continuous or recurrent symptoms of:

abdominal pain or discomfort that is:

- relieved by defaecation
- and/or associated with a change in stool frequency
- and/or associated with a change in stool consitency

together with

two or more of the following on at least a quarter of occasions or days:

- abdominal bloating (sansation of distension)
- passage of mucus
- sensation of incomplete evacuation, urgency or straining
- altered stool from (pelletty/stringy/loose/watery)
- altered stool frequency (often early morning frequency, or erratic pattern)

Table 5.2 Indicators of potential organic disease

- New onset of symptoms in patient aged >40 years
- Nocturnal symptoms with frequent awakening
- Steady, prograssive course from date of onset
- Absence of abdominal bloating
- Anorexia
- Weight loss
- Stools that are difficult to flash away
- Rectal bleeding
- Anaemia
- Elevated inflammatory markers (ESR, plasma viscosity, or Creactive protein)

When to refer to outpatients

Patients with indicators of organic disease (Table 5.2) should be referred for investigation, as should patients who have had an unexplained change in their symptom pattern over the age of 40 years. It is relatively unusual for symptoms of IBS to *start* after the age of 40, although older patients with IBS may be seeking medical attention for the first time. Otherwise, IBS is a condition that is best diagnosed and managed in a primary care setting. Patients with characteristic symptoms should be referred only if there is no response to all the manoeuvres suggested (pp. 80–84, Treatment strategy).

Management

Explaining the diagnosis to the patient

The doctor should endeavour to establish a firm diagnosis of IBS on the first visit. The manner in which this is done and the way in which it is explained to patients have a tremendous influence on the patients' reaction to the disorder, their cooperation and ultimate response to treatment. A useful approach is to explain that there *is* something wrong, but that it is not a disease; rather that the bowels are 'out of tune' or 'more sensitive' than normal. Symptoms not infrequently follow an episode of gastroenteritis, when the term 'postinfective irritable bowel' can be used.

The disorder can be explained in terms of poor coordination of the muscles of contraction of the gut. Helpful descriptions (unfortunately without much objective evidence) include explaining peristalsis as a sequence of contractions which, when poorly coordinated, cause segmentation that provoke spasm and pain, or trap gas, resulting in the sensation of bloating.

Descriptions of the typical characteristics of an irritable bowel are often recognized with relief by the patient. The relation to stress in some people (by enteric nerves communicating through the spinal cord with the brain) and the triggering of symptoms by some foods, will also be familiar to many. It is reassuring to state that there is no risk of cancer or serious disease. Finally, it is helpful to explain that, although symptoms may continue for many months or years, they can be relieved, even if they cannot always be cured.

Treatment strategy

The therapeutic approach should be based on five principles:

- a positive diagnosis
- consideration of the patient's agenda
- dietary manipulation
- drug therapy
- long-term care.

Positive diagnosis. (See above, and Table 5.1.)

Patient's agenda. As only a minority of patients with IBS seek medical attention, it is important to establish why the patient has sought help at this particular time. Fear of cancer or other serious disease, stressful life events and other psychosocial concerns should be sympathetically probed. Up to 40% of patients seeking treatment of IBS in one study reported sexual abuse as children. Early and careful attention to the patient's psychosocial concerns (employment prospects; marital disharmony; difficulties with housing, parents or children) is effective and may be of lasting benefit. Dyspareunia is frequently reported by women (up to 70%) and may be a reason why more women than men seek medical attention for their symptoms.

Dietary manipulation. A high-fibre diet is most appropriate for constipation-predominant IBS, or when there is alternating constipation and diarrhoea. *Fibre,* as unprocessed bran, isphagula or psyllium, is hydrophilic and should be consumed with

plenty of fluid. Mixed unrefined sources of fibre (fruit, vegetables, wholemeal bread) are more palatable than bran added to food, but sachets of isphagula (Fybogel or Regulan) may be necessary. Fibre may exacerbate bloating or flatulence and should not be considered a panacea.

Some patients have a *specific food intolerance* that can be reproducibly identified. The mechanism is unknown, but it is not a food allergy (defined as IgE-mediated type 1 hypersensitivity) or food fad (which is not a reproducible cause of symptoms on blind testing). In one controlled study, two-thirds of patients responded partly or completely to an exclusion diet. Wheat, caffeine in tea or coffee, oranges, cucumber or food additives are often implicated. Sorbitol or fructose are artificial sweeteners that may provoke flatulence. When a food is identified as a provoking factor, avoidance brings relief. If the patient suspects a food intolerance but cannot identify the food by excluding one food at a time at home, then referral to a dietitian for a formal exclusion diet may be helpful.

Drug therapy. No drug is of universal value in IBS and a pronounced placebo response (40–70%) makes it difficult to conduct controlled trials. A common sense approach is necessary, directed at symptom patterns (Table 5.3). *Antidiarrhoeal agents* are pragmatic for diarrhoea-predominant irritable bowel, but often need to be combined with increased fibre intake to prevent frequent pelletty motions. *Antispasmodics* are most appropriate for pain and should be used in full doses before changing drugs, although response is unpredictable and may be transient. A drug to which a response has declined can sometimes be reintroduced with benefit after an interval.

Pain can also be treated by *tricyclic agents* in low doses; these drugs are most helpful when pain and diarrhoea are prominent, because they have an anticholinergic action on the bowel. Preliminary reports suggest that serotonin-reuptake inhibitors (such as sertraline) may have a beneficial effect in constipation-predominant irritable bowel. It is essential to explain that such agents are being used to act on the enteric nerves, starting at paediatric doses, rather than for any antidepressant effect. Patients will otherwise think that the doctor believes that symptoms are ‘all in the mind’. Even though a central action may be beneficial in some patients, it helps nobody to dismiss symptoms as psychological. Anxiety and depression should, of course, be treated in their own right.

Table 5.3 Drug treatment of symptom patterns in IBS

Diarrhoea-predominant IBS	*Antidiarrhoeal agents* (loperamide up to 12 mg/day, codeine phosphate up to 120 mg/day, Lomitil up to 6 tabs daily). Add *fibre* (Fybogel Regulan 2 sachets daily) for pelletty motions. *Tricyclics* (amitriptyline 10 mg at night, increasing to 20–30 mg as tolerated, especially with pain. Motival 1–3 tabs daily, or imipramine 10–25 mg daily are less sedative).
Constipation - predominant IBS	*Fibre* (Fybogel or Regulan 2 sachets daily) and fluids, Stool softener (lactulos (20–60 ml daily) on a regular basis, or Laxoberal 10–20 ml daily if not tolerated), *Antispasmodics* (mebeverine up to 270 mg, alverine citrate 120 mg, or colpermin 2 caps, all three times daily) may help pain.
Pain-predominant	*Antispasmodics* (mebeverine up to 270 mg, mg, alverine citrate 120 mg, or

IBS	Colpermin 2 caps, all three times daily).
	Tricyclics (amitriptyline line 10 mg at night, increasing to 20–30 mg. Motival 1–3 tabs daily, or imipramine 10–25 mg daily as tolerated).
Non-ulcer dyspepsia	*Antiapasmodics* mebeverine up to 270 mg, alverine citrate 120 mg, or Colpermin 2 caps, all three times daily).
	Acid suppression (cimetidine up to 800 mg daily) may help help symptoms, but eradication therapy for *Helicobacter* has no perdictable benefit.
	Prokinetic (metoclopramide or domperidone 10–20 mg tds) for nausea.

Long-term care. For many troubled patients with IBS, cure is an unrealistic goal. Some patients benefit from regular brief visits, and continuity is best provided by the family doctor. For occasional patients who have been to many specialists and have concomitant organic disease, regular review in outpatients may reassure, and prevent further referral. It may benefit to put patients in touch with a *self-help organization* such as the IBS Network (Appendix). Assistance from clinical psychologists, psychiatrists or a pain clinic may help, and some patients find relief from practitioners of alternative medicine. In a retrospective study of 25 patients who received hypnotherapy after conventional medical treatment had failed, compared with a control group of 25 patients on the hypnotherapy waiting list, abdominal pain, bloating, psychological well-being, number of visits to the GP and absence from work were highly significantly better in the hypnotherapy group.

Continuing care by the family doctor

Questions to ask

Fundamental questions to confirm a diagnosis of IBS include the duration and pattern of pain, association with altered bowel habit and bloating, relief by defaecation, and lack of features of organic disease such as anorexia, weight loss or bleeding (Tables 5.1 and 5.2, pp. 78–79).

During follow-up visits, reviewing the symptom pattern will alert the doctor to any change in symptoms. Follow-up visits provide the opportunity to explore psychosocial concerns (p. 80) and to providecounselling.

Preliminary investigations

All patients should have their *full blood count* and *inflammatory markers* (C-reactive protein, plasma viscosity or ESR) checked early in their presentation, or when there is a change in symptom pattern. For constipation-predominant symptoms, it is worth considering checking the calcium and thyroid function. For diarrhoea-predominant symptoms, sigmoidoscopy and biopsy should be performed unless the diarrhoeal spells last less than a couple of days. Stool culture is rarely helpful unless there are atypical features that do not fit with an irritable bowel, such as nocturnal diarrhoea.

Other aspects

The psychosocial concerns of individual patients and continuity of care for patients with IBS are best managed by family doctors. In this way, unnecessary hospital visits or investigations (which are often arranged by junior hospital staff to the anxiety of patients that there may still be something amiss) can be limited.

Precipitate referral should be avoided. In the authors' specialist practice, patients are often discharged after a single outpatient visit, limited investigation having been arranged and advice on a treatment strategy having been given. The results and any further advice are then sent to the family doctor by letter. The doctor can then follow the strategy and explain the results of investigations to the patient as they are performed. This shared-care approach places the family doctor 'in the driving seat', with the gastroenterologist as a facilitator to arrange appropriate investigations, confirm the diagnosis and (it is hoped) reassure the patient.

Hospital visits

Assessment

Retaking the *history* and examining the patient in a careful, sympathetic and thorough manner makes subsequent explanation and reassurance much easier. The clinical pattern of symptoms that indicate IBS should be confirmed (Table 5.1) and unusual features identified, as these may indicate the need for further investigation. The *results of all investigations to date* should be reviewed, paying particular attention to the mean corpuscular volume (MCV), platelet count and results of inflammatory markers, as these may be the only indicator of underlying pathology. If the symptoms are characteristic and preliminary investigations normal, time should be spent in explaining the diagnosis (p. 79), exploring concerns and discussing the treatment strategy (p. 80), before discharging the patient to the care of the GP.

Further investigations

It may be necessary to perform investigations to exclude underlying pathology (Table 5.4), but tests should never be requested as a means of getting rid of the patient while hoping that another doctor will see the patient next time! If there is any doubt, further investigationsshould be discussed with a senior colleague.

Frequency of review

Junior hospital staff may be reluctant to discharge patients, for concern about underlying pathology. The authors' view is that the consultant gastroenterologist has a responsibility to see patients with IBS at the first or second visit, to address patients' concerns, limit investigations and recommend a treatment strategy that can be pursued by the family doctor. It is not a view that is universally shared, but it helps control the size of outpatient clinics!

Special situations and prognosis

Symptoms in the presence of organic disease

For a condition with a prevalence of 15–20% in the general population, a proportion of patients will have concomitant pathology. A careful history is the best way of distinguishing between pain due to IBS and that caused by co-existent gall stones, colonic diverticulosis or Crohn's disease. Judgement is necessary to decide which symptoms are related to known disease, but continuous abdominal discomfort, a sensation of abdominal distension, or symptoms that do not fit with the common pattern of the disease, are likely to be due to IBS. Careful interpretation of investigations can help: for instance, the absence of a thick-walled

Table 5.4 Investigation in suspected IBS according to the symptoms pattern and associated features

All patients	Rectal examination, full blood count, ESR or CRP
Age >40 yeaes, anaemia or rectal bleeding	Sigmoidoscopy and barium enema
Diarrhoea	Sigmoidoscopy and rectal biopsy (to exclude microscopic colitis)
	Consider: Thyroid function testsLactos breath test (or trial of lactose-free diet)
	Distal duodenal biopsy (if stools difficult to flush, or iron deficient) Small bowel radiology (if CRP elevated, or weight loss) Urine for laxative assay
Constipation	Thyroid function tests and serum calcium *Consider:* Transit studies (if bowels open <1/week)
Upper abdominal pain	*Helicobacter* serology if age <50 years Endoscopy if age >50 years, or if serology is positive Ultrasound if pain is periodic

gall bladder in the presence of gall stones means that chronic cholecystitis is unlikely and gall stones are more likely to be incidental. A normal CRP in a patient with Crohn's disease makes active disease less likely, but there are several other causes of symptoms in such patients, of which IBS is only one (Table 7.4, p. 128).

Refractory symptoms

Persistent symptoms despite treatment are taxing to both patient and doctor. It is wise to go over the history carefully again, including reexamination. Further investigation is not justified unless the symptom pattern has changed or clinical signs (such as weight loss) have developed. Explanations to provide insight and assistance in coping with symptoms may provide sufficient reassurance.

Persistent symptoms may be due to failure to treat constipation adequately, or failure to alter the diet. For patients with symptoms related to eating or with some food intolerance, referral to the *dietitian* for a formal exclusion diet may help. If pain predominates, referral to the *pain clinic* is appropriate. Clinical depression should be treated, or the patient referred to a *psychiatrist*. *Alternative treatment,* such as hypnotherapy, may have a role. If the confidence of the patient has been lost, referral to a colleague may help by confirming the diagnosis and reinforcing the management plan.

Non-visceral abdominal pain

Chronic abdominal wall pain or referred pain (usually from the back) may be misdiagnosed as IBS. Wall pain is often focal, and *Carnet's sign* is useful: a finger is placed on the site of maximum pain and the patient is asked to tense the abdominal muscles. This exacerbates abdominal wall pain but has little influence on the intensity of visceral pain such as that associated with IBS. Local anaesthetic infiltration may provide dramatic relief. Referred pain should always be considered when symptoms persist; examination of back movement is often overlooked.

Prognosis

Symptoms in IBS resolve or improve in about 50% of patients after 12 months; a minority (about 5%) deteriorate and the remainder remain unchanged. Intermittent symptoms are likely, often related to stressful life events. There is no mortality and patients should be reassured of the benign nature of the disorder.

Summary

Diagnosis More than 3 months with symptoms of:

- abdominal pain or discomfort relieved by defaecation, and/or associated with a change in stool frequency or consistency, together with two or more of the following on at least one-quarter of occasions:
- abdominal bloating, passage of mucus, sensation of incomplete evacuation, altered stool form, or altered stool frequency, for which no other cause is evident (Table 5.1, p. 78).

Referral criteria

New patients: New symptoms at age >40 years, or indicators of disease such a weight loss, anaemia, rectal bleeding (Table 5.2, p. 79).

Review: Unexplained change in pattern of symptoms.

Investigations Full blood count, ESR or C-reactive protein, sigmoidoscopy.
Barium enema if age >40 years. Otherwise limited (Table 5.4, p. 87).

Treatment

All patients	**Diarrhoea-predominant**	**Constipation-predominant**	**Pain-predominant**
Five principles:	Loperamide up	High-fibre diet,	Mebeverine

■ positive diagnosis	to 12 mg/day ±isphagula 2	plenty of fluids ±isphagula 2	270 mg or alverine
■ patient's agenda	sachets/day. Amitriptyline	sachets/day ±lactulose	citrate 120 mg or Colpermin
■ dietary manipulation	10–30 mg or Motival 1–3	20–60 ml/day	2 caps, all three
■ drug therapy	tabs/day.		times/day
■ continuing care			±amitriptyline 10–30 mg

Key points

- About 15–20% of the population symptoms of irritable/bowel syndrome, but only 20% of these seek medical attention.
- Some enquiry should be in to the factors precipitating presentation and underlying concerns, rather than assuming that relief of symptoms is the only goal,
- The first aim of management is to make a positive diagnosis with limited investigatton. This can often be achieved by recognizing the criteria for diagnosis (Table 5.1), together with a check on the full blood count and inflammatory markers.
- The treatment stragery should be discussed with the patient and should include a cambination of dietary manipulation, an increase in fibre, antispasmodic or tricyclic drugs, and addressing the psychosocial concenrs
- Referral should be considered only if symptoms are atypical, or preliminary investing abnormal, or If symptoms persist despite the combinaed treatment strategy.

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Chapter 6
Abnormal liver function tests and chronic liver disease

Abnormal liver function tests

Abnormal serum concentrations of *hepatic enzymes* ('liver function tests', Table 6.1) are a common finding that may be due to any systemic viral illness, or may reflect more serious pathology, including metastases or chronic liver disease. They may be detected while investigating patients with non-specific symptoms, as an incidental finding in blood donors, or during a routine check-up. Overt jaundice can be considered as part of the spectrum of abnormal liver function tests, necessitating expeditious investigation.

Very often the cause will be suggested by the history and clinical examination and by reviewing the medication record. Some cases in which a viral or drug-induced cause can be identified can be managed without referral. Other cases need hospital resources and it is usually the gastroenterologist who has readiest access to diagnostic and therapeutic procedures such as endoscopic retrograde cholangiopancreatography (ERCP), rendering the concepts of 'medical' and 'surgical' jaundice obsolete.

Common causes

The patterns of abnormal liver function tests are best divided into three—pre-hepatic, hepatocellular and cholestatic (Table 6.1). Jaundice becomes clinically detectable when the serum bilirubin exceeds 50 μmol/l.

The aspartate transaminase (AST) concentration is less specific than that of alanine transaminase (ALT) for hepatocellular damage, but the ALT is not as commonly measured in automated assays. Alkaline phosphatase (ALP) is biliary in origin if the γ-glutamyl transpeptidase γGT) is also elevated, but if the γGT is normal, a high ALP will usually arise from bone (Paget's disease, metastases or osteomalacia).

Although there may be considerable overlap in the biochemical patterns from different causes (Table 6.2), these patterns provide a good clue to diagnosis and also guide appropriate investigation. As the normal range represents only 95% of the normal population, a minor excess of a single enzyme concentration may not indicate hepatic pathology; this is particularly true of γGT.

Drug-induced causes of liver dysfunction are many and deserve special mention. An asymptomatic elevation in liver enzymes is the usual presentation. Hepatotoxic effects may be dose dependent (*paracetamol* >10 g/24 hours, or *tetracycline* >4 g/24 hours) or, more

Table 6.1 Interpreting liver function tests

Test	Normal	Pre-hepatic	Hrpatocellular	Cholestatic
AST (IU)	<35	<35	50–10,000	35–400
ALP (IU)	<120	<120	<120–400	>300
γGT (IU)	15–40	15–40	15–200	800–1000†
Bilirubin (μmol/l)	3–17	18–150	<17–350	17–750
Albumin (g/l)	40–50	40–50	20–50	30–50
Prothrombin time (see)	13–15	13–15	15–45†	15–45*
INR†	1.0–1.3	1.0–1.3	1.0–1.3†	1.0–1.3*

Hepatic enzymes are more correctly markets of liver dysfunction. The serum albumin and prothrombin time provide a better index of liver function.
*Decreases in response to parenteral vitmin K 10 mg.
†International mormalized ratio.

Table 6.2 Principal causes of abnormal liver function tests and janndice

	Pre-hepatic	Hepatocellular	Cholestatic
Common	Neonatal	Viral hepatitis	Common bile duct
	Gilberts	Alcohol	stones
	syndrome	Drug-induced	Pancreatic cancer
Uncommon	Heamolysis	Hepatic	Primary biliary
		metastases	cirrhhosis
		Cardiac failure	Selerosing
		Autolmmune	cholangitls
		hepatitis	cholangiocarcinoma
		Haema-chromatosis	Benign stricture
		Hepatoma	
		Thyroid or other	
		endocrine diesase	

commonly, idiosyncratic. In particular, *Augmentin* or *non-steroidal anti-inflammatory drugs* can cause cholestasis or a hepatocellular pattern, as can *azathioprine,*

anticonvulsant or *antituberculous* chemotherapy. For a complete list of causes, other textbooks (see Further reading) or the local drug information service shoud be consulted.

Minor elevations in AST (up to threefold) after starting potentially hepatotoxic drugs are not necessarily an indication for stopping the drug, as improvement often occurs. However, there can also be rapid deterioration, so close monitoring is essential. Jaundice is a definite indication for stopping any potentially hepatotoxic medication; liver enzymes may take many weeks to return to normal after stopping a drug.

Initial assessment

A systematic clinical approach to a patient with abnormal liver function tests or jaundice is important. The *sequence of any symptoms* should be established, because this often helps distinguish hepatocellular from cholestatic causes. Preceding anorexia, nausea, distaste for cigarettes and flu-like symptoms are characteristic of viral hepatitis. Dark urine with pale stools and itching indicates cholestasis. Abdominal pain suggests gall stones when the pattern is cholestatic, although stretching of the liver capsule from hepatomegaly may also cause pain in acute hepatitis. Rigors indicate cholangitis, which is a medical emergency, while weight loss favours malignancy.

Specific questions should focus on *drugs* (prescribed, over-the-counter, or herbal remedies), *alcohol intake, injections* (drug abuse, transfusions, tattoos), *travel abroad, occupation* (alcohol-related, industrial exposure), *family history of liver disease, contact with jaundiced patients,* and *sexual relations*.

It is usually possible to make an educated guess after examination about whether there is acute or chronic liver disease, although no clinical sign is invariably associated with either. Age and associated illness are important clues. Young adults may have Epstein-Barr virus-associated hepatitis, while drug treatment for chronic disease, or metastases from a previous malignancy, may be implicated in others.

Patients with acute liver disease tend to be well nourished and have tender hepatomegaly. Chronic liver disease is more commonly associated with leuconychia, loss of muscle bulk, telangiectases, splenomegaly, or ascites, but the depth of any jaundice is not a reliable indicator of the cause.

Investigations

The number of investigations performed before referral depends on the symptoms (none, mild, or severe), clinical circumstances (age, and associated illness), availability of outpatient investigations and degree of abnormality in the liver function tests. Patients who are jaundiced and in whom viral hepatitis has been excluded are best admitted for investigation or seen urgently in outpatients. Patients with a mild derangement in hepatic enzymes, or who have positive hepatitis C virus serology but normal liver function tests, can be referred routinely. For these reasons, the sequence of investigations shown in Figure 6.1 covers both initial and specialist investigation.

When to refer to outpatients

Most patients with abnormal liver function tests warrant referral for a specialist opinion, except those with isolated hyperbilirubinaemia due to Gilbert's syndrome (which affects about 4% of the population), or isolated elevation in γGT in the absence of symptoms. The γGT is the hepatic enzyme most readily induced by alcohol or drugs (such as anticonvulsants), but a single measurement is not a reliable marker of alcohol consumption.

Initial management of patients with minor derangements of liver function may best be a period of observation and repeating the tests after a period (about 6 weeks) of abstinence, or after changing drug therapy. Otherwise, preliminary investigations along the lines of Figure 6.1 are appropriate for most patients prior to referral.

Chronic liver disease

Chronic hepatitis and cirrhosis are stages in the progression of many liver diseases of different aetiology (Table 6.3). *Chronic hepatitis* is a histological diagnosis, defined as chronic hepatic inflammation persisting for more than 6 months. The histological features are snapshots in a dynamic process: the features (inflammatory infiltrate, disruption of the limiting plate around the portal tract, bridging hepatocyte necrosis) were previously divided into persistent, lobular and active chronic hepatitis, in ascending order of severity. In recognition of the dynamic process and the fact that a variety of causes may cause similar histological features, chronic hepatitis is now described by aetiology, grade and stage. The grade is a measure of the severity of the inflammatory process and the stage refers to the degree of fibrosis. Some causes, including viral, autoimmune, alcohol, drugs and metabolic disorders, are specifically amenable to treatment.

Cirrhosis is also a histological diagnosis that is the end stage of the process of hepatic damage. It is defined as disruption of normal hepatic architecture by fibrosis with nodular regeneration. Fibrosis implies irreversible liver damage, but progression to decompensated liver disease or, in some circumstances, hepatoma, can often be delayed by treatment.

Presentation

Establishing the diagnosis

The initial indicator of chronic liver disease is the finding of abnormal liver function tests (Table 6.1, p. 94). These may be detected following acute hepatitis, or as an incidental finding while investigating the patient's non-specific symptoms. The derangement is often minor, except in autoimmune active chronic hepatitis when the transaminases may be markedly elevated, or in chronic intrahepatic cholestasis due to primary biliary cirrhosis or primary sclerosing cholangitis, when there is a striking elevation in the alkaline phosphatase concentration.

