Hyperthermia in Oncology

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Clifford L. K. Pang
GUANGZHOU UNIVERSITY OF CHINESE MEDICINE, CHINA

Translated by Dr. Kaiman Lee

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Foreword by Dr. Ralph W. Moss

Out of the hundreds of complementary and alternative medicine (CAM) treatments that have been proposed for treating cancer, only a few have been scientifically verified. Some of these treatments are now making the transition into the realm of conventional medical practice. Put another way, mainstream oncology is absorbing treatments and ideas from the realm of CAM. In doing so, it will inevitably change for the better. The result is a new type of treatment, "integrative oncology."

The most effective cancer treatment includes not just the triad of surgery–radiation–chemotherapy but also hyperthermia, immunotherapy, and traditional Chinese medicine (TCM). These three once "alternative treatments" have come together in the outstanding work of Professor Clifford Pang, in the creation of his pioneering Clifford Hospital in Guangzhou, China, and now in this fascinating book on cancer treatment.

Clifford L. K. Pang, MD, is president of the International Clinical Hyperthermia Society and chairman of the World Federation of Chinese Medicine Societies—Special Committee of Natural Therapy (WFCMS-SCNT). Since 2000, he has been the board chairman and chief executive officer of the innovative Clifford Hospital in Guangzhou. This hospital has won many awards and has achieved United States Joint Commission International accreditation and a grade of AAA from the Chinese hospital accreditation agency.

Given this strong background, it is clear that no one is better qualified to bring about the integration of Eastern and Western medicine, and of CAM and conventional oncology, than Dr. Pang.

In particular, Dr. Pang has focused on the development of heat therapy, or hyperthermia. He points out in this work that hyperthermia has Eastern, as well as Western, roots. For instance, Chinese doctors used medicated baths, medical fumigation, hot spring baths, moxibustion, sand baths, and cupping jars, all of which involve the therapeutic use of heat. He relates that the use of stone needles and fire led to the development of acupuncture therapy, so these two fundamental CAM treatments are related in their origin.

Progress of hyperthermia has been slow. Thankfully, there have been genuine scientists, such as Prof. Pang, who were interested in this topic, and ultimately they proved to even the most skeptical critics that hyperthermia was a scientifically valid adjunctive therapy, which is not conspicuously effective by itself but works very well when combined with other treatments, including chemotherapy, radiation therapy, and TCM.

Today, as Dr. Pang points out, hyperthermia is researched as part of the broader field of thermal medicine, i.e., the modulation of temperature (through either heat or cold) to beneficially affect patients. In this broader sense, thermal medicine covers not just classical hyperthermia but also cryotherapy (freezing) and radiofrequency ablation (melting), as well as various new forms of nanotechnology such as heating minute iron or gold particles that are introduced into cancer cells.

The acceptance of hyperthermia rests on the completion of rigorous phase II and III clinical trials, mainly in Germany and Holland. Yet, as an American, I must confess to a deep sense of frustration as I read these scientific articles and editorials. A Utah-based company makes the hyperthermia equipment in question; but, with rare exceptions, U.S. hospitals do not buy, install, or use this type of machine. It is high time for American oncologists to take these studies to heart and get serious about the potential of heat therapy as an adjunctive treatment for many kinds of cancer. It is wonderful that this type of treatment is made available to patients in China at the Clifford Hospital in Guangzhou.

To speak frankly, there is a leadership gap in hyperthermia. Professor Pang has set out to remedy this deficiency. He brings unique qualifications to this study. First of all, he is a scholar of both Western and Eastern approaches to cancer. This is exceptionally rare. Thus, in discussing each form of cancer he is able to simultaneously provide the reader with the optimal treatment from each tradition, seamlessly integrating the two most important medical philosophies in the world today.

Second, he is a practicing physician in a large and thriving hospital. This gives him practical knowledge that is lacking in most scholars who rely entirely on books and articles for their knowledge. There is no substitute for actual experience in knowing firsthand what works and what doesn't work. This integration of practice and theory is essential for true knowledge. As my friend and mentor, the Nobel laureate Albert Szent-Gyorgyi, MD, PhD, once said: "Facts alone are apt to be dull things and need to be tied together by theories or applied to practical problems if they are to be made reasonably palatable."

Dr. Clifford Pang brings the reader of this wonderful book face to face with the outstanding scientific work on cancer, East and West, and interprets this in the light of practical experience. There is quite simply no other book that has done this task of integration in such a clear and lucid fashion. This book is indispensable for the library of any person who is seriously interested in the topic of integrative oncology.

Ralph W. Moss, PhD
State College, Pennsylvania

Foreword by Dr. Andras Szasz

Hyperthermia in oncology has a long-standing history, having roots in ancient medicine. Numerous books have been published about this topic, but the present *Hyperthermia in Oncology* is unique. It is written by an authentic doctor, Dr. Clifford Pang, who uses hyperthermia together with leading Western medicine, traditional Chinese medicine (TCM), and natural medicine treatments for oncology treatments.

Life is based on energetically open systems, where environmental conditions determine their equilibrium. The living system is complexly controlled, forming homeostasis. Diseases break the relative equilibrium and risk the relative stability of the system, which could be detected by various TCM approaches. The human body in many ways tries to reestablish homeostasis by enhancing the negative feedback controls. Multiple actions of human physiology try to compensate and correct the damage caused by diseases. The central dogma of TCM is based on the correction processes to find equilibrium again. Dr. Pang shows how to support natural homeostatic control by the synergy of TCM with hyperthermia.

To cure a disease, most of the medical approaches act with changes of conditions (diets, medicaments, and other supplies) trying to constrain the body back to the previously working equilibrium. However, in many cases, this works against natural homeostasis; the constrained action induces new negative feedback from the living object. The living organism starts to fight against our constraints together with fighting against the disease itself. This is the problem with classical hyperthermia, which introduces a new constrained effect—the heating out from natural homeostasis. This constraint induces new physiological feedback, forcing the body to "fight on two fronts": against the disease and against the healing action. The presented synergy of TCM and hyperthermia as the amalgamation of natural therapies helps internal corrective actions to reestablish the healthy state.

Richard Nixon, former president of the United States, declared a war against cancer in 1971. Since then, tremendous efforts have been used in the "pitched battle," but the fight is a stabilized warfare instead of a hands-down win. There are multiple reasons for the lack of success, and probably a change in paradigm is necessary to move ahead. This book makes it. Dr. Pang amalgamates the best Western medical knowledge with long-living proven traditional practices. The possible synergy of hyperthermia and traditional therapies was apparent, but a study that seriously deals with this topic was missing till now. Dr. Pang introduces an approach as complex as its target, the human body. He knows well the simple rule of the roots of medicine: He treats not a disease of an individual but an individual with a disease. He knows well the enormous complexity of the human being and its complex interactions with the environment, and he applies this unique knowledge to win the war.

Dr. Andras Szasz
Professor of physics and biophysics
Head, Biotechnics Department, St. Istvan University, Budapest, Hungary
Chief scientific officer, Oncotherm GmbH, Troisdorf, Germany

Foreword by Gerald Batist

Hyperthermia has ancient origins, and identifying its proper place in modern cancer therapeutics has been a challenge. It is through the type of work undertaken by Prof. Pang at the Clifford Hospital that we hope to derive an optimal definition of the mechanisms of action of hyperthermia and greater clarity on how to integrate it into modern and multiple traditional treatments to the benefit of patients.

This book documents Professor Pang's scholarship in this field, and his efforts to use evidence-based approaches to explore the potential benefits and the proper use of hyperthermia. The Clifford Hospital is an excellent environment, given its patient-centered approach to care. Professor Pang is taking on a major challenge in his exploration and study of hyperthermia; on the one hand there is the complexity of "personalized" or individualized treatments, as well as integration with a host of other traditional and modern approaches, and on the other hand he is attempting to use modern clinical research approaches to make comparisons of outcomes, both beneficial outcomes and side effects.

As a matter of fact, comparing outcomes from individualized, and therefore different, treatments is becoming a general challenge for research in cancer therapeutics, even in the West, so this book provides important insights that could be useful even beyond the scope of hyperthermia. As we attempt to discuss individual cancer treatments based on molecular signatures and characteristics of both the tumor and the host in each individual patient, we are increasingly engaging in the very approaches described by Dr. Pang, though he uses different criteria for selecting and designing treatment for each patient. A novel "adaptive" design, in which the patients become their own controls or are matched to others with similar phenotypes, is the current preoccupation of clinical trialists and, in this sense, we can learn much from Professor Pang and his colleagues.

Gerald Batist MDCM, FRCP (C), FACP
Minda de Gunzburg Professor of Oncology, McGill University
Director, Segal Cancer Centre

Preface

Hyperthermia in oncology (hereafter referred to as "hyperthermia") is the rational application of hyperthermia in combination with therapeutic techniques, including detoxification, medical ozone therapy, traditional Chinese medicine (TCM), acupuncture/moxibustion, psychology, qigong, and medicated/nutritional diet.

Hyperthermia applies various heat sources into a patient's body for the purpose of cancer treatment. Some scholars term it "cancer warming," "heat killing," or "heat penetration." In recent years, hyperthermia in oncology has enjoyed rapid development, with a large amount of clinical data becoming available. Although it may not necessarily be an independent treatment method for cancer, it has certainly played a significant synergistic and complementary role in surgery, chemotherapy, and radiotherapy. It has demonstrated its effects in improving a cancer patient's quality of life and survival time, reducing cancer recurrence, and even preventing cancer and other diseases.

Hyperthermia in Oncology is a summary of years of experiences from the outcomes of clinical treatments of cancer patients in Clifford Hospital, Guangzhou, China. It validates the unique effects of hyperthermia treatment with a large quantity of evidence-based data from medical research and clinical practice. The differentiating characteristic of this book is the systematic documentation of "evidence-based medicine" and "individualized treatment regimen." Hyperthermia is used as the prime treatment vehicle, and it is integrated with conventional cancer treatment technologies, such as chelation detoxification technology, ozone therapy, TCM, acupuncture/moxibustion, medicated diet, qigong therapy, and psychological treatment. Thus, the book offers a new, integrative cancer treatment approach.

Under the strict guidance of evidence-based procedures, theories of natural medicine, and objective clinical observations, every cancer patient is afforded an individualized therapeutic plan. Any hyperthermia treatment plan is tailored to the patient's characteristics, such as cancer location, pathological type, its stage, and its biological behavior. A typical integrative hyperthermia treatment keeps one eye on the tumor and the other on the patient. Timely adjustments are made according to the patient's changing conditions at different phases of tumor growth. Each plan is scientific, rational, and practicable. The goal is to achieve the highest protection of normal tissues, greatly enhance the therapeutic effect, and improve the quality of life of the cancer patient.

Hyperthermia, as described in this book, is a breakthrough in cancer treatment among the long-standing surgery, radiotherapy, and chemotherapy. It emphasizes patient rehabilitation in a wholly integrated way, thereby avoiding many cases of overtreatment or inappropriate treatment.

Our foundation of cancer therapy is based on the full comprehension of various medical techniques and taking advantage of their complementary strengths. Hyperthermia serves as a logical model and direction for future development of cancer therapy.

The objectives for writing this book are to promote hyperthermia as a viable cancer treatment method and to encourage innovations in cancer treatment techniques. An abundance of successful clinical cases are cited in the book. The amount and type of heat applied to patients are analyzed where hyperthermia is used in conjunction with surgery, radiotherapy, chemotherapy, biotherapy, and TCM.

Standard operation procedures for cancer treatment, management process, syndrome recognition, and preventive measures are documented. Guidance for evaluating clinical therapeutic effects, postoperation assessments, and dietary adjustments is also provided in detail.

The book exemplifies the theoretical system of hyperthermia in oncology. It serves as a guide for clinicians in the effective use of hyperthermia and in the application of hyperthermia in integrative cancer therapy.

Clifford L.K. Pang
Guangzhou, China

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My sincere gratitude goes to those experts, including Zhang Tao, Wang Xiaoguang, Lu Yimin, Zhang Xinting, Ou Junwen, Zhang Zili, Li Hengmou, Wang Junhua, Chen Pengfei, Wendy Man Lai Hung, Zhang Hongyu, and Wang Zhen, who assisted me in the development of this book and to the professors who so graciously wrote the forewords. And my sincere appreciation goes to Dr. Kaiman Lee for the translation of this book. Much remains to be improved and developed in the science of hyperthermia in oncology. I would like to share their progress and relevant information in Western, Chinese, and natural medicines, through various means, as they become available. Any and all feedback from the readers shall be gratefully received (e-mail: cpang@cliffordgroup.com).

Clifford L.K. Pang

About the author

Hyperthermia in Oncology is written by Clifford L.K. Pang, MD, PhD, past president (2013) of the International Clinical Hyperthermia Society (ICHS), chairman of the Specialty Committee of Natural Therapy of the World Federation of Chinese Medicine Societies, and president of Clifford Hospital. Clifford Hospital is the first Chinese hospital accredited by the Joint Commission International. Clifford Hospital has also been awarded National Triple-A Grade, the highest accreditation level in the official hospital appraisal in China.

This book is based on the essence of a multitude of international traditional medicine approaches, the development of modern medical sciences, and actual clinical cases. Scientific and objective analyses of the amount and types of heat in effective hyperthermia applications are documented where they are used in combination with surgery, radiotherapy, chemotherapy, biotherapy, and traditional Chinese medicine. It includes guidance for bedside maneuver during treatment, evaluating therapeutic effects, postoperative assessment, and dietary adjustments.

Based on actual cases that are detailed and accurately described, this book is scientific, creative, practical, and trailblazing. It will help medical researchers and clinicians understand the use of hyperthermia in oncology. As a practical reference for integrative applications of hyperthermia and nontoxic cancer treatment methods, it can well serve students in Western and Chinese medicine, cancer patients, and professionals with a general interest in medicine and hyperthermia.

Professor Clifford L.K. Pang, MD, PhD, has devoted almost a decade to the theory and clinical practice of hyperthermia for cancer treatments. He has created an integrative green therapy for cancer treatment, combining hyperthermia with chelation detoxification, ozone therapy, traditional Chinese medicine (TCM), acupuncture and moxibustion, psychology, qigong, and medicated nutrition.

His published works include *A Study of Non-Toxic Integrative Cancer Treatments* and *Non-Toxic Integrative Cancer Treatments—a New Approach for Cancer Prevention and Treatments*.

He has been instrumental in several scientific studies such as "Effects of natural therapies when combined with hyperthermia on immune functions of advanced cancer patients" and "Research on the combined application of TCM and Western medicine in treating middle-stage and late-stage colon cancer."

His research findings have been widely communicated in academic conferences in China and abroad. As the president of ICHS in 2013, Prof. Pang demonstrated his commitment to this research area.

Prof. Pang was a member of the Chinese People's Political Consultative Conference (10th and 11th sessions). In the recent past, Prof. Pang was the director of the Chinese Hospital Association (second session), standing director of the China Association of Chinese Medicine (fifth session), director of Continuing Education Base for National Clinical Tumor Prevention with TCM, vice director of Tumor Committee under the Guangdong Association of Integrative Traditional and Western Medicine (fourth session), and vice chairman of Guangdong Hospital Association (eighth session). Prof. Pang is currently president of Clifford Hospital, professor and advisor of doctoral candidates in Guangzhou University of Chinese Medicine, president of the World Federation of Chinese Medicine Societies—Specialty Committee of Natural Therapy, and director of the Song Qingling Foundation. The China Academy of Traditional Chinese Medicine awarded Prof. Pang awards such as "Outstanding President of China TCM Hospitals" and "China Top Ten Hospital Merit Award."

The author's main purposes of writing this book are expanding the application of hyperthermia treatment and nontoxic integrative treatment for cancer patients, strengthening their resistance and immunity against cancers, and improving their quality of life and prolonging their survival.

1 Overview of hyperthermia in oncology

1.1 DEFINITION OF HYPERTHERMIA IN ONCOLOGY

"Hyperthermia" is derived from the Greek words "hyper" and "therme," meaning "hyperpyrexia" or "overheating." It is one of the physiotherapies that take various thermal sources as media to spread heat throughout a human body for therapeutic purposes. There are three common hyperthermia methods: high-frequency diathermy, radiant heat therapy, and conductive heat therapy. In traditional Chinese medicine (TCM), hyperthermia is a branch of external therapy of Chinese medicines, which includes stone needle, burning acupuncture, medical fumigation, medicated bath, hot wax therapy, moxibustion, etc. In modern medicine, hyperthermia makes use of not only various media to transfer heat to the human body through transmission modes such as conduction, convection, and radiation, but also the electromagnetism principle that allows the human body to absorb energy in the electromagnetic field and convert it into thermal energy.

Cancer hyperthermia, which some researchers would call "mild-temperature cancer therapy," "high-temperature cancer therapy," or "cancer diathermy," is a technology, treatment approach, and physical method in which the biological tissues of a tumor are heated to exterminate cancer cells. Cancer hyperthermia makes use of the characteristics of the tumor tissue itself, such as distemperedness, slower thermolysis than that of normal tissues during heating, and sensitivity of malignant tumor cells to hyperpyrexia. Hyperpyrexia is generated through modes such as high-frequency diathermy, radiant heat, and conductive heat to kill cancer cells or let them die out gradually, while normal tissues remain intact.

In the application of traditional and modern hyperthermia technologies for therapy, the electromagnetic heat or radiation heat can kill cancer cells; eliminate chronic inflammations; improve circulation, metabolism, and nutrition of partial tissues; positively adjust immunity; raise the functions of the nervous, genital, and endocrine systems; relieve pain and muscular spasms; remove edema and tissue swelling; improve blood circulation; and so on. In view of these properties, hyperthermia has been extended from the field of tumor treatment to the treatment of noncancerous diseases and conditions, such as various chronic inflammations; hypofunction of local tissues; local pain and muscular spasms; hypofunction of local circulations; various primary immunity diseases such as asthma, chronic bronchitis, and arthritis; local tissue edema; infection; recovery of injuries from falls, fractures, contusions, and strains; protection for the genital system; and health protection for other organs and tissues.

1.2 ORIGIN AND DEVELOPMENT OF HYPERTHERMIA IN ONCOLOGY

Since the beginning of civilization, heat was used to cure diseases. Such treatment methods were recorded in the histories of ancient Greece, Egypt, China, and India. The use of hyperthermia in the West can be traced back to 5000 years. For example, doctors in Egypt frequently used heat to treat breast tumors. In Greece, the famous doctor Hippocrates (460–370 BC, regarded as father of medicine) (Figure 1.1) used hyperthermia for the treatment of tumors as well. His famous motto about hyperthermia was, "An operative therapy can be used if drug therapy is not effective, and hyperthermia can be used if operative therapy does not work, but there is no further method available if hyperthermia does not work." Since 1866, there had been frequent reports that malignant tumors of some sufferers had been eliminated due to previous episodes of erysipelas,

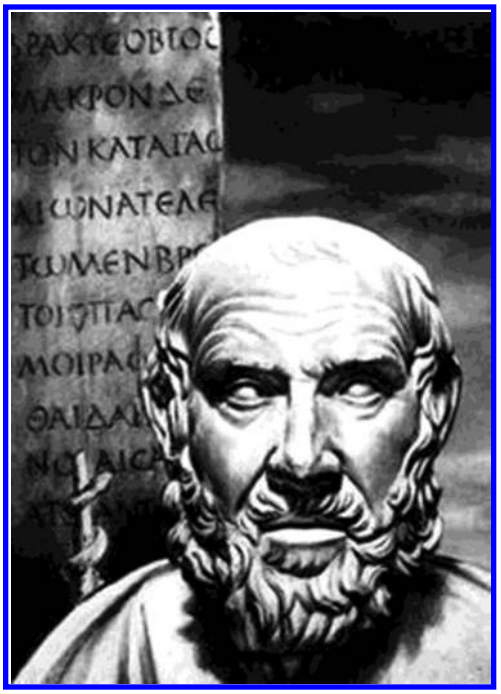

Figure 1.1 Hippocrates, famous ancient Greek doctor (460–370 BC).

serious infection, or high fever. Subsequently, there had been researchers who had frequently reported cases in which hyperthermia, when integrated with other therapies or treatments, could be used to improve the curative effect of such treatment on tumors, or heal tumors.

Thousands of years ago, diseases in China were treated by methods such as medicated bath, medical fumigation, hot bath, hot spring bath, moxibustion, sand bath, and cupping jar. Doctors treated diseases using stone needle and fire, based on which acupuncture therapy was developed. Qianjin moxibustion was adopted for Luo Li (scrofula, which might be a tubercle or tumor), as recorded in *the Medical Secrets from the Royal Library*, which might be the earliest record of hyperthermia. In modern times, a fire needle or small brand iron is used to treat surgical diseases, of which some are superficial tumors.

As for cancer hyperthermia, the ancient use of fire needle, moxibustion, brand iron, and medicated bath together was further developed into whole-body hyperthermia by infecting erysipelas in the nineteenth century. It developed slowly and was not applied clinically until the 1980s. In 1975, the first international conference for thermal treatment of cancers was held in Geneva. The American Cancer Society held its first conference for thermal treatment of cancers in 1978, after which the conference has been held once every year. In China, the first national cancer hyperthermia conference was held in Beijing in 1981. Since then, many hyperthermia apparatuses have been developed, one after another, in China and abroad, and meaningful curative effects have been achieved in medical experiments and clinical applications.

As for hyperthermia biology, China has obtained significant research achievements in terms of tumor apoptosis induced by low fever, heat-shock protein (HSP), hyperthermia and immunity, hyperthermia and heating tolerance, molecule-based thermal biology, and so on. In 1970s, China started the research and application of cancer hyperthermia technology, and then in the early 1980s, obtained meaningful achievements in comprehensive radio-frequency (RF) diathermy and microwave diathermy treatments. Currently, cancer hyperthermia has entered a new developmental phase in China, with wide clinical applications of techniques such as basic hyperthermia, intraperitoneal chemohyperthermia, and whole-body hyperthermia.

1.3 RESEARCH STATUS ON HYPERTHERMIA IN ONCOLOGY

China is one of the earliest countries applying hyperthermia for disease control and treatment, but its heating technology has developed slowly for a long period. Meanwhile, similar technologies have been developing rapidly in Western countries, and new hyperthermia heating technologies have emerged continuously. In the recent 20 years, cancer hyperthermia technology has progressed rapidly. Regarding its clinical application and its synergic actions when combined with other therapies, a large number of research findings have been reported and some optimal therapeutic effects have been achieved. And, it has been widely applied clinically, especially to tumors. In addition, the fundamental research on hyperthermia relative to heating technology, thermometry, thermal dosimetry, thermal biology, and so on has become a hot topic at present.

1.3.1 Research on cancer hyperthermia technology

1.3.1.1 HEATING TECHNOLOGY

In the past 20 years, the routine hyperthermia temperature of about 43°C has been shifted to hyperthermia conversion with different mechanisms, such as thermal gasification (over 200°C), thermoablation (over 60°C, mainly applied to superficial solid tumor, intraoperative and interstitial hyperthermia by endoscope), traditional hyperthermia (41.5°C–45°C), and medium- to high-temperature hyperthermia (39.5°C–41.8°C). The research on hyperthermia technology aims mainly at local (superficial, cavitary, deep, and interstitial) parts, deep region, limbs and trunk, whole body, and so on. Different energy sources, such as microwave, RF, ultrasonic wave, and light beam, are mostly physical factors of nonionization radiation.

1.3.1.1.1 Whole-body hyperthermia

Whole-body hyperthermia is a therapy that adopts the biophysics method to raise the body temperature uniformly, using the heat effect to kill cancer cells and to restrict and prevent cancer recurrence and metastasis. At present, clinical whole-body heating methods using hyperthermia instruments include mainly extracorporeal circular heating, microwave heating cabin, infrared radiation cabin for heating, and endogenic field whole-body hyperthermia system.

In recent years, a large amount of animal experiments and clinical practices have shown that the human body can withstand a whole-body hyperthermia at a temperature of 41.8°C for a long period (60–240 minutes) without any obvious toxic and adverse reaction. At present, the synergic effect from combining hyperthermia with chemoradiotherapy has been recognized widely as providing certain clinical therapeutic benefits. In 2008, Hegewisch Becher et al.[1] reported their stage II clinical research on metastatic colorectal cancer therapy using whole-body hyperthermia (41.8°C) combined with the FOLFOX plan (once every 2 weeks), and the results showed that the total therapeutic response rate reached 20% in 44 cases with noticeable therapeutic effects (CR: two cases, PR: six cases). The condition of 23 patients was stable, with a median survival time of up to 70 weeks and a median progressive time of up to 21 weeks. Such results support the theory that patients can benefit from combination therapy. Whole-body hyperthermia (41.8°C–42.5°C) combined with epirubicin and interferon-α as reported by Ismail Zad et al.[2] was used for advanced renal cancer in children. The therapeutic result of the median follow-up survey of 22 months shows that the conditions of all the patients were stable.

In 2006, a comprehensive hyperthermia therapy work of a team in Germany established therapeutic specifications for adults. They started multicenter stage III clinical experiment with hyperthermia combined with chemotherapy for tumors. It was implemented in Germany in accordance with stage I and II experimental results for whole-body hyperthermia (>41.5°C) combined with chemotherapy for malignant tumors.

Research by Feyerabend et al.[3] found that hyperthermia with proper temperature (41.5°C) increased the blood flow and oxidation of tumors. The combination of hyperthermia with radiation therapy was more effective than any therapy alone in improving the radiation susceptibility of tumors. Malignant pleural and peritoneum effusion are severe complications in the treatment of advanced malignant tumors. They can result in death due to water–electrolyte imbalance, and respiratory and circulatory failure.

Hu Chunhong et al.[4] selected 64 patients suffering from malignant pleural and peritoneum effusion and divided them into two groups. Group A of 34 patients received intracavitary chemotherapy alone and group B of 30 patients received intracavitary chemotherapy in combination with whole-body hyperthermia. The purpose was to study and research therapeutic effects, and toxic and adverse effects of the intracavitary chemotherapy combined with whole-body hyperthermia on malignant intracavitary effusion. The result showed that the effective rate of group A was up to 61.76% and that of group B was up to 86.67%. But, there was no statistical difference in toxic and adverse effects incurred by chemotherapeutic drugs between the two groups. Some researchers have pointed out that hyperthermia can induce HSP70 expression, increase immunogenicity of tumor cells, and induce immunity excitation, thus causing tumor apoptosis.

Heating allows the expression of HSP70 in tumor cells to increase rapidly in a short time. As a "molecular chaperone," HSP can combine with polypeptide to join in the tumor immunity response of the human body, assist the formation of tumor antigens, and ultimately generate tumor immunity. Some researchers have shown that the occurrence of hyperthermia-induced apoptosis is consistently associated with the reduction of cells in G_1 phase. It therefore infers that tumor apoptosis induced by hyperthermia occurs in the G_1 phase of the cell cycle. Hyperthermia kills tumor cells is an expression indicating that through the strength of relevant apoptosis genes, hyperthermia induces tumor apoptosis. At present, primary research on the combination of hyperthermia with genetic therapy have certain achievements, but further research is still required to provide a basis for clinical applications. Therefore, whole-body hyperthermia in combination with immunity and genetic therapies has wide prospects as well.

1.3.1.1.2 Local or regional hyperthermia

Local or regional hyperthermia method is based on hyperthermia technologies such as ultrasonic wave, microwave, RF, endogenetic field, and thermal perfusion. In accordance with the temperature rise classification of tumor tissues, local hyperthermia can be classified into three types: (1) Thermotherapy: The temperature is raised to 42°C–46°C for a long period, which generates irreversible cell damage in tumor tissues. This is usually used as an auxiliary therapy. (2) High-temperature therapy: It is a thermoablation with temperature of 46°C–70°C, which can result in the necrosis and coagulation of tumor tissues, excite the immunity system of the body, and strengthen its immunity. (3) Thermal resection therapy: The temperature is raised to over 70°C, which can destroy tumor tissues directly by having them widely coagulated or carbonized. The substances released by the necrosed tumor tissues enter the blood, which may lead to shock syndromes. Regional hyperthermia is applied mostly with intervention hyperthermia equipment, such as ductus arteriosus thermocoagulation and ductus thermal chemotherapy.

The synergetic action of combining local or regional hyperthermia with radiation chemotherapy has gone through wide clinical observations and verifications, and the combination with TCM treatment has achieved certain therapeutic effects. As for the current clinical therapy of malignant tumors, local or regional hyperthermia is mainly used in comprehensive therapy in combination with other therapies.

The Society for German Pediatric Oncology and Hematology (GPOH) carried out multicenter clinical research on 34 patients (average age of 11) with advanced soft-tissue sarcomas and Ewing tumors. These patients received chemotherapy combined with deep regional hyperthermia in the peripheral electromagnetic RF induction system or BSD system. The result showed, among 25 locally advanced patients, 12 patients exhibited no evidence of disease (NED), of which 7 patients had their cancer completely remitted. The control time for tumor was 7–64 months. Malignant pleural and peritoneum effusion are severe syndromes of advanced malignant tumor, for they can result in death due to water–electrolyte imbalance, and respiratory and circulatory failure.

The Medical Research Council of the United Kingdom and Canadian Princess Margaret Hospital cooperated to carry out five random comparison experiments to research the therapeutic effect of hyperthermia combined with radiotherapy. Stage III clinical experiments of hyperthermia on 148 cases of reoccurrence of breast cancers showed that the tumor temperature or heat effect was positively statistically correlated with the complete remission rate of tumor and was also greatly related to the disease-free survival time and curative ratio. Accordingly, the higher the temperature was, the greater the heat effect was; the higher the complete remission rate of disease was, the longer the disease-free survival was; and the longer the local reoccurrence time was,

the higher the complete cure rate was. As for stage III clinical research of therapeutic effect evaluations of hyperthermia combined with radiotherapy on head and neck cancer, 41 patients who suffered head and neck tumors (lymph node staging: N_2/N_3) were chosen, and they were randomly divided into two groups: radiotherapy alone group and radiotherapy combined with hyperthermia group. The result showed that the complete elimination rates of two groups were up to 41% and 83%, respectively; their local reoccurrence remission rates were up to 24% and 68%, respectively; and 5-year survival rates were up to 0% and 53%, respectively.

1.3.1.2 TEMPERATURE MEASUREMENT TECHNOLOGY

Currently, the temperature measurement technology mainly includes two types: invasive and noninvasive temperature measurements.

1.3.1.2.1 Invasive temperature measurement

Invasive temperature measurement is also called intrusive thermometry. The equipment consists of a medical thermoelement or thermal electric resistance detecting head (Figure 1.2). When measuring temperature, the temperature-measuring detecting head is placed into the tissues of the living body through a needle or cannula. Invasive temperature measurement mainly has the following problems: The range of measured temperature is restricted by the number of detecting heads as well as the structures of tissues; since the temperature measurement focuses on the temperature of some limited points of the tissue, it is difficult to reflect the general temperature of the body; the temperature measurement accuracy of detecting heads can be greatly impacted by energy source such as high-frequency electromagnetic wave, and the poor accuracy sometimes even causes difficult readings; the sensor wire is likely to affect the distribution of the magnetic field while heating; and invasive temperature measurement brings pain to the patient; and besides, measuring the temperature inside tumors may cause the risk of tumor metastasis. The study of invasive temperature measurement mainly focuses on reducing mutual influences between the detecting heads and the magnetic field through the development of varieties of new materials.

1.3.1.2.2 Noninvasive temperature measurement

Noninvasive temperature measurement, also called nonintrusive thermometry, is the development direction and research hot spot of the temperature measurement technology, with main research based on microwave, including microwave radiometer method and CT analysis method; ultrasonic wave, including projection mode and reflection mode, such as sound velocity–based nonintrusive thermometry, and ultrasonic nonlinear parameter–based nonintrusive thermometry; and electromagnetic wave, such as magnetic resonance (MR)–based nonintrusive thermometry (T_1 and M_0 methods, D method, and proton resonance frequency [PRF] method).

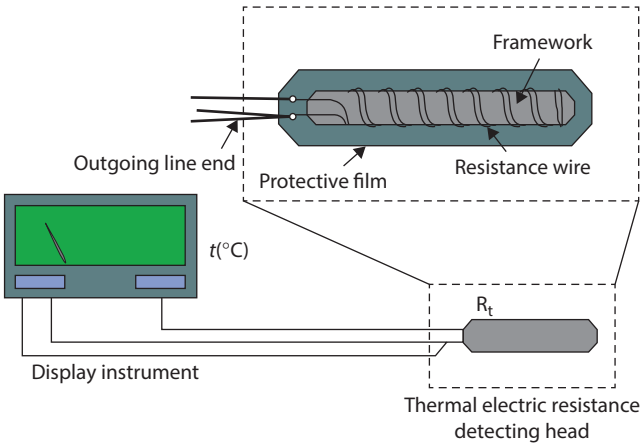

Figure 1.2 Working principle of thermal electric resistance.

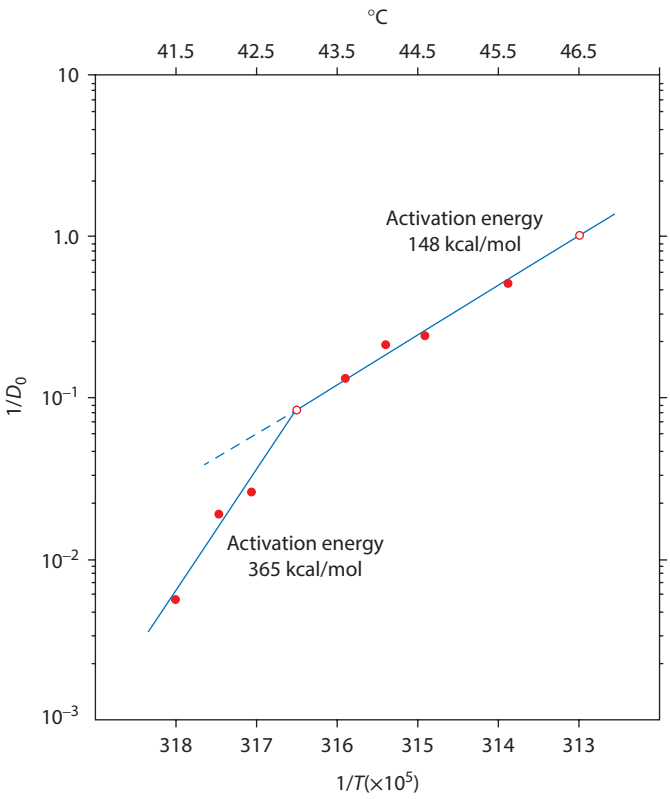

Figure 1.3 Arrhenius analysis of cell survival curve.

1.3.1.3 THERMAL DOSIMETRY

The basic physical quantities reflecting the heat effect of cancer hyperthermia are heat and time and those reflecting the thermal-dose biological effect are temperature and time. Different heating temperature and heating time will essentially result in different curative effects on the same tumor. At present, there has been a lot of research on the relations between temperature and time, aiming to prove that a *log-linear reaction* (Arrhenius curve diagram for typical thermobiological effects) (Figure 1.3) exists between heating temperature and time when the relations between different temperatures and cell survivals are evaluated. Such curve diagram shows an obvious slope change at about 43°C, indicating double-reaction curves and an existence of one "break." Some researchers have shown that cell injuries incurred under temperature of less than 43°C and higher than 43°C are different. When the temperature is at or higher than 43°C or less than 42.5°C, the toxic effects on cells are different, representing heat tolerance of the cells. When the temperature is below 43°C, heat tolerance can change further during heating. When the temperature is at 43°C, there is no development in heat tolerance during heating. In addition, at lower temperature, and with each 1°C rise in heating temperature, the heating time to obtain the same biological effect can be reduced by half. At higher temperatures, the heating time for that can be reduced by two-thirds. This shows that the heating temperature is more influential than the heating time, and both are considered two thermal dosage factors.

At present, the common modes of thermal dose expression used for clinical cancer hyperthermia are described in Sections 1.3.1.3.1 through 1.3.1.3.3.

1.3.1.3.1 Equivalent thermal dose

The calculation of equivalent thermal dose is restrained by temperature measurement technology. Meanwhile, three processes are considered: (1) temperature rise time, (2) therapeutic temperature time, and (3) temperature drop time. According to the research result of cytology, Sapareto and Dewey have put forward

the concept of equivalent thermal dose, in which different temperature–time ratios are converted into 43°C/subequivalent (Equivalent 43°C [Eq43]). They pointed out that if the prescription temperature was lower than 43°C, the heating time should be prolonged; if the prescription temperature was higher than 43°C, the heating time should be shortened so as to rectify the biological effect caused by overly high temperature. Kapp and Cox[5] have pointed out that it is necessary to adopt an independent factor (which is equal to logarithmic series in the Arrhenius diagram) to evaluate the relationship among various heating therapy schemes, which can be described by temperature equivalent factor (TEF).

1.3.1.3.2 Highest temperature (T_{max}), lowest temperature (T_{min}), and average temperature (T_{ave}) of tumor

Researchers have shown that T_{min} and T_{ave} are obviously related to fading rate and local control time of tumors, whereas T_{max} is associated with normal tissue injuries. Hiraoka et al., who works for the University of Tokyo in Japan, have used multiple factors to analyze and prove that T_{min}, T_{ave}, size of tumor, pathological type, and T_{min} Eq43 relate to the number of times and therapeutic effects of hyperthermia. Multivariable log analysis shows that only the depth of a tumor (<3 cm and ≥3 cm) is related to the remission rate of the tumor. At present, as it is hard to repeat this parameter, extensive clinical application is not recommended.

1.3.1.3.3 Tenths-digit trace code of tumor temperature

In 1989, Leopold et al. put forward the concept of spatial temperature distribution, which described the tumor temperature in any peripheral region. In 1992, they took the three-dimensional spatial temperature distributions as a description of functions in mathematics at temperature-measuring spots of tumors. They considered that although the three-dimensional temperature distributions were still important targets, describing the temperature in accordance with the temperature frequency distributions was widespread and repeatable in most cases, such as T_{90}, $T_{50,}$ and T_{20}. T_{90} means a numerical value when 90% of all the temperature values at all the temperature-measuring spots of the tumor reach the same temperature. The concepts of T_{50} and T_{20} are analogous. This temperature analysis has been named tenths-digit trace code of tumor temperature (T_{index}). Their research indicates that the cumulative time of T_{90}, average time of T_{90}, cumulative time of $T_{50,}$ and average time of T_{50} are obviously associated with tumor prognosis ($p < .001$).

1.3.1.3.4 T_{90} 43°C cumulative equivalent minute

T_{90} 43°C cumulative equivalent minute (CEM 43°C T_{90}) is defined as T_{90} per minute or a certain period during therapy, and it is converted into minutes accumulated at 43°C. Oleson et al.[6] used the concept of equivalent thermal dose to convert accumulative minutes of T_{90} or T_{50} into the equivalent minutes at 43°C. They were taken as the parameters of estimated therapeutic effect to avoid the requirements of specifying the threshold temperature and predicate the therapeutic results of cancer patients.

1.3.1.4 THERMAL BIOLOGY

In the past 20 years, breakthrough progress has been made in the research on thermal biology of molecules, cells, and blood vessels. Clinically, it is a subject of biological research on thermochemotherapy and thermoradiotherapy, and on cavities and vascular stents. It is also a subject of biological research on thermal seed implantation technology, micron medium technology, nanometer target-oriented medium biotechnology, combination technology of hyperthermia and gene, viral hyperthermia technology, therapeutic technology combining hyperthermia with TCM, and so on.

1.3.2 Research on cancer hyperthermia mechanism

1.3.2.1 CHARACTERISTICS OF TUMOR MICROENVIRONMENT AND MICROCIRCULATION

As a tumor tissue is abnormal, its blood vessel tissue is also different from the normal ones. Its structural characteristics (Figure 1.4) are as follows: structural disorder and disordered blood vessel pattern (in

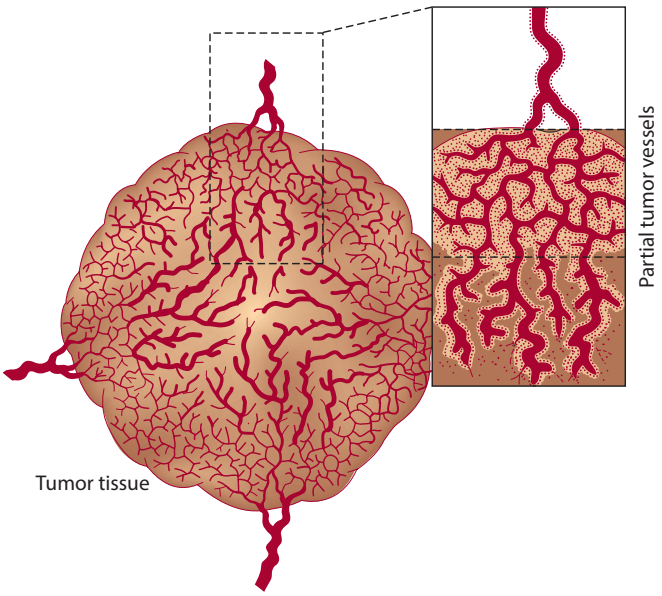

Figure 1.4 Schematic of tumor blood vessels.

addition, the microvessels are prolonged, pressed, and show an expansive, contorted, and disordered coil pattern due to random growth of the tissue, which easily form thrombus or occlusion); broad blood vessel sinus; arterial and venous fistulas existence; high blood flow resistance; the insufficiently distributed blood vessel region presents unsound structure of the vessel wall and lack of elastic basement membrane, showing edema of endothelial cells, overflow of blood cells, and even no basal lamina; easy angiorrhexis under high temperature and increased pressure; unsound vascular nerve receptor, which has the worse perception capacity of temperature and cannot adjust the temperature effectively through the nervous system; and a large number of sinusoids existing in blood capillaries, which stay in an opening state even under normal condition, so the temperature is higher than that of normal tissues.

1.3.2.2 PATHOLOGICAL CHANGE OF TUMOR MICROCIRCULATION UNDER HYPERTHERMIA

The characteristics of the abovementioned tumor tissue can result in low blood flow in the tumor tissue, stagnation of blood flow, lack of oxygen in the tissue, low pH, and increase in venous pressure in the tumor. The low perfusion in the tumor, low inflow of raw materials, and low drainage of metabolic products together can result in a lack of oxygen in the center of the tumor tissue and the necrosis of the center. During heating, when the temperature of the tissue rises by 1°C, the cell metabolism will increase by about 10%–15%. As the structure of the tumor vascular system is unable to fulfill the requirement for metabolism, it can result in injury of the endothelium of blood vessels and in weakness on the flexibility of erythrocytes. It can also result in the increase of microvascular capacity, increase of internal pressure, reinforcement of permeability, liquid exudate entering mesenchyme, tumefaction of tissue nuclei, destruction of nuclear membranes, damage of cell organs, and death of cells. In short, the effects of hyperthermia on tumor blood vessels include the destruction of tumor blood vessels, embolism of tumor blood vessels, and restriction in the formation of new tumor blood vessels.

1.3.2.3 HYPERTHERMIA AND IMMUNITY

The occurrence of cancer is mostly associated with systemic and local immune protection functions being out of control. The functional condition of the body's immune system determines the growth and diffusion of cancer to a very large extent. The increase of the immune state of the body has important significance in

controlling primary cancer, increasing long-term survival rate, and controlling recurrence. The anticancer immune mechanism is a very complicated one. On the basis of the mechanisms currently mastered, T lymphocytes, B lymphocytes, NK cell with strong capacity of killing cancer cells, and mononuclear macrophages have important functions of defense against and attack on tumors. Hyperthermia can strengthen the functions of these cells directly or through the humoral immune function. Moreover, it can control the growth and restoration of tumor cells through the same humoral immune function, which leads to the expression of HSP, caused by hyperthermia stimulation that can start the anticancer immune effect.

1.3.2.4 HEAT SHOCK PROTEIN, HEAT TOLERANCE, AND IMMUNITY

HSPs are a group of molecular chaperone proteins with strong activity under heat stress, by which heat tolerance is generated. If it is manifested in the cells, the heat tolerance of the cells can occur within a certain period. If it is manifested outside the cells, it can make the immune system generate a strong anticancer effect in killing the tumor cells. High-temperature therapy can influence the expression and immune response of HSPs. This phenomenon broadens the approach of tumor treatments and arouses the concerns and research of many scientists and doctors. Further research on the detailed mechanisms is still required.

HSPs are highly conserved proteins. They survive in an appropriate protein-folding style, and can strengthen the survival capacity of the cells. The dynamic equilibrium change of cells can activate the synthesis of these HSPs as a self-defense mechanism. Because the malignant cells are not in a normal state, but in an emergency state, a large number of HSPs exist to help malignant cells to survive. As one of homologues of HSP90, GRP94 can also be the metastasis medium of malignant cells.

Many therapies for malignant tumors can induce HSPs, such as hyperthermia, chemotherapy, radiation therapy, and phototherapy. Other nonthermal effects (such as magnetic stimulation) can also induce the synthesis of HSPs. The excessive manifestation of HSPs can protect tumor cells against apoptosis, and reduce the therapeutic effect through tolerance of radiotherapy and chemotherapy drugs. Accordingly, HSP expression in biopsy specimens can provide a good clinical clue for therapeutic tolerance.

Heat tolerance phenomenon refers to thermal resistance of the cells generated after heating the first time to a certain temperature and for a certain amount of time. Without mastering its rules, not only the sensitivity of the tumor to the second hyperthermia would be influenced, but also the following chemotherapy and radiotherapy, and the clinical therapeutic effect, could be affected. Heat tolerance is not the cell's original genetic characteristic but a temporary phenomenon of the cell that protects itself from damage. Heat tolerance occurs within 7–10 hours after heating for the first time, and decays 24 hours later. It becomes very weak 48 hours later, and almost dies away 72 hours later. Tolerance occurrence, tolerance degree, and tolerance decay time are related to the first heating. Low pH, low oxygen partial pressure, low nutrition state, and factors that affect thermal anticancer effect can impact the occurrence of heat tolerance. Heat tolerance of cells in stage S is the lowest. There is no significant difference in heat tolerance between tumor cells and normal cells, but heat tolerance diminishes fastest in the proliferation of active cells. These characteristics have important clinical significance in guiding the interval of administering hyperthermia, and in applying radiotherapy combined with chemotherapy.

In the realm of HSPs, it has been confirmed that the manifestation of HSP70 on the surface of a cell membrane can promote apoptosis and activate the immune system to fight against cancer. It results in the constant destruction of cancer cells that can release more HSPs to activate the anticancer immune effect. The effect of HSP70-promoting apoptosis may be associated with its activation of P53 protein and Rb cancer suppressor protein. Many members of the HSP family take part in cell surface antigen manifestation and cause anticancer immune response, which have important discussion values.

1.3.2.5 DIRECT EFFECT OF HYPERTHERMIA ON CANCER CELLS

Tests have shown that hyperthermia can kill cancer cells directly and depress the synthesis of DNA, RNA, and proteins. Hyperthermia can damage the normal functions of cell membranes by changing their permeability, resulting in the overflow of proteins, changing the nuclear chromatin structures, and leading to the dissolution or death of cancer cells. Hyperthermia can increase the activity of the cell lysosomes, which can cause the death of cancer cells because of dissolution. The imperfect internal structure of the cancer tissue

restricts the respiration of the cancer cells under high temperature, and the enhancement of the anaerobic glycolysis causes declination of pH, strengthening of lysosomal activity, and dissolution or death of cancer cells. At the same time, cellular microenvironment changes also have beneficial influences on hyperthermia destruction effect; i.e., an acidic environment can improve thermal destruction. Studies have shown that if the pH of a medium containing cancer cells is lowered from 7.0 to 6.4, then the success rate of the animal inoculation is lowered from 100% to 0%. Because of the depression in the synthesis of proteins, the proliferation of cancer cells is also depressed, resulting in the death of cancer cells. All of them are mostly sensitive to the proliferation of cells in stage S. The characteristic can be different from that in other stages by up to 10–100 times. Such a feature has important clinical significance.

1.3.2.6 EFFECT OF HYPERTHERMIA ON ELIMINATION OF INTRINSIC TOXINS

There are a large number of metabolites and harmful chemicals excreted through the human skin, respiratory tract, urine, and stool. Over 500 types of metabolic wastes and harmful and toxic chemicals are excreted by the human body, of which over 140 types are excreted from the lungs and the respiratory tract, and about 180 types are excreted through the skin, the latter of which include some carbon dioxide, ammonia, hydrogen sulfide, uric acid, urine toxins, bacteria, viruses, sugar, salt, potassium, calcium, water, denatured fat globules, necrotic bacteria, stale proteins, sweat glands secretions, and so on.

The skin is the largest part of the human body, spreading all over the body and providing protection. It is both an absorbing organ and an excretory organ. Chinese doctors in ancient times realized that some illnesses could be discharged or removed through the skin. In recent years, however, the method of treatment for some serious diseases through skin-sweating in the field of TCM has been partially lost. Through tests, it is found that some metabolic wastes can be excreted from the skin for the purposes of disease removal, anti-disease, and healing of diseases.

When whole-body hyperthermia is used, plenty of sweat is excreted from the body, and the pores that are not opened in regular times are open widely. With the excretion of a large amount of sweat, metabolic wastes and toxins in the body can be excreted to prevent and heal the diseases.

1.3.3 Clinical application research on cancer hyperthermia

1.3.3.1 HYPERTHERMIA AND SURGICAL TREATMENT

Hyperthermia combined with surgical treatment applied to malignant tumors has wide applications and significant therapeutic values. Surgical operation plays an important role during cancer therapy. However, it is known that cancer is a systemic disease that cannot be cured by physical resection alone. Among all cancer sufferers, the patients who are fit for surgical treatments are less than 30% in total. However, as one of the indispensable means of integrative treatments, surgical operations could reach a positive result with half the effort if they were combined with hyperthermia. Sections 1.3.3.1.1 through 1.3.3.1.3 elaborate on preoperative, intraoperative, and postoperative hyperthermia.

1.3.3.1.1 Preoperative hyperthermia

1.3.3.1.1.1 Preoperative thermal chemotherapy

Clinically, neoadjuvant chemotherapies for tumor are widespread and widely applied to osteosarcoma, breast cancer, nasopharyngeal carcinoma, non-small-cell lung cancer (NSCLC), gastric cancer, cervical cancer, esophagus cancer, colorectal cancer, bladder cancer, and so on. They have important clinical significance in creating surgical conditions, and preventing and curing postsurgical recurrence and distant metastasis. Many cancer patients can benefit from neoadjuvant chemotherapies before a surgical operation. However, their limited therapeutic effects are not satisfactory. The toxic and adverse effects of full-dose chemotherapy and influences on the prognosis of patients reveal their disadvantages and insufficiencies. The combination of chemotherapy with hyperthermia before surgical operation can improve the therapeutic effects, reduce the chemotherapeutic doses, and reduce toxic and adverse effects. It has significant values for long-term therapeutic effects and patient's survival quality. It has been recognized gradually in the academic field.

1.3.3.1.1.2 Preoperative hyperthermic perfusion

Most cancers in various systems of the body, such as in the abdominal and pelvic cavity, reach an advanced stage when diagnoses are made with lower therapeutic resection rate. It is sometimes difficult to find the lymphatic metastasis or the miliary metastases, for which the therapeutic resection and radical therapy rates can be improved, and the therapeutic risks can be reduced if a preoperative intraperitoneal chemohyperthermia is made before surgery. As for clinical surgery, it is often found that a tumor cannot be resected after laparoscopic or thoracoscopic surgery, which unfortunately makes a well-prepared surgery turn out to be just "open and close." Such a phenomenon is unavoidable, but preoperative hyperthermic perfusion can reduce its occurrence rate and reduce the probability of occurrence or make up for the open and close surgery to create the conditions for reoperation.

1.3.3.1.1.3 Preoperative hyperthermia and radiotherapy

During therapy of esophagus and rectal carcinomas, if preoperative hyperthermia and radiotherapy are conducted, the long-term survival rate, resection rate, or radiation efficiency can be improved significantly.

1.3.3.1.1.4 Preoperative combination therapy of hyperthermia, radiotherapy, and chemotherapy

It is of great therapeutic significance to adopt a preoperative combination therapy of hyperthermia, radiotherapy, and chemotherapy for a malignant tumor in pelvic cavity, which can obviously reduce the tumor stage, raise the resection rate, reduce the local recurrence rate of advanced tumor, and prolong survival period.

1.3.3.1.2 Intraoperative hyperthermia

Intraoperative hyperthermia generally focuses on the regional thermochemotherapy, and the commonly used one is intraperitoneal hyperthermic perfusion chemotherapy, with two main purposes: first, to use hyperthermia, such as applied to intraoperative hyperthermic perfusion chemotherapy, for advanced malignant tumors in abdominal and pelvic cavities and second, as for the niduses, which cannot be removed by surgery, it aims to prevent postsurgical recurrence. In addition, another mode of hyperthermia is associated with the cauterization of niduses by electrotome.

1.3.3.1.3 Postoperative hyperthermia

Postoperative hyperthermia is performed under the following conditions: (1) intraperitoneal hyperthermic perfusion chemotherapy is used for any unresected and residual or possibly residual malignant tumor in the abdominal cavity; (2) postoperative thermochemotherapy can prevent and cure the recurrence and metastasis of the tumor; (3) postoperative thermoradiotherapy can prevent and cure the recurrence and metastasis of the tumor; (4) preoperative therapy combined with hyperthermia, chemotherapy, and radiotherapy can prevent and cure the recurrence and metastasis of the tumor; and (5) postoperative hyperthermia is used in combination with TCM and other nontoxic integrative treatments.

1.3.3.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy plays an important role in tumor therapy; the failure of radiotherapy is usually a result of poor local control and recurrence. As for how to improve the effect of radiotherapy, the combination of hyperthermia with radiotherapy is of great interest.

The synergy effect mechanism of hyperthermia and radiotherapy is as follows: (1) Radioresistant cells in S-phase (DNA synthesis stage) are most sensitive to hyperpyrexia. (2) Hypoxic and innutritious cells and those in the low-pH environment are sensitive to hyperpyrexia, but resistant to radioactive rays. Radiotherapy exerts a stronger killing effect on peripheral oxygen-rich cancer cells but a weaker one on the hypoxic cells in the cancer center, and accordingly, the tumor often reoccurs in the tumor center after radiotherapy. But the hypoxic cells are sensitive to hyperpyrexia because of two reasons. First, the heat cannot be removed by blood circulation when the cells are heated, because of insufficient blood supply to the hypoxic cells, thus easily resulting in hyperpyretic accumulation. Second, high temperature aggravates

cellular hypoxia state, thus depressing cellular respiration. The increase of intracellular anaerobic glycolysis results in the accumulation of lactic acid and the reduction of pH value to strengthen the killing effect of the hyperpyrexia on cancer cells. (3) Hyperthermia aims to enhance the radiation effect by interfering sublethal cell injury or repairing potentially lethal damage. Heating can restrain cancer tissues from repairing any sublethal cell injury caused by rays; such effect often occurs during the first radiotherapy and then hyperthermia, and is realized through the reduction of DNA repair enzyme. (4) Hyperthermia before radiotherapy can improve the oxygen content of the cells around the tumor and increase the radiation sensitivity.

Hyperthermia can increase the sensitivity of radiotherapy before, during, or after the radiotherapy. Experiments have shown that the combination of hyperthermia with radiotherapy has a better effect, but radiotherapy damages both the cancer and the normal tissues. At present, it is thought that hyperthermia within 1–4 hours after radiotherapy may provide a maximum therapeutic result, and reduce side effects caused by radiotherapy.

1.3.3.3 HYPERTHERMIA AND CHEMOTHERAPY

Laboratorial and clinical research has shown that the effects of hyperthermia and chemotherapeutic drugs can be divided into synergistic, additive, and subtractive effects. As for actual clinical application, the combination of these effects are applied commonly to achieve purposes such as increase of therapeutic effect, reduction of chemotherapeutic drug application dosages, and lessening of the toxic and side effects of these chemotherapeutic drugs.

Synergistic and additive effect mechanisms of hyperthermia and chemotherapy are as follows: (1) High temperature changes the metabolism of the drugs in the body. The metabolic interaction of the drugs changes under high temperature. For example, in the liver and kidney tissues, heating weakens or stops the inactivation function of the therapeutic activity of cyclophosphamide, with a result that the therapeutic activity of the drug is enhanced, and the lasting time of the therapy is prolonged relatively. (2) The perfusion applied to tumor blood vessels is changed under high temperature, therefore the blood flow stagnates in the tumor tissues, and the concentration of the drug in the tumor tissues is increased due to convergence. (3) High temperature changes the permeability of the cancer cell membrane. When the temperature rises, the permeability is enhanced; therefore, the drug enters the cancer cells easily, and its concentration can be increased so that the therapeutic effect can be strengthened accordingly. (4) High temperature can enhance the cytotoxic effect of chemotherapy drugs on cancer cells. The cytotoxicity of many chemotherapy drugs is enhanced under high temperature, but is obviously weakened under normal temperature, and the therapeutic effects are restricted as well. (5) Because of the characteristics of blood vessels and histological features in the cancer cell, the cell is sensitive to hyperthermia internally and to radiotherapy externally; so, the effect of radiotherapy and chemotherapy can be strengthened if they are applied simultaneously. (6) Hyperthermia can prevent the occurrence of chemotherapeutic drug resistance and even the sensitivity to the chemotherapy drugs with drug resistance can be regained.

1.3.3.4 HYPERTHERMIA AND HERBAL MEDICINE

The thermal sensitization caused by the combined treatment of herbal medicines and hyperthermia has two meanings. First, herbal medicines can be used to control tumor heat tolerance factors and increase the sensitivity of hyperthermia for cancer treatment. Second, hyperthermia can enhance the reaction of herbal medicines to play greater anticancer effect, especially for those patients who cannot receive chemotherapy or are not sensitive to chemotherapy. The combination of herbal medicines with hyperthermia can increase the sensitivity of hyperthermia and enhance the anticancer effect of herbal medicines.

The combination of hyperthermia with TCM applied to cancers is under exploration at present. Broadly speaking, plant-based anticancer drugs such as camptothecin, vincristine, etoposide, and paclitaxel in chemotherapy belong to the scope of TCM. At present, some researchers have confirmed that cantharidin, *Isodon rubescens*, oridonin, irisquinone, scorpion venom, and so on show synergetic effect with hyperthermia. Zhang Li adopted the combination of Fuzheng Guben Decoction (a Chinese patent medicine) with microwave hyperthermia for 32 patients with advanced NSCLC, and the result showed that the therapy group was better than the control group, regarding clinical symptoms, quality of life, survival time, and survival rate ($p < .05$).

There was no statistically significant difference between the treatment group and the control group in terms of recent therapeutic effect ($p > .05$). The combination of herbal medicines with microwave hyperthermia had better therapeutic effect on advanced NSCLC as for improving the clinical symptoms and quality of life, and prolonging the survival time. Li Dengbao et al.[7] carried out hyperthermia in 28 patients with cancer in the bladder cavities by *Isodon rubescens* solution and found an increase in $CD4^+$ and $CD4^+/CD8^+$ lymphocytes, whereas soluble interleukin-2 receptor (sIL-2R), localized on cancer cells, decreased, showing that the immune function of the patients could be improved. Li Siwen et al.[8] applied herbal tumor-removing pastes combined with microwave hyperthermia on 136 patients with superficial lymph node metastasis. The effective rate of the treatment group was 82%, which is significantly higher than that of the control group. The Karnofsky Performance Status (KPS) of the treatment group is significantly higher than that of the control group as well. Zhang Dongwei et al.[9] used the external application of herbal medicines combined with microwave hyperthermia for superficial hemangiomas, which has an obvious therapeutic effect as compared with microwave hyperthermia alone. This therapy requires further study and discussion.

In accordance with Chinese medicine, it is believed that the human life is not only in the physical body, but it also contains the invisible vital force; that is, in the terms of TCM, fire and heat, which can be generalized to yang qi. Qi blood and body fluid can run only by yang qi. If yang qi is weak, heat is insufficient and the driving force is low; therefore, body fluid, essence, and vital energy will run slowly and even stop. And the weak yang qi in turn will easily bring in pathogenic cold. Because of weak yang qi and heat insufficiency in the body, lack of warm driving, condensation of pathogenic cold, and tangible abdominal masses can form, which is a key cause for tumor formation that is recognized by TCM. Through statistical analysis of 1000 patients with cancer, some researchers had found that 80% of the patients suffered from cold. Modern hyperthermia aims to penetrate heat into the human body from outside to inside, allowing the "warmth" to reach the malignant places directly without hurting the vital energy. Yang qi scatters and dispels the cold. Its accuracy, speed, and efficiency are too wonderful for words to describe, and no drug can be compared to it. Of course, the cancer mechanism (weak yang qi and cold accumulation) is just one of the main causes. The combination of herbal medicines with hyperthermia also considers factors such as deficiency and excess of viscera of the patient, differences among sputum, damp syndrome, toxin and blood stasis, different pulse symptom after body heating, and so on, in addition to the combination of "internal hyperpyrexia" with "external heating" (hyperthermia). As for herbal medicine preparation, oral application, static drop, external application, injection in tumor, and injection in cavity combined with hyperthermia are available, and they can be applied versatilely according to conditions.

Heat tolerance is a research focus of thermal biology in recent years. Repeated heating of cells generates heat tolerance, which affects the sensitivity of cancer cells to reheating. Herbal medicines are applied to reduce heat tolerance, particularly of cancer cells, and protect normal cells' resistance to heat, which is a significant theme. As for heating in combination with drugs in cancer therapy, the development of a particular type of drug—that is, a non chemotherapeutic drug without anticancer effect or with weak anticancer effect under normal temperature—is promising, which becomes a drug with strong anticancer activity after being heated. It could even exceed the anticancer effect under the combined application of heating and chemotherapy drugs. In this regard, herbal medicines have a huge potential. Through compression among the thermal synergic action of seven drugs (totaling five types), some researchers have found that some Chinese herbal medicines, such as matrine, can improve the heating therapeutic effect of MA737 small breast cancer and induce much more apoptosis. Furthermore, TCM theory holds that hyperthermia may hurt yin. Herbal medicines are used to adjust qi and yin for mutual reinforcement so that the therapy can be smoother and more successful.

1.3.3.5 HYPERTHERMIA AND CANCER-TARGETED THERAPY

Broadly speaking, cancer targeted therapy can be divided into organ-level solid tumor–targeted therapy technology and cellular molecule level–targeted therapy technology.

Organ-level solid tumor–targeted therapy technology includes tumor-targeted ablation therapy (cryoablation, RF ablation, and microwave ablation), interstitial laser therapy, high-intensity-focused ultrasound therapy, ablation-targeted outer radiation therapy, radioactive particle implantation in target for irradiation therapy, endovascular therapy, and local drug injection therapy. On the cellular molecule level, cellular molecule–targeted therapy aims at malignant phenotype molecules of the tumor cells; acts on the specific

cell receptor that promotes the growth and survival of the tumor; and acts also on signal transduction channels, formation of new blood vessels, and adjustment of cell cycle, thus achieving the anticancer effect by depressing the growth of tumor cells or promoting apoptosis. Meanwhile, it does not affect the normal cells around the tumor, so molecule-targeted therapy is also known as a "biological missile." Different from traditional cytotoxic chemotherapy, the tumor molecule–targeted therapy has a specific anticancer effect with significantly reduced toxicity, which creates a new field of tumor chemotherapy and has a broad development prospect.

Similar to many cancer therapies, the combination of hyperthermia with cancer-targeted therapy is applied in cancer therapy. In accordance with evidence-based medical mode for therapy and experience summary, reasonable and perfect individualized integrative treatment schemes can be formed gradually, which have clinical significance in improving the therapeutic effect on cancer and raising the survival quality of patients.

1.3.3.6 STUDY ON THERAPY OF NONCANCEREOUS DISEASES BY HYPERTHERMIA

Hyperthermia has also been widely applied in the clinical therapy of noncancerous diseases with sound therapeutic effects for especially dysmenorrhea, hyperplasia of prostate, various inflammations, bony joint disease, strain, obesity, and so on, as previously reported.

1.4 DEVELOPMENT TREND OF HYPERTHERMIA IN ONCOLOGY

With cancer being recognized increasingly, hyperthermia has become the fifth main systemic therapy after surgery, chemotherapy, radiotherapy, and biotherapy. At present, a multidisciplinary and integrative treatment of cancer has become a development trend. Hyperthermia, as a safe, effective, supplementary therapy for cancer, can be widely combined with chemotherapy, biotherapy, and TCM therapy; it has obtained satisfactory achievements and has wide development prospects.

At present, there is no completely effective therapy for cancer. Clinically, the integrative therapeutic mode is often selected. As the fifth cancer therapy method, hyperthermia can improve the anticancer effect resulting from many other approaches, in addition to the thermal effect.

Hyperthermia can induce cancer cell apoptosis and necrosis and can change its growth cycle to achieve the purpose of cancer therapy. In addition, hyperthermia has a direct cytotoxic effect, and can change the microenvironment of cancer and the signal transduction pathways of specific cells, can induce the expression of genes as well as proteins related to apoptosis, and so on. Many clinical experiments in phase II and III prove that hyperthermia combined with chemotherapy and/or radiotherapy has a better therapeutic effect on many cancers. At present, in terms of hyperthermia promotion mechanism of body immunity and the combination of hyperthermia with immunity therapy, more mature fundamental and clinical research is required.

Hyperthermia has a lethal effect on cancer cells. How to increase the temperature difference of the cancer tissue and cause the lethal effect on cancer tissue effectively and widely without damaging normal tissues is a bottleneck that is restraining the clinical application and development of hyperthermia. Aiming at this technology, nanometer magnetic media are becoming a research hot spot gradually at present. In 1957, Gilchrist et al.[10] first described the concept of magnetic induction hyperthermia, where the magnetic media are distributed in the cancer tissue and then externally AC magnetic fields are applied. Through the development of over 50 years, and according to the research reports published recently, the research on magnetic medium hyperthermia relating to prostatic cancer, brain tumor, and head and neck tumors, as well as esophagus cancer, has entered a clinical phase; research on other cancers has reached the clinical prophase and the animal-based test stage.

With the emergence of magnetic induction hyperthermia technology in recent years, the magnetic-targeted thermosensitive liposome-mediated thermal chemotherapies are of interest widely. Materials such as thermosensitive long-circulating lipidosome, thermosensitive immune liposome, multipolymer thermosensitive liposome, and magnetic thermosensitive liposome have come out in succession. As for the stability, controllability, and safety of these new materials and their clinical therapeutic effects, further research is

required. For the patients with combined intestinal obstruction, especially those with tumor at the connecting border of sigmoid colon of the left-sided colon, an obstruction can easily occur due to tumor, which would block the perfusion pathway of herbal machines; therefore, it is difficult to implement retention enema of TCM. How can it both resolve the stenosis of the intestinal tract and kill the tumors to maximum extent?

In 2005, Terumi et al.[11] conducted hyperthermia, with supports in the biliary tract, at 42°C totaling 40 minutes on patients with carcinoma of the bile duct, proving that the reduction of bile duct stenosis and enhancement of radiotherapy and chemotherapy effects are possible. In 2006, Freudenberg et al.[12] made primary discussions on safety and proper temperature in the case that esophageal supports were used for intrinsic hyperthermia, and conducted a series of tests. They manufactured and used a support, which was made of synthetic and thermoplastic material wrapped with platinum wire outside, and then conducted some research on the support, with a result showing that esophageal tumor tissue could be killed within 12 mm around the support when it was heated to 46.5°C. Although the above two studies were still in the testing stage on animals, we can imagine that the synergistic effect of hyperthermia and TCM for cancer therapy has been confirmed at present. If we apply the magnetic induction support for deep RF hyperthermia, combining TCM for carcinoma of the large intestine, it not only strengthens the killing effect of hyperthermia on the cancer but also resolves the obstruction problem in the intestinal cavity, while how to resolve the engineering science and material science for the therapy and ensure the safety of the therapy will require further research.

The resolution of temperature measurement problems and the accurate quantization of temperature in the therapeutic region can provide direction for the design of the hyperthermia schemes, which are favorable for the verification and development of new technology. Further, the noninvasive temperature measurement of hyperthermia is a development trend of temperature measurement and control technology. If new and effective noninvasive temperature measurement technologies can be developed, or the temperature measurement media can be protected from being affected by the heat source, the development of hyperthermia technology can be promoted greatly.

In addition, to reduce the toxic and side effect of cancer therapy and advocate "nontoxic integrative treatments," the combination of TCM with hyperthermia can be a new development direction of hyperthermia. Although there have been reports about the clinical therapeutic effect and survival time of RF local hyperthermia combined with TCM used for cancer, there have been few clinical studies regarding the control of cancer metastasis through the combination of hyperthermia with the specific syndrome-type therapy of TCM based on syndrome differentiation. On the basis of this theory, clinical research is carried out on the combination of hyperthermia with Fuzheng Guben Decoction of TCM for the therapy and restriction of metastasis of cancer. If further research can be done on the related expressions of different syndrome types and the effect of TCM on the molecular biology of cancer, and the influence of different prescriptions for therapy of TCM based on syndrome differentiation on the killing effect on immune cells and cancer cells can be understood, the combination of hyperthermia with therapy of TCM based on syndrome differentiation will have important clinical significance on cancer therapy.

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2

Categories and methods of hyperthermia in oncology

2.1 CATEGORIES AND METHODS OF TRADITIONAL HYPERTHERMIA

In traditional medicine, hyperthermia technology focuses mainly on thermotherapy. In ancient times, human beings learned to relieve pains by heat conduction, that is, by transferring the heat to different parts of the body through exposure of the body to hot water, hot sand, hot oil, grain, salt, or other solids and liquids. The earliest conductive hyperthermia adopted hot springs and sand heated by sunshine; then, human beings started to place toasted stones at the affected areas to relieve pain; after they learned how to use fire. Hippocrates, a doctor in ancient Greece, fed hot water into the animal bladder for making a hot-water bag to treat sciatica and local inflammation in the rectum. Wu Shiji, a famous medical expert in the Qing dynasty, was good at herbal medicine for external therapy, and he detailed therapeutic methods, such as solarization, fumigation, and hot compress, for diseases in his work *Theoretical Rhythmical Prose*. After the Liberation, physical therapies in China developed rapidly, such as hot wax therapy and hot salt therapy, which have been widely used in various hospitals.

There are many traditional thermotherapies, typically including paraffin therapy, mud therapy, and sand therapy. Some therapies are performed by heat generated from herbal medicine (Kanli coarse sand therapy), chemical reaction (chemical hot bag therapy), electricity (electrothermal therapy), and so on. Additionally, there are common folk therapies in China, including salt stir-fry therapy, alcohol and vinegar therapy, and so on.

2.1.1 Paraffin therapy

Paraffin has the advantages of plasticity, glutinousness, and ductility, and it is suitable for therapy on joints. In the process of refrigeration, the volume of paraffin can be reduced by 10%–20%, which enhances the compression on the treated area gradually.

Therapeutic effects of paraffin include thermal effect, mechanical effect, and promotion of wound healing.

Indications: (1) Motor system diseases, such as muscular fibrositis, myospasm, soft tissue contusion, rheumatic or rheumatoid arthritis, osteoarthritis, traumatic arthritis, and articular dysfunction prior to the application of kinesitherapy; (2)various chronic inflammations, such as chronic adnexitis, chronic colitis, refractory wound, and ulceration; (3) hyperplasia scar; (4) various neuralgias and peripheral nerve paralysis; and (5) frostbite.

2.1.2 Mud therapy

Mud therapy is a method in which mud is heated to a proper temperature to act on the body for therapy on diseases.

Therapeutic methods: Mud bath, mud cake, mud compression, embolism, indirect mud therapy, and mud therapy combining other physical therapies.

Indications: (1) Motor system: subacute and chronic inflammations such as rheumatic, rheumatoid arthritis, bursitis, chronic bursitis, tenosynovitis, and myotenositis; slow fracture union; prevention and cure of articular contracture, muscle cramp, and so on. (2) Nervous system: neuritis, neuralgia, multiple spinal radiculitis, peripheral nerve trauma sequela, spinal and spinal membrane trauma sequela, convalescence and sequela of poliomyelitis, and so on. (3) Vascular diseases: varicosity, peripheral neuritis, thrombotic phlebitis,

and so on. (4) Internal diseases: chronic nephritis, chronic hepatitis, and so on. (5) Urogenital system diseases: chronic prostatitis, chronic epididymitis, pelvic inflammatory disease, ovarian insufficiency, and menstrual disorder; (6) ENT (ear, nose, and throat) diseases: chronic paranasal sinusitis, chronic tympanitis, and so on. (7) Others: scar, synechia, trophic ulcer, and so on.

2.1.3 Hot and wet compression therapy

This includes hot bag, wet compress, and so on. Hot bag therapy is a therapeutic method in which the heat and vapor emitted from silica gel heated in the bag act on the affected place; it is also called foment therapy.

Wet compress is one of the simplest thermal therapies, suitable for families and hospitals with incomplete medical equipment. As for the specific method, a fabric such as towel with strong water absorption is soaked in hot water and then compressed on the affected part after water content is extruded.

Indications: Chronic inflammation, scar, synechia, muscle cramp, and neuralgia.

2.1.4 Aero thermotherapy

Aero thermotherapy, also called dry and hot air treatment, is a hyperthermia using strong dry thermal air flow to act on the affected parts or the whole body. Its characteristic is absence of water content, and is easier for patients to withstand high-temperature therapy.

This therapy is applicable to joint stiffness, muscle cramp, and the promotion of water exudate absorption; it is also used to make patients sweat and strengthen their metabolisms.

2.1.5 Sand bath therapy

Sand bath therapy means that sea sand, river sand, or field sand is taken as a medium to transfer heat to the body for therapeutic purpose. Sand has a strong capacity of absorption, and it can be used widely in the seashores or regions with sand.

Therapeutic effects: Thermal effect, mechanical effect, enhancement of body metabolism, promotion of cardiac and vascular movement and respiration, promotion of sweating, promotion of absorption of inflammations, and growth of injured tissues.

Therapeutic methods:

1. Whole-body therapy: sand bath field and sand bath apparatus
2. Local therapy

Indications: It is applied to patients requiring plenty of sweating and strengthening metabolisms, and those having various arthritides, posttrauma neurosis, neuralgia, pelvic inflammatory disease, and so on.

2.1.6 Kanlisha coarse sand granule therapy

It is derived from external hot bag compression therapy. Its pharmaceutical ingredients mainly include divaricate saposhnikovia root, rhizome of Sichuan lovage, speranskia herb, Chinese angelica root, acetic acid, and clean iron powder (less than 2 mm in diameter).

Therapeutic effects: Thermal effect combining drugs for dispelling wind, promoting blood circulation, promoting the circulation of qi, enhancement of metabolism, and relieving inflammations and pains.

Indications: Chronic arthritis; muscle fibrositis; trauma of joint, muscle, and ligament; periarthritis humeroscapularis; protrusion of intervertebral disc; neuritis; neuralgia, and so on.

2.1.7 Chemical thermal bag therapy

It adopts chemical materials such as sodium acetate, which releases heat to act on the body, to meet the therapeutic purpose.

2.1.8 Electrothermal therapy

It includes electric heating bag therapy, heat therapeutic apparatus, thermomagnetic Han Tong Bao, and so on, which are all heating devices for external compression, making use of the heat effect of electric current, and its heating principles are similar with those of common products such as electric blankets and hand warmers.

2.1.9 Dry foment therapy

It includes hot water bag therapy, hot brick therapy, salt stir-fry therapy, and so on.

2.1.10 Hot ironing therapy

Hot ironing therapy is one of the simple folk physical therapies among Chinese people with a long history: heat herbal medicines or other heat-transferring materials, and then wrap them in a cloth bag and move it back and forth or swing it on the affected parts, thus reaching the therapeutic effect of spasmolysis, easing pains, and detumescence. Common methods include *Tetradium ruticarpum* compress method (therapy on lumbar myalgia, frequent micturition, dysmenorrhea, etc.); medical therapy for dispelling wind, activating blood (medicines contain red peony root, Chinese angelica root, Chinese angelica, notopterygium root, angelica root, cassia twig, and large-leaved gentian, which can treat joint pain caused by wind cold); vinegar compress (therapy on dysmenorrhea, and cramping of feet and legs); salt compress (applied to the abdomen for diarrhea with spleen deficiency and abdominal pain); scallion compress (therapy on hypogastrium pain caused by the stagnation of cold and qi, flatulence, and urinary stoppage); and ginger compress (therapy on deficient cold of spleen and stomach, vomiting, hiccup, and anepithymia, caused by syndrome of internal stagnation of fluid dampness).

2.1.11 Alcohol and vinegar therapy

Take 5 g each of herba schizonepetae, divaricate saposhnikovia root, frankincense, myrrh, and pepper. Grind them into powder and mix with a small amount of 75% alcohol and vinegar into a paste, which is wrapped with gauze and applied to the affected part. Then, a wax bag, wax cake, or hot water bag is put on the surface of the affected part, or infrared rays are used for local radiation and heating. This therapy can expel wind and disperse cold, activate blood and absorb clots, soften stiffness and dissolve agglomeration, remove dampness and generate heat, dredge channels and collaterals, and relieve spasm and pain. Moreover, its indications are the same as those of Kanlisha coarse sand therapy.

2.1.12 Medicated bath therapy

Medicated bath therapy is one of the external therapies of traditional medicine. It is a whole-body or local bath method using liquid medicine or medicated liquid, in various modes. The local bath is also named "scalding," "steaming and washing," "hip bath," "foot bath," and so on, of which scalding is more popular. The application principle of the medicated bath therapy is the same as that of oral administration, and it also follows the prescription principles through the treatment based on syndrome differentiation.

2.2 CATEGORIES AND METHODS OF MODERN HYPERTHERMIA

Modern hyperthermia technology has various classifications, which are not unified completely, and the classifications from different scholars are as follows: whole-body hyperthermia and local or regional hyperthermia in accordance with heating range. Four classifications are available in accordance with therapeutic

temperature: (1) Mid- to low-temperature hyperthermia: It means that the local cancer tissue is heated to 39°C–42°C, which lasts for 60–90 minutes. It is used for whole-body hyperthermia, for which the body is usually heated to 38°C–40°C. This hyperthermia aims to strengthen the body's blood perfusion; blood stasis of the cancer issue; blood vessel permeability; and oxygen partial pressure (PO_2); and to improve the metabolic activity of heated parts and drug in take, as well as the sensibility of radiotherapy and chemotherapy. (2) Conventional hyperthermia: It is used for local hyperthermia, which means that the cancer is heated to 42°C–45°C, lasting 45–90 minutes. When it is used for whole-body hyperthermia, it is also named mid- to high-temperature hyperthermia, which means that the body is heated to 39.5°C–41.8°C, lasting 180–240 min. It is based on the mechanism that cancer cells are more sensitive to heat than normal cells. It can also be used to strengthen the sensitivity of the cancer tissues to radiotherapy and chemotherapy. (3) High-temperature hyperthermia: The temperature of cancer tissues under high-temperature hyperthermia is 45°C–60°C, lasting 30–60 minutes. The temperature range has a stronger killing effect on both cancer cells and normal cells, resulting in the necrosis and coagulation of the tissues and cells. Research indicates that these dead and coagulate tissues and cells can stimulate the immune system of the body, and enhance the immunity of the body to cancer. (4) Thermoablation: It damages cancer tissues directly by heat, and its temperature is 60°C–90°C, lasting 5–10 minutes. This therapy has a stronger damage effect on both cancer cells and normal cells, resulting in the wide coagulation and even carbonization or gasification of the cancer tissues. In accordance with the heating sources, it can be classified as infrared hyperthermia, radio-frequency hyperthermia, microwave hyperthermia, ultrasound hyperthermia, and so on. The classification can also be based on the locations of the hyperthermia.

Whole-body hyperthermia and local or regional hyperthermia are described in detail in Sections 2.2.1 and 2.2.2.

2.2.1 Whole-body hyperthermia

Whole-body hyperthermia refers to the method in which the body temperature is increased to the therapeutic temperature by various means, which lasts for a certain period. It is usually combined with chemotherapy and radiotherapy to sensitize the therapeutic effect, which are named thermal chemotherapy and thermal radiotherapy, respectively. Moreover, it can be applied alone for cancer therapy.

There is no specific standard for the temperature range of whole-body hyperthermia. At present, the body's temperature for cancer hyperthermia is mostly kept within 39.5°C–41°C and not beyond 41.8°C, which is named whole-body mid- to high-temperature hyperthermia. However, there is also another whole-body hyperthermia by which the body's temperature is kept at 38°C–40°C, which is named whole-body mid- to low-temperature hyperthermia.

There are many kinds of heating methods for whole-body hyperthermia, mainly including three categories described in Sections 2.2.1.1 through 2.2.1.3.

2.2.1.1 Surface heating method

Radiation or conduction is adopted to transfer heat into a body through the body's surface so that the whole-body temperature rises. Few examples are as follows: infrared radiation (Figures 2.1 and 2.2), wrapping by thermal blanket, embedding by liquid paraffin, hot water bath, and microwave heating combining infrared radiation for whole-body hyperthermia. At present, the infrared radiation heating is a common therapy.

2.2.1.2 Extracorporeal blood circulation heating method

A surgery is performed to build up arteriovenous shunt or veno–venous shunt, so as to connect with an extracorporeal circulation machine and a heat exchanger. The heat exchanger is used to heat up the blood outside of the body. Plenty of heat is spread throughout the body by blood circulation so that the body temperature rises. The heating speed is faster by extracorporeal blood circulation, but it will result in great wounds, with side effects such as intravascular coagulation and thrombus, so its clinical application is affected.

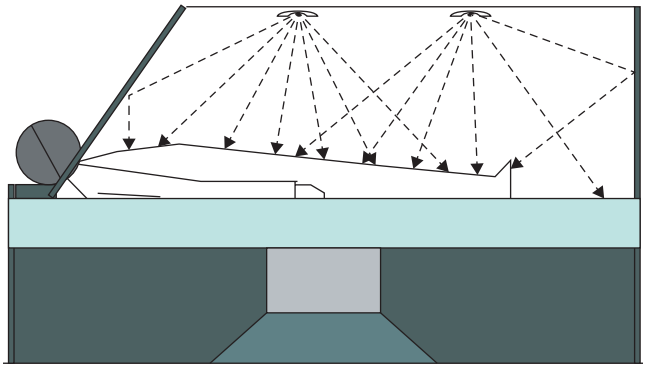

Figure 2.1 Schematic of infrared whole-body hyperthermia.

Figure 2.2 Infrared whole-body hyperthermia.

2.2.1.3 BIOLOGICAL PYROGEN METHOD

The body is injected with microorganisms or biological products such as the injection of Coley toxin and short *Corynebacterium*, which causes a temperature rise of the body. Because this method cannot estimate the extent of reaction of the body to pyrogen, it is hard to control the temperature; with such great risks, it is rarely applied at present.

2.2.2 Local or regional hyperthermia

Local or regional hyperthermia means a hyperthermia in which the heating range is restricted to a local part or partial region of the body, without obvious temperature rise of the whole body. Its heat sources include microwave, radio frequency, ultrasonic waves, and so on. The heating technology is divided into conventional heating technology and targeted heating technology.

2.2.2.1 CONVENTIONAL HEATING TECHNOLOGY

2.2.2.1.1 Microwave heating

We usually call the electromagnetic wave with a frequency of 300–3000 MHz microwave. The frequencies of microwave hyperthermia recognized medically include 2450 MHz, 915 MHz, and 434MHz. Microwaves

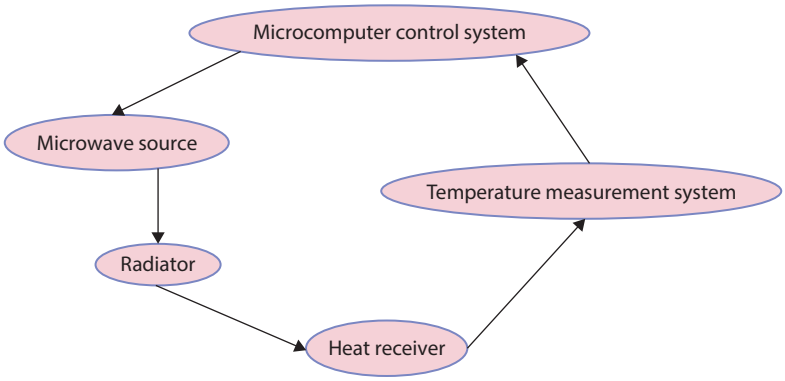

Figure 2.3 Schematic of microwave heating.

enter the body mainly by fluctuation. The mediums with different properties are attenuated due to absorption when they are propagated, and reflection and refraction occur at the interface so that most of the energy is near the body surface. After the biological tissue is radiated by the microwaves, also termed "absorption of microwave energy," the polar molecules in these tissue cells are in an excited state, leading to high-speed oscillations. Then, they generate frictions against adjacent molecules, and the microwave energy is converted into heat energy.

High temperature produced by microwaves has a selective cancer inhibition effect. Normal tissues have larger blood flows; after they are heated, the blood vessels can expand and the blood flow can increase to take away the heat. While the tumor tissue's blood flow velocity is relatively slow, the blood flow is low, the circulation is poor, and the heat gathers together, all of which results in the congestion, oxygen deficit, and internal respiration depression of the tumor tissue. PH value in the tumor falls. The temperature in the tissue is about 3–7°C higher than that in the adjacent normal tissues. Accordingly, when the tumor tissue is at lethal temperature, the normal tissues have not reached the damage temperature. Restricted by heating depth, microwave hyperthermia is mainly used for various superficial tumors and cavity tumors, such as superficial lymph node metastatic carcinoma, skin cancer, malignant melanoma, and other tumors in the superficial places of the body. Some specifically produced radiators can be applied to corresponding tumors in the body cavity (Figure 2.3), such as nasopharyngeal radiator, esophageal radiator, cervical radiator, and rectum radiator.

2.2.2.1.2 Radio-frequency heating

The frequencies of radio-frequency electromagnetic waves commonly used in medicine include 40.68 MHz, 27.12 MHz, and 13.56 MHz, as well as 8 MHz and about 100 MHz. They act on tissues by high-frequency oscillation current and adopt the two modes of ohm loss and medium loss so that the electric energy is absorbed by tissues, resulting in temperature rise. Thanks to its obvious advantages over microwave hyperthermia in heating depth, RF is a main heating method for mid-depth in the current conventional hyperthermia (Figure 2.4). The radio-frequency heating technology is divided mainly into capacitive heating, inductive heating, as well as capacitive and inductive combined heating. Capacitive heating aims to put the heating position between two and three polar plates and add radio frequencies at the polar plates, or many pairs of linear electrodes are inserted into the body tissues and added with radiation voltage so that the radio-frequency current generates joule heat and medium loss heat through the tissues. The depth of capacitive heating is better than that of microwaves, but its distribution of electric field is emanative, unsuitable for metal temperature-measuring devices; it is now widely applied clinically. Inductive heating means that induction coils are put on the body surface and energized with radio-frequency current so that the eddy current magnetic field generated by radio-frequency current can induce the eddy current for heating in the body. Its heating depth is less than that of capacitive heating, but it will not overheat fat. Capacitive and inductive heating is a hybrid heating mode with capacitivity and induction, and is still under the research phase at present.

Figure 2.4 Radio-frequency hyperthermia machine.

2.2.2.1.3 Ultrasonic heating

When ultrasounds are propagated in the human body, the mechanical waves result in the oscillation of the material particles, thus generating heat effect raise the temperature rise and heat the tissues. Ultrasonic heating features advantages of no radiation to the body and simple protection, applicability for superficial tissue therapy and deep tissue therapy, short single therapeutic time, no wound, and little influence on the whole body.

2.2.2.2 TARGETED HEATING TECHNOLOGY

2.2.2.2.1 Percutaneous microwave coagulation therapy

A microwave needle radiator is inserted into the cancer nidus by ultrasound or CT-guided percutaneous paracentesis, which is then heated up by microwave radiation (>50°C) for a certain period (several minutes). It results in the coagulation, denaturation, and permanent death of the tumor tissues in the area, which forms a spherical coagulation necrosis zone with a clear boundary, and kills cancerization tissues locally. Microwave coagulation therapy (MCT) is characterized by a highly centralized therapeutic temperature, complete destruction of tissues in the targeted zone, and relative safety of tissues outside the targeted zone. The transmural necrosis of vascular walls occurs after exposure to the microwave effect; endothelial cells disintegrate and thrombi form in the blood vessels, all of which can incur the further ischemic necrosis of the tumor tissues around the necrotic blood vessels. As for MCT, its therapeutic temperature is high and the heating range is relatively wider; multiple points can be made available with shorter therapeutic time and smaller traumas. Existing problems of MCT include the following: Due to the influences of respiration, puncture needle artifact, puncture operation error, and so on, an incomplete therapy on the part of smaller foci can be incurred. As for bigger tumors, leakage of focus space may be present due to puncture needle arrangement, and the fibers in the tumor can restrict the dispersion of hyperthermia so that the foci remain. Other problems are no fixed solidification time, output power, temperature standard, single-ablated effective volume, controllable ablation range, prevention and protection needed for medical care personnel, and so on.

2.2.2.2.2 Radio-frequency ablation

Iconography is used to lead a special puncture needle with a sheath to penetrate into the focus place; the cluster electrode at the needle tip emits intermediate-frequency radio waves to stimulate plasma concussion and pyrexia of the tissue cells so that the temperature in the therapeutic zone is more than 60°C with 100°C–120°C (Figures 2.5 and 2.6) at its center. Radio-frequency ablation (RFA) can result in the coagulation and necrosis of tumor tissues in the high-temperature targeted zone, which can influence the functions of the tumor cell membrane; increase the enzymatic activity of lysosomes in the tumor cells; affect the normal

Figure 2.5 Radio-frequency ablation electrode for tumor.

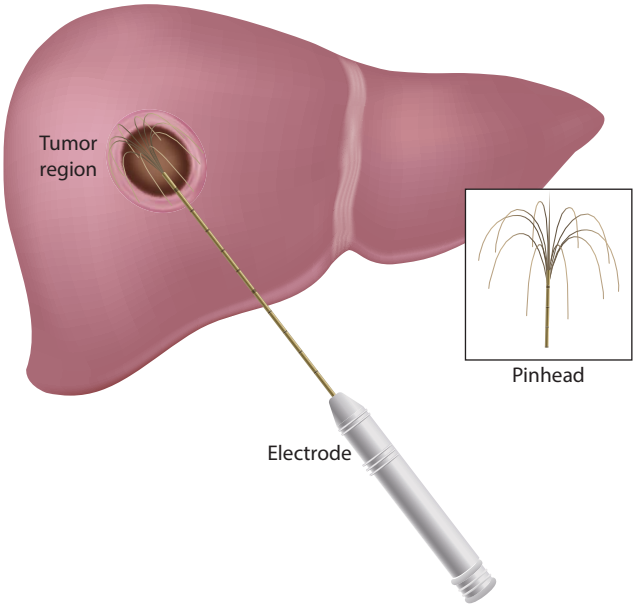

Figure 2.6 Schematic of radio-frequency ablation for tumor.

functions of multiple cell organelles; make the vascular tissues around the tumor coagulate, reduce, or blockade the blood supply for the tumor; prevent the tumor from dispersion; and stimulate the body to generate specific antibodies to kill and restrict the growth and dispersion of tumors that cause the apoptosis of tumor cells. The radio frequency is characterized by strong penetration into the body tissues, high-heat efficiency, minimal invasion, less misery, and little adverse effect. Presently, there are still some problems in radio-frequency therapy to be resolved urgently, such as no complete avoidance of residual tumor, lack of effective monitoring means to identify coagulation and necrosis, as well as focus residue after surgery and nonideal therapeutic effect on tumors with a diameter greater than 5 cm.

2.2.2.2.3 Interstitial laser photo-coagulation

High-power focused laser is used for direct radiation to eliminate tumors by means of evaporation and atomization of tumor tissues. As for interstitial laser photo-coagulation (ILP), the probe with the pore canal is inserted into the targeted tissues of the tumor directly through a percutaneous puncture, the optical fibers are implanted through the pore canal and protruded out of the probe for several millimeters, and the laser energy brought in is spread over the ambient tissues so that thermal coagulation and necrosis of the tumor tissues occur. Clinically, it is divided into cutting mode, evaporation mode, coagulation mode, and so on.

2.2.2.2.4 High-intensity focused ultrasound

Because of the characteristics of ultrasonic sound beam of aggregation and penetrativity, the extrinsic low-energy ultrasounds are aggregated into the intrinsic tumor-targeted zone, and the high-intensity ultrasonic waves are collected in the focus place so as to cover all the targeted zones from point to line, line to surface, and then surface to layer. Afterward, such mechanisms as transient high-temperature solidification effect (>70°), cavitation effect (cell breakage), destruction of capillaries, and mechanical effect can result in the coagulation, denaturation, necrosis, final absorption, and disappearance of the tumor niduses in the focus place, without damage to the normal tissue structures around the lesion (Figure 2.7). High-intensity focused ultrasound (HIFU) has no radiation on the body and its protective method is simple, so it can be applied to not only superficial tissue structures but also intrinsic deep tissues, with the characteristics of shorter

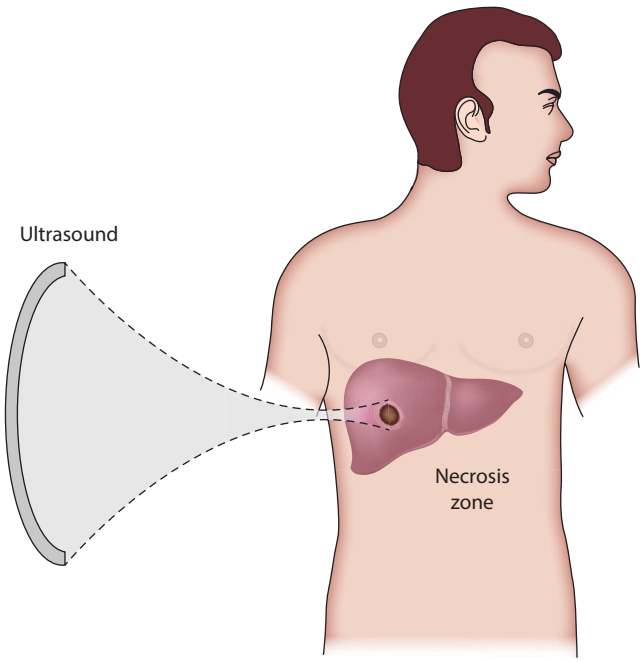

Figure 2.7 Schematic of high-intensity focused ultrasound.

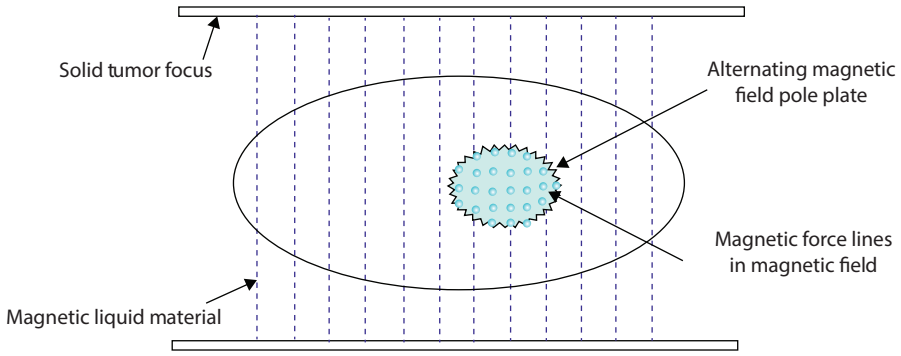

Figure 2.8 Schematic of magnetic induction therapy.

therapeutic time, small trauma, and accurate orientation. However, due to the possible residual cells in the targeted zone, the problem of displacement size of focuses and some visceral organs movement, to some extent during therapy, can cause difficulties in the confirmation of targeted points, which results in no effective therapy for the organs blocked by air or bone. Also, it cannot be applied to the tumors that cannot be observed by B ultrasound, or those with internal exuberant blood flow.

2.2.2.2.5 Magnetic induction hyperthermia

As for magnetic induction hyperthermia (MIH), magnetic media are to be distributed in the tumor tissue properly and accurately by various methods, and the tumor tissue is put in an alternating magnetic field (Figure 2.8). Then, the heat medium generates heat by mechanisms such as induction eddy, hysteresis loss, and Nell relaxation. The heat reaches the ambient tumor tissue through heat transfer by controlling various heating parameters, which allows the therapeutic zone to reach the temperature required to kill the tumor. The technology is developed on the basis of radio-frequency heating technology, and can increase the temperature difference between tumor tissue and ambient normal tissues, improve the therapeutic effect of heating, and relieve the complications incurred by hyperpyrexia of normal tissues. The technology is under development at present with sound application prospects.

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3

Physical technology and biological basis of hyperthermia in oncology

3.1 INTRODUCTION

Hyperthermia makes use of the sediments of relevant physical energies in tissues to generate heat effect, making the temperature of the cancer tissue to rise to an effectively therapeutic temperature, and is maintained for a certain period, which leads to growth obstruction and death of tumor cells without damage to cancer cells. Physical factors, such as high temperature, mechanical vibration, infrared ray, ultrasound, microwave, and radio frequency (RF), can generate heat effect on the body. Various tissues, body fluid, and so on in the body are composed of various molecules and electrical ions. Molecules include polar and nonpolar molecules. When body tissues are acted by extra electric magnetic fields, the internal free electrons and ions can generate ohmic heating effect, and the polar or nonpolar molecules that are polarized due to the magnetic field can generate inductive heat effect. In the alternating electric field, ions and polar molecules can generate molecular twisting, which results in frictional heating. Cancer hyperthermia adopts mainly electric field and magnetic field heat effects. High-frequency magnetic field aims mainly to heat the muscles or other tissues with small resistance, without fat being overheated. The frequency of the high-frequency electric field is lower, the generation of heat is larger, and the heat in the electric field is generated from the surface of the body. The heat characteristic of body tissues is associated with water content, and it may change with water loss during therapy.

3.2 PHYSICAL TECHNOLOGIES OF HYPERTHERMIA IN ONCOLOGY

3.2.1 Microwave technology

Microwave heating on the tissues relies mainly on molecular friction and secondary on tissue electrolyte effect; it has selectable heating effect on water and water-containing substances that can absorb microwave energy. Microwaves can generate heat in a medium that consumes energy of the electric field, and then heat effect can be available on the organisms. The substances composed of polar molecules can absorb the microwaves well. Water molecules show a strong polarity, so the sweat can absorb microwaves. Water-rich tissues, such as muscle tissue, brain tissue, skin, and viscera, absorb the microwaves strongly but penetrate shallowly, whereas tissues lacking water, such as fat and bone, absorb less microwaves than water-rich tissues. Cancer cells contain abundant water. Microwaves are converted into heat energy after irradiation on cancer tissues. When the cancer cell is heated to 41.4°C–43°C, the synthesis of RNA and DNA (of cancer cells) can be depressed, resulting in their death. Under microwaves, the heat production and temperature rise of tissues are influenced by electric field distribution and tissue properties. The thermal properties of the tissues and nerve–blood circulation cooling mechanism will determine the temperature distribution of the tissues. When hyperthermia is applied, cancer cells and normal tissues are heated to different extents. The blood circulation of the normal tissues is faster and the heat in the tissues disperses quickly. The low oxygen tension of the cancer cells causes its pH value to be lower and makes it sensitive to heat. In the cancer cells, temperature rise is faster and the blood circulation is relatively worse, resulting in higher local temperature in the cancer tissue, hence more susceptible to thermal destruction and necrosis.

3.2.2 Radio-frequency technology

When RF acts on body tissues, the ions, molecules with electric charge, electric doublets in the tissue, and so on vibrate back and forth under high-frequency electromagnetic field so that the electric energy is converted into heat, called endogenous heat. RF heating contains both joule heat factor and dielectric loss heat production factor. Under the radio-frequency (RF) electromagnetic waves, both normal and cancer tissues can absorb the energy of the electromagnetic waves. Because of poor heat dispersion of the cancer tissue and its sensibility to hyperpyrexia, the cancer tissue has higher temperature than normal tissues, thus can be killed without causing damage to the normal tissue. Because the effect of RF heating is deeper, it is also known as RF diathermy.

3.2.3 Ultrasonic technology

Ultrasonic waves are propagated in the manner of longitudinal waves, causing particle vibration. Because of friction viscous loss, heat conduction loss, and remittent process of some molecules, some orderly ultrasonic vibration energy is converted into disorderly molecular thermal motion energy, which is the main function of ultrasonic cancer therapy.

3.2.4 Laser technology

Laser can kill cancer directly through irradiation on the body surface or focus on the cavity surface. It generates photochemical reactions through the activation of a photosensitizer to achieve the purpose of therapy (photodynamic therapy). Laser-induced interstitial thermotherapy (LITT) is a minimally invasive therapy for solid tumors. During the therapy, optical fibers are implanted into the tumor under the guiding of iconography, and then the high-energy laser energy with a certain wavelength enters into the tumor tissue around the fiber tip through light-guide fiber transfer. Photons are absorbed by tissue chromophores and the energy of the photons is transferred to heat energy to make the tissue temperature rise, resulting in the coagulation and necrosis of the tumor tissue.

3.2.5 Magnetic induction technology

Magnetic induction heating aims to cause tissue heating through eddies present in the tissue, which are formed by alternating magnetic field produced by the induction coils. Any metal objects in alternating magnetic field can generate induction current, called eddy. When the eddy flows in the metal, heat is generated. If we put a ferromagnet (heat seeds) in the cancer tissue and set a high-frequency electromagnetic field, the ferromagnet can generate eddy current and heat so that the nearby cancer tissue is heated. For every ferromagnetic material, there is a critical temperature, called the curie point, above which the magnetism disappears completely and the ferromagnet becomes a paramagnet. So, the application of curie point can control the heating temperature of the magnetic media in tissues. In an alternating magnetic field, when ferromagnetic induction heating is higher than the curie point, the ferromagnet loses its magnetism and thus its capacity of further heating. When the temperature drops below the curie point, the ferromagnetic recovers its magnetism for continuous heating, thus reaching the temperature through automatic temperature control for cancer therapy. This technology is still under study.

The advantages of cancer hyperthermia technology lie in its minimal invasion or no invasion, as well as immunological enhancement. It has become an important therapy means after surgery, radiotherapy, and chemotherapy, and it is of great significance for clinical therapy of cancer. As an important means for integrative treatments of cancer, thermal ablation technology under the guiding of iconography, such as RF, microwave, high-intensity-focused ultrasound (HIFU), and laser, as well as conventional hyperthermia technology that induces apoptosis of cancer cells by heating, are worthy of further study and clinical popularization.

3.3 BIOLOGICAL BASIS OF HYPERTHERMIA IN ONCOLOGY

3.3.1 Heating damages to tissues

Temperature is one of the important factors affecting the survival of cells. High temperature can depress the synthesis and repair of cell DNA, RNA, and proteins; change the fluidity and permeability of cell membranes; and result in cytoplasmic destruction. Cells can adapt to the adverse effects of the external environment through their own capacity of regulation and defense. They can control their own states for counteraction according to the extent of the adverse effects, by integrating genetic mechanisms and even taking the initiative to induce the death of cells. During hyperthermia, the lethal effect on cells is closely related to the temperature and time of thermal stimulation. When the temperature in the biological tissues is higher than 40°C, blood flow of the tissue accelerates. The normal body temperature is 37°C, so when the tissue is heated to 37°C–42°C, it is generally difficult to observe any significant effect. Table 3.1 shows the effect of heating on tissues when the temperature is higher than 43°C.

Thermal effect is the medical application basis of laser and is an important lethal factor. Laser irradiation can cause the phenomena such as erythema, denaturalization of proteins, blood coagulation, evaporation of water in cells, and carbonization of tissues. In tissues irradiated by laser, we can find that cell nuclei are pulled flat and all layers of cells are elongated, which results in inserted-type cavitations, indicating that there are changes in tissue structures related to heat during the thermal effect of the laser. The influences of RF on tissues depend on the heating temperature, which is mainly shown by the roles of different temperatures in the damage of tissues and in immune enhancement during cancer therapy. Microwave therapy adopts external and endogenous thermal effects. The external thermal effect can enhance the metabolic process of cells, improve blood circulation, and raise the regeneration of tissues. The endogenous thermal effect includes hyperpyrexia therapy and tissue coagulation therapy. Local hyperpyrexia of microwaves can activate the immune system of the body. Tissue coagulation therapy is to make microwaves directly act on the local tissues of the body to realize hyperpyrexia in a small scope and generate coagulation. It results in the necrosis and fall of partial tissues, as well as blood coagulation of the tissues at the same time. Ultrasonic heating causes more damages to tissues than HIFU therapy, and it is a minimally invasive cancer therapy technology. By the characteristics of ultrasonic wave such as tissue penetration and focusing, this technology can make the extrinsic high-intensity ultrasonic waves focalize at the cancer so that the temperature of tissues in the targeted zone rises to 65°C instantly, resulting in coagulation and necrosis, without any damage to tissues penetrated by ultrasonic waves and those around the targeted zone. Magnetic induction

Table 3.1 Heat effect of different temperatures on tissue

Temperature (°C)	Heat Effect
43–45	Time dependency and reversibility, increase of tissue perfusion and permeability, rise of drug concentration and/or activation, improvement of drug metabolism rate, enhancement of cell cycle effect, rise of pH, strengthening of the sensitivity of tissues to radiotherapy
>47	Reduction of enzymatic activity
50–60	Denaturization and coagulation of proteins
90–100	Desiccation and dehydration of tissues
>100	Water molecules in tissues start boiling and evaporate, resulting in nonreversible damages
>150	Carbonization of tissues
>300	Vaporization of tissues
>500	Tissue begins to burn with appearance of firelight

Source: Data courtesy of Hans Olav Rolfsnes, Dan Neumann, and Prof. Paul Stauffer, University of California, San Francisco.

hyperthermia aims to distribute magnetic media into the cancer tissues properly and precisely. Under the action of external alternating magnetic field, the media begin to heat under induction to suppress and kill the cancer tissue after reaching a certain temperature.

3.3.2 Heating damages to cells

Heating can affect both cell nuclei and cytoplasm. It can act on cell nuclei directly, causing loss of cellular polymerase activity, and can also act indirectly on DNA synthesis, chromosomal and intracellular components, cytoskeletons, and so on, causing a series of reactions. A cell membrane has a phospholipid bilayer, and its viscosity varies with temperature. Any factor increasing the membrane fluidity will exacerbate the damage caused by high temperature. Membrane damage is likely to be one of the reasons for apoptosis. The killing energy of hyperthermia is consistent with that of protein damage and synthesis depression. The cell cannot continue its division after the damage of cell membrane, so it will die at phase G. The high temperature of 45°C can induce chromosomal aberrations and damage to DNA-related enzymes, resulting in cell death. Tumor cells are sensitive to heat. When they are heated to 43°C for 30 minutes, cell apoptosis occurs, and when they are heated to 46°C or more for 30 minutes, cell necrosis occurs. Figure 3.1 shows the differences between cell necrosis and apoptosis.

Necrotic process: Cellular swelling, rupture, nuclear chromosome pycnosis, and cracking.

Apoptosis: Cell condensation, condensation of nuclear chromosome into the crescent, cracking into DNA fragments, invagination and segmentation of cell membranes, wrapped in the formation of apoptotic bodies, which then are phagocytized.

High temperature has follow-up effects on the cells. Cell activity decreases after stimulation with high temperature, which is most obvious after 6–18 hours, and then they start their self-repair. Tests show that the cells are blocked at phase G_2 within 6–24 hours after the heat treatment. Continuous hyperpyrexia treatments

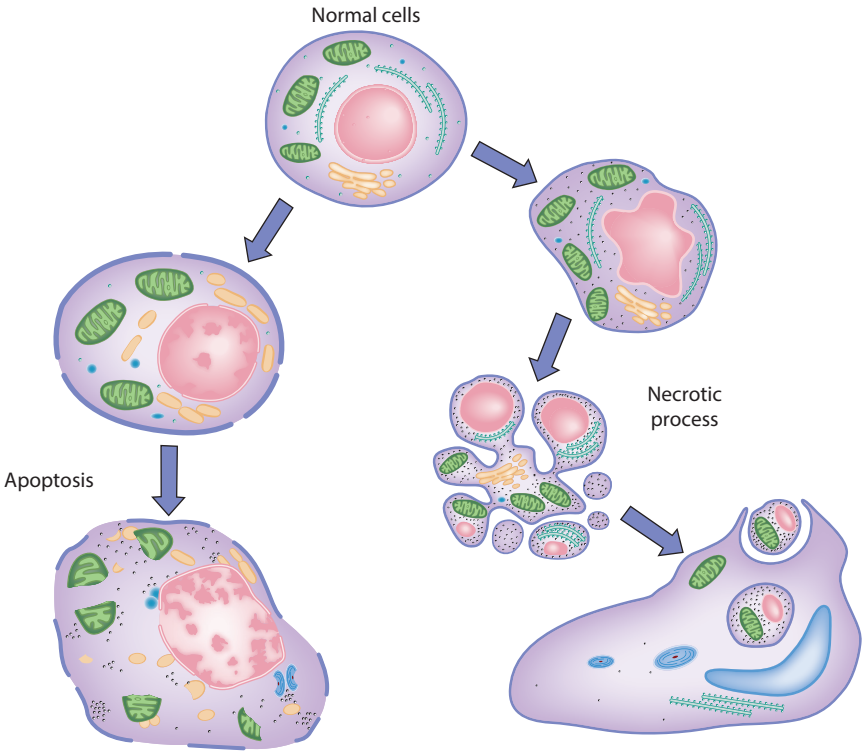

Figure 3.1 Differences between cell necrosis and apoptosis.

allow cells to generate tolerance. The cell thermal tolerance mechanism is not definitive now, and it is a representation of the body's self-protection mechanism. As for high-temperature-inducing apoptosis, the changes of cell nuclei and mitochondria are the most significant. Mitochondrial damage is the central link of apoptosis, and in the early apoptosis period, there appear an interruption of electron transfer chains of the mitochondria, obstruction of energy generation, increase of membrane permeability, reduction of transmembrane potential, opening of membrane permeability pores, and so on. The opening of hole canals balances the ion concentration inside and outside the membranes, loss of H^+ transmembrane gradient, and uncoupling of the respiratory chain, which result in the high permeability of mitochondrial matrix, expansion of its volume, release of cytochrome C into the cytolymph, promotion of enzyme chain reactions of caspases family after the release of cytochrome C, and some apoptosis promotion factors, and ultimately cell apoptosis occurs.

Cytoskeletons are distributed in the fibrous protein on the medial sides of cell nuclei and cell membranes, including microfilaments, microtubules, and intermediate filaments, and take part in many physiological functions in the cells. These cytoskeletons are distributed widely in cells, sensitive to heating, and involved in several cell functions. The changes of cytoskeletons are observed to predict the toxicity of the cells heated. Cytoskeletons can still change after heating and cause influences on the vital activities of the cells.

After thermal stimulation, the cells express a large amount of heat shock proteins (HSPs) and form thermal tolerance to protect cells from damage. HSPs can be taken as a molecular companion to mediate intramolecular or intermolecular protein interactions. Studies show that high temperature allows the cells to release NO-mediated endogenous cytokines and induce the expression of nitric oxide synthase (iNOS), which is favorable to the vasodilatation in an elderly body, tissue nutrition, and the intrinsic antipathogenic and anticancer capacity.

3.3.3 Influences of high-temperature hyperthermia on cancer

In recent years, with the development of molecular biology and its wide application in the field of hyperthermia, the study of hyperthermia mechanisms has been promoted at the molecular level. Studies show that the molecular mechanism about hyperthermia on cancer includes mainly three aspects: killing effect of hyperthermia on cancer cells, depression effect of hyperthermia on the invasion and metastasis of cancer, and immunoregulation effect of hyperthermia on cancer.

3.3.3.1 Killing effect of hyperthermia on cancer cells

The main mechanism about the killing effect of conventional hyperthermia on cancer cells aims to induce apoptosis. Studies have shown that hyperthermia can induce apoptosis through pathways of mitochondria and dead receptor (exogenous). Relevant genes of cancer include mainly tumor suppressor gene (including wild-type *p53*, *bax*, *TNF*, *Fas*, etc.), oncogene (mutagenic *p53*, *bcl-2*), and downstream gene (*IGF-1*, *PCNA*, *c-myc*, *c-fos*, etc.). Hyperthermia induces apoptosis mainly through these pathways of mitochondria, dead receptor, oxidative stress, and intracellular increase of Ca^{2+}.

The mechanism of radio-frequency ablation (RFA) aims to directly cause the coagulation and necrosis of cancer cells and induce apoptosis.

3.3.3.2 Depression effect of hyperthermia on cancer invasion and metastasis

At present, research on the mechanism of cancer invasion and metastasis focuses mainly on cancer angiogenesis and matrix metalloproteinase (MMP). Angiogenesis is one of the main conditions for the hyperplasia, metastasis, and dispersion of cancer. The regulation on MMP and its depression factors maintains a balance in the body, which can depress hyperplasia and adhesion, invasion, and metastasis of cancer. Hyperthermia can depress the invasion and metastasis of cancer by changing the expressions of the vascular endothelial growth factors (VEGFs), MMP, fibrinolysin, and adhesion factors.

Experimental evidence shows that the invasion and metastasis of cancer cells are regulated by MMPs and their depression factors (tissue inhibitor of metalloproteinases [TIMPs]), both of which maintain balance in the body and have important effects on the hyperplasia, migration, invasion, and apoptosis of cancer.

MMPs favor the invasion and metastasis of cancer cells. TIMPs are antagonistic to MMPs, and depress the invasion and metastasis of cancer cells. Studies show that heating can change the activity of MMPs and decrease their expressions; reduce the ablation and degradation of the basement membranes and extracellular matrixes; and depress the growth, invasion, and metastasis of cancer. Moreover, depression of MMPs is temperature dependent; the higher the temperature, the more obvious the depression; therefore, the possibility of blood vessel or lymph node metastasis is reduced.

3.3.3.2.1 Vascular endothelial growth factor

The tumor angiogenesis is an important condition for the occurrence, growth, invasion, and metastasis of cancer. VEGF plays an important role in the occurrence and development of many tumors. Hyperthermia can depress the expressions of tumor-derived VEGF and its products, and thus block the hyperplasia of tumor vascular endothelial cells and reconstruction of their extracellular matrixes to reach the depression purpose of cancer growth and metastasis. In addition, hyperthermia can activate the expression of the depression factor 1 that reduces the formation of fibrinolysin by promoting the expression of plasminogen so that the number of tumor blood capillaries decrease, which in turn depresses the growth of cancer and reduces the metastasis of cancer.

3.3.3.2.2 Transforming growth factor-β

Transforming growth factor-β (TGF-β) can stimulate the hematopoietic microenvironment to induce the formation of new blood vessels, and has a favorable effect on the invasion of cancer cells. Studies show that hyperthermia can decrease TGF-β1 level in the serum, which obviously depresses tumor angiogenesis, reduces the blood supply to cancer, limits the growth of cancer, and blocks the development of cancer from the tumor angiogenesis stage.

3.3.3.2.3 Urokinase-type plasminogen activator receptor

Urokinase-type plasminogen activator receptor (uPAR) can conduct and participate in cell adhesion, differentiation, hyperplasia, migration, and the formation of new blood vessels and lymphatic vessels of tumors. Studies show that heating can promote the expression of plasminogen activator inhibitor-1 (PAI-1), which is the main depressor of uPAR and tissue-type proenzyme. Through the suppression of such two factors, PAI-1 can depress the invasion and metastasis of cancer.

3.3.3.2.4 E-cadherin

E-cadherin is an I-type glycoprotein, and can mediate intercellular adhesion. Its loss can cause the falling, invasion, and metastasis of primary cancer cells. It is reported that hyperthermia can promote the expression of E-cadherin and affect the metastasis of cancer cells indirectly.

3.3.3.3 IMMUNOREGULATORY EFFECT OF HYPERTHERMIA ON CANCER

Low cancer immunogenicity is one of the reasons for cancer immune escape. Hyperthermia can activate cancer immunity. It can change the immune system of the body significantly, reverse cancer immune escape, promote the body's anticancer immune function, and allow the cell immune function to play an important role in anticancer.

Currently, the immunomodulatory effect of thermal stimulation includes mainly the following mechanisms: heating can result in the necrosis of part cancer cells and the necrosis products can stimulate the immune system. As an antigen, the denatured proteins of cancer cells and their decomposition products stimulate the immune system to produce cancer immune response. High temperature increases the lipid fluidity of cancer cell membranes to expose antigen determinant mounted on the cell membrane phospholipid bilayer, thus increasing the antigenicity of cancer cells and strengthening the killing effect of the humoral immune function. Local hyperthermia can also destruct or remove the inhibition effect of blocking factor on the immune system so as to recover the body's immune response to cancer, promote the generation of HSPs by cancer cells, cause the induction of immune responses by nonspecific inflammations, promote cytokine secretions, and improve immunity.

3.3.3.3.1 Heating effect

Hyperthermia produces thermal effects by the sedimentation of relevant physical energy in tissues so that the temperature of the cancer tissue rises to an effective therapeutic temperature and lasts for certain period, the purpose of which is to cause growth obstruction and death of cancer cells without any damage to normal tissues. Physical factors, such as high temperature, mechanical vibration, infrared rays, ultrasound, microwave, and RF, can generate thermal effects on the body. Various tissues and body fluids in the human body are composed of different molecules and charged ions. Molecules are described as polar and nonpolar molecules. When the external electromagnetic field acts on the human tissues, the internal free electrons and ions produce an ohmic thermal effect, while polar or nonpolar molecules that are polarized due to the electromagnetic field can generate a thermal induction effect. In alternating electric field, ions and polar molecules can generate molecular twisting to result in frictional heating. Cancer hyperthermia uses mainly electric field and magnetic field thermal effects. The high-frequency magnetic field is used mainly to heat the muscle or other tissues with small resistance without occurrence of fat overheating. The high-power electric field has a lower frequency but generates more heat, and the heat of the electric field is generated from the surface of the body. The thermal characteristic of the human tissue is associated with water content and changes with water loss during therapy.

3.3.3.3.2 Microwave heating

The microwave heating of tissues depends mainly on molecular friction, followed by the electrolytic effect of tissues. It has a selective heating effect on water and water-containing substances that can absorb microwaves. Microwave heating can generate heat through consumption of the electric field by the dielectric material itself, and can generate thermal effects on the living beings. The substances composed of polar molecules can soundly absorb the microwaves. The water molecule has a strong polarity, so the sweat substances can absorb microwaves. Water-rich tissues, such as muscle tissue, brain tissue, skin, and viscera, have strong absorption capacity of microwaves but penetrate shallowly, whereas tissues that lack water, such as fat and bone, absorb less heat. Cancer cells contain abundant water; therefore, microwaves are converted into heat energy after irradiation on the cancer tissue. When the cancer cell is heated to 41.4°C–43°C, the cell RNA and DNA syntheses are depressed, resulting in its death. The heat production and temperature rise under microwave effect are influenced by cancer cell electric field distribution and tissue properties. Its thermal properties and nerve–blood circulation cooling mechanism determine the temperature distribution of tissues. When hyperthermia is applied, cancer cells and normal tissues are heated to different extents. However, the blood circulation of normal tissues is faster and the heat dissipates quickly. Although the low oxygen tension of the cancer cell determines its lower pH value, sensitivity to heat, faster temperature rise, and relatively poor intratumoral blood circulation result in higher local temperature in the cancer tissue, hence it is more susceptible to thermal destruction and necrosis.

3.3.3.3.3 Radio-frequency hyperthermia

When RF acts on the body tissues, ions, charged molecules, and electric doublets in tissues vibrate back and forth under the high-frequency electromagnetic field so that electric energy is consumed and converted into heat, called endogenous heat. RF heating contains both joule heat factor and dielectric loss heat production factor. Under RF electromagnetic waves, both normal tissues and cancer tissues can absorb electromagnetic energy, but the temperature of the cancer tissues is higher than that of normal tissues because of poor heat dispersion in the cancer tissues and the sensibility of cancer cells to hyperpyrexia; thus, the cancer tissues are killed by hyperpyrexia without any damage to normal tissues. Because the heating effect of RF is deeper, it is also known as RF diathermy.

3.3.3.3.4 Ultrasonic wave vibration

Ultrasonic waves propagate in the medium in the manner of longitudinal waves, causing particle vibration. Because of friction viscous loss, heat conduction loss, and intension process of some molecules, part of the orderly acoustic vibration energy is converted into disorderly energy of molecular thermal motion, which is the main effect of ultrasound cancer therapy.

3.3.3.3.5 Laser power

Laser can generate a killing effect through irradiation on the focuses on the body surface or cavity surface. It generates chemical reactions through the activation of a photosensitizer to achieve the therapeutic effect (photodynamic therapy). Laser-induced interstitial thermotherapy (LITT) is a minimally invasive therapy for solid tumors. Under the guiding of iconography, optical fibers are implanted into the tumor when the therapy is performed. High-power laser energy with a certain wavelength enters into the tumor tissues around the fiber tip through light-guide fibers. Photons are absorbed by tissue chromophore and converted into heat energy, resulting in the temperature rise of the tissue, and then coagulation and necrosis of the tumor tissue.

3.3.3.3.6 Magnetic induction heating

Magnetic induction heating is a process of heating tissues through eddies present in the tissue, which are formed by an alternating magnetic field generated by the induction coils. Any metal objects in the alternating magnetic field can generate induction current, called eddy. When the eddy flows in the metal material, it heats up the material. If we put a ferromagnet (hot seed) in cancer tissues and set a high-frequency electromagnetic field, the ferromagnet generates an eddy current so as to heat the nearby cancer tissues. As for any ferromagnet, there is a temperature point, called the curie point, above which the magnetism disappears completely and the ferromagnetic becomes a paramagnet. So, the application of the curie point can control the heating temperature of the magnetic medium in tissues. In an alternating magnetic field, when the inductive temperature of the ferromagnetic is at the curie point, ferromagnet loses its magnetism and the capacity of further heating. When the temperature falls below the curie point, the ferromagnetic recovers its magnetism and continues heating, thus realizing the automatic temperature control and temperature rise for tumor therapy. At present, this technology is still under study.

The advantages of hyperthermia technology lie in its minimal invasion or no invasion, and immune enhancement; therefore, it has become an important therapeutic means for cancer after surgery, radiotherapy, and chemotherapy. It is of great significance for clinical therapy of cancer. As important means for integrative cancer treatments, thermal ablation technology under the guiding of iconography, such as RF, microwave, HIFU, and laser, as well as conventional hyperthermia, which induce apoptosis of cancer cells by heating, are worthy of further research and clinical popularization.

3.4 SAFETY OF NORMAL TISSUES UNDER CANCER HYPERTHERMIA

The biological characteristics of the cancer tissue are the basis of cancer hyperthermia. Defects in the histology of the cancer tissue lead to its blood supply insufficiency, hypoxia, warm orientation, and lack of thermal tolerance. The blood supply of cancer tissues only totals 2%–15% of normal tissues. Such significant difference in blood circulation is the basis for various heating methods in cancer hyperthermia.

Because of the anatomical characteristics of cancer blood vessels, the blood flow is slower than the adjacent normal tissues. After heating the targeted tissues, blood vessels of normal tissues, due to the good blood supply, begin to dilate, and the blood flow accelerates to take away heat. So, the temperature increase is not significant. Because of the anatomical defects (poor sensitivity, morphological abnormalities, and rudiment) of cancer tissues, the blood flow is slow. Cancer blood vessels also have some changes after diathermy, such as cell membrane hardening in the acidic environment, endothelial cell degeneration, increase of vascular permeability, and increase of adhesion of leukocytes on the vessel walls, all of which can cause blood stasis and even vascular occlusion. When blood flow is measured in lung cancer, renal cancer, and colorectal cancer by the isotope dilution method, it is found that the blood flow per gram of cancer tissues is only 1%–15% of the tumor-adjacent normal tissues. The larger the cancer, the slower the blood flow per gram of cancer tissues. Therefore, heat dispersion is difficult through blood circulation. Under hyperpyrexia, heat accumulates, resulting in significant temperature rise of the cancer. Its temperature is significantly higher than the adjacent normal tissues with a temperature difference of 5°C–10°C, and the temperature in the center of the cancer

is higher than in other parts of the cancer. For example, when the normal tissues near the cancer are heated to 38°C, the temperature inside the cancer can be 43°C–48°C. Therefore, hyperthermia can kill cancer cells without damage to normal tissues.

Because of the abnormal hyperplasia of cancer cells and physical defects caused by its development, the cancer tissue is more easily damaged by heat than normal tissues. As long as we have a good control of heating power and time, making the temperature in a range where cancer cells can be destructed while the normal cells survive, a safe and effective therapy can be assured.

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4

Hyperthermia in oncology and nontoxic integrative treatments

Hyperthermia currently plays an increasingly important role and exerts its increasingly greater effect in the field of cancer therapy. It has become the fifth cancer therapy after surgery, radiotherapy, chemotherapy, and biological therapy. However, it should be noted that cancer hyperthermia cannot replace surgery, chemotherapy, or radiotherapy as an independent cancer therapy scheme. Modern medicine emphasizes integrative treatments for cancer, namely, a combination of surgery, chemoradiotherapy, and biological therapy with emerging therapy technologies such as hyperthermia. Through clinical practices in Clifford Hospital for many years, the author has explored new approaches and methods for cancer therapy through a combination of various traditional therapies with modern ones for integrative application, characterized by uniqueness, minimal invasion, and no toxic side effects, and has proposed the concept of "nontoxic integrative cancer treatments" and enriched the integrative cancer therapy system. Hyperthermia is an important component of nontoxic integrative treatments, and it can be used together with other nontoxic treatments such as modern chelation therapy, medical ozone therapy, cell biological therapy, herbal medicine, acupuncture, psychotherapy, and naturopathy so as to exert their anticancer effects. Hyperthermia combined with other integrative cancer treatments can improve the life quality of cancer patients significantly, prolong their survival time, and reduce the risk of tumor recurrence and metastasis. It is even of great significance in the prevention of tumors and other diseases.

4.1 HYPERTHERMIA INTEGRATED WITH TRADITIONAL CHINESE MEDICINE

4.1.1 Cancer hyperthermia and traditional Chinese medicine

Hyperthermia and traditional Chinese medicine (TCM) treatments are both nontoxic treatments and easily accepted by patients. They have unique advantages in tumor therapy. The combination of the two therapies has synergistic effects. In recent years, with the proposal of herbal medicine hyperthermia, the combined application of hyperthermia with herbal medicine has already been widely used for various benign and malignant tumors, and it is especially prominent in the therapy of cancerous pains. Generalized, "Chinese herbal hyperthermic therapy = extrinsic hyperthermia + external application of Chinese herbs + internal application of Chinese herbs + Chinese herbal tea." Currently, the application of "extrinsic hyperthermia + external application of Chinese herbs" is popular. The combination of extrinsic hyperthermia with acupoint application of herbal medicine is named as thermal stimulation therapy of Chinese herbal medicine.

There are two implications in the generation of thermal sensitization by herbal medicine during the process of herbal medicine combined with hyperthermia for cancer therapy. Herbal medicine is used to control tumor heat tolerance factors and increase the sensitivity of hyperthermia on cancers. Hyperthermia can accelerate the reaction speed of herbal medicine to exert its greater anticancer effect. There are broad development prospects of the organic combination of hyperthermia with herbal medicine, especially for patients who are not sensitive to chemotherapy or those who cannot take chemotherapy. This is because of the two advantages of the combination of herbal medicine with hyperthermia. It can increase the sensitivity of hyperthermia, and the application of hyperthermia can increase the anticancer effect of herbal medicine. Hyperthermia has

an immune induction function, which can improve the immunity of the organism. Especially when whole-body hyperthermia is used, it can improve the systemic circulation and make smooth the flow of qi and blood, thus improving functions of the body and promoting metabolism. This facilitates the elimination of intrinsic toxins and harmful substances. Meanwhile, it can be combined with herbal medicines with the effect of supplementing qi and nourishing yin, as well as activating blood circulation to dissipate blood stasis, which can adjust the balance of body between yin and yang so as to reach the therapeutic effect of supporting healthy energy to eliminate evil aspects. Also, the two therapies can generate a synergistic effect in terms of adjustment of immunity, improvement of functions of the body, and elimination of toxins. The external application and internal application of herbal medicine can supplement each other, especially for the digestive tract cancer patients who cannot take oral medications or those who have poor absorption after oral application. Because the selectable herbal medicine for intravenous injection is limited at present, the internal therapy principle is applicable for external therapy; therefore, it is of great significance to seek for effective external therapies.

There are records of moxibustion on garlic used for cancer hyperthermia in a book on TCM called *Wai Tai Mi Yao*, published in the year 752. Acupuncture is an external therapy in TCM. Modern hyperthermia is a kind of warm-heating therapy and is used for cancer therapy through in vitro heating. TCM believes that human life not only is a physical body but also contains invisible vitality, which, in terms of TCM, refers to fire and heat and is summarized as yang qi. Another ancient book, *Su Wen Sheng Qi Tong Tian Lun*, points out, "Yang is like the sky and sun to the earth. The dissipation of Yang costs the vitality and the vigor of human beings." The blood and fluids of human body is only promoted by Yang Qi. If Yang Qi is not enough, the driving force is weak and the movement of body fluid essence slows down or even stops. The human body is vulnerable to pathogenic cold invasion if Yang Qi is poor. As said in *Ling Shu Bai Bing Shi Sheng Lun*, "Small intestine is the organ that food passes and where the nutritions are absorbed, the invasion of pathogenic cold in mesentery and blood vessels causes its disfunction . . . then its accumulation causes the disease." *Su Wen Ju Tong Lun* points out, "The accumulated illness breaks out due to the invasion of pathogenic cold, and it becomes more serious if no treatment is administered for a long time." Further, it says, "Sudden illnesses are often derived from pathogenic cold; if internal injuries are caused by infuriation, Qi ascends, which results in the obstruction of Qi transportation, no operation of warm Qi; dispersion of blood clotting; and leakage of body fluid, all of which cause illnesses for the long term." Accordingly, tangible syndromes form through accumulations, which is an important cause for the formation of cancer. Some researchers have made statistics from 1000 cancer patients and found that 80% of the patients showed syndromes caused by cold factors. As for modern hyperthermia, heat is penetrated from outside to inside the body. "Heating" only acts on the affected site without damage to vital qi, whereas yang qi scatters and dispels cold. Its accuracy, speed, and power are too wonderful for words to describe, and no drug can be compared with it. Of course, yang qi deficiency and cold accumulation is just one of the main causes. The combination of herbal medicine with hyperthermia is not only related to the combination of "internal heating" (internal application of "warm drugs" with "external heating" (hyperthermia) but also involved with all the factors such as asthenia or sthenia of viscera, sputum, dampness, toxin, blood stasis, chilliness degrees in four seasons, toxin elimination effects, and the change of pulse and symptoms after heating the body. The combination of hyperthermia with oral medicine, perfusion, external application, intratumoral injection, and intracavitary injection can be applied widely according to conditions.

Some non-chemotherapeutic drugs can be used in combination with hyperthermia to treat cancer. These drugs have no or little anticancer effect. But if they are heated, they can develop strong anticancer activities. Thus, they have great development prospects. They exceed the anticancer effect of even the combination of heating with chemotherapeutic drugs. In this respect, herbal medicine has great potential and we have found its sound clinical prospects. Through the comparisons of thermal synergistic actions of seven drugs totaling five types, some researchers have found that some Chinese herbal medicines can induce apoptosis of more cells. For example, matrine can improve the therapeutic effect of MA737 on small breast cancer. Therefore, the combination of cancer hyperthermia with herbal drugs has wide development prospects and requires our further research.

4.1.2 Research on herbal medicines for common cancer

4.1.2.1 RESEARCH WITH THEORETICAL BASIS

Basic experimental studies on common cancer started in 1965. The Beijing Institute of Traditional Chinese Medicine reported animal experiments on *Chinese cantharides* and *Huechys sanguinea*, and their clinical effects, at the national academic conference of oncology. This report attracted the attention of the medical community in China. In the late 1980s, the Cancer Hospital of Shanghai Medical University studied the pharmacological action of drugs nourishing the spleen and benefiting qi on liver cancer cell kinetics, estrogen receptors, and liver precancerous lesions. In the experiment, a nude mouse was inoculated with human liver cancer and it was found that the hyperplasia index of cancer cells was reduced in the fluid cell apparatus. In the experiment of inducing liver cancer in white rats, it was found that herbal medicines nourishing the spleen and benefiting qi could reduce the incidence of liver cancer and had little influence on estrogen receptors. In the early 1990s, the Longhua Hospital of Shanghai University of Traditional Chinese Medicine researched the prevention effect of herbal medicines nourishing the spleen on gastric cancer of animals. The experimental results showed that the TCM medical prescription and its decomposed recipes, which mainly nourish the spleen, supplemented with heat clearing, detoxification, phlegm resolution, lump dissolution, and stasis removal, can prevent the occurrence and incidence of gastric cancer.

The Guang'anmen Hospital of China Academy of Chinese Medical Sciences has developed a "prescription nourishing spleen and benefiting kidney." An animal experiment proved that the prescription could relieve the toxic reaction of chemotherapy, reduce the mortality of tumor-bearing mice during chemotherapy, protect karyocytes and multifunctional hematopoietic stem cells in the bone marrow, improve the immune system and adrenocortical functions, play an synergic action on the tumor-depressing effect of chemotherapeutic drugs, depress the blood flow of cancer cells and the metastasis of lymph, and obviously prolong the survival time of tumor-bearing mice.

Zhejiang Provincial Hospital of TCM has conducted research on *semen coicis* (herbal medicine) used for cancer therapy. The main effective ingredient of *semen coicis* for cancer therapy is coixenolide. Experimental research has showed that if the herbal medicine was made into intravenous emulsion, it can depress cancer cells directly. The emulsion had a significant depression effect on a variety of experimental animals with lung cancer, liver cancer, and colon cancer. This lipid prescription can provide high-energy nutritive elements totaling eight times higher than 10% of glucose solution and obviously improved immunity of the body.

Artesunate is a kind of anticancer drug extracted from southernwood. In vitro and in vivo experimental studies show that the anticancer mechanism of artesunate is related to its direct killing effect on cancer cell strains, related to the induction of apoptosis, or even related to its inhibition of tumor angiogenesis, and so on. The molecular mechanism in inducing apoptosis is related to the lower adjustment of *bcl-2* gene, and the influence on the activity of topoisomerase, etc., through the approach of p53 nondependence. Artesunate intravenous injections and intramuscular injections have positive anticancer effects on liver cancer and nasopharyngeal cancer of mice; their effective doses and modes are different in different studies. Further research is needed to determine the best application mode and dose.

4.1.2.2 COMMON CLINICAL SYNDROME RESEARCH

The TCM syndromes of cancer in a special development stage have their own characteristics. These syndromes reflect not only the status and degree of the body's internal yin, yang, qi, and blood disorders but also the nature, location, and extent of the environmental disorder in the body. The TCM syndrome type of cancer patients usually reflects accurate diagnosis and guides the rational choice of drugs. It can provide a more comprehensive and accurate basis for the development of cancer treatment options. Cancer is a complex disease; it is a local performance of systemic disease. In addition to the modern medical diagnosis like anatomic site, histological type, cytology, and others, all kinds of clinical syndromes at different stages of disease need to be considered, such as various deficiencies, qi stagnation, blood stasis, tanning, and toxic heat. During, or before and after, the applications of abrasive therapies like surgery, radiotherapy, and chemotherapy, and depending on different performances of clinical syndromes, syndrome differentiation treatments are taken. Local and

systemic treatments are combined and targeted. The therapy is comprehensive, and the effect is significantly improved. Due to the pathological injuries caused by a variety of cancers, which varies from person to person, and due to illness, all kinds of syndromes and the performance law need to be grasped based on the theory of TCM. We need to find out how many kinds of syndromes (syndrome type) there are and the intrinsic links among these syndromes. These syndromes are comprehensive reflections of the patient's body's pathophysiological, biochemical, and pathological changes. In different stages of the same disease, these changes are different, so the clinical syndromes change along with the course. It is stressed in Chinese medicine treatment that the overall concept needs to be considered. It attaches importance to the macroregulation of the patient's physiological function. On the basis of dialectical rules of TCM, treatments are formulated from person to person. The use of herbal medicines aims to improve the internal environment of the body in a direction that is not suitable for cancer recurrence and metastasis.

In recent years, some researchers have found in cancer syndrome studies that certain biochemical indexes were only related to certain syndromes and have nothing to do with the pathological types of cancer patients. For example, the determination of serum gastrin shows that it is lower if spleen syndrome and qi and blood are deficient. But it is not low if qi stagnancy and blood stasis syndromes are present; its value can even increase when phlegm dampness is present. The content of serum gastrin in blood has nothing to do with diseases such as gastric cancer, intestinal cancer, and breast cancer, which shows that the syndromes of TCM have a close relation with the physiological changes and also shows the significance of TCM syndrome differentiation. At present, TCM syndrome differentiation on which more research has been conducted includes syndrome of blood stasis due to qi deficiency, syndrome of qi stagnation and blood stasis, qi blood deficiency syndrome, syndrome of hyperactivity of fire due to yin deficiency, qi and yin deficiency with phlegm and blood stasis, syndrome of water overflow due to yang deficiency, syndrome of yin–yang disharmony, syndrome of phlegm dampness due to spleen deficiency, syndrome of yang deficiency of spleen and kidney, and syndrome of noxious heat damaging yin.

4.1.2.3 PHARMACOLOGICAL RESEARCH ON ANTICANCER HERBAL MEDICINES

During the cancer treatment process, TCM emphasizes pharmacological research against cancer, and many researchers have revealed the anticancer effects of various herbal medicines from different aspects. In recent years, a series of achievements have been made in the research on anticancer herbal medicines and their effective ingredients, with a large number of herbal medicines being discovered with anticancer effects, which have been playing significant roles in treating cancer with syndrome differentiation clinical TCM.

According to the effects and functional characteristics of herbal medicines, their applications during anticancer therapy can be summarized into the following categories: drugs for reinforcing the vital energy and consolidating the constitution, drugs for clearing heat and removing toxicity, drugs for promoting circulation and removing stasis, drugs for resolving phlegm and removing stasis, and purgative drugs.

The anticancer mechanisms of herbal medicines mainly include the following: direct depression of cancer, adjustment of the body's immune function, obstruction of carcinogens and antimutagenic effect, depression of hyperplasia of cancer cells, induction and differentiation of apoptosis effect, reduction of radiotherapeutic and chemotherapeutic toxic reactions, depression of cancer metastasis, anti-inflammatory and toxin-expulsion effect, oxidation-resistant and free radical–scavenging effect, and radiation-resistant effect.

4.1.3 Clinical research in traditional Chinese medicine on cancer

4.1.3.1 CANCER THERAPY WITH ANCIENT PRESCRIPTIONS

Liuwei Dihuang Pill: It is composed of *prepared rehmannia root, medical dogwood, common yam rhizome, oriental water plantain rhizome, tree peony bark*, and *Poria cocos Wolf.* It is a kidney yin–nourishing fundamental prescription, suitable for cancer patients with symptoms after chemotherapy such as dizziness and tinnitus, dysphoria with feverish sensation in chest, tidal fever and night sweating, soreness and weakness of waist and knees, thirsty mouth, red tongue with scant liquid and a little fur, and fine and sunken

string-like pulse. This prescription can depress the immunologic function of antihormone, confront hormone and cyanide mustard on normal cells of the body, promote the immunity of cells, and enhance the immunity and monitoring functions of T cells. It also allows active hyperplasia of the germinal center of animal's spleen and lymph after chemical carcinogen treatment; it strengthens the phagocytic activity of the mononuclear phagocyte system and increases the survival time of tumor-bearing cells at the earlier period of inoculation.

Yougui Pill (drink): It is composed of *aconite preparation, cinnamon, prepared rehmannia root, medical dogwood, deer-horn glue, barbary wolfberry fruit, dodder seed, eucommia bark*, and *angelica*. It is a common medicine for warming and recuperating kidney yang, suitable for cancer patients after chemotherapy with pale or dark complexion, thin figure, cold limbs, soreness of waist and back, myasthenia of limbs, thin sloppy stool, frequent nocturia, impotence and seminal emission, pale tongue and fat figure, and fine and sunken pulse. This prescription has an obvious improvement effect on the phagocytic rate of phagocytes and conversion rate of T cells in cancer patients. A large dose of cortisone is applied to the shaping of mice (syndrome of yang deficiency of kidney), resulting in volumetric atrophy and a decrease in lymphocytes. After the application of Yougui Pill, lymphocytes in the spleen increase and the lymph node of the thymus and the N-Ease response of the adrenal cortex are strengthened accordingly, showing that Yougui Pill can strengthen the immune effect on cells.

Yupingfeng Powder: It is composed of *astragalus root, white atractylodes rhizome*, and *ledebouriella root* and is a fundamental prescription for nourishing the lung, benefitting vital energy, and consolidating superficies; it is suitable for patients after chemotherapy with deficiency of lung qi and insecurity of the defensive exterior. It is often applied to prevent and cure the diseases of patients with chilliness, frequent sweating, shortness of breath, chronic cough, liability of cold, and pale tongue with whitish fur. This prescription aims to lower the higher immune response and raise the lower immune response of patients. As a main ingredient of this prescription, *astragalus root* can improve the defensive power of the nasal mucosa surface; enhance the capacity of leukocytes in inducing interferon; and promote the phagocytic function, formation of immune globulins, and increase in T cell quantity and conversion of lymphocytes.

Sijunzi Decoction: It is composed of pilose asiabell root, white atractylodes rhizome, Indian bread, and prepared liquorice root. It is the fundamental prescription and representative prescription for tonifying qi and nourishing spleen and is suitable for patients with symptoms such as shortness of breath and hypodynamia, lusterless complexion, poor appetite, abdominal swelling at noon or night, thin sloppy stool, pale tongue that has white and moist fur, and slow or weak pulse. This prescription can well promote the conversion rate of lymphocytes and formation of active rosettes.

Shengmai Drink: It is composed of ginseng, lilyturf root, and *Schisandra chinensis* (Turcz.) Baillon. It is a famous prescription for benefiting qi and nourishing yin suitable for patients with lung deficiency and deficiency of both qi and yin after chemotherapy, including symptoms such as dry cough, less sputum, anemophobia, sweating, low voice, shortness of breath, light-red tongue, white furred tongue, and weak pulse. This prescription can enhance the immune function of cells depressed by cellular immune depressors (including anticancer chemotherapy drugs) and has an obvious activation effect.

Bazhen Decoction: It is composed of Sijunzi Decoction and Siwu Decoction (Chinese angelica root, rhizome of Sichuan lovage, white peony root, and prepared rehmannia root). It is a fundamental prescription for benefiting qi and nourishing blood, suitable for patients with spleen deficiency and deficiency of both qi and yin after chemotherapy, including symptoms such as shortness of breath, a sallow complexion, pale nails, dizziness, poor appetite, thin and sloppy stool, pale tongue with thin coating, and fine and sunken pulse. The Siwu Decoction can promote immune function of cells and phagocytic function of phagocytes when it is used to tonify the blood.

Xuefu Zhuyu Decoction: It is composed of Chinese angelica root, dried rehmannia root, peach kernel, safflower, rhizome of Sichuan lovage, red peony root, achyranthes root, fructus aurantii, licorice root, and Chinese thorowax root. The pharmacological research indicates that due to this decoction, cancer cells can be depressed by self immunocompetent cells, reduce the coagulation of blood platelets, and decrease the metastasis of cancer.

4.1.3.2 TRADITIONAL CHINESE MEDICINE INJECTION FOR CANCER THERAPY

The clinical effect of TCM injection on cancer has been preliminarily confirmed. The anticancer TCM injection acting on the human body is characterized by multiple directions and multiple targets, in line with the mechanism of multiple factors and multiple links of pathogenesis. Although the direct depression effect of TCM injection is weak compared with chemically synthesized drugs, its application range is wider due to its advantages such as less toxic and side effects, uneasy generation of drug resistance, and obvious integrative anticancer effect. The research on its effect mechanism will provide a theoretical basis for clinical therapies so as to direct clinical applications. In recent years, research on the anticancer mechanism of TCM injection has mainly included cytotoxic effect on cancer cells, depression of new blood vessel formation, antimetastasis effect, synergic action and toxic reduction of radiotherapy and chemotherapy, reversion of multiple drug resistance, induction of cell differentiation, and immune adjustment.

4.1.3.3 EXTERNAL APPLICATION OF TRADITIONAL CHINESE MEDICINE FOR CANCER THERAPY

There are records about external application for cancer therapy in *The Medical Classic of the Yellow Emperor*, and external application has been developed and gradually become mature in the past dynasties. Wu Shiji, a famous therapist in the Qing Dynasty, thought, "The external therapy principle is also the internal treatment principle; the drug used for external therapy is also used for internal treatment, with differences between them depending on therapeutic methods." The medical principles and properties are identical, but the therapeutic methods are as variable as magic, because they can be used not only for refractory diseases but also as first aids in endless fields. Also, external therapy is characterized by no prohibition, no obstruction, no containment, and no adhesion.

4.1.3.3.1 Effect

External therapy of TCM is characterized by obvious effects, no invasion, cheapness, easy acceptance, easy popularization, and no addiction; therefore, it is of increasing interest to patients. At present, a variety of clinical methods are used integratively for root diseases, and they can not only "eliminate pathogenic factors" but also "strengthen the vital Qi," highlighting the characteristics of TCM therapy. When cancer enters the advanced stage, it is difficult for the patient to take oral medications because of poor gastrointestinal function, which can affect the drug absorption and effect of drugs. At this point in time, external therapy of TCM has its unique advantages. The applications of external therapy of TCM during tumor therapy are mainly summarized as follows:

Anticancer and acesodyne: Cancer pain is one of the most agonizing symptoms. For patients with advanced cancer and is also an important factor affecting the quality of life; pain brings physical and mental sufferings to cancer patients. Accordingly, the effective control of cancer pain is one of the most difficult challenges during tumor therapy. The external application of TCM has better analgesic effects on cancers. Its effect is persistent but slow, with few side effects.

Inducing diuresis for removing edema, used for tumor complications such as pleural effusion and ascitic fluid: Malignant pleural effusion and ascitic fluid are common complications in malignant cancer patients, most of which result from disease progression or recurrence; they are also regarded as the initial clinical representation of cancers. Pleural effusion is usually present in lung cancer, breast cancer, and lymphoid tumor. Ascitic fluid is common in liver cancer, gastric cancer, colorectal cancer, ovarian cancer, and peritoneal cancer. The Western medicine therapies on malignant pleural effusion and ascitic fluid are mainly based on constitutional drug administration and intracavitary and intraperitoneal injection of drugs, which have certain therapeutic effects on some patients. In addition, the therapeutic effect can be improved and pains can be relieved if they are combined with the external application of herbal medicines.