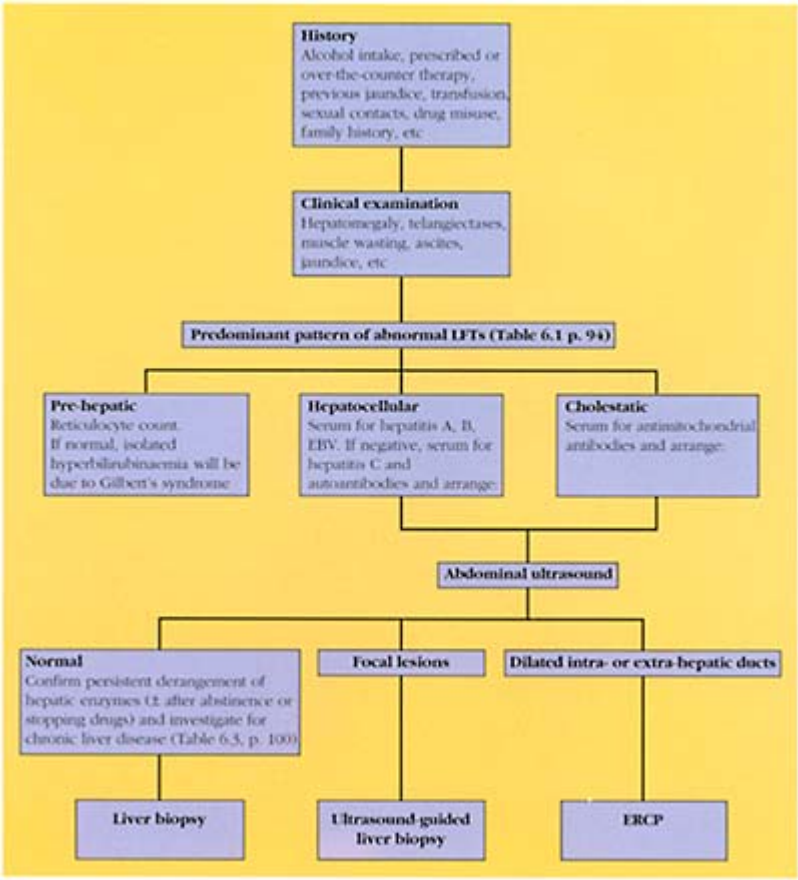

Figure 6.1 *Investigating abnormal liver function tests (LFTs).*

Identifying the cause of chronic liver disease

The history will often give a clue to the diagnosis (alcohol abuse, associated arthralgia in a young woman in autoimmune liver disease, itching in a middle-age woman in primary biliary cirrhosis), but serological and other investigations apart from liver biopsy are needed to confirm the diagnosis (Table 6.4). This table gives substantial detail, emphasizing the need to review all available information before determining a specific diagnosis.

Explaining the diagnosis to the patient

Hepatobiliary function (protein synthesis, metabolism of nutrients or toxins, and bile secretion) should be explained, according to the level of understanding of the patient. The

cause, extent and reversibility of liver damage can then be discussed, pointing out that the vast proportion of hepatic function is 'reserve capacity'.

Complications and available treatment can then be addressed. Advice on *diet, drugs and alcohol* is often expected, but the degree of dogmatism depends on the cause. Fluid and salt restriction are

Table 6.3 Causes of chronic liver disease and potential treatment

Aetiology	Treatment
Hepatitis B	Interferon-α
Hepatitis C	Interferon-α
Alcohol	Abstinence; alcohol counselling
Autoimmune	Prednisolone
Prolonged chotecasis	
■ primary biliary cirrhosis	Ursodeoxycholic acid; transplant Relieve biliary obstruction; transplantation
■ other intra- and extra-hepatic causes	
Metabolic	
■ haemochromatosis	Venesection
■ copper overload (Wilson's)	Penicillamine
■ α_1-antitrypsin deficiency	Transplant
■ galactosaemia, tyrosinaemia	Dietary exclusion (milk, tyrosine)
Drugs (e.g. methotrexate, amiodaroae)	Identify and stop
Hepatic venous obstruction	
■ Budd–Chiari syndrome	Identify cause; anticoagulation
■ cardiac failure	Treat cause (e.g. constrictive pericarditis)
Cryptogenic	None; transplantation

Table 6.4 Diagnosis of specific causes of chronic liver disease

*Viral hepatitis**	
■ *B*	HBsAg and HBeAg positive. Viral DNA by PCR rarely indicated. Orcein stain positive on liver biopsy.
■ *C*	HCV antibody by ELISA, confirmed by RIBA testing. HCV RNA by

	PCR is indicated for monitoring interfecon therapy. Lymphoid follicles characteristic on biopsy.
Alcohol	History, random alcohol γGT, raised MCV, elevated IgA. Fatty infiltration, megamitochondria, Mallory's hyaline on biopsy.
Autoimmune	Antismooth muscle antibody titre >1:80, antinuclear antibody >1:80. Elevated IgG titre, predominance (8:1), associated thyroiditis.
Metabolic	
■ *Haemocbromatosis*	Serum ferritin >1000 μg/l (also in alcoholics or chronic inflammation) Fe/TIBC ratio >80%, HLA A3 positive. Perl's stain positive on biopsy.
■ *Wilson's*	Serum caeruloplasmin <0.2 g/l. Increased urinary copper (>0.1 mg/ 24 hourse). Increased liver copper.
■ α_1-*antitrypsin deficiency*	serum α, α antirrypsin <0.2 g/l, Pizz Serum α_1-antitryspin <0.2 g/l, PiZZ phenotype on electrophoresis. PAS positive globules on biopsy.
Cholestasis	
■ *Primary biliary cirrbosis*	Antimitochondrial antibody titre>1:250, M2 antigen specific. Elevated serum IgM. Bile duct, proliferation, lymphoid aggregates and granulomas on biopsy.
■ *PSC*	ERCP. Sigmoidoscopy abd biopsy (80% associated with ulcerative colitis).
Drugs	History. Amiodarone, methotrexate, nitrofuration, α-methyldopa, etc. Wide variety of feature on biopsy
Hepatic venous obstruction	
■ *Budd-chtari syndrome*	Prothrombotic states (tumour, polycythaemia, antiphospholipid syndrome). Dropper ultrasound or hepatic venography.
■ *Veno-occlusive disease*	Biopsy shows occlusion and hyaline necrosis of small hepatic veins.
■ *Constructive pericarditis*	Clinical signs, echocardiogram.
Cryptogenic	All other causes excluded (15–30%)

*Hepatatis A and other hepatrotopic viruses (e.g. Epstein-Barr virus, herpesvirus, arboviruses) cause acute, but not chronic liver diesase. Abbreviations: ELISA, enzyrne-linked immunosorbent assay; ERCP, endoscopic retrograde cholangiopancreatography; Fe/TIBC, iron/total iron-binding capacity; HBs (or e) Ag, hepatitis B s- (or e-) antigen; HCV, hepatitis C virus; Ig. immunoglobulin; MCV, mean corpuscular volume, PAS, periodic acid-shiff; PCR, polymerase chain reaction; PSC. primary sclerosing cholangitis; RIBA. radioimmunobiot assay.

important for ascites, as is protein restriction during encephalopathy, but for most patients a well balanced diet avoiding foods that upset them is sufficient. Complete abstinence from alcohol is fundamental in alcohol-induced chronic liver disease, but for other causes

there is no evidence that a small amount of alcohol (an arbitrary 2-4 units/week) does any harm. The patient or relatives may find it helpful to have the address of an organisation such as the *British Liver Trust* (Appendix) for additional patient-based information.

Management

The principles of management are similar, whatever the aetiology. The five principles are as follows:

- document the diagnosis as accurately as possible by serology and liver biopsy
- assess hepatic function
- treat the underlying cause, whenever possible
- treat complications (portal hypertension or hepatocellular failure) promptly
- consider the place of liver transplantation.

Assessing hepatic function

An attempt should be made to evaluate current hepatic function and the consequences of portal hypertension, and then to determine the progression of the underlying disease.

Hepatocellular function is most simply assessed by the serum albumin and prothrombin time (or international normalized ratio, INR). Jaundice, encephalopathy or ascites indicate liver cell failure.

Portal hypertension is evaluated by examining for ascites, splenomegaly, and oesophageal varices, or by ultrasound. There are, however, no non-invasive measurements that directly correlate with portal pressure. This is unfortunate, because there appears to be a threshold for bleeding from oesophageal varices, which occurs when the portal pressure gradient exceeds 12 mmHg.

The *progression* of chronic liver disease is assessed by serial measurements of the INR, albumin and hepatic enzymes, clinical evaluation of ascites, liver and spleen size, and repeat liver biopsy in selected patients (such as those given specific treatment for the underlying aetiology). Transaminases alone are unreliable: they are a useful index of activity in autoimmune chronic hepatitis, but do not correlate with histological activity in hepatitis C.

Specific treatment of the underlying cause

An increasing number of conditions are amenable to specific treatment (Table 6.3), although the response is variable. Detailed treatment protocols are beyond the scope of this text and, in many cases, are still evolving, but some options can be given.

Treatment of *chronic hepatitis B or C* with *interferon-α* may be considered for patients with histological evidence of active chronic hepatitis, early cirrhosis, or (for those with hepatitis B) persistent hepatitis B e-antigen. The response depends on the dose, duration and the genotype of the virus. Local expert advice needs to be sought, because treatment protocols are evolving and costly. Virtually every patient experiences flu-like symptoms, but only 5–10% have to stop treatment. The response is monitored by transaminases, molecular markers of virus replication and liver biopsy. Transaminase concentrations

frequently return to normal during treatment, but do not necessarily predict viral clearance or a histological response. As a rule, hepatitis B is more susceptible to interferon than hepatitis C. Histological progression may be prevented, but cirrhosis is not reversed. For hepatitis C, viral clearance has been reported in up to 65%, but only 20–40% have a sustained response after treatment ceases; genotype 1 (especially type 1b) responds less well than do genotypes 2 and 3. The latter is more common in the UK. Other *antiviral agents,* including lamivudine in chronic hepatitis B and ribavarin in hepatitis C, are being evaluated, either as sole or as adjunctive therapy. Prednisolone does not alter the response to interferon-α.

For chronic *alcoholic liver disease,* abstinence is fundamental. Interventional counselling has a treatment benefit in up to 40% of patients (FRAMES: Feedback to patient about risks; personal Responsibility for change; Advice; Menu of options for change; Empathic interviewing; Self-efficacy). At least 25% will continue to drink, irrespective of therapy and 50% who become abstinent return to clinically significant drinking within 1 year. Naltrexone 50 mg daily has been reported to halve the incidence of recidivism in two placebo-controlled trials when combined with psychosocial support, without the side effects of disulfiram (Antabuse).

In chronic *autoimmune liver disease, prednisolone* is highly effective. Therapy should be continued for 1–2 years, starting at a dose of 30–40 mg/day for 1 month, then decreasing by 5 mg every month until a maintenance dose of 5–15 mg/day is established, keeping transaminases within the normal range. If there are unacceptable side-effects from steroids, *azathioprine* 1–2 mg/kg/day can be given as well, although this is ineffective as sole treatment. After 2 years, repeat liver biopsy is indicated and, for those with low histological activity, steroids can be withdrawn while carefully monitoring the transaminases every 2–4 weeks. Relapse, which can be severe, occurs in 60–70% and in these patients continued steroids are needed.

For patients with *primary biliary cirrhosis, ursodeoxycholic acid* 750 mg/day improves alkaline phosphatase, bilirubin and some aspects of liver histology, with a trend towards improved survival and decrease in liver transplantation. Immunosuppressive agents (prednisolone, azathioprine, cyclosporin, methotrexate) are too toxic for minimal benefit and colchicine has not fulfilled early potential. No treatment has been shown to alter the progress of *primary sclerosing cholangitis*. Liver transplantation (below) is potentially curative for both conditions.

Haemochromatosis is readily treated by *venesection* every 1–2 weeks until the serum ferritin is less than 500 µg/l, or the iron/total iron binding capacity (Fe/TIBC) ratio is less than 50%. Monthly venesection is then performed until normal values are achieved (ferritin <200 µg/1, Fe/TIBC ratio <30%), followed by maintenance venesection every 2–3 months. Copper overload in *Wilson's disease* is treated with *penicillamine* 1–2 g/day. Improvement may take up to 2 years and is monitored by transaminases, clinical state (neuropsychiatric signs, handwriting) and repeat liver biopsy. Urinary copper excretion and serum caeruloplasmin are unsatisfactory for monitoring treatment.

Treatment of complications

Even if the aetiology cannot be treated or does not respond, there is a substantial potential for ameliorating the complications of chronic liver disease.

Ascites. Free fluid in the peritoneal cavity accumulates in chronic liver disease when the liver fails to metabolize endogenous vasodilators. Splanchnic arteriolar vasodilation is thought to decrease renal blood flow and trigger salt and water retention through activation of the renin-angiotensin-aldosterone system. Portal hypertension then acts as the driving force to produce ascites.

A *stepped care approach* is designed to produce a weight loss of 0.5–1.0 kg/day (Figure 6.2). More rapid weight loss leads to hypovolaemia and renal failure unless peripheral oedema is also present. When ascites is refractory to *diuretics* or is causing respiratory embarrassment, *paracentesis* with intravenous colloid replacement is safe. Complete removal of ascites does not improve prognosis and may cause electrolyte imbalance or renal failure (hepatorenal syndrome). If the patient is comfortable, it is best to leave a small amount of ascites, especially during hot weather when insensible losses increase.

Spontaneous bacterial peritonitis is a frequent and serious complication of ascites, especially in those with advanced cirrhosis or low-protein ascites (<10 g/l). Abdominal pain is often absent and signs may be minimal. Increasing ascites or encephalopathy should suggest the diagnosis, which is confirmed by a total ascitic polymorphonuclear leucocyte count greater than 250/ml. Most infections are due to enteric Gram-negative bacteria (e.g. *Streptococcus faecalis, Escherichia coli*) and if this is suspected, the patient should be admitted directly to hospital. Intravenous cefotaxime 1 g twice daily for 5 days is the treatment of choice. Recurrence is frequent (74% at 2 years) and prognosis is poor (below).

Encephalopathy. Encephalopathy indicates hepatocellular dysfunction with portal-systemic venous shunting. The mechanisms are unclear, but may be due to neurotoxins of intestinal origin that are normally metabolized by the liver (ammonia, mercaptans, phenols), or the presence of false neurotransmitters (octopamine) acting on inhibitory receptors. Receptors such as γ-aminobutyric acid (GABA) are closely related to receptors for benzodiazepines, which may explain their neurodepressant effect.

In chronic liver disease, the development of encephalopathy usually has a *provoking cause* (Table 6.5). Treatment of the cause is crucial, complemented by *dietary protein restriction* (<60 g/day) and *lactulose* 60–120 ml daily adjusted to achieve two or three soft stools daily. Neomycin (2–6 g/day) is no more effective than lactulose and risks oto- or nephrotoxicity. When the patient has recovered, dietary protein restriction can be relaxed, although lactulose may be

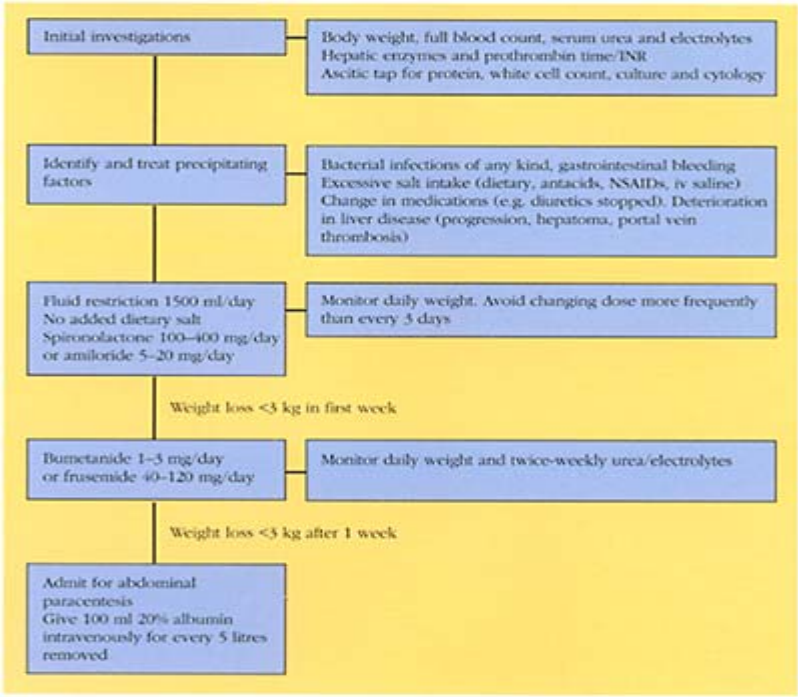

Figure 6.2 *Stepped-care approach for the management of ascites.*

Table 6.5 Factors precipitating bepatic hepatic deeompensation in chrouie liver disease

Infection	■ urinary tract, chest
	■ spontaneous bactrial preitonitis
Intestinal bleeding	■ varices, ulcer, erosions
Drugs	■ excess diuretics, benzodiazepines, opiates
Alcohol abuse	
Progression of underlying desease	
Excessive dietary protein	
Hepatocellular carcnoma	

continued in low doses (20–40 ml/day), as this may delay recurrence. Chronic or recurrent encephalopathy are poor prognostic signs and suitability for liver transplantation should be considered.

Oesophageal varices may be a consequence of portal hypertension, but only 30% bleed. Bleeding may be catastrophic and immediate admission is appropriate for any patient with liver disease and signs of gastrointestinal bleeding. Endoscopic sclerotherapy or banding is the treatment of choice to control bleeding, but opinion varies about subsequent management. Most gastroenterologists will repeat sclerotherapy at intervals of 1–2 weeks until varices have been obliterated, and start a non-selective (β-blocker to reduce portal venous pressure. Surgical or percutaneous shunting (transjugular intrahepatic portal-systemic shunt, TIPSS) more effectively decompress portal pressure, but increase the risk of encephalopathy. Although all these measures reduce the risk of further haemorrhage, there is no consistent evidence that they improve mortality.

Transplant. Although liver transplantation should always be considered for patients with end-stage liver disease, it can often be dismissed as an option, owing to continued alcohol abuse, comorbid disease, or, in some circumstances, age alone. It can, however, be very difficult to decide when to refer patients for transplant and, if in doubt, the clinical situation should be discussed with a transplant centre (Appendix). Some broad guidelines are given in Table 6.6.

Table 6.6 Relative indications and contraindieations for liver transpiant in chronioc liver disease

Relative indications

- End-stage liver disease (janudice, ascites, ±encephalopathy) despite active medical treatment.

  Bilirubin >100 μmol/l in primary bialary clothosis
- Ascites refractory to both spironolactone and a loop duretic
- After two separate episodes of variceal heamonhage
- Recurrent or chronic encephalopathy
- One episode of documented spontaneous bacterial peritonitis

Relative contraindications

- Active hepatitis B or C infection (viral DNA or RNA in serum)
- Malignancy (unifocal hepaucellular or filrolarmetlar turnours in young patients may be an exception)
- Recent or contimued alcohol abuse (abstinence for <6 months)
- psychological inability to comphy with post transplant treatment and monitoring (involving regular medication, weekly blood tests, and liver biopsies)
- Age >60 years (but carefulty selected older patients have done well)

Continuing care by the family doctor

Although specific treatment for the cause of the liver disease varies, and some conditions are extremely rare, the principles of assessing hepatic function, portal hypertension and the pattern of change should guide every consultation.

Frequency of review

This depends on the treatment and stage of the liver disease. After specific treatment has been initiated, such as interferon-α for viral chronic hepatitis, or prednisolone for autoimmune chronic hepatitis, patients should be reviewed every 1–2 weeks. This allows side-effects to be assessed and transaminases to be checked. Similarly, when the patient has started to receive treatment for ascites as an outpatient, close monitoring of weight and electrolytes every week is essential. Once transaminases or ascites have stabilized, the frequency of review can be reduced. Patients with stable cirrhosis can be reviewed every 3–6 months.

Questions to ask

Bearing in mind the above principles, regular assessment of general well-being, weight, clinical examination and blood tests will evaluate hepatic function, portal hypertension and the progression of the disease. *Specific questions* should relate to the underlying condition: control of itching in primary biliary cirrhosis, myalgia or arthralgia in autoimmune liver disease and alcohol intake in alcoholics are examples. Regular abdominal *examination* to assess the liver, spleen size and ascites should be recorded.

The opportunity should be taken to perform *blood tests* on most visits, including monitoring of urea, electrolytes, transaminases, alkaline phosphatase, bilirubin and albumin, supplemented by random blood ethanol measurement if appropriate. The results should be communicated to the hospital specialist, by asking the laboratory on the request form to send a copy. The family doctor should always be alert to early signs of encephalopathy, which may be subtle (personality change, altered sleep pattern, mild disorientation), before drowsiness, asterixis or fetor occur.

When to refer for review

Patients with chronic liver disease will usually be regularly reviewed in outpatients. Requests for an urgent review should follow increasing ascites, rising transaminases (especially in autoimmune chronic liver disease), or unexpected clinical deterioration. The development of encephalopathy is usually an indication for admission.

Hospital visits

The purpose of regular review is to assess the pattern of change in liver function tests, hepatocellular function and portal hypertension, so that complications can be detected at an early stage and decisions about further treatment, including transplantation, can be facilitated.

Assessment

The *evidence for the diagnosis* (e.g. serology, histology) should be reviewed and the *pattern of change* in liver function tests recorded on a flow chart. Specific monitoring results (such as viral nucleic acids during interferon therapy, ferritin or Fe/TIBC ratio in haemochromatosis) should also be reviewed. *Examination* should document the weight, liver and spleen size, signs of chronic liver disease, ascites and any features of encephalopathy.

Decisions can then be made about further investigation (e.g. ultrasound, repeat liver biopsy), continuing specific treatment and the timing of review. Surveillance by endoscopy to detect varices, or by ultrasound and α-fetoprotein measurements to detect hepatomas in patients with cirrhosis, have not been shown to alter the outcome. It is always helpful to give the patient request forms to have blood taken (liver function tests, other specific monitoring tests) a week or two *before the next appointment,* taking care to mark the forms 'copy to the family doctor'.

Frequency of review

It is not possible to be dogmatic, but patients with deteriorating liver function or ascites, or in whom specific treatment has been started, should be reviewed at short intervals (2–4 weeks), whereas those with stable cirrhosis can be reviewed every 6–12 months.

Special situations

HCV infection detected in blood donors

Initial screening of blood donors is by a simple enzyme-linked immunosorbent assay (ELISA) test for antibodies to hepatitis C virus (HCV). This is very sensitive, but not always specific, so the result has to be confirmed by recombinant immunoblot assay (RIBA). Most such patients will also have evidence of active viral replication if serum is analysed by the polymerase chain reaction (PCR) for the presence of viral nucleic acid. PCR analysis is usually restricted to monitoring the response to interferon therapy.

When the blood transfusion service contacts the family doctor about a positive result, the patient should be seen and referred for a specialist opinion. The *implications* are that up to 70% develop chronic liver disease, although only 20–40% develop cirrhosis and this may take 20–30 years to develop. Sensitive questioning about the *source* of HCV

infection is necessary: the main source is shared needles or equipment during intravenous drug misuse. Transfusion of blood or components abroad, or prior to the introduction of routine screening in the UK in 1991, or of clotting factors prior to virus-inactivation procedures in 1984, are other sources although transfusion-infected patients have generally had a small viral load. Sexual transmission is rare (<5%), but partners should be tested and barrier methods of contraception discussed. The results of transaminase assessment and clinical evidence of liver disease should be included in the referral letter.

Further *counselling* will be given by the specialist and treatment options discussed. In view of the expense of interferon therapy, local treatment protocols depending on liver histology and possibly the HCV genotype may be available. The authors' practice is to offer treatment to patients with lobular inflammation, bridging necrosis, or early cirrhosis with an active inflammatory infiltrate, taking into account the domestic stability and wishes of the patient. There seems little value in starting treatment in itinerant patients with low compliance.

Prognosis

The prognosis of chronic liver disease depends on the aetiology. In *alcoholic cirrbosis,* 70% will survive 5 years if they abstain, but for those who continue drinking, only 30% will survive. Patients with histology showing *viral chronic persistent hepatitis* have an excellent prognosis, with little chance of progression to cirrhosis.

In contrast, more than 70% with *viral chronic active hepatitis* will develop cirrhosis within 10 years and once *viral cirrhosis* has occurred, 5-year survival is only 70%. For *autoimmune chronic active bepatitis,* an early study showed a 63% 10-year survival in patients treated with prednisolone, compared with 27% in controls. As transplantation was not then available, current figures will be better.

In asymptomatic *primary biliary cirrhosis,* data from the 1980s show a 12-year median survival after diagnosis; once jaundice has developed, survival is less than 2 years. In asymptomatic *primary sclerosing cholangitis,* median survival is 10–15 years after diagnosis. If *haemochromatosis* is diagnosed before cirrhosis has occurred, complete regression of liver disease with a normal life expectancy can be anticipated. This emphasizes the importance of screening family members with blood tests for iron/iron-binding capacity and liver biopsy, if appropriate. Once cirrhosis has occurred, a hepatoma will develop in about 15%. The median survival after hepatoma has developed is 12 weeks.

The development of *complications* from chronic liver disease is a poor prognostic sign and, where appropriate, liver transplantation should be considered. Once refractory ascites needing paracentesis develops, only 20% survive 3 years. Following spontaneous bacterial peritonitis, 1-year survival is less than 40%. Hypoalbuminaemia, a prolonged prothrombin time and recurrent cholangitis in chronic cholestatic liver disease are also indications that transplant should be considered.

Survival following *liver transplantation* continues to improve. This is influenced by the timing of referral (those referred early do better), aetiology of liver disease and associated disease. For primary biliary cirrhosis, more than 80% survive 1 year and the

vast majority of these will survive 5 years. For primary sclerosing cholangitis, 1-year survival is 75–85%.

Summary

Abnormal liver function tests

Identify the pattern Distinguish between

- *pre-hepatic* (elevated bilirubin, normal hepatic enzymes),
- *hepatocellular* (predominantly elevated AST) and
- *cholestatic* (predominantly elevated ALP and γGT)

Clinical assessment Careful history (sequence of events, drugs, alcohol, travel, contacts etc). Look for features of chronic liver disease (muscle wasting, telangiectases, etc).

Initial investigation *Pre-hepatic.* reticulocyte count.
Hepatocellular. hepatitis serology, autoantibodies, ultrasound.
Cholestatic: antimitochondrial antibodies, ultrasound.

Referral criteria Asymptomatic isolated elevation in bilirubin or γGT: reassure and do not refer. Asymptomatic, minor derangement (AST< twofold elevated): repeat LFTs after abstinence and refer routinely if abnormality persists. Symptomatic, AST or ALP>twofold elevated: urgent outpatient referral. Jaundice, hepatitis serology negative: discuss admission for investigation.

Chronic liver disease

Diagnosis Defined by aetiology, grade of inflammation and stage of fibrosis (histology of liver biopsy, serology and biochemical tests, Table 6.3)

Referral criteria *New patients:* any patient with abnormal liver function tests and positive serology, or abnormal LFTs persisting for more than 6–12 weeks after abstinence from alcohol.
Review: unexpected increase in transaminases, development of ascites, jaundice or unexpected deterioration. Encephalopathy is an indication for admission.

Monitoring Weight, general well-being and blood tests (hepatic enzymes, albumin, bilirubin, prothrombin time). Specific tests for the aetiology (e.g. ferritin, caeruloplasmin). Frequency depends on the clinical state. Every 1–2 weeks for ascites or after initiating specific treatment, to every 3–6 months in stable cirrhosis.

Treatment

Disease specific	**Ascites**	**Encephalopathy**

Table 6.3 and p. 104.	Identify/treat provoking factor. Ascitic tap. Restrict fluid to 1500 ml/day. No added salt. Spironolactone 100–400 mg/day. Bumetanide 1–4 mg/day. Paracentesis and intravenous albumin if refractory.	Identify/treat provoking factor (infection/bleed/ drugs/hepatoma). Lactulose 60–120 ml/day Protein restriction (<60 g/day) Start empirical antibiotics if no cause identified.

Key points

- Abnormal liver function tests are common and often durg-induced. Asymptomatic patients with and isolated elevation in γGT do not need further investigation.
- The history and pattern of agbnormal liver function tests give a good due to the cause (Tabel 6.2)
- Chronic liver disease is rare in general practice, but good management can improve the quality and length of life.
- Specific diagnostic and treatment of chgronic liver disease are complex, but general managment principles are similar Each consultation should be guided by the need to assess hepatic function and the control of protal hypertension, and to evaluate the pattern of change.

Further reading

Batts KP, Ludwig J. Chronic hepatitis. An update on terminology and reporting. *Am J Surg Pathol* 1995; **19:** 1409–17.

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Chapter 7
Inflammatory bowel disease

The management of ulcerative colitis and Crohn's disease is quintessentially that of shared care. Patients are often young (two-thirds present aged less than 40 years) and there are frequently implications for employment and insurance as a result. Patients are generally well when in remission, but have unpredictable relapses of embarrassing and disabling symptoms. These relapses can be rapidly alleviated by prompt treatment and the risk of serious complications can be reduced by continuity of care. Despite similarities in the initial treatment of ulcerative colitis and Crohn's disease, subsequent management may differ radically, especially with respect to surgery. Every attempt should therefore be made to obtain a specific diagnosis by considering the symptoms, and the endoscopic, histological and radiological features of each patient. The principal diagnostic differences are summarized in Table 7.1. In the 10% of patients in whom the conditions cannot be distinguished, the term 'indeterminate colitis' (having features of both) is better than an indiscriminate label of inflammatory bowel disease.

Presentation

Ulcerative colitis is an inflammatory disorder of the colonic mucosa for which bloody diarrhoea is the hallmark. In contrast, Crohn's disease is a transmural inflammatory disorder with a predilection for the distal ileum and a tendency to form strictures or fistulae. Consequently, Crohn's usually presents as diarrhoea without bleeding,

Table 7.1 Principal diagnostic differences between ulcerative colitis and Crohn's disease

	Ulcerative colitis	**Crohn's disease**
symptoms and signs		
■ Bloody diarrhoea	90–100%	25–50% even in Crohn's colitis
■ Abdominal pain	Mild	often severe
■ Weight loss	Only in servere disease	Frequent; may be sole feature
■ Abdomas mass	Almost never	Common
■ Perianal disease	Exceptional	30–40%
Sigmoidoscopy		
■ Rectal sparing	Never if untreated	Frequent
Histology		

■ Inflammation	Diffuse mucosal	Focal and transmural
■ Cellular infiltrate	Poltmorphs	Lymphocytes
■ Glandular architecture	Distorted	Preserved
■ Goblet cells	Depleted	Normal
■ Granulomas	Absent	Diagnostic
Imaging		
■ Disease distribution	Confined to the colon	Throughout the intestine
■ Pattem	Continuous, from rectum	Discontinuous, skip lesions
■ Mucosa	Superficial ulceration	Deep fissures
■ Symmeuy	Symmetrical inflammation	Asymmetrical
■ Strictures	Very rare	Common
■ Fistulae	Never	Common

but with abdominal pain and weight loss. Both conditions are characterized by relapses and remission and, although the mechanisms of inflammation are increasingly understood, the triggering factor(s) remain unknown.

Traditionally, about 1 in 500 of the population are thought to be affected by ulcerative colitis or Crohn's disease. More recently, using computerized records in primary care of hospital-diagnosed cases in one area of the UK, evidence suggests that the prevalence may be nearer 1 in 250. Ulcerative colitis is about twice as common as Crohn's disease. This may be because many patients with proctitis (representing up to 48% of patients presenting with ulcerative colitis) are managed by family doctors and do not feature in other epidemiological studies. These new prevalence data need to be confirmed.

Establishing the diagnosis

For *ulcerative colitis,* sigmoidoscopy and rectal biopsy will always be abnormal during active disease (Figure 7.1), although therapeutic enemas may cause relative rectal sparing.

For *Crohn's disease,* there is no single definitive test (Figure 7.2). Sigmoidoscopy and rectal biopsy should always be performed, as granulomas may be identified in up to 10% of patients with a macroscopically normal rectal mucosa. Small bowel radiology is appropriate if abdominal pain is a prominent feature, looking for ileal or small bowel strictures. A barium follow-through is often adequate, but a small bowel enema gives better mucosal definition, although it is less comfortable for the patient because an orojejunal tube is used to introduce contrast. Colonoscopy may show characteristic aphthoid or serpiginous ulcers with intervening normal colonic mucosa, and biopsies can be taken. The role of a barium enema is now limited, unless fistulae are suspected.

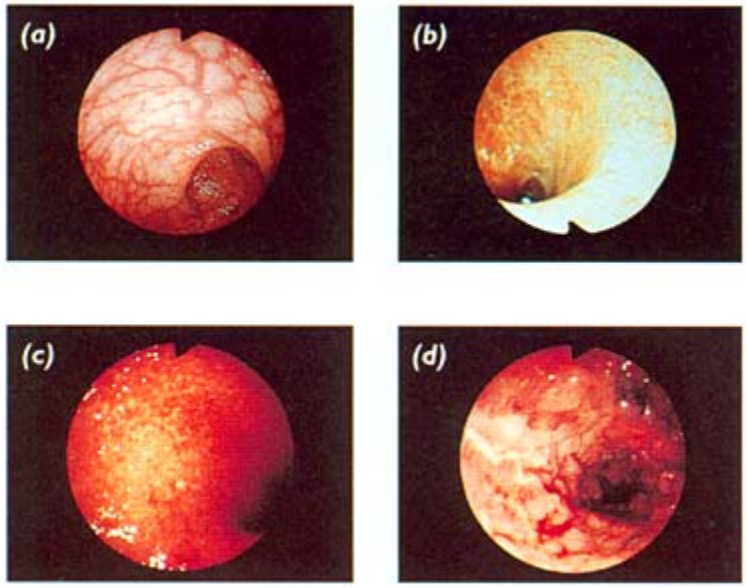


Figure 7.1 *Establishing the diagnosis in ulcerative colitis by sigmoidoscopy.*

When to refer to outpatients

New patients presenting with *bloody diarrhoea* should always be referred for further investigation if stool cultures are negative. The referral letter should state the number of bloody stools per day, the

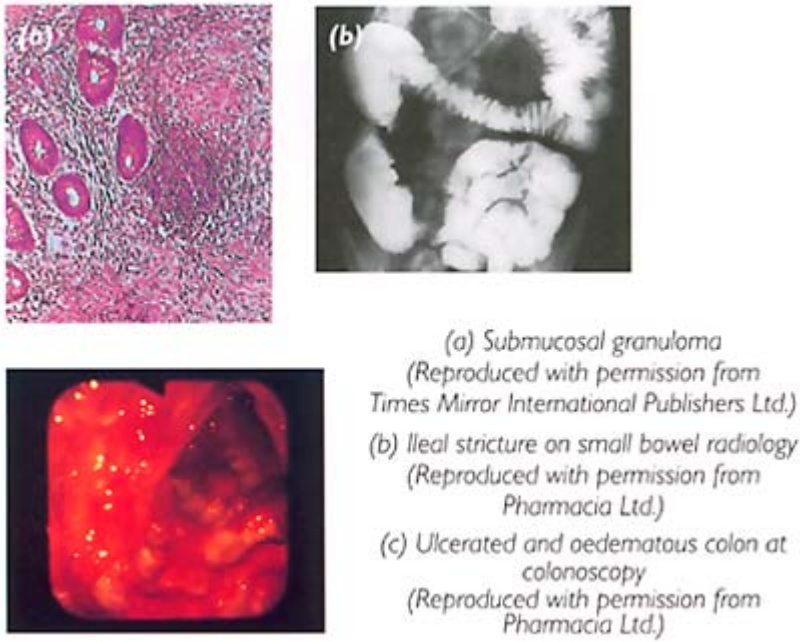


Figure 7.2 *Establishing the diagnosis in Crohn's disease by biopsy, small bowel radiology and colonoscopy.*

pulse rate, temperature, haemoglobin and erythrocyte sedimentation rate (ESR). If the criteria for a potentially severe attack (see Table 7.3) are met, the gastroenterologist should be telephoned. In patients presenting with *diarrhoea without bleeding,* those with negative stool cultures should be referred if diarrhoea persists for more than 3 weeks.

Early *review* of patients with established ulcerative colitis or Crohn's disease should be requested if a relapse fails to resolve on local steroid or mesalazine enemas within a couple of weeks, or if symptoms recur within 6 weeks of finishing a course of steroids. Most gastroenterologists with an interest in inflammatory bowel disease run an 'open access' clinic, which patients can telephone to make an early appointment.

Management

The principles of management are prompt control of active disease, maintenance therapy to extend remission, detection of complications and selection of patients for surgery. Continuity of care provided by a gastroenterologist in close cooperation with surgical and general practice colleagues establishes the confidence of patients and allows most to lead a normal life. Patient education is essential to ensure early presentation in the event of a relapse.

Explaining the diagnosis to the patient

Once the diagnosis has been established, it is important to explain the distribution, likely pattern of disease, treatment options and prognosis, in terms that the patient can understand. Much of the 'IBD neurosis' that was a feature of colitis or Crohn's disease can be attributed to the lack of a sympathetic explanation of miserable symptoms, delay in diagnosis, poor continuity of care or failure to treat active disease promptly.

Some facts may help explain the diagnosis (Table 7.2). It is also helpful to describe a strategy for the initial treatment of a relapse, to provide a telephone number for an open-access appointment and to give details of the National Association for Colitis and Crohn's Disease (Appendix).

Table 7.2 Explaining ulcerative colitis and Crohn's disease

	Ulcerative colitis	Crohn's diesase
Epidemiology		
■ Incidence	1–2 per 10,000, stable	0.6 per 10,000, increasing
■ Prevalence	10–27 per 10,000	5–16 per 10,000
Potential causes		
■ Inheritance	10–20% have affected relative, especially in Crohn's	
■ Infections	No definite link	??Measles
	?*E. colf*	??Mycobacteria ??Others
■ Diet	No link	No definite link
■ Smoking	Decreases risk	Increases risk
■ Immunological	Epithelial and T-cell interactions influenced by treatment	
Pattern		
■ Intermittent relapses	90%	90%
■ Annual relapses	20%	40%
■ Continuous symptoms	10%, only in first 5 years	Inadequate data
■ Remission	50% at any one time	40% at any one time
■ Remission for 1 year after relapse	30%	20%
■ Continued remission after 1 year	80%	70%
■ Prolonged remission	50–60% up to 10 year	Inadequate data
■ Effect of maintenace therapy	Fourfold reduction in relapses	Twofold reduction in relapses

Ulcerative colitis Crohn's diesase

Prognosis		
■ Life expectancy	Normal	Normal
■ Risk of colecomy	9–35% in 1st 5 years, than 1%/year	5% for Crohn's colitis
■ Risk of surgery	9–35% in 1st 5 years, than 1%/year	50% at 5 years, than 10% each 5 years
■ Risk of more than one operation		12% at 5 years, 23% at 10 years, 26% at 15 years
■ Clinical relapse after surgery		20% at 2 years, 30% at 3 years, 50% at 5 years
■ Risk of colorectal cancer	?10% in pancolitis after 20 years	Similar in extensive Crohn's colitis
■ Risk of other cancer	Not increased	<1% small bowel cancer
■ Effect on employment	>90% working after 10 years	>80% working after 10 years

Defining the distribution of disease

In ulcerative colitis, *colonoscopy* should be performed at an early opportunity after initial treatment, but not in severely active disease when there is a danger of colonic perforation. There is now rarely any role for barium enema in evaluating ulcerative colitis, because colonoscopy more accurately defines the extent of disease, allows biopsies to be taken and avoids radiation exposure (Figure 7.3).

In Crohn's disease, the whole intestinal tract should be evaluated by *small bowel radiology* and *colonoscopy*. When the diagnosis has initially been established by one of these investigations, the other should still be performed to assess fully the distribution of disease. (Figure 7.4).

Assessing disease activity

Simple, objective assessment of disease activity is essential, because patients can look misleadingly well and active disease is not the only cause of symptoms.

In *ulcerative colitis,* bloody stool frequency is broadly related to disease activity. The criteria in Table 7.3 have stood the test of time and help to define appropriate treatment.

Activity in *Crohn's disease* is more difficult to assess. Active disease should be determined by the history (usually diarrhoea with pain, anorexia or other systemic features) and confirmed by an elevated Creactive protein or other inflammatory markers (ESR, plasma viscosity). It is important to recognize that there are several causes of diarrhoea or pain in patients with Crohn's other than active disease (Table 7.4).

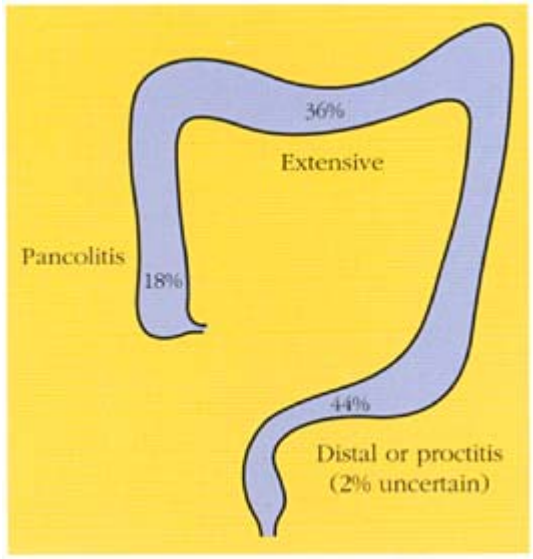


Figure 7.3 *Macroscopic distribution of ulcerative colitis at presentation In 1161 patients. (From Langholz E, Munkholm P, Davidsen M, Binder V. Course of ulcerative colitis: analysis of changes in disease activity over years. Gastroenterology 1994;* ***107:*** *3–11.) Proctitis: Limited to the rectum Distal: rectosigmoid, up to the splenic Extensive: up to hepatic flexure Pancolitis: Entire colon*

Treatment of active disease

For active *ulcerative colitis,* prompt and decisive treatment (Table 7.5) brings rapid relief to the patient and reduces the risk of complications,

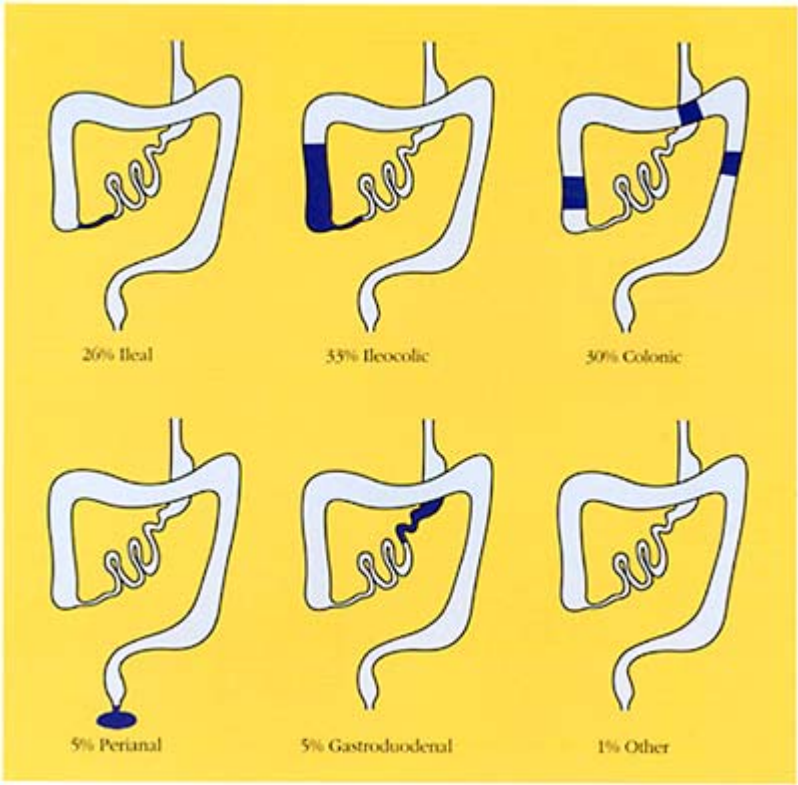


Figure 7.4 *Distribution of Crohn's disease in 373 patients. (From Munkholm P, Langholz E, Davidsen M, Binder V. Intestinal cancer risk and mortality in patients with Crohn's disease. Gastroenterology 1993;* ***105:****1716–23.)*

so oral steroids with enemas are recommended even for mild relapses. Foam enemas (such as Colifoam™, Predfoam™ or Asafoam™) tend to be better tolerated than liquid enemas (such as Predsol™ or Pentasa™ enemas), especially in proctitis, although liquid enemas may be preferable for more extensive left-sided disease.

Table 7.3 Assessing disease activity in ulcerative colitis

Feature	Mild	Moderate	Severe
Bloody motions (no/day)	<4	4–6	>6

Temperature	Apyrexial	Intermediate	>37.8°C on 2/4 days
Pulse rate	Normal	Normal	>90 bpm
Haemoglobin	Normal	Intermediate	<10.5 g/dl
ESR (mm/hour)	<30	<30	<30

(From Truelove SC, Witts IJ. Cortisone in ulcerative colitis. Final report on a therapeutic trial, *Br Med J* 1995; **2:**1041–5,)

Table 7.4 Causes of symptoms other than active Crohn's diesase

Abdominal pain		**Diarrhoea**
Obstruction	■ fibrotic stricture	small intestianal bacterial overgrowth
	■ adhesions	Hypolactasia
Abscess (usually with active disease)		Bile-salt malabsorption after ileocolic resection
Gall stones (after ileal resection)		Short bowel after resection
Renal caculi (hyperroxaluria after ileal resection)		Irritable bowel syndrome
Steroid-induced peptic ulceration		
Pancreatitis (azathioprine, steroids)		
Irritable bowei syndrome		
Other causes unrelated to Crohn's diesase		

It is quite reasonable for patients with distal colitis or proctitis to use steroid or mesalazine enemas as 'first aid' for a couple of weeks, prior to starting steroids if symptoms have not completely resolved. There is some evidence that mesalazine foam enemas are more effective than steroid foam enemas, but they are also more expensive. Indeed, mild disease of limited extent often settles with such local treatment, without the need to resort to systemic therapy. However, all too often patients are expected to put up with symptoms that are poorly controlled by local treatment and salicylates for many weeks or months, which is unnecessary.

Using the regimes below, about 75% enter remission within 2 weeks, compared with 60% after 4–6 weeks using salicylates and local steroids (Figure 7.5). Shorter courses of steroids are associated with an increased risk of relapse. Enemas give benefit in addition to oral steroids.

Table 7.5 Treatment of active ulcerative colitis

	Mild attacks	**moderate attacks**	**severe attacks**
Prednisolone	20 mg/day for	40 mg/day for	Admit for iv
	1 month	1 week,	and pr
	15 mg/day for	30 mg/day for	hydrocortisone
	1 week,	1 week,	(p. 138).

	10 mg/day for 1 week, 5 mg/day for 1 week, then stop.	then as for mild attacks	Refer by telephone to gastroenterologist.
Mesalazine or steroid foam enemas	Once or twice daily while bleeding, then at night for 2 weeks.	As for mild attacks.	
Salicylate therapy	Continue unchanged.	Continue unchanged.	

Active *Crohn's disease* is initially treated in a similar way. Vomiting, severe pain, tachycardia or hypoalbuminaemia usually indicate a severe attack, needing hospital admission for intravenous steroids (p. 138). Milder attacks can usually be treated on an outpatient basis with prednisolone 40 mg/day for 1 week, 30 mg/day for 1 week, then 20 mg/day for 1 month, before reducing by 5 mg/day every 1–2 weeks. Maintenance steroids are not indicated, but there is a group in whom steroid withdrawal is difficult. Alternatives to steroids are discussed below (p. 144). A low-residue diet is advisable if colicky abdominal pain persists.

Maintenance of remission

For *ulcerative colitis,* long-term maintenance therapy is almost always indicated, since salicylates reduce the risk of relapse by a factor of four. The new salicylates have not been shown to be more effective than sulphasalazine and all are three or four times more expensive. Steroids have no place in maintaining remission.

Sulphasalazine 1 g twice daily remains the first choice for many gastroenterologists, except for patients who are sensitive to sulphonamides; this dose is tolerated by 80% of patients. Common side-effects include headaches, nausea and rashes. Reversible oligospermia occurs in men and alternative therapy should then be considered. Serious side-effects are extremely rare (agranulocytosis, pneumonitis, hepatotoxicity and Stevens-Johnson syndrome), but for this reason some gastroenterologists prefer to start with one of the newer salicylates.

Olsalazine 500 mg twice daily with meals is an alternative for people who cannot tolerate sulphasalazine, although higher doses (1 g twice daily) are better for distal disease that has recently relapsed. Olsalazine may cause diarrhoea in about 10%, which is distinguished from active disease by sigmoidoscopy and the lack of bleeding. *Pentasa* 500 mg three times daily is an alternative if olsalazine cannot be tolerated. *Asacol* 400 mg three times daily is also as effective as sulphasalazine, but may not be as effective as olsalazine for distal disease.