Softening and resolving hard mass for dispelling cancer: The softening and resolution of hard mass is classified in dispelling therapy in the principle of TCM. "Dispelling any hard mass" is a common method for treating pathological symptoms during TCM therapy, such as accumulation, abdominal mass, osteoma

osseous tumor, and breast cancer. As for the therapy, its drug administration is not extremely strong, but its long-term application can depress the vital qi. It can be applied properly under better body conditions of early cancer patients, with positive therapeutic significance. As for intermediate-advanced cancers, however, the vital qi is much weaker because the diseases have rooted deeply for a long time, and overdispelling often causes even weaker vital qi. Therefore, as for the application of these drugs, indications must be mastered soundly and their applications must depend on the body conditions of patients.

4.1.3.3.2 Routes of administration

For external therapy, drug administration is mainly made through routes such as skin and mucous membranes.

Transdermal drug delivery: The drugs are assisted by a skin penetrant to penetrate into the epidermis, enter capillaries, and then enter the blood and tissues through the capillaries; afterward, they gather in the tumor location with rich blood vessels and exert their effects.

Umbilical compress therapy: It has the same advantages as transdermal drug delivery, and the umbilicus has high absorption and utilization rate of drugs. It has its own uniqueness for therapy on some diseases. Therefore, umbilical compress therapy can be used to relieve the pains caused by tumor infiltration and oppression on liver and part of intercostal nerves, upper and middle abdominal organs, and visceral peritoneum and viscera layers.

Acupoint injection: As for acupoint drug administration, it brings about both quick drug effect and doubling of drug effect. Experiments show that meridian acupoint administration can amplify and enhance the effect of drugs.

Mucosal administration: The administration is made mainly through mouth, eyes, nasal mucosa, vagina, and rectal mucosa. The absorption rate of mucosal administration is better than skin; with relatively stable drug effect and particularly high concentration of drugs in the administration sites, the drug effect is increased. However, we need to pay attention to the irritation and damage caused by drugs on skin and mucous membranes to avoid the increase in sufferings of patients.

Gargling or fumigation and washing therapy: Gargling means that drugs are boiled into decoction, which is gargled in mouth and disgorged without swallowing. It is mainly used for patients with oropharyngeal cancers, oral mucous membrane response caused by radiotherapy or chemotherapy, oral cancer, and nasopharyngeal carcinoma. Considering its special anatomical location, sipping application, mouthwash, blowing the nose, and medical gas fumigation can be applied from time to time to increase the concentration of drugs in the focus site. Materials such as mints, fortune eupatorium herb, and raw licorice are commonly used.

Fumigation and washing: Fumigation and washing therapy means that drugs are boiled into hot decoction, which is then used to fumigate and wash the skin or affected places. For patients with brachioneus caused by radical treatment of breast cancer and lower leg swelling caused by lower limp inguinal region lymph node metastasis, fumigation and washing as well as dipping of affected legs for detumescence can be conducted by a decoction with *rhizome of Sichuan lovage, frankincense, myrrh, plantain seed*, and *Indian bread* so as to relieve suffering.

Enema: Enema is a method in which drugs are made into liquid and injected into diseased regions through an enema syringe, which is inserted into the affected parts. For patients with colorectal cancer, apply enema with a decoction of *dandelion, coptis root, sargentgloryvine stem, prepared rhubarb, Gleditsia sinensis*, and *pleione rhizome*, so that the drugs reach the affected areas and act on the foci directly through mucous membranes, which can attack evil toxicities, fight against cancers, and relieve pains, thus improving the quality of life.

Foot bath: Cancer patients with high blood pressure or head sweating or asthma can take foot baths with a decoction of *anemarrhena rhizome, cassia bark, peach kernel*, *rhizome of Sichuan lovage*, and *Cyathula officinalis* to disperse internal heat and induce qi for recovery.

Esophageal paste: When patients have difficulty in swallowing, they can triturate *notoginseng, sal ammoniac, root of subprostrate sophora*, and *arnebia root*, which are combined with lotus root starch for swallowing; this can be helpful in improving the esophageal obstruction symptom.

External application of plaster: The Longhua Hospital affiliated with Shanghai University of TCM, the third factory of Shanghai TCM Pharmaceutical Factory, has developed toad venom paste to treat malignant tumors. This prescription is a TCM adhesive plaster composed of 18 drugs, such as *bufonis venenum, aconite root, prickly ash root, lilac flower, cassia bark, asarum, Paris polyphylla,* and *safflower.* This plaster can be used for various cancer pains, with sound therapeutic effect.

4.1.4 Traditional Chinese medicine detoxification therapy

TCM detoxification therapy for cancer means that toxins in the human body after medication can be exhausted through various channels such as the nose and mouth, as well as two lower orifices, so as to reach the purpose of therapy. Therefore, it is necessary to conduct further research from the original meaning of "toxin," tumor etiology and pathogenesis, and the basic principles of detoxification therapy to result in new progresses and breakthroughs of TCM therapy on cancer.

There are eight detoxification therapies in TCM, namely, sweating, emetic therapy, purgative therapy, mediation method, warming method, heat-clearing method, resolving method, and tonifying method. Their effects are not only in eliminating toxins, but they can also treat the diseases.

Cancer is derived from evil toxins, with prevailing pathogenic factors. Clinically, it is found that cancer is characterized by fierce disease condition, rapid change, high mortality, long course of disease, and uneasy radical treatment. According to the aforementioned characteristics and viewing from the angle of TCM, the tumor mortality of human body results from severe dysfunction of the viscus under evil toxins. The body loses the balance between yin and yang, with prevailing pathogenic factors, which then form a pathological state in which yin and yang are too strong or too weak, yin cannot control yang or otherwise, yin and yang are mutually damaged, or yin and yang die out. If the pathogenic factors continue to prevail, it will result in further development of dysfunction, separation of yin from yang, and even death.

Accordingly, TCM detoxification therapy is used to treat cancer; eliminate blood stasis by catharsis and adjust yin–yang disharmony, so as to reach the purpose of recovery of yin–yang balance; and cure cancer by expelling pathogenic factors, rectifying deviations, and correcting maladies.

4.1.4.1 Toxin-expelling approaches

Toxin expulsion by TCM is conducted through the following ways: discharging fire and relaxing the bowels, diuretic dampness detoxification, sweating, diet detoxification, emetic detoxification, and acupuncture bloodletting.

4.1.4.2 Toxin-expelling methods

Incidences of cancer keep rising, which are associated with the accumulation of harmful substances in the human body. TCM believes that substances that can hurt people are called toxins. Toxins are divided into noxious dryness, virulent fire, damptoxin, yin poisoning, poison of alcohol, epidemic pathogenic factor, and so on.

Counteracting toxin with toxin: It means that some poisonous herbal medicines are used to attack pathogenic factors by their severe characteristics and counteract cancers by toxins. Because cancers are inveterate evil diseases and their pathogenic factors are rooted deeply, it is very necessary to counteract them. Therefore, some poisonous drugs are usually applied, and the procedure is called counteracting toxin with toxin.

The method of counteracting toxin with toxin must be applied under the condition that vital qi still exists and can be tolerant. When it is applied clinically, the dosage, usage, and application time of drugs must be well considered to achieve the expected effect.

Removing toxin with toxin: It uses toxic drugs to expel tumor tissues out of the body through skin and the seven apertures, most of which are expelled through the two lower orifices. Common herbal medicines such as *rheumofficinale, Chinese blister beetle, scorpion, centipede, arisaema*, and *raw pinellia* have a high clearance rate for tumor tissues. *Raw pinellia* and *cantharidin* have significant effects on lung cancer and bladder cancer. If combined with the use of *rheumofficinale*, it has the functions of resolving hard lumps and eliminating toxins.

Detoxification by toxin: Malignant cancer patients, especially those with middle-advanced tumors, often suffer from symptoms such as fever, lump enlargement and local causalgia, pain, thirst, constipation, reddened tongue with yellow fur, and rapid pulse, all of which are symptoms of pathogenic heat and toxic stasis, for which the therapy of clearing heat and removing toxicity must be applied.

4.1.5 Traditional Chinese medicine immune therapy

The Medical Classic of the Yellow Emperor first proposed some arguments: "If the vital Qi itself was sufficient and the vital essence and energy remain in the body without leakage, how can a disease happen"; "if the vital Qi is present, no pathogenic factor can invade"; "if pathogenic factors gather sufficiently, the vital Qi must be weak"; and so on. It proposed the basic therapeutic principle of strengthening vital qi to eliminate pathogenic factors.

As for cancer, once normal cells of the body have become "dissidents," the body's immune system will exclude these mutant cells through the immunologic rejection reaction, to avoid the occurrence of any tumor. Vital qi coordinates meridians and qi and blood in the viscera, and they are interdependent and interinhibitive: the "interrestriction can generate mutual balance" so that the viscera is harmonious, the meridians are clear, and qi and blood flow freely without the formation of any phlegm and blood stasis to avoid the occurrence of any accumulation.

In a word, any "non-self" substance that can stimulate the body to produce immunologic rejection reaction can be called a "pathogenic factor." Immune reaction just means "competition between vital Qi and pathogenic factors." Vital qi and immune function, competition between vital qi and pathogenic factors, and immune reaction are the cognitions of TCM on immunity. The cognitions of TCM on human immunity are mainly based on discussions of the relations between defensive qi and immunity; lung, spleen and kidney, and immunity; meridian, qi and blood, and immunity; strengthening vital qi to eliminate pathogenic factors and immunity; and so on.

4.1.5.1 HERBAL MEDICINES WITH IMMUNE FUNCTION

In recent years, new progress in research on herbal medicine has been seen in terms of promoting and regulating the immune function of human body. It is generally believed that all the drugs used in TCM that support healthy energy have immunologic enhancement. As for research on herbal medicines from the angle of tumor immunity, most of them include the following types: supplementing and strengthening body resistance, promoting blood circulation and removing blood stasis, clearing heat and removing toxicity, softening and resolving hard mass, resolving phlegm, animal drugs, and aromatic resuscitation.

Medicines for supplementing and strengthening body resistance: Commonly used herbal medicines include *ginseng, codonopsis pilosula, astragalus root, asparagus cochinchinensis, acanthopanax root, psoralea fruit, glossy privet fruit, semen coicis, wolfberry fruit, tortoise plastron, freshwater turtle shell, juglans maxim's branch*, and *cordyceps sinensis*, of which *ginseng*, *acanthopanax root*, and *glossy privet fruit* can enhance the immunity of the body. Pharmacological research has found that this type of medicines can regulate the immune function of the body and strengthen the nonspecific immune function of the body.

Medicines for promoting blood circulation and removing blood stasis: Such medicines mainly include *red peony root, root of red-rooted salvia, safflower, podophyllotoxin, Japanese dock root, herb of Chinese sage, crisped dock root, Tripterygium wilfordii*, and *garden balsam seed*. These herbals have been proved to have some depression effect on some tumor cells through experiments on animals.

Medicines for clearing heat and removing toxicity: Such medicines mainly include *Hedyotic diffusa, Solanum lyratum Thunb, black nightshade, barbed skullcap herb, radix sophorae subprostratae, radix actinidiae argutae, rhizoma bistortae, hornet nest, flavescent sophora root*, *rhizome of many leaf Paris, kirilow groundsel herb, Baikal skullcap root*, and *buffalo horn*.

There are a variety of medicines for clearing heat and removing toxicity, with different properties and relatively particular therapeutic orientations. Some medicines can excite the reticuloendothelial system and enhance the phagocytic capacity of cells; for example, buffalo horn can increase the number of lymphocytes

and excite the adrenal cortex and hornet nest can improve the function of T lymphocytes and depress humoral immune function.

Medicines for softening and resolving hard mass: Such medicines mainly include *pseudobulb of appendiculate cremastra*, *brunellae spica, raw oysters, and ranunculus ternatus thunb*, and so on. The medicines for softening and resolving hard mass and dispelling phlegm have depression effects on tumor cells such as S180, WK256, S37, and so on. The medicines for dispelling phlegm, such as pinellia tuber, *Chinese honeylocust spine, fructus trichosanthis, rhizoma arisaematis, sal ammoniac*, and *air potato yam*, have depression effects on the tumor cell S180, and *pinellia tuber* also has immunologic adjuvant function.

Animal medicines: Such medicines include *donkey-hide gelatin, tortoise plastron, pilose antler, batryticated silkworm*, and *freshwater turtle shell*, and so on, all of which can improve the lymphocyte transformation rate and have similar immunologic adjuvant functions. *Pilose antler* can promote the formation of hemolysin antibodies of mice and improve their serum agglutinin potency and has obvious activation effect on the depression of the monocyte–macrophage system caused by hydrocortisone and cyclophosphamide. It can also strengthen the phagocytic indexes of phagocytes in livers and spleens of mice and increase the thymic weight of mice. The medicine shows enhancement effects on the immunity of cells and blood fluid of the body to a different extent, which may be the important pharmacological basis of pilose antler in "generating essence Qi and tonifying marrow, nourishing blood and benefiting Yang." Batryticated silkworm has a depression effect on tumor cell S180, freshwater turtle shell can prolong the survival time of antibodies, and placenta lipopolysaccharides can enhance the immunity of cells and body fluid.

Aromatic resuscitation medicines: Such medicines include *musk*, which can enhance the immunity of cells. Research on Chinese patent drugs like Meihua Dianshe Dan have proved that the medicines can increase the weight of normal mice and tumor-bearing immune organs and can antagonize the immunosuppressive effect of cyclophosphane. They can also improve the peritoneal macrophages' phagocytic function of normal mice, mice depressed by cortisol, and tumor-bearing mice.

4.1.5.2 IMMUNE MECHANISM

In accordance with the immunity-activating condition, herbal medicines with immune effect can be divided into three categories: medicine promoting the reticuloendothelial system, medicine promoting the immunity of body fluid, and medicine promoting the immunity of cells.

Herbal medicines promoting the reticuloendothelial system: Such medicines include those tonifying qi, nourishing yin, activating blood circulation to dissipate blood stasis, and clearing heat and removing toxicity, such as ginseng, *astragalus root, Codonopsis pilosula, bighead atractylodes rhizome, liquorice, glossy ganoderma*, Chinese yam, and Solomon's seal. They can significantly enhance the phagocytic function of the endothelial system and sterilization ability of the spleen. Its mechanism is to enhance the body's nonspecific immune response. Yin-nourishing drugs like turtle shell and oyster have significant functions of stimulating the phagocytosis of the reticuloendothelial system. Blood circulation–promoting and blood stasis–removing drugs like the root of red-rooted salvia, *radix paeoniae rubra, peach kernel, rhizoma sparganii*, and *curcuma zedoary* can excite the reticuloendothelial system to release a large number of macrophages, improve the vitality of serum opsonin, and enhance phagocytosis of leukocytes. Heat-clearing and detoxifying drugs like honeysuckle, common andrographis, *cordate houttuynia, subprostrate sophora, flos chrysanthemi indici, coptis chinensis*, and *Scutellaria baicalensis* can promote phagocytosis.

Medicine promoting the immunity of body fluid: Includes medicines regulating specific and nonspecific immunities of the body fluid. Such medicines include *astragalus mongholicus* and ginseng, which can increase γ-globulin; *platycodon root*; and *flosdaturae*, which can increase lysozyme activity.

Medicine promoting the immunity of cells: Mainly refers to herbal medicines with induction effect of interferon, such as *astragalus mongholicus, dulcamara, acanthopanax root, rhiizoma dioscoreae from Hena of China, radix glehniae, placentahominis, dendrobe, towel gourd, pericarpium trichosanthis, gentiana scabra bunge, root of red-rooted salvia*, and so on.

4.2 HYPERTHERMIA INTEGRATED WITH CHELATION AND DETOXIFICATION THERAPY

4.2.1 Cancer hyperthermia and chelation detoxification

Vitamin C is the most necessary and common vitamin for the human body. Recent studies have shown that it has anticancer effects under proper dose, which is directly related to the metabolite of vitamin C in the human body; this is called the "hydrogen peroxide" (H_2O_2) theory. Based on this theory, the combination of hyperthermia with vitamin C has a synergistic effect. First of all, in the early stage of heating the circulation of both normal tissues and cancer tissue can be improved and drug perfusion can be increased accordingly. At this time, with the application of vitamin C, blood circulation passages of normal tissues that are usually unopened can be opened sufficiently when hyperthermia is applied, and drug perfusion is increased relatively. Then, vitamin C will exert its effect on the scattered cancer cells, remove the free radicals and harmful cell factors, maintain the intrinsic environment stability, and enhance immunity. In the later stage of heating, due to imperfect growth of blood vessels in the cancer tissue, low blood flow in the tumor tissue, blood stasis, tissue hypoxia, fall of pH value, rise of intratumor venous pressure, low intratumor perfusion, low inflow of raw materials, and low discharge of metabolites, hypoxia of the tumor tissue center and necrosis will occur. Hence, the anticancer effect of hyperthermia can be realized, which forms a complementary relation with vitamin C. So, the combination of hyperthermia and a large dose of vitamin C can exert a better effect only at the early stage of hyperthermia. Clinically, it is found that the combination of hyperthermia with a large dose of vitamin C during radiotherapy and chemotherapy can obviously increase the radiotherapeutic effect and relieve toxic and side effects. It can especially relieve liver injuries due to chemotherapy and the damage on normal tissues in the area of radiotherapy.

In addition to vitamin C therapy, colon cleansing detoxification therapy is also an important part of detoxification therapies. Colon cleansing detoxification therapy contributes to the positive regulation of immunity by removing intrinsic toxins and plays an important role in prevention and curing of tumors. In addition to the anticancer effect, hyperthermia can also improve the metabolism of normal tissues. The combination of whole-body hyperthermia with colon cleansing detoxification therapy can effectively improve metabolism; promote the discharge of metabolic wastes; and benefit the prevention of occurrence, recurrence, or metastasis of tumors.

4.2.2 Development history of chelation and detoxification therapy

Chelation and detoxification therapy is derived from Western medicine and is a natural therapy. The word *chelation* comes from Greek, meaning that a crab bites something without any damage to itself. Hippocrates, the originator of Western medicine in ancient Greece, proposed the therapeutic concept of chelation and detoxification therapy. He hoped that there were some methods that could eliminate toxins from the human body without any adverse effect on the health and organ functions of the human body. More than 10 centuries have passed and although harmful toxins are continuously being found and their damages to human health are clearly increasing, no ideal chelation and detoxification therapy has been found. The main reasons include the following: the body's own detoxification functions are limited and the liver, as the most important detoxification organ, can remove part of the pathogen toxins such as bacteria and viruses, as well as toxic products, through metabolism, but unfortunately the liver itself can suffer damages to different extents during detoxification. For some toxins, particularly heavy metals such as lead, mercury, arsenic, cadmium, thallium, and barium and radioactive elements such as radium, uranium, strontium, and X-ray, the liver and other organs have no detoxification function available. Therefore, all of them can not only result in death due to acute and severe poisoning but also accumulate slowly in bones, viscera, and nervous tissues to form chronic poisoning, which can endanger the body, and cause difficulties to the therapy.

In 1893, Prof. Alfred Werner, a Swiss chemist and winner of the Nobel Prize, began preliminary research on chelation and detoxification therapy. He explained the biochemical mechanism and clinical representation of human body poisoning resulting from the combination of heavy metals including lead and mercury with special proteins in the human body. He began with animal experiments and obtained reliable laboratory evidence; then, he cooperated with clinical doctors. His research achievements first proved that some heavy metals entering the human body from the outside were poisonous substances, which could be combined with special proteins in the human body to cause damages to human organs and tissues, while the human body had no detoxifying function against the heavy metals and their conjugates. Even though there was no special antidote for heavy metals, Werner's research indicated the direction of chelation and detoxification therapy and resolved key theoretical problems. For this reason, he is called the father of chelation and detoxification therapy by later generations.

The chelation and detoxification therapy for cancer has significantly progressed over the years. In the 1970s, medical experts led by the famous American scientist Cameron and two-time winner of the Nobel Prize Prof. Pauling first used chelation and detoxification therapy combining large doses of vitamin C during integrative cancer treatments and achieved good therapeutic effects. The chelation and detoxification therapy for cancer has reliable evidence and experimental medicine bases. According to Prof. Pauling et al., a large scale of clinical epidemiological data proved that a lot of poisonous heavy metals, such as lead, mercury, cadmium, arsenic, and nickel, are carcinogenic substances and might cause cancer in organs and tissues such as respiratory tract, digestive tract, mammary gland, skin, and blood. In recent years, research has shown that some cancers in some places are abnormally accumulated with heavy metals. Therefore, when surgeries, chemotherapies, and radiotherapies are applied to patients with cancer, a large dose of vitamin C can be used to expel the intrinsic toxins. For patients with heavy metals exceeding the standard, ethylenediaminetetraacetic acid (EDTA) therapy combining vitamin C (which is a chelating agent itself) must be applied to remove the heavy metals, which can not only enhance the therapeutic effect and promote the healing of surgical incisions but also relieve the side effects of radiotherapy and chemotherapy. For some patients, especially patients in the advanced stage or those with severe bone marrow suppression and severely damaged immunity, chelation and detoxification therapy combining vitamin C can improve the constitutional conditions, relieve bone marrow suppression, enhance the immunity, prolong the survival period, and improve the life quality. Prof. Stevens conducted in-depth research on the relationship between heavy metals and cancer, confirming that the combination of heavy metals with proteins in cells of the body can generate gene mutation. Chelation and detoxification therapy is applied to depress or remove gene mutation of cells and prevent or control early on the carcinogenesis of cells.

In conclusion, chelation and detoxification therapy has experienced a long and tortuous journey from idealism to reality, and it did not develop rapidly until the recent half century. Clinical indications have expanded gradually, the quality of pharmaceutical preparations has been improved continuously, and the clinical effect has been recognized widely. The application of chelation and detoxification therapy during tumor therapy has progressed significantly. It is also an important part of nontoxic integrative treatments and plays an important role in modern therapy of cancer.

4.2.3 Trace elements, heavy metals, and cancer

4.2.3.1 Importance of trace elements on human health

Under normal conditions, there are some special trace elements in the human body such as sodium, potassium, calcium, magnesium, phosphorus, iron, copper, zinc, and selenium, all of which play important roles in the metabolic processes of the human body. Therefore, they are considered the essential trace elements of the human body.

In 1996, it was first reported in the medical field that supplementation of selenium can prevent cancer, which was followed by many similar reports. Navarro believed that supplementation of selenium can prevent prostate cancer and lung cancer to some extent. In 2005, Prof. Trumbo, serving in the U.S. Food and Drug Administration (FDA), analyzed selenium and clinical epidemiological data on tumor prevention and

reached a preliminary conclusion: long-term regular selenium supplementation can reduce the risks of prostate cancer, lung cancer, and colon cancer. Currently, it is proposed that selenium supplementation is required during integrative treatments on cancer patients, for which single selenium preparation can be applied, and it is better to use compound preparation of a variety of vitamins and essential trace elements. It can be replenished daily and applied for a long time. If selenium deficiency of the human body is found, selenium can be supplemented through parenteral nutrition. Now, scientific research regarding the prevention and therapy of cancers through supplementation of selenium is still continuing, and it is expected that impressive achievements will be available in the next few years.

4.2.3.2 HEAVY METALS AND CANCER INCIDENCE

4.2.3.2.1 Carcinogenic mechanism of heavy metals

Since the mid-1970s, the medical field has paid much attention to research and investigation of cancers caused by heavy metals. Over 20 heavy metals have been used for animal experiments for long-term tracing, based on which it is now widely recognized that arsenic, cadmium, chromium, nickel, thallium, and beryllium have carcinogenic effects and lead, mercury, tungsten, and cobalt have synergistic carcinogenic effects. All of them can cause malignant tumors in humans and animals. In the medical field, carcinogenic effects of heavy metals have been identified for a long time, and their effects in the occurrence of cancers have been clarified gradually.

Any cancer occurring in the epithelial tissue is named cancer; cancerization first occurs in a single cell. The main differences between cancer cells and normal cells include the following: cancer cells have resistance to apoptosis, while apoptosis is a death form of normal cells; cancer cells have an uncontrollable differentiation capacity, which is called "immortality," whereas normal cells can grow and die orderly under the control of the body; cancer cells are not sensitive to the antigrowth factors of the body, whereas normal cells are controlled by the antigrowth factors; cancer cells have the capacity of altered differentiation, whereas normal cells do not; cancer cells have the ability to invade and destruct neighboring tissues and cells, and they also have the capacity of metastasis to distant places; and cancer cells can secrete special substances to stimulate blood vessels' proliferation of cancerous tissues and speed up metastasis. Cancerization starts with a single cell and clones repeatedly to form cancer cell lines and then cancer tissues. As a whole, cell cancerization is caused by cell gene mutation. Some heavy metals have been confirmed to cause gene mutations of normal cells, which is the main cancerogenic mechanism of heavy metals.

4.2.3.2.2 Common carcinogenic heavy metals

4.2.3.2.2.1 Carcinogenic toxicity of arsenic

Arsenic is an active and widespread heavy metal, with the atomic number 33. In the chemical elements, arsenic is a protean toxic element. Sometimes it seems to occur in the nonmetallic form; this characteristic is called allotropic form. It is usually known from the poison "white arsenic," with the chemical name of arsenic trioxide. Toxicity of arsenic manifests in many ways; it has contact toxicity, causing inflammation and necrosis of the mucous membranes of the skin, and mostly it causes damages to the viscera, such as heart, liver, kidney, bone marrow, and brain. The human body has no detoxification function for arsenic, which can cause acute and chronic poisoning. Insurmountable environmental pollution provides a good opportunity for the toxicity of arsenic to spread, and consequently the contamination of drinking water has become a serious global problem. Studies show that incidences of cancer, especially gastrointestinal cancer, are significantly increased after the arsenic poisoning of large populations.

Arsenic is the number one direct carcinogen widely recognized by the World Health Organization (WHO) and the U.S. FDA. Arsenic can significantly depress the oxidative phosphorylation of the glucose metabolism process and reduce the production of adenosine triphosphate (ATP). Arsenic is an important factor and a free radical to trigger oxidative stress and can cause systemic inflammatory injuries. More seriously, arsenic can enter the cells to attack and damage chromosomes and DNA, causing gene mutation and thereby leading to cell canceration.

4.2.3.2.2.2 Carcinogenic toxicity of lead

Lead is an industrial product existing virtually everywhere. Vehicle exhaust is the largest lead pollution source, and the real "unleaded gasoline" is just a theoretical myth. Food and water pollution are common hiding places for lead. Lack of consciousness of environmental protection is the important reason for lead contamination. Chemicals, textiles, building materials, and furniture are the main sources of lead contamination. Therefore, it is difficult to prevent lead poisoning at present.

Lead is easy to accumulate in the human body, resulting in damages to the bone, heart, and lung and depressing the hematopoietic function. Lead is a direct carcinogen. It is found clinically that the incidences of lung cancer, skin cancer, kidney cancer, bladder cancer, and leukemia among patients with chronic lead poisoning are 2.5 times higher than those with no lead poisoning. If the patients are smoking, carcinogenicity is significantly enhanced; especially on lung cancer, it has a strong induction effect, which has been proved in animal experiments. Because lead is the most common heavy metal in environmental pollution and is difficult to be completely avoided in daily life, it is really necessary to carry out regular examinations, find excessive lead or lead poisoning as early as possible, and adopt chelation and detoxification therapy in time.

4.2.3.2.2.3 Carcinogenic toxicity of mercury

Mercury is an ancient metal known to humans from historic times. According to historical records, the Chinese and Egyptians found and used this metal in around 1500 BC, and it was named "quicksilver" for a long time due to its polymorphism. Up to now, mercury is still related to the human life. For example, medical sphygmomanometer and thermometer, as well as filling material commonly used for dental purposes, cannot work without mercury. Similarly, there is much mercury pollution in chemical, building material, cosmetic, weaving, and dyeing industries. Moreover, it can easily invade the human body from the respiratory tract or skin to cause acute or chronic poisoning due to its polymorphism and volatility; it can cause acute or chronic poisoning. There is a safe range specified by the WHO of the United Nations: the mercury in each kilogram of muscle of the human body shall not exceed 0.5 mg.

According to clinical and laboratory observations, mercury enters the human body easily and continuously through the respiratory tract, digestive tract, and skin due to its polymorphism and especially high volatility. The mercury content in poor-quality skin care products, hair dyes, and clothes has exceeded the health standards by 10–20 times. The carcinogenic toxicity of mercury has been confirmed: it can cause carcinogenesis of skin, kidney, bone marrow, nervous system, and connective tissues, and there are some common cases of leukemia and multiple myeloma caused by mercury poisoning. Therefore, the mercury content in blood must be inspected regularly and chelation and detoxification therapy should be applied to remove the mercury if it exceeds the standard to ensure health of the human body.

4.2.3.2.2.4 Carcinogenic toxicity of cadmium

Cadmium is a heavy metal with direct carcinogenic toxicity; its atomic number is 48. Purified cadmium is soft and can be cut with a knife. Cadmium is an important raw material in battery manufacturing, plastic industry, and electroplating process. For example, nickel–cadmium batteries are still widely used and cadmium exists in TV and computer components. Research and observation over many years show that cadmium is absolutely toxic to the human body and is not required by human tissues and metabolism. Even under a low concentration, it has strong toxicity. Cadmium has a strong tendency to accumulate, so it is difficult to be cleared completely. A major mechanism of cadmium poisoning lies in that it can block the metabolic enzymes activated by zinc ions and magnesium ions; these enzymes play important roles in liver function and cell oxygen exchange function.

In clinical practices, cadmium poisoning can lead to respiratory refractory infections and renal failure, as well as severe osteoporosis. In recent years, it was found that cadmium can cause lung cancer, bone cancer, kidney cancer, breast cancer, and malignant lymphoma. Moreover, the concentration of cadmium found in the pathological tissue of breast cancer patients is about five times higher than that in normal tissues. Therefore, it is significantly important to remove carcinogenic heavy metals during integrative treatments on cancer patients.

4.2.3.2.2.5 Carcinogenic toxicity of chromium

Chromium is a special heavy metal, and its atomic number is 24 in the periodic table of elements. It is very active and easily oxidizes in air to form diverse compounds, mainly including divalent, trivalent, and hexavalent compounds, whereas monovalent, tetravalent, and pentavalent compounds are relatively rare. Trivalent compounds are the most stable and nontoxic. The chemical characteristic of hexavalent compounds is the strongest, and their toxicity is also the highest. On the other hand, metabolism in the healthy human body does require a little trivalent chromium, which plays important roles in aspects such as normal glycometabolism, cardiovascular function, and coenzyme activity, so it is an essential trace element for the human body. In compound preparations of vitamins and trace elements, produced and sold widely in the United States, Switzerland, and the United Kingdom, traces of trivalent chromium are present. It is a strong oxidant, particularly used to clean and disinfect glassware, and it seems that no preferable compound now can replace it. The human body requires only a little trivalent chromium, and the rest of the chromium compounds are toxic to the human body.

4.2.3.2.2.6 Carcinogenic toxicity of thallium

Thallium is a very special and diversified heavy metal, with atomic number 81 in the periodic table of elements. It is used widely and has very strong toxicity; it is broadly recognized as a direct carcinogen. Thallium has significant polymorphism; its compounds can be colorless, odorless, and tasteless. Although the United States and many other countries expressly prohibit the use of thallium, many rodenticides and forest pests' preparations still adopt thallium. It still exists in industries such as photo and optical materials, semiconductor, and glass manufacturing due to its special electrical conductivity. The number of isotopes of thallium is up to 25, which are very active in the field of medicine. Radioisotope thallium-201 (half-life of 73 hours) is commonly used for diagnosis and condition assessment of cardiovascular disease. For nuclear magnetic resonance equipment, thallium is also used to manufacture key materials for conservation of high-temperature superconducting magnetic sources and nuclear magnetic imaging.

The toxicity of thallium includes skin contact toxicity, important organ damage, and fatal neurological toxicity. Carcinogenicity toxicity of thallium is more common in people who come into contact with thallium and its compounds, and they may suffer from skin cancer, lung cancer, liver cancer, brain cancer, and neurofibromatosis. According to research, thallium can cause genetic damage and mutations of many cells in the human body and can directly attack and damage cell mitochondria and nucleus. Carcinogenicities of thallium and arsenic are strong. In view of its strong toxicity but wide application in the industrial and medical fields, thallium poisoning including acute and chronic forms, and its clinical representations being complex and diversified, there is no effective antidote for it. All practitioners and medical personnel should be on the alert and pay attention to thallium poisoning.

4.2.3.3 HEAVY METAL DETOXIFICATION FOR CANCER PREVENTION

The increasingly serious heavy metal pollution is one of the main reasons for cancer incidence. Lead, mercury, arsenic, cadmium, nickel, and chromium are the main cancerogenic heavy metals recognized internationally. Their main cancerogenic mechanism is that their toxicities can cause genetic mutations of normal tissues and cells and lead to the decline of immune surveillance and regulation capacity of the human body, resulting in the cancerization of cells and occurrence of cancer due to the failure of the body to remove cancer cells. In recent years, in accordance with discoveries of medical scientists in the Occident, the contents of heavy metals such as arsenic, cadmium, and nickel are higher in the pathological tissues of patients with lung cancer, breast cancer, gastrointestinal cancer, and so on than in those with normal tissues. Additionally, clinical epidemiology investigations made by the medical and health fields of all countries have further shown that cancer incidence in areas polluted seriously by heavy metals is 10–15 times higher than that in areas without pollution. Presently, it has been confirmed that arsenic can lead to lung cancer, bone cancer, skin cancer, and pancreatic carcinoma; lead can result in lung cancer, leukemia, and gastrointestinal cancer; mercury can cause kidney cancer and myeloma; cadmium can cause lung cancer, breast cancer, and prostate cancer; nickel can cause skin cancer and lung cancer; and chromium can cause bone cancer and blood cancer. If the contents of many heavy metals exceed the standards, carcinogenic effect is obviously enhanced.

Research in recent years indicates that reduction of heavy metals entering the body and removal of poisonous heavy metals from the body are effective in preventing relevant cancers. Because the human body does not yet have any active detoxification and sound excretion effect on heavy metals, advanced equipments must be used to inspect the contents of heavy metals and microelements in the human body. Then, customized therapeutic schemes can be proposed to remove the heavy metals according to actual conditions. Safe and effective drugs without any side effects are applied to clear away various harmful heavy metals. Meanwhile, beneficial microelements and vitamins are replenished so as to promote physical health, enhance clinical therapeutic effects on cancer, improve life quality of patients, and prolong their survival time.

4.2.4 Cancer therapy mechanism of chelation and detoxification therapy

The mechanism of chelation and detoxification therapy mainly includes chelation of heavy metals, rectification of calcium overload, prevention and treatment of premature cellular senility, and removal of free radicals.

4.2.4.1 Chelation of heavy metals

Chelation and detoxification therapy means intravenous infusion of the amino acid EDTA, which is a nonbiological amino acid synthesized artificially. EDTA itself is not metabolized but is taken as a chelating agent after it enters the body. It reaches various tissues and organs through blood circulation and is chelated with various metals accumulated in blood vessels and whole-body tissues, such as calcium, iron, copper, lead, aluminum, mercury, arsenic, cadmium, and nickel, so as to form dissolvable, nontoxic, and stable conjugates that are then discharged out of the body through the kidney, removing the harmful heavy metals accumulated in the human body and realizing the effect of chelation and detoxification.

4.2.4.2 Rectification of calcium overload

Chelation of EDTA with $Ca^{2}+$ in the blood is applied to reduce calcium ions and prevent the coagulation of blood, so as to realize the anticoagulation effect, reduce blood viscosity, improve the blood circulation, and prevent the formation of thrombus and occurrence of cardiovascular diseases. The chelation of EDTA with $Ca^{2}+$ combining other anticoagulation drugs can realize the effect of dissolving the thrombus.

The chelation of EDTA with harmful substances deposited on vascular walls, such as calcium, lipid, mucopolysaccharide, and heavy metals, for the removal of "wastes" on the vascular walls, can effectively prevent and cure arteriosclerosis, hypertension, hyperlipidemia, obesity, and other cardiovascular diseases.

EDTA is chelated with excessive $Ca^{2}+$ (calcium overload change) accumulated in other tissues and organs to reduce calcium overload. The calcium in tissues and bones is redistributed through the feedback and regulation effects of systems such as the endocrine system and the nervous system, so as to meet the physiological requirements and realize the prevention and therapy of diseases such as osteoporosis, arthritis, and sclerosis.

4.2.4.3 Prevention of premature senility and death of cells

According to research conducted in recent years, calcium overload in cells is a representation of cell aging, especially in brain cells and nervous tissues. Patients with hypertension combined with arteriosclerosis may easily suffer from the aforementioned pathological phenomenon, and it is found through long-term tracing observations that the incidence of dementia is very high. Through the chelation of EDTA with $Ca^{2}+$ accumulated in tissues and organs, the $Ca^{2}+$ in the cells of the body is unloaded and the $Ca^{2}+$ gathered in cell mitochondria is reduced relatively, so as to prevent the aging and death of cells and improve the health of the human body. The latest medical research shows that the basic reason for the death of cells is calcium overload in mitochondria. Mitochondria play an important role in regulating the steady state of calculus in cells. The

rise of cytoplasmic calcium concentration by any cause may lead to excessive calcium being accumulated in mitochondria, which shows a state of high permeability, thus resulting in the tumefaction and destruction of mitochondria and the exhaustion of cell energy.

At the same time, abundant $Ca^{2}+$ in the mitochondria will be released and when $Ca^{2}+$ in the cytoplasm increases beyond its bearing capacity, calcium ion, as the second messenger of the organism, can activate various proteolytic enzymes and phospholipases, disintegrating the cell membrane and resulting in the death of cells. On the other hand, when $Ca^{2}+$ in the mitochondria increases, the cell will not reach necrosis if the time is short and mitochondria can provide sufficient energy for the cell. However, mitochondria will release cytochrome C and apoptosis-inducing factor, both of which can lead to cell apoptosis. Therefore, chelating EDTA with $Ca^{2}+$ accumulated in tissues and organs can reduce the concentration of calcium ions within the cells of the organism, which is good for health.

4.2.4.4 ELIMINATION OF FREE RADICALS IN THE BODY

Humans produce many types of free radicals in the process of metabolism and these free radicals are harmful to the body's organs and tissues, especially because they cause hypoxia and dysfunction of tissues and cells. The damage to the body caused by free radicals is also a main reason leading to the aging and death of cells. EDTA can chelate well with free radicals accumulated in the tissues and organs of the human body, so that the amount of free radicals in the body decreases while the cells' lifespan and vitality increase correspondingly. This can prevent the death and aging of a lot of cells and improve the patient's health.

4.2.5 Clinical application of chelation and detoxification therapy in cancer therapy

Chelation and detoxification therapy has been well-documented and widely used in clinical settings for a long time. However, this therapy must be applied more carefully to cancer patients, because most of them have often received routine cancer therapies, such as surgery, radiation therapy, and chemotherapy, that have side effects such as bad performance status, immune dysfunction, bad appetite, dormancy, and psychological problems, resulting in difficulties to the therapy. We should pay attention to therapeutic "individualization," follow the principle of "evidence-based medicine," adjust the therapeutic procedure and drugs to be dispensed according to the therapeutic responses, and objectively check results on the patients.

4.2.5.1 INDICATIONS OF CHELATION AND DETOXIFICATION THERAPY

Indications of chelation and detoxification therapy mainly include the following: heavy metal poisoning or content exceeding medical standards, hypercalcemia, digitalis-poisoning arrhythmia, arteriosclerosis, coronary disease including angina and hemadostenosis observed from coronary angiogram, occlusive angiopathy (including arteries and veins), and degenerative joint disease.

Therapies must be applied to cancer patients who have blood copper, blood iron, serum magnesium, or blood zinc beyond the standard values. Even though such trace elements are necessary for ordinary metabolism, it their concentrations are high they can directly damage the functions of cells and visceral organs. So, chelation and detoxification therapy must be applied to eliminate excessive microelements.

4.2.5.2 CONTRAINDICATIONS OF CHELATION AND DETOXIFICATION THERAPY

From the clinical angle, chelation and detoxification therapy is very safe with few contraindications. At present, the following are considered contraindications:

Favism: Known as glucose-6-phosphate dehydrogenase deficiency disease, it is often seen in children and is a genopathy due to irritability to specific materials (such as broad bean flower), which may be hereditable. Therefore, it is named favism; it is represented as a seasonal hemolytic anemia. This disease can be confirmed by laboratory examinations. Chelation and detoxification therapy can be applied to children less than 12 years old.

End-stage renal failure: As the poisonous substances after chelation are mainly expelled out of the body through the kidney and the chelating agent itself has no toxicity, the kidney will be heavily loaded, for the conjugates produced by heavy chelation are expelled through the kidney in a short time. Accordingly, and in principle, for patients with end-stage renal failure (uremia period) chelation and detoxification therapy is never applied. If the patients are receiving hemodialysis therapy, chelation and detoxification therapy can still be applied and the chelates can be removed safely during hemodialysis.

Patients with severe bleeding tendency and cancer can suffer from cachexia and multiple organ failure.

4.2.6 Mechanism of vitamin C therapy on cancer

Large doses of vitamin C can be applied to cure malignant tumors, which was preliminary reported by Cameron in the 1970s. However, because research on pharmacology, pharmacokinetics, cell biochemistry, and immunohistochemistry were relatively lagging at the time, there were many divergent views on the anticancer mechanism of vitamin C therapy. In the past 10 years, basic research and clinical application of vitamin C for malignant cancer therapy have achieved great progress and realized encouraging results.

4.2.6.1 Pharmacological research of vitamin C

4.2.6.1.1 Pharmacological effect of vitamin C

Vitamin C is an essential vitamin for human metabolism. Vitamin C can be synthesized in livers and intestines of mammals and can be stored in the body for a long time. However, the human body lacks a key enzyme (G, luco-lactone dehydrogenase) necessary for the synthesis of vitamin C, so the human body has to get it from outside the body. The normal plasma value of vitamin C totals 0.6–1.4 mg% (1 mg% = 56.7 mmol/L), and it is considered deficiency of vitamin C if the plasma value is less than 0.2 mg%. Normal vitamin C is used and rapidly decomposed in the human body. Due to the limited storage capacity, vitamin C can stay under relative deficiency for no more than 72 hours. It must be replenished from foods or health products; otherwise, scurvy symptoms will occur, such as swelling and bleeding of gums, ecchymosis, abdominal pain and diarrhea, hypodynamia and insomnia, and ease of infection. The physiological requirement for vitamin C is about 100–200 mg/day. The main pharmacological effects of vitamin C include removal of free radicals, antagonism of oxidative stress response, nonspecific detoxification, improvement of cardiac and hepatic functions, improvement of blood coagulation, proper reduction of blood pressure, and depression of viruses. Vitamin C is an important enzymatic factor for elastase and collagen synthesis enzyme in blood vessels and connective tissues and is of great importance in maintaining normal structures and functions of systemic artery vessels.

4.2.6.1.2 Experiment on vitamin C for normal cell safety

Vitamin C used clinically for the treatment of cancer requires large doses, which causes concern about whether it has any killing effect on normal cells. Numerous research has been done on the safety of its application. Nemoto et al. observed the depression effect of vitamin C on cell growth of different mammals. They carried out respective and simultaneous standard cultivations of liver cells and cartilage cells of normal guinea pig, normal white rat's splenocytes (LT4Tr), brain cells (RCR1), bone marrow cells (UMR106), embryonic cells (3T6), human's leukemia cells (HL60), and pheochromocytoma cells (PC12) of mouse and added 0.1–15 mmol/L sodium vitamin C to the cell culture medium, which were without sodium vitamin C as control. Both the culture mediums were incubated for 48 hours to inspect the survival rates of various cells and the activity of catalase in the cells. The results showed that no apoptosis or necrosis of normal cells; besides, when the concentration of vitamin C was up to 0.2 mmol/L or more RCR1, PC12, and 3T6 cells decreased slightly. However, even when the concentration of vitamin C totaled 4 mmol/L the number of liver cells remained unchanged. Different reactions of animal cells to vitamin C are related to the activity of catalase in the cells, because vitamin C can generate hydrogen peroxide (H_2O_2) in the cells. The activity of catalase in normal liver cells is significantly higher than that in other cells, suggesting that it is not sensitive to vitamin C.

In recent years, the research by Chen et al. has gained authority. The human Burkitt lymphoma cell strains (JLP-119) and three breast cancer lines (MCF7, Hs5871, and MB587t) provided by the U.S. typical standardization cell bank were compared with six healthy persons' lymphocytes, monocytes, fibroblasts, and mammary gland cells, and all of the cells were cultivated in vitro. Vitamin C was freshly prepared into sodium salt, with a pH of 7, and the tumor cells and normal cells in the culture mediums were subjected to 2.5×10^5/mL of 0.3–20 mmol/L vitamin C sodium, which were added to the mediums, and incubated for 1 hour. Then by observing ED50 (cell survival rate of 50%), it was found that the doses of vitamin C in the majority of tumor lines (5/9) ED50 were less than 5 mmol/L, whereas normal cell strains were all alive even under the high dose of 20 mmol/L, which proved that large doses of vitamin C had no damaging effect on normal cells.

Vitamin C is harmless to normal cells, which is a basic difference from many chemotherapeutic drugs, and has great significance in clinical applications. It shows that vitamin C has a selective killing effect to malignant cells and has no adverse effect on metabolism and viscera functions of the body. Therefore, vitamin C can be applied to patients with various middle-advanced cancers; it is very safe to apply a large dose of vitamin C in curing cancer, and the patients' drug adaptability is improved as well.

4.2.6.1.3 Experimental research on direct cytotoxic effect of vitamin C

In some in vitro culture experiments on malignant lymphoma cell strains of the human body, Helgestad et al. found that the cancer cells were highly sensitive to vitamin C and could be killed within 2 hours under a concentration of 50 mmol/L. They thought that it was the direct cytotoxic effect of vitamin C. Kadaswami et al. took squamous cancer strains for in vitro cultivation; they were divided into two groups, one using vitamin C alone and the other using vitamin C combining flavonoids, for cancer-depressing experiments. The results showed that vitamin C could depress the growth of cancer cells while vitamin C combining flavonoids had a synergistic effect, capable of significantly enhancing the depression of the growth of squamous cancer cells and resulting in the death of some cancer cells. Kao et al. from Japan conducted research on the effects of vitamin C on leukemia cells and lymphoma cells; after purified in vitro cultivation of two cell strains, vitamin C was added into the mediums. Afterward, it was found that vitamin C could depress the growth of leukemia cells and directly lead to the death of lymphoma cells under the same concentration (over 10 mmol/L). The death of cancer cells was mainly in the form of necrosis, with apoptosis phenomenon of a few cells. The cell toxicant effect of vitamin C depended on dose and time. A small dose and a short action time can weaken its depression or killing capacity on cancer cells.

To research the cell toxicant effects of the application of vitamin C alone and its combination with antioxidants (lipoic acid), Casciari et al. made a hollow fiber standard cultivation of colon cancer cell strains (SW620 HFST) of the human body, with the cultivation of normal human lung tissue and skin fibroblasts as the control. After the dose of vitamin C in the culture fluid reached 11.2 mmol/L and after the culture was incubated for 48 hours, examination and analysis were done by flow cytometer. The results found that the apoptosis rate of colon cancer cell strains was up to 42.9% and their necrosis rate was up to 24.4%, indicating that lipoic acid can enhance the effect of vitamin C and the aforementioned dose of vitamin C had no damage to normal cells.

4.2.6.2 FUNDAMENTAL RESEARCH ON VITAMIN C FOR CANCER THERAPY

Fundamental research on vitamin C for cancer therapy has been carried out for a long time. In recent years, it is widely recognized in the academic field that the anticancer activity of vitamin C has been clearly explained with three great mechanisms, which are discussed in Sections 4.2.6.2.1 through 4.2.6.2.3.

4.2.6.2.1 Direct cell toxicant effect

It is believed that vitamin C itself and its metabolites (vitamin C free radicals) have a direct cell toxicant effect on cancer cells, which can lead to growth depression and death of tumor cells; in this case, the death form of tumor cells is mainly necrosis.

4.2.6.2.2 Growth-promoting effect of hydrogen peroxide

It is believed that vitamin C itself is an H_2O_2-promoting agent with strong activity in the body. H_2O_2 inside and outside cancer cells can lead to the death of the cancer cells, with the main death forms of apoptosis and then necrosis. Most authors believe that the hydrogen peroxide theory is the main anticancer mechanism of vitamin C.

4.2.6.2.3 Inductive effect of cancer cell autoschizis

It occurs when large doses of vitamin C and vitamin C combined with vitamin K3 are used. This death form is different from necrosis and apoptosis.

4.2.6.3 HYDROGEN PEROXIDE MECHANISM OF VITAMIN C AGAINST CANCER

Clement et al. confirmed that vitamin C showed its direct cytotoxic effect on in vitro culture experiments on cancer cells. The strength of this effect was related to the concentration of hydrogen peroxide generated by vitamin C in a culture medium. In recent years, medical scientists in many countries have worked together to conduct further research on the anticancer mechanism of vitamin C and virtually perfected the hydrogen peroxide mechanism. Moreover, they have further researched the anticancer synergy effect of vitamin C and vitamin K_3.

The outstanding research by Chinese scientists Chen et al. has made important contributions to confirmation of the anticancer mechanism of vitamin C. They have made in vitro cancer cell cultivations and conducted cat experiments successively; they have also quantitatively inspected the contents of vitamin C and ascorbate free radicals in cells and blood and around tumors and in extracellular fluid through three different administration approaches (intravenous injection, intraperitoneal injection, and oral application) and the advanced "ultra-micro-inspection technology." Their conclusions are as follows: (1) when the concentration of vitamin C in the culture medium is more than 25 μmol, the cancer cells can be killed. The vitamin C dosage applied to the experimental animal is up to 0.5 g/kg; the blood drug level can kill cancer cells, and this dose can be referred to clinically. (2) In animal experiments, the main mechanism of vitamin C in killing cancer cells or causing their apoptosis is the formation of hydrogen peroxide (H_2O_2) and ascorbate free radicals around cancer cells; the two metabolites of vitamin C have direct cytotoxic effects. (3) Only intravenous injection of vitamin C can achieve an effective anticancer drug concentration, whereas oral application has no anticancer effect due to its lower concentration. (4) Normal blood contains catalase and superoxide dismutase (SOD), which can restrain the generation of hydrogen peroxide and ascorbic acid free radicals in blood, so the intravenous injection of vitamin C cannot cause any damage to the blood cells. The cancer cells do not contain the two aforementioned enzymes, so they are unable to resist the killing effect of vitamin C. (5) The ability of vitamin C to generate H_2O_2 and ascorbic acid radicals inside the body shows a dosage dependency, while H_2O_2 is parallel to the ascorbic acid free radicals in terms of generation volume.

After intravenous injection of vitamin C, the metabolic pathways in blood, extracellular fluid, and cancer cells are well understood. In blood, due to the functions of catalase and SOD, the catabolic metabolism of vitamin C is depressed, and the generation of hydrogen peroxide and ascorbic acid radicals is difficult. However, vitamin C can enter the extracellular fluid in prototype form through the capillary walls. In the extracellular fluid (including intercellular substance), vitamin C begins to decompose due to the lack of impact of the two aforementioned enzymes, losing a negative electronic charge and forming ascorbic acid radical (Asc–). Then the active electron deoxidizes a protein-core metal ion (the protein-centered metal), which is now considered as the element that deoxidizes the trivalent iron into a divalent iron ion. During this process, it can form highly active oxygen ions, which then aggregate with hydrogen ions in the extracellular fluid to create hydrogen peroxide. It has been confirmed that the hydrogen peroxide and ascorbic acid radicals have a high selectivity to tumor cells. After entering cancer cells, they block ATP metabolism of cancer cells from three pathways. The apoptosis or necrosis of cancer cells can occur once they lose the energy for metabolism, because the metabolism of cancer cells is very strong, incapable of bearing any "hunger." However, vitamin C and its metabolites block the energy sources of cancer cells, which results in their "death due to hunger."

4.2.7 Clinical application of vitamin C therapy in cancer therapy

4.2.7.1 VITAMIN C THERAPY FOR CANCER THERAPY

Vitamin C therapy has been clinically applied in cancer treatment for over 30 years and is contained in a large number of foreign literatures. Yeom et al., scholars from South Korea, have done a prospective study on vitamin C therapy in improving the life quality of cancer patients. They observed 39 cases of cancer patients, including 20 males and 19 females, with an average age of 53.5 years, of whom 10 patients were with gastric cancer, 9 were with colon cancer, 7 were with lung cancer, 4 were with breast cancer, 2 were with bile duct cancer, 1 was with liver cancer, and 1 was with cervical cancer and 5 were with other cancers. All 39 patients suffered from cancer metastases. Previous therapy conditions were as follows: surgery combining chemotherapy for 19 patients (48.7%), surgery combining radiotherapy for 3 (7.7%), surgery combining radiotherapy and chemotherapy for 4 (10.3%), chemotherapy alone for 11 (28.2%), surgery alone and radiotherapy for 1 (each 2.6%). Short-course and high-dose vitamin C therapy was adopted, namely, intravenous injection of vitamin C twice in the first week, 10 g each time, with an interval of 3 days; oral application of vitamin C totaled 4 g/day in the second week. The Patients' Life Quality Questionnaire formulated by the Federation of European Cancer Treatment and Research was used to assess the improvement of life quality of patients before and after therapy, with life quality scores totaling 36 ± 18 and 55 ± 16, respectively, which had statistically significant differences ($P < .001$); the function scores and symptom scores were improved significantly after therapy.

4.2.7.1.1 Workup and assessment before therapy

Before formal application of vitamin C therapy, it is necessary to comprehend the patient's diagnosis (including TNM stage, pathological diagnosis, and immunohistochemical examination); the patient's previously received therapies, especially surgery, radiotherapy, and chemotherapy situations; whether there is any concomitant disease or not; the patient's heart, liver, kidney, lung, and hematopoietic functions; the nutritional status of the whole body; the patient's psychological quality assessment; and so on.

4.2.7.1.2 Laboratory and special examinations

Conventional laboratory examination items include the following: routine blood, urine, and stool examinations; blood biochemistry, including blood fat, blood sugar, liver and renal function, electrolytes, liver enzymes, and myocardial enzymes; trace elements and heavy metals; various tumor-associated antigens; humoral and cellular immune functions; and so on. Bone marrow examinations must be made for patients with malignant hematological cancer. As for thyroid function, sex hormone function, and other endocrine functions, examinations can be made according to actual conditions.

Other examination items include the following: (1) compulsory items: electrocardiogram, echocardiography, pulmonary function, and abdominal ultrasound; (2) extenuatory items: X-ray, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET)-CT, and radioisotope. The examinations of viscera and locations should be determined according to clinical conditions. In principle, if patients have not received the aforementioned examinations for more than 3 months, one or two examinations can be selected according to the patients' conditions. (3) Special items: tumor biopsy; chemotherapy drug sensitivity test, which requires more sophisticated equipment and technical conditions and is applied to patients with special conditions according to actual conditions so that it cannot be used widely.

4.2.7.1.3 Administration time of vitamin C therapy

Vitamin C, as an anticancer drug, can be used alone and applied in the early, medium, and advanced stages of cancer. If it is combined with radiotherapy or chemotherapy, vitamin C therapy can be applied before, during, or after radiotherapy and chemotherapy. Because vitamin C can enhance the effects of radiotherapy and chemotherapy and reduce toxic side effects, it is suggested that vitamin C therapy be applied within a week before radiotherapy and chemotherapy and stopped within a week after radiotherapy and chemotherapy so as to get better results.

4.2.7.1.4 Dosage and treatment course of vitamin C therapy

The principles of vitamin C used for cancer therapy include high dosage and long treatment course. It is divided into intensive treatment period and consolidated treatment period. The former refers to initial treatment cases and it mainly aims at eliminating or controlling tumors, while the consolidative treatment period is to prevent recurrence and metastasis. According to foreign literatures, vitamin C treatment is used alone in the intensive treatment period; the dosage for adults may not be less than 30 g each time. The recommended dosage is 30–60 g each time; after dilution, it is applied for 1–1.5 hours through intravenous injection (Figure 4.1) two to three times per week. As for special cases, the dosage can be increased to 100 g each time, and 15–20 times within one treatment course. After this treatment course, the whole-body conditions and therapeutic effect of patients should be assessed clinically; then the dosage can be adjusted appropriately. The next treatment course can be applied after 1 to 2 months of rest; the intensive treatment period requires five to six treatment courses in principle. In the consolidated treatment period, vitamin C of 30–60 g is recommended with intravenous infusion each week. There is no rule on treatment courses; the long-term medication is proposed generally.

When vitamin C is combined with radiotherapy and chemotherapy, it mainly aims to enhance the therapeutic effects and reduce the side effects. Its dosage is different from the application of vitamin C alone as an anticancer drug. Small dosage is usually applied, and common dosage is applied every other day. The drug administration is made within 1 week before radiotherapy and chemotherapy, and this treatment course is stopped within 1 week after the completion of radiotherapy and chemotherapy.

4.2.7.1.5 Precautions

When radiotherapy and chemotherapy are applied simultaneously, the chemotherapeutic drugs and radiotherapeutic dosages should be reduced appropriately so as to avoid or relieve the toxic and side effects. During vitamin C therapy, hard-shell seafood (seashells, crab, etc.) should be prohibited to avoid or reduce the hypersensitivity reactions of patients to vitamin C. Although vitamin C allergy is very rare, it could be very serious in the event of illness. In the intermittent days of vitamin C therapy, oral administration of vitamin C 2 g/day is required. Even after the therapy, oral administration of vitamin C 1 g/day for at least 3 months is required, because acute vitamin C deficiency of the body will occur when administration is suddenly stopped.

Clinically, as for dermatitis, dermatomyositis, neuritis, glossopharyngeal nerve recurrent laryngeal nerve paralysis, and hemorrhagic enteritis caused by radiotherapy, liver and kidney dysfunction, severe anemia or bone marrow suppression, spiritual depression, and gastrointestinal dyspepsia syndrome and conditions further caused by chemotherapy, integrative treatments combining vitamin C with herbal medicines can relieve the radiotherapeutic and chemotherapeutic side effects of most patients and significantly improve their quality of life.

Figure 4.1 Chelation and detoxification therapy.

4.2.7.2 ENHANCEMENT OF CHEMOTHERAPEUTIC EFFECT WITH VITAMIN C THERAPY

For many years, it was believed that vitamin C is a sensitizer for a variety of chemotherapeutic drugs. In this century, the medical field has strengthened the scientific research in this respect. Dedy et al. has proved through research that vitamin C can enhance the effect of chemotherapeutic drugs during therapy on cervical cancer. The reason for the generation of this effect is that vitamin C has the effect of stabilizing and depressing the gene *p53*. Casciari et al. made a hollow fiber cultivation of human colon cancer cells (SW620 strains) with different concentrations of vitamin C alone, doxorubicin alone, and vitamin C combined with doxorubicin (proportion of 10,000:1). They observed and found that the apoptosis and necrosis of cancer cells caused by vitamin C were associated with its concentrations; vitamin C could significantly enhance the effect of doxorubicin in killing cancer cells. In multiple myeloma research, Jennifer et al. found that vitamin C could increase over two times the anticancer effect of trivalent arsenic preparation. Moreover, Bahlis et al. adopted the combination of vitamin C with arsenic preparations for drug-resistant multiple myelomas, which realized a desired therapeutic effect.

Because vitamin C itself has an anticancer effect, it can enhance the anticancer effect of many chemotherapeutic drugs. White believes that the large dose of vitamin C has become a chemotherapy sensitizer, and an important alternative anticancer drug during integrative cancer treatments.

4.2.7.3 SYNERGISTIC EFFECT OF VITAMIN C AND RADIOTHERAPY

The synergistic effect of vitamin C and radiation therapy has attracted much attention for many years. First, the main mechanism of radiotherapy on cancer is the formation of free radicals; the metabolism of vitamin C in the body also generates vitamin C free radicals. These two types of free radicals have synergistic effects on cancer. Second, both vitamin C and radiotherapy have cytotoxic effects, but their actions on the targeted points of cancer cells are not identical. The targeted points of vitamin C are in the cell membrane, mitochondria, and nuclear DNA, whereas those of radiotherapy are mainly located in the cytoplasm and nucleus DNA. Therefore, cancer cells can be attacked fully and be besieged on all sides under the combination of the two therapies, without any space for survival. Calderon et al. researched the synergistic effect of vitamin C and radiation therapy. First, they molded a liver cancer animal model of mice (transplantable liver tumor). When the tumor volume reached or slightly exceeded 1000 mm^3, the tested mice were divided into radiotherapy alone group, oral application group of vitamin C and vitamin K_3, oral application group of vitamin C and vitamin K_3 combining radiotherapy, and blank control group. The radiotherapy dosage was 20 Gy for each X-ray irradiation, and the tumor volume was measured twice a week for a total of six times in 3 weeks. The final measurement results of the average tumor volume showed the following: the blank control group rose to 9000 mm^3, the radiotherapy alone group rose to 6000 mm^3, and the vitamin C and vitamin K_3 group rose to 8300 mm^3; all of these therapeutic effects were not satisfactory. The average tumor volume in the group of oral application of vitamin C and vitamin K3 combining radiotherapy only rose to 2100 mm^3, which had a statistically significant difference ($P < .05$), showing a relatively ideal anticancer effect. It is virtually certain that vitamin C can enhance the effect and reduce the side effects of radiotherapy.

4.2.8 APPLICATION OF VITAMIN B_{17} IN CANCER THERAPY

In the recent half-century, vitamin B_{17} is widely researched and applied as a botanical drug; it is also one of the vitamin-based anticancer drugs that are quietly distinctive and prospective.

Vitamin B_{17} was discovered by Dr. Ernst Theodor Krebs Jr. during the screening and purification of many anticancer plants. It is essentially purified laetrile containing a small amount of cyanate, a kind of hypertoxic substance, causing people to be somewhat fearful of its toxicity. Krebs et al. have conducted a lot of experimental research and have made practical observations proving that vitamin B_{17} is safe. First, vitamin B_{17} comes from natural plants and it is completely different from potassium cyanide, an artificially synthesized poisonous agent. Second, in daily foods for people, small amounts of laetrile cannot be converted into potassium cyanide. Additionally, the production mechanism of potassium cyanide in the human body is as

follows: when vitamin B_{17} touches tumor tissue, it can be converted into potassium cyanide under the effect of β-glucosinolate (G, lucosidase) and kill the cancer cells. Potassium cyanide thus generated cannot enter normal cells, so no toxicity against normal cells and tissues can be generated.

4.2.8.1 ANTICANCER MECHANISM OF VITAMIN B_{17}

Vitamin B_{17} is an important one in the vitamin B family. Its main functions in the human body include the following: as a coenzyme in a variety of metabolic enzyme systems, it promotes the synthesis and metabolism of protein, fat, and sugar to store nutrients and energy for the body; it strengthens the functions of liver, kidney, brain, and nervous system; it enhances the immunity of the body, especially resistance to virus infection, and strengthens the natural cell-killing activity of the human body; and it strengthens the hematopoietic function of bone marrow. Vitamin B_{17} also has special resistance to malignant tumors, so it plays an important role in integrative cancer treatments.

The anticancer theory of vitamin B_{17} proposed by Krebs includes two parts: killing process and mechanism of cyanide and hydride on cancer cells, and nontoxic metabolism of cyanide and hydride in the human body.

In Krebs' opinion, human cancers originate from primitive embryonic cells that are equivalent to stem cells. Cyanide and hydride are the main components of vitamin B_{17}. They stably exist in the human body, with a half-life of about 24 hours, and they can maintain their biological activity for a long time. Vitamin B_{17} has a special affinity for primitive embryonic cells. When cells suffer from cancerization, vitamin B_{17} shows its killing or depression effect on the cancer cells. First, it can gather around cancer cells, forming a higher drug concentration. Then a very important enzyme, glucosinase, comes into play when vitamin B_{17} attacks the cancer cells. This enzyme can reconstruct the chemical structure of vitamin B_{17} and makes B_{17} become bioactiviated. During this process, benzaldehyde is generated. The activated vitamin B_{17} can penetrate the cancer cell membranes in coordination with benzaldehyde. At this time, the concentration of vitamin B_{17} inside the cancer cells can be more than 3000 times higher than that inside normal cells. It has a stronger cytotoxic effect and is able to destroy the respirator of cells, mitochondria, resulting in the death of cancer cells or cancer depression for a long time. It is necessary to emphasize that with good application safety vitamin B_{17} does not damage normal cells.

4.2.8.2 EVALUATION OF THERAPEUTIC EFFECT OF VITAMIN B_{17} DURING CANCER THERAPY

At the Ninth International Cancer Academic Conference, Benedetto, an Italian scholar, summarized and reported the clinical therapeutic effect of B_{17} during cancer treatments. Benedetto et al. received and cured 150 patients with advanced cancer in the San Cottoleng Hospital, Turin, Italy; Dosio Hospital, Miland, Norway; and Tumor Center of Louvain University, Italy, from 1954 to 1966; all of the patients were failures in other therapies, including 25 breast cancer patients, 20 colon cancer patients, 24 urinary tract (including prostate) cancer patients, and 10 ovarian cancer patients.

The therapeutic dosage of vitamin B_{17} for adults totaled 100 mg/day on average, and the largest dosage was up to 500 mg/day, which was applied through slow intravenous injection (with the former method). Three standard therapeutic courses were taken as a complete evaluation period, and the disease condition evaluations before and after therapy included symptomatic remission degree, blood, functions of heart/liver/kidney, immune reaction, X-ray picture, intravital tissue examination, and so on. According to laboratory indexes and the symptomatic remission degree of patients, therapeutic effect evaluation included four grades: excellent (+), good (+), valid (+−), and invalid (−). Results showed that 135 patients completed the therapy period, including 28 patients with excellent therapeutic effect, 39 with good effect, 23 with valid effect, 45 with invalid effect, and 90 above the valid effect grade (66.6%). Through further analyses, it was found that after the paracentesis was applied to 15 carcinogenic pleural effusion patients for pumping effusion and then vitamin B_{17} was applied for intrapleural injection, the pains of the said patients were relieved and the therapeutic effects were maintained for over 3 weeks. As for advanced cancer patients who had suffered from failures in other therapies, such a therapeutic effect was satisfactory.

4.2.9 Application of colon cleansing detoxification therapy in cancer therapy

In recent decades, the effects of environmental pollution on human beings have spread all over cities and even the countryside during the constant improvement of economies and rapid development of modern industries. Some bad lifestyle diets promote wide applications of pesticides, chemical fertilizers, food additives, and hormones, resulting in accumulation of toxins in the human body. After ingestion by the human body, they are harmful to health, destroy normal physiological functions, and result in or promote the occurrence of cancer and various chronic diseases, and they are classified as foreign poisons. In the theory of TCM, "toxin" is the main pathogenesis of cancer; thus the treatments of cancer and chronic diseases in TCM focus on eliminating toxins and dispelling factors that could cause toxins to build up in human body. Clifford Hospital adopted natural colon cleansing therapy and applied pure, natural, and organic garden stuffs that are not processed and have no additive, preservative, or pigment. It promotes the elimination of toxicants through urine and stool. In addition, it improves the detoxification capacity of the liver, thus producing alkaline body conditions in cancer patients to realize the effects of preventing and depressing the growth and metastasis of cancer.

4.2.10 Composition of natural colon cleansing therapy

4.2.10.1 Oral application of garden stuff beverage

It is composed of the five cereals, various organic green vegetables, various organic fruits, ginger, garlic, onion, aloe, seaweed, sea salt, olive oil, and so on.

4.2.10.2 Coffee enema

The use of coffee enema can be traced back 2000 years. During the First World War, due to the lack of anesthetics and due to the analgesic effect of coffee enema, the German army adopted the coffee enema to relieve the pains of patients during surgery. Later, medical specialists found that coffee enema can not only clean the bowels and discharge residual stool but also alleviate pains and promote the effect of detoxification of the liver. Basically, coffee enema is identical with general enemas. During clinical applications in Clifford Hospital, we used superior organic coffee imported from Peru, which did not contain chemosynthetic pesticides, chemical fertilizers, hormones, antibiotics, or food additives, so as to ensure the safety and effectiveness of the therapy process.

4.2.9.2.1 Functions of coffee enema

Caffeine promotes the secretion of glutathione enzyme, and the latter is the most important enzyme in detoxicating the liver and eliminating free radicals. The caffeine and theophylline contained in coffee can expand the blood vessels of intestinal walls and alleviate enteritis. The coffee injected through coffee enema cleans the large intestines on the left side near anus, a place most susceptible to the accumulation of residual stool and having the strongest fecundity of malignant bacteria. The coffee taken orally can stimulate the gastric wall, and the sterilization ingredients contained are not beneficial to good bacteria on large intestines. Coffee enema disposes the daily discharged toxins from the liver to facilitate and maintain the health of the liver, which explains the significance of coffee enema in cancer patients.

4.2.9.2.2 Therapeutic effect of coffee enema

Coffee enema can improve constipation by increasing beneficial bacteria in intestinal tracts and maintaining the balance of intestinal bacteria; help to improve allergy symptoms such as hives; promote blood circulation and lymph circulation to improve various skin problems; promote metabolism and assist in the control of body weight; improve symptoms such as chronic fatigue, headache, or shoulder pain by the elimination of intrinsic toxicants; and help to improve liver function and maintain the good state of the body.

4.2.9.2.3 Indications of coffee enema

It is applicable to patients with subhealth conditions, chronic fatigue syndrome, constipation, incomplete liver function, and tumors in various parts.

4.2.9.2.4 Contraindications of coffee enema

Contraindications include patients with hemorrhoidal bleeding, patients with delicate health, pregnant women, children, and patients who are unconscious.

4.3 HYPERTHERMIA INTEGRATED WITH MEDICAL OZONE THERAPY

Medical ozone is a kind of active oxygen; it is called medical ozone in medical applications and ozone in industrial applications, and the two are different. Ozone is naturally formed or produced with air as its raw material under a high-temperature electric discharge. It contains poisonous nitrogen oxide and is widely used for water processing, air sterilization, and the oxidation process. Medical ozone does not contain nitrogen oxide; it must be produced with medically pure oxygen using medical ozone production equipment.

Medical ozone therapy for cancer has a history of more than 20 years and is mainly based on three theories. In 1996, Warburg, a Nobel Prize–winning German doctor, proposed the theory that cancer occurrence and development were due to anoxia at the cell level. Watson and Crick, Nobel Prize winners and DNA double-chain structure discoverers, believed that cancer was caused by a virus. In 1974, Varro from Germany discovered that cancer cells were sensitive to hydrogen peroxide, which could reduce the metabolism standard of cancer cells so that the growth of tumors could be depressed. Research has demonstrated that hydrogen peroxides originating from medical ozone have a sensitization effect on radiotherapy and chemotherapy and can relieve their side effects. Hydrogen peroxides can also directly kill and eliminate cancer cells by enhancing the killing and elimination effect of macrophages and neutrophilic granulocytes. It can also induce the body to release tumor necrosis factors (TNFs) and the immune surveillance system of the body to kill the viruses causing cancer.

Medical ozone therapy is one of the main methods for nontoxic integrative cancer treatments. Cancer is the disease with the highest clinical mortality rate; sometimes, traditional surgeries, radiotherapies, and chemotherapies fail to cure cancer. Additionally, these three procedures are limited by many factors: when surgery, radiotherapy, and chemotherapy are ineffective, or radiotherapy and chemotherapy are applied excessively, some inevitable toxic and side effects can cause further breakdown of the patients. Therefore, the medical field has been searching for new, effective anticancer therapies with less toxic and side effects; hence, medical ozone therapy is applied in cancer therapy.

In recent years, medical ozone therapy has been widely applied to auxiliary therapy on cancer, for malignant fibrous sarcoma, lung cancer, colon cancer, liver cancer, and breast cancer, with reliable therapeutic effects. During clinical application, Clifford Hospital adopted the medical ozone integrated therapy on cancer, obtained satisfactory therapeutic effects, and accumulated some clinical experience.

4.3.1 Cancer hyperthermia and medical ozone therapy

Hyperthermia and medical ozone therapy are often integrated in cancer therapies. Both have the functions of killing cancer cells, enhancing body immunity, and killing the viruses causing cancer through different approaches and have sensitization and synergistic effects on radiotherapy and chemotherapy. The author has used medical ozone therapy, including extracorporeal blood oxygenation and ozonation (EBOO), medical ozone major autohemotherapy, medical ozone minor autohemotherapy, medical ozone saline infusion, medical ozone gas infusion (rectum and vaginal infusion), medical ozone package, and medical ozone oil. Clinical observations have shown that the combination of hyperthermia with medical ozone therapy not only has anticancer effects but also can improve patients' mental state, fatigue, dormancy, and appetite. Their toxic and side effects have not yet been found. There remains a lot of room for study and discussion.

Medical ozone therapy has shown advantages in cancer therapy; there has been some research on its effect mechanism on the immune system and apoptosis induction mechanism on cancer cells. Hyperthermia has a direct lethal effect on cancer cells and an immune induction effect on cancer affected areas and whole body. It can also induce the apoptosis of cancer cells, in accordance with the medical

ozone therapy in terms of the anticancer mechanism. In current clinical applications, the integrative treatment plan combining cancer hyperthermia with medical ozone therapy has obtained certain preliminary effects; it can relieve the symptoms of patients effectively and improve their life quality. However, its synergistic effect mechanism requires further research. Additionally, during therapy on benign diseases medical ozone shows an amazing therapeutic effect on skin injury, nonunion of surgery incision, nervous lesion of diabetes and angitis, and so on. Infrared hyperthermia also has anti-inflammatory functions, improves circulation, and promotes wound healing. Its clinical application still requires further research.

4.3.2 Cancer therapy mechanism of medical ozone therapy

The anticancer mechanism of medical ozone therapy mainly includes the regulation effect of medical ozone and its metabolites on the immune system, direct anticancer effect of hydrogen peroxide, and anticancer effect of the oxygen free radicals that are produced.

4.3.2.1 Regulation effect of medical ozone and its metabolites on the immune system

4.3.2.1.1 Immune lethal effect

Medical ozone and its active metabolites can induce the human body to produce cytotoxic T lymphocytes and natural K cells and make use of the immune function of the body to attack and eradicate cancer cells.

4.3.2.1.2 Immune induction effect

Medical ozone and its active metabolites can enter the immunocompetent cell clearances or the cells; activate nuclear factor-κB, so as to further activate nucleus mRNA; promote the synthesis of specific proteins; and finally release idiosyncratic cytokines. The cytokines are moved to various lymphoid organs of the body by the blood circulation to transfer information and activate other immunocompetent cells, generate further cascade-type immune reactions, and exert the anticancer effect of medical ozone.

4.3.2.1.3 Induction of multiple cell factors

Medical ozone and its metabolites can induce multiple cell factors, such as various endogenous interferons (IFN-α, IFN-β, and IFN-γ), interleukins (IL-2, IL-4, IL-6, IL-8, and IL-10), colony stimulating factors of granulocyte and monocyte (GM-CSF), and transforming growth factors (TGF-β1). GM-CSF can cause leukocytes to increase, whereas the interferon blocks the replication of viruses and the endogenous interferon avoids the miscellaneous components of the artificially synthesized interferon, so as to relieve some of the toxic and side effects incurred. Meanwhile, IL-2 and IFN-α can activate the basic immune and regulatory functions; activate T lymphocytes, macrophages, neutrophilic granulocytes, and eosinophilic granulocytes; activate antibody-dependent cell-mediated cytotoxicity (ADCC); and finally kill the cancer cells.

Research has demonstrated that medical ozone can induce the body to release TNF-α, which is an important factor of immune system surveillance and for killing cancer. Based on this principle, autologous blood transfusion after ozonation has been applied in clinical therapy on cancer.

4.3.2.2 Anticancer effect of hydrogen peroxide

Medical ozone enters the human body and contacts the body fluid to generate hydrogen peroxide. The anticancer effect of hydrogen peroxide has been proved to be multifaceted; previously, the cancer therapy process of hydrogen peroxide was associated with the sensitization of radiotherapy and chemotherapy. Observation of cancer histology shows that there are two types of cells: one is a cell that is proliferating well, and the other is a cell that has died or is dying. Considering the two extremes, there is a steady decline of oxygen tension; it can be expected that there is an area where cells are under the state of oxygen tension that is high enough to enable the cells to form clones but low enough to protect the cells from the influences of ionizing radiation. Cells in this area can be protected in radiation therapy due to their low oxygen tension, and some of them will provide positions for cancer regeneration. Based on these views, it can be assumed that this relatively small number of hypoxic cells exists in the tumor and can affect the success rate of radiation therapy under some clinical conditions.

4.3.2.2.1 Sensitization effect of radiotherapy and chemotherapy

Some foreign research has confirmed that intra-arterial injection of hydrogen peroxide can provide the body with much more active oxygen to improve arterial blood oxygen pressure and strengthen the sensitivity of cancer cells to radiations; if the hydrogen peroxide solution is directly injected into the tumor site, it can increase the oxidation of the local tumor. On the one hand, it can keep the tumor cells in the oxidation environment, losing their survival space; on the other hand, it can make the hypoxic part of tumor cells oxygenate again to enhance the sensitivity of the tumor to radiations.

According to the research of the Institute of Cancer of Baylor University, the arterial injection of hydrogen peroxide not only has the effect of radiotherapy sensitization but also improves cancer staging and is beneficial to surgery. Research has also confirmed that if hydrogen peroxide is combined with chemotherapeutic drugs for tumor therapy, the tumors of most patients can disappear or diminish. The arterial injection of hydrogen peroxide combining radiotherapy and chemotherapy for tumor therapy has significant synergistic effects. Whether it is the reduction rate, improvement of symptoms, or long-term survival rate of patients, the combination of hydrogen peroxide with radio- and chemotherapy is better than chemotherapy alone on patients.

4.3.2.2.2 Directly killing cancer cells

After entering the human body, medical ozone reacts with the body fluid to generate hydrogen peroxide. According to research, hydrogen peroxide can kill cancer cells directly as a cytotoxic factor, regulate the activity of the anticancer antibody in the body, and enhance the anticancer function of the body. Research has also found that normal human cells can generate peroxidase through their own regulating mechanism to avoid damage after the medical ozone enters the human body, and generates hydrogen peroxide; but the cancer cells lack the capacity of generating peroxidase.

Hydrogen peroxide can also enhance the capacity of macrophages and neutrophilic granulocytes in killing and eliminating cancer cells. When any cancer cell exists, the normal cells of the body can secrete hydrogen peroxide to eliminate the cancer cell; the exogenous hydrogen peroxide enhances this effect. Research has also shown that catalase can activate low-level hydrogen peroxide, change the cytotoxin quantity of Hodgkin' s disease, and kill the cancer cells of Hodgkin's disease.

4.3.2.3 GENERATION OF OXYGENIC FREE RADICALS FOR ANTICANCER

Free radicals can damage normal cells and result in their cancerization; they can also kill cancer cells for cancer treatment. In certain developmental stages of the cancer, the free radical content in some types of cancer cells is reduced, so the equivalent free radicals or substances that can generate free radicals are delivered to cancer cells and normal cells. Due to the lack of Mn-SOD, cancer cells cannot clear the free radicals, so the cancer cells are easily killed by the free radicals. At present, the known anticancer drugs such as bleomycin, mitomycin, and anthracycline antibiotics all work using this method.

During medical ozone cancer therapy, a large amount of oxygenic free radicals are generated directly. They improve the free radical level in cancer cells while the cancer itself has no mechanism for elimination of free radicals, thus resulting in the apoptosis of the cancer cells. Contrarily, normal cells have mechanisms for eliminating free radicals and can avoid any damage, which may be the main effect mechanism of medical ozone for cancer therapy.

In the process of nontoxic integrative cancer treatments, medical ozone therapy fights against cancer cells by generating free radicals or increasing free radicals. Detoxification therapy, such as VitC therapy, plays a role in counteracting free radicals. Is there any contradiction between two such therapies? Clifford Hospital has conducted 5 years of clinical observations on patients who received medical ozone therapy while receiving detoxification therapy simultaneously. There was no contradiction or dispute available between the two. On the contrary, they both play complementary roles; the large number of free radicals generated in medical ozone therapy can be scavenged by VitC, thus avoiding damage to the body. Also, VitC does not incur any influence on the free radical level in the cancer cells and the therapeutic effects of medical ozone. However, the applications of the aforementioned two therapies must be kept at a certain time interval. The effect mechanism of VitC on cancer is different from that of medical ozone, but both of them are not repugnant.

4.3.3 Common methods of medical ozone therapy on cancers

Medical ozone therapy has been widely used for treating various cancers in China and other countries. Through medical ozone therapy, 60% of patients have obtained long-term remission of symptoms, 20% have improved significantly, and 70% have reduced pains. It can also be used for patients with cancer reoccurrence.

4.3.3.1 MEDICAL OZONE RECTAL INFUSION

Medical ozone rectal infusion is the most mature therapy. It has a significant therapeutic effect on ulcerative colitis and is more effective than traditional colitis therapies. The rectal infusion of the mixed gas O_2–O_3 is a simple and inexpensive ozone-delivering method. It is not dangerous and has obvious advantages without any side effects.

The concentration of medical ozone is very important in inducing local or whole-body effects. Generally, the concentration of medical ozone must not be more than 40 μg/mL. Otherwise, the therapy usually causes spasmodic pains, especially during its use for patients with ulcerative colitis or after rectal infusion; it will bring indications of a dangerous stimulation to regional intestinal tracts. If the mucus layers are washed, medical ozone with high concentration can destroy the enteral epithelial cells directly, because medical ozone can induce the occurrence of mutation. Therefore, it is suggested that 3–5 μg/mL should be applied at the beginning of therapy; it can be gradually increased to 30 μg/mL if patients have a good tolerance. It has been recorded that the common concentration of medical ozone can be 70–80 μg/mL to stop bleeding; however, it is inadvisable due to the occurrence of cytotoxic damage. Since medical ozone can induce tolerance, it is reasonable that the concentration can be increased to 30 μg/mL within 2 to 3 weeks. Whether the highest concentration of 40 μg/mL is appropriate depends on the pathological types, tolerance of patients, and daily observed information obtained through sound clinically controlled research. The therapy can be done every day or every other day and continued two to three times per week while maintaining a medium concentration of medical ozone.

4.3.3.2 EXTRACORPOREAL BLOOD OXYGENATION AND OZONATION

EBOO (Figure 4.2) refers to a therapeutic method in which blood is drawn out through venous blood vessels for direct ozonation and then fed back through the venous blood vessels. EBOO is the main method for medical ozone therapy and no toxic or side effects have been reported in our several-years-long applications, and some of its technical problems have been solved. The dosage and concentration of medical ozone can be precisely controlled in EBOO, which is very important for cancer patients. EBOO is a process of circulation from vein to vein, which avoids arteriopuncture, with higher technical operation requirements.

Figure 4.2 Extracorporeal blood oxygenation and ozonation.

For EBOO, the most apparent problem during the process of operation is coagulation; that is, the blood drawn coagulates in vitro and cannot be reinfused into the body. After some improvements of the techniques, a small dose of heparin was shown to ensure a normal operation process and is appropriate for advanced cancer patients, and it will not cause any complication including bleeding. Of course, it is not the first choice for patients with a bleeding tendency.

EBOO can generate a large amount of oxygenic free radicals in a short time, which will improve the free radical level in the local tumor, induce apoptosis of cancer cells, and reach the effect of killing cancer cells. Because the body has a strong antioxidant function and reduction of free radicals, EBOO has no obvious influence on the body. In other words, EBOO is safe and effective due to the progress and improvement of its operational technique.

4.3.3.3 MEDICAL OZONE MAJOR AUTOHEMOTHERAPY

Medical ozone major autohemotherapy refers to a therapy in which venous blood of 100–150 mL is mixed with medical ozone gas in vitro and then fed back to the body. This therapy is characterized by simple operation, no complication, short therapy time, and easy acceptance by patients. In the 1960s, the therapy was proposed by Hans Wolff, with indications including cardiocerebrovascular disease, peripheral blood flow disorder, acute and chronic viral disease (hepatitis B, hepatitis C, and herpes), metabolic disorder (hyperlipemia and diabetes), and various infectious diseases. There is less application experience of medical ozone major autohemotherapy in the tumor department, considering that tumor therapy requires many more doses of medical ozone during cancer therapy, but this therapy is not able to provide enough ozone; therefore, EBOO is always required. Further research is required regarding whether medical ozone major autohemotherapy can provide enough doses of ozone.

In the process of medical ozone major autohemotherapy, the main problem is related to the storage of blood after its extraction out of the body. Any plastic bag is forbidden because medical ozone can result in the oxidation, decomposition, and damage of the plastic bag and the phthalate composition of the plastic bag can cause lesions to the body; therefore, a glass bottle or a special antioxidant blood bag must be used.

In the process of medical ozone major autohemotherapy, there is no blood coagulation or air embolism, or hemolysis. During the operation, we have to pay attention to the mixing time between medical ozone and blood, totaling 5 minutes, to maximize the reduction of chances of foam and hemolysis. In current clinical research, there have been few reports regarding cases of thrombus and hemolysis, showing that this therapy is effective and safe.

4.3.3.4 MEDICAL OZONE MINOR AUTOHEMOTHERAPY

Medical ozone minor autohemotherapy differs from medical ozone major autohemotherapy mainly in blood volume, generally totaling 3–5 mL, and the application methods between them are different. Minor autohemotherapy mainly adopts gluteal injection or acupoint injection after sufficient mixing with ozone.

4.3.3.5 VAGINAL MEDICAL OZONE THERAPY

Medical ozone therapy on vaginal infection is sufficiently successful. For each patient, an appropriate therapy is necessary. Medical ozone therapy has obvious effects on the cure and prevention of chronic pelvic inflammatory disease, vaginal cancer, cervical cancer, ovarian cancer, and adnexal carcinoma. Medical ozone therapy applied to patients treated with radiotherapy or chemotherapy can strengthen the effect of radiotherapy and chemotherapy, can relieve toxic and side effects, and has obvious prevention effect on enteritis and vaginitis caused by radiotherapy and chemotherapy.

We must pay attention to the concentration of medical ozone applied, because an exceedingly high concentration may cause serious damages to vaginal mucosa.

4.3.3.6 MEDICAL OZONE ENVELOPING THERAPY

Medical ozone enveloping therapy is mainly applied to lesions, such as hypoxia, ulceration and necrosis of skin, four limbs and blood vessels, and so on, with indications including cutaneous cancer, radiation injury of skin, skin trauma, infection, and diabetes.

4.3.3.7 MEDICAL OZONE OLIVE OIL OR MEDICAL OZONE SALINE

The main indications of medical ozone olive oil include traumatic wound, mucosal lesion, mucocutaneous damage after radiotherapy, skin tumor, and oral cancer. Normal saline solution is sufficiently mixed with medical ozone and then infused into the body of the patient. Such an operational method can be taken as a supplement for EBOO and medical ozone major autohemotherapy. Because normal ozonized saline solution has a lower dissolution concentration of medical ozone, it cannot replace EBOO and medical ozone major autohemotherapy; it can only be applied under the specific condition that enough blood fails to be drawn from patients who require medical ozone therapy. The indications of this method include various cancers or nerve diseases and inflammatory diseases or infectious diseases.

4.4 HYPERTHERMIA INTEGRATED WITH CELL THERAPY

Cell therapy, also known as cancer adoptive immunotherapy, is to induce, activate, and expand in vitro the progenitor cells of self or xenogenous anticancer effect cells through IL-2, anti-CD3 monoclonal antibody, and activators such as specific polypeptides and then transfuse them to cancer patients so as to improve their anticancer immunity and realize the purpose of therapy and prevention from recurrence. Through several decades of development, cancer adoptive immunotherapy has used cell preparations successively, such as natural killer (NK) cells, lymphokine-activated killer (LAK) cells, and tumor-infiltrating lymphocytes. At present, the most widely used cells clinically are the third generation of adoptive immune cells, including dendritic cell (DC), cytokine-induced killer (CIK) cell, and DC-CIK, which have been widely applied to clinical therapy on patients with viral hepatitis and cancers. The immune cells, after inductive cultivation, enter the human body and then target and kill the cells infected by virus and cancer cells (especially tiny focus-based cancer cells). They can actively stimulate the immune function of the body itself, secrete a large number of cytokines, and ultimately reach certain therapeutic effects: hepatitis B surface antigens can turn negative; E antigen and E/antibody can be converted into each other; the reoccurrence and metastasis of cancer can be depressed; the remission rate of cancer can be raised; the remission time of cancer can be prolonged.

In the modern medical model, antagonistic methods are usually adopted for therapy on diseases, so there are many insufficiencies and defects. The application and development of cell therapy have opened a new disease therapy mode in the medical field: living tissues are adopted to reconstruct and regenerate diseased and aged tissues for the purpose of achieving healthy recovery.

At present, there is no literature or report about the interaction relationship between hyperthermia and cell therapy, but both of them are usually applied to integrative cancer treatments clinically without any obvious adverse reaction.

4.4.1 Cancer hyperthermia and DC-CIK

In recent years, research has shown that the anticancer mechanism of hyperthermia can promote the immune function of the body and strengthen the anticancer effect in addition to promoting the necrosis and apoptosis of cells by destroying DNA using high temperatures. The main representations are as follows: hyperthermia can promote the hyperplasia and activity of nonspecific killer cells such as NK cells, and macrophages; positively regulate T cell subpopulations; and promote the expressions of cancer-depressing cell factors like IL-2, and so on. Additionally, further research has shown that heat shock protein (HSP) plays a core role in the body immunity improvement of hyperthermia. HSP is a very conservative protein synthesized by stress, especially thermal stress induction cells, and can be classified into families such as HSP110, HSP90, HSP70, HSP60, small-molecule HSP, and ubiquitin in accordance with its homology and molecular weight.

Research has found that the degeneration and necrosis of cancer cells can occur, and their products decomposed by the body can be taken as antigenic peptides to stimulate the immune response of the body after heating the cancer cells. High temperatures can increase the fluidity of plasma membrane bilayers to expose the antigenic determinants inlaid bilayers and increase the antigenicity of cancer cells. Hyperthermia can also destroy the depression effect of blocking factors on the immune system to recover the body's immune

response to cancer. When hyperthermia is conducted, the cancer cells can secrete a large number of HSPs and form HSP–antigen peptide complexes with various tumor antigens so as to participate in the immune response. It is done in the following ways: (1) participating in the processing and presentation of tumor antigens, (2) participating in the growth and differentiation of immune cells, (3) participating in the homing of lymphocytes, and assisting the assembly of immune globulins.

With the support of the aforementioned theoretical research, the combined application of hyperthermia with DC-CIK therapy is supposed to be a more effective anticancer approach. Zhu Liming adopted the tumor antigen–pulsed DC vaccines combining hyperthermia for therapy on advanced non–small cell lung cancer. The local sound field hyperthermia was applied within 1 day before DC feedback, which had a better effect. Guo et al. adopted the intratumoral injection to treat nine patients with malignant melanoma after hyperthermia. The results showed: for the combined application, one patient with complete remission, three patients with local remission and four patients with stable disease condition; for the DC alone group, one patient with local remission and three patients with stable disease condition; which indicates obviously that the therapeutic effect of the combined application group is better than that of the DC alone group.

4.4.2 Mechanism of cell therapy on cancer

4.4.2.1 Cytokine-induced killer

In 1991, Schmidt Wolf first reported the CIK cell, which is a group of heterogeneous cell populations with $CD3^+$ $CD56^+$ T cells as main effect cells obtained by peripheral blood mononuclear cells (PBMC) in the peripheral blood, through the induction of various cell factors such as CD3 monoclonal antibody and IL-2 in vitro. Because it has not only T cell surface signs but also NK cell surface signs, it has the anticancer activity of T lymphocyte as well as the non-MHC restrictive cancer-killing activity of NK cell. In clinical applications, it has a sound therapeutic effect on solid tumors and partial blood system cancers. Its main functional mechanism includes the following aspects:

Direct killing effect: It can identify and combine with target cells by surface antigens and then release particles in the cytoplasm (perforin, cells dissolved element, etc.) to kill the cancer cells directly.

Indirect killing effect: After CIK enters the body, it can release a large number of cancer-depressing cytokines (IL-2, IFN, TNF, etc.) to kill cancer cells indirectly by regulating the immune function of the body. It induces the apoptosis of cancer cells.

Reversion of multidrug resistance: Some research has shown that CIK can reverse the multidrug resistance of cancer cells by reducing the expression of *P-gp* to provide further theoretical bases for the combined application of CIK and chemotherapy.

4.4.2.2 Dendritic cell

DC is the antigen presenting cell currently considered as having the strongest function and can acquire, process, and present antigens effectively. Any immature DC has strong transfer ability, whereas any mature DC can activate the initial type of T cells effectively, staying in the central link of initiating, regulating, and maintaining immune response. In recent years, research has shown that DC is closely associated with the occurrence and development of cancer cells; the more DC infiltrates in most solid tumors, the better the patients' prognosis. DC cells can become mature in vitro through the induction of certain cell factors after they separate out PBMCs. Meanwhile, tumor-associated antigens or antigenic peptides are applied to impact and sensitize DC in vitro for the preparation of tumor DC vaccines, which are fed back or vaccinated into the host, thus inducing the anticancer immunoreaction of specific CTLs.

4.4.2.3 DC-CIK

Research has shown that DC and CIK can strengthen the multiplication capacity and killing activity of CIK after cocultivation, and the in vitro cocultivation of DC-CIK can pass the complex immune and depression passages in the body of patients with cancer, so it can generate better therapeutic effects than in vivo

application of DC vaccine or CIK alone. Zhan Hailun et al. discussed the killing activity of DC-CIK cells on kidney cancer after cocultivation of antigen sensitization DC and CIK. The cocultivation group of antigen sensitization DC and CIK, cocultivation group of nonsensitization DC and CIK, and CIK alone group showed their killing activities on 786-0 cells of (70.64 ± 8.26)%, (53.40 ± 7.33)%, and (46.64 ± 6.01)%, respectively, demonstrating that DC-CIK cells can improve the killing specificity and killing activity of CIK cells on kidney cancer after cocultivation of primary sensitization DC and CIK.

4.4.3 DC-CIK INDICATIONS

4.4.3.1 INCLUSION STANDARD

It is applicable to most solid tumors and blood system cancers and has better therapeutic effects on cancers with strong immunogenicity, such as kidney cancer, prostatic carcinoma, and malignant melanoma. It is applicable to most malignant cancer patients who along with their families ask for T cell and NK cell therapy and fully understand the relevant indications and complications. It is applicable to small load tumors, in combination with other treatment means after radical cure or cytoreductive surgery.

4.4.3.2 CONTRAINDICATIONS

Contraindications include the following: (1) patients with NK/T cell lymphoma and T cell leukemia; (2) patients with autoimmune diseases; (3) patients with severe systemic infection or severe local infection who require anti-infection healing; (4) patients with dysfunction of important organs such as combined heart, lung, liver, and kidney; (5) patients with blood coagulation dysfunction such as hemophilia; (6) patients with severe allergic constitution or severe allergic history; (7) patients with low levels of leukocytes ($<1.5 \times 10^9$/L) or agranulocytosis ($<0.5 \times 10^9$/L) or severe anemia; (8) patients with shock or systemic failure and abnormal vital signs or who are not able to receive an examination; and (9) patients in the gestational period and breast-feeding period.

4.4.3.3 PRUDENCE STANDARDS

Prudence standards include the following: (1) patients with unrealistic expectation, (2) patients with relatively stable cardiovascular disease and lung disease, (3) patients with blood transfusion history within 3 months, and (4) patients with an expected survival period less than 3 months.

4.4.4 CLINICAL APPLICATIONS

Cancer adoptive immunotherapy (Figure 4.3) has become the fourth major means of cancer treatment and is widely applied clinically after surgery, radiotherapy, and chemotherapy. Clinical data show that DC-CIK cell

Figure 4.3 Cell therapy.

therapy is applicable to patients with low tumor load after surgery, radiotherapy, and chemotherapy and has particular advantages in clearing residual minimal lesions and preventing the recurrence and metastasis of cancer. For those advanced patients without contraindications and with failure of radiotherapy and chemotherapy, DC-CIK cells can improve immune functions effectively, improve tumor-bearing survival quality, and prolong survival time.

4.4.4.1 KIDNEY CANCER

Forty-five patients with kidney cancer at the clinical stage of $T_{1\text{-}3}N_{0\text{-}1}M_0$, all of whom were treated with laparoscopic radical nephrectomy, were randomly divided into three groups: the DC-CIK treatment group, IFN-α treatment group, and control group. As a result, the specific values of CD3+, CD4+, and CD4+/CD8+ in the DC-CIK therapy group and IFN-α therapy group rose significantly compared to those before surgery. Long-term tracking interviews showed that all the patients in the immunotherapy groups (treatment groups) survived. There was no patient with recurrence and metastasis in the DC-CIK group, whereas there were four patients with recurrence or metastasis and three patient deaths in the control group. There were significant differences in survival rates in 3 and 5 years between immunotherapy group and control group, demonstrating that immunotherapy could improve the immune status of patients with kidney cancer to some extent and raise the comprehensive therapeutic effect on kidney cancer after early kidney cancer surgery and that DC-CIK cell immunotherapy had the same therapeutic effect as IFN-α immunotherapy in preventing the recurrence of kidney cancer but with fewer side effects. Zhang Peng et al. applied CIK therapy to 80 patients with advanced metastatic kidney cancer. The progression-free survival rates of the CIK therapy group for 1, 2, and 3 years were 47%, 28%, and 17%, respectively, in contrast with the IL-2 and IFN conventional immunotherapy group, which had respective rates of 36%, 15%, and 10%. The total survival rates of the CIK therapy group for 1, 2, and 3 years were 87%, 67%, and 59%, respectively, which also were significantly superior to the values of 55%, 37%, and 18%, respectively, in the conventional immunotherapy group. Li Jianwang et al. adopted autologous DC-CIK combining sorafenib for 26 patients with metastatic renal cell carcinoma, with results showing a disease control rate up to 72.7% and an objective effective rate up to 19.12% and with median survival time and median no-progress time totaling 25 and 14 months, respectively, suggesting that DC-CIK therapy combining sorafenib has an obvious effect on metastatic renal cell carcinoma.

4.4.4.2 LIVER CANCER

For early liver cancers, surgery is mainly applied. CIK therapy is combined after the operation, which can not only remove the residual foci but also improve the immunity of the body, helping the patient to recover as soon as possible. In addition, for patients with advanced liver cancer there have been reports showing that hepatic arterial embolism chemotherapy combining CIK therapy can improve the effect of interventional liver cancer chemotherapy significantly and reduce the toxic effects of chemotherapeutic drugs on liver. The median survival rates of the combined application group and the control group totaled 22 months (95% confidence interval [CI], 7–37) and 10 months (95% CI, 8–12), respectively. The survival rates of the two groups in half a year, 1 year, and 2 years totaled 85.71%, 58.35%, and 48.62% and 69.05%, 32.74%, and 3.97%, respectively. The survival periods of the combined application group were obviously longer than those of the control group. Compared with hepatic arterial embolism chemotherapy alone, the aforementioned combination may improve the long-term survival rate of patients with primary liver cancer. Patients with medium and advanced liver cancer, due to serious damage in liver functions, cannot tolerate chemotherapy, radiotherapy, chemotherapy, and interventional therapy. CIK therapy can improve the quality of life and prolong the survival time of patients who survive with cancer.

4.4.4.3 LUNG CANCER

Peng Dawei et al. applied the autologous DC-CIK therapy combining pemetrexed therapy to cure non–small cell lung cancer in the elderly, which was compared with the effect of pemetrexed therapy alone, with the following results: the clinically beneficial rates of the combined therapy group and the chemotherapy alone group were 66.67% and 56.52%, respectively, and their median survival rates were 9.3 and 8.7 months, respectively, showing that the combined therapeutic effect was better.

4.4.4.4 COLON CANCER

Li Sha et al. compared the effects of a chemotherapy alone group with those of a chemotherapy combined with DC/CIK therapy group for colon cancer, and the results showed that the local recurrence rate of the combined administration group was lower than that of the single chemotherapy group and the immunity of the organism of the former is higher than that of the latter, but there were no obvious differences in survival rates between the groups for 1 and 2 years.

4.4.4.5 MALIGNANT PLEURAL EFFUSION

Xiong Ruihua et al. compared the therapeutic effect of pleural infusion chemotherapy drugs with a perfusion of CIK for malignant pleural effusion treatment; the results showed that the total clinical effective rate after administration of perfusion chemotherapy drugs was up to 52.94%, whereas the clinical effective rate after perfusion of CIK totaled 81.25%, and the perfusion of CIK was safer and could improve the patient's life quality effectively.

4.4.4.6 HEMATOLOGICAL CANCER

Zhou Dongfeng et al. used chemotherapy combined with DC-CIK cell therapy to treat 47 infants with acute leukemia who were followed up for 5–72 months. It was found that 36 infants were under continuous and complete remission among 38 negative minimal residual disease sufferers and 8 infants became negative after reinfusion therapy among 9 minimal residual disease–positive sufferers, showing that DC-CIK therapy had an advantage in the treatment of acute leukemia in infants, including the clearing of minimal residuals.

4.4.5 Concomitant reactions and treatment

4.4.5.1 FEVER

After reinfusion, patients may show fevers of less than 38.5°C within 1 to 2 hours, with or without chills. There are many reasons for fevers caused by cell therapy, such as infectious pyrogens (e.g., bacteria and endotoxins) and immunologic factors (such as residual cytokines, cytokines released by immune response, and mediators of inflammation). The clinical treatment is done in the same way for the transfusion reaction. If the body temperature of the patient does not exceed 39°C, physical cooling can be applied. However, if the body temperature exceeds 39°C, the fever lasts for over 6 hours, or the patient feels any obvious discomfort, the stored cell samples must be delivered for inspection to rule out any infection, and it must be treated as an acute infection if it is indeed an infection.

4.4.5.2 ANAPHYLACTIC REACTION

Symptoms of mild allergy are skin pruritus, skin redness, or maculopapule. It is mainly caused by heterologous proteins and cells. It can relieve itself without any treatment. If the allergy is severe or the symptoms continue, antianaphylaxis symptomatic therapy can be applied.

4.5 HYPERTHERMIA INTEGRATED WITH ACUPUNCTURE THERAPY

Acupuncture's role in integrative anticancer treatments is currently attracting the attention of more and more people, and it has become one of the common approaches for cancer prevention and treatment. The characteristic of acupuncture therapy (Figure 4.4) is its natural regulation of overall body functions. Especially for the advanced cancer patients who are not suitable for surgery or chemotherapy, acupuncture therapy can be used for its more unique advantages and play an irreplaceable role in cancer prevention and treatment. Acupuncture has no toxic side effects and can reduce toxicities and side effects of radiotherapy and chemotherapy, promote the functional recovery of the body after surgery, improve the general body conditions of patients, and mobilize the particular immunocompetence of the human body, which have been verified clinically and with remarkable therapeutic effects.

Figure 4.4 Acupuncture.

4.5.1 Cancer hyperthermia and acupuncture therapy

Hyperthermia and acupuncture have therapeutic effects in improving immunity and reducing the side effects of chemotherapy. In clinical applications, cancer therapy emphasizes integrative treatments and acupuncture has unique advantages in improving the life quality of patients. Cancer hyperthermia has shown its therapeutic effects of improving the life quality of patients and prolonging their survival periods, which have been confirmed clinically. The combination of the two therapies reflects the integrative cancer treatment principle and the nontoxicity principle and also shows the TCM principle of people orientation, strengthening vital qi, and eliminating pathogenic factors. As an overall therapy, their therapeutic principles and functions are complementary and have certain clinical therapeutic effects. Whether the combination of the two therapies has a superimposition effect or a synergistic effect requires further verifications on random large samples.

4.5.2 Fundamental research on acupuncture treatment of cancer

4.5.2.1 FUNDAMENTAL THEORIES OF TCM MERIDIANS

Acupuncture and moxibustion are important components of TCM, which is based on an integral view. The integrity of acupuncture refers to certain acupuncture points of the body, which can influence the functions of multiple organs and play multifaceted, multilinked, multilevel, and multiway regulation roles in the functions of various systems and organs of the body. For example, local stimulations of microneedles, such as auricular acupuncture, scalp acupuncture, hand acupuncture, foot acupuncture, nose acupuncture, tongue acupuncture, and eye acupuncture, can excite channel qi, thereby generating overall regulatory functions of the body and curing various systemic diseases.

In the integral view of TCM, the human body is a complete organic integration and all the parts constituting the human body are indivisible, supplementing each other in function and affecting each other in pathology. Meridian is the generic name of channels and superficial venulles and is also a passage running qi blood, connecting viscera and limbs and joints, and linking the up and down as well as the intrinsic and extrinsic. The meridians run all over the human body and organize the viscera, organs, apertures, and flesh and bones into an organic integration. The meridians include twelve regular meridians, eight extra meridians, internal branches of twelve meridians, musculature of twelve meridians, skin areas of the twelve meridians, and collaterals and subcollaterals (including superficial collaterals and minute collaterals). Because the meridian

system connects the viscera inside and the flesh and bones outside, appropriate stimulation on acupuncture points, excitation on the conduction and induction of the meridian, dredging of meridian, and regulation of yin–yang and qi blood can strengthen vital qi and eliminate pathogenic factors, rectify the ebb or flow and excess or deficiency of qi blood in the viscera, and regulate the balance of yin and yang, so as to reach the purpose of treatment of diseases.

4.5.2.2 INTEGRITY AND BIDIRECTION OF ACUPUNCTURE IMMUNITY REGULATION EFFECT ON CANCER

The integral views of TCM acupuncture and moxibustion as well as modern immunology are the theoretic bases of the immune regulation effect of acupuncture. The human body has the balancing capacity of automatic immune regulation to maintain a stable internal environment, and acupuncture for disease treatment is realized through regulation of the immune function of the unbalanced body by integral bidirectional regulations. The advantages of acupuncture lie in its capability of overall functional regulation and bidirectional regulation of the organism's immune defense function, enhancing the normal body's immune function, raising low immunity, depressing hyperactive immune responses, recovering disordered physiological functions, and reconstructing the balance and stability of the internal environment. As a result, acupuncture can adjust the disordered viscera functions of cancer patients and regulate the imbalanced immune function so as to exert an overall anticancer effect. As a natural therapy, due to its advantages of bidirectional regulation on cancer immunity function, it plays an important role in anticancer therapy and is quite a promising therapy during cancer immunotherapy.

4.5.2.3 REGULATION OF IMMUNE FUNCTION

A large number of clinical observations and research has shown that acupuncture can improve the immunity and immunosurveillance functions of the body, enhance the activities of NK cells and LAK cells with anticancer effects, and raise the immune levels of cancer patients. As for the intricate phenomenon in some patients with low cellular immune function and high humoral immune function, acupuncture can coordinate the immune response in different immune links to achieve normalization and reach immune balance, namely, the vital qi balance of TCM.

There are two main pathways of acupuncture for cancer treatment: one is indirect therapy on cancer, that is, it can improve the immune function of the human body for anticancer effect; the other is the direct action on cancer for killing cancer cells and dissolving the cancer. The immunomodulatory effect of acupuncture rests on not only a single link but also multilevel, multiaspect regulations of nerve, body fluid, cell, and molecules. It is better than the unilateral regulation of Western immune preparations. Acupuncture can affect the whole process of cancer occurrence and development. It has a unique role in improving clinical symptoms, prolonging survival periods, and preventing cancerization of normal tissues.

4.5.2.4 REGULATION EFFECT OF ACUPUNCTURE ON IMMUNOLOGIC CELLS

Among anticancer immunologic effects, cellular immunity plays a more important role than humoral immunity. Cells participating in antitumor immunosurveillance mainly include T lymphocytes, macrophages, NK cells, LAK cells, peripheral white blood cells, and red blood cells. Acupuncture has various regulation effects on the activities and functions of immunologic cells.

4.5.2.5 REGULATION EFFECT OF ACUPUNCTURE ON IMMUNE MOLECULES

The regulation of acupuncture on immune molecules mainly represents the regulation effect on cell factors like IL-2, immunoglobulin, complements, lectin, hemolysin, bactericidin, precipitin, and plasma bactericidin.

4.5.2.6 DEPRESSION OF CANCER CELL GROWTH

Shi Yin et al. found that acupuncture on the acupoints of Dazhui and Zusanli in mice could increase phagocytosis of peritoneal macrophages, the content of IL-1, and the percentage of helper T cells and could also inhibit sarcoma to some extent. Pei Jian observed that serum lymphocyte stimulation index, activity of killer (NK) cells, and activity of LAK cells in the tumor-bearing mice group were significantly lower than those in

the normal serum control group. NK activity and LAK activity in the Dazhui moxibustion group were much higher than those in the tumor-bearing mice serum group and nonacupoint moxibustion control group, indicating that clearing the cancer-originated immunosuppressive factors was the important mechanism in moxibustion anticancer immune response. Yang Zhixin et al. found that moxibustion on the Dazhui acupoint could significantly depress the growth of malignant lymphoma, with depression rates of up to 41.08%; prolong the survival periods of mice; improve phagocytosis capacity; and improve the killing activity of peritoneal macrophages and IL-1 induction capability. Studies by Liang Jun et al. showed that moxibustion of the Dazhui acupoint could depress the growth of cancer cells, improve the activity of macrophages and NK cells, and improve lymphocyte transformation and mixed lymphocyte proliferative responses. Through experiments on moxibustion on the Guanyuan acupoint against transplanted liver cancer in mice, Zhai Zundang showed that moxibustion could improve the cytotoxic activity of NK cells and the activity of ADCCs of peritoneal macrophages, raise the effect of spleen lymphocytes in converting and secreting leukocyte IL-2, and obviously stabilize the proportion of the spleen T lymphocyte subgroup. Also, it had an obvious depression effect on the growth of cancer in the early stage, revealing that the immunomodulatory effect of moxibustion is an important anticancer mechanism. Through experimental observations of the moxibustion effect on depression of transplanted tumors S180 in mice, Yang Youmi showed that moxibustion could promote the generation of antibodies, improve the immune function and functional activity of the reticuloendothelium, activate the phagocytic activity of macrophages, and protect glucose metabolism of tumor-bearing bodies through the enhancement of immune function, thus stabilizing the internal environment of tumor-bearing bodies to depress the growth of tumors and support and protect the tumor-bearing human bodies.

Experimental studies also showed that after moxibustion on Dazhui and Guanyuan the cancers were significantly lighter than in the control group, the intrinsic cancer cell growth was not active, some cells were severely damaged, and there was an enveloping layer between cancer and peripheral tissues. Yang Youmi et al. reported that moxibustion on Dazhui in mice could generate a certain protective effect on the tumor-bearing body, depress the growth of tumors, and reduce the weight of tumors. The experiments by Sun Lanying showed that the moxibustion on Dazhui could prevent the growth and outward expansion of tumors in mice with solid tumors and ascites tumors. The moxa-moxibustion on Guanyuan could significantly prolong the survival of mice that had been vaccinated with HAC (mouse ascites hepatoma) tumor cells and also had significant depression effect on the growth of tumors. It is now believed that the depression effect of acupuncture on the growth of tumors is closely related to the fact that acupuncture can activate the immune system and the phagocytosis of macrophages and can enhance the anticancer immune response capacity of the tumor-bearing body.

4.5.2.7 DISSOLUTION EFFECT ON CANCER

Acupuncture therapy has the function of shrinking and dissolving cancer. There are two forms of disappearance of cancer: first, large tumors gradually reduce in size and then disappear; second, large tumors dissolve into some small cancer foci and then disappear gradually. The electrothermic needle is clinically applied to some superficial malignant tumors and has shown satisfactory therapeutic effects. Xia Yuqing et al. applied electric acupuncture to 100 patients with skin cancer, and two to three therapeutic courses resulted in 56 patients whose cancer disappeared completely, 36 patients whose cancer were reduced partially, and 8 patients whose cancer had no change or had deterioration, with a total efficiency of up to 92%. Tang Xuezheng et al. conducted research on the depression effect of electrothermic needles on three kinds of mice with transplantable cancers (gastric cancer, breast cancer, and liver cancer) by inserting electrothermic needles into the centers of the cancer, with a heat of 135–96 cal for 40 minutes. The results showed that the survival rates of treatment groups were much longer than the control group. The curative ratio of gastric cancer of the mice was 70%–100%; the curative ratios of breast cancer of the three kinds of mice were 50%–60%, 76%–83.3%, and 84.8%–90.6%, and the curative ratios of liver cancer of the three kinds of mice were 70%–88.2%, 88.2%–90%, and 84.2%–94.4%. There was no metastasis in the treatment group when the experiment was repeated. Experiments show that the principle of cancer therapy by using the electrothermic needle rests with the high-temperature cauma directly stimulating the tumor, so as to result in the shrinkage of tumor tissues, coagulation and necrosis of cancer cells, and ultimately scabbing and falling. In

addition, moxibustion is used to directly act on the region of cancer; similarly, high-temperature cauma can also kill the cancer. This therapy has great significance in superficial tumor treatment. Animal experiments show that acupuncture has a significant depression effect on the growth of transplanted cancer of animals and can improve the survival rate and survival time of tumor-bearing animals.

Fundamental research on the anticancer effect of acupuncture conducted in Japan presented the increased depression rate of subcutaneous transplanted tumor cells in animals receiving moxibustion; the skin tissue extracts of moxibustion-tested parts had anticancer substances with anticancer factors, which were nonspecific reactions to the physical stimulation of the body. Junin Noma made observations and therapies on the solid cancer of tumor-bearing mice by moxibustion. When the tumors proliferated to 10 mm × 10 mm, the mice were divided into a moxibustion group and a control group, with five mice in each. In the moxibustion group, a moxa cone was applied to the cancerous protuberance skin for therapy. After 3–6 weeks, all the cancerous protuberances disappeared in the moxibustion group, whereas the cancerous protuberances significantly increased in the control group.

4.5.2.8 PREVENTION OF CANCER CELL METASTASIS

Acupuncture has the function of anticoagulation and fibrinolysis and can maintain the balance of the blood coagulation and fibrinolysis system. Accordingly, acupuncture can reduce the blood viscosity of patients with cancer and improve the high coagulation state of cancer patients, for which the acupoints activating blood circulation to dissipate blood stasis can be selected such as Sanyinjiao, Zusanli, Hegu, Taichong, Xuehai, Baihui, Yangyingquan, Dazhui, Pishu, and Geshu. Modern research shows that these acupoints can expand capillaries, increase blood flow, promote penetration of immunocompetent cells into the cancer, depress the growth of cancer cells, inhibit platelet aggregation, promote fibinolysis, and destroy the agglutination of fibrins around cancers and in foci, so as to prevent cancer cells from nidation and block the cancer from metastasis.

4.5.2.9 BIDIRECTIONAL REGULATION OF ENDOCRINE SYSTEM

The disorder of hormone levels and the endocrine balance in the body are closely associated with the occurrence and development of cancer. Clinical studies by Zheng Kuishan et al. show that heat-reinforcing acupuncture can obviously improve the adrenal cortex structure and function of mice with insufficiency of kidney yang, enhance the cortical hormone levels in plasma, depress the atrophy of the adrenal cortex, and promote the metabolism of substances and hormone synthesis process in cells, which shows that acupuncture can enhance the adrenocortical function and regulate the adrenocortical hormone. Research conducted by Xu Zheng et al. shows that patients with hyperplasia of mammary glands can suffer from disorder of cell immune function and sexual hormones, which can be regulated by acupuncture. Research performed by Yang Jinhong shows that acupuncture can regulate the abnormally increased or reduced estradiol (E2) and estriol (E3) levels in patients with cancer to some extent and reduce elevated testosterone levels. In addition, the regulation of acupuncture on estrogen can reduce formation of high-level serum follicle-stimulating hormone, increase the reduced progesterone, and especially and significantly increase the decreased estradiol (E2). Research also shows that acupuncture on Shenshu and Guanyuan can significantly increase the luteotropin and testosterone hormones of white rats with insufficiency of kidney yang. Wu Yujun et al. conducted auricular acupuncture excitation experiments, with results showing that auricular acupuncture could regulate the secretion of growth hormone bidirectionally. Therefore, acupuncture has a bidirectional regulation effect on hormone levels in the body and can be applied for the treatment of diseases related to hormones, such as breast cancer and prostate cancer.

4.5.2.10 REGULATION OF INTRACELLULAR cAMP CONTENT AND cAMP/cGMP RATIO

Cyclic adenosine monophosphate (cAMP) and cyclic guanosine phosphate (cGMP) are key links representing the relative balance of yin and yang in cells. cAMP plays an important role in the body and is closely associated with the occurrence and development of cancer. Cancerization is related to cAMP content in cells; low cAMP content and abnormal ratio of cAMP/cGMP in cells of the body can lead to disorder of cell proliferation and differentiation function. For a cancer patient, the lower the cAMP content in cancer cells, the more

serious the disease condition, while the increase of cAMP content or improvement of cAMP/cGMP ratio can depress the proliferation of cancer cells, make the cancer cells convert into normal cells, and depress cancer growth. In recent years, much extensive research has shown that acupuncture is able to regulate yin and yang, adjust the balance and stability of the internal and external environments of the body, and enhance cAMP content and cAMP/cGMP ratio. The cAMP/cGMP ratio plays a major role in regulating the balance of the internal and external environments of patients with cancer. Guo Yaojie took mice vaccinated with Sl80 sarcoma as animal models and then conducted moxibustion with moxa cones on Zhongwan to observe the depression effect of moxibustion on cancer, and results showed that moxibustion could depress the increase of tumors in cancer mice, improve the ratio of cAMP to cGMP plasma in cancer mice, and strengthen the cytotoxic activity of spleen NK cells. Animal experiments also show that injection of cAMP into primary or transplantable cancer in the body can depress cancer growth. Therefore, cAMP has an effect on cancer cells in promoting differentiation and depressing proliferation.

In conclusion, a large number of clinical practices and modern medical research results show that acupuncture therapy on diseases has three major functions: abirritation, enhancement of defense and immune effects of the body, and regulation on various systems of the body. These three functions are required for cancer therapy. The acupuncture therapy on cancer includes two approaches: indirect therapy on cancer, namely, strengthening the body's anticancer immune functions, and directly acting on the cancer to kill cancer cells and dissolve the cancer. The immunoregulatory effect of acupuncture does not act on any link singly but conducts multilayer and multilink regulations on nerve, body fluid, cell, and molecule at different levels, so it is better than the single regulation of Western medicine immune preparations. The anticancer effect of acupuncture is mainly to improve the immune function of the body; allow the obvious rise of conversion rates of the body's immune cells, such as T cells and lymphocytes; and enhance the activity of NK cells, LAK cells, and macrophages. The enhancement of these immune cells is very important for cancer patients, and it can kill the cancer cells in the human body naturally and promote the apoptosis of cancer cells. At the same time, the disordered viscera functions of the body are regulated and the function of the body in generating normal cells is recovered through the regulations of acupuncture, while abnormally proliferating cancer cells become aged and gradually die and cancer foci thereby stop growing and then shrink until they disappear. Acupuncture can affect the whole process of cancer occurrence and development and has particular effects on improving the clinical symptoms, prolonging the survival periods, and preventing the canceration of normal tissues. This discussion presents the current recognition of the therapeutic effect mechanism of acupuncture in cancer treatment.

4.5.3 Clinical research on the anticancer effect of acupuncture

4.5.3.1 Prevention and treatment of bone marrow depression caused by radiotherapy and chemotherapy

Radiotherapy and chemotherapy can easily cause bone marrow suppression and hematopoiesis dysfunction of the bone marrow and reduction of leukocytes in patients accompanied by infections, thus influencing the successful operation of chemotherapy. At present, clinically, GM-CSF treatment is usually applied, with common drugs of rhG-CSF, rHuG-CSF, G-CSF, and so on. These medicines have definite therapeutic effect on the increase of leukocytes, but they have disadvantages such as high price and poor patient compliance. The combination of acupuncture with moxibustion is clinically adopted to prevent the arrest of bone marrow incurred after chemotherapy, with satisfactory therapeutic effects.

Acupuncture on acupoints: Zusanli, Sanyinjiao, Hegu, Neiguan, Pishu, Shenshu, Taixi, and so on. *Moxibustion on acupoints:* Guanyuan, Qihai, Dazhui, Geshu, Pishu, and Shenshu. Due to the reduction of leukocytes, patients with cancer often present clinical characteristics such as deficiency of spleen and kidney or deficiency of both qi and blood, for which we select the Stomach Channel of Foot-Yangming points, Zusanli, Pishu, and Weishu to regulate the spleen and stomach and strengthen the vital energy. Select Sanyinjiao at the intersecting point of the spleen, liver, and kidney meridians to regulate spleen and stomach, benefit liver and

kidneys, replenish essence and blood, and cultivate marrow. Select Shenshu to warm yang, tone the kidneys, and cultivate bone marrow. Select Xuehui and Geshu of the eight influential points to enrich and regulate blood and activate blood circulation. And select Dazhui at the intersecting point of Du channel and Liuyang meridian to strengthen yang qi. The multipoint application of acupuncture can strengthen spleen and stomach, nurse the middle Jiao, benefit liver and kidneys, cultivate bone marrow, nourish blood, and support vital energy. Also, the combination of acupuncture with moxibustion can strengthen their effects. Moxibustion can enhance leukocytes and increase their phagocytosis, increase erythrocytes in blood, improve microcirculation, boost the production of antibodies, and enhance the immune function of the body and the reticuloendothelial activity.

Acupoint injection: Zusanli (both), Sanjinjiao (both), and Dazhui should be selected. Astragalus (2 mL) is injected into two acupoints each time. After routine disinfection of local skin, select a 5-mL injector with a number 5 pinhead to suck the drug solution of 4 mL, and puncture into Zusanli, Sanyinjiao, or Dazhui by rapid needle insertion method, which should be done without returning blood and to the extent that the patient can tolerate local swelling of acupuncture points. Apply 2 mL for each acupoint, once per day, with five times and 2 days off as a course, continuing until 1 week after chemotherapy. The therapy can strengthen patients' sensitiveness to needles and improve the regulation effect of acupoints on the body. Moreover, it can rapidly replenish qi due to the synergistic effect of the drugs on acupoints and meridians. Astragalus root has the effect of replenishing and benefiting qi and blood and improving yang qi. Astragalus is used for acupoint injection, which is a new therapy combining acupuncture with drugs. It is combined with the mechanical effect of acupuncture, pharmacological action of drugs, and the opening and closing as well as conduction of acupoints to strongly stimulate the body so as to recover its normal functions and eliminate the bone marrow suppression effect caused by chemotherapy.

4.5.3.2 PREVENTION AND TREATMENT OF GASTROINTESTINAL REACTIONS INDUCED BY RADIOTHERAPY AND CHEMOTHERAPY

Nausea or vomiting is a common side effect caused by radiotherapy and chemotherapy, mainly due to the fact that radiotherapy and chemotherapy can stimulate the mucous membranes of the stomach and esophagus and result in symptoms such as nausea, vomiting, anorexia, and epigastric distension. Long-term inadequate food intake can lead to decreased immunity of the body and exacerbated disease condition, thus influencing the successful operation of chemotherapy. TCM believes that the nausea and vomiting are the results of the disorder of qi and blood in the human body, phlegm endogenesis, impairment of the spleen, and the stomach and ascent–descent disorder caused by chemotherapeutic drugs. Therefore, acupoints like Zhongwan and Fenglong are selected and the even reinforcing–reducing method is adopted for therapy to regulate the spleen and stomach and improve the disorder of qi and blood. It is better to apply acupuncture early, such as from 5 days before chemotherapy to its completion.

Acupuncture on acupoints: Zhongwan, Neiguan, Zusanli, Shangjuxu, Yanglingquan, Hegu, and Quchi are selected, one to two times per day with needle retention of 30 minutes, by the even reinforcing–reducing method, because patients are asthenic after chemotherapy and their tolerance to strong stimulation is reduced. When manipulating the needles, the lifting–inserting method and the rotating method are combined, and the acupuncture therapy must reach a certain stimulation amount; only then can therapeutic effect be achieved. The acupuncture amount is mainly composed of the two factors of stimulation intensity and stimulation time. There are two needling manipulations for the stimulation time, intermittent and continuous needling manipulations, and the stimulation intensity of the continuous needling manipulation is higher than that of the intermittent needling manipulation. Clinically, however, considering that the patients are asthenic after chemotherapy, the intermittent needling manipulation is applied. For patients with serious vomiting during chemotherapy, it should be combined with acupoint injection including Zusanli, zhongwan, and so on. For patients who are afraid of acupuncture, Clifford Hospital adopts moxibustion alone for Zusanli, Guanyuan, Zhongwan, Neiguan, and so on, which can reduce the counterflow and check vomiting.

Acupuncture can prevent and cure chemotherapy-induced nausea and vomiting because of its moderate stimulation of Zhongwan, which is the Front-mu acupoint of the stomach, where the channel qi of the viscera congregates, and acupuncture on this acupoint can regulate the visceral function and dredge qi channels

and blood. Neiguan has function for dredging qi channels and eliminating adverse qi and is an important acupoint for stopping vomiting. Zusanli is the lower confluent acupoint of the stomach viscera, and combined therapy on the internal viscera is applied to regulate visceral qi and reduce adverse qi. The combination with the Yuan-primary point of Hand-Yangming Large Intestine Meridian Hegu acupoint, confluent Quchi, and the lower confluent acupoint Shangjuxu can nourish the spleen, dedge qi channels, normalize the stomach, reduce adverse qi, and stop vomiting. For the intractable vomiting induced by chemotherapy, acupuncture on Zusanli and Neiguan combined with acupoint injection and auricular therapy can be applied. Metoclopramide dihydrochloride injection of 10 mg or vitamin B_6 of 2–4 mL can be chosen as drugs. The two points of unilateral Zusanli and contralateral Neiguan are injected as one group each time, alternating the two groups, which can attain an obvious therapeutic effect.

4.5.3.3 PREVENTION AND TREATMENT OF ULCERATIONS OF ORAL CAVITY AND XEROSIS INDUCED BY RADIOTHERAPY AND CHEMOTHERAPY

Acupuncture has a good therapeutic effect on ulcerations of the oral cavity and xerosis induced by radiotherapy and chemotherapy. According to the disease conditions of patients, the reducing method is used for excess syndromes and the reinforcing method is used for deficiency syndromes. Its therapeutic mechanism is probably due to promoting the release of neuropeptides and inducing the secretion of the salivary gland.

Acupuncture on acupoints: Lianquan, Jiache, Hegu, Neiting, Quchi, Zusanli, and Tongli. Because both Hand-Yangming and Foot-Yangming meridians are in the mouth, Jiache, Neiting, and Zusanli of the Foot-Yangming stomach meridian are combined to dredge pathogenic heat. Hegu and Quchi belong to Hand-Yangming meridian points, which can clear stomach heat and dredge the channels. Lianquan is a point of the Conception Vessel Meridian and has an effect on clearing heat and relieving sore throat. Tongli belongs to Hand-Shaoyin Heart Meridian, whereas tongue is the seedling of the heart and the heart opens up from the tongue. The combination of all the points can regulate heart and yin, clear heat and relieve sore throat. For excessive heat, Dazhui is combined; for dry mouth and tongue, Jinjin and Yuye are combined; and for hectic fever, Jianshi, Taixi, and Sanyinjiao are combined with auricular point therapy and a three-edged needle is applied simultaneously. The auricular points selected include Shenmen, mouth, heart, spleen, stomach, and Erjian; the three-edged needle is used to puncture Jinjin, Yuye, and Shaochong and for patients with large ulceration areas, Sifeng is added, or these acupoints are injected with vitamin B_1 or vitamin B_6.

4.5.3.4 ACUPUNCTURE FOR CANCER COMPLICATIONS

4.5.3.4.1 Therapy on cancer pain

Pain is one of the main symptoms of medium and advanced cancer. According to statistics, its clinical incidence totals over 70%. In various advanced cancers, the patients suffer from pains to different extents due to the increase of tumor bodies and oppression or encroachment of adjacent organs, nerve endings, or nerve trunk, such as causalgia, vague pain, swelling pain, dragging pain and pertinacious pain, as well as continuous sharp pain. These pains are associated with their locations, growth modes, and increase in speed, with characteristics including ability to last long and linear exacerbation, and the pains are increasingly more severe with the progression of the diseases, which not only bring great sufferings to patients, resulting in their loss of confidence in continued therapy, but also influence the implementation of anticancer therapy schemes, resulting in the rapid progression of cancer. Accordingly, relieving pains is an important aspect in improving the survival quality of patients with medium and advanced cancer. The abirritation of acupuncture shows its great advantages in relieving cancer pains and is characterized by controlling cancer pains, convenient application, and no addiction, as well as perfect abirritation. TCM believes that the pathogenesis of cancer pains is a result of stagnation of qi and blood stasis, coagulated phlegm, and blocked meridians, which incurs the pathogen prevailing with asthenia of vital qi and deficiency of qi and blood. Acupuncture therapy focuses on dredging meridians and regulating qi and blood, so it can achieve good results in pain relief. The acupuncture therapies on cancer pains mainly include body acupuncture, electric acupuncture, and acupoint injection.

4.5.3.4.2 Therapy on uroschesis after surgery

After surgeries of colon cancer, ovarian cancer, and uterine cancer, the common complication is uroschesis, which is included in the TCM range of "retention of urine." Its focus is located in the bladder, but it is closely related to lung, spleen, kidney, and the three cavities. The abundant lung qi can dredge the water passages leading to the bladder, the abundant spleen qi can ascend lucidity and descend turbidity, and the abundant kidney yang can unlock the water passages. Due to poor vital qi of cancer patients, the deficiencies of qi and blood and kidney qi are more obvious after wide excision. The problems, including deficiency of qi and blood, deficiency of kidney qi, disorder of the three cavities, and dysfunction of gasification in bladder, result in difficult urination and then uroschesis. Acupuncture therapy through acupoints focuses on strengthening kidneys, benefiting essence, improving vital qi and original qi, and passing of urine with satisfactory clinical therapeutic effects.

4.5.3.4.3 Therapy on intractable hiccups

Due to long-term reduction of diet while undergoing surgery or chemoradiotherapy, medium and advanced cancer patients are physically weak and their stomach qi is adynamic, yin and yang in viscera are impaired, functional activities of qi are out of normality, and stomach qi reverses upward. As a result, they are prone to intractable hiccups, which are difficult to be cured in a short time. Intractable hiccups are a common symptom of advanced cancer patients and an inducement of serious complications, such as massive hemorrhage of the upper digestive tract, so it should be treated as soon as possible. Applying acupuncture therapy on such a disease can get a rapid therapeutic effect. The treatment focuses on regulating the disordered functional activities of qi, namely, regulating the balance between ascending and descending functional activities of qi in the viscera, harmonizing stomach by descending adverse qi, and raising clear qi and lowering pathogenic qi. Also, when acupuncture is applied, the patients should be told to regulate respiration using the universal breathing method (a kind of breathing method of TCM exercise) so that they can concentrate their essence, qi, and mentality on the acupoints punctured to strengthen the sensing of essence and qi and centralize qi in the foci. In accordance with the physical conditions and mental states of patients, different reinforcing and reducing methods are adopted to obtain therapeutic effects.

4.5.3.4.4 Therapy on paralytic intestinal obstruction

Paralytic intestinal obstruction is a common complication of medium and advanced cancer patients, more often found in advanced tumors such as gastric cancer, pancreatic carcinoma, colon cancer, and ovarian cancer. It results from wide metastasis of cancer, encroachment of peripheral tissues and organs, deficiency of vital qi in advanced tumors, dysfunctions of gastrointestinal peristalsis, or disorders of visceral functions. TCM believes that this disease belongs to "bowel bilges" and "tympanites," mainly caused by disorders of large intestine's conduction, obstruction of visceral qi, swelling of cumulated qi, no recovery of visceral functions after surgery, inverse and disordered functional activities of qi due to stasis of heat, stagnation of qi, exhaustion of body fluid, and deficiency of qi. Acupuncture therapy focuses on activating qi and dredging stagnation and regulating gastrointestinal functions. In addition, acupoint injection, auricular point therapy, and so on are combined, which will bring better therapeutic effects.

4.5.3.5 PROMOTION OF CANCER PATIENT RECOVERY

Acupuncture can obviously improve the clinical symptoms of cancer patients, such as common sleep dysfunctions, anorexia, digestive dysfunctions, gastrointestinal dysfunctions, and pain syndromes. Combined with psychotherapy, acupuncture can also enhance the confidence of patients in recovery and play important longer term roles in improving the clinical symptoms of cancer patients and their life quality.

Acupuncture can promote the recovery of cancer patients' visceral functions. For example, after breast cancer surgery the backflow of ipsilateral upper limb lymph fluid is often obstructed and the limbs suffer from swelling and pain. After facial jaw surgery, symptoms such as restriction of mouth opening and facial nerve paralysis often appear. After intracranial tumor ablation, symptoms such as hypomnesia, slurred speech, and paralysis of limps often appear. After head and neck tumor radiotherapy, patients often suffer from dryness of

mouth and tongue, tinnitus, and toothache, as well as radiation myelitis, radiation pneumonitis, and pulmonary fibrosis. Acupuncture plays an important role in the rehabilitation therapy of tumors. Through stimulating acupoints and dredging meridians, acupuncture can regulate the body's yin and yang, qi and blood, as well as visceral functions so that the overall rehabilitation of cancer patients can be realized.

The reasons for cancer occurrence under exterior carcinogenesis factors mainly are that the cellular immune function of the body is low and the immune surveillance system function cannot distinguish between normal cells and tumor cells. Therefore, improvement of cellular immune function is a vital part of the prevention and treatment of "endopenia." For effective prevention of recurrence and metastasis, it is important to enhance the immunity of patients and regulate the functions of viscera, yin and yang, qi and blood, and meridians to realize the stability of the internal environment in addition to thorough radical surgeries leaving no residual cancer cells. Thus, as one of the important measures for tumor prevention, it is necessary to regulate the body's internal environment, keep it balanced and stable, and enhance the antidisease capacity of the body. Acupuncture can enhance and activate the body's immune surveillance system and play its unique roles in the prevention of metastasis and recurrence of cancer. Acupuncture can also dredge the meridians, regulate the balance of yin and yang, harmonize qi and blood, tone liver and kidneys, nourish spleen and benefit qi, strengthen vital qi and consolidate the constitution, support the body's vital qi, adjust visceral functions, sufficiently exert the general internal antidisease capacity, and ultimately achieve the prevention and treatment purposes. Accordingly, prevention and therapy are effective measures in reducing the recurrence or metastasis of cancer.

4.5.3.6 AURICULAR POINT THERAPY FOR CANCER TREATMENT

Auricular points can act as the auxiliary diagnosis points of tumors. Meridian theories are applied to the diagnosis of tumors, which are highly regarded and widely applied. The human body is a unified entirety, and any local pathologic change may be a reaction to general pathological changes. The positive characteristics of the ears of cancer patients mainly present the thickening and bulging of relevant positions at the auricle and the abnormal color of specific skin areas. Research has found seven acupoint signals representing different properties in the auricle acupoint including tumor 1, tumor 2, tumor 3, tumor 4, endocrine, adrenal gland, and subcortex. They directly reflect the existence and properties of tumors, presenting staging of tumors and pointing out that when the positive indexes of tumor 1 and tumor 4 increase malignant tumors may be present. The intensity and occurrence rule of signals measured from tumor 1 to tumor 4 can be used to determine whether there is any tumor and determine whether the tumor is benign or malignant. Thus, it is believed that the decline of the average positive current values of acupoints and the change of subcortical positive indexes are important bases in tumor diagnoses.

Auricular point therapy has a sound therapeutic effect on tumors, because it has the function of regulating the immune function. Auricular points are associated with viscera in terms of the immune system. Auricular point therapy can not only enhance the immunologic function of the body fluid but also improve the immunologic function of cells. It has a comparably good therapeutic effect on cancer pains. In accordance with the "meridian point–viscera relationship theory," acupuncture on auricular points, auricular-plaster, auricular point injection can attain the effects of dredging meridians, regulating the viscera, and improving the flow of qi and blood.

4.6 CANCER HYPERTHERMIA AND MEDICATED DIET NUTRITION THERAPY

4.6.1 Cancer hyperthermia and medicated diet nutrition

Hyperthermia can improve the body conditions of cancer patients and relieve the adverse reactions after radiotherapy and chemotherapy; hence, it is propitious for the intake of oral nutrients by patients. It can also promote the dissemination and adoption of nutrients throughout the body and facilitate the improvement of the physical state of patients to support medicinal diet nutrition therapy (Figure 4.5).

Figure 4.5 Medicinal Diet & Nutrition.

4.6.2 Nutritional imbalance and incidence of cancer

At present, the research results of cancer pathogenesis show that dietary factors play a nonnegligible role in cancer occurrence. The American National Cancer Institute and the World Cancer Institute indicate that the occurrence of 30%–40% of cancers can be prevented effectively by reasonable diet management. The occurrence and development of cancer can be divided into start-up period, cancer-promoting stage, and canceration progress period. The former two periods are relatively benign growth periods of cancer during which rational dietary nutrition can reverse the pathologic changes. Some nutritional ingredients can effect antioxidation, depress the generation of tumor blood vessels, and improve body immunity with sound therapeutic values. Modern medicine has researched and proved that nutritional factors in foods are associated with the incidence of cancer (Table 4.1) and that carcinogenic substances or precursors are contained in some foods (Table 4.2).

Table 4.1 Relationship between food nutritional factors and malignant tumors

Malignant tumor	Carcinogenic substances	Carcinogenic factors	Protective or depressive factors
Esophagus cancer, oral cancer	Tobacco, salted or preserved foods	Alcohol	Foods rich in vitamins A and C
Gastric cancer	Dried salted fish, salted vegetables and smoked fish, high nitrate levels in food and water (nitrite + carcinogenic precursor)	Low intake of salt, fresh fruits, vegetables, and vitamin C	Intake increase of fresh fruits and vegetables; vitamins A, B, and C
Colon cancer	Carcinogenic substances formed when meat and fish are fried or roasted (heterocyclic amines)	High-fat diet, cholic acid	Wheat bran and corn fiber, some fresh vegetables such as cabbage, cauliflower, olive, and vegetable and microelement selenium
Pancreatic carcinoma	Tobacco, fried meat and fish	Alcohol, coffee, high-fat diet	Fresh fruits and vegetables
Breast cancer	Fried meat and fish	High-fat diet, endocrine disorder	Low-fat diet
Prostatic cancer		High-fat diet	Low-fat diet, complement with moderate selenium and zinc

Table 4.2 Cancerogenic substances or precursors contained in foods

Cancerogenic substances	Source	Tumor position
Acrylonitrile	Food packaging materials	Upper stomach, central nervous system, some glands
Aflatoxin	Moldy grain, milk, peanuts and corn, etc.	Esophagus, liver, kidney, lungs, colon
Arsenic	Marine products, meat, vegetables, and water	Undefined
Butyl hydroxy anisole	Conservants for grease, biscuit, chewing gum and nonalcoholic beverage	Upper stomach
Dibutyl hydroxy toluene	Same as above	Lungs
Nitrosamine	Nitrate and nitrite in foods	Multiple incidence parts (relating to high incidence of gastric cancer and esophagus cancer)
Polycyclic aromatic hydrocarbon	Contaminants in smoked foods and fish	Multiple incidence parts (higher incidence of gastric cancer and skin cancer)
Saccharin	Sweetening agent	Bladder cancer
Chloroethylene	Food packing materials	Multiple incidence parts (higher incidence of brain, liver, respiratory system)
Cadmium	Pollution of foods and drinking water	Skin
Lead	Pollution of canned food, paint, waste gas	Kidney

4.6.2.1 NUTRIENTS RELATING TO OCCURRENCE OF CANCER

4.6.2.1.1 Calorigenic nutrients

4.6.2.1.1.1 Gross heat budget

Excessive caloric intake may be an important cause for the occurrence of cancer. The recent forward-looking cancer prevention cohort studies show that the incidence of cancer caused by overweight and obesity in men is up to 14% and in women 20%. The epidemiological data indicate that corpulent and overweight groups suffer from obvious increases of esophagus cancer, gastric cancer, liver cancer, gallbladder cancer, pancreatic carcinoma, kidney cancer, carcinoma of large intestine, prostatic cancer, breast cancer, cervical cancer, and ovarian cancer. By increasing exercises and reducing weight, the dangers of carcinoma of the large intestine and breast cancer can be reduced. Analyses on 14 animal experiments internationally show that calorie intake control can not only reduce the incidence of spontaneous tumors in laboratory white rats by 55% but also restrict the growth of artificially implanted tumor cells and prolong the survival periods of the white rats. An investigation on epidemiology in Switzerland indicates that among women with anorexia the rate of nulliparous women suffering from breast cancer is 23% lower than that among common women with normal diets, while it is reduced by 76% compared to multiparas. Therefore, the excessive intake of total calories increases the risk of cancer occurrence in the human body.

4.6.2.1.1.2 Glucose

Modern research has proved that the glycemic index in diet shows positive correlations with the occurrence of cancer. The glycemic indexes of refined sugar and cereals are usually high, totaling over 75. The refined rice and flour that are usually consumed are the main sources of carbohydrates. Because of the removal of wheat germ and wheat bran, the cellulose in the refined powder is reduced by 78%, vitamin B and vitamin E

are reduced by 74%, and mineral substances are reduced by 69%, compared with the unprocessed varieties. Comparison research in America has found that the risks of esophagus cancer, gastric cancer, endometrial cancer, ovarian cancer, and carcinoma of the large intestine increase with the rise of glycemic index in the diet.

In recent years, glycosylated hemoglobin has been more widely used to clinically observe the relationship with the occurrence of cancer than glycemic index. A large cohort study in America shows that carcinoma of the large intestine rises when glycated hemoglobin is higher than normal, body mass index > 30 kg/m^2. A large number of clinical observations show that more diabetic patients suffer from endometrial cancer and pancreatic carcinoma than persons with normal blood sugar.

In daily diets, be sure to reduce the intake of refined rice and flour and increase the intake of coarse grains and cereals, and the proper increase of foods with glycemic indexes less than 55 will help to prevent the occurrence of pancreatic carcinoma, endometrial cancer, and colorectal cancer.

4.6.2.1.1.3 Protein

The intake of proteins plays an important role in the occurrence of cancer. A retrospective epidemiological investigation shows that an excessively low intake of proteins can increase the risk of esophagus cancer, gastric cancer, and liver cancer, and the protein intake of patients surveyed was less than that of the control group before the occurrence of cancer. A prospective observation report in Japan shows lower incidence of gastric cancer in those who regularly drink milk compared with those who do not. The investigation and research on epidemic diseases conducted by the Shanghai Second Medical University show that persons who often eat bean products and drink soybean milk have a relatively lower risk of gastric cancer. On the contrary, an excessive intake of proteins can also increase the risk of cancer.

During as early as the 1970s, Armstrong and Doll found that the higher the total intake of proteins, particularly animal proteins, the higher the incidence of breast cancer, colorectal cancer, pancreatic carcinoma, and endometrial cancer when they investigated the relationship between mortality rates of 14 kinds of cancers and dietary nutrients in 32 countries. Animal experiments also achieved the same conclusions: researchers divided Syvian mice into two groups; both were given the carcinogen *N*-2 hydroxypropyl-2 oxygen propyl-nitrosamines totaling 220 mg/kg, with one group being fed foods with protein covering 20% of the total calories and the other group being fed foods with protein covering 8% of the same. The incidences of pancreatic cancer in the first group and the second group of animals were up to 46% and 13%, respectively, indicating that the increase of protein intake enhances the incidence of pancreatic carcinoma. Accordingly, both the overhigh and overlow intakes of dietary protein can increase the risk of cancer incidence.

4.6.2.1.1.4 Lipids

A large number of results of epidemiological research shows that the excessive intake of dietary animal fat can increase the risk of breast cancer, colorectal cancer, prostatic cancer, and pancreatic carcinoma. The results of animal experiments present the following: ω-3 (EPA or DHA) aliphatic acid has an effect of prevention on the occurrence of cancer, whereas excess ω-6 (arachidonic acid) aliphatic acid is considered one of the factors promoting the occurrence of cancer.

To date, most research related with fat has focused on the relationship between polyunsaturated fatty acids and breast cancer. Six foreign large comparison studies show the following results: the incidence of breast cancer decreases when the proportion of ω-3 aliphatic acid/ω-6 aliphatic acid increases in diets. ω-3 Aliphatic acid and ω-6 aliphatic acid have completely different effects on the breast cancer suppressor genes *BRCA1* and *BRCA2*. After adding ω-3 aliphatic acid in the culture medium of breast cancer cells, the expressions of tumor suppressor genes *BRCA1* and *BRCA2* were enhanced, whereas ω-6 aliphatic acid had no effect. Most researchers believe that the mechanism of ω-3 aliphatic acid in reducing the incidence of breast cancer lies in that EPA and arachidonic acid compete for peroxidases in the prostaglandins, restraining the arachidonic acid from synthesizing prostaglandin E2, while prostaglandin E2 reduces the body's anticancer capacity by restraining the activity of NK cells. Therefore, fish oil with rich ω-3 aliphatic acid can depress cancers through the depression of the synthesis of prostaglandin E2.

There are always different opinions on the relationship between cholesterol and cancer incidence. Epidemiological investigations in 65 counties of China found that the rise of plasma cholesterol increases the risk of lung cancer, liver cancer, colorectal cancer, leukemia, and brain tumor. However, a foreign prospective research indicates that the level of plasma cholesterol shows a negative correlation with the occurrence of cancer. Accordingly, it is advocated to properly control the intake of cholesterol-rich foods as a measure for preventing cancer by maintaining plasma cholesterol in the normal range.

4.6.2.1.2 Vitamin

Vitamins are classified into vitamins A, B, C, D, and E, of which the B family has the most vitamin members, with the most complex functions. Vitamin C is the most active in clinical therapy and medical care and has attracted the most attention. Vitamins A, C, and E have been named antioxidative vitamins.

In recent years, more and more clinical, epidemiological, and laboratory research is indicating that vitamins play important roles in the occurrence, metastasis, and deterioration of cancer. Vitamins have important and irreplaceable effects in maintaining the soundness of epithelial tissue, sound immunity of the body, normal immunologic surveillance of the body, and normal regulation of microcirculation and vascular hyperplasia and endocrine function of glands. The occurrence of cancers, especially those in the epithelial tissue, is closely related to the dysfunction discussed here. Vitamin deficiency has become an important pathogenic factor for the occurrence of cancer. Similarly, for some cancer patients the rational supplementation of vitamins, especially essential ones (which cannot be synthesized in the body) for the human body, plays very significant roles in recovering the patients' physical strength, enhancing immunity, relieving cancer metastasis, improving the life quality, and prolonging lives.