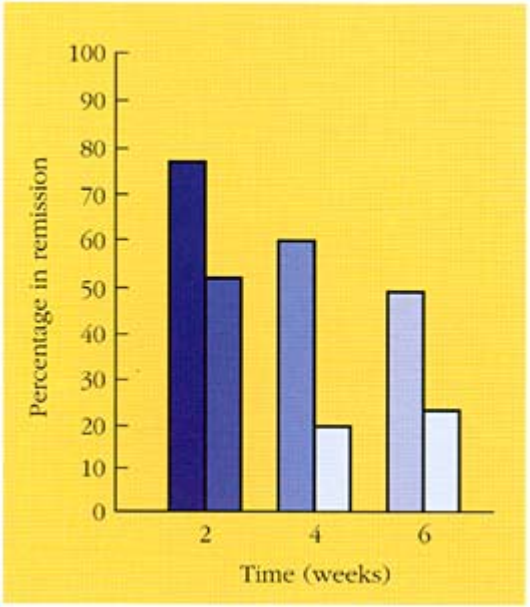


Figure 7.5 *Comparison of steroids and salicylates (prednisolone 20 mg; sulphasalazine (SASP) 6 g; olsalazine 2 g; Asacol 2.4 g) in mild to moderate attacks of ulcerative colitis Symptomatic remission occurs in 76% of patients treated with oral and rectal steroids for 2 weeks, compared with 48% of patients treated with Asacol and steroid enemas for 6 weeks. All treatments are, however, better than placebo ( ). (See Further reading for sources of data in full.)*

For *Crohn's disease* in remission, maintenance therapy is now advised by many gastroenterologists, although higher doses of the newer salicylates appear to be needed for ileal disease. The site of release of 5-aminosalicylic acid (5-ASA) differs between the compounds, as does the serum concentration. Since 5-ASA has a local action on the intestinal epithelium and is potentially nephrotoxic, the lower the serum concentration the better (Figure 7.6). The mechanism of salicylate-associated nephrotoxicity, however, remains controversial and may be a hypersensitivity reaction independent of dose. All salicylates should be avoided or used with great caution in renal impairment.

Asacol 800 mg three times daily has halved the risk of relapse in some well conducted studies and is the only salicylate licensed for maintenance therapy of ileocolic Crohn's disease in the UK. However, bearing in mind the lower serum 5-ASA concentration and convenience of twice daily dosing, some gastroenterologists prefer *Pentasa* 1 g twice daily (500 mg tablets are available), which is principally indicated within 3 months of a relapse of Crohn's disease or surgery. Sulphasalazine 1 g twice daily is acceptable when disease is limited to the colon.

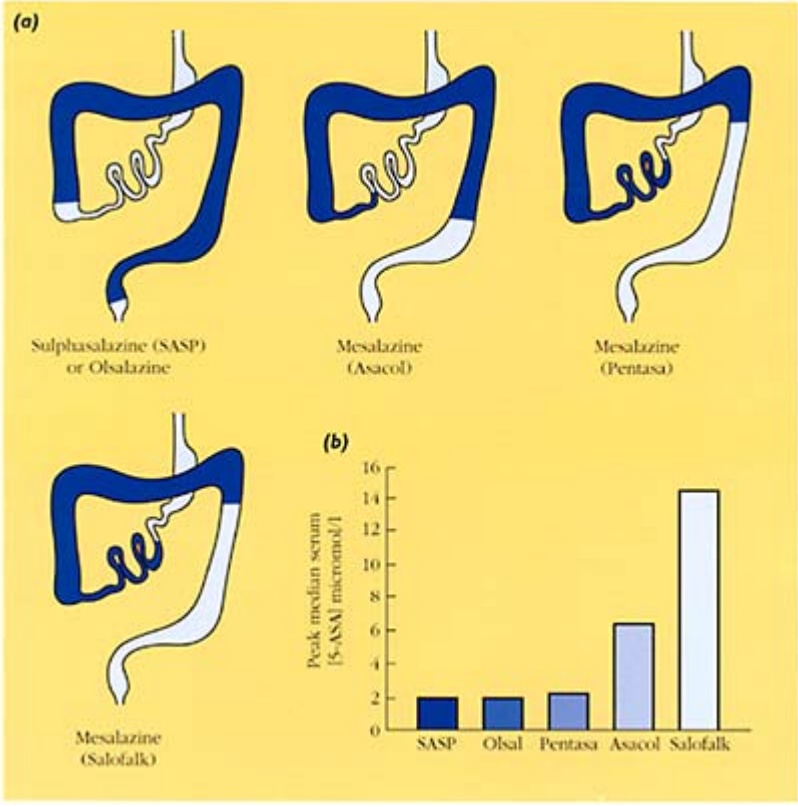


Figure 7.6 *(a) Schematic diagram comparing the intestinal release of salicylate compounds. (b) 5-Aminosalicylic acid (5-ASA), the active component of maintenance therapy, works through a local action on the intestinal epithelium and side-effects are largely related to systemic absorption. There are appreciable*

differences between compounds in the site of release and absorption.

Continuing care by the family doctor

Patients are best reviewed regularly, to identify persistent symptoms and to detect side-effects of treatment. The family doctor is often in the best position to assess the impact of the condition on employment.

Frequency of review

A review midway between hospital visits is usually appropriate. When the patient has relapsed, intervals may be as short as every 1–4 weeks; when in remission for longer than 6 months, visits every 6–12 months are sufficient.

Questions and investigations

Specific questions should be asked about bowel frequency, visible rectal bleeding, timing and nature of abdominal pain, general well-being and any side-effects from treatment. Most patients can expect a good quality of life without pain. Symptoms such as a bowel frequency greater than three times daily, especially if nocturnal, should not be dismissed as 'typical' for a patient with inflammatory bowel disease, without considering treatable causes (Table 7.4).

When new symptoms develop, the *full blood count* and *C-reactive protein* should be checked to assess disease activity, especially in Crohn's disease. For patients in remission, it is sufficient to check a full blood count, *creatinine and liver function tests* every 6–12 months. Blood dyscrasias can occur very rarely with any of the salicylates, but are much less common during sulphasalazine treatment of ulcerative colitis than during that of rheumatoid arthritis. Unexplained anaemia, deterioration in renal function or the development of cholestatic liver function tests may be the first sign of complications such as carcinoma, drug nephrotoxicity or primary sclerosing cholangitis. Patients on *azathioprine* should have their full blood count monitored every 4–6 weeks, because 5% develop neutropenia.

Follow-up appointments should not just focus on the presence or absence of symptoms, but also take into account how the patient feels about their qualilty of life. This is affected by many factors including degree of continence, sexual problems, social difficulties from flatus or urgency, employment and relationship issues. Even if problems cannot be solved, they should be acknowledged and not ignored. Access to other professionals (counsellor, continence adviser, social services) should be made possible.

Figure 7.7 *Shared-care diary.*

Shared-care diary

If family doctors are going to complement hospital care (and vice versa), communication is vital. A shared-care diary carried by the patient is one way of facilitating this. A useful diary designed for this purpose is provided by SmithKline Beecham Pharmaceuticals (Figure 7.7). Family doctors—but not necessarily gastroenterologists—will be familiar with the concept from obstetric care. Treatment changes, results of blood tests and investigations can be documented.

Other aspects

When patients are stabilized, 3-month prescriptions for maintenance therapy are best given, to reduce the cost to individual patients.

The early stages of a relapse should be treated according to a locally agreed enema/oral steroid protocol. For practices without facilities for proctoscopy, steroid or mesalazine enemas alone can be given, pending review in outpatients under an open-access policy. If symptoms have not resolved within a couple of weeks on primary treatment, patients should be referred back for early review.

Hospital visits

Long-term follow up in a specialist clinic, even for those with quiescent disease, is usually appropriate for a number of reasons. First, the severity of disease is frequently underestimated by non-specialists and regular follow-up provides an immediate point of

contact; second, cancer not infrequently presents in patients who have been lost to follow-up; and third, in the event of complications (such as cancer, severe relapse leading to surgery, or primary sclerosing cholangitis) management is greatly facilitated if confidence between patient and specialist has been established during follow-up. The balance between hospital and primary care follow-up is affected by the patients' confidence in the doctors concerned, degree of severity of the condition and convenience of the hospital.

Assessment

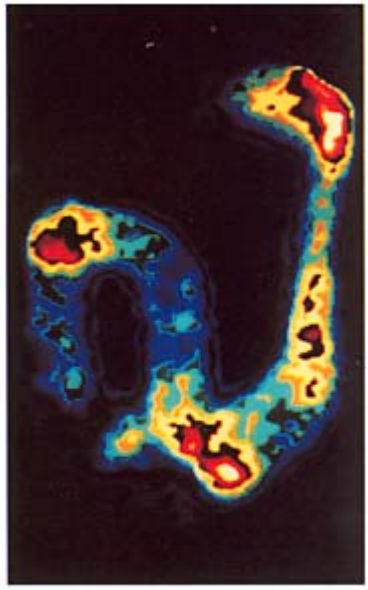
It greatly facilitates assessment if the date of onset of symptoms, site and extent of disease, presence or absence of positive histology, date of last small bowel/colonic examination and the chronology of operations or complications has been summarized. If this has not been done recently, the first couple of minutes should be spent doing this.

At each review, present symptoms and extra-intestinal manifestations, the weight and abdominal signs should be recorded. Sigmoidoscopy is necessary only if recurrent symptoms have developed in patients with colitis, to confirm active disease. It is advisable to ensure that the patient has some understanding of the extent of disease and the reason for maintenance therapy, as well as knowing what to do in the event of a relapse. Questions should be asked about the general quality of life and the impact of any symptoms on social, occupational and family relationships.

Further investigations

Patients have many investigations over a lifetime, so radiological investigations should be performed only when they will affect decision-making. Patients often find investigations undignified, embarrassing, or very unpleasant, so this should be considered. For ulcerative colitis, *colonoscopy,* rather than a barium enema, is indicated. Colonoscopy best determines the extent of disease, and is indicated if anaemia develops in a patient with quiescent colitis, or to reassess the extent of active disease in refractory distal colitis (p. 142), or if the rectal mucosa is normal despite recurrent symptoms. The role of surveillance colonoscopy is hotly debated (p. 143) but should, in any case, be limited to patients with pancolitis for more than 10 years.

After diagnosis of Crohn's disease, *small bowel radiology* is indicated only if surgery is being considered, such as for obstructive abdominal pain despite initial medical treatment. For active disease, the *C-reactive protein* is currently the most sensitive marker. In patients with symptoms of active disease but with normal inflammatory markers, an isotope-labelled *white blood cell scan* may confirm disease activity (Figure 7.8).



Slide No. 26. ^{99m}Tc–labelled white blood cell scan in patient with Crohn's disease. Reproduced with permission from Pharmacia Ltd.

Figure 7.8 *^{99m}Tc-labelled white blood cell scan in a patient with active Crohn's disease*

Frequency of review

A rough (and empirical) guide to the frequency of review is given in Table 7.6. Factors such as disease complexity, previous response to treatment, travelling distance to the hospital, overbooking of outpatient clinics and established shared-care protocols will need to be considered.

Indications for hospital admission

Patients with *severe ulcerative colitis* (bloody stool frequency >6/day with pyrexia, tachycardia, anaemia or high ESR; Table 7.3, p. 128)

Table 7.6 Rough guide to reviewing patients

	Ulcerative colitis	Crohn's disease
Active disease	2–6 weeks	2–4 weeks
After inpatient treatment	2–6 weeks	2–6 weeks
Remission after treatment	3 months	6–12 weeks

Remission 3–6 months	6 months	3–6 months
Remission >6 months	12 months	6–12 months

should always be admitted for intensive medical treatment. Mortality in this group was 30–40% before steroid therapy and is still about 5%, although it is less than 1% in specialist centres. Sometimes it may be appropriate to admit elderly patients with moderate attacks of ulcerative colitis who have difficulty in managing at home.

In *Crohn's disease,* patients with vomiting, severe abdominal pain, pyrexia or hypoalbuminaemia usually need admission for intensive medical treatment. It is vital to remember that steroids can mask physical signs (including those of perforation) and that a superficial impression may be misleading.

Intensive treatment for severe disease

For ulcerative colitis, a rigorous '5-day' regime of intravenous fluids (3000 ml/24 hours, with 80 mmol KCl/24 hours), intravenous hydrocortisone 100 mg four times daily and rectal hydrocortisone has a 70% chance of inducing remission. Heparin should be given subcutaneously to reduce the risk of thromboembolism and the patient should be transfused if anaemic. The benefit of withdrawing food has not been proven, but patients are often anorexic and the response to reintroducing food after 5 days on intravenous fluids may help decide whether remission has really been achieved.

For intensive treatment of *severe Crohn's disease,* the same regimen is followed but without rectal steroids unless there is rectal involvement. Intravenous metronidazole 500 mg three times daily is appropriate if there is pyrexia or leucocytosis, since infection may mimic or complicate active Crohn's disease.

For both conditions, *investigations on admission* are similar. An urgent full blood count, assessment of electrolytes, grouping and saving of serum, and abdominal radiography should be performed. Stool should be sent for culture and *Clostridium difficile* toxin assay, and if there is pyrexia, blood cultures are necessary.

Response to treatment should be monitored by the temperature, pulse rate and stool frequency. Deterioration at any stage or failure to respond after 5 days are usually indications for surgery, because perforation increases mortality to 30% if surgery is inappropriately delayed. Some gastroenterologists continue treatment for much longer, especially in those who make a partial response. Prospective studies have shown, however, that such patients continue to have symptoms and 60% come to colectomy within the next few months.

For those who respond to intensive treatment, food can be reintroduced after 5 days, with oral prednisolone (40 mg/day) and steroid enemas twice daily. If there is no increase in bowel frequency, pulse or temperature, sulphasalazine 1 g twice daily (or olsalazine 500 mg twice daily, or mesalazine 500 mg three times daily, if intolerant) can be reintroduced and the patient discharged to be followed up in 2–4 weeks. Oral steroids can be tapered, as in Table 7.5 (p. 129).

Indications for surgical referral

Joint management by a gastroenterologist and colorectal surgeon with special interests in inflammatory bowel disease produces the best results. The team approach ideally involves care on a gastroenterology ward with specialist nurses, including responsibility for stoma care.

In ulcerative colitis, *colectomy* is indicated in patients who have any of the following:

- severe colitis unresponsive to intensive medical treatment
- continuous symptoms (often with general ill health and anaemia) despite treatment
- frequent relapses, poorly responsive to medical treatment, that materially affect the patient's life
- dysplasia on colonic biopsies
- frank malignancy.

Although some patients (and their doctors) are prepared to tolerate a certain level of symptoms that limit social and working life, the *advantages and disadvantages of colectomy* if real remission cannot be achieved should be discussed. Colectomy for ulcerative colitis means that immunosuppressive drugs are no longer required; it eliminates the risk of colorectal cancer (p. 146) and can be expected to relieve the patient of the unpredictable urgency of defaecation that is so socially limiting. On the other hand, it involves a major operation (mortality 1–2%) and at least a temporary ileostomy.

An *ileo-anal pouch* is indicated for patients with ulcerative colitis who have good continence even during spells of active disease and who do not want a permanent ileostomy. The procedure is usually performed in two or three stages (Figure 7.9). Good results are obtained in 90% of patients in experienced hands, but poor function can be just as debilitating as active colitis. *Proctocolectomy and a permanent ileostomy* as a single procedure may be preferred by some older patients.

In *Crohn's disease,* unlike ulcerative colitis, surgery does not offer a potential cure. It is indicated for symptomatic disease despite medical treatment, for intestinal obstruction from strictures, or for complications such as fistulae, abscesses or perforation. The principles are bowel preservation by *stricturoplasty* for short strictures or *limited resection* of the most diseased area by an experienced surgeon. Resistant colonic or perianal disease may be treated by a *defunctioning ileostomy,* proceeding to proctocolectomy only if symptoms recur when continuity is restored after 12–18 months. Ileo-anal pouch formation is absolutely contraindicated, because fistulae and sepsis develop. Interestingly, patients with 'indeterminate colitis' (when it is not possible to distinguish between ulcerative and Crohn's colitis) appear to follow the pattern of ulcerative colitis and usually do well with a pouch.

Early relapse and indications for azathioprine

Early relapse can be defined as recurrent symptoms as steroids are reduced below 15 mg/day, or within 6 weeks of completing a course of steroids (Table 7.5). This is usually an indication for early specialist review and consideration of azathioprine therapy.

A further course of steroids is worth giving first, but reducing the dose below 20 mg more slowly (by 5 mg/day every 2–4 weeks). If a further relapse occurs, then steroids should be increased to 20 mg/day for 1 month and azathioprine 2 mg/kg/day started, because it takes 3–4 weeks to take effect. Prednisolone can then be withdrawn by 5 mg/day every 2 weeks. Azathioprine is best continued for 3–4 years if tolerated, because it reduces the risk of relapse in both ulcerative colitis and Crohn's disease. Patients may be reluctant to stop azathioprine if they remain well, and should be involved in the decision-making, since there is a slightly increased risk of relapse when it is withdrawn. A blood count every 4–6 weeks is necessary to detect the 5% risk of agranulocytosis. Co-trimoxazole and allopurinol interact with azathioprine to increase bone marrow suppression, so are best avoided.

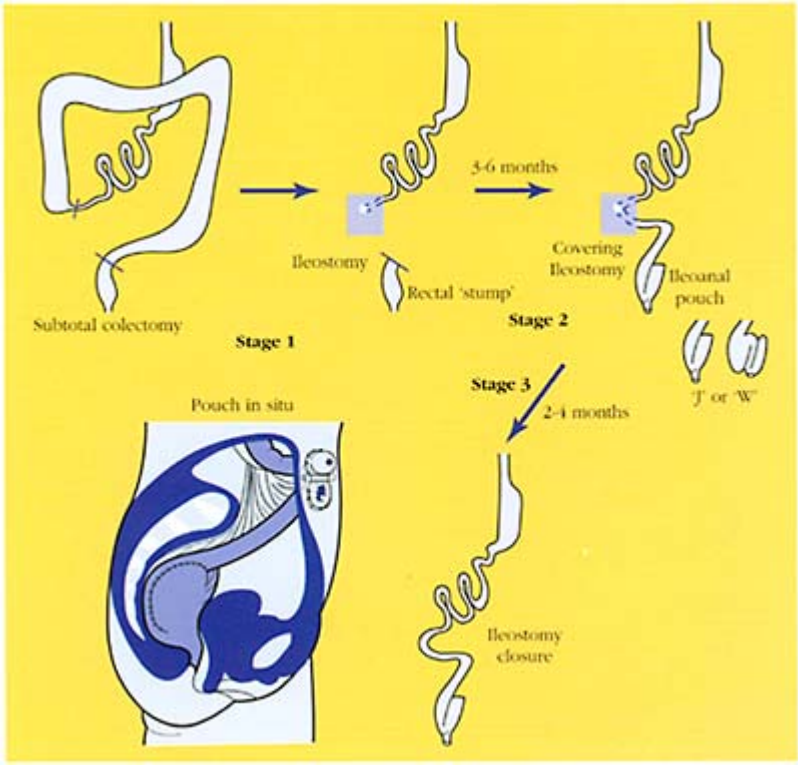


Figure 7.9 *lleoanal pouch formation for ulcerative colitis. Stages 1 and 2 are often combined, except in urgent colectomy for severe disease, or if the diagnosis (ulcerative colitis vs. Crohn's colitis) needs to be confirmed.*

Special situations and prognosis

Refractory distal colitis and proctitis

Limited ulcerative colitis can, paradoxically, be refractory to treatment and, although not dangerous, can cause disabling symptoms. Refractory disease can be defined as persistent symptoms despite steroid therapy, and is usually an indication for early specialist review.

Persistent, active disease should be confirmed by sigmoidoscopy. The first approach is to treat as for a moderate relapse, but using *5-aminosalicylic acid* 5-ASA, (mesalazine) rather than steroid *enemas*. Foam enemas (Asacol™) are usually better tolerated than liquid (Pentasa™) enemas. It is not clear why high local concentrations of 5-ASA can be more effective than steroids in this situation. If symptoms persist after another 2–4 weeks, a *plain abdominal X-ray* should be performed to look for proximal constipation. A laxative (such as one sachet of Picolax™) can be given, as anecdotal experience suggests that proximal constipation delays resolution of distal inflammation. If symptoms are still present after another 2–4 weeks, *colonoscopy* is appropriate to reassess the extent of disease and exclude a carcinoma. Colectomy is occasionally necessary, even in distal disease, but the whole colon must still be removed if recurrence is to be prevented.

For highly localized disease (<10 cm), local therapy with mesalazine suppositories rather than enemas may be better tolerated [available as 250 mg and 500 mg (Asacol™) or 1 g (Pentasa™) suppositories]. Anecdotal reports suggest that lignocaine gel twice daily, arsenic (Acetarsoal™) suppositories, bismuth enemas or cyclosporin enemas can be effective.

Pregnancy and contraception

Ideally, conception should be planned during an established period of remission. Although fertility may be reduced during active disease, it is not otherwise affected unless Crohn's disease has caused tubal obstruction. It is important that both the patient and obstetricians understand the need to continue *maintenance therapy* during pregnancy to reduce the risk of relapse. Sulphasalazine does not alter folate metabolism *in vivo* and published reports confirm the safety of sulphasalazine, olsalazine or mesalazine during pregnancy. *Active disease* should be treated normally, as the risk to the pregnancy of active disease is greater than that of side-effects. Both salicylates and low doses (less than 10 mg) of steroids may be given safely during breast-feeding. The combined contraceptive pill does not appear to alter the pattern of either ulcerative colitis or Crohn's disease.

Diet

In *ulcerative colitis,* no diet has been shown to alter the pattern of disease, although a high-fibre diet may help avoid proximal constipation in patients with proctitis. Furthermore, a lactose-free diet may reduce stool frequency in patients with concomitant hypolactasia, which is one cause of persistent diarrhoea after treatment of active disease.

In *Crohn's disease,* good nutrition is an important aspect of management, but this is usually achieved by controlling active disease. Fibre should be avoided when there are

obstructive symptoms. It is now generally accepted that either *elemental* or *polymeric* diets are effective treatment for active Crohn's disease when given as sole nutrition for 6–12 weeks. Polymeric diets are more palatable, but neither is as effective as oral steroids. Their main roles are as the primary treatment of ileocolic Crohn's disease in children, where growth failure may be corrected. In adult patients, a liquid diet may be appropriate for those who have a relapse after several operations despite maintenance therapy, or who have unacceptable side-effects (such as psychosis) from steroids, or as a means of medically defunctioning the colon in severe perianal disease.

Cancer surveillance

Colonoscopic surveillance every 3 years for patients with pancolitis for more than 10 years has been recommended, but efficacy is not proven (p. 165, chapter 8). Most cancers present in patients not being followed up in a gastroenterology clinic, or between dates of surveillance. Until an effective practical policy can be advised, it seems reasonable to perform a colonoscopy after 8–10 years to reassess the extent of disease. In patients with pancolitis, prompt colonoscopy is indicated if anaemia develops, or for a refractory relapse, or to investigate a change in symptom pattern.

Withdrawing long-term steroids

When disease is quiescent and steroids have been given continuously for more than a year, doses below 5 mg/day should be decreased at a rate equivalent to 1 mg/day each month, if hypoadrenalism is to be avoided. *Steroid-induced pseudorheumatism* (arthralgia, myalgia) is common in these circumstances. Paracetamol, NSAIDs, amitriptyline, or reintroduction of steroids may be tried in that order, but symptoms resolve after several months.

Alternatives to steroids and new treatment

Patients, especially young women, are often understandably concerned about steroid-induced side-effects. Most, however, accept that decisive treatment of active disease with a defined course of steroids (Table 7.5) is preferable to prolonged symptoms through under-treatment. Care should be taken to explain that short term side-effects (cosmetic, acne, dyspepsia, altered sleeping pattern, labile mood) resolve when steroids are withdrawn and that long-term effects (osteoporosis, avascular necrosis, dermal thinning) are usually a consequence of treatment for many months or years.

Budesonide-CIR (9–12 mg/day) is a steroid with poor systemic bioavailability that delivers a high concentration of steroid to the ileocaecal region. It is more effective than placebo for mild-to-moderate Crohn's disease and causes less adrenal suppression than prednisolone. Other controlled-release preparations designed to deliver poorly absorbed steroids to the colon, such as prednisolone metasulphobenzoate, are being developed for treatment of colitis.

Pentasa 4 g/day or a liquid *polymeric diet* for 6 weeks are also effective for mild to moderately active Crohn's disease. They are less effective than prednisolone, but offer an option for patients keen to avoid steroids.