4.6.2.1.3 Trace elements

The human body is composed of dozens of elements, of which those with contents accounting for less than 0.01% of the total body weight and with daily demand less than 100 mg are called trace elements. There are 41 elements such as iron, copper, zinc, iodine, and so on with the total amount occupying 0.05% of the human body. Trace elements have various functions in the body, but they mainly exert their effects through the formation of conjugated proteins, enzymes, hormones, and vitamins. With extensive research being done on the biological effects of trace elements, they have become increasingly important. Recently, there has been much progress in the research on trace elements and carcinogenesis. Some of the most researched trace elements are detailed in Sections 6.6.2.1.4 and 6.6.2.1.5.

4.6.2.1.4 Dietary fiber

Dietary fibers include nonstarch polysaccharides (cellulose, hemicellulose, pectins, gum, and viscose), lignins, resistant starch, and resistant oligosaccharides. The mechanisms of dietary fiber in preventing intestinal cancer are as follows: (1) bulking the feces and shortening the storage time in the large intestine and diluting carcinogenic substances; (2) adhering to cholic acid or other carcinogenic substances; (3) bacteria cause the dietary fiber to decompose to produce short-chain fatty acids, reduce the fecal pH value, and depress the production of carcinogenic substances; (4) changing the microbial population in the large intestine; and (5) increasing the intestinal antioxidants.

4.6.2.1.5 Digestive enzymes

Most patients diagnosed with cancer often suffer from digestive disorders. The destroyed digestive function can impact the effect of nutritional auxiliary therapy. If the body cannot deliver food nutrients effectively to the small intestines for absorption, any food, regardless of how nutritious it is, is useless. Digestive enzymes play an important role in this process and even though they cannot affect the cancer directly, they can help the body to digest the nutrients more effectively so as to prevent nutritional deficiencies. A study in America shows that the digestive enzymes can not only help cancer patients absorb carbohydrates and proteins from small intestine mucosa but also improve the digestive function of healthy groups, of which protease has the most significant effect.

According to Wald et al., animal studies show that oral protease can prevent the metastasis of small cell lung cancer to other visceral organs. They divided white rats into four groups. The primary tumors of all the animals were ablated by surgery. The first group was the control group, the second group was given rectum protease supplements on the day of ablation, the third group was given the supplements 6 days before the surgery, and the fourth group was given the supplements on the day the white rats were induced as tumor models. Eighteen days later, 90% of the white rats in the control group died from tumor metastasis to other parts. After acceptance of the rectal digestive enzymes, only 30% of the white rats in the second group died from tumor metastasis on the 25th day. In the third group, which was given protease before surgery, only 10% suffered from tumor metastasis. For all the animals in the fourth group, there was no tumor metastasis in visceral organs within 1 month. Similarly, a multicenter study in Germany showed that side effects were significantly relieved in women with cervical cancer replenished with digestive enzymes during radiotherapy. Moreover, compared with those in whom digestive enzymes were not replenished, the metastasis rates were reduced and survival periods prolonged.

4.6.2.2 NUTRITIOUS DIETS FOR CANCER PREVENTION

Reasonable dietary nutrition intake can not only have effects on disease prevention but also improve the immunity of the body and fight against diseases. Reducing the intake of the previously mentioned carcinogenic substances (Tables 4.1 and 4.2) and maintaining a balanced diet are basic premises in cancer prevention. Through the work of many years, some famous nutritionists in America reached an accordant conclusion: diet must be kept in balance without bias toward any single nutrient. The human body is just like a balance, requiring a variety of nutrients in specific quantities to avoid imbalance. In many carcinogenic factors and cancer-protective factors, it seems that some of them are contradictory. Some factors may cause one kind of cancer, but they may be favorable factors in preventing another kind of cancer. Moreover, natural foods ingested in our daily life may contain both anticancer nutrients and cancerogenic elements. After all, the foods ingested per day are not single nutrient tablets. Therefore, how to keep a balanced diet so as to prevent and cure diseases is one of the topics that challenge health authorities of all countries in the world.

The dietary guidelines issued by the U.S. government in 2005 recommended eating fruits and vegetables for up to twice the quantity (600–800 g/day) recommended in the dietary guidelines issued in 2000 and suggest replacing refined or processed corn with corn-based foods with rich high fibers and high nutrients so as to prevent certain cancers.

4.6.3 NUTRITIONAL DISORDERS OF CANCER PATIENTS

Malnutrition with protein deficiency is a common phenomenon in patients with medium and advanced malignant tumors. According to statistics, more than 50% of the hospitalized cancer patients are malnourished, weight loss being its most prominent clinical representation. The nutritional status of the patients is loosely associated with cancer type, cancer location, and different cancer stages. The incidences of malnutrition and cachexia are high in patients with digestive tract cancer and advanced cancer.

4.6.3.1 CANCER CACHEXIA

Cachexia is derived from Greek *kakaos Hexis*, meaning "the body is under a bad condition." It is usually found in a variety of chronic or end-stage diseases. About one-third to two-thirds of various cancer patients suffer from cachexia, which once it occurs is difficult to reverse. Cachexia is a complex metabolic state appearing in people with progressive nutritional status deterioration characterized by consumption of adipose tissue and thin body tissue groups. It often exhibits anorexia, progressive marasmus, muscle atrophy, anemia, low blood sugar, hypoproteinemia, low immunologic function, metabolic change and obstruction, and so on. Cancer cachexia can result in the progressive decline of body weight and the exhaustion of skeletal muscles and visceral protein. It can damage the structure and function of tissues, harm enzyme generation and immunologic function, and increase the susceptibility for parasitifer. Usually, it can be found in various cancer patients, mostly patients with lung cancer, gastric cancer, and pancreatic carcinoma, with incidences of up to 60%, and its incidence in medium and advanced patients can be as high as 80%. It is more common in the elderly

and children. Such patients usually have severe weight loss. The consumption of thin tissue groups can incur the reduction of sensitivity and tolerance of cancer patients for tumor therapy, not only making it difficult to achieve the desired effect in anticancer therapy but also resulting in the death of cancer patients eventually.

The occurrence mechanism of cancer cachexia is not yet defined, and it was believed that cancer cachexia had a constant relationship with cancer location. However, many recent studies show that the occurrence mechanism of cachexia is very complex and it cannot be explained clearly by a single factor. It is related not only to the local influence of cancer but also to systemic metabolic disorders caused by tumors. On the whole, the occurrence of cancer cachexia is due to many factors associated with cancer. Generally speaking, cancer cachexia is the result of multiple reasons and interactive factors. It is presently believed that the incidence of cachexia is closely associated with decreasing nutrient intake of the body, metabolism disorders of nutrient absorption, action of cytokines, and negative effects incurred as a result of cancer therapy.

4.6.3.2 ANOREXIA AND CALORIC INTAKE REDUCTION

Anorexia is the common chief complaint of cancer patients, about 33%–75% of whom can suffer from such a problem. Over 50% of patients with digestive system tumors exhibit the phenomenon of anorexia, which is not just a complex eating disorder. Loss of appetite is part of the causes of eating disorders and also one of the main causes for malnutrition of cancer patients.

4.6.3.3 ENERGY METABOLISM CHANGES

Changes in energy metabolism are mainly manifested by the following aspects:

Energy consumption change: The malnutrition of cancer patients is generally attributed to the reduction of energy intake and the increase of energy consumption.

Metabolic change of glucose: The metabolic abnormality of glucose in cancer patients is mainly exhibited as the reduction of glucose stored in the body and its increase of consumption, as well as the enhancement of glyconeogenesis activity and the glucose use disorder of peripheral tissues.

Metabolic change of proteins: The metabolic change of proteins in cancer patients is exhibited as the reduction in protein synthesis, increase in decomposition, increase in conversion rate, and abnormality of plasma aminogram.

Fat metabolism change: Cachexia is mainly associated with fat consumption of the body, found in various stages of cancer.

4.6.3.4 RELEVANT MEDIUM FUNCTIONS OF CACHEXIA

The mediums participating in the process of cancer cachexia generally fall into two categories: one comprises the endogenous factors secreted by the body, including TNF-α, IL-1, IL-6, IFN-γ, and LIF, and the other comprises the catabolic substances generated during the growth of cancer, such as LMF and PIF. The former mainly affects the appetite of the individual and has an effect of depressing the appetite. The latter results in the loss of weight by strengthening fat decomposition of fat tissue without influencing appetite and participates in the process of tumor cachexia.

4.6.3.5 INFLUENCE OF CANCER THERAPY ON PATIENT NUTRITION

When patients with various types of tumors are receiving therapies such as surgery, radiotherapy, and chemotherapy, their nutritional conditions are being influenced (Table 4.3). In the perioperative period, preoperative fasting and abnormal intake of foods after surgery can influence the absorption of various nutrients. The stress reactions incurred by surgical wounds can result in the negative balance of nitrogen. The resection on different parts can also incur complications such as swallowing dysfunction, reduction of gastric acid secretion, absorptive hypofunction, deficiency of interior factors, and absorptive dysfunction of water and electrolytes, directly influencing the nutritional condition and life quality of patients.

The influences of chemotherapy on the nutritional condition of patients involve various mechanisms. The direct influences on the body during chemotherapy can disturb the metabolism of cells, DNA synthesis, and cell reduplication in the body. The effect of chemotherapy on the digestive tract mucous membrane can incur the inflammation of the digestive tract and ulceration and ultimately result in absorptive hypofunction of the

Table 4.3 Influences of various therapeutic processes on patient nutrition

Therapies	Nutritional problems
Radiotherapy	
Mouth and pharynx radiotherapy	Gustation impairment, dry mouth, throat irritation.
Lower neck and mediastinal radiotherapy	Difficulty in swallowing, esophagitis
Abdominal and pelvic radiotherapy	Acute and chronic enteritis, malabsorption, diarrhea, intestinal tract stenosis, and obstruction
Surgical therapy	
Radical surgery on mouth and pharyngeal portion	Difficulty in chewing and swallowing
Radical surgery for esophageal cancer	Reduction of gastric acid secretion, diarrhea, loss of appetite
Gastric cancer resection	Maldigestion and malabsorption, deficiency of gastric acid, intrinsic factors and R protein, hypoglycemia
Pancreatectomy	Malabsorption
Jejunum resection	Reduction of absorptive rates of various nutrients
Ileum resection	Deficiency of vitamin B_{12}, malabsorption of dissoluble vitamins and fats
Colostomy	Imbalance of water and electrolytes
Drug therapy	
Cellular toxicity chemical drugs	Vomiting, nausea, diarrhea, bone marrow depression
TNF	Vomiting, nausea, diarrhea
IFN	Anorexia, nausea, vomiting, and diarrhea

body. The indirect influences of the chemotherapy process and drugs on the body include anorexia, nausea, vomiting, and gestation changes, which will lead to a negative balance of nitrogen and consumption of thin tissue groups.

The influence of radiotherapy on the nutritional condition of patients is mainly on the digestive system and is related to the dose of radiation and the irradiation area. Radiotherapy generates rapid depression of bone marrow, resulting in anemia and leukopenia of the organism, decreased immune function, and increased susceptibility to diseases. Moreover, radiotherapy can precipitate the dysfunction of protein synthesis and increase catabolic rate, superhigh metabolism of the body, negative balance of nitrogen, and loss of weight.

4.6.4 Nutritional support for cancer patients

Of the 1.8 million new cancer patients reported each year in China, over 80% suffer from weight loss and malnutrition; the medium and advanced cancer patients have higher incidences of malnutrition. There are many causes for malnutrition, mainly including the following: malnutrition is caused by the metabolic change of tumor tissues, namely, the energy metabolism of cancer patients is about 10% higher than that of normal people, the weight of cancer patients is obviously reduced, and the energy consumption is a nonnegligible reason in addition to absorptive deficiency caused by anorexia. Malnutrition is caused by the progress of the diseases themselves, namely, disease development, occurrence of complications, or oppression of the tumor on digestive tract. Other causes of malnutrition are malnutrition caused by nutrient loss and synthetic dysfunction; malnutrition caused by tumor therapies, such as surgical trauma, radiotherapy, and chemotherapy; and malnutrition caused by mental and social problems.

The nutritional support for cancer patients is different in properties from that for benign diseases, and not all cancer patients can benefit from the nutritional support therapy. In different periods of tumor development, different individuals are provided with appropriate nutritional supports, which have great influences on the progress and consequence of the disease. For patients with malnutrition accompanied by immune dysfunction, both the incidence of complications and the mortality rates after surgery rise. For cancer patients

with malnutrition who require surgery, nutritional support in the perioperative period is highly necessary. It is similarly important for cancer patients treated with radiotherapy or chemotherapy and accompanied by malnutrition or abnormal eating. Analyses of several sample cases found that the survival rates of patients without weight loss were obviously higher than those of patients with weight loss, and the prognosis for those with malnutrition was obviously worse than for those with proper nutrition. The following groups of data sufficiently reflect the importance of nutritional support: about 20% of gastric cancer patients suffer from the first symptom of progressive loss of weight, and the survival period of patients with stable weight is twice that of patients with weight loss. If the range of weight loss of gastric cancer patients is within 6%–18%, the anticancer therapy and nutritional support should be conducted simultaneously, which can realize a certain therapeutic effect on 50% of patients, while single cancer therapy without nutritional support can realize the same therapeutic effect on only 20% of patients. More than 50% of the advanced cancer patients die from malnutrition.

When developing nutritional support schemes for cancer patients, objective, integral, and comprehensive nutritional assessments should be performed, and the results obtained should be utilized for nutritional therapy.

4.6.4.1 NUTRITIONAL ASSESSMENT ON CANCER PATIENTS

After cancer patients are hospitalized, an integral, comprehensive, and objective nutritional assessment should be done on them, usually adopting the combination of subjective global assessment with body composition assessment. In accordance with the assessment results, the nutritional condition is generally divided into five grades: good nutrition, medium nutrition, mild malnutrition, moderate malnutrition, and serious malnutrition. For mild malnutrition, timely nutrition-intervening measures should be taken. In addition, malnutrition is divided into marasmus-type malnutrition, protein malnutrition, and mixed malnutrition.

4.6.4.2 NUTRITIONAL INTERVENTION FOR CANCER PATIENTS

In cancer patients, nutritional support therapy is as important as anticancer therapy. An appropriate nutritional therapy can improve the nutritional status of the patients, enhance the patients' immunity and anticancer capability, improve their life quality, strengthen the cancer patients' tolerance to surgical therapy, lessen or avoid any infection after surgery, accelerate wound healing after surgery, enhance the tolerance capacity of the cancer patients to radiotherapy or chemotherapy, and relieve toxic and side effects.

Medium and advanced cancer patients suffer from malnutrition that is obviously accompanied by low immunologic function, specifically exhibited as low activity of NK cells and TH (T assistance) cells and the rise of TS (T depression) cell levels. This low immunity is mainly influenced by tumor-depressing factors, while the invasive therapies greatly influence the immunologic functions of the body. As for nutritional judgment and necessity and effectiveness of the support, one must first check whether the patients' nutritional condition and life quality are improved, as well as for influences on the prognosis. For patients with malnutrition accompanied by immunologic function depression, the incidence of complications and mortality rates can rise. Therefore, for most patients with malnutrition who require surgical therapies, nutritional support in the perioperative period is extremely necessary; similarly, nutritional support is important for cancer patients with malnutrition or abnormal intake of foods.

4.6.4.3 IMPLEMENTATION OF NUTRITIONAL SUPPORT

Cancer patients in the progressive stages always have different degrees of disorders or malnutrition, and such conditions can directly impact the whole therapeutic process. Patients with chronic consumptive diseases should not expect a complete full-body recovery in a short period. They must be made aware that the improvement and correction of malnutrition will go through a relatively slow and long process.

The approaches for nutritional support can be divided into enteral nutritional support and parenteral nutritional support, which are organic components of the integrative treatments. When gastroenteric functions and the therapy allow it, enteral nutrition can be selected first. Parenteral nutrition can be considered only when the gastroenteric functions cannot act or when there is any therapeutic restriction. For patients who fail to recover the intake of foods through the mouth for a long time after surgery but still have intact gastrointestinal tract function, intraoperative stomach or jejunostomy can be adopted to give enteral nutritional support after surgery. After the internal environment becomes stable, a short period of parenteral nutritional support can be made available after surgery.

4.6.4.4 DIETETIC CONTRAINDICATIONS OF CANCER PATIENTS

Cancer patients during radiotherapy and chemotherapy often face some problems, such as what they shall or shall not eat. Some patients may be concerned about some "stimulating foods" that can result in the reoccurrence or metastasis of cancer, on which we shall keep objective and scientific attitudes.

The occurrence and development of cancer cells will certainly go through stages of initiation and cancer promotion, then the stage of cell progression, and finally cancer formation. At the initiation stage of cancer, initiating agents, such as aflatoxin, nitrosamines, and benzopyrene, induce the cells to mutate into latent cancer cells, and they exist mainly in moldy, pickled, roasted, and smoked foods. Meanwhile, the imbalance between cocarcinogenic factors (such as intake of too much protein and fat or insufficient intake of some micronutrients) and nutrients, low immunologic function, or lots of chemical cancer-promoting agents such as gluside and 3,4-benzopyrene in foods will make the latent cancer cells get out of control in splitting and under a limitless hyperplasia they ultimately form cancer. As for time, the initiation of cancer cells can be completed in a short time (even in several minutes), whereas the cancer-promotion stage requires a long time (several years and even decades), so the cancer-promotion stage is worthy of more attention from the cancer prevention angle and its development can be delayed with appropriate and targeted diet and nutrition.

4.6.5 Effects of medical food and diet therapy in cancer treatments

Cancer is a systemic disease, and it not only infiltrates locally, transfers elsewhere, and destroys normal tissues but also brings about a series of nutritional disorders and metabolic disorders in patients. Clinically, doctors often focus on anticancer therapy, such as surgery, radiotherapy, and chemotherapy but neglect the nutritional issue. However, the nutritional condition is closely related to the therapeutic effect. For patients with good nutritional condition, surgical safety is higher and their tolerances to radiotherapy and chemotherapy are improved. So, a rational and nutritional diet for a cancer patient has positive significance in receiving better therapies, mobilizing and protecting the disease resistance capacity, improving the immunologic function, and promoting recovery as well as prolonging survival time.

4.6.5.1 CHARACTERISTICS OF A MEDICATED DIET

Diet refers to dietary therapy and is also named as diet treatment, therapeutic diet, health-preserving diet, and medicated diet. It is generally divided into three types: first, applicable foods alone, such as rice, vegetables, melons, fruits or drink, porridge, cooked food, soup, thick soup, beverage, candies, and preserved fruit made from the aforementioned items; second, various foods with drugs, which are customarily called medicated diets; and, third, foods to which necessary nutrients are added, such as vitamins, inorganic salts, and trace elements, which are often called "fortified foods."

Medicated diet is not an ordinary nutritional food and is neither a simple TCM added with drugs nor their random combination. Medicated diet provides "palatable effective medicine" by taking into consideration and retaining the features of food: color, smell, flavor, and so on. Therefore, it has not only the efficiency of medicine but also the delicacy of food and can be used to prevent and cure disease, protect and strengthen the body, and prolong life.

Although medicated diet is associated with supplementation, it is not blind supplementation; it is rather a special combination of Chinese drugs, food, and condiments that provides supplementation but without intemperance, stagnation, or overabundance and complies with the principles of TCM.

Under TCM theory, food and medicine share a common origin and each food has its own characteristics, with coldness, hotness, warmth, and coolness, similar to herbal medicine. Therefore, the prescriptions of medicated diets will not achieve the desired therapeutic effects if the diets do not incorporate the natures and flavors as well as the channel tropisms of foods.

4.6.5.2 MEDICATED DIETS FOR CANCER PATIENTS

The specific selection of medicated diets for cancer patients must be determined by the disease and therapeutic conditions of the cancer patients. In addition to the common characteristics of ordinary medicated diets,

medicated diets for cancer patients have their own characteristics, that is, they must be rich in nutrition, easy for digestion, and suitable for the disease conditions and tastes of cancer patients. For example, surgical treatment often leads to deficiency of qi and blood, asthenia of spleen and stomach, nutritional deficiency, and body dysfunction. Therefore, the selection of medicated diets aims to supplement nutrition properly, regulate the functions of spleen and stomach, arouse stomach qi, recover the source of vital function, and strengthen the foundation of acquired constitution. Also, radiotherapy and chemotherapy often cause symptoms of hot toxins impairing yin, and yin deficiency inducing hyperactivity of internal heat, so the application of medicated diets for cancer patients shall follow the principle of dialectical application of diets.

4.7 HYPERTHERMIA INTEGRATED WITH PSYCHOTHERAPY

4.7.1 Cancer hyperthermia and psychotherapy

Cancer therapy emphasizes integrative people-oriented therapies. In the processes of cancer development and cancer therapy, the mutual convergence and influences of physical–psychological diseases and psychophysiological disorders exist; so the therapy should not only aim to cure the physical disease but also include psychotherapy, which plays an important role in the whole therapy. The combination of cancer hyperthermia with psychotherapy represents a nontoxic integrative treatment of "body–mind harmonization," which focuses on humanistic care during therapy on the physical diseases and exerts the immunoregulatory effects of the two therapies on cancer from two aspects, body and spirit, so as to maximize the therapeutic effect.

As an important component of nontoxic integrative treatment, cancer psychotherapy plays an increasingly greater role in combination with surgery, chemotherapy, and radiotherapy, thus expanding into new territories and opening new application fields for psychotherapy.

4.7.2 Psychosocial factors and cancer

4.7.2.1 PSYCHOSOCIAL FACTORS

4.7.2.1.1 Psychological factors of cancer

These factors include an introverted personality, a depressive mood, and adverse psychological reactions (such as anxious mind, a depression mentality, excitability, and declining recognition ability).

4.7.2.1.2 Social factors of cancer

These factors include unfavorable life events (such as death of spouse, divorce, pregnancy, parodynia, abortion, unemployment, financial difficulty, and death of an immediate family member), long-term nervous rhythm of life, and tense human relationships.

4.7.2.2 PSYCHOSOCIAL FACTORS FOR THERAPY AND RECOVERY

A sound mental state is the foundation of cancer therapy. Overcoming mental disorders is crucial to successful cancer therapy while bad mental factors are closely associated with the incidence of cancer. The psychological status of cancer patients has significant effect on their recovery. A good frame of mind is an indispensable part of cancer recovery; on the opposite, a bad mental state can aggravate treatment and recovery.

4.7.2.3 PSYCHOSOCIAL FACTORS FOR PREVENTION OF CANCER

In introspect, it is recognized that the destruction of the living environment by the human race and bad living habits have resulted in the wide occurrence of cancers all over the world. For the individual, the change of bad living habits is the best therapy for cancer. Also, the elimination of bad emotions is extremely important, and for this the following methods can be attempted: aerobic exercise, color therapy, music therapy, conversation therapy, spirit relaxation, tranquility of the mind, and regulation of lifestyle.

4.7.3 Psychological and neural immunity and cancer

In 1984, Paul J. Rosch proposed that hormone levels and immune condition of the body can influence the occurrence and development of cancers when the physicochemical effect of carcinogenic factors causes body cells to mutate, and the central nervous system can regulate the hormone levels and immune condition of the body. Because psychological factors can change the activities of the nervous, endocrine, and immune systems in the body, the psychological factors can change the occurrence and development of cancers by changing the activities in the nervous, endocrine, and immune systems.

4.7.3.1 Relationship between psychosocial factors and immunologic functions

4.7.3.1.1 Effects of stress events on immunologic function

Stressful events are related to changes in the body's immunologic function. Batrop found that any stressful event experienced by individuals can affect the activity of NK cells; the NK cell activity of the widowed could be reduced and the dissociative reaction of lymphocytes decreased. Glarser conducted tests on the antibody levels of the EBV in 45 male students 3 to 4 weeks before and during exams. The results showed that the students' EBV antibody titer increased during the exam and that the immunologic function of the students with poor social supports decreased more significantly. Eliyahu once researched the influences of stress on pulmonary metastasis of male mice with breast cancer. For the mice stimulated by acute stress, the cell toxicant effect of NK cells on cancer cells was reduced, and the lung metastasis of cancer was two times higher than that of unstimulated mice. Also, only stress effects occurring within 1 hour before the injection of cancer cells were able to promote increase in cancer metastasis, whereas no such effect was observed within 24 hours of injection of cancer cells.

4.7.3.1.2 Effects of individual traits on immunologic function

Individual traits are related to the immunologic function of the body. Jemmott discovered through research that anyone who can strongly affect others and has self-control has lower activity of NK cells, and this phenomenon is more obvious when the person encounters stressful events. Miller investigated 276 healthy adults and found that the NK cell activity of adults with lower extroversion levels is higher and the relationship between the extroversion score and the NK cell activity is correlated to the adrenaline level. Shea once conducted a personality survey on 39 women and tested their quantities of T lymphocytes and delayed skin hypersensitivity levels. The results showed that the immunologic reaction levels of women with high nervousness levels were higher. Studies by Cohen showed that acute and persistent stress could result in changes in healthy women's NK cell activity and T lymphocyte classification counts and such changes were associated with the optimistic and pessimistic tendencies of the individual.

4.7.3.1.3 Effects of emotional changes on immunologic function

Emotional representations are related to the immunologic function. In clinical studies, many researchers found that depression had inhibitory effects on immunologic function. Herbert analyzed relevant research and found that depression could reduce the dissociative reactions of the individual's lymphocytes and the activity of NK cells and affect leukocyte levels; it was shown that the more serious an individual's depression, the greater the activity changes of NK cells. Miller investigated the immunologic functions of 32 depressed women and compared them with the functions of 32 healthy women, with the results showing that the dissociative reaction of lymphocytes of depressed women decreased; the activity of NK cells of old depressed patients was reduced, whereas the activity of NK cells of young depressed patients was increased.

4.7.3.1.4 Effects of psychosocial factors on immunologic function

Depression can lead to the decrease of NK cells in cancer patients, increase of peripheral blood granulocytes, and reduction of percentages of $CD4^+$ and $CD8^+$ cells, but the change in $CD4^+/CD8^+$ ratio is small. The levels

of IgG and IgM are obviously reduced and their decrease of immunologic functions is significantly associated with patient emotions, such as patients' depression and anxiety. Although there are different opinions about whether the emotions of cancer patients are associated with immunologic function, there is an accordant opinion that negative emotions (such as depression and anxiety) can result in the continuous rise of corticosteroid concentration in the blood, resulting in the depressions of the phagocytic activity of phagocytes, the differentiation and hyperplasia of T cells, and the antibody excretion capacity of cells, changes that can lead to continuous development and occurrence of cancer cells. Therefore, targeted effective therapeutic measures should be taken to release the negative emotions of patients, fully mobilize the recovery potential of patients, and enhance their immunity, thereby benefiting the life qualities of patients and maximizing the therapeutic effects.

4.7.3.2 CANCER PSYCHOLOGY–NERVE–ENDOCRINE–IMMUNE AXLE

Psychosocial factors promote the occurrence and development of cancers, which is realized through the psychophysiological approach, namely, the cancer psychology–nerve–endocrine–immune channel.

A large number of experiments indicate that electric shock, traumatic malignant stimulations, and repetitious and concentrated conditional reflex experiments can cause excess or universal stresses of the nervous system and promote the "spontaneous" growth of cancer. The removal of the cerebral cortex or use of central depressants (such as barbital sodium) can promote the development of transplantable cancer and cause premature death of animals, whereas caffeine and small doses of strychnine can delay or block the occurrence of cancer. The derogation of the dorsomedial hypothalamic nucleus and paraventricular nucleus can lead to the proliferous degradation of the thyroid gland adenoid, the destruction of the dorsal side hypothalamus can prolong the survival period of transplantable cancer, and the band-shaped destruction of the front-side hypothalamus can cause the decrease of the antibody titer and the depression or delay of anaphylaxis. These experimental data show that hypothalamus plays an important role in the effect of psychosocial factors on cancer, and the hypothalamus and immunoreaction may be influenced by many processes of the autonomic nervous system and nervous endocrine.

Psychosocial factors initiate the neuroendocrine system and immune system loop so as to impact the occurrence and development of cancer. At present, as for the function of psychological and social factors in the occurrence of cancer, some people believe that the body generates a nonspecific reaction after stimulation that leads to the reduction of the body's immune surveillance and killer cells, and the decrease of T lymphocytes, as well as the promotion of occurrence and development of cancer with the participation of carcinogenic factors through the effect of the nerve–endocrine–immune channel. Many study results in China and abroad indicate that psychological factors are important factors in promoting the development of cancer, which is more obvious when patients lack social support.

4.7.3.3 PSYCHOTHERAPY AND IMMUNOLOGIC FUNCTION

In recent years, music therapy, cognitive behavior intervention therapy, and catharsis therapy have been applied to some cancer patients to obtain different types of effects. As a natural and noninvasive therapy, music therapy is applied in clinical oncology. Patients can listen to graceful, lively, and cheerful sound waves while they are receiving invasive chemotherapy. The music sound waves act on their brains and raise the excitability of the nerve cells. In turn, the body can secrete certain substances through the regulations of nerve and nervous body fluid, such as hormones, enzymes, and acetylcholine, which play important roles in regulating blood flow, improving blood circulation, enhancing gastrointestinal peristalsis, promoting the secretion of digestive juices such as spittle, and strengthening metabolism, thereby effectively mitigating worries and improving sleep patterns and other constitutional symptoms of the patients. The cognitive education about emotional catharsis and knowledge of cancer allows cancer patients to relieve their negative emotions and divert their attentions from the disease situation, which can not only control and rectify the negative automatic thoughts and attendant behaviors of the patients toward cancer and chemotherapies but also change their latent dysfunctional anxieties. It will improve stimulation of immunologic mechanisms that are vital to successful treatment and recovery.

4.7.4 Common psychological reactions of cancer patients

4.7.4.1 Mental disorders of cancer patients in different stages

Generally speaking, all cancer patients suffer from some form of mental disorder. According to different premorbid personalities, cultural level, illness conditions, family backgrounds, social and economic conditions, and clinical manifestations vary. Symptom improvement during therapy can often relieve the psychological pressures on patients, whereas adverse reactions of the body often enhance emotional disorders such as anxiety and depression. Common mental states include fear, pessimism, mental depression, mental fragility, sensitivity, anxiety, hostility, denial, acceptance, and hope.

4.7.4.1.1 Mental disorders in the preliminary diagnosis stage

There are some basic manifestations of anxiety, uneasiness, and fear during this period, along with doubt and helplessness, as patients await the confirmation or reversal of the initial diagnosis. Often, the patient denies such information and will not accept it, which is the most common psychological defense. Such contradictory emotional states can persist until the actual situation is known and, conjoined with other adverse manifestations, can thus disrupt the patient's sleep, aggravate the patient's condition, enlarge the cancer, and result in the metastasis of cancer cells.

4.7.4.1.2 Mental disorders in the confirmed diagnosis stage

Common mental disorders include shock, fear, denial, doubt, anger, frustration, and acceptance and adaptation.

4.7.4.1.3 Mental disorders in the therapy stage

With a person's adaptation to the role of being a patient, the nervous, depressive, and sad mental states can be relieved temporarily, but new psychological problems can occur due to side effects or disease changes during therapy and the emotions of the patient can also change accordingly.

When it is confirmed that metastasis of the cancer has not occurred, surgical resection is the preferred method. Subsequently, the patient will accept surgical therapy, gain confidence in the therapy, and voluntarily cooperate with the medical stuff in the resection of the cancer.

Due to their serious therapeutic reactions and toxic side effects when receiving chemotherapy or radiotherapy, the patient can suffer from nausea, vomiting, fatigue, phalacrosis, decrease of leukocytes and platelets, traumatism of liver and kidney functions, and so on, all of which can lead to adverse psychological reactions and even the idea of suicide due to the unwillingness of the patient to continue to suffer and the patient's loss of confidence in the therapy.

Some patients who suffer from surgeries, radiotherapies, and chemotherapies and patients in whom the metastasis of foci or increase of original foci due to certain causes is found during reexaminations may suffer from more serious psychological problems such as total despair and hopelessness.

Due to domestic problems or inability to pay the therapeutic fees, they can suffer from additional psychological problems, worry about losing both life and wealth, and refuse to continue the therapies. Or, the patients themselves can have strong survival appetencies but poor family conditions and incapability of bearing medical fees can result in despair.

All of the aforementioned psychological problems can influence the therapeutic effects on cancer, so it is necessary to understand them early and have them resolved.

4.7.4.1.4 Mental disorders in the late stage

After cancer treatments, recurrence or metastasis is the most frightening event for patients. Even some patients' mental states may worsen compared with the time of the first diagnosis, which can include insomnia, reduction of appetite, and anxiety and even depression. If the patients have actively cooperated during the surgery, chemotherapy, radiotherapy, immunotherapy, or other treatments but unfortunately the patients' conditions have not improved but rather deteriorated, they can fail to control their mental sorrow and desperation and can even display anger, hostility, sense of persecution, anxiety, depression, and irritability.

4.7.4.1.5 Mental disorders in medium and advanced stages

Medium- and advanced-stage cancer patients often suffer from cachexia, but most maintain their mental awareness even though their bodies are seriously adynamic. Thus, they not only suffer from the disease itself, but also bear the emotional pain of inevitable parting from their family forever. Further, the emotional pain will eventually lead to self-blaming when the patients witness the desperation of their close friends and family members. In their long-term sufferings, the patients understand that they will not survive much longer, and they mentally prepare for death. However, there are also some patients who are afraid of being abandoned, being incapacitated, and losing their dignity or are afraid of death itself.

4.7.5 Psychotherapy for cancer patients

Psychotherapy on cancer patients mainly aims to support and improve their life quality, with specific objectives including the following: reduce emotional symptoms such as anxiety and depression; encourage patients to express in words their irritable feelings such as anger, fear, rage, and disappointment; learn the behavioral skills against diseases; learn to live normally again; reduce the emotional irritability of families or spouse; remove any taboo on discussions of death; and learn relaxation skills to alleviate insomnia, pain, and nausea.

Common psychotherapies include cognitive therapy, behavior therapy, hint and hypnosis therapy, and supportive therapy.

4.8 HYPERTHERMIA INTEGRATED WITH TRADITIONAL NATURAL THERAPY

4.8.1 Cancer hyperthermia and traditional natural therapy

Traditional natural therapy plays an important auxiliary role in preventing, curing, and healing cancer, and it mainly achieves the situation of "relative equilibrium of Yin and Yang" through the improvement of living condition and emotions, and regulation of immunity and body condition. Hyperthermia can improve the immunity of the body and play an important role in three-level prevention against cancer; moreover, the combination of hyperthermia with traditional natural therapy is an innovation in the field of cancer therapy, which is beneficial to the long-term therapy on cancer.

4.8.2 Introduction to traditional natural therapies

4.8.2.1 QIGONG BREATHING EXERCISE THERAPY

Here, qigong refers to medical qigong, which is nonmedicated health-building therapy through the physiological and psychological processes of exercises such as regulating body, breathing and mental activities, relaxing limbs, adjusting respiration, and stabilizing spirit consciousness so as to regulate the balance of yin and yang in viscera. The effect of qigong breathing exercise therapy is to enhance and replenish the original qi of the human body, improve the quality of the body, self-regulate and self-control the life process by the guiding effect of consciousness so as to coordinate the body to adapt to the environment, keep the stability of inner and outer environments, exert the inherent potential of the human body, and realize the effects of prevention and cure of diseases while nourishing the body and prolonging life.

Qigong breathing exercise therapy has the therapeutic effect of strengthening vital qi to eliminate pathogenic factors. First, qigong breathing exercise therapy focuses on "regulation of mental activities" to reach the superior skill of "conversion of qi into vitality" and "conversion of vitality into the original Qi" by regulating mental activities to achieve calmness, because the "Heart" (mental activities) in the "Office of Monarch" exerts the main domination effect on five organs so that the five organs are coordinated, and the regulation of mental activities removes the adverse effects of emotional factors so as to reach a therapeutic effect of "relieving Qi stagnancy in the liver." Second, the long-term regulation of mental activities can lead

Figure 4.6 Medical qigong.

qi consciously, to reach the "Qi running after consciousness"; then, the "Qi leading the blood flow" becomes available. Moreover, the smoothness of qi and blood can mobilize the vital qi of the human body, completely remove pathogenetic toxic qi, and drive the meridian qi to remove pathogenetic factors such as phlegm, dampness, blood stasis, and stagnation and mobilize the essential substances to nourish and moisten the damaged visceral tissues.

Qigong exercise emphasizes the "absorption of body fluid and conservation of essence Qi" to ensure the storage of essence qi in the human body. Qigong exercise can play the role of heart, governing mental activities and making the mental power bright, to reach the best regulation and control of life movement and process, realize the "increasing vigorousness of vital Qi and gradual breakdown of pathogenic factors," and achieve the purpose of treating cancer (Figure 4.6).

4.8.2.2 KINESIATRICS

With the conversion of the biomedicine mode to the biologic–psychologic–social medicine mode, the knowledge of the harm from the side effects of synthetic drugs, and the constant occurrence of iatrogenic diseases and drug-induced diseases, people are increasingly being advocated to recover their original simplicity and return to nature. Natural therapy has attracted great concern and attention from people all over the world. At present, natural therapy is prevailing in many countries and regions of Europe, America, and Asia. Kinesiatrics is one of the common natural therapies for health preservation and protection and prevention and cure of diseases. Modern medical research and clinical practice show that many movement modes, such as traditional guiding, "five-animal" exercise, "eight-sectioned" exercise, shadow boxing, muscle–bone strengthening exercise, physical exercise, and jogging, that were performed by ancient Chinese have better auxiliary therapeutic effects on cancer patients in preventing cancers and protecting health and have great significance in relieving clinical symptoms, improving life quality, and prolonging survival periods.

In recent years, the influences of movement on the immune system have been increasingly recognized by sports science workers and the medical field. Kinesiatrics not only can strengthen various tissues and organic functions of the body, improve the adaptation and tolerance capacity of the body to the environment, enhance the defense capacity of the body, and improve work efficiency and protect health but also has an obvious regulation effect on systems such as the nervous system, endocrine system, and immune system, thereby playing an important role in preventing tumors. Modern medical research and experiments have proved that kinesiatrics can attain anticancer effect directly or indirectly by means of regulating the immunologic functions of the body, increasing the oxygenic absorption of the body, promoting the metabolism of the body, and adjusting the mental state.

4.8.2.3 INEDIA THERAPY

Inedia is a former cultivation method of vital energy of Chinese Taoism, well known in China, together with guidance, intake of qi, and alchemy. It is also called cereal give-up, cereal rejection, grain rejection, foodstuff cease, and colon cleansing, meaning no eating of five cereals; but it does not mean not to eat anything and, least of all, fasting or no beverage or food. Only such understanding can eliminate the fear of many people and relieve their psychological loads.

TCM believes that the visceral diseases in the human body depend on the changes of qi blood and yin–yang. Inedia reaches a particular effect in developing the potential of the human body and regulating the balance of yin–yang and qi blood. Modern qigong Inedia, also called qi-intaking Inedia, is a cultivating method suitable for modern people, based on Chinese traditional qigong theories and methods and adopting the research achievements of modern Inedia in China and abroad, and it has special effects of qigong and fasting.

Inedia therapy has main functions such as removing pathogenetic factors and eliminating toxins, improving the antidisease capacity of the body, regulating the balance of acid and alkali in the body, and preventing cancer.

4.8.2.4 MASSAGE THERAPY

Massage is one of the earliest therapies for prevention and cure of diseases. TCM medical massage is popular all over the world, with characteristics of long history, numerous schools, rich techniques, strong skills, wide indications, and significant therapeutic effects. Under the directions of TCM meridian acupoint theory, massage adopts various techniques for certain positions on the surface of the human body to promote meridian dredging and unobstructed flow of qi and blood, and for prevention and cure of diseases. Massage is a natural therapy that has unique therapeutic rules and has attracted wide attention due to its wide therapeutic range, safety, effectiveness, and absence of toxicity and side effects.

The essence of the massage technique is the application of an external force, which can be applied locally to cause changes in local joint positions and soft tissue properties (such as muscle and aponeurosis), so as to rectify the pathological state of the body. It can also generate secondary whole responses through stimulation of the meridian that changes the pathological state, so as to activate the whole regulation function of the meridian system, leading to recovery (Figure 4.7). The main therapeutic effects include the following: dredging the meridian, promoting blood circulation to remove blood stasis, strengthening vital qi to eliminate pathogenic factors, reinforcing the vital essence and strengthening the primordial qi, and regulating the circulation and function of the nervous system.

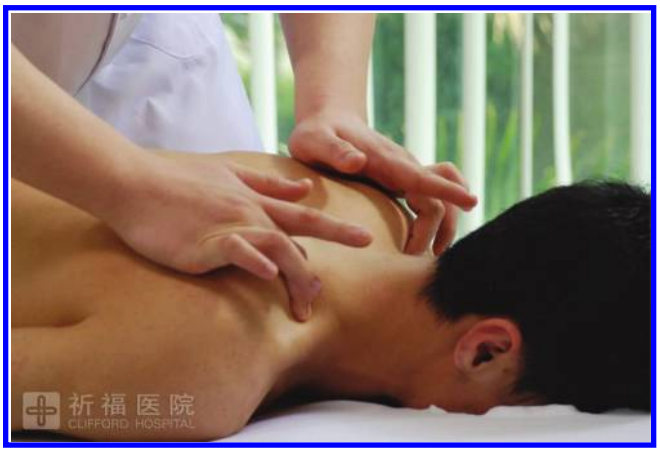

Figure 4.7 Massage therapy.

4.9 HYPERTHERMIA INTEGRATED WITH SYSTEMIC BIOFEEDBACK THERAPY

Cancer hyperthermia and systemic biofeedback therapy are consistent with the physical or biological foundation, but both have their own therapeutic characteristics. They can supplement each other during cancer therapy, showing a synergistic effect. They can also supplement each other with effects and are often combined clinically to play important roles in cancer therapy, in accordance with different disease types and different conditions of different patients.

Systemic biofeedback therapy integrates international biological resonance technology and TCM meridian theory and produces highly concentrated pulse electromagnetic fields through the electromagnetic induction principle. They penetrate the deep target tissue region and act on extracellular matrixes directly, so as to regulate the energy balance of the body; clear the blocked areas of the body; dredge blood vessels and meridians; block the formation and development of diseases without any invasion, pain, or side effects, activate the self-repair function of cells and regulate the immunologic functions of the body; strengthen and improve the self-regulation and self-repairing activities of the body; and eventually achieve the dynamic balance of metabolism (Figure 4.8).

The electromagnetic system of the human body is closely associated with the occurrence of diseases. Studies in the fields of modern physics and biophysics find that the biochemical process in the living tissue is controlled by an information system characterized by electromagnetic oscillations. These electromagnetic oscillation forces not only control the biological system but also cause some electromagnetic resonance phenomena. The electromagnetic oscillation is not only necessary to maintain life functions but also closely related to the incidence of disease and can even become a cause of diseases. Maintaining the harmony of the body's electromagnetic oscillation information system depends on the resonance capacity of cells, tissues, organs, and the whole body. After the derangement or complete loss of such capacity, the transmission of the electromagnetic information will be incoherent and inappropriate; hence, the healthy physiological process deviates toward the pathological process, wherein pathological electromagnetic waves reflecting a particular organ, tissue, or region will produce a "wrong working pattern." If this process is not rectified in time, this pattern will be solidified into a pathological pattern, namely, disease.

The human body has more than 70 trillion cells, of which healthy cell membranes bear a voltage of 70 mV and asthenic or nutrient-deficient cells only bear 30 mV. It is difficult for the cell membrane with a voltage of 30 mV to input enough nutrients into the cell, resulting in the death of the cell. The key to prolonging cell life is to increase the electric potentials of cell membranes. In addition, the systematic biofeedback therapy can help the body get much more energy, reduce the death of cells, and strengthen the resistance of the body.

Figure 4.8 Systemic biofeedback therapy.

Systemic biofeedback therapy can effectively regulate the metabolic balance of cell nutrients, promote the repair and regeneration of any wound, realize the reconstruction of damaged tissues and cells, and normalize physiological working patterns. Also, it shows effects of clearing intrinsic toxins (especially heavy metals), improving the detoxification function, and relieving and eliminating various acute or chronic pains and inflammatory reactions. It has significant clinical values in promoting the recovery of cancer patients, improving their symptoms and survival quality.

4.10 HYPERTHERMIA INTEGRATED WITH CONSTITUTIONAL ALKALINIZATION THERAPY

4.10.1 Cancer hyperthermia and constitutional alkalinization therapy

Nontoxic integrative cancer treatments emphasize strengthening vital qi to eliminate pathogenic factors, to improve the body's capacity for resisting extracorporeal pathogenic factors, and to depress the hyperplasia of cancer cells through improvement of the body's immunologic functions; they include important components aimed at maintaining the healthy internal environment of the body, especially the acid–base balance. Some studies show that a stable strongly alkaline body is beneficial to the immunologic function. The thermal effect and extrathermal effect of hyperthermia has a positive immunologic regulation function and can depress the hyperplasia and metastasis of cancer while it kills the cancer directly by heat. During clinical practice and research on nontoxic integrative cancer treatments in Clifford Hospital, the author combined hyperthermia with constitutional alkalinization therapy organically, attaining certain therapeutic effects, especially for some medium and advanced patients who had lost their opportunity for surgery and had poor sensitivities to radiotherapy and chemotherapy. Their life quality improved and their survival periods were prolonged. In addition, the combination of low-temperature whole-body hyperthermia with constitutional alkalinization therapy can be applied for preventing cancer, improving health, and so on because both of them have positive immunologic regulation effects.

4.10.2 Regulation of intrinsic acid–base balance as a new hope for cancer therapy

In the process of normal metabolism, the human body generates acid and alkaline substances continuously and ingests them from foods, so the pH level changes constantly. However, due to certain acid–base balance ability, the human body can keep a relative balance between acid and alkali under normal conditions, which is named the acid–base balance, with a healthy balance range of (pH value) 7.35–7.45, averaged as 7.41 and showing weak alkalinity. If the pH in the body is (often) lower than 7.35, it will be considered an acid constitution. Immune cells in the human body have an optimal pH range of 7.35–7.45, in which the resistance of immune cells is the strongest and the immunologic function of the body is the best. When the pH value is lower, the activity of immune cells can be reduced greatly and the immunologic function will be weakened accordingly, under which condition the activity of some viruses and bacteria are the strongest. According to an investigation on the healthy conditions of urbanites, the pH values of blood in over 80% of urbanites are often at the lower part of the healthy range. When the body fluid is overly acidic, the resistance of immune cells is reduced and body metabolism can slow down; hence, wastes cannot be easily discharged and the visceral load increases. A Japanese study shows that most cancer patients have acid constitutions. Therefore, some medical experts propose that acidification of the body is likely to be one of the causes for the occurrence of cancer.

As early as the 1920s, this theory became one of the hot topics of discussion. Otto Warburg (winner of the Nobel Prize for medicine in 1931), who was a biochemist in Germany at that time, proposed that the energy metabolism in abnormal cells was one of the main causes of cancers. Cells could get energy through

the aerobic respiration of mitochondria or the glucolysis in the cytoplasm. Warburg believed that the cells inducing tumors existed in an acidic external environment, which made cells transfer from the aerobic respiration energy supply to the glycolysis energy supply, ultimately leading to the malignant development of cells.

Under normal conditions, surplus acid or alkaline substances are moved out of the human body by the autologous regulation function, to reach alkalescence. Although there have not been definitive scientific studies proving the quantitative relation between diets and acid–base level in the human body, practices have proved that the intake of more alkaline foods can be directly beneficial to the acid–base balance of the body. The Japanese simply refer to acidic foods as "semi-health foods" and alkaline foods as "health foods." Acidic constitutions are the consequence of eating foods with high fat, high protein, and high heat, but we can match them with alkaline foods. For example, some seaweeds can be included when meats are stewed, and some radishes can be added while beef is baked, so as to neutralize the acid–base level of foods.

4.10.3 Diet therapy for alkaline constitution

A food in the mouth can taste acidic, acerbic, or otherwise through responses of the taste sense, but these acidic and alkaline tastes cannot indicate whether such food is acid forming or alkali forming in the body. For example, oranges and carambolas taste acidic, but they are alkaline foods. Another example is that rice and noodles show no taste, but they are acidic foods. Accordingly, any reaction of the taste organs does not represent the essential acidity or alkalinity of foods.

Therefore, the differentiation between acidity and alkalinity in a food cannot depend on the intuitive reaction or subjective sensation of the food in the mouth. Generally speaking, any food containing more inorganic ingredients such as sulfur, iodine, and phosphorics can be recognized as an acidic food, whereas it is an alkaline food if it contains more ingredients such as sodium, calcium, potassium, magnesium, iron, and copper. Because such foods after ingestion and absorption in the human body can generate influences on the acid–base level of the blood, they are associated with the health of the human body.

In order to maintain the acid–base balance in the body, it is appropriate to include more vegetal foods such as natural fruit in the daily diet, with an applicable proportion of meat and vegetables as 1:4 or 3:7. Additionally, bad habits must be avoided, such as overstraining of cerebration, eye strain, staying up late, and alcoholic intemperance, because all of these behaviors can consume a large number of amino acids and fats in the body within a short time, increase the acidic substances in the metabolites, and affect the pH value of the body.

Accordingly, common acidic and alkaline foods in our daily life are summarized as follows:

- Acidic foods include chicken, pork, beef, cheese, egg yolk, fish roe, oyster, eel, carp, crucian carp, abalone, shrimp, rice, flour and flour products, barley flake, peanut, fried bean curd, asparagus, sake, and beer.
- Alkaline foods include bean curd, soybean, green bean, spinach, lettuce, turnip, radish, bamboo shoots, sweet potato, potato, onion, eggplant, cucumber, watermelon, kelp, orange, carambola, banana, apple, grape, persimmon, milk, protein, coffee, strawberry, and kale.

4.10.4 Bicarbonate therapy

4.10.4.1 DEVELOPMENT OF BICARBONATE THERAPY

In 2000, Moss in Arizona first applied the bicarbonate therapy clinically to cancer patients with good therapeutic effects. Since 2003, Simonsini in Italy has started to research and clinically apply bicarbonate therapy to medium and advanced cancer patients. Drug application approaches include oral application, venous injection, and intervention. Since 2004, Sirkus has widely applied the bicarbonate therapy to cancers and found that the oral application is better. Integrating patients' conditions, approaches such as oral application, venous and local injection, intervention, and celiac infusion have been applied to systemize and standardize bicarbonate therapy.

4.10.4.2 MAIN MECHANISMS OF BICARBONATE THERAPY ON CANCER

1. Change the internal environment of tumor cells, destroy the function of the mitochondrion, and depress the respiration of cells to result in the death of cancer cells.
2. Change the permeability of tumor cell membranes, allowing chemotherapeutic drugs to enter the cells so as to exert their effects.
3. Alkalinize the cancer tissue, change the microenvironment of the cancer, and depress the spontaneous metastasis of the cancer, inhibiting infiltration and growth.
4. Through the combination with a radioactive element called uranium, form a nontoxic substance without radiation, which is then discharged out of the body through the viscera to relieve the side effect of radiotherapy.
5. Rectify acid-oriented substances, strengthen the physical condition of patients, reduce any infection and physical energy consumption, improve the life quality of patients, and prolong the survival periods of patients.

4.10.4.3 COMPREHENSIVE BICARBONATE THERAPY SCHEME

4.10.4.3.1 Assessment before drug application

4.10.4.3.1.1 Diagnosis and therapeutic assessment

It should include confirmed cancer diagnosis, position, stage and grade, pathology, metastasis condition, immunohistochemistry, and gene examination; therapies performed previously (surgery, radiotherapy, chemotherapy, intervention, target orientated therapy, biological therapy, and natural therapy); and special examinations conducted previously, such as CT, MRI, PET-CT, radiography, ultrasonic examination, and cardiogram.

4.10.4.3.1.2 Systemic disease condition assessment

It should include nutritious assessment, pain assessment, life index, body weight, routine tests, uric pH value, biochemical tests, liver and kidney functions, blood coagulation function, relevant antigens of tumor, and blood gas analysis (arterial and venous pH values).

4.10.4.3.1.3 Pathological changes and functional assessments of main viscera and tissues

Check whether there are any metastasis; pathological changes of heart, liver, lung, kidney, and brain; bone metastasis; and bone marrow depression.

4.10.4.3.2 Intravenous drip rapid alkalization scheme

Within 3 days before chemotherapy, bicarbonate solution should be prepared at 2.5% concentration and injected at the dose of 150 mg/kg/day, by methods including intravenous drip, once a day for 3 days as a course. Then, it could be applied by itself or in combination with chemotherapeutic drugs.

For example, a colon cancer patient with 60 kg body weight would require 7.2 g of bicarbonate each time, which equates to a bicarbonate injection of 300 mL with a concentration of 2.5%.

4.10.4.3.3 Oral application of bicarbonate

The dose for an adult totals 100 mg/kg/day. A powder agent can be put into drinking water or fruit juice of 500 ml for slow drinking, once a day, or tablets can be divided into three portions for oral application, requiring more water constitution, with 8 days as a therapeutic course; the latter can be applied with radiotherapy and chemotherapy simultaneously. As for cancer patients, long-term oral application of bicarbonate can be considered at 2 to 3 g/day, which can obviously relieve the side effects of radiotherapy and chemotherapy, strengthen the therapeutic effect and immunologic function, and reduce any opportunity for infection.

When intravenous injection and oral application of bicarbonate are applied, the pH value (paper strip method) of urine or sputum should be inspected once every morning; a pH value of sputum over 7.4 and a pH value of urine over 7.0 are required. After the completion of such a therapeutic course, the pH values

of arteries and veins should be inspected and compared with those before therapy; the pH is required to be over 7.35.

4.10.4.3.4 Local or acupoint injection around tumor

For skin cancer, tumor colli (primary or metastasis), and superficial lymph node metastases, first apply routine disinfection, keeping away from blood vessels; then, use a thin needle for a multipoint bicarbonate injection of 2.5%–5%, with about 2 mL for each point and a total volume not more than 10 mL for one injection, once every other day with 8 days as a course.

4.10.4.3.5 Intervention injection

A catheter is inserted through the artery to inject the drug at 5%, 20–30 mL each time, lasting 10 minutes. This therapy has a good therapeutic effect on liver cancer, and if any chemotherapeutic drug is applied simultaneously the bicarbonate solution is injected first, once a month with three continuous injections as a course.

4.10.4.3.6 Peritoneal perfusion

Peritoneal perfusion is safe and effective. It can be applied with chemotherapy drugs. A volume of 100 mL of 5% sodium bicarbonate injection heated to 37°C is perfused slowly into the abdominal cavity within 1 hour. It is performed in combination with abdominal massage to achieve uniform distribution of the liquid in the abdominal cavity. If the patient complains about abdominal pain, 10 mL of 2% lidocaine can be added inside or the concentration can be reduced to 2.5% with the same dose. If chemotherapy drugs are simultaneously applied, sodium bicarbonate is applied first; 20 minutes later, the chemotherapy drugs are perfused, once or twice a week for eight times as a course. If peritoneal perfusion of sodium bicarbonate is combined with hyperthermia, RF local hyperthermia at the abdomen can be carried out after perfusion.

4.10.4.3.7 Retention enema of sodium hydrogencarbonate or rectosigmoid administration

A volume of 100–150 mL of 1.25%–2.5% sodium hydrogencarbonate solution is applied for retention enema. Retain for 15–20 minutes, or 50 mL of sodium bicarbonate with the same concentration is set to the junction of the rectosigmoid with a fine silica tube for slow infusion (10–15 drops/min). Patients should feel comfortable, and quick alkalization of the liver, intestine, pancreas, and spleen can be achieved.

4.10.4.3.8 Other administration approaches of bicarbonate

Bicarbonate solution with the concentration 1.25% is applied. The administration approaches include mouth rinse (for buccal, pharyngeal, and tonsillar tumors), which can be conducted at any time, and ultrasonic atomization for absorption, 10 mL each time, one to two times a day for 8 days as a course (for laryngeal carcinoma, nasopharyngeal carcinoma, lung cancer, etc.).

4.10.4.3.9 External skin application

For external application (skin cancer, etc.), the concentration is up to 5%, three times a day for 1 month as a course. It can be alternated with other skin medicines.

4.11 HYPERTHERMIA INTEGRATED WITH CRYOSURGICAL THERAPY

4.11.1 Cancer hyperthermia and cryosurgical therapy

Cryosurgery is a product integrating space rocket guidance technology with modern medical cryogenic freezing tumor therapy. The refrigerant (argon gas) and the heating medium (helium gas) circulate and inflate rapidly on the knifepoint, which can not only freeze pathological tissues to –140°C within 50 seconds but also unfreeze and heat them to 45°C rapidly so that the tumor cells burst to death. Also, because of the disruptive

death of tumor cells, the antigens in tumor cells enter the blood and stimulate the body's immunologic system to generate cellular immune responses and body fluid immune responses and enhance the immunity of the body. It is a unique, new, and high-tech medical procedure used all over the world, integrating multiple technologies such as ultra-low-temperature refrigeration of –150°C, intervention hyperthermia, high-temperature-difference reversion of 200°C, and immunologic enhancement. It is superior to hyperthermia or cryotherapy used alone and is more complete and effective in killing cells. Moreover, it was developed in succession to radiofrequency ablation therapy, microwave, laser, focused ultrasound technology, and Gamma Knife, with significant advantages in curing solid tumors such as in lung cancer, liver cancer, breast cancer, and renal cancer, representing an advanced level of cancer therapy that is used all over the world. Argon–helium targeted therapy technology is honored in the Occident as a nontoxic cancer treatment. Cancer hyperthermia has anticancer effects such as killing of cancer cells, positive immune regulation, as well as anti-inflammation, and improvement of blood flow in normal tissues. The addition of cancer hyperthermia to cryosurgical therapy is usually performed 1 to 2 weeks after cryosurgical therapy, to alleviate the pain of patients after cryosurgical therapy, promote the absorption of necrotic substances, improve the circulation of normal tissues and the metabolism, have synergistic effect with the cryosurgical positive immune regulation, relieve any adverse effects after cryosurgical therapy, enhance the therapeutic effect, and improve the life quality of patients.

4.11.2 Theoretical basis and development of cryosurgical therapy

Refrigeration is divided into three stages: Overlow temperature, freezing, and thawing. To guarantee that cancer cells are destructed thoroughly, four factors play a decisive role, minimum temperature, freezing speed, freezing time, and freezing frequency. Within –10°C to –15°C, ice crystals begin to form in the cytoplasm, leading to the death of cell tissues. Based on this principle, the freezing effect depends on the freezing speed. When temperature drops, if the freezing speed is slow the ice first formed in the cell tissue clearances can absorb water from the cells. The dehydration in cells can obstruct freezing internally, so as to protect the cells from necrosis to some extent. Therefore, rapid freezing in cells is a key process of refrigeration. After the refrigeration process, thawing commences and it can damage the cell tissue. During the temperature rise to –20°C from –40°C, ice crystals can expand, resulting in the busting of the ice balls formed during refrigeration, which can cause the same high destruction as the refrigeration process itself. Multiple freezing–thawing cycles can thus increase the destructive effect of cryosurgery.

4.11.2.1 Cell destruction mechanism by fast cooling

Stage I (temperature from –4°C to –21°C) refers to the formation of ice crystals outside cells. In the initial freezing stage, the water inside the cells flows out, resulting in the rise of osmotic pressure in the cells and dehydration in the cells. The cells losing water become wizened, and the cell membranes and cell organelles are damaged accordingly.

Stage II (temperature below –21°C) refers to the formation of ice crystals in cells. When the freezing speed is rapid enough and the temperature further decreases, ice crystals form in the cells. The cell organelles, such as chondriosome and endoplasmic reticulum, can be damaged irreversibly and then the cell membranes can also be damaged, ultimately resulting in the death of the cell.

4.11.2.2 Two cell destruction mechanisms by temperature rise (especially between –40°C and –20°C)

The cell destruction mechanisms are as follows:

1. Small ice crystals in cells are recrystallized or syncretized with each other to form bigger ice crystals while having a stronger destructive effect on the cells.
2. Ice crystals in the clearances outside the cells are dissolved into a low permeability state; then, water reenters the cells to generate the swelling of cells and this results in the destruction of cell membranes.

4.11.2.3 DESTRUCTION OF CAPILLARIES

Refrigeration results in the shrinkage of blood vessels, decrease of blood flow, coagulation of blood platelets, formation of microthrombus, blockage of blood flow and blood and oxygen deficiency in tissues, and damage to targeted cells.

4.11.2.4 IMMUNOLOGIC REGULATION FUNCTION

After repeated freezing and thawing of cancer cells, tumor cells fracture and cell membranes dissolve to promote the release of antigens in cells and those in a shielding stage, relieve the immunosuppressive effect of the cancer in the body, and improve the anticancer immunity, so as to switch on its lethal immune effect on cancer cells.

4.11.3 Advantages of cryosurgical therapy

4.11.3.1 OBVIOUS EFFECT

This targeted therapy is applied in a precise location, and its extremely low temperature can destroy the pathological tissues thoroughly.

4.11.3.2 MINIMALLY INVASIVE THERAPY

It is characterized by fewer traumas, lesser suffering, fewer complications, lesser influences on viscera organs, faster recovery of patients, and shorter hospitalization times compared to traditional methods of therapy.

4.11.3.3 HIGH SAFETY

The complete penetration process of the probe is monitored by video to protect important organs from collateral injury, the thermal pool effect of blood vessels can protect these blood vessels from trauma, and the probe is only frozen at the tip so as to prevent the freezing of normal tissue in its puncture path.

4.11.3.4 WIDE INDICATIONS

It can be applied to old and weak patients as well as in advanced cancer cases that cannot be cured or fail to recover by other therapies.

4.11.3.5 REAL-TIME MONITORING

It includes full video monitoring of the surgery, full video monitoring of freezing and thawing, and full monitoring of tissue temperature.

4.11.3.6 REPEATABILITY

It can be applied repeatedly to consolidate and increase the therapeutic effect.

4.11.3.7 SIMPLE OPERATION

It is applied under local anesthesia, and its orientation and puncture operations are simple.

4.11.3.8 COMBINED APPLICATION

It can be conducted not only alone but also combined with radiotherapy, chemotherapy, and surgery.

4.11.3.9 NONTOXIC TREATMENT

It is a physical therapy without any of the toxic and side effects of radiotherapy and chemotherapy and with minimal injury to normal tissue cells.

4.11.4 Indications and contraindications

In 1999, the China National Medical Administration Bureau approved the application of cryosurgical therapy in China. Wu Mengchao, Tang Zhaoyou, and Hao Xishan, famous academicians in China, as well as other domestic specialists applied such technology to the therapy of over 20,000 patients with medium and

advanced liver cancer, lung cancer, breast cancer, pancreatic carcinoma, brain tumor, prostatic cancer, and kidney tumor, all of which showed obvious effects.

Broadly speaking, as long as puncture freezing does not injure large blood vessels, or important nerves and organs near the viscera, this therapy can be applied without restriction by tumor properties. Except for therapy on liver cancer and lung cancer, cryosurgical therapy can be applied to liver angioma, kidney cancer, postoperative colon cancer reoccurrence, prostatic cancer, benign prostate hyperplasia, breast cancer unsuitable for surgery, oral carcinoma, face and neck tumors, tumors in systemic soft tissues, glioma within 4 cm of brain template and the top, and tumors that can be punctured in the abdomen and pelvic cavity. Each therapy is usually within 6 cm; otherwise, it must be applied separately several times. For patients who suffer from the metastasis of multiple organs, have worse systemic body conditions, and have liver or lung insufficiency, this therapy is not appropriate.

4.11.5 Clinical applications

4.11.5.1 LIVER CANCER

Liver cancer is one of the most common malignant tumors for which surgical resection is the most preferred therapeutic method, as widely acknowledged. When found with liver cancer, only about 20% of patients can receive such surgeries, with survival periods calculated only in months. Cryosurgical therapy is an ultra-low-temperature refrigeration surgery that can freeze any pathogenetic tissue to –140°C within 60 seconds and defreeze the ice balls quickly to raise their temperature to 45°C rapidly, and thus it can destroy the tumors thoroughly. Clinical therapeutic results have proved that a precise refrigeration resection can destroy the tumor cells in the liver with high precision, so as to increase the survival rate. It is applicable for patients who suffer from medium and advanced liver cancers that cannot be ablated, tumor reoccurrence after surgery, liver function decompensation, low leukocytes and blood platelets, and so on for which any surgery or chemotherapy is not suitable. It is also applicable for patients with small liver tumors in certain locations that cannot be ablated by surgery. This therapy is inadvisable for patients suffering from tumor with areas exceeding 70% of the liver volume, excess of ascites, jaundice, bleeding tendency, and hepatic failure. Complications: first, it can cause the rupture of the hepatic capsula. When the refrigeration is close to the liver surface, it may arouse bleeding. So, it is better to perform the intraoperative refrigeration under direct vision to arrest bleeding. If endemic refrigeration is required, it is better conducted in a manner in which the cryoprobe gets through one part of the normal liver tissue and then enters the focus. Second, hysteretic bleeding, though not common, is the key complication, often found in about 1% of patients. Such complication may be due to the fact that some patients will suffer from thrombocytopenia after a large number of liver tissues are frozen. Third, the ultralow clinical temperature is a latent complication for which a device must be adopted to control the temperature by circulating warm gas for applying heat around the patient's body and combining traditional temperature control technologies, such as the combination of heating liquid with absorption of gas, so as to reduce the problems incurred by the ultralow temperature. Fourth, unexpected myoglobinuria after refrigeration surgery, in most cases, is only limited to 1–3 days after surgery. In serious cases, myoglobinuria can cause acute tubular necrosis and renal failure. Also, myoglobinuria arouses a reduction in kidney function, which is obviously associated with the freezing volume. Therefore, before freezing any big tumor it is necessary to consider the influences on kidney function. For all such cases (especially when the myoglobins become heavier after refrigeration), be sure that hydrate inhibitor and hydragogue are used to maintain the discharge and alkalize the urine. Fifth, bile duct and vascular fistula problems; the biliary tracts and small blood vessels cannot take away the coldness, so they are easily frostbitten by the ice balls. It is reported that 6% of cases can result in damage to the main biliary tract. Therefore, the needle-inserting paths must be chosen carefully to avoid these structures and a heat insulator is placed between the ice balls and the biliary tract to protect the hepatic portal region.

4.11.5.2 ADVANCED LUNG CANCER

Cryosurgical therapy is applied to advanced lung cancer, with surgical approaches including percutaneous puncture under guidance of CT, B-type ultrasonic guidance after CT positioning, X-ray fluoroscopic guidance after CT positioning, and direct-vision thoracotomy. The primary therapeutic effect is the obvious

reduction on CT value of the focus, which is found immediately after surgery and can be over 45 Hu less than that before the surgery. Moreover, as long as the targeted point is designated properly before surgery the ice balls can cover over 1 cm beyond the edge of the tumor, which reaches the effect of surgical resection. For about 3 months afterward, the tumor gradually reduces till it disappears. The complications induced by lung cancer cryosurgery include pneumothorax in up to 10% of patients, hemothorax in up to 1% of patients, pulmonary closure, pleural effusion, and slight hemoptysis, all of which will mostly disappear 1 week later. In addition, pay attention to the influences of central lung cancer cryosurgery on the great vessels and heart.

4.11.5.3 PROSTATIC HYPERPLASIA AND PROSTATIC CANCER

For routine cryotherapy for prostatic hyperplasia and prostatic cancer, the procedures during surgery are more complex, with characteristics of long cryogenic times, difficult application of accurate cryogenic depth and width, common complications of prostatic urethral necrosis, constrictive bladder neck, uroclepsia, impotence, and rectal injury. As for transurethral prostate electrocision, there are also various complications reported, including envelope perforation and constrictive urinary exosmosis accounting for 17%, postoperative bleeding accounting for 3.9%, temporary incontinence accounting for 3.8%, permanent urinary incontinence accounting for 0.1%, and constrictive urethrae accounting for 2.1%. Percutaneous puncture cryosurgical therapy can allow accurate positioning, monitoring the temperature and size of ice balls, and controlling the cryogenic range, with fewer traumas, no bleeding, and light reaction. Moreover, the recovery of patients after surgery is improved.

4.11.5.4 BRAIN TUMORS

To date, therapy on brain glioma remains a stubborn problem for neurosurgery because glioma shows an infiltrative growth and has no obvious boundary with normal brain tissues and it is difficult to resect a glioma completely. Additionally, it has poor sensitivities to radiotherapy, chemotherapy, and immunobiological therapy, with reoccurrence rates of no more than 8 months. As for intracranial tumors with small size and unobvious volume, the stereotaxic technique can be used to insert an argon–helium knife into the tumor center for cryosurgery by percutaneous drilling of the skull, and such a method is characterized by less bleeding and little trauma. For intracranial tumors with big areas, irregular forms, and obvious volumes, direct-vision cryosurgery and resection under craniotomy are applied. It is worthy of attention that the therapy must avoid important functional areas such as the brain stem, and median line structure.

Cryosurgery therapy technology (Figure 4.9) is mainly used on solid tumors. It cannot be applied to cavity tumors, such as esophagus cancer and gastric cancer, because the refrigeration can make the cavities generate fistulas. In addition, current cryosurgery often adopts orientation-guiding devices, such as CT, X-ray

Figure 4.9 Cryosurgery.

machines, and B-type ultrasonic diagnosis apparatus, and it can be used under laparoscope and thoracoscope guidance. CT is mainly used for guidance on lung cancer, with the advantage that the distance of the needle-inserting point from the focus and the needle-inserting angle can be accurately measured, but it has difficulties in real-time monitoring of the needle during the procedure and is highly expensive. B-type ultrasonic diagnosis apparatus is used mainly for liver tumors and peripheral lung tumors near the breast wall, with the advantage that the distance of the needle-inserting point from the focus and the angle of needle insertion can be accurately measured. At the same time, one can carry out real-time monitoring for the procedure and at low expenses.

However, because B-type ultrasonic diagnosis apparatus is influenced by subjective factors of the operator during scanning and cannot reconstruct three-dimensional images of the scanning layer, it lacks a degree of integrity. In addition, B-type ultrasonic image quality and resolution ratio can directly influence the needle-inserting accuracy. At present, cryosurgical (computer treatment planning system) TPS is under research, and if the video data are processed properly, they can reflect the three-dimensional image of the tumor at any point and angle of the body surface to visually display the refrigeration effect more clearly and to more precisely direct the clinical operation.

Generally speaking, cryosurgery therapy technology is a purely physical therapy featuring the advantages of thorough destruction of tumors with definite therapeutic effect; no induction of cancer cell diffusion or microinvasion; no suffering during therapy; fast recovery; no damage to normal tissues; effective regulation of secretion of cytokines and antibodies; more obvious improvement of immunologic function in the patient; significant enhancement of long-term survival rate, as well as lower therapy expenses; shorter hospitalization times; and so on. A reasonable application of such therapy during cancer therapy can bring about a better therapeutic effect on any patient.

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5

Clinical applications of hyperthermia in cancer treatments

5.1 INTRODUCTION

Cancer hyperthermia, although generating no toxic and side effects, can increase the immunity of the body, kill cancer cells, activate cancer immunity through the expression of heat shock proteins outside the cell membranes, sensitize radiotherapy and chemotherapy, and reduce toxic and side effects caused by radiotherapy and chemotherapy; thus, achieving the purpose of increasing both the therapeutic effect and the tolerance of patients. In addition, the application of hyperthermia combined with surgery, biotherapy, and traditional Chinese medicine (TCM) has been reported extensively. Research shows that cancer hyperthermia can be combined with various other comprehensive means to reduce the reoccurrence of tumors, alleviate cancerous pains, and improve patients' recoveries and survival quality and time, and is one of the more important integrative nontoxic cancer treatments.

According to the heating target property, cancer hyperthermia heating technology can be divided into conventional heating technology and targeted heating technology. This chapter mainly focuses on the conventional cancer heating technology. At present, the conventional method is the most widely applied clinical cancer hyperthermia technology, which can be classified into whole-body hyperthermia and local or regional hyperthermia. At present, whole-body hyperthermia is mainly realized by infrared superficial heating, and it can be divided into medium-low temperature hyperthermia and medium-high temperature hyperthermia. The medium-low temperature hyperthermia is safer, whereas the medium-high temperature hyperthermia is more complex, has certain requirements for the functional condition of all the visceral organs, and may entail certain risks during therapy. They both are mainly used for cancer patients in various stages, including those who have poor sensitivities to conventional cancer radiotherapy, show no therapeutic effect of chemotherapy, or are resistance to specific therapeutic drugs, as well as advanced cancer patients with wide cancer metastases. The combination of hyperthermia with chemotherapy can show a synergistic effect. Combinations of whole-body chemotherapy, local chemotherapy, and whole-body hyperthermia alone show sound therapeutic effects, such as depression of growth of cancers that show routine chemotherapy failure or drug resistance, improvement in clinical symptoms and survival quality as well as prolongation of survival time. Local or regional hyperthermia mainly adopts microwave, radio frequency (RF), and ultrasonic equipment to heat cancer. It is characterized by mature technique, sound safety, wide application range, and definite therapeutic effects. Hyperthermia and radiotherapy also have a synergistic effect, increasing the sensitivity of cancer to radiotherapy.

5.2 LOCAL AND REGIONAL HYPERTHERMIA

Local hyperthermia means a heating method in which the heating range is limited to pathologic changes in local tissues without temperature rise of the whole body. Although regional hyperthermia is another form of local hyperthermia, with heat sources such as microwave, RF, and ultrasonic waves, some researchers consider it as whole-body hyperthermia because it can cause the temperature rise of the whole body. The therapeutic range of regional hyperthermia includes early, medium, and advanced malignant tumors in various parts of the trunk, except for the head, neck, and limbs.

5.2.1 Microwave hyperthermia

A microwave is a radio wave with wavelength of 1 mm–100 cm and frequency of 300 MHz–300 GHz; the higher the frequency of the microwave, the shallower the penetration, and different tissues have different penetration depths. Common microwave frequencies include 2450, 915, and 433 MHz. Microwave hyperthermia is mainly applied to superficial tumors and those in the natural cavities. Different radiators have different purposes. An external microwave radiator is mainly applied to superficial tumors and an intracavitary microwave radiator is mainly for the nasopharynx, esophagus, uterine neck, rectum, prostate, and so forth, in accordance with different body cavities. Microwave hyperthermia has fewer side effects and complications, involving only local burning.

Contraindications of microwave hyperthermia: In any patient using a cardiac pacemaker, as for any local body heating, the microwave hyperthermia must be applied under strict monitoring and implemented according to specific conditions.

5.2.2 Radio-frequency hyperthermia

RF is a radio wave band. It is a heating method whereby a high-frequency electromagnetic field is used to cause the vibratory friction of particles (such as charged ions and molecules) to convert electric energy into heat energy, which results in the temperature rise of tissues. RF is also called diathermy. It is mainly used to heat deep tissues. At present, some researchers conduct whole-body hyperthermia using the regional RF hyperthermia technology, maintaining a temperature of 39.5°C–41.5°C for more than 2 hours.

5.2.3 Ultrasonic heating

An ultrasonic wave is a high-frequency mechanical vibration. It acts on the particles of the tissue cells by means of sound waves, and then these particles generate movement frictions that produce heat in accordance with the frequency of sound waves. It is also called internal heat source. However, ultrasounds can decay rapidly in the air and absorb plenty of heat in bone tissues; so ultrasounds cannot be used for tissues with air and impenetrable bone tissues.

The high-intensity focused ultrasound (HIFU) hyperthermia, tissue hyperthermia, and intracavitary hyperthermia researched and developed in China can kill the main focus, but because they have no advantage for other foci beyond the main focus, they can be complemented with regional hyperthermia covering a large area.

5.3 ENDOCELIAC CHEMOHYPERTHERMIA

Endoceliac chemohyperthermia refers to the method wherein the liquid with chemotherapeutic drugs is infused into the body cavity and kept for a certain amount of time using the heating equipment, aiming to cure cancer. The current common chemohyperthermias include intraperitoneal chemohyperthermia (IPCH), intrapleural hyperthermic infusion chemotherapy, bladder chemohyperthermia, and pericardial cavity chemohyperthermia, which are under research. Endoceliac chemohyperthermia is characterized by high concentrations of local drugs and low systemic toxicity. It is the most recognized, fully developed, and common hyperthermia.

5.3.1 Intraperitoneal chemohyperthermia (IPCH)

5.3.1.1 GENERAL DESCRIPTION

IPCH, as a relatively developed method applied clinically, aims to heat the liquid with the chemotherapeutic drug, which is filled into the abdominal cavity and kept in constant temperature. Under the condition of high temperature, the liquidity of cancer cell membranes increases, and then the chemotherapeutic drug with

synergetic effect enters and congregates there. Since the concentration of the drug in the abdominal cavity tissue is much higher than that in plasma, it can kill any intraperitoneal metastatic carcinoma focus without great systemic toxicity; so it is widely applied to the intraperitoneal digestive tract, gynecological cancer, and ascites. The 2009 National Comprehensive Cancer Network (NCCN) Guidelines upgraded the intraperitoneal chemotherapy to first-class evidence, which is to be taken as the frontline treatment for patients with advanced ovarian cancer. Because of the absorption function of the peritoneal cavity, the drug concentration in the portal system is up to 10 times that of peripheral blood, which is a favorable factor for therapy of liver and pancreatic cancer, and has sound effects on primary and metastatic liver cancers as well as pancreatic carcinomas, and can prevent liver-oriented metastasis of the cancer in the digestive tract.

The peritoneum is a semipermeable membrane with two-way permeability. It has a great absorption function on liquid and small granules. Under normal circumstances, the peritoneum secretes a little liquid to lubricate the surface of the intraperitoneal viscera to reduce the friction damage during movement. Peritoneal fluid contains water, electrolyte and other solutes, and various cells. Moreover, macrophages and lymphocytes in the peritoneum are related to the cell immunity. Peritoneum is infused with plentiful chemotherapeutic liquor, which is ideally distributed to any part of the abdominal cavity so that it can maximally contact with any free cancer cell or focus. In the animal experiments, the transperitoneal transfusion can incur that not only water, electrolytes, and urea can penetrate the peritoneum rapidly, but also endogenous and exogenous toxic substances can be absorbed freely.

The common chemotherapeutic drugs for IPCH include cisplatin (CDDP), 5-fluorouracil (5-FU), mitomycin (MMC), and oxaliplatin (L-OHP), of which cisplatin and 5-FU are widely applied. Hyperthermia has sensitization and synergetic effects on the chemotherapeutic drugs infused in the peritoneum without increasing their side effects. IPCH can be combined with bicarbonate infusion, or intraperitoneal bicarbonate infusion alone can be applied to patients who cannot tolerate chemotherapy. (Refer to Section 4.11 of Chapter 4 for specific methods.)

There are various forms of IPCH. Using a special IPCH apparatus, the perfusate is heated outside the body and its temperature is maintained through its circulation in the intraperitoneal tracts, but such method is somewhat fussy. The author adopts two methods: IPCH under RF local hyperthermia and under whole-body hyperthermia, which are introduced in detail in the next section.

The indications of IPCH mainly include treatment of peritoneal wide metastatic carcinoma (including derivable from gastric cancer, carcinoma of the large intestine, ovarian cancer, biliary cancer, pancreatic carcinoma, and peritoneal pseudo mucous gland cancer); prevention of postoperative peritoneal metastasis of gastric cancer, carcinoma of the large intestine, ovarian cancer, biliary cancer, pancreatic carcinoma, peritoneal pseudo mucous gland cancer; and treatment of malignant ascites. Its contraindications include patients with intraperitoneal wide synechia, abdominal cavity with large quantity of cancer, complete intestinal obstruction, end-stage cachexia, and severe cruor-promoting disorder.

As for abdominal cancers, whether primary or metastasis, this treatment is difficult once it loses the surgical opportunity, or postoperative recurrence occurs. Except for a few cancers that cannot be given effective radiotherapy and chemotherapy, the survival quality of most patients can be improved. However, IPCH is able to provide an effective therapeutic approach and even has a sensitization effect on chemotherapeutic drugs.

5.3.1.2 INTRAPERITONEAL CHEMOHYPERTHERMIA UNDER LOCAL HYPERTHERMIA

The IPCH under RF local hyperthermia is completed by extracorporeal deep RF heating, featuring simplicity, convenience, and safety.

Specific operation method: Before treatment, a routine intraperitoneal puncture for indwelling the catheter is conducted. Routine antiemetic drugs are applied within half an hour before perfusion of chemotherapeutic drugs. Physiological saline about 100–200 mL is infused to confirm that the catheter is unobstructed and its position is proper, getting ready for perfusion of the drugs into the abdominal cavity when the treatment is made. The physiological saline and chemotherapeutic drugs are placed in a water bath box and preheated to 45°C–48°C for standby. Later, 500–1000 mL physiological saline is perfused into the abdominal cavity for a 10-minute observation to reconfirm whether the intraperitoneal catheter position is proper, then the heated

perfusate is infused into the abdominal cavity. After the completion of the chemotherapeutic drug perfusion, perfusion of 1000–2000 mL physiological saline into the abdominal cavity is continued. Subsequently, the extracorporeal deep RF hyperthermia apparatus is used for closure heating so that the abdominal cavity maintains a temperature of 42°C–43°C for 60–90 minutes.

5.3.1.3 INTRAPERITONEAL CHEMOHYPERTHERMIA UNDER WHOLE-BODY HYPERTHERMIA

There are few reports on IPCH under whole-body hyperthermia. Clifford Hospital adopts IPCH during infrared whole-body hyperthermia because the heating time of such method is long enough and its temperature can be measured precisely; the improvement condition of the intraperitoneal and constitutional circulation system and cell permeability are different from extracorporeal RF local hyperthermia; and the absorption and exertion of therapeutic effects have obvious advantages. Meanwhile, because of the repeated distribution and great loss of body fluid during whole-body hyperthermia, the liquor perfused in the abdominal cavity infiltrates easily around, and the chemotherapeutic drugs are prone to enter the focus region. In addition, an abundance of intraperitoneal perfusate can supplement the loss of body fluid under whole-body hyperthermia.

Specific operation method: Before treatment, a routine intraperitoneal puncture for indwelling the catheter is conducted and 100–200 mL physiological saline is infused to confirm that the catheter is unobstructed and its position is proper, getting ready for perfusion of the drugs into the abnormal cavity when the treatment is made. Then, physiological saline and chemotherapeutic drugs are placed in a water bath box and preheated to 45°C–48°C for standby. Later, whole-body hyperthermia under deep sedation is implemented, and after the hyperthermia commences, a routine antiemetic drug is applied and the heated 500–1000 mL physiological saline is perfused into the abdominal cavity to reconfirm whether the intraperitoneal catheter position is proper. Subsequently, when the core temperature of the body exceeds 39°C, the heated chemotherapeutic drugs and 1000–2000 mL physiological saline are injected through the catheter into the abdominal cavity to complete whole-body hyperthermia. The whole-body hyperthermia totals 6–8 hours so that the hyperthermic perfusion heating can maintain a temperature of over 39.5°C for over 180 minutes.

5.3.2 Intrapleural chemohyperthermia

As for the intrapleural chemohyperthermia, researchers adopt various methods and different apparatuses, but certain risks are present because of various physical limitations, such as vacuum sealing of the chest cavity, whereas the therapeutic result is invigorative and its efficiency on a malignant hydrothorax can be as high as 88%–100%.

Indications of intrapleural chemohyperthermia include (1) cancer hydrothorax accompanied by non-small-cell lung cancer, (2) diffused cancer focuses in the pleura, (3) breakage of tumor during therapy, (4) less residue of recurrent cancer after resection, and (5) recurrence and metastasis after surgery. Its contraindications include (1) patients with poor constitutional condition (KPS score < 60); (2) patients with severe cardiopulmonary dysfunction; (3) patients with tumor metastasis in the liver, brain, and bone; (4) patients with tuberculosis at tumor position; (5) fever, body temperature >38°C, or accompanied by active infection; (6) leukocytes or blood platelets less than normal and patients with bleeding tendency.

Main methods include two classifications: One is with ingress and egress of the catheter under narcosis, and where a homeothermic water bath box and an extracorporeal circulating pump are used for intrapleural circulating perfusion of saline; the other is, after the intrapleural perfusion of chemotherapeutic drugs, a chemohyperthermia based on closure-type heating is conducted immediately, and such method is characterized by simple operation, high safety, wide application, and satisfactory effect.

5.3.3 Bladder chemohyperthermia

Bladder cancer is a common urinary system cancer, and one of its biological behavior characteristics is its easy reoccurrence and evolution after surgical resection, with reoccurrence rates of up to 60%–85%, of which

30% have evolved into invasive carcinoma. After the transurethral resection of the bladder tumor (TURBT), 10%–67% patients can suffer from reoccurrence within 12 months, and 24%–84% can suffer from it within 5 years after surgery, which may be related to new cancer and implantation of cancer cells or the incomplete resection of the primary cancer.

Through modern hyperthermic technology, bladder chemohyperthermia aims to heat the perfusate continuously and maintain it for a certain period. The sensitization and synergetic effects of hyperthermic chemotherapy, which, with the definite anticancer mechanism and pharmacokinetics advantage, can effectively kill free cancer cells in the bladder, eliminate smaller residual cancer foci, prevent and cure the bladder cancer and its postoperative reoccurrence, and improve the clinical therapeutic effect on bladder cancer. Accordingly, it is a therapeutic method characterized by economy, effectiveness, simple operation, fewer toxic and side effects, fewer complications, and being readily repeatable. Hyperthermia system can raise the temperature in the bladder to 42°C–43°C, which can kill cancer cells or cause their apoptosis directly, expand the blood vessels in the cancer tissues, increase the membrane permeability of chemotherapeutic drugs, and increase the drug concentration in cancer cells. It has a sensitization effect on chemotherapy. Moreover, it can kill the cancer cells in phase S of chemotherapy. Other methods include electrochemical perfusion therapy and photodynamic therapy.

Bladder perfusion therapy is a key therapy for bladder cancer. The postoperative instantaneous perfusion chemotherapy has become a frontline chemotherapy application for bladder cancer. The bladder chemohyperthermia can not only improve the therapeutic effects, but it is characterized by simplicity, safety, and fewer side effects. The latest research shows that the instantaneous perfusion chemotherapy has greater advantages than the continuous perfusion chemotherapy, and it has become the first-line chemotherapy application for bladder cancer, wherein 30 mg mitomycin or 50 mg Adriamycin is applied as the perfusion drug within 24 hours after surgery. Later, the risk of recurrence within 2 years is reduced by about 50% and by more than 15% for recurrence within 5 years. It has obvious advantages in comparison with continuous perfusion chemotherapy; for example, chemotherapy perfusion is only required for once, and it relieves the economic burden of patients with reliable therapeutic effects. Moreover, the newly emerged gemcitabine is expected to become a new medicine for perfusion therapy because of higher disease-free survival (DFS) and lower adverse reaction rates.

Perfusion therapy and immunotherapy for bladder cancer, such as application of bacillus Calmette–Guérin (BCG) can prevent the recurrence of cancer, reduce the evolution risks of cancer, and decrease the case fatality rates. It has better therapeutic effects in comparison with the perfusion of other chemotherapeutic drugs. As for its disadvantage, it can increase the toxic reactions. Interferon is another drug for immunotherapy, but the therapeutic effect of perfusion alone is limited.

Indications for bladder chemohyperthermia include postoperative patients with non–muscle invasive bladder cancers bladder cancer in situ, corpora mammillaria tumors that are distributed widely and with ablation difficultly, palliative therapy of invasive bladder cancer that does not tolerate any surgery or multiple superficial bladder cancer that cannot receive any surgery or fails to receive any surgery because of poor body condition, preoperative cooperative therapies on invasive bladder cancers, and prevention of high-risk patients from cancer evolution.

Its contraindications include invasive tumors that have penetrated the bladder wall, urinary tract infections, and bladder inflammation.

5.4 WHOLE-BODY HYPERTHERMIA

5.4.1 Whole-body hyperthermia and methods

As mentioned in the sections above, whole-body hyperthermia refers to a hyperthermia method whereby various heating methods are used to raise the temperature of the human body to reach the therapeutic temperature that is maintained for a certain period. As for the temperature range of whole-body hyperthermia, a higher temperature and range above 41°C were preferable previously, but it was never higher than 41.8°C.

However, based on clinical application research and with both therapeutic effect and safety considered, the cancer hyperthermia has been mostly able to maintain the body temperature within 39.5°C–41.8°C. Some researchers advocate maintaining a temperature of 38°C–40°C, which is named as medium-low temperature whole-body hyperthermia.

The heating methods for whole-body hyperthermia are divided into three categories: (1) biological method, (2) extracorporeal circulation method, and (3) superficial heating method. The biological method aims to heat the body by injection of microbial or biological agent, such as early injection of Coley toxin or short Corynebacterium. It is rarely applied at present because the sensitive reaction degree of the human body to the pyrogen is unpredictable and the heating temperature and time cannot be easily controlled, resulting in high risk. The extracorporeal circulation method, i.e., to take some of the blood out of the body and heat it in vitro to a predetermined temperature with a special device, and then recirculate it into the body to achieve elevated body temperature, is not easily popularized because of expensive equipment and elaborate procedural requirements. The superficial heating method refers to a heating method whereby thermal energy is transferred to the body by radiation or conduction, such as infrared radiation, hot water bath, hot wax bath, and electric blanket wrapping. However, hot water bath, hot wax bath, and electric blanket wrapping have been rarely applied since 1980s because of their various defects. Infrared radiation has been widely applied clinically due to its definite heating effect, fewer side effects, easy monitoring, and lower cost.

5.4.2 Physiological changes during whole-body hyperthermia

Considering the infrared whole-body hyperthermia, the body receives plentiful heat to make the body temperature rise when whole-body hyperthermia is conducted. During the clinical therapies implementation at Clifford Hospital, the author usually took 39.5°C–41°C as the therapeutic temperature range, with a maximum temperature of not more than 41.8°C and total time for a course of up to 6–8 hours. The body fluid lost is plentiful because of the longer therapeutic time course, profuse sweating, and respiratory acceleration. The rise of the body temperature strengthened the metabolism of the body, and the metabolism rate was twice as high when the body temperature reached 41.8°C compared to that at 37°C. Also, whole-body hyperthermia had great influences on the respiratory and circulatory systems. The wide opening of the systematic blood vessel network caused the repeated distribution of blood, acceleration of blood flow, increase of skin sweating, and the loss and replacement of body fluids. It resulted in blood flow insufficiency, faster fluid replacement, and fluctuations such as relative increase of blood volume. It brought certain influences to the stability of blood pressure, increase of heat rate, reduction of blood pressure, respiratory acceleration, and increased respiratory and circulatory burdens. The imbalance of electrolytes is also common during whole-body hyperthermia. Some researchers have shown that with the decrease of serum phosphate, serum magnesium, the internal environment change of the body can generate certain influences on some important organs, such as the heart, lung, kidney, and brain, all of which can cause serious tachycardia, ventricular arrhythmia, ventricular premature beat, and so forth, so it is extremely important to maintain the stability of respiration and circulation as well as electrolytes when whole-body hyperthermia is conducted. The redistribution of body fluids during whole-body hyperthermia can lead to edema of various degrees in different body areas. Accordingly, the prevention and treatment of the occurrence of serious cerebral edema and pulmonary edema are some of the most important safety considerations in whole-body hyperthermia.

As for the medium-low temperature whole-body hyperthermia, the body fluid redistribution is not obvious because of its short therapeutic time and little rise of body temperature; and there are fewer influences on respiration and circulation.

5.4.3 Implementation of whole-body hyperthermia

5.4.3.1 Medium-low temperature whole-body hyperthermia

Because of its high safety factor, the medium-low temperature whole-body hyperthermia shows a low requirement for cardiopulmonary function; anesthesia or sedation is not required because the patient is conscious

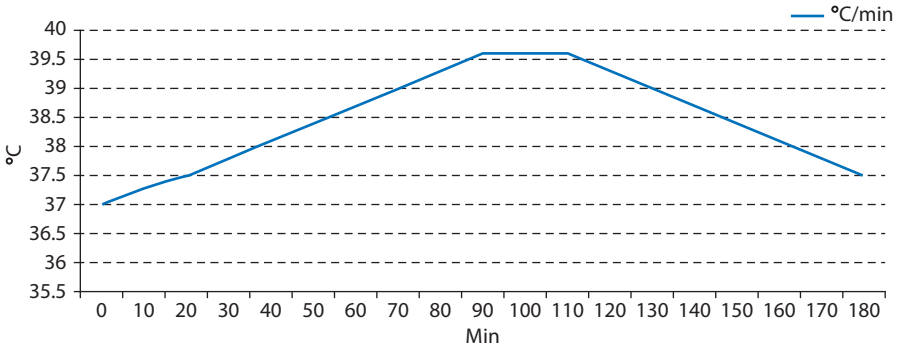

Figure 5.1 Time/temperature curve for medium-low temperature whole-body hyperthermia.

during the therapy, and body fluid replacement can be accomplished with oral rehydration salts, which is more and more widely applied clinically.

5.4.3.1.1 Preparations before hyperthermia

Before hyperthermia, conventional visits and assessments of patients are conducted to understand the patients' diseases, complications, drug applications, allergic histories, daily activities, individual smoking, drinking histories, and so forth, as well as functions of the heart, lung, liver, kidney, and so forth.

Patient education before hyperthermia: Explain to the patients the therapeutic process possible attributable sensations and physical reactions. Tell them about the preparations before therapy and reactions and precautions during and after therapy, such as, drink sufficient water within 1–3 days before therapy to improve the amount of water stored in the body, relieve the bowels as much as possible on the therapy day, take off all jewelry, and have family members prepare beverages for drinking after the hyperthermia.

5.4.3.1.2 Implementation of medium-low temperature hyperthermia

After the patient enters the hyperthermia chamber, conventional oxygen inhalation must be arranged, and a multifunctional monitor is connected to monitor the patient's electrocardiograph (ECG), blood pressure (BP), heart rate (HR), respiratory rate (RR), and SPO_2, which are recorded into hyperthermia record list within 10 minutes. As for the temperature monitoring, the anal temperature is generally considered as the core temperature index. Because the temperature range of the therapeutic target is safe and the patient is conscious and able to relate feelings and reactions during the therapy, no multipoint temperature measurement is required.

During hyperthermia, the patient can listen to music, watch TV, or chat to relax, and thereby improve their tolerance to the hyperthermia. Meanwhile, the patient is assisted with drinking water and wiping perspiration. For indispositions occurring during hyperthermia, such as palpitations and dysphoria, no special treatment is usually required but a pause for conciliation is exercised. In accordance with the tolerance degree, the patient is wrapped for temperature preservation for about 60 minutes and when the core temperature rises to 38°C–39°C (the body temperature of the average patient can rise 0.3°C–1.0°C), then the wrapping is opened gradually before completion of the therapy, so that the body temperature of the patient is reduced and recovers as slowly and smoothly as possible (Figure 5.1).

After the completion of the therapy, the patient must drink water and fruit juice for water replenishment and get sufficient rest, and no other special treatment is required.

5.4.3.2 MEDIUM-HIGH TEMPERATURE WHOLE-BODY HYPERTHERMIA

5.4.3.2.1 Anesthesia for medium-high temperature whole-body hyperthermia

During treatment of medium-high temperature whole-body hyperthermia, the endotracheal intubation under general anesthesia and moderate and deep sedation is mostly adopted. The endotracheal intubation under general anesthesia, just like surgical anesthesia, has a complex process and more potential complications.

It is thus more prone to be replaced by the moderate and deep sedation, which operate simply and are controlled easily. It can meet the requirements of whole-body hyperthermia and has been widely applied increasingly in recent years. Therefore, this chapter advocates the moderate and deep sedation methods.

5.4.3.2.1.1 Assessments and preparations before anesthesia

Similar to conventional preparations before general anesthesia, patient visits and assessments are conducted before hyperthermia, to understand the patient's daily activities, existing diseases, complications and drug application conditions, patients' surgical anesthesia histories (inquiry about any past accidents or adverse reactions during surgical anesthesia), drug allergy history, individual smoking and drinking histories, and so forth. It is also done to understand the functions of the heart, lung, liver, kidney, endocrine, as well as ensuring the unobstructed conditions of air passages and paying attention to whether patients have any history of "sleep apnea syndrome." The patients are assessed according to ASA (American Society of Anesthesiologists) guidelines, and those with ASA I–II are chosen since those over III have greater therapeutic risks. A TCM doctor is asked for assessment if necessary. The patients may be provided with a "qi-toning decoction" before hyperthermia and a "yin-nourishing decoction" later, in accordance with the assessments of the doctor.

Patient educations before hyperthermia: Drink sufficient water within 1–3 days before whole-body hyperthermia. Consume liquid foods on the evening before hyperthermia, and any food or drink is forbidden 8 hours and 6 hours, respectively, prior to the hyperthermia. Relieve the bowels on the current morning of the hyperthermia. Wear special all-cotton clothes for the hyperthermia. Take off jewelry and other metals as well as artificial teeth. Have family members prepare beverages; and never leave the hospital in the evening after hyperthermia nor drive a car. A 10-minute moderate exercise is required before hyperthermia. The medium-high temperature hyperthermia totals 6–8 hours. Remember to obtain a signed informed consent form for whole-body hyperthermia and the hyperthermia sedation.

The requirement of whole-body hyperthermia for anesthesia is different from that of surgery. Its requirement for acesodyne is low even if patients have some subjective discomfort during the whole-body hyperthermia. But with safety and few toxic and side effects it can still attain its purpose if the presetting temperature and time for hyperthermia is relatively well met.

Common drugs for moderate and deep sedation: Propofol, midazolam, and other optional drugs such as promethazine and benzodiazepine. Common drugs maintaining the balance of body fluid and electrolytes: Ringer's solution, lactated Ringer's solution, 10% glucose, hydroxyethyl starch, 5% sodium bicarbonate, physiological saline, vitamin C, vitamin B_6, potassium aspartate and magnesium aspartate, 10% KCI, and so forth. Spare drugs and first-aid kit equipped with a full set of standard configurations: intubation devices and materials, nasopharyngeal and buccal air passages, breathing bag, and aspirator. Monitoring system: multifunctional monitor and temperature measuring station. Liquid infusion system: infusion pump, anesthetic microinfusion pump, liquid tee, injection syringe. Other preparations: cotton protective clothing, ice cap, ice water bag, oxygen tube, urine tube, urine bag, and so forth.

5.4.3.2.1.2 Selection and application of anesthetics

As for the selection of anesthetics, the requirements include rapid metabolism in the body, short half-life and easy control of deepness so as to realize no pain to the patient and achieve the purposes of safety, and fewer complications and side effects. When anesthetic induction is required, the intravenous injection of midazolam totaling 1–2 mg is conducted. It is a sedative drug that can be metabolized rapidly, causing the patient to fall into a sleep, and the recovery period is shorter. In addition, during the recovery period, flumazenil can also be applied. It is one of the main antagonists for moderate and deep sedation. Propofol injection is a fugitive intravenous alkylphenol-type anesthetic which can spread to the whole body rapidly after injection, incurring a sleep state within 40 seconds. Access to the anesthesia is rapid and smooth. Even though it has a depression effect on the respiratory and circulative systems, the therapy can still be completed during the sleep of the patient as long as the dose is controlled well. The anesthesia recovery of this drug is also rapid and most patients can be awake within about 10 minutes with no special discomfort. The drug dose should be maintained at 2–4 mg/kg/h, and it can be pumped by injection pump through the peripheral vein or deep vein catheter. For patients accompanied with pains, this drug can be combined with a few doses of opium-like drugs, such as fentanyl.

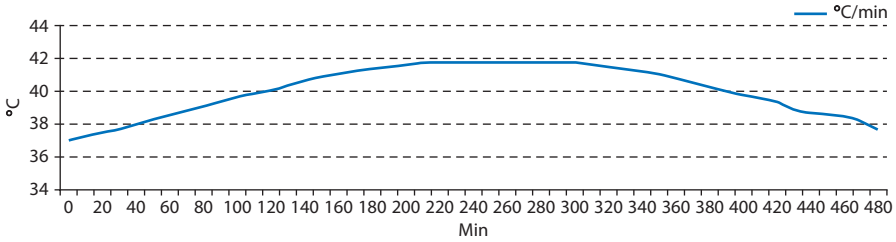

Figure 5.2 Time/temperature curve for medium-high temperature whole-body hyperthermia.

5.4.3.2.2 Medium-high temperature whole-body hyperthermia

The complete process of medium-high temperature hyperthermia falls into three stages: (1) temperature rise stage, (2) stationary stage, and (3) temperature drop stage (Figure 5.2). Temperature measurement aims to measure the rectal temperature, which is the main referable index of the core temperature in the human body. Venous anesthesia covers three stages of the hyperthermia and it plays a vital role in ensuring a safe hyperthermia.

5.4.3.2.2.1 Temperature rise stage

The temperature rise stage refers to a period in which the body temperature rises because of heating to the target temperature. Heating is stopped after it reaches the setting temperature, and then the body temperature rise is maintained, with greater temperature rise amplitude differences in different bodies. (The author has calculated statistics of 96 persons, which show temperature rise amplitude differences totaling 0.3°C–1°C, with an average value of 0.6°C.) Under most circumstances, when the heating stops, the higher the temperature value is, the longer the relative platform stage is. In accordance with the tolerance of a patient, the venous anesthesia starts when the temperature rises to a certain value and maintained, which is infiltrated throughout the temperature rise stage, platform stage, and temperature drop stage.

5.4.3.2.2.2 Stationary stage

The stationary stage refers to a stage in which body temperature does not rises and is kept relatively stable after it has risen to a certain temperature value. It is the stage with the highest temperature and the maximum load on various visceral organs in the whole therapeutic course. The heart rate is the fastest when the temperature rises to the highest value, totaling about 130 beats/min on average.

5.4.3.2.2.3 Temperature drop stage

The temperature drop stage refers to a therapeutic stage where in the temperature drops gradually after the platform stage. The time in the temperature drop stage means the time required for the temperature to drop to 38 °C from the platform stage. In such stage, anesthesia is removed and the patient is awakened, and subsequent temperature measurement after 38°C has no clinical significance. During the whole therapy, body fluid losses and blood pressure drops are greatest during this stage, for which vasoactive agents to maintain blood pressure and fluid replenishments are continuously applied.

5.4.3.2.3 Surveillance and management of medium-high temperature whole-body hyperthermia

5.4.3.2.3.1 Vital signs and temperature monitoring

After the patient enters hyperthermia chamber, the oxygen absorption and continuous multifunctional surveillance instrument must routinely monitor ECG, BP, HR, RR, and SPO_2 of the patient, and central venous pressure (CVP) surveillance is conducted if necessary. Temperature surveillance generally takes the anal temperature as the core temperature index while multipoint surveillances are made on the superficial temperatures, such as at the external auditory meatus, breast, abdomen, and front-side position of thigh.

5.4.3.2.3.2 Respiration and circulation management of whole-body hyperthermia

During the whole-body hyperthermia, the influences on the respiratory and circulatory systems are the most critical; therefore, any improper observation and treatment can cause serious consequences.

Respiratory system: During whole-body hyperthermia, pay close attention to observations of respiratory functions, including respiratory movement, respirations, and color of skin mucous membrane. In addition, for maintaining an unobstructed respiratory system, one can adopt head tilt, neck lift, chin lift or a lower jaw elevator, and an oral pharynx or nasal pharynx breather pipe could be used if necessary to prevent any obstruction caused by glossocoma or excessive excretions. Be prepared for high-sensitivity reactions such as laryngeal spasm and bronchospasm, which are incurred by sputum and absorption of sputum. For any laryngeal spasm, its simulation should be removed immediately. Although the face mask is pressurized for oxygen absorption, a muscle relaxant shall be injected and endotracheal intubation be conducted if necessary. Any bronchospasm should be treated by venous injection of lidocaine, isoprenaline, and terbutaline.

Circulatory system: The reduction of blood pressure is a common complication when whole-body hyperthermia is applied. Common causes are peripheral vasodilatation and blood flow deficiency. It is also influenced by sedation drugs and rare irritability or transfusion reactions, for which symptomatic treatments are required, such as fluid expansion, increasing vascular resistance and reducing the volume of venous blood (e.g., application of phenylephrine), enhancement of stroke volume (e.g., application of dopamine), and decreasing depth of anesthesia. After entering the platform stage, tachycardia usually occurs when the heart rate exceeds 130 beats/min, and β-receptor blocking agents should be applied according to specific conditions (e.g., esmolol). When the heart rate is abnormal, a timely treatment or first aid should be applied according to the specific circumstances.

5.4.3.2.3.3 Fluid replacement strategies for medium-high temperature whole-body hyperthermia

As for the medium-high temperature whole-body hyperthermia under mid-deep sedation, the fluid replacement is more complex, and aims to correct the deficiency by both the quality and quantity of supplementation. The rate of replacement depends on the cardiopulmonary function, which requires early and steady supplementation. According to our clinical treatments, venous carbohydrate supplementation of 150–250 g should be conducted first when whole-body hyperthermia starts, then the crystalloid infusion of Ringer solution or sodium lactate Ringer injection is applied (colloid is injected according to the proportion of 3–4:1, with total volume of less than 30 mL/kg), at a rate of about 500–800 mL/h. Later, supplemented with 2 g vitamin C and 2 g vitamin B_6 while observing the urine volume, and 2–3 g of potassium is added as required. For the maintenance of fluid equilibrium, the liquid supplementation instructions, including applications, monitoring, and precautions are referred.

5.4.3.2.4 Adverse reactions and follow-up treatments after medium-high temperature whole-body hyperthermia

After hyperthermia, the patients should be sent back to the wards, and then continuous vital sign surveillance should be conducted for the next 12 hours. Patients can suffer from swelling of limbs after whole-body hyperthermia, considering the increase of microcirculation during hyperthermia and the redistribution of body fluid, but can recover normally 24–48 hours later, during which the micturition of patients increases, and no special treatment is necessary because they can eat and drink normally.

After the medium-high temperature whole-body hyperthermia, there may be side reactions as follows: (1) Burns usually appear in the lower abdomen, front inner side of thigh, blood pressure sleeve location on upper limb, convex position of sacroiliac, heel, and occiput, mainly showing phlyctena, with area <2 cm^2, for which a conventional treatment on burns should be applied. (2) Cold sores can appear around the lips within 1–3 days after therapy, for which special treatment is not necessary. (3) The general asthenia can continue for 3–7 days, for which no special treatment is required. (4) A burning sensation during urination may occur for 1–2 days; it is suggested to carry out an examination if it lasts beyond 2 days. (5) The

body temperature may rise after therapy to as high as 39°C for some individuals, but no special treatment is necessary for such condition.

5.4.3.2.5 Contraindications of medium-high temperature whole-body hyperthermia

The contraindications of the medium-high temperature whole-body hyperthermia include Karnofsky performance status (KPS) score < 70; heart function hypoplasia (over II) accompanied with myocardial infarction disease history and serious arrhythmia; large tumor or metastatic tumor in the brain accompanied with high skull pressure; seriously infected persons; serious liver and kidney dysfunction; bleeding tendency; serious endocrinal and metabolic diseases, such as hyperthyroidism and hematoporphyrin; serious dehydration, electrolyte disturbance, and excessive obesity; poor respiratory condition that causes breathing difficulty; and insanity.

5.5 INFORMED CONSENT FOR HYPERTHERMIA TREATMENT

Cancer hyperthermia includes whole-body hyperthermia, local (or regional) hyperthermia, in combination with radiotherapy and/or chemotherapy. In addition to educating patients on the principles of hyperthermia, therapeutic process, precautions, and how to cooperate with medical personnel, all medical personnel shall follow the principle of informed consent. Tell the patients about the purposes and methods of hyperthermia, possible adverse reactions or unexpected circumstances, emergency measures, and possible consequences of adverse reactions or unexpected circumstances. The patients should sign an informed consent, which shall cover the patient's general information, diagnosis, cancer hyperthermia method, purpose or possible benefit, existing risks or complications and unexpected circumstances, other optional methods, and rejection of possible consequences. The informed consent shall be complied in the language understood by the patient, so that it is "comprehended sufficiently" and "chosen independently" by the patient, and it shall comply with the principle of "complete notice."

5.5.1 Conventional contents of informed consent

5.5.1.1 GENERAL INFORMATION

It should include the patient's name, gender, age, department, number of ward bed, and outpatient number/hospital admission number.

5.5.1.2 RELEVANT THERAPEUTIC CONTENTS

It shall include the clinical diagnosis, operator's name, therapeutic regimen, temperature control range of whole-body hyperthermia, contraindications, risk assessment, therapeutic benefits, possible adverse consequences caused due to rejection of any therapy, and so forth.

5.5.2 Notice of possible complications and accidents

5.5.2.1 INFORMED CONSENT FOR WHOLE-BODY CANCER HYPERTHERMIA

All patients should be told of possible complications or accidents during whole-body hyperthermia, including but not limited to (1) after therapy: tachycardia, breathing acceleration, disturbances of blood pressure fluctuations or heart rhythms during therapy, and headaches, fatigue, asthenia; (2) lung and brain edema or other tissue edemas to some extent; (3) skin burns with possible phlyctena; and (4) other possible unpredictable complications or accidents.

5.5.2.2 INFORMED CONSENT FOR ANESTHESIA OF WHOLE-BODY HYPERTHERMIA

As for the anesthesia treatment for cancer hyperthermia, an endotracheal intubation for general anesthesia or moderate-to-deep sedation anesthesia is usually adopted, and because the endotracheal intubation for general anesthesia can cause many hyperthermia complications, the moderate-to-deep sedation anesthesia

has been increasingly applied. In the process of informed consent, all patients should be told of the possible complications or accidental risks during the moderate-to-deep sedation anesthesia, including but not limited to the following: (1) sedative allergies and hypersensitive reactions causing respiratory or cardiac arrest; (2) circulatory system complications: low blood pressure, shock, hypertension, arrhythmia, heart failure, and so forth; (3) respiratory system complications: respiratory depression, respiratory tract obstruction, laryngeal spasms, and hypoxemia; (4) any vomit inhaled into the trachea because of backflow may cause suffocation or aspiration pneumonia; and (5) other unpredictable accidents or complications.

5.5.2.3 INFORMED CONSENT FOR LOCAL OR REGIONAL HYPERTHERMIA

5.5.2.3.1 Informed consent for conventional heating technology

During local or regional hyperthermia, the conventional heating technology for microwave and deep RF local hyperthermia is highly safe, but complications can occur due to skin burn or phlyctena. As for RF local hyperthermia, it may incur fatty sclerosis caused by subcutaneous fat denaturation under heat exposure, but usually of low incidence, light degree, and no serious consequence.

5.5.2.3.2 Informed consent for targeted heating technology

As for the local hyperthermia with different targeted heating technologies, the mechanisms, such as transient high-temperature hot solidification effect, are adopted to cause the focal spots to coagulate, degenerate, necrotize, atrophy, and disappear ultimately due to absorption. The expected result is that the core tissue in the targeted region is destructed completely while the tissues beyond the targeted region are kept relatively safe from injury and pathological changes. In addition to possible anesthesia complications, there is a possibility of injuries to peripheral normal tissues.

5.5.2.4 INFORMED CONSENT FOR HYPERTHERMIC CHEMOTHERAPY

Hyperthermia is often combined with chemotherapeutic drugs that may cause some side reactions or complications because of the different therapeutic drugs, and in that case such relevant information is to be included in the informed consent form.

5.5.2.5 INFORMED CONSENT FOR INTRACAVITARY CHEMOHYPERTHERMIA

Intracavitary chemohyperthermia combined with hyperthermia, chemotherapy, and intracavitary perfusion each presents risks for complications, including intraperitoneal perfusion, intrapleural, so that the informed consent form should include pertinent information regarding possible adverse reactions and complications during intracavitary perfusion therapy.

5.5.3 Informed consent for cancer hyperthermia

A referable model for the informed consent form developed by Clifford Hospital for infrared whole-body hyperthermia is presented below. Others can formulate their own informed consents and file them in accordance with special conditions and apparatus types and characteristics.

Clifford Hospital Informed Consent for Infrared Whole-Body Hyperthermia

Name: Gender: Age: Dept.: Number of sickbed:

Outpatient number/hospital admission number:

Clinical diagnosis: _____ Name of operator:

Diagnostic basis: _____

Therapeutic scheme: _____ Temperature control range: _____ Date: _____

Contraindication: ☐ No ☐ Yes _____

Risk assessment: ☐ Low risk ☐ Moderate risk ☐ High risk

Therapeutic benefit: ☐ Complete healing ☐ Obvious improvement ☐ Remission of disease progression ☐ Pain relief ☐ Retrieval of pathogenic organ function ☐ Reducing possibilities for future serious problems ☐ Others _____

Adverse consequences due to therapeutic rejection: ☐ Disease deterioration ☐ Loss of comprehensive therapy opportunity ☐ Reduction of life quality ☐ Acceleration of organic function damage ☐ Others_____

Optional other therapies: ☐ Surgery ☐ Chemotherapy ☐ Radiotherapy ☐ Intervention ☐ TCM ☐ others:

Possible or complications during therapy include but are not limited to: _____

In accordance with your disease conditions, a doctor can give you hyperthermia advice, and present relevant items that are listed in detail. Although hyperthermia is a relatively safe therapy, there are still some possible complications or adverse reactions because of different physical conditions and key visceral function differences, including but not limited to the following:

☐ It may cause heart rate and respiratory accelerations, blood pressure fluctuations or heart rate disturbances during therapy, and headaches, fatigue, asthenia after therapy, which usually are remedied on their own, but in severe cases, can be life-threatening for the patient with constitutional abnormity.

☐ Skin burns that may cause phlyctena.

☐ A minority of patients may suffer from subcutaneous fat scleroma and liquefaction causing pains after therapy.

☐ Hyperthermia can enhance the chemotherapy effect as well as partially increase the toxic and side effects of drugs.

☐ Transfusion may cause adverse drug reactions, liquid leakage, and transfusion reactions, etc.

☐ Therapeutic effects may not satisfy the patient due to individual physical differences or high expectations.

☐ Others:_____

Your Obligations:

① All patients must provide their true disease histories, express real desires, and actively participate in and closely cooperate with all the therapies.

② All patients should pay medical expenses as required.

③ Abide by the current regulations of the hospital.

Your Rights:

① Final decision on whether any therapy is chosen or not.

② Right to give up any therapy.

③ Right to access other therapies.

④ Right to require the hospital to provide comparable services.

⑤ Right to know conditions such as disease condition, anticipant effect, therapeutic risk, medical expenses.

⑥ Right to protect personal privacy.

⑦ Right to consult doctors and other medical personnel.

Patient's comments:

Patient's signature:_____ Family member signature:_____

Relationship to the patient:_____ Date and time_____

Please give reasons if any patient fails to sign but his or her family member sign:_____

Signature of doctor:_____ Date and time:_____

5.6 RISK ASSESSMENT AND CONTINGENCY PLAN FOR HYPERTHERMIA TREATMENT

5.6.1 Infrared whole-body hyperthermia

As for infrared whole-body hyperthermia for a cancer patient, a medium-high temperature hyperthermia is usually adopted, with therapeutic temperatures in the range of 39.5°C–41.8°C, and therapeutic time of 6–8 hours. During the therapy, the patient's body temperature rises gradually, and the resulting loss and redistribution of the body fluids would cause much interference on the respiration and circulation of the patient, causing greater respiratory and circulative fluctuations and bringing higher therapeutic risks accordingly.

5.6.1.1 RISK ASSESSMENT

5.6.1.1.1 Assessment before whole-body hyperthermia

Before any hyperthermia, sufficient assessments must be made, especially functional assessments of the respiratory, circulatory, and urinary systems of the patient. Also, the blood routine, blood biochemistry, and blood coagulation should be examined to determine the liver function, kidney function, bleeding, and blood coagulation.

5.6.1.1.2 Preparations of hyperthermia and facilities

Before initiating hyperthermia, recheck must be done to ascertain that all the hyperthermia facilities are in good condition.

5.6.1.2 EMERGENCY PLAN FOR WHOLE-BODY HYPERTHERMIA

5.6.1.2.1 Acute respiratory tract obstruction

If acute respiratory tract obstruction is caused by glossocoma, the head is placed in a lateral position immediately; a neck tilt, jaw lift, or lower jaw elevator is used to raise the lower jaw so as to maintain an unobstructed respiratory tract and reduce the level of obstruction; and intubation is used in the oral-pharyngeal air tract or trachea if necessary.

If it is caused by excessive secreta, the head is placed in a lateral position immediately to clean the secreta in the respiratory tract and keep it unobstructed.

5.6.1.2.2 Hypersensitive reaction of respiratory tract

It means that the respiratory tract is abnormally sensitive to physical, chemical, or pathological stimulations and generates abnormal reactions to the stimulation.

Laryngeal spasm (laryngeal stridor): After its occurrence, remove the abnormal stimulating factors, pressurize the mask for oxygen absorption and deepen the anesthesia, inject a muscle relaxant into a vein, and then use intubation in the trachea if necessary.

Bronchospasm (expiratory dyspnea): After its occurrence, the salbutamol aerosol should be inhaled in the form of a spray, a greater dose is applied if necessary to deepen the anesthesia, and the venous injection, such as of isoproterenol, can be applied if necessary.

5.6.1.2.3 Acute pulmonary edema

It is mostly cardiogenic, caused by too rapid transfusion, and is left with ventricular failure. Once it happens, decelerate the transfusion, strengthen the heart, expand the blood vessels, promote urination, improve the colloidal osmotic pressure, apply glucocorticoid, provide oxygen supply and respiratory support, and so forth.

5.6.1.2.4 Tachycardia

When HR is 130–150 beats/min, close attentions should be paid. A fugitive β-receptor retarder (e.g., esmolol) should be pumped in to the vein to keep the heart rate within 120–130 beats/min, which is more proper.

5.6.1.2.5 Drop in blood pressure

When the blood pressure is up to 30% more than that before therapy, or the mean arterial pressure (MAP) is lower than 50 mmHg, dopamine at 5–15 μg/(kg·min) is selected to maintain the stability of blood pressure. Generally speaking, it is safe to keep the MAP above 60 mmHg.

5.6.2 Infrared whole-body hyperthermia combined with chemotherapy

5.6.2.1 RISK ASSESSMENT

Combining chemotherapy with whole-body hyperthermia increases the risks because of the application of chemotherapeutic drugs and their side effects.

5.6.2.2 APPLICATION REQUIREMENTS FOR CHEMOTHERAPEUTIC DRUGS

1. All drug administration personnel shall wear uniforms, masks, caps, gloves, and protective glasses/goggles as required. Replace them if they are damaged.
2. Wash hands before wearing gloves and after taking them off. After the completion of drug administration, all the materials that have contacted drugs directly, such as syringe, syringe needle, transfusion apparatus, and drug packaging bags (bottles), shall be discarded into the designated red plastic buckets that are collected and disposed of by the Department of Environmental Protection after sealing.

5.6.2.3 EMERGENCY PLAN FOR THE LEAKAGE OF CHEMOTHERAPEUTIC DRUGS

After the accidental leakage or discharge of any chemotherapeutic drug, any improper disposal may cause adverse consequences to patients, medical personnel, and the environment.

1. When an operator's eyes are infected, use physiological saline to wash them for minimum 10 minutes, and then promptly consult an ophthalmologist for further treatment.
2. When other parts are infected, take off the polluted clothes and gloves immediately, wash the contaminated areas with detergent and clean water. Use plenty of clean water to wash the contaminated skin for 15 minutes, and then consult a doctor if necessary. All the contaminated clothes and bedclothes shall be sealed in a yellow bag, stored in the contamination room, with descriptive labels, which is then collected by the Department of Environmental Protection for special disposal.
3. After any chemotherapeutic drug leaks on the equipment, furniture, or floor, evacuate all personnel and post a warning sign, "Danger, Keep Out!" to restrict other personnel from entering the contaminated area. All personnel in charge of clean up or disposal shall wear gloves, masks, caps, glasses/goggles, and shoe covers for individual protection. Later, proper absorbent paper, stick, or blanket with strong absorbency shall be used to absorb or clean off the drug completely, and together with all the disposable protective pads, broken glass, drug packaging bags (bottles), and injection syringe should be placed into red plastic buckets and sealed for disposal. Any contaminated equipment, furniture, or floor area should be washed by clean water, and then cleaned three times by detergent from small to big areas. Then the detergent must be washed off by clean water and properly disposed. The disposable gloves, masks, caps, and shoe covers are discarded into designated yellow garbage bags that are disposed of as medical wastes.
4. Wash hands and record the following information: Name of drug, probable leakage amount, and causes for leakage, and treatment methods for staff, patients, and other personnel exposed to the leakage environment. The causes of the therapeutic drug leakage are analyzed in a timely manner so that improvement measures could be implemented.

5.6.2.4 EMERGENCY PLANS FOR TOXIC AND SIDE EFFECTS OF CHEMOTHERAPEUTIC DRUGS

During whole-body hyperthermia, be alert to side effects of chemotherapeutic drugs including nausea, vomiting, allergic reactions, and cardiotoxicity, all of which can be life-threatening if no immediate action is taken.

5.6.2.4.1 Vomiting reaction

Immediate treatment of any nausea with vomiting: First the perfusion of any therapeutic drug is to be stopped. Then the patient's head should be placed in a lateral position to remove the vomitus in the respiratory tract that is kept unobstructed. Finally, venous injection of an antiemetic can be conducted, such as granisetron (3 mg).

5.6.2.4.2 Anaphylaxis

After diagnostic confirmation, immediately stop the perfusion of the chemotherapeutic drug. Carry out an anaphylactic therapy immediately.

5.6.2.4.3 Cardiotoxicity

Cardiotoxicity due to anthracycline-based anticancer drugs is the most common. ECG monitoring should be conducted during their applications, and the occurrence of any arrhythmia should be observed and treated during the hyperthermia. Immediately stop the drug application and rectify the arrhythmia once it occurs.

5.6.3 Intraperitoneal chemohyperthermia

IPCH aims mainly to combine infrared whole-body hyperthermia with extracorporeal RF local hyperthermia. In addition to emergency plans for toxic and side effects caused by infrared whole-body hyperthermia and therapeutic drugs, a common accident involves the improper position of the catheter in the subcutaneous tissue or intestinal canal. However, if operation-strict procedures are followed, there are generally no serious consequences.

5.6.3.1 CATHETER IN THE SUBCUTANEOUS TISSUE

When the catheter is in the subcutaneous tissue, local abdominal pains and local protuberances may occur during therapy. However, if physiological saline is dripped during puncture and 500 mL physiological saline is dripped before perfusion of any chemotherapeutic drug, they can be found and treated as soon as possible. An ultrasonic examination may be conducted to confirm the diagnosis before the treatment.

Emergency plan for erroneous injection of therapeutic drugs into the subcutaneous tissue: Common chemotherapeutic drugs for IPCH include platinum (such as cisplatin and oxaliplatin) and 5-FU. When it is diagnosed that a chemotherapeutic drug is injected into the subcutaneous tissue erroneously, stop the injection immediately; then a cold compress or wet compress of $MgSO_4$ (50%) is applied in accordance with the therapeutic drug injected. If the patient suffers from severe pains, lidocaine 2% (100 mg) or procaine 2% (2 mL) plus dexamethasone (5 mg) can be applied for local closure. Subsequently, close observations must continue. If any extravasation injury is near the skin, it can form an ulceration, which usually occurs within 3–10 days. For any local necrosis caused by deeper ulceration, it can be absorbed gradually, with observation time of not less than 10 days.

5.6.3.2 CATHETER IN THE INTESTINAL CANAL

When the catheter is in the intestinal canal, no obvious discomfort is felt at the beginning of therapy, so it is not found easily if a little physiological saline is dripped during puncture. However, if the 500 mL physiological saline is dripped before perfusion of the therapeutic drug and the dysentery symptom occurs mostly within 10 minutes, then it can be found and treated as soon as possible. If it cannot be confirmed, an ultrasonic examination can be conducted.

Emergency plan for erroneous dripping of therapeutic drugs into the intestinal canal: After definite diagnosis of a therapeutic drug that has erroneously dripped into the intestinal canal, stop dripping the drug; replace it with 1000–2000 mL physiological saline for continuous dripping and washing, so that the drug is diluted in the intestinal tract and discharged from the anus. After the completion of the washing, pull out the catheter and maintain observations for 3–5 days.

5.7 CANCER HYPERTHERMIA AND INTEGRATIVE TREATMENT PRESCRIPTION

5.7.1 Single hyperthermia and indications

The methods and applications of hyperthermia depend on the location and pathology type of cancer (Table 5.1).

5.7.2 Hyperthermia combining surgery

Surgery is a preferred therapy for various cancers. It plays an important therapeutic role, so various conditions are created for surgery. A comprehensive therapy is conducted in the preoperative period to improve the effect of cancer therapy, which is extremely important. The adjuvant therapies of hyperthermia during the preoperative period include (1) preoperative hyperthermia: preoperative hyperthermia alone, preoperative hyperthermic chemotherapy, preoperative hyperthermal perfusion, preoperative hyperthermia combined with radiotherapy and chemotherapy, and so forth; (2) intraoperative hyperthermia: focusing on regional hyperthermia, common IPCH, intraoperative electrotome burning foci, and so on; (3) postoperative

Table 5.1 Commonly used hyperthermia treatments

Cancer location	Therapeutic method
Malignant tumors (except brain tumor) without contraindications	Whole-body hyperthermia or whole-body hyperthermia combining other therapies
Depth of superficial tumors <3 cm	915 MHz common microwave radiator ultrasound
Depth of superficial tumors <3 cm	Focused radiator microwave, intraoperative multihead ultrasound
Brain tumor	Interstitial hyperthermia, extracorporeal deep RF hyperthermia Ultrasound after craniotomy, low-power RF
Metastasis of nasopharyngeal carcinoma carotid <3 cm	Intracavitary microwave, ultrasound, extracorporeal deep RF hyperthermia
Esophagus cancer	Intracavitary microwave, intracavitary RF, extracorporeal deep RF hyperthermia
Lung cancer	Whole-body hyperthermia, extracorporeal deep RF hyperthermia
Liver cancer	Intraoperative hyperthermia, extracorporeal deep RF hyperthermia
Pancreatic carcinoma, gastric cancer, ovarian cancer	Intraoperative interstitial hyperthermia, endoscopic interstitial and regional hyperthermia Extracorporeal deep RF hyperthermia
Rectal cancer	Intraoperative hyperthermia, IPCH Extracorporeal deep RF hyperthermia
Bladder cancer	Intracavitary hyperthermia, regional hyperthermia, hyperthermal perfusion Extracorporeal deep RF hyperthermia
Uterine neck, cervical cancer	Regional hyperthermia, hyperthermic perfusion, RF, ultrasound, focused ultrasound
Prostatic cancer	Intracavitary hyperthermia, regional hyperthermia, extracorporeal deep RF hyperthermia
Limb osteosarcoma	Interstitial heating, regional hyperthermia, extracorporeal deep RF hyperthermia Intraoperative hyperthermia, isolative perfusion, ring induction heating

hyperthermia: for any patient who does not require any radiotherapy or chemotherapy, single hyperthermia combining other integrative treatments can be applied to prevent any reoccurrence or metastasis.

5.7.2.1 PREOPERATIVE HYPERTHERMIC CHEMOTHERAPY

According to the neoadjuvant chemotherapy scheme before surgery, chemotherapy is combined with whole-body hyperthermia or RF local hyperthermia in the cancer area to reach the purpose of hyperthermic chemotherapy. Preoperative chemohyperthermia can be conducted for 4–6 times in accordance with the patient's condition. As for hyperthermia, the extracorporeal deep RF hyperthermia can be selected and a whole-body hyperthermia can also be applied. In accordance with the radiotherapy scheme, the RF local hyperthermia is conducted within 1–4 hours after the radiotherapy, once every other day.

5.7.2.2 INTRAOPERATIVE HYPERTHERMIA

To decrease the chance of cancer plantation and metastasis during the intraperitoneal surgery, the surgeons often adopt the chemohyperthermia method wherein a recirculating chemohyperthermia machine is mostly adopted to maintain the perfusate at about 45°C, lasting for 60–90 minutes.

5.7.2.3 POSTOPERATIVE HYPERTHERMIA

Each RF local hyperthermia lasts for 1 hour, once every 2–3 days, with 15 times as a course of treatment. Each whole-body hyperthermia lasts for 6–8 hours, with its therapeutic temperature maintained at 40°C–41.8°C for minimum 180 minutes, once every 10–14 days. If the RF local hyperthermia is combined with whole-body hyperthermia, it can be conducted in the interval between two times whole-body hyperthermia. For any radiotherapy or chemotherapy after surgery, it can be combined with hyperthermic chemotherapy, hyperthermic radiotherapy, or hyperthermia combined with radiotherapy and chemotherapy in accordance with the therapeutic scheme for hyperthermia before surgery. Postoperative hyperthermia can be conducted after taking the stitches out of the postoperative wound and ruling out hyperthermia contraindications, after the chief surgeon's assessment of the surgical recovery, after lab examinations discloses no bleeding tendency, and after the comprehensive assessment of the patient by the physician in hyperthermia center. Especially for patients with a rich blood supply around the surgical wound, complex surgery and larger wounded area, it is necessary to carry out cautious assessments of the commencement times and therapeutic schemes of the hyperthermia.

5.7.3 HYPERTHERMIA COMBINED WITH CHEMOTHERAPY

5.7.3.1 HYPERTHERMIA COMBINED WITH WHOLE-BODY CHEMOTHERAPY

Chemotherapy can be combined with RF local hyperthermia or whole-body hyperthermia. Each RF local hyperthermia lasts for an hour, once every 2–3 days. Each whole-body hyperthermia lasts for 6–8 hours, with its therapeutic temperature maintained at 39.5°C–41.8°C for minimum 180 minutes, once every 10–14 days. If RF local hyperthermia is combined with whole-body hyperthermia, it can be conducted in the interval between two times whole-body hyperthermia. If chemotherapy is combined with RF local hyperthermia, the RF local hyperthermia can be conducted after the therapeutic drug administration. If chemotherapy is combined with whole-body hyperthermia, the chemotherapeutic drug can be infused during whole-body hyperthermia that is conducted on the first drug administration of each chemotherapy period. A RF local hyperthermia can be conducted every other day in the interval between two chemotherapies. During the therapy, routine allopathy-supporting therapies are conducted to prevent and cure any adverse reactions.

5.7.3.2 INTRACAVITARY CHEMOHYPERTHERMIA

5.7.3.2.1 Intraperitoneal hyperthermic perfusion

After preheating the chemotherapeutic drug, a routine drainage tube is left in the abdominal cavity to infuse the preheated chemotherapeutic drug into the abdominal cavity. Then RF local hyperthermia or whole-body hyperthermia is carried out. Each perfusion period totals 10–15 days, during which RF local hyperthermia

alone can be conducted every other day. During the therapy, routine allopathy-supporting therapies are conducted to prevent and mitigate any adverse reactions.

5.7.3.2.2 Intrapleural hyperthermic perfusion

After preheating the chemotherapeutic drug, a routine drainage tube is left in the thoracic cavity to infuse the preheated chemotherapeutic drug into the thoracic cavity. Then RF local hyperthermia is carried out. Each perfusion period totals 10–15 days, during which RF local hyperthermia alone can be conducted every other day. During the therapy, routine allopathy-supporting therapies are conducted to prevent and mitigate any adverse reactions.

5.7.3.2.3 Intravesical hyperthermic perfusion

After preheating the chemotherapeutic drug, a catheter is left routinely to infuse the preheated chemotherapeutic drug into the bladder. Then RF local hyperthermia is carried out. The perfusion period must be subject to the designated period, with intervals including 1 week, 2 weeks, and 1 month, respectively. During the perfusion, RF local hyperthermia alone is conducted every other day. During the therapy, routine allopathy-supporting therapies are conducted to prevent and mitigate any adverse reactions. It is usually used for bladder cancer.

5.7.4 Hyperthermia combined with radiotherapy

Targeting patients with radiotherapy indication or those without hyperthermia contraindication, a radiotherapy regimen is formulated at first, namely, radiotherapy and hyperthermia are conducted simultaneously. As for RF local hyperthermia combined with radiotherapy, the local hyperthermia is conducted every other day after the radiotherapy. As for whole-body hyperthermia combined with radiotherapy, whole-body hyperthermia is conducted, once every 10–14 days after radiotherapy. During the period between two times whole-body hyperthermia, local hyperthermia is conducted every other day, also right after radiotherapy. During the therapy, routine allopathy-supporting therapies are conducted to prevent and mitigate any adverse reactions.

5.7.5 Hyperthermia combined with other physiotherapies

Hyperthermia has effects such as antiphlogistic, odynolysis, promotion of exudate absorption, and improvements in immunity and metabolism. It can be combined with physical therapies such as recovery therapy, external application therapy, cryotherapy, electrotherapy, and electromagnetic therapy. Each combination shows an additive or synergistic effect on benign diseases such as inflammation, local pain, and muscle spasm, and subsidence of local circulatory function, local tissue edema, infection, recovery of traumatic injury, primary immune disease, malignant diseases and their complications, such as cancer pain.

Hyperthermia and other physiotherapies can be conducted synchronously, targeting complications, such as malignant disease and cancer pain, which can be treated according to hyperthermia scheme for malignant diseases. As for benign diseases, RF local hyperthermia is conducted once per day, 40 minutes each time, with 10 times as a therapeutic course. Whole-body hyperthermia is conducted once a week, lasting about 2–3 hours at a temperature of 38°C–40°C, with five times as a therapeutic course.

5.7.6 Hyperthermia combined with vitamin C therapy

Combined application scheme for hyperthermia with vitamin C: Local hyperthermia lasts for an hour, once every 2–3 days with 10–15 times as a course. Whole-body hyperthermia lasts for 6–8 hours with its therapeutic temperature maintained at 39.5°C–41.8°C for not less than 180 minutes, once every 10–14 days. If local hyperthermia is combined with whole-body hyperthermia, it can be conducted every other day in the interval between two times whole-body hyperthermia, with vitamin C injected while hyperthermia is being conducted.

5.7.7 Hyperthermia combined with traditional Chinese medicine therapies

5.7.7.1 HYPERTHERMIA COMBINING ORALLY TAKEN CHINESE MEDICINE

According to the tumor symptoms of qi stagnation, blood stasis, abdominal mass and cold stagnation, TCM is applied to drive out cancer toxins and regulate immunity, and it can be combined with cancer hyperthermia. Each RF local hyperthermia lasts for an hour, once 2–3 days with 5–10 times as a course. Whole-body hyperthermia lasts for 6–8 hours with its therapeutic temperature maintained at 39.5°C–41.8°C for not less than 180 minutes, once every 10–14 days. If RF local hyperthermia is combined with whole-body hyperthermia, it can be conducted every other day in the interval between two times whole-body hyperthermia. Orally taken TCM is used for treatment based on syndrome differentiation in accordance with the specific conditions of a patient, one dose a day to be divided for the morning and evening consumption. Because of the requirement for fasting and no drinking on the day before whole-body hyperthermia, a dose of TCM should be strongly decocted and taken orally after the completion of whole-body hyperthermia.

5.7.7.2 HYPERTHERMIA COMBINED WITH CHINESE MEDICINE INFUSED IN BODY CAVITY AND LUMENS

5.7.7.2.1 Herbal liquid rectal infusion combined with local hyperthermia

TCM directly touches or is close to the diseased region is combined with local heating to increase the therapeutic effect, once per 2–3 days, for 1 hour each time, with 10 times as a course of treatment.

Indications: It is applied to various tumors, of which colon cancer (descending colon cancer, sigmoid colon cancer, and rectal cancer) and prostatic cancer are the easiest to administer using TCM.

5.7.7.2.2 Hyperthermic perfusion of traditional Chinese medicine preparation into bladder

Some researcher adopt a *Rabdosia rubescens* solution for intra-bladder hyperthermic perfusion for patients with bladder cancer, which increases $CD4^+$ and $CD4^+/CD8^+$, while sIL-2R decreases, showing that it can improve the immunological functions of these patients.

5.7.7.3 HYPERTHERMIA COMBINED WITH EXTERNAL APPLICATION OF CHINESE MEDICINE

The external application of TCM is a main method for the external therapy of TCM. It attains the healing purpose through drug potency, which is infiltrated into the local area and transferred throughout the viscera to dredge qi movement and strengthen vital qi so as to dispel pathogenic factors. Therefore, it plays an important role in clinical therapy. The external application of drugs adopts the skin administration, and the means of absorption approaches of these drugs through the skin mainly include the following: (1) Arterial passage: Drugs are absorbed through horny layer and epidermis deep layer, and then they enter the blood circulation through one or more approaches. (2) Hydration: After the external application of herbal drugs, they are stimulated by 42°C–43°C heat. The affected region applied with drugs can form a closure state that prevents fluid escape through sweating and evaporation, so that the water content of the horny layer increases, its expansion shows a state of multiple holes, and the local blood flow accelerates, all of which are beneficial to the infiltration of the drugs. (3) Surfactant effect: The substance acts like aluminum soap as a surfactant, which can promote the absorption of the passive diffusion and strengthen the permeability of the epidermis lipid membrane to the drugs. (4) Auxoaction of the aromatic drugs.

How to improve the permeability of drugs to the skin is a key to obvious therapeutic effects. Modern research shows that the factors influencing the transdermal absorption of the drugs are closely associated with the inherent transmissibility of the skin except the physical and chemical properties, and the horny layer of the skin is a main obstruction of transdermal absorption. To strengthen the drug absorption of the skin, the horny layer must be softened to accelerate drug infiltration, and heat stimulation of the epidermis is an effective means for softening the horny layer.

5.7.7.3.1 External application of drugs plus radio-frequency local hyperthermia or whole-body hyperthermia

In accordance with the specific conditions of a patient, herbal drugs are prescribed for treatment based on syndrome differentiation. The drugs are powdered and mixed with alcohol, acid, or honey to form a paste, which is stuck on the body surface at the pathological areas with dressing. External application is conducted after the deep or whole-body hyperthermia. RF local hyperthermia lasts for an hour each time, once every 2–3 days, with 10–15 times as a course. Whole-body hyperthermia lasts for 6–8 hours each time with the therapeutic temperature maintained at 39.5°C–41.8°C for minimum 180 minutes, once every 10–14 days. If RF local hyperthermia is combined with whole-body hyperthermia, it can be conducted every other day in the interval between two times whole-body hyperthermia.

5.7.7.3.2 Whole-body external application of herbal drugs plus medium-low temperature whole-body hyperthermia

Herbal drugs are powdered and packed into specially made vests and bellybands to wrap around a patient, then the medium-low temperature hyperthermia is conducted, once a week, for 2–3 hours each time, at 38°C–40°C, with five times as a course. It is mainly used for benign diseases.

5.7.7.4 HYPERTHERMIA COMBINED WITH TRADITIONAL CHINESE MEDICINE TECHNOLOGIES (ACUPUNCTURE, MOXIBUSTION, MASSAGE, CUPPING THERAPY, BEE VENOM THERAPY, AND AURICULAR POINT)

During cancer therapy, TCM technologies, such as acupuncture, moxibustion, massage, cupping therapy, bee venom therapy, and auricular point, can strengthen the vital qi to eliminate pathological factors, strengthen immunity, regulate the energy balance of the human body, improve the functions of the organism, and so on. Both single and combined applications play important roles during cancer therapy. Especially, TCM technologies are characterized by simplicity, convenience, cheapness, and effectiveness, which have no side effects or toxicities, and are real "green therapies." Hyperthermia is combined with TCM technologies, in accordance with the principle of nontoxic integrative cancer treatments—eliminating pathological factors without injury to the vital qi and strengthening the vital qi without pathological factors remaining. Although the additive action between hyperthermia and TCM technologies has been shown clinically, it still requires further observations and generations, including research on its synergetic effects.

5.8 INTEGRATIVE HYPERTHERMIA REGIMENS FOR COMMON COMPLICATIONS OF CANCER

5.8.1 Pain

5.8.1.1 GENERAL INTRODUCTION OF CANCER PAIN

Cancer pain is a feeling caused after the repair or regulation information from the pain position is transferred to the central nerve. It is one of the causes of suffering for a patient with advanced cancer. It comprises of many factors, including physical, psychological, social, and mental. Pain is one of the most common and uncontrollable symptoms in cancer patients. According to statistics of WHO, there are 10 million new cancer patients each year around the world, of which 6 million people die of their cancers, 50% have the symptoms of cancer pain, and 70% advanced cancer patients have a main symptom of pain. Studies show that the incidence of patients with cancer pain is about 50% in China. The pain caused primarily because of the tumor covers about 80%. Tumor therapies can also incur pain, with incidence of about 10%. The remaining 10% is not associated with cancer.

5.8.1.2 CLASSIFICATION OF CANCER PAIN

The causes of cancer pain can be divided into three categories: (1) pain caused directly by cancer covers about 88%; (2) pain caused by cancer therapy covers about 11%; (3) pain caused indirectly by cancer covers about 1%.

Clinically, there are a few cancer patients who suffer from pains not connected with their cancer; for example, a patient with lung cancer suffers from lumbosacral pain because of the coinstantaneous protrusion of intervertebral disc, which is a noncancer pain. Therefore, the pain causes of cancer patients must be diagnosed clearly.

5.8.1.3 PAIN DIRECTLY CAUSED BY CANCER

Tissue damage: When cancer invades pleura, peritoneum, or marrow to cause pressure increase and even a pathological fracture, the patient can suffer from pain, such as bone ache caused by bone metastasis or bone cancer. A lung cancer that invades the pleura can incur chest pain. Any tumor at the apex of lung invading arms can cause shoulder–arm pain, and so forth.

Oppression: Brain tumors can cause headaches and cranial nerve pain. Nasopharyngeal carcinoma neck metastasis can oppress the brachial or cervical nerve plexus, causing pain in the neck, shoulder, and arm. Retroperitoneal tumor oppressing the lumbar and abdominal nerve plexuses can cause lumbar and abdominal pains. The nerve tissue under oppression by the tumor often coexists with the invader.

Obstruction: When the hollow viscera are obstructed by tumor, discomfort and spasms can occur. The spasm can be severe when viscera is obstructed completely, such as in gastric cancer, intestinal cancer, and pancreas-head carcinoma. In addition, the metastasis of breast cancer toward the axillary lymph node can oppress the axillary lymph and blood vessels, which causes swelling pain of the diseased arm.

Tension: When primary and liver metastatic tumors grow quickly, the liver capsule is stretched and tautened excessively, which can incur severe pain of the right upper abdomen.

Others: The long-term nonhealing tumor ulceration causing infection can incur severe pain.

5.8.1.4 PAIN CAUSED DURING CANCER THERAPY

There are many pain symptoms after therapy, some of which are described as follows: (1) brachial plexus nerve pain after resection of lung and mammary gland; (2) complications after gastrointestinal surgery; peripheral neuritis and aseptic femoral head necrosis after chemotherapy; (3) complications after long-term application of hormonal drugs: pseudo-rheumatoid arthritis after drug discontinuation, general tiredness, and fatigue, and wide soreness of muscle joints, with immediate elimination after reuse of hormonal application; (4) complications of radiotherapy: radioactive enteritis, secondary malignant abdominal or pelvic tumors, and perineal pain; (5) common pain caused by fiber hyperplasia and denaturation after radiotherapy on brachial plexus and lumbar plexus; (5) secondary primary neurofibroma because of pathological changes of bone marrow and radiotherapy, and so forth.

5.8.1.5 PAIN INDIRECTLY CAUSED BY CANCER

An adynamic patient can suffer from pain due to local infections that are caused by bedsores and low organic immunity. In addition, bone metastasis, which is caused by prostate, lung, breast, and thyroid carcinomas, can cause severe abdominal pain.

5.8.1.6 PAIN CAUSED BY INVASIVE DIAGNOSIS

Some special diagnoses, such as cardiac or cerebral angiography, gastroscope, esophagoscope, hepatic-intestinal artery angiography, laparoscope, enteroscope, and cystoscope, can stimulate and damage relevant receptors, which then cause pain.

5.8.1.7 PAIN CAUSED BY PSYCHOLOGICAL FACTORS

A patient's emotions and psychological factors can cause nonnegligible influences on the sense of pain. Any patient with cancer can suffer from physical and mental stimulations, feel exhausted and lose the capacity for work and self-living, and when he or she must rely on others, additional emotional and mental changes may result, which can affect the degree of pain.

5.8.1.8 THERAPEUTIC METHODS

Cancer pain usually subsides with therapies such as drug treatment, hyperthermia, and internal and external applications of herbal drugs. Any surgical therapy must consider the general physical condition and survival

period of a patient. After a definite diagnosis of pain causes, assessments of the analgesic effects and pain-relieving degree of relevant therapies must be available, so as to formulate the proper therapeutic schemes and administration doses.

5.8.1.8.1 Hyperthermia and cancer pain

Local or whole-body hyperthermia can relieve pain of different causes, and TCM can effectively relieve any circulating obstruction leading to pain. After hyperthermia, blood flow can increase, blood vessels expand, capillaries are opened because of stimulations by vascular active substances such as bradykinin or histamine; then local blood flow is improved and the pains are relieved effectively. Generally, hyperthermia is combined with medical acesodyne, which can raise the analgesic effect to 30%–50%.

To help ensure sound patient conditions and tolerance to whole-body hyperthermia, it is recommended to adopt the medium-high temperature whole-body hyperthermia once a week for a total of 4–6 times. On the day before whole-body hyperthermia, nutritional support must be given. Food must be abstained for 8 hours and water for 4 hours before hyperthermia. It is necessary to monitor the body temperature, blood pressure, and pulse during hyperthermia, and then, a timely fluid replacement is made to maintain the balance of water and electrolytes. Later, the electrolytes are rechecked within 1–3 days to maintain the balance of water and electrolytes. In the interval periods of whole-body hyperthermia, proper local hyperthermia can be added in accordance with the patient's general condition and tolerance.

For any patient who cannot tolerate the medium-high temperature whole-body hyperthermia, local hyperthermia or medium-low temperature hyperthermia can be conducted in the pain region. Local hyperthermia is conducted every other day, with 20 times as a course for a total of over three courses. Medium-low temperature hyperthermia is conducted once per week, for a total of 12 times.

5.8.1.8.2 Drugs and cancer pain

"Three-Step Therapy" of drug treatment for cancer pain:

Step I. Non-opium analgesic: It is used for patients with slight cancer pain, mainly including aspirin, acetaminophen (Panadol), and so forth, which can be combined with adjuvant drugs according to specific situations.

Step II. Weak opium analgesic: It is used for patients who are not satisfied with the analgesic effect of non-opium analgesics or for moderate cancer pain patients, mainly including codeine, which is suggested to be combined with the drugs in Step I. Because the two types of drugs have different functional mechanisms, namely, the drugs in Step I are mainly used for the peripheral nervous system whereas those in Step II are mainly for the central nervous system, the combination of these two drugs can enhance the analgesic effect. Adjuvant drugs can also be applied as required.

Step III. Strong opium analgesic: It is used for therapy on moderate or severe cancer pain, and applied when the therapeutic effects of drugs in Step I and II are poor, mainly including morphine. Adjuvant drugs can also be applied according to specific conditions.

Other than with the above drugs, pains can be alleviated according to different disease causes. If they are caused by bone metastases, it is appropriate to adopt hyperthermia combining non steroidal and zoledronic acid salt for acesodyne. If they are caused by nerve compression or cerebral edema, adopt hyperthermia in combination with hormone for dehydration.

5.8.1.8.3 Surgical therapy

Surgical therapy plays an important role during cancer therapy, and it is a necessary and effective therapy for the obstructive pain caused by tumor oppression and stimulation.

5.8.1.8.3.1 Anesthesia methods

Anesthesia methods include five major types: peripheral nerve block, myofascial trigger point injection, autonomic nerve block, intrathecal nerve block, and nitric oxide drug anesthesia. The anesthetic is injected locally to block the peripheral nerve, relieving the limited pain, and it is simple and feasible. If the local anesthetic

is not effective, consider anhydrous alcohol and phenol to destroy the nerve and achieve nerve-destructive block for acesodyne (anesthetic surgery). As for the cancer pain in viscera, the intraperitoneal ganglion block is effective. For the cancer pain caused by the infiltration of brachial plexus and lumbosacral plexus, as well as that of head, neck, and face, the sympathetic ganglion block can get a therapeutic effect.

5.8.1.8.3.2 Neurosurgery method

It can be divided into three categories: nerve destruction, nerve stimulation, and resection or separation of peripheral nerve and nerve roots, all of which are used to cure the pains in the sensory area. Neurosurgery is applied to relieve cancer pains through three forms: implanted drug pump, resection or separation of nerve roots, and nerve stimulation. During the nerve resection, the percutaneous spinal cord ventro-column resection is commonly used and it is applied to the single lower limb pain caused by rectal and pelvic tumors invading the nerve plexus, with an estimated survival period of 2–3 years or less. Thalamus resection aims to block the thalamic pain pathway; pituitary gland ablation is almost completely effective for breast cancer pain. As for the general pain of bone metastases, chemical hypophysectomy can make 80% patients relieved, but often cause complications such as diabetes insipidus and cranial nerve paralysis. Deep nerve stimulation is effective for both central and afferent nerve pain, without damage to the movement function, and it has certain application prospects. Intravenous analgesia pump (intravenous application of propofol plus midazolam) or analgesia pump in the vertebral canal can be applied if necessary.

5.8.1.8.3.3 Orthopedic method

When positive x-ray film shows that more than half of the bone cortex is destructed, about 2/3 patients can suffer from pathological fracture; therefore, a fixation (including splint, suspension) must be applied when the long bone destruction exceeds 3 cm, even though there is not any pathological fracture. Once a pathological fracture occurs, an internal or external fixation must be applied. As for bone cancer of four limbs, the method of reconstruction after cancerous section resection can be adopted to restore most or part of the limb functions, eliminate or relieve pains, reduce the cripple-causing rate, prolong life, and improve the quality of life of the patients.

5.8.1.8.4 Oral administration and external treatment for cancer pain

According to the comprehensive analysis of data gained by four diagnostic methods (watch, listen, ask, and touch), determine the treatment based on differentiation of symptoms and signs, with pain-relieving therapeutic methods including dispelling cold, clearing away heat, promoting qi, activating blood circulation, dispersing phlegm, eliminating dampness, toning deficiency, arresting discharge, and dispelling melancholy.

5.8.1.8.4.1 Internal therapy

In accordance with the TCM theory, to determine the treatment based on differentiation of symptoms and signs, the pain causes are differentiated as blood stasis, heat toxin, qi stagnation, and turbid phlegm, and then relevant therapies are selected. For the blood stasis type, it is used for activating blood circulation to relieve pain, by a representative prescription of Taohong four-material decoction (angelica, rhizome of Sichuan lovage, Chinese peony, and dried *Rehmannia* root). For the heat toxin type, it is used for softening and resolving hard mass for catharsis to relieve pain, by a representative prescription of fried turtle shell pill. For the qi stagnation type, it is used for regulating vital qi to relieve pain, by a representative prescription of chai hu liver smoother. For the turbid phlegm type, it is used for purging the lung and reducing phlegm to relieve pain, by a representative prescription of lung-draining decoction with seeds of pepper weed and Chinese date.

5.8.1.8.4.2 External therapy

The external therapy for cancerous pain is rich in contents. For example, a herbal drug prescription, such as centipede, wall lizard, nux vomica, prepared Sichuan aconite root, *Arisaema*, toad venom, myrrh, and borneol, for internal application is applied to pathological places (most drugs are aromatic or poisonous) to activate blood circulation and break blood stasis. Most of these are paste or powder prescriptions, such as toad venom paste, which can be used for external acupoint application, embrocating and straight sequence

of herbal drug, and so forth. External therapy of herbal drugs are used with exterior drug administration, which can avoid the multilink inactivation when the orally taken drugs are absorbed in the alimentary canal, as well as toxic and side effects caused by oral application of some drugs. It has obvious advantages especially for patients with medium and advanced pain.

5.8.1.8.5 Acupuncture and cancer pain

Acupuncture focuses on selecting acupoints based on syndrome differentiation, to relieve any acute pain and to improve the immunological function, thus depressing the reoccurrence and metastasis of tumors.

5.8.1.8.6 Medical ozone acupoint injection and cancer pain

Acupoint therapy has an obvious analgesic effect. It is characterized by reducing cancer by depressing the growth of cancer cells. Also, it reduces the sufferings of patients, delays the development of diseases, and improves the quality of life of patients.

As a gas, medical ozone has good solubility, and is easily absorbed through muscle and subcutaneous tissue. After entering the human body, one part is decomposed into oxygen and produces hydrogen peroxide through redox reaction. Oxygen can increase acupuncture's sense of qi arrival in the acupoint tissue, stimulating the body to enhance its integral immune level. It can be combined with red erythrocytes in the blood capillaries. Hydrogen peroxide is also taken as a strong immune-stimulating factor in an acupoint to obviously enhance the immune effect of acupoint therapy. Medical ozone acupoint injection can be applied to relieve pains effectively.

5.8.1.8.7 Radiotherapy and cancer pain

The pain remission rate caused by radiotherapy's oppression on cancer or infiltration into the nerve is 70%–85%. If the primary focus is sensitive to radiotherapy, the effect is better. Especially for local osseous metastasis, local radiotherapy can not only depress and even kill tumor, but also reduce the pain greatly, so it has a unique therapeutic effect. The analgesic indications of radiotherapy mainly include metastatic bone cancer, spinal metastasis, oppression of tumor on the spinal nerve root, brain tumor, invasion of lung cancer on brachial plexus, and invasion of gastric cancer and pancreatic carcinoma on the postperitoneum.

5.8.1.8.8 Chemotherapy and cancer pain

Chemotherapy is mainly applied to patients with multiple bone metastases. Especially, it can show a rapid effect on pains caused by oppression or infiltration into the nerve tissue by cancers such as lymphoma, small-cell lung cancer, and leukemia, which are sensitive to chemotherapy.

5.8.1.8.9 Cell analgesia, gene therapy, and cancer pain

Cell analgesia therapy aims to implant the autologous cells or cell strains cultivated in vitro into the body. It relieves pains or improves pain thresholds through these cells, analogous to a "biological micro pump," which continuously secretes analgesic substances. These implanted cells can secrete pain-resistance proteins, and regulate factors of pain-resistance proteins, enzymes, or signal transducing factors, so as to enhance the expression of pain-resistance proteins. In research related to pain, gene therapy includes mainly two aspects, promotion of pain-resistance gene expression and decrease of pain gene expression, which can intervene in the biological behaviors of pain specifically, so as to attain therapeutic purposes.

5.8.1.8.10 Qigong and cancer pain

Qigong therapy can smoothen qi and blood, thus beneficial in eliminating or relieving cancer pain. If qigong is combined with the acupoint-pressing massage therapy, it can have a better therapeutic effect. Also, the psychological implications of qigong can relieve cancer pain and benefit the spleen.

5.8.1.8.11 Psychotherapy and cancer pain

It is applied to patients with light and moderate cancer pain, who are of lucid consciousness, normal mind, and appropriate physical condition. Patients can get relevant information from education, as well as

communications with doctors, other patients, and families, which could guide them to correctly recognize their body senses of reality, rectify wrong or misconceived cognitions, change the reactions of their bodies to pains, and ultimately generate such sense that the cancer pain is being controlled. Methods include hypnotism, attention transfer, relaxation exercise, biofeedback regulation, psychotherapy, and cognitive behavioral therapy, which can enhance the capacity of patients in coping with pain, and reducing the levels of fear, anxiety, and depression in patients.

5.8.2 Pleural effusion

5.8.2.1 General introduction of malignant pleural effusion

In cancer-based pleural effusion, malignant cells can be found in pleural effusion in most cases. If the pleural effusion is accompanied with metastatic nodules on the surface of mediastinum or pleura, irrespective of whether the malignant cells are found in the pleural effusion, the malignant pleural effusion is diagnosed. In clinical pleural effusion, about 40% are caused by malignant tumors, including common lung cancer, breast cancer, and lymphoma. The cancer types have certain differences between males and females. Common cancers in males include lung cancer, lymphoma, and gastrointestinal tract tumor; those in females include breast cancer, female genital duct cancer, lung cancer, and lymphoma. Malignant pleural effusion comprises 38%–53% of the total; pleural metastatic cancer and pleural diffuse malignant mesothelioma are the main reasons for producing malignant pleural effusion.

5.8.2.2 Pathogenesis

5.8.2.2.1 Common pathogenic factors

Malignant pleural effusions are pleural cancer metastases in the parietal layer and/or visceral layer. These metastatic cancers break the blood capillaries that lead to the leakage of fluid or blood, which usually causes bloody pleural effusion.

5.8.2.2.2 Drainage disorder in the lymphatic system

The drainage disorder in the lymphatic system is a main mechanism for producing malignant pleural effusion. The tumors involving the pleura, even if they occur primarily in or transferred to the pleura, can block the lymphatic vessels on the surface of the pleura, so that the normal pleural effusion circulation is destructed to produce pleural effusion. The lymphatic drainage of the parietal layer pleura mainly enters the malignant tumor cells in the mediastinal lymph node. It is blocked in any position between pleural minipores and mediastinal lymph nodes, including formation of cancer cell embolisms and metastasis of mediastinal lymph nodes in the lymphatic vessels, which can cause the reabsorption disorder of liquid in the chest cavity, and result in pleural effusion.

5.8.2.2.3 Large number of proteins in cancer cells entering the chest cavity

The tumor tissue on the pleura grows rapidly, and the cells are prone to fall off. The lack of blood circulation can result in necrosis and decomposition of cancer cells in the pleural cavity, and then the proteins in the cancer cells enter the chest cavity. Thus, the osmotic pressure of the colloid in the pleural cavity rises and causes pleural effusion.

5.8.2.2.4 Increase of pleural permeability

Any cancer invading pleura in the visceral layer and parietal layer, and the plantation of cancer cells in the pleural cavity, can cause inflammatory reaction of the pleura and permeability increase of the blood capillaries. If any liquid is infiltrated in the pleural cavity, the primary lung cancer or lung-metastatic cancer can lead to obstructive pneumonia, producing similar parapneumonic effusion.

5.8.2.2.5 Decrease of intrapleural pressure and increase of pleural capillary hydrostatic pressure

Lung cancer causes bronchial obstruction, incurs distal atelectasis, and results in the decrease of the intrapleural pressure. When the intrapleural pressure decreases to –4.7 kPa (–48 cmH_2O) from –1.176 kPa (–12 cmH_2O),

there will be about 200 mL of body fluid accumulated in the pleural cavity. The malignant cancer in the lung can invade the vena cava or pericardium, leading to venous backflow obstruction, the increase of the pleural capillary hydrostatic pressure, and then the generation of pleural effusion.

5.8.2.2.6 Others

Cancer cells invade blood vessels to form cancer embolus, which then produce the pulmonary embolism and pleural exudation. Cancer consumption can cause hypoproteinemia and the reduction of the plasmatic colloid osmotic pressure, resulting in pleural effusion. After radiotherapy on the chest or mediastinal, exudative pleural cavity effusion can occur.

5.8.2.3 THERAPEUTIC METHOD

Whether or not to carry out a positive therapy depends on the degree of the respiratory symptom caused by the malignant pleural effusion. If the patient has no respiratory symptoms or the patient has been in the middle-advanced stage, no special local therapy is required. If the clinical condition is uncertain, pleural puncture alone may be suitable. If the patient's respiratory symptom is not improved after removing a certain amount of pleural effusion, the disease condition of the patient may be caused by potential lung diseases, such as pulmonary emphysema and primary or secondary malignant tumor in the lung. Under this circumstance, it is not appropriate to conduct a local therapy. The cancer chemotherapy and radiotherapy causing pleural effusion are beneficial for eliminating the pleural effusion and improving the respiratory tract symptoms. As for the pleural effusion caused by lymphoma, lung cancer, or breast cancer blocking the lymphatic vessels, radiotherapy can eliminate the block pathogenesis, and rebuild and improve dynamics of the pleural fluid, showing a better therapeutic effect. As for the pleural effusion that affects the pneumodynamics and threatens life, pleural puncture is helpful for controlling the symptom before no other effective therapies are made.

5.8.2.3.1 Etiological therapy and basic therapy

Active therapy on primary diseases: For some patients with hydrothorax, the intake of sodium salt shall be restricted in their daily diet, and a reasonable nutrition shall be supplemented for patients with poor nutrition, especially paying attention to the appropriate intake of amino acids and protein.

5.8.2.3.2 Pleural puncture for pumping liquid and closed thoracic drainage

It is not necessary to treat small effusion that can be absorbed naturally. A medium amount of effusion or more can cause an oppression symptom, for which a pleural puncture must be applied to pump the effusion, 2–3 times per week. The pumping amount of effusion must not be excessive and rapid, to avoid the pleural shock and homolateral expansionary pulmonary edema.

Because of its simplicity, convenience, and rapid remission of symptoms, pleural puncture for pumping liquid is the most fundamental therapeutic means, which must be repeated due to rapid increase of hydrothorax in the tumor. As for patients with more hydrothorax and non packed hydrothorax, blind puncture is usually adopted; otherwise, puncture under the direction of ultrasounds is safer.

Pleural puncture is conducted by the central vein by placing a catheter for drainage, which can pump hydrothorax maximally. This method is characterized by controlling drainage speed, no influence by body position during drainage, less occurrence of electrolyte disturbances, and so forth.

5.8.2.3.3 Pharmacotherapy

5.8.3.3.3.1 Common pharmacotherapy

If hydrothorax is excessive and there are obvious dysfunctions of respiration and circulation, oral and venous urinative drugs should be considered.

5.8.3.3.3.2 Treatment based on syndrome differentiation

Malignant pleural effusion belongs to "xuan yin (the disease caused by the pathogenic fluid-retention stagnated in the chest) in TCM. Evil flow in chest and hypochondrium blocks the three cavities, and excessive

fluid accumulates in the body to form hydrothorax. It shows yin symptoms including visible phlegm retention and blood coagulation. Such cloudy phlegm-carrying toxins can result in the obstruction of water passages for the three cavities and excessive fluid retention, the treatment for which must dispel phlegm and resolve masses, promote qi, alleviate water retention, and protect the vital qi.

Common herbal preparations include elemene emulsion injection, matrine injection, and lentinan, and oil seed *Bruceae* ointment. Chinese herbal medicine emphasizes preparations with characteristics of clearing heat, removing toxicity, removing blood stasis, and retaining water. It also combines with characteristics of strengthening and consolidating body resistance. It includes common *Hedyotis diffusa*, herba *Scutellariae barbatae*, Chinese honeylocust spine, burred tuber, zedoary, Asiatic plantain seed, betelnut peel, peppergrass, Mongolian snakegourd, peach kernel, safflower, ginseng, pilose asiabell root, and *Astragalus* root.

Phlegm stasis resistance type: The prescription includes Daotan Decoction combining Qingzao Jiufei Decoction, plus perilla fruit, fried semen raphani, zedoary, pleione rhizome, pangolin scale, Mongolian snakegourd, rhizoma pinelliae preparata, air potato yam, agaric, raw milkvetch root, and raw semen coicis.

Qi and yin deficiency type: The prescription includes Sijunzi Decoction combining Dryness Relieving and Healing Lung Decoction, plus *Hedyotis diffusa*, oriental water plantain rhizome, raw oyster shell, hairy vein agrimony, and radix notoginseng.

Liver and kidney yang deficiency type: The prescription includes Zhenwu Decoction plus *Astragalus* root and shell of areca nut.

Liver and kidney yin deficiency type: The prescription includes Yiguan Decoction, plus white peony root, turtle shell, and radix bupleuri.

Spleen and stomach deficiency type: The prescription includes Zhishi Xiaopi Powder plus *Astragalus* root.

5.8.3.3.3.3 Simple recipe and empirical prescription

Single recipe: Aucklandia root plus oral application of powdered spurge capsule, and so on.

Proved prescription: Guiqitingbai Decoction, Yiqi Juan Drink Decoction, and so forth, which are used to cure malignant hydrothorax, showing a better therapeutic effect. Also, some custom-made prescriptions (raw ephedra, balloonflower root, mulberry bark, peppergrass, Chinese date, shell of areca nut, and plantain seed) have certain therapeutic effects in ventilating lung qi for diuresis.

5.8.3.3.3.4 Local drug administration

Clinically, pleural drug administration is usually applied to cure pleural effusion, and these drugs can be herbal preparation, biological preparation, or chemical drugs and antibiotics.

Herbal preparation: At present, common preparations include Elemene Emulsion Injection, Kanglaite Injection, Matrine Injection, and Bruceolic Oil Emulsion. They not only have a direct anticancer effect, but also can cause chemical inflammations, promote pleural adhesions and hypertrophy, and reduce pleural permeability after injection into the chest cavity, so as to decrease hydrothorax seepage. They can also produce anticancer effects and cause depression of the hydrothorax through many approaches such as immunological regulation effects.

Biological preparation: It is mainly injected in the chest cavity to cure malignant hydrothorax, mainly including interleukin-2, interferon α-2b, ribonucleic acid (BP cord), thrombin, urokinase, BCG vaccine, Sapylin, α-mannan peptide, *Staphylococcus aureus* preparation (highly agglutinative staphylococcin, staphylococcal enterotoxin C injection), nocadia rubra cell wall skeleton (N-CWS), *Corynebacterium parvum* preparation, and so forth. It shows main side effects such as fever and causalgia. After injection of these drugs, they can stimulate the body to produce abundant T-cells, lymphokines, interleukins, interferons, tumor necrosis factors, colony stimulating factors, and so forth, so as to directly kill cancer cell. They can also directly stimulate the medium-grained cells and lymphocytes to release fiber cell–stimulating factors, arouse pleural fibrosis, and further depress the production of hydrothorax.

Pleural perfusion chemotherapy: It is one of the main approaches for malignant hydrothorax, with advantages including cavitary drug administration, high local drug concentration, and vigorous exertion of

its anticancer effects. The chemotherapeutic drugs can also arouse a chemical inflammation between two layers of pleura on the chest wall, which results in pleural adhesion, and the obstruction and fixation of the pleural cavity so as to reach the purpose of controlling the hydrothorax. Chemotherapeutic drugs that can be injected in the chest cavity include cisplatin, mitomycin, arsenious acid, *bleomycin*, 5-FU, hydroxy camptothecin, etoposide, doxorubicin, and mitoxant.

Administration method: After extraction of the hydrothorax, it is better to adopt physiological saline or water for injection, totaling 20–40 mL, to dissolve the drug, which is then injected into the chest cavity through drainage tube or puncture tube, to prevent the drugs from being injected or permeated into the chest wall or subcutaneous tissue. Within 1–2 hours after injection, the body position must be changed every 15 minutes, so that the drug is distributed uniformly in the chest cavity. The choice and dosage of the drug should depend on the patient's general condition, liver and kidney functions, blood routine, body surface area, and sensitivity of the primary cancer to the drug. The repeating frequency should depend on the therapeutic effect or the patient's condition and bone marrow, and so forth. Local pleural administration can cause high pleural drug concentration, but less influence on the whole body, and show a worse effect in controlling the primary or other metastatic focuses.

5.8.3.3.3.5 Other drug treatments

Drug treatments should aim to enhance the general immunity, improve the integral condition, and rectify any hypoproteinemia for positive anti-infection therapy. As for any severely infected chest cavity, it must be infused with a more sensitive antibiotic.

5.8.3.3.4 Hyperthermia

First of all, pleural local hyperthermia can obviously enhance the permeability and sensitivity of any therapeutic drug. Second, hyperthermia itself has an anticancer effect, causing polar molecules in the water to move and generate heat rapidly under its electromagnetic field, while the cancer cells in the malignant pleural effusion are distributed dispersedly and are more sensitive to hyperthermia. Third, local hyperthermia can increase the conductivity of the vessels, cause the expansion of blood vessels and lymphatic vessels in local tissues, benefit the permeation of the chemotherapeutic drug, and increase its antitumor effect. Also, the high heat can induce necrosis of cells. The cytoplasm zymogen in the hydrothorax can activate the concentration increase of depression factors, which depresses the activity of the fibrinolytic system, increases the sediment possibility of the celluloses on the pleural surface, and promotes the formation of chemical inflammation of the pleura.

Hyperthermia combined with pleural perfusion chemotherapy has a more obvious therapeutic effect than chemotherapy alone in curing malignant pleural effusion, and it can improve the quality of life of patients, and there is no obvious difference of toxic and side effects from chemotherapy alone. In addition, hyperthermia can be combined with biological preparations, through which the side effects of hyperthermia are few, and fewer patients suffer from causalgia, empyema and fatty scleroma, which usually occur in females and obese people. The pleural perfusion of various drugs is combined with local or whole-body hyperthermia, which can obviously improve the efficiency and the quality of life of patients. Generally, the perfusion of drugs must not be conducted until the entire hydrothorax is drained as much as possible, and the local thoracic hyperthermia is conducted within 0.5–2 hours; on the one hand, to sensitize the drugs, and on the other hand, to relieve the toxic and side effects of the chemotherapy. In accordance with the patient's condition, one perfusion is generally conducted within 1–2 weeks. As for hyperthermia, it is recommended that it must be conducted every other day, totaling 20 times in a therapeutic course, except for its synchronous therapy with the perfusion of drugs.

5.8.3.3.5 Acupuncture and moxibustion

Methods: Acupuncture, moxibustion, acupoint injection, auricular needle, medical moxibustion, and so forth. The application of acupuncture, moxibustion, or medicinal moxibustion can show certain effects such as ventilating lung qi for dissipating phlegm.

5.8.3.3.5.1 Acupuncture

Acupoint selection: Lung Shu, Spleen Shu, and Kidney Shu. The acupuncture is conducted once a week, totaling five times in a therapeutic course.

5.8.3.3.5.2 Moxibustion therapy

The selection of acupoints is the same as the above, one to three times each day, and two to three acupoints are selected each time.

5.8.3.3.5.3 Acupoint injection

It can adopt the *Astragalus* injection once per day.

5.8.3.3.6 Medical ozone therapy

After the drainage through pleural puncture, 40–60 mL medical ozone saline with high concentration is injected into the chest cavity, or the pumped hydrothorax is mixed with medical ozone saline and then infused into the chest cavity again, which shows a more definite therapeutic effect on the hydrothorax because of various causes.

In addition, medical ozone acupoint injection can also be applied, selecting Fei (Lung) Shu, Pi (Spleen) Shu, and Shen (Kidney) Shu. Two to three acupoints are selected each time, and each acupoint is injected with medical ozone gas of 2–4 mL once every 2–3 days.

5.8.3.3.7 Surgical therapy

For patients with refractory malignant pleural effusion, assess their condition to determine if pleural resection can be adopted to remove the pathological bases causing hydrothorax, relieve the stimulations of pleural inflammation and cancer invasion to the intercostal nerve, realize the effect of relieving chest pain, alleviate the cancer load of the body to some extent, remove immunosuppressive factors effectively, improve and raise the immunological state of the body effectively, and create sound conditions for anticancer therapy.

5.8.4 Seroperitoneum

5.8.4.1 GENERAL INTRODUCTION OF MALIGNANT SEROPERITONEUM

Seroperitoneum means that the ascites exceeds its normal value and shows retention. Malignant seroperitoneum is a presentation of an advanced tumor. Once any malignant seroperitoneum occurs, the median survival time is from a few weeks to several months, with a 1-year survival rate of less than 10%. Patients with ovarian cancer and lymphoma after prognosis have longer survival time. The survival time of breast cancer patients is longer than that of patients with gastrointestinal cancer.

5.8.4.2 PATHOGENESIS

Most cancer patients may suffer from seroperitoneum at different stages of the disease, with common causes including the following: (1) Hypoalbuminemia: It is mostly associated with malnutrition, tumor consumption, abnormality of kidney function causing the urinary leakage, for which the ascites is transudate, and the ascites shows a yellow clear liquid; also, the cells are fewer and the protein content is lower in the hydrothorax. (2) Peritoneal metastasis of cancer: Many middle-advanced tumors can result in wide peritoneal metastases when the ascites is mostly hematic and is only transudate, its proteins and cells exceed their normal values, and there are many cancer cells in the hydrothorax. (3) Blood vessels, such as portal vein, splenic vein, and inferior vena cava, suffer from embolism or oppression. Primary liver cancer or liver metastasis carcinoma is relatively common, the ascites is mostly transudate, and the protein and cell contents are relatively less in the hydrothorax. (4) Lymphatic circumfluence block: It is mainly caused by the mass effect of tumor metastasis oppressing lymphatic vessels, and the ascites may be transudate or liquid leakage or their mixture. (5) Abnormal hormone levels: For example, lung cancer includes abnormal amine precursor uptake decarboxylase (APUD) cell secretion. There are also many causes such as secretory abnormality

of various hormones and inactivation dysfunction, which are incurred by middle-advanced cancer invading the liver, kidney, and adrenal gland and/or causing dysfunction; so the ascites caused is mostly liquid leakage. (6) Infection: Any of the cancer patient's low immunity, tumor obstruction, metastasis, and various punctures, especially abdominal puncture, can result in bacterial translocation, infection, and so forth. Most bacteria are gram-negative bacilli, but also include other bacteria such as pathological bacterium, Eumycota, and tubercle bacillus. (7) Other: For example, some cytokines can increase the permeability of blood vessels, such as interleukin-2, tumor necrosis factor, interferon-α, vascular endothelial growth factor, and matrix metalloproteinases (MMPs), all of which also play important roles in the formation of malignant hydrothorax.

5.8.4.3 THERAPY

At present, common therapies include whole-body chemotherapy, IPCH or intraperitoneal perfusion of biological reaction regulator (Chinese patented medicine), radiation therapy, and symptomatic support.

5.8.4.3.1 Basic therapy

It includes restriction on the intake of sodium salt and routine oral application or venous injection of drugs for diuresis, such as spironolactone, hydrochlorothiazide, and furosemide. When the ascites affects a patient's breathing, circulation, or daily life, the intraperitoneal puncture for drainage must be conducted, with discharge of ascites less than 5000 mL for the first time, then less than 8000 mL. The discharge speed should not be too fast. Diuretic drugs can be applied in the abdominal cavity: furosemide plus dopamine (2:1) are injected in the abdominal cavity, which produce a better effect on the reduction of ascites than venous diuretic drugs, and with fewer complications that can cause the electrolyte disorders.

5.8.4.3.2 Albumin supplementation

It is applied to patients with hypoalbuminemia.

5.8.4.3.3 Hyperthermia combined with drugs

Different chemotherapeutic drugs are selected according to the primary cancers, and common drugs include mitomycin, FU, doxorubicin, and cisplatin. Specific operation approaches: after sufficient drainage of hydrothorax, generally, the intraperitoneal perfusion of dexamethasone (5–10 mg) and lidocaine (100 mg) is conducted to prevent intraperitoneal adhesion and reduce the stimulating pain of the chemotherapy. Then, the intraperitoneal perfusion of the chemotherapeutic drug and sodium bicarbonate (50–100 mL) is administered, and the abdominal local hyperthermia is conducted subsequently. One perfusion of the chemotherapeutic drug is conducted every 10–14 days, totaling 4–6 times, and meanwhile, the support therapies, such as venous fluid replacement and gastric protection for prevention of any vomit, is prepared. IPCH is beneficial in sensitizing the therapeutic effect and relieving the adverse reactions of the chemotherapy, such as vomiting and bone marrow depression. It is recommended that hyperthermia is conducted once every other day, totaling 20 times in a therapeutic course.

5.8.4.3.4 Portal vein shunt

For vascular obstruction, generally, if patients' conditions are good and their survival periods are longer by estimation, the portal vein shunt (PVS) can be applied but assessments should be required, and the PVS cannot improve the survival quality of the patient or prolong his or her survival period in many cases.

5.8.4.3.5 Intraperitoneal radioisotope therapy

It is applied to patients with metastasis of the abdominal cavity. Radioisotopes ^{131}I, ^{32}P should be selected for the intraperitoneal perfusion therapy. Radioactive elements have strong penetration capacity (8 mm) in tissues and longer half-life (14 days), so they are often applied with a dose of 20 mCi.

5.8.4.3.6 Concentrated ascites feedback of seroperitoneum

To prevent loss of a large number of proteins, the ascites can be concentrated and fed back to the abdominal cavity, which can get a certain therapeutic effect.

5.8.4.3.7 Intraperitoneal medical ozone injection

After discharge of the ascites, medical ozone saline is injected, and in consideration of the ascites, circulate medical ozone for filtration and feedback, which can be combined with the concentrated ascites for feedback. Especially, it is applied to patients with spontaneous peritonitis, abdominal cavity infection, and peritoneal metastasis.

5.8.4.3.8 Immunotherapy

It adopts intraperitoneal perfusion of interleukin-2, *Streptococcus* A group for injection, tumor necrosis factor and nocadia rubra cell wall skeleton, interferon-α; and *Corynebacterium parvum*, which have produced sound effects on most therapies of cancerous ascites.

5.8.4.3.9 Infection resistance

It is applied to infectious peritoneal inflammatory ascites, and it can be applied throughout the body by intraperitoneal perfusion of antibiotics.

5.8.4.3.10 Traditional Chinese medicine

5.8.4.3.10.1 Treatment based on syndrome differentiation

Syndrome of qi stagnation and dampness

Syndromes: Abdominal swelling, swelling without hardness, flank ruffian swelling or pain, less urination, dry stools, belching, flatus causing relieving swelling, appetite, fatigue, stringy pulse, and thin white or white grease tongue fur.

Recipes: Radix bupleuri (10 g), trifoliate orange (9 g), cyperus tuber (9 g), Guangzhou turmeric root-tuber (9 g), fruit of five leaf *Akebia* (20 g), plantain seed (10 g), oriental water plantain rhizome (15 g), agaric (10 g), Indian bread peel (12 g), white *Atractylodes* rhizome (10 g), and so forth.

Syndrome of dampness due to spleen deficiency

Syndromes: Decrease of food intake, swelling due to intake of food, thin sloppy stools, frequent stools, fatigue, qi deficiency and lack of speech, edema of lower limbs, thin white tongue fur, pink tongue texture, and tooth marks on its edge.

Recipes: Pilose asiabell root (15 g), white *Atractylodes* rhizome (12 g), Indian bread (12 g), fried *Astragalus membranaceus* (20 g), oriental water plantain rhizome (9 g), agaric (9 g), barbed skullcap herb (30 g), plantain seed (10 g), amomum fruit (6 g), and *Costus* root (9 g).

Syndrome of spleen and kidney yang deficiency

Syndromes: Abdominal swelling (especially at night), less urination, sluggish intake of foods, swollen and cold limbs, thin sloppy stools, backache and dizziness, pale complexion, pale and swollen tongue, little tongue fur, and thin and sunken pulse.

Recipes: Prepared monkshood piece (6 g, fried first), pilose asiabell root (20 g), white *Atractylodes* rhizome (10 g), dried ginger (6 g), Shorthorned Epimedium Herb (15 g), Indian bread peel (20 g), oriental water plantain rhizome (9 g), barbed skullcap herb (30 g), plantain seed (9 g), and agaric (10 g).

Syndrome of liver and kidney yin deficiency

Syndrome: Abdominal swelling (especially at night), less urination, thin body statue, feverishness in palms and soles, low fever in the afternoon, dry mouth and lips, back pain and dizziness, dry stool, red tongue with less fluid, less fur or no fur, and stringy pulse with less strings.

Recipes: Anemarrhena rhizome (10 g), bark of Chinese corktree (6 g), dried *Rehmannia* root (12 g), asiatic cornelian cherry fruit (10 g), Chinese yam (10 g), Indian bread (12 g), oriental water plantain rhizome (9 g), moutan bark (30 g), and fried turtle shell (9 g, fried first).

Syndrome of qi and yin deficiency

Syndromes: Abdominal swelling, less urination, thin body, dryness, heat, afternoon chilliness, spontaneous sweating day and night, less food and gastrectasia, thin stool, prone to catching a cold, red tongue with less fur, and thin and sunken pulse.

Recipes: Heterophylly falsestarwort root (12 g), white *Atractylodes* rhizome (9 g), fried *Astragalus* root (30 g), *Asparagus* root (9 g), lilyturf root (9 g), shell of areca nut (9 g), barbed skullcap herb (20 g), oriental water plantain rhizome (9 g), and plantain seed (10 g).

5.8.4.3.10.2 External application of herbal drugs

Herbal drugs, such as kansui root and spurge, are powdered to apply on the belly button. Raw *Astragalus* root (40 g), zedoary (40 g), morning glory seed (50 g), peach kernel (50 g), and safflower (50 g) are cooked in water until a state of thin paste and then applied on the belly button externally.

Raw leech (5 g), centipede (5 pcs), morning glory seed (10 g), kansui root (10 g), semen coicis (20 g), and immature bitter orange (30 g) are powdered and applied on the belly button.

Herbal drugs, including cinnamon, asarum, fistular onion stalk, ginger peel, kansui root, spurge, and flower of lilac daphen, are powdered and applied on the belly button. Some moleplant seeds and two dog buttons are selected; the moleplant seeds are decladed and deoiled; they are then powdered together. Later, they are dipped in vinegar for 2 days until becoming a paste. The abdominal wall is first scrubbed using warm water, and the prepared paste drug is then applied on the belly button of the patient.

Herbal drugs, including kansui root (5 g), borneol (5 g) and lilac flower (5 g), dragons blood (6 g), black catechu (6 g), frankincense (6 g), and myrrh (6 g); are powdered together, then proper amount of vinegar is applied to mix them into a paste, and applied on the belly button, with one drug replacement within 24 hours.

Herbal drugs, such as agaric (15 g), plantain seed (12 g), shell of areca nut (15 g), pokeberry root (5 g), semen coicis (15 g), and zedoary (15 g), are powdered together, then added with honey, and applied on the belly button, with one replacement per day, and 10 days as one therapeutic course.

Kansui root (10 g) and alum (20 g) are powdered together. Later, the kansui root powder is mixed with raw flour paste and applied on the Shenque acupoint of the belly button. At the same time, the alum powder is mixed with boiled rice uniformly and the mixture is stuck in the Yongquan acupoints of the soles of two feet, with one replacement every 3 days, and 5 times in a therapeutic course.

5.8.4.3.10.3 Intravenous injection of herbal drugs

Injections, such as *Astragalus* injection, alkaloids *Sophora flavescen* injection, and coix seed oil injection, can reduce the ascites effectively and have anticancer and immunity-regulating effects.

5.8.4.3.11 Acupuncture therapy

It applies acupoints for acupuncture, moxibustion, or medicinal moxibustion. It shows a better effect of inducing diuresis for removing edema, and its clinical application is simple with definite effects, so it is being popularized. Acupuncture: Its main acupoints include Zhongwan, Zusanli, Sanyinjiao, Shuifen, and Qihai. Auxiliary acupoints: They include Zhongji, Shuidao, Guanyuan, YInlingquan, and Tianshu. Apply once or twice each day, and five times in one therapeutic course. Moxibustion therapy: Select acupoints such as Shenque, Guanyuan, Qihai, Zhongwa, and Zusanli; apply one to three times each day, within two to three acupoints each time. Acupoint injection: It shall adopt *Astragalus* injection; two acupoints are selected each time, including Zusanli plus Sanyinjiao, Qihai plus Yinlingquan, and Shuifen plus Zhongwan, totaling once a day. Auricular acupuncture therapy: Select acupoints such as subcortical, spleen, abdomen, Shenmin, adrenal gland, liver, kidney, and sympathetic.

5.8.4.3.11.1 Superior vena cava syndrome

Superior vena cava syndrome is a life-threatening acute syndrome in the medical oncology. It is common clinically and caused by influences that block blood partially or completely when it flows back to the right atrium from the superior vena cava. It can cause patients to suffer from acute or subacute dyspnea and swelling of face and neck. Through clinical examinations, the venous returns of face, neck, upper limbs, and thorax are blocked, showing blood stasis and edema, the further progress of which can cause oxygen deficit and rise of intracranial pressure. A rapid radiotherapy should be applied, especially to the small-cell carcinoma of the lung; radiation therapy is a key therapeutic method. The therapy for the superior vena cava syndrome aims to not only relieve the symptom, but also cure the primary tumor as far as possible. It is for patients with

wide metastasis who require an immediate effect, and chemotherapy is more advisable than radiotherapy. The patient must restrict the intake of sodium salt and liquid. The diuretics show sound effect on relieving the edemas on neck, face, and upper limbs, while the oxygen-absorbing remission can cause dyspnea. In addition, the glucocorticoid hormone can relieve any inflammatory reaction caused by edema around tumor and radiotherapy.

Although a routine therapy by Western medicine is applied, herbal medicine features a treatment based on syndrome differentiation that has a certain effect, and the integrative treatments can improve the clinical effect. The combination of RF local hyperthermia with radiotherapy and chemotherapy shows a synergistic effect. Hyperthermia has effects such as reduction of cancer load, improvement of circulation, and elimination of edema, which can relieve the oppression symptom and alleviate the adverse reactions of radiotherapy. Its combination with a routine therapy of Western medicine can improve therapeutic effects. In addition, hyperthermia is combined with therapies such as expulsion of toxins, which can improve the immunity of the patient, relieve any adverse reaction of radiotherapy and chemotherapy, and it shows certain advantages in aspects such as symptomatic treatment and etiological treatment.

Local hyperthermia is applied to the superior vena cava syndrome, totaling 60 minutes each time and once again every other day. After the remission of symptoms, it should be applied 8–10 times to solidify the therapeutic effect, and then the maintenance therapies can be reduced to 2–3 times each week. Hyperthermia and chelation detoxification therapy can be conducted simultaneously. The chelation detoxification therapy is applied by the administration of large doses of vitamin C, totaling 1–1.5 g/kg according to the patient's body weight, for which the venous injection is applied every other day. The intravenous drop infusion for chelation detoxification therapy requires over 2 hours and the dosage should be increased if there is not any adverse reaction.

5.9 OPPRESSION SYMPTOM CAUSED BY CANCER METASTASES

Cancer metastases result in the following situations: (1) When cancer cells invade the recurrent laryngeal nerve, they can result in vocal cord paralysis and husky voices, tumor oppression, and short breath and sensitive dry cough caused by invasion on the trachea and bronchus. (2) The invasion on the vagus nerve can cause an acceleration of heart rates. (3) The invasion on the brachial plexus can cause arm soreness, pain, and abnormal sensation. (4) The oppression on the superior vena cava can lead to the superior vena cava compression syndrome. (5) Cancerous metastasis in important organs can cause complications such as yellow abscess, ascites, liver failure, dyspnea, and coma. For respiratory tract obstruction caused by the oppression on the trachea, consider a trachea support implanted to improve the respiratory condition. For the oppression on the superior vena cava, radiotherapy can be applied and local hyperthermia can be conducted to increase the radiotherapy effect. After radiotherapy, local hyperthermia should be conducted within 2 hours, aiming, first, to sensitize the therapeutic effect of the radiotherapy, and second, to relieve any local skin damage, fibrosis, and local tissue adhesion. An implanted frame is contraindication for hyperthermia, and chelation detoxification therapy, medical ozone, and Chinese medicine can relieve the side effects of radiotherapy and enhance the anticancer effect.

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6

Integrative hyperthermia treatments for different types of cancer

Modern cancer therapy emphasizes integrative treatments. With the transformation of the medical model from biomedical model to biopsychosocial medical model, cancer therapy is no longer a single treatment for diseases but is the best mode that stresses participation of a variety of means and disciplines and is people-oriented. It not only focuses on cancer control and prolonging survival but also pays more attention to the patient's overall quality of life by adopting measures suitable to the patient, place, and time. It emphasizes a combination of treatment methods customized for the patient and strives to obtain comprehensiveness in diagnosis and treatment of cancer diseases.

Surgery, radiotherapy, chemotherapy, biological therapy, traditional Chinese medicine (TCM), and so on are the primary means for cancer treatment. In recent years, with the rise and rapid development of hyperthermia techniques, hyperthermia has become the fifth main means for cancer therapy following surgery, radiotherapy, chemotherapy, and biological therapy. Domestic and international clinical research and observations have shown that hyperthermia for cancer has documented beneficial effect with no significant side effects. With synergistic interactions with a variety of tumor therapies, it is now playing an important role in the integrative treatments of cancer.

The author has achieved gratifying results at Clifford Hospital after years of clinical practice of combining hyperthermia with conventional cancer treatments. With his staff, the author has creatively put forward the concept of "Nontoxic Integrative Cancer Treatments." It includes medical ozone therapy, chelation and detoxification therapy, traditional Chinese medicine, acupuncture, cell therapy, systemic biofeedback therapy, diet nutrition, alkaline therapy, minimal invasion, and other "green therapies," with nontoxic or low toxic side effects, that are organically combined with hyperthermia and conventional cancer treatments. The author has continuously recruited foreign experts for guidance on new international technologies and methods and has carried out "Combined Therapy for Cancers and Expert Consultation System" in Clifford Hospital, emphasizing that multidisciplinary experts with multiple specialties should join the effort for cancer treatment. They are to discuss and design optimized antineoplastic protocols based on the disease itself and with the consideration of the patient's individual genetic background, physical condition, living environment, psychology, and other factors. They then fully participate in the implementation and revision of treatments to ensure standardization and internationalization of treatments and management. As shown in clinical validations, the Nontoxic Integrative Cancer Treatments and Expert Consultation System have brought new hope to innumerable cancer patients, especially those with medium-advanced cancers. It embodies dialectics of scientific treatments for cancer and ensures the most appropriate combined therapy to achieve the purpose of controlling cancers, extending survival time, and improving the quality of life of the patients.

6.1 SUPERFICIAL TUMORS

The common superficial tumors are lymph node metastases, thoracic and abdominal wall metastatic carcinoma, breast cancer, vulvar cancer, malignant melanoma, and so on. Because technologically it is not difficult to apply local heating on the surface of the tumor, early clinical hyperthermia trials basically started on superficial tumors, which confirmed the effectiveness of hyperthermia and laid the foundation for promoting the development of hyperthermia to heat deep tumors and the whole body.

The general manifestation is a local mass with or without pain and discomfort, and mass oppression or ulceration appears in the late stage. Surgical removal is preferred. If metastasis occurs, address mainly the primary disease. Systemic chemotherapy or radiotherapy can be considered if the patient's primary disease is chemotherapy sensitive; chemotherapy commonly uses combined therapy. For patients with advanced cancer, consider applying integrative treatments of hyperthermia, chelation detoxification, oxygen, and traditional Chinese medicine.

Superficial tumors that are treated clinically by hyperthermia mainly include head and neck lymph node metastases, chest wall invasion after mammary cancer operation, malignant melanoma, and some superficial soft tissue sarcomas. Heating methods applied clinically are mainly microwave, radio-frequency local hyperthermia, and infrared whole-body hyperthermia.

6.1.1 Hyperthermia and surgical treatment

Patients with early superficial tumor lesions that are localized and without peripheral invasion and metastasis, and those with clear indications for surgery, can choose to have radical surgery. Nontoxic integrative treatment can be conducted during the perioperative period, such as medical ozone, chelation detoxification, TCM, acupuncture, and herbs. It can significantly improve the patient's tolerance to surgery, promote postoperative rehabilitation, and prevent occurrence of postoperative implantation metastasis and other circumstances.

Hyperthermia can start to be applied after the postoperative wound is completely healed, after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, after laboratory tests reveal no bleeding tendency, and after comprehensive assessment of patients by their hyperthermia center physician. It is recommended to have whole-body hyperthermia four to six times at intervals of 10–14 days. Choose microwave hyperthermia for local hyperthermia, once every other day, 20 times as a course of treatment for a total of three courses.

Pay attention to monitoring of body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Apply local hyperthermia during intermission periods of whole-body hyperthermia.

For patients who cannot tolerate whole-body hyperthermia, local hyperthermia for lesions or systemic middle-low temperature hyperthermia can be carried out once every other day for local hyperthermia 20 times as a course of treatment for a total of three courses. Carry out systemic middle-low temperature hyperthermia once a week for a total of 12 times.

For patients with metastatic superficial tumors with a solitary nodule who are in good general condition and whose expected survival times are more than 6 months or whose tumors affect activities, surgery may be considered. Implement hyperthermia and other integrative treatments after surgery targeting the original disease.

6.1.2 Hyperthermia and radiotherapy

Hyperthermia may be implemented after radiotherapy for some superficial tumors sensitive to radiotherapy. Combined application of hyperthermia with radiotherapy may increase the sensitivity of tumor cells to radiotherapy, thereby reduce the radiation dosage required to kill the tumor, and reduce skin and hematological toxicity induced by radiotherapy.

For combination order, using radiotherapy first and then hyperthermia is appropriate. It is mostly advised to carry out local hyperthermia within 2 hours after radiotherapy. Implement local hyperthermia once every other day in full cooperation with radiotherapy.

6.1.3 Hyperthermia and chemotherapy

For patients with primary diseases sensitive to chemotherapy, systemic chemotherapy may be considered, which commonly uses combined therapy. Simultaneous application of whole-body hyperthermia with

chemotherapy and simultaneous coordination with the cycle of chemotherapy are recommended for patients who are assessed to be in generally good condition and able to tolerate whole-body hyperthermia. Typically, six to eight courses are needed and local hyperthermia can be applied during the intermission periods of the whole-body hyperthermia.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body hyperthermia can be carried out in the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Simultaneously carry out hyperthermia and chemotherapy cycles for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

For patients who cannot tolerate whole-body hyperthermia, local hyperthermia or whole-body hyperthermia with middle-low temperature can be carried out. Local hyperthermia can be alternately conducted between the primary tumor and the metastases and may continue in the intermission periods of chemotherapy, once every other day. The total number of coordinated local hyperthermias is about 30–40 times during chemotherapy. Conduct whole-body hyperthermia with middle-low temperature once a week for a total of 12 times.

6.1.4 Hyperthermia and chelation detoxification therapy

Chelation detoxification therapy can be given from the time of the physical operation to chemotherapy to patients with physical weakness and low immunity after the operation. It promotes physical recovery and regulates the immune system, and it can kill residual tumor cells or inhibit early metastasis.

Local hyperthermia and chelation detoxification therapy: According to extensive research information, the combined application of hyperthermia and chelation detoxification can increase efficacy. Conduct local hyperthermia and chelation detoxification therapy at the same time. Carry out continuous intravenous infusion for over 2 hours once every other day 20 times as a course of treatment for a total of three courses.

6.1.5 Hyperthermia and medical ozone therapy

Patients' blood circulation is accelerated and cell activity increased after hyperthermia. As a result, it is better to conduct medical ozone therapy again within 2 hours after hyperthermia to increase the effect of medical ozone therapy in killing cancer cells, enhance the role of body immunity, and increase the efficacy of medical ozone. Extracorporeal blood oxygenation and ozonation (EBOO) is preferred once every other day with 20 times as a course of treatment. Reduce to once a week after three courses of treatment, and carry out long-term maintenance treatment; or, choose medical ozone saline infusion once every other day, with 10–14 days on a course of treatment for a total of three courses. Conduct medical ozone major autohemotherapy once every other day, 12 times as a course of treatment for a total of three treatments.

6.1.6 Hyperthermia and other treatments

The combined application of other integrative treatments such as TCM, acupuncture, DC-CIK (Dendritic Cell, DC; Cytokine-Induced Killer, CIK) cell therapy, systemic biofeedback treatment, and alkaline treatment with hyperthermia can increase the effectiveness and safety of the treatment.

TCM: Conduct treatment based on syndrome differentiation. For example, Chinese medicine treatment of skin cancer includes internal treatment and external treatment.

6.1.6.1 INTERNAL TREATMENT

Etiology and pathogenesis of skin cancer are mostly liver qi depression, liver fire and blood dryness, and the combination of wind and toxicity. The treatment should focus on soothing liver-qi stagnation, nourishing liver and blood, and reinforcing primordial qi; the prescriptions recommended are Gardenia Liver Decoction, Xiaoyao Powder, Buzhong Yiqi Decoction, and Shixuan Powder.

6.1.6.2 EXTERNAL TREATMENT

Externally apply Veratrum Ointment, stick with old toad after laparotomy, externally rub with mashed portulaca or its burnt ash and lard oil, triturate eritrichium pedumculare and extract juice for scrubbing, or smash fresh burdock roots and Chinese violet for external application. All of these have a certain effect. External rubbing of plaster-containing arsenicals and intramuscular injection of cinobufotalin have also shown good effects.

6.1.6.3 ACUPUNCTURE TREATMENT

Take skin cancer as an example. Common syndromes of skin cancer are qi stagnation, blood stasis, and phlegm coagulation. The therapeutic principle should focus on promoting blood circulation, removing blood stasis, clearing heat, and eliminating phlegm.

Acupuncture on acupoints: Feishu, Zhongfu, Taiyuan, Zusanli, Pishu, Geshu, Yinlingquan, Fenglong, Taichong, Xuehai, and Weizhong. Methods: all use mild reinforcing–reducing method. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Pishu, Geshu Feishu, Guanyuan, and Zusanli. Methods: take two points each time with the moxa stick; perform moxibustion for 10 minutes per point, once per day. Take 2 days off after five moxibustion treatments, with 10 times as a course of treatment.

Ear acupoints: Subcortex, heart, Erjian, Jiaogan, liver, lung, Shenmen, Fengxi, adrenal gland, and the corresponding parts of lesions. Methods: stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.1.6.4 DC-CIK CELL THERAPY

Malignant melanoma on the body surface is one of the tumors with strong immunogenicity. It occurs on the body surface and is easy to be accessed. Use the patient's own tumor tissue for individualized antigen peptide to prepare specific DC-CIK, which has a clear treatment effect. The number of CIK cells for each reinfusion should reach at least 1×10^{10}, twice a week, with four times as a course of treatment. Conduct periodic review after transfusion. If there is no recurrence, implement an additional treatment every 2 to 3 months.

6.1.6.5 SYSTEMIC BIOFEEDBACK THERAPY

Conduct it three times a week, 15 times as a course. Adjust to one or two times a week after two to three courses for long-term treatment.

Malignant melanoma can gain good effects in immunotherapy, which can effectively improve the immune effect of the treatment and better improve patient survival time and quality of life. Whole-body hyperthermia may be considered: carry out four to six times at intervals of 10–14 days, and conduct DC-CIK cell therapy during the off period.

6.1.6.6 ALKALIZATION TREATMENT

Alkalization treatment adopts the combination therapy of food therapy and sodium bicarbonate. Refer to Section 4.10 for food therapy recipes. Sodium bicarbonate therapy can adopt local or point injection around the tumor. Avoid blood vessels with routine disinfection. Inject 2.5%–5% sodium bicarbonate with a thin needle at multiple points, about 2 mL for each point, for a total of not more than 10 mL each time once every other day with eight times as a course of treatment.

6.1.7 Hyperthermia and herbal medicines

6.1.7.1 HERBAL BATH

Proven prescription 1: Thirty grams each of *Fructus Cnidii*, *Solanum nigrum*, *Patrinia scabiosaefolia Fisch.*, and *dandelion* for decoction and bathing of the affected area, one or two times per day. Efficacy: invigorates

blood circulation, eliminates toxic substances, and removes food retention. It is applicable to patients with skin cancer forming ulcers or outward cauliflower tumor, infection, discharge of pus and juice, fetor, and nastiness.

Proven prescription 2: Erhuang Decoction: *Cortex phellodendri* 30 g, and *wintergreen barberry root* 30 g. Decoct them for external washing or wet compress. Efficacy: clears heat, moistens dryness, and purges fire for detoxification. Applicable to postoperative wound infection of breast cancer, skin flap necrosis, radiodermatitis or local swelling, or ulceration caused by venous leakage of chemotherapeutic drugs.

Proven prescription 3: Sanhuang Lotion: take 30 g each of *Cortex phellodendri*, *rhubarb*, *Radix scutellariae*, and *Sophora flavescens Ait*. Decoct them and wash the affected area. Efficacy: purges fire for detoxification, relieves itching, and induces astringency. It is applicable for radiodermatitis, skin ulceration, watering, and itching induced by radiotherapy for breast cancer.

6.1.7.2 GRILLING METHOD

Proven prescription 1: Millipede Compound Paste: *millipede* (Malu) 6 g, *fresh nettle root* 6 g, *castor seed* 2 g, *stele lime* 1 g, and tobacco leaf powder 1 g. After the millipede is soaked with 95% ethanol, smash it; add the mud of castor seed, stele lime, and tobacco leaf powder. Mix thoroughly. Finally, add the pounded *nettle root* and reconcile evenly. First wash the cancer wound with hydrogen peroxide or physiological saline, coat it with the paste, and then bake the affected area for 20 minutes with divine lamp. Change dressing daily or every other day. Efficacy: activates blood and removes toxicity. It is applicable to skin cancer.

Proven prescription 2: Shengji Yuhong Plaster: *sesame oil* 500 g, *Angelica* 60 g, white wax 60 g, *Glycyrrhiza uralensis* 36 g, *Angelica sinensis* 15 g, *calomelas* 12 g, *Resina draconis* 12 g, and *Lithospermum erythrorhizon* 6 g. Decoct them into plaster. Spread it on the affected area and irradiate for 20 minutes with divine lamp, once a day. Efficacy: activates blood circulation, eliminates necrosis, moistens skin, and promotes granulation. It is applicable to patients with radiation-induced unhealed skin ulcers, postoperative wound infection or flap necrosis, and ulceration of advanced breast cancer tumors.

6.1.7.3 MOXIBUSTION THERAPY

Proven prescription 1: Grind equal amounts of *Squama manitis* (fried with earth) and *Cantharides* to powder. Coat it on affected area and conduct indirect garlic moxibustion with a moxa cone the size of a soybean. Efficacy: resolves phlegm coagulation and treats lymphoma.

Proven prescription 2: Mash the root of raw *Phytolacca americana* to make a cake. Place it on the affected area. Conduct moxibustion with three to four moxa cones. Efficacy: resolves phlegm coagulation and treats lymphoma.

Proven prescription 3: Grind Jiangxi fermented soybean cake into fine powder, and mix it with rice wine to make a pancake the size of a coin, about 6 mm thick. Place it on the affected area and conduct moxa cone moxibustion above the cake, with three to four moxa cones each time. Efficacy: resolves phlegm coagulation and treats lymphoma.

6.1.8 Hyperthermia indications

Patients with Karnofsky performance scores (KPSs) more than 70 points can take whole-body hyperthermia. The general condition of the body should be rigorously assessed for hyperthermia, and select patients with grades ASA I to II. Patients with no large area of ulceration can receive local hyperthermia. If local skin is uneven, a water pillow can be used for treatment.

6.1.9 Hyperthermia contraindications

The main contraindications of whole-body hyperthermia include patients with KPSs less than 70 points; patients with heart failure (above degree II), a history of myocardial infarction, severe arrhythmia, and large intracranial tumors or metastases; patients with signs of high intracranial pressure; and patients with severe liver and kidney dysfunction and bleeding tendencies.

Contraindications of local hyperthermia include local skin damage, bleeding tendency, cachexia, and pacemakers in the treatment areas.

6.1.10 Introduction of a typical case

The patient named Lu, male, 45 years old, was admitted on December 22, 2007 to Clifford Hospital due to "postoperation of the left scrotal skin cancer, chemotherapy for five months, and paroxysmal abdominal pain for 20 days." The patient itched on the skin of his scrotum in July 2007, and repeated scratching resulted in an ulcer that could not be healed. Later, the local skin was resected in Queen Mary Hospital of Hong Kong and pathologically confirmed as "Skin Exocrine Cancer, Ki-67 (+)." At that time, several lymph nodes were found migrating in the abdominal cavity, seen in an abdominal magnetic resonance imaging (MRI). Taxol, cisplatin, methotrexate, and gemcitabine chemotherapies were given (specific program was unknown), as well as tamoxifen treatment. In October 2007, the abdominal cavity was reviewed with the abdominal MRI, showing several lymphadenoceles in bilateral groins, retroperitoneum, and abdominal cavity, with paroxysmal abdominal pain accompanied by shortness of breath, malaise, profuse sweating, and mild edema of the right lower extremity. As a result, he was admitted for further treatment.

Physical examination: Several lymph nodes about 2 cm × 3 cm in size could be reached in bilateral groins. Some were fused and hard with poor mobility and slight tenderness. The right lower extremity had mild edema. The KPS was 80.

Auxiliary examination: Abdominal computed tomography (CT) was carried out after admission. Several lymph nodes were swelling in bilateral groins, retroperitoneum, and abdominal cavity. It was considered to be lymph node metastasis of skin cancer. Blood routine examination: red blood cell (RBC) 4.3×10^{12}/L, Hb 121 g/L, white blood cell (WBC) 6.1×10^{9}/L, and PLT 138×10^{9}/L. Biochemistry: ALT 38 U/L, AST 25 U/L, TBIL 26 U/L and DBIL 14.5 U/L, ALB 38 g/L; ALP 53 U/L, GGT 321 U/L, Cr 56 μmol/L, Ua 235 μmol/L, BUN 6.2 mmol/L, and GLU 4.31 mmol/L. Electrolytes and blood lipids were normal. Tumor markers: CEA 6.1 ng/mL, AFP 5.6 ng/mL, CA-125 4 U/mL, CA-153 3.8 U/mL, CAl9-9 13 mL/L, and TSGF 11.2 U/mL. Immunology items were as follows: IgM (immunoglobulin) 0.7 g/L, and others are normal. Trace elements were normal.

Diagnosis: Scrotum skin exocrine cancer and postoperative chemotherapy, phase III (lymph node metastasis in groins, retroperitoneum, and abdominal cavity).

Integrative treatment prescription: The patient suffered from scrotum skin exocrine cancer. The disease is rare, and there are no mature treatment options. Abdominal lymph node metastases were found during his first visit in Hong Kong. After the primary lesion was resected, a variety of chemotherapy drugs were given. Tamoxifen endocrine therapy was conducted, considering that it was a secretory tumor, but the patient's condition was not able to be controlled. The patient's physical condition was weak after multiple courses of chemotherapy. As a result, TCM treatment and acupuncture treatment were given. The patient showed fatigue, shortness of breath, spontaneous perspiration, mild edema of the right lower limb, loose stool, pink tongue, thin and white tongue coating, slow and sunken pulse, and proven deficiency of both qi and blood. The TCM treatment focused on invigorating qi and blood, draining toxins and astringing sores with the prescription of modified Shiquan Dabu Decoction.

Medications: The specific medications were as follows: *ginseng* 10 g, *Radix rehmanniae Preparata* 12 g, *Atractylodes macrocephala Koidz* 15 g, *Poria cocos* 15 g, *Angelica sinensis* 10 g, *Radix paeoniae Alba* 15 g, *Ligusticum chuanxiong Hort* 10 g, *Radix astragali* 30 g, *Cinnamomum cassia Presl* 5 g, *Radix glycyrrhizae Preparate* 10 g, ginger three slides, Chinese date 8 pieces, one dose per day. Decoct in water for oral dose.

Acupuncture on acupoints: Take Feishu, Zhongfu, Taiyuan, Zusanli, Pishu, Geshu, Yinlingquan, Fenglong, SP10, Weizhong, Linggu, and Dabai for acupuncture. Even reinforcing–reducing method was used for all points. The needles were retained for 20 minutes, once per day. Took 2 days rest after five acupuncture treatments.

Moxibustion on acupoints: Pishu, Geshu, Feishu, Guanyuan, and Zusanli. Selected two points each time and conducted moxibustion for 10 minutes, once per day. Took 2 days rest after five moxibustion treatments.

Auricular acupoints: Took Pizhixia, heart, Erjian, Jiaogan, liver, Shenmen, Fengxi, Shenshangxian, and corresponding parts of lesions, twice a week, and alternated ears.

Meanwhile, alternation of chelation detoxification and intravenous medical ozone were conducted as well as local hyperthermia on the right groin. After 1 week of treatment, the size of the patient's abdomen was reduced, symptoms of shortness of breath and fatigue were significantly improved, and right lower limb edema was eliminated. Whole-body hyperthermia and intraperitoneal chemotherapy were given (a total of four times). The drugs for peritoneal perfusion were cisplatin + mitomycin. Conventional pretreatment was conducted before and after treatment as well as symptomatic and supportive treatment to prevent adverse reactions. Abdomen local hyperthermias were implemented during the interim periods of whole-body hyperthermia. The patient was treated for 50 days before discharge.

Treatment effects: After 50 days of active treatment while being hospitalized, the patient's symptoms of abdominal pain, fatigue, and profuse sweating completely disappeared. Three lymph nodes about 1 cm × 2 cm could be reached at the bilateral groins through physical examination, with middle hardness, fine mobility, and no tenderness. The KPS was 90. The abdomen was reviewed, and CT showed that lymph nodes at the groin, retroperitoneum, and abdominal cavity were significantly reduced after treatment. Subsequently, the patient adhered to the integrative treatments as an outpatient in the hospital, consisting of 5-day treatment every 15 days. To date, the patient's diet and sleep have been normal and he continues to participate in normal work in Hong Kong.

6.1.11 Related research in China and abroad

Li Chuanyun has applied out-of-body hyperthermia treatment to 27 patients, with the surface temperature controlled at 41°C–43°C for about 45 minutes, two times per week, and 3 weeks as a course of treatment. Short-term efficacy: complete remission (CR) rate, 80.8%; partial remission (PR) rate, 10.2%; and no therapeutic value, 9%. In addition to a mild recent radiotherapy and chemotherapy response, patients showed no obvious discomfort. Zhao Yanli et al. conducted randomized controlled trials and clinical observation of 50 cases of patients with superficial malignant tumors. The treatment group was given microwave hyperthermia combined with chemotherapy, and the control group was given single chemotherapy. Hyperthermia was two or three times a week, 3–10 times as a course of treatment. The heating time was 50 minutes each time, and skin temperature of the tumor surface was 42°C–45°C. Different chemotherapy regimens were selected according to different disease categories; they were mainly FVP, FP, CHOP, and CAP. Regimens for both groups were basically the same. Hyperthermia and chemotherapy were carried out simultaneously for combined chemotherapy, or chemotherapy first and then hyperthermia. The efficiency of the treatment group was 74% and the control group 56%; $P < .01$. Arcanmgeli et al. reported that the overall response rate was 95% after thermochemotherapy on 43 patients with cervical lymph node metastasis.

6.2 INTRACRANIAL TUMORS

Intracranial tumors are divided into primary brain tumors and metastatic brain tumors. Brain tumors can occur at any age, approximately 85% being seen in adults. Tumor location is age related and intracranial supratentorial neoplasms are in the majority for adults and infants under 1 year, of which more than 50% are astrocytomas and glioblastomas. Intracranial infratentorial neoplasms are in the majority for children 1–12 years old. The most common is medulloblastoma, followed by astrocytoma and glioblastoma. Brain tumor can be broadly divided into neuroepithelial tumor (mostly astrocytoma), meningiomas, pituitary tumor, neurilemmoma, craniopharyngioma, brain metastases, vascular tumors, congenital tumor, and so on according to histology. Patients with malignant brain tumors (glioma degrees III and IV, medulloblastoma, and brain metastases), compared with tumors in various systems of the body, have shorter survival times, higher mortality rates, more difficult treatments, and a poorer prognosis.

Clinical manifestations are not the same and depend on lesion location, histological type, growth rate, and so on. About 90% of patients manifest dizziness, headache, insomnia, and poor memory. Severe headaches

accompanied by nausea and vomiting suggest that the tumor has reached the advanced stage of intracranial hypertension. Also, some patients may have sensory disturbance, hemianopia, seizures, and other symptoms.

Because overheating of the intracranial tumor can lead to cerebral edema, hyperthermia treatment for intracranial tumor should consist of gradual increases in power and treatment duration. For solid tumors, begin at 60% power and 50% treatment duration.

6.2.1 Conventional treatments

6.2.1.1 Surgical treatment

The hope for surgical cure is greater if brain tumors are more benign with more integrative capsule and are easier to be peeled off, as well as having a shorter duration. However, for tumors with higher degrees of malignancy or other metastatic cancers, palliative operation can be carried out, such as tumor resection, decompression, ventriculocisternostomy, and ventriculovenous shunt. Gamma Knife, X knife, and so on can also be chosen for cytoreductive therapy. For small and medium-sized intracranial tumors with less obvious occupied effect, cryocare therapy can be implemented through percutaneous drilling. For large-scale and irregularly shaped tumors with obvious occupied effect, combination therapy of Ar-He cryoablation with surgical resection can be carried out under direct vision by craniotomy. The surgery can be divided into radical surgery and palliative surgery. Before and after surgery, medical ozone, chelation detoxification, acupuncture, TCM, and other nontoxic integrative treatments can be actively implemented. Focus on regulating immunity, improving preoperative body state, promoting recovery after operations, and reducing the risk of metastasis and recurrence.

6.2.1.2 Radiotherapy

Radiotherapy is one of the important means of adjuvant therapies for brain tumors. Studies have shown that conducting radiotherapy after surgery results in longer survival times than surgery alone. Begin usually 1 to 2 weeks after surgery, and the treatment will take about 4–8 weeks. Determine the range of irradiation and the dosage according to different pathological diagnoses, differentiations, and image results of medical examination of tumors.

6.2.1.3 Chemical treatment

Most drugs cannot pass the blood–brain barrier, and the brain tumor is not sensitive to chemotherapy. As a result, chemotherapy is ineffective. Combined chemotherapy is usually used. Chemotherapy for brain tumors is subject to a number of restrictions. Chemotherapy drugs can only pass vascular endothelial cells through the lipid solubility of the drug and then enter tumor cells for effect. Such a pattern affects the speed and efficiency of the drug.

6.2.1.4 Hyperthermia

For many brain tumors, local hyperthermia can not only directly inhibit tumor growth and promote apoptosis of tumor cells but also help anticancer drugs penetrate the blood–brain barrier, to obtain a good therapeutic effect. If radiotherapy is necessary, combining hyperthermia can reduce radiation damage to brain cells and contribute to the function recovery of normal cells. Whole-body hyperthermia is not conducted under normal circumstances. If there is no postoperative tumor mass effect, whole-body middle-low hyperthermia may be given to improve immune function.

Hyperthermia for intracranial tumor is mainly local hyperthermia. The RF (radio frequency) local hyperthermia machine with automatic tuning function can be used. As intracranial cancer hyperthermia may increase the risk of cerebral edema, some therapeutic measures for reducing cerebral edema and intracranial pressure need to be taken before treatment of patients accompanied with cerebral edema or high cranial pressure. The treatment time and intensity should gradually increase, starting from low values. Generally, begin at 60% of the power for solid tumors. The treatment duration begins at two-thirds of the solid tumors.

6.2.1.5 CHELATION DETOXIFICATION THERAPY

A lot of vitamins can penetrate the blood–brain barrier and therefore be able to produce anticancer effects. Combining with hyperthermia at the same time, the effect is more obvious. Chelation detoxification therapy adopts intravenous infusion in clinical practice and effectively removes heavy metals in the body, and other toxins. Recommend conducting chelation detoxification treatment once every other day, with 20 times as a course of treatment. It is best to apply with local hyperthermia, and three continuous courses can bring obvious effect.

6.2.1.6 MEDICAL OZONE THERAPY

Medical ozone therapy can increase the oxygen supply to brain cells; promote the apoptosis of brain tumor cells; inhibit the growth of brain tumors; reduce brain cell edema caused by a variety of treatments; and stabilize mitochondria, Golgi apparatus, and the nucleus of normal cells to avoid damage to normal brain tissues. Medical ozone saline intravenous infusion and medical ozone autohemotherapy can be involved throughout the treatment. Recommend conducting EBOO treatment once every other day, with 20 times as a course of treatment. After three courses of treatment, change to once a week for consolidated therapy or adopt medical ozone saline intravenous infusion and medical ozone autohemotherapy for long-term maintenance.

6.2.1.7 TRADITIONAL CHINESE MEDICINE

The syndrome of phlegm dampness and stasis is commonly seen in brain cancer patients. The prescription of modified Ditan Decoction is used. Use the prescription of Tongluo Sanjie Decoction for the syndrome of phlegm-blood accumulation. Use the prescription of Longdan Xiegan Decoction for the syndrome of excess heat of liver and gallbladder. Use the prescription of Lingjiao Gouteng Decoction for the syndrome of endogenous liver wind. Use the prescription of modified Tongqiao Huoxue Decoction for the syndrome of qi stagnation and blood stasis. Use the prescription of Jinkui Shenqi Pill for the syndrome of spleen yang deficiency and kidney yang deficiency. Chinese formulated products commonly used include Angong Niuhuang Pill, Qingkailing Injection, Bruceolic Oil Emulsion Injection, and Elemenum Emulsion Injection.

6.2.1.8 ACUPUNCTURE

Acupuncture on acupoints: Taiyang, Baihui, Dazhui, Touwei, Fengchi, Hegu, Shangxing, and Zusanli. Methods: even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days rest after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Yuanguan, Baihui, Zusanli, and Dazhui. Methods: select two points each time. Conduct moxibustion 10 minutes for each point. Use the two groups alternately, once a day. Take 2 days rest after five moxibustion treatments, with 10 times as a course of treatment.

Auricular acupoints: Shenmen, Jiaogan, subcortex, cheeks, forehead, liver, and adrenal gland. Methods: four to six points are selected each time. Penetrate with filiform needle. Retain the needle for 30–60 minutes after fast twist, once a day with 10 times as a course of treatment, or stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes twice a week. Alternate both ears, with 10 times as a course of treatment.

6.2.1.9 DIET, NUTRITION, AND SO ON

Nutrition therapy is extremely important when brain tumors affect the feeding center, or the digestive system center of patients is abnormal. It is necessary to ensure proper nutritional intake to maintain the patient's physical strength and immunity. Qigong, psychology, music therapy, and other treatments contribute to the rehabilitation of patients with brain tumors, especially when patients have obvious neurological symptoms affecting sleep and mood disorders.

6.2.1.10 OTHERS

Because brain tumors are often accompanied by cerebral edema, nerve damage, and other complications, along with simultaneously conducting nontoxic integrative treatments, we should also support and appropriately

select Western medicines for nourishing nerve cells and use Western medicines such as mannitol for dropping intracranial pressure to achieve symptomatic relief. Resolve complications quickly and in a timely manner to relieve symptoms, and strive for a comprehensive and integrated treatment time. Combining with DC-CIK cell therapy helps to improve the treatment outcome. The combined systemic biofeedback treatment can help relieve symptoms and improve quality of life. Conduct treatment three times a week, with 15 times as a course of treatment. After two to three courses, adjust to one or two times a week for long-term treatment.

6.2.2 Combination of hyperthermia with conventional treatments

6.2.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

If part of the brain tumor has indications for surgery, surgery can be chosen. Gamma Knife, X knife, cryocare, and other cytoreductive therapies can also be applied. As hyperthermia itself has the functions of killing tumors and boosting local immune functions, the application of hyperthermia can be combined before and after surgery. During the implementation of medical ozone, chelation detoxification, TCM, acupuncture treatment, and other nontoxic integrative treatments before and after surgery, combining hyperthermia for comprehensive treatment is conducive to the improvement of efficacy and reduces the probability of metastasis and recurrence. Intracranial cancer hyperthermia is mainly local hyperthermia. Local hyperthermia can be carried out after Gamma Knife or X knife after excluding hyperthermia contraindications through assessment of surgical site recovery by physicians, laboratory tests of no bleeding tendency, and comprehensive assessment of the patient by the hyperthermia center physician. Conduct once every other day, and each treatment time is from 40 minutes to 1 hour (start at 40 minutes and gradually increase to 1 hour based on patients' tolerance, and then maintain it). Generally, 20 times forms a course of treatment.

Local hyperthermia can be directly carried out for patients with no surgical indications, once every other day, with 20 times as a course of treatment for a total of three courses. Patients with no intracranial edema and signs of high intracranial pressure can directly receive local hyperthermia. Patients with intracranial edema but without obvious signs of high intracranial pressure can first receive dehydration therapy with mannite and, after the use of dexamethasone 1 to 2 mg, undergo local hyperthermia. Patients with significantly high intracranial pressure are required to reduce the intracranial pressure before local hyperthermia can be carried out.

6.2.2.2 HYPERTHERMIA AND RADIOTHERAPY

The combination of hyperthermia and radiotherapy can reduce the radiation damage to the brain cells, contribute to the functional recovery of normal cells, and increase the sensitivity of tumor cells to radiotherapy. The side effects of radiotherapy can be appropriately reduced if radiotherapy is conducted at the same time.

Radiotherapy followed by hyperthermia is appropriate as the combination order, with local hyperthermia being carried out within 2 hours after radiotherapy. Implement hyperthermia once every other day. Hyperthermia supports radiotherapy during the whole course.

6.2.2.3 HYPERTHERMIA AND CHEMOTHERAPY

For many brain tumors, local hyperthermia can not only directly inhibit tumor growth and promote apoptosis of tumor cells but also help anticancer drugs penetrate the blood–brain barrier to obtain a good therapeutic effect. Studies have shown that the combination of hyperthermia and chemotherapy has a synergistic interaction. Local hyperthermia is mainly adopted for brain tumors; it is conducted at the same time as chemotherapy or after the end of chemotherapy administration. Local hyperthermia can be carried out during chemotherapy once every other day, and each treatment lasts for 40 minutes to 1 hour (start at 40 minutes and gradually increase to 1 hour based on the patient's tolerance, and then maintain it). A total of about 30–40 times of hyperthermia treatment are to be carried out. At present, there is no evidence that hyperthermia can increase side effects of chemotherapy. Implement conventional prevention of adverse reactions during the treatment. Due to the tension felt by the patients in hyperthermia treatment process or individual

patient discomfort caused by the rise of head temperature, which can aggravate the patient's adverse reactions to chemotherapy, psychological comfort and treatment education should be provided before and after the treatment. Be sure to ask about the patient's feelings during the course of treatment from time to time to promote smooth treatment.

6.2.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Simultaneously delivering chelation detoxification therapy during hyperthermia treatment process has a synergistic effect. Intravenous infusion over 2 hours is needed for chelation detoxification therapy, with 20 times being a course of treatment for a total of three courses.

6.2.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing tumor cells, enhance the effect on immunity, and increase the efficacy of medical ozone. Medical ozone therapy may promote apoptosis of brain tumor cells; inhibit the growth of brain tumor; reduce edema of brain cells caused by a variety of treatments; and stabilize mitochondria, Golgi apparatus, and the nucleus of normal cells to avoid damage to normal brain tissues. Medical ozone therapy selects EBOO, once every other day, 20 times as a course of treatment for a total of three courses. Change to once a week after the end of treatment for consolidated therapy.

6.2.2.6 HYPERTHERMIA AND OTHER TREATMENTS

Glioma has poor sensitivity to radiotherapy and chemotherapy and has a certain effect in immunotherapy. Combining other treatments such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback therapy treatment, and other integrative treatments with the application of hyperthermia can increase the effectiveness and safety of the treatment.

6.2.2.7 HYPERTHERMIA AND HERBAL MEDICINES

Fumigation therapy: Snakeweed vapor. Diffusa 100 g, *Rhizoma amorphophalli* (konjac) 100 g, *Prunella vulgaris* 100 g, fried *Fructus xanthii* 60 g, *Polygala tenuifolia* 60 g, *Acorus tatarinowii Schott* 60 g, *Rhizoma paridis* 60 g, and *borneol* 20 g. Add suitable amount of water and boil the mixture for about 10 minutes on a small fire. Lean the hot soup toward patient's mouth and nose and have the patient naturally inhale the steam of the drug. Efficacy: detoxification, removal of stasis, and elimination of phlegm for resuscitation. It is applicable to brain tumor patients.

6.2.3 Introduction of a typical case

A patient named Li, female, aged 28 years, was admitted on December 26, 2008, to Clifford Hospital due to more than 2 years of intracranial space occupation and more than a month of headaches and dizziness with aggravation for 1 day. The patient was found to have left intracranial space occupation during examination in December 2006. At that time, she had no headaches, dizziness, nausea, vomiting, blurred vision, and hearing loss, so no special treatment was provided. In early November 2008, the patient suffered from headaches and dizziness as well as periodic nausea and vomiting, promoting her to visit a local hospital for treatment. The cranial CT examination revealed the following: "tumors on the right thalamus and parietal lobe, possible glioma, abnormal signal projection on the left parietal lobe, and obvious edema zone." On November 5, 2008, "resection of intracranial tumor" was performed. Postoperative pathology: oligoastrocytoma level 2. Postoperative recovery was good. More than a month later and due to a hard journey, the patient experienced aggravated headaches and dizziness, with nausea and vomiting, and was then admitted to the Clifford Hospital's emergency department.

Physical examination: Symptoms seen on the admission day included headache, dizziness, nausea, and vomiting; walking was affected. There was no tinnitus; there was numbness and movement disorder, poor appetite, good sleep, smooth discharge at urination and defecation, pink tongue, sublingual vein cyanosis,

thin and white fur, and weak and unsmooth pulse. General condition was fine through physical examination. Two surgical scars 7 cm long in a curved shape were visible on the top right of the head. Superficial lymph nodes were not palpable as swelling. Neck was soft without resistance. Breathing sounds of double lung were clear, and wet and dry rales were not heard. Heart rate was 72 times per minute with regular rhythm and without noise. Abdomen was soft. Liver and spleen were not palpable under ribs. There were no tenderness and rebound tenderness in the whole abdomen. Bowel sounds were normal. Four limbs could move freely and without movement disorder. Physiological reflex existed. Pathological signs were not elicited. Blood routine was checked on admission: WBC 3.56×10^9/L, RBC 3.43×10^{12}/L, HGB 113 g/L, and PLT 281×10^9/L; biochemistry: GGT 159 U/L, urea 2.49 mmol/L, and Cr 133 μmol/L.

Auxiliary examination: Head CT (taken at Hainan Provincial People's Hospital on December 8, 2008) showed postoperative right parietal glioma. Compared to the old film, surgical area had edema with a little accumulation of blood. There were no significant changes in the lesion on the left parietal lobe. There was a small quantity of effusion on the right top of the frontal and temporal lobes. There was accumulation of blood under the scalp of the right occipital–parietal lobe. She had sphenoiditis and mastoiditis on the right side.

Diagnosis: Postoperative cerebral astrocytoma.

Integrative treatment prescription: After admission, tumor experts conducted consultations and considered that the patient was in the postoperative recovery phase. First, they reduced the intracranial pressure, increased WBCs, complemented nutrition, and conducted symptomatic treatments. Then, they gave temozolomide 150 mg qd × 5/28 days for oral chemotherapy, TCM, acupuncture, local hyperthermia, chelation detoxification, Keliu mixture, medical ozone, and other comprehensive treatments. The patient's symptom belonged to the type of blood stasis obstructing the interior, and as a result herbal medicines for activating blood, reducing swelling, resolving phlegm, and removing blood stasis were used.

Medications: The prescription was the mixture of brain tumor potion and Sanlengjian Pill. Specific medication: *Rhizoma sparganii* 15 g, *Fructus Polygoni orientalis* 10 g, *Rhizoma curcumae* 15 g, *Radix paeoniae Rubra* 15 g, *Poria cocos* 15 g, raw *Semen coicis* 30 g, scorpion 5 g, *centipede* 5 g, *Hedyotis diffusa Willd* 30 g, and Liuwei Dihuang Pill 12 g, one dose per day. Decocted in water for oral intake.

Acupuncture on acupoints: Taiyang, Baihui, Dazhui, Touwei, Fengchi, Hegu, Shangxing, Zusanli, Sanchongxue, and Waisanguan. Methods: even reinforcing–reducing method was used for acupuncture. Retain the needle for 20 minutes, once a day. Took 2 days rest after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Baihui, Zusanli, and Dazhui. Methods: selected two points each time. Conducted moxibustion 10 minutes for each point. Used the two groups interchangeably, once per day. Took 2 days rest after five treatments of moxibustion.

Auricular acupoints: Shenmen, Jiaogan, subcortex, cheek, forehead, liver, and adrenal gland. Methods: stick auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week. Alternated both ears.

Local hyperthermia was conducted on the head once every other day. At the same time, gave chelation detoxification therapy once every other day, Keliu mixture one dose per day, and medical ozone therapy once every other day (conducted alternately with chelation detoxification). After 1 week of treatment, the patient's various symptoms basically disappeared. Treatments of hyperthermia, chelation detoxification, EBOO, acupuncture, and TCM were continued. She was discharged a month later because her condition had improved. Integrative outpatient treatments were continuously implemented after 1 week of discharge from the hospital for more than 3 months. She was in a stable condition and did not show symptoms of high intracranial pressure. During this period, 36 treatments of hyperthermia were carried out as well as 45 treatments of chelation detoxification therapy and medical ozone therapy.

Treatment effects: After the combined treatment, the patient's symptoms were completely relieved. Her diet was normal when she was discharged, and she gained 3 kg in weight. Her four limbs moved freely. She could take care of herself. One week after discharge, she came back to the hospital for oral chemotherapy with temozolomide + nontoxic integrative treatments (including TCM, chelation detoxification, hyperthermia, medical ozone, Clifford Anticancer Composition, and acupuncture). She adhered to the treatment for 3 months and was then given a brain MRI, prompting changes of "postoperative right parietal cerebral astrocytoma." By comparing with the MRI film of December 8, 2008 (film taken outside the hospital), it was found

that the lesion was reduced; thus, she was recommended to continue nontoxic integrative treatments. She was followed up for more than 4 years and no obvious discomfort was reported. Continued improvement was found in image reviews. The patient worked and lived normally. In 2011, the patient spontaneously labored a child and both mother and child were healthy.

6.2.4 Related research in China and abroad

Qiu Jianwu et al. observed the impact of the temperature of 45°C combined with cisplatin on the proliferation and apoptosis of U251 human glioma cells through in vitro testing with randomized control. The results showed that the temperature of 45°C combined with cisplatin could inhibit proliferation of U251 human glioma cells and induce apoptosis.

The team of Hüseyin Sahinbas et al. conducted a clinical retrospective study of deep hyperthermia for glioma treatment and used 13.56 MHz RF heating, power of 40–150 W, and more than 90% of the treatment time was maintained at 40°C or above for hyperthermia. Studies have shown that hyperthermia alone or combination of hyperthermia and chemotherapy can extend the survival time of patients with glioma. Also, the patients have good tolerance, with no significant adverse reactions. Local hyperthermia can improve the anticancer effect of molecular biology.

Studies by Hauck et al. have shown that hyperthermia can increase five to eight times the level of the mucin chimeric monoclonal antibody ch81C6 taken in by the tumor-bearing mouse glioma cell line D54. In addition, studies by Hirschberg et al. have also shown that hyperthermia can enhance the effect of photodynamic therapy for glioma treatment.

Studies by Aoki et al. have found that when they used thermosensitive liposome to encapsulate doxorubicin for rat glioma treatment, and when the tumor center was heated to 43°C, the drug concentration was higher than free doxorubicin and the experimental animals survived significantly longer.

6.3 ORAL CANCER

Oral cancer is a general term for malignant tumors occurring in the oral cavity. Most oral cancers are squamous cell carcinomas. Generalized oral cancers refer to cancers occurring in the area below the orbit and above the neck and can occur in any part of the tongue, cheek, jaw, and periodontal tissue. Oral cancers in the narrow sense mainly refer to all the tissues that can be seen in the oral cavity. Common clinical oral cancers include lip cancer, carcinoma of gingiva, tongue cancer, soft and hard palate cancer, jaw cancer, carcinoma of mouth floor, oropharyngeal cancer, salivary gland carcinoma, maxillary sinus carcinoma, and mucocutaneous cancers occurring on facial skin. Predilection age is between 40 and 70 years. The incidence for men is one to five times higher than that for women. Smoking and drinking are the most important risk factors that lead to oral cancers. Early symptoms include unexplained lumps in the mouth or neck; limited tongue movement that results in difficulties in chewing, swallowing, or speaking; loss of sensation and numbness in hemitongue; partial swelling and pain of jaw bone or limitation of opening mouth; recurrent lip ulceration; and scab. The prognosis is poor due to the difficulty of oral cancer surgery and the complex anatomy.

6.3.1 Conventional treatments

6.3.1.1 SURGERY

Surgery is the preferred treatment method for the vast majority of early oral cancers. For patients with advanced oral cancers, combined treatment must be performed to achieve good therapeutic effect. Surgery can be used under the following conditions: there is no distant metastasis and the primary tumor and neck metastases can be resected within secure borders; radiotherapy has poor effect on lesions; and oral function damage caused by surgical resection is not predicted to be severe, or a considerable degree of compensation can be achieved by reconstruction or other means with the consent of the patient.

6.3.1.2 RADIOTHERAPY

Radiotherapy alone for oral cancers can be applied, and it can be combined with surgery and chemotherapy. The radical effects of radiotherapy alone for early oral cancer are basically similar to those of radical surgery. Some patients who are inoperable due to poor health (such as severe cardiovascular and cerebrovascular diseases) are in the advanced stage. Those with postoperative recurrence or metastasis can receive radiotherapy to achieve the palliative effects of tumor reduction and prolonged survival time. For the majority of middle-advanced patients, radiotherapy should be used as part of integrative treatments because preoperative, intraoperative, and postoperative radiotherapy can significantly reduce the rate of local recurrence and raise survival rate.

6.3.1.3 CHEMOTHERAPY

The majority of head and neck cancers are squamous cell carcinomas with low sensitivity to chemotherapy. Single chemotherapy is rarely used in the treatment of head and neck cancers, but it is often used with radiotherapy or surgical treatment for comprehensive application or combined with radiotherapy. It is used for the palliative treatment of advanced head and neck cancers or recurrent carcinomas.

6.3.1.4 HYPERTHERMIA

Hyperthermia has a synergistic interaction with chemoradiotherapy in addition to having a direct killing effect on cancer cells. Thermoradiotherapy can improve the surgical resection rate and reduce the recurrence rate before oral cancer surgery and can be effective in reducing the recurrence rate or increasing the rate of tumor control, and prolonging survival time after the surgery. Oral cancers are less sensitive to chemotherapy; the sensitizing effect of hyperthermia on chemotherapy has a crucial role in advanced patients in palliative chemotherapy. Hyperthermia has a positive immunomodulatory effect on the body and can effectively control metastasis. Local hyperthermia and whole-body hyperthermia also have a positive effect on oral cancer lymph node metastasis. Studies have shown that interstitial hypertherapy using ThermoSeed, which has increased in use in recent years, has gratifying effects in the treatment of oral cancer.

6.3.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can not only clear heavy metals and other toxins from the body but also enhance immune function; reduce the incidence of surgical infections; reduce radiotherapy-induced leukopenia, radiation dermatitis, and other side effects; and reduce other complications caused by bone marrow suppression after chemotherapy. Oral cancers have poor prognosis. Chelation detoxification therapy should be applied at the early stage in the treatment of oral cancers, and throughout the whole process of treatment, focusing on the combination of chemoradiotherapy and hyperthermia. Chelation detoxification therapy that is applied "at the early stage, with enough quantity, throughout the whole process, and integratively" can effectively extend survival time and improve the quality of life of patients.

6.3.1.6 MEDICAL OZONE THERAPY

Medical ozone has positive immunomodulatory and anticancer effects and can be carried out at the early stage and throughout the whole process of treatment. EBOO is mostly applied at the early stage once every other day, with 20 times as a course of treatment for a total of three courses. Patients in poor physical condition or with active bleeding are subject to medical ozone saline infusion once every other day, with 12 times per course of treatment for a total of three courses, or medical ozone autohemotherapy once every other day, with 12 times per course of treatment for a total of three courses. Also, medical ozone acupoint injection can be applied once every 3 days, with eight times for one course of treatment. Long-term maintenance therapy is allowed. Medical ozone saline can effectively alleviate radiotherapy-induced stomatitis, ulcers, pharyngitis, and so on and is used two to five times per course of treatment. Medical ozone olive oil is used for the treatment of radiotherapy-induced skin damage, all kinds of wounds, and skin rashes; it is applied to the affected area one to four times a day. Medical ozone saline aerosol inhalation is used for radioactive inflammation of the mouth.

6.3.1.7 TRADITIONAL CHINESE MEDICINE

For the symptom of virulent fire and blood stasis, Daochi Powder is given; for the symptom of excessive noxious heat, Berberine Detoxification Decoction is given; and for the symptom of deficiency of vital energy with blood stasis, modified Bazhen decoction is given. Chinese formulated products commonly used are Liushen Pill, Xihuang Pill, Pientzehuang Pill, and Meihuadianshe Pill. For external treatment, Superior Sore Throat Powder, Pearl Bingpeng Powder, Shuicheng Paste, Rose Powder, Gold Elixir, and Babylon Weeping Willow Flower Powder are used.

6.3.1.8 ACUPUNCTURE

The principle of acupuncture focuses on clearing away heat and toxic substances as well as reducing swelling and resolving mass.

Acupuncture on acupoints: Hegu, Dicang, Chengjiang, Zusanli, Jiache, Sanyinjiao, Jinjin, Yuye, Lianquan, Yingxiang, and Neiting.

Methods: even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once per day. Take 2 days rest after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Xiaguan, Hegu, Jiache, Dicang, Lianquan, Laogong, Quchi, Sanyinjiao, and Taixi.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Heart, mouth, tongue, throat, spleen, stomach, Jiaogan, forehead, and temporal bone.

Methods: Select four to six points each time. Penetrate with filiform needle. Retain the needle for 30–60 minutes after fast twist, once a day with 10 times as a course of treatment, or stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, two times a week. Alternate ears, with 10 times as a course of treatment.

6.3.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Early-stage nutrition is provided mainly through medicated diet conditioning. For patients with radiotherapy inflammation and difficulty in swallowing, indwell gastric tube or conduct fistulization for nutritious meal injection. For medium-advanced patients who can eat, nutrition is mainly given through medicated conditioning. Those who cannot eat, if necessary, are given total parenteral nutrition. Meanwhile, combine qigong, sports, and music therapy to strengthen psychological adjustment and enhance the patient's self-healing powers and confidence in the treatment.

6.3.1.10 OTHERS

If common bleeding, radioactive inflammation, and other complications that seriously affect the quality of life result from oral cancer radiotherapy, nontoxic integrative treatments or Western medicine treatments must be applied in a timely manner during the course of treatment to rapidly relieve these complications and relieve the pain in the shortest possible time. In recent years, it has been reported that the combination of biological immune therapy with surgery and chemotherapy has a certain effect in the treatment of oral cancers.

6.3.2 Combination of hyperthermia with conventional treatments

6.3.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

If early-stage oral cancer has no neck lymph node metastasis, surgery is possible. For medium-stage patients, radiotherapy can be carried out first and then surgical treatment. Whole-body medium-high temperature hyperthermia may be given after the postoperative wound is completely healed, after excluding hyperthermia contraindications through the assessment of surgical site recovery by physicians, if laboratory tests reveal no bleeding tendency, and after the comprehensive assessment of the patient by the hyperthermia center

physician to prevent recurrence and metastasis. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Local hyperthermia can be used in the intermission periods of whole-body hyperthermia.

If the patient cannot tolerate whole-body hyperthermia, oral and maxillofacial local hyperthermia or systemic middle-low temperature hyperthermia can be implemented. Local hyperthermia is carried out once every other day, with 25–30 times as a course of treatment. Local hyperthermia can be applied in combination with other approaches in long term treatment. Whole-body middle-low temperature hyperthermia is carried out once a week, for a total of 12 times.

6.3.2.2 HYPERTHERMIA AND RADIOTHERAPY

Medium-advanced oral cancer patients who have no chance of operation can receive radiotherapy. The combination of hyperthermia and radiotherapy may increase the sensitivity of tumor cells to radiotherapy and reduce skin and hematologic toxicity caused by radiotherapy. The order of radiotherapy followed by hyperthermia is appropriate, and many advocate that an interval time of less than 2 hours is appropriate. Hyperthermia mainly adopts oral and maxillofacial local hyperthermia, once every other day and combined with radiotherapy for the whole process. From a clinical point of view, combining hyperthermia with radiotherapy can significantly reduce bone marrow suppression and skin damage caused by radiotherapy, and it is conducive to the successful completion of treatment. The first course of hyperthermia is maintained up to 2 weeks after the end of radiotherapy. Adjust to whole-body hyperthermia in the recovery period. From a clinical point of view, combining hyperthermia with radiotherapy can significantly reduce bone marrow suppression, skin lesions, and tissue damage caused by radiotherapy and is conducive to the successful completion of treatment.

6.3.2.3 HYPERTHERMIA AND CHEMOTHERAPY

Oral cancers have certain sensitivity to chemotherapy, and combination chemotherapy is mostly used for treatment. Hyperthermia has a sensitizing effect to chemotherapy and can be combined for application. Whole-body hyperthermia can be carried out in the first day of chemotherapy. Chemotherapy is implemented simultaneously during the whole-body hyperthermia process and whole-body hyperthermia is combined with chemotherapy treatment, once every 2 to 3 weeks. Local hyperthermia can be given during the intervals of whole-body hyperthermia to improve the efficacy of chemotherapy and reduce the side effects of chemotherapy. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during the whole-body hyperthermia process, and give symptomatic treatment in a timely manner. Antiemetic drug treatment should be given before chemotherapy. It is safe under normal circumstances. If the patient vomits seriously during hyperthermia, it is necessary for timely treatment. When (rare) vomiting is severe, whole-body hyperthermia needs to be suspended. Simultaneously conduct the hyperthermia and chemotherapy cycle for six to eight courses. Local hyperthermia can be carried out during the intermission periods of whole-body hyperthermia and during radiotherapy.

If whole-body hyperthermia is not suitable, oral and maxillofacial local hyperthermia or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day. Chemotherapy may be continued during intermission periods of hyperthermia. Take 1 week rest after two chemotherapy treatments. Conduct whole-body medium-low temperature hyperthermia once a week, for a total of 12 times.

Combined local hyperthermia for the whole process is carried out during chemotherapy. After completion of chemotherapy treatment, local hyperthermia alone can be carried out for 20 times as a course, and for long-term maintenance therapy. Take 15 days rest and continue to the next course of treatment after the end of each course.

6.3.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelating detoxification therapy can effectively remove toxins from the body, and the vitamin it contains can reduce the side effects induced by radiotherapy and isotope therapy. Be sure that intravenous infusion is not less than 2 hours during the course of the treatment, with 20 times being a course of treatment for a total of three courses. Simultaneously conducting hyperthermia and chelation detoxification has a synergistic

enhancement effect. Patients treated with radiotherapy can remain on chelation detoxification treatment for 2 weeks after the end of radiotherapy or isotope therapy and then change to twice a week and maintenance for 3 months. After 3 months, health rehabilitation can be given once a week. Simultaneously conducting chelation detoxification treatment and thermoradiotherapy can fully maximize the synergistic effect.

6.3.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing tumor cells, enhance the effect on immunity, and increase the efficacy of medical ozone. We propose giving EBOO treatment for medical ozone therapy as soon as possible, once every other day, with 20 times as a course of treatment, for a total of three courses. Change to once per week after the end of treatment for consolidated therapy. Medical ozone saline intravenous injection and autohemotherapy have synergistic anticancer effects; they enhance immunity and reduce the side effects of radiotherapy. Usage: once every other day. Conducting hyperthermia 1 day before medical ozone therapy can increase the sensitivity of medical ozone therapy to cancer cells.

6.3.2.6 HYPERTHERMIA AND OTHER TREATMENTS

The cancer treatment that requires integrative treatments includes other treatments, such as cryocare therapy, TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, psychological adjustment, qigong, sports, and music therapy. All these can improve the self-healing capacity and, combined with the application of hyperthermia, can increase treatment efficacy and safety.

DC-CIK cell therapy: DC-CIK can be an adjuvant therapy and applied in combination with chemotherapy. For the combined application of DC-CIK with radiotherapy, adopt the principle that DC-CIK reinfusion is conducted at the intervals of radiotherapy. For example, on the day when radiotherapy is to be conducted, collect the patient's peripheral blood for DC-CIK culture before the start of radiotherapy, and conduct reinfusion at the interval of radiotherapy. One day before chemotherapy, collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, i.e., 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct consolidated therapy every 2 to 3 months. After combination application, immunity of the patient should be significantly higher than with chemotherapy alone.

Systemic biofeedback therapy: This is performed three times a week, with 15 times as a course of treatment. Adjust to one or two times a week after two to three courses of treatment for long-term treatment.

Alkalization treatment can be effective as anticancer treatment, and mouthwash or inhalation of 1.25% sodium bicarbonate solution can control oral cancers and reduce the adverse reactions to radiotherapy.

6.3.2.7 HYPERTHERMIA AND HERBAL MEDICINES

6.3.2.7.1 Fumigation

Proven prescription 1: Selaginella doederleinii 30 g, raw oyster 30 g (Predecoct), *Rhizoma amorphophalli* 30 g (Predecoct), *Flos lonicerae* 15 g, seaweed 15 g, *Radix sophorae Tonkinensis* 12 g, *Prunella vulgaris* 12 g, and *Fructus xanthii* 9 g. Decoct drugs into steam, and have the patients inhale the steam through the mouth. Efficacy: clears away heat and toxic substances, resolves phlegm and softens hard masses, and reduces swelling. It is applicable to patients with the syndrome of heat toxin and coagulated phlegm of oral cancer.

Proven prescription 2: Ercao Shuanghua Decoction: take 30 g each of *Hedyotis diffusa* and *Flos lonicerae*, *Prunella vulgaris* 20 g, and ginseng 3 g. It is applicable to patients with oral cancer after radiotherapy.

Proven prescription 3: Soldago decurrens Lour 30 g, *Scutellaria barbata* 30 g, *Scrophularia ningpoensis* 30 g, *Paris polyphylla Sm.* 30 g, *Radix sophorae Tonkinensis* 15 g, *Fructus arctii* 15 g, *Cremastra appendiculata* 15 g, *Nidus vespae* 15 g, *Prunella vulgaris* 12 g, *Bombyx batryticatus* 12 g, *Gekko* 9 g, *Puffball* 6 g, *Platycodon grandiflorum* 6 g, and *Licorice roots* 6 g. Decoct drugs into steam, and have the patients inhale the steam through both nose and mouth. Efficacy: clears throat heat and removes dampness. It is applicable to patients with the syndrome of accumulated dampness toxicity in the initial-medium term of oral cancer.

Proven prescription 4: Galla chinensis 60 g, *Cremastra appendiculata* 60 g, *Fructus viticis Negundo* 30 g, *Euphorbia pekinensis* 15 g, *Paris polyphylla Sm.* 15 g, *Realgar* 15 g, and musk 1 g. Decoct drugs into steam, and have the patients use both nose and mouth to inhale the steam. Efficacy: removes blood stasis and breaks junction, removes toxins, and induces resuscitation. It is applicable to oral cancer patients with swelling and pain in the throat.

Proven prescription 5: Dandelion 30 g, *Radix isatidis* 20 g, *Rhizoma coptidis* 6 g, *Scutellaria baicalensis Georgi* 15 g, *Cortex moutan* 15 g, *Radix rehmanniae* 15 g, *Bezoar* 10 g, *Radix paeoniae Rubra* 15 g, and *Eclipta alba* 15 g. Decoct it with water for oral dose, and have the patients use both mouth and nose to inhale while steaming. Efficacy: clears away heat and toxic substances, removes phlegm, and resolves mass. It is applicable to oral pharyngeal tumor patients with the syndrome of accumulation of dampness, heat, and blood stasis.

Proven prescription 6: Flos chrysanthemi Indici 30 g, *Herb rubi Parvifolii* 20 g, *Zanthoxylum nitidum* 20 g, *Rhizoma paridis* 20 g, *Radix gentianae* 15 g, *Radix codonopsitis* 20 g, and *Fructus xanthii* 20 g. Decoct with water. Place the hot decoction near the patient's mouth and nose, and have the patient naturally inhale the nature of the drug. Efficacy: clears away heat and toxic substances, diminishes inflammation, and relieves pain. It is applicable to oral cancer after radiotherapy.

Proven prescription 7: Houttuynia cordata Thunb 60 g, *Flos lonicerae* 30 g, *Smilax glabra Roxb* 30 g, *dandelion* 30 g, *Scutellaria baicalensis Georgi* 15 g, and *Paris polyphylla Sm.* 15 g. Add 1000 mL of water into the drug, and decoct it to 300 mL. Put the liquid medicine into the bottle of spray machine, and make the gas orifice point at the oral cavity for inhalation. Use once a day continuously for 5–7 days. Efficacy: clears away heat and toxic substances. It is applicable to patients with oral coinfection.

6.3.2.7.2 Moxibustion therapy

It is applicable to cancer patients with long illness, yang deficiency, and weakness for enhancement of immunity.

Acupoints: The first group of acupoints includes Dazhui, Shenshu (both), and Pishu (both). The second group of acupoints includes Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both).

Herbal cake making: Take equal amounts of Radix Astragali, *Angelica sinensis*, Fructus Psoraleae, Curculigo Orchioides, and rhubarb, and smash them into powder. Filter with a 120 mesh sieve and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm.

Moxibustion: Place the moxa cone with a diameter of 2 cm and a height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints each time, with two groups of points alternated, once every other day, with 24 times as a course of treatment.

Efficacy: Enforces spleen and nourishes kidney for muscularity and general health.

6.3.2.8 HYPERTHERMIA INDICATIONS

Hyperthermia can be applied for any cancers that are suitable for surgery and chemoradiotherapy.

6.3.2.9 HYPERTHERMIA CONTRAINDICATIONS

Patients whose skins have visible damage; patients who have fever with body temperatures above 38.5°C; patients with bleeding tendency; and oral cancer patients with apparent ulcers, tissue decay, or hemorrhage who cannot receive interstitial hyperthermia.

6.3.3 Introduction of a typical case

A patient named Li, 65 years old, was admitted on August 29, 2009, to Clifford Hospital due to "3 months of the pain on the left side of the tongue." From mid-May 2009, the patient felt pain on the left side of the tongue with no obvious inducement. After self-medication (details were unknown), he had not improved. Later, the pain worsened. A new biological biopsy of the tongue was carried out in another hospital, and the pathology results showed (back of the tongue) well-differentiated squamous cell carcinoma. The patient was recommended to have surgical resection after consultation with the hospital. The hemitongue and part of the

mandible needed to be resected. Also, speech and swallowing function might have been greatly affected after surgery. Later, the patient came to Clifford Hospital for treatment.

Physical examination: A neoplasm with the size of approximately 3 cm × 1.5 cm was visible at the left edge of the tongue base. Surface protrusion was about 0.3 cm. Ulcers were visible with tenderness.

Auxiliary examination: Blood routine and liver and kidney function were generally normal. Neck and nasopharynx CT showed that the left edge of the tongue base had pathological changes, which were considered as tongue cancer by combining with pathology. The tongue tonsil thickened. There were several pieces of small lymph node shadows at districts II and III of the bilateral carotid. Abnormal calcification shadows could be seen under the skin and outside the right parotid gland.

Diagnosis: Well-differentiated squamous cell carcinoma of tongue.

Integrative treatment prescription: Integrative treatments of "cryosurgical treatment + radiotherapy + chemotherapy + local hyperthermia + chelation detoxification therapy + medical ozone therapy + TCM treatment" were developed after expert consultation. On September 4, 2009, tongue cancer cryocare cryotherapy was carried out under the condition of endotracheal intubation and general anesthesia. On October 2009, a TP regimen of systemic chemotherapy was given. At the same time, local hyperthermia, chelation detoxification, medical ozone major autohemotherapy, TCM, and acupuncture treatments were given. At that stage, the tongue was dark with white fur. The pulse was thready and quick. TCM syndrome differentiation belonged to qi deficiency and blood stasis. The principle of treatment was to invigorate spleen and replenish qi, as well as to promote blood circulation and remove blood stasis.

Medications: The proposed prescriptions were as follows: *Atractylodes macrocephala Koidz* 30 g, *Poria Cocos* 30 g, *Radix glycyrrhizae Preparate* 6 g, *Alisma orientalis* 30 g, *Ramulus cinnamomi* 6 g, *Perilla seed* 15 g, *Prunella vulgaris* 15 g, *cowherb seed* 30 g, *Hedyotis diffusa Willd* 30 g, *Scutellaria barbata* 15g, *Agrimonia pilosa Ledeb* 30 g, *Lophatherum gracile Brongn* 10 g, *Juncus effusus L.* 10 g, *Radix rehmanniae* 15 g, and *Mentha haplocalyx Briq* 6 g, one dose a day and decocted with water for oral intake.

Acupuncture on acupoints: Quchi, Hegu, Neiguan, Zusanli, Yinlingquan, Sanyinjiao, Taixi, Taichong, Zhaohai, and Waisanguan. Methods: even reinforcing–reducing method was used for acupuncture with needle retention of 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Qihai, Shenque, and Zusanli. Methods: took two points each time. Conducted moxibustion with a moxa stick. Took 10 minutes of moxibustion for each point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Spleen, mouth, kidney, liver, endocrine, subcortex, Jiaogan, Erjian, and adrenal gland. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

After two courses of chemotherapy, the tumor of the patient shrank. From November 12, 2009, onward, radiotherapy was conducted. The total radiation dosage was 50 Gy. Local hyperthermia was given during radiotherapy, once every other day. Chelation detoxification was given during hyperthermia once every other day. The herbal medicine and acupuncture remained unchanged. Four courses of TP regimen were given after radiotherapy. Whole-body medium-low temperature hyperthermia and chelation detoxification therapy were given on the next day of chemotherapy. EBOO treatment was given once every other day. TCM and acupuncture treatment were continued during chemotherapy. At that stage, TCM syndrome differentiation was stasis toxin and internal resistance. The purpose of treatment was to activate blood circulation and resolve blood stasis and toxin. The proposed prescription was as follows: *Perilla seed* 30 g, *oyster* 30 g, *Prunella vulgaris* 30 g, *cowherb seed* 30 g, *Hedyotis diffusa Willd* 30 g, *Scutellaria barbata* 15 g, *Houttuynia cordata Thunb* 30 g, *Cortex lycii* 30 g, *rhizoma belamcandae* 10 g, and *Rhizoma paridis* 10 g, one dose per day, decocted with water for oral administration. Acupuncture was continued according to the original program. After treatment, the tumor disappeared. The patient continued outpatient treatment and received local hyperthermia, chelation detoxification, medical ozone, TCM, and acupuncture treatments after discharge.

The patient had psychotherapy at the beginning of hospitalization to increase his confidence in the treatment. Also, the patient gradually began practicing qigong and sports therapy to increase his self-healing powers.

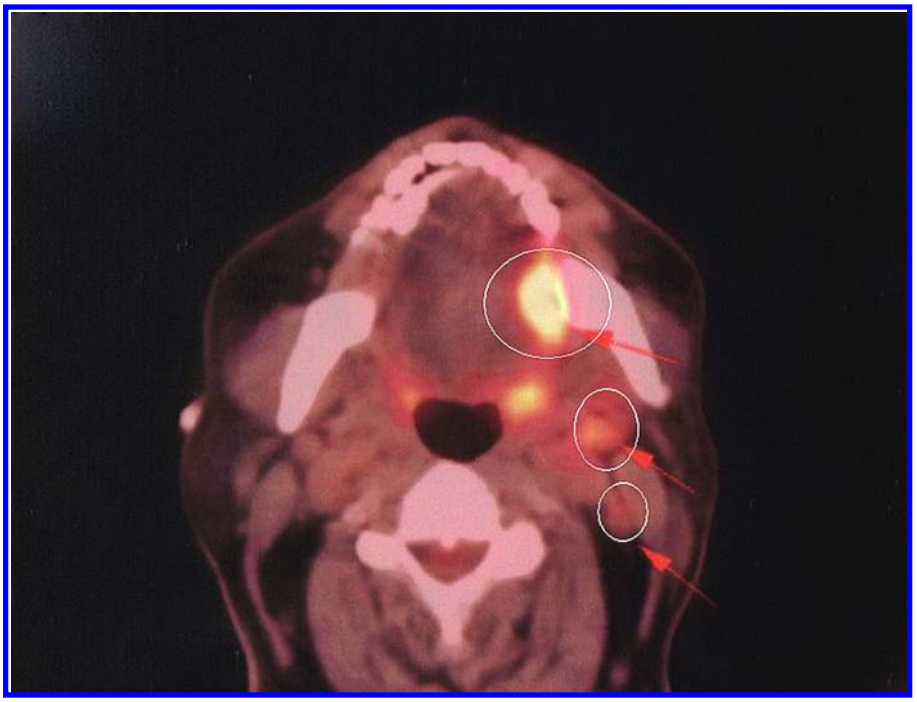

Figure 6.1 Before treatment. Apparent mass was visible on the tongue base before treatment. Multiple neck lymph node metastases were visible.

Treatment effects: The patient had intermittent hospitalizations. When he had chemotherapy, he was hospitalized. When he had radiotherapy, it was conducted as an outpatient. A total of 4 times of whole-body medium-low temperature hyperthermia, 60 times of local hyperthermia, 55 times of chelation detoxification therapy, and 20 times of EBOO were given. After treatment, the tumor disappeared, tongue movement was good, and speech was clear. The patient had tongue and mouth ulcers, and after symptomatic treatment was given they gradually improved. Since then, the patient had been insisting on integrative treatments at the outpatient department once a month and once every 3 months for review. After more than 3 years, no recurrence and metastasis were seen (Figures 6.1 and 6.2).

6.3.4 Related research in China and abroad

Leng Weidong et al. have explored the effect of hyperthermia on cell resistance of *Tca8113* and resistant Tca8113 and CBDEA through experimental studies. The results showed that *MDR1*, *MRP1*, and *GST-π* resistant gene expression levels of *Tca8113*/CBDEA cells were significantly decreased 4 hours and 24 hours after hyperthermia ($P < .01$); *MDRl-* and *MRP1*-resistant gene expressions of *Tca8113* cell were also decreased significantly ($P < .05$) at 4 hours and 24 hours; and *GST-π* was significantly decreased at 24 hours ($P < .01$). The concentration of Adriamycin (ADM) in the tumor cells was increased significantly after hyperthermia ($P < .01$). Hyperthermia inhibited the expression of the resistance gene and increased intracellular drug concentration. Hyperthermia may be an effective means to reverse the resistance of tumor cells and to improve the effect of chemotherapy.

Bianli et al. have explored the relationship between the maxillofacial squamous cell apoptosis induced by hyperthermia and *Bcl-2* and Bax protein expression through experimental studies. The results showed that the cell number of the maxillofacial squamous carcinoma cell apoptosis was significantly increased after treatment, *Bcl-2* gene protein expression was significantly decreased, and Bax gene protein expression was significantly increased. Hyperthermia induced maxillofacial squamous carcinoma cell apoptosis by downregulating *Bcl-2* gene protein expression and upregulating Bax gene protein expression.

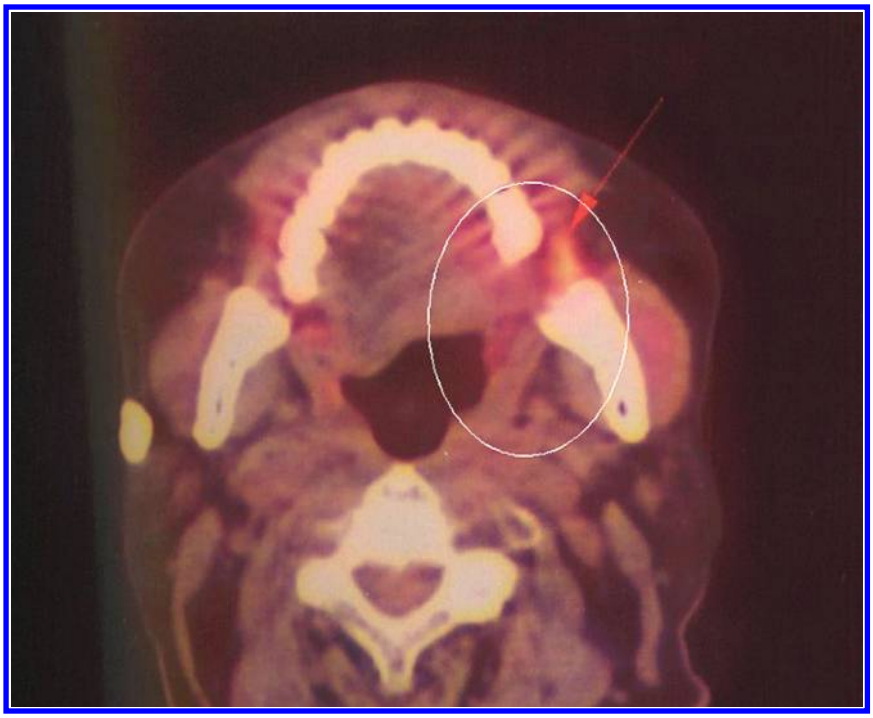

Figure 6.2 After treatment. The mass on the root of the tongue and neck lymph node metastases disappeared.

Zhang Jie et al. have adopted microwave plus hyperthermia to treat mandible invaded by tumor through clinical studies and explored the short-term efficacy and complications. Hyperthermia was carried out during surgery. Heat targeted bone segment by using microwave transducer. The results showed that local swelling in patients was not obvious after surgery, the drainage volumes were small, and obvious pain did not appear. Wounds healed well in seven cases and patients were discharged after 2 weeks; three patients showed wound dehiscence in the mouth 2 weeks after the surgery, and mandibular tissues were exposed. Bone tissue treated by hyperthermia underwent pathological fracture in approximately 1 to 2 months. All patients were followed up with no recurrence. The short-term effect of mandibular bone segment invaded by tumor through microwave heat treatment was acceptable. With strictly selected indications, no significant side effects occur. The long-term efficacy remains to be observed.

Prevost et al. conducted heating by applying microwaves into tissues in 24 cases of tongue cancer patients, of which 21 cases showed complete eradication and the rest had varying degrees of damage.

Tohnai et al. implanted iron–platinum hot seed at the Curie point of 68°C in eight cases of oral cancer for interstitial hyperthermia. They conducted hyperthermia once a week for about 45 minutes for a total of three to six times. At the same time, they conducted chemotherapy through the superficial temporal artery. They implemented tumor resection once hyperthermia and chemotherapy ended. Seven cases showed CR, and one case was PR. All patients after tumor resection were not found with residual tumors through tumor histopathological examination, indicating that the combination of interstitial hyperthermia with chemotherapy is an effective treatment for oral cancer.

6.4 NASOPHARYNGEAL CARCINOMA

Nasopharyngeal carcinoma is one of the common cancers in China, most commonly found in the Guangdong province of China. Nasopharyngeal carcinoma accounts for 31.77% of the local cancers, and the average annual mortality rate ranks third among cancer deaths in the province. Currently, the

nasopharyngeal cancer cure rate is approximately 40%–70%. How to further improve the efficacy of nasopharyngeal carcinoma treatment is a very important issue nowadays. The combination of hyperthermia with other treatments can ensure the smooth progress of treatment and reduce local recurrence rate. A lot of work remains to be done to ensure a 5-year survival rate.

Clinical manifestations of the cancer are complex and changeable because the primary site of nasopharyngeal cancer is the nasopharyngeal cavity. The cancer invades the skull base upward, involving the left and right sides of the pharynx, metastasizing to the neck downward and metastasizing to the bone, liver, lungs, and other distant organs. The common clinical symptoms are nasal congestion, blood in nasal discharge, sensation of ear fullness and blocking, hearing loss, diplopia and headache, and so on. The World Health Organization (WHO) has divided it into three types: type I is keratinized squamous cell carcinoma, type II nonkeratinized squamous cell carcinoma, and type III poorly differentiated carcinoma or undifferentiated carcinoma. Cervical lymph node metastasis is the most common in nasopharyngeal carcinoma. The occurrence sites of distant metastasis are bone, liver, and lung.

6.4.1 Conventional treatments

6.4.1.1 SURGERY

The anatomical structure of the location of primary nasopharyngeal carcinoma is complex, being closely linked with important nerves, blood vessels, and other tissues and organs around the base of the skull. Also, nasopharyngeal carcinoma has a strong aggressive nature and easily involves the surrounding tissue structure, as well as having a higher lymph node metastasis rate, and the site lacks a cutting edge necessary for surgery. As a result, surgery is difficult for complete eradication. Surgery is mainly used for patients with local lesions that are residual or recurrent, cervical lymph nodes that are residual or recurrent, and so on after radiotherapy.

6.4.1.2 RADIOTHERAPY

Because the vast majority of nasopharyngeal carcinomas are poorly differentiated squamous cell carcinomas that are relatively sensitive to radiotherapy, radiotherapy is the preferred treatment for nasopharyngeal carcinomas. Radiotherapy should be preferred for the primary treatment of nasopharyngeal carcinoma. In general, radiotherapy can cure nasopharyngeal carcinoma, and the 5-year survival rate can reach 50%–70%. Even for recurrent nasopharyngeal carcinoma, a 10%–20% 5-year survival rate can be achieved after a reasonable reprocess treatment. Radiotherapy alone is conducted for early-stage nasopharyngeal carcinoma, including external exposure or external exposure plus intracavitary afterloading therapy. Comprehensive chemoradiotherapy can be selected for medium-advanced cases, including concurrent chemoradiotherapy, induction chemotherapy, or adjuvant chemotherapy. For cases with distant metastasis, adopt mainly chemotherapy, supplemented by radiotherapy. For nasopharyngeal carcinoma patients with recurrence, radiation or an integrative treatment program should be developed, depending on the time and site of recurrence after radiotherapy.

6.4.1.3 CHEMOTHERAPY

The majority of nasopharyngeal carcinomas are poorly differentiated squamous cell carcinomas, prone to distant metastases, and are medium sensitive to chemotherapy. Chemotherapy, as an adjuvant therapy for medium-advanced cases, may improve the local control rate and reduce the incidence of distant metastasis. For widely distant metastasis that has occurred in advanced nasopharyngeal carcinoma, chemotherapy can achieve good palliative effect and can be combined with radiotherapy for comprehensive use or concurrent chemoradiotherapy. Commonly used combination methods are induction chemotherapy, concurrent radiotherapy, adjuvant chemotherapy, and so on.

6.4.1.4 HYPERTHERMIA

Hyperthermia is also a clinically feasible means for radiosensitization in addition to having anticancer and local immune functions. The existing clinical results suggest that the effect of hyperthermia combined with radiotherapy or integrative treatments of hyperthermia, radiotherapy, and chemotherapy for nasopharyngeal

carcinoma cervical lymph node metastases is better than the effect of radiotherapy alone. And, hyperthermia applied to the primary cancer has the potential to bring therapeutic gain for cervical lymph node metastases. Also, clinical studies have shown that whole-body hyperthermia combined with chemotherapy for nasopharyngeal carcinoma multiple bone metastases has a better palliative treatment effect.

6.4.1.5 CHELATION DETOXIFICATION THERAPY

Chelating detoxification therapy can effectively remove toxins from the body; the vitamins contained within can reduce the side effects induced by radiotherapy and isotope therapy. Be sure that intravenous infusion is not less than 2 hours during the course of treatment, with 20 times as a course of treatment for a total of three courses. Simultaneously conducting hyperthermia and chelation detoxification has a synergistic enhancement effect. The timing of chelation detoxification therapy in the treatment of advanced nasopharyngeal carcinoma is particularly important. Chelation detoxification therapy should be conducted as early as possible after the diagnosis to ensure early enough full dose for the entire process, combined with hyperthermia and other therapies.

6.4.1.6 MEDICAL OZONE THERAPY

For early-stage nasopharyngeal carcinoma, EBOO is mostly applied once every other day, with 20 times as a course of treatment for a total of three courses. Patients in poor condition or with active bleeding are subject to medical ozone saline infusion once every other day, 12 times as a course of treatment for a total of three courses; medical ozone autohemotherapy once every other day, 12 times per course of treatment; or medical ozone acupoint injection once every 3 days, 8 times per course of treatment. Medical ozone saline can effectively alleviate radiotherapy-induced stomatitis, ulcers, pharyngitis, and so on. Provide two to five times as a course of treatment. Medical ozone olive oil is used for the treatment of radiotherapy-induced skin damage, all kinds of wounds, and skin rashes and is applied to the affected areas one to four times a day. Medical ozone saline atomizing inhalation is for radioactive inflammation of the mouth and nasopharynx. Medical ozone saline can also be applied to rinse the nasal cavity, paranasal sinuses, maxillary sinus, and other parts. For medium-advanced nasopharyngeal carcinoma, EBOO is still the first choice. If the patient is excessively weak with abnormal coagulation function, major autohemotherapy or medical ozone saline intravenous injection can be chosen. Rinse the cancer area directly with medical ozone saline through conchoscope. It can achieve hemostasis and reduce edema, and so on; also, it can achieve the effect of cancer reduction.

6.4.1.7 TRADITIONAL CHINESE MEDICINE

Modified Qingjin Huatan Pill is given for the syndrome of lung-heat and phlegm coagulation. Modified Xiaolei Pill is given for the syndrome of qi stagnation and phlegm and blood stasis. Longdan Xiegan Decoction is given for the syndrome of fire toxicity and internal resistance. Shengmai Powder with Jiawei Zengye Decoction is given for the syndrome of deficiency of both qi and yin. Commonly used Chinese formulated products are Biyanlin tablets, Biyanqingdu granules, and Xiaojin pellets.

6.4.1.8 ACUPUNCTURE

6.4.1.8.1 Early nasopharyngeal carcinoma

Because the syndrome is mainly lung heat, the therapeutic principle should focus on clearing away heat and removing throat dampness.

Acupuncture on acupoints: Lieque, Quchi, Hegu, Shangyingxiang, Taiyuan, and Shangxing.

Methods: Even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

6.4.1.8.2 Medium-advanced nasopharyngeal carcinoma

Because the syndrome is mainly toxic heat stagnating in the body, the therapeutic principle should focus on clearing away heat and toxic substances as well as removing swelling and lumps.

Acupuncture on acupoints: Hegu, Quchi, Zusanli, Dazhui, Baihui, Yingxiang, Tinghui, Taixi, and Feishu.

Methods: Even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Zusanli, Guanyuan, Dazhui, Pishu, Shenque, and Shenshu.

Methods: Take two points each time with a moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Internal nose, external nose, throat, Jiaogan, forehead, temporal bone, adrenal gland, and lung.

Methods: Select four to six points each time. Penetrate with filiform needle. Retain the needle for 30–60 minutes after fast twist, once a day with 10 times as a course of treatment, or stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.4.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Early nutrition is mainly through medicated diet conditioning for nasopharyngeal carcinoma. For patients with radiation esophagitis and dysphagia, indwell gastric tube or conduct fistulization for nutritious meal injection. It is to be combined with qigong practice, adequate exercise, music therapy, and other therapies, as well as psychological counseling to adjust the patient's attitude to fight against tumors with optimism and confidence. For patients with medium-advanced cancers who can eat, nutrition is provided mainly through medicated diet conditioning, supplementing enough amino acids, vitamins, digestive enzymes, and so on. If digestive tract obstruction occurs, total parenteral nutrition may be considered. At the same time, combine qigong, sports, music therapy, and so on, as well as psychological counseling adjustment to enhance the patient's confidence and self-healing powers.

6.4.1.10 OTHERS

Because bleeding, ear infections, headaches, and other complications that seriously affect the quality of life are commonly seen due to the nasopharyngeal condition itself or after radiotherapy, nontoxic integrative treatments or targeted Western medicines must be applied in a timely manner during the course of treatment to quickly alleviate these complications. For example, use thrombin, mannitol, and other drugs to relieve the suffering of patients in the shortest possible time.

6.4.2 Combination of hyperthermia with conventional treatments

6.4.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

The majority of nasopharyngeal carcinoma cases can achieve good results by chemoradiotherapy, and some patients can recover. A very small number of patients still have localized mass or regional lymph node residues after chemoradiotherapy, and surgery may be appropriate. After the postoperative wound is completely healed, whole-body or local hyperthermia can be carried out, excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of the patient by the hyperthermia center physician. If patients are assessed to be in good general condition and are able to withstand whole-body hyperthermia, whole-body hyperthermia can be combined with chemotherapy cycles for a total of six times. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Local hyperthermia can be added during the intermission periods of whole-body medium-high temperature hyperthermia.

For patients not suitable for whole-body medium-high temperature hyperthermia, local hyperthermia in the nasopharynx or whole-body medium-low temperature hyperthermia can be carried out. Local hyperthermia is carried out every other day, 20 times as a course for at least three courses. Local hyperthermia can be applied in combination with other approaches in long-term treatment. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.4.2.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy is one of the preferred primary means for treating nasopharyngeal carcinoma. The combination of hyperthermia and radiotherapy may increase the sensitivity of cancer cells to radiotherapy and reduce skin and hematologic toxicity caused by radiotherapy. The order of radiotherapy followed by hyperthermia is appropriate, and many advocate that the interval time of 2 hours is appropriate. Local hyperthermia is applied once every other day, and combined with radiotherapy for the whole process. From a clinical point of view, combining with hyperthermia during radiotherapy significantly reduces bone marrow suppression and skin damage caused by radiotherapy and is conducive to the successful completion of the treatment. The first course of hyperthermia is maintained up to 2 weeks after the end of radiotherapy. Adjust to whole-body hyperthermia in the recovery period. From a clinical point of view, combining with hyperthermia during radiotherapy can significantly reduce bone marrow suppression, skin lesions, and tissue damage caused by radiotherapy and is conducive to the successful completion of the treatment.

6.4.2.3 HYPERTHERMIA AND CHEMOTHERAPY

The majority of patients in phase II and above need concurrent chemoradiotherapy or a "sandwich therapy" of chemotherapy + radiotherapy + chemotherapy. If the former is used, the radiotherapy synchronization method can be applied and local hyperthermia is mainly used for hyperthermia. If the latter is used and patients are assessed to be in a good general condition, combined whole-body hyperthermia can be carried out with the cycles of chemotherapy. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during the whole-body hyperthermia process, and give symptomatic treatment in a timely manner. When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body hyperthermia can be carried out during the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if rare vomiting is severe. Simultaneously carry out the hyperthermia and chemotherapy cycles for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

For patients not suitable for whole-body medium-high temperature hyperthermia, local hyperthermia for the nasopharynx or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, and it can be continued at chemotherapy intervals. Take 1 week off between two courses of chemotherapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

Combined local hyperthermia for the whole process is carried out during chemotherapy. After completion of chemotherapy treatment, local hyperthermia alone can be carried out for 20 times as a course and take 15 days off after three courses of treatment. Thereafter, maintenance therapy can be carried out for the long term.

6.4.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given to cancer patients who are receiving chemotherapy. It can promote physical recovery and regulate immunity, and kill residual cancer cells or inhibit early metastasis.

Carry out chelation detoxification therapy once every other day, with 20 times as a course of treatment for a total of three courses. If combined with blood detection for patients who have excessive heavy metals, a chelating agent can be added, and at the same time note that intravenous infusion should not be less than 2 hours. Simultaneously conducting hyperthermia and chelation detoxification can increase the chelation detoxification efficacy.

6.4.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance effect on immunity, and increase the efficacy of medical ozone. We propose to give EBOO treatment for medical ozone therapy as soon as possible, once every other day, with 20 times as a course of treatment for a total of three courses. Change to once per week after the end of treatment for consolidated therapy.

6.4.2.6 HYPERTHERMIA AND OTHER TREATMENTS

Cancer treatment needs integrative treatments, and the combined applications of TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, and alkaline treatment with hyperthermia can increase the effectiveness and safety of the treatment.

DC-CIK cell therapy: NPC is a cancer related to EB (Epstein-Barr) virus infection and rather sensitive to chemoradiotherapy. DC-CIK can be an adjuvant therapy and applied in combination with chemotherapy. One day before chemotherapy, collect the patient's peripheral blood for DC-CIK preparation and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect peripheral blood again for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct a consolidated therapy every 2 to 3 months. For the combined application of DC-CIK with radiotherapy, adopt the principle that DC-CIK reinfusion is conducted at the intervals of radiotherapy. For example, on the day when radiotherapy is to be conducted, collect the patient's peripheral blood for DC-CIK culture before the start of radiotherapy and conduct reinfusion at the interval of radiotherapy. The patient's immunity is markedly elevated after combination application by comparing with simply chemotherapy. Meanwhile, the anti-(Epstein-Barr virus) antibody is significantly decreased in the titer. The specific mechanism is not clear.

Systemic biofeedback therapy: Perform three times a week, with 20 times as a course of treatment. Adjust to once or twice a week after three courses for long-term treatment.

Alkalization treatment: Dietotherapy to alkalize the body and sodium bicarbonate therapy can be applied. Refer to Section 4.10 for food therapy. The working concentration of sodium bicarbonate therapy is 1.25% solution; ultrasonic atomizing inhalation is applied, 10 mL each time, one to two times a day, with 8 days as a course of treatment.

Reasonable nontoxic integrative treatment taken for nasopharyngeal carcinoma can significantly improve the cure rate, effectively reducing the side effects of radiotherapy, enhancing the quality of life of cancer patients, inhibiting tumor progression, and prolonging survival time.

6.4.2.7 INTRACAVITARY HYPERTHERMIA

Because the growth area of nasopharyngeal carcinoma is hidden within complex anatomical structures, but located in the natural orifice, cavity heating is a possible way to achieve better hyperthermia treatment effect. It must be noted that intracavitary tumor growth will lead to the change of the cavity structure, even occlusion of the cavity, and to the increased difficulty of the radiation placement operation. Therefore, there are not enough cases for relevant clinical reports and experience so far; there are some reports, but they fail to reach a satisfactory level.

6.4.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.4.2.8.1 Fumigation

Proven prescription 1: Selaginella Doederleinii 30 g, raw oyster 30 g (Predecoct), *Rhizoma amorphophalli* 30 g (Predecoct), *Flos lonicerae* 15 g, seaweed 15 g, *Radix sophorae Tonkinensis* 12 g, *Prunella vulgaris* 12 g, and *Fructus xanthii* 9 g. Add drugs and decoct them into steam. Have the patients inhale the steam through both nose and mouth. Efficacy: clears away heat and toxic substances, resolves phlegm and softens hard masses, and reduces swelling and resolves mass. It is applicable to nasopharyngeal carcinoma patients with the syndrome of heat toxicity and coagulated phlegm.

Proven prescription 2: Ercao Shuanghua decoction: *Hedyotis diffusa* 30 g, *Flos lonicerae* 30 g, *Prunella vulgaris* 20 g, and ginseng 3 g. It is applicable to patients with oral cancer after radiotherapy.

Proven prescription 3: Soldago decurrens Lour 30 g, *Scutellaria barbata* 30 g, *Scrophularia ningpoensis* 30 g, *Paris polyphylla Sm.* 30 g, *Radix sophorae Tonkinensis* 15 g, *Fructus arctii* 15 g, *Cremastra appendiculata* 15 g, *Nidus vespae* 15 g, *Prunella vulgaris* 12 g, *Bombyx batryticatus* 12 g, *Gekko* 9 g, *Puffball* 6 g, *Platycodon grandiflorum* 6 g, and *Licorice roots* 6 g. Add drugs and decoct them into steam. Have the patients inhale the steam through both nose and mouth. Efficacy: clears throat heat and removes dampness. It is applicable to nasopharyngeal carcinoma patients with the syndrome of heat toxicity and coagulated phlegm at the initial-medium term.

Proven prescription 4: Galla chinensis 60 g, *Cremastra appendiculata* 60 g, *Jinzimo* 30 g, *Euphorbia pekinensis* 15 g, *Paris polyphylla Sm*. 15 g, *Realgar* 15 g, and musk 1 g. Decoct the drugs into steam. Have the patients inhale the steam through both nose and mouth. Efficacy: removes blood stasis and breaks junction, removes toxins, and induces resuscitation. It is applicable to oral cancer patients with swelling and pain in throat.

6.4.2.8.2 Moxibustion therapy

It is applicable to cancer patients with long illness, yang deficiency, and weakness and is capable of immunity enhancement.

Acupoints: The first group of acupoints includes Dazhui, Shenshu (both), and Pishu (both). The second group of acupoints includes Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both).

Herbal cake making: Take equal amounts of *Radix astragali*, *Angelica sinensis*, *Fructus psoraleae*, *Curculigo orchioides*, and *rhubarb*, and smash them into powder. Filter with 120 mesh sieve, and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm.

Moxibustion: Place the moxa cone with a diameter of 2 cm and height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints each time, with two groups of points alternated, once every other day, with 24 times as a course of treatment.

Efficacy: Enforces spleen and nourishes kidney for muscularity and general health care.

6.4.2.9 HYPERTHERMIA INDICATIONS

Hyperthermia can be applied for all cancers suitable for surgery and chemoradiotherapy.

6.4.2.10 HYPERTHERMIA CONTRAINDICATIONS

Intracavitary hyperthermia is not suitable for patients with visible damage of the skin; patients having fever with body temperatures above 38.5°C; patients with bleeding tendency; or nasopharyngeal carcinoma patients with apparent ulcers, tissue decay, and hemorrhage.

6.4.3 Introduction of a typical case

A patient named Li, male, 39 years old, was admitted on January 4, 2007, to Clifford Hospital due to "more than 2 years after chemoradiotherapy for nasopharyngeal carcinoma." The patient was found with left submandibular tumor and neck lymph nodes in October 2004 and diagnosed with nasopharyngeal poorly differentiated squamous cell carcinoma and bone metastases at clinical stage IV. He underwent radical radiotherapy and six courses of chemotherapy. He experienced headaches, thirst, dry mouth and throat, swelling and aching of gums, swelling pain in cheeks, hearing loss, mental fatigue, and anorexia when she was admitted to the hospital.

Physical examination: His weight was 46 kg, and she was in a poor general condition. He was thin. Superficial lymph nodes were not enlarged. Heart, lung, liver, and spleen were normal. His neck skin became hard due to radiation injury. He had decreased hearing in her left ear. The tongue was red with less fur. The pulse was thready and rapid. The KPS was 70.

Auxiliary examinations: Blood routine: Hb 102 g/L, RBC 3.2×10^{12}/L, WBC 3.1×10^{9}/L, PLT 194×10^{9}/L; ECT Emission Computed Tomography examination showed nasopharyngeal carcinoma with skull metastasis.

Diagnosis: Nasopharyngeal carcinoma recurrence and bone metastases after chemoradiotherapy.

Integrative treatment prescription: The patient was given intravenous nutrition, acupuncture, and TCM once a day after admission to the hospital. At the same time, medical ozone and other integrative treatments were given as well as local hyperthermia, once every other day. After 1 week, his symptoms of headaches, mental fatigue, and anorexia were improved. First, TP program for two courses of chemotherapy was implemented. Added one treatment of whole-body medium-low temperature hyperthermia for each course of chemotherapy and stopped local hyperthermia 3 days before and after whole-body hyperthermia. For the rest of the time, local hyperthermia was conducted once every other day. After two courses of chemotherapy, radiotherapy (a total of 35 times) + local hyperthermia (once every other day for a total of 21 times) was given.

After radiotherapy, four courses of chemotherapy of TP program + whole-body hyperthermia + local hyperthermia treatments were implemented. Chinese medicine and acupuncture treatments accompanied chemoradiotherapy throughout the whole process. Because the patient was with red tongue, less fur, and thready and rapid pulse, and the syndrome was deficiency of both qi and yin, the TCM treatment was implemented to supplement qi and nourish yin as well as drain toxins and resolve mass.

Medications: The prescription was supplemental Shengmai Powder. The specific medications were as follows: *Radix pseudostellariae* 15 g, *Ophiopogon japonicus* 15 g, *Schisandra chinensis* 12 g, *Rhizoma pinelliae Praeparatum* 12 g, *Bile arisaema* 12 g, *Cremastra appendiculata* 15 g, *Agrimonia pilosa Ledeb* 30 g, *Selaginella doederleinii* 12 g, *Cortex moutan* 10 g, *Gardenia jasminoides Ellis* 10 g, *Fructus xanthii* 15 g, and *Flos magnoliae Liliflorae* 10 g, one dose a day. Drugs were decocted with water for oral dose.

Acupuncture treatment: The principle of acupuncture was to drain toxins and resolve mass.

Acupuncture on acupoints: Hegu, Quchi, Zusanli, Dazhui, Baihui, Yingxiang, Tinghui, Taixi, Feishu, and Waisanguan. Methods: even reinforcing–reducing method was used for acupuncture. Retained the needle for 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Zusanli, Guanyuan, Dazhui, Pishu, Shenque, and Shenshu. Methods: took two points each time. Conducted moxibustion with the moxa stick. Conducted moxibustion for 10 minutes per point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Internal nose, external nose, throat, Jiaogan, forehead, temporal bone, adrenal gland, and lung. Methods: stuck auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

Treatment effects: The patient received a total of about 6 months of treatments (intermittent hospitalization). Because the patient was in poor general condition, had poor diet, and had headaches, mental fatigue, and other symptoms when he was admitted to the hospital, the main treatment was to improve the symptoms as well as correct malnutrition. Small doses or base quantum for medical ozone and chelation detoxification were used, and the therapeutic dose was gradually increased after the relief of symptoms such as headaches and mental fatigue. We applied treatment by looking into both the root cause and the symptoms. While applying chemoradiotherapy for cancer treatment, we adhered to combining TCM, chelation detoxification, medical ozone, whole-body hyperthermia, local hyperthermia, and other treatments so that we achieved anticancer effect and effectively reduced chemotherapy side effects. After 2 months of treatment, the symptoms of dry mouth and swelling and pain of gums disappeared. Hearing was slightly restored, and 3 kg of weight was gained. The KPS was 90. After discharge, he still insisted on taking herbal medicines and returned to the hospital and received nontoxic integrative cancer treatments for 3 days every 2 weeks, which were adjusted to 3 days treatment per month after 3 months of treatment. After 7 months, CT lesions basically disappeared. ECT showed the skull metastasis of nasopharyngeal carcinoma with no significant change compared with the previous scan. No new metastases occurred. The patient continued to pay regular visits. His condition remained stable, and no recurrence or new metastases have been seen.

6.4.4 Related research in China and abroad

Wang Shaofeng et al. conducted a randomized controlled study of 105 patients with larger neck lymph node metastasis of nasopharyngeal carcinoma; CR rates of the thermoradiotherapy group and the radiotherapy alone group were 60% and 42.9%, respectively. Wu Jingbo et al. implemented controlled clinical studies on the cavity microwave combined with emission treatment, and the results showed that the thermoradiotherapy group had a higher rate of CR compared with the radiotherapy alone group. Liu Shixi et al. have reported that with the implementation of hyperthermia when conducting conventional irradiation DT40Gy, CR of the thermoradiotherapy group was 82.6% and CR of the radiotherapy alone group was 54.2%. The rate and extent of cancer regression in the thermoradiotherapy group were superior to that of the radiotherapy alone group.

Deng Jingfeng et al. have conducted clinical studies on whole-body hyperthermia combined with chemoradiotherapy treatment for patients with nasopharyngeal carcinoma III and IVA. The treatment group received whole-body hyperthermia combined with chemoradiotherapy, and the control group received radiotherapy combined with chemotherapy. Both groups received 6-MV X-ray external irradiation radiotherapy

and systemic chemotherapy. The group with hyperthermia combined with radiotherapy and chemotherapy received whole-body hyperthermia on the same day when cisplatin chemotherapy was conducted, once every 3 weeks. The treatment temperature was set at 39.8°C–40.5°C. Intravenous infusion of cisplatin chemotherapy drug was given when the treatment temperature was reached, and the temperature was kept constant for 2 hours. The results have shown that the CR of the treatment group was higher than that of the control group, with statistical significance; the radiotherapy dose for regression of nasopharyngeal cancer and cervical lymph node in the treatment group was lower than that in the control group, with statistical significance, but side effects of both groups had no statistical discrepancies.

Clinical studies by Margin et al. have shown that combination with local hyperthermia can improve local efficacy of radiotherapy. Also, studies by Manning et al. have confirmed that microwave hyperthermia alone can not only have the effect of anticancer but also increase the sensitivity of cancer cells to radiation. Combination treatment of nasopharyngeal carcinoma and cervical lymph node metastasis has significant effect.

6.5 THYROID CARCINOMA

Thyroid carcinoma is cancer of the thyroid tissue. The incidence of thyroid carcinoma accounts for 1.3% of systemic cancers. Incidence of thyroid carcinoma, especially of poorly differentiated thyroid carcinoma, is also high in the endemic areas of nodular goiter. Thyroid carcinoma is the solid malignant tumors with the fastest growing incidence in the past 20 years and has an average annual growth of 6.2% since the mid-1980s and after the accident of Chernobyl in the former USSR.

Because thyroid carcinoma has a variety of different pathological types and biological characteristics, its clinical manifestations are not the same. It can exist with multiple thyroid nodules, the majority of which are asymptomatic. A nodule or mass in the anterior cervical region is usually found by chance. Some masses that have been in existence for many years may rapidly grow or have recent metastasis. Some patients have no main complaints for a long time and pay no attention until cervical lymph node metastasis, pathologic fractures, hoarseness, disordered breathing, difficulty in swallowing, and even Horner syndrome exhibit at the advanced stage. Local signs are not the same. There may be asymmetric nodules or masses of thyroid or masses inside the gland, up and down after swallowing. The mass is fixed until the surrounding tissue or trachea is invaded.

General types of thyroid carcinomas are papillary carcinoma (including mixed papillary follicular carcinoma), follicular carcinoma, medullary carcinoma (solid body accompanied by amyloid thyroid tumors), undifferentiated carcinoma, and rare anaplastic carcinoma. Generally, thyroid carcinoma is not highly malignant. If appropriate treatment is conducted, the patient can achieve normal life expectancy.

6.5.1 Conventional treatments

6.5.1.1 SURGERY

Surgery is an important means for thyroid carcinoma treatment. According to the different pathological types and violation range of the cancer, methods are also different. The main form of surgery includes thyroid single leaf plus isthmus resection, subtotal thyroidectomy or total thyroidectomy, and combined radical operation of thyroid carcinoma. If the following conditions occur, total thyroidectomy or nearly complete resection surgery should be considered: (1) cancer diameter greater than 1 cm; (2) contralateral presence of thyroid nodules to cancer; (3) local or distant metastases; (4) patients with a history of head and neck radiotherapy; and (5) first-degree relatives of patients having differentiated thyroid carcinoma history. Older patients (>45 years) have a higher recurrence rate. Even if the cancer diameter is less than 1–1.5 cm, we still recommend the aforementioned operation. Expanding the resection margin may improve the survival rates of high-risk and low-risk patients.

6.5.1.2 RADIOTHERAPY

Sensitivity to radiation varies greatly for various types of thyroid carcinoma, which is almost proportional to the degree of differentiation of thyroid carcinoma; the better the differentiation the poorer the

sensitivity, whereas the poorer the differentiation the higher the sensitivity. Thyroid carcinoma radiotherapy mainly includes external radiotherapy and internal radiotherapy. External radiotherapy: differentiated thyroid carcinoma is not sensitive to radiation, and thyroid adjacent organs such as the thyroid cartilage, organs, and spinal cord have low tolerance. As a result, external radiotherapy alone is not conducted under normal circumstances, or it is only taken as adjuvant therapy. External radiotherapy is mainly for undifferentiated carcinoma treatment. Internal radiotherapy: I^{131}-ray (mainly β-ray) has the effect of destroying thyroid tissue, and differentiated thyroid carcinoma has the function of uptaking I^{131}. Thus, it is used in the clinical treatment of differentiated thyroid carcinoma, especially hematogenous metastases (lung and bone).

6.5.1.3 CHEMOTHERAPY

Differentiated thyroid carcinoma has poor response to chemotherapy. Only selective combinations with other treatments are used for some patients with locally advanced and unresectable or distant metastasis. Doxorubicin is the most effective. Its response rate can be 30%–45%, and it can prolong life. The patient can have long-term survival even when the carcinoma foci are not reduced. In contrast, undifferentiated carcinoma is more sensitive to chemotherapy, and combination chemotherapy is commonly used.

6.5.1.4 ENDOCRINE THERAPY

Thyroid hormone can inhibit thyroid-stimulating hormone secretion, which inhibits proliferation of thyroid tissue and differentiated cancer and has a better therapeutic effect on papillary carcinoma and follicular carcinoma. Thus, doses of thyroid hormone, which can inhibit thyroid-stimulating hormone secretion, are conventionally given after surgery for the aforementioned types of thyroid carcinoma and have some effect in preventing cancer recurrence and metastases but have no effect on undifferentiated carcinoma. Generally, in China dried thyroid tablets of 80–120 mg are applied daily to maintain a high thyroid hormone level.

6.5.1.5 HYPERTHERMIA

Hyperthermia has the effect of directly killing cancers and can effectively control the growth of thyroid carcinoma. Cellular immune function is enhanced after hyperthermia, which can improve the efficacy of cancer treatment. Hyperthermia has a synergistic sensitizing effect on chemoradiotherapy and can also reduce adverse reactions of chemoradiotherapy. Clinical studies have shown that efficacy of thermoradiotherapy and thermochemotherapy for thyroid carcinoma is superior to that of chemoradiotherapy alone. Whole-body hyperthermia has a good effect on thyroid local control as well as prevention of recurrence and metastasis and can be combined with systemic chemotherapy. Neck RF local hyperthermia can be used alone, and it can also be used in combination with radiotherapy. For patients with combined distant metastasis, hyperthermia can effectively relieve symptoms, improve quality of life, and prolong survival time. Studies have shown that whole-body thermochemotherapy has higher pain relief rates for patients with thyroid carcinoma combined with bone metastasis than chemotherapy alone.

6.5.1.6 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can effectively inhibit cancer cell growth and metastasis and can also reduce the side effects of radiotherapy and isotope therapy. The course of treatment is once every other day, and treatment is maintained until 2 weeks after the end of radiotherapy or isotope therapy and is then changed to therapy twice a week for 3 months. Health rehabilitation can be given once a week when the condition is stable after 3 months. Ensure to arrange chelation detoxification and hyperthermia at the same time as far as possible to maximize the synergistic effect.

6.5.1.7 MEDICAL OZONE THERAPY

EBOO treatment or medical ozone saline intravenous injection, major autohemotherapy, and so on should be given as soon as possible to obtain synergistic anticancer effect, enhance immunity, and reduce the side effects of radiotherapy. Usage is once every other day. Alternately apply with chelation detoxification therapy; the course of treatment is the same as that of chelation detoxification.