Cyclosporin (4 mg/kg/day intravenously) has been shown in a controlled trial to induce remission in patients with severe ulcerative colitis unresponsive to steroids, who would otherwise need colectomy. Experience in the UK is not as favourable as in the USA, and cyclosporin should be used only in specialist centres, probably for patients with refractory limited disease or in patients facing colectomy during a severe first attack. A controlled trial has not shown any benefit in active Crohn's disease.

Other approaches include *methotrexate* (15 mg/week), which may induce remission in Crohn's disease otherwise refractory to steroids. Use should be limited to specialist centres in view of potential side-effects. *Fish oil* capsules (Purepa™) may halve the risk of relapse in Crohn's by modifying the release of pro-inflammatory leukotriene-B4, among other mediators. It is available only on a named-patient basis in the UK, pending further trials.

In the future, specific antagonists to tumour necrosis factor, or interleukin-10 therapy may have a role, but one of the advantages of the multiplicity of actions of steroids is that they influence at several stages the complex events that cause intestinal inflammation.

Prognosis

Recent population-based studies on the long-term morbidity and mortality from ulcerative colitis and Crohn's disease are encouraging. This is important, not only from the patient's point of view but in advising on insurance risk, because life-assurance companies calculating risks have used data from tertiary referral centres that are skewed towards patients with more severe disease.

Survival. There appears to be no increase in mortality from ulcerative colitis after the first year. However, in one population-based study from Copenhagen, the relative risk of death in 1161 patients during the first year was 2.4. For Crohn's disease there also appears to be no overall increase in mortality compared with the general population. However, patients aged 20–29 years at diagnosis had a threefold, and those with extensive small bowel disease had a sixfold, increase in relative mortality. These two groups constitute about 10% of patients with Crohn's disease.

Surgery. For ulcerative colitis, the colectomy rate varies with the local approach to management of refractory disease. Following an approach similar to that advocated above, the cumulative colectomy rate in 1161 patients 10 years after diagnosis was 24%, and 32% after 25 years. Within the first 5 years of diagnosis, the colectomy rate was 9% for distal colitis, 19% for substantial colitis and 35% in total colitis. After 5 years, the colectomy rate was 1%/year and did not differ between patient groups.

For Crohn's disease, about 50% have an operation within 5 years of diagnosis, 60% after 10 years, 70% after 15 years and 80% after 20 years. Patients with ileocaecal disease are more likely to need surgery within 5 years (78%) than when disease affects other locations (44%). About 10% of patients with Crohn's colitis have a permanent ileostomy after 10 years. After 15 years, 30% of patients have had no surgery, 34% have had one operation and 36% have had two or more operations.

Cancer. Patients with total ulcerative colitis for more than 10 years have an increased risk of colorectal cancer. It also appears that patients with Crohn's colitis of equivalent extent and duration have a similarly increased risk. Reports vary, but a lifetime risk of 2% in the general population may be increased to 20% after pancolitis for 25 years. The

risk is not increased for left-sided or distal disease. However, in the best epidemiological study to date, the risk of cancer was not increased in 1161 patients. This was owing to good follow-up and early colectomy for refractory symptoms, but is reflected in the relatively high colectomy rate overall. The risk of small bowel cancer appears to be increased in small intestinal Crohn's disease, as is anal canal carcinoma in perineal disease, although both remain rare.

Pattern. Disease activity in ulcerative colitis is intermittent in 90% and continuous in 10%, although the latter usually come to colectomy. About 50% of patients are in remission at any one time. Although 50–60% remain in remission for several years, 20% will have a relapse every year. Relapses in the first 2 years after diagnosis mean that continuing disease activity over the next 5 years is likely.

Working capacity. Apart from the year of diagnosis, 90–95% of patients with ulcerative colitis maintain working capacity after 10 years. On the other hand, of the 3% of patients incapable of work in the second year of disease, two-thirds remain incapable of work after 10 years.

Summary

Referral criteria	New patients	■	diarrhoea lasting more than 3 weeks.
		■	bloody diarrhoea when no pathogens isolated.
	Review patients	■	deteriorating symptoms after 2 weeks' treatment (open access).
General	Distinguish between ulcerative colitis and Crohn's disease by history, colonoscopy, biopsies and small bowel radiology.		
Clinical	7.3, p. 128) by history and Confirm diesaes activity by history and sigmoidoscopy (UC) or C-reactive protein (CD).		

Treatment

Active ulcerative colitis

Mild	**Moderate**	**Severe**
Prednisolone 20 mg/day for 1 month, 15 mg/day 1 week, 10 mg/day 1 week, 5 mg/day 1 week, with steroid or mesalazine enemas twice daily.	Prednisolone 40 mg/day 1 week, 30 mg/day 1 week, then as for mild UC.	Admit for iv steroids if >6 bloody stool/day with pulse >90 bpm, temp >37.8, Hb <10.5 g/dl.

Active Crohn's disease

Mild relapse	**Severe relapse**
As for moderate UC but reduce steroids below 20 mg/day by 5 mg/day every 1–2 weeks.	Admit for iv steroids and metronidazole if vomiting, pyrexial, or in severe pain

Early relapse	Early specialist review.

Further course of steroids, reduce dose below 20 mg day by 5 mg/day every 2–3 weeks.

Further relapse

Prednisolone 20 mg/day 1 month.
Start azathioprine 2 mg/kg/day, then withdraw prednisolone by 5 mg/day every 2–4 weeks.

Maintenance therapy

Ulcerative colitis	**Crohn's disease**
Sulphasalazine 2 g/day, Olsalazine 1 g/day or Asacol 1.2 g/day.	Pentasa 2 g/day, Asacol 2.4 g/day.

Key points

- It is possible to distignuish between ulcerative colitis and Crohn's disease in 90% of cases, after taking the clinical, endoscopic, radiological *and* histological featuers into accout. When there is doubt, 'indeterminate colitis' (having features of both) is a better term than 'inflammatory bowel disease.'
- Objective assessment of the degree of activity in ulcerative colitis is essential, by recording the stool frequency, pulse, temperature, haemoglobin and inflammatory markers (Table 7.3).
- Decisive treatment of active ulcerative colitis with oral and rectal corticossteroids is usually preferable to oral salicylates and enemas.

- There are many causes of pain or diarrhoea in patients with Crohn's disease, other than active disease (Table 7.4)
- The main role of salicylated (sulphasalazine, olsaiazine or mesatazioe) in ulcerative colitis is maintenance therapy. Higher doses are needed to maintain retniseion in Crohn's disease.
- The risk of coloroctal cancer in either ulcerativeor or Crohn's colitis is increased only for those with extensive disease of long (>10 years) duration. The role of surveillance colonoscopy remains debatable.
- The majority of patients with either ulcerative colitis or Crohn's disease continue working and have a normal life expectancy. Support from patient-based orgnaizations such as the National Association for Colotis and Crohn's Disease in the UK (Appendix) may be halpful.

Further reading

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Chapter 8
Colonic polyps and cancer

Colonic polyps

A polyp is defined as an elevation above a mucosal surface. Several types may be found within the colon, but only adenomatous polyps are clinically important in terms of malignant potential (Table 8.1).

Adenomatous polyps

The commonest neoplastic polyp found in the colon is the adenoma. This term covers tubular (pedunculated, common), tubulovillous and villous adenomas. Adenomas are found in 25–30% of the 50–70-year age-group in the Western world, but are rare in the developing world. Although genetic factors are important in their pathogenesis (e.g. familial adenomatous polyposis; FAP), environmental factors such as diet have a major influence on the development of colonic adenomas. The evidence for this assertion is largely based on studies from Japan, where the incidence of colonic adenomas is low; following emigration, the incidence of colonic polyps increases dramatically.

The perceived wisdom is that most, if not all, colonic carcinomas originate as adenomas (the adenoma-carcinoma sequence). Indeed, 5–10% of adenomas will show histological evidence of carcinomatous change at the time of excision. Prior to frank carcinoma, histological changes of *dysplasia* may be identified, which are initially low grade and then high grade. The rate of growth of adenomas is usually slow and the time interval for development of a carcinoma in an adenoma

Table 8.1 Colonic polyps

Neoplastic polyps	Histology	Type	Comment
Adenomas	Tubular Tubulovillous (may occur on any type) Villous	Pedunculated Sessile Villiform	All have malignant potential, Especially polyps with villous pattern, or >1.0 cm, or if multiple
Non-neoplastic polyps			
Metaplastic Hamartomatous	2–5 mm Variable size	Sessile	Very commonvery rare. Peutz-Jeghers (p. 157) or incidental juvenile polyps
Inflammatory	Variable size	Sessile, cylindrical	Ulcerative colitis 'pseudo-polyps'

	or pedunculated	Usually multiple
Lipomas Pneumatosis Neurofibromas Leiomyomas		Rare causes of submucosal polypold lesions in the colon

is several years, and may be 10 years or more. Accurate data on this are difficult to determine, since polyps, once identified, are usually removed. The *risk of carcinoma* developing in a polyp is associated with size (more common in polyps >1 cm), histology (much more common in villous adenomas) and number (more common when more than five). However, some polyps, and possibly a majority, will not undergo malignant change: whereas 25–30% of older people will have an adenoma, only 3% develop colonic cancer. In contrast, patients with FAP have a 100% lifetime risk of developing colonic cancer.

Large colonic polyps can cause *symptoms* due to bleeding (rectal bleeding, anaemia), abdominal pain or a change in bowel habit. Villous adenomas in the rectum can cause local symptoms, including mucous discharge or tenesmus, and have a tendency to cause hypokalaemia. Small colonic polyps usually cause no symptoms and are often a chance finding in a patient having a sigmoidoscopy, barium enema or colonoscopy during investigation of a change in bowel habit that is related to a motility disorder.

Principles of treatment

The principles of treatment of colonic adenomas depend on accurate histological diagnosis. Once this is established, it is important to ensure that the entire colon is polyp free and that the patient is subsequently followed up appropriately.

Polyps should be removed in their entirety for *histological diagnosis,* because it is often not possible to distinguish macroscopically between an adenoma (with malignant potential, requiring follow-up) and a metaplastic polyp (with no malignant potential, not requiring follow-up). Once an adenoma has been confirmed, it is imperative to make sure that the colon is adenoma free, which in practice means a full colonoscopy with polyp removal by snare or hot biopsy. Small adenomas may be overlooked on barium enema and can occasionally be missed at colonoscopy.

In a minority of patients the polyp will show dysplasia or definite malignant change. Careful histological scrutiny will determine whether the carcinoma has invaded the stalk, or if excision is incomplete, in which case local surgical excision is needed. In some patients with only a small focus of malignant cells, decisons regarding surgery can be more difficult and, in the elderly or infirm, the potential benefits may well be outweighed by the risks.

Follow-up

Adenomas recur in 30–40% of patients, and carcinomas recur in about 5%. For this reason, patients who have had an adenoma should have at least one colonoscopy. The

optimum timing for follow-up colonoscopy remains a matter of debate but, given the slow-growing nature of adenomas, a check colonoscopy at 2–3 years seems reasonable. For patients with more than five polyps, large (>1cm) polyps or villous histology, or if excision is thought to be incomplete, the check colonoscopy may be earlier (6–12 months). If further adenomas are found, the patient should continue to have colonoscopies every 2–3 years. If no adenomas are found, the interval can be increased to 5 years for as long as the patient is considered a candidate for surgery. Surveillance is usually continued until the age of 75–80 years.

The family doctor's role in the follow-up of patients with adenomas includes checking for symptoms or signs that indicate the unexpected development of colonic cancer. Further rectal bleeding, anaemia or a change in bowel habit are indications for immediate referral for further colonoscopy. Family doctors also have an important role in ensuring that patients do not 'slip through the net'. Follow-up colonoscopy may not occur, owing to an administrative oversight, or patients may default from follow-up, especially as the interval between examinations increases. A related role of the family doctor in this situation is to communicate any major change in the patient's medical condition that may make further colonoscopy inappropriate—such as the development of serious cardiorespiratory or cerebrovascular disease. This not infrequently occurs, because often patients are elderly. Such an approach keeps the default rate to a minimum, encouraging the most effective use of a limited resource.

Complications and prognosis

The main complication of adenomas is malignant change. Once the colon has been cleared of adenomas and the patient entered into a surveillance programme, the prognosis is excellent. Patients may not understand that repeated colonoscopy is designed to prevent carcinomas occurring and think that each procedure will detect a cancer. It is clearly important that the polyp-cancer sequence is explained.

Of more concern in terms of affecting the incidence of colorectal cancer is how to identify polyps in the first place. This raises issues regarding population screening (p. 161).

Familial adenomatous polyposis (FAP)

FAP is characterized by multiple (>100) adenomatous polyps in the colon. Adenomas may also occur in the small bowel, duodenum and ampulla of Vater. *Gardner's syndrome* is a variant of FAP in which mesodermal tumours such as osteomas, desmoids or sebaceous cysts also occur. The incidence of FAP is about 1 in 10,000 live births. It is an autosomal dominant condition, although 30% of cases are sporadic, without a family history of colorectal cancer. The *polyposis gene* is located on the q21–22 region of chromosome 5 and the syndrome is usually caused by one of several mutations in this area.

Patients with FAP have many hundreds or thousands of adenomas in the colon. These start to grow in adolescence and increase in size and number. If these are undetected, the patients usually present in their mid-30s with colorectal cancer, and the lifetime risk of

cancer without colectomy is 100%. There is also an increased risk of malignant change in duodenal polyps and those in the ampulla of Vater.

Treatment principles

The main aim in managing patients with FAP is to make an early diagnosis. This allows a tailored treatment and follow-up plan to be devised and affords an excellent prognosis. This is usually achieved by meticulous screening of the family members of an index case; the development of colorectal cancer in a relative of an index case must be regarded as a treatment failure.

Screening for FAP

Screening for FAP *in utero* is possible, by the use of gene probes to detect deletions of the q21–22 region of chromosome 5. More usually, first-degree relatives of an index case (children or siblings) are screened by *flexible sigmoidoscopy or colonoscopy in adolescence* (11–14 years). Genetic markers for screening are not yet universally used, because of the number of mutations that may occur, resulting in about a 5% false-negative rate.

In addition, an expert ophthalmological opinion should be sought to detect *congenital hypertrophy of the retinal pigment epitbelium* (CHRPE). This is a condition in which there are multiple areas of pigmentation in the peripheral retina and which seems to be specifically associated with FAP. The retinal changes may appear several years before adenomas develop. However, the sensitivity and specificity of this rather subtle sign is not 100% and its significance should be interpreted only in conjunction with sigmoidoscopy and gene study findings.

Patients diagnosed as having FAP should have a colectomy. The timing is flexible to a certain extent, but the operation is probably best performed before the age of 20 years. The operation of choice is a total colectomy and ileo-anal pouch formation. Some patients still opt for a proctocolectomy and terminal ileostomy, or a colectomy and ileorectal anastomosis. In the latter case, long-term sigmoidoscopic follow-up is required, because a significant risk of rectal carcinoma remains. The details of all patients should be sent to the FAP Registry (St Mark's Hospital, Northwick Park, Harrow, Middlesex, telephone 0181 235 4000).

All first-degree and probably all second-degree relatives should be screened for FAP. The family doctor can provide valuable help in this process, as well as being a source of advice and support. It is also important for the family doctor to be alert to any symptoms or signs indicating malignant change. Apart from anaemia or rectal bleeding, this includes upper abdominal pain and jaundice, even after colectomy. Symptoms must be investigated promptly.

Prognosis

In patients with FAP who are detected by screening, the incidence of colonic cancer at the time of presentation is about 5%. This contrasts with those patients with FAP who present with symptoms, where the incidence of cancer is 60–70%. Although colectomy

prevents colorectal cancer, associated complications such as duodenal or ampullary carcinoma, or desmoid tumours, will affect the prognosis in a minority. Such patients are best managed in conjunction with a specialist centre such as St Mark's Hospital (London), for the back-up and support given by a team of experienced nurses and doctors.

Peutz-Jeghers syndrome

This is a rare, dominantly inherited condition comprising perioral pigmentation and hamartomatous polyps of the gastrointestinal tract. The polyps contain a mixture of normal intestinal tissues. There is a slightly increased risk of cancer, mainly of the upper gastrointestinal tract, as the polyps sometimes contain foci of adenomatous tissue, which has a malignant potential. Removal of accessible polyps in the lower and upper gut by snare diathermy is probably sensible. Large polyps in the small intestine should also be considered for surgical removal, as they may bleed or cause intussusception.

Juvenile polyps

These hamartomatous polyps are a rare cause of rectal bleeding or intussusception in childhood. Patients with isolated polyps do not appear to be at increased risk of cancer. In contrast, when colonic polyps are multiple there is a substantial risk of colorectal cancer, and regular colonoscopies are advisable.

Colorectal cancer

Colonic cancer accounts for nearly 20,000 deaths per annum in the UK and is the second most common cause of death from malignant disease. Almost all cancers are thought to develop in pre-existing colonic adenomatous polyps, and the global variation in the incidence of colorectal cancer mirrors that of colonic polyps. Colonic cancer can occasionally occur without proceeding through the 'polyp-cancer' sequence, such as in patients with long-standing ulcerative colitis.

Dietary and genetic factors have an important role in pathogenesis. Apart from FAP, where there is a 100% lifetime risk of colorectal cancer (p. 155), other family groups are at increased risk. *Hereditary non-polyposis colorectal cancer* (HNPCC) is a dominantly inherited condition with an increased incidence of cancers in the right side of the colon. The putative gene appears to be on chromosome 2, but penetrance is sometimes incomplete. HNPCC (also known as *Lynch syndrome*) accounts for less than 10% of colorectal cancer and one variant (type 2) is associated with ovarian, breast and endometrial carcinoma occurring in the same family.

The molecular basis of sporadic colorectal cancer is slowly being unravelled. It appears that inactivation of tumour suppressor genes, such as *p53,* and activation of oncogenes, such as K-*ras* or C-*myc,* lead to loss of control of epithelial growth and repair. Separate steps in the process take many years to occur, before carcinogenesis ensues.

Treatment principles

Colonic carcinoma is usually a slow-growing cancer. There is some evidence that suggests that early diagnosis and intervention significantly improves prognosis (Table 8.2). Therefore, the most important aspect of managing patients with colorectal cancer is prompt diagnosis and referral for definitive therapy.

Family doctors have a fundamental role in the early recognition and diagnosis of colorectal carcinoma. Symptoms depend on the site of the tumour. Rectal cancers present with rectal bleeding, mucus discharge, urgency or tenesmus. Sigmoid cancers also tend to present with rectal bleeding and may cause pain, as well as a change in bowel habit. However, right-sided tumours often present with none of the above and frequently present late with abdominal pain or iron deficiency anaemia. Clearly, any of the above symptoms necessitates

Table 8.2 Modified Duke's classification and prognosis in colorectal cancer

Classification	Description	5-year survival (%)
A	Tumour limited to bowel wall	95–100%
B	Penetration of bowel wall, no nodes involved	65–75%
C	As B, plus node involvement	30–40%
D	Distant metastases	<1%

prompt referral, but many of the early symptoms of colorectal cancer are non-specific. Consequently, any significant change in bowel habit in a patient over the age of 40 should be regarded as suspicious until proved otherwise. Rectal examination should never be deferred, as an appreciable proportion of cancers are palpable with the fingertip. Negative occult blood tests do *not* exclude a cancer.

The definitive diagnosis of colorectal carcinoma is achieved by a combination of digital examination, rigid or flexible sigmoidoscopy and barium enema. The advantage of flexible over rigid sigmoidoscopy is that the whole of the distal colon, sometimes up to the splenic flexure, can be examined; this area accounts for 60–70% of cancers. Furthermore, with a barium enema it is surprisingly easy to miss small lesions in the sigmoid colon, especially if it is tortuous or if there is diverticulosis.

The most sensitive investigation for patients suspected of having colorectal cancer is colonoscopy, especially if there is visible rectal bleeding. This technique is, however, time consuming and expensive: nevertheless, it does allow biopsies to be taken from any suspicious lesion. Approximately 15% of patients over the age of 50 presenting with rectal bleeding will be found to have colorectal cancer.

The best treatment for colorectal cancer is surgical resection, if possible. This usually involves removal of the tumour with wide excision margins, together with related vascular and lymphatic fields. The use of staple guns means that rectal cancers down to 5–10 cm from the anal margin can usually be resected without the need for a colostomy. Colonic cancers have been resected with the assistance of laparoscopy, resulting in a smaller surface scar, but the role of this technique remains to be established. Local

transanal excision of some rectal cancers is possible and effective palliation of unresectable rectal cancers can be achieved with lasar ablation. In patients with Dukes' C carcinoma, adjuvant therapy with 5-fluorouracil and folinic acid achieves about a 30% reduction in mortality.

Follow-up

Following surgery, patients require colonoscopic surveillance. The purpose is to detect local recurrence and to remove any new polyps. There is no general agreement about optimum timing and frequency of such examinations. A colonoscopy within a year of resection and then at intervals of 2–3 years is a reasonable compromise. Serial blood tests for carcinoembryonic antigen (CEA) can be a useful way of detecting recurrence at an early stage.

Follow-up by the family doctor

It is important to consider the psychological as well as the physical impact on patients following surgery. Attention should be paid to how the patient has come to terms with the condition, especially if a colostomy has been necessary. Depending on the age and history of the patient, consideration should be given to screening family members (p. 164). Any symptoms or signs suggestive of recurrence between hospital visits should be followed by prompt re-referral.

Prognosis

With the exception of the moderate improvement in survival of patients with Dukes' C cancers treated with adjuvant chemotherapy, the prognosis for colorectal cancer has remained essentially unchanged for 25 years (Table 8.2). It is for this reason that attention should be directed at earlier diagnosis.

Screening for colorectal cancer

For a screening test to be clinically useful it must ultimately result in a reduction in mortality from the condition screened (Table 8.3). For a screening test to be politically digestible, it must have a reasonable cost-benefit ratio. Unfortunately, population screening for colorectal cancer has not been shown to meet either of these criteria to date. This may be because screening is prone to lead-time bias, where screening brings forward the time of diagnosis without moving back the time of death.

Table 8.3 Criteria for screening

- The condition screened for should be an important one
- There should be recognized latent or early symptomatic stage
- There should be a suitable test or examination

- The test or examination should be acceptable to the population
- The facilities for diagnosis and treatment should be available
- The natural history of condition should be understood
- There should be an acceptable treatment for patients with the disease
- There should be an agreed policy on whom to treat
- The cost of case finding should be balanced in relation to civil expenditure on medical on care as a whole
- Case finding should be a continuing process

(From Wilson R. Some principles of early diagnosis and detection. In: Teeling-Smith G, ed. *Proceedings of the colloquium Magdalen College, Oxford, 1965*. London Office of Health Economics, 1976.)

Population screening for colorectal cancer

The rationale for screening asymptomatic individuals for colorectal cancer is that it is possible to detect lesions (polyps) at a stage before cancer has occurred and that early colorectal cancer (Dukes' A) is still potentially curable (Table 8.2). The reasonable hypothesis is that early diagnosis by screening will ultimately reduce mortality. The best technique for population screening has yet to be determined. All techniques suffer from a low take-up rate by the population (Table 8.3), although this may be improved by education. The present options are faecal occult blood testing (FOB) or flexible sigmoidoscopy.

There are currently four large double-blind trials using FOB testing as a screening tool (Table 8.4). The major problem with FOB testing is that it has a relatively poor sensitivity and specificity, although it is cheap and practical. This means that 20–50% of cancers will be missed by false-negative results and many unnecessary colonoscopies performed for false-positive results. All four studies have shown an increased detection of early (Dukes' A/B) lesions. The unresolved question is whether this will result in improved outcome, or whether screening simply detects slow-growing tumours with a good prognosis (lead-time bias). Only one of the studies has shown a reduction in mortality compared with controls (Table 8.4). Furthermore, almost 10% of FOB tests were positive in any one year, resulting in a huge

Table 8.4 Controlled trials of population screening for colorectal cancer with FOB tests

Study	Compliance (%)	Test positivity (%)	Reduction in cancer mortality (%)
Sweden	65	6	–
Denmark	67	1	–
UK	54	2	–

(Nottingham)			
USA (Minnesota)	75	10	33

colonoscopy workload. As a result, well over half the study group had a colonoscopy at some stage. It could be argued that the reduction in mortality reflected the large proportion of the study group who had a colonoscopy, rather than being the result of FOB screening.

Smaller studies have evaluated flexible sigmoidoscopy for screening. There is some evidence that it reduces mortality from distal colorectal cancer. Given the limitations of FOB testing, a once-only flexible sigmoidoscopy at the age of 55 years has been suggested. The rationale is that the average age of diagnosis of colorectal cancer is in the late 60s (Table 8.5) and that the adenoma-carcinoma sequence takes 10–15 years to complete. A flexible sigmoidoscopy at age 55 would identify most 'polyp-formers', who can then have more intensive surveillance. The clinical effectiveness and cost-benefit ratio of this remain to be determined, but it has been suggested that it is likely to be more effective than mammographic screening for breast cancer. A cost 'guesstimate' is approximately £10,000 per cancer death prevented.