6.5.1.8 TRADITIONAL CHINESE MEDICINE

For the syndrome of phlegm and qi stagnation, the prescriptions recommended include modified Sihai Shuyu Pill. For the syndrome of phlegm, blood, and poison stagnation, the prescriptions recommended include modified Haizao Yuhu decoction. For the syndrome of phlegm fire and blood stagnation, the prescription recommended is modified Liver-clearing Aloe Pill. For the syndrome of deficiency of both qi and blood, the prescriptions recommended include Shengmai Powder combined with modified Huoxue Xiaoying Decoction.

6.5.1.9 ACUPUNCTURE

Thyroid carcinoma is mainly caused by a poor emotional state, stagnation of qi due to depression of the liver, and phlegm and dampness coagulation. The therapeutic principle should focus on soothing liver qi stagnation, regulating qi, eliminating goiter, promoting blood circulation, removing phlegm, and resolving mass.

Acupuncture on acupoints: Zusanli, Yanglingquan, Yinlingquan, Futu, Tianding, and Neiguan. Add Taichong, Qimen, and Fenglong for patients with liver qi stagnation and phlegm coagulation, and add Sanyinjiao, Baihui, Hegu, and so on for patients with qi stagnation and blood stasis.

Methods: Even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Zusanli, Guanyuan, Dazhui, and Jianyu.

Methods: Take two points each time with a moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Endocrine, adrenal gland, subcortex, thyroid, liver, heart, and Shenmen.

Methods: Select four to six points each time. Penetrate with filiform needle. Retain the needle for 30–60 minutes after fast twist, once a day for 10 times as a course of treatment, or stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.5.1.10 MEDICATED DIET, NUTRITION, AND SO ON

Nutrition is a major treatment for advanced cancer. In addition to necessary medicated conditioning, enough nutrients need to be supplemented. Patients with eating difficulty may be given nasal feeding of enteral nutrition or total parenteral nutrition. At the same time, include psychological adjustment, qigong, sports, music, and so on to keep the patient calm, positive, and optimistic so as to enhance self-healing ability, which can delay the progression of cancer.

6.5.1.11 OTHERS

We recommend patients at the early stage to actively practice qigong, tai chi, and so on and to use TCM to regulate emotions. Guide patients to attain peace of mind and to overcome panic and desperation, so that they can face the disease with a positive, optimistic, and open-minded disposition. Also, combine music therapy and sound wave therapy to alleviate psychological pressure.

6.5.2 Combination of hyperthermia with conventional treatments

6.5.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Differentiated thyroid carcinoma has a favorable prognosis, and thorough surgical resection can achieve radical results. If differentiated thyroid carcinoma presents metastasis in the rest of the body, the effect of alleviating the disease can also be achieved by undergoing I^{131} therapy after thyroid resection. Thus, surgery is the most important means of treatment for differentiated thyroid carcinoma. After the postoperative wound is completely healed, whole-body hyperthermia may be given after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing

no bleeding tendency, and comprehensive assessment of the patient by the hyperthermia center physician, to prevent recurrence and metastasis. If patients are assessed to be in good general condition, it is recommended to conduct whole-body hyperthermia for a total of six times. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Local hyperthermia can be added at the intermission periods of whole-body hyperthermia.

For patients not suitable for whole-body hyperthermia, local hyperthermia or whole-body medium-low temperature hyperthermia can be carried out. Local hyperthermia is adopted for the neck once every other day, with 20 times as a course of treatment. Local hyperthermia can be applied in combination with other approaches in long-term treatment with 1 week taken off between two courses. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.5.2.2 HYPERTHERMIA AND RADIOTHERAPY

For differentiated thyroid carcinoma patients without distant metastasis, radiotherapy can be carried out after surgery. At the same time, local hyperthermia on the neck can be conducted to improve the cure rate. The order of radiotherapy followed by hyperthermia is appropriate, and many advocate that an interval time under 2 hours is appropriate. Conduct hyperthermia once every other day, combined with radiotherapy during the whole process. From a clinical point of view, combining with hyperthermia during radiotherapy significantly reduces bone marrow suppression and skin damage by radiation and is conducive to the successful completion of the treatment. The first course of hyperthermia is maintained for 2 weeks after the end of radiotherapy. Adjust to whole-body hyperthermia during the recovery period.

6.5.2.3 HYPERTHERMIA AND CHEMOTHERAPY

Hyperthermia has a sensitizing effect to chemotherapy, which can be combined for application. Whole-body hyperthermia can be carried out during the first day of chemotherapy. Chemotherapy is implemented simultaneously in the whole-body hyperthermia process, and whole-body hyperthermia is combined with chemotherapy treatment, once every 2 to 3 weeks. Local hyperthermia can be given during the intervals of whole-body hyperthermia to improve the efficacy and reduce the side effects of chemotherapy. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during the whole-body hyperthermia process, and give symptomatic treatment in a timely manner. Antiemetic drug treatment should be given before chemotherapy. It is safe under normal circumstances. If the patient vomits seriously during hyperthermia, it is necessary to give timely treatment. When (rare) vomiting is severe, whole-body hyperthermia needs to be suspended. Simultaneously conduct the hyperthermia and chemotherapy cycle for six to eight courses. Local hyperthermia can be carried out during the intermission periods of whole-body hyperthermia and during radiotherapy.

For patients not suitable for medium-high whole-body hyperthermia, local hyperthermia or whole-body medium-low temperature hyperthermia can be carried out. Local hyperthermia is adopted on the neck, once every other day, with 20 times as a course of treatment. Local hyperthermia can be combined for a long time. Take 1 week off between two courses. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

Combined local hyperthermia for the whole process is carried out during chemotherapy. After completion of the chemotherapy treatment, local hyperthermia alone can be carried out for 20 times as a course and for long-term maintenance therapy.

6.5.2.4 HYPERTHERMIA AND ENDOCRINE THERAPY

Because the level of thyroxine is lower after thyroid gland excision surgery, appropriate thyroxine must be complemented exogenously to maintain normal physiological function. At the same time, giving a certain amount of thyroxine can reduce thyroid-stimulating hormone in feedback and reduce tumor recurrence and metastasis. Simultaneously carry out endocrine therapy and whole-body hyperthermia once every 2 weeks. It is recommended to have six treatments. Conduct local hyperthermia once every other day during the intermission periods of whole-body hyperthermia.

6.5.2.5 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelating detoxification therapy can effectively remove toxins from the body, and the included vitamin can reduce the side effects induced by radiotherapy and isotope therapy. It is noted that intravenous infusion should not be less than 2 hours during the course of treatment, with 20 times as a course of treatment for a total of three courses. Simultaneously conducting hyperthermia and chelation detoxification has a synergistic enhancement effect. Patients treated with radiotherapy remain on chelation detoxification treatment 2 weeks after the end of radiotherapy or isotope therapy and then change to twice a week and maintain the treatment for 3 months. After 3 months, health rehabilitation can be given once a week. Simultaneously conducting chelation detoxification treatment and thermoradiotherapy can fully maximize the synergistic effect.

6.5.2.6 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing tumor cells, enhancing the effect on immunity, and increasing the efficacy of medical ozone. We propose to give EBOO treatment for medical ozone therapy as soon as possible, once every other day, with 20 times as a course of treatment for a total of three courses. Change to once per week after the end of treatment for consolidated therapy. Medical ozone saline intravenous injection and autohemotherapy have synergistic anticancer effects, enhance immunity, and reduce the side effects of radiotherapy. Usage: once every other day. Conducting hyperthermia 1 day before medical ozone therapy can increase the sensitivity of medical ozone therapy to cancer cells.

6.5.2.7 HYPERTHERMIA AND OTHER TREATMENTS

Cancer treatment requires integrative treatments, such as TCM; acupuncture; DC-CIK cell therapy; systemic biofeedback treatment; alkaline treatment; as well as psychological adjustment, qigong, sports, and music therapy to improve mood, self-healing capacity, and treatment efficacy and safety when combined with the application of hyperthermia.

DC-CIK cell therapy: DC-CIK can be an adjuvant therapy and applied in combination with chemotherapy. The combination application of DC-CIK with radiotherapy also adopts the principle that DC-CIK reinfusion is conducted during the intervals of radiotherapy. For example, on the day when radiotherapy is to be conducted collect the patient's peripheral blood for DC-CIK culture before the start of radiotherapy, and conduct reinfusion at the interval of radiotherapy. One day before chemotherapy, collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second course of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct a consolidation therapy every 2 to 3 months. After the combination application, the immunity of the patient should be significantly higher than chemotherapy alone.

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Adjust to once or twice a week after two to three courses for long-term treatment.

Alkalization treatment adopts the combination of food therapy and sodium bicarbonate therapy. Refer to Section 4.10 for food therapy recipes. Sodium bicarbonate therapy can adopt local or acupoint injection around the tumor. Conduct routine disinfection and avoid blood vessels. Inject 2.5%–5% sodium bicarbonate with a thin needle at multiple points, about 2 mL for each point, for a total of not more than 10 mL each time, once every other day, with eight times as a course of treatment.

6.5.2.8 HYPERTHERMIA INDICATIONS

Hyperthermia can be applied for any cancers that are suitable for surgery and chemoradiotherapy.

6.5.2.9 HYPERTHERMIA CONTRAINDICATIONS

Patients with visible damage to the skin, patients accompanied by fever with body temperatures above 38.5°C, or patients with local tissue decay and hemorrhage or bleeding tendency cannot receive hyperthermia.

6.5.3 Introduction of a typical case

A patient named Zhang, female, 26 years old, was admitted on June 24, 2007, to Clifford Hospital due to the discovery of medullary thyroid carcinoma nearly 18 months after total thyroidectomy and the discovery of multiple double-pulmonary metastases for 9 months with chest pain, cough, and bloody sputum for 7 months. In early 2006, the patient found a mass in the left neck and experienced hoarseness. Through physical examination, it was found that there was a 3 cm × 4 cm mass in the left thyroid area, which was hard and fixed, and there were multiple lymph nodes in the left neck. The diagnosis was medullary thyroid carcinoma at clinical stage III. Treatment with total thyroidectomy plus lymphadenectomy and oral thyroxine tablets was carried out. In September 2006, the patient showed repeated dry cough, and the examination showed bilateral pulmonary multiple metastases. In November 2006, the patient showed emaciation, chest tightness and breathlessness, irritability, head and neck pain, chest pain, cough, bloody sputum, shortness of breath, slightly yellow sputum in cough, hoarseness, breathing discomfort, dysphagia, as well as constipation and brown urine. The aforementioned symptoms were recurrent and were not alleviated. The patient was admitted later for further treatment.

Physical examination: The patient was in poor general condition and thin, with a weight of 49 kg, and had a pale appearance. Superficial lymph nodes were not palpable and enlarged. The neck incision healed well. The heart rate was regular. The breathing sounds of the left lung decreased. Liver and spleen were normal. Tongue was red with yellow fur. The pulse was thready and quick. Her KPS was 40.

Auxiliary examinations: Blood routine: Hb 90 g/L, RBC 28 × 10^{12}/L, WBC 3.5 × 10^{9}/L, and PLT 150 × 10^{9}/L. Lung CT showed the following: both lungs had multiple soft tissue mass shadows and the biggest was approximately 3.2 cm × 4.0 cm. Lung metastases were considered. Cervical CT showed multiple neck lymph nodes swelling after thyroidectomy.

Diagnosis: Medullary thyroid carcinoma and lung metastases.

Integrative treatment prescription: Because the patient was at the advanced stage of medullary thyroid carcinoma, she was in poor general condition. Also, the prognosis was poor due to the highly malignant tumor and lung metastasis. The patient immediately received the Western medicine treatments of intravenous nutrition for hemostasis, relieving cough, and dissipating phlegm and anti-infection, in combination with local hyperthermia, chelation detoxification, medical ozone major autohemotherapy, TCM, acupuncture, and other integrative treatments. After 7 days of continuous treatment, chest tightness, cough, sputum, headache, and other symptoms were improved. EBOO, whole-body medium-high temperature hyperthermia, chelation detoxification therapy, and so on were gradually administered. TCM and acupuncture were appropriately adjusted at any given time.

TCM treatment: The syndrome differentiation belonged to the syndrome of liver depression, transforming into fire during the patient's early admission. The patient was cured by eliminating heat and purging fire, as well as clearing away toxic substances and resolving mass. *Medicines of Radix bupleuri* 10 g, *Rhizoma dioscoreae Bulbiferae* 10 g, *Radix paeoniae Alba* 15 g, *Radix trichosanthis* 10 g, *Ligusticum chuanxiong Hort* 15 g, *Pericarpium trichosanthis* 10 g, *Fritillaria thunbergii Miq* 10 g, *Pericarpium citri Reticulatae Viride* 15 g, *Bile arisaema* 15 g, *Squama manitis* 10 g, seaweed 15 g, *Salvia miltiorrhiza* 15 g, *Prunella vulgaris* 15 g, and *Solanum nigrum* 20 g one dose a day were used. After more than 1 week of modified treatment, the symptoms were improved significantly. The tongue turned light and the pulse became thready and relaxed. Changed to the treatment of invigorating spleen, replenishing qi, clearing away toxic substances, and resolving mass with medicines of *Codonopsis pilosula* 15 g, *Atractylodes macrocephala* Koidz 20 g, *Pericarpium citri Reticulatae* 10 g, *Poria cocos* 10 g, *Dolichos lablab* 15 g, *Fritillaria thunbergii Miq* 10 g, seaweed 15 g, *Rhizoma dioscoreae Bulbiferae* 10 g, *Solanum nigrum* 20 g, *Arisaema cum Bile* 15 g, *Agrimonia pilosa Ledeb* 30 g, and lily 15 g, one dose a day. Modifications according to the symptoms were conducted until discharge. Application of TCM treatments were continued after discharge for more than 3 months.

Acupuncture treatment: Acupuncture on acupoints: Zusanli, Yinlingquan, Quchi, Taiyuan, Tai Chong, Feishu, Dazhui, Fenglong, Linggu, and Dabai. Acupuncture methods: even reinforcing–reducing method was used for acupuncture. Retained the needle for 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Took Zusanli, Guanyuan, Dazhui, Pishu and Feishu. Moxibustion methods: selected two to three points each time. Conduct with a moxa stick for 10 minutes at each point, once a day or once every other day.

Auricular acupoints: Took internal nose, external nose, throat, Jiaogan, forehead, temporal bone, adrenal gland, lung, and tumor-specific area. Methods: stuck auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

The patient had psychotherapy at the beginning of hospitalization to increase her anticancer confidence. Meanwhile, the patient gradually began practicing qigong, sports therapy, and so on to increase her self-healing powers.

Treatment effects: The patient had been hospitalized for 60 days. Three times of whole-body hyperthermia, 20 times of local hyperthermia, 25 times of chelation detoxification, and 16 times of EBOO were given. The general condition improved significantly after combined treatment. The weight was increased to 56 kg. Chest tightness and pain, chest pain, cough, hemoptysis, and other symptoms disappeared. Occasionally, the patient had hoarseness but could take care of it herself. Multiple lung metastases were seen by CT review. The metastatic lesions were narrowed compared with the original ones. The maximum lesion was 1.2 cm × 2.0 cm, and no new metastases occurred. Blood routine: RBC 4.2×10^{12}/L, Hb 123 g/L, and WBC 3.7×10^{9}/L. Thyroid function: FT3 3.2 pmol/L, FT4 15.4 pmol/L, and thyroid-stimulating hormone 4.7 mIU/L. Her KPS was 100. The patient insisted on treatment as an outpatient afterward and received comprehensive treatments once a month. Conducted review once every 3 months.

6.5.4 Related research in China and abroad

Liu Qinjiang et al. have explored the effects of RF on thyroid carcinoma cell sodium/iodide symporter expression through clinical research. Results showing positive iodine uptakes by whole-body scan were four cases (4/29) before RF, 19 cases (19/29) 2 weeks after RF, and 12 cases (12/29) 4 weeks after RF, respectively. After RF was conducted for 4 weeks, serum Ig levels in 5 cases were elevated, those in 17 cases were lowered, and there was no change in seven cases. A total of 25 cases (25/29) were effective for treatment and 15 cases were cured (15/29). It indicated that thyroid carcinoma cells showed iodine intake because the sodium/iodide symporter lost expression induced by RF, which improved the clinical efficacy of I^{131} for the treatment of differentiated thyroid carcinoma.

Liu Yanpeng et al. have proved, by clinical studies, that whole-body thermochemotherapy for the treatment of thyroid multiple bone metastases can effectively relieve pain, control metastases, and prolong survival time. At the same time, it can reduce the side effects of chemotherapy compared with chemotherapy alone.

Foreign studies have shown that thermoradiotherapy can increase the response rate and survival rate in patients with head and neck cancer and lymph node metastasis. Valdagni has reported the results of a randomized study of 44 patients with $N_{2\text{-}3}$ head and neck cancer. The same dose was applied for the radiation treatment. Hyperthermia was conducted within 20–30 minutes after radiotherapy. The temperature in the tumor was 42.5°C, lasting for 30 minutes. The results showed that the two groups had significant differences in the rate of CR (83% vs. 41%), survival rate without local recurrence (68% vs. 24%), and 5-year overall survival rate (53% vs. 0%).

6.6 ESOPHAGEAL CANCER

China is the country where esophageal cancer morbidity and mortality are the highest. Linxian of Henan Province is a high-risk area of esophageal cancer in China. Generally, the incidence in males is significantly more than that in females. The highest incidence by age is from 60 to 64 years, and ages 50–69 years account for 60%. In general, 20% of patients can receive surgery, with a resection rate of about 80%, and the postoperative 5-year survival rate is 30%. The survival rate using advanced radiotherapy is less than 10%. The effect of

chemotherapy alone is poor, which explains the importance of early diagnosis and treatment of esophageal cancer as well as the necessity to enhance the integrative treatment of surgery by including other treatments.

The pathology of early esophageal cancer can be substantially divided into insidious type, erosive type, plaque type, and papillary type. The medium-advanced stage is divided into medullary type, fungating type, ulcerative type, and constrictive type. According to the histological features of esophageal cancer, it can be divided into esophageal squamous cell carcinoma, adenocarcinoma, adenoacanthoma, small cell undifferentiated carcinoma, and sarcoma, of which squamous cell carcinoma accounts for more than 90%. Because the esophagus has no serosal layer, the cancer can easily spread to adjacent organs, such as trachea, bronchus, lung, pleura, pericardium, aorta, and so on, through the loose external coat of the esophagus after penetrating the muscular layer. In addition, metastasis of esophageal cancer is also accessible to peripheral lymph nodes and remote regions through lymph node metastasis, blood-borne metastasis, and other ways.

Esophageal cancer is occult in onset and is asymptomatic in the early stage. Some patients have esophageal foreign body sensation, or food passes slowly or the patient has a choking feeling. Also, it can be expressed as retrosternal burning, prickly, or referred pain when swallowing. Patients with advanced esophageal cancer often go to the hospital due to acataposis, dysphagia, or inability to eat and often experience vomiting, upper abdominal pain, weight loss, and other symptoms.

6.6.1 Conventional treatments

6.6.1.1 SURGERY

Because early esophageal lesions are small with shallow infiltration, surgery combined with integrative treatment means can often achieve a cure. For middle and lower part esophageal cancer, surgical resection is preferred when combined with chemotherapy, radiotherapy, and other symptomatic and supportive treatments. Endoscopic dissection or partial surgical removal can be applied for precancerous lesions or early cancer recognized by gastroscopy. Surgical treatment in combination with radiotherapy or chemotherapy is recommended when cancer cells have deep infiltration in the esophageal wall. For patients with esophageal cancer of stages I, II, and III ($T_3N_1M_0$ and partial $T_4N_1M_0$) and recurrent esophageal cancer after radiotherapy but not distant metastasis, surgery treatment can be conducted for patients who are able to tolerate surgery in general. Because the late lesion is difficult to be resected, and to relieve symptoms such as feeding problems, cytoreductive, bypass, or gastrostomy surgery can be carried out. Clinical data show that the operation can achieve radical resection purpose for early- and mid-stage carcinoma. For patients with advanced esophageal cancer who cannot eat, or for patients with esophageal stenosis or esophageal fistula, endoscopic stenting can be used to relieve esophageal obstruction. Complete esophageal resection should be combined with routine regional lymph node dissection. For patients in the perioperative period, especially when patients have postoperative low immunity and are more prone to remnants or exfoliated cancer cell growth and metastasis, chelation detoxification (once every other day) and medical ozone (EBOO once every other day for patients in good condition and intravenous medical ozone saline for weak patients) can be applied. At the same time, apply TCM and acupuncture to improve immunity and prevent metastasis. Corresponding postoperative hyperthermia is given to achieve the purpose of cure, whereas other nontoxic integrative treatments, such as TCM, chelation and detoxification, and so on, are given to reduce toxicity and enhance effects. For patients in the medium-advanced term, the effects of chemotherapy, surgery, and radiotherapy are poor, and nontoxic integrative treatments of hyperthermia, chelation detoxification, medical ozone, and TCM are preferred.

6.6.1.2 RADIOTHERAPY

Indications for esophageal cancer radiotherapy are wide. Except for esophageal fistula formed by esophageal perforation; distant metastasis; apparent cachexia; and severe heart, lung, and liver diseases, radiotherapy can be carried out. Radiotherapy includes radical radiotherapy and palliative radiotherapy. Because the trauma of cervical and upper thoracic esophageal cancer surgery is major with a high incidence of complications while radiotherapy damage is small and efficacy is greater than surgery, radiotherapy should be preferred. If the patient's general condition is acceptable, the patient can comfortably eat a semiliquid or liquid

diet. Thoracic esophageal cancer is without supraclavicular lymph node metastasis and distant metastasis; without trachea invasion, esophageal perforation, and signs of bleeding; with lesion lengths less than 7 to 8 cm; and without medical contraindications; with the aforementioned conditions, radical radiotherapy can be carried out. Other patients may have palliative radiotherapy aimed at alleviating esophageal obstruction, improving feeding difficulty, reducing pain, improving quality of life, and prolonging survival time. If the patient cannot tolerate surgery, or the tumor is judged to be unresectable, and if the symptom of dysphagia is mild, radiotherapy can be carefully selected. If the dysphagia symptom is obvious and seriously affects eating, laser treatment should be used, especially when the stenosis is in the middle or lower esophagus, which is caused by the pedunculated tumor projecting within the lumen of the esophagus. If the annular stenosis is in the thoracic esophagus, foreign researchers recommend probe dilatation plus built-in tube surgery. At the same time, conduct adjuvant radiotherapy (external exposure and brachytherapy).

6.6.1.3 CHEMOTHERAPY

As a systemic treatment, chemotherapy is an important part of the integrative treatments of esophageal cancer. Esophageal cancer chemotherapy is divided into palliative chemotherapy, neoadjuvant chemotherapy (preoperative), and adjuvant chemotherapy (postoperative). Esophageal cancer chemotherapy mostly uses a cisplatin and 5-fluorouracil combination chemotherapy program. While esophageal cancer palliative chemotherapy has been using a cisplatin and 5-fluorouracil combination program, in the past 5 years there have been studies to explore the efficacy of a new generation of chemotherapy drugs for esophageal cancer treatment, mainly focusing on palliative chemotherapy in advanced esophageal cancer. These commonly used drugs include capecitabine, TS-1, taxanes, vinorelbine, camptothecin, nedaplatin, and carboplatin.

6.6.1.4 HYPERTHERMIA

Hyperthermia can directly kill residual cancer cells; promote cancer cell apoptosis; regulate the body to produce tumor necrosis factor (TNF), interleukin (IL)-2, and other immune factors; enhance the anticancer effect itself; enhance sensitivity to chemotherapy; inhibit primary or metastatic lesions from continuous proliferation; and prevent metastasis. The combination of whole-body hyperthermia with chemotherapy is recommended for the early stage, in which it can modulate the immune function and enhance the ability of anticancer effect. If it is difficult for the patient to tolerate whole-body hyperthermia, whole-body medium-low temperature hyperthermia can be given. For medium-advanced patients with KPSs of 80 points or above, whole-body hyperthermia can be given. Patients without abnormal cardiopulmonary function can consider having high-temperature hyperthermia. If it is not suitable for the patient to have whole-body hyperthermia, local deep hyperthermia could be offered once every other day.

6.6.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can not only effectively remove toxins from the body and improve immune function but also reduce the side effects of chemotherapy and enhance chemosensitivity. Simultaneous use of chelation detoxification with hyperthermia can have a synergistic effect. Application of chelation detoxification can have the inhibitory effect of reducing cancer recurrence and metastasis, repair the damage of various tissues and organs, and improve cell function. The patient with a generally acceptable condition is given therapeutic amounts once every other day. Twenty times of chelation detoxification for medium-advanced patients are considered to be a course of treatment, and three continuous courses can achieve the best effect. After the condition becomes stable, gradually decrease chelation detoxification to once per week for 3 continuous months.

6.6.1.6 MEDICAL OZONE THERAPY

It can stimulate improvement to the immune system itself, directly kill the early cancer cells present in the blood or lymph, and reduce the side effects of chemotherapy. It can also promote the healing of surgical wounds. We especially recommend EBOO once every other day. For the patient with weak constitution or with coagulation disorder, autohemotherapy or intravenous medical ozone saline can be used once every other day. At the same time, medical ozone acupoint injection can be carried out once every 3 days. For specific point

selection, refer to the acupoints mentioned in Section 6.6.1.8. For medium-advanced patients with recurrence and metastasis, if the general condition of the patients is still good, KPSs are more than 60 points, and bleeding tendency and active bleeding do not exist, EBOO is preferred once every other day, with 20 times as a course of treatment. If the patient is in poor general condition but has no active bleeding, intravenous medical ozone can be given once every other day, with 20 times as a course of treatment. Medium-advanced patients can be given medical ozone acupoint injection once every 3 days till a stable condition is achieved.

6.6.1.7 TRADITIONAL CHINESE MEDICINE

For the syndrome of liver stagnation and phlegm coagulation, a modified Xuefu Zhuyu Decoction is given. For the syndrome of blood stasis and sputum block, Xuanfu Daizhe Decoction plus modified Sini Powder are given. For the syndrome of yin deficiency and internal heat, Yiguan Decoction plus modified Yangwei Decoction are given. For the syndrome of deficiency of qi and declination of yang, Danggui Buxue Decoction plus modified Ginseng Guizhi Decoction are given. Chinese formulated products commonly used are Pingxiao Capsule, Huachansu Injection, Yadanzi Emulsion, Antike, Zengshengping Tablet, Tongdao Powder, and so on.

6.6.1.8 ACUPUNCTURE

6.6.1.8.1 Early esophageal cancer

The syndrome is mainly qi stagnation and coagulated phlegm. The therapeutic principle should focus on soothing the liver and regulating the circulation of qi, as well as removing phlegm and resolving mass.

Acupuncture on acupoints: Neiguan, Shangwan, Tanzhong, Sanyinjiao, and Yanglingquan.

Methods: Even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

6.6.1.8.2 Medium-advanced esophageal cancer

The syndrome is mainly phlegm and blood stasis, or deficiency of both qi and yin. The therapeutic principle should be to supplement qi and nourish yin, reverse adverse flow of qi, control nausea and vomiting, and relieve chest stiffness to regulate qi.

Acupuncture on acupoints: Geshu, Neiguan, Shanzhong, Zusanli, Zhongwan, Sanyinjiao, Taixi, Ganshu, and Qihai.

Methods: Even reinforcing–reducing method is used for acupuncture with needle retention for 20 minutes, once per day; take 2 days off after 5 times, with 10 times as a course.

Moxibustion on acupoints: Guanyuan, Shenque, and Zusanli.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after 5 times of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Esophagus, stomach, cardia, liver, subcortex, Jiaogan, spleen, and mouth.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.6.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Medicated diet is mainly for the early stage. Enteral or total parenteral nutrition can be considered to be given according to the nutritional status of patients when surgery, whole-body hyperthermia, and chemotherapy are conducted, to prevent malnutrition and establish a therapeutic sensitizing effect.

For patients in the medium and advanced stages who often have difficulty eating, intravenous infusion of high nutrition should be carried out in combination with other integrative treatments to prolong survival time and improve quality of life. For patients with gastrointestinal obstruction, total parenteral nutrition should be given for support. For esophageal cancer patients in the medium-advanced stage, the therapy

should be the same as that for early esophageal cancer and be in combination with qigong, music therapy, psychotherapy, and so on to calm heart, regulate breathing, and calm the nerves for relieving pain.

6.6.1.10 OTHERS

For patients in the early stage, we recommend them to actively practice qigong, tai chi, and so on and use TCM to regulate emotions. Guide patients to have peace of mind and to overcome panic and desperation, so that they can face the disease with a positive, optimistic, and open-minded attitude. Also, combine music therapy and sound wave therapy to alleviate psychological pressure. Because esophageal cancer at the medium-advanced stage has more complications that could seriously affect the patient's quality of life, such as dysphagia due to gastrointestinal obstruction and irritating cough caused by cancer compression, central antibechic can also be applied to alleviate these complications and minimize the suffering of patients. Note that if esophageal stent implantation has been implemented, local hyperthermia cannot be reused after the installation of the esophageal stent.

6.6.2 Combination of hyperthermia and conventional treatments

6.6.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Surgery is one of the primary means for esophageal cancer treatment. After the postoperative wound is completely healed, whole-body hyperthermia or local hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of the patient by the hyperthermia center physician. If patients are assessed to be in good general condition and can tolerate whole-body hyperthermia, six to eight times of whole-body medium-high hyperthermia can be conducted in combination with chemotherapy cycles. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Local hyperthermia can be added at the intermission periods of whole-body hyperthermia.

For patients not suitable for whole-body medium-high hyperthermia, local hyperthermia of the chest or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, with 20 times as a course for long-term concomitant treatment. Carry out whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.6.2.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy is one of the preferred primary means for treating esophageal cancer. The combination of hyperthermia and radiotherapy may increase the sensitivity of cancer cells to radiotherapy, reduce fibrosis of the esophagus, and reduce skin and hematologic toxicity caused by radiotherapy. The order of radiotherapy followed by hyperthermia is appropriate, and many advocate that the interval time of less than 2 hours is appropriate. It is appropriate to conduct local hyperthermia once every other day in combination with radiotherapy for the whole process. From a clinical point of view, combining with hyperthermia during radiotherapy significantly reduces fibrosis of the esophagus, bone marrow suppression, and skin damage caused by radiotherapy and is conducive to the successful completion of the treatment.

6.6.2.3 HYPERTHERMIA AND CHEMOTHERAPY

The therapeutic effect of chemotherapy alone on esophageal cancer is not ideal. Chemotherapy for esophageal cancer is mostly applied as postoperative chemotherapy or in combination with radiotherapy. When combining radiotherapy, the radiotherapy synchronization method can be adopted, and local hyperthermia is mainly applied as well. When applying postoperative chemotherapy, if patients are assessed to be in good general condition, whole-body hyperthermia can be combined for each chemotherapy cycle. Preparation before hyperthermia and observation during hyperthermia are the same as mentioned earlier.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body hyperthermia can be carried out in the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Simultaneously carry out hyperthermia and chemotherapy cycles for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy, and during the intermission periods of radiotherapy, once every other day.

For patients not suitable for whole-body hyperthermia, local hyperthermia of the chest or whole-body medium-low temperature hyperthermia can be carried out. Local hyperthermia is conducted once every other day and can be continued during the intermission periods of chemotherapy. Take 1 week off after two treatments of chemotherapy. Combine local hyperthermia during chemotherapy, with 20 times as a course of treatment. Take 15 days off after three courses of treatment, and then continue to have maintenance therapy to consolidate the curative effect. Local hyperthermia can be a long-term concomitant therapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.6.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Cancer patients receiving chemotherapy can be given chelation and detoxification therapy to remove toxins from the body, promote physical recovery, and regulate the immune system. Note that chelation detoxification needs infusion of more than 2 hours. Local hyperthermia or whole-body hyperthermia can be simultaneously applied with chelation and detoxification to improve efficacy.

6.6.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance the effect on immunity, and increase the efficacy of medical ozone. We propose giving EBOO treatment for medical ozone therapy as soon as possible, once every other day, with 20 times as a course of treatment for a total of three courses. Change to once per week after the end of treatment for consolidated therapy.

6.6.2.6 HYPERTHERMIA AND OTHER TREATMENTS

Cancer treatment needs integrative treatments. The combination of hyperthermia with TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, and colon cleansing therapy can increase the efficacy and safety of treatment.

DC-CIK cell therapy: (1) For early esophageal cancer after radical operation, combined DC-CIK transfusion can effectively remove small residual lesions and reduce recurrence. The number of CIK cells for each reinfusion should reach at least 1×10^{10}, once per month with four times as a course of treatment. Conduct periodic review after transfusion, and if there is no recurrence an additional treatment is carried out once every 6 months. Collecting tumor tissue during the operation for the preparation of individual peptides and DC vaccines to culture together with CIK can provide better efficacy. (2) For patients who need postoperative adjuvant chemotherapy, DC-CIK treatment can also be combined and the efficacy is greater than chemotherapy alone. Treatment program: 1 day before chemotherapy, collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct a consolidated therapy every 2 to 3 months.

Systemic biofeedback therapy: 3 times a week, with 15 times as a course of treatment. Adjust to once or twice a week after two to three courses of treatment for long-term treatment.

Alkalization treatment effect: Oral sodium bicarbonate therapy can be used. For adults, take 100 mg/kg/day. Powder can be added to 500 mL of drinking water or fruit juice and drunk slowly, once a day. The tablet can be divided into the amount for three doses and for direct oral administration. The patient needs to drink more water, with 8 days as a course of treatment. Simultaneously apply with chemoradiotherapy. Patients with cancer can take sodium bicarbonate 2 to 3 g/day for long-term oral administration, which

can significantly reduce chemotherapy side effects, enhance the efficacy and immune function, and reduce chances of infection. When taking sodium bicarbonate by intravenous and oral administration, measure urine or saliva pH values once every morning (slip method) to ensure that the saliva pH value is above 7.4 and the urine pH value is above 7. After the end of treatment, measure the intravenous or arterial pH value and compare it with the value before treatment; pH should be more than 7.35, as required.

Colon cleansing therapy: Patients without feeding difficulty can take fruit and vegetable drinks with the coffee enema; patients with feeding difficulty can take a single coffee enema, but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, give parenteral nutrition for support.

Reasonable nontoxic integrative treatment taken for the treatment of esophageal cancer can significantly improve the cure rate, effectively reduce the side effects of radiotherapy, ensure the quality of life of cancer patients, inhibit cancer progression, and prolong survival time.

6.6.2.7 INTRACAVITARY HYPERTHERMIA

For cancers with lengths less than 8 cm, intracavitary heating can be applied. Pay attention to the positioning and the distance of the spiral coil of radiator in the cavity. So far, notwithstanding some reports, a satisfactory result has not been obtained. Intracavitary hyperthermia includes intracavitary microwave hyperthermia, intracavitary radio-frequency hyperthermia, intracavitary microwave high-temperature solidification, and so on.

6.6.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.6.2.8.1 Bath

Proven prescription 1: Ramulus cinnamomi 60 g, *Acanthopanax senticosus* 50 g, and *Glycyrrhiza uralensis* 5 g. Add water to drugs and boil for 30 minutes. Remove slag and take juice. Immerse feet for 30 minutes once a day, with 10 days as a course of treatment. Efficacy: supplements qi to warm yang and mainly cures a variety of fatigue. It is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 2: Radix astragali 450 g, *Radix codonopsis* 300 g, *Radix polygoni Multiflori Preparata* 300 g, *Ligusticum chuanxiong Hort* 300 g, *Fructus alpinia Oxyphylla* 300 g, *Semen cuscutae* 300 g, *Atractylodes macrocephala Koidz* 300 g, and *Carthamus tinctorius L.* 200 g. Put all drugs into the wok and add the proper amount of water. Boil for 50 minutes. Remove slag and take juice. Blend with 450g of white wine. Take bubble bath for 40 minutes, once a day with 10 days as a course of treatment. It tones the lung, spleen and kidney and is mainly a cure for a variety of types of fatigue. It is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 3: Stems and leaves of *Panax ginseng* 30 g, *Atractylodes macrocephala Koidz* 30 g, *Radix saposhnikoviae* 20 g, yam 20 g, and *Glycyrrhiza uralensis* 6 g. Add drugs and the proper amount of water. Boil twice and each time for 30 minutes. Combine filtrate and immerse feet for 30 minutes once a day, with 15 days as a course of treatment. Efficacy: Invigorates spleen and replenishes qi. It is applicable to long-term weakness of cancer patients who lack resistance.

Proven prescription 4: Rhodiola 800 g, *Semen coicis* 500 g, *Acanthopanax senticosus* 400 g, *Radix astragali* 300 g, *Cyrtomium fortunei* 300 g, *Schisandra chinensis* 300 g, *Angelica sinensis* 200 g, and *Ligusticum chuanxiong Hort* 200 g. Boil twice and for 50 minutes each time. Combine filtrate and immerse feet for 40 minutes once a day, with 15 days as a course of treatment. Efficacy: supplements qi and nourishes yin as well as invigorates qi and promotes blood circulation. It is applicable to long-term weakness in cancer patients who lack resistance.

6.6.2.8.2 Moxibustion therapy

It is applicable to cancer patients with long illness, yang deficiency, and weakness and is capable of enhancement of immunity.

Acupoints: The first group of acupoints includes Dazhui, Shenshu (both), and Pishu (both). The second group of acupoints includes Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both).

Herbal cake making: Take equal amounts of *Radix astragali*, *Angelica sinensis*, *Fructus psoraleae*, *Curculigo orchioides*, and *rhubarb*, and smash them into powder. Filter with 120 mesh sieve and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm.

Moxibustion: Place the moxa cone with a diameter of 2 cm and a height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints each time, with two groups of points alternated, once every other day with 24 times as a course of treatment.

Efficacy: Enforces spleen and nourishes kidney, and for muscularity and general health.

6.6.2.9 Hyperthermia indications

Patients with more than 2 weeks after surgery and well-healed wounds, and patients with locally advanced esophageal cancer who can accept chemo- and radiotherapy. If intracavitary hyperthermia is used, the patient shall be able to have a semiliquid diet based on the degree of obstruction. Advanced patients in need of local treatment to relieve symptoms are required to have KPSs greater than 60 points.

6.6.2.10 Hyperthermia contraindications

Severe ulcerative esophageal cancer (with caution in the implementation of intracavitary hyperthermia); esophageal cancer patients with active bleeding; patients with bleeding tendency; and patients with esophageal perforation, esophageal fistula, mediastinal-esophageal fistulae, and mediastinitis, as well as cachexia.

6.6.3 Introduction of a typical case

A patient named Hong, male, 49 years old, was admitted on June 19, 2007, to Clifford Hospital due to "20 months after esophageal cancer operation, progressive weight loss accompanied with hoarseness for more than 2 months, and progressive dysphagia for 20 days." Because the patient had repeated upper abdominal pain accompanied with vomiting, in October 2005, CT was performed, which showed the possibility of lower esophageal malignancy. Endoscopy showed neoplasm in the lower esophagus, and pathological feedback showed moderately differentiated squamous cell carcinoma. Then, radical resection of the esophageal cancer was carried out under general anesthesia and the surgery went smoothly. Pathological examination revealed esophageal squamous cell carcinoma, infiltration of muscle coming up to the serosa layer, no cancer invasion in the upper and lower cut ends, and no lymph node metastasis. Postoperative recovery was good, and chemoradiotherapy was not conducted. In April 2007, the patient presented weight loss of about 10 kg within 2 months, hoarseness, poor appetite, and occasional vomiting. The patient showed dysphagia 20 days before admission. Later, the patient was admitted to the hospital for further treatment.

Physical examination: Normal development, body weight loss, weight 49 kg, moderate anemia, no superficial lymph node enlargement, and normal heart and lung auscultation. Abdomen was flat without tenderness. Liver and spleen were not palpable.

An approximately 15-cm surgery scar was on the breast. Petechiae could be seen on the left side of the abdomen and waist. The KPS was 70.

Auxiliary examination: Blood routine: RBC 2.8×10^{12}/L, Hb 85 g/L and WBC 4.2×10^{9}/L. Biochemistry: ALT 32 U/L, AST 21 U/L, TP 67 g/L, ALB 35.5 g/L, ALP 221 U/L, GGT 125 U/L, TBIL 17.8 μmol/L, DBIt 4.0 μmol/L, Cr 31 μmol/L, Ua 236 μmol/L, BUN 3.1 mmol/L, GLU 4.11 mmol/L, TG 0.36 mmol/L, GHO 2.56 mmol/L, K^+ 3.8 mmol/L, Na^+ 139 mmol/L, Cl^-102 mmol/L, and Ca^{2+}1.96 mmol/L. Tumor markers: CEA 3.7 ng/mL, AFP 6.6 ng/mL, CA-125 12 U/mL, CA-153 12 U/mL, CAl9-9 27 mL, and TSGF 31.7 U/mL. Five items of immunity and trace elements were normal. Abdominal ultrasound showed no abnormalities. Gastroscopy showed that the anastomosis had swelling, and erosion and the pathological report revealed biopsy cancer at the anastomosis (moderately differentiated squamous cell carcinoma). Esophageal barium meal: postoperative change of the lower esophagus and mucosal barium filling defect at anastomosis. Electrocardiogram (ECG) and chest x-ray were normal. Fecal occult blood: (+ +).

Diagnosis: Recurrence after resection of esophageal cancer.

Integrative treatment prescription: The patient faced recurrence after resection of esophageal cancer. His general condition was poor and KPS was 70 with nausea, vomiting, and significant weight loss, most likely because the esophageal stricture caused difficulty in feeding after tumor recurrence and the tumor consumption caused severe malnutrition. As a result, the patient was immediately given nutritional support after hospitalization, i.e., total parenteral nutrition and medicated nutritional supplements. To treat the cancer,

local hyperthermia of the chest was given once every other day. Hyperthermia was conducted simultaneously with chelation detoxification therapy. Intravenous medical ozone saline treatment was carried out once every other day and alternated with hyperthermia and chelation detoxification. And, systemic biofeedback therapy was conducted once every other day. Combined TCM and acupuncture treatments were carried out throughout the treatment. The patient had a dark red tongue and white and greasy fur, and the symptom belonged to stagnation of phlegm and qi. The purpose of TCM treatment was to alleviate mental depression and repress upward perversion of qi, as well as to reduce phlegm and resolve masses.

Medications: The prescription was Xuanfu Daizhe Decoction and modified Sini Powder with specific medicines: *Inula japonica* 15 g, *Ruddle* 15 g, *Radix bupleuri* 15 g, *Fructus aurantii* 15 g, *Radix curcumae* 15 g, *Pericarpium citri Reticulatae* 10 g, *Pinellia ternata* 15 g, *Radix sophorae Tonkinensis* 10 g, *Paris polyphylla Sm.* 15 g, *Radix paeoniae Alba* 15 g, *Gecko* 6 g, and *Nidus vespae* 10 g, one dose a day and taken by decoction.

Acupuncture treatment: Acupoints: Geshu, Neiguan, Shanzhong, Zusanli, Zhongwan, Sanyinjiao, Taixi, Ganshu, and Qihai and Waisangun. Methods: even reinforcing–reducing method was used for acupuncture. Retained the needle for 20 minutes, once per day. Took 2 days off after five acupuncture treatments.

Moxibustion: Acupoints: Zhongwan, Guanyuan, Shenque, and Zusanli. Methods: Took two points each time. Conducted moxibustion with the moxa stick. Carried out moxibustion on one point for 10 minutes, once a day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Esophagus, stomach, cardia, liver, subcortex, Jiaogan, spleen, and mouth. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

The patient's symptoms of nausea and vomiting disappeared after 1 week. The dosage was increased for chelation detoxification therapy three times a week for 6 consecutive weeks. Intravenous medical ozone saline injection was used for 2 consecutive weeks; systemic biofeedback therapy was used for 2 consecutive weeks. TCM and acupuncture remained unchanged. After 2 weeks, the patient's mental condition was improved and his weight had increased to 52 kg; his blood routine was as follows: RBC 3.5×10^{12}/L, Hb 105 g/L, and WBC 4.7×10^{9}/L. At that time, intravenous medical ozone saline was adjusted to EBOO for 18 treatments, and the hyperthermia was changed to the combination of whole-body medium-high temperature hyperthermia and local hyperthermia. The whole-body hyperthermia was conducted once every 2 weeks for a total of four times. Local hyperthermia was conducted 3 times a week and once every other day for a total of 27 times. Systemic biofeedback therapy was conducted 3 times a week and once every other day for a total of 27 times. Chelation detoxification was conducted simultaneously with hyperthermia. Acupuncture was continued as in the original treatment, and TCM was modified on the basis of the original prescription. After 3 months of treatment, it could be seen by endoscopy that the anastomotic mild swelling and erosive lesions were significantly reduced.

After discharge, the patient continued to receive local hyperthermia, EBOO, chelation detoxification, TCM, acupuncture, feedback system biological treatment, medicated conditioning, and other nontoxic integrative treatments as an outpatient, once a week.

Treatment effects: After 3 months of comprehensive treatments dominated by hyperthermia, the patient's nausea, vomiting, anorexia, weight loss, anemia, and other symptoms were markedly improved. The patient's mind-set was significantly improved, weight had increased by 9 kg, diet was normal, sleep was better, anemia was basically corrected, and KPS was 100. The patient continued adhering to integrative treatments of 1 week per month to consolidate the effect, prevent recurrence and metastasis, and improve immunity.

6.6.4 Related research in China and abroad

Hongmei et al. conducted a randomized controlled trial of 20 cases of patients with esophageal cancer after radiotherapy and explored the effects of hyperthermia radiotherapy on the subtype of T-helper cell (Th1/Th1) of esophageal cancer patients with radiotherapy. Local endogenetic thermotherapy was used for heating, two times a week for 4 to 5 weeks of treatment. The results showed that local endogenetic thermotherapy could promote the body to reverse from Th2 cells to Th1 cells and adjust Thl/Th2 cells balance.

Morita et al. have also confirmed in clinical studies of the treatment of esophageal cancer patients that combined hyperthermia could activate the patient's immune system and improve the clinical efficacy, compared with chemotherapy alone. Jing Yiqiang conducted a randomized controlled trial of 98 cases of esophageal cancer patients and observed the clinical efficacy of hyperthermia plus radiotherapy in patients with esophageal cancer. The results showed that the hyperthermia combined with radiotherapy group was superior to the radiotherapy alone group in treatment efficacy and the difference was statistically significant.

Hu Yonghong has also confirmed by clinical studies of patients with inoperable esophageal cancer that hyperthermia combined with radiotherapy was superior to radiotherapy alone.

Dai Bing et al. conducted a randomized controlled trial of short-term efficacy in patients with medium-advanced esophageal cancer by hyperthermia combined with chemotherapy. Hyperthermia temperature was controlled at 38°C–40°C and maintained for 60–70 minutes for each treatment. Each patient received two treatments a week. The control group underwent chemotherapy of the "PF scheme." The efficacy was evaluated after treatment (two cycles). The CR and PR of the hyperthermia combined with chemotherapy group were 10.8% and 40.5%, respectively, which were significantly better than the control group. The 1-year survival rate was 74.1%, which was significantly higher than that for the control group, 42.1%, and had statistical significance.

Saeki et al. have reported the results for 294 esophageal cancer cases who received chemoradiotherapy plus intracavitary heating before surgery, and the results showed that postoperative tissue sample efficiency of the chemotherapy plus intracavitary heating group was better than the single chemotherapy group; the 3-year and 5-year survival rates of preoperative hyperthermia combined with chemoradiotherapy in patients with T_4 cancer were 26.5% and 15.9%, respectively, whereas they were 0% for patients without hyperthermia.

6.7 LUNG CANCER

Lung cancer is one of the most common cancers in China. Its clinical manifestations are complex. It can be broadly grouped into four categories: symptoms of primary cancer, symptoms of intrathoracic spread, symptoms of distant spread. and extrapulmonary manifestations. Symptoms and signs are accompanied with the site of occurrence, cancer size, pathological type, metastasis, and so on. Common symptoms are cough, hemoptysis or bloody sputum, chest pain, chest tightness, and others. Some patients manifest symptoms of shortness of breath, wheezing, and localized pneumonia due to airway obstruction.

The WHO has briefly divided histological manifestation of lung cancer into squamous cell carcinoma (epidermoid carcinoma), adenocarcinoma, large cell carcinoma, small cell undifferentiated carcinoma, and mixed type, of which the first three categories are collectively referred to as non–small cell lung cancer.

The main treatments are surgery, radiotherapy, and chemotherapy, but no matter which treatment is used the treatment efficiency is not satisfactory. As a result, integrative treatment is of paramount importance. A wide range of thermal methods can be applied to the treatment of lung cancer; but whether it is interstitial coagulation hyperthermia or out-of-body heating, when used alone it is difficult to form an effective treatment temperature. Generally, radiotherapy or chemotherapy is combined.

6.7.1 Conventional treatments

6.7.1.1 SURGERY

Non–small cell lung cancer patients at phase I, II, or IIIa; patients with no clear surgical contraindications; and patients with clear indications for surgery can choose to have surgical treatment. Patients who are not suitable for surgery can select cryosurgery, radio-frequency ablation, or some other minimally invasive treatment.

6.7.1.2 RADIOTHERAPY

Small cell undifferentiated carcinoma is the most sensitive to radiotherapy among the various types of lung cancers, followed by squamous cell carcinoma and adenocarcinoma. It is commonly used for patients with a wide range of diseases, with distant metastasis or a bad general condition, or not suitable for surgical

treatment to improve symptoms and prolong life. Comprehensive application of radiotherapy can also be adopted with surgery. According to the location and extent of the cancer source as well as the expected difficulty of surgery, preoperative radiotherapy can improve the resection rate. If small cell undifferentiated carcinoma patients are suitable for surgical resection, preoperative radiotherapy can improve efficacy. For patients with lymph node metastasis and positive surgical margins, radiotherapy has a positive meaning. For patients who are unresectable due to old age or poor cardiac function, radiotherapy alone can be considered. For patients at phase IIIb who are not suitable for surgery due to existing mediastinal vital organ invasion or supraclavicular lymph node metastasis, radiotherapy; chemotherapy; or a comprehensive treatment of radiotherapy, chemotherapy, and hyperthermia can be conducted according to the pathology. Local conformal radiotherapy is safer because it improves the efficiency of the target dose. As a result, conformal radiotherapy technology is preferred for radiotherapy. The application of preventative brain radiotherapy for small cell lung cancer can reduce the number of brain metastases or delay brain metastases.

6.7.1.3 CHEMOTHERAPY

Small cell undifferentiated lung cancer is the most sensitive to chemotherapy among the various types of lung cancers and the efficacy is the best, followed by squamous cell carcinoma. Adenocarcinoma has the lowest sensitivity. In recent years, several drugs that act at different cell cycles are chosen for combination application. Anticancer perfusion for preoperative bronchial artery intubation can also reduce the cancer source and increase the resection rate. Postoperative chemotherapy is routinely given. Whole-body hyperthermia and local hyperthermia are applied according to the situation after hyperthermia assessment. Chemotherapy commonly uses a combination program. Postoperative chemotherapy is given for small cell lung cancer and non–small cell lung cancer except for phase Ia, and radiotherapy is given to patients with postoperative residues.

6.7.1.4 HYPERTHERMIA

A wide range of thermal methods can be applied to the treatment of lung cancers, including whole-body hyperthermia; regional hyperthermia; interstitial coagulation hyperthermia; RF local hyperthermia; thermochemotherapy; thermoradiotherapy; combination of hyperthermia, radiotherapy, and chemotherapy; and intrapleural perfusion hyperthermic chemotherapy. Hyperthermia has the effect of enhancing chemoradiotherapy, the effect of using high temperatures to kill cancer cells, and the effect of promoting cancer immunity. Temperatures above 60°C can make the lung cancer tissue inactive in situ. Out-of-body heating, whether it is interstitial solidification hyperthermia or microwave or radio-frequency heating, is local heating. Hyperthermia alone has difficulty in achieving an effective treatment temperature throughout the entire tumor, and the cancer-surrounding parts tend to be of lower temperatures. Although intrapleural perfusion hyperthermic chemotherapy can reach above 42°C in the chest, its effect of killing cancer cells is still not satisfactory. Therefore, a combination therapy of radiotherapy, chemotherapy, and hyperthermia is mostly used for outpatients. Whole-body hyperthermia or regional hyperthermia can make the temperature more uniform, usually maintaining it at 40°C–42°C. Clinical studies have shown that hyperthermia has some therapeutic effect in advanced lung cancer; intrapleural perfusion hyperthermic chemotherapy has a better palliative treatment effect; and the combination treatment of radiotherapy, chemotherapy, and hyperthermia has some effect in patients with recurrence after radiotherapy.

6.7.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given, from the period of operation to chemotherapy, to the patient with physical weakness and low immunity after operation. On the one hand, it promotes physical recovery and regulates the immune system and, on the other hand, it can kill residual tumor cells or inhibit early metastasis.

6.7.1.6 MEDICAL OZONE THERAPY

For medical ozone therapy, EBOO is the preferred treatment, which is to be applied once every other day. At the same time, medical ozone acupoint injection is given. Select Feishu, Zhongfu, Chize, Zhigou, and Zusanli. Select two to four points each time and 2–5 mL for each point. If the physical condition cannot

tolerate EBOO, intravenous medical ozone saline, major autohemotherapy, minor autohemotherapy, and so on can be used. If the physical condition is weak and cannot tolerate EBOO, intravenous medical ozone saline or oxygen autohemotherapy can be chosen.

6.7.1.7 TRADITIONAL CHINESE MEDICINE

The following syndromes are commonly seen at the early stage. For yin deficiency and internal heat, the prescriptions recommended are Shashen Maidong Decoction combining modified Baihe Gujin Decoction. For the syndrome of qi stagnation and blood stasis, the prescriptions recommended are Taohong Siwu Decoction combining modified Wuling Powder. Syndromes for the medium-advanced stage are commonly seen as follows. For the syndrome of turbid phlegm obstructing lung, the prescriptions recommended are Daotan Decoction plus Tingli Dazao Xiefei Decoction. For the syndrome of deficiency of lung–spleen qi, the prescription recommended is modified Xiangsha Liujunzi Decoction. For the syndrome of spleen and kidney deficiency, the prescription recommended is Lizhong Decoction combining modified Shishen Pill.

6.7.1.8 ACUPUNCTURE

6.7.1.8.1 Early lung cancer

Early lung cancer usually presents an excess of syndromes. The therapeutic principle should focus on eliminating pathogens and resolving mass as well as dispersing lung qi and dissipating phlegm.

Acupuncture on acupoints: Fengmen, Feishu, Taiyuan, Chize, Lique, and Hegu.

Methods: Even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

6.7.1.8.2 Lung cancer at medium-advanced stage

Lung cancer at the medium-advanced stage mainly presents the syndrome of retention of phlegm heat in the lung or qi stagnation, and blood stasis. The therapeutic principle is to clear away heat and toxic substances, as well as resolve phlegm and soften hard mass.

Acupuncture on acupoints: Feishu, Zhongfu, Chize, Zhigou, Zusanli, Quchi, Hegu, and Fenglong. Add Xingjian, Xuehai, Taichong, and Geshu for the syndrome of qi stagnation and blood stasis.

Methods: Even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Feishu, Dazhui, Guanyuan, and Zusanli.

Methods: Take two to three points each time. Conduct moxibustion with the moxa stick, 10 minutes for each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course.

Auricular acupoints: Lung, chest, subcortex, Shenmen, trachea, endocrine, Jiaogan, and tumor-specific area.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.7.1.9 MEDICATED DIET, NUTRITION, AND SO ON

It is recommended to give total parenteral nutrition the day before thermochemotherapy. Then, mainly adopt oral medicated diet and supplementary nutrients. Pay attention to chemotherapy-induced gastrointestinal side effects. In addition to the adjustment of TCM, apply appropriate vitamins, minerals, and other elements. Nutrition is an important treatment factor for medium-advanced lung cancer. Enough nutrients also need to be included in addition to the necessary medicated diet conditioning. If necessary, total parenteral nutrition is given. At the same time, pay attention to psychological counseling, qigong, sports, music, and other therapies to keep the patient calm, positive, and optimistic as well as to improve the self-healing ability. Encourage patients to continue their daily living in spite of their affliction.

6.7.1.10 OTHERS

The prognosis of most patients at the early stage is acceptable. Patients at the medium-advanced stage have a predicted period of survival. Give appropriate psychological counseling to patients to reduce their

psychological fear of cancer, and recommend them to practice qigong. Adhering to proper exercise can help patients recover faster.

6.7.2 Combination of hyperthermia with conventional treatments

6.7.2.1 EARLY LUNG CANCER

6.7.2.1.1 Hyperthermia and surgical treatment

Patients with localized early lung cancer lesion, no surrounding invasion and metastasis, and clear indications for surgery can have radical surgery. Positive nontoxic integrative treatment must be carried out in the perioperative period. Medical ozone, chelation detoxification, TCM, acupuncture, medicated diet, and so on can significantly improve the patient's tolerance to surgery, promote postoperative rehabilitation, and prevent postoperative metastasis. After the postoperative wound is completely healed, hyperthermia can be carried out after excluding hyperthermia contraindications through the assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of the patient by the hyperthermia center physician.

Patients who are assessed to be in good general conditions with KPSs above 70 points and who can tolerate whole-body hyperthermia can receive whole-body hyperthermia once every 2 weeks: six times per course of treatment for a total of three courses. Pay attention to body temperature monitoring, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Local hyperthermia can be added at the intermission periods of whole-body hyperthermia.

Patients who cannot tolerate whole-body medium-high temperature hyperthermia can receive local hyperthermia of the chest, or whole-body medium-low temperature hyperthermia. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. Carry out the second course of treatment after an interval of 10 days. After three courses, deep hyperthermia can be applied in combination with other approaches in long-term treatment. Carry out whole-body medium-low temperature hyperthermia once a week, for a total of 12 times.

6.7.2.1.2 Hyperthermia and radiotherapy

Patients with postoperative residual non–small cell lung cancer or with superior vena cava syndrome need radiotherapy. Patients who refuse surgery or have surgical contraindications can have radical radiotherapy. The combination of hyperthermia with radiotherapy is applicable to patients who are not suitable for surgery or whose cancer is difficult to be completely removed by surgery. The order of radiotherapy followed by hyperthermia is appropriate. Many advocate hyperthermia to be carried out within 2 hours after radiotherapy. Hyperthermia is conducted once every other day and combined for the whole process of radiotherapy. The clinical results showed that thermoradiotherapy had good efficacy in alleviation of clinical symptoms, cancer shrinkage, and reduction of pleural effusion or ascites. Hyperthermia of the first course is maintained up to 2 weeks after the end of radiotherapy. Adjust to whole-body hyperthermia during the recovery period.

6.7.2.1.3 Hyperthermia and chemotherapy

Because small cell lung cancer is more sensitive to chemotherapy, in addition to surgery, thermochemotherapy is preferred. For limited-stage small cell lung cancers, it is recommended to simultaneously conduct thoracic radiotherapy and chemotherapy. Thoracic radiotherapy can be carried out simultaneously at the beginning of the first or second cycle of chemotherapy.

Postoperative chemotherapy is usually carried out for non–small cell lung cancer except for phase Ia. Thermochemotherapy is routinely given after the operation. Whole-body hyperthermia or local hyperthermia is applied according to the situation after hyperthermia assessment. Chemotherapy commonly uses a combination program.

The combination application of chemotherapy and whole-body hyperthermia means that whole-body thermochemotherapy is carried out simultaneously with chemotherapy cycles. Whole-body medium-high temperature hyperthermia can be carried out in the first day of each chemotherapy cycle. Antinausea drugs

are routinely given before chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Whole-body hyperthermia and chemotherapy cycles are implemented simultaneously. Conduct combined local hyperthermia at the intervals of chemotherapy once every other day. Thermochemotherapy can have six to eight courses. After the end of chemotherapy, whole-body hyperthermia is conducted once every 10 days for a total of six times for consolidation effect.

If patients cannot tolerate whole-body medium-high hyperthermia, local hyperthermia of the chest or whole-body medium-low temperature hyperthermia can be carried out and synchronized with chemotherapy cycles. Local hyperthermia is simultaneously carried out in the first day of each course of chemotherapy and then once every other day. It may be continued during intermittence of chemotherapy. Take 1 week off after two chemotherapy treatments. The total number of combined local hyperthermia treatments during chemotherapy is about 60–80 times, and at later stages it may be continued for long-term treatment. Whole-body medium-low temperature hyperthermia is simultaneously carried out in the first day of each course of chemotherapy and then once per week. Continue 12 times of treatment after the end of chemotherapy.

The combination application of hyperthermia with chemotherapy can increase sensitivity to chemotherapy and increase the efficiency of chemotherapy to 85.6%; the incidence of side effects can be reduced to below 30%.

6.7.2.1.4 Hyperthermia and chelation detoxification therapy

Patients who are weak with postoperative low immunity can receive chelation detoxification and medical ozone therapy in the perioperative period when patients have not yet accepted chemotherapy. On the one hand, these treatments can promote physical recovery and regulate immunity and, on the other hand, kill residual tumor cells or inhibit early metastasis. For patients who lose the chance for surgery due to widespread metastasis and are not suitable for chemotherapy, chelation detoxification therapy can alternate with chemotherapy for better clinical efficacy and has no toxic side effects.

Chelation detoxification therapy consisting of intravenous infusions effectively removes heavy metals and other toxins from the body. Recommend having chelation detoxification therapy once every other day, with 20 times as a course of treatment. It is best applied simultaneously with local hyperthermia. When consecutively carried out for three courses, apparent effects can be seen.

6.7.2.1.5 Hyperthermia and medical ozone therapy

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing tumor cells, enhance effect on immunity, and increase the efficacy of medical ozone. We propose giving EBOO treatment for medical ozone therapy as soon as possible, once every other day, with 20 times as a course of treatment for a total of three courses. Change to once per week after the end of treatment for consolidated therapy.

6.7.2.1.6 Hyperthermia and other treatments

Cancer treatment needs integrative treatments. The combined application of TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, and alkaline treatment with hyperthermia can increase the effectiveness and safety of treatment.

DC-CIK cell therapy: Early postoperative DC-CIK consolidated therapy. Surgery is the preferred method for early-stage non–small cell lung cancer. Combining postoperative DC-CIK treatment can eliminate residual small lesions and reduce recurrence. Take and keep cancer tissue during the operation, and obtain antigen peptides of autologous cancer cells from the patient and prepare targeting DC-CIK, which can yield better efficacy. After the primary wound healing, collect 50–60 mL of autologous peripheral blood of the patient and prepare DC-CIK. When the reinfusion number of CIK cells reaches at least 1×10^{10}, reinfuse once a month, four times being a course of treatment. Conduct review on a regular basis after reinfusion. If there is no recurrence, additional treatment is carried out once every 6 months.

Combination treatment with chemotherapy: Studies have shown that DC-CIK can reverse multidrug resistance of chemotherapy drugs, reduce the toxicity of the chemotherapy, and improve the anticancer efficacy of chemotherapy drugs. The progression-free survival time and overall survival time were obviously prolonged.

One day before chemotherapy, collect the patient's peripheral blood for DC-CIK preparation and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct a consolidated therapy every 2 to 3 months.

Integrative treatments dominated by DC-CIK treatment: Elderly patients, patients at the medium-advanced stage with poor body condition and unable to tolerate chemoradiotherapy, or patients who reject chemotherapy are more suitable for integrative treatments dominated by DC-CIK treatment. After the preparation of a batch of cells, one or multiple infusions can be carried out according to the patient's tolerance (once per day, continuous transfusion). DC-CIK treatment is applied every 2 weeks. Each treatment course includes 4 sessions. Assess the efficacy. If it is effective, conduct a consolidation therapy every 2 to 3 months.

For malignant pleural effusion caused by primary and metastatic lung cancer, pleural infusion of DC-CIK is also able to demonstrate better therapeutic effect than infusion of chemotherapy drugs alone. Collect peripheral blood of patients and prepare DC-CIK. After draining pleural effusion, infuse DC-CIK 2×10^9 to 3×10^9 per time through the pleural drainage tube once a day, and continuously infuse for 4 days as a cycle.

Systemic biofeedback therapy: Three times a week with 15 times as a course of treatment. Adjustable to once or twice a week after two to three courses of treatment for long-term treatment.

Alkalization treatment effect: Patients without respiratory dysfunction can use intravenous administration of sodium bicarbonate. Refer to Section 4.10 for methods and details. Pay attention to the monitoring of blood gas analysis in patients during the application of alkalization treatment. Alkalize the body in combination with food therapy. Refer to Section 4.10 for details.

Because prognosis of most early lung cancers is acceptable, give appropriate psychological counseling to patients to reduce their psychological fear of cancer and recommend that patients practice qigong, adhere to appropriate exercise, and carry out long-term medicated conditioning.

6.7.2.2 MEDIUM- AND ADVANCED-STAGE LUNG CANCER

Most patients at the medium and advanced stages need chemotherapy or radiotherapy. Hyperthermia in combination with chemotherapy and radiotherapy is the same as mentioned earlier. Hyperthermia cycle extends longer than that for early lung cancer. We recommend that after combination treatment of hyperthermia with chemoradiotherapy continue to carry out hyperthermia combined with chelation detoxification, medical ozone, TCM, and other integrative treatments.

6.7.2.2.1 Hyperthermia and chelation detoxification therapy

Whole-body hyperthermia can improve immunity; promote tumor cell apoptosis; and regulate the body to produce TNF, IL-2, and other immune factors that are involved in the anticancer effect. Patients who are in generally good condition with KPSs above 70 points and who can tolerate whole-body hyperthermia can be given whole-body hyperthermia once every 10–15 days, with six times as a course of treatment. Patients in poor general condition are given local hyperthermia once every other day for long-term maintenance. Local hyperthermia is applied by radio-frequency capacitive heating, namely, RF local hyperthermia; the generation of subcutaneous fat induration is greatly reduced, and the power for treatment tolerance by patients is significantly increased. Microwaves for local hyperthermia through surface radiation are applied for superficial lesions of lung cancer, such as supraclavicular lymph node metastasis.

Combining chelation detoxification therapy during the hyperthermia treatment process has a synergistic effect. Chelation detoxification therapy needs infusion of more than 2 hours, with 20 times as a course of treatment for a total of three courses. Single chelation detoxification can be carried out during the intervals of hyperthermia.

6.7.2.2.2 Hyperthermia and medical ozone therapy

Medical ozone therapy is better conducted within 2 hours after hyperthermia. For medical ozone therapy, EBOO is the preferred treatment, which is applied once every other day, with 20 consecutive times as a course of treatment for a total of three courses. Change to once very week after the end of treatment for consolidation therapy.

6.7.2.2.3 Other Therapies

Nontoxic integrative treatments dominate other treatments for medium-advanced lung cancers. In addition to hyperthermia, chelation detoxification, medical ozone, TCM, acupuncture, and systemic biofeedback, we emphasize diet plus qigong plus sports as the supplementary treatments to improve overall immunity and encourage patients to survive despite the cancers.

6.7.2.3 INTEGRATIVE TREATMENTS FOR COMMON COMPLICATIONS OF LUNG CANCER

6.7.2.3.1 Respiratory tract obstruction

For patients with complete obstruction, tracheotomy, intubation, and sputum aspiration are given to keep the airway open and anti-infective therapy is immediately given. Radiotherapy combined with local hyperthermia is carried out for the primary lesion. For cancers with endogenous growth, photodynamic knife can be given for ablation; for external pressure type, tracheal stent is given. Pay attention to cardiac function, and when cardiac function is impaired the application of cardiac diuretic can be considered.

6.7.2.3.2 Malignant pleural effusion and pericardial effusion

Most lung cancer patients have malignant pleural effusion and pericardial effusion. Improvement of symptoms after the first drainage and reproduction rate of effusion are the important factors for consideration in the choice of treatments. Local treatment adopts intrapleural injection of chemotherapeutic drugs or biotherapeutics, such as cisplatin, mitomycin, IL-2, *Corynebacterium parvum*, N-CWS, KLT, and elemene. It can be combined with hyperthermia for the treatment of perfusion. Patients with the combination of pleural effusion and pericardial effusion can receive pleural or pericardial cavity hyperthermic perfusion chemotherapy. In this method, after the effusion is drained clean heat chemotherapy drugs to about 40°C at first, infuse into the cavity, and then give deep hyperthermia. Heat for more than 1 hour to ensure the proper temperature of chemotherapy drugs, reduce chemotherapy side effects, and increase the effect of chemotherapy drugs.

6.7.2.4 HYPERTHERMIA AND HERBAL MEDICINES

6.7.2.4.1 Fumigation

Proven prescription 1: Elixir: *Flos daturae* 25 g, *Semen coicis* 20 g, *Realgar* 15 g, *Pearl* 10 g, *Bezoar* 2 g, musk 1 g, and *Venenum bufonis* 1.5 g are ground into powder, placed in a special fumigation instrument, and turned into steam 1 minute after being powered; patients can directly inhale. Efficacy: regulates the flow of qi to eliminate phlegm, promotes blood circulation, and removes blood stasis. It is applicable to lung cancer patients with blood stasis and sputum block.

Proven prescription 2: Flos lonicerae 15 g, *Prunella vulgaris* 15 g, *Rhizoma imperatae* 15 g, *Agrimonia pilosa Ledeb* 15g, *mulberry leaves* 10 g, *Flos chrysanthemi Indici* 10 g, *Radix isatidis* 10 g, *Radix sophorae Tonkinensis* 10 g, *Lithospermum erythrorhizon* 10 g, *Scutellaria barbata* 10 g, *boat-fruited Sterculia Seed* 10 g, *Platycodon grandiflorum* 10 g, *Mentha haplocalyx Briq* (add later) 7 g, and *Borneol* 3 g. Put the drugs together and boil. Have the patient inhale the hot steam of the liquid medicine. Efficacy: clears away heat and toxic substances, activates blood, and resolves mass. It is applicable to lung cancer patients with symptoms of cough, asthma, phlegm, hoarseness, dry mouth, and nasopharynx.

6.7.2.4.2 Bath

Proven prescription 1: Sappanwood 50 g, *Camphora* 50 g, *Ramulus cinnamomi* 15 g, *Old radix Lithospermi* 15 g, *Fructus liquidambaris* 15 g, *Rhizoma homalomenae* 15 g, *Lycopodii herba* 15 g, *Olibanum* 10 g, *Myrrha* 10 g, *Carthamus tinctorius L.* 10 g, *Chaenomeles speciosa Nakai* 10 g, and *Rubus obcordatus* 10 g. Decoct them with water for oral application, and immerse (wash) joints of the affected part in the hot decoction. Efficacy: promotes blood circulation to dispel cold and remove meridian obstruction. It is applicable to patients with the syndrome of joint and bone pain caused by bone metastatic carcinoma.

Proven prescription 2: Rhizoma cyperi Rotundus L. 10 g, *Angelica sinensis* 10 g, *Myrrha* 10 g, *Natrii Suleas* 10 g, *Cortex acanthopanacis* 10 g, *Pericarpium citri Reticulatae Viride* 10 g, *Zanthoxylum bungeanum Maxim.*

10 g, clove 3 g, musk 0.3 g, Old Shallot 3 g, *Cortex lycii* 3 g, and *Cortex moutan* 6 g. Decoct them with water for oral application, and immerse (wash) joints of the affected part in the hot decoction. Efficacy: promotes blood circulation to dispel cold and removes meridian obstruction. It is applicable to patients with the syndrome of joint and bone pain caused by bone metastatic carcinoma.

Proven prescription 3: Ramulus cinnamomi 60 g, *Acanthopanax senticosus* 50 g, and *Glycyrrhiza uralensis* 5 g. Add water to drugs and boil for 30 minutes. Remove slag and take juice. Immerse feet for 30 minutes once a day, with 10 days as a course of treatment. Efficacy: supplements qi to warm yang, mainly cures a variety of fatigue, and is applied to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 4: Radix astragali 450 g, *Radix codonopsis* 300 g, *Radix polygoni Multiflori Preparata* 300 g, *Ligusticum chuanxiong Hort* 300 g, *Fructus alpinia Oxyphylla* 300 g, *Semen cuscutae* 300 g, *Atractylodes macrocephala Koidz* 300 g, and *Carthamus tinctorius L.* 200 g. Put all drugs into the wok, and add a proper amount of water. Boil for 50 minutes. Remove slag and take juice. Blend with 450 g of white wine. Take bubble bath for 40 minutes once a day, with 10 days as a course of treatment. Efficacy: tones lung, spleen, and kidney, as well as strengthening spirit and mainly curing a variety of types of fatigue, and is applied for physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 5: Stems and leaves of *Panax ginseng* 30 g, *Atractylodes macrocephala Koidz* 30 g, *Radix saposhnikoviae* 20 g, yam 20 g, and *Glycyrrhiza uralensis* 6 g. Add drugs and a proper amount of water. Boil twice and each time for 30 minutes. Combine filtrate and immerse feet for 30 minutes once a day, with 15 days as a course of treatment. Efficacy: invigorates spleen and replenishes qi. It is applicable to long-term weakness of cancer patients who lack resistance.

Proven prescription 6: Rhodiola 800 g, *Semen coicis* 500 g, *Acanthopanax senticosus* 400 g, *Radix astragali* 300 g, *Cyrtomium fortunei* 300 g, *Schisandra chinensis* 300 g, *Angelica sinensis* 200 g, and *Ligusticum chuanxiong Hort* 200 g. Boil twice and each time for 50 minutes. Combine filtrate and immerse feet for 40 minutes once a day, with 15 days as a course of treatment. Efficacy: supplements qi and nourishes yin, as well as invigorating qi and promoting blood circulation. It is applicable to long-term weakness in cancer patients who lack resistance.

Proven prescription 7: Take 20 g each of *Ligusticum chuanxiong Hort*, *Erythrina variegata L.*, *Speranskia tuberculata*, *Cortex acanthopanacis*, *Caulis spatholobi*, and *Retinervus luffae Fructus* and 15 g each of *Angelica sinensis*, *Carthamus tinctorius L.*, and *Lycopodii herba*. Add water and boil them together for 30 minutes. Fumigate and wash the affected area one or two times a day for 30 minutes each time. Efficacy: activates blood, relaxes veins, and relieves pain. It is applicable for activating blood, relaxing veins, and relieving pain and to cancer patients with the syndrome of limb joint and bone pain.

6.7.2.4.3 Grilling method

Xiaoliu Cream: 30 g of *Angelica sinensis*, *Lithospermum erythrorhizon*, safflower, *Resina draconis*, *Radix astragali*, and dandelion as well as musk 2–5 g. Add water 2500 mL to the six herbal medicines and boil for 60–90 minutes, decocting it into cream. Add musk. Uniformly flatten it on a cloth, and externally apply at the site of cancer pain and bind with bandages. Use infrared lamp to bake for 30 minutes once a day. Efficacy: promotes blood circulation to relieve pain. It is suitable for advanced lung cancer patients with pain.

6.7.2.4.4 Moxibustion therapy

It is applicable to cancer patients with long illness, yang deficiency, and weakness and capable of immunity enhancement.

Acupoints: The first group of acupoints includes Dazhui, Shenshu (both), and Pishu (both). The second group of acupoints includes Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both).

Herbal cake making: Take equal amounts of *Radix astragali*, *Angelica sinensis*, *Fructus psoraleae*, *Curculigo orchioides*, and *rhubarb*, and smash them into powder. Filter with 120 mesh sieve, and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm.

Moxibustion: Place the moxa cone with a diameter of 2 cm and a height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints each time, with two groups of points alternated, once every other day, with 24 times as a course of treatment.

Efficacy: Enforces spleen and nourishes kidneys and for muscularity and general health care.

6.7.2.5 HYPERTHERMIA INDICATIONS

Patients with well-healed postoperative wounds, patients who have received chemoradiotherapy, and patients with advanced cancer.

6.7.2.6 HYPERTHERMIA CONTRAINDICATIONS

Patients with a fever over 38.5°C; patients with bleeding tendency accompanied by respiratory acidosis or alkalosis and cachexia.

6.7.3 Introduction of a typical case

A patient named Dai, male, 69 years old, was admitted on October 5, 2010, to Clifford Hospital due to "space-occupying lesion in the left upper lobe of the lung [having been] found, and with cough and hemoptysis for 6 days." The patient showed fever, cough, expectoration, and excessive blood-tinged sputum 6 days before admission to the hospital. The patient went to a local hospital and was given anti-infection therapy (specific drugs were unknown). Chest X-ray and CT examination revealed space-occupying lesions in the left upper lung, and lung cancer and obstructive pneumonia were considered. After treatment, the patient's fever stopped and cough and expectoration were reduced. The patient was transferred to Clifford Hospital for further treatment. Past medical history: the patient had a history of hypertension and took a hypotensor for treatment. At the time of admission, his blood pressure was stable. The patient was hospitalized in Clifford Hospital due to cerebral infarction and discharged in March 2009 when the condition got better. The patient had an 8-year history of diabetes and took oral repaglinide and Glucophage for treatment. The patient had a history of smoking for years, two packs a day, and quit smoking the last 3 years. The patient had no history of hepatitis, tuberculosis, heart disease, and so on.

Physical examination: The patient was in good mental condition, with hoarseness, herpes around the lips, cough, sputum, and some sputum tinged with a small amount of blood. The patient had a good diet and did not have wheezing, chest tightness, and other discomforts. The patient had pink tongue, thin white fur, and thready and weak pulse. Physical examination: barrel chest and thoracic symmetry. Breathing sounds at the left upper lung with percussive flatness were not detected by auscultation. A few fine, thin, and moist rales could be heard at the left lower lung. Breathing sounds were clear at the right lung, wet and dry rales not being heard. There was no uplift in the precordium. The apex beat was at the left fifth interspace and about 2 cm inside the central line of collarbone. The border of cardiac dullness was normal. Heart rate was 94 beats/min, with regular rhythm. Pathological murmurs were not heard in each cardiac valve area. The KPS was 90.

Auxiliary examination: CT: (1) Space-occupying lesion in the left upper lung was considered to be a possibility of lung cancer; other symptoms were supraclavicular fossa, mediastinal lymph node metastasis, pericardial effusion, and a small amount of left pleural effusion. Biopsy with tracheoscopy was recommended. (2) Obsolete lacunar lesions were at the left basal ganglia and the left thalamus. Fiber-optic bronchoscopy: left lung cancer. Pathology report: squamous cell carcinoma.

Laboratory tests: Blood routine: RBC 3.74×10^{12}/L, Hb 102 g/L, WBC 11.00×10^{9}/L, N 82.4%, and PLT 549×10^{9}/L; blood biochemistry: ALT 47 U/L, AST 33U/L, TP 60.5 g/L, ALB 34.0 g/L, ALP 215 U/L, GGT 87 U/L, TBIL 12.2 μmol/L, DBIL 34.5 μmol/L, Cr 99 μmol/L, Ua 277 μmol/L, GLU 7.01 mmol/L, TG 1.13 mmol/L, GHO 2.85 mmol/L, K^+ 3.97 mmol/L, Na^+ 140.90 mmol/L, Cl^- 103.80 mmol/L, and Ca^{2+} 2.09 mmol/L. The five tumor markers were as follows: CEA 3.93 ng/mL, CA15-3 6.06 U/mL, TPSA 2.81 ng/mL, CA19-9 19.38 U/mL, and AFP 0.61 ng/mL. The remainder was normal.

Diagnosis: Left lung squamous cell carcinoma and multiple lymph node metastasis ($T_3N_3M_0$, stage IIIb).

Integrative treatment prescription: The patient refused chemotherapy; as a result, TCM, acupuncture, detoxification, hyperthermia, medical ozone, and other comprehensive treatments were given. The patient was with yin deficiency and phlegm heat, as well as a complication of deficiency and excess of vital qi and etiological factors. The principle of TCM was to nourish yin and clear away lung heat, reduce phlegm, and resolve masses.

Medications: Modified Qingjin Sanjie Decoction was given. The specific medication is as follows: *Gecko* 6 g, *Semen coicis* 30 g, *Agrimonia pilosa Ledeb* 30 g, *Prunella vulgaris* 15 g, *Platycodon grandiflorum* 12 g,

Fritillaria thunbergii Miq 15 g, *Polyporus umbellatus* 20 g, *Radix adenophorae* 30 g, *Ophiopogon japonicus* 15 g, *Carapax trionycis* 30 g, *Radix rehmanniae* 20 g, and *Schisandra chinensis* 10 g, one dose a day and decocted with water for oral dose.

Acupuncture on acupoints: Took Feishu, Zhongfu, Chize, Zusanli, Quchi, Fenglong, Xuehai, Taichong, Linggu, Dabai, and Waisanguan. Even reinforcing–reducing method was used for acupuncture. Retained the needle for 20 minutes, once per day. Took 2 days off after five acupuncture treatments.

Moxibustion acupoints: Feishu, Dazhui, Guanyuan, and Zusanli. Took two points each time and conducted moxibustion for 10 minutes per point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Lung, chest, subcortex, Shenmen, trachea, endocrine, and Jiaogan. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

At the same time, a combination of parenteral nutrition with medicated diet conditioning to strengthen supportive treatment was conducted; local hyperthermia of chest three times a week and chelation detoxification three times a week, simultaneously with hyperthermia, were conducted. The medical ozone therapy selected was EBOO, twice a week, and it was conducted at the intervals of hyperthermia. After 1 month of hospitalization, the patient had improved and was discharged. After a 1-week break, the patient came to the hospital again for treatment.

Treatment effects: After 1 month of treatment in the hospital, the patient's general condition had improved significantly. Cough and hemoptysis had gradually reduced. Speech was clearer than before. Weight gain was 3 kg. Diet, urine, and stool were basically normal. The KPS was 100. The patient adhered to treatment as an outpatient and by intermittent hospitalization. In the 2-year follow-up after being discharged from hospital, the patient was in recovery. Lung CT was reviewed 10 months and 22 months after treatment, and the lesions were significantly reduced and in stable condition. The patient is still being followed up (Figures 6.3 through 6.5).

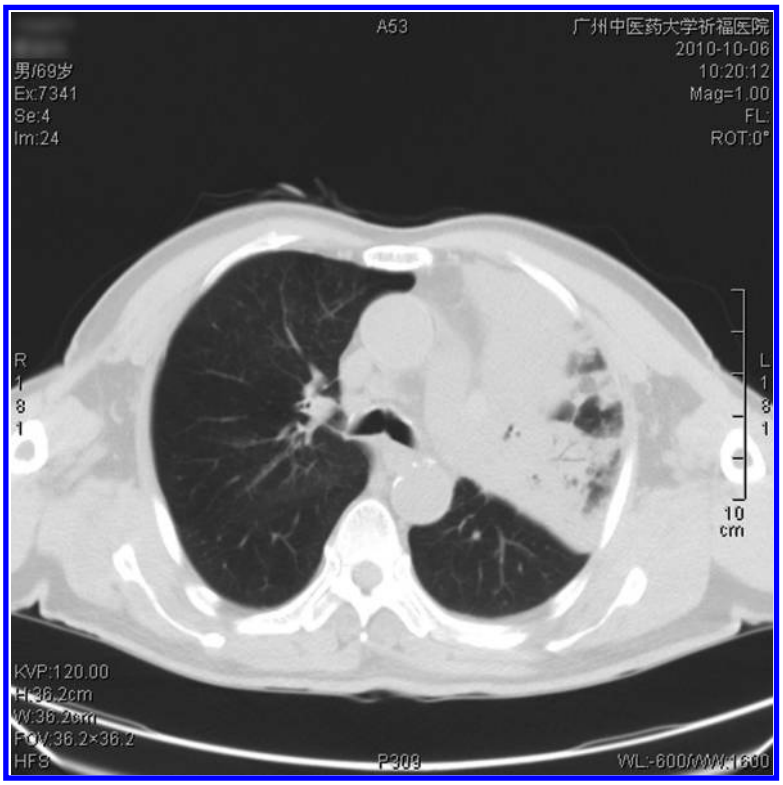

Figure 6.3 Before treatments: October, 2010, CT.BMP.

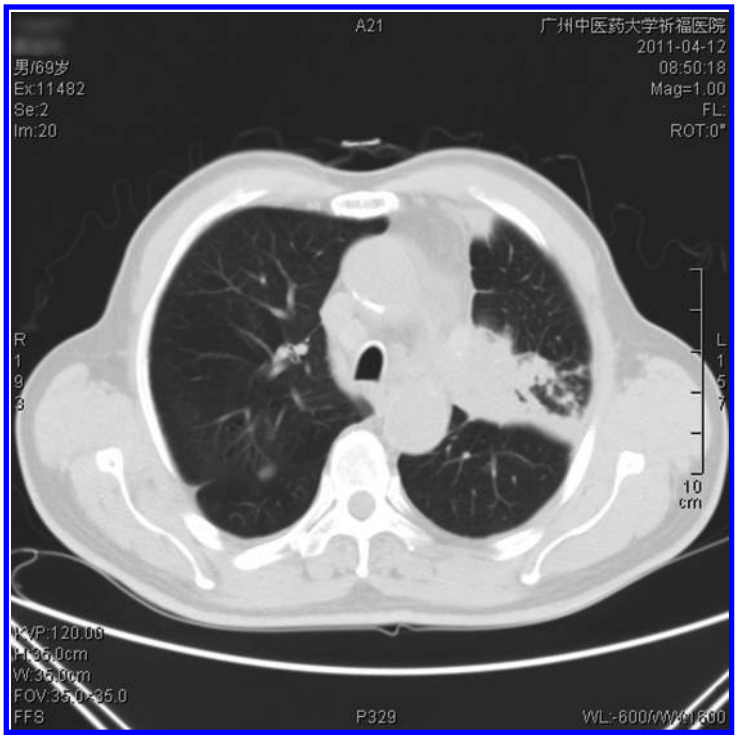

Figure 6.4 After treatments: April, 2011, CT.BMP.

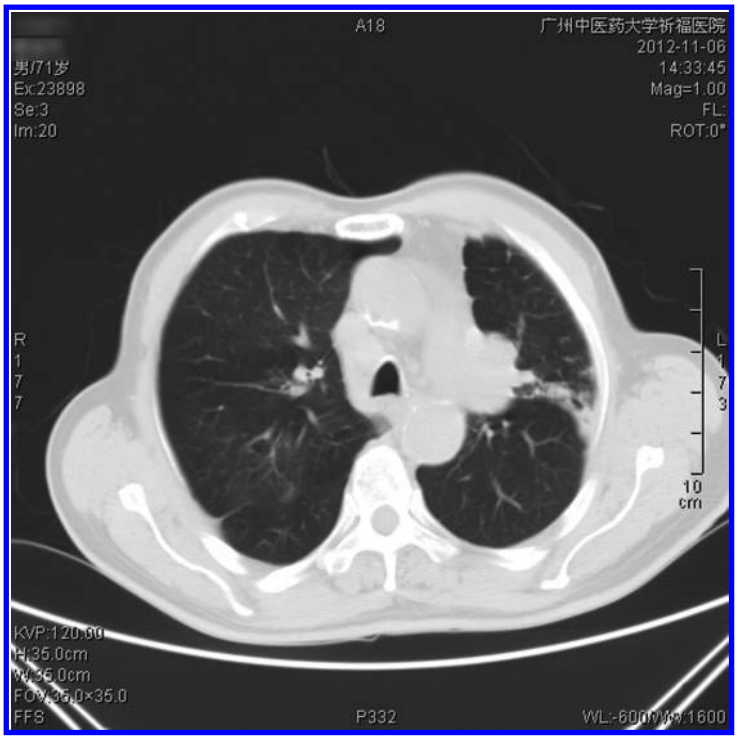

Figure 6.5 After treatments: November, 2011, CT.BMP.

6.7.4 Related Research in China and Abroad

Bian Chun'an et al. reported an experimental study of hyperthermia effect on P-glycoprotein (P-gp) expression in A549 cells. Results showed that hyperthermia can inhibit the expression of P-gp, which may be a means to reversing multidrug resistance of tumor cells. The combination of hyperthermia and Chinese patent medicines in clinical applications has also demonstrated a positive effect.

Li Xiaojiang et al. have applied hyperthermia in combination with pleural injection of lentinan powder in the treatment of lung cancer malignant pleural effusion and achieved better clinical efficacy, and no significant adverse reactions were seen.

Kang Yanxia et al. have conducted an experimental study on how hyperthermia enhances the toxic effect of Navelbine on human lung cancer cells. Results showed that 42°C hyperthermia can significantly enhance the toxicity of the chemotherapy drug Navelbine, and its mechanism may be related to the interference with the cell cycle. Studies have shown that hyperthermia can promote chemotherapy drug–induced apoptosis. Cisplatin is the most commonly used anticancer drug clinically and is one of the most effective drugs in the treatment of non–small cell lung cancer.

Sorenson et al. have speculated that cisplatin (DDP) causes mainly the arrest of cells in the G_2 phase. Sun Shengjie et al. have conducted an experimental study on how 42°C hyperthermia enhances the toxicity of DDP on human lung cancer cells PLA-801D. Results showed that the 42°C hyperthermia can significantly enhance the toxicity of chemotherapy drugs (DDP). The combination mode of thermochemotherapy at the same time is the best, and its mechanism may be related to the interference with the cell cycle.

Zhavrid et al. have compared the treatment effects of two groups with advanced small cell lung cancer. The control group received chemotherapy and radiotherapy only and the treatment group received whole-body hyperthermia with the temperature of 41°C at the same time for 3 to 4 hours, and results found that the efficiency of the treatment group was higher than that of the control group (79.5% and 63.5%, respectively) and that 1-year and 2-year survival rates of the treatment group were significantly higher than those of the control group (40.6% and 22.2%, 15.9% and 5.1%, respectively).

6.8 BREAST CANCER

Breast cancer is a cancerous disease caused when breast ductal and lobular epithelial cells, due to a variety of carcinogenic factors, lose their normal characteristics and lead to dysplasia, thus exceeding the limits of self-healing. It has the highest incidence among female cancers with complex pathological types. Because it is a systemic disease, patients with low degrees of cell differentiation can have systemic metastasis at an early stage.

Breast mass is the most common manifestation of breast cancer. The symptom of nipple discharge mostly means benign change. But patients more than 50 years old with unilateral nipple discharge should be alerted to the possibility of breast cancer. Nipple retraction, nipple itching, scaling, erosion, ulceration, scab, and eczema-like changes are often clinical manifestations of mammary Paget's disease. Some patients present breast skin and contour changes. For example, when the cancer invades the Cooper ligament of the skin a "dimple syndrome" can be formed, cancer cells blocking subcutaneous lymphatic capillaries can result in skin edema, and depressions at the hair follicles can form the "orange peel" syndrome. When the skin is widely invaded, many hard nodules or small cords are formed in the epidermis or even integrated into pieces. If lesions extend to the back and to contralateral chest wall, breathing can be restricted and corset cancer can be formed. Inflammatory breast cancer can present significantly enlarged breasts with skin congestion, redness, and swelling and with increased local skin temperature. In addition, advanced breast cancer can present skin ulceration and form cancerous ulcers. Some patients present with swollen lymph nodes: the ipsilateral axillary lymph nodes can undergo swelling. Advanced breast cancer can transfer to contralateral axillary lymph node metastasis and cause swelling; moreover, the ipsilateral and contralateral supraclavicular lymph nodes are palpable in some cases.

Common pathological types are noninvasive cancer (including ductal carcinoma in situ and lobular carcinoma in situ) and invasive cancer (including invasive ductal carcinoma, invasive lobular carcinoma,

carcinoma simplex, medullary carcinoma, hard carcinoma, mucinous adenocarcinoma, and papillary carcinoma). The overall development of breast cancer is slow, and after active treatment most patients have shown better long-term efficacy. Prognostic factors are mainly primary cancer size and local infiltration; lymph node metastasis; pathological type of cancer and degree of differentiation; intratumoral microvessel density; vascular, lymphatic cancer thrombus; patient's immune function; tumor molecular biological morphology and expression; and so on. Detection of hormone receptors by immunohistochemistry is also a reference index for prognosis. If ER and PR are positive, prognosis is relatively good. If ER and PR are negative, prognosis is relative poor. DNA aneuploidy or increased cell ratios at S-phase or positive CEA prompt poor prognosis.

6.8.1 Conventional treatments

6.8.1.1 SURGERY

Surgical resection has been the main treatment of breast cancer. The current surgical approach is developed toward the narrower resection, including breast-conserving surgery and sentinel lymph node biopsy. Patients of stages I and II should be applied with modified radical mastectomy; patients of stage III can do preoperative chemotherapy first and then modified radical mastectomy. Part of the patients of stage I can receive breast-conserving surgery and postoperative radical radiotherapy.

6.8.1.2 RADIOTHERAPY

Radiotherapy is the main component of breast cancer treatment and is one of the means for local treatment. Patients with cancer combined with lymph node metastasis, patients with positive surgical margin, and patients with breast-conserving surgery are required to do radiotherapy. At present, most experts do not advocate radiotherapy alone for curing breast cancer. Radiotherapy is mostly used in integrative treatments, including adjuvant therapy before or after radical surgery, and palliative treatment of advanced breast cancer. In the past 10 years, local excision in parallel with integrative treatments has been mainly carried out for early-stage breast cancers. Radiotherapy plays an important role in narrowing the scope of surgery.

6.8.1.3 CHEMOTHERAPY

A primary cancer with diameter greater than 1 cm is required to carry out adjuvant chemotherapy. Preoperative chemotherapy can promote retreat of local breast cancer and metastases, expand surgical indications, and narrow the scope of surgery. It can also reduce the activity of cancer cells, prevent the spread of cancer cells during surgery, control micrometastases undetectable clinically, reduce breast cancer metastasis, and augment cancer sensitivity to chemotherapy regimens used. The efficacy of adjuvant chemotherapy in combination with routine chemotherapy is better than that of single-agent chemotherapy, and early postoperative application is preferable. Because the side effects of chemotherapy used in breast cancers are significant, the treatment period should not extend too long. Postmenopausal patients with positive lymph node metastasis generally do not have to use adjuvant chemotherapy except when there are high-risk factors for recurrence. If there are high-risk factors for recurrence, adjuvant combination chemotherapy should be applied. For patients who are node positive and hormone receptor positive, adjuvant combination chemotherapy should be used.

6.8.1.4 ENDOCRINE THERAPY

Endocrine therapy is one of the means for breast cancer systemic therapy. Endocrine therapy plays a very important role for hormone-dependent recurrent and metastatic breast cancer, and adjuvant treatment of early breast cancer. It can even be used for high-risk healthy women to prevent breast cancer, which depends on whether patients have entered menopause or not, as well as the condition of ER and PR receptors. For postmenopausal hormone receptor–positive patients, postoperative adjuvant endocrine therapy is optional. Patients after 5 years of surgery can have anastrozole or letrozole; after the use of tamoxifen for 2 to 3 years, sequentially use exemestane or anastrozole for 2 to 3 years. After the use of tamoxifen for 5 years increase the use of letrozole for 5 years, and patients who cannot tolerate aromatase inhibitor treatment due to various

reasons can still use tamoxifen for 5 years. Premenopausal patients who are hormone receptor positive have the following options for postoperative adjuvant endocrine therapy. First use tamoxifen for 2 to 3 years, and after menopause patients can switch to an aromatase inhibitor. If patients are still premenopausal after the use of tamoxifen for 2 to 3 years, they can continue to use tamoxifen for 5 years. If patients enter menopause after 5 years, then use letrozole for 5 years as intensive follow-up treatment. Some premenopausal patients who are not suitable for treatment with tamoxifen or who have a high risk of recurrence and metastasis factors can consider using aromatase inhibitors as adjuvant therapy after ovaries are castrated.

6.8.1.5 HYPERTHERMIA

Hyperthermia in combination with chemotherapy and radiotherapy can enhance the sensitivity of therapy, improve cancer control rates, and enhance the chemoradiotherapy-sensitizing effect for recurrence of breast cancer. For breast cancer patients at stage I who do not need postoperative chemotherapy, it can be added in the whole-body medium-low temperature mode to improve immunity and reduce the risk of postoperative recurrence. The application of whole-body hyperthermia and local hyperthermia combined with chemotherapy and radiotherapy for patients at stage II or above can improve the cancer control rate and can enhance the chemoradiotherapy-sensitizing effect for recurrence of breast cancer. When breast cancer patients present skin damage, such as orange peel–like appearance or ulceration or upper extremity lymphedema, hyperthermia combined with radiotherapy can significantly improve the control rate. When advanced patients present widespread metastasis at lung, liver, bone, and so on, as well as emergence of pain, whole-body hyperthermia can significantly improve symptoms, reduce pain, and improve the patients' quality of life. Microwave hyperthermia, RF local hyperthermia, regional hyperthermia, and whole-body hyperthermia can be applied.

6.8.1.6 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can not only effectively remove toxins from the body, and improve immune function, but also reduce the side effects of chemotherapy and enhance sensitivity to chemotherapy. Specific usage: once every other day with 20 times as a course of treatment. Change to once per week after 1 week when the condition is stable. Rehabilitation can be extended. Just like other infusions, pay attention to slow infusion rate for patients with heart dysfunction. Chelation detoxification therapy is one of the main treatments for patients with advanced breast cancer. The application of appropriate doses alternating with chemotherapy can have great benefits for the survival of patients and their quality of life.

6.8.1.7 MEDICAL OZONE THERAPY

Medical ozone therapy may increase oxygen content of cancer lesions. It not only can directly kill cancer cells, unspecifically increase immune system function, and promote the release of TNF but also has significant radiosensitizing effect and can improve the sensitivity of cancer cells to chemotherapy. Treatment methods: use EBOO once every other day, with 20 times as a course of treatment, or select medical ozone saline infusion once every other day, with 10–14 days as a course of treatment. Use medical ozone major autohemotherapy once every other day, with 12 times per treatment. Use medical ozone minor autohemotherapy once every other day, with 12 times per treatment. Use medical ozone acupoint injection once every other day, with 12 times as a course of treatment.

6.8.1.8 TRADITIONAL CHINESE MEDICINE

For the syndrome of stagnation of qi due to depression of the liver, modified Xiaoyao Powder is given. For the syndrome of disharmony of Chong and Conception Channels, modified Zhibai Dihuang Pill is given. For the syndrome of stagnation of heat and toxin, modified Wuwei Xiaodu Decoction is given. For the syndrome of deficiency of both blood and qi, modified Ginseng Tonic Decoction is given. Chinese formulated products commonly used are Xiaojin Dan, Xihuang Pill, Xiaoxing Pill, Pingxiao Capsule, and so on.

6.8.1.9 ACUPUNCTURE

The syndrome of stagnation of qi due to depression of the liver appears mostly at the early stage. The therapeutic principle should focus on soothing the liver and regulating the circulation of qi, as well as removing phlegm and resolving mass.

Acupuncture on acupoints: Qimen, Shanzhong, Zusanli, Xingjian, and Fenglong.

Methods: even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The type of accumulated heat toxicity or deficiency of both qi and blood is mainly for the medium-advanced stage. The therapeutic principle should focus on clearing away heat and toxic substances, removing blood stasis and relieving pain, replenishing qi and blood, and strengthening healthy qi to eliminate pathogens.

Acupuncture on acupoints: Zusanli, Sanyinjiao, Zhongwan, Taixi, Guanyuan, Qihai, Shenshu, and Pishu.

Methods: even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Guanyuan, Dazhui, Zusanli, Sanyinjiao, Ganshu, Pishu, and Shenshu.

Methods: Take two to four points each time. Conduct moxibustion with the moxa stick with 10 minutes for each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Breast, chest, stomach, liver, endocrine, subcortex, adrenal gland, Yuanzhong, Naodian, Jiaogan, and tumor-specific area.

Methods: Select four to six points each time. Penetrate with filiform needle. Retain the needle for 30–60 minutes after a fast twist, once a day, with 10 times as a course of treatment. Or stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.8.1.10 MEDICATED DIET, NUTRITION, AND SO ON

Medicated diet is mainly for the early stage. Total parenteral nutrition is given 1 day before thermochemotherapy. Pay attention to rational nutrition collocation. Patients at medium-advanced stage who still can eat are given medicated conditioning. Appropriately apply megestrol acetate and multienzyme tablets for oral administration to improve appetite, supplemented with amino acids, and so on. If patients have difficulty in feeding, total parenteral nutrition is given, and at the same time complications are treated.

6.8.1.11 OTHERS

Qigong, tai chi, music, and mental therapy of TCM support the patient's mental health and increase confidence in the treatment.

6.8.2 Combination of hyperthermia with conventional treatments

6.8.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Early breast cancer patients with localized lesions, without surrounding invasion and metastasis, and with clear indications for surgery can choose to have radical surgery. Nontoxic integrative treatments can be actively carried out during the perioperative period, such as medical ozone, chelation detoxification, TCM, acupuncture, medicated diet, and so on, which can significantly improve the patient's tolerance to surgery, promote postoperative rehabilitation, and prevent occurrence of postoperative metastasis. Hyperthermia can be conducted 2 weeks after the postoperative wound heals.

For patients at stage II or above who are assessed to be in good general condition, have KPSs of 70 points or above, and are able to tolerate whole-body hyperthermia, after the postoperative wound is completely healed whole-body medium-high hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of the patient by the hyperthermia center physician, once every 2 weeks with six times as a course of treatment for a total of three courses. Local hyperthermia can be added at the intermission periods of whole-body hyperthermia.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia or whole-body medium-low temperature hyperthermia can be carried out at the breast area, including the

ipsilateral superior and inferior clavicles as well as the axillary area. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. Conduct the second course after an interval of 10 days. After three courses, local hyperthermia can be used for long-term treatment. Carry out whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.8.2.2 HYPERTHERMIA AND RADIOTHERAPY

Breast cancer patients with lymph node metastasis or breast-conserving surgery should undergo radiotherapy. For some patients who refuse surgery or whose tumor cannot be completely resected, radiotherapy can also be carried out. The combination of hyperthermia and radiotherapy may increase the sensitivity of tumor cells to radiotherapy and reduce skin and hematologic toxicity caused by radiotherapy. The order of radiotherapy followed by hyperthermia is appropriate, and many advocate that an interval time under 2 hours is appropriate. It is appropriate to conduct local hyperthermia once every other day in combination with radiotherapy for the whole process. The first course of hyperthermia is maintained for up to 2 weeks after the end of radiotherapy. Adjust to whole-body hyperthermia during the recovery period.

6.8.2.3 HYPERTHERMIA AND CHEMOTHERAPY

The majority of patients at stage II and above need systemic chemotherapy. Chemotherapy commonly uses a combination program. Whole-body hyperthermia can be combined with the chemotherapy cycles for application. Conduct a total of six times. Local hyperthermia can be added at the intermission periods of whole-body hyperthermia.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body hyperthermia can be carried out during the first day of chemotherapy. Pay attention to medications of antinausea drugs before chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Simultaneously carry out hyperthermia and chemotherapy cycles for six to eight courses. Local hyperthermia can be carried out intermittently with chemotherapy.

For patients who cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia or whole-body medium-low temperature can be carried out. Local hyperthermia is conducted once every other day, and it can be continued intermittently with chemotherapy. Take 1 week off after every two chemotherapy treatments. The total number of combined local hyperthermia treatments during chemotherapy is about 60–80 times. After the end of the thermochemotherapy, local hyperthermia can be used for long-term treatment. Whole-body medium-low temperature is carried out once a week for a total of 10 times.

6.8.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given, from the end of operation to the end of chemotherapy or radiotherapy, to the patient with physical weakness and low immunity after the operation. On the one hand, it can promote physical recovery and regulate the immune system and, on the other hand, kill residual cancer cells or inhibit early metastasis. Note that chelation detoxification needs infusion for more than 2 hours. Local hyperthermia or whole-body hyperthermia can be simultaneously applied with chelation and detoxification to improve efficacy.

6.8.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

Medical ozone therapy may increase the oxygen content of cancer lesions. It not only can directly kill cancer cells, nonspecifically increase immune system function, and promote the release of TNF but also has significant radiosensitizing effect and can improve the sensitivity of cancer cells to chemotherapy. The patients' blood circulation is accelerated and cell activity increased after hyperthermia. It is proposed that medical ozone therapy be carried out again within 2 hours after the hyperthermia. EBOO is preferred, once every other day, with 20 times as a course of treatment for a total of three courses. Or, choose medical ozone saline intravenous infusion once every other day, with 10–14 days taken as a course of treatment. Use medical ozone major autohemotherapy, once every other day, with 12 times as a course of treatment.

6.8.2.6 HYPERTHERMIA AND OTHER TREATMENTS

The combination of TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, and alkaline treatment with hyperthermia can increase efficacy and safety of treatment.

DC-CIK cell therapy: (1) DC-CIK consolidates treatment after radical resection: after early breast cancer radical resection, DC-CIK transfusion can effectively remove residual small lesions and reduce recurrence. The number of CIK cells for each reinfusion should reach at least 1×10^{10}; conduct once per month, with four times as a course of treatment. Conduct periodic review after transfusion; if there is no recurrence, an additional treatment is carried out once every 6 months. Collecting cancer tissues during the operation for preparation of individual peptides and DC vaccines, which are cultured together with CIK, can obtain better efficacy. (2) DC-CIK in combination with other methods: after radical mastectomy, DC-CIK can also be combined with conventional chemoradiotherapy, endocrine therapy, and other integrative treatments. Treatment program: one day before chemotherapy collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct a consolidation therapy every 2 to 3 months. DC-CIK in combination with radiotherapy can also be applied using reinfusion in the intervals of radiotherapy. For example, on the day when radiotherapy is to be conducted, collect the patient's peripheral blood for DC-CIK culture before the start of radiotherapy and conduct reinfusion at the interval of radiotherapy. DC-CIK can be combined with endocrine therapy and conducted simultaneously.

Systemic biofeedback therapy: Three times a week, with 20 times as a course of treatment. Adjust to once or twice a week after two to three courses of treatment for long-term treatment.

Alkaline treatment: Adopt external application of sodium bicarbonate or local or acupoint injection. Conduct routine disinfection, and avoid blood vessels. Inject 2.5%–5% sodium bicarbonate with a thin needle at multipoints, about 2 mL for each point, for a total of not more than 10 mL for one time, once every other day, with eight times as a course of treatment.

6.8.2.7 HYPERTHERMIA AND HERBAL MEDICINES

6.8.2.7.1 Bath

Proven prescription 1: Erhuang decoction: *Cortex phellodendri* 30 g, wintergreen barberry root 30 g. Decoct them for external washing or wet compress. Efficacy: clears heat, moistens dryness, and purges fire for detoxification. It is applicable to postoperative wound infections of breast cancer, skin flap necrosis, radiodermatitis, and local swelling or ulceration caused by venous leakage of chemotherapeutic drugs.

Proven prescription 2: Sanhuang Lotion: take 30 g each of *Cortex phellodendri*, *rhubarb*, *Scutellaria baicalensis Georgi*, and *Sophora flavescens Ait*. Decoct them, and use the decoction to wash the affected area. Efficacy: purges fire for detoxification, relieves itching, and induces astringency.

6.8.2.7.2 Grilling method

Shengji Yuhong Plaster: Sesame oil 500 g, *Angelica* 60 g, white wax 60 g, *Glycyrrhiza uralensis* 36 g, *Angelica sinensis* 15 g, *calomelas* 12 g, *Resina draconis* 12 g, and *Lithospermum erythrorhizon* 6 g. Decoct them into plaster. Spread it on the affected area and irradiate for 20 minutes with infrared lamp, once a day. Efficacy: activates blood circulation, eliminates necrosis, moistens skin, and promotes granulation. It is applicable to patients with unhealed radiation-induced skin ulcers, postoperative wound infections, or flap necrosis and ulceration in advanced breast cancer tumor.

6.8.2.8 HYPERTHERMIA INDICATIONS

Patients with KPSs of 60 points or above can use hyperthermia. Critically assess the general condition during whole-body hyperthermia.

6.8.2.9 HYPERTHERMIA CONTRAINDICATIONS

Local skin damage, patients with bleeding tendency, and cachexia.

6.8.3 Introduction of a typical case

A patient named Kathy from the United States, female, 59 years old, was admitted to Clifford Hospital on October 18, 2007, due to "four years with right breast invasive ductal carcinoma, which has progressively increased, 3 months of weight loss, one week of skin redness and swelling." On October 2003, the patient accidentally discovered a mass in the right breast, which was hard and had the size of a peanut without pain. Prior to that time, the patient had been taking estrogen for more than 3 years. The patient was diagnosed with breast invasive ductal carcinoma in a hospital in North Carolina by local tissue biopsy, with PR (+), ER (+), and CerbB2 (+ + +). The patient refused to accept invasive treatment, including surgery and chemoradiotherapy. She has always received natural therapies such as vitamin C, medical ozone, massage, hydriatrics, and others, and the disease was relatively stable. The mass gradually increased in size in the 3 months before admission, and the entire right breast was hard with skin redness and swelling. The patient was obviously fatigued, with shortness of breath and palpitations after mild activity. The patient had recurrent paroxysmal coughs. The patient came to Clifford Hospital for further treatment. The patient had lost 10 kg of weight during the 3 months before admission. Her mental state was poor during the course of the disease. Appetite generally remained good. Urine and stool were normal.

Physical examination: The patient's appearance and mental state were poor. She was thin and weighed 51 kg. There were bilateral breast surface swelling, local spot ulceration covered with pus, bilateral nipple retraction, and particle surface similar to strawberry. Several lymph nodes were palpable at bilateral axillary and left supraclavicular fossa, and the largest was approximately 2 cm × 2 cm × 1.5 cm, was hard with poor mobility, and presented clear boundary with the surrounding tissue. A 2 cm × 1.5 cm × 1.5 cm mass was palpable at the sixth intercostal space of the right posterior axillary line, hard with poor mobility, and without clear boundary to the skin around. The heart rate was 112 beats/min with regular rhythm, and no noise was heard. Dullness was heard by percussion at the gap between the double inferior lung and the fifth intercostal space, and breathing sounds were significantly reduced. The patient could not sleep in the right lateral position. There were pitting swellings at the right upper forearm and the upper arm, and mild swelling at the lower limbs. Her KPS was 60.

Auxiliary examination: Pathology of the hospital in Carolina: right breast invasive ductal carcinoma grade II with ER (+), PR (+), and CerbB2 (+ + +). Blood routine: RBC 3.1×10^{12}/L, Hb 93 g/L, WBC 4.2×10^{9}/L, and PLT 153×10^{9}/L. Biochemistry: ALT 37 U/L, AST 32 U/L, TP 58 g/L, ALB 27.3 g/L, ALP 157 U/L, GGT 88 U/L, TBIL 13.2 μmol/L, DBIt 5.0 μmol/L, Cr 35 μmol/L, Ua 335 μmol/L, BUN 5.3 mmol/L, GLU 5.25 mmol/L, TG 0.28 mmol/L, GHO 3.46 mmol/L, K^+ 3.95 mmol/L, Na^+ 141 mmol/L, Cl^- 107 mmol/L, and Ca^{2+} 2.01 mmol/L. The five items of immune function and trace elements were normal. CEA 48 ng/mL, AFP 7.09 ng/mL, CA 12-5(OV) 34.99 U/mL, CA199 35.94 U/mL, and CA 153(BR) 238 U/mL. Thoracic and abdominal CT showed that there were multiple metastases in the lung, liver, and chest. There was a 5 cm × 4.5 cm × 4 cm pedunculated mass in the left pleural cavity, connecting to the parietal pleura. There were bilateral pleural effusions with a great quantity of effusion in the right pleural. No significant bone metastases were seen in the whole-body bone scan. ECG: sinus rhythm, heart rate of 115 beats/min, and right bundle branch block.

Diagnosis: Invasive ductal carcinoma of the right breast, stage IV (left internal mammary, lung, liver, chest, skin, and other metastases).

Integrative treatment prescription: The patient presented liver, lungs, chest, skin, and lymph node and other multiple metastases when admitted to the hospital. There were moderate malnutrition, breast surface ulceration infection, and bilateral pleural effusion. It was considered that edema of the right arm was caused by chest wall lymphatic flow obstruction. Bilateral lower extremity edemas were caused by hypoalbuminemia. The patient was given debridement and medical ozone cupping treatment on bilateral breast after admission. The surface of the ulcer healed after 3 days. The swellings were eased significantly. After giving pleural drainage of pleural effusion, injected cisplatin 30 mg + IL-2 4,000,000 U, once every week. Bilateral chest local hyperthermia was given after injection, and local hyperthermia was carried out once every other day. At the same time, letrozole 2.5 mg a time was given, once per day for oral administration. Bilateral pleural effusions basically disappeared after 2 weeks. Then, whole-body medium-high hyperthermia was conducted once every 10 days and in conjunction with chelation detoxification therapy, once every other day.

Local hyperthermia was given in the interim periods of whole-body hyperthermia. A total of four treatments of whole-body hyperthermia and 20 times of local hyperthermia were conducted. Close attention was paid to nutritional support when the patient was admitted to the hospital. At the same time, EBOO was applied once every other day, alternating with chelation and detoxification therapy; TCM and acupuncture treatment were applied throughout the treatment. The patient presented dark red tongue, thin yellow greasy fur, and thready and unsmooth pulse. The syndrome belonged to the stagnation of heat and toxin when combined with the patient's symptoms. The therapeutic principle is to clear away heat and toxic substances, as well as removing blood stasis and promoting the reduction of swelling.

Medications: The prescription of modified Wuwei Xiaodu Decoction was given. Specific medication: *Flos lonicerae* 30 g, *dandelion* 15 g, *Viola yedoensis Makino* 15 g, *Begonia fimbristipula Hance* 15 g, *Semen persicae* 10 g, *Carthamus tinctorius L.* 10 g, *Nidus vespae* 6 g, and *Chinese Honeylocust Spine* 10 g, one dose a day. Decocted with water for oral administration.

Acupuncture on acupoints: Zusanli, Sanyinjiao, Zhongwan, Taixi, Guanyuan, Qihai, Shenshu, Pishu, and Sanchongxue. Methods: even reinforcing–reducing was mainly conducted. Retained the needle for 20 minutes, once per day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Dazhui, Zusanli, Sanyinjiao, Ganshu, Pishu, and Shenshu. Methods: took two points each time. Conducted moxibustion with a moxa stick. Conducted moxibustion for each point for 10 minutes once a day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Breast, chest, stomach, liver, endocrine, subcortex, adrenal gland, Yuanzhong, brain point, and Jiaogan. Methods: stuck auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

The patient was discharged after 2 months of hospitalization, and she continued Chinese medicine treatment after discharge.

Treatment effects: After more than 60 days of integrative treatments, the patient's ulcers and swelling on the breast disappeared. The huge mass in the right breast was softened and reduced significantly (Figure 6.6, Figure 6.7). Limb edemas disappeared, and fatigue was improved significantly. There was no palpitation when she went up and down the stairs. Her heart rate was 80–90 beats/min. Lymph nodes at bilateral axillary and left supraclavicular fossa were significantly reduced, and the largest was about 1 cm × 1.5 cm × 1.5 cm, and softened. She had a better diet, and her weight increased to 62 kg. She could lie in the supine position, and her activities were normal. Multiple metastases in the bilateral lungs and liver were reduced compared with the previous ones through a review of chest and abdomen CT, and there were no new lesions. The left pleural cavity lesion was 3.5 cm × 4.2 cm × 3.4 cm. RBC 4.2×10^{12}/L, Hb123 g/L, ALB 36.5 g/L, CEA 15 ng/mL, AFP 7.09 ng/mL, CA 12-5(OV) 20 U/mL, CA199 30 U/mL, and CA 153(BR) 88 U/mL. The KPS was 90. Follow-ups lasted for more than 8 months after discharge. We maintained e-mail contact with the patient. The patient continued to take letrozole 2.5 mg each time, once per day, and her condition has remained relatively stable (Figures 6.6 and 6.7).

6.8.4 Related research in China and abroad

Studies of Kouloulias et al. have shown that adjuvant hyperthermia with chemoradiation has a positive effect in the treatment of breast cancer.

Song Xiangwei et al. found through experimental studies that elemene in combination with hyperthermia induced apoptosis of breast cancer MCF-7 cells and had effect on cell cycle. Results showed that elemene combined with hyperthermia can significantly increase the MCF-7 cell proliferation inhibition rate and inhibit the conversion process of MCF-7 cells from phase G_1 to phase S, as well as induce apoptosis and subcellular structure change.

Li Yongqiang et al. have confirmed through experimental study that microwave hyperthermia (41°C, 2 hours) can induce apoptosis of human breast cancer cell line MCF-7, and the number of apoptotic cells can increase with time.

Shen Jianbin et al. have conducted intraoperative thermochemotherapy on 31 patients with breast cancer and carried out concurrent control of 30 patients with surgery alone. Results showed that local

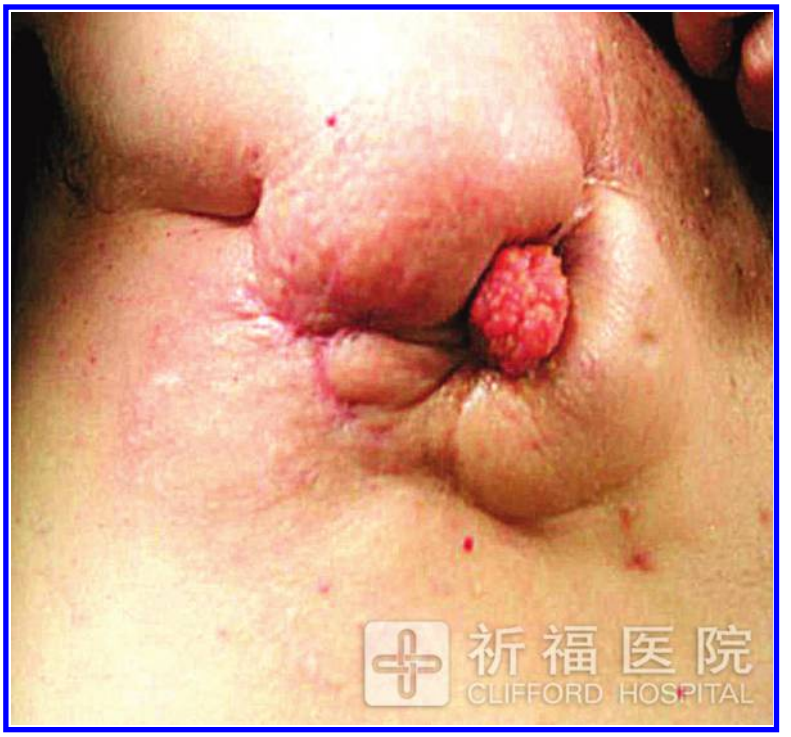

Figure 6.6 Before treatments: photo of mammary.

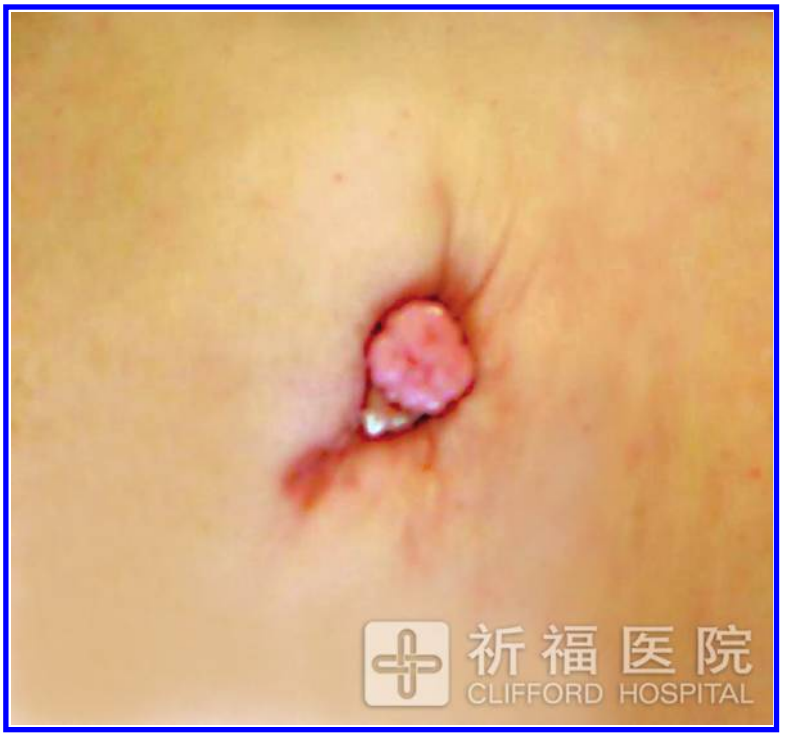

Figure 6.7 After treatments: photo of mammary.

hyperthermia and chemotherapy taken during surgery can reduce postoperative metastasis and local recurrence of breast cancer and help to improve the 5-year cure rate.

Zhang Lin et al. have conducted experimental studies and shown that hyperthermia has a resistance reversal effect for breast cancer cell lines cultured in vitro and enhances the sensitivity of chemotherapy drugs. Its mechanism may be that hyperthermia downregulates the expression of P-gp at the level of translation.

Clinical studies by Li Gong et al. have shown that local hyperthermia combined with radiotherapy can improve the local control rate of recurrence of breast cancer and can especially reduce the radiation dose in the area that had received radiotherapy.

Studies by Welz et al. have shown that chest wall radiotherapy combined with hyperthermia is an effective method for the treatment of chest wall recurrence of breast cancer.

Experimental studies of Xie Xiaoxue et al. have shown that hyperthermia at temperatures 43°C, 45°C, and 47°C can downregulate TGF-β1, downregulate VEGF protein expression in MCF-7 cells, and inhibit secretion and activity of MMP-2 and MMP-9, thereby inhibiting human breast cancer cell invasion and metastasis.

6.9 LIVER CANCER

Liver cancer refers to malignant tumors in the liver, including the two types of primary liver cancer and metastatic liver cancer. Primary liver cancer can be divided into hepatocellular carcinoma, intrahepatic cholangiocarcinoma, and mixed liver carcinoma based on cell typing. It can be divided into nodular, bulky, and diffuse liver cancers according to tumor morphology. Primary liver cancer is one of the most common malignant tumors clinically, ranking fifth among world malignancies. At present, the number of liver cancer patients in China accounts for about 55% of the world total. This cancer has become a major killer, seriously threatening the health and lives of people in China, and the danger cannot be overlooked or underestimated. Also, it is difficult to be discovered in the early stage; therefore, when newly diagnosed and initially treated most patients have already lost the chance for a successful operation.

Early symptoms of the disease are concealed. Clinical manifestation is mainly liver pain, which can radiate to the right shoulder. With the progress of the disease, there may be fever, fatigue, anorexia, diarrhea, weight loss, and so on.

6.9.1 Conventional treatments

6.9.1.1 SURGERY

Surgery is the preferred treatment for liver cancers. Patients with indications for surgery should grasp the earliest opportunity for surgery. Patients with a clear diagnosis that lesions are confined to a leaf or half of the liver; patients of stages I and II with good compensatory liver function; and patients with good heart, lung, and kidney function who can also tolerate surgery are key indications for surgery. Surgical resection is preferred for cases of local lesions and combined sclerosis that is not serious, especially in the early stages of small liver cancer. Chemotherapy pump is indwelled via the hepatic artery and portal vein during surgery. Chemotherapy drugs, vitamin C, and so on are locally infused through the pump after surgery. Combining chelation detoxification, medical ozone, TCM, hyperthermia, and other treatments can further improve the curative effect. For multinodular cancer patients who are not suitable for surgery, and with liver function of level Child A, TACE, cryopreservation, radio-frequency ablation, and other interventional therapies are preferred. For patients with unresectable medium-advanced hepatocellular carcinoma; patients with postoperative cancer recurrence, liver function discompensation, and excessively low WBCs and platelets, who are also not suitable for surgery or chemotherapy; as well as patients with small hepatocellular carcinomas that are located in specific unresectable sites, accurate cryosurgical methods can effectively and accurately destroy liver cancer cells to improve survival rates. For small hepatocellular carcinoma, liver transplantation can be considered. Preoperatively and postoperatively (including before and after the intervention), providing positive chelation detoxification, medical ozone, TCM, and other nontoxic integrative treatments can further

inhibit cancer cell growth and proliferation and protect liver function. They can not only create favorable conditions for surgery or intervention and enhance the therapeutic effect but also reduce the damage of surgery or interventional therapies to the patient so as to promote wound healing as quickly as possible.

6.9.1.2 RADIOTHERAPY

It was believed previously that liver cancer had poor sensitivity to surgery and the effect was not ideal. But now, with the development of modern radiotherapy techniques, early cases have been reported showing that if larger doses of radiotherapy can be tolerated, efficacy can be significantly improved from that in the past. Many early-stage inoperable liver cancers can obtain radical treatment through modern radiotherapy with minor liver dysfunction.

6.9.1.3 CHEMOTHERAPY

For unresectable liver cancers, transcatheter arterial chemoembolization is preferred and is mainly applicable to multinodular cancer patients with liver function of level Child A. For multinodular hepatocellular carcinoma with tumor thrombus at the main portal vein, and if liver function is good and collateral circulation is rich, it can also be applied. For patients with systemic multiple metastases, if their general condition is good, systemic chemotherapy can be considered. For patients in poor general condition, combined therapy that focuses on supportive care is appropriate.

6.9.1.4 HYPERTHERMIA

Hyperthermia can inhibit or kill cancer cells. Because most liver cancer patients have deficiency of both qi and yin and whole-body hyperthermia can easily cause profuse sweating and impair yin, local hyperthermia is recommended. Appropriate whole-body hyperthermia can also be chosen in cases of clear indications for hyperthermia, and after TCM assessment; but before and after hyperthermia, herbal medicines should be adjusted to mitigate possible adverse effects. In 1987, the local high-temperature curing treatment of liver cancer was reported for the first time in China; based on this, research studies on high-temperature tumor-curing vaccines have been conducted and the immune effects of hyperthermia in cancer therapy were confirmed on an experimental basis. In recent years, domestic and overseas research aiming to seek minimally invasive or noninvasive treatments of liver cancer have found relatively effective ways of utilizing hyperthermia in clinical applications: microwave/RF local hyperthermia, arterial catheter, thermal coagulation therapy, radio-frequency ablation, percutaneous arterial catheter thermochemotherapy, percutaneous ultrasound-guided laser (simply thermal conductivity), microwave curing, degradable starch microspheres for hepatic arterial embolization thermochemotherapy, isolated liver perfusion, and high-intensity focused ultrasound.

6.9.1.5 CHELATION DETOXIFICATION THERAPY

Chelation and detoxification therapy can effectively remove toxins from the body. Vitamins has a better hepatoprotective effect. Therefore, vitamin therapy is the most recommended detoxification therapy in the treatment for liver cancer. Chelation therapy is usually applied once every other day, with 20 times as a course of treatment, with an infusion time of more than 2 hours. For patients with severe heart and lung function disorders, the amount of liquid should be appropriately reduced and the infusion rate should be slowed. Chelation detoxification should be combined with hyperthermia at the same time, or conducted before hyperthermia, which can produce a sensitizing effect. Preoperative chelation detoxification helps to control subclinical lesions or micrometastases, prevents cancer cell transition and diffusion during metastasis, as well as preventing recurrence caused by rapid proliferation of postoperative residual cancer cells. Postoperatively patients are low in immunity, and chelation detoxification is conducive to the recovery of immune functions. Chelation detoxification therapy is particularly needed after local infusion chemotherapy because chelation detoxification can reduce the side effects of chemotherapy drugs. At the same time, it can produce a sensitizing effect and prevent recurrence and metastasis caused by rapid proliferation of postoperative residual cancer cells. Chelation detoxification therapy can also inhibit the proliferation and metastasis of cancer cells in patients with medium-advanced hepatocellular carcinoma. The drug composition of chelation

detoxification is vitamin C and reduced glutathione, which have good hepatoprotective effects, and combining with TCM syndrome differentiation it is preferred for patients with advanced hepatocellular carcinoma. It is recommended that dosage can reach twice the usual therapeutic amount, once every other day, until the condition is stable and then can be adjusted to one to two times a week. Chelation detoxification therapy for advanced hepatocellular carcinoma patients has no treatment restrictions.

6.9.1.6 MEDICAL OZONE THERAPY

It has significant effects in promoting liver functional recovery, inhibiting hepatitis virus replication, and promoting hepatitis B virus antigen negative conversion. At the same time, it has significant tumor inhibition and direct killing effects. Patients with weak constitutions should be given intravenous medical ozone saline or major autohemotherapy, usually once every other day. Patients with good constitutions and without coagulation abnormalities should be given EBOO usually 2 or 3 times a week, with 20 times as a course of treatment. Medical ozone therapy must be alternated with chelation detoxification and cannot be scheduled on the same day. The majority of medium-advanced liver cancer patients are physically weak, accompanied by coagulation abnormalities, so it is recommended that after careful evaluation of the patient at first use medical ozone saline for transition treatment once or twice. If the patient can tolerate it, then perform transition to EBOO treatment, once every other day, and alternately conduct chelation detoxification. At the same time, give medical ozone acupoint injection. If the patient has hemorrhagic tendency with a weak constitution, use intravenous medical ozone saline and minor autohemotherapy once every other day, with 16 times as a course of treatment.

6.9.1.7 TRADITIONAL CHINESE MEDICINE

Conduct syndrome differentiation according to the patient's condition, stage of disease, complications, and variations in body responses. The syndrome of qi stagnation and blood stasis is commonly seen in the early stage. Prescriptions recommended are Xiaochaihu Decoction plus modified Dahuang Zhechong Pill. The syndrome of wetness heat of liver and gallbladder is commonly seen in the medium-advanced stage. Prescriptions recommended are Yinchenhao Decoction plus modified Gexia Zhuyu Decoction. For the syndrome of yin deficiency of liver and kidneys, the prescription recommended is modified Yiguan Decoction.

6.9.1.8 ACUPUNCTURE

The syndrome of liver qi depression mainly appears at the early stage of liver cancers. The therapeutic principle should focus on soothing the liver and regulating the circulation of qi, as well as softening and resolving hard mass.

Acupuncture on acupoints: Ganshu, Neiguan, Yanglingquan, Taichong, and Pigen. If the syndrome of liver depression and phlegm stagnation is seen, add Xingjian and Fenglong to regulate liver qi, remove phlegm, and resolve mass.

Methods: Even reinforcing–reducing method is used for acupuncture, with needle retention of 20 minutes once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The syndromes of wetness heat of liver and gallbladder as well as yin deficiency of liver and kidneys mainly appear at the advanced stage of liver cancer. The therapeutic principle should focus on clearing away heat and eliminating dampness, eliminating foot ulcers, reducing swelling and resolving mass, nourishing the liver and kidneys, and invigorating spleen for diuresis.

Acupuncture on acupoints: The main points are Ganshu, Qimen, Pishu, Shenshu, Zusanli, Taixi, and Sanyinjiao. If the syndrome of yin damage by heat toxin is seen, Chongquan and Shuiquan can be added to cool blood and nourish yin, as well as clear away heat and toxic substances.

Methods: Even reinforcing–reducing method is used for acupuncture, with needle retention of 20 minutes once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Guanyuan, Zusanli, Ganshu, Shenshu, and Pishu.

Methods: Take two to four points each time. Conduct moxibustion with the moxa stick and take 10 minutes for each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Liver, Pishu, diaphragm, hepatitis point, Erjian, endocrine, adrenal gland, subcortex, Jiaogan, Shenmen, and tumor-specific area.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.9.1.9 MEDICATED DIET, NUTRITION, AND SO ON

The liver is the body's most important metabolic organ; the occurrence and development of liver cancer is closely related to the levels of the body's nutrition and metabolism. Liver cancer patients must be given nutritional assessment and rational nutritional support. Patients able to eat normally are subject to nutritional medicated diet combined with infusion to supplement sugar, salt, vitamins, amino acids, and so on; patients with poor nutrition and poor intake are given total parenteral nutrition for maintaining normal energy metabolism. Medium-advanced hepatocellular carcinoma patients have poor nutrition and many have been complicated by hepatic decompensation, thus requiring higher nutritional support. Replenished daily amounts of protein and other nutrients need to be calculated cautiously; otherwise, they are not conducive to the rehabilitation of patients, will increase the burden on the liver, and can even induce hepatic failure and hepatic coma. Patients who can eat should focus on taking a medicated diet. Patients who eat less can combine oral administration or intravenous nutrition. Patients who cannot eat should receive total parenteral nutrition.

6.9.1.10 OTHERS

Patients with liver disease often show irascibility and irritability. In particular, when patients enter the medium-advanced stage the majority of them are frustrated and depressed, and their moods are worsened because pain and other symptoms cannot be relieved. At this point of time, it is a must to encourage the practice of qigong and to apply music therapy, TCM therapy, or Western psychotherapy, and so on to keep the patients calm and peaceful, as well as with positive and optimistic attitudes in conjunction with other treatments, all of which can help in their rehabilitation.

6.9.2 Combination of hyperthermia with conventional treatments

6.9.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Early-medium liver cancer patients with focal lesions, liver function of level Child A-B, and clear indications for surgery should focus on radical surgery. Small hepatocellular carcinoma patients can be considered for liver transplantation. Patients who cannot tolerate or who refuse surgery may be considered for minimal invasion such as transcatheter arterial chemoembolization/chemotherapy, or radio-frequency ablation. In the perioperative period, medical ozone, chelation detoxification, TCM, acupuncture, herbs, and other nontoxic integrative treatments should be actively employed. These can significantly improve the patient's tolerance to surgery and reduce the occurrence of intraoperative and postoperative metastasis, which can promote postoperative rehabilitation as soon as possible. After the postoperative wound is completely healed, hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of the patient by the hyperthermia center physicians.

Liver cancer hyperthermia contraindications are especially worth noting: hyperthermia is not suitable for patients with very large cancers of liver mass (volume is greater than 70%), which comes with the risk of spontaneous rupture; patients with hemorrhagic tendency; patients with jaundice, ascites, severe cirrhosis, accompanied with severe hepatic dysfunction, severe heart, liver, lung, or kidney dysfunction, and other organic diseases; and patients with one of the syndromes of yin deficiency or deficiency of both qi and yin according to TCM syndrome differentiation. Only with strict control of liver cancer hyperthermia indications and contraindications can hyperthermia provide the greatest degree of efficacy for liver cancer and reduce unnecessary medical risks as much as possible.

Whole-body hyperthermia can improve immunity; promote cancer cell apoptosis; and regulate the body to produce TNF, IL-2, and other immune factors involved in the anticancer effect.

If patients are assessed to be in good general condition and are able to withstand whole-body hyperthermia, it is recommended to carry out whole-body hyperthermia, once every 2 weeks, with six times as a course of treatment. Pay attention to the monitoring of body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give timely fluid infusion to maintain water–electrolyte balance and other symptomatic treatments. Review electrolytes and so on 1–3 days after the whole-body hyperthermia. Continue to supplement energy to maintain water-electrolyte balance. Local hyperthermia can be appropriately added at the intervals of whole-body hyperthermia according to the general condition and tolerance of patients.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the liver area or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. Conduct the second course after an interval of 10 days. After three courses, local hyperthermia can be taken as long-term concomitant therapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.9.2.2 HYPERTHERMIA AND CHEMOTHERAPY

Transcatheter arterial chemoembolization is commonly used for chemotherapy of liver cancers. Because liver cancer has low sensitivity to chemotherapy, generally we do not advocate systemic intravenous chemotherapy. To improve the effect of interventional chemotherapy, enhance the sensitivity of chemotherapy. It is more desirable to conduct local hyperthermia at the liver area within 2 hours after interventional chemotherapy. Because the majority of liver cancer patients are usually diagnosed at the medium-advanced stage with symptosis, local hyperthermia is often combined with chemotherapy for most situations.

In recent years, China has approved arsenic trioxide as one of the primary advanced liver cancer chemotherapy programs. Clifford Hospital has effectively combined insulin-mediated small doses of arsenic trioxide intravenous chemotherapy with medical ozone and hyperthermia and achieved good results in clinical practice. Specific methods: rule out contraindications of chemotherapy through comprehensive assessment, and obtain the informed consent of patients. An empty stomach is required before chemotherapy. Carry out medical ozone major autohemotherapy before chemotherapy, then give insulin to control blood glucose at about 3.6 mmol/L (it is better to control blood glucose when the hypoglycemia reaction has just appeared, and according to individual circumstances), and then give a small dose of arsenic trioxide 10–15 mg for intravenous chemotherapy once a day for 5 consecutive days. Conduct routine antiemetic hepatic protection and stomach protection, to be supplemented with high glucose and trace elements before chemotherapy. It is appropriate to conduct local hyperthermia at the liver area within 2–4 hours after chemotherapy. If the patient is in generally good condition and can tolerate whole-body hyperthermia, it is advised to have whole-body medium-low temperature hyperthermia.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body medium-high hyperthermia can be carried out simultaneously during the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Simultaneously carry out hyperthermia and chemotherapy cycles for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the right upper abdomen or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, and continue it at the intervals of chemotherapy. Take 1 week off after each cycle (5 consecutive days) of chemotherapy. A total of about 60–80 times of combined local hyperthermia is carried out during chemotherapy. Local hyperthermia can be taken as long-term maintenance therapy after the end of chemotherapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 10 times.

6.9.2.3 HYPERTHERMIA AND TARGETED THERAPY

The new molecule-targeted drug sorafenib (Nexavar) coming out in recent years can delay cancer progression and prolong survival to a certain extent. Domestic and overseas clinical trial results have shown that sorafenib can prolong survival time by 2 to 3 months, and the rate of delaying the development of the disease was 73%, but the drug is comparatively expensive. At the same time, diarrhea, rash, hypertension, hand–foot syndrome, and other more serious adverse reactions may occur. If patients took targeted Nexavar combined with local hyperthermia, medical ozone, chelation detoxification therapy, and other nontoxic integrative treatments at the same time, the efficiency can be increased by about 8%–12% and adverse reactions can be reduced by about 30%–45%.

6.9.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given from the end of operation to the period of chemoradiotherapy to the patient with postoperative physical weakness and low immunity. On the one hand, it promotes physical recovery and regulates the immune system and, on the other hand, it can kill residual cancer cells or inhibit early metastasis. Local hyperthermia or whole-body hyperthermia can be simultaneously applied with chelation detoxification to improve efficacy.

6.9.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance effect on immunity, and increase the efficacy of medical ozone. Treatment methods: use EBOO once every other day for 20 times as a course of treatment. Alternatively select medical ozone saline infusion once every other day, with 10–14 days as a course of treatment for a total of three courses. Use medical ozone major autohemotherapy once every other day, 12 times per treatment. Medical ozone minor autohemotherapy must be taken once every other day, 12 times per treatment. Use medical ozone acupoint injection once every other day, for 12 times as a course of treatment. Conduct at least three courses for long-term maintenance therapy.

6.9.2.6 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. Other treatments such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, colon cleansing therapy, and so on in combination with hyperthermia can increase the effectiveness and safety of the treatment.

6.9.2.6.1 DC-CIK cell therapy

Surgical treatment is preferred for early liver cancer. Combination with postoperative DC-CIK treatment can not only eliminate residual small lesions but also improve patients' immunity and reduce recurrence. Take and keep cancer tissue during the operation and obtain antigen peptides of autologous cancer cells from the patient and prepare targeting DC-CIK, which can specifically kill cancer cells and have a better efficacy. Condition assessment: collect the test data on cancer foci image examination, tumor antigens, immune function, liver, kidney and blood routine, and infectious diseases of blood to assess patients' systemic conditions. Rule out contraindications, and obtain a signed informed consent for DC-CIK treatment from the patient. Specific methods: (1) collect 50–60 mL autologous peripheral blood of the patient, and prepare DC-CIK and submit to the laboratory for isolating and inducing culture. Collect cells after 12–14 days and conduct reinfusion intravenously. Rigorously test the patient's vital signs during and after the reinfusion process by following the protocols of blood transfusion. The number of CIK cells for each reinfusion should reach at least 1×10^{10}; conduct once per month, with four times as a course of treatment. Conduct periodic review after transfusion, and if there is no recurrence an additional treatment is carried out once every 6 months. (2) Transcatheter arterial chemoembolization is often preferred for advanced hepatocellular carcinoma. Studies have shown that the combined application of transcatheter arterial chemoembolization with DC-CIK treatment can significantly improve the interventional treatment efficacy of liver cancer and reduce recurrence. For medium-advanced hepatocellular carcinoma patients, simultaneously conduct

intervention embolization and perfusion of DC-CIK in combination with the method of intravenous infusion of DC-CIK. The volume of cell infusion and duration of treatment are the same as those of postoperative consolidated therapy. (3) Advanced patients often cannot tolerate chemotherapy, interventional therapy, and other treatments with significant toxicity due to poor liver function. In such cases, it is favorable for patients to apply DC-CIK in combination with conservative treatments. After the preparation of a batch of cells, one or multiple infusions can be carried out according to the patient's tolerance, with every 2 weeks as a treatment batch and four consecutive batches as a course. Assess the efficacy. If it is effective, conduct a consolidation therapy every 2 to 3 months. For patients with ascites, intravenous reinfusion of DC-CIK combined with intraperitoneal perfusion DC-CIK can also be applied for treatment.

6.9.2.6.2 Systemic biofeedback therapy

Systemic biofeedback therapy: Three times a week, with 20 times as a course of treatment. Adjust to once or twice a week after two to three courses for long-term treatment.

Because the prognoses of most early liver cancers are favorable, give appropriate psychological counseling to reduce patients' psychological fears of cancer and recommend them to practice qigong and to adhere to appropriate exercise as well as to receive long-term medicated conditioning.

6.9.2.6.3 Alkalization therapy

Dietotherapy or sodium bicarbonate therapy can be applied to alkalize the body.

Sodium bicarbonate intervention: Implant 5% sodium bicarbonate through arterial interventional catheter, 20–30 mL each time, lasting for 10 minutes. This has better effect on liver cancer. If simultaneous chemotherapy drugs are applied, sodium bicarbonate should be injected first, once a month, with three consecutive times as a course of treatment.

Peritoneal perfusion of sodium bicarbonate: It is considered safe and effective. It can be applied with chemotherapy drugs. It is noted that 100 mL of 5% sodium bicarbonate injection heated to 37°C is perfused slowly into the abdominal cavity within 1 hour combined with abdominal massage to achieve uniform distribution of liquid in the abdominal cavity. If the patient complains of abdominal pain, 10 mL of 2% lidocaine can be added inside or the concentration can be reduced to 2.5% with the same dose. If chemotherapy drugs are also applied, sodium bicarbonate is applied first; 20 minutes later, the chemotherapy drugs are perfused, once or twice a week with eight times as a course of treatment. If peritoneal perfusion of sodium bicarbonate is combined with hyperthermia, RF local hyperthermia at the abdomen can be carried out after perfusion.

Retention enema of sodium hydrogen carbonate or rectosigmoid administration: About 100–150 mL of 1.25%–2.5% sodium hydrogen carbonate is applied for retention enema. Retain for 15–20 minutes, or 50 mL of sodium bicarbonate with the same concentration is set to the junction of the rectosigmoid with a fine silica tube for slow infusion (10–15 drops/min). Patients should feel good, and the purpose of quickly alkalizing the liver, intestine, pancreas, and spleen can be achieved.

6.9.2.6.4 Colon cleansing therapy

Patients can take fruit and vegetable drinks with the coffee enema; a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support.

6.9.2.7 HYPERTHERMIA AND HERBAL MEDICINES

6.9.2.7.1 Bath

Proven prescription 1: Ramulus cinnamomi 60 g, *Acanthopanax senticosus* 50 g, and *Glycyrrhiza uralensis* 5 g. Add water to the drugs, and boil for 30 minutes. Remove slag and take juice. Immerse feet for 30 minutes once a day, with 10 days as a course of treatment. Efficacy: supplements qi to warm yang. Mainly cures a variety of types of fatigue and is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 2: Ramulus cinnamomi 60 g, *Acanthopanax senticosus* 50 g, and *Glycyrrhiza uralensis* 5 g. Add water to the drugs, and boil for 30 minutes. Remove slag and take juice. Immerse feet for 30 minutes once a day, with 10 days as a course of treatment. Efficacy: supplements qi to warm yang. It mainly cures a variety of types of fatigue and is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 3: Stems and leaves of *Panax ginseng* 30 g, *Atractylodes macrocephala Koidz* 30 g, *Radix saposhnikoviae* 20 g, yam 20 g, and *Glycyrrhiza uralensis* 6 g. Add proper amount of water to the drugs. Boil twice, lasting 30 minutes each time. Combine filtrate and immerse feet for 30 minutes once a day, with 15 days as a course of treatment. Efficacy: invigorates spleen and replenishes qi. It is applicable to cancer patients with long-term weakness and lack of resistance.

Proven prescription 4: Rhodiola 800 g, *Semen coicis* 500 g, *Acanthopanax senticosus* 400 g, *Radix astragali* 300 g, *Cyrtomium fortunei* 300 g, *Schisandra chinensis* 300 g, *Angelica sinensis* 200 g, and *Ligusticum chuanxiong Hort* 200 g. Boil twice, lasting 50 minutes each time. Combine filtrate and bathe for 40 minutes once a day, with 15 days as a course of treatment. Efficacy: supplements qi, nourishes yin, invigorates qi, and promotes blood circulation. It is applicable to cancer patients with long-term weakness and lack of resistance.

6.9.2.7.2 Grilling method

Proven prescription 1: Yongquan Plaster: one piece of large and raw *Radix aconiti Lateralis Preparata*; one pair of big *Syngnathus*; 9 g each of *Lysimachia foenum-graecum*, *Squama Manitis*, and *Cynomorium songaricum Rupr*; sesame oil 600 g; plus yellow lead 200 g. Boil them into paste, which is mixed well with 15 g each of actinolite and musk and 9 g each of Cordyceps Sinensis, ginseng, Sichuan pepper, and clove fruit. Spread out 1 g to the size of a coin each time and paste to the centers of both feet, and then bake for 0.5–1 hour in the affected area with the infrared lamp. Efficacy: reinforces liver and kidney. It is applicable to middle-aged and old-aged patients having masses in the abdomen due to renal asthenia with general debility and to tumors in various parts of the body.

Proven prescription 2: Aweihuapi Plaster: decoct *ferula*, *Rhizoma sparganii*, *Rhizoma curcumae*, rhubarb, *crude Sichuan aconite root*, *Olibanum, Momordica cochinchinensis*, dung beetle, *Rhizoma cyperi*, *aloe vera*, *Resina draconis*, and *camphor* for plaster. Heat the mixture to soften it for external application and paste it in the umbilical region or the affected area, and then irradiate for 30 minutes with the Magic Lamp once a day. Efficacy: regulates the flow of qi and promotes blood circulation, softens and resolves hard mass, as well as relieving chest and abdominal distention and disintegrating abdominal mass. It is applicable to patients who have chest and abdominal distention and abdominal mass with the symptoms of qi stagnancy and who have blood stasis in liver, gallbladder, stomach, and intestines and gynecological diseases.

6.9.3 Introduction of a typical case

A patient named Xian, male, 62 years old, was admitted on April 28, 2007, to Clifford Hospital due to "icteric skin and sclera for more than 20 days, and abdominal distension accompanied with lower extremity edema for 3 days." The patient was feeling fatigued and went to a local clinic seeking medical attention. The patient was diagnosed with "hepatitis" and the doctor recommended further examination and treatment, but the condition was not considered serious. The patient found that he had lower extremity edema, poor appetite, and abdominal distension 3 days before coming to the Outpatient Department of Clifford Hospital seeking medical attention. Abdominal ultrasound prompted right hepatic lobe multiple nodules, the largest being 4 cm × 5 cm × 5.5 cm, and abdominal CT results suggested left hepatic lobe atrophy and abnormal low-density lesion in the upper segment of the right hepatic lobe with a cross-sectional area of about 5.4 cm × 6.2 cm. A sublesion with a diameter of about 6 mm was seen behind the lesion, which was considered primary liver cancer, liver cirrhosis, and ascites. The patient was then admitted to the hospital for further treatment. During the course of the disease, the patient's mental state was poor and he had poor appetite, a sense of malaise, mild abdominal distension, general sleep disruptions, and occasional dark black stools.

Physical examination: Moderate icteric skin and mucus on the whole body. Skin rash, subcutaneous hemorrhage points, and ecchymosis were not found. Several spider moles could be seen at the neck and the upper chest. The abdomen was relatively full without abdominal vein distention and soft abdominal muscles. No tenderness and rebound tenderness on the whole abdomen and no liver tenderness were found. Liver and spleen were not palpable. Negative Murphy's sign and shifting dullness (+) were found. Mild edema of both lower extremities was found. His KPS was 60.

Auxiliary examination: Blood routine test: RBC 5.5×10^{12}/L, Hb 125 g/L, WBC 5.3×10^{9}/L, and PLT 224×10^{9}/L. Biochemistry: ALT 775 U/L, AST 585 U/L, TBIL 217 U/L, DBIL 154.5 U/L, ALB 26.7 g/L, ALP 256 U/L, GGT 357 U/L, Cr 12 μmol/L, Ua 125 μmol/L, BUN 2.7 mmol/L, GLU 6.21 mmol/L, TG 0.54 mmol/L, GHO 3.78 mmol/L, K^+ 3.5 mmol/L, Na^+ 137 mmol/L, Cl^- 101 mmol/L, and Ca^{2+} 1.78 mmol/L. Tumor indexes: CEA 3.7 ng/mL, AFP 1276.6 ng/mL, CA-125 12 U/mL, CA-153 12 U/mL, CAl9-9 27 mL, and TSGF 31.7 U/mL. The five items of immune function were normal. Copper: 3.55 mmol/L; zinc, lead, mercury, cadmium, nickel, and so on were normal. Serum ammonia was 143 μmol/L. The five items of hepatitis B were as follows: HBsAg (+), HBsAb (–), HBcA (–), HBeAg (+), HBeAb (+), and HBV-DNA 3.37×10^{5} copies/mL. Abdominal CT examination: left liver lobe atrophy and abnormal low-density lesion at the upper segment of the right liver lobe are with a cross-sectional area of about 5.4 cm × 6.2 cm. A sublesion was seen behind the lesion with a diameter of about 6 mm. Impression: primary liver cancer, liver cirrhosis, and ascites. Esophagogastric varices were seen by gastroscope. A small amount of the right pleural effusion was seen by the chest X-ray. ECG was normal.

Diagnosis: (1) Primary liver cancer ($T_3N_0M_0$) and (2) posthepatitic cirrhosis of chronic hepatitis B (decompensated period).

Integrative treatment prescription: The patient showed significantly abnormal liver function, massive ascites, hypoproteinemia, and elevated blood ammonia when he was admitted to the hospital. Had the disease progressed, liver failure and even liver coma, hepatorenal syndrome, upper gastrointestinal hemorrhage, and so on could have resulted. Accordingly, chelation detoxification, protecting liver and lowering transaminase, eliminating jaundice, reducing blood ammonia, acid making, correcting hypoproteinemia, and other positive symptomatic treatments were given and appropriate nutritional support was added. Reasonable proportions of liver ammonia, MCT/LCT lipid emulsion, and glucose were given. TCM syndrome differentiation and treatment: the early symptoms were xanthochromia, icteric sclera, ascites, lower extremity edema, poor appetite, red tongue with yellow greasy fur, and wiry pulse. The syndrome belongs to stagnation of qi due to depression of the liver, as well as water and dampness retention. The therapeutic principle should focus on soothing the liver and regulating the circulation of qi, as well as removing dampness and eliminating jaundice.

Medications: Pericarpium citri Reticulatae Viride 10 g, *Radix curcumae* 20 g, *Rhizoma cyperi* 20 g, *Fructus aurantii* 10 g, *Angelica sinensis* 15 g, *Panax notoginseng* 6 g, *Nacre* 30 g, *Fructus tritici Ievis* 60 g, *Radix glycyrrhizae Preparata* 10 g, *Fructus trichosanthis* 30 g, *Bulbus allii Macrostemi* 15 g, *Acorus calamus* 15 g, *Salvia miltiorrhiza Bge.* 20 g, *radix puerariae* 30 g, *Mentha haplocalyx Briq* 6 g, *Curcuma longa* 10 g, *Radix paeoniae Rubra* 60 g, and *Herba artemisiae Scopariae* 30 g, one dose a day and decocted with water for oral administration.

Local hyperthermia was applied to the abdomen once every other day. After 2 consecutive weeks of treatment, xanthochromia and icteric sclera were significantly reduced and ascites and lower extremity edema disappeared, but paroxysmal palpitation appeared. ECG showed paroxysmal supraventricular tachycardia, which prompted the stopping of hyperthermia and the adjusting of the herbal medicines. TCM syndrome differentiation belonged to deficiencies of both qi and yin. The prescriptions recommended were Sijunzi Decoction plus modified Shengmai Powder and chelation detoxification once every other day as well as EBOO, also once every other day, with both alternated for treatment. After 1 week of treatment, the patient showed no skin and sclera xanthochromia and no palpitations, but had poor appetite. Syndrome differentiation belongs to deficiency of spleen and stomach. The prescriptions recommended were Xiangsha Liujunzi Decoction plus herbs that can invigorate the spleen and increase appetite. The patient orally took Pei-yuan decoction, one packet a day. All symptoms disappeared after treatment, and we continued to conduct local hyperthermia once every other day.

Acupuncture: Took Ganshu, Qimen, Pishu, Shenshu, Zusanli, Taixi, Sanyinjiao, Taichong, Yinlingquan, Yanglingquan, Waisanguan, and Shangsanhuang. Even reinforcing–reducing techniques were used and retained the needle for 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Zusanli, Ganshu, Shenshu, and Pishu. Took two points each time and conducted moxibustion for 10 minutes per point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Took liver, spleen, diaphragm, hepatitis point, Erjian, endocrine, adrenal gland, subcortex, Jiaogan, and Shenmen. Stuck auricular points with cowherb seed twice a week, and alternated ears.

The symptom of decompensated liver cirrhosis was more obvious than when the patient was admitted to the hospital. The treatment at that time focused on temporary emergency solutions by referring to Western medicine, such as hepatic protection, acid making, supplementation of albumin, and reducing aminopherase and blood ammonia. We waited until the patient had passed the dangerous period and gradually increased the intensity of treatment step by step.

Treatment effects: The patient's mental state had improved markedly with normal appetite, without fatigue and abdominal distension, and with soft yellow stools, and lower extremity edema had disappeared after 2 months of hospitalization. No icteric skin or mucus on the entire body was found by physical examination. The lesion was 5.4 cm × 5.5 cm by review. No effusion and enlarged lymph nodes were found in the abdominal cavity. Compared with pretreatment, occupying lesions of the liver had narrowed. Liver function tests: ALT 35 U/L, AST 47 U/L, TBIL 39 U/L, DBIL 18.5 U/L, ALB 20.5 G/L, AFP 173 UG/L. His KPS was 100. We conducted regular follow-ups, and the patient returned to normalcy in terms of mental state, appetite, and sleep. The patient returned to the hospital every 20 days for a 10-day treatment and insisted on taking herbal medicines. The treatment was adjusted to 1 week of treatment in the hospital every month after 3 months and 3 days of treatment after half a year. We conducted one-and-a-half years of follow-ups after discharge. The lesions remained relatively stable with no enlargement, and no new lesions were confirmed by abdominal CT at outpatient reviews. Liver function was normal, and AFP and other indicators were basically normal.

6.9.4 Related research in China and abroad

Chen Jinglong et al. have conducted clinical studies on hyperthermia combined with TACE for the treatment of liver cancer. Results showed that the effective rate in the combined group was 51.7% and that in the TACE alone group was 36.0% according to the WHO solid tumor evaluation standard, and comparison of the two groups had a statistical difference ($P < .05$). The 1-year survival rate was 58.8% in the combined group and 47.35% in the TACE group. The comparison difference had statistical significance ($P < .05$). Comparison of the analgesic efficiency of the combined group with that of the TACE group had statistical significance (75% vs. 28.6%, $P < .05$). In vitro high frequency hyperthermia in combination with TACE had a certain effect in the treatment of advanced liver cancer. No serious adverse reactions appeared in the course of treatment, and it was demonstrated to be noninvasive, safe and reliable, and worthy of clinical application.

Nikfarjam et al. have found through the study of heating liver tumor cells that the apoptosis was sustained for 96 hours and reached its peak at 24 hours.

Yan Xiuxin et al. have applied local endogenetic thermotherapy combined with chemotherapy for the treatment of primary liver cancer. The effective rate was 59.0%; median survival time was 14 months; 1-year survival rate was 68.1%; and 2-year survival rate was 27.2%, with relatively mild toxic and side effects, which were mainly bone marrow suppression of degrees I and II, gastrointestinal reactions, and occasional fever and high blood pressure.

Experimental studies of Zhang Li et al. have shown that radiotherapy combined with hyperthermia had synergistic effect for hepatocellular carcinoma cell killing, and its mechanism may induce apoptosis by upregulating the expression of P53 protein.

Zhang Jingyu et al. have studied the multidrug resistance effect of hyperthermia combined with arsenic trioxide (As_2O_3) on rat liver cancer through experiments and explored its feasibility as liver cancer adjuvant therapy. The results showed that As_2O_3 and hyperthermia had significant inhibition in vivo for rat liver cancer. The combination application had a synergistic effect, and its mechanism may be related to the inhibition of the expression of the multidrug resistance gene (*MDR1*).

6.10 GASTRIC CANCER

Gastric cancer is the most common cancer of the digestive tract and is among the forefront of all human malignancies. More than 1 million new cases of gastric cancer are reported annually in the world, of which China accounts for 42% and deaths of about 0.8 million, accounting for 35%. China is one of the countries

with the highest incidence of gastric cancer, with morbidity and mortality more than twice the world's average levels. About 90% of early gastric cancer patients can survive more than 5 years or be cured after appropriate treatment, while the 5-year survival rate of very advanced gastric cancer patients is less than 5% after treatment. Due to various reasons, the early diagnosis rate of gastric cancer in China is less than 10%, and about 50% of advanced gastric cancers exist with peritoneal recurrence and metastasis. The application of hyperthermia and hyperthermal perfusion chemotherapy has increased the efficacy and 5-year survival rate of gastric cancer patients.

The gastric predilection site is the gastric antrum. The vast majority is adenocarcinoma according to histopathological classification, and the rest comprise undifferentiated carcinoma, signet-ring cell carcinoma, hard cancer, squamous cell carcinoma, carcinoid, and so on. Diffusion of gastric cancer is mainly by direct extension and lymphatic metastasis, as well as metastasis through blood channels in the advanced stage. Direct extension can arrive at the greater omentum, pancreas, liver, transverse colon, transverse mesocolon, parietal peritoneum, and so on. Lymphatic metastasis occurs earlier, mainly located in the lesser and greater gastric curvature, inferior and superior pylorus, side of cardia, splenic hilum, spleen, hepatic artery, left gastric artery, lymph nodes, posterior pancreaticoduodenal side, side of celiac artery, abdominal aorta, fossa transversalis hepatis, mesenteric root, surroundings of the middle colic artery, and left supraclavicular lymph nodes. Hematogenous metastasis can reach liver, lung, bone, brain, kidney, spleen, and other organs and can also be planted to the greater omentum, peritoneum, and other organ surfaces.

Early gastric cancer may have no obvious symptoms. Upper abdominal fullness is often the earliest symptom of advanced gastric cancer, sometimes accompanied by belching, acid regurgitation, and vomiting. If carcinoma foci are located in the cardia, the patient may feel swallowing obstruction; if carcinoma foci are located in the pylorus and obstruction appears, the patient may vomit corrupted food. According to statistics, about 50% of elderly patients have significant loss of appetite, increasing weight loss and fatigue, and 40%–60% of patients would seek medical care due to weight loss. In about 10% hematemesis appears among patients with gastrointestinal hemorrhage, in about 35% melanemia appears, and in about 60%–80% persistent fecal occult blood may be present (small quantities and invisible to the naked eye but can be found by testing).

6.10.1 Conventional treatments

6.10.1.1 SURGERY

Surgery is the major and traditional treatment of gastric cancer, including mainly gastric cancer resection and cleaning of lymph nodes that are most likely to be metastasized by gastric cancer. Surgical treatment is preferred for early gastric cancer, and part of patients at phase III can also achieve surgical conditions by preoperative chemotherapy for surgical treatment. Patients who show obstruction can also receive palliative surgical treatment.

6.10.1.2 RADIOTHERAPY

Because the sensitivity of gastric adenocarcinoma is low to radiation, radiotherapy alone is ineffective and, thus, is complementary in the treatment of gastric cancer. Radiotherapy is divided into preoperative radiotherapy, intraoperative radiotherapy, postoperative radiotherapy, palliative radiotherapy (i.e., relieve obstruction or pain without prolonging life), and so on. Studies have shown that radiotherapy in the treatment of gastric cancer has a certain value as a remedial measure. Foreign studies have suggested that postoperative chemoradiotherapy can improve the treatment of gastric cancer and long-term efficacy. Further clinical exploration is needed.

6.10.1.3 CHEMOTHERAPY

Preoperative chemotherapy, also known as neoadjuvant chemotherapy, is mainly for gastric cancer patients at preoperative stages II and III and mostly applies combined chemotherapy protocols. Generally, conduct one to three cycles and the route of medication is dominated by intravenous or oral administration. Intraoperative

chemotherapy is mainly to prevent surgically induced iatrogenic tumor dissemination and to eliminate residual foci. Intravenous administration can be applied. In recent years, intraperitoneal administration has been encouraged. The purpose of postoperative chemotherapy is to prevent recurrence and metastasis. In principle, early postoperative gastric cancer does not need chemotherapy, whereas medium-advanced patients need chemotherapy; chemotherapy commonly adopts combined therapy, focusing on intravenous and oral administration of chemotherapy drugs. In recent years, early postoperative intraperitoneal chemotherapy has been encouraged, which can be effective in preventing postoperative peritoneal recurrence and prolonging survival time. For advance gastric cancer patients who are inoperable with nonradical surgery or cannot be reexcised due to radical recurrence, combined therapy including chemotherapy treatment can be applied. It should be noted that the treatment of advanced gastric cancer should focus on prolonging survival time and improving quality of life; indications for chemotherapy need to be cautiously assessed.

6.10.1.4 HYPERTHERMIA

Hyperthermia for gastric cancer includes mainly perioperative hyperthermia, postoperative maintenance treatment, and hyperthermia for medium-advanced gastric cancer. Currently, RF deep hyperthermia combined with intraperitoneal hyperthermic perfusion chemotherapy is commonly applied clinically.

6.10.1.5 CHELATION DETOXIFICATION THERAPY

Giving chelation detoxification after surgery together with chemotherapy can not only supplement liquids but also stabilize cell membranes and organelles of normal cells. At the same time, it can reduce the side effects of chemotherapy and enhance sensitivity to chemotherapy, as well as improving immunity and inhibiting or killing residual cancer cells. Generally, a base quantum is often given as the amount for the first time. The dose is gradually increased to a therapeutic dose after two to three times. If the condition permits after several times, each chelation detoxification dose can be redoubled, with 20 times as a course of treatment. It is recommended to maintain the application of small doses for patients with poor liver and kidney functions.

6.10.1.6 MEDICAL OZONE THERAPY

After entering the body, medical ozone, on the one hand, directly increases the amount of oxygen supply to normal tissue cells and improves the normal metabolism of cells and, on the other hand, directly kills early cancer cells in the blood or lymph that may promote metastasis or micrometastasis and induce the release of TNFs, as well as IL-immune factors to activate the immune system. The application of medical ozone at the same time can also reduce the side effects of chemotherapy and can promote the reduction of inflammation, as well as healing of surgical wounds. For patients in good physical condition, EBOO can be applied once every other day, with 20 times as a course of treatment. Patients in weak physical conditions can select medical ozone autohemotherapy and venous medical ozone water once every other day, with 12 times as a course of treatment. For medium-advanced gastric cancer patients, it is recommended that it is best to start the first application with intravenous medical ozone saline followed by transition to EBOO after one or two applications, with 20 times as a course of treatment, in conjunction with medical ozone injection. Select Shangwan, Zhongwan, Zusanli, and other points, and inject 2–5 mL of medical ozone gas at each point. For patients with active bleeding, or with weaker constitutions, only intravenous medical ozone can be applied, once every other day or once every 3 days. Be sure that if simultaneously applying chelation detoxification, the interval should be more than 24 hours.

6.10.1.7 TRADITIONAL CHINESE MEDICINE

The syndrome of liver–stomach disharmony and syndrome of deficiency of stomach heat and yin deficiency are often seen in the early stage. The prescriptions recommended are, respectively, Chaihu Shugan Powder and Maimendong Decoction plus modified Zhuyeshigao Decoction. The syndrome of yang deficiency of spleen and stomach, syndrome of phlegm and blood stasis, and syndrome of deficiency of both qi and blood are

often seen in medium-advanced gastric cancer. The prescriptions recommended are, respectively, Huangqi Jianzhong Decoction plus Lizhong Decoction, Gexiazhuyu Decoction plus Erchen Decoction, and modified Shiquan Dabu Decoction.

6.10.1.8 ACUPUNCTURE

Early gastric cancer is mainly exhibited as a syndrome of liver–stomach disharmony, and the therapeutic principle should focus on soothing the liver and regulating the circulation of qi, as well as regulating the stomach and calming the adverse rising energy.

Acupuncture on acupoints: Zhongwan, Neiguan, Zusanli, Sanyinjiao, Yanglingquan, and Taichong.

Methods: Even reinforcing–reducing method is used for acupuncture with needle retention of 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The syndrome of phlegm and blood stasis and the syndrome of deficiency of both qi and blood are mainly seen in medium-advanced gastric cancer; we should focus on resolving phlegm and removing blood stasis, softening and resolving hard mass, invigorating the spleen and replenishing qi, as well as nourishing yin and blood.

Acupuncture on acupoints: The main points are Zhongwan, Feishu, Zhangmen, Pishu, Sanyinjiao, Zusanli, and Qihai. If the syndrome of deficiency of stomach yin is seen, Yinxi, Diji, and Taixi can be added.

Methods: Reinforcing method is used for acupuncture. Retain the needle for 20 minutes once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Guanyuan, Shenque, Zusanli, Zhongwan, Dazhui, Pishu, and Shenshu.

Methods: Take two to three points each time. Conduct moxibustion with the moxa stick with 10 minutes for each point, once a day, with 10 times as a course of treatment.

Auricular acupoints: Stomach, spleen, liver, subcortex, Jiaogan, Shenmen, cerebral point, duodenum, endocrine, adrenal gland, and tumor-specific area.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.10.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Medicated diet is mainly for the early stage. If patients belong to the syndrome of qi deficiency and deficiency of spleen and stomach, Radix Astragali, *Atractylodes macrocephala* Koidz, ginger, Pericarpium Citri Reticulatae, hawthorn, and other products for strengthening the spleen and replenishing qi are given as herbal gruels, soups, or other dishes along with rice for conditioning. Total parenteral nutrition therapy is given before thermochemotherapy for inadequate nutritional intake caused by loss of appetite. Nutritional support treatment is dominant in medium-advanced gastric cancer. For patients who are able to eat, medicated conditioning is given and appropriate amino acids are added (oral administration or intravenous application). For patients who are unable to eat, total parenteral nutrition should be given.

6.10.1.10 OTHERS

Patients should actively practice qigong, tai chi, and meditation. Regulate emotions by TCM, and guide patients to achieve peace of mind and overcome panic and desperation. Use a positive, optimistic, and open-minded approach to treat diseases. At the same time, combine music therapy and sound-wave therapy to alleviate the psychological pressures of patients.

6.10.2 Combination of hyperthermia with conventional treatments

6.10.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

The main treatment methods of Western medicine for gastric cancer are surgery and chemotherapy. Because gastric cancer is insensitive to radiotherapy, it is rarely used. For early gastric epithelial carcinoma foci without invasion into lamina propria mucosae, endoscopic mucosal layer removal may be considered. For

early-medium gastric cancer patients with localized lesions, generally good conditions, and clear indications for surgery, radical surgery is mainly conducted. Local hyperthermia can be carried out before and after surgery to prevent proliferation and metastasis of cancer. For patients with T_2 and above, preoperative adjuvant chemoradiotherapy, postoperative chemoradiotherapy, molecular targeted therapy combined with chelation detoxification, medical ozone, TCM, acupuncture, and other nontoxic integrative treatments can be applied. Generally, after the postoperative wound is completely healed, local hyperthermia or whole-body hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician. For patients with peritoneum and abdominal viscera lymph node metastasis, intraperitoneal hyperthermic perfusion chemotherapy, as well as insulin-mediated thermochemotherapy, can also be applied.

Whole-body hyperthermia can improve immunity; promote cancer cell apoptosis; and regulate the body for production of TNF, IL-2, and other immune factors involved for anticancer effects.

If patients are assessed to be in good general condition and are able to withstand whole-body hyperthermia, it is recommended to carry out whole-body hyperthermia twice a week, with six times as a course of treatment. Pay attention to the monitoring of body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give timely fluid infusion to maintain water–electrolyte balance and other symptomatic treatments. Review electrolytes and so on 1–3 days after whole-body hyperthermia. Continue to supplement energy to maintain water–electrolyte balance. Local hyperthermia can be appropriately added at the intervals of whole-body hyperthermia according to the general condition and tolerance of patients.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the liver area or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. Conduct the second course after an interval of 10 days. After three courses, local hyperthermia can be taken as long-term concomitant therapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.10.2.2 HYPERTHERMIA AND CHEMOTHERAPY

Western medicine treatment of gastric cancer focuses on surgery, chemotherapy, and targeted therapy. Because gastric cancer is relatively insensitive to chemotherapy, no fixed chemotherapy is applied, mainly referring to colorectal cancer chemotherapy. Early gastric cancer patients without any metastasis (stage I) need no chemotherapy but surgery combined with hyperthermia, chelation detoxification, medical ozone, TCM, acupuncture, and other nontoxic integrative treatments. Preoperative chemotherapy can be applied for medium (stages II and III) gastric cancer to reduce stage and localize the lesion to facilitate complete surgical resection and postoperative conventional chemotherapy. A variety of effective adjuvant treatments, including biological treatment, chemoradiotherapy combined with hyperthermia, and nontoxic integrative treatments, are applied before surgery for advanced gastric cancer, followed by radical or cytoreductive surgery according to circumstances. Conduct postoperative thermochemotherapy; intravenous or intraperitoneal hyperthermic perfusion chemotherapy can be applied. For patients who cannot tolerate surgery, palliative surgery and postoperative recurrence can be considered applying the integrative treatment program of intraperitoneal hyperthermic perfusion chemotherapy and combined nontoxic treatments.

The common program of systemic chemotherapy for gastric cancer is oxaliplatin plus fluorouracil/S-1/Xeloda. When chemotherapy is applied with whole-body hyperthermia, whole-body hyperthermia is simultaneously carried out with chemotherapy cycles and a total of six to eight courses are needed. Whole-body medium-high hyperthermia can be carried out simultaneously during the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner.

Whole-body hyperthermia needs to be suspended if rare vomiting is severe. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

For patients who cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the right upper abdomen or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day and continue at the intervals of chemotherapy. Take 1 week off after each cycle (5 consecutive days) of chemotherapy. A total number of about 60–80 times of combined local hyperthermia is carried out during chemotherapy. Local hyperthermia can be taken as long-term maintenance therapy after the end of chemotherapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

Insulin-mediated small-dose intravenous chemotherapy combined with medical ozone and hyperthermia in clinical practice has good effects. Specific methods: rule out contraindications of chemotherapy through comprehensive assessment, and obtain the informed consent of patients. An empty stomach is required before chemotherapy. Carry out medical ozone major autohemotherapy before chemotherapy, and then give insulin to control blood glucose at about 3.6 mmol/L (it is better to control blood glucose when the hypoglycemia reaction has just appeared, and according to individual circumstances). Then, intravenous chemotherapy with a small dose of oxaliplatin plus fluorouracil (10%–30% of conventional amount) is given. Implement conventional nausea and vomiting control and stomach protection, and supplement with glucose and trace elements. Conduct chemotherapy within 2–4 hours after hyperthermia. It is recommended to apply whole-body medium-high temperature hyperthermia for patients in generally good condition with the ability to tolerate whole-body medium-high hyperthermia.

Intraperitoneal hyperthermic perfusion chemotherapy is suitable for the following gastric cancer patients: (1) tumor has not yet invaded the serosa, but the patient has received radical resection of advanced gastric cancer with free intraperitoneal cancer positive; (2) invasion into serosa or accompanied with peritoneal micrometastasis; (3) postoperative gastric cancer recurrence or after resurgery; and (4) gastric cancer peritoneal metastasis accompanied with ascites, excluding patients with severe cardiovascular system and respiratory disorders and significant liver and kidney dysfunctions. Common chemotherapy agents for intraperitoneal hyperthermic perfusion chemotherapy are cisplatin plus fluorouracil, cisplatin plus mitomycin, oxaliplatin plus fluorouracil, paclitaxel, and so on. Refer to Chapter 5, Section 5.3.1 for specific procedures.

6.10.2.3 HYPERTHERMIA AND TARGETED THERAPY

Currently, the types and effects of gastric cancer therapeutic drugs are limited; only about 20%–30% of patients are candidates for these targeted drugs. Combination applications with chemotherapy drugs can increase the 5-year survival rate by about 5%–10% and can be used in integrative cancer treatments with hyperthermia.

6.10.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given from the end of operation to the period of chemotherapy to the patient with postoperative physical weakness and low immunity. On the one hand, it promotes physical recovery and regulates the immune system and, on the other hand, it can kill residual cancer cells or inhibit early metastasis. Chelation detoxification needs infusion of more than 2 hours. Local hyperthermia or whole-body hyperthermia can be simultaneously applied with chelation detoxification to improve efficacy.

6.10.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance effect on immunity, and increase the efficacy of medical ozone. Treatment methods: use EBOO once every other day, with 20 times as a course of treatment, or select medical ozone saline infusion once every other day, with 10–14 days as a course or treatment for a total of three courses. Use medical ozone major

autohemotherapy once every other day, 12 times per course. Use medical ozone minor autohemotherapy once every other day, 12 times per course. Use medical ozone acupoint injection once every other day, with 12 times as a course of treatment. Conduct at least three courses of the respective treatment for long-term maintenance therapy as applicable.

6.10.2.6 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. Others such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, Qingchang therapy, and so on in combination with hyperthermia can increase the effectiveness and safety of the treatment.

6.10.2.6.1 DC-CIK cell therapy

For early gastric cancer, after radical operation DC-CIK reinfusion can effectively remove residual small lesions and reduce recurrence. The number of CIK cells for each reinfusion should reach at least 1×10^{10}. Conduct once per month, with four times as a course of treatment. Conduct periodic review after transfusion, and if there is no recurrence an additional treatment is carried out once every 6 months. Collecting cancer tissue during the operation for the preparation of individual peptides and DC vaccines, which are cultured together with CIK, can obtain better efficacy. For patients who need postoperative adjuvant chemotherapy, DC-CIK treatment can also be combined and the efficacy is superior to chemotherapy alone. Treatment program: one day before chemotherapy, collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct a consolidation therapy every 2 to 3 months.

6.10.2.6.2 Systemic biofeedback therapy

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Adjust to once or twice a week after two to three courses for long-term treatment.

6.10.2.6.3 Alkalization treatment

Dietotherapy or sodium bicarbonate therapy can be applied to alkalize the body.

Oral sodium bicarbonate therapy: For adults, take 100 mg/kg/day. Powder can be added in 500-mL drinking water or fruit juice and drunk slowly, once per day. The tablet can be divided into three doses for direct oral administration. Drink more water, with 8 days as a course of treatment. Simultaneously apply with chemoradiotherapy. Patients with cancer can take sodium bicarbonate 2 to 3 g/day for long-term oral administration, which can significantly reduce chemotherapy side effects, enhance the efficacy and immune function, and reduce chances of infection.

When taking sodium bicarbonate by oral administration, measure urine or saliva pH value once every morning (slip method) and ensure that the saliva pH value is above 7.4 and the urine pH value is above 7.0. After the end of treatment, measure arteriovenous pH value and compare it with the value before treatment; pH should be more than 7.35, as required.

Because prognoses of most early gastric cancers are favorable, give appropriate psychological counseling to patients to reduce their psychological fear of cancer and recommend patients to practice qigong and to adhere to appropriate exercise as well as to receive long-term medicated conditioning.

6.10.2.6.4 Colon cleansing therapy

Colon cleansing therapy: Patients who have no feeding difficulty can take fruit and vegetable drinks with the coffee enema. Patients with feeding difficulty can take the enema by itself, but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support.

6.10.2.7 ADVANCED GASTRIC CANCER

The majority of patients in the advanced stage are unresectable. Patients suitable for intraperitoneal hyperthermic perfusion chemotherapy should combine hyperthermic peritoneal perfusion chemotherapy with some optimal supportive treatments. Optimal supportive treatments include nutrition; relieving pain and other symptoms; and local hyperthermia, chelation detoxification, medical ozone, TCM syndrome differentiation, and other nontoxic integrative treatments. Patients who are in good general condition with KPSs above 70 points and who can tolerate whole-body hyperthermia can be given this treatment once every 10–15 days, with six sessions as one course of treatment. Patients in poor general condition are given local hyperthermia once every other day for long-term maintenance. Local hyperthermia is applied by radio-frequency hyperthermia. Combining chelation and detoxification therapy during the hyperthermia treatment process has a synergistic effect. The chelation and detoxification therapy is implemented as one session of infusion for more than 2 hours, with 20 sessions as one course of treatment for a total of three courses. Single chelation and detoxification can be carried out during the intervals of hyperthermia. The cycle of hyperthermia for advanced gastric cancer should be longer than the cycle for early gastric cancer. In addition to hyperthermia, chelation detoxification, medical ozone, acupuncture, and TCM can be combined. We emphasize dietotherapy plus qigong plus sports as supplementary treatments to improve overall immunity, and we encourage patients to continue to live their lives in spite of the disease.

6.10.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.10.2.8.1 Medicated ironing (hot medicinal compress)

Proven prescription 1: Powder for drawing out poison and resolving mass: *Euphorbia helioscopia* 60 g, *toad cortex* 50 g, *Eupolyphaga* 20 g, *Rhizoma curcumae* 20 g, *Rhizoma sparganii* 20 g, *gecko* 20 g, *Angelica sinensis* 20 g, *Carthamus tinctorius L.* 10 g, *Ligusticum chuanxiong Hort* 20 g, *Rhizoma corydalis* 20 g, *Olibanum* 20 g, *Myrrha* 20 g, *crude Sichuan aconite root* 20 g, *Radix aconiti Kusnezoffii* 20 g, *Radix angelicae Pubescentis* 20 g, *Radix aucklandiae* 20 g, *Ephedra* 20 g, *Euphorbia pekinensis* 20 g, ferrous sulfate 20 g, and *Euphorbia kansui* 10 g. After drug processing, grind the mixture into finer powder and mix well. Load with bags and steam for 30 minutes. Sprinkle 50–100 mL of wine after steaming. Wrap with a dry towel, and apply hot compress on lesion area. When temperature is appropriate, remove the towel and maintain a certain temperature and humidity. Apply hot compress two to three times a day, 30 minutes each time. Every package of medicine can be reused for 5 days. Efficacy: warms yang, promotes blood circulation, eliminates heat, purges fire, clears away toxic substances, and resolves mass. It is applicable to gastric cancer patients with syndromes of cold as well as qi stagnancy and blood stasis in the stomach.

Proven prescription 2: Xiaoji Zhitong Plaster: the same amount for *ferula*, *Paris polyphylla Sm.*, *Rhizoma kaempferiae*, *clove*, *camphor*, and *Realgar*. Grind drugs into fine powder. Mix well and seal it for use. Scissor adhesive plaster according to the range of the pain. Paste proper amount of medicinal powder on the shin above the gastric cavity, and then use a hot towel of about 60°C to apply on the plaster for 30 minutes, three times a day. Change the dressing every 5–7 days. Efficacy: promotes the circulation of qi, removes qi stagnation, and stops pain. It is applicable to gastric cancer patients with the syndrome of pain.

6.10.2.8.2 Bath

Proven prescription 1: Stems and leaves of *Panax ginseng* 30 g, *Atractylodes macrocephala Koidz* 30 g, *Radix saposhnikoviae* 20 g, yam 20 g, and *Glycyrrhiza uralensis* 6 g. Add drugs to proper amount of water. Boil twice and for 30 minutes each time. Combine the filtrate and immerse feet for 30 minutes once a day, with 15 days as a course of treatment. Efficacy: invigorates spleen and replenishes qi. It is applicable to cancer patients with long-term weakness and lack of resistance.

Proven prescription 2: Rhodiola 800 g, *Semen coicis* 500 g, *Acanthopanax senticosus* 400 g, *Radix astragali* 300 g, *Cyrtomium fortunei* 300 g, *Schisandra chinensis* 300 g, *Angelica sinensis* 200 g, and *Ligusticum chuanxiong Hort* 200 g. Boil twice, 50 minutes each time. Combine the filtrate and immerse feet for 40 minutes once a day, with 15 days as a course of treatment. Efficacy: supplements qi, nourishes yin, invigorates qi, and promotes blood circulation. It is applicable to cancer patients with long-term weakness and lack of resistance.

6.10.2.8.3 Grilling method

Aweihuapi Plaster: Decoct *ferula*, *Rhizoma sparganii*, *Rhizoma curcumae*, *rhubarb*, *crude Sichuan aconite root*, *Olibanum*, *Momordica cochinchinensis*, *dung beetle*, *Rhizoma cyperi*, *aloe vera*, *Resina draconis*, and *camphor* into a paste. Heat to soften it for external application, paste it in the umbilical region or the affected area, and then irradiate for 30 minutes with Magic Lamp, once a day. Efficacy: regulates the flow of qi and promotes blood circulation, softens and resolves hard mass, relieves chest and abdominal distention, and disintegrates abdominal mass. It is applicable to patients who have chest and abdominal distention and abdominal mass with the symptoms of qi stagnancy and blood stasis in liver, gallbladder, stomach, and intestines and with gynecological diseases.

6.10.3 Introduction of a typical case

A patient Dai, female, 56 years old, was admitted on December 29, 2006, to Clifford Hospital due to "epigastric pain with melena for 1 year and aggravation for 1 week." On December 2005, the patient exhibited epigastric pain and distending pain without obvious incentives, which were obvious after eating and at night; no radiating pain, accompanied with acid regurgitation, belching, heartburn, no fever, no nausea, no vomiting, no diarrhea, and no recurrent melena. After taking herbal medicines by herself (details were unknown), she had no significant improvement. The aforementioned symptoms got worse 1 week before admission to the Outpatient Department of Clifford Hospital. Gastroscopic and abdominal CT examinations revealed "gastric cancer with multiple metastases at the right lobe of liver, pancreas, retroperitoneal lymph node as well as vein tumor thrombi at the main portal vein, the left and right branch of splenic vein and the mesentery." The pathology showed "average differentiated adenocarcinoma of stomach." The patient was transferred to the Oncology Department of Clifford Hospital for treatment because she was inoperable. The patient was in a generally good mental state with poor appetite and sleep, normal urine, tar-like loose stools, and more than 10 kg of weight loss in the past 8 months.

Physical examination: Thin, weight of 37 kg, moderate anemia, mucosal pallor and pale whole-body skin, abdominal fullness under xiphoid, a palpable mass sized about 5 cm × 6 cm × 7 cm and hard with obscure boundary, poor mobility, obvious tenderness, and no significant rebound tenderness. There was succussion splash in the gastric cavity as well as active bowel sounds. The KPS was 30.

Auxiliary examination: Abdominal CT showed soft tissue masses at the gastric body and the gastric antrum, which were considered to be gastric cancer with multiple metastases at the right lobe of liver, pancreas, and retroperitoneal lymph nodes; vein tumor thrombi at the main portal vein, left and right branches of splenic vein, and mesentery; cavernous transformation of the liver portal vein; and a small amount of effusion at the rectouterine fossa (as shown in Figures 6.8 and 6.9). Pathology showed average differentiated adenocarcinoma of the stomach. Five tumor markers were as follows: CEA 1183.6 ng/mL, AFP 143.22 ng/mL, and CA199 194.32 U/mL. Blood routine: WBC 19.03 × 10^9/L, NEUT 73.6%, RBC 3.19 × 10^{12}/L, HGB 76 g/L, and HCT 0.246. Biochemistry: ALT 69 U/L, AST 78 U/L, TP 65 g/L, ALB 31.3 g/L, ALP 157 U/L, GGT 231 U/L, TBIL 21.5 μmol/L, DBIt 6.5 μmol/L, Cr 24 μmol/L, Ua 144 μmol/L, BUN 3.7 mmol/L, GLU 5.21 mmol/L, TG 1.11 mmol/L, GHO 3.42 mmol/L, K^+ 4.1 mmol/L, Na^+ 137 mmol/L, Cl^- 97 mmol/L, and Ca^{2+} 1.78 mmol/L. The five immunological items and trace elements were normal.

Diagnosis: Gastric cancer (average differentiated adenocarcinoma, stage IV) accompanied with multiple metastases at the right lobe of liver, pancreas, retroperitoneal lymph node, as well as vein tumor thrombi at the main portal vein, left and right branches of splenic vein, and mesentery.

Integrative treatment prescription: The patient had obvious weight loss, moderate anemia, and poor physical condition when she was admitted. Blood transfusion was applied for active correction of anemia, total parenteral nutrition (TPN) was given to strengthen nutrition, and acid making and gastric mucosa protection was applied to prevent continued bleeding, and herbal medicines such as Huangqi Jianzhong Decoction plus modified Lizhong Decoction were applied: *Radix astragali* 20 g, dried ginger 10 g, *Poria cocos* 12 g, *Radix paeoniae Alba* 12 g, *Atractylodes macrocephala Koidz* 12 g, *Pinellia ternata* 12 g, *Pericarpium citri Reticulatae* 10 g, *Evodia rutaecarpa* 6 g, orange peel 6 g, *Semen coicis* 30 g, *Glycyrrhiza uralensis* 6 g, *Panax notoginseng* 12 g, *Rhizoma imperatae* 12 g, stir-baked malt 12 g, and *Semen cuscutae* 10 g, one dose per day.

It is decocted with water for oral administration. Blood routine was reexamined after 4 days of treatment and showed HGB 93 g/L and WBC 8.25 × 10^9/L. She was without significant abdominal pain, gastrointestinal bleeding stoppage, and yellow rotten stool. At that time, whole-body medium-high temperature hyperthermia was applied and simultaneously intraperitoneal drug hyperthermic perfusion was conducted. The drug for perfusion was cisplatin plus 5-fluorouracil. Granisetron was given before and after treatment to stop vomiting. Chelation detoxification was given after hyperthermia to reduce the side effects of chemotherapy and increase the sensitivity to chemotherapy. Because whole-body hyperthermia easily leads to the loss of large amounts of liquid, herbal medicines were adjusted before and after hyperthermia, focusing on strengthening the spleen, nourishing yin, and supplementing blood.

Medications: The prescriptions recommended were Guipi Decoction and modified Danggui Buxue Decoction: Poria Cocos 25 g, Pericarpium Citri Reticulatae 15 g, *Angelica sinensis* 10 g, *Glycyrrhiza uralensis* 10 g, baked *Glycyrrhiza uralensis* 10 g, *Radix paeoniae Alba* 15 g, *Radix* 10 g, *Codonopsis pilosula* 25 g, *Salvia miltiorrhiza* 10 g, *Atractylodes macrocephala* Koidz 12 g, *Radix rehmanniae* 25 g, Chinese yam 25 g, *Radix bupleuri* 10 g, and *Scutellaria baicalensis Georgi* 10 g. Made water pills to orally take 10 g, three times a day. The patient had mild nausea and no leukopenia, diarrhea, or abdominal pain after hyperthermia.

Acupuncture on acupoints: Zhongwan, Neiguan, Weishu, Zhangmen, Pishu, Sanyinjiao, Zusanli, Guanyuan, Taixi, and Waisanguan. Methods: reinforcing method was applied. The needle was retained for 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Took Guanyuan, Shenque, Zusanli, Zhongwan, Dazhui, Pishu, and Shenshu. Methods: took two to three points each time. Conducted moxibustion with a moxa stick lasting 10 minutes for each point, once per day or once every other day.

Auricular acupoints: Stomach, Pishu, liver, subcortex, Jiaogan, Shenmen, Naodian, duodenum, endocrine, adrenal gland, and tumor-specific area. Methods: stuck auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

Herbal medicines and acupuncture were applied during the whole process of the treatment. The aforementioned treatment program was applied for 5 weeks. At the intervals, whole-body hyperthermia and peritoneal perfusion were conducted three times each in combination with a variety of treatments such as nutrition, chelation detoxification, medical ozone, acupuncture, and TCM. The patient's condition was improved markedly, hemoglobin was stabilized at about 95 g/L, weight was increased by 0.6 kg/week, black stools did not appear, and appetite returned to normal. At that time, adjusted peritoneal perfusion drugs and cisplatin plus mitomycin were given. The patient showed leukopenia with WBC reduced to 1.2 × 10^9/L after adjusting treatment. GM-CSF was applied as well as herbal medicines: *Sunburn radix Astragali* 30 g, *Angelica sinensis* 15 g, *Eucommia ulmoides* 15 g, *Cornu cervi Degelatinatum* 15 g, *Semen persicae* 10 g, safflower 10 g, *Fried atractylodes macrocephala Koidz* 15 g, *Fructus corni* 15 g, Donkey-hide Glue (molten) 15 g, *Carapax trionycis* (Predecoct) 15 g, *Carapax trionycis* (Predecoct) 15 g, *Salvia miltiorrhiza* 10 g, with three slides of ginger, five pieces of jujube as the guide, one dose a day. Decocted with water for oral administration. The original program for chelation detoxification, and medical ozone was maintained. Conducted acupuncture and simultaneously Astragalus injection was given at the acupoint of Zusanli. Leukopenia was stabilized and WBCs were normal after 3 days. Conducted this program for more than a month. Conduct whole-body hyperthermia once every 10 days, and combined with medical qigong therapy in the course of treatment.

Treatment effects: The patient was hospitalized for 81 days. After integrative treatments, the patient showed significantly improved mental state, acceptable appetite and sleep, and normal urine and stool. There were no nausea and vomiting and no abdominal pain. Weight had increased by 12 kg and was maintained at 56 kg. TCM treatments were continued, and others were stopped. The whole abdominal enhanced CT prompted after treatment showed that the sizes of primary lesions and hepatic lymph node metastasis range were significantly narrowed. Vein tumor thrombi at the portal system, splenic vein, and mesentery were significantly reduced (as shown Figures 6.10 and 6.11). Five tumor markers after treatment: CEA 329.8 ng/mL, AFP 7.09 ng/mL, CA 12-5(OV) 34.99 U/mL, CA199 35.94 U/mL, and CA 153(BR) 56.45 U/mL (all were significantly reduced compared with the values on admission). Blood routine showed the following results: WBC 3.70 × 10^9/L, NEUT 58.9%, RBC 1.61 × 10^{12}/L, HGB 89 g/L, and HCT 0.26. Hemogram returned to normal, and anemia improved. The KPS was 90 (Figures 6.8 through 6.11).

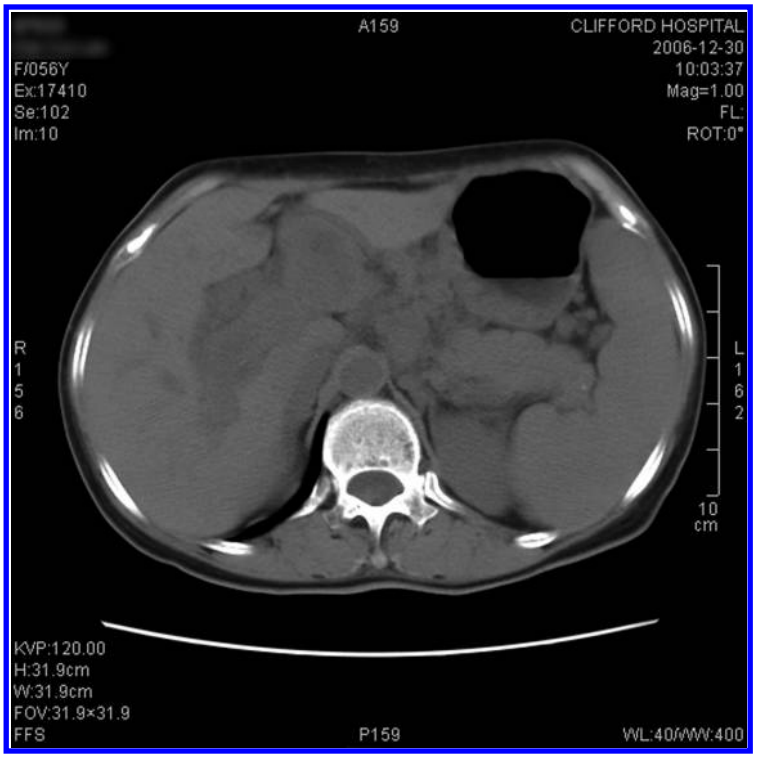

Figure 6.8 Before treatments: abdominal CT Scan (1).

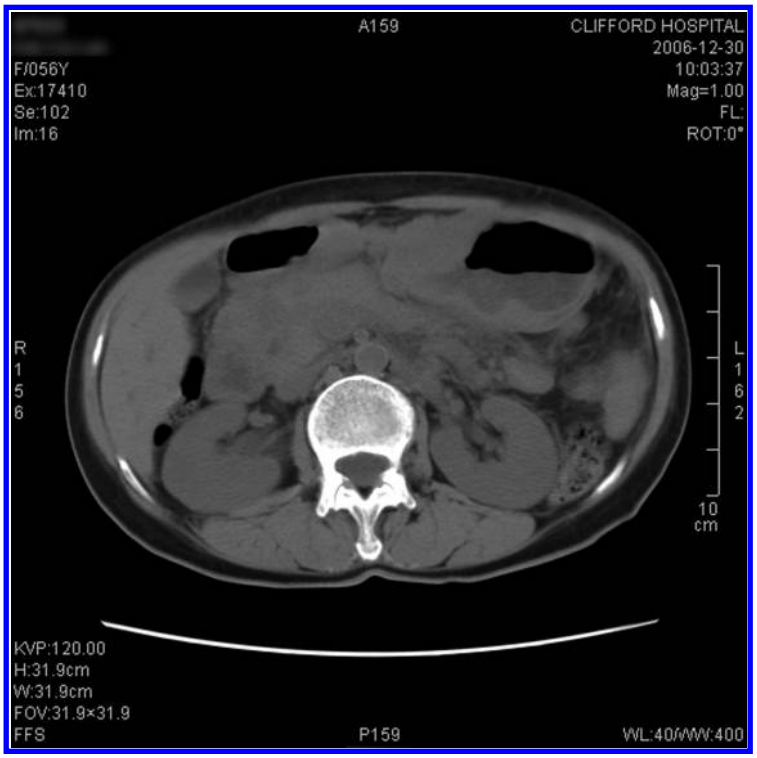

Figure 6.9 Before treatments: abdominal CT Scan (2).

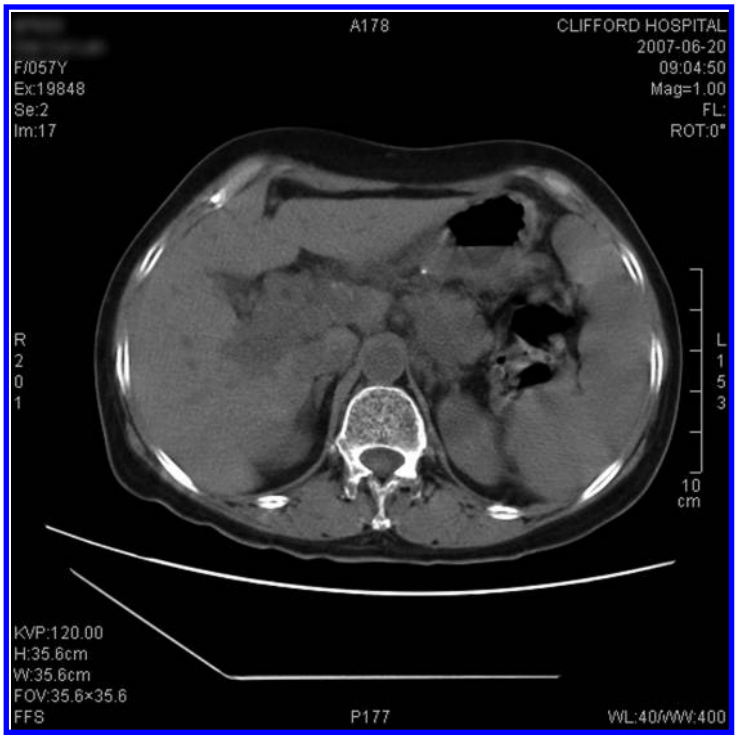

Figure 6.10 After treatments: abdominal CT Scan (1).

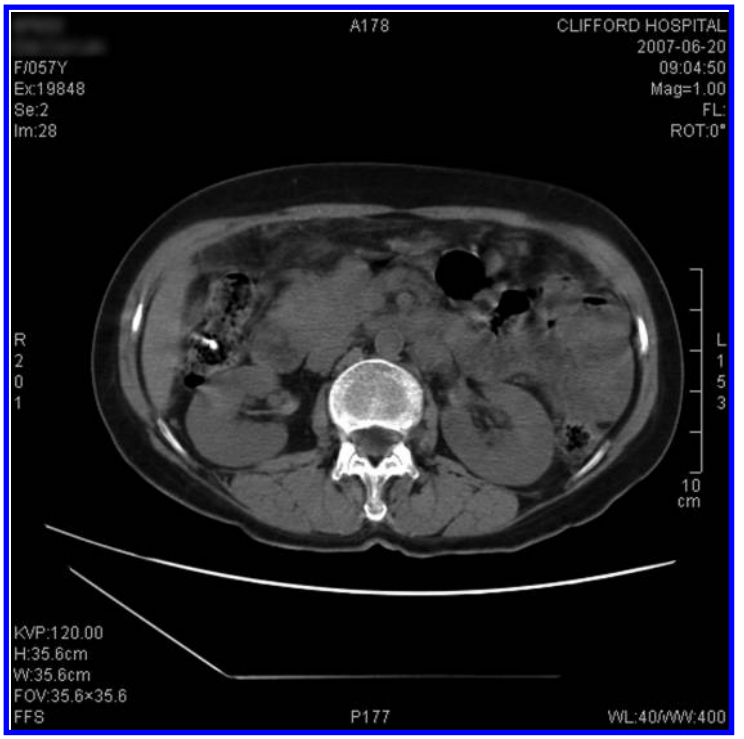

Figure 6.11 After treatments: abdominal CT Scan (2).

6.10.4 Related research in China and abroad

Li Caiyun et al. have investigated the inhibition effect of combined hyperthermia on human gastric cancer living cells through experimental studies; the results showed that the combined application of 43°C hyperthermia with the conventional chemotherapy drug 5-fluorouracil had better inhibition rates of human gastric cancer living cells than chemotherapy ($P < .01$) and the combined application of 43°C hyperthermia with the conventional chemotherapy drug 5-fluorouracil had stronger toxic effects on human gastric cancer living cells.

Hegewisch-Becker et al. have confirmed through in vitro experiments that hyperthermia enhances chemotherapy efficacy of oxaliplatin by increasing the formation of DNA compounds.

Mohamed et al. have reported that whole-body hyperthermia could increase the anticancer activity of oxaliplatin and increase the concentration of chemotherapeutic drugs in animal tumor tissues by more than three times.

Peng Shun et al. have conducted clinical observations of whole-body chemotherapy in combination with local hyperthermia for the treatment of advanced gastric cancer, with the results showing that among 33 patients, four cases (12.1%) showed CR and 13 cases (39.4%) showed PR with an efficiency (CR+ PR) of 51.5%. The main toxicities were gastrointestinal reactions, bone marrow suppression, and neurosensory toxicity. The efficacy of the FOLFOX4 program of chemotherapy combined with hyperthermia for advanced gastric cancer has been confirmed, and its toxicity can be tolerated.

Clinical studies of Wang Yishan et al. have shown that intensity-modulated conformal radiotherapy combined with hyperthermia and chemotherapy could more effectively control the development of advanced gastric cancer. Under certain conditions, the higher the radiation dose, the better the treatment efficacy. On the premise that the patient's body can tolerate the dose, microwave hyperthermia frequency was positively correlated with the efficacy.

Du Caiju et al. have conducted clinical observations of herbal medicines combined with thermochemotherapy, and the results showed that the disease control rate in the chemotherapy plus hyperthermia group was higher than that in the chemotherapy alone group ($P < .05$); the efficiency (RR) rate and disease control rate of the herbal medicines combined with chemotherapy and hyperthermia group were higher than those of the chemotherapy group and chemotherapy plus hyperthermia group ($P < .01$). KPSs and body mass indexes were higher after the treatment in herbal medicines combined with chemotherapy and hyperthermia group than those in the chemotherapy group and chemotherapy plus hyperthermia group ($P < .05$). The pain score had decreased in the chemotherapy plus hyperthermia group after treatment compared with the same group before treatment ($P < .05$). Scores of nausea, vomiting, pain, loss of appetite, and fatigue in the herbal medicines combined with chemotherapy and food therapy group after treatment were lower than those of the same group before treatment ($P < .05$). Scores of nausea, vomiting, pain, loss of appetite, and fatigue were decreased in the herbal medicines combined with chemotherapy and hyperthermia group after treatment compared with the chemotherapy group and chemotherapy plus hyperthermia group ($P < .01$).

Zhao Changlin et al. have applied whole-body hyperthermia combined with intraperitoneal hyperthermic perfusion chemotherapy in the treatment of advanced gastric cancer. The results of clinical studies showed that whole-body hyperthermia combined with intraperitoneal hyperthermic perfusion chemotherapy was superior to whole-body chemotherapy alone in terms of clinical outcomes, symptom reduction, extension of survival time, and so on ($P < .05$).

6.11 PANCREATIC CARCINOMA

Pancreatic carcinoma, manifesting as occult and rapid onset, is the tumor with the worst prognosis among malignant abdominal tumors. It often occurs among the elderly, and the incidence in developed countries is higher than that in developing countries. With the improvement of living standards in China and changes in diet structure in recent years, the incidence of pancreatic carcinoma has shown an upward trend and the disease now tends to occur at a younger age. The incidence of pancreatic carcinoma has risen from 20th to 12th among cancers.

The histological types of pancreatic carcinoma can be divided into catheter cell carcinoma, acinar cell carcinoma, pancreatic islet cell carcinoma, and other types (such as undifferentiated carcinoma, pancreatoblastoma, carcinosarcoma, etc.). There are two common categories: one is ductal cell carcinoma, accounting for about 90% of pancreatic carcinomas, and the other is pancreatic acinar cell carcinoma, accounting for about 10% of pancreatic carcinomas. Because the pancreas itself has no envelope, it is easy to incur early diffusion. Its modes of metastases are mainly pancreatic diffusion, invasion to peripancreatic tissues, lymphatic metastasis, hematogenous metastasis, and metastasis along the nerve tract.

Jaundice and abdominal pain are the most common among the first symptoms of pancreatic carcinoma, followed by weight loss, upper abdominal fullness, back pain, fatigue, as well as individual heat.

6.11.1 Conventional treatments

6.11.1.1 SURGERY

Based on cancer locations, surgery can be broadly divided into pancreaticoduodenectomy, distal pancreatectomy, and total pancreatectomy. On the whole, pancreatic surgery is a major operation and requires high levels of technology and surgeon experience, as well as integrative treatments before and after surgery. If possible, surgery should be carried out in hospitals with extensive pancreatic surgery experience.

For patients not suitable for radical resection due to tumor or health reasons, appropriate surgical intervention might provide significant effect in prolonging survival and improving quality of life. In this case, the common surgical interventions include gastroenterostomy and choledochojejunostomy. It should be emphasized that with the advancement of medical science the technology of catheter and stent is increasingly widely being used and the performance of open palliative choledochojejunostomy has been significantly reduced for simple biliary obstruction.

6.11.1.2 RADIOTHERAPY

The majority of pancreatic carcinomas are cancers occurring on the pancreatic ductal epithelium, with infiltrative growth, high degree of malignancy, poor prognosis, and higher postoperative recurrence rates. Radiotherapy is suitable for patients with localized lesions but has poor clinical efficacy for patients with metastasis. Because the pancreas is deeply located, the sensitivity of pancreatic carcinoma to radiation is lower; dosage required to kill the cancer cells is high; and radiosensitivity of peripancreatic organs such as liver, kidney, intestines and stomach, spinal cord, and others is higher than the pancreas and hence they are susceptible to radiation damage. As a result, radiotherapy is not regarded as the primary treatment clinically and is mainly applied for inoperable integrative treatments of locally advanced pancreatic carcinoma and integrative treatments of postoperative residual cancer or recurrence, as well as palliative reduction treatment of advanced pancreatic carcinoma. In recent years, with the advancement of radiotherapy it is applied in some cases as neoadjuvant radiotherapy before surgery for improving surgical treatment or increasing the resection rate.

6.11.1.3 CHEMOTHERAPY

Pancreatic carcinoma has poor sensitivity to chemotherapy, so chemotherapy is generally not preferred nor is it applied alone. Chemotherapy is mainly applied as neoadjuvant or adjuvant therapy, or for locally advanced unresectable and metastatic pancreatic carcinoma. There is evidence that pancreatic carcinoma postoperative adjuvant chemotherapy may extend survival. Adjuvant chemotherapy for pancreatic carcinoma should begin about 1 month after radical resection, and its purpose is to prolong survival, improve quality of life, and increase the effects of other treatments. It can also be applied as palliative chemotherapy for patients who did not receive radical treatment. In recent years, there have been more applications of neoadjuvant chemotherapy with the purpose of preoperatively improving surgical outcomes or increasing the resection rates.

For pancreatic carcinoma, the commonly used chemotherapy drugs are gemcitabine or TS-1 (S1) used alone or in combination with 5-fluorouracil, TS-1, oxaliplatin, and so on.

6.11.1.4 HYPERTHERMIA

Due to its insidious onset and poor prognosis, combined therapy in the treatment of pancreatic carcinoma is particularly important. Hyperthermia, as an emerging anticancer therapy, in combination with existing treatments provides a new approach for the treatment of pancreatic carcinoma, achieves clinically positive effects, and plays an important role in the integrative treatments of pancreatic carcinoma. For pancreatic carcinoma that cannot be completely removed by operation, interstitial high frequency electromagnetic wave coagulation therapy can be carried out, which includes interstitial microwave therapy and interstitial RF coagulation treatment. Interstitial microwave therapies for pancreatic carcinoma mainly include microwave coagulation therapy, intraoperative microwave coagulation therapy, and ultrasound-guided microwave coagulation therapy. For patients with advanced pancreatic carcinoma, clinical studies have shown that out-of-body high-intensity focused ultrasound hyperthermia combined with chemotherapy has a positive effect. In addition, in recent years studies have shown that intraperitoneal hyperthermic perfusion chemotherapy combined with external high frequency diathermy for the treatment of advanced, unresectable pancreatic carcinoma also has a satisfactory clinical outcome.

6.11.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can effectively remove toxins from the body and improve immune function and also reduce the side effects of chemotherapy and enhance chemosensitivity. The simultaneous application of chelation detoxification with hyperthermia can have a synergistic effect. The application of chelation detoxification can have inhibitory effects on tumor recurrence and metastasis, can repair the damage in various tissues and organs, and can improve cell functions. The pathogenetic condition of medium-advanced pancreatic carcinoma develops quickly, and if patients can tolerate the therapeutic amounts after receiving two to three applications of chelation detoxification therapy and are also with normal renal function, the chelation detoxification dose can be increased to two times the therapeutic amount for 20 times of consecutive use, once every other day. Administer it twice a week after the patient's condition has become stable and improved. Reduce to once a week after 6 consecutive weeks to maintain satisfactory results.

6.11.1.6 MEDICAL OZONE THERAPY

Treating early pancreatic carcinoma patients with medical ozone therapy can improve the immune system and inhibit cancer development. Medical ozone therapy can incorporate major autohemotherapy, vein medical ozone saline, EBOO, medical ozone acupoint injection, and so on. Different methods are applicable to patients with different physical conditions, but the principles behind the therapeutic effects are the same. Usage: once every other day, with 20 times as a course of treatment; alternate it with chelation detoxification and hyperthermia and avoid using it on the same day. For medium-advanced pancreatic carcinomas, the amount of medical ozone therapy should be determined after the assessment of patients' physical conditions. Intravenous medical ozone saline can be given first and then EBOO is given after one or two times of venous medical ozone saline, once every other day for 20 consecutive times. For patients in weak physical condition, intravenous ozone saline or major autohemotherapy can be applied once every other day, with 12 times as a course of treatment. The aforementioned treatments must be alternated with chelation detoxification. At the same time, medical ozone acupoint injection is given once every other day. Selection of points is the same as that in acupuncture.

6.11.1.7 TRADITIONAL CHINESE MEDICINE

The syndrome of qi stagnation and blood stasis can be seen in the early stages of pancreatic carcinoma, and the prescriptions recommended are Xuefu Zhuyu Decoction and modified Yueju Pill. For the syndrome of deficiency of stomach yin, the prescriptions recommended are Yiguan Decoction and modified Biejiajian Pill. The syndrome of splenic asthenia and accumulation of dampness is more common in advanced pancreatic carcinoma, and the prescription recommended is modified Xiangsha Liujunzi Decoction. For the syndrome of excessive dampness, heat, and toxin, the prescription recommended is modified Yinchenhao Decoction. For the syndrome of qi and dampness stagnation, the prescriptions recommended are Erchen Decoction and modified Pingwei Powder. For the syndrome of yin deficiency and toxic stasis, the prescriptions recommended are Yiguan Decoction and Biejiajian Pill.

6.11.1.8 ACUPUNCTURE

Early pancreatic carcinoma mainly manifests the syndromes of qi stagnation and blood stasis as well as spleen–stomach dampness heat. We should focus on clearing heat and eliminating dampness, as well as regulating qi to dissipate blood stasis.

Acupuncture on acupoints: Zusanli, Xiajuxu, Shangjuxu, Yanglingquan, and Diji. When Fu qi is obstructed in patients, add Tianshu, Qihai, and Zhongwan. If the syndrome of adverse rising of stomach qi is seen in patients, add Neiguan, Hegu, and Taichong for regulating qi and stopping pain as well as reducing adverse flow of qi and preventing vomiting.

Methods: Even reinforcing–reducing technique is used. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The syndrome of medium-advanced pancreatic carcinoma is mainly spleen and kidney deficiency, and the therapeutic principle should focus on invigorating the spleen and nourishing kidneys.

Acupuncture on acupoints: Zusanli, Sanyinjiao, Zhongwan, Tianshu, Pishu, Shenshu, and Guanyuan.

Methods: Even reinforcing–reducing technique is used. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Guanyuan, Zusanli, Ganshu, Shenshu, and Pishu.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Liver, Pishu, diaphragm, pancreaticobiliary point, Erjian, endocrine, adrenal gland, subcortex, Jiaogan, and Shenmen.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.11.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Medicated diet is mainly for the treatment of early pancreatic carcinoma; it focuses on increasing appetite and supplementing nutrition. Digestive enzymes and megestrol acetate can be given to aid digestion and improve appetite. Medium-advanced patients who can eat can receive oral administration, which can be appropriately supplemented with amino acids, and so on. If there is obstruction, total parenteral nutrition can be given. If the condition permits, it is best to utilize a fistula to give nutritional meals. Combine with other therapies to prolong survival time and improve quality of life. At the same time, give qigong, music therapy, as well as mental therapy to relax the patient and to relieve pain.

6.11.1.10 OTHERS

In recent years, sorafenib, erlotinib, cetuximab, bevacizumab, and other targeted therapy drugs have been tentatively applied for pancreatic carcinoma, but the effects are far from satisfactory and we still need further exploration. Qigong, tai chi, music, and mental therapy can adjust the patient's psychology, contributing to the treatment of the disease.

6.11.2 Combination of hyperthermia with conventional treatments

6.11.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

The main treatments of Western medicine for pancreatic carcinoma are surgery and chemotherapy. Radiotherapy is rarely used for pancreatic carcinoma due to the poor sensitivity. For pancreatic carcinoma at phases I and II with localized lesions and for patients in fairly good condition as well as having clear indications for surgery, radical surgery is mainly applied. Local hyperthermia can be carried out two to three weeks before and after surgery to prevent cancer diffusion and metastasis. For patients who are considered inoperable at stages III and IV and above, palliative surgery can be conducted, such as cholangioenterostomy via

biliary decompression and drainage. Postoperative chemotherapy combined with hyperthermia, chelation detoxification, medical ozone, TCM, acupuncture, and other special nontoxic integrative treatments can be carried out. Generally, after the postoperative wound is completely healed local hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests disclosing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician. For patients with peritoneum and abdominal viscera lymph node metastasis, intraperitoneal hyperthermic perfusion chemotherapy can be applied and application of insulin-mediated thermochemotherapy can also be considered.

Whole-body hyperthermia can improve immunity; promote cancer cell apoptosis; and regulate the body for production of TNF, IL-2, and other immune factors involved in anticancer effects.

If patients are assessed to be in generally good condition and are able to withstand whole-body hyperthermia, it is recommended to carry out whole-body hyperthermia twice a week, with six times as a course for a total of three courses. Be sure to monitor body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give timely fluid infusion to maintain water–electrolyte balance and other symptomatic treatments. Review electrolytes and so on 1–3 days after whole-body hyperthermia. Continue to supplement energy to maintain water–electrolyte balance. Local hyperthermia can be appropriately added at the intervals of whole-body hyperthermia according to the general condition and tolerance of patients.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the liver area or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. Conduct the second course after an interval of 10 days. After three courses, local hyperthermia can be taken as long-term concomitant therapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.11.2.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy is mainly used for the integrative treatment of inoperable locally advanced pancreatic carcinoma, postoperative neoplasm residual or recurrent cases, as well as palliative cases and reduction of advanced pancreatic carcinoma. In recent years, there have been more applications of neoadjuvant chemotherapy for preoperatively improving surgical outcomes or increasing the resection rates. Conducting local hyperthermia at the radiation area within 2 hours after radiotherapy can effectively reduce the side effects of radiotherapy, such as skin damage, local soft tissue fibrosis, and so on. Conduct local hyperthermia once every other day. The first course of hyperthermia is maintained until 2 weeks after the end of radiotherapy. Change to whole-body hyperthermia in the rehabilitation period.

6.11.2.3 HYPERTHERMIA AND CHEMOTHERAPY

The purpose of pancreatic carcinoma chemotherapy is to prolong survival time and improve quality of life and increase the effects of other treatments, including postoperative adjuvant chemotherapy and palliative chemotherapy for patients who have not received radical treatment. In recent years and in some large-scale pancreas centers, there have been more applications of neoadjuvant chemotherapy for the purpose of preoperatively improving surgical outcomes or increasing resection rates.

For pancreatic carcinomas, the commonly used chemotherapy drugs are gemcitabine or TS-1 (S1) alone, or in combination with 5-fluorouracil, TS-1, oxaliplatin, and so on.

When advanced pancreatic carcinoma is diagnosed, 40% of cases are inoperable due to local development, 40% have external pancreatic metastasis, and only 20% of cases can receive surgery. As a result, 80% of pancreatic carcinomas are indications for chemoradiotherapy. In the early years, luorouracil chemotherapy alone was applied, with an effective rate of 10%. Combining with mitomycin would not improve the effect of chemotherapy, and combining with cisplatin may slightly improve the efficacy. In recent years, gemcitabine has become the preferred chemotherapy drug for pancreatic carcinoma, with a single-agent effectiveness rate of 13%–18%.

The common regimen for pancreatic carcinoma systemic chemotherapy is to combine gemcitabine, fluorouracil, S-1, and so on with platinum. Clifford Hospital has effectively combined insulin-mediated small doses of intravenous chemotherapy with hyperthermia and medical ozone and achieved clinically good

results. Specific methods: rule out contraindications of chemotherapy through comprehensive assessment, and obtain the informed consent of patients. An empty stomach is required before chemotherapy. Carry out medical ozone major autohemotherapy before chemotherapy, and give insulin to control blood glucose at about 3.6 mmol/L (it is better to control blood glucose when the hypoglycemia reaction has just appeared, and according to individual situations); then give a small dose of oxaliplatin plus fluorouracil (10%–30% of conventional amount) for intravenous chemotherapy. Implement conventional nausea and vomiting control, stomach protection, and high glucose and essential nutrients supplementation. Conduct local hyperthermia 2–4 hours after chemotherapy. For patients who cannot tolerate or who refuse surgery, if they are in good general condition, in addition to whole-body hyperthermia, intraperitoneal hyperthermic perfusion chemotherapy can be considered. It is recommended to apply whole-body medium-high temperature hyperthermia for patients in good general conditions and who are able to tolerate whole-body medium-high hyperthermia.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body medium-high hyperthermia can be carried out simultaneously on the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if vomiting is severe. Simultaneously carry out hyperthermia and chemotherapy cycles for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the right upper abdomen or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, and continue it during the intermission periods of chemotherapy. Take 1 week off after each cycle (5 consecutive days) of chemotherapy. A total number of about 60–80 times of combined local hyperthermia is carried out during chemotherapy. Local hyperthermia can be taken as long-term maintenance therapy after the end of chemotherapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.11.2.4 HYPERTHERMIA AND TARGETED THERAPY

With the study of pancreatic carcinoma–related genes and signaling pathways, targeted therapy has become a new approach for the treatment of pancreatic carcinoma. Targeted drugs reported currently for pancreatic carcinoma are erlotinib, cetuximab, bevacizumab, and so on, but the effects are far from satisfactory and further exploration is still needed. If financial conditions are good, hyperthermia and other nontoxic treatments in combination with targeted therapy can be considered to increase targeted therapy efficiency and reduce the side effects of targeted drugs.

6.11.2.5 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given from the end of operation to the period of chemotherapy to patients with postoperative physical weakness and low immunity. On the one hand, it promotes physical recovery and regulates the immune system and, on the other hand, it can kill residual cancer cells or inhibit early metastasis. Local hyperthermia or whole-body hyperthermia can be simultaneously applied with chelation and detoxification to improve efficacy.

6.11.2.6 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance the effect on immunity, and increase the efficacy of medical ozone. Treatment methods: use EBOO once every other day, with 20 times as a course of treatment. Alternatively, select medical ozone saline infusion once every other day, with 10–14 days as a course of treatment. Use medical ozone major autohemotherapy once every other day, with 12 times per course. Use medical ozone minor autohemotherapy once every other day, with 12 times per course. Use medical ozone acupoint injection once every other day, with 12 times as a course of treatment. Medical ozone treatments should be conducted for at least three courses, and long-term maintenance therapy is applicable.

6.11.2.7 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. Other treatments such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, colon cleansing therapy, and so on in combination with hyperthermia can increase the effectiveness and safety of the treatment.

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Change to once or twice a week after two to three courses of treatment for long-term treatment.

Alkalization therapy: Dietotherapy or sodium bicarbonate therapy can be applied to alkalize the body.

Peritoneal perfusion of sodium bicarbonate is safe and effective. It can be applied together with chemotherapy drugs. About 100 mL of 5% sodium bicarbonate injection heated to 37°C is perfused slowly into the abdominal cavity within 1 hour, to be combined with abdominal massage to achieve uniform distribution of liquid in the abdominal cavity. If the patient complains about abdominal pain, 10 mL of 2% lidocaine can be added inside or the concentration can be reduced to 2.5% with the same dosage. If chemotherapy drugs are also applied, sodium bicarbonate is applied first and 20 minutes later chemotherapy drugs are perfused; this is done once or twice a week, with eight times as a course of treatment. If peritoneal perfusion of sodium bicarbonate is combined with hyperthermia, RF local hyperthermia at the abdomen can be carried out after perfusion.

Retention enema of sodium hydrogen carbonate or rectosigmoid administration: About 100–150 ml of 1.25%–2.5% sodium hydrogen carbonate is applied for retention enema. Retain for 15–20 minutes, or 50 mL of sodium bicarbonate with the same concentration is set to the junction of rectosigmoid with a fine silica tube for slow infusion (10–15 drops/min). Patient should feel good and the purpose of quickly alkalizing liver, intestine, pancreas, and spleen can be achieved.

Colon cleansing therapy: Patients can take fruit and vegetable drinks with the coffee enema, which is conducive to the discharge of toxins and metabolic waste; but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, give parenteral nutritional support.

In addition to hyperthermia, chelation detoxification, medical ozone, acupuncture, and TCM, we emphasize dietotherapy plus qigong plus sports as supplementary treatments to improve overall immunity. Provide encouragement to patients to continue with their lives despite the presence of the disease.

6.11.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.11.2.8.1 Bath

Proven prescription 1: Ramulus cinnamomi 60 g, *Acanthopanax senticosus* 50 g, and *Glycyrrhiza uralensis* 5 g. Add water to the drugs and boil for 30 minutes. Remove slag and take juice. Immerse feet for 30 minutes once a day, with 10 days as a course of treatment. Efficacy: supplements qi to warm yang. It mainly cures a variety of fatigue and is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 2: Radix astragali 450 g, *Radix codonopsis* 300 g, *Radix polygoni Multiflori Preparata* 300 g, *Ligusticum chuanxiong Hort* 300 g, *Fructus alpinia Oxyphylla* 300 g, *Semen cuscutae* 300 g, *Atractylodes macrocephala Koidz* 300 g, and *Carthamus tinctorius L.* 200 g. Put all drugs into the wok and add proper amount of water. Boil for 50 minutes. Remove slag and take juice. Blend with 450 g of white wine. Take bubble bath for 40 minutes once a day, with 10 days as a course of treatment. Efficacy: tones lungs, spleen, and kidneys, as well as strengthening spirit. It is mainly a cure for a variety of types of fatigue and is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 3: Stems and leaves of *Panax ginseng* 30 g, *Atractylodes macrocephala Koidz* 30 g, *Radix saposhnikoviae* 20 g, yam 20 g, and *Glycyrrhiza uralensis* 6 g. Add drugs and the proper amount of water. Boil twice and for 30 minutes each time. Combine filtrate and immerse feet for 30 minutes once a day, with 15 days as a course of treatment. Efficacy: invigorates spleen and replenishes qi. It is applicable to cancer patients with long-term weakness and low immunity.

6.11.2.8.2 Moxibustion therapy

It is applicable to cancer patients with long illness, yang deficiency, and weakness, and it can enhance immunity.

Acupoints: The first group of acupoints includes Dazhui, Shenshu (both), and Pishu (both). The second group of acupoints includes Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both).

Herbal cake making: Take equal amounts of *Radix astragali*, *Angelica sinensis*, *Fructus psoraleae*, *Curculigo orchioides*, and *rhubarb*, and smash them into powder. Filter with 120 mesh sieve, and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm.

Moxibustion: Place the moxa cone with a diameter of 2 cm and a height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints each time, with two groups of points alternated, once every other day, with 24 times as a course of treatment.

Efficacy: Reinforces spleen and nourishes kidneys for muscularity and general health.

6.11.3 Introduction of a typical case

A patient named Lei was admitted on September 4, 2007, to Clifford Hospital due to "postoperative pancreatic carcinoma for 1 year and abdominal pain accompanied with anorexia, and weight loss for more than 2 months." The patient was admitted to Toronto Hospital, Canada, on September 2006; CT examination results showed a 5.7 cm × 3.6 cm × 4 cm mass in the tail of the pancreas. At that time, partial pancreatectomy was carried out in the Canadian hospital and intraoperative multiple lymph nodes in the abdominal cavity were found with gastric wall invasion. No other postoperative treatments were given. The patient was reexamined 6 months before the admission to Clifford Hospital. CT showed that there were neoplasms near the left renal artery as well as multiple liver metastases. On July 2007, the patient exhibited recurrent dull abdominal pain accompanied with anorexia, an obviously thin physique, and a weight loss of 8 kg and then came to Clifford Hospital from Canada for further treatment.

Physical examination: Weight of 48 kg; a visible abdominal surgical scar with local crowning, which was hard with ill-defined boundary and pressing pain. Lung breathing sounds were clear, and wet and dry rales were not heard. The border of cardiac dullness was normal with a heart rate of 60 beats/min and regular rhythm. Pathological murmur was not heard at each valve area of the heart. The KPS was 50.

Auxiliary examination: Blood routine test: RBC 3.1×10^{12}/L, Hb 103 g/L, WBC 4.7×10^{9}/L, and PLT 235×10^{9}/L. Biochemistry: ALT 125 U/L, AST 87 U/L, TBIL 32 U/L, DBIL 15.5 U/L, ALB 16.8 g/L; ALP 312 U/L, GGT 127 U/L, Cr 8 μmol/L, Ua 313 μmol/L, BUN 3.6 mmol/L, GLU 6.62 mmol/L, TG 0.17 mmol/L, GHO 1.65 mmol/L, K^+ 3.64 mmol/L, Na^+ 139 mmol/L, Cl^- 99 mmol/L, and Ca^{2+} 2.21 mmol/L. Five items of immune function were normal, and of the minerals copper, zinc, lead, mercury, cadmium, nickel, and so on were normal. Serum ammonia: 21 μmol/L. The five tumor markers were as follows: CEA 127.6 ng/mL, AFP 9.09 ng/mL, CA 12-5(OV) 13.72 U/mL, CA-199 47.14 U/mL, and PSA 3.1 U/mL. Abdominal CT: A 3 cm × 2 cm mass could be seen at the tail of the pancreas with lymphadenectases at the abdominal wall, liver, abdomen, and retroperitoneum. Results of ECG and chest X-ray showed no abnormality.

Diagnosis: Postoperative pancreatic carcinoma and recurrence, accompanied by lymph node metastasis and liver metastasis.

Integrative treatment prescription: When the patient was admitted, the main symptoms were poor appetite, weight loss, and pain, but the mental state was acceptable. Supplemented with trypsin and a combined medicated diet for the replenishment of fat emulsions, amino acids, and so on as treatment. Simultaneously conducted malnutrition correction and treatments for cancer. Gave local hyperthermia and simultaneously conducted chelation detoxification in combination with local hyperthermia alternating with EBOO. The therapeutic principle of herbal medicines should focus on soothing the liver and regulating the circulation of qi, as well as dissipating dampness and eliminating stagnant blood. Prescription given: *Radix bupleuri* 10 g, *Radix paeoniae Alba* 20 g, *Fructus aurantii* 15 g, *Pogostemon cablin* 10 g, *Magnolia officinalis* 10 g, *Rhizoma pinelliae Praeparatum* 10 g, *Amomun kravak Pierre ex Gagnep* 10 g, *Caulis bambusae in Taeniam* 10 g, *Herba eupatorii* 10 g, *Platycodon grandiflorum* 6 g, *areca* 6 g, *Ruddle* 20 g, Dragon's Teeth (Apatite) 30 g, *Rhizoma corydalis* 10 g, and *Radix glycyrrhizae Preparata* 6 g, one dose a day. Decocted with water for oral administration. During the course of treatment, the patient presented dull abdominal pain, dry mouth, hiccups, fatigue, constipation, red tongue with little saliva, and rapid and thready pulse. The therapeutic principle of herbal medicines should focus on nourishing yin, dispersing stagnant liver qi, and dissipating blood stasis.

Medications: Glehnia littoralis 15 g, *Ophiopogon japonicus* 15 g, *Radix trichosanthis* 12 g, *Fructus toosendan* 10 g, *Rhizoma anemarrhenae* 10 g, *Cortex lycii* 12 g, *Carapax trionycis* 12 g, *Donkey-hide Glue* 12 g, *Fructus polygoni Orientalis* 12 g, *Semen Persicae* 12 g, *Rhizoma curcumae* 10 g, *Radix paeoniae Rubra* 10 g, *Hedyotis diffusa Willd* 30 g, prepared *rhubarb* 6 g, and *Glycyrrhiza uralensis* 3 g. Decocted with water for oral administration, one dose a day, with each dose for two administrations. Increased the dosage of chelation detoxification and changed to once every other day. Added Peiyuan Decoction for oral administration, one dose per day. At the same time, recommended to the patient to do proper mild exercise daily but to avoid sweating.

Acupuncture: Took Zusanli, Shangjuxu, Sanyinjiao, Zhongwan, Tianshu, Pishu, Shenshu, Guanyuan, Sanchongxue, and Waisanguan. Even reinforcing–reducing techniques were used. Retained the needle for 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Zusanli, Shenshu, and Pishu. Took two points each time and conducted moxibustion for 10 minutes on each point, once a day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Took liver, spleen, diaphragm, pancreaticobiliary point, Erjian, adrenal gland, subcortex, and Jiaogan, twice a week, alternating ears.

Treatment effects: After the patient was hospitalized for 45 days of integrative treatments, his mental state got better, pain was obviously relieved, food intake was normal, body weight had increased to 56 kg, and quality of life was significantly improved. He participated in regular recreational activities, and the KPS was 90. The patient was reexamined 2 months after hospitalization by abdominal CT, which showed that no recurrence of lesions was seen in the residual pancreas and at the head of the pancreas the number of multiple intrahepatic low-density lesions had not significantly increased from before admission and the sizes were reduced over the previous ones. The patient continued to adhere to outpatient treatment, during which chelation detoxification therapy was applied twice a week, medical ozone therapy was applied once a week, and hyperthermia was applied once a week. The patient was reexamined after 5 months. The abdominal CT showed postoperative liver metastases of pancreatic carcinoma. Compared with the previous CT, the following were observed: the number of liver metastases had decreased and the volume was also reduced; blood routine reexamined was normal. Liver function: alkaline phosphatase 135 U/L and r-GT 99 U/L. Tumor markers: CEA 37.5 ng/mL, CA-199 21.03 U/mL, and the rest were normal. The patient lived a normal life without obvious discomfort and remained on a weekly outpatient treatment program.

6.11.4 Related research in China and abroad

Liu Liyan et al. conducted experimental studies on the synergistic and inhibitory effects of selective cyclooxygenase-2 inhibitor celecoxib combined with hyperthermia on W1990 cells of human pancreatic carcinoma. The results showed that celecoxib combined with hyperthermia had synergistic and inhibitory effects on the W1990 cell growth of pancreatic carcinoma. The combined application can induce apoptosis and cell cycle arrest by upregulating the expressions of *HSP70, bax, p16, and p27kipl*.

Zhang Nianhua et al. evaluated the application value of peritoneal perfusion chemotherapy in combination with local endogenetic thermotherapy for the treatment of malignant ascites caused by pancreatic carcinoma through a clinical study on 76 advanced pancreatic carcinoma patients. The results showed that for advanced pancreatic carcinoma patients with malignant ascites, peritoneal perfusion chemotherapy combined with local endogenetic thermotherapy had better efficacy than conventional intraperitoneal chemotherapy alone and that it can prolong the survival time of patients without increasing adverse reactions.

Sui Lili et al. have conducted a randomized controlled study on 30 patients with inoperable advanced pancreatic carcinoma and explored the short-term effects of local endogenetic thermotherapy combined with chemotherapy for unresectable advanced pancreatic carcinoma. For hyperthermia in patients, rectal temperature was maintained at 39°C–40°C; it was conducted twice every cycle, 120 minutes each time, with 21 days as a cycle. The results showed that local endogenetic thermotherapy combined with chemotherapy has the effect of improving the efficacy of chemotherapy, does not increase the incidence of adverse reactions, can effectively control pain, and can improve quality of life.

Maluta et al. have carried out clinical studies on local hyperthermia combined with chemotherapy in the treatment of advanced pancreatic carcinoma. The results showed that hyperthermia combined with chemotherapy for patients with advanced pancreatic carcinoma is safe and effective and can prolong the survival time.

6.12 COLORECTAL CANCER

Colorectal cancer is the general term for colon and rectal cancer; it has poor prognosis and a high mortality rate. Cancers on the mucosa epithelium are collectively referred to as colorectal cancer and are the most common cancer of the gastrointestinal tract, second only to gastric cancer and esophageal cancer. The cancer originating from mesenchymal tissue is called sarcoma, accounting for 1% of the intestinal malignant lesions. The 5-year survival rate after surgical resection can reach 40%–60% on average. Early detection; early diagnosis; and early treatment, primarily standardized surgical treatment, are still the key for improving the curative effect of colorectal cancer.

According to national statistics, the majority of patients are 40–50 years old and the median age group is about 45 years. Patients under the age of 40 years account for one-third of all cases, and patients under the age of 30 years accounts for about 10%. The high onset age of colorectal cancer is 60–70 years, and in some high onset countries about 6% of patients are under the age of 30 years. The incidence age of colorectal cancer in China is 10–15 years earlier than that abroad, and patients under 30 years account for 11%–13%, which is a key concern in China.

Changes in defecation routines and properties of feces are often the earliest symptoms, such as increased number of defecations; diarrhea; constipation; and feces with mucus, pus, and blood. Abdominal pain is usually dull pain without clear position or abdominal discomfort, accompanied by flatulence, and so on. Weight loss, anemia, as well as acute and chronic intestinal obstruction appear in the medium-advanced stage. The mass, hard with unsmooth surface and less activity, is palpable in the abdomen of some patients.

6.12.1 Conventional treatments

6.12.1.1 SURGERY

Radical resection can be applied to the majority of the primary cancers, and the objective is to remove the intestinal segment where the cancer is located (including the range of proximal 10 cm and distal 7 cm and the corresponding mesentery and its lymph nodes). The range for specific radical resection and its surgical mode are determined by the location of the cancer. If patients cannot receive radical surgery, palliative resection can still be applied to alleviate the symptoms and improve the patients' quality of life. In recent years, many surgeons have applied resection under endoscopy for early colorectal cancer and have achieved better efficacy.

6.12.1.2 RADIOTHERAPY

The main purposes of colorectal cancer radiotherapy and chemoradiotherapy are for adjuvant therapies and palliative treatments. The indications for adjuvant therapy are colorectal cancers at stages II and III; the indications for palliative treatment are tumor locoregional recurrence and/or distant metastasis. For some who cannot tolerate surgery or are adamant about anus preservation, radical radiotherapy or chemoradiotherapy can be tried. It is not recommended to apply radiotherapy for cancers of phase I. Radical surgery is recommended for the following cases: after local excision, when the postoperative pathological stage is T_2, when the maximum tumor diameter is greater than 4 cm, if the tumor-occupying perimeter of intestine is greater than one-third the size of intestine, if adenocarcinoma is poorly differentiated, if there is neural invasion, and if there is intravascular cancer embolus. If patients refuse surgery or are inoperable, it is recommended to apply postoperative radiotherapy. For rectal cancer clinically diagnosed as stage II or III, it is recommended to carry out preoperative radiotherapy or preoperative concurrent chemoradiotherapy. Patients who are pathologically diagnosed with rectal cancer at stage II or III after radical resection and without receiving preoperative chemoradiotherapy must receive postoperative concurrent chemoradiotherapy. Locally advanced unresectable rectal cancer (T_4) must first receive preoperative concurrent chemoradiotherapy and must be reevaluated

after chemoradiotherapy to qualify for radical surgery. For local recurrence of rectal cancer, surgery is the first choice; if surgery is impossible, chemoradiotherapy is recommended. For initially treated rectal cancer of stage IV, it is recommended to carry out chemotherapy alone or chemotherapy combined with primary lesion radiotherapy. Reassess resectability after treatment. For metastases, if necessary, palliative reduction radiotherapy can be carried out. As far as recurrence and metastasis of colorectal cancer is concerned, and for patients with resectable local recurrence, it is recommended to have surgical resection first and then consider whether postoperative radiotherapy should be conducted. For unresectable patients with local recurrence, it is recommended to first have preoperative concurrent chemoradiotherapy and then seek surgical resection. For advanced rectal cancer cases, apply small doses of radiotherapy, which sometimes can have temporary effects of hemostasis and analgesia.

6.12.1.3 CHEMOTHERAPY

Patients at stages II and III are required to have adjuvant chemotherapy, and if advanced patients are in good general condition palliative chemotherapy can be carried out. For colorectal cancer patients at stage II, confirm the presence or absence of the following risk factors: poor histological differentiation (grade III or IV), T_4, vascular lymphatic invasion, preoperative intestinal obstruction or intestinal perforation, and insufficiency of lymph nodes detected from specimens (fewer than 12 pieces). It is recommended to conduct follow-ups for patients without high risk factors or to conduct chemotherapy with single-agent thymidine phosphorylase. It is recommended to conduct adjuvant chemotherapy for patients with high risk factors. For rectal cancers at $T_{3\text{-}4}$ or $N_{1\text{-}2}$, less than or equal to 12 cm from the anal edge, it is recommended to carry out preoperative neoadjuvant chemotherapy. If preoperative neoadjuvant radiotherapy is not conducted, adjuvant chemoradiotherapy is recommended.

6.12.1.4 HYPERTHERMIA

Hyperthermia heating technologies for colorectal cancer include intracavitary hyperthermia and out-of-body hyperthermia. According to pathological observations, preoperative thermoradiotherapy or thermochemoradiotherapy for killing cancer cells is significantly better than preoperative single radiotherapy alone. In recent years, in vitro heating intraperitoneal hyperthermic perfusion chemotherapy has been widely used clinically and has been commonly used for medium-advanced patients with good effects.

6.12.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be applied before and after surgery, and its effectiveness is to help patients improve immunity, preoperatively inhibit tumor growth or metastasis, postoperatively inhibit or kill residual tumor cells, reduce the side effects of chemotherapy, and enhance chemosensitivity. Chelation detoxification therapy in clinical practice adopts intravenous infusion and effectively excludes heavy metals and other toxins from the body. Chelation detoxification can be used as the main treatment for advanced colorectal cancer and usually starts with the therapeutic dose. If patients can tolerate two or three treatments, the dosage can be increased to two times the therapeutic one. Conduct treatment once every other day, with 20 times as a course of treatment.

6.12.1.6 MEDICAL OZONE THERAPY

Medical ozone can activate the body's own immune function, directly kill the early cancer cells in blood or lymph that may produce metastasis or micrometastasis, increase oxygen supply, reduce the side effects of chemotherapy, and promote the healing of surgical wounds. EBOO is preferred, once every other day, with 20 times as a course of treatment. Patients in poor physical conditions can change to major autohemotherapy, minor autohemotherapy, venous medical ozone saline, medical ozone acupoint injection, and so on, once every other day, with 20 times as a course of treatment. Colorectal cancer patients can also be given concurrent rectal insufflation of medical ozone gas in addition to the aforementioned medical ozone therapies, which has direct effect on cancer or stump after surgery, can kill cancer cells, and inhibit cancer recurrence and metastasis. For medium-advanced patients, medical ozone therapy varies from person to person and venous medical ozone saline, EBOO, rectal insufflation of medical ozone gas and other modes can

be selected. If the general condition of patients is acceptable, the preferred method is still EBOO, once every other day, with 20 times as a course of treatment. If the general condition of patients is poor with coagulation disorders, venous medical ozone saline, major autohemotherapy, or minor autohemotherapy can be given, once every other day. Medical ozone gas point injection can be used for Tianshu, Dachangshu, Zusanli, and other acupoints according to the disease. Take two to four points each time, and inject 2–5 mL of medical ozone gas at each point, once every other day.

6.12.1.7 TRADITIONAL CHINESE MEDICINE

The syndrome of dampness invasion of lower energizer is commonly seen at the early stage and the prescription recommended is Huaihua Diyu Decoction or Qingchang Drink, or modified Windflower Decoction. For the obstruction of pathogenic factors, the prescription recommended is Wuwei Xiaodu Decoction or modified Huanglian Jiedu Decoction. For the syndrome of blood stasis obstruction in the interior, the prescription recommended is modified Xuefu Zhuyu Decoction. For advanced stage with the syndrome of yin deficiency of liver and kidney, the prescription recommended is modified Zhibai Dihuang Pill. For the syndrome of deficiency of spleen yang and kidney yang, the prescriptions recommended are Shenlingbaizhu Powder and modified Sishen Pill. For the syndrome of deficiency of both qi and blood, the prescriptions recommended are Guipi decoction and modified Bazhen Decoction.

Medium-advanced colorectal cancer mainly exhibits syndromes of dampness heat, blood stasis, and toxins, as well as deficiency of spleen yang and kidney yang. The therapeutic principle should focus on invigorating spleen for eliminating dampness, removing toxins, eliminating stagnant blood, reinforcing spleen, and nourishing kidneys, as well as inducing astringency and relieving diarrhea.

6.12.1.8 ACUPUNCTURE

The syndrome of early colorectal cancer is mainly the stagnation of liver qi. The therapeutic principle should focus on regulating qi flow for activating stagnancy, as well as relieving Fu qi.

Acupuncture on acupoints: Tianshu, Dachangshu, Zhongwan, Zusanli, and Shangjuxu.

Methods: Even reinforcing–reducing method is used. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The main syndromes of medium-advanced colorectal cancer are dampness heat and stasis toxins and deficiency of spleen yang and kidney yang. The therapeutic principle should focus on invigorating spleen for eliminating dampness, removing toxins and eliminating stagnant blood, toning kidneys and spleen, as well as inducing astringency and relieving diarrhea.

Acupuncture on acupoints: Tianshu, Dachangshu, Zusanli, Qihai, Pishu, and Shenshu. If the syndrome of deficiency of spleen yang and kidney yang is seen, add Shenshu, Mingmen, and Guanyuan to activate yang, invigorate primordial energy, and reinforce kidney qi. If the syndrome of yin deficiency of liver and kidney is seen, add Sanyinjiao, Taixi, Shenshu, and Ququan to nourish yin and saliva, as well as to regulate and reinforce liver and kidneys.

Methods: Even reinforcing–reducing method is used. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Guanyuan, Zusanli, Zhongwan, Shenshu, and Pishu. Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Large intestine, Pishu, Jiaogan, subcortex, low rectal segment, endocrine, Shenmen, and adrenal gland.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.12.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Medicated diet is mainly given for the cancer at the early stage. Total parenteral nutrition is given 1 day before thermochemotherapy to ensure adequate nutritional intake and to prevent loss of appetite caused

by gastrointestinal reactions after thermochemotherapy, which can result in immune system damage. For medium- and advanced-stage patients who have no obstruction and can eat, it is recommended to give medicated diet and increase oral amino acids for supplementing rational nutrition. For patients with obstruction, consider giving total parenteral nutrition in conjunction with other therapies to prolong survival time and improve quality of life.

6.12.1.10 OTHERS

Actively practice qigong and tai chi. Strongly recommend to patients to make the necessary psychological adjustments to overcome negative emotions and alleviate psychological pressures by themselves. If necessary, psychiatrist treatment is given to help the transition to a normal and healthy state of mind.

6.12.2 Combination of hyperthermia with conventional treatments

6.12.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

For patients with localized colorectal cancer lesions of stages I and II, and in good general condition as well as with clear indications for surgery, radical surgery is mainly conducted. Local hyperthermia can be carried out before and after surgery to prevent tumor diffusion and metastasis. For patients at stage III to IV or above in good general condition, conduct preoperative adjuvant chemotherapy for two cycles combined with hyperthermia, chelation detoxification, medical ozone, TCM, acupuncture, and other characteristic nontoxic integrative treatments. For patients who are assessed as able to be given cytoreductive surgery or diversion surgery to remove the obstruction, generally, after the postoperative wound is completely healed, chemotherapy combined with local hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests disclosing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician.

Whole-body hyperthermia can improve immunity; promote tumor cell apoptosis; and regulate the body for the production of TNF, IL-2, and other immune factors involved in the anticancer effect.

If patients are assessed to be in good general condition and able to withstand whole-body hyperthermia, it is recommended to carry out whole-body hyperthermia twice a week, with six times as a course of treatment. Be sure to monitor body temperature, blood pressure, pulse, and other vital signs during hyperthermia and give timely fluid infusion to maintain water–electrolyte balance and other symptomatic treatments. Review electrolytes, and so on 1–3 days after whole-body hyperthermia. Continue to supplement energy to maintain water–electrolyte balance. Local hyperthermia can be appropriately added at the intervals of whole-body hyperthermia according to the general condition and tolerance of patients.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the upper abdomen or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. Conduct the second course after an interval of 10 days. After three courses, local hyperthermia can be taken as long-term concomitant therapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.12.2.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy is often used as an additional means to surgery and chemotherapy to reduce the probability of tumor recurrence. The efficacy is still not satisfactory, and generally radiotherapy is rarely used for colon cancer.

Preoperative radiotherapy can shrink the tumor, increase resection rate, and reduce regional lymph node metastasis and the intraoperative diffusion and local recurrence of cancer cells.

Postoperative radiotherapy: Postoperative radiotherapy is suitable for cases with radical surgery, for example, the cancer penetrates the intestinal wall and invades regional lymph nodes and lymphatic and blood vessels, and there are postoperative tumor residuals but without distant metastasis.

Radiotherapy alone: For advanced rectal cancer cases, conducting radiotherapy with a small dose can sometimes achieve a temporary remedial and analgesic effect.

The order of thermal radiotherapy is recommended to be radiotherapy followed by hyperthermia. Local hyperthermia at the chemotherapy area is conducted within 2 hours after the end of radiotherapy and as soon as possible. It can increase sensitivity of the radiotherapeutic effect and significantly reduce local skin damage and fibrosis. The first course of hyperthermia is maintained until 2 weeks after the end of radiotherapy. Change to whole-body hyperthermia during the rehabilitation period.

6.12.2.3 HYPERTHERMIA AND CHEMOTHERAPY

According to the NCCN Guidelines and program of FOLFOX, oxaliplatin plus fluorouracil plus calcium folinate is the preferred standard program of category I and oxaliplatin plus capecitabine is recommended as category 2A. For patients who cannot take oxaliplatin, capecitabine alone or fluorouracil plus calcium folinate can be used. It is not recommended to use irinotecan combined with bevacizumab, and cetuximab for nonmetastatic colon cancer.

Systemic chemotherapy combined with intraperitoneal hyperthermic perfusion chemotherapy may be considered for chemotherapy. Generally, conventional chemotherapy lasts four to six cycles, combining with local and whole-body hyperthermia during chemotherapy. Give intraperitoneal hyperthermic perfusion chemotherapy for two to four cycles after conventional chemotherapy. Intraperitoneal chemotherapy has the pharmacokinetic characteristics of high selective regional chemotherapy and can maintain a constant high concentration of anticancer drugs in peritoneal fluid, portal vein blood, and peritoneal lymphatic system, as well as the liver. In this treatment, the free cancer cells that are exfoliated during surgery in the abdominal cavity, as well as minimum cancer lesions and common abdominal locations of recurrence and metastases, can be soaked in the high concentration of anticancer drug solution and can be directly attacked. The most common sites of postoperative colorectal cancer recurrence are the vicinity of primary cancer and its lymph nodes, and the most common diffusion sites are liver and abdominal cavity. Therefore, abdominal local chemotherapy is an important means of controlling postoperative recurrence and metastasis. If postoperative recovery is good and patients are in good general condition, local hyperthermia combined with whole-body hyperthermia can be carried out.

When conducting the combined application of conventional chemotherapy and whole-body hyperthermia, whole-body medium-high hyperthermia can be selected for combined application with chemotherapy at the same time, and simultaneously conduct whole-body hyperthermia and chemotherapy for six to eight courses. Whole-body medium-high hyperthermia can be carried out simultaneously on the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

Insulin-mediated small dose of intravenous chemotherapy combined with medical ozone and hyperthermia in clinical practice has obtained good results. Specific methods: rule out contraindications of chemotherapy through comprehensive assessment and obtain the informed consent of patients. An empty stomach is required before chemotherapy. Carry out medical ozone major autohemotherapy before chemotherapy, give insulin to control blood glucose at about 3.6 mmol/L (it is better to control blood glucose when the hypoglycemia reaction has just appeared, and according to individual circumstances), and then give intravenous chemotherapy with a small dose of oxaliplatin plus fluorouracil plus calcium folinate (10%–30% of conventional amount). Implement conventional nausea and vomiting control, stomach protection, and high glucose supplementation as well as trace elements. Conduct hyperthermia within 2–4 hours after chemotherapy. It is recommended to apply whole-body medium-high temperature hyperthermia for patients in good general condition and who are able to tolerate whole-body medium-high hyperthermia.

For patients who cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the right upper abdomen or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day and continue during the intermission periods of chemotherapy. Take 1 week off after each cycle (5 consecutive days) of chemotherapy. A total number of about 60–80 times of combined local hyperthermia is carried out during chemotherapy. Local hyperthermia can be taken

as long-term maintenance therapy after the end of chemotherapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.12.2.4 HYPERTHERMIA AND TARGETED THERAPY

With the study of colorectal cancer–related genes and signaling pathways, targeted therapy has become a new approach for the treatment of colorectal cancer. Targeted drugs reported currently for colorectal cancer are erlotinib, cetuximab, bevacizumab, and so on, but the effects are far from satisfactory and further exploration is still needed. If the financial conditions are good, hyperthermia and nontoxic integrative therapies in combination with targeted therapy can be considered to increase targeted therapy efficiency and to reduce the side effects of targeted drugs.

6.12.2.5 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given from the end of operation to the period of chemotherapy to the patient with postoperative physical weakness and low immunity. On the one hand, it promotes physical recovery and regulates the immune system and, on the other hand, it can kill residual tumor cells or inhibit early metastasis. Chelation detoxification needs an infusion of more than 2 hours. The therapeutic dosage can be gradually increased if there is the absence of adverse reactions, and taken 20 times as a course of treatment for a total of three courses. Local hyperthermia or whole-body hyperthermia can be simultaneously applied with chelation and detoxification to improve efficacy.

6.12.2.6 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance effect on immunity, and increase the efficacy of medical ozone. Treatment methods: use EBOO once every other day, with 20 times as a course of treatment, or select medical ozone saline infusion once every other day, with 10–14 days as a course of treatment. Use medical ozone major autohemotherapy once every other day, with 12 times per course. Use medical ozone minor autohemotherapy once every other day, with 12 times per course. Use medical ozone acupoint injection once every other day, with 12 times as a course of treatment. Conduct treatment for at least three courses, and long-term maintenance therapy is applicable.

6.12.2.7 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. Other treatments such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, colon cleansing therapy, and so on in combination with hyperthermia can increase the effectiveness and safety of the treatment.

6.12.2.7.1 DC-CIK cell therapy

DC-CIK consolidated treatment after radical resection: After radical resection for early colorectal cancer, combined DC-CIK transfusion can effectively remove residual small lesions and reduce recurrence. The number of CIK cells for each reinfusion should reach at least 1×10^{10}; conduct once per month, with four times as a course of treatment. Conduct periodic review after transfusion, and if there is no recurrence an additional treatment is carried out once every 6 months. Collecting cancer tissue during the operation for preparation of individual peptides and DC vaccines, which are cultured together with CIK, can obtain better efficacy.

6.12.2.7.2 DC-CIK combined with chemotherapy

For patients who need adjuvant chemotherapy after radical resection, or due to recurrence and metastasis, combined DC-CIK therapy can have the effect of improving immunity and increasing the sensitizing effect of chemotherapy. Treatment program: one day before chemotherapy collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, i.e., 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. Conduct efficacy assessment. If it is effective, conduct a consolidated therapy every 2 to 3 months.

6.12.2.7.3 DC-CIK perfusion for the treatment of malignant ascites

For malignant ascites due to metastases of colon cancer, gynecological cancer, and other cancers, perfusion of DC-CIK can inhibit intra-abdominal metastases, reduce ascites, and have a better effect than single infusion of chemotherapy drugs. Collect peripheral blood of patients and prepare DC-CIK. After ascite drainage, perfuse DC-CIK 2×10^9/time to 3×10^9/time through the abdominal drainage tube once per day, with 4 days of continuous infusion as a cycle.

6.12.2.7.4 Systemic biofeedback therapy

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Change to once or twice a week after two to three courses for long-term treatment.

6.12.2.7.5 Alkalization treatment

Alkalization therapy: Dietotherapy or sodium bicarbonate therapy can be applied to alkalize the body.

Peritoneal perfusion of sodium bicarbonate is safe and effective. It can be applied together with chemotherapy drugs. About 100 mL of 5% sodium bicarbonate injection heated to 37°C is perfused slowly into the abdominal cavity within 1 hour, combined with abdominal massage to achieve uniform distribution of liquid in the abdominal cavity. If the patient complains about abdominal pain, 10 mL of 2% lidocaine can be added inside or the concentration can be reduced to 2.5% with the same dose. If chemotherapy drugs are also applied, apply the sodium bicarbonate first and 20 minutes later the chemotherapy drugs, once or twice a week with eight times as a course. If peritoneal perfusion of sodium bicarbonate is combined with hyperthermia, RF local hyperthermia at the abdomen can be carried out after perfusion.

Retention enema of sodium hydrogen carbonate or through rectosigmoid administration: About 100–150 mL of 1.25%–2.5% sodium hydrogen carbonate is applied for the retention enema. Retain for 15–20 minutes, or 50 mL of sodium bicarbonate with the same concentration is set to the junction of rectosigmoid with a fine silica tube for slow infusion (10–15 drops/min). Patients should feel good, and the purpose of quickly alkalizing liver, intestine, pancreas, and spleen can be achieved.

6.12.2.7.6 Colon cleansing therapy

Patients without eating difficulty can take fruit and vegetable drinks with coffee enema; patients with eating difficulty can take the coffee enema by itself, but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support. It is banned for patients with bowel obstruction.

In addition to hyperthermia, chelation detoxification, triatom oxygen, acupuncture, and TCM, we emphasize dietotherapy plus qigong plus sports as supplementary treatments to improve overall immunity. Encourage patients to continue with their daily lives in spite of the disease.

6.12.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.12.2.8.1 Medicated ironing (hot compress)

Take 15 g each of *Angelica sinensis*, *Cinnamomum cassia Presl*, *Evodia rutaecarpa*, *Olibanum*, *Myrrha*, and *Asarum*. Grind them to fine powder and fry, and then wrap the mixture with cloth and put it on the navel for hot compress. Efficacy: dissipates dampness and activates stagnancy, warms meridians and disperses cold, and relieves menalgia, as well as regulating qi and blood. It is applicable to patients who suffer from abdominal and pelvic cancers (colon cancer, colorectal cancer, ovarian cancer, cervical cancer, etc.) with the syndromes of wet and cold coagulation.

6.12.2.8.2 Bath

Proven prescription 1: Sappanwood 50 g, *Camphora* 50 g, *Ramulus cinnamomi* 15 g, *Old radix Lithospermi* 15 g, *Lulutong* 15 g, *Rhizoma homalomenae* 15 g, *Lycopodii herba* 15 g, *Olibanum* 10 g, *Myrrha* 10 g, *Carthamus tinctorius L.* 10 g, *Chaenomeles speciosa Nakai* 10 g, and *Rubus obcordatus* 10 g. Decoct the mixture with

water, and immerse (wash) joints of the affected part in the hot decoction. Efficacy: promotes blood circulation to dispel cold and remove meridian obstructions. It is applicable to patients with the syndrome of joint and bone pain caused by bone metastatic carcinoma.

Proven prescription 2: Radix astragali 450 g, *Radix codonopsis* 300 g, *Radix polygoni Multiflori Preparata* 300 g, *Ligusticum chuanxiong Hort* 300 g, *Fructus alpinia Oxyphylla* 300 g, *Semen cuscutae* 300 g, *Atractylodes macrocephala Koidz* 300 g, and *Carthamus tinctorius L.* 200 g. Put all drugs into the wok, and add proper amount of water. Boil for 50 minutes. Remove slag and take juice. Blend with 450 g of white wine. Take bubble bath for 40 minutes once a day, with 10 days as a course of treatment. Efficacy: tones lungs, spleen, and kidneys, as well as strengthening spirit. It mainly cures a variety of fatigue and is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 3: Stems and leaves of *Panax ginseng* 30 g, *Atractylodes macrocephala Koidz* 30 g, *Radix saposhnikoviae* 20 g, yam 20 g, and *Glycyrrhiza uralensis* 6 g. Add drugs and proper amount of water. Boil twice and for 30 minutes each time. Combine filtrate and immerse feet for 30 minutes once a day, with 15 days as a course of treatment. Efficacy: invigorates spleen and replenishes qi. It is applicable to patients with long-term weakness and low immunity.

6.12.2.8.3 Grilling method

Proven prescription 1: Yongquan Plaster: one piece of large and raw *Radix aconiti Lateralis Preparata*; one pair of big *Syngnathus*; 9 g each of *Lysimachia foenum-graecum, Squama manitis*, and *Cynomorium songaricum Rupr*; sesame oil 600 g; plus yellow lead 200 g. Boil them into paste, which is mixed well with 15 g each of *actinolite* and musk and 9 g each of *Cordyceps sinensis*, ginseng, Sichuan pepper, and clove fruit. Spread out 1 g the size of a coin, and paste to both sole centers and then bake for 0.5–1 hour in the affected area with the Magic Lamp. Efficacy: reinforces liver and kidney. It is applicable to middle-aged and old-aged people with disease-producing mass in the abdomen due to renal asthenia and general debility and is also applicable to tumors in various parts of the body.

Proven prescription 2: Aweihuapi Plaster: decoct *ferula*, *Rhizoma sparganii*, *Rhizoma curcumae*, *rhubarb*, *crude Sichuan aconite root*, *Olibanum*, *Momordica cochinchinensis*, dung beetle, *Rhizoma cyperi*, *aloe vera*, *Resina draconis*, and camphor into a paste. Heat to soften it for external application, paste it in the umbilical region or affected area, and then irradiate for 30 minutes with the infrared lamp once a day. Efficacy: regulates the flow of qi and promotes blood circulation and softens and resolves hard mass, as well as relieving chest and abdominal distention and disintegrating abdominal mass. It is applicable to patients who have chest and abdominal distention and abdominal mass with the symptom of qi stagnancy and blood stasis in liver, gallbladder, stomach, and intestines and with gynecological diseases.

6.12.2.9 HYPERTHERMIA INDICATIONS

Hyperthermia can be applied for patients in good general condition.

6.12.2.10 HYPERTHERMIA CONTRAINDICATIONS

Patients accompanied by intestinal infections or obvious bleeding; need to be cautious if there are nonpeptide metal and metal objects in the treated area; need to be cautious in patients with bleeding tendency; need to be cautious in patients with large surgical ranges; and patients in poor general condition and having KPSs less than 60 points.

6.12.3 Introduction of a typical case

A patient named Yuan, male, 53 years old, was admitted on June 28, 2006, to Clifford Hospital due to "postoperative of colon cancer for more than 2 years, 9 months after interventional chemotherapy for liver metastases and abdominal pain for 2 weeks." On June 2004, the patient was diagnosed with colon cancer by colonoscopy and right colon palliative resection and colon polypectomy were carried out. Liver metastasis was seen during the surgery and the tumor, approximately 6 cm × 7 cm, was located in the upper segment of sigmoid to the side of mesocolon; most of it had grown outside the enteric cavity (inside the mesenterium), and it had

not yet invaded surrounding tissues and organs. Two pedicled polyps were visible in the vicinity of the proximal and distal colon. Lesions in the colon segment as well as polyps were removed. Postoperative pathology: moderately differentiated adenocarcinoma of ulcerative type of the sigmoid colon, invading the surrounding tissues of the intestinal wall. The two polyps were tubular adenomas with one of canceration. A postoperative program of 5-fluorouracil plus calcium folinate plus oxaliplatin for chemotherapy was given. On September 2005, enhanced abdominal CT of the patient showed increased and enlarged intrahepatic metastases compared with the previous scan and interventional chemoembolization for hepatocellular carcinoma was given. In early June 2006, the patient was reexamined with CT and it showed that intrahepatic metastases had continued to grow, the largest being 4 cm × 3.2 cm. The patient was admitted to Clifford Hospital for further treatment due to abdominal pain for 2 weeks. On admission, the main complaints were right upper abdominal pain and discomfort, poor mental state, and without difficulty of sleep. Urine and stool were normal.

Physical examination: No jaundice and no cyanosis in the whole-body skin mucus membrane. No rash and subcutaneous bleeding were found. A surgical scar of about 15cm could be seen in the middle of the abdomen with local tenderness. Superficial lymph nodes were not enlarged. Cardiopulmonary auscultation was normal. The abdomen was relatively full with no abdominal vein distention. Abdominal breathing activities were not limited with soft abdominal muscles. No whole abdominal tenderness and rebound tenderness were found. There was no tenderness in the hepatic region. The liver dullness border was normal. The liver and spleen were inpalpable, and Murphy's sign was negative. There was no shifting dullness. No tenderness and percussion pain in the kidney area. Bowel sounds were normal. Vascular murmur was not heard. The patient's KPS was 90.

Auxiliary examination: RBC 4.3×10^{12}/L, Hb 126 g/L, BC 5.9×10^{9}/L, and PLT 267×10^{9}/L. Biochemistry: ALT 26 U/L, AST 21 U/L, TBIL 29 U/L, DBIL 14 U/L, ALB 36.7 g/L, ALP 467 U/L, GGT 358 U/L, Cr 6 μmol/L, Ua 168 μmol/L, BUN 5.7 mmol/L, GLU 5.89 mmol/L, TG 1.52 mmol/L, GHO 3.74 mmol/L, K^+ 3.8 mmol/L, Na^+ 137 mmol/L, Cl^- 102 mmol/L, and Ca^{2+} 1.22 mmol/L. Five items of immune function were normal, and trace elements such as copper, zinc, lead, mercury, cadmium, and nickel were normal. Serum ammonia was 39 μmol/L. Five tumor markers were as follows: CEA 329.8 ng/mL, AFP 17.09 ng/mL, CA 12-5(OV) 3.99 U/mL, CA199 5.94 U/mL, and PSA 56.45 U/mL. Intrahepatic metastases continued to grow and increase as was shown by abdominal CT, with the largest being 4 cm × 3.2 cm.

Diagnosis: Hepatic metastases after postoperative chemotherapy of colon cancer and interventional treatment.

Integrative treatment prescription: After the patient was admitted to the hospital and after a comprehensive assessment, it was recommended to give nontoxic integrative treatment in combination with irinotecan plus Erbitux for treatment, but the patient refused chemotherapy and biological therapy and only accepted nontoxic integrative treatment. Chelation detoxification was given. Local hyperthermia and chelation detoxification were simultaneously conducted. Hyperthermia was conducted in the abdomen and hepatic region twice a week for a total of 37 times. EBOO was applied twice every week and was alternated with chelation detoxification. At the same time, TCM and acupuncture therapy were given. The patient's tongue was dark red with yellow greasy fur. Pulse was wiry and quick. The syndrome was stagnation of toxic stasis in the body. The therapeutic principle should focus on promoting qi and activating blood, as well as removing stasis and eliminating accumulation.

Medications: The prescription recommended was modified Gexia Zhuyu Decoction. Specific medication: *Radix angelicae Sinensis Tail* 12 g, *Radix paeoniae Rubra* 12 g, *Semen persicae* 10 g, *Carthamus tinctorius L*. 6 g, *Rhizoma sparganii* 10 g, *Rhizoma curcumae* 10 g, *Scutellaria barbata* 30 g, *Radix linderae* 10 g, *Rhizoma corydalis* 12 g, *Patrinia scabiosaefolia Fisch*. 15 g, *Polygonum cuspidatum* 10 g, and *Purslane* 15 g, one dose a day. Decocted with water for oral administration. Acupuncture treatment: the main syndromes of medium-advanced colorectal cancer are dampness heat and stasis toxin and deficiency of spleen yang and kidney yang. The therapeutic principle should focus on invigorating spleen for eliminating dampness, removing toxins, eliminating stagnant blood, and toning kidneys and spleen, as well as inducing astringency and relieving diarrhea.

Acupuncture on acupoints: Linggu, Dabai, Tianshu, Dachangshu, Zusanli, Qihai, Pishu, Shenshu, and Waisanguan. If the syndrome of deficiency of spleen yang and kidney yang is seen, add Shenshu, Mingmen,

and Guanyuan to activate yang, invigorate primordial energy, and reinforce kidney qi. If the syndrome of yin deficiency of liver and kidney is seen, add Sanyinjiao, Taixi, Shenshu, and Ququan to nourish yin and saliva, as well as to regulate and reinforce liver and kidneys.

Methods: Even reinforcing–reducing method was used. Retained the needle for 20 minutes, once per day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Zusanli, Zhongwan, Shenshu, and Pishu. Methods: took two points each time with a moxa stick for moxibustion. Conducted moxibustion for 10 minutes above each point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Large intestine, Pishu, Jiaogan, subcortex, lower rectal segment, endocrine, Shenmen, and adrenal gland. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

Treatment effects: Although the patient was with hepatic metastasis of advanced colonic carcinoma when he was admitted, he had no obvious symptoms and signs. The patient was hospitalized for 97 days and had no obvious discomfort during the application of green comprehensive treatment. After treatment, the patient's mental state was good, the right upper abdominal pain disappeared, diet was normal, and sleep was fine. Abdominal CT for reexamination showed that intrahepatic metastases had no significant changes compared with the previous scans and lesions were not increased; laboratory: CEA 156.5 ng/mL. The patient returned as outpatient for two applications each of chelation detoxification, medical ozone, local hyperthermia, and acupuncture treatments every 20 days after discharge and took herbal medicines. Abdominal CT for reexamination 3 months after discharge showed that intrahepatic metastases had decreased compared with the previous scans. The biggest was 1.5 cm × 1.2 cm in size, and no new lesions were found. Rechecked CEA, 76.3 ng/mL. Conducted follow-ups for 2 years and 8 months after discharge and the patient's condition remained stable. Conducted regular outpatient treatments and reviews.

6.12.4 Related research in China and abroad

Hu Zhanghua et al. have observed the efficacy and adverse effects of hyperthermia combined with systemic chemotherapy in the treatment of advanced colorectal cancer in clinical studies. The results showed that compared with conventional systemic chemotherapy the efficiency, disease progression–free survival time, and overall survival time of hyperthermia combined with systemic chemotherapy were significantly improved, with the difference being statistically significant ($P < .05$) and with no increase in adverse effects.

Wu Xueyong et al. have conducted clinical studies on hyperthermia combined with CapeOx chemotherapy for the treatment of advanced colorectal cancer. The results showed that PR was 14 cases out of 24 patients with advanced colorectal cancer in the study group with RR 58.3%; PR was 9 cases out of 29 patients with RR 31.0% in the control group. The difference between the two groups was significant ($P < .05$). The median PFSs (progression free survival) of the study group and the control group patients were 6.5 months (95% confidence interval [CI]: 4.4–8.6 months) and 5.6 months (95% CI: 4.6–6.3 months), respectively, and the difference between the two groups was significant ($P < .05$). Common adverse reactions were peripheral nerve abnormalities, gastrointestinal toxicity, hand-foot syndrome, and neutropenia, but all were relatively minor.

Clifford Pang applied RF deep hyperthermia combined with the prescription of Fuzheng Guben of TCM for the treatment of patients with colon cancer. The results showed that the combined application of hyperthermia and herbal medicine is better than the application of hyperthermia alone or herbal medicine treatment alone in terms of clinical efficacy, improvement of patient's quality of life, and extension of survival time ($P < .05$).

Currently, intraperitoneal hyperthermic perfusion chemotherapy in the treatment of colorectal cancer is being widely used clinically in China and abroad. Experts at the annual meeting of surgical oncology in the United States have recommended intraperitoneal hyperthermic chemotherapy as the standard treatment for metastatic colorectal cancer and pelvic tumor peritoneal metastasis.

Wang Yuandong et al. have applied whole-body hyperthermia combined with the program of oxaliplatin in the treatment of advanced colorectal cancer. Clinical studies have shown that whole-body hyperthermia combined with oxaliplatin, fluorouracil, and calcium folinate for the treatment of advanced colorectal cancer has significant therapeutic effect and tolerable toxicity.

6.13 KIDNEY CANCER

Kidney cancer, also known as renal cell carcinoma, originates from renal tubular epithelial cells. It may occur in any part of the renal parenchyma but mostly at the upper and lower ends, with some invading the whole kidney. Incidence of cancer to the left and right kidneys has equal chance. The clinical appearance rate of hematuria, back pain, and abdominal mass, known as the "kidney cancer triad," is less than 15%, which often indicates that the lesion has entered the advanced stage. The majority of patients show only one or two symptoms of the triad.

The prognosis is mainly related to factors such as tumor size, histological type, clinical stage, degree of differentiation, and so on. Clinical stage and treatment as well as state of the patient's own immune function are the key factors affecting prognosis. Malignancy of clear cell carcinoma is low and the prognosis is good. Malignancy of granular cell carcinoma is higher and the prognosis is poorer. Differentiation of spindle cell carcinoma is the worst and the prognosis is also the worst.

Surgery is the main treatment for kidney cancer; but there is the possibility of postoperative recurrence or metastasis, and kidney cancer has had poor sensitivity to chemotherapy. As a result, the combination application of hyperthermia and naturopathy with TCM has better prospects in improving symptoms, bettering the quality of life, and prolonging survival time.

6.13.1 Conventional treatments

6.13.1.1 SURGERY

Radical nephrectomy is the most basic method of treatment for renal cell carcinoma. In recent years, nephron sparing surgery has been advocated. The scope of renal parenchyma resection from the cancer margin is 0.5–1.0 cm. It is stated in the European Association of Urology Guidelines on Renal Cell Carcinoma that as long as the complete cancer is resected the thickness of the edge does not affect the rate of cancer recurrence.

6.13.1.2 RADIOTHERAPY

It is not recommended to have radiotherapy because kidney cancer has low radiosensitivity. Palliative radiotherapy for local recurrence of the tumor bed, regional or distant lymph node metastasis, and bone or lung metastasis can achieve the purpose of relieving pain and improving quality of life.

6.13.1.3 CHEMOTHERAPY

Kidney cancer also has low chemosensitivity, and chemotherapy is not generally considered. If the pathological type is sarcoma, the programs of gemcitabine or capecitabine can be given for chemotherapy.

6.13.1.4 HYPERTHERMIA

In recent years, hyperthermia has gradually been tried in the treatment of kidney cancer, and the clinical applications of the technology are minimally invasive thermal ablation and high-intensity focused ultrasound. Noninvasive microwave or radio-frequency deep heating has obtained a certain effect and is mostly used as auxiliary treatment.

6.13.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can effectively remove toxins from the body and improve immune function. It is best to conduct it simultaneously with hyperthermia for better efficacy. Chelation detoxification therapy is one of the preferred methods for the treatment of advanced renal cell carcinoma, and the dosage varies from person to person and is applied once every other day. Conduct the treatment once or twice per week after the patient's condition is more stable. Long-term patients need to adhere to sufficient amounts of medications, and it is better to conduct hyperthermia simultaneously. Be sure to monitor renal function when applying chelation detoxification therapy for kidney cancer. For patients with end-stage renal failure

(uremia stage), in principle chelation detoxification therapy is no longer applicable. If the patient undergoes hemodialysis therapy, chelation detoxification therapy can still be implemented because chelates can be safely cleared during the dialysis process.

6.13.1.6 MEDICAL OZONE THERAPY

Medical ozone therapy can stimulate autoimmunity, kill cancer cells directly, increase the oxygen supply for normal tissue cells, and promote the healing of surgical wounds. Usage: medical ozone major autohemotherapy, 10 times as a course of treatment for two to three times a week; intravenous medical ozone saline, 12 times as a course of treatment for two to three times a week; and EBOO, 20 times as a course of treatment for two to three times a week. Be sure to avoid using chelation detoxification on the same day, generally, alternating days. For medium-advanced renal cell carcinoma, EBOO is the preferred treatment; EBOO is to be applied once every other day, with 20 times as a course of treatment. For patients with physical difficulty tolerating it, with coagulation abnormalities, less blood volume, or venous return obstruction, intravenous medical ozone or major autohemotherapy can be given once every other day, with 12 times as a course of treatment for two to three times a week. At the same time, medical ozone acupoint injection can be applied. The selected points are the same as those with acupuncture on acupoints.

6.13.1.7 TRADITIONAL CHINESE MEDICINE

The syndrome of deficiency of both spleen and kidney can appear at the early stage. The prescriptions recommended are Siwu Decoction plus modified Yougui Drink. For the syndrome of dampness and heat stagnation in kidney, the prescription recommended is modified Bazheng Powder. For the syndrome of exuberance of heart fire, the prescriptions recommended are Xiaoji Yinzi and modified Daochi Powder. The syndrome of blood stasis obstruction in the interior is mostly seen at the medium-advanced stage, and the prescription recommended is modified Taohong Siwu Decoction. For the syndrome of deficiency of both blood and qi, the prescription recommended is modified Bazhen Decoction.

6.13.1.8 ACUPUNCTURE

The main syndromes of early kidney cancer are stagnation of pathogenic dampness and heat. The therapeutic principle should focus on clearing heat and eliminating dampness, as well as stimulating the circulation of blood and effecting relaxation in muscles and joints.

Acupuncture on acupoints: Pangguangshu, Zhongji, Yinlingquan, Shenshu, Sanyinjiao, Taixi, and Zusanli.

Methods: Even reinforcing–reducing method is used. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The main syndrome of medium and advanced kidney cancer is deficiency of both spleen and kidney. The therapeutic principle should focus on reinforcing spleen and nourishing kidneys, as well as benefiting qi and nourishing blood.

Acupuncture on acupoints: Shenshu, Pishu, Sanyinjiao, Zusanli, Guanyuan, Qihai, and Zhongji.

Methods: Reinforcing method is used. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Shenshu, Guanyuan, Zhongji, Zusanli, and Shenque. Methods: take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Kidney, bladder, Jiaogan, Pishu, subcortex, Sanjiao, endocrine, and adrenal gland.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.13.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Focus on a medicated diet for nutrition. Rationally supplement amino acids, digestive enzymes, and trace elements. Medium-advanced patients need to be strengthened with nutritional support treatment. Patients

who can eat can be given medicated conditioning, supplemented with enough amino acids, vitamins, and digestive enzymes. For patients who have difficulty in eating, total parenteral nutrition can be given for supplementing appropriate proportion of amino acids, fat emulsion, and so on.

6.13.1.10 OTHERS

Actively practicing qigong, exercising sensibly, TCM, and a psychologically adjusting attitude for maintaining a good state of mind can achieve the best prognosis and are important parts of the therapeutic regimen.

6.13.2 Combination of hyperthermia with conventional treatments

6.13.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Surgery is the main treatment for kidney cancer, and radical surgery should be applied for early kidney cancer. Perioperative nontoxic integrative treatments such as medical ozone, chelation detoxification, TCM, acupuncture, and medicated diet must be carried out, which can significantly improve the patient's tolerance to surgery, promote postoperative rehabilitation, and prevent postoperative metastasis. After the postoperative wound is completely healed, hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician.

For early-stage patients in good general condition, whole-body medium-high temperature hyperthermia is given as far as possible. For patients with less tolerance, whole-body medium-low temperature hyperthermia is given. Hyperthermia heating destroys cancer tissue structures and is not affected by tumor histological properties; therefore, it can be applied for advanced cancer and recurrent cancer. The key is to make the cancer and the cancer area that is not sensitive to chemoradiotherapy reach an effective temperature of not less than 41.5°C, while the surrounding tissues, including subcutaneous tissue, are less affected or are not affected. Hyperthermia alone can be used or can be applied together with radiotherapy or nontoxic integrative cancer treatments. Whole-body medium-high temperature hyperthermia is conducted, six times being a course of treatment. Conduct whole-body hyperthermia once every 10–14 days, for three courses of treatment. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. After three courses, local hyperthermia can be administered as long-term concomitant therapy.

6.13.2.2 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Kidney cancer is not sensitive to chemoradiotherapy, and our experience is that local hyperthermia or whole-body hyperthermia application combined with chelation detoxification has synergistic and enhanced efficacy. For patients who are in good general condition and can tolerate whole-body hyperthermia, we recommend whole-body medium-high temperature hyperthermia twice a week, with four to six times as a course of treatment for a total of three courses.

6.13.2.3 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increases after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance effect on immunity, and increase the efficacy of medical ozone. Treatment methods: use EBOO once every other day, with 20 times as a course of treatment, or select medical ozone saline infusion once every other day, with 10–14 days as a course of treatment. Use medical ozone major autohemotherapy once every other day, 12 times per course. Use medical ozone minor autohemotherapy once every other day, 12 times per course. Use medical ozone acupoint injection once every other day, with 12 times as a course of treatment. Conduct respective treatment for at least three courses, applicable for long-term maintenance therapy.

6.13.2.4 HYPERTHERMIA AND OTHER TREATMENTS

For kidney cancer cases with recurrence, stage IV or unresectable, biological treatment is applied according to their types: Clear cell type and non–clear cell type. Clear cell type is the principal type: choose high-dose IL-2 and/or sorafenib, sunitinib, interferon (IFN), and other biological agents for treatment; bevacizumab can also be applied in the treatment of medium-advanced renal clear cell carcinoma. Non–clear cell type: sorafenib, sunitinib, and so on can be applied for treatment. Combining with hyperthermia can enhance the effect of immunotherapy during treatment.

Other treatments such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback therapy, and colon cleansing therapy in combination with the application of hyperthermia can increase the effectiveness and safety of treatment.

DC-CIK cell therapy: Kidney cancer is one of the cancers with strong immunogenicity. DC-CIK treatment, especially DC-CIK coincubated with renal cell carcinoma antigen, can effectively control cancer growth as well as inhibit metastasis and recurrence. Adoptive immunotherapy for kidney cancer is the Food and Drug Administration (FDA)'s first approved biological treatment program that is entering the clinical trial stage.

DC-CIK postoperative consolidation therapy: For early kidney cancer, immune cells with specific tumoricidal activity obtained by collecting tumor tissues during radical resection for preparation of individual peptides, which are then cultured together with DC-CIK, are reinfused into the body to effectively remove residuals of small lesions, and the efficacy has been confirmed. The number of CIK cells for each reinfusion should reach at least 1×10^{10}; it should be applied once a month, with four times as a course of treatment. Conduct periodic reviews after transfusion, and if there is no recurrence an additional treatment is carried out once every 6 months.

Combined treatment with chemotherapy: For kidney cancer that cannot be radically resected, after the tumor burden is reduced by freezing, minimal invasion, or other means DC-CIK can also be combined with chemotherapy for application to inhibit cancer progression and to prolong survival time with the presence of cancer. Treatment protocols: one day before chemotherapy collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue the process in this manner, with four consecutive times forming a course of treatment. After efficacy assessment, if it is effective conduct a consolidation therapy every 2 to 3 months.

Systemic biofeedback therapy: Three times a week, with 20 times as a course of treatment. Change to once or twice a week after two to three courses of treatment for long-term treatment.

Colon cleansing therapy: Patients can take fruit and vegetable drinks with the coffee enema, but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support.

6.13.2.5 HYPERTHERMIA AND HERBAL MEDICINES

6.13.2.5.1 Medicated ironing (hot compress)

Proven prescription 1: Take 15 g each of *Angelica sinensis*, *Cinnamomum cassia Presl*, *Evodia rutaecarpa*, *Olibanum*, *Myrrha*, and *Asarum*. Grind to fine powder and fry, and then wrap the mixture with a cloth and put it on the navel for hot compress. Efficacy: dissipates dampness and activates stagnancy, warms meridian and disperses coldness, deoppilates meridians and blood vessels to relieve pain, and regulates qi and blood.

Proven prescription 2: Ginger 120 g, *Evodia rutaecarpa* 90 g, *Zanthoxylum bungeanum* 60 g, *Cinnamomum cassia Presl* 30 g, and onion 30 g. Fry the drugs together. Wrap in cloth and iron the lower back sore area. If it gets cold, fry again. Iron for 30 minutes each time, two to three times a day. Efficacy: warms the kidneys to strengthen yang. It is applicable to patients with lumbago caused by deficiency of kidney after surgery.

6.13.2.5.2 Bath

Proven prescription 1: Ramulus cinnamomi 60 g, *Acanthopanax senticosus* 50 g, and *Glycyrrhiza uralensis* 5 g. Add water to drugs and boil for 30 minutes. Remove slag and take juice. Immerse feet for 30 minutes once

a day, with 10 days as a course of treatment. Efficacy: supplements qi to warm yang. Mainly cures a variety of types of fatigue and is applicable to physical fatigue caused by chronic wasting in cancer patients.

Proven prescription 2: Radix astragali 450 g, *Radix codonopsis* 300 g, *Radix polygoni Multiflori Preparata* 300 g, *Ligusticum chuanxiong Hort* 300 g, *Fructus alpinia Oxyphylla* 300 g, *Semen cuscutae* 300 g, *Atractylodes macrocephala Koidz* 300 g, and *Carthamus tinctorius L.* 200 g. Put all drugs into the wok and add proper amount of water. Boil for 50 minutes. Remove slag and take juice. Blend with 450 g of white wine. Take bubble bath for 40 minutes once a day, with 10 days as a course of treatment. Efficacy: tones lungs, spleen, and kidneys, as well as activating spirit. Mainly cures a variety of types of fatigue and is applicable to physical fatigue caused by chronic wasting in cancer patients.

6.13.2.5.3 Grilling method

Yongquan Plaster: A large and raw *Radix aconiti Lateralis preparata*; a pair of big *syngnathus*; 9 g each of *Lysimachia foenum-graecum*, *Squama manitis*, and *Cynomorium songaricum Rupr*; as well as sesame oil 600 g plus yellow lead 200 g. Boil them into paste, which is mixed well with 15 g each of *Actinolite* and musk and 9 g each of *Cordyceps sinensis*, ginseng, Sichuan pepper, and clove fruit. Spread out 1 g to the size of a coin each time and paste to both sole centers, and then bake for 0.5–1 hour in the affected area with the Magic Lamp. Efficacy: reinforces liver and kidneys. It is applicable to the middle-aged and elderly with disease-producing mass in the abdomen due to renal asthenia and general debility and is applicable to tumors in various parts of the body.

6.13.2.5.4 Moxibustion

It is applicable to cancer patients with long illness, yang deficiency, and weakness for enhancement of immunity.

Acupoints: The first group of acupoints includes Dazhui, Shenshu (both), and Pishu (both). The second group of acupoints includes Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both).

Herbal cake making: Take equal amounts of *Radix astragali*, *Angelica sinensis*, *Fructus psoraleae*, *Curculigo orchioides*, and *rhubarb*, and smash them into powder. Filter with 120 mesh sieve, and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm.

Moxibustion: Place the moxa cone with a diameter of 2 cm and a height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints each time, with two groups of points alternated, once every other day, with 24 times as a course of treatment.

Efficacy: Reinforces spleen and nourishes kidneys for muscularity and general health.

6.13.2.5.5 Steam therapy

Speranskia tuberculata 30 g, *Lycopodii herba* 30 g, *Erythrina variegata* L. 30 g, *Chinese star jasmine stem* 30 g, *Folium Artemisiae Argyi* 30 g, *sappanwood* 20 g, *Carthamus tinctorius L.* 20 g, *Caulis spatholobi* 20 g, *Rhizoma corydalis* 20 g, *Faeces trogopterori* 20 g, *Ramulus cinnamomi* 20 g, *Radix curcumae* 20 g, *Radix angelicae Pubescentis* 20 g, and *Achyranthes bidentata* 20 g. Boil drugs inside a fumigating bed; the patient lies down in the bed for systemic or local fumigation.

6.13.3 Introduction of a typical case

A patient named Xie, male, 40 years old, was admitted on August 7, 2007, to Clifford Hospital due to "postoperative resection of the left kidney cancer for more than 3 years; postoperative kidney transplantation for nearly two years; kidney cancer metastasis and chemotherapy for more than 1 year; abdominal distension and increased bloated legs for 20 days." The patient was treated in 1984 for acute nephritis, which was changed to chronic nephritis. Serum creatinine checked in 1997 was 170 mmol/L, and herbal medicines were given for treatment. In July 2003, creatinine rose to 700 mmol/L and dialysis treatment was conducted. Hematuria appeared at the end of 2003, and no significant occupying lesions were seen on repeated checks. On June 13, 2004, left renal occupation was shown by abdominal CT and left kidney resection was carried out. Postoperative pathology showed "transitional cell carcinoma of renal pelvis." No further treatment was

conducted after surgery. Right kidney transplantation was carried out in September 2005, and the patient started taking cyclosporine for antirejection therapy after surgery. From June 2006, the patient switched to Leipaming for oral administration. Postoperative urine volume remained above 1000 mL daily. In May 2006, the patient had lower back pain and left supraclavicular lymph node metastasis. Chemotherapy was conducted 10 times since June 2006. Abnormal liver function was found during chemotherapy, and hepatic protection treatment was carried out. After femoral venous catheter chemotherapy, the patient showed swellings of the lower limbs, with the right lower limb being more severe. Twenty days before admission, the patient felt abdominal distension, which was aggravated after eating; increased lower limb edemas; no nausea and vomiting; no acid regurgitation; and loose stools and defecation after application of drugs. Since the occurrence of the disease, the patient had been in a negative mental state but without any conscious disturbance and difficulty in sleeping.

Physical examination: A surgical scar about 15 cm in length could be seen at the left and right lower abdomen. There was abdominal distension, and abdominal breathing activities were not limited. Abdominal muscles were soft. Liver and spleen were not palpable. Mild tenderness was in the navel area. Murphy's sign was negative. Transplanted kidney was palpable at the right lower abdomen. Shifting dullness was positive. Moderate pitting edemas were at the lower limbs, which were severe at the right lower extremity. The KPS was 50.

Auxiliary examination: Positron emission tomography (PET)-CT examination, which was done 1 month ago, showed the following: (1) postoperative transitional cell carcinoma of renal pelvis; the left kidney was absent, the right kidney was atrophic with multiple cysts, and the transplanted kidney in the right iliac fossa had normal development. (2) Small high metabolic lesions could be seen at the left supraclavicular fossa, which were considered as small lymph node metastasis foci. (3) Multiple high metabolic lesions could be seen at the side of lesser curvature; hepatic portal area; and retroperitoneal area of the upper, middle, and lower abdomen, which were considered as multiple lymph node metastasis foci. (4) Multiple small high metabolic lesions in the pancreas were considered as pancreatic tumor infiltration. (5) Obsolete inflammation could be seen in the left lung; small calcification foci could be seen in the right lobe of the liver; and small amount of fluid was found in the pelvic cavity. Blood routine: RBC 3.1×10^{12}/L, Hb 101 g/L, WBC 4.65×10^{9}/L, and PLT 97×10^{9}/L. Biochemistry: ALT 34 U/L, AST 37 U/L, TBIL 32 U/L, DBIL 16 U/L, ALB 28 g/L, ALP 89 U/L, GGT 112 U/L, BUN 12.8 mmol/L, Cr 32 μmol/L, Ua 176 μmol/L, and GLU 6.1 mmol/L. Tumor markers were normal. Eight items of immune function were as follows: IgM 12.8 g/L, IgG 4.3 g/L, TG 1.96 mmol/L, GHO 6.13 mmol/L, K^+ 3.7 mmol/L, Na^+ 136 mmol/L, Cl^- 92 mmol/L, and Ca^{2+} 2.01 mmol/L. Trace elements such as copper, zinc, lead, mercury, cadmium, and nickel were normal.

Diagnosis: Kidney cancer (transitional cell carcinoma of renal pelvis of stage IV), postoperative left kidney resection, and postchemotherapy metastasis; postoperative right renal transplantation.

Integrative treatment prescription: The patient was under the conditions of postoperative kidney cancer resection and postchemotherapy multiple metastases as well as postoperative renal transplantation. Kidney cancer is not sensitive to chemotherapy. As a result, multiple chemotherapies for the patient were ineffective and lesions still progressed. Also, immunotherapy could not be applied because the patient had postoperative renal transplantation. Using nontoxic integrative treatment was imperative. First, gave albumin; amino acid 9R compound injection; erythropoietin to support the symptomatic treatment; indwelling peritoneal drainage tube; and levigated *Polyporus umbellatus* 15 g, *Semen plantaginis* 12 g, *Pericarpium arecae* 15 g, *Phytolacca acinosa Roxb* 5 g, *Semen coicis* 15 g, *Rhizoma curcumae* 10 g, and other herbal medicines. Added honey and externally applied at the perinavel region once a day. The patient was with abdominal fullness, particularly at night; difficulty in micturition, anorexia and fatigue, cold extremities with edema, pale complexion, swollen tongue in pale color with a little fur, and thready and weak pulse were present. The differentiation was yang deficiency of spleen and kidney.

Medications: Used herbal medicines such as cooked *Radix aconiti Lateralis Preparata* 6 g (predecocted), *Codonopsis pilosula* 20 g, *Atractylodes macrocephala Koidz* 10 g, *Rhizoma zingiberis* 6 g, *Herba epimedii* 15 g, *Poria cocos* 20 g, *Alisma orientalis* 9 g, *Scutellaria barbata* 30 g, *Semen plantaginis* 9 g, and *Polyporus umbellatus* 10 g for reinforcing spleen and nourishing kidneys as well as inducing diuresis and reducing edema.

At the same time, while local hyperthermia in the abdomen was given chelation detoxification was applied, once every other day, and alternated with EBOO.

Acupuncture: Took Shenshu, Pishu, Sanyinjiaoyin, Zusanli, Guanyuan, Qihai, Zhongji, Taichong, Yinlingquan, Sanchongxue, and Waisanguan. Reinforcement method was used. Retained the needle for 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Took Shenshu, Guanyuan, Zhongji, Zusanli, Sanyinjiao, and Shenque. Took two points each time. Conducted moxibustion on each point for 10 minutes, once a day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Took kidney, bladder, Jiaogan, Pishu, subcortex, Sanjiao, endocrine, and adrenal gland, twice a week, alternating ears.

After 2 weeks of treatment, the symptom of abdominal distension in the patient was reduced. The waist was narrowed. Lower extremity edemas had disappeared. Laboratory tests: Hb 118 g/L, BUN 9.6 mmol/L, ALB 34 g/L, and Ca^{2+} 2.21 mmol/L. A small amount of ascites in the abdominal cavity was shown in ultrasound, which was significantly reduced compared with the amount at the time of admission.

Continued to apply the aforementioned medicines at the umbilical region. At this time, the patient showed red tongue with thin and yellow fur, as well as a thready and rapid pulse. Herbal medicines such as Liuwei Dihuang Decoction plus *Scutellaria barbata*, *Lygodium japonicum*, and *Agrimonia pilosa Ledeb* were applied. Continued to apply chelation detoxification, hyperthermia, medical ozone, acupuncture, and other integrative treatments.

Treatment effects: The patient was hospitalized for 65 days. After 2 weeks of treatment, abdominal distension and lower limb edemas disappeared. Ascites were significantly reduced. The patient's symptoms and signs were significantly improved. Anemia was corrected. Renal function was returned to near normal. Consolidated treatment was continued on this basis. Abdominal CT rechecked before discharge showed that "the number of lymph nodes at the side of lesser curvature, the hepatic portal area and the retroperitoneal area of the upper, middle and lower abdomen were reduced in comparison with those on April 12, and the diameter of the largest was 2 cm, which was narrower than before; the pancreatic metastases was less than before. There was no intra-abdominal effusion." Liver and kidney functions and the five tumor markers were normal. The KPS was 90. After discharge, the patient came back to the hospital regularly for 1 week of treatment per month. Conducted follow-ups for more than 1 year after discharge. The condition became more stable.

6.13.4 Related research in China and abroad

Gervais et al. conducted radio-frequency hyperthermia on 42 renal cell tumors in 34 patients. As a result, 31 exogenous tumors were ablated (the average size was 3.2 cm) and only five had complete radio-frequency hyperthermia out of the remaining 11 because the tumors were located in the renal sinus. The results showed that radio-frequency hyperthermia had a significant treatment effect on endogenous and exogenous tumors with diameters less than 5.0 cm but had poor efficacy on kidney cancer that was partially located in the renal sinus with diameters greater than 3.0 cm. Complications: two cases of minor bleeding, two cases of heavy bleeding, and one case of ureteral blockage.

Onishi et al. conducted treatment on nude mice bearing human cells of kidney cancer with a combination of microwave hyperthermia and interferon; they found that with the combined application of microwave hyperthermia and IFN-α tumors completely disappeared in five mice among 10, and five had prolonged survival times.

An Shixing et al. have conducted short-term efficacy observations on the combined application of high-intensity focused ultrasound and interferon for the treatment of advanced kidney cancer. The results showed that the efficacy assessment of the hyperthermia group by CT review was significantly better than that of the chemotherapy group, and the difference between the two groups was statistically significant ($P < .05$). The short-term efficacy of high-intensity focused ultrasound in combination with interferon was satisfactory for the treatment of advanced kidney cancer. It was safe to use and without significant adverse reactions.

6.14 BLADDER CANCER

Bladder cancer is a kind of cancer that originates in the bladder mucosa, mainly in the bladder trigone, both sides of the wall, and the neck. Bladder transitional cell carcinoma accounts for more than 90% of all bladder cancers, whereas adenocarcinoma, squamous cell carcinoma, and leiomyosarcoma are rare. Bladder cancer is mainly exhibited as lymph node metastasis and local spread, and blood dissemination can be found at the advanced stage.

Painless gross hematuria is the most common symptom and it can appear in more than 80% of patients, 17% of which have severe hematuria, but there are 15% that may begin with only microscopic hematuria. Hematuria mostly occurs throughout the whole process with intermittent seizures and can also be manifested as initial hematuria or terminal hematuria. Urinary frequency, urgency, dysuria, and other irritation signs of the bladder can appear, and urinary tract obstruction, bladder pain, lower limb edema, and other symptoms may also occur in advanced patients. The common sites of distant metastases are liver, lung, and bone.

6.14.1 Conventional treatments

6.14.1.1 SURGERY

Bladder cancer treatment focuses on surgical excision. Surgical treatments are divided into transurethral resection of cancer, bladder incision to remove cancer, partial cystectomy, and radical cystectomy. An appropriate surgical approach is chosen according to pathology of the cancer, cancer location, and general condition of the patient. The standard treatment of early cancer is traditional surgery or endoscopic complete resection. Radical cystectomy and colonic bladder replacement can be carried out for cancers that are too big or too difficult for endoscopic resection or recurrent cancers.