Screening high-risk groups

As the effectiveness of population screening remains to be established, it may be best to concentrate on screening people at higher risk of colorectal cancer.

Table 8.5 Colorectal cancer: age at diagnosis in the UK (1987)

Age (years)	Percentage of all colorectal cancer
<40	1
40–49	4
50–59	11
60–69	25
70–79	35
>80	24

Familial adenomatous polyposis

Screening of relatives is discussed in the section on familial adenomatous polyposis (p. 156).

Hereditary non-polyposis colorectal cancer (HNPCC)

The importance of family history in increasing the risk of colorectal cancer is shown in Table 8.6. It seems appropriate to screen patients with a strong family history by colonoscopy, but the timing and frequency of examinations remains unknown. Many gastroenterologists offer colonoscopic screening from the age of 20–25 years if the family history suggests that the risk of developing colorectal cancer is 10% or greater. Examinations are often done at 5-year intervals if no polyps are found. Although this is apparently reasonable and often requested by relatives of patients, there is no evidence that it works. The small mortality inherent in colonoscopy (about 0.05%) should be remembered.

Once a family history indicates a heritable risk of malignancy, there is an obligation to act on the information. The family doctor is in a privileged position to identify patients at risk, through health screening checks, or when new patients are booked. Indeed, if a family history is not taken or no appropriate action is taken, it may be considered negligent. The availability of local endoscopic resources has to be taken into account.

Table 8.6 Family history and risk of colorectal cancer

Family history	Risk	
None	1:50	(2%)
One first-degree relative aged >45 years	1:17	(6%)
One first- and one second degree relative (any age)	1:12	(8%)
One first-degree relative aged >45 years	1:10	(10%)
Two first-degree relative affected	1:6	(17%)
Familial adenomatous polyposis	1:2	(50%)

Inflammatory bowel disease

Patients with a total colitis due to ulcerative colitis or Crohn's disease have an increased risk of developing colorectal cancer. About 5–10% of such patients will develop cancer 20 years after the onset of symptoms. The clinical impression is that the risk is higher in patients with poorly controlled symptoms, or if the onset occurred in childhood. However, one large population-based study on over 1100 patients has shown that the risk of colorectal cancer is not increased when an active medical and surgical approach to management is taken, although the colectomy rate in patients with pancolitis was high (35%). It is generally agreed that there is little, if any, increased risk of cancer for patients with left-sided disease.

Cancers develop in areas of dysplasia and are often flat rather than polypoid and may be multifocal. Screening by colonoscopy every 1–3 years for patients with extensive disease and symptoms for more than 10 years has been proposed and is widely practised. Serial biopsies are taken and, if dysplasia is detected, then patients are offered a

colectomy. Two major studies have failed to demonstrate the effectiveness of this approach and no consensus has been achieved. A great deal depends on the inclinations of the individual patient. Some gastroenterologists recommend early colonoscopy if symptoms change or a relapse becomes refractory, or if anaemia develops. The problem is that precancerous dysplasia is asymptomatic and that cancer complicating colitis has a poor prognosis.

Summary

Colonic adenomas

Adenoma→ identified	Full colonoscopy and polyp removal	→ Surveillance colonoscopy at 2–3 years, then 2–3 years if further polyps found, or 5 years if colon clear, until age 75–80 years or major illness intervenes. Check at 6–12 months if polyps are multiple (>5), large (>1cm), have villous histology, or if excision incomplete

Familial adenomatous polyposis

First- or second-degree relative of index case with FAP, age 11–14 years	Gene study, flexible sigmoidoscopy	→ *FAP:* Colonoscopy every 2 years until definitive surgery (late teens)
	Fundoscopy for CHRPE	→ *Negative.* Repeat flexible sigmoidoscopy every 2–5 years until age 45–50 years.

Colorectal cancer

Prompt investigation of rectal bleeding, change in bowel habit age >40 years, or iron deficiency anaemia is essential. Definitive investigation includes rectal examination and barium enema or colonoscopy. Early diagnosis improves 5-year survival: Dukes' A (95–100%), compared with Dukes' C (30–40%). Treatment is primarily surgical, but chemotherapy improves survival in Dukes' C group.

Screening

Population screening of asymptomatic individuals has not yet been shown to be effective. Relatives of patients with colorectal cancer at less than 45 years of age, or those with two first-degree relatives affected, may reasonably be offered colonoscopic surveillance after the age 20–25 years.

Key points

- Colorectal cancers arise from adenomatous colonic polyps, patients with colonic adenomas greater than 1 cm in diameter, villous histologym or multiple (>5) polyps are at greatest risk.
- A family histroy is essential and action must be taken on the information. Any individual with a first-degree relative aged less than 45 years who has developed colorectal cancer, or with two first-degree reletives who have had colorectal cancer, should be offered colonoscopic screening.
- Negative facal occult blood testing does *not* exclude colorectal cancer.
- Population screening by occult blood testing or flexible siginoidoscopy has not yet been shown to be effective.

Further reading

Houlston RS, Murday V, Harcopos J *et al.* Screening and genetic counselling for relatives of patients with colorectal cancer in a family cancer clinic. *Br Med J* 1990; **301:** 366–8.

Ross P, Rigg A, Cunningham D. Understanding colorectal cancer. *Hosp Update* 1996; 160–6.

Chapter 9
Other disorders:
iron deficiency anaemia, coeliac diesease and chronic pancreatitis

Some conditions remain that lend themselves to shared care, but do not fit readily into previous chapter headings. Patients with iron deficiency anaemia present a common gastroenterological problem, as anaemia is often detected during investigation of non-specific symptoms. Much of the initial evaluation and subsequent care can be managed in the community. On the other hand, patients with coeliac disease or chronic pancreatitis are traditionally reviewed frequently in the gastroenterology outpatient department. Although these disorders are uncommon in the community, they share the common characteristics of variable periods of stability that can be extended if appropriately supervised, but with a potential for serious complications if inappropriately managed. Shared care in these circumstances is entirely appropriate, with the emphasis on good liaison between primary and specialist care.

Iron deficiency anaemia

Iron deficiency should not be attributed to an uncomplicated peptic ulcer, hiatus hernia, ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) or oesophagitis, without investigation of the colon. Indeed, iron deficiency should be considered as attributable to a caecal neoplasm in post-menopausal women or men past middle age, until proved otherwise. In teenagers suspected of having anorexia nervosa, iron deficiency should provoke a search for Crohn's disease. However, the cause of iron deficiency can not be identified in up to 20% of patients, despite detailed and appropriate investigation.

Unfortunately, many patients with iron deficiency are not investigated. In one UK health district of 290,000 population, 130 new cases of iron deficiency anaemia in patients over the age of 50 years were identified from laboratory records in a 6-month period. In 21 patients the source was clearly not from the gastrointestinal tract but, of the remaining 109, only 19% had investigation of both upper and lower gastrointestinal tract, 21% of the upper alone and 7% of the lower gastrointestinal tract alone. In 50%, no investigation had been performed, or only faecal occult blood tests. By 18 months after presentation, nine cases of colorectal cancer, five of gastric cancer and 11 of peptic ulcer had been diagnosed; two patients had died from colorectal cancer that had not been detected when iron deficiency anaemia first presented. There is no reason to suppose that this health district is in any way different to others.

Common causes

Chronic blood loss of more than 20 ml/day from the gastrointestinal tract or uterus will ultimately lead to iron deficiency anaemia. Failure of absorption or inadequate iron intake need to be considered as, occasionally, do other causes of a microcytic, hypochromic anaemia (Table 9.1).

Initial assessment

A careful *history* is mandatory. Specific questions should enquire about evidence of bleeding (visible rectal bleeding, or menorrhagia in women), abdominal symptoms (dyspepsia, altered bowel pattern), dietary intake (frequency of eating red meat), previous anaemia (recurrent iron deficiency in adults may be due to coeliac disease), drug ingestion (NSAIDs) and weight loss (which may indicate neoplasia or malabsorption).

Clinical examination should look for signs of iron deficiency (cheilitis, koilonychia), telangiectasia in the mouth (hereditary haemorrhagic telangiectasia can present as iron deficiency in adults) and 3

Table 9.1 Common causes of a microcytic hypochromic anaemia

Blood loss	Colonic neoplasm (large polyp or tumour)
	Menorrhagia
	Peptic ulcer
	Ingestion of NSAIDs
	Inflammatory bowel disease
	Large hiatus hernia with oesophagitis
	Angiodysplasia
Malabsorption	Coeliac disease
	Previous gastric surgery
	Blind loop syndrome
Dietary	Vegetarian
Other	Renal carcinoma
	Chronic disease
	Thalassaemia trait
	Sideroblastic anaemia

an abdominal mass (neoplasm, Crohn's disease). A rectal examination is essential: the aphorism that 'if you don't put your finger in it, you put your foot in it' is worth remembering before referral!

Investigations before referral

The *full blood count* is the starting point. A hypochromic (MCH<27 pg), microcytic (MCV<80 fl) anaemia (Hb<14 g/dl in men or <12 g/dl in women) is not always due to iron deficiency, which should be confirmed by measuring the *serum ferritin*. A low serum ferritin (<15 µg/1) is diagnostic of deficient iron stores, but in inflammatory conditions the ferritin may be only at the lower limit of normal (30 µg/l). A low serum iron (<10 µmol/l) and high *total iron-binding capacity* (TIBC) (>70 µmol/l) also confirm iron deficiency and some laboratories prefer these investigations to measurement of the ferritin in the first instance.

Faecal occult blood tests may help confirm gastrointestinal blood loss but, as blood loss may be intermittent or absent and investigation of the gastrointestinal tract is appropriate (except when anaemia is clearly due to menorrhagia), some gastroenterologists consider this superfluous. Looking for occult blood is occasionally helpful when deciding how far to subject a patient to gastrointestinal investigation if a dietary cause of anaemia is suspected, or when there is doubt about the amount of menstrual loss, but false negatives and false positives are common.

Referral criteria

As a rule, *any patient* with iron deficiency anaemia should be referred for gastrointestinal evaluation unless there is clearly a gynaecological cause. Doubt sometimes arises in a general practitioner's mind when a patient has no abdominal symptoms. Mild, recurrent anaemia, however, is the commonest presentation of adult coeliac disease and treatment is very rewarding. The other *common dilemma* is in the *elderly*. There is a natural reluctance to impose invasive investigation on elderly patients, but some judgement is necessary before simply prescribing iron. An abdominal CT scan is a non-invasive way of diagnosing a colonic neoplasm and may help future management, even in patients for whom surgery is inappropriate. It is also sensible to check the urine for blood; renal carcinoma occasionally causes iron deficiency anaemia, which may confuse the unwary.

Out-patient investigations

The *full blood count* and *iron indices* should be re-examined before initiating a search for a cause of iron deficiency. Thrombocytosis indicates inflammation, or acute-on-chronic bleeding. In chronic disease, hypochromia or microcytosis are mild and the TIBC is characteristically low (<45 µmol/1). In thalassaemia trait, the microcytosis is often profound (<60 fl) and the serum ferritin normal, which is an indication for measuring HbA2 (normal <2%).

If *malabsorption* is suspected, the folate, B12, prothrombin ratio [international normalized ratio] (INR 1.0:1.1), calcium and albumin are best measured on the first outpatient visit.

Investigation of the oesophagus, stomach, duodenum and whole colon is needed, although initial investigation is guided by upper or lower abdominal symptoms. It is most convenient to perform *upper gastrointestinal endoscopy* and *colonoscopy* during one visit to the endoscopy unit. *Distal duodenal biopsies* should *always* be taken if the endoscopy does not reveal the cause of iron deficiency, to exclude coeliac disease at an early stage.

The advantage of colonoscopy over a barium enema is that it avoids radiation, allows biopsies to be taken of any colonic lesion and allows the cause to be treated if bleeding is due to polyps or angiodysplasia. However, the local waiting time for colonoscopy may exceed that for a *barium enema,* which may then be the preferable way of excluding a neoplasm. Depending on the experience of the endoscopist, a barium enema obtains views of the caecum more reliably than colonoscopy but, if polyps are detected, patients have to undergo a second procedure.

Anaemia of obscure aetiology

When the cause of iron deficiency anaemia has not been diagnosed after these investigations, it can present a difficult problem. Before further investigation, it is wise to *retake the history* and to *review the results,* to ensure that obvious causes (dietary insufficiency, menstrual loss) or pitfalls (renal carcinoma, haemoglobinopathy) have not been overlooked. Discussion with the haematologists about examination of the bone marrow to exclude sideroblastic anaemia is appropriate if blood loss cannot be confirmed.

For patients who are asymptomatic, it is then reasonable to stop iron therapy and repeat the full blood count in 3–6 months. Should anaemia recur, then *further investigations* are warranted.

A *colonoscopy* should be performed or repeated after careful preparation, to look for angiodysplasia or telangiectasia in the proximal colon. If this is negative, *small bowel radiology* is appropriate. A small bowel enema is more sensitive than a barium follow-through in identifying mucosal pathology. Although Crohn's disease is usually associated with a high platelet count and raised inflammatory indices, it occasionally presents with iron deficiency and weight loss, especially in adolescents. *Isotope scans* may identify chronic blood loss from one region of the intestine, or heterotopic gastric tissue in a Meckel's diverticulum, but are rarely productive. Similarly, *mesenteric angiography* rarely helps in the absence of acute bleeding, although an arteriovenous malformation may be identified. Finally, *enteroscopy* to examine the small bowel may be appropriate if frequent transfusion is needed. This can be performed either with a purpose-designed enteroscope or at laparotomy.

Coeliac disease

Coeliac disease is defined as small intestinal villous atrophy that resolves when gluten is withdrawn from the diet (Figure 9.1). Gluten is a group of proteins derived from wheat, barley and rye, but not from oats, rice, or maize. The toxic component is α-gliadin, but the exact mechanism of damage remains unknown.

Coeliac disease may present at any age, but in adults the most common presentation is now recurrent iron deficiency anaemia. Diarrhoea may be intermittent or absent and non-specific symptoms (bloating, flatulence, lethargy) may have been attributed to irritable bowel syndrome. Symptomatic malabsorption with steatorrhoea may be provoked by infection, pregnancy or surgery.

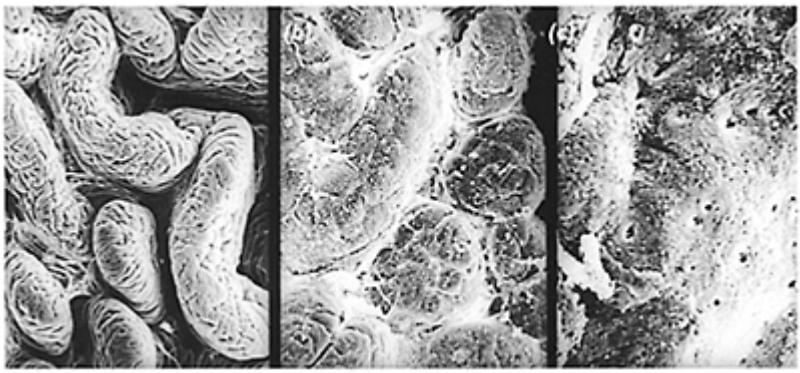

Figure 9.1 *Scanning electron micrographs of villous architecture. (a) Normal, (b) partial villous atrophy and (c) total villous atrophy.*

Management

Establishing the diagnosis. There is no alternative in adults to a *small intestinal biopsy* (usually from the distal duodenum at endoscopy) followed by a second biopsy after 3–6 months on a gluten-free diet to document resolution of villous atrophy. Clinical improvement after gluten withdrawal may be coincidental if villous atrophy is due to a transient cause, such as infection with *Giardia lamblia,* and the implications of a lifelong gluten-free diet are considerable. There is no need for a subsequent gluten challenge in adults.

Antibody tests vary in sensitivity and specificity between laboratories. Some have claimed a predictive value approaching 100%, especially for anti-endomysial immunoglobin A (IgA) or anti-reticulin IgA antibodies, but anti-gliadin antibodies are generally of little value. All tend to disappear during gluten exclusion, which may lead to false-negative results, although this has been advocated as a means of monitoring the diet. Their role in screening patients or family members for potential coeliac disease has yet to be determined.

Explaining the diagnosis to the patient. The clinical features of coeliac disease were first described by Samuel Gee in 1888, but it was an alert Dutch paediatrician, Willelm Dicke, who first observed the beneficial effect of excluding wheat, rye and barley when bread was rationed in the Second World War. The fundamental importance of meticulous *gluten withdrawal* should be explained, including, if necessary, the fact that there is good evidence that a strict diet decreases the risk of malignant complications. All patients should see a dietitian with their partner and be encouraged to join the *Coeliac Society* (Appendix), which provides a versatile recipe book, among other benefits.

The toxic role of gluten and its effect on small intestinal villi is readily explained, if necessary with diagrams of normal and flat intestinal mucosa. Iron deficiency is common, because iron is absorbed in the duodenum and proximal small intestine which is the area

predominantly affected by villous atrophy. About 10% have an affected first-degree relative. This implies that 90% of children of patients with coeliac disease will be unaffected.

Treatment strategy. *A lifelong gluten-free diet* is central to treatment (Table 9.2): 85% respond and patients often feel dramatically better within a few days. The management of poor responders is discussed below (p. 178).

Nutritional supplements (iron, folate) are needed if the patient is anaemic, and specific deficiencies may need treating. For hypocalcaemia, give calcium 2 g daily (50 mmol Ca^{2+}, as 4 tabs Calcichew™ or 2 tabs Sandocal-1000™) until the serum calcium is corrected, monitoring every 2 weeks. Effervescent calcium gluconate releases too little elemental calcium to be practicable (20 tabs release 50 mmol Ca^{2+}).

Table 9.2 Guidelines for a gluten-free diet

Aviod	■ Any products of wheat, bariey, rye
	■ Bread, Cakes, biscuits, pastry, crispbread
	■ Wheat cereals (e.g. weetabix, Puffed wheat).
	■ Pasta
	■ Packet soups, gravy powder, stock cubes, curry powder, mustard, sauces
	■ Chocolate, ice ceram, sweets
Allowed	■ Any fish, meat, poultry, game (but no breadcrumbs or batter and beware sauces)
	■ Any cheese, eggs, milk, dairy products
	■ Any vegetables, potatoes, rice or fruit
	■ Cornfiakes, Rice Krispies
	■ Bread, cakes, or biscuits made from gluten-free flour

Continuing care by the family doctor

Patients will visit the surgery for prescriptions of gluten-free products (Figure 9.2), such as bread (e.g. Juvela, Glutafin, Lifestyle, Rite Diet, Ultra), pasta (Aglutella, Aproten, Ener-G), biscuits (Glutano, Nutricia, Polial) and flour. In the UK, prescriptions for these products should be endorsed ‘ACBS’.

Specific questions about dietary compliance and general well-being should be asked. The full blood count should initially be checked every 3 months, with more frequent monitoring of calcium and folate if supplements are being given (above). Membership of the Coeliac Society should be confirmed: patients who do not take the trouble to do this are unlikely to be complying with the diet.

Early review by a gastroenterologist should be requested if there is weight loss, persistent diarrhoea, or persistent anaemia.

Hospital visits

The *evidence* for the diagnosis should be reviewed, especially in those patients in whom the diagnosis was made some years previously: a histological response to gluten withdrawal may not have been documented and symptoms from a wheat-sensitive irritable bowel

Figure 9.2 *Examples of prescribable gluten-free products.*

syndrome may have been labelled inappropriately as coeliac disease. *Enquiry* about the strictness of the gluten-free diet (especially when eating out) and further emphasis on the importance of life-long gluten exclusion are important.

Results of the full blood count, ferritin and folate are a reasonable guide to the state of the intestinal mucosa once a histological response has been confirmed. These should be checked at least annually, with a request form being given to the patient for a blood test 1–2 weeks prior to their appointment (copy to the family doctor).

Persistent or recurrent symptoms should be thoroughly investigated, because of the risk of small intestinal lymphoma or carcinoma. Tests should include those for immunoglobulins (in case of hypogammaglobulinaemia or IgA deficiency), and C-reactive protein (elevated in Crohn's disease or lymphoma), small bowel radiology and a colonoscopy. Abdominal CT scan looking for retroperitoneal lymphadenopathy, multiple small intestinal biopsies (a paediatric colonoscope allows more distal biopsies than an ordinary endoscope) and, occasionally, laparotomy and full-thickness small intestinal biopsy may be necessary.

Special situations

Poor response to gluten withdrawal is usually due to failure to adhere to a gluten-free diet (Table 9.3). This is also the most common cause of recurrent symptoms after an initial response. A dietitian should carefully review compliance. Some coeliacs, especially adolescents, tolerate moderate amounts of gluten with few symptoms. The clue is usually persistent iron or folate deficiency, but the absence of symptoms makes it more difficult to emphasize the importance of complete gluten exclusion. Other coeliacs have a dramatic sensitivity to tiny amounts of gluten, such as that found in communion wafers.

If compliance is good, excluding milk and milk products (yoghurt, cottage cheese) may help in cases of secondary hypolactasia. Response can be reassessed in 2 weeks. If this does not help, *Giardia lamblia* should be looked for in stool samples and hypogammaglobulinaemia excluded on blood tests. Empirical

Table 9.3 Causes of a poor response to ghiten exclusion in villous atrophy

Poor dietary compliance
Concomitant hypolactasia
Infection (*Giardia lamblia,* other parasites)
Associated endocrine disease (e.g. Addison's)
Untreated mutritional deficiency (iron, folate, calcium, magnesium, zinc)
Co-existing disease (such as pancreatic insufficiency, Crohn's disease)
Small intestinal lymphoma
Hypogammaglobulinaemia
Ulcerative jejunitis, collagenous sprue, or reasons unknown

treatment with metronidazole 800 mg three times daily for 3 days sometimes helps, even if infection cannot be documented. Further investigation for a lymphoma or small bowel carcinoma is then indicated (above) and only once these have been excluded should prednisolone 20 mg/day be given. Response should be assessed by repeat intestinal biopsy after 3 months. Some still do not respond and are found to have subepithelial collagen deposition (collagenous sprue), although this is rare. Poor responders tend to be found in the end to have a low-grade T-cell small intestinal lymphoma.

Prognosis

Life expectancy is normal in those who respond and adhere to a gluten-free diet. This must be emphasized, because it is the main reason for assiduously following up patients with stable coeliac disease. Those who do not adhere to a strict diet have a higher risk of malignancy.

The three principal complications are malignancy (intestinal T-cell lymphoma, small bowel and oesophageal adenocarcinoma), refractory villous atrophy and ulcerative jejunitis. The incidence is uncertain, but probably less than 5%. In a study of 210 patients in Birmingham, followed for more than 15 years, there was a twofold relative risk of cancer. Nine developed lymphoma, three had oesophageal carcinoma and six had cancer elsewhere in the gastrointestinal tract, including the mouth and pharynx. Patients who had maintained a strict glutenfree diet for more than 5 years had the same incidence of cancer as the general population. The risk appeared to be confined to those on a reduced-gluten or normal diet.

Chronic pancreatitis

In chronic pancreatitis, irreversible glandular destruction usually follows episodes of acute pancreatitis, but may occur without an identifiable attack. The prevalence is increasing in Europe, where it is more common in men and due to alcohol (Table 9.4). Acini are replaced by fibrous tissue causing ductular distortion, exocrine insufficiency and, in some patients, atrophy of the islets with diabetes mellitus.

Early disease is asymptomatic, but the three *clinical features* are pain, weight loss and steatorrhoea due to exocrine insufficiency, sometimes with glucose intolerance. *Abdominal pain,* which may be anterior and radiate into the back, or primarily posterior, may be the

Table 9.4 Causes of chronic pancriatitis

Alcohol (80%; 40–50% have associated liver disease)
Gall stones (may co-exist, but uncommonly cause chronic pancreatitis)
Duct obstruction (papillary stenosis, tumour or stricture)
Congenital (pancreas divisum or annular pancreas; a hereditary from has been described)
Cystifc fibrosis
Idiopathic

only feature. Pain is improved by abstinence in 75% and resolves as fibrosis replaces inflammation, but this often takes years. Painless chronic pancreatitis occurs in a few patients, who present with exocrine insufficiency. *Weight loss* is due to malabsorption and limited food intake due to associated pain. It is exacerbated by protein catabolism, because deficient pancreatic proteases (trypsin) cause protein malabsorption.