6.14.1.2 RADIOTHERAPY

Radiotherapy has been defined as an exact treatment of bladder transitional cell carcinoma or as adjuvant therapy after cystectomy. The main advantage of radiotherapy is that it may retain normal bladder function and sexual function. Furthermore, radiotherapy is also an option for patients who are not suitable for surgical treatment. For patients who select radiotherapy, it is possible to preserve the bladder by combining neoadjuvant chemotherapy and radiotherapy. The purpose of preoperative or postoperative radiotherapy is to prevent local recurrence.

6.14.1.3 CHEMOTHERAPY

Chemotherapy is most commonly used in treating metastatic bladder cancer, or locally advanced bladder cancer that cannot rely on surgical resection. Systemic chemotherapy can be applied as neoadjuvant chemotherapy for preoperative bladder cancer, postoperative adjuvant chemotherapy, and palliative chemotherapy for advanced metastatic bladder cancer. For early patients with a tendency toward formation of new lesions in the bladder, preventive or adjuvant intravesical chemotherapy can be applied. Perfusion drug options are bacillus Calmette-Guérin, interferon, sapylin, and Brucea Javanica oil, which are comparatively effective immune agents. For advanced bladder cancer patients with metastasis, systemic chemotherapy may be considered.

6.14.1.4 HYPERTHERMIA

Hyperthermia combined with radiotherapy or chemotherapy has synergistic killing effect on cancer cells. Clinical application has shown that hyperthermia combined with radiation or chemotherapy may further improve efficacy. Heat therapies for bladder cancer are bladder irrigation with hot water, radiation diathermy by intrabladder microwave, surface diathermy by RF, and high-energy focused ultrasound method, in which the latter two are most commonly used.

6.14.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can improve immune function, has synergistic effect when combined with surgery and intravesical chemotherapy, and has great significance in the prevention of cancer recurrence and metastasis; it is conducted once every other day, with 12 times as a course of treatment. Alternate it with medical ozone systemic therapy.

6.14.1.6 MEDICAL OZONE THERAPY

EBOO is preferred once every other day, with 20 times as a course of treatment. Medical ozone saline can be used for rinsing the bladder after surgery and with intravesical chemotherapy, which not only can relieve frequent urination, dysuria, and other symptoms after perfusion but also has the effects of directly killing residual tumor cells, sterilization, and inhibition of tumor recurrence. At the same time, medical ozone gas acupoint injection can be implemented once every other day, with 12 times as a course of treatment. The selection of points is the same as with acupuncture. For patients in poor physical conditions and with coagulation dysfunction, intravenous medical ozone saline can be used once every other day, with 12 times as a course of treatment, or medical ozone major autohemotherapy can be used once every other day, with 12 times as a course of treatment. At the same time, giving medical ozone saline to rinse bladder and medical ozone gas rectal insufflation have a good effect of controlling bleeding and infection and inhibiting further growth of cancer.

6.14.1.7 TRADITIONAL CHINESE MEDICINE

The syndrome differentiation of early bladder cancer belongs to insufficiency of kidney qi, and the prescription recommended is modified ginseng and Clamshell Powder. For the syndrome of stagnation of qi due to depression of the liver, the prescription recommended is modified Chenxiang Powder. For the syndrome of deficiency of spleen qi, the prescription recommended is modified Buzhong Yiqi Decoction. For the syndrome of dampness invasion of lower energizer, the prescription recommended is modified Bazheng Powder. The syndrome differentiation of advanced bladder cancer belongs to deficiency of spleen and kidney. The prescriptions recommended are modified Siwu Decoction plus modified Zuogui Decoction. For the syndrome of internal heat due to yin deficiency, the prescription recommended is modified Zhibai Dihuang Decoction. For the syndrome of blood stasis obstructing in the interior, the prescription recommended is modified Taohong Siwu Decoction.

6.14.1.8 ACUPUNCTURE

The main syndrome of early bladder cancer is dampness invasion of lower energizer, and the therapeutic principle should focus on clearing heat and eliminating dampness as well as regulating the lower Jiao.

Acupuncture on acupoints: Pangguangshu, Yinlingquan, Weiyang, Zhongji, Sanyinjiao, Shuidao, Baihuanshu, and Tianshu.

Methods: Even reinforcing–reducing method is used for acupuncture; retain needle for 20 minutes once a day; and take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The main syndrome of medium-advanced bladder cancer is deficiency of both spleen and kidney. The therapeutic principle should focus on invigorating spleen for eliminating dampness, as well as regulating and reinforcing liver and kidneys.

Acupuncture on acupoints: Yinlingquan, Zhongji, Sanyinjiao, Taixi, Shenshu, Zusanli, and Guanyuan.

Methods: Even reinforcing–reducing method is used for acupuncture; retain needle for 20 minutes once a day; and take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Pangguangshu, Sanyinjiao, Guanyuan, Shenmai, and Kunlun. For excess syndrome, add Zhongji and Fuliu for moxibustion. For deficiency syndrome, add Shenshu, Pishu, and Sanjiaoshu for moxibustion. Methods: take two points each time. Conduct moxibustion with the moxa stick for 10 minutes on each point, once a day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Bladder, Shenmen, Jiaogan, endocrine, subcortex, spleen, and kidney.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.14.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Most patients at the early stage have acceptable general conditions, with no significant malnutrition and with normal diet, so it is recommended to give herbal diet therapy as the adjuvant treatment. Appropriately add trace elements and vitamins to improve immunity. For advanced bladder cancer patients with weight loss, poor eating or without eating, intestinal obstruction, and other symptoms, total parenteral nutrition therapy should be considered to enhance physical conditions and disease resistance.

6.14.1.10 OTHERS

Guide early-stage patients to practice qigong, tai chi, and so on, as well as to conduct aerobic exercise with relatively mild exertion, combined with music, psychology, and other therapies to adjust the patients' states of mind to improve the cure rate. For medium-advanced patients, qigong, music, sports, psychology, and other therapies can complement each other along with the aforementioned integrative treatments, which help to activate or enhance the patients' own immune systems to monitor and inhibit cancer, stabilize state of mind, improve sleep, and improve survival quality.

6.14.2 Combination of hyperthermia with conventional treatments

6.14.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

The standard treatment of early cancer is traditional surgery or endoscopic complete resection. Preoperatively and postoperatively intravesical therapy should be applied. Radical cystectomy and colonic bladder replacement can be carried out for cancers that are too big or too difficult for endoscopic resection, or early recurrent cancer. After the postoperative wound is completely healed, hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests disclosing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician.

For early patients in good general condition, whole-body medium-high temperature hyperthermia can be given as far as possible, with six times as a course for whole-body hyperthermia, once every 10–14 days for a total of three courses. For patients who cannot tolerate whole-body medium-high temperature hyperthermia, whole-body medium-low hyperthermia can be carried out once a week for a total of 10 times.

6.14.2.2 HYPERTHERMIA AND RADIOTHERAPY

RF diathermy combined with radiotherapy is suitable for larger masses of cancer. The effect is better if the cancer is located in the anterior wall and side wall of the bladder and less effective if the cancer is located in the bladder neck and the triangular space. It shows good effect for a single focus of cancer and poor effect for multiple foci. Hyperthermia is conducted within 2 hours before or after radiotherapy and hyperthermia duration is 60 minutes each time, once every other day, with six to eight times as a course of treatment. Radiotherapy should be carried out first and then therapeutic diathermy to reduce any radiation reaction of the skin. The sequence of radiotherapy and hyperthermia treatment has had no significant effect on efficacy. The first course of hyperthermia should be maintained until 2 weeks after the end of radiotherapy. Change to whole-body hyperthermia during the rehabilitation period.

6.14.2.3 HYPERTHERMIA AND CHEMOTHERAPY

For postoperative bladder cancer, systemic chemotherapy is generally not considered and intravesical chemotherapy is mostly applied. Generally, intravesical chemotherapy combined with local hyperthermia is carried out. Chemotherapy drugs are retained for 2 hours before discharge. During the whole process of

the treatment, intravesical chemotherapy should be applied for more than 20 times, lasting for 2 years or so. It is recommended that after each hyperthermic chemo perfusion, local hyperthermia should continue to be carried out once every other day for at least more than two times, which can enhance the efficacy of infusion chemotherapy.

If patients are assessed to be in good general condition and can tolerate whole-body hyperthermia during infusion chemotherapy treatment, whole-body medium-high temperature hyperthermia is recommended twice a week for a total of 8 to 10 times. For patients who cannot tolerate whole-body medium-high temperature hyperthermia, whole-body medium-low hyperthermia can be carried out once a week for a total of 10 times.

6.14.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification, medical ozone, and other therapies can be given from the end of bladder cancer operation to the start of chemotherapy, which can promote physical recovery and regulate immunity. Generally, conduct chelation detoxification therapy once every other day, with 20 times as a course of treatment, for a total of three courses. Chelation detoxification needs infusion of more than 2 hours, and if there is absence of adverse reactions gradually increase the therapeutic dosage. Hyperthermia can be applied simultaneously with chelation detoxification to improve efficacy.

6.14.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing tumor cells, enhance effect on immunity, and increase the efficacy of medical ozone. Select EBOO once every other day, with 20 times as a course of treatment. Medical ozone saline can be used for rinsing the bladder after surgery, with intravesical chemotherapy, which not only can relieve frequent urination, dysuria, and other symptoms after perfusion but also has the effects of directly killing residual cancer cells, sterilization, and inhibition of cancer recurrence. At the same time, medical ozone gas point injection can be implemented once every other day, with 12 times as a course of treatment. The selection of points is the same as with acupuncture.

6.14.2.6 HYPERTHERMIA AND OTHER TREATMENTS

Bladder cancer is mostly prone to local recurrence. Combined TCM, acupuncture, systemic biofeedback treatment, alkaline treatment, and colon cleansing therapy can reduce cancer recurrence and metastasis and combined with hyperthermia can increase the efficacy and safety of treatment.

Systemic biofeedback therapy: Conduct three times a week for 15 times as a course of treatment. Adjust to once or twice a week after two to three courses of treatment for long-term treatment.

Alkaline treatment: Dietotherapy or sodium bicarbonate intravesical instillation can be applied to alkalize the body. Sodium bicarbonate intravesical instillation uses 5% sodium bicarbonate solution poured into the bladder and the treatment mode is the same as that with bladder hyperthermic peritoneal perfusion chemotherapy, which is mostly used for patients who cannot tolerate hyperthermic peritoneal perfusion chemotherapy or during the intervals of hyperthermic peritoneal perfusion chemotherapy.

Colon cleansing therapy: Patients can take fruit and vegetable drinks with the coffee enema, but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support.

6.14.2.7 HYPERTHERMIA AND HERBAL MEDICINES

6.14.2.7.1 Bath

Proven prescription 1: Sappanwood 50 g, *Camphora* 50 g, *Ramulus cinnamomi* 15 g, old *Radix lithospermi* 15 g, *Fructus liquidambaris* 15 g, *Rhizoma homalomenae* 15 g, *Lycopodii herba* 15 g, *Olibanum* 10 g, *Myrrha* 10 g, *Carthamus tinctorius L.* 10 g, *Chaenomeles speciosa Nakai* 10 g, and *Rubus obcordatus* 10 g. Decoct the mixture with water, and immerse (wash) joints of the affected part in the hot decoction. Efficacy: promotes blood circulation to dispel cold and remove meridian obstruction. It is applicable to patients with the syndrome of joint and bone pain caused by bone metastatic carcinoma.

Proven prescription 2: Rhizoma cyperi Rotundus L. 10 g, *Angelica sinensis* 10 g, *Myrrha* 10 g, *Natrii suleas* 10 g, *Cortex acanthopanacis* 10 g, *Pericarpium citri Reticulatae Viride* 10 g, *Zanthoxylum bungeanum Maxim.* 10 g, clove 3 g, musk 0.3 g, old Shallot 3 g, *Cortex lycii* 3 g, and *Cortex moutan* 6 g. Decoct the mixture with water, and immerse (wash) joints of the affected part in the hot decoction. Efficacy: promotes blood circulation to dispel cold and remove meridian obstruction. It is applicable to patients with the syndrome of joint and bone pain caused by bone metastatic carcinoma.

6.14.2.7.2 Grilling method

Proven prescription: Fructus gleditsiae Abnormalis 30 g, honey 15 g. *Grind Fructus gleditsiae Abnormalis* into fine powder and blend with honey. Pour into the umbilical hole. Heat the navel with Magic Lamp (a kind of specialized heating device commonly used in TCM thermal therapies) once a day and for 30 minutes each time. Efficacy: activates blood circulation and resolves mass, as well as relieving stuffy nose and eliminating metabolic waste. It is applicable to bladder cancer with the syndrome of phlegm and blood stasis.

6.14.2.7.3 Moxibustion

Proven prescription 1: Dazhui, Shenshu (both), and Pishu (both). The second group of points is as follows: Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both). Take equal amounts of *Radix astragali*, *Angelica sinensis*, *Fructus psoraleae*, *Curculigo orchioides*, and *rhubarb*, and smash them into powder. Filter with 120 mesh sieve, and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm. Place the moxa cone with a diameter of 2 cm and a height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints each time, alternating the two groups of points, once every other day, with 24 times as a course of treatment. Efficacy: reinforces spleen and nourishes kidneys for muscularity and general health. It is applicable to cancer patients with long illness, yang deficiency, and weakness for enhancement of immunity.

Proven prescription 2: Lettuce moxibustion therapy: take proper amount of lettuce, and after mashing mix with salt. Fill it into the navel and conduct moxibustion with three medium moxa cones on it, three times a day. Efficacy: warms stomach, relaxes the bowels, resolves mass, and promotes urination and clears stagnation. It is applicable to uroschesis caused by advanced bladder cancer.

6.14.3 Introduction of a typical case

A patient named He, male, 31 years old, was admitted on November 20, 2006, to Clifford Hospital due to "intermittent gross hematuria for more than 3 years." From October 2003, the patient began to have intermittent gross hematuria, like water after washing meat, about once per month, mostly after activities, and with total hematuria. Hematuria may disappear on its own, with no dysuria and no waist and abdominal pain and discomfort. Later, the patient came to Clifford Hospital for confirmation of diagnosis and treatment. Bladder CT examination showed a cauliflower-like mass of 4.2 cm × 3.2 cm in the left rear wall of the bladder and no pelvic lymph node metastasis was found. The mental state of the patient was acceptable, with normal diet, poor sleep, and normal stool.

Physical examination: There were no positive signs. The KPS was 90.

Auxiliary examination: B-mode ultrasound showed bladder-occupied lesion. A cauliflower-like tumor of 3 cm × 2.5 cm with pedicle was found under cystoscopy, located at the left side of the bladder wall and approximately 1.5 cm from the left ureteral orifice. It was reported as bladder transitional cell papilloma. Blood routine test: RBC 4.2×10^{12}/L, Hb 123 g/L, WBC 5.2×10^{9}/L, and PLT 156×10^{9}/L. Biochemistry: ALT 24 U/L, AST 16 U/L, TBIL 27 U/L, DBIL 11 U/L, ALB 39 g/L, ALP 33 U/L, GGT 31 U/L, Cr 47 μmol/L, Ua 159 μmol/L, BUN 5.1 mmol/L, and GLU 4.25 mmol/L. Electrolytes and blood lipids were normal. Tumor markers: CEA 3.2 ng/mL, AFP 6.5 ng/mL, CA-125 6 U/mL, CA-153 2.5 U/mL, CA-l99 6 mL/L, TSGF 6.24 U/mL, IgM 8.6 g/L, TG 1.55 mmol/L, GHO 6.42 mmol/L, K^+ 3.65 mmol/L, Na^+ 139 mmol/L, Cl^- 99 mmol/L, and Ca^{2+} 2.3 mmol/L. Trace elements such as copper, zinc, lead, mercury, cadmium, nickel, and others were normal.

Diagnosis: Bladder transitional cell carcinoma of level 1 to 2.

Integrative treatment prescription: Performed preoperative preparation after admission. Transurethral resection of bladder tumor was carried out. Bladder transitional cell carcinoma of level 1 to 2 was reported in the postoperative pathology. The bladder was rinsed with medical ozone saline after surgery for 1 consecutive week. After treatment, contraindications were excluded by hospital experts' consultation, and whole-body hyperthermia combined with intravesical chemotherapy was conducted in the fifth week after surgery and mitomycin 40 mg each time was applied once a week for a total of eight times. Whole-body medium-high temperature hyperthermia was conducted at the first and fifth times and local hyperthermia was carried out once every other day. Later, this was changed to whole-body hyperthermia and intravesical chemotherapy once a month for a total of 12 times. Chelation detoxification therapy, medical ozone, TCM, acupuncture, and other integrative treatments were given in combination. The patient had symptoms including frequent and urgent micturition, burning in urinary canal, tongue with yellow fur, and gliding and quick pulse, which were collectively referred to as "damp invasion of lower energizer" syndrome in TCM. The therapeutic principle should focus on clearing heat and eliminating dampness, as well as cooling blood to stop bleeding.

Medications: The prescription recommended was modified Bazheng Powder. Specific medication: *Pink Herb* 15 g, *Polygonum aviculare* 15 g, *Semen plantaginis* 10 g, *Herba pyrrosiae* 15 g, *talc* 20 g, *Medulla tetrapanacis* 10 g, *rhubarb* 6 g, *Gardenia jasminoides Ellis* 10 g, *Glycyrrhiza uralensis root tip* 6 g, *Sophora flavescens Ait* 15 g, *Radix rehmanniae* 30 g, *Pollen typhae* 10 g, and *Herba cirsii* 15 g, one dose a day. Decoct with water for oral administration.

Acupuncture on acupoints: Yinlingquan, Zhongji, Sanyinjiao, Taixi, Shenshu, Zusanli, Guanyuan, and Waisanguan. Methods: even reinforcing–reducing method was used for acupuncture. Retained the needle for 20 minutes, once a day. Took 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Pangguangshu, Sanyinjiao, Guanyuan, Shenshu, Pishu, and Sanjiaoshu. Methods: took two points each time. Conducted moxibustion with a moxa stick for 10 minutes on each point, once a day. Took 2 days off after five treatments of moxibustion, with 10 treatments as a course of treatment.

Auricular acupoints: Bladder, Shenmen, Jiaogan, endocrine, subcortex, spleen, and kidney. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

Treatment effects: The patient was in stable condition without hematuria. No abnormalities were shown by regular cystoscopy. CT examination showed no signs of recurrence and metastasis. The test results showed no abnormalities. One year later, the patient started coming back to the hospital for 1 week of integrative treatments every 3 months. Treatment options were whole-body hyperthermia, chelation detoxification, medical ozone, TCM, acupuncture, and so on. The patient has been in good physical condition for more than 6 years. His KPS was 100. Periodic reviews are conducted.

6.14.4 Related research in China and abroad

Colombo et al. have reported that intravesical local hyperthermia combined with chemotherapy can achieve better effects of prevention and treatment of superficial bladder transitional cell carcinoma.

Li Penghui has conducted clinical observation on the application of high frequency hyperthermia combined with intravesical instillation of Pirarubicin to prevent postoperative recurrence of bladder cancer. The results showed that high frequency hyperthermia combined with intravesical instillation of Pirarubicin can delay the recurrence time, can reduce the relapse rate, has no significant adverse reactions, and can improve the quality of life of patients compared with Pirarubicin chemotherapy alone.

Xu Ping has applied modified Polypori Umbellati Decoction combined with 41.8°C whole-body hyperthermia in the treatment of advanced bladder cancer and has conducted clinical observation of 43 cases, of which 16 cases had marked effectiveness, accounting for 37.3%; 17 cases had no changes, accounting for 39.7%; and 10 cases had progressed, accounting for 23.0%.

Xu Peiyuan et al. have applied Rabdosia liquid hyperthermia combined with mitomycin intravesical therapy for the treatment of superficial bladder cancer recurrence and have conducted a nonrandomized concurrent control study. The results showed that the effect of Rabdosia liquid hyperthermia for the prevention of superficial bladder transitional cell carcinoma recurrence was reliable.

Zhu Yunsheng et al. have applied high frequency hyperthermia combined with mitomycin intravesical instillation for preventing the recurrence of bladder cancer and have conducted clinical observation, with the results showing that 3-year and 9-year recurrence rates of hyperthermia combined with mitomycin intravesical instillation and mitomycin-alone intravesical instillation were 25% and 45% and 50% and 85%, respectively. The difference was statistically significant ($P < .01$). The relapse time of high-frequency hyperthermia combined with intravesical instillation of mitomycin chemotherapy was delayed and recurrence rate was low compared with mitomycin chemotherapy alone. There were significant clinical significances for improving the quality of life and prolonging survival time.

6.15 PROSTATE CANCER

Prostate cancer is a common cancer in men, with incidences growing at an annual rate of 3%. The incidence is increased with age and the mortality rate is about 20%, characterized by obvious geographical and ethnic differences in the incidence rate. It is the highest in the regions of the Caribbean and Scandinavia and the lowest in China, Japan, and other countries. Prostate cancer rates of African-Americans are the highest in the world. The cause of prostate cancer is not clear so far and is associated with the impact of prostatic gonorrhea, virus and chlamydia infections, sexual activity intensity, and hormones. In addition, a high-fat diet and occupational factors (too much exposure to cadmium) also have certain relationships with the onset.

Early prostate cancer can have no warning symptoms other than elevated serum PSA values found by screening and (or) prostatic abnormal changes found by digital rectal examination. Once the symptoms appear, it often has become late progressive prostate cancer. It manifests as progressive dysuria (urinary thinned, urinary skewed, urinary bifurcated, or urinary prolonged), urinary frequency, urgency, dysuria, and vesical tenesmus. When it is severe, urinary dribbling and urinary retention occur. For advanced progressive prostate cancer, fatigue, weight loss, body pain, and other symptoms may appear. Because pain seriously affects diet, sleep, and mentality, in the long term the general condition is increasing frailty with weight loss, fatigue, and anemia, ultimately systemic failure and cachexia.

The treatment of early prostate cancer includes radical prostatectomy, radical radiotherapy, and watchful waiting; the treatment of advanced cancer mostly applies palliative treatment such as endocrine therapy and chemoradiotherapy. Because surgery can lead to urinary incontinence and impotence, radiotherapy may be complicated by acute gastrointestinal reactions, sexual dysfunction, urinary symptoms, urethral stricture, urinary incontinence, as well as genital and lower extremity edema. Endocrine therapy can only kill the hormone-dependent cancer cells and narrow cancer and prostate volume; it cannot completely eliminate it. The side effects of chemotherapy are significant with poor efficacy. In recent years, people have begun to look for new treatments with effectiveness and with fewer side effects and hyperthermia is one of them.

6.15.1 Conventional treatments

6.15.1.1 SURGERY

Radical prostatectomy (referred to as radical resection) is the most effective method for the treatment of localized prostate cancer, with three main operations, namely, traditional perineal, retropubic, and laparoscopic radical prostatectomy, developed in recent years. Timing of surgery: patients with transrectal biopsy should wait for 6–8 weeks, and patients with transurethral resection of prostate should wait for 12 weeks before surgery, so as to avoid the inflammatory response causing rectal and surrounding tissue damage. Also, nerve-sparing surgery is easier. In addition, percutaneous cryoablation has accurate positioning, minimal trauma during surgery, and good postoperative recovery. It has also been widely used clinically.

6.15.1.2 RADIOTHERAPY

Radiotherapy for prostate cancer patients has many advantages such as good efficacy, broad indications, and fewer complications and is suitable for all patients at each stage. The local control rate and 10-year disease-free survival rate of early patients ($T_{1\text{-}2}N_0M_0$) through radical radiotherapy are similar to those of radical

prostatectomy. The therapeutic principle of locally advanced prostate cancer ($T_{3-4}N_0M_0$) focuses on adjuvant radiotherapy and endocrine therapy. Palliative radiotherapy can be carried out for metastatic cancer to relieve symptoms and improve quality of life. In recent years, three-dimensional conformal radiotherapy and intensity-modulated radiotherapy are increasingly used in prostate cancer treatment and have become mainstream technologies in radiotherapy. Prostate cancer pelvic spread or lymph node metastasis can lead to pelvic pain, constipation, lower limb swelling, ureter blockage or hydronephrosis, and so on. Palliative radiotherapy can significantly improve these symptoms. Palliative radiotherapy for bone metastases of prostate cancer can significantly alleviate the symptoms of pain and spinal cord compression.

6.15.1.3 CHEMOTHERAPY

It is applied for endocrine-refractory metastatic prostate cancer patients to delay cancer growth and prolong the lives of patients. Studies have confirmed that docetaxel can effectively prolong the survival time of endocrine-refractory metastatic prostate cancer patients, whereas cabazitaxel can further extend the survival time of patients failed by the treatment of docetaxel. Many clinical trials are studying new drugs and drug combinations, aiming to find treatment means with more effectiveness and less adverse reactions.

6.15.1.4 ENDOCRINE THERAPY

Prostate cells without androgen stimulations will undergo apoptosis. Any treatment of androgen activity inhibition may be referred to as androgen deprivation therapy. Deprivation of androgen is primarily through the following strategies: (1) inhibition of testosterone secretion: surgical castration or medical castration (luteinizing hormone–releasing hormone analogs [LHRH-A]). (2) Block combination of androgen with receptor: application of antiandrogen drugs competitively closes the combination of androgen and prostate cells androgen receptor. The combination of the two can achieve the purpose of maximum androgen blockage. Other strategies include inhibition of adrenal gland source androgen synthesis as well as inhibition of the conversion of testosterone to dihydrotestosterone, and so on. Endocrine therapy aims to reduce the concentration of androgen in the body, inhibit adrenal gland source androgen synthesis, inhibit the conversion of testosterone to dihydrotestosterone, and block the combination of androgen with its receptor so as to suppress or control prostate cancer cell growth. Endocrine therapy methods include the following: castration, maximum androgen blockage, intermittent hormonal therapy, neoadjuvant endocrine therapy before radical treatment, and adjuvant endocrine therapy.

6.15.1.5 HYPERTHERMIA

Prostate cancer is mainly adenocarcinoma, and hyperthermia combined with radiotherapy may improve the outcome. In recent years and among prostate hyperthermias, in addition to conventional local hyperthermia there are still other heating technologies focusing on local ultrahigh temperatures such as microwave, radio frequency, ultrasound, and so on. Hyperthermia can directly promote tumor cell apoptosis, inhibit continuous proliferation of primary or secondary lesions, and inhibit metastasis and has a better therapeutic effect on prostate cancer and benign prostatic hyperplasia. It is recommended to apply whole-body hyperthermia and local hyperthermia alternately. Conduct whole-body hyperthermia once every 10–14 days, with six times as a course of treatment. Conduct local hyperthermia once every 2 days, with 20 times as a course of treatment. Simultaneously applying chelation detoxification therapy can have a synergistic effect; but be sure to avoid simultaneous application with medical ozone therapy, and it is best to have an interval of 2 hours or more. Hyperthermia can be carried out as long-term maintenance therapy.

6.15.1.6 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can improve immune function; can reduce chemoradiotherapy side effects such as nausea, vomiting, diarrhea, loss of appetite, weakness, fatigue, leukopenia, thrombocytopenia, and alopecia; and has the effect of directly killing cancer cells to induce cancer cell apoptosis, which is of great significance for prevention of tumor recurrence and metastasis. Usage: conduct hyperthermia at the same time as far as possible, once every other day with 20 times as a course of treatment. For medium-advanced patients whose physical conditions are not suitable for chemoradiotherapy, chelation detoxification therapy

can be strengthened to alternate with chemotherapy, once every other day with 20 times as a course of treatment. After the condition becomes stable, treatment frequency and therapeutic dose can be gradually reduced and, finally, chelation detoxification is given for long-term health treatment with a base quantum maintained to ensure that patients survive with cancer.

6.15.1.7 MEDICAL OZONE THERAPY

EBOO is preferred once every other day, with 20 times as a course of treatment. Be sure to conduct chelation detoxification alternately and avoid scheduling treatment on the same day. Carry out systemic medical ozone treatment and at the same time give medical ozone acupoint injection, once every other day or once every 3 days, with 12 times as a course of treatment for a total of four courses. Because medium-advanced prostate cancer patients have been shown to have physical weakness, select medical ozone saline intravenous infusion as the first treatment. After one or two times, carry out EBOO as the strengthened treatment two to three times a week. For patients with moderate physical weakness or accompanied by coagulation disorder, intravenous medical ozone saline is applied once every other day or ozone minor autohemotherapy is applied once every other day. It is recommended for long-term application without treatment restrictions.

6.15.1.8 TRADITIONAL CHINESE MEDICINE

For the syndrome of damp invasion of lower energizer, the prescription recommended is modified Bazheng Powder; for the syndrome of unconsolidation of renal qi, the prescription recommended is modified Jinkui Shenqi Pill; for the syndrome of kidney yang deficiency, the prescription recommended is modified Zuogui Decoction; for the syndrome of deficiency of kidney yin, the prescription recommended is modified Liuwei Dihuang Pill; and for the syndrome of stagnation of blood and toxic stasis, the prescription recommended is Wuwei Xiaodu Decoction.

6.15.1.9 ACUPUNCTURE

The main syndrome of early prostate cancer is damp invasion of lower energizer, and the therapeutic principle should focus on clearing heat and eliminating dampness as well as opening up qi movement.

Acupuncture on acupoints: Yinlingquan, Sanyingjiao, Pangguangshu, Zhongji, Shenshu, and Guanyuan.

Methods: Reinforcing method is used. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course.

The main syndrome of medium-advanced prostate cancer is the deficiency of both spleen and kidney qi and the therapeutic principle should focus on enforcing spleen and nourishing kidney, as well as reinforcing lower Jiao.

Acupuncture on acupoints: Shenshu, Pangguangshu, Pishu, Zusanli, Sanyinjiao, Taixi, Guanyuanshu, and Sanjiaoshu.

Methods: Reinforcing method is used. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course.

Moxibustion acupoints: Guanyuan, Zhongji, Shenque, Zusanli, and Guanyuanshu.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Prostate, kidney, bladder, urethra, Sanjiao, subcortex, endocrine, spleen, and Jiaogan.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.15.1.10 MEDICATED DIET, NUTRITION, AND SO ON

Early nutritional support focuses on an herbal diet. Rationally complement with amino acids, digestive enzymes, and trace elements. For medium-advanced cancer patients who can eat, a medicated diet is to be given continuously and amino acids, trace elements, and so on are appropriately supplemented; for patients who are restricted in eating or totally unable to eat, total parenteral nutrition should be given as much as possible to ensure an adequate supply of nutrition and energy.

6.15.1.11 OTHERS

Actively practice qigong, and rationally do exercise. Aerobic exercise requiring relatively low physical strength can be conducted. Adjusting attitude and maintaining a good state of mind can achieve the best prognosis. For medium-advanced patients, we should urge to actively practice qigong, give psychological music therapy, and so on to regulate emotions and guide them to have peace of mind and to overcome panic and desperation as well as to relieve psychological pressure so that they can face the disease with a positive, optimistic, and open-minded attitude.

6.15.2 Combination of hyperthermia with conventional treatments

6.15.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Whole-body medium temperature hyperthermia or local hyperthermia can be carried out after the postoperative wound is completely healed, excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, getting laboratory tests revealing no bleeding tendency, and a comprehensive assessment of the patient by the hyperthermia center physician. For patients who have been evaluated to be in good general condition and can tolerate whole-body hyperthermia, whole-body medium-high temperature hyperthermia can be carried out for a total of six times. Be sure to monitor body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Local hyperthermia can be added during the intermission periods of whole-body hyperthermia. For patients who cannot tolerate whole-body medium-high hyperthermia, prostatic local hyperthermia or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, with 20 times as a course of treatment. Local hyperthermia can be a long-term concomitant treatment. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

Some advanced patients choose castration as the surgical option. If the prostate tumor is not resected, according to postoperative evaluation of the general condition, whole-body hyperthermia and local hyperthermia may be given.

6.15.2.2 HYPERTHERMIA AND RADIOTHERAPY

Most of the advanced prostate cancers are accompanied by bone metastases and other distant metastasis and have lost the opportunity for radical surgery. For patients with clear indications after assessment, external radiotherapy can be implemented, simultaneously conducting local or whole-body hyperthermia with radiotherapy to enhance the effect of radiotherapy and reduce radiotherapy side effects. Hyperthermia heating destroys cancer tissue structure without being affected by cancer histologic properties and can be applied in prostate cancer progression and recurrence. The key is to make the cancer and the cancer areas that are not sensitive to chemoradiotherapy reach an effective temperature of not less than 42.5°C, while the surrounding tissue, including subcutaneous tissue, is less affected or not affected.

The combination order of radiotherapy–hyperthermia is appropriate. Conduct local hyperthermia within 2 hours after radiotherapy, once every other day. It is appropriate if local hyperthermia is conducted once every other day in combination with radiotherapy for the whole process. Hyperthermia of the first course is maintained till 2 weeks after the end of radiotherapy. Adjust to whole-body hyperthermia during the recovery period.

6.15.2.3 HYPERTHERMIA AND CHEMOTHERAPY

Chemotherapy can be used after endocrine therapy has failed in prostate cancer, but the efficacy of chemotherapy is poor. In most cases, endocrine therapy needs to be combined to achieve a certain effect. Combined hyperthermia can improve the efficacy of chemotherapy to a certain extent.

The application of different types of hyperthermia depends on the body condition of the patient. It is recommended to apply whole-body hyperthermia and local hyperthermia alternatively. Whole-body hyperthermia applies whole-body medium-high temperature hyperthermia once every 10–14 days, with six times as a

course of treatment. Conduct local hyperthermia once every 2 days, with two times as a course of treatment. After three courses, local hyperthermia can be taken as long-term accompanying treatment. For patients who cannot tolerate whole-body medium-high hyperthermia, whole-body low temperature hyperthermia can be carried out once a week for a total of 12 times.

6.15.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

During the period of radiotherapy for cancer patients, chelation detoxification, medical ozone, and other therapies may be applied, on the one hand, to promote physical recovery and regulate the immune system and, on the other hand, to kill residual cancer cells or to inhibit early metastasis. Chelation detoxification adopts intravenous infusion, which needs to last for more than 2 hours once every other day, with 20 times as a course of treatment for a total of three courses. The therapeutic dose can be gradually increased if there is an absence of adverse reactions. Local hyperthermia or whole-body hyperthermia can be simultaneously applied with chelation detoxification to improve efficacy.

6.15.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patients' blood circulation is accelerated and cell activity increased after hyperthermia. It is proposed that medical ozone therapy be carried out within 2 hours after hyperthermia. EBOO is preferred once every other day, with 20 times as a course of treatment for a total of three courses. But be sure to conduct chelation detoxification alternately and avoid scheduling treatment on the same day. Carry out systemic medical ozone treatment and at the same time give medical ozone acupoint injections once every other day or once every 3 days, with 12 times as a course of treatment for a total of four courses, which can increase the effect of killing cancer cells, enhance the effect on immunity, and increase the efficacy of medical ozone.

6.15.2.6 HYPERTHERMIA AND ENDOCRINE THERAPY

Prostate cells will undergo apoptosis without androgen stimulations. As a result, endocrine therapy is the main treatment for prostate cancer. The combination of hyperthermia and endocrine therapy can cause prostate cancer cell apoptosis in different ways and effectively improve the efficacy for prostate cancer.

Local hyperthermia is carried out during endocrine therapy for prostate cancer so as to accelerate the speed of apoptosis of prostate cancer cells. Conduct local hyperthermia once every 2 days for long-term application, and it should not be limited by the number of treatments.

6.15.2.7 HYPERTHERMIA AND OTHER TREATMENTS

Prostate cancer treatment applies reasonable integrative treatments such as TCM, herbal medicines, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, and colon cleansing therapy. Combination application with hyperthermia can increase the effectiveness and safety of treatment, significantly improve the cure rate, effectively reduce the side effects of radiotherapy, ensure the quality of life of cancer patients, inhibit tumor progression, and prolong survival time.

6.15.2.7.1 DC-CIK cell therapy

Prostate cancer, as one of the strong immunogenic cancers, is also very suitable to be treated by DC-CIK.

Postoperative DC-CIK consolidation therapy: For early prostate cancer, collect cancer tissues during radical resection and prepare individual peptides that are cultured together with DC-CIK to obtain immune cells with specific tumoricidal activity, the reinfusion of which into the body can effectively remove residual small lesions, and the efficacy is clear. The number of CIK cells for each reinfusion should reach at least 1×10^{10}, once per month with four times as a course of treatment. Conduct periodic review after transfusion, and if there is no recurrence an additional treatment is carried out once every 6 months.

Combined treatment with chemotherapy: For prostate cancer that cannot be treated with radical resection or prostate cancer with recurrence and metastasis, after the cancer burden is reduced by freezing, minimal invasion, and other means DC-CIK can also be combined with chemotherapy for application to inhibit tumor progression and prolong survival time with the cancer. Treatment protocols: one day before

chemotherapy collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation. Continue in this manner, and four consecutive times form a course of treatment. For efficacy assessment, if it is effective conduct a consolidated therapy every 2 to 3 months.

6.15.2.7.2 Systemic biofeedback therapy

Three times a week, with 20 times forming a course of treatment. Change to once or twice a week after two to three courses for long-term treatment.

6.15.2.7.3 Alkaline treatment

Dietotherapy or sodium bicarbonate therapy can be applied to alkalize the body.

Rapid alkalinization method by intravenous infusion of sodium bicarbonate: 3 days before chemotherapy, with a dose of 150 mg/kg/day prepare the sodium bicarbonate injection at a concentration of 2.5%. Conduct intravenous infusion within 2 hours once a day, a total of 3 consecutive days forming one course of treatment. Afterward, it can be used alone or with chemotherapy drugs at the same time. For example: for a colon cancer patient who weighs 60 kg, 7.2 g of sodium bicarbonate should be applied each time, which is about 300 mL of sodium bicarbonate parenteral solution with 2.5% concentration.

Sodium bicarbonate therapy for oral administration: For adults, take 100 mg/kg/day. Powder can be added to 500 mL of drinking water or fruit juice, which can be drunk slowly once per day. The tablet can be divided into the amount for three doses and for direct oral administration. One needs to drink more water, for 8 days as a course of treatment. Simultaneously apply with chemoradiotherapy. Patients with cancer can take sodium bicarbonate 2 to 3 g/day for long-term oral administration, which can significantly reduce chemotherapy side effects, enhance the efficacy and immune function, and reduce chances of infection.

When taking sodium bicarbonate by intravenous and oral administration, detect urine or saliva pH value once every morning (slip method) and it is required for the saliva pH value to be above 7.4 and the urine pH value to be above 7.0. After the end of treatment, detect the intravenous or arterial pH value and compare it with the value before treatment; the pH should be more than 7.35, as required.

6.15.2.7.4 Colon cleansing therapy

Patients can take fruit and vegetable drinks with the coffee enema; but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutrition for support.

6.15.2.8 INTRACAVITARY HYPERTHERMIA

Prostate cancer is located in the natural cavity path of the body; therefore, intracavitary heating is a treatment that can possibly achieve a better hyperthermia effect. Generally, transurethral microwave therapy is used. With the development of technology, prostate hyperthermia can now be completed with the latest hyperthermia equipment in the outpatient department and under local anesthesia. Furthermore, the growth of prostate cancer in the cavity will lead to narrowed cavity structure, elongated urethra, and even lumen occlusion. Placement of the radiator has certain technical requirements and has the risk of leading to ascending urinary tract infection and urinary incontinence. Therefore, select the appropriate treatment according to the actual situation of patients and the technical conditions of the hospital.

6.15.2.9 HYPERTHERMIA AND HERBAL MEDICINES

6.15.2.9.1 Medicated ironing (hot compress)

Prescription for fennel medicated ironing: Cumin 15 g and *Evodia rutaecarpa* 15 g. Fry the drugs with salt or rice wine. Wrap with a cloth and iron on the lower abdomen or umbilical region. Repeat several times so that the drug fever arrives at the lower abdomen. Iron for 30 minutes each time, and perform this once each in the morning, at noon, and in the afternoon. Efficacy: warms yang and removes stasis. Applicability: prostate cancer, testicular cancer, and cervical cancer.

6.15.2.9.2 Bath

Proven prescription 1: Sappanwood 50 g, *Camphora* 50 g, *Ramulus cinnamomi* 15 g, old *Radix lithospermi* 15 g, *Fructus liquidambaris* 15 g, *Rhizoma homalomenae* 15 g, *Lycopodii herba* 15 g, *Olibanum* 10 g, *Myrrha* 10 g, *Carthamus tinctorius L.* 10 g, *Chaenomeles speciosa Nakai* 10 g, and *Rubus obcordatus* 10 g. Decoct the drugs with water, and immerse (wash) joints of the affected part in hot decoction. Efficacy: promotes blood circulation to dispel cold and remove meridian obstruction. It is applicable to patients with the syndrome of joint and bone pain caused by bone metastatic carcinoma.

Proven prescription 2: Take 20 g each of *Ligusticum chuanxiong Hort*, *Erythrina variegata L.*, *Speranskia tuberculata*, *Cortex acanthopanacis*, *Caulis spatholobi*, and *Retinervus luffae Fructus* and 15 g each of *Angelica sinensis*, *Carthamus tinctorius L.*, and *Lycopodii herba*. Add water and boil together for 30 minutes. Fumigate and wash the affected area one or two times a day for 30 minutes each time. Efficacy: activates blood, relaxes veins, and relieves pain. It is applicable to cancer patients having the syndrome of limb joints and bone pain.

6.15.2.9.3 Steam therapy

Proven prescription 1: Decoctions of *Speranskia tuberculata*: *Ramulus cinnamomi* 12 g, *Saposhnikovia divaricata* 12 g, *Angelica dahurica* 12 g, *Zanthoxylum bungeanum* 12 g, *Folium artemisiae Argyi* 12 g, *Lycopodii herba* 12 g, *Speranskia tuberculata* 12 g, *Rhizoma et Radix notopterygii* 15 g, *Radix angelicae Pubescentis* 15 g, *Cortex acanthopanacis* 15 g, *Erythrina variegata* L. 15 g, and *Ramulus mori* 30 g. Put the drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: promotes blood circulation to remove meridian obstruction. It is applicable to cancer patients with bone metastases and with neck, shoulder, and back-of-leg pain.

Proven prescription 2: Prescription for relieving rigidity of muscles and promoting blood circulation: *Lycopodii herba* 30 g, *Speranskia tuberculata* 30 g, *Radix paeoniae Alba* 30 g, *Clematis chinensis Osbeck* 25 g, *Radix aconiti* 20 g, *Radix aconiti Kusnezoffii* 20 g, *Asarum* 20 g, *Chaenomeles speciosa Nakai* 20 g, *Erythrina variegata* L. 20 g, *Olibanum* 15 g, *Myrrha* 15 g, and vinegar 200 mL. Put the drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: promotes blood circulation to remove meridian obstruction. It is applicable to cancer patients with bone metastases and with neck, shoulder, and back-of-leg pain.

Proven prescription 3: Prescription for fumigating washing and ironing paralysis: crude *Sichuan aconite root* 15 g, *Health Aconitum* 15 g, *Speranskia tuberculata* 15 g, *Clematis chinensis Osbeck* 15 g, *Rhizoma curcumae* 15 g, *Herba taxilli* 15 g, *Chinese Honeylocust Spine* 15 g, *Cruel Semen Strychni* 10 g, *Asarum* 10 g, *Herba epimedii* 10 g, stir-baked *Radix paeoniae Alba* with Vino 20 g, and *Arisacma consanguineum* 12 g. Put the drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: promotes blood circulation to remove meridian obstruction. It is applicable to cancer patients with bone metastases and with neck, shoulder, and back-of-leg pain.

Proven prescription 4: Speranskia tuberculata 30 g, *Lycopodii herba* 30 g, *Erythrina variegata L.* 30 g, *Chinese star jasmine stem* 30 g, *Folium artemisiae Argyi* 30 g, *sappanwood* 20 g, *Carthamus tinctorius L.* 20 g, *Caulis spatholobi* 20 g, *Rhizoma corydalis* 20 g, *faeces trogopterorum* 20 g, *Ramulus cinnamomi* 20 g, *Radix curcumae* 20 g, *Radix angelicae Pubescentis* 20 g, and *Achyranthes bidentata* 20 g. Boil the drugs inside the fumigating bed, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: warms yang and dredges collaterals. It is applicable to cancer patients with the syndrome of yang deficiency arthromyodynia.

6.15.2.10 HYPERTHERMIA INDICATIONS

Hyperthermia can be given for localized prostate cancer or localized bone metastases.

6.15.2.11 HYPERTHERMIA CONTRAINDICATIONS

KPS less than 60 points; poor general condition accompanied by severe heart, liver, lung, kidney, and other organic diseases; patients with poor postoperative wound healing or local skin damage; and patients accompanied by severe coagulation disorder. Prostate cancer accompanied by significant bleeding or patients with urinary tract obstruction should not accept intracavitary hyperthermia.

6.15.3 Introduction of a typical case

A patient named Liao, male, 67 years old, was admitted on October 31, 2006, to Clifford Hospital due to "intermittent hematuria with dysuria for nearly seven months." In March 2006, the patient exhibited urine in pale red, accompanied by tingling, slender urine, without frequent urination, and urgency of micturition. The patient was taking herbal tea and anti-inflammatory drugs (specific drugs and doses were unknown) by himself and did not come to the hospital seeking medical services. In June 2006, his urine gradually changed from pale red to dark red, most obvious in the first part of urine as well as the last part of urine. No frequent urination, urinary urgency, and urinary cloud were exhibited, and daily urine output was normal. Then the patient went to a urology specialty clinic of Kowloon, Hong Kong, and it was revealed by cystoscopy that there were no abnormalities. Prostate cancer antigen (PSA): 174 ng/mL (significantly higher than normal); urinalysis: occult blood (+++). Prostate biopsy showed prostate adenocarcinoma. Prostate MRI showed a 1 cm × 2 cm inhomogeneous occupation at the prostate right lobe and left ischial permeability sclerosis destruction, highly suspicious of metastatic cancer and T8 compression fracture. It was recommended to have prostate and testicular resection. The patient refused surgery, radiotherapy, and chemotherapy and then came to Clifford Hospital for treatment. Conditions at admission: urine intermittently presented a pale red color, with the first part of urine as well as the last part of urine most obvious, accompanied by mild dysuria, urinary frequency, and urgency and nocturia five to six times, which seriously affected sleep. The patient had lumbosacral pain discomfort when doing activity. Stool was normal, and appetite was acceptable.

Physical examination: General condition was good. Superficial lymph node had no enlargement. No abnormal syndrome was detected in physical examination; mild tenderness was felt in spinal column and pelvis. The KPS was 90.

Auxiliary examination: RBC 4.7×10^{12}/L, Hb 136 g/L, WBC 5.9×10^{9}/L, and PLT 176×10^{9}/L. Biochemistry: ALT 24 U/L, AST 26 U/L, TBIL 26 U/L, DBIL 11.7 U/L, ALB 41 g/L, ALP 36 U/L, GGT 32 U/L, Cr 67 μmol/L, Ua 356 μmol/L; BUN 5.21 mmol/L, GLU 6.31 mmol/L, TG 0.69 mmol/L, GHO 5.17 mmol/L, K^+ 3.9 mmol/L, Na^+ 141 mmol/L, Cl^- 103 mmol/L, and Ca^{2+} 2.31 mmol/L. Tumor markers: CEA 2.69 ng/mL, AFP 7.6 ng/mL, CA-125 13 U/mL, and PSA 194.15 ng/mL. The five items of immune function were normal; urine routine: RBC 800 pcs/UL.

Prostate MRI showed prostate cancer and possible multiple bone metastases at the left iliac bone, sacral 4, the left ischium, and inferior ramus of pubis. Whole-body bone scan showed that multiple bone metabolisms were extremely active at the left ischium, pubis, iliac bone, and right sacrum and presented the possibility of bone metastases as well as eight thoracic compression fractures.

Diagnosis: Prostate cancer with bone metastases.

Integrative treatment prescription: After admission, the patient was given endocrine therapy (Zoladex + Fugerel), herbal medicines, acupuncture, hyperthermia, chelation detoxification, medical ozone, and other integrative treatments. Whole-body medium-high temperature hyperthermia was carried out once a week for a total of six times. Local hyperthermia was conducted at the prostate region twice a week for a total of 15 times and alternated with whole-body hyperthermia. Combined chelation detoxification was carried out each time when hyperthermia was conducted. EBOO treatment was conducted twice a week, separated with hyperthermia for a total of 14 times. After a course of treatment, the patient's symptoms of hematuria, urgency, and dysuria completely disappeared, and the patient had nocturia once at night. Sleep quality was improved, and sacral pain and discomfort were improved and without bone pain. PSA was decreased to 2.59 ng/mL. Abdominal CT reexamination: lesion range was narrowed at the left ischium. Herbal medicines and acupuncture treatment were combined throughout the whole treatment process. The patient exhibited pink tongue, thin white fur, and deep and thready pulse, and the syndrome belonged to spleen and kidney deficiency. The therapeutic principle should focus on nourishing and warming kidney yang, as well as eliminating dampness and diuresis.

Medications: The prescription recommended was modified Zhenwu Decoction. Specific medication: cooked *Aconitum carmichaeli* 10 g, *Atractylodes macrocephala Koidz* 15 g, *Poria cocos* 15 g, *Radix paeoniae Alba* 10 g, ginger 15 g, *Solanum nigrum* 20 g, *Solanum lyratum Thunb.* 30 g, and *Alisma Orientalis* 15 g; one dose a day, decocted with water for oral administration.

Acupuncture treatment: The main syndrome of medium-advanced prostate cancer is deficiency of both spleen and kidney, and the therapeutic principle should focus on reinforcing the spleen and nourishing the kidney, as well as reinforcing the lower Jiao.

Acupuncture on acupoints: Shenshu, Pangguangshu, Pishu, Zusanli, Sanyinjiao, Taixi, Guanyuanshu, Sanjiaoshu, and Waisanguan. Methods: reinforcing method was used. Retained the needle for 20 minutes, once per day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Zhongji, Shenque, Zusanli, and Guanyuanshu. Methods: took two points each time with a moxa stick for moxibustion. Conducted moxibustion for 10 minutes above each point, once per day. Took 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Prostate, kidney, bladder, urethra, Sanjiao, subcortex, endocrine, Pishu, and Jiaogan. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

Treatment effects: The patient was hospitalized for 42 days. After integrative treatment, the patient's condition was stable and general conditions were good with smooth urination and without frequent micturition, urgency, and hematuria. The KPS was 100. Prostate MRI review showed a 1 cm × 2 cm inhomogeneous occupation at the prostate right lobe. Combined with the history, it was considered to be prostate cancer. Compared with the previous one, the prostate lesion was not enlarged. The left ischial permeable hardened damage was seen by ECT check, and compared to the previous piece it was slightly reduced and highly suspicious of metastatic cancer. There was a T8 compression fracture. PSA test prompted 1.01 ng/mL (↑) and blood testosterone 27 ng/dL. The patient was discharged for convalescing through care, rest, and nourishment according to the situation. After discharge, the patient received regular review. One week of integrative treatments was conducted every 2 months as outpatient. Six months after discharge, the prostate lesion, rechecked by MRI, was narrowed compared with the previous result. Follow-ups have been conducted for more than 6 years and PSA has remained in the normal range.

6.15.4 Related research in China and abroad

Maluta et al. have applied appropriate conformal radiotherapy in combination with hyperthermia for the treatment of 144 patients with locally advanced prostate cancers, and the results showed that the overall 5-year survival rate was 87%.

Zhang Dingrong et al. have conducted clinical observation of three-dimensional conformal radiotherapy combined with radio-frequency hyperthermia for the treatment of locally advanced prostate cancer, and among 21 cases of prostate cancer patients primary lesion CR was 33.3%, PR was 42.9%, stability and progress (SD + PD) was 23.8%, and the total effective rate (CR + PR) was 76.1%, without adverse reactions of grade 3 or higher.

Studies by Xiang Zuolin et al. have confirmed that three-dimensional conformal radiation therapy combined with radio-frequency hyperthermia for treatment of locally advanced prostate cancer has good short-term efficacy with a low complication rate.

Van Vulpen et al. have reported that the survival rate of biochemical index was increased to 70% after 3 years of three-dimensional conformal radiotherapy combined with radio-frequency hyperthermia.

6.16 CERVICAL CANCER

As the most common female genital tract malignancy, cervical cancer is the only one among gynecological cancers with a clear cause, is associated with persistent infection of high-risk human papillomavirus (HPV), and is the third most common cancer among global women after breast cancer and colorectal cancer. It ranks number two among cancers, preceded only by breast cancer in developing countries. In 2008, there were 529,800 estimated new cases of cervical cancer in the world, among which there were 255,100 deaths, and 85% of the new cases were in developing countries.[1] With the launch of cervical cancer screening, cervical cancer

incidence and mortality rates in developed countries decreased significantly. The incidence of cervical cancer has significant regional differences. In China, cervical cancer is mainly distributed in the central region; it is higher in rural areas than in urban areas and higher in mountain areas than in the plains. The national high incidences are in Tonggu of Jiangxi, Wufeng of Hubei, and Lueyang of Shanxi.

The most common pathological type is cervical intraepithelial cervical squamous cell carcinoma, followed by endocervical adenocarcinoma and rare glandular squamous cell carcinoma, adenoid cystic adenocarcinoma, and small cell undifferentiated carcinoma. Tumors grow locally and infiltrate parametrium as well as pelvic organs and occur as pelvic lymph node metastases.

The earliest symptoms are vaginal bleeding and vaginal discharge. Prognosis of early patients is good. Carcinoma violates pelvic connective tissue; compresses bladder, rectum, and sciatic nerve; and affects lymphatic and venous return and urinary frequency; advanced patients can suffer from frequent micturition, urgency, anal heaviness and distension, constipation, lower abdominal pain, sciatica, and lower limb swelling pain. If carcinoma compresses or violates the ureter, hydronephrosis and uremia can occur. Cachexia often appears due to long-term consumption at the end stage.

6.16.1 Conventional treatments

6.16.1.1 SURGERY

For cases of CIN I and CIN II, generally, conservative treatment is applied, including laser, microwave, freezing, and other treatments. For cases of CIN III, hysterectomy is mostly carried out. If patients are young and have fertility requirements, cervical conization can be applied. Conduct periodic review after conservative treatment.

Radical surgery is suitable for cervical cancers of stages Ib and II, and radical hysterectomy and pelvic lymph node dissection can be adopted, including resection of the uterine double annex and extended hysterectomy and radical hysterectomy. Effects of radiotherapy and surgery of the latter two are similar, depending on patients' conditions. If it is considered before surgery that resection is difficult, or there is concern that metastasis and planting may be caused in the surgical procedure, neoadjuvant radiotherapy of preoperative brachytherapy can be given, and local hyperthermia can be given at the time radiotherapy is carried out. For stages Ib and IIa, efficacies of surgery and radiotherapy are similar, and the selection of treatment required depends on medical equipment and technology as well as the patient's specific circumstances. Generally, surgical treatment is mostly advocated, especially for young patients in need of retaining ovarian function, with pregnancy or pelvic inflammation, as well as for adenocarcinoma patients who are less sensitive to radiotherapy. Extensive cervical resection and pelvic lymph node dissection can be carried out for young patients of stage Ia_2 who want to preserve fertility, patients with foci less than 2 cm at stage Ib_1, and patients without lymph node metastasis. Obese patients, frail elderly, and patients with chronic diseases of the heart and lung are contraindications for surgery, and radiotherapy should be considered. For medium or locally advanced patients, if it is considered before surgery that resection is difficult or there is concern that metastasis and planting may be caused by the surgical procedure, preoperative and postoperative green treatments should be given to facilitate rehabilitation of the body after surgery and prevent cancer recurrence.

6.16.1.2 RADIOTHERAPY

Radiotherapy is suitable for stage Ib and patients at various phases afterward, and even for stage IV it can play a palliative role. The common methods are intracavitary irradiation and external irradiation. Intracavitary irradiation mostly uses brachytherapy with radioactive sources such as ^{137}Cs and ^{192}Ir, mainly for cervical primary lesions. External irradiation uses $^{60}Cobalt$, linear accelerator, and so on, focusing on metastases, excluding primary tumor metastasis, and including pelvic lymph nodes.

6.16.1.3 CHEMOTHERAPY

Chemotherapy is mainly an adjuvant therapy for cases of advanced or recurrent metastasis. In recent years, interventional chemotherapy has been applied as adjuvant therapy to surgery or radiotherapy. Preoperative

neoadjuvant chemotherapy is applicable to patients at phases Ib_2 and IIa_2 with large foci or young patients of phase IIb who want to reserve ovarian function by surgery or to narrow lesions first and then undergo surgery. Postoperative adjuvant therapy focuses on radiotherapy, and currently the methods of chemotherapy are also applicable.

6.16.1.4 HYPERTHERMIA

Microwave or radio-frequency heating treatment is commonly used for hyperthermia of cervical cancer, and both intracavity heating and in vitro heating have good effects. According to clinical studies in China and abroad, the clinical efficacy of hyperthermia for the treatment of advanced cervical cancer is confirmed. Compared with radiotherapy alone, the rate of 5-year survival time can be improved.

6.16.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can directly kill cancer cells, induce apoptosis of cancer cells, and improve immune function and also has a synergistic effect with radiotherapy. In particular, it can reduce radiotherapy-induced leukopenia and other side effects. Use it once every other day, with 20 times as a course of treatment. Change to once every week after three courses for long-term maintenance. As with other infusions, pay attention to the infusion rate for patients with cardiac insufficiency and lung metastasis.

6.16.1.6 MEDICAL OZONE THERAPY

Use EBOO once every other day, with 20 times per course for a total of three courses. For patients who are in poor physical condition or cannot tolerate EBOO, medical ozone saline infusion is given once every other day, with 10–14 times as a course of treatment. Use ozone major autohemotherapy once every other day, with 12 times as a course of treatment. Use ozone minor autohemotherapy once every other day, with 12 times as a course of treatment. Use medical ozone acupoint injection once every other day, with 12 times as a course. At least three courses for each therapy are conducted. According to the specific circumstances of patients, vaginal medical ozone insufflation or medical ozone saline rinse, once every day, is conducted after radiotherapy to reduce vaginal injury after radiotherapy.

6.16.1.7 TRADITIONAL CHINESE MEDICINE

For the syndrome of stagnation of qi due to depression of the liver, modified Xiaoyao Powder is given; for the syndrome of dampness heat and stasis toxin, Liuwei Dihuan Pill is given; and for the syndrome of yang deficiency of spleen and kidney, modified Senate Baizhu Powder is given. Commonly used Chinese formulated products include Xihuang Pill, Guizhi Fuling Pill, Xiaojin Dan, Pingxiao Capsule, Dahuang Zhechong Pill, and Elemene Injection.

6.16.1.8 ACUPUNCTURE

The therapeutic principle should focus on regulating Chong and Ren channels, as well as promoting the flow of qi and blood.

Acupuncture on acupoints: Guanyuan, Zhongji, Zigong, Ligou, Sanyinjiao, and Taichong. Add Qimen and Zhangmen for the syndrome of stagnation of qi due to depression of the liver; add Yinlingquan and Dadu for the syndrome of dampness heat and stasis toxin; add Ganshu and Shenshu for the syndrome of yin deficiency of liver and kidney; and add Shenshu and Mingmen for the syndrome of yang deficiency of spleen and kidney.

Methods: Even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days rest after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion therapy: Take Guanyuan, Zhongji, Shenque, Zusanli, Guanyuanshu, and Baihuanshu.

Methods: Take two to four points each time. Conduct moxibustion with the moxa stick.

Take 10 minutes for each point once every other day, with 10 times as a course of treatment.

Auricular acupoints: Zigong, Luanchao, Penqiang, kidney, Pizhixia, Neifenmi, spleen, Jiaogan, liver, Erjian, and tumor-specific area.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.16.1.9 MEDICATED DIET, NUTRITION, AND SO ON

For early-stage patients who can eat, focus on medicated diet conditioning. Patients with nutritional imbalance can be given total parenteral nutrition, in which fat-soluble vitamins, water-soluble vitamins, and essential minerals and trace elements can be included.

6.16.1.10 OTHERS

Pay attention to the patient's emotional state, and help instill methods that will promote a positive mental attitude and healthy lifestyle habits in patients; qigong, tai chi, music, and the mental therapy of TCM can be used.

6.16.2 Combination of hyperthermia with conventional treatments

6.16.2.1 HYPERTHERMIA AND SURGERY

Generally, after the postoperative wound is completely healed, combined local hyperthermia and whole-body hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician.

Whole-body hyperthermia can improve immunity, promote cancer cell apoptosis, and regulate the body for the production of TNF, IL-2, and other immune factors involved in anticancer effects, inhibition of primary or secondary lesions for continuous proliferation, as well as inhibition of metastasis. Hyperthermia can effectively kill the virus and is of great significance for the etiology treatment of cervical cancer. It is recommended to apply whole-body hyperthermia and local hyperthermia alternatively. Whole-body hyperthermia applies whole-body medium-high temperature hyperthermia once every 10–14 days, with six times as a course of treatment. Pay attention to the monitoring of body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give fluid infusion to maintain water–electrolyte balance and other symptomatic treatments in a timely manner. Review electrolytes, and so on 1–3 days after whole-body hyperthermia. Continue to supplement energy to maintain water–electrolyte balance. Local hyperthermia can be appropriately applied at the intervals of whole-body hyperthermia according to the general condition and tolerance of patients. For patients who cannot tolerate whole-body medium-high hyperthermia, a whole-body medium-low temperature hyperthermia can be used once a week for a total of 12 times.

Abdominal in vitro RF deep hyperthermia can be carried out for local hyperthermia once every 2 days, with 20 times as a course of treatment. After three courses of treatment, if it has no treatment restrictions it can be applied in combination with other approaches in long-term treatment.

6.16.2.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy is one of the effective methods for the treatment of cervical cancer, suitable for stage Ib and patients at various phases afterward; even for stage IV, it can play a palliative role. The common methods are intracavitary irradiation and external irradiation. Intracavitary irradiation mostly uses brachytherapy with radioactive sources of ^{137}Cs, ^{192}Ir, and so on, mainly for cervical primary lesions. External irradiation uses ^{60}Co, linear accelerator, and so on, focusing on metastases, excluding primary tumor metastasis, and including pelvic lymph nodes. Local hyperthermia is suggested to be conducted within 2 hours after the end of radiotherapy, once every other day, throughout the course of treatment of radiotherapy. It can sensitize the effect of radiotherapy and significantly reduce local skin damage, fibrosis, and local tissue adhesion.

6.16.2.3 HYPERTHERMIA AND CHEMOTHERAPY

Over the past decade, chemotherapy as an adjuvant therapy for advanced or recurrent cases has achieved a certain effect. Preoperative neoadjuvant chemotherapy is applicable to patients in stages Ib_2 and IIa_2 with large foci, or young patients of stage IIb who want to reserve ovarian function by surgery and to narrow lesions and then undergo surgery. Postoperative adjuvant therapy focuses on radiotherapy and, currently, the methods of chemotherapy are also applicable. Effective drugs are cisplatin, cyclophosphamide, ifosfamide, doxorubicin, bleomycin, taxanes, and so on. Triple or quadruple chemotherapy dominated by cisplatin is mostly applied, which is administered by intravenous or regional arterial cannula. Conduct conventional chemotherapy for four to six cycles. It is suggested to have medium-high temperature hyperthermia for whole-body hyperthermia, synchronized with the cycle of chemotherapy for four to six times. Local hyperthermia can be conducted in the intermittence of chemotherapy once every 2 days and can also be taken as long-term concomitant therapy.

For patients who cannot tolerate systemic chemotherapy at all or who refuse systemic chemotherapy, Clifford Hospital has effectively combined insulin-mediated small doses of intravenous chemotherapy with medical ozone and hyperthermia and achieved good results in clinical practice. Specific methods: rule out contraindications of chemotherapy through comprehensive assessment and obtain the informed consent of patients. An empty stomach is required before chemotherapy. Carry out medical ozone major autohemotherapy before chemotherapy, and then give insulin to control blood glucose at about 3.6 mmol/L or so (it is better to control blood glucose when the hypoglycemia reaction has just appeared, and according to individual circumstances); then give a small dose of cisplatin + bleomycin for intravenous chemotherapy (10%–30% of normal amount) twice a week, for a total of 2–4 weeks. Conduct routine antiemetic hepatic protection and stomach protection, with supplementation of high glucose and trace elements before chemotherapy. It is appropriate to conduct local hyperthermia within 2–4 hours after chemotherapy. If the patient is in good general condition and can tolerate whole-body hyperthermia, it is advised to apply whole-body medium-low temperature hyperthermia. For patients who cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the right upper abdomen can be carried out, once every other day, and continued during the intermission period of chemotherapy, and the combined local hyperthermia can be applied 60–80 times during small-dose intravenous chemotherapy.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body medium-high hyperthermia can be carried out simultaneously on the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Simultaneously carry out the hyperthermia and chemotherapy cycle for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

6.16.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy can be given from the end of the operation to the period of chemotherapy to patients with postoperative physical weakness and low immunity. It can promote physical recovery and regulate the immune system, and kill residual cancer cells or inhibit early metastasis. Note that chelation detoxification needs infusion of more than 2 hours. Hyperthermia can be simultaneously applied with chelation detoxification to improve efficacy.

6.16.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing tumor cells, enhance the effect on immunity, and increase the efficacy of medical ozone. The specific program of medical ozone therapy is as follows:

For patients with good vascular conditions, EBOO is proposed to be carried out once every other day, with 20 times per course of treatment for a total of three courses.

For patients with hypovolemia, medical ozone major autohemotherapy can be carried out once every other day, with 12 times as a course of treatment. Use ozone minor autohemotherapy once every other day, with 12 times per course. Use medical ozone acupoint injection once every other day, with 12 times as a course. At least three courses are conducted for each therapy.

For patients who are in poor physical conditions or who cannot tolerate EBOO or major and minor autohemotherapy, medical ozone saline infusion is given once every other day, with 10–14 days as a course for long-term maintenance therapy. According to the specific circumstances of patients, vaginal medical ozone insufflation or medical ozone saline rinse, once every day, is conducted after radiotherapy to reduce vaginal injury after radiotherapy.

6.16.2.6 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. Other treatments such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, colon cleansing therapy, and so on in combination with hyperthermia can increase the effectiveness and safety of the treatment.

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Change to once or twice a week after two to three courses of treatment for long-term treatment.

Alkaline treatment: Intravenous or oral sodium bicarbonate therapy can be used, combined with a medicated diet, to alkalize constitution. For medium-advanced patients accompanied by intra-abdominal metastasis, sodium bicarbonate peritoneal perfusion therapy can also be carried out. Please refer to Section 4.10 for details.

Colon cleansing therapy: Patients can orally take fruit and vegetable drinks with the coffee enema; but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support.

In addition to hyperthermia, chelation detoxification, medical ozone, acupuncture, and TCM, we emphasize dietotherapy plus qigong plus sports as supplementary treatments to improve overall immunity. We also encourage, support, and educate our patients on leading a productive and fulfilling life despite their affliction.

For medium and advanced patients who can eat, focus on medicated diet conditioning. Patients with nutritional imbalances can be given total parenteral nutrition, in which fat-soluble vitamins, water-soluble vitamins, and essential minerals and trace elements can be included. Pay attention to the emotional states of patients, and establish in them the attitude of active participation in the treatment and correct living habits thereafter.

Through adjustment of body, breathing, and heart, qigong can stimulate the meridian qi of the human body, restore healthy energy, and adjust qi and blood, which are conducive to reinforcing the vital energy and consolidating the constitution as well as enhancing body immune functions. When combined with other nontoxic integrative treatments, it enhances anticancer effects.

Music therapy can make patients feel happy and refreshed; improve sleep; relieve anxiety, fear, depression, and other negative moods; and thereby enhance the quality of life.

6.16.2.7 INTRACAVITARY HYPERTHERMIA

Intracavitary hyperthermia can be used for cervical cancer hyperthermia. In general, intracavitary hyperthermia is preferable for tumor lesions confined to the cervix because it can reach a sufficiently high heating dose. However, for patients with lesions in a wider range, pelvic invasion, or obvious lymph node metastasis, it is best to select in vitro RF local hyperthermia or whole-body high temperature hyperthermia to benefit from a wider heating area for reducing local cervical and pelvic lesions.

6.16.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.16.2.8.1 Medicated ironing (hot compress)

Proven prescription 1: Take 15 g each of *Angelica sinensis*, *Cinnamomum cassia Presl*, *Evodia rutaecarpa*, *Olibanum*, *Myrrha*, and *Asarum*. Grind to fine powder and fry, and then wrap it with cloth and put it on the navel for a hot compress. Efficacy: dissipates dampness and activates stagnancy, warms meridians and

disperses coldness, induces menstruation to relieve menalgia, and regulates qi and blood. It is applicable to patients who suffer abdominal and pelvic cancers (colon cancer, colorectal cancer, ovarian cancer, cervical cancer, etc.) and having the syndromes of hysteresis and cold coagulation.

Proven prescription 2: Prescription for fennel medicated hot compress: *fennel* 15 g and *Evodia rutaecarpa* 15 g. Fry drugs with salt or rice wine. Wrap them with a cloth and iron on the lower abdomen or umbilical region. Repeat for several times so that the drug fever arrives at the lower abdomen. Iron for 30 minutes each time, and conduct one time each in the morning, at noon, and in the afternoon. Efficacy: warms yang and removes stasis. Applicability: prostate cancer, testicular cancer, and cervical cancer.

6.16.2.8.2 Bath

Prescription of modified Yinjia Pill: Solanum nigrum 60 g, *Pollen typhae* 60 g, *Smilax glabra Roxb* 30 g, *Sargentgloryvine stem* 30 g, *dandelion* 30 g, *Cortex ailanthi* 30 g, *Rhizoma curcumae* 25 g, *Atractylodes macrocephala Koidz* 20 g, *Cimicifuga foetida* 15 g, and *Platycodon grandiflorum* 15 g. Decoct for hip bath and fumigate external genitalia. Efficacy: clears away heat and toxic substances, as well as activating blood and resolving mass. Applicability: cervical cancer patients with the syndrome of noxious heat and blood stasis.

6.16.2.8.3 Grilling method

Awei Huapi Plaster: Decoct *ferula*, *Rhizoma sparganii*, *Rhizoma curcumae*, *rhubarb*, *crude Sichuan aconite root*, *Olibanum*, *Momordica cochinchinensis*, dung beetle, *Rhizoma cyperi*, *aloe vera*, *Resina draconis*, and *camphor* into a paste. Heat it to soften it for external application, paste it in the umbilical region or the affected area, and then irradiate for 30 minutes with the infrared lamp once a day. Efficacy: regulates the flow of qi and promotes blood circulation, softens and resolves hard mass, relieves chest and abdominal distention, and disintegrates abdominal mass. It is applicable to patients who have chest and abdominal distention and abdominal mass with the symptom of qi stagnancy and blood stasis in liver, gallbladder, stomach, and intestine or gynecological diseases.

6.16.2.9 HYPERTHERMIA INDICATIONS

Early, medium, and advanced cervical cancers have indications for hyperthermia. Except when having contraindications, all cervical cancer patients can undergo hyperthermia.

6.16.2.10 HYPERTHERMIA CONTRAINDICATIONS

Accompanied by systemic infection or cervical local severe infection, or bleeding tendencies; poor general condition; and KPS less than 60 points.

6.16.3 Introduction of a typical case

A patient named Li, female, 60 years old, was admitted on October 27, 2008, to Clifford Hospital due to "irregular vaginal bleeding accompanied by increased vaginal discharge for more than a month." After admission to the hospital, colposcopy and biopsy were conducted, showing cervical squamous cell carcinoma. PET/CT showed the following: (1) cervical high metabolic occupation, which was in line with changes in cervical cancer; (2) no significant violations in the uterine body and bladder; (3) fatty liver; (4) pleural thickening at the right side oblique fissure; and (5) imaging of other parts of the body showed no abnormality. On October 31, 2008, "wide hysterectomy and pelvic lymph node dissection" was carried out. A cervical lesion of approximately 2.5 cm × 2 cm × 1 cm with a fine pedicle of about 0.5 cm was found under direct vision during surgery, located in the bottom left of the cervix. Postoperative pathology results showed the following: (1) exogenous, polypoid endometrial adenocarcinoma with squamous cell carcinoma (adenosquamous carcinoma) in the cervical canal transitional zone, with moderate-poor differentiation. The cancer infiltrated the whole cervix wall layer, with the biggest diameter of 2.0 cm. The cancer from the vaginal wall cutting edge was 3.0 cm, and no cancer invasion was at the vaginal wall cutting edge. (2) Uterine smooth muscle lipoma. (3) Endometrial polyps, postmenopausal atrophic endometrium and focal cystic atrophy. (4) Chronic cervicitis with squamous metaplasia and retention cysts. (5) Both ovaries and fallopian tube tissue. (6) The left obturator lymph

node, 1/7; left internal iliac lymph nodes, 0/1; left external iliac lymph node, 0/7; right common iliac lymph nodes, 0/1; right external iliac lymph nodes, 0/1; and right iliac and right obturator lymph nodes, 0/7.

Physical examination: The patient was previously healthy and claimed no history of hepatitis, tuberculosis, high blood pressure, diabetes, heart disease, and so on.

Diagnosis: Postoperative cervical cancer and adenosquamous carcinoma of stage III.

Integrative treatment prescription: after surgery, the patient had sensations of heaviness and distension in the lower abdomen and occasional abdominal cramps after eating, accompanied by fatigue, lower abdominal distension, no nausea and vomiting, acceptable appetite, occasional constipation, occasional diarrhea, pink tongue, thin white fur, and wiry pulse. Body weight of the patient did not significantly reduce since the onset. The patient refused postoperative chemoradiotherapy. Clifford Hospital gave the following treatment after experts' consultation: local hyperthermia, three times a week; whole-body medium-low temperature hyperthermia, twice a month; chelation detoxification therapy, three times a week, simultaneously conducted with hyperthermia; systemic biofeedback treatment, three times a week; EBOO, once a week, combined with the mixture of Keliu; herbal medicines; acupuncture; and other integrative treatments. The syndrome of the patient belonged to stagnation of qi due to depression of the liver. The therapeutic principle should focus on soothing the liver, as well as cooling the blood to remove pathogentic heat.

Medications: The prescription recommended is modified Xiaoyao Powder. Specific medication: *Radix Bupleuri* 15 g, *Angelica sinensis* 10 g, *Radix paeoniae Alba* 15 g, *Atractylodes macrocephala Koidz* 15 g, *Poria cocos* 25 g, *Radix glycyrrhizae Preparata* 6 g, *Cortex moutan* 6 g, *Gardenia jasminoides Ellis* 6 g, *Hedyotis diffusa Willd* 20 g, and *Scutellaria barbata* 20 g, one dose a day. Decoct with water for oral administration.

Acupuncture on acupoints: Sanyinjiao, Zusanli, Qihai, Guanyuan, Pishu, Shenshu, Ganshu, Taixi, Linggu, Dabai, and Waisanguan. Methods: even reinforcing–reducing method was used for acupuncture. Retained the needle for 20 minutes, twice a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Zhongji, Shenque, Zusanli, Guanyuanshu, and Baihuanshu; and add Mingmen, Pishu, and Shenshu for patients with kidney yang deficiency. Methods: took two points each time and conducted moxibustion with a moxa stick. Conducted moxibustion for 10 minutes on each point, once every day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Zigong, Luanchao, Penqiang, kidney, Pizhixia, Neifenmi, spleen, Jiaogan, liver, and Erjian. Stuck auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

The patient was discharged with good recovery after hospitalization for 2 months. The patient adhered to returning to the hospital for hyperthermia and chelation detoxification, and medical ozone therapy, once every 2 to 3 weeks after discharge, as well as for the combination of Keliu, herbal medicines, acupuncture, systemic biological feedback treatment, and other integrative treatments.

Treatment effects: After 2 months of hospitalization, the sensation of heaviness and distension in the lower abdomen of the patient was improved, and the patient had no abdominal pain and diarrhea. The condition was under better control. Her mentality was significantly improved. Diet was acceptable. Urine and stool were normal. Skin and mucus membranes were in blush. Her KPS was 100. The patient could work and live normally. Tumor indexes reviewed showed that liver and kidney functions were normal. No abnormalities were shown in the abdomen and pelvic cavity by CT. Follow-up was conducted for 4 years, and no recurrence was seen. Currently, the patient is still under follow-up.

6.16.4 Related research in China and abroad

Li Kaixin et al. have conducted a clinical study of deep hyperthermia combined with concurrent chemoradiotherapy for the treatment of locally advanced cervical cancer, and the results showed that the CR rate, efficiency at the end of treatment, local control rate at the end of treatment, local tumor control rate, and 1-year cancer-free survival rate at the end of the external irradiation were 80%, 100%, 90%, 50%, and 90%, respectively, in the thermochemoradiotherapy group. They were significantly higher than in the other two groups ($P < .05$), whereas no significant difference was seen between the chemoradiotherapy group and the thermoradiotherapy group ($P > .05$). The 1-year survival rate had no significant difference in the three groups

($P > .05$). The main side effects were gastrointestinal reactions and myelosuppression, in which the thermoradiotherapy group was significantly lower than the chemoradiotherapy group ($P < .05$). No significant difference was seen between the thermochemoradiotherapy group and the other two groups ($P > .05$).

The in vitro studies of Liu Yusheng et al. indicated that hyperthermia can interfere with the repair of potentially lethal and sublethal radiation by rays. Radiotherapy combined with hyperthermia can be more effective in inhibiting the growth of cervical cancer Hela cells and colony formation.

The Netherlands has carried out a classic test of the combined application of radiotherapy and hyperthermia for the treatment of patients with locally advanced cervical cancer using local hyperthermia. The trial was carried out with up to 12 years of follow-up, and the results showed that comprehensive treatments combined with hyperthermia have brought significant improvements to short-term treatment efficacy and long-term survival.

Franckena et al. has summarized the case results of radiotherapy and hyperthermia for the treatment of primary locally advanced cervical cancer (FIGOIB stage IIa) in which 378 locally advanced cervical cancer patients received thermoradiotherapy with external exposure meter doses of 46.0–50.4 Gy, combined with breech-loading brachytherapy, and with hyperthermia once a week. The CR was 77% and the 5-year local control rate, disease-specific survival rate, and late toxicity of level 3 or above were 53%, 47%, and 12%, respectively. Multivariate analysis found that hyperthermia is a prognostic factor in addition to the common prognostic factors. Conclusion: the observation results of CR showed that local control rate and survival rate were similar to those of the previous randomized, deep hyperthermia experiments of the Netherlands.

Kong Yamei et al. have conducted efficacy observation of regional hyperthermia combined with chemotherapy for the treatment of locally recurrent cervical cancer. The hyperthermia output power was 1200–1000 W, and the rectal temperature was constantly maintained at 40.5°C–41.5°C. The heated treatment time was about 40 minutes, two times per week at intervals of 72 hours for eight times per course. Chemotherapy was simultaneously carried out with hyperthermia. Routine hyperthermia was conducted if chemotherapy was not carried out. The results showed that the effective rate for the chemotherapy alone group was 36.6% and that for the thermochemotherapy group was 61.7% ($P < .05$); the incidence of leukopenia of degree III + IV was significantly higher in the chemotherapy alone group than in the thermochemotherapy group ($P < .05$); and the thermochemotherapy group did not appear to have serious adverse reactions.

Harima et al. have reported a randomized study of radiotherapy alone or combination of hyperthermia and radiotherapy in 40 cervical cancer patients with stage IIIb. The CR rate was 80% in the thermoradiotherapy group and 50% in the radiotherapy alone group. The 3-year survival rates were 58.2% and 48.1%, respectively. Cancer-free survival rates were 63.6% and 45%, respectively. Local control rates were 79.7% and 48.5%, respectively. Five patients exhibited varying degrees of side effects in the group of radiotherapy combined with hyperthermia, of which two patients displayed mild subcutaneous fat necrosis; one case of mild colitis, one case of mild proctitis, and one case of intestinal obstruction of colon were reported 15 years after the end of the treatment. The radiotherapy alone group had no significant side effects.

6.17 OVARIAN CANCER

Ovarian cancer is a kind of malignant tumor of the ovaries, in which 90%–95% is primary ovarian cancer and the remaining 5%–10% is ovarian metastases from primary cancers at other parts. Although the incidence of ovarian cancer is lower than that of cervical and endometrial cancer, ranking third among gynecological malignancies, the mortality rate is more than the sum of cervical cancer and endometrial cancer, the highest in gynecological cancers, and is the most serious threat to women's health. Early ovarian cancer is usually absent of symptoms, and even if it is not symptoms are not specific and the role of screening is limited. Thus, early diagnosis is difficult and 60%–70% of cases are advanced by the time patients seek medical services, and the efficacy for advanced cases is poor. The 5-year survival rate of ovarian cancer is 30%–40%. How to improve the efficiency of treatment of ovarian cancer is a serious challenge

faced by the gynecologic oncology community in recent years. Thermochemotherapy and intraperitoneal hyperthermic perfusion chemotherapy have achieved good results.

Common histopathologic types are epithelial ovarian cancers (including serous carcinoma, mucinous carcinoma, endometrial carcinoma, malignant Brenner tumor, and transitional cell carcinoma), ovarian sex cord stromal tumors (including granulosa cells, theca cells, and fibroblasts), and malignant ovarian germ cell tumors (embryonal carcinoma, endodermal sinus tumor, immature teratoma, and asexual cell tumor). Due to the ovarian enriched lymphatic and blood supply, ovarian cancer is prone to abdominal lymph nodes and liver metastases.

Early ovarian cancer is often asymptomatic, and some patients inadvertently stumble on palpable masses in the lower abdomen or such masses are accidentally found by gynecological examination. Patients often feel abdominal discomfort, but there is generally no significant abdominal pain. When complications occur, such as torsion, rupture, or infection, patients can feel lower abdominal pain. Some patients may present menstrual disorders or amenorrhea. Loss of appetite, indigestion, and other gastrointestinal symptoms often appear in some patients. With the increase of cancer and ascites, some patients may have a sense of increased waist circumference; some even consider it to be obesity and, hence, may try to reduce weight. There may be fatigue, weight loss, and anemia in advanced ovarian cancers.

6.17.1 Conventional treatments

6.17.1.1 SURGERY

Ovarian cancer at the early stage produces abdominal planting and lymphatic system metastasis, that is, subclinical spread. The vast majority of patients should seize the opportunity for surgical treatment. Surgery is not only the most effective treatment but also the necessary means for confirming the diagnosis and defining staging. Once it is suspected as ovarian cancer, early surgery should be carried out. Systemic operational examination and staging are stressed for early ovarian cancer. Correct staging is not only the premise for determining treatment but also a significant basis for estimating prognosis and efficacy comparison. As a result, once ovarian cancer is suspected, early surgery should be carried out. In principle, hysterectomy, adnexectomy, omentectomy, and pelvic and paraaortic lymph node dissection are carried out for early ovarian cancer. For advanced cancer, tumor cells cytoreductive surgery can be carried out to resect the primary tumor and metastases as much as possible and minimize the number of cancer cells. For young patients who have fertility requirements and meet the criteria, conservative surgery to preserve fertility can be carried out. If the first operation is not very complete, with only biopsy or partial resection, or it is considered that the cancer stage is too advanced and surgery cannot achieve satisfactory cytoreduction, surgery should be carried out after one to three courses of chemotherapy. For patients with postoperative residual cancer less than 2 cm, especially cancer less than 1 cm, prognosis is significantly improved. Whether to reoperate on recurrent cancers remains controversial, and comprehensive consideration should be given according to the patient's specific circumstances.

6.17.1.2 RADIOTHERAPY

Ovarian cancers vary a lot in radiosensitivity. Endodermal sinus tumor of the ovary, immature teratoma, and embryonal carcinoma are the most insensitive. Epithelial ovarian cancer and granular cell carcinoma are moderately sensitive. Dysgerminoma is the most sensitive and can be controlled by radiotherapy after surgery. Because early ovarian cancers result in peritoneal metastasis, the irradiation range includes the abdominal and pelvic cavity.

6.17.1.3 CHEMOTHERAPY

Chemotherapy is the main means of adjuvant therapy for ovarian cancers. It not only can tolerate the disease but also has the potential to completely eliminate the cancer. As a result, patient survival time is significantly prolonged. Chemotherapy is mostly used after surgery to kill residual lesion cancer cells that are difficult to be resected completely. Except for certain patients with cancers of stages Ia and Ib as well as those with postoperative borderline tumor who cannot receive chemotherapy, patients should have chemotherapy. Most ovarian

cancers are more sensitive to chemotherapy. Epithelial carcinoma is commonly treated with a TP program (taxol plus carboplatin or cisplatin), and germ cell tumors and specific gonadal stromal cells tumors are treated with a BEP program (bleomycin plus etoposide plus cisplatin) and a VPB program (vincristine plus cisplatin plus bleomycin).

Because ovarian cancers have intraperitoneal spread, in addition to conventional intravenous administration intraperitoneal administration can also be used for chemotherapy.

6.17.1.4 HYPERTHERMIA

Ovarian cancer hyperthermia focuses on local hyperthermia, thermochemotherapy, and intraperitoneal hyperthermic perfusion chemotherapy. Basic and clinical studies have demonstrated that the efficacy of ovarian cancer hyperthermia combined with chemotherapy is significantly increased compared to chemotherapy alone. In the past 20 years, preoperative thermochemotherapy and intraoperative and postoperative intraperitoneal hyperthermic perfusion chemotherapy have produced good effects.

6.17.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification has the effect of directly killing cancer cells and can also improve immunity. It is recommended to give a full dose and full course of chelation detoxification therapy in the preoperative period, or before and after chemoradiotherapy, to ovarian cancer patients at an early stage; simultaneously applying hyperthermia can help achieve satisfactory effects, increase cure rates, improve the tolerance of the body to surgery and chemoradiotherapy, and reduce chemoradiotherapy side effects.

6.17.1.6 MEDICAL OZONE THERAPY

The significance of the application of medical ozone therapy for early ovarian cancer is that it can regulate immune function, directly kill remaining cancer cells, and inhibit cancer recurrence and metastasis. Usage: EBOO is preferred once every other day, with 20 times per course of treatment. For patients in poor physical condition, medical ozone saline infusion or medical ozone major autohemotherapy and medical ozone minor autohemotherapy are given once every other day, with 12 times as a course of treatment. Be sure that the medical ozone systemic treatment is not used at the same day as chelation detoxification. Combining medical ozone therapy application theory with the TCM acupoint theory, medical ozone acupoint injection can be given to enhance the effect of the treatment of cancer. According to the acupuncture points selected, take three to five points each time and inject 2–4 mL medical ozone gas once every 2 to 3 days, with 12 times as a course of treatment. At the same time, medical ozone vaginal or rectal insufflation can also be given. Apply topical treatment to inhibit tumor recurrence and metastasis. For medium-advanced ovarian cancer patients who are in good general condition, EBOO treatment can be given once every other day to help suppress tumor progression. For patients in poor general condition and with coagulation disorders, intravenous medical ozone saline, major autohemotherapy, and medical ozone acupoint injection can also be given; medical ozone vaginal insufflation also has a certain effect in cancer control.

6.17.1.7 BIOLOGICAL TREATMENT

Biological treatment for ovarian cancers is a kind of treatment using cytokines, such as IL-2, IFN-α, and TNFα, and is widely used in patients with ovarian cancer. The efficacy of IL-2 and TNFα in conjunction with other drugs for the treatment of ovarian cancer hydrothorax and seroperitoneum is significant. The method is easy to use and can be applied by direct intramuscular injection or intravenous infusion as well as by direct thoracic and abdominal cavity perfusion. Adoptive immunotherapy, such as multi-factor-induced killer cells CIK, adopts immunotherapy for cancer patients to help eliminate minimal residual lesions, prevent tumor recurrence, and prolong survival time.

6.17.1.8 TRADITIONAL CHINESE MEDICINE

Syndrome differentiation of the early stage mostly belongs to the syndrome of stagnation of pathogenic dampness and heat. The prescription recommended is modified Longdan Xiegan Decoction. For the syndrome of

qi stagnation and blood stasis, the prescriptions recommended are Xiaoyao Powder plus modified Taohong Siwu Decoction. Syndrome differentiation of advanced ovarian cancers mostly belongs to the syndrome of phlegm dampness and coagulation, and the prescriptions recommended are Sijunzi Decoction plus modified Haizao Yuhu Decoction.

6.17.1.9 ACUPUNCTURE

The syndromes of early ovarian cancers are mainly qi stagnation and blood stasis. The therapeutic principle should focus on promoting blood circulation to remove meridian obstruction, as well as softening and resolving hard mass.

Acupuncture on acupoints: Sanyinjiao, Hegu, Taichong, Yanglingquan, Xuehai, Zusanli, Baihui, and Pishu.

Methods: even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course.

The syndromes of medium-advanced ovarian cancers are mainly phlegm dampness and coagulation, as well as deficiencies of both qi and blood. The therapeutic principle should focus on invigorating the spleen for eliminating dampness, eliminating phlegm and softening indurated mass, and replenishing qi and the blood, as well as toning deficiency and reinforcing the primary qi.

Acupuncture on acupoints: Zusanli, Sanyinjiao, Guanyuan, Pishu, Shenshu, Zhongwan, Yinlingquan, and Diji. Methods: even reinforcing–reducing method is used for acupuncture. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with10 times as a course of treatment.

Moxibustion on acupoints: Guanyuan, Sanyinjiao, Zusanli, and Zhongwan. Methods: take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five times of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Luanchao, Penqiang, Zigong, adrenal gland, Pizhixia, Neifenmi, liver, kidney, and spleen.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.17.1.10 MEDICATED DIET, NUTRITION, AND SO ON

Nutritional support of early ovarian cancer patients focuses on medicated diet and food therapy. Before conducting chemotherapy or whole-body hyperthermia, total parenteral nutrition can be given 1 day in advance to replenish the consumption of hyperthermia. Because advanced ovarian cancer patients are often accompanied by malnutrition, parenteral nutrition is mostly given. Actively give nutritional support and supplement with enough protein, vitamins, trace elements, and so on to support the body's tolerance to a variety of anticancer therapies.

6.17.1.11 OTHERS

Adhere to the practice of qigong and tai chi. Take music therapy and psychotherapy to reduce psychological stress or fear, which facilitates the rapid and comprehensive rehabilitation of patients. Medium-advanced patients should also pay attention to psychological adjustments, and anticancer confidence, and be encouraged to practice qigong; music therapy; and the regulation of breathing, body, and heart to improve their self-healing powers. All these will help to extend survival time and improve quality of life.

6.17.2 Combination of hyperthermia with conventional treatments

6.17.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Western medicine treatment of ovarian cancers focuses on surgical treatment, with adjuvant therapies of chemotherapy, radiotherapy, and immunotherapy, and if combined with hyperthermia can achieve synergistic effects.

Preoperative and postoperative local hyperthermia can be carried out to prevent the spread and metastasis of cancer. For patients of stages III and IV and above and with good general condition, preoperative adjuvant chemotherapy can be carried out for two cycles. At the same time, the combination of hyperthermia, chelation detoxification, medical ozone, herbal medicines, acupuncture, and other nontoxic integrative treatments can improve immune function and further inhibit cancer growth and metastasis.

For patients who are assessed to be able to have cytoreductive surgery or patients undergoing palliative operation with the purpose of removing the obstruction, generally, after the postoperative wound is completely healed, chemotherapy combined with hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician.

Hyperthermia can improve immunity; promote cancer cell apoptosis; and regulate the body for production of TNF, IL-2, and other immune factors involved in the anticancer effect.

Hyperthermia can involve the alternation of whole-body hyperthermia and local hyperthermia. It is recommended to have whole-body medium-high temperature hyperthermia for whole-body hyperthermia, twice a week for a total of four to six times. RF local hyperthermia can be applied once every 2 days, with 20 times as a course of treatment. Conduct the second course after an interval of 10 days. Long-term concomitant treatment can be carried out after three courses. Be sure to monitor body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and timely give fluid infusion to maintain water–electrolyte balance and other symptomatic treatments. Review electrolytes and so on 1–3 days after whole-body hyperthermia. Continue to supplement energy to maintain water–electrolyte balance. Local hyperthermia can be appropriately added at the intervals of whole-body hyperthermia according to the general condition and tolerance of patients.

6.17.2.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy is one of the adjuvant therapies for ovarian cancers. Palliative radiotherapy for median and advanced, or refractory, lesions can reduce the patient's pain and prolong life. Hyperthermia can enhance the effect of radiotherapy and reduce the side effects of radiotherapy. It is recommended to carry out local hyperthermia within 2 hours after the end of radiotherapy, once every other day, accompanying the full process of radiotherapy.

6.17.2.3 HYPERTHERMIA AND CHEMOTHERAPY

For patients of stages III and IV, it is recommended to have systemic chemotherapy combined with intraperitoneal hyperthermic perfusion chemotherapy. For patients in good general condition, whole-body hyperthermia combined with intraperitoneal hyperthermic perfusion chemotherapy can be considered. Generally, conventional chemotherapy lasts for four to six cycles, combining with local and whole-body hyperthermia during chemotherapy and giving intraperitoneal hyperthermic perfusion chemotherapy for two to four cycles. Intraperitoneal chemotherapy has the pharmacokinetic characteristic of high selective regional chemotherapy and can maintain a constant high concentration of anticancer drugs in peritoneal fluid, portal vein blood, and peritoneal lymphatic system, as well as the liver. In this treatment, the free cancer cells that are exfoliated during surgery in the abdominal cavity, as well as minimum cancer lesions and common abdominal locations of recurrence and metastases, can be soaked in the high concentration of the anticancer drug solution and can be directly attacked. The most common sites of postoperative ovarian cancer recurrence are in the vicinity of the primary tumor and its lymph nodes, and the most common disseminated sites are the liver and abdominal cavity. Therefore, abdominal local chemotherapy is an important means to control postoperative recurrence and metastasis. If postoperative recovery is good and patients are in good general condition, local hyperthermia combined with whole-body hyperthermia can be carried out.

For patients who are completely unable to tolerate systemic chemotherapy, insulin-mediated small doses of intravenous chemotherapy combined with chelation detoxification, medical ozone, and hyperthermia can be used, which has achieved better results in clinical practice. Specific methods: rule out

contraindications of chemotherapy through comprehensive assessment and obtain the informed consent of patients. An empty stomach is required before chemotherapy. Carry out medical ozone major autohemotherapy before chemotherapy and then give insulin to control blood glucose at about 3.6 mmol/L or so (it is better to control blood glucose when the hypoglycemia reaction has just appeared, and according to individual circumstances), and then give a small dose of taxol plus cisplatin (10%–30% of the regular amount)/intravenous chemotherapy, twice a week for a total of 2–4 weeks. Conduct routine antiemetic hepatic protection and stomach protection, with supplementation of high glucose and trace elements. It is appropriate to conduct hyperthermia at intervals of 2–4 hours after chemotherapy. If the patient is in good general condition and can tolerate whole-body hyperthermia, whole-body medium-high temperature hyperthermia can be applied and accompanied by low-dose, RF local hyperthermia (the preferred local hyperthermia) once every other day.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body medium-high hyperthermia can be carried out simultaneously on the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Simultaneously carry out the hyperthermia and chemotherapy cycle for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

For patients who cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the right upper abdomen or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, and continue at the intervals of chemotherapy. Take 1 week off after each cycle (5 consecutive days) of chemotherapy. A total of about 60–80 times of combined local hyperthermia is carried out during chemotherapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

The therapeutic value of intraperitoneal chemotherapy for ovarian cancers has obtained more and more attention, and indications are as follows:

- Relatively small residual tumor after initial surgery
- Early-stage patients with high risk factors (G_2 and G_3 of stage I and stage II) with small lesions remaining in the abdomen
- Patients (stage III and poorly differentiated G_3) with high recurrence risk factors during consolidated therapy after pathological CR
- Remedial treatment for the second positive exploratory laparotomy
- Patients with massive ascites

6.17.2.4 HYPERTHERMIA AND IMMUNOTHERAPY

The study is still in the exploratory stage, aiming to improve host immune function, prevent tumor growth, and kill and clear cancer cells. Under the integrative treatments of hyperthermia, TCM, acupuncture, EBOO, and DC-CIK cell therapy, NK cells and T cell subsets of the patient may be increased by 3%–8% than that before treatments, which implies the improvement of immunity of the patient. In addition, adjuvant therapies such as medicated diet plus qigong plus sports also should be stressed to improve overall immunity and encourage patients to continue with a productive and satisfying lifestyle despite the presence of cancer.

6.17.2.5 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Patients who are weak and have postoperative low immunity can receive chelation detoxification and medical ozone therapy in the postoperative period. They can promote physical recovery and regulate immunity, and kill residual cancer cells or inhibit early metastasis. For the application of chelation detoxification therapy, carry out intravenous infusion once every other day. Please note that chelation detoxification needs infusion of more than 2 hours. The therapeutic dose can be gradually increased if there is absence of adverse reactions; 20 times form a course of treatment for a total of three courses.

6.17.2.6 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 1 hour after hyperthermia can increase the effect of killing cancer cells, enhance the effect on immunity, and increase the efficacy of medical ozone. The significance of the application of medical ozone therapy is that it can regulate immune function, directly kill remaining cancer cells, and inhibit cancer recurrence and metastasis. Usage: EBOO is preferred once every other day, with 20 times as a course for a total of three courses. For patients in poor physical condition, medical ozone saline infusion or medical ozone major autohemotherapy and medical ozone minor autohemotherapy are given, once every other day with 12 times as a course of treatment. It is noted that medical ozone systemic treatment is not used in the same day as chelation detoxification. Combining medical ozone therapy application theory with TCM acupoint theory, medical ozone acupoint injection can be given, which can enhance the effect of treatment of cancer.

6.17.2.7 HYPERTHERMIA AND OTHER TREATMENTS

Herbal medicines of TCM, acupuncture, systemic biofeedback treatment, alkaline treatment, and colon cleansing therapy can also play important roles in the treatment of ovarian cancers. Combination with hyperthermia can increase the efficacy and safety of treatment.

Systemic biofeedback therapy: Three times a week with 15 times as a course of treatment. Adjust to once or twice a week after two to three courses for long-term treatment.

Alkaline treatment: Intravenous or oral sodium bicarbonate therapy can be used, combined with a medicated diet to alkalize constitution. For medium-advanced patients with intra-abdominal metastasis, sodium bicarbonate peritoneal perfusion therapy can also be carried out. Please refer to Section 4.10 for details.

Colon cleansing therapy: Patients can take fruit and vegetable drinks with the coffee enema, but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support.

6.17.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.17.2.8.1 Medicated ironing (hot compress)

Proven prescription: Take 15 g each of *Angelica sinensis*, *Cinnamomum cassia Presl*, *Evodia rutaecarpa*, *Olibanum*, *Myrrha*, and *Asarum*. Grind to fine powder and fry; then wrap it with cloth and put it on the navel for a hot compress. Efficacy: dissipates dampness and activates stagnancy, warms meridian and disperses coldness, induces menstruation to relieve menalgia, and regulates the qi and blood. It is applicable to patients who suffer abdominal and pelvic tumors (colon cancer, colorectal cancer, ovarian cancer, cervical cancer, etc.) and from syndromes of hysteresis and cold coagulation.

6.17.2.8.2 Grilling method

Awei Huapi Plaster: Decoct the following into a paste: *ferula*, *Rhizoma sparganii*, *Rhizoma curcumae*, *rhubarb*, *crude Sichuan aconite root*, *Olibanum*, *Momordica cochinchinensis*, dung beetle, *Rhizoma cyperi*, *aloe vera*, *Resina draconis*, and *camphor*. Heat to soften it for external application, paste it in the umbilical region or the affected area, and then irradiate for 30 minutes with the Magic Lamp, once a day. Efficacy: regulates the flow of qi and promotes blood circulation, softens and resolves hard mass, as well as relieving chest and abdominal distentions and disintegrating abdominal mass. It is applicable to patients who have chest and abdominal distention and abdominal mass, with symptoms of qi stagnancy and blood stasis in liver, gallbladder, stomach, intestine, and gynecological diseases.

6.17.2.9 HYPERTHERMIA INDICATIONS

It is applicable to patients who have had well-healed postoperative wounds, patients who receive chemoradiotherapy, and patients who are at the advanced stage.

6.17.2.10 HYPERTHERMIA CONTRAINDICATIONS

Patients with fevers higher than 38.5°C; skin damage in heated area; patients with bleeding tendency; and cachexia.

6.17.3 Introduction of a typical case

A patient named Mo, female, 69 years old, was admitted on July 3, 2006, to Clifford Hospital due to "fatigue and abdominal discomfort for more than one year, aggravated and accompanied with abdominal distension for more than 20 days, and vomiting for one day." On July 2005, the patient underwent a comprehensive examination in a hospital in Guangzhou due to fatigue and abdominal discomfort, and a 5.2 cm × 3.9 cm × 4.6 cm mass was found in the left adnexa uteri, which was ill defined and with pelvic fluid. The patient was given "cytoreductive surgery + pelvic lymph node dissection + appendectomy" in the hospital. Postoperative pathological examination: embryonal carcinoma of the left ovary; no lymph node cancer. An embryonal carcinoma nodule with a diameter of 0.3 cm could be seen at the right ovary tissue. The patient was given chemotherapy 10 days after surgery in the hospital (specific program was unknown). Due to severe chemotherapy reaction, the patient refused to continue it and took herbal medicines by herself (details were unknown). The symptoms varied in degrees; she exhibited aggravated abdominal pain for more than 20 days before admission, accompanied by abdominal distention. The patient experienced frequent vomiting 1 day before admission to Clifford Hospital seeking medical treatment. After admission, the following results were shown by CT: postoperative changes of ovarian cancer, massive ascites, a metastasis mass in the right side of the abdominal cavity, and retroperitoneum lymph node metastases.

Physical examination: Clear mind, poor mentality, macritus, body weight of 51 kg, semirecumbent posture, abdominal distension, a palpable 3 cm × 4.6 cm × 3.8 cm mass at the right abdomen, shifting dullness (+), and lower extremity edema. Her KPS was 50.

Auxiliary examination: The following results were shown by pelvic CT: postoperative changes of ovarian cancer, massive ascites, a 3 cm × 1.7 cm × 3.8 cm metastasis mass at the right side of the abdominal cavity, and retroperitoneum lymph node metastases. Pathology showed "embryonal carcinoma of the left ovary." Tumor markers were as follows: CEA 116 ng/mL; AFP 50 ng/mL, and CA199 194.32 U/mL. Blood routine: WBC 8.3×10^9/L, NEUT 74%, RBC 3.8×10^{12}/L, and HGB 89 g/L. Abdominal plain film showed incomplete intestinal obstruction. Electrolytes: K^+ 3.37 mmol/L↓, Na^+ 130.2 mmol/L↓, Cl^- 98 mmol/L, ALT 25 U/L, AST 46 U/L, TBIL 30 U/L, DBIL 16 U/L, ALB 34.5 g/L, ALP 67 U/L, GGT 58 U/L, Cr 79 μmol/L, Ua 153 μmol/L, BUN 7.0 mmol/L, and GLU 5.90 mmol/L.

Diagnosis: Embryonal carcinoma of the left ovary at stage IV (with abdominal and retroperitoneum lymph node metastases).

Integrative treatment prescription: After admission, symptomatic and supportive treatment, decompression, fasting, paracentesis, total parenteral nutritional support, correction of electrolyte disorders, and so on were conducted. Chelation detoxification was applied once a day. The patient had smooth stool after 3 days and then a liquid diet was given. Intravenous ozone saline and chelation detoxification were applied alternately. TCM and acupuncture were combined throughout the whole course of treatment. The patient exhibited a dark purple tongue with petechia and a thready and unsmooth pulse, which belonged to the syndromes of qi stagnation and blood stasis. The treatment focused on promoting qi and activating blood, as well as removing blood stasis and lumps.

Medications: The prescription recommended was modified *Curcuma phaeocaulis Valeton* Powder. Specific medication: *Rhizoma curcumae* 15 g, *Rhizoma sparganii* 15 g, *Fructus aurantii* 12 g, *Carapax trionycis* (Predecoct) 30 g, *Ramulus cinnamomi* 10 g, *areca* 15 g, *rhubarb* 10 g, *Radix aucklandiae* (add later) 10 g, *Radix paeoniae Rubra* 15 g, *Angelica sinensis* 15 g, *Radix bupleuri* 15 g, *Semen persicae* 10 g, and *Carthamus tinctorius L.* 10 g, one dose a day, decocted with water for oral administration.

Acupuncture on acupoints: Zusanli, Sanyinjiao, Guanyuan, Pishu, Shenshu, Zhongwan, Yinlingquan, Diji, and Wansanguan. Methods: used mild reinforcing–reducing method and retained the needle for 20 minutes, once per day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Sanyinjiao, Zusanli, and Zhongwan. Methods: took two points each time with a moxa stick for moxibustion. Conducted moxibustion for 10 minutes above each point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Luanchao, Penqiang, Zigong, adrenal gland, Pizhixia, Neifenmi, liver, kidney, and spleen. Methods: stuck auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

After 1 week, abdominal distension of the patient was reduced and ascites were reduced. The patient showed basically normal eating with an HGB of 101 g/L. Whole-body hyperthermia plus intraperitoneal chemotherapy was given. Intraperitoneal drugs: cisplatin 100 mg plus IL-2 one million units, once every 10 days. Applied abdominal and pelvic local hyperthermia at the interval period, once every other day. Simultaneously conducted hyperthermia and chelation detoxification and applied EBOO alternately. Conducted continuous treatment for 4 weeks. Guidance in qigong and psychotherapy was given.

Treatment effects: After the integrative treatments for 35 days, the mentality of the patient was improved markedly. Urine and stool were normal. No nausea and vomiting were found. Diet was normal. There was no abdominal distension. Weight increased by 3 kg. The whole abdominal enhanced CT scan showed the following after treatment: postoperative changes of ovarian cancer and a 1.5 cm × 1.2 cm × 1.1 cm metastasis mass at the right abdominal cavity. Retroperitoneum lymph node metastases were significantly reduced. Blood routine after treatment: WBC 6.2×10^9/L, NEUT 68%, RBC 4.2×10^{12}/L, and HGB 110 g/L. Abdominal plain film showed no fluid level and normal electrolytes. Tumor markers were as follows: CEA 58 ng/mL, AFP 28 ng/mL, and CA199 33 U/mL. Currently, the patient maintains a body weight of 59 kg, with normal diet, no black stools, and no pain, and can complete usual housework. Her KPS was 90. The patient is still insisting on taking herbal medicines and returns to the hospital once every 20 days for 1-week treatments of whole-body hyperthermia, chelation detoxification, EBOO, acupuncture, and other integrative treatments.

6.17.4 Related research in China and abroad

Li Zhibin et al. have conducted clinical observation of in vitro high frequency hyperthermia combined with gemcitabine and cisplatin for the treatment of recurrent ovarian cancer. They carried out chemotherapy for two cycles on the second day of medication (at the intermission periods) and conducted abdominal external high frequency hyperthermia twice a week, lasting 60 minutes each time. Results showed that the total effective rate was 65.2%, five cases of CR (21.7%) and 10 cases of PR (43.5%). The adverse reactions were mainly neutropenia and thrombocytopenia. In vitro high frequency hyperthermia combined with cisplatin and gemcitabine for treatment of recurrent ovarian cancer is an effective program, and its adverse reactions can be tolerated.

Qian Haihong et al. have conducted clinical research on chemotherapy combined with abdominal high frequency hyperthermia in treating advanced ovarian cancer with ascites. In their research, intravenous chemotherapy of docetaxel and intraperitoneal chemotherapy of carboplatin combined with abdominal high frequency hyperthermia was applied and the clinical efficacy and toxicity were observed. High frequency hyperthermia was conducted 2 hours after intraperitoneal carboplatin and, afterward, once every other day with 21 days as one cycle. The effective rate of conventional chemotherapy group was 55.6%, whereas that of the high frequency hyperthermia group was 87.5%; the difference between the two groups was statistically significant ($P < .05$). For KPS, improvement rate for the conventional chemotherapy group was 61.1% and that for the high frequency hyperthermia group was 93.8%; the difference between the groups was statistically significant ($P < .05$). The main side effects during chemotherapy were gastrointestinal reactions, leukopenia, thrombocytopenia, and hair loss; the difference was not statistically significant ($P > .05$). Starting from the second cycle of chemotherapy, patients with recession of ascites in the high frequency hyperthermia group were significantly increased compared with the conventional chemotherapy group; the difference between the two groups was statistically significant ($P < .05$), indicating that docetaxel systemic chemotherapy and carboplatin intraperitoneal chemotherapy combined with abdominal high frequency hyperthermia can significantly improve the treatment of patients with advanced ovarian cancer ascites, improve the quality of life of patients, and control growth of ascites without an increase in side effects.

Chatzigeorgion et al. selected 20 patients with peritoneal metastasis of recurrent ovarian cancer for cytoreductive surgery and persistent hyperthermic intraoperative intraperitoneal chemotherapy. The study found that no complications occurred during surgery and intraperitoneal hyperthermic perfusion chemotherapy. The average time of ascites disappearance was 21 months (3–109 months) and the average survival time of patients with residual tumor diameter less than 1.5 cm was 29 months, whereas for those with diameter greater than or equal to 1.5 cm it was 7 months; the difference was significant ($P < .05$). Results showed that persistent hyperthermic intraoperative intraperitoneal chemotherapy for the treatment of patients with recurrent ovarian cancer can prolong the survival time of patients, while reducing the incidence of malignant ascites.

Gori et al. have conducted a randomized grouping of 29 ovarian cancer patients at stages IIIb and IIIc. First, they carried out cytoreductive surgery and six courses of taxol and DDP program for chemotherapy; then they conducted open intraperitoneal hyperthermic perfusion chemotherapy, heated DDP (100 mg/m), and conducted perfusion for 60 minutes, with abdominal temperature maintained at 41°C–43°C. Compared with the control group without IPC, the results showed a good 5-year survival and a lower recurrence rate.

6.18 ENDOMETRIAL CARCINOMA

Endometrial cancer is a group of endometrial epithelial cancers and is most commonly found in perimenopausal and postmenopausal women. In China, with the improvement of social and economic conditions the incidence of endometrial cancer is also increasing year after year and is now second only to cervical cancer, ranking second in malignancy of the female reproductive system.

According to pathogenesis and the characteristics of biological behavior, endometrial cancer can be divided into estrogen-dependent type (type I) and non-estrogen-dependent type (type II). Most of estrogen-dependent endometrial cancers are endometrioid carcinomas, a small part of which is mucinous adenocarcinomas. Non-estrogen-dependent endometrial cancers include serous carcinoma, clear cell carcinoma, and so on.

The clinical manifestations are mainly vaginal bleeding, vaginal discharge, lower abdominal pain, and abdominal mass. Advanced cancer patients with cancer infiltration oppressing iliac vessels can experience ipsilateral lower limb edema and pain. The lesion infiltration oppressing the ureter causes ipsilateral hydronephrosis and hydroureter and even leads to renal atrophy. Continuous bleeding can lead to secondary anemia. Cancer long-term consumption can lead to weight loss, fever, cachexia, and other symptoms of systemic failure.

6.18.1 Conventional treatments

6.18.1.1 SURGERY

Surgery is the main treatment for endometrial cancer. Surgical procedures for early-stage patients are surgical–pathological staging, accurately determining the extent of disease and prognosis, resecting uterus with lesions and possible metastatic lesions, and determining the choice of postoperative adjuvant therapy. For stages I and II, radical surgery is focused. For stage III or IV, reduction of cancer should be tried as much as possible to create the conditions for postoperative chemoradiotherapy. A considerable number of early endometrial cancer patients can be cured through standard surgery. But for patients with high risk factors of recurrence through surgical–pathological staging, or for advanced patients, certain adjuvant therapies are required. Because endometrial cancer patients are often older and have more complications, such as hypertension, diabetes, obesity, and other cardiovascular and cerebrovascular diseases, we need to assess body tolerance of specific patients in detail and give individualized treatment.

6.18.1.2 RADIOTHERAPY

Radiotherapy is one of the effective methods for the treatment of endometrial cancers. Radiotherapy alone is only suitable for patients who are frail, patients with serious medical complications who cannot tolerate surgery or have contraindications for surgery, as well as patients above stage III who are unfit for surgery,

including intracavitary and external irradiation. Postoperative adjuvant radiotherapy is often used in clinical applications. Indications for postoperative radiotherapy are as follows: lymph node metastasis or suspicious lymph node metastasis as shown by surgical detection; uterine myometrial invasion greater than 1/2 or G_2, G_3; special histological types, such as serous carcinoma and clear cell carcinoma; and cancer residual at the vaginal cutting edge. For the first three cases, whole pelvic irradiation is given; for the last case, brachytherapy needs to be added.

6.18.1.3 CHEMOTHERAPY

Chemotherapy alone is rarely used for the treatment of endometrial cancers; but it is commonly used for special types of endometrial cancer, such as serous and clear cell carcinoma recurrent cases, and for patients with high risk factors for recurrence after surgery, such as patients with G_3 and those who are ER/PR negative.

6.18.1.4 HORMONE THERAPY

Indications: Advanced or recurrent patients, endometrial cancer patients who want to retain fertility, conservative surgery combined with high-dose progesterone for preserving ovarian function, and postoperative adjuvant therapy for patients with risk factors.

6.18.1.5 HYPERTHERMIA

High-intensity focused ultrasound and local hyperthermia by microwave or radio-frequency heating is commonly applied clinically. Extensive clinical practice has proved that the efficacy of radiotherapy combined with hyperthermia is significantly higher than that of radiotherapy alone in patients.

6.18.1.6 CHELATION DETOXIFICATION THERAPY

The therapeutic effects of chelation detoxification therapy for treatment of uterine cancers include direct cancer cell killing, induced apoptosis of cancer cells, improvement of immune function, as well as a synergistic effect with radiotherapy; the effects include, in particular, reduction of side effects of radiotherapy-induced leukopenia and others. Chelation detoxification and local hyperthermia can be performed simultaneously once every other day, with 20 times as a course of treatment for three courses. When patients are in stable condition, the frequency of treatment can be gradually reduced, and it can be taken for long-term maintenance therapy.

6.18.1.7 MEDICAL OZONE THERAPY

Use EBOO once every other day, with 20 times as a course of treatment for a total of three courses. For patients in poor physical condition or who are unable to tolerate it, medical ozone saline infusion is given once every other day, with 10–14 days as a course of treatment, or medical ozone major autohemotherapy is given once every other day, with12 times as a course of treatment. According to the specific circumstances of patients, vaginal medical ozone insufflation or medical ozone saline rinse can also be chosen after radiotherapy, once a day, which has a clear effect in alleviating the vaginal injury after radiotherapy.

6.18.1.8 TRADITIONAL CHINESE MEDICINE

The syndrome of stagnation of qi due to depression of the liver is common at the early stage. The prescription recommended is modified Xiaoyao Powder; for the syndrome of blood stasis obstruction in the interior, the prescription recommended is a modified Shaofu Zhuyu Decoction. The syndrome of yin deficiency of liver and kidney is commonly seen in the medium-advanced stage, and the prescription recommended is a modified Zhibai Dihuang Pill. For the syndrome of deficiency of vital qi as well as interior invasion by heat toxicity, the prescription recommended is a modified Fuzheng Jiedu Decoction.

6.18.1.9 ACUPUNCTURE

The main syndrome of early uterine cancer is stagnation of qi due to depression of the liver. The therapeutic principle should focus on relieving the depressed liver, as well as regulating Chong-Ren.

Acupuncture on acupoints: Qihai, Likou, Xingjian, Sanyinjiao, Taichong, Xuehai, and Yanglingquan.

Methods: All use mild reinforcing–reducing method. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

The main syndromes of medium-advanced uterine cancer are yang deficiency of spleen and kidney and yin deficiency of liver and kidney. The therapeutic principle should focus on nourishing yin and clearing heat, reinforcing the liver and kidney, invigorating the spleen, and replenishing qi, as well as warming and toning the spleen and kidney.

Acupuncture on acupoints: Sanyinjiao, Zusanli, Qihai, Guanyuan, Pishu, Shenshu, Ganshu, Taichong, Mingmen, Taixi, Dadu, and Dadun.

Methods: Use mild reinforcing–reducing method for acupuncture. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Guanyuan, Zhongji, Shenque, Zusanli, Guanyuanshu, and Baihuanshu. For patients with the syndrome of yang deficiency of spleen and kidney, Mingmen, Pishu, and Shenshu are added. Zhongji is added for excess syndrome.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with10 times as a course of treatment.

Auricular acupoints: Zigong, Luanchao, Penqiang, Pinzhixia, Neifenmi, Pishu, Jiaogan, liver, and Erjian.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.18.1.10 MEDICATED DIET, NUTRITION, AND SO ON

Nutritional supportive treatment focuses on medicated diet and food therapy for adjustment. For medium-advanced patients who can eat, focus on medicated diet conditioning by oral administration. Total parenteral nutrition is given to patients with serious nutritional imbalances, to which fat-soluble vitamins, water-soluble vitamins, and essential minerals and trace elements should be added.

6.18.1.11 OTHERS

Combine with qigong, tai chi, music, and mental therapy of TCM to maintain calmness, positivity, and optimism in patients and to improve their self-healing ability and delay tumor progression. Through adjustment of body, breathing, and heart, qigong can stimulate the meridian qi of the human body, restore vital energy, and adjust qi and blood, which are conducive to reinforcing the vital energy and consolidating the constitution, as well as enhancing body immunity, and can jointly have an anticancer effect by combining with other nontoxic integrative treatments. Psychological therapy and music therapy can make patients feel happy and refreshed and have good regulative effects for improving sleep and relieving anxiety, fear, depression, and other negative moods, hence enhancing the quality of life of cancer patients.

6.18.2 Combination of hyperthermia with conventional treatments

6.18.2.1 HYPERTHERMIA AND SURGERY

Surgical treatment is a basic method for treatment of early carcinoma of the corpus uteri. For medium or locally advanced patients, if it is considered before surgery that resection is difficult or there is worry that metastasis and planting may occur during the surgical procedure preoperative and postoperative nontoxic integrative treatments should be given, to facilitate the postoperative rehabilitation of the body and prevent cancer recurrence. Generally, after the postoperative wound is completely healed local hyperthermia or whole-body hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, after laboratory tests reveal no bleeding tendency, as well as after the exclusion of contraindications of hyperthermia and after a comprehensive assessment of patients is made by the hyperthermia center physician.

Whole-body hyperthermia can improve immunity; promote cancer cell apoptosis; and regulate the body for production of TNF, IL-2, and other immune factors involved in the anticancer effect.

If patients are assessed to be in good general condition and are able to withstand whole-body hyperthermia, it is recommended to carry out whole-body hyperthermia once every two weeks, with six times as a course. Be sure to monitor body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give timely fluid infusion to maintain water–electrolyte balance and other symptomatic treatments. Review electrolytes, and so on 1–3 days after whole-body hyperthermia. Continue to supplement energy to maintain water–electrolyte balance. Local hyperthermia can be appropriately added at the intervals of whole-body hyperthermia according to the general condition and tolerance of patients.

If patients cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the liver area or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day, with 20 times as a course. Conduct the second course after an interval of 10 days. After three courses, local hyperthermia can be taken as long-term concomitant therapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.18.2.2 HYPERTHERMIA AND RADIOTHERAPY

Radiotherapy is one of the effective methods for the treatment of endometrial cancers. For patients with massive vaginal bleeding, in poor general condition, having many complications, and who are unable to tolerate surgery in the short term, to start with conduct radiotherapy for hemostasis and control of disease progression. Hysterectomy plus adnexectomy can be carried out until the patient's general condition improves. Local hyperthermia should be carried out as soon as possible, half an hour after the end of radiotherapy and within 2 hours once every other day, accompanying the full course of radiotherapy. It can sensitize the effect of radiotherapy and alleviate local skin damage, fibrosis, and local tissue adhesion.

6.18.2.3 HYPERTHERMIA AND CHEMOTHERAPY

Chemotherapy alone is rarely used in the treatment of endometrial cancer, but it is commonly used for special types of endometrial cancer. Drugs used for chemotherapy are mainly platinum, taxol, Adriamycin, and doxorubicin. Currently, combination chemotherapy is commonly applied. Chemotherapy programs are AP, TP, TAP, and so on. Generally, conventional chemotherapy is conducted for four to six cycles and whole-body hyperthermia can be synchronized with the cycle of chemotherapy for a total of four to six times. Local hyperthermia can be carried out during the intermission periods of chemotherapy, once every 2 days, and can also be applied in combination with other approaches in long-term treatment.

For patients who are completely unable to tolerate systemic chemotherapy or who refuse systemic chemotherapy, Clifford Hospital has effectively combined insulin-mediated small doses of intravenous chemotherapy with medical ozone and hyperthermia and achieved good results in clinical practice. Specific methods: rule out contraindications of chemotherapy through comprehensive assessment and obtain informed consent of patients. An empty stomach is required before chemotherapy. Carry out medical ozone major autohemotherapy before chemotherapy and give insulin to control blood glucose at about 3.6 mmol/L or so (it is better to control blood glucose when hypoglycemia reaction has just appeared, and according to individual circumstances), and then give small-dose TP program (10%–30% of conventional amount)/intravenous chemotherapy, twice a week for 2–4 weeks. Conduct routine antiemetic, hepatic protection and stomach protection, with supplementation of high glucose and trace elements. Conduct hyperthermia within 2–4 hours after chemotherapy. If the patient is in good general condition and can tolerate whole-body hyperthermia, it is appropriate to have whole-body medium-high temperature hyperthermia.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body medium-high hyperthermia can be carried out simultaneously in the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. Simultaneously carry out the hyperthermia and chemotherapy cycle for six to eight courses. Local hyperthermia can be implemented during the intermission periods of chemotherapy.

For patients who cannot tolerate whole-body medium-high temperature hyperthermia, local hyperthermia at the right upper abdomen or whole-body medium-low temperature hyperthermia can be carried out. Conduct local hyperthermia once every other day and continue at the intervals of chemotherapy. Take 1 week off after each cycle (5 consecutive days) of chemotherapy. A total of about 60–80 times of combined local hyperthermia is carried out during chemotherapy. Conduct whole-body medium-low temperature hyperthermia once a week for a total of 12 times.

6.18.2.4 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Because patients are prone to postoperative physical weakness and low immunity after chemoradiotherapy, chelation detoxification therapy and medical ozone can be given from the end of operation to the period of chemotherapy; they can promote physical recovery and regulate the immune system, kill residual tumor cells, and inhibit early metastasis. Conduct chelation detoxification therapy by intravenous drip once every other day. It is noted that chelation detoxification needs infusion for more than 2 hours. Hyperthermia can be simultaneously applied with chelation and detoxification to improve efficacy. The therapeutic dose can be gradually increased if there is an absence of adverse reactions, taking 20 times as a course of treatment for a total of three courses.

6.18.2.5 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance the effect on immunity, and increase the efficacy of medical ozone. The specific program of medical ozone therapy is as follows: (1) for patients with good vascular condition, use EBOO once every other day, with 20 times per course of treatment for a total of three courses. (2) For patients with hypovolemia, medical ozone major autohemotherapy can be carried out once every other day, with 12 times as a course of treatment. Use medical ozone minor autohemotherapy once every other day, with 12 times per course. Use medical ozone acupoint injection once every other day, with 12 times as a course, and three courses are conducted for each therapy. (3) For patients in poor physical condition or unable to tolerate EBOO or major and minor autohemotherapy, medical ozone saline infusion is given once every other day, for 10–14 days as a course of treatment, which can be taken for long-term maintenance therapy. According to the specific circumstances of patients, vaginal medical ozone insufflation or medical ozone saline rinse, once every day, is conducted after radiotherapy to reduce vaginal injury after radiotherapy.

6.18.2.6 HYPERTHERMIA AND ENDOCRINE THERAPY

Progestin preparation has treatment effect on about one-third of medium and advanced or recurrent endometrial cancer patients and is particularly best suited for lung metastasis. Approximately 35% of patients had significant reaction, but the effect on pelvic recurrence or persistence of lesions was not good. Highly efficient progesterone hormones currently consist of many types, such as megestrol acetate, medroxyprogesterone acetate, hexanoate progesterone, and acid hydroxy progesterone with an antiestrogen drug tamoxifen. The cases that show treatment effect of progesterone are mainly patients whose receptors tested positive. Routinely give medroxyprogesterone acetate 160 mg twice a day for long-term use, which has the effect of increasing appetite and improving patients' quality of life. Conducting hyperthermia at the same time with endocrine therapy has the effect of improving the quality of life as well as survival time for some patients.

6.18.2.7 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. Other treatments such as TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, alkaline treatment, colon cleansing therapy, and so on, in combination with hyperthermia, can increase the effectiveness and safety of the treatment.

DC-CIK cell therapy: After early gynecologic malignancy radical resection, DC-CIK transfusion can effectively remove residual small lesions and reduce recurrence. The number of CIK cells for each reinfusion should reach at least 1×10^{10}, once per month, with four times as a course of treatment. Conduct periodic

review after transfusion, and if there is no recurrence an additional treatment is carried out once every 6 months. Postoperative DC-CIK can be combined with conventional chemoradiotherapy, endocrine therapy, and other integrative treatments. Treatment protocols: one day before chemotherapy collect the patient's peripheral blood for DC-CIK preparation, and conduct reinfusion 10–12 days after chemotherapy. One week after reinfusion, that is, 1 day before the second cycle of chemotherapy, collect again peripheral blood for DC-CIK preparation; continue this for four times as a course of treatment, and assess the efficacy. If it is effective, then conduct a consolidated therapy once every 2 to 3 months. DC-CIK in combination with radiotherapy also applies the principle that DC-CIK reinfusion is conducted in the interval of radiotherapy. For example, on the day when radiotherapy is to be conducted collect the patient's peripheral blood for DC-CIK culture before the start of radiotherapy and conduct reinfusion at the interval of radiotherapy. DC-CIK can be combined with endocrine therapy.

Systemic biofeedback therapy: Three times a week, with 20 times as a course of treatment. Change to once or twice a week after two to three courses of treatment for long-term treatment.

Alkaline treatment: Intravenous or oral sodium bicarbonate therapy can be used with medicated diet to alkalize constitution. Medium and advanced patients accompanied by intra-abdominal metastasis can also be given sodium bicarbonate peritoneal perfusion therapy. For details, please refer to Section 4.10.

Colon cleansing therapy: Patients can take fruit and vegetable drinks with the coffee enema; but a clinical nutritionist should be invited for nutritional status monitoring and, when necessary, to give parenteral nutritional support.

In addition to hyperthermia, chelation detoxification, medical ozone, acupuncture, and TCM, we emphasize dietotherapy plus qigong plus sports as supplementary treatments to improve overall immunity. Encourage and instruct patients in ways of dealing with their disease in their daily living.

6.18.2.8 HYPERTHERMIA AND HERBAL MEDICINES

6.18.2.8.1 Grilling method

Proven prescription: Yongquan Plaster: one piece of large and raw *Radix aconiti Lateralis Preparata*; one pair of big *Syngnathus*; 9 g each of *Lysimachia foenum-graecum*, *Squama manitis*, and *Cynomorium songaricum Rupr*; sesame oil 600 g; and Yellow Lead 200 g. Boil them into paste, which is mixed well with 15 g each of *actinolitum* and musk and 9 g each of *Cordyceps sinensis*, ginseng, Sichuan pepper, and clove fruit. Spread out 1 g to the size of a coin each time and paste to the centers of both feet, and then bake for 0.5–1 hour in the affected area with the Magic Lamp. Efficacy: reinforces liver and kidney. It is applicable to middle-aged and old-aged patients with diseases producing masses in the abdomen due to renal asthenia and general debility (applicable to tumors in various parts of the body).

Aweihuapi Plaster: Decoct *ferula*, *Rhizoma sparganii*, *Rhizoma curcumae*, *rhubarb*, crude *Sichuan aconite root*, *Olibanum, Momordica cochinchinensis*, dung beetle, *Rhizoma cyperi*, *aloe vera*, *Resina draconis*, and *camphor* into a paste. Heat the mixture to soften it for external application, paste it in the umbilical region or the affected area, and then irradiate for 30 minutes with the Magic Lamp, once a day. Efficacy: regulates the flow of qi and promotes blood circulation, softens and resolves hard mass, relieves chest and abdominal distention, and disintegrates abdominal mass. It is applicable to patients who have chest and abdominal distention; abdominal mass; and symptoms of qi stagnancy and blood stasis in liver, gallbladder, stomach, and intestine and gynecological diseases.

6.18.2.8.2 Steam therapy

Taohong Huoxue Decoction: Radix astragali 30 g, *Radix paeoniae Rubra* 20 g, *Angelica sinensis* 20 g, *Ligusticum chuanxiong Hort* 20 g, *Semen persicae* 20 g, *Carthamus tinctorius L.* 20 g, *Ramulus cinnamomi* 25 g, *Radix puerariae* 20 g, *Pericarpium citri Reticulatae* 20 g, and *Salvia miltiorrhiza* 30 g. Put the drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic fumigation. Efficacy: invigorates qi and blood, promotes blood circulation, and removes blood stasis. It is applicable to cancer patients having the syndromes of qi deficiency and blood stasis.

6.18.2.9 HYPERTHERMIA INDICATIONS AND CONTRAINDICATIONS

For patients who are accompanied by systemic infection or cervical local severe infection, bleeding tendencies, poor general condition, and a KPS less than 60 points, it is not appropriate to apply hyperthermia, but other patients can be treated with hyperthermia or with other treatments for combination application.

6.18.3 Introduction of a typical case

A patient named Li, female, 59 years old, was admitted on January 27, 2010, to Clifford Hospital due to "postoperative endometrial cancer for 15 months, abdominal distension and abdominal pain with weight loss for 4 months, aggravating for two days." On October 2008, the patient underwent hysterectomy + adnexectomy plus partial vaginectomy plus lymphadenotomy of paraaortic lymph nodes due to endometrial cancer. The patient received 24 treatments of radiotherapy within 1 month after surgery and experienced stool irregularity and constipation alternated with diarrhea after radiotherapy. On September 2009, the patient showed recurrent abdominal distension and abdominal pain radiating to the back, which was aggravated after drinking water and having food. The sense of abdominal distension was present throughout the whole abdomen. Gastric acid returned, and loud bowel sounds could be heard. Vomiting of the stomach contents occurred. Abdominal distension and abdominal pain could be alleviated after vomit or stool discharge. The patient had poor appetite and ate less. On December 8, 2009, X-ray taken at another hospital showed possible intestinal obstruction. Abdominal CT scan plus enhancement showed a small amount of ascites, small bowel expansion, effusion, and intestinal obstruction. Colonoscopy showed proctitis and schistosome eggs. Diagnosis was "proctitis, schistosomiasis, chronic gastritis, and intestinal obstruction." After antischistosome regulation of intestinal function and anti-inflammatory treatment were given, the patient was discharged after the symptoms were alleviated. On January 6, 2010, mesenteric contrast examination revealed intestinal obstruction, which was considered to be caused by adhesions. The patient was with persistent symptoms and could only have a liquid diet, resulting in weight loss, malaise, and palpitation. The patient had intensified abdominal distension and abdominal pain 2 days before admission, accompanied by frequent vomiting, which was why the patient came to Clifford Hospital. The patient was admitted as outpatient due to "postoperative incomplete intestinal obstruction of endometrial cancer."

Physical examination: Body weight of 45 kg, poor nutrition, marasmus, and clear lung breathing sounds. Wet and dry rales were not heard. The heart rate was 85 beats/min, with regular rhythm. Pathological murmurs were not heard at the auscultation area of the heart valve. The abdomen was soft, with visible intestinal shape at intervals, which could be relieved by itself after about a few minutes. There was lower abdominal tenderness (+) and no rebound tenderness. High-profile sounds of air over the water could be heard.

Auxiliary examinations: Blood routine: WBC 3.91×10^9/L, RBC 2.8×10^{12}/L, HGB 67 g/L, and PLT 120×10^9/L. Biochemistry: ALT 55 U/L and AST 95 U/L. Bilirubin and protein were normal. CHOL 2.04 mmol/L and LDL 0.72 mmol/L. Determination of blood trace elements: Ca 2.03 mmol/L and Fe 8.8 μmol/L. Tumor marker: CA12-5 148.60 U/mL. On January 22, 2010, PET/CT results reported the following: (1) postoperative endometrial adenocarcinoma after radiotherapy, and retroperitoneum multiple high metabolic enlarged lymph nodes, considered to be lymph nodes metastases; (2) no residual tumor and no signs of recurrence in the local pelvic surgery area; (3) incomplete small bowel obstruction and pelvic fluid; (4) fatty liver; (5) left and right coronary artery calcification; and (6) PET/CT imaging showed no abnormalities in other parts of the body.

Diagnosis: (1) Postoperative endometrial cancer, (2) incomplete intestinal obstruction, (3) radiation enteritis, and (4) schistosomiasis.

Integrative treatment prescription: The patient could not eat when she was admitted. Gastrointestinal decompression and intravenous nutritional support were given immediately after admission. Treatment focused on nontoxic integrative treatments. Chelation detoxification, medical ozone, herbal medicines, acupuncture, systemic biofeedback therapy, and other integrative treatments were given. The patient exhibited dark tongue, petechia, and a deep and unsmooth pulse. The syndrome belonged to toxin and blood stasis stagnating in the body. The treatment focused on promoting blood circulation and removing blood stasis, as well as removing lumps and relieving pain.

Medications: The prescription recommended was a modified Shaofu Zhuyu Decoction. Specific medication: *Angelica sinensis* 15 g, *Radix Paeoniae rubra* 15 g, *Foeniculum vulgare Mill* 15 g, ginger 10 g, *Rhizoma corydalis* 9 g, *Myrrha* 12 g, *Ligusticum chuanxiong Hort*. 9 g, *Cinnamomum cassia Presl* 6 g, *Faeces trogopterpri* 12 g, *Cattail Pollen* 9 g, *Rhizoma sparganii* 10 g, and *Rhizoma curcumae* 10 g, one dose a day, decocted with water for oral administration.

Acupuncture on acupoints: Neiguan, Sanyinjiao, Zusanli, Shangjuxu, Yinlingquan, Tianshu, Qihai, Shenshu, Taichong, Taixi, and Waisanguan. Methods: even reinforcing–reducing methods were used. Retained the needles for 20 minutes, once a day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Guanyuan, Zhongji, Shenque, Zusanli, Guanyuanshu, and Baihuanshu. Methods: took two points each time with a moxa stick for moxibustion. Conducted moxibustion for 10 minutes above each point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Zigong, Penqiang, Yaodizhui, kidney, Pizhixia, adrenal gland, Neifenmi, Jiaogan, liver, and Erjian; stuck auricular points with cowherb seed. The patient was asked to press by herself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

After 9 days of aggressive treatment, intestinal obstruction of the patient was gradually reduced and hemoglobin was raised to 85 g/L from 67 g/L. The patient smoothly took a small amount of porridge and water and had defecation once every 2 days. Chelation detoxification was given once every other day, synchronized with local hyperthermia. Systemic biofeedback treatment was conducted three times a week, EBOO twice a week, medical zone rectal infusion once a day, intraperitoneal hyperthermic perfusion of cisplatin 40 mg once every 2 weeks, with four sessions in total.

The patient was discharged after 2.5 months of treatment. The patient continued to receive outpatient local hyperthermia, systemic biofeedback therapy, chelation detoxification, and medical ozone therapy. During hospitalization, the patient had always insisted on practicing qigong and had been taking megestrol.

Treatment effects: After more than 70 days of hospitalization, the symptom of intestinal obstruction was relieved and mentality was significantly improved. Diet was acceptable, and urine and stool were normal. Skin and mucus membranes were in blush, and weight was increased to 52 kg. The KPS was 90. Recheck: CA12-5 38.50 U/mL. Blood routine: WBC 4.8×10^9/L, RBC 4.2×10^{12}/L, HGB 90/L, and PLT 150×10^9/L. In May 2010, the review of PET/CT results was reported: (1) postoperative endometrial adenocarcinoma after radiotherapy and retroperitoneum multiple high metabolic enlarged lymph nodes, considered to be lymph node metastasis. Compared with the PET/CT of January 22, metabolism was significantly lower and metabolic lesions were significantly reduced. (2) No residual tumor and signs of recurrence in the local pelvic surgery area. (3) Small bowel obstruction was basically relieved; pelvic fluid. (4) Fatty liver. (5) Left and right coronary artery calcification. (6) PET/CT imaging showed no abnormalities in other parts of the body.

The patient continued to have local hyperthermia, systemic biofeedback therapy, chelation detoxification, medical ozone, TCM, herbal medicine, and other integrative treatments after being discharged from hospital. Review showed that CA125 gradually returned to normal. To date, intestinal obstruction has not been detected by follow-up examinations. Till now, tumor indexes are normal, multiple reviews of the abdomen have been conducted, and no swelling lymph nodes have been seen by CT.

6.18.4 Related research in China and abroad

Kurpeshev et al. have reported that RF combined with lower doses of radiotherapy for the treatment of endometrial cancer received satisfactory results. At the same time, it could reduce radiation reaction of adjacent normal tissues and organs.

Zaporozhan et al. have observed the effect of postoperative γ radiation and shortwave radiation on cellular immunity in 81 cases of endometrial cancer patients and found that shortwave radiation had immune-stimulating and immunomodulatory effects and could restore the patient's normal immune function.

In 1996, Ueki et al. used laser thermal balls for treatment of early endometrial cancer, with the results that histological changes were up to 4–6 mm, the surface of foci was smooth after treatment, and the majority of cancer infiltrations did not exceed one-fourth of the myometrium, but its clinical utility value needed

further study. The studies by Rau et al. have shown that for advanced cancer patients with abdominal and pelvic metastases who cannot accept systemic chemotherapy, the efficacy of local hyperthermal perfusion chemotherapy combined with RF diathermy for treatment was determined.

6.19 TUMORS OF LIMBS, BONES, AND SOFT CONNECTIVE TISSUES

Limb cancers are mainly bone cancer, soft tissue sarcoma, malignant melanoma, and so on.

Osteosarcoma, a kind of common bone cancer also known as osteogenic sarcoma, originates in mesenchymal tissue and is characterized to produce spindle-shaped stromal cells of bone-like tissue. Osteosarcoma commonly occurs at the metaphyseal segment of the limb long bones and the most common sites are distal femur, proximal tibia, and humerus, whereas flat bone is less involved. According to different histological types, osteosarcomas can be divided into osteoblastoma type, chondroblastoma type, myofibroblastoma type, small cell type, giant cell-rich type, and telangiectasia type. Prominent clinical manifestations of this disease are swelling, tenderness, and masses. Distant metastases are prone to occur in the early stage. The majority of patients already have the presence of tiny metastases when seeking medical services. Lung metastasis is the most common, followed by bone. Bone cancers are divided into primary and secondary categories. Almost all of the bone cancers are with hematogenous metastasis. Therefore, in most cases, only surgery combined with systemic chemotherapy treatment can cure primary bone cancers. Because most bone cancers are not sensitive to chemoradiotherapy, hyperthermia in combination with chemoradiotherapy as well as with integrative treatment is needed to improve the therapeutic effect. For secondary tumors, refer to the treatment protocol of the primary disease and add local hyperthermia at the metastatic sites and the corresponding anti–bone metastasis treatment.

Soft tissue tumors refer to tumors originating from mesenchymal tissue, such as fibrous tissue, striated muscle, fat, synovium, mesothelium, blood vessel, and so on and are divided into benign, malignant, and intermediate tumors. The common soft tissue sarcomas with higher concentration of incidence are divided into fibrosarcoma, synovial sarcoma, rhabdomyosarcoma, liposarcoma, leiomyosarcoma, and mesothelioma. Soft tissue sarcoma can occur at any age and in any part of the body but more commonly in limbs, where incidence accounts for about 40% for lower limbs, about 30% for torso and retroperitoneum, 15% for upper limbs, and 15% for head. In addition, a few occur in internal organs. The disease often presents invasive growth, is not always easy to be completely resected, and has a high recurrence rate. Distant metastasis is another feature of soft tissue sarcoma and is mainly hematogenous metastasis. Metastatic sites are lung, bone, brain, liver, and so on. Lungs are the most common metastatic sites of limb sarcomas, which also have metastasis through the lymphatic system.

Malignant melanoma is a highly malignant tumor derived from melanocytes. Due to the distribution of melanoma cells in skin, eyes, mucus membrane surfaces, and nervous system, malignant melanoma can occur in skin, mouth, digestive tract, respiratory tract, reproductive system and mucus membranes, eye ciliary body, iris, choroid, choroidal meninges, and so on, of which approximately 90% occurs in the skin. For men it commonly occurs on the trunk, head, and neck, and for women it commonly occurs in the limbs. Cutaneous malignant melanomas mainly have four pathological types such as superficially disseminated, nodular, freckle-like, and acral freckle–like. If the disease is detected early, diagnosed early, and properly treated, many patients can be cured; but the disease is highly malignant and tumor stimulation can cause tumor metastasis, which is prone to hematogenous dissemination and poor prognosis.

Because hyperthermia applications for limb malignancies (including bone cancers, soft tissue sarcoma, malignant melanoma, etc.) are similar, they will be put together for discussion.

6.19.1 Conventional treatments

6.19.1.1 SURGERY

Surgical resection is the primary means for the treatment of osteosarcomas. Amputation and disarticulation are the most common methods. However, with the progress of chemotherapy in recent years, some

researchers have begun applying resection of tumor segment or total femur resection, with artificial prosthetic for replacement. Limb salvage has become a major operation. Conduct preoperative standardized chemotherapy for 6–8 weeks, and then implement tumor resection. Resection margin is required to be radical or extensive. Artificial joint replacement is commonly used for bone defects. If limb salvage is not suitable or in the case that there is no condition for limb salvage, amputation should be decisively implemented, but postoperative chemotherapy has to be applied. Chondrosarcoma treatment focuses on surgery, and the efficacy depends on the breadth of tumor resection and malignancy of histological grade. Ewing's sarcoma is very sensitive to radiation and chemotherapy. In current treatment protocols, the most advocated is neoadjuvant chemotherapy combined with extensive or radical resection of tumor. The therapeutic principle of treatment for bone malignant fibrous histiocytoma is similar to that of osteosarcoma.

Surgical treatment is an important means for limited soft tissue sarcomas. For ideal local excision, tumors of all positions must be removed together with the surrounding normal tissue and we often have to give up some of the normal organizational structure to ensure complete resection. Surgical resection should include the site of biopsy and the nearby skin and partial muscles. For muscle tumor, the affected muscle should be excised completely. Only when lymph node involvement is shown clinically can lymph node dissection be carried out. For soft tissue tumors that cannot be completely excised, debulking surgery can be applied, and postoperative integrative treatments are combined to improve quality of life and prolong survival time. Amputation is applicable for advanced patients with a giant tumor accompanied by massive ulcer hemorrhage that cannot be stopped; patients accompanied by severe infections such as sepsis, tetanus, and so on that endanger their life; patients with a tumor that grows rapidly and causes severe pain and is difficult to control with medication; or patients who cannot be saved by using other methods due to pathological fractures, loss of activity, and other serious conditions.

The most important treatment for malignant melanoma is surgical removal of skin lesions. For malignant melanoma in situ, the recommended resection margin from the lesion or biopsy scar is 0.5–1 cm. For lesions with a thickness less than 1 mm, a margin of 1 cm can also be accepted. For lesions with a thickness of 1 to 2 mm, a margin of 2 cm is strived for. For lesions with a thickness of 2–4 mm, a margin of 2 to 3 cm is recommended. For postoperative patients (stage IIb or IIc) with the thickness of primary foci exceeding 4 mm or regional lymph node metastasis patients (stage III) who had lymph node dissection, it is recommended to strive for a resection margin of 3 cm. Postoperative adjuvant therapy can help reduce the risk of recurrence and metastasis and improve the quality of life.

6.19.1.2 RADIOTHERAPY

Radiotherapy can only be an adjuvant therapy for the treatment of bone cancers. Radiotherapy is ineffective for chondrosarcoma. Ewing's sarcoma is sensitive to radiotherapy. For cases that are inoperable and surgery can only result in marginal or intralesional resection, radiotherapy and chemotherapy can be carried out.

The majority of soft tissue sarcoma patients should receive preoperative or postoperative radiotherapy, but there is also research evidence showing that smaller primary tissue sarcoma does not necessarily require radiotherapy after complete resection. Radiotherapy is often combined with limb salvage surgery for the treatment of soft tissue sarcomas to get the best local control. Radiotherapy can be given as preoperative or postoperative external irradiation or tissue interstitial irradiation (brachytherapy).

For malignant melanomas, when lesions cannot be excised or distant organ metastases occur adjuvant radiotherapy can be considered. For patients with only skin or lymph node metastasis, sometimes local radiotherapy can be considered.

For bone metastases, 89SiCl, 131I, 186Re-HEDP, 153Sm, and other isotopes are accumulated at a high concentration at the tumor site, which plays a further role in inhibiting tumor destruction of bone by internal radiation.

6.19.1.3 CHEMOTHERAPY

Osteosarcoma chemotherapy focuses on following the principles of drug combination, neoadjuvant chemotherapy, and dose intensity. Chemotherapy is ineffective for chondrosarcomas. Ewing's sarcoma is sensitive to chemotherapy, so chemotherapy and radiotherapy can be combined. Chemotherapy combined with surgery

is mainly used for malignant fibrous histiocytoma of bone. Chemotherapy can be local or systemic chemotherapy. Local chemotherapy includes intra-arterial infusion chemotherapy and regional perfusion, of which the regional perfusion effect is better.

The value of soft tissue sarcoma systemic chemotherapy depends on the type of tumor. For Ewing's sarcomas and rhabdomyosarcomas, chemotherapy can be carried out before surgery. After surgical resection, adjuvant chemotherapy should be carried out. For other tissue types of soft tissue sarcomas, the value of systemic chemotherapy is still controversial.

For malignant melanoma patients with the presence of distant metastases (stage IV), chemotherapy and biological treatment are mainly conducted and local radiotherapy, disease reduction surgery, and palliative surgery can also be considered. Currently, drugs approved by the U.S. FDA for the treatment of advanced melanoma include dacarbazine and high-dose interferon α-2b. Temozolomide is the analog of DTIC, which can penetrate the blood–brain barrier. It can also be tried for the treatment of advanced melanoma, especially for patients presenting brain metastases.

6.19.1.4 HYPERTHERMIA

For limb, bone, and soft tissue tumors, basic research and clinical practice have confirmed that, regardless of the heating mode, the clinical effects of hyperthermia are obvious. Currently, limb heating perfusion and other integrative treatments with hyperthermia have been accepted by many medical centers and some clinical experiences have been obtained conducive to limb salvage surgery. Methods of limb, bone, and soft tissue hyperthermia have been developed for preoperative/intraoperative hyperthermia, thermoradiotherapy, thermochemotherapy, and so on.