In asymptomatic alcoholics, 54% have been reported to have abnormal exocrine function after secretin-pancreozymin testing, but steatorrhoea develops only once 90% of exocrine function has been lost. *Steatorrhoea* is recognized by bulky, offensive stools that are difficult to flush away, but may not be noticed if patients unconsciously reduce fat intake. It is caused by defective secretion of lipase and bicarbonate. Fat-soluble vitamin malabsorption may be sufficient to cause hypocalcaemia, osteomalacia, or a prolonged prothrombin time. *Glucose intolerance* and, eventually, frank diabetes occur in 30%. Acute pancreatitis with attendant complications may still occur in chronic disease.

Management

Establishing the diagnosis. A *plain abdominal X-ray* may show pancreatic calcification, but an abdominal *ultrasound scan* (for thin patients) or *CT scan* (for fat patients) should be the initial investigation, looking for pancreatic atrophy, calcification or calculi. Serum amylase activity is unhelpful and is often normal even during acute attacks in chronic alcoholic pancreatitis. Similarly, faecal fat excretion is unhelpful as this does not distinguish pancreatic from intestinal causes of malabsorption.

Endoscopic pancreatography *(ERCP)* is the 'gold standard', revealing duct distortion and side-branch dilatation (Figure 9.3). Pancreatic function tests are not routinely performed, especially when clinical malabsorption is present, as they rarely alter management. They are indicated when there are minimal changes on ERCP, or to assist diagnosis when ERCP is not readily available. The pancreolauryl (fluorescein dilaurate) test is most widely available.

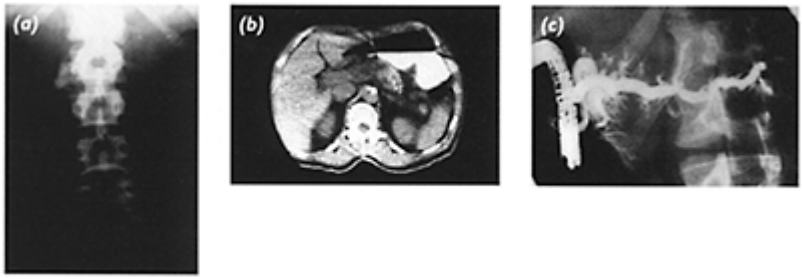

Figure 9.3 *Establishing the diagnosis in chronic pancreatitis. (a) Plain X-ray. Calcification is identifiable in the pancreas. (b) CT scan. The pancreas is atrophic. (c) ERCP. The pancreatic duct is irregular with dilated side branches.*

Explaining the diagnosis to the patient. The role of the pancreas in digesting fat and other nutrients should be distinguished from its endocrine function, because patients usually equate pancreatic malfunction with diabetes. Absolute abstinence must be counselled if alcohol is the established or suspected cause. It is important to emphasize that enzyme supplements should be taken during, rather than before or after, a meal. Chronic pancreatitis does not predispose to carcinoma.

Treatment strategy. The aim is to control pain, restore nutrition and maintain glucose control. Very occasionally, surgery to remove calculi, treat complications, or resect a focal chronic pancreatitis in the distal pancreas may be necessary.

Pain control is usually achieved with analgesics (dihydrocodeine), pancreatic enzyme supplements and avoidance of alcohol. Opiates such as pethidine may be required during severe pain, but dependence is common, possibly because of a susceptible personality in

those who also abuse alcohol. If this is the case, the local pain team should be involved. When pain is persistent or recurrent, the ultrasound and ERCP should be repeated, because pancreatic duct strictures or calculi may be the cause. Coeliac plexus block provides temporary relief, sometimes for months. Early hypotension and, later, impotence, or total visceral anaesthesia are potential complications. Recurrent blocks are often necessary, but relief is occasionally permanent. The assistance of a psychologist to teach coping strategies for pain is helpful for patients with unrealistic expectations.

Exocrine insufficiency is treated by a low-fat diet (30–40 g/day) and pancreatic enzyme supplements. No one type (Creon, Nutrizym, Pancrease, Pancrex) is of proven superiority to another, although enzyme preparations are unpalatable when sprinkled on food. If more than 10 capsules daily are needed, then high-potency preparations (Creon 25,000, or Nutrizym HP™ 1–3 caps with each meal or snack) are more convenient, although some cases of colonic stricture have been reported in children with cystic fibrosis taking these preparations. If steatorrhoea persists despite a low-fat diet and enzyme supplements, acid suppression with an H2-receptor antagonist or proton-pump inhibitor may help, although these are not otherwise necessary (Table 9.5). Medium-chain triglyceride supplements (Trisorbon™) are not very palatable, but may help to improve fat absorption if a low-fat diet, enzyme supplements and acid suppression fail to control steatorrhoea.

Table 9.5 Causes of presistent steatorrhoea in chronic pancreatitis

Problem	Management
Poor dietary compliance with a low-fat diet	Review by dietitian
Insufficient enzyme supplements	Change to high-potency preparation
Talking the capsules at the wrong time	Capsules must be taken *during* meals
Misdiagnosis	Consider Crohn's, coeliac disease

Endocrine insufficiency quite commonly causes glucose intolerance that can be managed by avoiding refined sugars, but frank diabetes is uncommon. Oral hypoglycaemics are usually ineffective, but insulin must be used with caution. Sugar control is more labile than in diabetes from other causes, probably owing to the lack of glucagon. Careful monitoring of blood sugars is needed, with close liaison between patient and diabetic team.

Surgery is indicated for localized chronic pancreatitis or pancreatic calculi causing severe intractable pain, but should be performed only by an experienced pancreatic surgeon. Total pancreatectomy for diffuse chronic pancreatitis has an unacceptable morbidity and a substantial number still have persistent pain. The decision balancing the quality of life with persistent pain against the complications of surgery is always difficult,

because pain often remits spontaneously after several years. A joint decision between physician, surgeon and patient is necessary.

Continuing care by the family doctor

Relevant *questions* concern pain control, stool frequency, character of the motions and alcohol intake. Weight should be documented and, if decreasing, blood glucose should be checked. Serum calcium and albumin provide a rough guide to nutritional sufficiency but, if there is steatorrhoea, the prothrombin time (for vitamin K deficiency) alkaline phosphatase and γ-glutamyl transpeptidase (γGT) (in case of osteomalacia or common bile duct stricture) should also be checked.

The family doctor plays a key role in managing chronic pain by exploring psychological issues, ensuring realistic expectations and monitoring excessive use of opiates. A pain management chart may be helpful and amitriptyline (up to 150 mg daily) may be more effective than ordinary analgesics.

Referral for review is indicated if there is weight loss or persistent steatorrhoea, or if diabetes develops. Acute exacerbation of pancreatitis is recognized by severe abdominal pain with vomiting and is usually an indication for direct admission. The serum amylase may not be elevated if sufficient acini have already been replaced by fibrosis.

The *frequency of review* depends on pain control and nutritional state, but regular review every 3–6 months helps to ensure continued abstinence and provides an opportunity to check on blood tests (above and Table 9.6).

Hospital visits

The *purpose* of outpatient review is to manage complications (below), ensure nutritional sufficiency and support the family doctor in managing patients with chronic pain. Once the diagnosis of chronic pancreatitis has been made, patients whose symptoms are controlled and who do not have endocrine insufficiency can be discharged to the care of their family doctor.

Special situations

Complications of chronic pancreatitis, apart from exocrine and endocrine insufficiency, include jaundice, portal hypertension, gastrointestinal bleeding and pseudocysts.

Jaundice may be caused by distortion of the common bile duct or associated cirrhosis, but pancreatic carcinoma is a more common cause. The risk of cancer is probably not increased, but can be difficult to distinguish from chronic pancreatitis in the early stages. Rapidly progressive symptoms and weight loss are likely to be due to cancer. *Portal hypertension* due to splenic or portal vein thrombosis is rare, but needs to be distinguished from associated alcoholic cirrhosis, because surgical decompression occasionally helps. *Bleeding* from associated varices or periductular vessels is rare. *Pseudocysts,* which may become infected (abscess) or rupture (causing ascites), are a complication of acute pancreatitis but may supervene in chronic pancreatitis if the cause—usually alcohol—is not addressed. Pain is the presenting feature, and ultrasound

with aspiration establishes the diagnosis; conservative management with total parenteral nutrition and percutaneous or endoscopic drainage is usually preferable to surgery.

Table 9.6 Outpatient check-list when reviewing patients with chronic pancreatitis

Review evidence for the diagnosis (CT scan or ERCP report)

Ask about pain control, stool frequency and character, alcohol intake

Record any change in weight

Examine nutritional status (subcutaneous fat, muscle bulk, glossitis, cheilitis) and for complieations (hepato/splenmegaly or ascites from portal or splenic vein thrombosis, epigastric mass from pesudocyst, jaundice, proximal myopathy, distal neuropathy from alchol or diabetes)

Check blood sugar, calcium, albumin, alkaline phosphatase, γGT, full blood count, random alchol if appropriate

Check drug therapy

Dietetic assessment if there is glucose intolerance or persistent steatorrhoea

Pain clinic referral if pain persists after focal causes have been excluded

Prognosis

A total of 85% of patients become pain free within 5 years. In alcoholic chronic pancreatitis, 80% survive 10 years if drinking stops, but this falls to less than half if drinking continues. Death occurs from the complications of acute-on-chronic attacks or cirrhosis, the cardiovascular complications of diabetes, drug dependence or suicide.

Summary

Iron deficiency anaemia

Definitive values	Anaemia (Hb <14 g/dl (men), <12 g/dl (women), that is hypochromic (MCH <27 pg) and microcytic (MCV <80 fl).
Confirm iron deficiency	Serum ferritin <15 μg/l, or serum iron <10 μmol/l and TIBC >70 μmol/l.
Take a careful history	Evidence of bleeding including menstrual loss, abdominal symptoms, dietary intake, previous anaemia or gastric surgery, drug ingestion.
Referral criteria	All patients who do not have menorrhagia. Perform a rectal examination.
Investigations	Endoscopy, distal duodenal biopsy and colonoscopy or barium enema, depending on local resources.
Further investigation	Review history and results before small bowel radiology, isotope scan, or other investigation.

Coeliac disease

Diagnosis	Small intestinal villous atrophy that responds to a gluten-free diet.
Referral criteria	*New patients:* any patient with unexplained iron deficiency anaemia, persistent diarrhoea, or gastrointestinal symptoms in a relative of a patient with coeliac disease.
	Review: persistent or recurrent symptoms despite a gluten-free diet, weight loss, recurrent anaemia.
Monitoring	Weight, general well-being, full blood count, folate, ferritin, calcium and albumin. Initially every 4–8 weeks, then 6–12 months when response to gluten withdrawal has been confirmed.
Treatment	Meticulous gluten-free diet for life and join Coeliac Society (Table 9.5). Poor response: review diet, exclude lactose, small bowel radiology (Table 9.6).

Chronic pancreatitis

Diagnosis	Abdominal pain, steatorrhoea, or diabetes associated with pancreatic atrophy and calcification on ultrasound/CT scan, or duct distortion at ERCP.
Referral criteria	*New patients:* abdominal pain, weight loss and diarrhoea in a heavy drinker. *Review:* severe persistent or recurrent pain despite enzyme supplements, low fat diet; weight loss, diabetes.
Monitoring	Weight, stool frequency, glucose, calcium, albumin, alkaline phosphatase. Initially every 4–6 weeks, then 3–6 months when stable.
Treatment	Complete abstinence from alcohol. Low-fat diet.
	Pancreatic enzyme supplements (e.g. Creon 2–4 caps during each meal).
	Regular analgesics (dihydrocodeine, consider amitriptyline).
	Referral to pain clinic, psychologist or diabetic team, as appropriate.

Key points

- Iron deficiency anaemia should not be attributed to an uncomplicated petic ulcer, hiatus herniam ingestion of non-steriodal anti-inflammatory drugs or oesophagitism without investigation of the colon.
- Confirm the presence of iron deficiency by measuring the serum ferritin before starting treatment, otherwise other causes of a hypochromic microcytic anaemia will be overlooked.
- Investigation for a source of gastrointestinal blood loss should include endoscopy, distal doudenal biopsy and a barium enema.
- Coeliac disease most commonly presents as recurrent or or efractory iron deficiency anaemia in adults.
- A meticulous guiten-free diet is necessary for life if the risk of complications (including malignancy) is to be reduced.
- Chronic pancreatitis commonly causes pain or exocrineinsufficiency, both of which can be halped by pancreatic enzyme supplements. Supplements should be taken during

rather than before or after, a meal.

Further reading

British Society of Gastroenterology. *Guidelines in Gastroenterology 1996.* See especially guidelines on coeliac disease and malabsorption.

Holmes GKT, Prior P, Lane MR, Pope D, Allan RN. Malignancy in coeliac disease—effect of a gluten-free diet. *Gut* 1989; **30:**333–9.

Lucas CA, Logan ECM, Logan RFA. Audit of the investigation and outcome of iron-deficiency anaemia in one health district. *J R Coll Physicians Lond* 1996; **30:**33–5.

Sahay R, Scott BB. Iron deficiency anaemia—how far to investigate? *Gut* 1993; **34:** 1427–8.

Chapter 10
Nutrition

Clinical surveys estimate that 15% of patients admitted to UK hospitals each year are malnourished (Figure 10.1) and 30–40% are undernourished. These patients have a longer hospital stay, a higher incidence of complications, including death, and a fourfold higher cost if a complication of their illness develops. Although undernutrition is usually the greatest concern, obesity—the malnutrition of affluence—also increases morbidity.

The short- and long-term *clinical benefits of supplementary nutrition* have been demonstrated in controlled trials (see references under Further reading p. 208). On an orthopaedic ward, patients with a fractured neck of femur were randomized to receive supplementary drinks (250 kcal and 20 g protein/day) in addition to food, or a normal ward diet: hospital stay decreased from 40 to 24 days, the

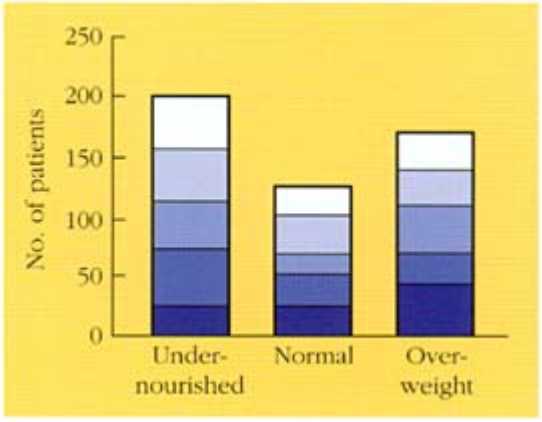

Figure 10.1 *Malnutrition in 500 hospital patients: undernourished (BMI<20), normal (BMI 20–25) or overweight (BMI>25) in elderly care (□), orthopaedics (■), chest medicine (■), general medicine (■) and general surgery (■). (From McWhirter JP, Pennington CR. Incidence and recognition of*

malnutrition in hospital. Br Med J *1994;* ***308:****945–8.)*

complication rate decreased from 37 to 16% and mortality decreased from 37 to 24%, in those receiving the supplements. A similar study, in 501 patients with general medical conditions on a geriatric ward, reduced the 6-month mortality from 19 to 9%. Parenteral nutrition is life saving for patients with intestinal failure, by allowing time for definitive treatment of the underlying disease to take effect.

The *decision to provide nutritional support* depends on the nutritional status (Table 10.1) and nature of the illness. In hospital, a decision to provide or withhold nutritional support ought to be made if eating is not anticipated for 7 days, or if dietary intake is inadequate in a malnourished patient. Some of the conditions justifying nutritional support (Table 10.1) are equally applicable in the community, although methods will differ.

Enteral feeding should always be used if the gut is functioning, by whatever access is possible (p. 196). Sip feeds are prescribable in the community and in hospital. Tube or gastrostomy feeding will be initiated in hospital. There has been an exponential increase in the

Table 10.1 Indications for nutritional support

General	Specific
Weight loss >10% in <3 months	Dysphagia (including stroke,
Moderate or severe malnutrition	neuromuscluar causes)
Unable to eat adequate oral diet	Persistent vomiting
No oral diet antiopated for >7 days	Crohn's disease (especially children, adolescents)
Severe anorexia	Short bowel syndrome
	Malignancy
	Complications of surgery
	Pancreatitis
	Sepsis
	Burns
	Multiple injuries

number of feeding gastrostomies, now that percutaneous endoscopic gastrostomy is widely available. Such patients are frequently discharged to community care, and this has considerable implications for the family doctor. *Parenteral feeding* is indicated only when enteral feeding is impossible owing to gut failure.

Nutritional assessment

Nutritional assessment is fundamental for any patient, particularly those with gastrointestinal disease, because neglecting the nutritional status of ill patients compromises survival. In hospital a variety of factors can effectively result in starvation, including surgery, prolonged investigation, or gastrointestinal pathology, all exacerbated by loss of appetite due to apprehension and unappetizing food. In a community setting, dietary inadequacy due to social isolation may contribute to nutritional deficiency, apart from malabsorption caused by gastrointestinal disease.

The *aim of assessment* is to recognize general (protein-calorie) malnutrition (Table 10.2), as well as specific deficiencies (Table 10.3). No single measurement is sufficient. Carefully conducted studies have shown that *clinical judgement* is better at predicting postoperative complications than single measures such as a low serum albumin. Similarly, *anthropometric measurements* (triceps skin-fold thickness or mid-arm muscle circumference) vary widely between observers, being both cumbersome and unreliable for individual patients in clinical practice. *Other objective measures* (such as serum transferrin or delayed cutaneous hypersensitivity) are affected by hepatic, renal or inflammatory disease, a variety of drugs and infection. Deficiencies of *vitamins and minerals* are usually mixed, so it is rarely necessary to do specific vitamin or trace element tests other than those in Table 10.3; it is more practical to treat suspected deficiency generously.

So, although it is difficult to be objective, identifying patients who are at risk from undernutrition should be straightforward (Table 10.2). The nutritional assessment can then be placed in the context of the patient's illness, so that supplementary nutrition can be prescribed to patients at risk, as part of the definitive treatment of their disease. The trouble is that this simple action is too often neglected.

Table 10.2 General assessment of undernutrition

Evaluate	■ Pattern of weight loss (continuing, stable) ■ dietary intake (solids, liquids, nil by mouth) ■ gastrointestinal symptoms (anorexia, nausea, vomiting) ■ functional capacity (ambulatory, bedridden) ■ physical signs (muscle wasting, loss of subcutanous fat, oedema, glossitis)
Look for broad markers of undernutrition	■ body mass index (<20 kg/m^2, Figure 10.2) ■ weight loss >10% of normal body weight in last 3 months ■ hypoalbuminaemia (<35 g/l)

It is often helpful to ask a *dietitian* to assess formally the difference between current intake and nutritional requirements. This is more readily available in hospital than the community and can be used to estimate the amount of nutritional supplement needed. Although this approach is logical, calculations to the nearest kilocalorie or millimole may introduce spurious accuracy, because the estimates are subject to a number of errors. Regular re-evaluation during nutritional supplementation is the best guide to the adequacy of replacement, and is an integral part of nutritional assessment.

Nutritional supplements

The simplest way to augment nutritional intake is to give general advice on meals and to prescribe sip-feed supplements.

General advice

Frequent, small meals, attractively presented, may help patients with early satiety. Taste is often impaired in patients with cancer or

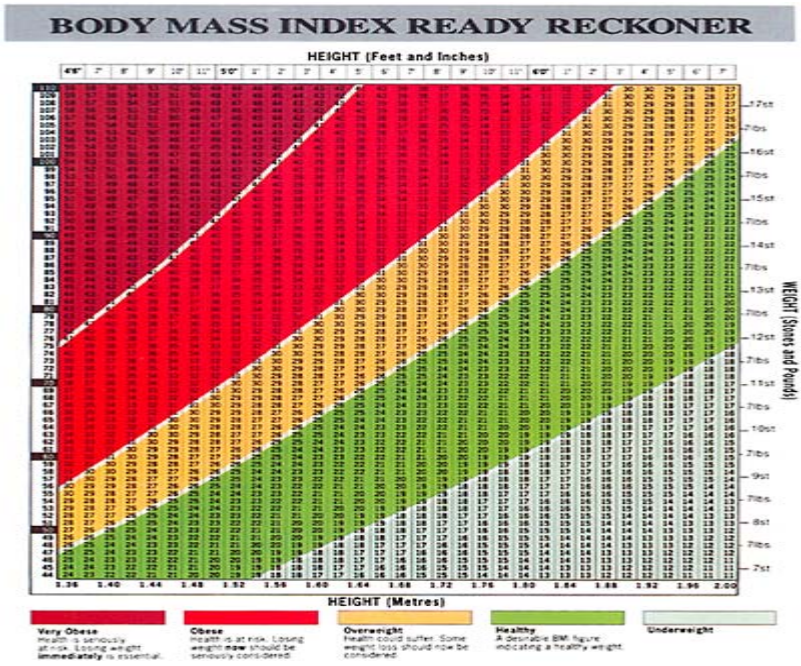

Figure 10.2 *Body Mass Index chart. Mortality increases twofold when body mass index (BMI, height/weight^2) exceeds 36 kg/m^2, and threefold when*

BMI exceeds 44 kg/m^2. (Adapted from Garrow JS. Obesity and related diseases. *Edinburgh; Churchill Livingstone, 1988.) © Servier Laboratories Limited, 1991.*

Table 10.3 Common laboratory tests for specific nutritional deficiencies

Full blood count (microcytosis or macrocytosis due to iron, folate or B12 deficiency)
Serum B12 concentration
Serum and red cell folate concentration
Serum ferritin (iron deficiency)
Prothroubin time (prolonged in vitamin K deficiency)
Serum calcium and phosphate (both low in vitamin D deficiency)
Serum magnasium and zinc

systemic disease, and food may need to be sweeter or more intensely flavoured to be appreciated. If red meat causes nausea, poultry or fish may remain palatable. Replacing beverages (tea, coffee, water) that contain no calories by a cup of liquid feed supplement with each meal will increase intake by 750 kcal daily. Appetite stimulants, such as a glass of sherry, are often recommended but of debatable benefit.

Sip-feed supplements

Palatability is the key to compliance and a variety should be tried to find the most acceptable brand (Table 10.4). These supplements significantly increase nutrient intake without significantly affecting the consumption of conventional food. Although any of the liquid enteral feed formulas can be used, commercial cartons are usually more palatable and convenient. Their extra cost is justified by better compliance, because less is wasted. Refrigeration improves palatability, especially if the patient has a dry mouth. The *amount* needed depends on the amount of other food being eaten and can be calculated with the help of a dietitian. If this is not available, most formulas contain 1.0 kcal/ml and a normal cup contains about 250 ml; two cups (cartons) will therefore provide 500 kcal and four cups 1000 kcal daily, which will usually be adequate. A *target* should be set and

Table 10.4 Selection of sip-feed formulas*

Supplements	Flavours	Energy (nearest 0.25 kcal/ml)	Net NHS cost (£; 1996)
Advera (237 ml can)	Orange, chocolate	1.25	2.26
Ensure Plus(200ml carton)	Caramel, raspberry, coffee, other	1.25	1.37
Fortijuice (200 ml carton)	Lemon+lime, peach+orange, other	1.25	1.50
Fortimel (200 ml carton)	Apricot, forest fruits, other	1.00	1.16
Fortisip (200 ml carton)	Vanilla, banana, mushroom, other	1.50	1.40
Protein Forte (200 ml carton)	Vanilla, strawberry, chocolate	1.00	1.05
Approved as supplements, or for sole source of nutrition			
Clinifeed favour (375 ml can)	Neutral	1.00	0.97
Enrich (250 ml can)	Vanilla, chocolate, with fibre	1.00	1.74
Ensure (250 ml can)	Chicken, mushroom, asparagus, other	1.00	1.47
Entera (250 ml can)	Butterscotch, vegetable cream, other	1.50	1.35
Fresubin (250 ml can)	Nut, peach, chocolate, mocha, other	1.00	1.09
Osmolite (250 ml can)	Neutral	1.00	1.49

*All are polymeric with vitamins and minerals, gluten-free and limited (or no) lactose, suitable for the majority of patients. See also Table 10.6 and comment about comparative costs.

reviewed after 3–5 days to confirm that a sufficient intake has been achieved. If it has not, formal enteral feeding should be started.

Home enteral feeding

Tube-feeding, either by a fine-bore nasogastric tube or after placement of a percutaneous endoscopic gastrostomy (PEG), is a practical method of managing the dietary requirements of patients in the community who are otherwise unable to eat. The tube will be inserted and feeding initiated in hospital, but the key components are liaison between

hospital and general practice team, training of the primary patient carer, provision of supplies and monitoring of nutritional status.

Indications

Oral intake must be inadequate for normal requirements and the proximal small intestine must be working. The majority of patients selected for a PEG will have neuromuscular dysphagia following a stroke or degenerative conditions such as motor neurone disease, multiple sclerosis or Parkinson's disease (Table 10.5). In 162 consecutive patients in Plymouth, the median duration of feeding was 9.8 months (range 1.5–38 months) in those still alive with the PEG in place at follow-up. The PEG was removed in 23% and needed changing in 8%.

Table 10.5 Indications for PEG insertion in 162 consecutive patients in Plymouth

Indication	Percentage
Stroke	47
Motor nearone disease	10
Head injury	6
Other neurological disease	22
Head and neck surgery	9
Other non-neurological disease	6

Which feed?

The choice is enormous and unnecessarily confusing. Feed formulas can broadly be divided into polymeric and elemental types. *Polymeric* formulas contain whole proteins, carbohydrates as glucose polymers and fat as long-chain fatty acids. *Elemental* formulas contain predigested nutrients in a directly absorbable form, with free amino acids *(monomeric)* or short peptides *(oligomeric),* glucose polymers and medium-chain triglycerides.

The theory is that patients with impaired absorption (such as short bowel syndrome or small intestinal Crohn's disease) will benefit from elemental diets. Oligomeric formulas are purported to be better absorbed and more palatable than monomeric formulas, because there are specific transport mechanisms for di- and tripeptides, whereas free amino acids make monomeric formulas hyperosmolar and unpalatable. *Other modifications* include variations in *energy density* (up to 2.0 kcal/ml), *electrolyte, nitrogen or fat content* (for hepatic encephalopathy or steatorrhoea), *lactose-free formulas* (for hypolactasia), additional *fibre* (purported to reduce the incidence of feed-associated diarrhoea), and *glutamine* content. Glutamine is the principal fuel of enterocytes and may benefit small intestinal integrity. Lastly, *disease-specific formulas* have been marketed for patients with hepatic, renal or pulmonary disease, for a variety of theoretical reasons.

The truth is that careful studies have not shown any difference in nutrient absorption or clinical benefit between polymeric and elemental (either monomeric or oligomeric) feeds. Furthermore, it has been difficult to demonstrate consistent benefit from the various modifications. Consequently, the choice can be limited to a polymeric feed for almost every patient and is reasonably guided by a local prescribing policy on account of cost (Table 10.6).

Percutaneous endoscopic gastrostomy (PEG)

The procedure takes 10–20 minutes to perform, under sedation with local anaesthetic infiltration into the epigastric skin. The 'pull-through' technique is most commonly used. Briefly, during endoscopy, a cannula is inserted through the epigastric skin into the

Table 10.6 Enternal feeding formulas*

Type	Examples	Net NHS Cost (£; per 500 ml, 1996)
Polymeric		
Lactose free, normal calorie	Clinifeed favour	1.90
	Ensure	2.94
	Fresubin	2.35
	Osmolite	2.98
Lactose free,	Fresenius OPD	3.99
normal calorie,	Nutrison standard	2.61
high nitrogen		
Lactose free,	Clinifeed Protein Rich	1.87
high calorie,	Ensure Plus	3.68
high nitrogen	Nutrison Energy-plus	2.76
	Fresubin High Energy	3.10
With medium-chain triglycerides	Liquisorbon MCT	2.80
Fibre enriched	Enrich	2.94
	Fresubin Isofibre	3.10
	Jevity	3.50
	Nutrison Fibre	2.67
Elemental		
Monomeric	Elemental 028 powder	3.82/100 g
	Elemental O28 cartons	6.25

Oligomeric	Peptamen	5.90
	Pepti 2000 LF	3.47
	Peptisorb	4.83
	Perative	5.69
	Reabilan	4.58

*The costs are stated to demonstrate the variablity between compounds at one point in time. It is appreciated that costs and comparisons may change.

stomach, which has been insufflated with air. A thread is inserted through the cannula and withdrawn through the mouth as the endoscope is removed. The gastrostomy tube is attached to the thread and pulled into position, where it is secured by an internal buffer and external clip. Feeding can start within 12 hours. A Luertype lock on the PEG connects to disposable plastic tubing attached through an infusion pump to the feeding bottle (Figure 10.3). If the PEG is removed, the fistulous track closes spontaneously within a few days. Complications relate to sedation during the procedure (peritonitis is exceptionally rare), or aspiration pneumonia after feeding has begun.

In the Plymouth health district serving 470,000 population, about 50 patients are being fed by PEG at any one time, for a median duration of 10 months.

Liaison between hospital and family doctors. PEG feeding is usually well established before discharge, because the patient's general condition is the governing factor. Consequently, the type and volume of feed (usually 125 ml/hour for 16 hours/day) will have been confirmed. There should be direct contact between the nurses on the ward and the district nurse, an initial supply of feed and plastic connectors, agreement on who is going to pay for plastics and feed (often the most difficult issue!) and a contact number for the carer to call if there are problems with the pump or feed.

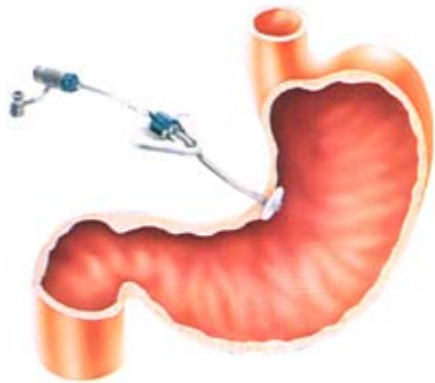

Figure 10.3 *Diagram of PEG and connections.*

Training of the carer and provision of supplies. The primary carer (family member, or residential or nursing home nurse) should be trained in the storage, connection and administration of the feed. This will be performed on the ward prior to discharge. The feed can be stored at room temperature (refrigeration promotes diarrhoea) and connected immediately after opening. Plastic connectors and any residual feed should be disposed of every 24 hours. An infusion pump delivers the feed at a set rate, which should not be exceeded because too much feed in the stomach promotes reflux and aspiration. Plastics and feed can be obtained by the local chemist, who should be given the product order numbers by the hospital before discharge.

Monitoring of nutritional status. It is usually impracticable to weigh the patient after discharge from hospital, but a clinical assessment (looking at subcutaneous fat and muscle bulk, and for oedema) should be made every 1–2 weeks. The serum electrolytes, albumin, calcium and full blood count should be checked every 2–4 weeks once feeding has been stabilized. Enteral feeds now contain sufficient vitamins (including folate) and minerals for normal requirements. If there are abnormal losses due to diarrhoea or vomiting, closer monitoring is needed.

Complications. Diarrhoea may be due to gastroenteritis, antibiotics, too-rapid administration of feed, or co-existing disease. Aspiration pneumonia is a real hazard in patients with free gastro-oesophageal reflux and an absent gag reflex. Feeding in a semi-recumbent position may reduce the risk. Tube blockage is the other common problem. The tube should be flushed with 20 ml water after every disconnection. Sometimes effervescent fluids will shift a blockage but, if this is persistent, or if the tube is leaking, the PEG has to be replaced.

Home parenteral nutrition

General points

Since home total parenteral nutrition (TPN) in the UK is given to less than 1 per 100,000 population, only some general points are made here. The usual *indication* is a short bowel (<100 cm), as a result of resection following mesenteric infarction or extensive Crohn's disease. A few patients have gut failure due to radiation enteritis, systemic sclerosis or autonomic neuropathy. The *decision* to start home TPN will have been taken after careful consideration in hospital, taking into account the prognosis, domestic circumstances and ability of the primary carer, and, it is hoped, after discussion with the patient's general practitioner.

The *principles* of TPN are that the daily nitrogen and energy requirements are calculated, depending on the weight of the patient and underlying disease. Nitrogen (usually around 14 g/day) is supplied by amino acids. Energy (usually 2000 kcal/day) is provided by equivalent amounts of lipid and glucose. Electrolytes, vitamins and trace elements are added into a single 2–3-litre bag and the solution administered through a tunnelled central venous line. This line enters the skin on the chest wall several centimetres away from the entry point into the vein, which reduces the incidence of line infections. Meticulous asepsis when connecting and disconnecting the feed is absolutely fundamental.

Complications once TPN has been established are infective (line, endocarditis), metabolic (hyperglycaemia, electrolyte imbalance), mechanical (venous thrombosis, catheter displacement, air embolus), or nutritional (deficiencies of trace elements, folate or essential fatty acids).

Some hospitals will supply their own home TPN, arranging education and training for the carer and district nurse, as well as backup facilities in case of pump failure or complications. There are, however, commercial companies (Appendix) who will take on all these responsibilities, at a price (about £120/day, 1996), once the patient's feeding regime has been stabilized in hospital.

Monitoring

The purpose of frequent monitoring is to limit the complications associated with TPN. Local protocols will vary, but regular clinical and biochemical monitoring is essential. The authors' own monitoring protocol is shown in Table 10.7. Clinical assessment of well-being, subcutaneous fat, muscle bulk and peripheral oedema complements the objective measurements.

Special diets

An imaginative dietitian is invaluable for helping patients to maintain special diets. Badly planned, badly presented or poorly understood diets result in poor compliance and are not worth prescribing. Details of the diet are beyond the scope of this chapter, but it is helpful to understand the general principles.

Table 10.7 Monitoring protocol for home parsenteral nutrition

Measurement	Daily	Twice weekly	Fortnightly	Monthly
Clinical				
Temperature	+			
Weight	+			
Cannula entry site	+			
Clinical assessment			+	
Biochemical				
Electrolytes		+		
Glucose		+		
Liver function tests		+		
Calcium and phosphate			+	
Full blood count			+	

Folate	+
Trace element	+

Weight reduction

Obesity can be *defined* as a weight exceeding the recommended weight for height by 20%, or a body mass index above 25 kg/m^2 (Figure 10.2). There is increasing evidence that obesity is related to a modification of insulin receptor expression, leading to insulin resistance and fat deposition, although many other factors contribute. Obesity exacerbates osteoarthritis, diabetes, cardiovascular disease and many other conditions, directly increasing the risk of death. Patients over 120 kg usually have a high metabolic rate and even higher food intake, despite frequent denials of excessive eating.

The *principles* of weight reduction are to set a realistic target weight, aiming for steady, moderate weight loss (about 0.5 kg/week). An intake low in fat and sugar but high in complex carbohydrates (fibre) is recommended, because fat has twice the energy density of protein or carbohydrate. *Early weight loss* is largely attributable to loss of body water due to breakdown of glycogen, and an inappropriately low carbohydrate intake can lead to breakdown of protein rather than fat. Prolonged dieting is necessary for any substantial loss of body fat and eating patterns must be permanently changed, or weight will be regained. Regular exercise increases *energy expenditure,* which must exceed intake until the target weight is reached.

Successful weight loss is improved by regular supervision, a weight chart posted in a prominent place and support from a skilled practice nurse, dietitian, or slimming organization (especially those that charge!). There are other approaches to obesity, including appetite suppressants (D-fenfluramine 15 mg twice daily), and surgical procedures (gastroplasty, nylon waist cord), but sideeffects are common and dietary compliance is still required with drug treatment.

High-fibre diet

A high-fibre diet is *indicated* for diverticulosis, most patients with constipation and some with irritable bowel syndrome. The *principles* are that fibre provides bulk, absorbs water and satisfies hunger. Fluid intake must be increased (to 1500 ml/day) to compensate for water retained by the increased fibre. Excessive flatulence from bacterial fermentation is the main *disadvantage,* but only intestinal strictures or constipation due to neurological disease (spinal cord damage, autonomic neuropathy) are *contraindications*.

Good *sources* of fibre are wholemeal (not ordinary brown) bread, wholegrain cereals, fresh vegetables, pulses (dried beans, lentils), wholemeal flour or pasta and fresh fruit. Unprocessed coarse bran can be added to soups, cereals, stewed fruit and home baking, if dietary changes are insufficient. Isphagula husk granules (Regulan, Fybogel) are more convenient and expensive than dietary changes or unprocessed bran.

Gluten-free diet

A strict gluten-free diet is indicated for coeliac disease (p. 174). The Coeliac Society (Appendix) provides an excellent recipe book, with the gluten content of most foods. The *principles* are to avoid wheat, barley, oats and rye, which means all ordinary bread, cakes, biscuits, pastry, pasta and crispbread, many cereals (Weetabix, Puffed Wheat), packet soups, chocolate, ice cream, and sweets. Essential *gluten-free products* are prescribable (p. 177).

Lactose-free diet

A lactose-free diet is *indicated* for hypolactasia, which should be suspected if diarrhoea persists after acute gastroenteritis, Crohn's disease, ulcerative colitis or coeliac disease. The *principles* are to *avoid* milk and soft milk products (yoghourt, milk shakes, cottage cheese), which are the only appreciable source of lactose. Many dairy products contain insufficient lactose to cause symptoms. Hypolactasia may be temporary, so milk can often be reintroduced at a later date. Soya milk, or 'live' yoghourt containing *Lactobacillus acidophilus,* which should digest lactose, are *allowed*.

Low-fat diet

A low-fat diet is unpalatable, but is *indicated* for steatorrhoea due to chronic pancreatitis, cholestasis or severe malabsorption, as well as for hyperlipidaemia. No benefit has been shown for other types of hepatobiliary disease (such as gall stones or acute hepatitis), although avoiding fatty foods (rather than a specific low-fat diet) may decrease post-prandial discomfort in some patients.

The *principles* are to reduce total fat intake to 30–50 g/day, or until steatorrhoea is controlled. Unsaturated fats should be substituted for saturated fats in hyperlipidaemia. *Medium-chain triglyceride* supplements are indicated only if calorie intake is insufficient following fat restriction (shown by continued weight loss). All fried food, butter, cheese, cream, whole milk and fatty meat or fish should be *avoided*. Skimmed milk, low-fat spreads, cottage cheese, chicken, turkey, white or smoked fish and any vegetables or fruit are *allowed*.

Exclusion diet

An exclusion diet is *indicated* for refractory irritable bowel syndrome (p. 88), especially if symptoms appear to be related to food. About 50% of patients respond well and more are improved. An experienced dietitian is needed to motivate the patient and to provide a systematic approach. The *principles* are that the diet is continued for 2 weeks, with a diary kept of food eaten and symptoms experienced. Foods are then reintroduced one at a time, if improvement has occurred. Individual items are tried at intervals of 2 days. Intelligent cooperation by the patient is clearly essential.

Foods *excluded* are cow's milk, butter, cheese, eggs, yoghourt, tea, coffee, alcohol, squashes, citrus fruits, bread, other yeast or wheat products, onions, potatoes, nuts and preservatives. Chicken, lamb, white fish, rice, soya milk and most vegetables are *allowed*.

Summary

Assess nutritional status	Body mass index (Figure 10.2), pattern of weight loss (>10% normal weight in <3 months), current intake (none, liquids, semi-solids) and specific deficiencies (iron, B12, etc.) (Tables 10.1, 10.2).
Sip-feed supplements	Indicated when nutrition is inadequate, but some oral intake is possible. 2–4 cartons of the most palatable supplement (Table 10.4).
Enteral feeding	Indicated when supplements fail or are inappropriate (e.g. neurological dysphagia), with normal proximal intestinal function. Fine-bore nasogastric tube for up to 6 weeks, or percutaneous gastrostomy. Simple polymeric feeds (Table 10.6) via continuous infusion up to 125 ml/hour usually appropriate. Elemental or oligomeric feeds rarely needed.
Parenteral nutrition	Indicated for gut failure in hospital. Monitoring for home TPN (Table 10.7).

Key points

- Some effort should be made to make a nutritional assessment on any patient with gastrointestinal disease. Patients at risk from undernutrition are readily indentified (Table 10.1)
- Routine sip-feed supplements halved the 6-month mortality in elderly patients with general medical conditions in one study.
- Nutritional support should always be enteral (as sip feeds, nasogastric or percutaneous gastrostomy) unless the gut is not functioning.

Further reading

British Association for Parenteral and Enteral Nutrition [BAPEN]. *Organisation of nutritional support in hospitals.* BAPEN, PO Box 922, Maidenhead, Berks SL6 4SH, 1994.

British Society of Gastroenterology. *Guidelines in Gastroenterology 1996.* See especially guidelines on nutrition.

Delmi M, Rapin C-H, Bengoa J-M et al. Dietary supplementation in elderly patients with fractured neck of femur. *Lancet* 1990; **335:**1013–6.

Larsson J, Unosson M, Ek A-C *et al.* Effect of dietary supplement of nutritional status and clinical outcome in 501 geriatric patients—a randomised study. *Clin Nut* 1990; **9:** 179–84.

Appendix

Useful addresses

The telephone numbers of local organizations can be found in the telephone directory under Social Service and Welfare Organizations, or Charitable and Benevolent Organizations. These are especially helpful for alcohol abuse, bereaved, hospices, services for the disabled and services for the elderly.

Alcohol abuse

Al-Anon

61 Great Dover Street, London SE1 4YF (Tel. 0171 403 0888).

Provides a 24-hour telephone helpline and offers group support for close friends and relatives of problem drinkers. There are local groups throughout the country.

Alcoholics Anonymous

PO Box 1, Stonebrow House, York YO1 2NJ (Tel. 01904 644 026) or 11 Redcliffe Gardens, London SW10 (Helpline Tel. 0171 352 3001).

Provides anonymous groups for the assistance of alcoholics and problem drinkers. Local numbers in the telephone directory.

Al-Ateen

61 Great Dover Street, London SE1 4YF (Tel. 0171 403 0888).

In conjunction with Al-Anon provides a helpline for young people aged 12–20 years whose lives have been affected by problem drinking.

Alcohol Concern (National Agency On Alcohol Misuse)

Waterbridge House, 32–36 Loman Street, London SE1 0EE (Tel. 0171 928 7377).

Concerned with the prevention and treatment of alcohol misuse.

Cancer

British Association of Cancer United Patients (BACUP)

121–123 Charterhouse Street, London EC1 6AA (Tel. 0800 181 199). Provides information and support for patients and relatives using a telephone and written answer service by experienced cancer nurses (10 a.m.–7 p.m. Mon–Thurs; 10 a.m.–5.30 p.m. Fri).

Cancer Relief Macmillan Fund

Anchor House, 15–19 Britten Street, London SW3 3TZ (Tel. 0171 351 7811).
Provides nursing services. Local number in the telephone directory.

Cancer-Link

17 Britannia Street, London WC1X 9JN (Tel. 0171 833 2451) or 9 Castle Terrace, Edinburgh EH1 2DP (0131 228 5557).
Patient-based organization, offering support on all aspects of cancer.

Family Cancer Clinic

Department of Clinical Genetics, Royal Free Hospital NHS Trust, Pond Street, London NW3 2QG (Tel. 0171 794 0500 ext 3702).
Referral centre and source of advice on patients and families with multiple tumours.

Marie Curie Memorial Foundation

28 Belgrave Square, London SW1X 8QG (Tel. 0171 235 3325). Runs 11 UK nursing homes and a nationwide domiciliary nursing service, especially night nursing. Provides urgent welfare needs in kind, advice and general information.

General

British Digestive Foundation

3 St Andrew's Place, Regent's Park, London NW1 4LB (Tel. 0171 486 0341).
Produces patient-orientated leaflets and supports research.

British Society of Gastroenterology

3 St Andrew's Place, Regent's Park, London NW1 4LB (Tel. 0171 387 3534).

Encourages education, training and audit in gastroenterology and gastrointestinal endoscopy.

Employment Medical Advisory Services

Director of Medical Services, Health and Safety Executive, Woodside House, 261 Low Lane, Horsforth, Leeds LS18 5TW (Tel. 0113 283 4200).

Part of the Health and Safety Executive with local offices and a Prestel Service, which enables users to send messages, as well as giving general information.

Primary Care Society for Gastroenterology

Secretariat: Mrs Ros Aukett, Primary Care Society for Gastroenterology, 16 Cheltenham Road, Gloucester GL2 0LS (Tel. 01452 304638).

Provides a forum for doctors to address the issues of education and research in gastroenterology in primary care.

Liver

British Liver Trust

Central House, Central Avenue, Ransomes Euro Park, Ipswich IP3 9QG (Tel. 01473 276 326).

Provides patient information leaflets and advice for patients with chronic liver disease.

Children's Liver Disease Foundation

138 Digbeth, Birmingham B5 6DR (Tel. 0121 643 7282).

Provides advice and emotional support for families with a child suffering from liver disease.

Liver Transplant Units

Birmingham

Liver Unit, Queen Elizabeth Hospital, Birmingham B15 2TH (Tel. 0121 472 1311 ext 3428).

Cambridge

Transplant Coordinator, Addenbrookes NHS Trust, Hills Road, Cambridge [Tel. 01223 217 251 (direct line)].

Leeds

Transplant Coordinator, St James' University Hospital NHS Trust, Becket Street, Leeds LS9 7TF (Tel. 0113 243 3144 ext 4553).

London

Transplant Coordinator, Liver Unit, King's Healthcare NHS Trust, Denmark Hill, London SE5 9RS [(Tel. 0171 737 4000 bleep 149 or Tel. 071 326 3254 (direct line)].

Transplant Coordinator, Liver Unit, Royal Free Hospital NHS Trust, Pond Street, London NW3 2QG [Tel. 0171 794 0500 (bleep)].

Primary Biliary Cirrhosis Support Group

Mrs Collete Thain, The Dean, Longniddry, East Lothian, EH3 20PN (Tel. 01875 853 552).

Provides patient information, advice and support.

Miscellaneous

Association for Glycogen Storage Disease

9 Lindop Road, Hale, Altrincham, Cheshire WA15 9DZ (Tel. 0161 980 7303).

Provides information and support for all persons and their families affected by glycogen storage disease.

Coeliac Society

PO Box 220, High Wycombe, Bucks NG11 2HY (Tel. 01494 437 278).

Provides advice and counselling concerning the disease and diet, and gluten-free recipe books, together with holidays and social activities.

Crohn's in Childhood Research Association (CICRA)

Parkgate House, 356 West Barnes Lane, Motspur Park, Surrey KT3 6NB (Tel. 0181 949 6209).

CICRA offers self-help support to young people with Crohn's disease or ulcerative colitis, their families and friends.

Eating Disorders Association

Sackville Place, 44–48 Magdalen Street, Norwich NR3 1JE (Tel. 01603 621 414).

Offers mutual support and sharing of information. Concerned to promote research

IBS Network

St. John's House, Hither Green Hospital, Hither Green, London SE13 6BU (correspondence only).

Provides information, advice and support for patients with irritable bowel syndrome.

National Association for Colitis and Crohn's Disease

98A London Road, St Albans, Hertfordshire AL1 1NX (Recorded message Tel. 01727 844 296).

Offers support and information for patients with inflammatory bowel disease and their families. Local groups throughout the country.

Oesophageal Patients' Association

16 Whitefields Crescent, Solihull, West Midlands B91 3NU (Tel. 0121 704 9860).
Provides leaflets and support for patients with oesophageal cancer.

Share-a-Care (National Register for Rare Diseases)

8 Cornmarket, Faringdon, Oxon.
Puts people with rare diseases in contact with others with the same disorder, as well as compiling a national register.

Nutrition

Medical Information (Nutrition Department), Pharmacia & Upjohn, Davy Avenue, Knowlhill, Milton Keynes MK5 8PH (Tel. 01908 603 790).
A commercial parenteral nutrition service is available; 48 hours notice is generally needed before initiating feeding, but delivery is thoughout the United Kingdom.

Stomas

British Colostomy Association (incorporating the Colostomy Welfare Group)

15 Station Road, Reading, RG1 1LG (Tel. 01734 391 537).
Composed of volunteers (who are all colostomists) who will visit in hospital or at home, pre- or postoperatively.

Hollister Stoma Care Advice Service

42 Broad Street, Wokingham, Berks RG40 1AB (Tel. 0800 521 377).
Offers confidential advice on any aspect of stoma care for patients and their carers.

Ileostomy Association of Great Britain & Ireland

Amblehurst House, Black Scotch Lane, Mansfield Notts N18 4PF (Tel. 01623 28099).
Advisory service for people with ileostomies by way of hospital and home visits. Many of the volunteers are ileostomists themselves.

Kingston Trust

The Drove, Kempshott, Basingstoke, Hants RG22 5LU (Tel. 01256 52320).

Provides homes for all types of stoma patients or those with other abdominal diseases who are in need of short-stay or permanent accommodation.

National Advisory Service for Parents of Children with a Stoma

51 Anderson Drive, Valley View Park, Darvel, Ayrshire KA17 0DE (Tel. 01560 322024).

Provides advice and support group for parents of children who have a stoma, ileostomy, colostomy, or urostomy.

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