6.19.1.5 CHELATION DETOXIFICATION THERAPY

Chelation detoxification therapy mainly focuses on the overall factors at disease onset, improves immune function, indirectly kills cancer cells, and induces cancer cell apoptosis, which are of great significance in the prevention of recurrence and metastasis. It can be applied at the same time with hyperthermia, once every other day, with 20 times as a course of treatment.

6.19.1.6 MEDICAL OZONE THERAPY

Medical ozone can not only conduct overall regulation against cancer etiology but also be carried out as local application for direct effect on the cancer. EBOO can be given for systemic application once every other day, with 20 times as a course of treatment. Patients in poor physical condition or with active bleeding are subject to medical ozone saline infusion, once every other day, with 12 times per course of treatment, or medical ozone major autohemotherapy, once every other day, with 12 times per course of treatment, or medical ozone acupoint injection, once every 3 days, eight times per course of treatment. Selection of points is the same as that in acupuncture. Medical ozone enveloping therapy on the skin or medical ozone olive oil coating as well as oxygen gas injection around the tumor can be used for local application, which can directly cause tumor necrosis and inhibit tumor surface bleeding, infection, and so on.

6.19.1.7 TRADITIONAL CHINESE MEDICINE

6.19.1.7.1 Bone cancers

For the syndrome of severe pathogenic cold blocking collaterals, the prescription recommended is modified Wutou Decoction; for the syndrome of accumulated toxic heat, the prescription recommended is Xijiao Dihuang Decoction plus modified Huanglian Jiedu Decoction; for the syndrome of stasis and toxin stagnating in the body, the prescription recommended is Shentong Zhuyu Decoction; and for the syndrome of spleen and kidney deficiency, the prescription recommended is modified Bazhen Decoction. Commonly used Chinese patent medicines are Xihuang Pill, Xinhuang Tablet, Pingxiao Capsule, and so on.

6.19.1.7.2 Soft tissue sarcomas

For the syndrome of phlegm-dampness-coagulation, the prescription recommended is modified Haizao Yuhu Decoction; for the syndrome of stagnation of heat and toxins, the prescription recommended is modified

Wuwei Xiaodu Decoction; for the syndrome of qi stagnation and blood stasis, the prescription recommended is modified Taohong Siwu Decoction; for the syndrome of deficiency of both qi and blood, the prescription recommended is Bazhen Decoction plus modified Huangqi Guizhi Wuwu Decoction. The commonly used Chinese patent medicines are Dahuang Zhechong Pill, Biejiajian Pill, Pingxiao Capsule, Xiaojin Dan, and so on.

6.19.1.7.3 Malignant melanomas

For the syndrome of excessive noxious heat, the prescription recommended is Wuwei Xiaodu Decoction plus modified Xinfang Huoming Decoction; for the syndrome of phlegm dampness retention, the prescription recommended is Erchen Decoction plus modified Haizao Yuhu Decoction; for the syndrome of stasis and toxins stagnating in the body, the prescription recommended is Taohong Siwu Decoction plus modified Simiao Yongan Decoction; and for the syndrome of deficiency of both qi and blood, the prescription recommended is Bazhen Decoction. The commonly used Chinese patent medicines are Liushen Pill, Xihuang Pill, Pingxiao Capsule, Liuwei Dihuang Pill, Elemene Injection, and so on.

6.19.1.8 ACUPUNCTURE

6.19.1.8.1 Bone cancers

The therapeutic principle of bone cancers focuses on toning kidney and strengthening bone, dredging meridians and relieving pain.

Acupuncture on acupoints: Juegu, Taixi, Sanyinjiao, Zusanli, Geshu, Xuehai, and Dazhui.

Methods: Use mild reinforcing–reducing method. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Dazhui, Zusanli, Shenzhu, Mingmen, Pishu, and Shenshu.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Pizhixia, Jiaogan, Shenmen, Zhen, adrenal gland, kidney, Pishu, stomach, and Erjian.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week; alternate ears, with 10 times as a course of treatment.

6.19.1.8.2 Soft tissue sarcomas and malignant melanomas

The therapeutic principle for treating soft tissue sarcomas and malignant melanomas focuses on promoting blood circulation and removing blood stasis, as well as clearing heat and resolving phlegm.

Acupuncture on acupoints: Feishu, Zhongfu, Taiyuan, Zusanli, Pishus, Geshu, Yinlingquan, Fenglong, Taichong, Xuehai, and Weizhong.

Methods: Use mild reinforcing–reducing method. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Pishu, Geshu, Feishu, Guanyuan, and Zusanli.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Pizhixia, heart, Erjian, Jiaogan, liver, lung, Shenmen, Fengxi, adrenal gland, and the corresponding parts of lesions.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.19.1.9 MEDICATED DIET, NUTRITION, AND SO ON

Be sure to use medicated diet and food therapy to enhance nutritional support; especially supplement sufficient amounts of vitamins, trace elements, and so on, which contribute to the rehabilitation of patients.

6.19.1.10 OTHERS

Patients are often depressed or irritable due to pain or limb movement disorder and lose confidence in cancer healing. Qigong therapy, psychotherapy, and so on can help patients improve their psychological state of mind to improve the body's reaction and to adjust the level of metabolism, as well as improving self-healing capabilities. With the advances in modern technology, some local physical therapies can be chosen to directly kill tumor cells, such as cryotherapy, laser vaporization, laser curing, and photodynamic therapy. But these methods only suppress the symptoms, and nontoxic integrative treatments must be applied after treatment to prevent cancer recurrence and metastasis.

6.19.2 Combination of hyperthermia with conventional treatments

6.19.2.1 HYPERTHERMIA AND SURGICAL TREATMENT

Surgery is the main treatment for limb, bone, and soft tissue tumor lesions. Because of its characteristic of easy metastasis, after the postoperative wound is completely healed whole-body hyperthermia can be carried out after excluding hyperthermia contraindications through assessment of surgical site recovery by the physician, laboratory tests revealing no bleeding tendency, and comprehensive assessment of patients by the hyperthermia center physician to prevent tumor recurrence and metastasis.

It is recommended to apply whole-body hyperthermia and local hyperthermia alternately: whole-body hyperthermia, adopting whole-body medium-high temperature hyperthermia once every 10–14 days, with six times as a course of treatment, and local hyperthermia, adopting external RF local hyperthermia once every 2 days, with two times as a course of treatment. After three courses, local hyperthermia is not limited by course and can be used for long-term treatment.

6.19.2.2 HYPERTHERMIA AND CHEMORADIOTHERAPY

Hyperthermia combined with systemic chemotherapy or radiotherapy may be considered. A number of studies have demonstrated that combined hyperthermia can increase the sensitivity of limb, bone, and soft tissue tumors to chemoradiotherapy.

If patients are assessed to be in good general condition and can tolerate whole-body hyperthermia, whole-body medium-high temperature hyperthermia can be carried out in combination with the chemotherapy cycle. Local hyperthermia can be added at the intermission periods of whole-body hyperthermia. Hyperthermia is simultaneously carried out with the chemotherapy cycle for six to eight courses. Local hyperthermia can be carried out at the intermission periods of chemotherapy once every other day, accompanying the whole process of chemotherapy.

For patients who cannot tolerate whole-body medium-high hyperthermia, local hyperthermia or whole-body medium-low temperature hyperthermia can be carried out. Local hyperthermia on the primary tumor and metastases can be carried out at intervals and can be continued during the intermission periods of chemotherapy. The total number of combined local hyperthermia carried out during the period of chemotherapy is about 30–40 times. Carry out whole-body medium-low hyperthermia once a week for a total of 12 times.

For symptomatic bone metastases, hyperthermia is used to relieve pain and restore function. It is selectively used for bone metastasis preventive radiotherapy at the weight-bearing location, such as spinal metastasis or femoral metastasis. The majority of patients with bone metastasis, even patients with medium-advanced cancer, are likely to tolerate local palliative radiotherapy. The organic combination of radiotherapy and hyperthermia with the application of medical ozone, chelation detoxification, and herbal medicines, at the same time, can not only reduce the side effects of radiotherapy but also produce a therapeutic synergy. The order of radiotherapy followed by hyperthermia is important for the application of hyperthermia combined with radiotherapy; local hyperthermia should be carried out within 2 hours after radiotherapy once every other day, accompanying the full course of radiotherapy.

6.19.2.3 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Whole-body hyperthermia and local hyperthermia help to ease the pain from bone metastases, and chelation detoxification is carried out simultaneously to inhibit further metastasis of the tumor and relieve bone destruction. Carry out chelation detoxification therapy once every other day, with 20 times as a course of treatment for a total of three courses. For patients who have excessive heavy metals in the blood, a chelating agent can be added and it must be noted that intravenous infusion should not be less than 2 hours. Simultaneously conducting hyperthermia and chelation detoxification can increase chelation detoxification efficacy.

6.19.2.4 HYPERTHERMIA AND MEDICAL OZONE THERAPY

The patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance effect on immunity, and increase the efficacy of medical ozone. Use EBOO once every other day, with 20 times per course of treatment for a total of three courses. For patients in poor physical condition or who are unable to tolerate it, medical ozone saline infusion is given once every other day, with 10–14 days as a course of treatment, or medical ozone major autohemotherapy is given once every other day, with 12 times as a course of treatment. According to the specific circumstances of patients, vaginal medical ozone insufflation or medical ozone saline rinse can also be chosen after radiotherapy, once a day, which have a clear effect in alleviating vaginal injury after radiotherapy.

6.19.2.5 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. The combined application of Chinese medicine, acupuncture, systemic biofeedback treatment, and alkaline treatment with hyperthermia can increase the effectiveness and safety of treatment.

Giving hyperthermia at the same time can further reduce side effects and achieve the best therapeutic effect.

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Adjust to one or two times a week after two to three courses of treatment for long-term treatment.

Alkaline treatment: Food therapy can alkalize the body. Adopt locally external application of sodium bicarbonate or acupoint injection therapy; conduct routine disinfection, and avoid blood vessels. Inject 2.5%–5% sodium bicarbonate with a thin needle at multiple points, about 2 mL at each point, for a total of not more than 10 mL at one time once every other day, with eight times as a course of treatment.

6.19.2.6 OTHER HYPERTHERMIAS

Continuous perfusion with hot water at constant temperature for in situ inactivation: Conduct locally radical curettage at the tumor bone lesions, and perfuse hot water at constant temperature into the cavity of residual tumor after curettage. Use the heat energy of hot water at constant temperature to heat and treat the tumor residual cavity. The surrounding normal tissues should be protected while using this method, and the tumor residual cavity should be fully soaked.

6.19.2.7 HYPERTHERMIA AND HERBAL MEDICINES

6.19.2.7.1 Bath

Prescription 1: Sappanwood 50 g, *Camphora* 50 g, *Ramulus cinnamomi* 15 g, old *Radix lithospermi* 15 g, *Fructus liquidambaris* 15 g, *Rhizoma homalomenae* 15 g, *Lycopodii herba* 15 g, *Olibanum* 10 g, *Myrrha* 10 g, *Carthamus tinctorius L.* 10 g, *Chaenomeles speciosa Nakai* 10 g, and *Rubus obcordatus* 10 g. Decoct drugs with water, and immerse (wash) joints of the affected part in the hot decoction. Efficacy: promotes blood circulation to dispel cold and removes meridian obstruction. It is applicable to patients with the syndromes of joint and bone pain caused by bone metastatic carcinoma.

Proven prescription 2: Rhizoma cyperi Rotundus L. 10 g, *Angelica sinensis* 10 g, *Myrrha* 10 g, *Natrii suleas* 10 g, *Cortex acanthopanacis* 10 g, *Pericarpium Citri reticulatae Viride* 10 g, *Zanthoxylum bungeanum* 10 g,

clove 3 g, musk 0.3 g, Old Shallot 3 g, *Cortex lycii* 3 g, and *Cortex moutan* 6 g. Decoct the mixture with water, and immerse (wash) joints of the affected part in the hot decoction. Efficacy: promotes blood circulation to dispel cold and removes meridian obstruction. It is applicable to patients with the syndromes of joint and bone pain caused by bone metastatic carcinoma.

6.19.2.7.2 Hot wax therapy

First knead the dough mud into a 1-cm thin long bar, and enclose the affected area. Sprinkle yellow wax shavings or externally apply yellow wax cake inside the circle. Put rubber or several layers of cloth on the periphery of the circle to prevent burns. When the yellow wax shavings are evenly distributed at 0.8–1.2 cm, bake above the yellow wax shavings with a copper spoon holding charcoal fire till the wax is melted. And then add the wax shavings till the dough circle is full, or coat with wax cakes in the circle until the thickness of the cake is like a coin. Cap with moxa and ignite the moxa till the wax is melted. Usually, this is conducted once a day. It has the effects of warming Middle Jiao to dispel cold, reducing swelling and relieving pain, improving motor function, and promoting tissue healing. It is applicable to cancer patients having limb joint pain and muscle neuralgia.

6.19.2.7.3 Steam therapy

Tougucao Decoction: Ramulus cinnamomi 12 g, *Saposhnikovia divaricata* 12 g, *Angelica dahurica* 12 g, *Zanthoxylum bungeanum* 12 g, *Folium artemisiae Argyi* 12 g, *Lycopodii herba* 12 g, *Speranskia tuberculata* 12 g, *Rhizoma et Radix notopterygii* 15 g, *Radix angelicae Pubescentis* 15 g, *Cortex acanthopanacis* 15 g, *Erythrina variegata* L. 15 g, and *Ramulus Mori* 30 g. Put the drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: promotes blood circulation to remove meridian obstruction. It is applicable to cancer patients with bone metastases and with neck, shoulder, and back-of-leg pain.

Shenjin Huoxue Decoction: Lycopodii herba 30 g, *Speranskia tuberculata* 30 g, *Radix paeoniae Alba* 30 g, *Clematis chinensis Osbeck* 25 g, *Radix aconiti* 20 g, *Radix aconiti Kusnezoffii* 20 g, *Asarum* 20 g, *Chaenomeles speciosa Nakai* 20 g, *Erythrina variegata* L. 20 g, *Olibanum* 15 g, *Myrrha* 15 g, and vinegar 200 mL. Put the drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: promotes blood circulation to remove meridian obstruction. It is applicable to cancer patients with bone metastases and with neck, shoulder, and back-of-leg pain.

Xunxi Yunbi Decoction: Crude *Sichuan aconite root* 15 g, *Health aconitum* 15 g, *Speranskia tuberculata* 15 g, *Clematis chinensis Osbeck* 15 g, *Rhizoma curcumae* 15 g, *Herba taxilli* 15 g, *Chinese Honeylocust Spine* 15 g, *Cruel semen Strychni* 10 g, *Asarum* 10 g, *Herba epimedii* 10 g, stir-baked *Radix paeoniae Alba* with Vino 20 g, and *Arisacma consanguineum* 12 g. Put the drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: promotes blood circulation to remove meridian obstruction. It is applicable to cancer patients with bone metastases and with neck, shoulder, and back-of-leg pain.

Proven prescription: Speranskia tuberculata 30 g, *Lycopodii herba* 30 g, *Erythrina variegata* L. 30 g, *Chinese star jasmine stem* 30 g, *Folium artemisiae Argyi* 30 g, *sappanwood* 20 g, *Carthamus tinctorius L.* 20 g, *Caulis spatholobi* 20 g, *Rhizoma corydalis* 20 g, *faeces trogopterorum* 20 g, *Ramulus cinnamomi* 20 g, *Radix curcumae* 20 g, *Radix angelicae Pubescentis* 20 g, and *Achyranthes bidentata* 20 g. Boil drugs inside the fumigating bed, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: warms yang and dredges collaterals. It is applicable to cancer patients with the syndrome of yang deficiency arthromyodynia.

6.19.2.8 HYPERTHERMIA INDICATIONS

Patients with KPSs of 60 points or above can use hyperthermia. The general condition needs to be critically assessed when conducting whole-body hyperthermia. If the local skin is uneven, a water pad can be added when conducting local hyperthermia.

6.19.2.9 HYPERTHERMIA CONTRAINDICATIONS

Local skin damage, bleeding tendency, and cachexia.

6.19.3 Introduction of a typical case

A patient named Feng, male, 73 years old, was admitted on February 8, 2009, to Clifford Hospital due to "weight loss for more than 1 year accompanied with anorexia and multiple body pain for 3 months." The patient exhibited weight loss without obvious inducement in January 2008. The patient had no fever or night sweats; no palpitations; excessive dreams at night; no polydipsia, polyphagia, or polyuria; and no abdominal pain, diarrhea, or other symptoms at the onset of the disease. The patient underwent endoscopy examination in another hospital; chronic gastritis was suggested, which was not specially treated. The patient lost about 40 kg of weight over more than 1 year after the onset of the disease (from 110 to 70 kg). Nearly 3 months before admission, the patient exhibited nonincentive anorexia and multiple body pains (severe at the chest and waist). He took morphine sulfate sustained-release tablets of 150 mg once every 12 hours for pain relief. He had shortness of breath, fatigue, weakness, and lower limb mild pitting edema. He exhibited no blurred vision, palpitations, chest pain or tightness, lower limb joint swelling, or varicose veins. He had acceptable sleep, poor appetite, and normal urine and stool. The patient was admitted as hospital outpatient due to "weight loss waiting for examination."

Physical examination: No obvious positive signs in heart, lung, or abdomen; bilateral ribs, thoracic, and lumbar multiple vertebral spinous process tenderness and percussion pain.

The patient showed normal blood routine, normal liver and kidney function, normal three items of rheumatoid and immunologic indexes, and normal six items of diabetes. Five tumor markers: CA199 92.75 ng/mL and others were normal. PET-CT showed the following: The metabolic rate of glucose was increased in the 4th, 6th, and the 11th ribs of the left side, the 11th thoracic vertebrae, and right pubis and ischium, which implies possible metastasis; T11 vertebral pathological fracture was observed. No abnormalities were found by gastrointestinal endoscopy. The results of bone marrow aspiration and biopsy were normal.

Diagnosis: Systemic multiple bone metastatic tumors.

Integrative treatment prescription: Multiple bone metastases were diagnosed by imaging. Because the patient was unfit for surgery and chemoradiotherapy, hyperthermia-based comprehensive treatment was applied to obtain good effect. Whole-body medium-low temperature hyperthermia was given once every 2 weeks, local hyperthermia was given at the right hip once every other day, and systemic biofeedback therapy was given three times a week. At the same time, chelation detoxification was given. EBOO was given twice a week. Herbal medicines and acupuncture treatment were combined throughout the whole treatment. The patient showed pale and plump tongue, white and slippery tongue fur, and slow and deep pulse, which belonged to the syndromes of yin cold coagulation and obstruction of collaterals by blood stasis. The treatment focused on warming yang to expel coldness, as well as promoting blood circulation to remove meridian obstruction.

Medications: The prescription recommended was Yanghe Decoction. Specific medication: *Radix rehmanniae Preparata* 30 g, *Ramulus cinnamomi* 10 g, *Radix aconiti Preparata* (Predecoct) 6 g, deer-horn gelatin (smelt) 15 g, *Asarum* 3 g, seed of *Brassica alba* 10 g, *Fructus psoraleae* 15 g, *Ephedra* 3 g, *Speranskia tuberculata* 15 g, *Angelica sinensis* 10 g, *Clematis chinensis Osbeck* 20 g, and *Glycyrrhiza uralensis* 6 g; one dose a day, decocted with water for oral administration.

Acupuncture on acupoints: Juegu, Taixi, Sanyinjiao, Zusanli, Geshu, Xuehai, Linggu, Dabai, and Waisanguan. Methods: mild reinforcing–reducing method was used. Retained the needle for 20 minutes, once per day. Took 2 days off after five acupuncture treatments.

Moxibustion on acupoints: Dazhui, Zusanli, Shenzhu, Mingmen, Pishu, and Shenshu. Methods: took two points each time with a moxa stick for moxibustion. Conducted moxibustion for 10 minutes above each point, once per day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Subcortex, Jiaogan, Shenmen, Zhen, adrenal gland, kidney, Pishu, stomach, and Erjian. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week, alternating ears.

Treatment effects: The patient was hospitalized for 59 days. Whole-body bone pain symptoms basically disappeared after active treatment without medication for stopping pain. With normal diet, the weight was kept at 70 kg. There was no obvious discomfort. The patient walked freely and could take care of himself. The

KPS was 90. PET-CT was done 3 months later, and glucose metabolism was reduced. The CA199 of 10 ng/mL was considered normal. The patient continued to adhere to outpatient treatment and received chelation detoxification twice a week, EBOO twice a week, local hyperthermia twice a week, systemic biofeedback therapy three times a week, and whole-body medium-low temperature hyperthermia once a month for 3 consecutive months. PET-CT was periodically done, and no new lesions were found. Follow-ups have been conducted for more than 4 years, particularly when the patient complained of pain or discomfort.

6.19.4 Related research in China and abroad

Matsumine et al. conducted curettage for metastatic bone cancer lesions, fixed with intramedullary nails or plates, and then filled the residual bone cavity with Fe_3O_4 phosphate bone cement. They externally applied an alternative electromagnetic field to induce high temperature 1 week after surgery. Radiology and functional assessment showed that this method was superior to surgery alone. Clinical trials were conducted in which titanium or stainless steel intramedullary nail fixation was carried out for pathologic fracture or metastatic bone cancers with fracture risk in patients. The diseased limb was put into the tubular metal circle with alternating current after a week and an alternating electromagnetic field was generated in the center of the coil, which made the intramedullary nails produce eddy current effects and develop high temperatures. This was performed twice a week and lasted for 10 minutes each time. The results showed that metastatic bone cancers were stopped in progression and new bone was formed in the lesions.

Luo Yimiao et al. used zoledronic acid plus radio-frequency hyperthermia for the treatment of metastatic bone cancers, and the results showed that in the bisphosphonate plus hyperthermia group pain in six cases was completely remissed (CR), pain in five cases was partially remissed (PR), and eight patients were stable (SD). In the bisphosphonate treatment group, two cases were completely remissed, five patients were stable, and six cases were partially remissed. The disease control rates (CR + PR + SD) were 82.6% for the treatment group and 52.0% for the control group ($P < .05$); CT or MRI showed that reductions of bone damage were 26.1% for the treatment group and 28.0% for the control group ($P > .05$). No significant differences were seen in liver and kidney function and blood changes of the two groups of ($P > .05$). This study suggested that the clinical efficiency of bisphosphonates plus radio-frequency hyperthermia for the treatment of metastatic bone pain and bone destruction was higher than that of bisphosphonate therapy alone, and there was no significant difference in side effects.

Hu Yongcheng et al. have conducted in situ hyperthermia in 89 cases of malignant bone cancers by the intraoperative microwave radiation plus chemotherapy method, of which there were 51 cases of osteosarcoma, 12 cases of parosteal osteosarcoma, nine cases of chondrosarcoma, six cases of giant cell tumor, and 11 cases of others. Tumor location: 68 cases near joints, 11 cases at the backbone, and 10 cases at flat bones. The 5-year survival rate of the total group was 60.5%. For 51 cases of osteosarcoma, there were a 5-year survival rate of 58.4%, a 10-year survival rate of 51.6%, and 9 cases of local recurrence. Nakano et al. explored through clinical research the possibility of limb salvage surgery through preoperative radiotherapy plus hyperthermia for the treatment of soft tissue sarcomas. The study included 13 patients and local hyperthermia was used, 1 hour each for a total of 10 times. The total amount of radiotherapy applied was 40–60 Gy by conventional fractionation. Surgery was conducted after 3 weeks. The results showed that 12 patients achieved limb salvage and no local recurrence was found after 27 months (median) of follow-up. Seven cases reached PR after thermoradiotherapy.

Xu Demen et al. have reported a clinical study of RF combined with radiotherapy for the treatment of bone and soft tissue sarcomas in 70 cases, which included 19 cases of fibrosarcoma; 10 cases of synovial sarcoma; seven cases each of osteosarcoma and rhabdomyosarcoma; six cases of neurofibrosarcoma; five cases of cartilage sarcoma; four cases of liposarcoma; two cases each of leiomyosarcoma, malignant hemangioendothelioma, and hemangiopericytoma; and 6 cases of other rare sarcomas. ^{60}Cobalt was used for radiotherapy, 2 Gy each time with a total amount of about 50 Gy. Hyperthermia was conducted 60 minutes after radiotherapy and lasted for 40 minutes each time, two to three times a week, and with 13.56-MHz radio-frequency hyperthermia. The research results showed that one case was effective with the tumor less than 5 cm; tumors in 12 cases were greater than or equal to 5 cm, of which eight cases were effective; and tumors in 25 cases were greater than or equal to 10 cm, of which16 cases were effective.

Rubins et al. have used radiation diathermy to conduct whole-body hyperthermia combined with carboplatin chemotherapy for the treatment of refractory sarcoma. Repeated contrast showed that whether carboplatin is combined with hyperthermia or not had no difference in myelosuppression and that when using melphalan combined with whole-body hyperthermia at 41.8°C, which was sustained for 60 minutes, the adaptability of patients was good. It was clinically shown that whole-body hyperthermia in the treatment of advanced patients plays a supporting role.

6.20 LYMPHOMA

Malignant lymphoma is a kind of cancer derived from lymphatic network organization and closely related to immunity; it mainly occurs in lymph nodes but can also occur outside lymph nodes and nonlymphoid tissues, such as lung, stomach, and intestines. It is divided into two categories: Hodgkin's lymphoma and non-Hodgkin's lymphoma. Its incidence increases year after year. Lymphoma is more sensitive to chemoradiotherapy, so treatment focuses on chemoradiotherapy. Generally, surgery is not considered.

6.20.1 Conventional treatments

6.20.1.1 RADIOTHERAPY

6.20.1.1.1 Hodgkin's lymphomas

Radiotherapy is mainly used for large masses before chemotherapy or residual cancer after chemotherapy. Hodgkin's lymphoma has metastasis from the primary site to the adjacent lymph nodes in sequence, except for a minority of cases with intervals in swollen lymph nodes. As a result, the radiotherapy area should also include the possible invaded lymph nodes and tissues, in addition to the involved lymph nodes and tissues.

6.20.1.1.2 Non-hodgkin's lymphomas

The multicentric occurrence tendency of non-Hodgkin's lymphoma makes multiple clinical stage values of non-Hodgkin's lymphoma and treatment effects of expanded irradiation inferior to Hodgkin's lymphoma, which decides that its treatment strategy should focus on chemotherapy.

6.20.1.2 CHEMOTHERAPY

6.20.1.2.1 Hodgkin's lymphomas

Controlled studies have shown that the efficacy of combination chemotherapy for Hodgkin's lymphoma is not less favorable than radiotherapy, it is even better than radiotherapy, and chemotherapy does not affect the child's development and also avoids laparotomy damage in patients for pathological staging. As a result, for Hodgkin's lymphoma patients at stages Ib, IIb, III, and IV, even if patients have mediastinal masses or belong to the type of lymphocytic depletion, chemotherapy must be used. For huge masses or residual tumors after chemotherapy, local radiotherapy can be added.

6.20.1.2.2 Non-Hodgkin's lymphomas

Chemotherapy is the primary treatment. The efficacy depends on pathological tissue types. According to the malignant degree of pathological classification, different combinations of chemotherapy are selected. Low-degree malignant group: stages I and II of the group after radiotherapy have no recurrence and the survival time can reach 10 years; however, stages III and IV of the group are not able to gain recovery whether chemotherapy or radiotherapy is applied or not. According to retrospective analysis, patients of this group should delay chemotherapy as late as possible. If the disease progresses or complications occur, COP or CHOP chemotherapy may be given. Intermediate-degree malignant group: once the diagnosis of various types of the group is clear and the clinical stages are stage III or IV and stage II involving a wide range, COP or CHOP must be given, one course of chemotherapy for each month for a total of 6–9 months; 70% of patients can

achieve CR. High-degree malignancy: intensive chemotherapy should be given. The progression of lymphoblast-type lymphoma and Burkitt-type lymphoma is very quick, and if it is not treated patients will die within several weeks or months. A program of second or third generation in combination with chemotherapy is better.

6.20.1.3 HYPERTHERMIA

Malignant lymphoma is very sensitive to radiation and chemotherapy. Heating also can enhance the sensitivity to radiation and chemotherapy drugs and overcome tumor resistance. Whole-body hyperthermia has a good effect on systemic malignant lymphoma and improves systemic immunity. Hyperthermia in combination with standard radiotherapy and chemotherapy has been applied clinically with some specific effects.

6.20.1.4 CHELATION DETOXIFICATION THERAPY

Chelation detoxification and hyperthermia applied at the same time can significantly increase efficacy and be more conducive to the removal of toxins. Chelation detoxification can also reduce the side effects of chemoradiotherapy. Whole-body hyperthermia plus chelation detoxification is preferred for lymphomas.

6.20.1.5 MEDICAL OZONE THERAPY

Medical ozone can stimulate the autoimmune system; directly kill cancer cells in blood, lymphatic vessels, and metastases; and reduce the side effects of radiotherapy and chemotherapy. In general, intravenous medical ozone saline is carried out three times a week. Conduct major autohemotherapy and EBOO two to three times a week. Medical ozone acupoint injection can also be selected, and the selection of points is the same as that for acupuncture.

6.20.1.6 TRADITIONAL CHINESE MEDICINE

For the syndrome of coldness and dampness coagulation, the prescription recommended is Yanghe Decoction. For the syndrome of qi and phlegm stagnation, the prescription recommended is modified Shugan Kuijian Decoction. For the syndrome of blood dryness and wind hotness, the prescription recommended is modified Qinggan Luhui Pill. For the syndromes of yin deficiency of liver and kidney and deficiency of both qi and blood, the prescriptions recommended are Liuwei Dihuang Pill and Herong Sanjian Pill.

6.20.1.7 ACUPUNCTURE

The therapeutic principle for lymphoma should focus on dispelling wind and removing obstruction in the meridians, clearing away toxic substances and resolving mass, nourishing liver and kidney, as well as benefiting qi and nourishing blood.

Acupuncture on acupoints: Tianjing, Yifeng, Shaohai, Zulinqi, Sanyinjiao, Xuehai, Geshu, and Zusanli.

Methods: Use mild reinforcing–reducing method. Retain the needle for 20 minutes, once per day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Tianjing, Zusanli, Guanyuan, and Dazhui.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Neck, Jiaogan, adrenal gland, Pizhixia, Shenmen, Zhen, liver, Pishu, and kidney.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.20.1.8 MEDICATED DIET, NUTRITION, AND SO ON

If patients have good general conditions and can orally take food, medicated diet of syndrome differentiation and food therapy are carried out for conditioning. If patients have difficulty eating, ostomy is needed to inject nutritious meals through the gastric tube. If medium-advanced patients have severe malnutrition and have difficulty eating, total parenteral nutrition is given.

6.20.1.9 OTHERS

Qigong, tai chi, music, and psychotherapy can be practiced to help patients cooperate with the treatment and fight against cancer with a calm, positive, and optimistic attitude.

6.20.2 Combination of hyperthermia with conventional treatments

6.20.2.1 HYPERTHERMIA AND RADIOTHERAPY

Local or whole-body hyperthermia is given after each radiotherapy session to enhance sensitization and synergism as well as reduce the side effects of radiation-induced myelosuppression and local normal tissue radiation injury. Local hyperthermia can be carried out once every other day, and the whole course is about 30–40 times.

Adjuvant therapies such as chelation detoxification, medical ozone, and Chinese medicine can be carried out during the treatment of radiotherapy and after radiotherapy.

6.20.2.2 HYPERTHERMIA AND CHEMOTHERAPY

Chemotherapy is appropriate for lymphoma cases of stages II to IV, in which the CHOP regimen is now widely used with higher clinically proven efficiency. Because blood supply of these cancer tissues is special, capillaries are fragile, and cooling capacity is poor, and when body temperature reaches 40.5°C, the local cancer tissue temperature can reach more than 45°C. A short period of sustained high temperatures can cause apoptosis to cancer cells, whereas normal cells are able to survive. Local hyperthermia is carried out to lymph nodes 20 minutes after each chemotherapy injection, 40 minutes each time, and twice a week. Malignant lymphoma is very sensitive to chemotherapy, and heating can also enhance the sensitivity of chemoradiotherapy as well as overcome tumor resistance to chemotherapy. Whole-body hyperthermia plus chemotherapy plus chelation detoxification therapy can increase efficacy and enhance tolerability. Whole-body hyperthermia can be combined with chemotherapy cycles. Whole-body hyperthermia can be applied once in each cycle, and local hyperthermia is given at the intermittent periods. For patients who cannot tolerate whole-body hyperthermia, local hyperthermia or whole-body medium-low temperature hyperthermia is given. Local hyperthermia is carried out once every other day, with 20 times as a course of treatment for a total of three courses. Whole-body medium-low temperature hyperthermia is carried out once a week for a total of 12 times.

6.20.2.3 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Chelation detoxification carried out simultaneously with hyperthermia can significantly increase efficacy and be more favorable to the elimination of toxins from the body. Whole-body hyperthermia plus chelation detoxification can increase efficacy and enhance tolerability. Chelation detoxification therapy is applied 3 times a week, with 20 times as a course for a total of three courses. Hyperthermia can be applied at the same time with chelation detoxification to improve efficacy.

6.20.2.4 HYPERTHERMIA AND MEDICAL OZONE THERAPY

Medical ozone therapy may be given after hyperthermia. Medical ozone therapy can stimulate the autoimmune system and directly kill cancer cells in blood, lymphatic vessels, and metastases and reduce the side effects of radiotherapy and chemotherapy. The blood circulation of the patient is accelerated and cell activity increased after hyperthermia. Application of medical ozone therapy within 2 hours after hyperthermia can increase the efficacy of medical ozone therapy. In general, intravenous medical ozone saline is carried out three times a week and major and minor autohemotherapy and EBOO are carried out two or three times a week, with 20 times as a course of treatment for a total of three courses. Medical ozone acupoint injection can also be used, and the selection of points is the same as that for acupuncture.

6.20.2.5 HYPERTHERMIA AND OTHER TREATMENTS

Other integrative treatments such as Chinese medicine, acupuncture, systemic biofeedback therapy, systemic biofeedback treatment, and alkaline treatment can be combined. DC-CIK cell therapy can be applied for some lymphomas, and its combination with hyperthermia can increase the effectiveness and safety of the treatment.

DC-CIK cell therapy: DC-CIK treatment can be a new adjuvant therapy for the treatment of non-T/NK cell lymphoma that is not sensitive to chemotherapy. Autologous DC-CIK treatment can effectively improve the patient's immunity and cause inhibitory effect.

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Adjust to one or two times a week after two to three courses of treatment for long-term treatment.

Alkaline treatment: Intravenous or oral sodium bicarbonate therapy can be used with medicated diet to alkalize constitution. For details, please refer to Section 4.10.

6.20.2.6 HYPERTHERMIA AND HERBAL MEDICINES

6.20.2.6.1 Moxibustion

Proven prescription 1: Grind equal amounts of *Squama manitis* (fried with earth) and *Cantharides* to powder. Coat it on affected area and conduct indirect garlic moxibustion with moxa cones the size of soybeans. Efficacy: resolves phlegm coagulation and treats lymphoma.

Proven prescription 2: Mash the root of raw *Phytolacca americana* to make cakes. Place the cake on the affected area. Conduct moxibustion with three to four moxa cones. Efficacy: resolves phlegm coagulation and treats lymphoma.

Proven prescription 3: Grind Jiangxi fermented soybean cake into fine powder and mix it with rice wine to make pancakes the size of coins with a thickness of about 6 mm. Place them on the affected area and conduct moxa cone moxibustion above the cake, with three to four moxa cones each time. Efficacy: resolves phlegm coagulation and treats lymphoma.

6.20.2.6.2 Steam therapy

Proven prescription 1: Taohong Huoxue Decoction: *Radix astragali* 30 g, *Radix paeoniae Rubra* 20 g, *Angelica sinensis* 20 g, *Ligusticum chuanxiong Hort* 20 g, *Semen persicae* 20 g, *Carthamus tinctorius L.* 20 g, *Ramulus cinnamomi* 25 g, *Radix puerariae* 20 g, *Pericarpium citri Reticulatae* 20 g, and *Salvia miltiorrhiza* 30 g. Put drugs into the fumigating bed for boiling, and let the patient lie down in the bed for systemic fumigation. Efficacy: invigorates qi and blood, as well as promoting blood circulation and removing blood stasis. It is applicable to cancer patients with the syndrome of qi deficiency and blood stasis.

Proven prescription 2: Speranskia tuberculata 30 g, *Lycopodii herba* 30 g, *Erythrina variegata L.* 30 g, *Chinese star jasmine stem* 30 g, *Folium artemisiae Argyi* 30 g, *sappanwood* 20 g, *Carthamus tinctorius L.* 20 g, *Caulis spatholobi* 20 g, *Rhizoma corydalis* 20 g, *faeces trogopterorum* 20 g, *Ramulus cinnamomi* 20 g, *Radix curcumae* 20 g, *Radix angelicae Pubescentis* 20 g, and *Achyranthes bidentata* 20 g. Boil drugs inside the fumigating bed, and let the patient lie down in the bed for systemic or local fumigation. Efficacy: warms yang and dredges collaterals. It is applicable to cancer patients with the syndrome of yang deficiency arthromyodynia.

6.20.3 Introduction of a typical case

A patient named Chen, male, 55 years old, was admitted on June 22, 2006, to Clifford Hospital due to "abdominal pain and the left lower back pain for more than 2 months." On April 2006, the patient showed nonincentive abdominal pain, presenting persistent distending pain accompanied by left lumbar sour pain, anorexia of stodge, nonacid regurgitation, belching, occasional nausea, and no diarrhea or fever. After the patient was treated for "gastritis" with painkillers and intravenous drip in the local hospital, the symptoms were not significantly alleviated. Electronic gastroscope examination revealed erosive gastritis with duodenal inflammation; upper abdominal MRI showed mass shadow at the right front top of the left kidney of retroperitoneum, and possible lymphoma. The patient took herbal medicines for 2 months, but they were ineffective.

Exploratory laparotomy was carried out in the Surgery Department of Clifford Hospital; it showed a mass of about 12 cm × 15 cm at the tail of the pancreatic body, with less smooth surface and hard. Masses were palpable at the side of hilar and abdominal aorta. No obvious tumor was palpable at the surface of the liver. Abdominal lymph node biopsy immunohistochemistry pathology report: diffuse large B-cell lymphoma (center cell type) with moderate malignancy. Diffuse large B-cell lymphoma: CD20(+), CD79a(+), Bcl-6(+), CD30(–), CD15(–), EMA(+), CD3(–), CD43(–), and ALK-1(–). The patient was transferred to the Oncology Department after the wound healed for further treatment. Since the onset of the disease, the patient had fever, night sweats, and a weight loss of more than 10 kg.

Physical examination: Marasmus and 42 kg body weight. Basic vital signs were normal. Superficial lymph nodes were not enlarged. No obvious abnormalities were found by heart and lung auscultation. A surgical scar of 10 cm length was seen approximately 3 cm below the navel. Abdominal breathing activity was slightly restricted. All abdominal muscles were soft. A fist-sized tumor was palpable at the left and middle of the abdomen, with moderate hardness, poor activity, and obvious tenderness and without rebound tenderness. There was no liver tenderness. The border of liver dullness was at its normal position. Liver and spleen were not palpable with shifting dullness (+).

Auxiliary examination: Abdominal MRI at the outpatient showed the following: (1) mass shadow at the right front top of the left kidney at retroperitoneum with a size of 11 cm × 16 cm, which was considered to be lymphoma; (2) splenomegaly and a small amount of fluid around the spleen; (3) possible involvements of the left kidney, abdominal aorta, and pancreas; and (4) a small amount of pleural effusion. Normal ECG and chest X-ray were shown. Blood routine: RBC 3.2×10^{12}/L, Hb 101 g/L, WBC 10.3×10^{9}/L, PLT 78×10^{9}/L. Biochemical test: ALT 65 U/L, AST 57 U/L, TBIL 21 U/L, DBIL 14 U/L, ALB 29.9 g/L, ALP 47 U/L, GGT 82 U/L, Cr 7 μmol/L, Ua 236 μmol/L, BUN 4.5 mmol/L, GLU 5.71 mmol/L, TG 0.69 mmol/L, GHO 4.38 mmol/L, K^+ 3.67 mmol/L, Na^+ 139 mmol/L, Cl^- 102 mmol/L, and Ca^{2+} 2.18 mmol/L. Tumor markers, five items of immunity, and the trace element copper were normal.

Diagnosis: Diffuse B-cell lymphoma (center cell type), intermediate malignance of stage IIIb.

Integrative treatment prescription: The patient was transferred to the Oncology Department after exploratory laparotomy. The pathological diagnosis was diffuse B-cell lymphoma. The patient had weight loss and hypoalbuminemia. The patient was given albumin after surgery, but the patient's eating was limited. The patient had malaise, a pale complexion, and pale lips. Albumin was reexamined and was still low (only 30 g/L). As a result, total parenteral nutrition and albumin infusion were actively given. At the same time, herbal medicines and acupuncture treatments were given. The patient showed red tongue, little coating, and a rapid and thready pulse. The syndrome belonged to deficiency of liver and kidney as seen from the clinical symptoms. The treatment principle focused on nourishing the liver and kidney, as well as softening and resolving hard mass.

Medications: The prescription recommended was modified Dabuyin Pill. Specific medication: *Radix Rehmanniae preparata* 20 g, *Cortex phellodendri* 10 g, *Rhizoma anemarrhenae* 10 g, *Carapax trionycis* 15 g, *Rhizoma pinelliae Preparatum* 15 g, donkey-hide gelatin (molten) 15 g, *Cortex lycii* 15 g, *Cortex moutan* 10 g, *Gardenia jasminoides Ellis* 10 g, *Prunella vulgaris* 15 g, and oyster (Predecoct) 30 g; one dose a day, decocted with water for oral administration.

Acupuncture on acupoints: Tianjing, Yifeng, Shaohai, Zulinqi, Sanyinjiao, Xuehai, Geshu, Zusanli, Linggu, Dabai, and Sancongxue. Methods: even reinforcing–reducing method was used with needle retention for 20 minutes, once a day. Took 2 days off after five times, with 10 times as a course.

Moxibustion on acupoints: Tianjing, Zusanli, Guanyuan, and Dazhui. Methods: took two points each time with a moxa stick for moxibustion. Conducted moxibustion for 10 minutes above each point, once a day. Took 2 days off after five treatments of moxibustion.

Auricular acupoints: Neck, Jiaogan, adrenal gland, Pizhixia, Shenmen, Zhen, liver, Pishu, and kidney. Methods: stuck auricular points with cowherb seed. The patient was asked to press by himself three to five times every day and press each point for 3–5 minutes, twice a week. Alternated ears.

After 8 days, the patient's general condition had improved and the patient could basically eat normally without obvious weakness. Albumin returned to normal.

CHOP-21 chemotherapy program was applied in combination with nontoxic integrative treatments. Consultation of the specialists ruled out the possibility of contraindication. Whole-body medium-low

temperature hyperthermia was carried out at the second day of chemotherapy. Abdominal local hyperthermia was given 3 days after whole-body hyperthermia, once every other day. At the same time, chelation detoxification and intravenous medical ozone were alternately carried out, once every other day. The patient only had grade I gastrointestinal reaction during chemotherapy. The blood routine test suggested myelosuppression of grade I. Metoclopramide was given for controlling nausea and vomiting, and GM-CSF was given for leucopenia. After six cycles of chemotherapy, abdominal radiotherapy of 36 Gy was given. Abdominal local hyperthermia was given during the period of chemotherapy once every other day. Herbal medicines and acupuncture were carried out throughout the entire process of treatment. The specific medication and acupoint selection were modified according to the syndromes and on the basis of the original prescription. The patient's mentality was good throughout the course of treatment. Eating was acceptable. The established treatment program was successfully completed.

Treatment effects: The patient was in poor general condition, with weight loss and hypoproteinemia, when he was admitted. The patient improved after symptomatic treatments were given. Hyperthermia combined with systemic chemotherapy and chelation detoxification and medical ozone were given to reduce the toxic side effects. After six cycles of treatments, the abdominal tumor was narrowed to two-thirds its original size, as reviewed by CT, and had no adhesion with surrounding organs. Pleural effusion disappeared. Tumors in the patient disappeared after continuous local radiotherapy plus hyperthermia therapy. The patient had a weight increase of 6 kg at discharge with soft abdomen, no palpable abdominal mass, and no tenderness, and he could participate in general household labor. His KPS was 100. The patient returned every month to the hospital after discharge for 5 days of local hyperthermia, chelation detoxification, medical ozone, herbal medicines, and other integrative treatments. Five years of follow-ups have been conducted. Annual reviews of upper abdominal CT and chest X-ray have found no abnormalities.

6.20.4 Related research in China and abroad

Wang Yang et al. have applied microwave hyperthermia combined with systemic chemotherapy for the treatment of 20 cases of malignant lymphoma, including five cases of Hodgkin's lymphoma and 15 cases of non-Hodgkin's lymphoma. There were nine cases of stage III and 11 cases of stage IV according to clinical staging. Lymph node microwave hyperthermia was carried out 20 minutes after each chemotherapy injection, lasting for 40 minutes, applied twice a week. Twenty patients received microwave hyperthermia 4–12 times and two to three courses of chemotherapy. The results showed CR in 16 cases and PR in four cases.

Li Dingjiu et al. have conducted integrative treatments by applying hyperthermia with intraperitoneal hyperthermic perfusion and systemic vein two-route chemotherapy in 11 patients with recurrent, refractory peritoneal malignant lymphoma, and they retrospectively analyzed the results of 15 cases of single intravenous chemotherapy. The results showed that the CR rate in the thermochemotherapy group was 45.5% (5/11) and in the chemotherapy alone group was 6.7% (1/15) ($P < .05$).

Yang Ke et al. have conducted clinical observation on dimensional conformal radiotherapy combined with thermochemotherapy and the hyperthermia used was local microwave heating, which was given before radiotherapy or 2 hours after radiotherapy, and the temperature was controlled at (42 ± 1)°C. The hyperthermia lasted for 30–40 minutes after achieving the required temperature, three times a week, with 2 to 3 weeks as a course of treatment. The results showed that the effective rate of simple three-dimensional conformal radiotherapy was 70.73%, effective rate of three-dimensional conformal radiotherapy combined with hyperthermia was 80.64%, and effective rate of three-dimensional conformal radiotherapy combined with thermochemotherapy was 84.62% when the radiotherapy amount was DT less than 40 Gy and the effective rate was 34.62%. The effective rate was 50.0% with 40 Gy < DT < 60 Gy, and the rate was 63.16% with DT greater than or equal to 60 Gy. The effective rate was 96.43% when microwave treatment was applied more than four times, and the rate was 66.67% when it was less than four times. There was significant difference ($P < .05$) in each group. Three-dimensional conformal radiotherapy when combined with chemotherapy could more effectively control lymphatic tumor progression. The amount of radiotherapy and efficacy were positively correlated. The microwave frequency of treatment and efficacy were positively correlated.

6.21 HEMOPATHY

Blood disease is a primary disease of the hematopoietic system, or a disease that affects the hematopoietic system, accompanied by blood abnormalities and characterized by anemia, bleeding, and fever. The hematopoietic system includes blood, bone marrow mononuclear phagocyte system, and lymphoid tissue. All that involves hematopoietic system pathology and physiology and its main manifestations of the disease belongs to the scope of hematologic diseases. Blood disease is clinically divided into three types: RBC disease, WBC disease, and bleeding and thrombotic disease. Common clinical diseases are leukemia, aplastic anemia, myelodysplastic syndrome, thrombocytopenia, multiple myeloma, lymphoma, bone fibrosis, hemophilia, thalassemia, and so on. Hematologic diseases mostly are refractory diseases. The incidence is insidious and symptoms are occult. Even if the patient is ill, he or she is often not aware of it. It is found mostly when the patient seeks medical treatment for other diseases or through health examination. Many hematologic diseases were considered incurable in the past due to the lack of effective therapy.

Hormones and chemotherapy are commonly used for the treatment of hematologic diseases, but the side effects are great, with low cure rates and easy recurrence. In recent years, the use of herbal medicines for the treatment of hematologic diseases has obtained certain beneficial effects. The use of hyperthermia combined with chemotherapy for the treatment of hematologic diseases is also under study.

6.21.1 Conventional treatments

6.21.1.1 ETIOLOGICAL TREATMENT

If the etiology is clear, timely separate the effect of etiological factors. The etiology of some diseases is unclear or unavoidable, and the treatment effect may be affected.

6.21.1.2 MAINTAINING NORMAL BLOOD COMPONENTS AND FUNCTIONS

Supplementary hematopoietic substances: For nutritional megaloblastic anemia, supplement with folic acid or vitamin B_{12}; for iron deficiency anemia, supplement with iron; and for vitamin K deficiency, supplement with vitamin K. Stimulate hematopoiesis: for chronic aplastic anemia, androgen and herbal medicine treatments are applied. Cytokines: erythropoietin (EPO) is used in the treatment of renal anemia and granulocyte colony-stimulating factor or granulocyte-macrophage colony-stimulating factor accelerates the recovery of leukopenia. Splenectomy has an exact effect on patients by hereditary spherocytosis cell histiocytosis and idiopathic thrombocytopenic purpura. Component transfusion: for severe anemia or blood loss, erythrocyte should be transfused. For thrombocytopenia with bleeding risk, supplement with blood platelets. For hemophilia A with active bleeding, factor VIII should be supplemented.

6.21.1.3 CHEMOTHERAPY

Over the years, combined chemotherapy has been widely used, in which herbal medicines are mostly used for medication in combination with chemotherapy or at the intermission periods of chemotherapy. A growing number of clinical studies have shown that combination therapy of Chinese medicine with Western medicine is superior to chemotherapy alone.

6.21.1.4 INDUCED DIFFERENTIATION AND INDUCED APOPTOSIS

Chinese researchers have applied all-trans retinoic acid to induce differentiation and arsenic trioxide to accelerate apoptosis; they provide very good results for treating acute promyelocytic leukemia, thus creating new ways to treat cancer.

6.21.1.5 PLASMA EXCHANGE AND THERAPEUTIC HEMAPHERESIS

Selectively remove some dysplasia ingredients in blood through a blood cell separator and achieve therapeutic purposes. For example, plasmapheresis is used for the treatment of multiple myelomas.

6.21.1.6 IMMUNOSUPPRESSION

Use immunosuppressive agents such as glucocorticoids and cyclosporine for the treatment of autoimmune hemolytic anemia, aplastic anemia, and so on.

6.21.1.7 ANTITHROMBOTIC AND THROMBOLYTIC THERAPY

For disseminated intravascular coagulation, use heparin to prevent further coagulation. Use heparin to prevent further consumption of clotting factor. To prevent platelet aggregation, use aspirin, and so on. In addition, urokinase, tttt-PA, and so on can be applied to dissolve fresh thrombus to restore blood flow.

6.21.1.8 HEMATOPOIETIC STEM CELL TRANSPLANTATION

It is a major advancement in treatment in modern hematology. It uses chemoradiotherapy of super high doses to maximize the removal of abnormal cells from the patient's body and then uses the donor's or autologous hematopoietic stem cell to rescue or reconstruct the patient's hematopoietic and immune function. It is a method for radical hematologic malignancies and some solid tumors and is widely applied currently in clinical practice. In addition, it can be used to treat aplastic anemia, myelodysplastic syndrome, genetic hereditary diseases, autoimmune diseases, and so on. According to the source of hematopoietic stem cells, it can be divided into bone marrow transplantation, peripheral blood stem cell transplantation, and cord blood transplantation. According to the difference in source of donor and immunology, it is divided into allogeneic transplantation, homogenic transplantation, autograft, and xenotransplantation.

6.21.1.9 HYPERTHERMIA

Studies have shown that whole-body hyperthermia can significantly improve the quality of life of patients with hematologic malignancies, clinical symptoms, and signs, and when combined with chemotherapy it can improve clinical efficacy.

6.21.1.10 CHELATION DETOXIFICATION THERAPY

Modern research shows that hematologic diseases are associated with ionizing radiation, exposure to chemicals, and poisons or drugs. The majority of patients with hematologic diseases have excessive heavy metals. Chelation detoxification formulas made of vitamins and chelating agents can get rid of toxic substances from their bodies. Chelation detoxification has a synergistic effect with chemotherapy and reduces chemotherapy-induced nausea and vomiting, diarrhea, loss of appetite, fatigue, and other side effects. It especially has significant attenuation for chemotherapy-induced skin pigmentation, and oral and gastrointestinal mucositis. Conduct it three times a week, with 20 times as a course of treatment for not less than three courses. When the condition is stable, change to once a week. After 12 times, reduce to once a month for consolidated therapy.

6.21.1.11 MEDICAL OZONE THERAPY

When medical ozone enters the body, it can be decomposed into oxygen ions, thus improving the oxygen carrying capacity of RBCs and anemia and, at the same time, stimulating hematopoiesis. Medical ozone therapy can reduce the side effects of chemotherapy, such as fatigue and insomnia. Usage: use EBOO or medical ozone saline intravenous drip three times a week and once every other day, applied with chelation detoxification alternately, with 20 times as a course of treatment for a total of three courses. After the end of treatment and when patients are in stable condition, change to once a week and then gradually reduce to once a month for consolidated therapy. Be cautious when applying this therapy to patients with signs of bleeding; when platelets are less than 20×10^9/L, it is not recommended.

6.21.1.12 TRADITIONAL CHINESE MEDICINE

The syndromes are mainly retention of heat toxicity, retention of damp heat, as well as stagnation of phlegm toxin in the body before chemotherapy. The treatment focuses on eliminating pathogens. Products for clearing away toxic substances as well as cooling blood are mostly selected. The prescriptions recommended are modified Xijiaodihuang Decoction, modified Ganlu Xiaodu Decoction, and modified Taohong Siwu

Decoction. The syndrome of damp heat and deficiency coexistence is mainly manifested during chemotherapy. The treatment focuses on eliminating pathogens to support healthy qi. Products for moisturizing and preventing dryness and resolving dampness with aromatic drugs are mostly selected. The prescriptions recommended are Yiguan Decoction and modified Erchen Decoction. The syndrome of deficiency of qi and blood is mostly manifested after chemotherapy. The treatment focuses on strengthening body resistance. The prescription recommended is Bazhen Decoction or Radix Ophiopogon Decoction. For patients with low blood, it is suitable to reinforce the liver and kidney, nourish blood, and promote blood circulation. The prescriptions recommended are Bazhen Decoction, Dangui Siwu Decoction, and modified Renshen Yangrong Decoction.

6.21.1.13 ACUPUNCTURE

The main syndrome of leukemia is deficiency of both qi and yin, or yin deficiency of liver and kidney. The therapeutic principle should focus on supplementing qi and nourishing yin, tonifying liver and kidney, as well as invigorating qi and blood.

Acupuncture on acupoints: Qihai, Qixue, Gaohuang, Dazhui, and Zusanli. For blood heat, add Hegu and Xingjian; for deficiency of both qi and yin, add Feishu, Xinshu, and Sanyinjiao; for deficiency of qi and blood, add Feishu, Xinshu, Pishu, and Yinlingquan; for yin deficiency of liver and kidney, add Ganshu, Shenshu, and Taixi; and for blood stasis stagnating in the body, add Ganshu, Pishu, Sanyinjiao, Xuehai, Yanglingquan, and so on.

Methods: Reducing method is used for Hegu and Xingjian due to blood heat, and reinforcing method is used for the rest. Retain the needle for 20 minutes, once a day. Take 2 days off after five acupuncture treatments, with 10 times as a course of treatment.

Moxibustion on acupoints: Dazhui, Qihai, Sanyingjiao, Gaohuang, Zhongwan, and Yanglingquan. For heat syndrome, add Hegu and Lieque; for deficiency of both qi and yin, add Yinlingquan and Sanyinjiao; for deficiency of both qi and blood, add Xinshu and Pishu; for yin deficiency of liver and kidney, add Ganshu and Shenshu; and for blood stasis stagnating in the body, add Feishu, Sanjiaoshu, Sanyinjiao, and Xuehai.

Methods: Take two points each time with the moxa stick for moxibustion. Conduct moxibustion for 10 minutes above each point, once per day. Take 2 days off after five treatments of moxibustion, with 10 times as a course of treatment.

Auricular acupoints: Heart, Pishu, liver, kidney, adrenal gland, Xueyedian, Shenmen, Pizhixia, Neifenmi, Jisui1, and Jisui2.

Methods: Stick auricular points with cowherb seed. Patients are asked to press by themselves three to five times every day and press each point for 3–5 minutes, twice a week. Alternate ears, with 10 times as a course of treatment.

6.21.1.14 MEDICATED DIET, NUTRITION, AND SO ON

Utilize medicated diet of TCM and modern nutrition knowledge to guide and regulate the patient's diet, and give individualized nutritional support programs. During chemotherapy, the patient should mainly keep a light diet, accompanied by Semen Coicis, Poria Cocos, and Pericarpium Citri Reticulatae boiled into soup to remove dampness and reduce phlegm; after chemotherapy, the diet should be accompanied by Astragalus Radix, Radix Adenophorae, jujube, and donkey-hide gelatin boiled into soup to supplement qi and nourish yin. If the patient has significant reaction on the day before chemotherapy or during chemotherapy, total parenteral nutrition can be given to strengthen the nutritional support therapy.

6.21.1.15 OTHERS

Eliminate the psychological barriers of cancer patients and their families, such as pessimism, despair, and so on. These negative emotions often affect treatment and prognosis. Health-care workers should frequently communicate with patients, conduct psychological counseling, and encourage patients to actively face the disease. At the same time, ask patients to practice qigong, regulate breathing and move qi for smooth systemic blood flow, and strive for peace and calmness of mind so as to achieve synergistic therapy and improvement of efficacy.

6.21.2 Combination of hyperthermia with conventional treatments

6.21.2.1 HYPERTHERMIA AND CHEMOTHERAPY

For the majority of patients with hematologic diseases, whole-body chemotherapy is needed. Hyperthermia combined with chemotherapy can enhance the sensitivity of chemotherapy, improve efficacy, and reduce the side effects of chemotherapy. If patients are assessed to be in good general condition and able to tolerate whole-body hyperthermia, whole-body medium-high hyperthermia can be carried out, combined with a chemotherapy cycle, for a total of six to eight times. Pay attention to monitoring of body temperature, blood pressure, pulse, and other vital signs during hyperthermia, and give symptomatic treatment in a timely manner. Apply local hyperthermia during the intermission periods of whole-body hyperthermia, every other day, accompanying the full course of chemotherapy.

When chemotherapy and whole-body hyperthermia are simultaneously applied, whole-body medium-high hyperthermia can be carried out simultaneously on the first day of chemotherapy. Pay attention to medications of antinausea drugs before administering chemotherapy drugs. Generally, it is safe. If the patient vomits seriously during the hyperthermia, he or she needs to be treated in a timely manner. Whole-body hyperthermia needs to be suspended if (rare) vomiting is severe. The hyperthermia and chemotherapy cycles are to be synchronized.

For patients who cannot tolerate whole-body medium-high temperature hyperthermia, whole-body medium-low temperature hyperthermia can be carried out. Hyperthermia at spleen, spine, and pelvis regionals can promote spleen and bone marrow hematopoiesis and can reduce pain. Conduct endogenous field and RF local hyperthermia once every other day, with 20 times as a course of treatment for a total of three courses. But be sure that for WBCs less than 1.0×10^9/L or patients with the syndrome of internal heat due to yin deficiency by syndrome differentiation, whole-body hyperthermia should not be applied.

6.21.2.2 HYPERTHERMIA AND CHELATION DETOXIFICATION THERAPY

Because patients are prone to postoperative physical weakness and low immunity, chelation detoxification therapy and medical ozone can be given from the end of operation to the period of chemotherapy. They can promote physical recovery and regulate the immune system and kill residual tumor cells or inhibit early metastasis. Conduct chelation detoxification therapy by intravenous drip once every other day, with 20 times as a course of treatment for a total of three courses. For patients assessed as having excessive heavy metals in blood, chelating agents can be added. It is noted that chelation detoxification needs infusion for more than 2 hours. Hyperthermia can be simultaneously applied with chelation and detoxification to improve efficacy.

6.21.2.3 HYPERTHERMIA AND MEDICAL OZONE THERAPY

Patient's blood circulation is accelerated and cell activity increased after hyperthermia. Carrying out medical ozone therapy within 2 hours after hyperthermia can increase the effect of killing cancer cells, enhance effect on immunity, and increase the efficacy of medical ozone. Treatment methods: use EBOO once every other day, with 20 times as a course of treatment, or select medical ozone saline infusion once every other day, with 10–14 days as a course of treatment for a total of three courses. Use medical ozone major autohemotherapy once every other day, with 12 times per course. Use medical ozone minor autohemotherapy once every other day, with 12 times per course. Use medical ozone acupoint injection once every other day, with 12 times as a course of treatment. Conduct at least three courses respectively, and they can be taken for long-term maintenance therapy.

6.21.2.4 HYPERTHERMIA AND OTHER TREATMENTS

Cancer therapy requires integrative treatments. Combining the application of TCM, acupuncture, DC-CIK cell therapy, systemic biofeedback treatment, and alkaline treatment with hyperthermia can increase the effectiveness and safety of treatment.

DC-CIK cell therapy: DC-CIK cells have reversal effect on K562/ADR cell multidrug resistance, significant killing effect on autologous primary leukemia cells, and significant inhibiting effect on G_0 phase of

leukemia cells, but they have no killing effect on normal hematopoietic stem cells. Therefore, DC-CIK can be used as an effective tool for removing residual leukemia cells and preventing recurrence. For patients who have acute myeloid leukemia of hematologic remission and acute B lymphocytic leukemia after chemotherapy or hematopoietic stem cell transplantation, applying DC-CIK treatment for one to three courses can achieve long-term CCR (clinical complete remission), and its efficacy is related to the leukemia load in the patient's body.

Systemic biofeedback therapy: Three times a week, with 15 times as a course of treatment. Adjust to one or two times a week after two to three courses for long-term treatment.

Alkaline treatment: Food therapy can be used for alkalizing constitution; please refer to Section 4.10 for details.

6.21.2.5 HYPERTHERMIA AND HERBAL MEDICINES

6.21.2.5.1 Bath

Proven prescription 1: Radix astragali 450 g, *Radix codonopsis* 300 g, *Radix polygoni Multiflori Preparata* 300 g, *Ligusticum chuanxiong Hort* 300 g, *Fructus alpinia Oxyphylla* 300 g, *Semen cuscutae* 300 g, *Atractylodes macrocephala Koidz* 300 g, and *Carthamus tinctorius L.* 200 g. Put all drugs into the wok and add proper amount of water. Boil for 50 minutes. Remove slag and take juice. Blend with 450 g of white wine. Take bubble bath for 40 minutes once a day, for 10 days as a course of treatment. This can tone the lung, spleen, and kidney, as well as strengthening spirit. It is mainly a cure for a variety of fatigue. It is applicable to physical fatigue caused by chronic consumption in cancer patients.

Proven prescription 2: Stems and leaves of *Panax ginseng* 30 g, *Atractylodes macrocephala Koidz* 30 g, *Radix saposhnikoviae* 20 g, yam 20 g, and *Glycyrrhiza uralensis* 6 g. Add proper amount of water to drugs. Boil twice, for 30 minutes each time. Combine filtrate and bathe for 30 minutes once a day, for 15 days as a course of treatment. Efficacy: invigorates spleen and replenishes qi. It is applicable to cancer patients having long-term weakness with low immunity.

Proven prescription 3: Rhodiola 800 g, *Semen coicis* 500 g, *Acanthopanax senticosus* 400 g, *Radix astragali* 300 g, *Cyrtomium fortunei* 300 g, *Schisandra chinensis* 300 g, *Angelica sinensis* 200 g, and *Ligusticum chuanxiong Hort* 200 g. Boil twice, for 50 minutes each time. Combine filtrate and bathe for 40 minutes once a day, for 15 days as a course of treatment. Efficacy: supplements qi and nourishes yin, and invigorates qi and promotes blood circulation. It is applicable to cancer patients having long-term weakness with low immunity.

6.21.2.5.2 Moxibustion

It is applicable to cancer patients with long illness, yang deficiency, and weakness and for the enhancement of immunity.

Acupoints: The first group of acupoints includes Dazhui, Shenshu (both), and Pishu (both). The second group of acupoints includes Shanzhong, Zhongwan, Shenque, Guanyuan, and Zusanli (both).

Herbal cake making: Take equal amounts of *Radix astragali*, *Angelica sinensis*, *Fructus psoraleae*, *Curculigo orchioides*, and *rhubarb*, and smash them into powder. Filter with 120 mesh sieve, and make herbal cakes with a diameter of 3 cm and a thickness of 0.8 cm.

Moxibustion: Place the moxa cone with a diameter of 2 cm and a height of 1.5 cm on the herbal cake. Conduct moxibustion with three moxa cones per point. Conduct moxibustion for one group of acupoints at a time, with two groups of points alternated, once every other day, with 24 times as a course of treatment.

Efficacy: Reinforces spleen and nourishes kidney for a strong and healthy body.

6.21.2.6 HYPERTHERMIA INDICATIONS

Hyperthermia can be applied to patients with KPSs of 60 points or above and without significant bleeding tendencies. The general condition needs to be critically assessed when applying whole-body hyperthermia.

6.21.2.7 HYPERTHERMIA CONTRAINDICATIONS

Local skin damage, obvious bleeding tendency, and cachexia.

6.21.3 Introduction of a typical case

A patient named Zhou, male, 60 years old, was admitted on May 21, 2006, to Clifford Hospital due to "limb petechiae, accompanied with fever and nausea for more than 20 days; and aggravation accompanied with abdominal pain and diarrhea for one day." The patient experienced paroxysmal abdominal pain after taking heated red rice wine more than 20 days before admission to the hospital and exhibited secondary limb ecchymosis, fever, interval nausea, no vomiting, no cough, no diarrhea, and no numbness of the limbs. At the time, symptoms did not appear to be serious. Abdominal pain of the patient got worse on the date of admission; it was accompanied by diarrhea, watery stools, tenesmus, nausea, vomiting, and fever. The highest body temperature of the patient was 39°C. The patient came to the Outpatient Department of Clifford Hospital for blood routine: WBC 43.48×10^9/L, RBC 2.8×10^{12}/L, HGB 87 g/L, and PLT 60×10^9/L; the patient was admitted due to "acute leukemia."

Physical examination: Clear mind; mental fatigue; and multiple scattered petechiae at the chest, abdomen, and limbs. Multiple lymph nodes were palpable at the neck and groin in the shape of beads, with toughness and without tenderness. Pulmonary signs were not positive. Abdomen was flat, and the right abdomen was hard. The superior border of the liver was normal. But the inferior border of the liver was 3–3.5 cm below the umbilicus, which is hard and with tenderness. A sausage-like mass was palpable in the right lower abdomen. Tenderness was obvious in the right lower abdomen, with rebound tenderness (±) without mobile dullness. Bowel sounds decreased. Intestine-like material could be seen at the anal prolapse. The KPS was 60.

Auxiliary examination: Blood routine: BC 43.48×10^9/L, RBC 2.8×10^{12}/L, HGB 87 g/L, and PLT 60×10^9/L. Biochemical test: LDH 361 U/L, HBDH 269 U/L, Cr 192 μmol/L, UA 438 μmol/L, ALT 35 U/L, AST 27 U/L, TBIL 16 U/L, DBIL 12 U/L, ALB 35 g/L; ALP 27 U/L, GGT 53 U/L, BUN 4.3 mmol/L, GLU 5.67 mmol/L, TG 0.35 mmol/L, GHO 4.65 mmol/L, K^+ 3.6 mmol/L, Na^+ 127 mmol/L, Cl^- 89 mmol/L, and Ca^{2+} 2.31 mmol/L. Tumor markers and the five items of immunity were normal. Trace elements such as copper, zinc, lead, cadmium, and nickel were normal, and mercury was 7.57 mmol/L. Ultrasound: a piece of heterogeneous mass was observed in the right lower abdomen, which is suspected to be inflammatory mass, and considered to be intestine originated. The nature of the mass was undetermined. The liver was significantly enlarged 3 cm below the belly button. Abdominal CT: the right-sided colon and appendix wall were thickened. A small amount of leakage occurred from the right lower abdomen, accompanied by mesenteric lymph node enlargement. Rectum and perirectal space changed, which may be considered to be possible leukemic bowel wall infiltration. Myelogram: bone marrow nucleated cells were proliferated; they were obviously active and mainly leukemia cell proliferation. Grain: red = 36.6:1; extreme proliferation of leukemia cells (primary particles) accounted for 87%, and erythroid proliferation inhibition accounted for 2.5/5. Histochemistry: leukemia cell positive rate was 39%, Shell (±), uncountable core, NAP positive rate of 0.91, and integration of 294.

Diagnosis: Acute nonlymphoblastic leukemia (M_2).

Integrative treatment prescription: The diagnosis of acute nonlymphoblastic leukemia (type M_2) was confirmed by bone marrow examination when the patient was admitted to the hospital. Anti-infection treatment was given with the consideration of intestinal infection. Rectal medical ozone insufflation was applied. After abdominal hyperthermia, abdominal pain and diarrhea were alleviated. At that time, the patient still had limb petechiae, so herbal medicines were given. The patient exhibited plump tongue with a pink, pale coating and a weak and thready pulse. According to the clinical symptoms, the syndrome belonged to deficiency of kidney yang and blood stasis stagnating in the body. The treatment focused on nourishing and warming kidney yang, as well as removing phlegm and resolving mass.

Medications: The prescription recommended was modified Shenqi Pill. Specific medication: dried *Radix rehmanniae* 20 g, yam 15 g, *Fructus corni* 12 g, *Alisma orientalis* 10 g, *Poria cocos* 10 g, *Cortex moutan* 10 g, *Radix aconiti Praeparata* 10 g, *Cinnamomum cassia Presl* 10 g, *Fructus psoraleae* 10 g, and *Euryale ferox Salisb* 15 g; one dose a day, decocted with water for oral administration.

Because the patient had low platelets, acupuncture treatment was temporarily not applied. Moxibustion and auricular therapy were given.

Moxibustion on acupoints: Dazhui, Qihai, Guanyuan, Zusanli, Sanyinjiao, Gaohuang, and Zhongwan. Take two points each time. Conducted moxibustion on each point for 10 minutes, once a day, and took 2 days off after five treatments of moxibustion.

Auricular acupoints: Heart, Pishu, liver, kidney, adrenal gland, Xueyedian, Neifenmi, Jisui 1, and Jisui 2. Stuck auricular points with cowherb seed twice a week and alternated ears.

Abdominal pain, diarrhea, fever, limb petechiae, and other symptoms disappeared after a week of treatment.

Blood routine was tested after symptoms were improved: WBC 122.2 × 10^9/L, RBC 3.4 × 10^{12}/L, HGB 103 g/L, and PLT 49 × 10^9/L; TA program was conducted for chemotherapy. Total parenteral nutrition was given daily during chemotherapy. Hyperthermia taboos were excluded by consultation of the panel. Whole-body medium-high temperature hyperthermia was given during the first day of chemotherapy. Abdominal local hyperthermia was given 3 days after whole-body hyperthermia, once every other day. Venous medical ozone and chelation detoxification were carried out alternately to improve the bone marrow hematopoietic microenvironment. Herbal medicines, moxibustion, and auricular therapy were combined for the whole treatment process, and drugs and acupoints were modified from the original prescriptions.

The patient presented myelosuppression of degree IV 10 days after chemotherapy; the minimum was 0.3 × 10^9/L, and the platelet count was a minimum of 10 × 10^9/L, accompanied by pulmonary infection. Filgrastim was given to increase WBCs. Antibiotics were applied for anti-infection. The patient's myelogram was completely remissed after 1 week, and the second cycle of chemotherapy was carried out as scheduled. Thereafter, the patient received six cycles of whole-body chemotherapy, combined with herbal medicines, chelation detoxification (a total of 28 times), and intravenous medical ozone (a total of 32 times) treatment for consolidation. The patient survived the marrow inhibitory period after chemotherapy, and chemotherapy was completed on time. After discharge, the patient adhered to whole-body medium-low temperature hyperthermia, chelation detoxification, medical ozone, and TCM treatment once every month. The condition remained stable, as was shown by periodic reviews. The patient could work as usual. After the platelets of the patient returned to normal, acupuncture was conducted on acupoints such as Qihai, Zusanli, Feishu, Sanyinjiao, Shenshu, Taixi, Pishu, Xuehai, Yanglingquan, Linggu, and Dabai. Mild reinforcing–reducing method was used with needle retention of 20 minutes, once per day. Took 2 days off after five acupuncture treatments. Moxibustion and auricular therapy remained unchanged.

Treatment effects: The patient was hospitalized for 70 days. After whole-body medium-high hyperthermia, abdominal local hyperthermia, and chemotherapy of TA program, myelogram was completely remissed and proliferation of bone marrow nucleated cells was obviously active. Grain: red = 2.24:1. Myeloid hyperplasia was active, accounting for 56%, and erythroid hyperplasia was active, accounting for 25%. The patient presented a mild fever, myelosuppression, and the lowest WBCs of 0.3 × 10^9/L after chemotherapy but no significant foci of infection; no nausea or vomiting; and no abdominal pain, diarrhea, or other discomforts. After symptomatic and supportive treatment, fever was reduced and WBCs rose to normal. The patient recovered quickly, and symptoms of abdominal pain, diarrhea, tenesmus, nausea, vomiting, and fever disappeared. Cervical lymph node and liver enlargement as well as abdominal mass disappeared. No obvious abnormalities were seen by abdominal CT review. Outpatient follow-up continued to be carried out after discharge. The patient returned to the hospital monthly for 1 week of integrative treatments and after a half year every 3 months for 1 week of treatment. Follow-up was carried out for more than 4 years after discharge. The patient's condition was relatively stable and without any discomfort, and WBCs were maintained at 2.5 × 10^9/L to 4.7 × 10^9/L. The KPS was 100.

6.21.4 Related research in China and abroad

Wei Hongmei et al. have done a research on human chronic leukemia cell line K562 by heating them to 40°C–41°C for 1 hour using a water bath, in which the cell apoptosis rate was still increasing after 48 hours.

Wei Hongmei et al. have conducted observation on safety, compliance, and effectiveness of heating, temperature measurement, and control techniques in a clinical study of 15 cases of hematological malignancy

patients through systemic whole-body hyperthermia treatment. The results showed that 15 cases of patients with hematologic malignancies can tolerate 40°C and 120 minutes of heating process, with good compliance. After 24 hours of systemic heating treatment, the patients' clinical symptoms and signs were markedly improved and the KPS increased by an average of 10 points. Before whole-body heating treatment and after 24 hours of treatment, difference comparison of the patient's blood routine, biochemistry, and other test indexes was not significant ($P > .05$). In a study by Deezagi et al., leukemia cell line (H-60, K562, and TF-1) was heated to 41°C–44°C for 2 hours. At total of 96 hours later, apoptosis was observed in the cells that were heated to 41°C–42°C, and the most obvious state of apoptosis was observed in the cells heated to 43°C–44°C.

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7

Nursing care techniques for hyperthermia in cancer treatment

7.1 INTRODUCTION

Cancer hyperthermia is divided into whole-body hyperthermia and local or regional hyperthermia based on the heating area. Whole-body hyperthermia refers to a hyperthermia method in which body temperature is raised to treatment temperature and then maintained for a certain amount of time through various means. Local or regional hyperthermia is used to heat the local lesion for cancer therapy mainly through microwave, radio frequency, and ultrasonic equipment. This chapter is mainly about nursing techniques in whole-body infrared hyperthermia; nursing techniques in local or regional hyperthermia and out-of-body radio frequency local hyperthermia are introduced.

7.2 NURSING IN WHOLE-BODY INFRARED HYPERTHERMIA

Whole-body infrared hyperthermia is used to raise body temperature and maintain it for a certain amount of time through infrared radiation. According to the target temperature, the therapy is divided into two temperature types: medium-low and medium-high. The former is mainly used for noncancerous diseases and the latter for cancers. This section describes the nursing techniques in the above two kinds of whole-body infrared hyperthermia.

7.2.1 Medium-low temperature

In this therapy, the body temperature is raised through infrared light to 38°C–40°C and maintained for a certain amount of time.

7.2.1.1 PRETREATMENT NURSING

7.2.1.1.1 Patient assessment

Assessment content: Vital signs, pain, skin integrity and scar tissue, weight, history of drug allergies, physical activity, mood, consciousness, oral communication ability, implants in the body, and so on.

7.2.1.1.2 Patient education

On the last day before the treatment, the patient needs to drink more water, get good sleep, and avoid fatigue. On the first day of the treatment, have normal meals to avoid fasting. Before treatment, empty stool and urine, wear pure cotton clothing designed for hyperthermia, and remove decorative jewelry and accessories from the body; during treatment, drink more water and fruit juice, and so on; after treatment, avoid wind to prevent cold. Soon after the treatment mild headache, tiredness, weakness, and so forth may occur, which will spontaneously disappear and need no special treatments; ensure getting sound rest and sleep.

7.2.1.1.3 Psychological nursing

Psychological care is essential for patients before the hyperthermia. They should be informed of the purpose, method, principle, role and process of hyperthermia; possible adverse reactions; precautions; and how to cooperate with the medical staff. They should be told that this therapy has significant effects and may result in rare but severe complications to help alleviate their concerns. To enhance patients confidence and remove their unhealthy psychological state, they should be invited to learn the working of whole-body hyperthermia instruments and be encouraged by other patients who have achieved good therapeutic effects, so that they can understand and recognize that hyperthermia is a safe and effective method of treatment, thereby becoming relaxed and happy to receive treatments and ensuring smooth implementation of hyperthermia.

7.2.1.1.4 Hyperthermia room preparations

Environment: Treatment rooms should be spacious and bright, and daily routine air disinfection should be done.

Drug: Rehydration saline (oral).

Instrument and article: Oxygenator, disposable water cups, straws, and so on.

Other equipments: Whole-body hyperthermia machine and multiparameter electrocardiogram (ECG) monitor.

Bed set: Big bath towel, small towels, pillow, and so on.

7.2.1.2 NURSING DURING HYPERTHERMIA

It refers to the whole nursing process, including patient's entry into the hyperthermia cabin, temperature rise, stay, and fall.

7.2.1.2.1 Monitoring vital signs

7.2.1.2.1.1 Temperature monitoring

Anal and abdominal surface temperatures must be regularly monitored. With the patient in lateral position, and with the front anal tube segment in a ready-to-use condition, temperature sensor is lubricated with paraffin, the nurse instructs the patient to deeply breathe and relax and, at the same time, slowly inserts the anal tube into the anus about 10 cm and fixes it on the hip with tape. The body surface thermometer is placed on the abdomen and affixed with tape. During monitoring of body surface temperature, reading is taken once every 10 minutes.

7.2.1.2.1.2 Respiratory monitoring

Patient's respiratory frequency, rhythm, and amplitude are observed. Oral mucosa, fingernail, earlobe, and facial skin color are checked to understand whether the patient has low oxygen and carbon dioxide accumulation. The monitor indicates the breathing conditions through the thoracic impedance values of the two electrodes. ECG electrode installation is quite important, because it directly affects the measured value. It is best to place one electrode in the midline of the right armpit and the other electrode diagonally on the left side of the chest (this site has the maximum activity area at breathing) to obtain the best respiratory wave. During respiratory monitoring, recording is taken once every 10 minutes.

7.2.1.2.1.3 Heart rate monitoring

ECG cable is connected for monitoring heart rate. In the process of treatment, with the increase of body temperature, heart rate will accelerate gradually. It is necessary to pay close attention to changes in the heart rate. During heart rate monitoring, recording is taken once every 10 minutes.

7.2.1.2.1.4 Blood pressure monitoring

With the patient in recumbent position, one limb is chosen to measure blood pressure. The limb on the transfusion side should not be chosen for blood pressure monitoring. In whole-body hyperthermia state, due to

vasodilation and large amounts of fluid loss, a drop in blood pressure easily occurs. It is necessary to measure the blood pressure every 10 minutes to observe and record the changes in blood pressure.

7.2.1.2.1.5 ECG monitoring

ECG monitoring can indicate heart rate, cardiac rhythm, and whether arrhythmia or ischemic happens, and so forth.

7.2.1.2.1.6 Blood oxygen saturation monitoring

It mainly indicates the blood oxygen state and predicts hypoxemia in a timely manner. The blood oxygen saturation sensor is placed in a suitable finger (short nail and good blood circulation). In high heat state, cell metabolism is strong and oxygen demand is increased. Conventionally, low flow oxygen 3 L/min is provided. Continuous monitoring and recording every 10 minutes should be done.

7.2.1.2.2 General conditions monitoring

In hyperthermia, palpitation, dizziness, headache, and so forth, may occasionally happen. The nurse should closely observe the patient's reactions, patrol, and inquire about the chief complaints of the patients. Any problem should be promptly dealt with.

7.2.1.2.3 Skin care

Correctly instruct and assist patients into hyperthermia cabin and pay attention to anti-scald measures. Place a soft pillow under the head, cover the body with a big bath towel, and isolate all metal tubes contacting with the body through the gauze to prevent any scald due to high temperature. A small towel is made available to the patient to wipe facial sweat in a timely manner.

7.2.1.3 NURSING AFTER HYPERTHERMIA

It refers to the nursing process after the following steps: hyperthermia is completed in the cabin, temperature has dropped close to normal, and patient has exited from the hyperthermia cabin.

Assessment before exit from the cabin: Whether the skin has red press marks, blisters, or other complications. If any, a symptomatic treatment should be timely made. After the exit from the cabin, the patient should change clothes, and blow-dry hair with a hair dryer.

Patient education after exit from the cabin: Instruct the patient to drink more water and have a light diet of high heat, high vitamin, and high protein content; inform the patient of adverse reactions that may occur after hyperthermia, such as dizziness, fatigue, and so forth, so as to relieve the patient's anxiety. Leave the bed only after the body temperature drops to normal, and prevention of any fall has been made.

7.2.2 MEDIUM-HIGH TEMPERATURE

This kind of therapy adopts infrared light to raise body temperature to 39.5°C–41.8°C and maintain it for a certain amount of time. Usually it requires anesthesia or deep sedation. Because of the complex process, it may cause a series of effects on the internal environment including the central nervous system, circulatory system, urinary system, blood system, immune system, and so forth. Therefore, nursing is difficult, needing strict nursing measures and technical skills.

7.2.2.1 NURSING BEFORE HYPERTHERMIA

7.2.2.1.1 Inquiry and assessment

Vital signs, pain, skin integrity and scar tissue, weight, history of drug allergies, physical activity, mood, consciousness, oral communication ability, implants, and so forth.

7.2.2.1.2 Patient education

One to three days before hyperthermia, the patient needs to drink more water to ensure that the body water storage is in good condition. In the last evening before hyperthermia, have a liquid diet. Within 8 hours and

6 hours before hyperthermia, do not eat and do not drink, respectively. Do aerobic exercise for 10 minutes before hyperthermia. After hyperthermia, do not leave the ward, and more importantly, do not drive any vehicle.

7.2.2.1.3 Psychological nursing

Most patients with malignant tumors have received several treatments of surgery, radiotherapy, and chemotherapy. Because of poor past curative effects coupled with high stress and anxiety, they have expectations and doubts concerning whole-body hyperthermia. Therefore, the first thing is to establish a good relationship between nurses and patients before treatment. Patients and their families should be given detailed explanations about the procedure of hyperthermia and matters needing attention during the treatment so as to ease their unhealthy psychological state and help eliminate fear and tension. Also, some successful cases should be presented, since communications with successfully cured patients in previous hyperthermia can help them eliminate psychological concern and establish confidence in the procedure. Special counseling may be needed according to the specific needs of each patient.

7.2.2.1.4 Hyperthermia room preparations

Environment: Treatment rooms should be spacious and bright, and daily routine air disinfection should be done. *Drug:* Intravenous rehydration fluids (including liquid glucose, Ringer solution, equilibrium liquid, and colloid), anesthetic drug, vascular active drug, narcotic antagonist. Article: body temperature sensor, distilled water ice pad, ambulance vehicle, binding belt, cotton pad, infusion device, tee connection tube, extension tube, oxygen device, sputum suction device, and so forth. Other equipment: whole-body hyperthermia machine, ECG monitoring equipment, defibrillator, thermometer, and so forth; Bed set: big bath towel, small towel, pillow, and so forth.

7.2.2.2 NURSING DURING HYPERTHERMIA

It refers to the whole nursing process, including entry into the hyperthermia cabin, temperature rise, stay and fall, and so forth. The patient is required to empty stool and urine, wear pure cotton clothing designed for hyperthermia, and remove body decorations, other metal items, and dentures.

7.2.2.2.1 Monitoring vital signs

The vital signs requiring monitoring include temperature, respiration, heart rate, blood pressure, and blood oxygen saturation.

Monitoring procedures are the same as whole-body hyperthermia (medium-low temperature).

7.2.2.2.2 Intravenous route preparation

Intravenous routes are established for drug delivery in accordance with the doctor's advice.

7.2.2.2.3 Skin care

The patient, after aerobic exercise, is instructed and assisted by the nurse to enter the treatment cabin. Anti-scald measures are adopted. Place a soft pillow under the head; cover the body with a big cotton towel; isolate metal tubes contacting with the body using gauze; and protect hands and feet with special cotton gloves and socks to prevent high-temperature scald. Protect artificial anus, wound, and postoperative scar healing site with double layers of cotton towel or cotton cushion. After sedation, affix the binding belt to the body making sure that its binding firmness does not affect blood circulation (the blood supply in the bound limb should be observed and recorded once per 10 minutes). Place a soft pillow under the knee and the waist back, to relieve the heel and sacral oppression so as to prevent skin burns due to compression time being too long. After sedation and rise of the body temperature to 39.0°C, turn the head and change the head pillow position every 15–20 minutes. Small towels should be available to wipe sweat in the head and face in a timely manner. Pay attention to prevent sweat getting into the eyes and ears.

7.2.2.2.4 Psychological nursing

Before sedation, the patient can enjoy music and watch TV so as to distract his attention. When necessary, the nurse can chat with the patient about some pleasant topics.

7.2.2.2.5 Respiratory tract nursing

During hyperthermia, keep patient's respiratory tract unobstructed, and observe patient's breathing and blood oxygen changes. If blood oxygen saturation is decreased to below 95%, check whether the blood oxygen saturation sensor is placed correctly, timely eliminate external causes, and assist the anesthesiologist in opening the respiratory tract and increasing oxygen flow rate; 8–10 L/min oxygen masks are used. Respiratory tract opening methods: (1) head side method; (2) neck-lift, chin-lift, and jaw-support method; (3) oropharyngeal or nasopharyngeal airway tubes and endotracheal intubation.

7.2.2.2.6 Accurate recording of urine output

After sedation, the female patients undergo aseptic urethral catheterization with 14# or 16# urine tube chosen; the male patients can use a urine bag tube or undergo aseptic urethral catheterization. If urethral catheterization is done, conventionally tetracaine mucilage is squeezed into urethra before the urine tube is inserted into it. Then urine tube is gently inserted to avoid urethral injury. In hyperthermia, the color and volume of urine should be continuously observed so as to guide the intravenous rehydration.

7.2.2.2.7 Proper use of chemotherapy drugs

When the body temperature is raised to 39.0°C, use chemotherapy drugs according to the doctor's instruction. Do a good job in protection of both patient and medical staff. Prohibit drug extravasations; once extravasation appears, be sure to immediately do a local sealing, and make the wet compression with 50% magnesium sulfate gauze so as to avoid local tissue necrosis.

7.2.2.2.8 Cooling care

Do not cool too fast. It is advisable to drop 1°C/hour. At the same time, a small towel is used to wipe sweat and a big bath towel to cover the chest so as to prevent the patient from catching cold.

7.2.2.2.9 Precautions after the treatment

After the treatment is completed and when body temperature is at 38°C, temperature sensor is removed, oxygen is supplied, and multifunctional ECG monitoring is done.

7.2.2.3 NURSING AFTER HYPERTHERMIA

7.2.2.3.1 Skin care

Maintain a clean and tidy bed unit, assess skin integrity and distal limb swelling (edema). Pay attention to keep patient warm, timely change sweated clothes and bedsheets, and blow-dry hair with a dryer. Timely change the dressing in venipuncture site and trocar paster or sticker to prevent skin infections in needled sites.

7.2.2.3.2 Venous passage nursing

The venous channel should be maintained unobstructed, and drugs administered according to the doctor's instruction.

7.2.2.3.3 Safe transport

The patient is sent to ICU on a flat cart. On the way, be sure to keep the patient warm and observe any significant changes in vital signs; oxygenate and ECG monitor for no less than 6 hours. When the vital signs are back to normal, the patient can be sent back to the common ward; if any abnormal condition occurs, be sure to promptly report to the doctor for relevant measures to be taken.

7.2.2.3.4 Diet

After hyperthermia, family members may give fruit juice, water, and other drinks to patients; it is advisable to give a bland light diet with high heat, high vitamin, and high protein, and to select nutritious and diverse meals. When necessary, venous nutrition supply can be made.

7.2.2.3.5 Psychological nursing

The patient is told that, after the hyperthermia, urethral orifice pain, distal limb edema, oral herpes, dizziness, fatigue, or late-onset blister in skin may appear, but these are normal phenomenon. The explanation can eliminate patients' anxieties.

7.2.2.3.6 Bed rest

The patient is instructed to have bed rest for 24 hours after hyperthermia, and empty stool and urine at bedside as much as possible using a bedpan and urinal, to prevent any potential of a fall.

7.2.3 Adverse reactions after hyperthermia

7.2.3.1 Skin burns

Skin burns frequently occur in lower abdomen, inside thigh, blood pressure cuff site in upper limb, sacrococcygeal protuberance, heel, occipital, and so forth. If only local skin redness or burning occurs, local cold compress can be applied under continuous observation; indeed, it generally disappears the next day. If there are any small blisters, topical use of moist burn cream can be applied and further observed. If large blisters occur on the next day, they are drained in aseptic conditions, followed by topical use of wet burn cream twice a day, and then a sterile dressing. Usually, the healing effect can be obtained within 1 week.

7.2.3.2 Digestive tract reactions

Patients undergoing thermochemotherapy often have nausea and vomiting mainly as side effects of chemotherapy drugs. Before and after chemotherapy, antinausea and sedation drugs can be taken by doctor's instruction to effectively reduce digestive tract reaction. Patients are encouraged to drink more water so as to better eliminate metabolites. Dietary guidance to patients: In case of strong sick feeling, do not force oneself to eat; in case of a desire, eat immediately according to the principle of eating little but often; it is advisable to have a slight and digestible diet with less fat, high heat, and high vitamins. Let the patient know some methods to inhibit nausea and vomiting, such as applying orange peel, raw ginger paste at Lieque acupoint, massage on Zusanli, and so forth. Keep the ward air fresh, timely dump vomit, and reduce odor stimulus.

7.2.3.3 Re-rise of body temperature

Patients, within 3 days after treatment, have varying degrees of temperature rise. Usually, their body temperature is below 39.0°C. In such case, it can be lowered by compression of ice and alcohol, sponge bath, and other physical cooling methods. Do not cool by drugs, since this method is not meaningful under the assumption that the temperature rise is a result of the regulation center in the body.

7.2.3.4 Oral herpes

One to three days after treatment, a few patients may have oral herpes. Antiviral ointment should be applied in the affected area.

7.2.3.5 Urethritis

One to two days after the treatment, some patients may have a burning sensation in the urethra. They must be instructed to drink more water, while no special treatment is needed.

7.2.3.6 Dizziness

Pay attention to rest after treatment, where no special treatment is needed.

7.3 Local or regional hyperthermia nursing

It is a nursing technique in local or regional hyperthermia mainly using in vitro radio frequency local hyperthermia.

7.3.1 Nursing before hyperthermia

7.3.1.1 PSYCHOLOGICAL CARE

Many patients do not know it as a new type of treatment, and have some doubt and fear on its process and effect. Before the hyperthermia, this treatment should be patiently explained to patients and their family members, including its advantages, operating methods, necessity, and feasibility, so that they can have a correct understanding, and actively cooperate with the medical staff. Medical protective measures should be taken for new patients who may be quite sensitive to this treatment. When necessary, family members should be allowed to accompany them to meet the psychological needs of patients and family members. During treatment, the staff should understand patients' cultural background differences and conduct doctor–patient communications in an effective manner, ensuring smooth progress of treatment.

7.3.1.2 PATIENT EDUCATION

Before local hyperthermia, patients should remove all metal objects and keep them safe (such as necklace, bracelet, and keys). Metal objects should not be brought into the treatment area; in case of a metal implant in the body (such as pacemaker, metal stent, and contraceptive ring), make sure to report it to the medical staff. These measures can let the treatment avoid metal sites and prevent burns caused by metal heat conduction. During treatment, telephone must not be used.

In the treatment, the patient should not be allowed to endure excessive heat. In case of local overheating or tingling, the patient must report it to the staff to make effective adjustments to prevent burns.

Before treatment, the patient should have a meal to prevent hunger or hypoglycemia; avoid eating too much. Especially, patients whose treatment site is in the chest and abdomen can easily suffer abdominal distension and discomfort during electrode positioning. Fully empty the stool and urine before treatment.

Before treatment, have the patient wear comfortable soft cotton clothing. Patients sweating more in treatment should carry an additional set of clothes or cotton towel. Also the staff should provide enough clothes and towels for the patients. After the treatment, timely wipe sweat, change clothes, avoid wind, and have the patient rest so as to prevent a cold.

Female patients with treatment sites in the lower abdomen should avoid treatment during the menstrual cycle, and those at childbearing age are told to pay attention to contraception during treatment.

7.3.1.3 HYPERTHERMIA ROOM PREPARATIONS

Keep the room clean and quiet with neat bed sets, fresh air, and proper indoor temperature and humidity.

7.3.2 Nursing during hyperthermia

7.3.2.1 OBSERVING AND REPORTING ON ADVERSE REACTIONS

Closely observe the patient's reactions, and initiate examinations and inquiries. In case of local overheating or sting, promptly report to the medical staff to make effective adjustments to prevent scald. In case of dizziness, promptly report to and assist the doctor.

7.3.2.2 SKIN CARE

If the patient sweats, timely wipe them away using cotton towels. Operate hyperthermia equipment at high power according to the manual. Wipe sweat or drink water after the equipment stops.

7.3.3 Nursing after hyperthermia

Skin care: Check whether the skin of the treatment site has redness or skin burns. If an elderly patient has dull skin, we should provide a full assessment. If there is the possibility of burns, immediately give wet ice bag compress for 10–20 minutes and a topical use of burn ointment, so as to reduce the harm of burns.

Keep warm: If the patient sweats, there may be a need to change clothes. Advise the patients and their family members to keep warm and prevent cold.

Rest and activity: After the treatment, advise the patient to have a short rest. After no discomfort is observed, the patient can leave the treatment bed with support. Take antifall measures during this period.

The patient should drink more warm water or juice to replenish fluids.

7.4 NURSING IN HYPERTHERMIC PERITONEAL PERFUSION

Hyperthermic peritoneal perfusion treatment is an effective means to treat primary, secondary, and cancerous ascites. In this technique, peritoneal perfusion fluid is kept at 40°C–43°C and maintained for a certain amount of time, to maintain high drug constant concentration at high temperature, making abdominal metastatic lesions of small carcinoma more fully contact with chemical drugs, and therefore, eventually clearing or killing cancer.

7.4.1 Psychological care before treatment

Before hyperthermic peritoneal perfusion chemotherapy, the nurse should carefully evaluate the patient's physical condition, make sure the treatment is safe, and inform the patient about it. explain in detail this treatment, including its advantages, operating procedures, and adverse reactions; thus, allowing the patient to believe in this therapy's necessity, have a proper attitude, and actively cooperate with the staff in treatment.

7.4.2 Nursing during abdominal puncture

Abdominal puncture should be strictly performed in an aseptic state to prevent abdominal infection. During the puncture process, closely observe the patient's condition and listen to the patient's complaints. If abdominal pain, cold sweat, or pale face occurs, immediately stop puncture and assist the doctor in symptomatic treatment. After puncture, connect the indwelling catheter to the blood transfusion device, and drip 100 mL physiological saline. Observe whether the patient has swollen skin, urinating urge, or abdominal pain, and ensure that the catheter remains in the abdomen. Affix it with sterile transparent paste. Instruct the patient to maintain a comfortable position and avoid strenuous exercise, so as to prevent the needle from coming out or puncturing the bowel and other organs.

7.4.3 Nursing during peritoneal perfusion

7.4.3.1 EVALUATION AND DISPENSATION BEFORE PERITONEAL PERFUSION

Before perfusion, 100–200 mL saline can be infused to reconfirm the catheter is in the abdomen. Closely observe drug perfusion in the process. If fluid infusion is not smooth, timely observe whether the perfusion tube is squeezed or folded; adjust the patient position; when necessary, report to the physician. Closely observe significant changes of patient's vital signs, talk to the patient, and heed his feelings. Pay attention to the complaints of the patient. If discomfort such as nausea, vomiting, abdominal distension, abdominal pain, bowel movement, urination urge, or other symptoms occurs, make sure to suspend fluid infusions and assist the physician in treatment. If tolerable thermal sensation occurs in the abdomen, tell the patient that this is a normal situation.

7.4.3.2 SAFE USE OF CHEMOTHERAPY DRUGS

In the use of chemotherapy drugs that may cause adverse effects on the skin, respiratory tract, digestive tract, and so forth, it is necessary to strictly follow the principle "three checks and seven reviews"; and operators must wear masks and double-layer gloves.

The infusion stand for chemotherapy drugs is kept at the end of the bed. Protective measures for both doctors and patients are taken. Saline solution is infused before and after chemotherapy drugs. As much as possible any drip-out of these drugs is avoided in taking the bottle and discharging air. After the operation is completed, all of the pollutants and used items are discarded into a yellow plastic bag, which is sealed and placed into the special red plastic barrel. After the barrel is labeled, it is collected by special staff for centralized disposal. If the drug leaks in the perfusion process, it should be immediately collected with a special bag in a proper manner.

7.4.3.3 PRETREATMENT BEFORE PERFUSION

Thirty minutes before perfusion of chemotherapy drugs, have a venous drip of saline 100 mL plus granisetron 3 mg to alleviate varying degrees of reaction of the gastrointestinal tract in the patient. The medical staff can timely communicate with the patient to give the patient a distraction. If nausea or vomiting occurs, suspend perfusion, help the patient remove the vomit to prevent it from entering the airway, and let him clean his mouth with warm water to ensure his comfort as much as possible.

7.4.3.4 PREVENTION OF ADVERSE REACTIONS

The perfusion may cause abdominal distension and pain because of much liquid lavage and local stimulation. To reduce or avoid these symptoms, conventionally inject 10 mL saline plus 5 mg dexamethasone plus 4000 IU chymotrypsin into the abdomen to obtain such effects as preventing abdominal adhesion by high concentrations of chemotherapeutic drugs, and reducing the high heat and stimulation of the abdominal wall by drugs occurring in a short time; assist patients in regularly changing positions. These measures can not only make the chemotherapy drug evenly distributed and fully contacted with abdominal organs and mucous membranes to better kill cancer cells, but also promote intestinal peristalsis to discharge gas from the anus and reduce abdominal pain.

7.4.4 Nursing during hyperthermia

After perfusion, in vitro hyperthermia in a deep position of the body through radio frequency is done. Before hyperthermia, reevaluate the patient, remove all metal objects, and explain the procedure so that the patient becomes fully prepared.

The conditions of the abdomen should be checked in the patient; for example, whether the surface of the skin has scars, damages, swelling, or indurations, or whether fat is excessive in the heating region. A cold distilled water bag can be placed to ensure that the electrical plate is fully matched with body surface. In hyperthermia process, closely observe the patient's condition, and tell the patient that when the skin is overheated or stabbing pain is felt, it is necessary to promptly report it to the medical staff, so that the power can be timely adjusted to prevent burns.

Because of local blood circulation acceleration, the patient may sweat and lose body fluids in the treatment; it is necessary to change clothes and drink warm boiled water after the treatment. After the treatment, the staff send the patient back to the ward using a wheelchair, and instruct the patient and his/her family members to keep warm and prevent cold.

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8

Therapeutic protocols of integrated hyperthermia treatment for noncancerous diseases

8.1 INTRODUCTION

In the clinical application of hyperthermia for cancer, Clifford Hospital has gradually found that hyperthermia also has a good clinical effect on noncancerous diseases. Some reports show that the clinical application of hyperthermia is not limited to cancer, and it has recently been gradually extended to the treatment for noncancerous diseases with the desired results obtained. Some of them are described below.

8.2 HYPERTHERMIA MECHANISMS FOR NONCANCEROUS DISEASES

8.2.1 Promotes local or systemic blood circulation

Hyperthermia can promote and improve the body's blood circulation and microcirculation, especially in the skin (more significant in face), and can accelerate metabolism, which results in stronger tissue repair function. It also strengthens metabolism in the liver and kidney, leading to better decomposition and elimination of toxins. In other words, there is a better effect in the regeneration, repair, absorption, and removal of the pathological product, achieving the goals of eliminating inflammation and restoring tissue functions.

8.2.2 Promotes cell immune function

The purpose of hyperthermia is to promote cellular immunity and leukocyte phagocytosis. In hyperthermia, T lymphocytes and natural killer (NK) cells gain better activity, phagocytes mature faster and are more aggressive, and immune cells have better chemotaxis. All of these lead to inhibition or removal of pathogens.

8.2.3 Promotes humoral immune function

Hyperthermia can promote humoral immune function, resulting in the increase of immunologically active proteins. Many unknown mechanisms are still unexplainable.

8.2.4 Promotes the increase of endocrine secretion

Hyperthermia promotes the increase of endocrine secretion, which is associated with increased blood circulation and metabolism. The mechanism needs further exploring.

8.3 DIFFERENCES BETWEEN MODERN HYPERTHERMIA AND TRADITIONAL HYPERTHERMIA

Modern hyperthermia stems from traditional hyperthermia. Their differences are described below.

8.3.1 Modern hyperthermia has strict temperature treatment indicators, whereas traditional hyperthermia does not

Modern hyperthermia must have multiple-site temperatures measured or temperature parameters as references; its regional therapy must have clear and accurate temperature indicators in the treatment area; and its whole-body hyperthermia must have overall accurate temperature indicators inside and outside the body. However, these are not needed in traditional hyperthermia.

8.3.2 Modern hyperthermia utilizes high-tech equipment

In modern hyperthermia, high-tech equipment is used, including ICU and monitors, whereas in traditional hyperthermia, the technical content is not high. The former has much laboratory data as the theoretical basis and the latter has little or none. Modern hyperthermia equipment represents the highest level of thermal medical science and technology, and is still in development and being perfected. But there is less equipment required in traditional hyperthermia.

8.3.3 Modern hyperthermia has a long duration time

With strict temperature indicators for modern hyperthermia, its operating duration time is very long, but traditional hyperthermia typically requires only 20–30 minutes. For example, in the modern therapy technique, whole-body hyperthermia for nontumor diseases has a duration of 2 hours or so and for malignant tumors 6–7 hours or longer.

8.3.4 Methods and indicators in modern hyperthermia

Indicators and methods are more specific in modern hyperthermia, but less so in traditional hyperthermia.

8.3.5 High-qualification requirements for physicians in modern hyperthermia

Modern hyperthermia requires physicians with high qualifications, especially in cancer treatment; there are higher standards for the physician's professional level and clinical experience.

8.3.6 Modern hyperthermia has more definitive curative effects

Modern hyperthermia has strict therapeutic indicators. If patient tolerance is poor, the treatment can also be supplemented by other drugs, thus ensuring a therapeutic effect.

8.3.7 Treatment scope and depth

Traditional hyperthermia is mainly for noncancerous diseases and generally not for cancers; its treatment depth is obtained mainly by heat conduction, so is very limited (just applied to superficial diseases). Modern hyperthermia is not only important in cancer treatment, but also applied for noncancerous diseases,

including those of traditional hyperthermia and in the deep sites of the body. Thus, modern hyperthermia largely extends the treatment range of diseases.

8.4 HYPERTHERMIA FOR NONCANCEROUS DISEASES

8.4.1 Gynecological inflammation

Common in females, it mainly refers to inflammation in reproductive organs, including vulvitis, vaginitis, cervicitis, and pelvic inflammation.

Local hyperthermia makes full use of radio frequency (RF) characterized by heat and high-frequency electromagnetic field with the following benefits: local vasodilation; stronger blood circulation; increased permeability of cells in blood vessels and tissues; improved nutrition in local tissues; stronger leukocyte phagocytosis function and enzyme activity; better elimination of metabolites or toxins, thereby facilitating absorption and disappearance of inflammation; elimination or inhibition of bacteria through heat accumulation; and enhanced immune system function. In addition, improved local blood circulation, increased cell metabolism, and increased permeability of cells in local blood vessels and tissues can increase the absorption of drugs, enhance drug action and absorption of local inflammatory exudates, and promote recovery from inflammation.

Therapeutic regimen: Administer local hyperthermia once a day and 40 minutes each time, with 10 times as a course for a total of two courses. After each treatment course, take 1 week off. At the same time, infusion of vitamin C can improve the efficacy. Also, conventional gynecological treatment and TCM drugs can be combined.

8.4.2 Primary dysmenorrhea

Primary dysmenorrhea refers to menstrual pain often being spasmodic, which occurs mainly in the lower abdomen. Other symptoms include headache, fatigue, dizziness, nausea, vomiting, diarrhea, and waist and leg pain. Primary dysmenorrhea is very common in young females and is not associated with apparent organic pelvic diseases.

Therapeutic regimen: Administer local hyperthermia once a day and 40 minutes each time, with 10 times as a course for a total of two courses. After each treatment course, take 1 week off. Administer whole-body hyperthermia once a week and about 2 hours each time, with temperature maintained at 38°C–39°C, five times as a course for a total two courses. After each treatment course, take 1 week off. For the combination of both, deep hyperthermia can be done every day during the whole-body hyperthermia period. Combining with herbal medicine (oral and external use), acupuncture, and/or moxibustion can improve the efficacy.

8.4.3 Prostatitis and prostatic hyperplasia

Prostatitis is caused by a variety of complex factors. Main clinical manifestations are urethral irritation and chronic pelvic pain involving pathological changes in immunity and neuroendocrine function. Prostatic hyperplasia is a common disease in older men caused by oppression of urethra and bladder orifice, clinically characterized by frequent urination, urgency, more frequent urination at night time, and micturition arduous; and can lead to complications such as urinary tract infection, blood in urine, and bladder calculi. The relevant cause is not very clear. There are four theories in which the most recognized theory relates to sex hormones (clinical drug treatment based on this theory is effective). On the other hand, scientists have discovered that in prostatic hyperplasia, chronic inflammatory cell infiltration is very common, which is a theoretical basis of hyperthermia for prostatic hyperplasia treatment.

In addition to the above anti-inflammatory effect, local hyperthermia for prostatitis and prostatic hyperplasia can reduce urethral resistance and urine reflux. The alternating electromagnetic field can generate an induced eddy current at the pelvic floor, which stimulates tissues and nerves to contract and relax. This can reduce muscle tension and sensory nerve excitability; alleviate perineal discomfort and pain; and

reduce urinary frequency, urgency, and urine pain symptoms. Prostate tissue is sensitive to temperature; at about 41°C, the chronically inflammatory prostate tissue can be found presenting vasodilation, faster blood flow, enhanced oxygen and nutrition supply, faster exudate removal, and faster removal of metabolites and chemicals responsible for pain and inflammation. As a result, local nutrition and metabolism are improved, local irritation is reduced, inflammation and edema of tissue are eliminated, and the prostate size is reduced, thus improving symptoms. Theoretical inference is that regular hyperthermia can delay the process of prostatic hyperplasia in elderly patients.

Therapeutic regimen: Administer local hyperthermia combined with chelate detoxification once a day and 40 minutes each time, with 10 times as a course for a total of two courses. After each treatment course, take 1 week off. Combining with Chinese medicine external treatment can improve the curative effect; at the same time, conventional urological treatment is combined. Severe hyperplasia of prostate not relieved in repeated treatment by drugs and heat still needs surgical intervention when necessary. Postoperative hyperthermia can promote wound recovery.

8.4.4 Lung infection

Pulmonary infection refers to parenchymal inflammation inclusively in terminal airway, alveolar cavity, and pulmonary interstitial tissues. Infection is the most common cause. It can also be caused by physical and chemical treatments, immune insufficiency, and drugs.

In the treatment of lung infections, hyperthermia plays a role of anti-inflammatory and immune-enhancement, the mechanism of which is the same as that in gynecological inflammation treatment, i.e., enhancing body immunity, enhancing inflammatory substance absorption, and drug sensitizing.

Therapeutic regimen: Administer local hyperthermia once a day, 40 minutes each time, and 10 times as a course with courses continuing until the infected lesion is absorbed. After each treatment course, take 1 week off. In the hyperthermia process, infusion of vitamin C can improve the treatment effect. Conventional internal medicine anti-infection treatment is combined.

8.4.5 Chronic lumbar muscle strain

Chronic lumbar muscle strain, also known as low back muscle fasciitis or functional lumbago, mainly refers to the local aseptic inflammation caused by chronic injury in lumbosacral muscle, fascia, ligaments, and other soft tissues. The symptom is the diffused pain on one side or both sides of the lumbosacral. It is one of the common chronic lumbar pains and is often related with the occupational environment.

The hyperthermia benefits include tissue temperature rise, capillary dilation, faster blood flow, enhanced metabolism, improved vitality, and regeneration of tissue cells. RF local hyperthermia can relieve pain and muscle spasm, eliminate edema and tissue swelling, activate blood, remove stasis, and so on. Infrared hyperthermia can reduce the excitability of the nerve system, kill pain, relieve muscle spasm, promote neural functional recovery, and so on.

Therapeutic regimen: Administer local hyperthermia once a day and 40 minutes each time, with 10 times as a course for a total of three courses. After each treatment course, take 1 week off. Administer whole-body hyperthermia, once a week, about 2–3 hours each time, at 38°C–40°C temperature, with five times as a course for a total of three courses. After each treatment course, take 1 week off. Local hyperthermia can be done daily during whole-body hyperthermia. Combination with TCM treatment techniques such as drug topical use, acupuncture, massage, and cupping can improve the curative effect. At the same time, combine rehabilitation exercise and other physical therapy.

8.4.6 Osteoarthritis

Osteoarthritis refers to noninflammatory degeneration of articular cartilage and joint marginal osteophyte formation because of old age or other reasons, such as trauma, congenital anomalies, and deformities of joints. Clinical symptoms include joint pain, restricted movement, and joint deformities.

Arthritis RF local hyperthermia can generate effects such as blood vessel wall permeability enhancement, local blood circulation improvement, edema elimination, elimination of substances causing pain, and inhibition of sensory nerve conduction to attain pain relief. The heat effect is to stimulate local joints; dilate blood vessels; promote blood circulation; improve local tissue metabolism of nutrients; regulate functions of local joint, nerve, muscle, and ligament; reduce the tension of muscle and connective tissue; enhance leukocyte phagocytosis; and regulate immune function.

Therapeutic regimen: Administer local hyperthermia once a day and 40 minutes each time, with 10 times as a course. Administer whole-body hyperthermia once a week, about 2–3 hours each time, at 38°C–40°C temperature, with five times as a course. RF local hyperthermia can be done daily during whole-body hyperthermia. After each treatment course, take 1 week off. After the symptoms are relieved, one additional course is taken to consolidate the treatment effect. Combination with TCM treatment techniques such as drug topical use, acupuncture, massage, cupping, and medicated diet can improve the treatment effect. At the same time, combine conventional physical therapy and drug therapy.

8.4.7 Rheumatic diseases

Rheumatic disease refers to a range of diseases affecting bones, joints, and the surrounding soft tissues, such as tendons, slippery bursa, and fascia. There are varieties of etiologies, such as infection, immunity, metabolism, endocrine, degeneration, geographical environment, and genetics.

Hyperthermia in rheumatic disease mainly plays a role in pain relief, immune regulation, and improvement of circulation function, thereby alleviating symptoms.

Therapeutic regimen: Administer local hyperthermia once a day and 40 minutes each time, with 10 times as a course for a total of five courses. The patient can rest for 1 week after completion of each course. Administer whole-body hyperthermia once a week, about 2–3 hours every time, at 38°C–40°C temperature, with five times a course for a total of five courses. After each treatment course, take 1 week off. Local hyperthermia can be done daily during whole-body hyperthermia. Combination with TCM treatments such as drug compress, acupuncture, massage, cupping, medicated diet, and bee needle can improve the treatment effect. Clinically, hyperthermia combined with medical ozone articular cavity injection, autohemotherapy, and other treatments can improve the treatment effect. At the same time, combine conventional physiotherapy and drug therapy.

8.4.8 Obesity

Obesity refers to a certain degree of obvious excess weight and being fat. It is caused by the accumulation of excessive body fat, especially triglycerides. Excessive food intake or changes in the metabolism of the body leads to accumulation of excessive body fat and being overweight, causing the change or incubation of body pathology and physiology.

Hyperthermia for obesity can increase the basal metabolic rate, lower blood insulin levels, and promote the decomposition and metabolism of the fat in the body.

Therapeutic regimen: Administer whole-body hyperthermia once a week, about 2 hours each time, at 38°C–39°C temperature, with five times as a course. Bowel cleaning treatment: 400–800 mL daily vegetable and fruit juices as meal alternatives, with 1 month as a course. Administer chelation detoxification therapy once a week with five times as a course. It is done simultaneously with hyperthermia. Hyperthermia can be maintained for a long time. Acupuncture treatment: Choose appropriate acupuncture, moxibustion, and catgut embedding according to the patient's syndrome. Oral Chinese medicine: The treatment is done according to the patient's syndrome. The treatment should be combined with diet, exercise, trace elements, and endocrine regulation. Therapeutic regimen: Administer whole-body hyperthermia once a week, about 2 hours each time, at 38°C–39°C temperature, with five times as a course. Bowel cleaning treatment: 400–800 mL daily vegetable and fruit juices as meal alternatives, with 1 month as a course. Administer chelation detoxification therapy once a week with five times as a course. It is done simultaneously with hyperthermia. Hyperthermia can be maintained for a long time. Acupuncture treatment: Choose appropriate acupuncture,

moxibustion, and catgut embedding according to the patient's syndrome. Oral Chinese medicine: The treatment is done according to the patient's syndrome. The treatment should be combined with diet, exercise, trace elements, and endocrine regulation.

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Appendix 1: General condition evaluation of cancer patients

A1.1 KARNOFSKY PERFORMANCE STATUS SCORE

Karnofsky (100-point method) performance status (Table A1.1).

Table A1.1 Karnofsky performance status

Performance Status	Scores
Normal, no signs and symptoms	100
Capable of normal activities; mild signs and symptoms	90
Barely capable of normal activities; some signs or symptoms	80
Capable of self-care; but inability to maintain normal life and work	70
Capable of self-care in most cases; but occasionally needs help	60
Always needs care	50
Incapable of self-care; needs special care and assistance	40
Incapable of self-care to a serious extent in the life	30
Seriously ill; needs to be hospitalized and have active support treatment	20
Critical illness; close to death	10
Death	0

A1.2 AMERICAN SOCIETY OF ANESTHESIOLOGISTS SCORE

ASA score: According to physical conditions and operational risks, American Society of Anesthesiologists (ASA) divides patients prior to anesthesia into five levels:

ASA I: No organic, physiologic, biochemical, or psychiatric disturbance.

ASA II: A patient with mild systemic disease that results in no functional limitation. Examples: well-controlled hypertension, uncomplicated diabetes mellitus.

ASA III: A patient with severe systemic disease that results in functional impairment. Examples: diabetes mellitus with vascular complications, prior myocardial infarction, uncontrolled hypertension.

ASA IV: Severe systemic disease that is a constant threat to life. Examples: congestive heart failure, unstable angina pectoris.

ASA V: Moribund condition in a patient who is expected to survive with or without operation. Examples: ruptured aortic aneurysm, intracranial hemorrhage with elevated intracranial pressure. Patients of Level I and II are in good anesthetic surgical tolerance with smooth anesthesia process. Patients of Level III could be with a certain danger during anesthesia, requiring thorough preparation before anesthesia, and effective preventive measures should be taken to prevent possible complications during anesthesia. Patients of Level IV are facing high risk in anesthesia. Patients of Level V are extremely critically ill with poor anesthesia tolerance, threatened by death at any time, and subject to high risk in anesthesia and surgery; thus, it is more important to do preparations before anesthesia (these preparations should be thorough, precise, and well considered).

A1.3 POSTANESTHESIA SCORE (TABLE A1.2)

Table A1.2 Anesthesia recovery score criteria (postanesthesia score [PAS]), 10 scores in total

Items	Score
Motoricity	2 = with four limbs moves independently or can follow instructions
	1 = with two limbs movable
	0 = with four limbs unmovable
Breath	2 = capable of deep breath and effective cough
	1 = with difficult, superficial, or blocked breath
	0 = with no spontaneous breath
Circulation	2 = before anesthesis: BP ± 20 mmHg
	1 = before anesthesis: BP ± 20–50 mmHg
	0 = before anesthesis: BP ± 50 mmHg
Consciousness	2 = completely conscious
	1 = able to be woken up
	0 = no response
Blood oxygen saturation	2 = breathing air: $SpO_2 > 92\%$
	1 = breathing O_2: $SpO_2 > 92\%$
	0 = breathing O_2: $SpO_2 < 92\%$

Criteria for exit from hyperthermia room: The total score should be 10 for a transfer from the hyperthermia center to the ward.

A1.4 CARDIAC FUNCTION CLASSIFICATION

According to the classification scheme issued by New York Heart Association (NYHA) in 1928, patients are divided into four classes, depending on their conscious activity:

I: With heart disease, but without activity restriction; without fatigue, palpitation, dyspnea, or angina after general activity at ordinary times.

II: With heart disease, with low-grade physical activity restriction; without subjective symptom at rest time, but with fatigue, palpitation, dyspnea, or angina after general physical activity.

III: With heart disease, with significant physical activity restriction; fatigue, palpitation, dyspnea, or angina could be caused by movements that are less than general activity.

IV: With heart disease, unable to engage in any physical activity; heart failure symptoms occurs at rest state and aggravates after physical activity.

A1.5 PULMONARY FUNCTION CLASSIFICATION CRITERIA (TABLE A1.3)

Table A1.3 Pulmonary function classification criteria

	VC or MVV%	FEV1.0%	SaO_2%	PaO_2 (mmHg)	$PaCO_2$ (mmHg)
Basically normal	>81	>71	>94	>87	<45
Sight reduction	80–71	70–61	>94	>87	<45
Significant reduction	70–51	60–41	93–90	87–75	<45
Severe reduction	50–21	<40	89–82	74–60	>45
Respiratory failure	<20		<82	<60	>45

A1.6 PAIN EVALUATION

Visual analog scale (VAS) pain evaluation (Table A1.4): The pain level is represented by 0–10, a total of 11 numbers; 0 represents painless, 10 most painful. Patients choose one of these 11 numbers according to their pain level.

Table A1.4 Visual analog scale

Level of Pain	Scores
No pain.	0
Mild pain that can be tolerated.	<3
Pain that affect sleep but can still be tolerated. The pain should be clinically relieved.	4–6
More intense pain that cannot be tolerated.	7–10

Appendix 2: Assessment on curative effect

Curative effect is evaluated according to the WHO criteria.

A2.1 EVALUATION OF MEASURABLE LESIONS

Complete remission (CR): All measurable lesions completely disappear in more than 4 weeks.
Partial remission (PR): Decrease in tumor volume being more than 50% in more than 4 weeks; serum tumor indicators significantly declined with statistical significance.
No change (NC): Increase in tumor volume being less than 25% or decrease less than 50% in more than 4 weeks.
Progress and development (PD): Tumor not able to be controlled and increase in tumor volume being more than 25%, or new lesions present, or blood tumor indicators significantly increased with statistical significance.

A2.2 EVALUATION OF LESIONS THAT CANNOT BE MEASURED

Complete remission (CR): All visible lesions disappeared, and this situation maintained at least for more than 4 weeks.
Partial remission (PR): Decrease in entire tumor estimated to be more than 50%, and this situation maintained for more than 4 weeks.
No remission (NR): Lesion has no significant change at least 6 weeks after treatment, increase in the tumor estimated to be less than 25%, or decrease in the tumor estimated to be less than 50%.
Progress and development (PD): New lesions present, or the increase in original lesions estimated to be more than 50%.

A2.3 EVALUATION OF QUALITY OF LIFE

Comprehensive evaluation is made according to Karnofsky performance status (KPS) and visual analog scale (VAS) scores.

Appendix 3: Common clinical prescriptions of traditional Chinese medicine

B

百合固金汤（《医方集解》）

Baihe Gujin Decoction (*Yifang Ji Jie* [*Collected Exegesis of Recipes*])

生地 熟地 麦冬 贝母 百合 当归 芍药 甘草 玄参 桔梗

Rehmannia glutinosa libosch, Radix Rehmanniae preparata, *Ophiopogon japonicus*, Fritillaria, *Lilium brownii* var. *viridulum*, Radix *Angelica sinensis*, *Paeonia lactiflora* Pall., *Glycyrrhiza uralensis* Fisch., Figwort root, *Platycodon grandiflorus*.

萆薢分清饮（《医学心悟》）

Bixie Fenqing Decoction (*Yixue Xinwu* [*Medicine Comprehended*])

川萆薢 黄柏 石菖蒲 茯苓 白术 莲子心 丹参 车前子

Dioscorea tokoro Makino, Cortex *Phellodendri chinensis*, *Acorus tatarinowii* Schott, *Poria cocos* Wolf, *Atractylodes macrocephala* Koidz., *Plumula nelumbinis*, *Salvia miltiorrhiza*, *Plantago* seedi (psyllium seed).

鳖甲煎丸（《金匮要略》）

Biejia Jian Pill (*Jinkui Yao Lue* [*Synopsis of the Golden Chamber*])

鳖甲 乌扇 黄芩 柴胡 鼠妇 干姜 大黄 芍药 桂枝 葶苈子 石韦 厚朴
丹皮 瞿麦 凌霄花 半夏 人参 蜚虫 阿胶 蜂房 赤硝 蜣螂 桃仁

Carapax trionycis, *Belamcanda chinensis*, *Scutellaria baicalensis georgi*, *Bupleurum chinense*, *Armadillidium vulgare* (Latreille), *Rhizoma zingiberis*, *Rheum palmatum* L., *Paeonia lactiflora* Pall., *Cassia* twig, *Lepidium apetalum* Willd, *Herba pyrrosiae*, Cortex *Magnoliae officinalis*, Cortex Moutan, *Dianthus superbus*, *Campsis grandiflora*, *Pinellia tube*r, Radix ginseng, *Eupolyphaga seu steleophaga*, Beehive, Red niter, *Catharsius molossus*, Semen persicae.

八正散（《太平惠民和剂局方》）

Bazheng Powder (*Taiping Huimin Heji Ju Fang* [*Prescriptions of the Bureau of Taiping People*])

木通 车前子 扁蓄 瞿麦 滑石 甘草梢 大黄 山栀 灯芯草

Akebia quinata, *Plantago* seedi (psyllium seed), *Polygonum aviculare* L., *Dianthus superbus*, Talcum, *Glycyrrhiza uralensis* Fisch., *Rheum palmatum* L., Cape Jasmine fruit, *Juncus effusus* L.

八珍汤（《正体类要》）

Bazhen Decoction (*Zhengti Leiyao* [*Traditional Classification Main and Points*])

人参 白术 茯苓 甘草 当归 白芍 川芎 熟地 生姜 大枣

Radix ginseng, *Atractylodes macrocephala* Koidz., *Poria cocos* Wolf, *Glycyrrhiza uralensis* Fisch., Radix *Angelicae sinensis*, Radix *Paeoniae alba*, *Ligusticum chuanxiong* Hort., Radix Rehmanniae Preparata, *Zingiber officinale* Roscoe, *Fructus jujubae*

补中益气汤（《脾胃论》）

Buzhong Yiqi Decoction (*Pi Wei Lun* [*Treatise on Spleen and Stomach*])

人参 黄芪 白术 甘草 当归陈皮 升麻 柴胡

Radix ginseng, *Radix astragali*, *Atractylodes macrocephala* Koidz., *Glycyrrhiza uralensis* Fisch., Radix *Angelicae sinensis*, *Pericarpium citri reticulatae*, *Cimicifuga foetida* L., *Bupleurum chinense*

C

柴胡疏肝散（《**景岳全**书》）
Chaihu Shugan Powder (*Jingyue Quanshu* [*Complete Works of Zhang Jingyue*])
柴胡 陈皮 枳壳 白芍 炙甘草 香附 川芎
Bupleurum chinense, pericarpium citri reticulatae, *Fructus aurantii*, Radix Paeoniae Alba, Radix Glycyrrhizae Preparata, *Rhizoma cyperi*, *Ligusticum chuanxiong* Hort.
柴胡疏肝汤（《**金匮翼**》）
Chaihu Shugan Decoction (*Jinkui Yi* [*Supplements of Jinkui Notes and Records*])
柴胡 陈皮 川芎 甘草 赤芍 香附 枳壳
Bupleurum chinense, pericarpium citri reticulatae, *Ligusticum chuanxiong* Hort., *Glycyrrhiza uralensis* Fisch., Radix *Paeoniae rubra*, *Rhizoma cyperi*, *Fructus aurantii*.
沉香散（《**金匮翼**》）
Chenxiang Powder (*Jinkui Yi* [*Supplements of Jinkui Notes and Records*])
沉香 石苇 滑石 当归 陈皮 白芍 冬葵子 甘草 王不留行
Lignum aquilariae resinatum, Herba pyrrosiae, Talcum, Radix *Angelica sinensis*, pericarpium citri reticulatae, Radix *Paeoniae alba*, *Malva verticillata* L., *Glycyrrhiza uralensis* Fisch., *Vaccaria segetalis*.

D

导**赤散**（《**小儿**药证**直**诀》）
Daochi Powder (*Xiaoer Yaozheng Zhi Jue* [*Key to Therapeutics of Children's Diseases*])
生地黄 木通 竹叶 甘草
Rehmannia glutinosa libosch, *Akebia quinata*, Folia bambusae, *Glycyrrhiza uralensis* Fisch.
大黄䗪虫丸（《**金匮要略**》）
Dahuang Zhechong Pill (*Jinkui Yao Lue* [*Synopsis of the Golden Chamber*])
大黄 䗪虫 水蛭 虻虫 蛴螬 桃仁 芍药 干漆 地黄 黄芩 甘草 杏仁
Rheum palmatum L., *Eupolyphaga seu steleophaga*, *Whitmania pigra* Whitman, Tabanus, Holotrichia, Semen persicae, *Paeonia lactiflora* pall., Resina Toxicodendri, *Rehmannia*, *Scutellaria baicalensis georgi*, *Glycyrrhiza uralensis* Fisch., Amygdalus Communis Vas.
当归补**血**汤（《**内外**伤**辨惑**论》）
Danggui Buxue Decoction (*Neiwai Shang Bianhuo Lun* [*Clarification of Perpexities about Internal and External Damage*])
黄芪 当归
Radix Astragali, Radix *Angelica sinensis*.
导**痰**汤（《**寿世保元**》）
Daotan Decoction (*Shoushi Baoyuan* [*Longevity and Life Preservation*])
陈皮 半夏 茯苓 白术 香附 青皮 黄芩 瓜蒌 砂仁 黄连 甘草
Pericarpium citri reticulatae, *Pinellia* tuber, *Poria cocos* Wolf, *Atractylodes macrocephala* Koidz., *Rhizoma cyperi*, *Vatica mangachapoi* Blanco, *Scutellaria baicalensis georgi*, *Trichosanthes kirilowii* Maxim., *Fructus amomi*, *Coptis chinensis* Franch., *Glycyrrhiza uralensis* Fisch.
涤**痰**汤（《**奇效良方**》）
Ditan Decoction (*Qixiao Liangfang* [*Wonderful Well-Tried Recipes*])
制南星 制半夏 炒枳实 茯苓 橘红 石菖蒲 人参 竹茹 甘草 生姜
Arisaema heterophyllum Blume, Rhizoma pinelliae preparata, roasted *Fructus aurantii immaturus*, *Poria cocos* Wolf, Exocarpium citri rubrum, *Acorus tatarinowii* Schott, Radix ginseng, Caulis bambusae in Taeniam, *Glycyrrhiza uralensis* Fisch., *Zingiber officinale* Rosc.

E

二陈汤（《**太平惠民和剂局方**》）
Erchen Decoction (*Taiping Huimin Heji Ju Fang* [*Prescriptions of the Bureau of Taiping People*])
法半夏 橘红 白茯苓 炙甘草
Rhizoma pinelliae preparata, Exocarpium citri rubrum, *Smilax china*, Radix glycyrrhizae preparata.

G

桂枝茯苓丸（《**金匮要略**》）
Guizhi Fuling Pill (*Jinkui Yao Lue* [*Synopsis of the Golden Chamber*])
桂枝 茯苓 丹皮 桃仁 赤芍
Cassia twig, *Poria cocos* Wolf, Cortex Moutan, Semen persicae, Radix *Paeoniae rubra*.

H

黄芪建中汤（《**金匮要略**》）
Huangqi Jianzhong Decoction (*Jinkui Yao Lue* [*Synopsis of the Golden Chamber*])
黄芪 白芍 桂枝 炙甘草 生姜 大枣 饴糖
Radix Astragali, Radix *Paeoniae alba*, *Cassia* twig, Radix glycyrrhizae preparata, *Zingiber officinale* Rosc., *Fructus jujubae*, *Saccharum granorum*.
海藻玉壶汤（《**外科正宗**》）
Haizao Yuhu Decoction (*Waike Zhengzong* [*Orthodox Manual of External Diseases*])
海藻 海带 昆布 陈皮 青皮 半夏 贝母 当归 川芎 连翘 独活 甘草
Sargassum, *Thallus laminariae* (Laminariaceae), *Thallus eckloniae* (Phaeophyta, Alariaceae), pericarpium citri reticulatae, Vatica mangachapoi Blanco, *Pinellia* tuber, Fritillaria, Radix *Angelica sinensis*, *Ligusticum chuanxiong* Hort., *Forsythia* suspense, Heracleum hemsleyanum Diels, *Glycyrrhiza uralensis* Fisch.

J

金匮肾气丸（《**金匮要略**》）
Jinkui Shenqi Pill (*Jinkui Yao Lue* [*Synopsis of the Golden Chamber*])
桂枝 附子 熟地 山萸肉 山药 茯苓 丹皮 泽泻
Cassia twig, Radix *Aconiti carmichaeli*, Radix Rehmanniae preparata, Fructus Corni, *Dioscorea opposita*, *Poria cocos* Wolf, Cortex Moutan, *Alisma plantago-aquatica*.

L

龙**胆泻肝**汤（《**兰室秘藏**》）
Longdan Xiegan Decoction (*Lanshi Micang* [*A Secret Book Kept in Chamber*])
龙胆草 黄芩 山栀子 泽泻 木通 车前子 当归 生地黄 柴胡 生甘草
Gentiana scabra Bunge, *Scutellaria baicalensis georgi*, *Gardenia jasminoides*, *Alisma plantago-aquatica*, *Akebia quinata*, Plantago seedi (psyllium seed), Radix *Angelica sinensis*, *Rehmannia glutinosa libosch*, *Bupleurum chinense*, *Glycyrrhiza uralensis* Fisch.

六味地黄丸（《**小儿**药证**直**诀》）
Liuwei Dihuang Pill (*Xiaoer Yaozheng Zhi Jue* [*Key to Therapeutics of Children's Diseases*])
熟地黄 山萸肉 山药 茯苓 丹皮 泽泻
Radix Rehmanniae preparata, Fructus Corni, *Dioscorea opposita*, *Poria cocos* Wolf, Cortex Moutan, *Alisma plantago-aquatica*.
理中汤（《伤**寒**论》）
Lizhong Decoction (Shanghan Lun [Treatise on Febrile Diseases])
人参 白术 干姜 炙甘草
Radix ginseng, *Atractylodes macrocephala* Koidz., *Rhizoma zingiberis*, Radix glycyrrhizae preparata.

M

麦门冬汤（《**金**匮**要略**》）
Maimendong Decoction (*Jinkui Yao Lue* [*Synopsis of the Golden Chamber*])
麦门冬 人参 半夏 甘草 粳米 大枣
Ophiopogon japonicus, Radix ginseng, *Pinellia* tuber, *Glycyrrhiza uralensis* Fisch., Polished round-grained rice, *Fructus jujubae*.

Q

清肺饮（《证**治**汇补》）
Qingfei Decoction (*Zhengzhi Hui Bu* [*Integrations and Supplements of Syndromes and Treatments*])
茯苓 黄芩 桑白皮 麦冬 车前子 山栀 木通
Poria cocos Wolf, *Scutellaria baicalensis georgi*, *Morus alba* L., *Ophiopogon japonicus*, Plantago seedi (psyllium seed), *Gardenia jasminoides*, *Akebia quinata*.
启膈散（《**医学心悟**》）
Qige Powder (*Yixue Xinwu* [*Medicine Comprehended*])
沙参 茯苓 丹参 川贝 郁金 砂仁壳 荷叶蒂 杵头糠
Adenophora stricta Miq., *Poria cocos* Wolf, *Salvia miltiorrhiza*, Bulbus fritillariae cirrhosae, *Curcuma aromatica* Salisb., *Fructus amomi* pelam, *Nelumbo nucifera* Gaertn., *Oryza sativa* L.
杞菊地黄丸（《**医**级》）
Qiju Dihuang Pill (*Yi Ji* [*Medical Level*])
枸杞子 菊花 熟地黄 山萸肉 山药 丹皮 泽泻 茯苓
Lycium barbarum L., *Chrysanthemum*, Radix Rehmanniae preparata, Fructus Corni, *Dioscorea opposita*, Cortex Moutan, *Alisma plantago-aquatica*, *Poria cocos* Wolf.
清瘟败**毒**饮（《**疫疹一得**》）
Qingwen Baidu Decoction (Yizhen Yide [A View of Epidemic Febrile Diseases])
生石膏 生地 犀角 川连 栀子 桔梗 黄芩 知母 赤芍 玄参 连翘 甘草 丹皮 竹叶
Calcium sulfate dihydrate, *Rehmannia glutinosa libosch*, Rhinoceros horn, *Coptis chinensis* Franch., *Gardenia jasminoides*, *Platycodon grandiflorus*, *Scutellaria baicalensis georgi*, *Anemarrhena asphodeloides*, Radix *Paeoniae rubra*, Figwort root, *Forsythia suspensa* Vahl, *Glycyrrhiza uralensis* Fisch., Cortex Moutan, Folia bambusae.
清燥救肺汤（《**医门法律**》）
Qingzao Jiufei Decoction (*Yimen Falv* [*Principle and Prohibition for Medical profession*])
桑叶 石膏 杏仁 甘草 麦冬 人参 阿胶 炒胡麻仁 炙批把叶
Folium Mori, calcium sulfate dihydrate, Amygdalus Communis Vas, *Glycyrrhiza uralensis* Fisch., *Ophiopogon japonicus*, Radix ginseng, rosted Sesame, Folium Eriobotryae preparata.

S

参蛤散（《济生方》）

Shenge Powder (*Jisheng Fang* [*Recipes for Saving Lives*])

蛤蚧 人参

Gekko gecko Linnaeus, Radix ginseng.

四海舒郁丸（《疡医大全》）

Sihai Shuyu Pill (*Yangyi Daquan* [*Encyclopedia of Surgical Treatments*])

海蛤粉 海带 海藻 海螵蛸 昆布 陈皮 青木香

Powder of sea clams, *Thallus laminariae* (Laminariaceae), *Sargassum*, *Sepia esculenta* Hoyle, *Thallus eckloniae* (Phaeophyta, Alariaceae), pericarpium citri reticulatae, *Aristolochia contorta* Bunge.

四君子汤（《**太平惠民和**剂**局方**》）

Si Junzi Decoction (*Taiping Huimin Heji Ju Fang* [*Prescriptions of the Bureau of Taiping People*])

人参 白术 茯苓 炙甘草

Radix ginseng, *Atractylodes macrocephala* Koidz., *Poria cocos* Wolf, Radix glycyrrhizae preparata.

参苓白术**散**（《**太平惠民和**剂**局方**》）

Shen Ling Baizhu Powder (*Taiping Huimin Heji Ju Fang* [*Prescriptions of the Bureau of Taiping People*])

人参 茯苓 白术 桔梗 山药 甘草 白扁豆 莲子肉 砂仁 薏苡仁

Radix ginseng, *Poria cocos* Wolf, *Atractylodes macrocephala* Koidz., *Platycodon grandiflorus*, *Dioscorea opposita*, *Glycyrrhiza uralensis* Fisch., *Dolicho lablab* L., Semen Nelumbinis, *Fructus amomi*, Job's tears seed.

生脉散（《**内外**伤**辨惑**论》）

Shengmai Powder (*Neiwaishang Bianhuo Lun* [*Clarification of Perpexities About Internal and External Damage*])

人参 麦冬 五味子

Radix ginseng, *Ophiopogon japonicus*, *Schisandra chinensls* (Turcz) Baill.

十全大补汤（《**太平惠民和**剂**局方**》）

Shiquan Dabu Decoction (*Taiping Huimin Heji Ju Fang* [*Prescriptions of the Bureau of Taiping People*])

熟地黄 白芍 当归 川芎 人参 白术 茯苓 炙甘草 黄芪 肉桂

Radix Rehmanniae preparata, Radix *Paeoniae alba*, Radix *Angelica sinensis*, *Ligusticum chuanxiong* Hort., Radix ginseng, *Atractylodes macrocephala* Koidz., *Poria cocos* Wolf, Radix glycyrrhizae preparata, Radix Astragali, Cinnamon Latin.

沙参麦冬汤（《**温病条辨**》）

Shashen Maidong Decoction (*Wenbing Tiaobian* [*Detailed Analysis of Epidemic Warm Diseases*])

沙参 麦冬 玉竹 桑叶 甘草 天花粉 生扁豆

Adenophora stricta Miq., *Ophiopogon japonicus*, *Polygonatum odoratum* (Mill.) Druce, Folium Mori, *Glycyrrhiza uralensis* Fisch., Radix trichosanthis, Purple Haricot.

四物汤（《**仙授理**伤续**断秘方**》）

Siwu Decoction (*Xianshou Lishang Xuduan Mifang* [*Secret Recipes of Treating Trauma and Fracture*])

熟地黄 当归 白芍药 川芎

Radix Rehmanniae preparata, Radix *Angelica sinensis*, Radix *Paeoniae alba*, *Ligusticum chuanxiong* Hort.

四神丸（《**内科摘要**》）

Sishen Pill (*Neike Zhaoyao* [*Abstract of Internal Medicine*])

补骨脂 五味子 肉豆蔻 吴茱萸 生姜 红枣

Psoralea corylifolia Linn., *Schisandra chinensls* (Turcz) Baill, *Myristica fragrans* Houtt., *Tetradium ruticarpum*, *Zingiber officinale* Rosc., *Fructus jujubae*.

T

桃红四物汤（《医宗金鉴》）
Taohong Siwu Decoction (*Yizong Jinjian* [*Golden Mirror of Medicine*])
桃仁 红花 地黄 芍药 当归 川芎
Semen persicae, *Carthamus tinctorius* L., *Rehmannia glutinosa libosch*, *Paeonia lactiflora* Pall., Radix *Angelica sinensis*, *Ligusticum chuanxiong* Hort.
葶苈大枣泻肺汤（《金匮要略》）
Tingli Dazao Xiefei Decoction (*Jinkui Yao Lue* [*Synopsis of the Golden Chamber*])
葶苈子 大枣
Lepidium apetalum Willd, *Fructus jujubae*.
通窍活血汤（《医林改错》）
Tongqiao Huoxue Decoction (*Yilin Gaicuo* [*Errors in Medicine Corrected*])
赤芍 川芎 桃仁 红花 老葱 生姜 红枣 麝香 黄酒
Radix *Paeoniae rubra*, *Ligusticum chuanxiong* Hort., Semen persicae, *Carthamus tinctorius* L., *Allium fistulosum*, *Zingiber officinale* Rosc., *Fructus jujubae*, *Moschus*, Yellow rice wine.
通幽汤（《兰室秘藏》）
Tongyou Decoction (*Lanshi Micang* [*A Secret Book Kept in Chamber*])
生地 熟地 桃仁 红花 当归 炙甘草
Rehmannia glutinosa libosch, Radix *Rehmanniae* preparata, Semen persicae, *Carthamus tinctorius* L., Radix *Angelica sinensis*, Radix glycyrrhizae preparata.

W

五味消毒饮（《医宗金鉴》）
Wuwei Xiaodu Decoction (*Yizong Jinjian* [*Golden Mirror of Medicine*])
金银花 野菊花 蒲公英 紫花地丁 紫背天葵子
Lonicera japonica Thunb., *Dendranthema indicum*, *Taraxacum mongolicum* Hand-Mazz, *Viola philippica*, *Begonia fimbristipula* Hance.

X

小柴胡汤（《伤寒论》）
Xiao Chaihu Decoction (*Shanghan Lun* [*Treatise on Febrile Diseases*])
柴胡 黄芩 半夏 人参 甘草 干姜 大枣
Bupleurum chinense, *Scutellaria baicalensis georgi*, *Pinellia* tuber, Radix ginseng, *Glycyrrhiza uralensis* Fisch., *Rhizoma zingiberis*, *Fructus jujubae*
旋覆代赭汤（《伤寒论》）
Xuanfu Daizhe Decoction (*Shanghan Lun* [*Treatise on Febrile Diseases*])
旋覆花 代赭石 半夏 生姜 人参 甘草 大枣
Inula japonica Thunb., *Ocherum rubrum*, *Pinellia* tuber, *Zingiber officinale* Roscoe, Radix ginseng, *Glycyrrhiza uralensis* Fisch., *Fructus jujubae*
血府逐瘀汤（《医林改错》）
Xuefu Zhuyu Decoction (*Yilin Gaicuo* [*Errors in Medicine Corrected*])
当归 生地 桃仁 红花 枳壳 赤芍 柴胡 甘草 桔梗 川芎 牛膝
Radix *Angelica sinensis*, *Rehmannia glutinosa libosch*, Semen persicae, *Carthamus tinctorius* L., *Fructus aurantii*, Radix *Paeoniae rubra*, *Bupleurum chinense*, *Glycyrrhiza uralensis* Fisch., *Platycodon grandiflorus*, *Ligusticum chuanxiong* Hort., *Achyranthes bidentata*.

犀角地黄汤（《千金要方》）

Xijiao Dihuang Decoction (*Qianjin Yaofang* [*Thousand Golden Prescriptions*])

水牛角 生地黄 牡丹皮 赤芍药

Cornu Bubali, *Rehmannia glutinosa libosch*, Cortex Moutan, Radix *Paeoniae rubra*.

小蓟饮子（《济生方》）

Xiaoji Decoction (*Jisheng Fang* [*Recipes for Saving Lives*])

生地黄 小蓟 滑石 通草 炒蒲黄 淡竹叶 藕节 当归 山栀 甘草

Rehmannia glutinosa libosch, herba cepbalanoplosis segeti, Talcum, *Tetrapanax papyrifer*, roasted Pollen Typhae, Herba Loophatheri, Nodus Nelumbins Rhizomatis, Radix *Angelica sinensis*, *Gardenia jasminoides*, *Glycyrrhiza uralensis* Fisch.

香砂六君子汤（《太平惠民和剂局方》）

Xiangsha Liu Junzi Decoction (*Taiping Huimin Heji Ju Fang* [*Prescriptions of the Bureau of Taiping People*])

人参 白术 茯苓 甘草 半夏 陈皮 木香 砂仁

Radix ginseng, *Atractylodes macrocephala* Koidz., *Poria cocos* Wolf, *Glycyrrhiza uralensis* Fisch., *Pinellia* tuber, pericarpium citri reticulatae, Radix Aucklandiae, *Fructus amomi*.

逍遥散（《太平惠民和剂局方》）

Xiaoyao Powder (*Taiping Huimin Heji Ju Fang* [*Prescriptions of the Bureau of Taiping People*])

柴胡 白术 白芍药 当归 茯苓 炙甘草 薄荷 煨姜

Bupleurum chinense, *Atractylodes macrocephala* Koidz., Radix *Paeoniae alba*, Radix *Angelica sinensis*, *Poria cocos* Wolf, Radix glycyrrhizae preparata, *Mentha haplocalyx* Briq., roasted *Zingiber officinale* Rosc.

Y

茵陈蒿汤（《伤寒论》）

Yinchenhao Decoction (*Shanghan Lun* [*Treatise on Febrile Diseases*])

茵陈蒿 栀子 大黄

Artemisia capillaries, *Gardenia jasminoides* Ellis, *Rheum palmatum* L.

一贯煎（《柳州医话》）

Yiguanjian (*Liuzhou Yihua* [*Liuzhou Medical Words*])

沙参 麦冬 当归 生地黄 枸杞子 川楝子

Adenophora stricta Miq., *Ophiopogon japonicus*, Radix *Angelica sinensis*, *Rehmannia glutinosa libosch*, *Lycium barbarum* L., *Melia toosendan* Sieb.

右归饮（《景岳全书》）

Yougui Decoction (*Jingyue Quanshu* [*Complete Works of Zhang Jingyue*])

熟地 山药 山萸肉 杜仲 枸杞子 炙甘草 制附子 肉桂

Radix *Rehmanniae* preparata, *Dioscorea opposita*, Fructus Corni, *Eucommia ulmoides*, *Lycium barbarum* L., Radix glycyrrhizae preparata, Radix *Aconiti lateralis* preparata, Cinnamon Latin.

阳和汤（《外科全生集》）

Yanghe Decoction (*Waike Quansheng Ji* [*Life-saving Manual of External Diseases*])

熟地黄 麻黄 鹿角胶 白芥子 肉桂 生甘草 炮姜炭

Radix Rehmanniae preparata, *Ephedra sinica* Stapf, Colla Cornus Cervi, Semen sinapis, Cinnamon Latin, *Glycyrrhiza uralensis* Fisch., charred rhizoma zingiberis recens.

越鞠丸（《丹溪心法》）

Yueju Pill (Danxi Xinfa [Danxi's Mastery of Medicine])

香附 苍术 川芎 栀子 神曲

Rhizoma cyperi, *Atractylodes lancea*, *Ligusticum chuanxiong* Hort., *Gardenia jasminoides* Ellis, Massa medicata fermentata.

益胃汤（《温病条辨》）
Yiwei Decoction (Wenbing Tiaobian [Detailed Analysis of Epidemic Warm Diseases])
沙参 麦门冬 生地 玉竹 冰糖
Adenophora stricta Miq., *Ophiopogon japonicus*, *Rehmannia glutinosa libosch*, *Polygonatum odoratum* (Mill.) Druce, candy sugar.

Z

知柏地黄丸（《医宗金鉴》）
Zhibai Dihuang Pill (*Yizong Jinjian* [*Golden Mirror of Medicine*])
知母 黄柏 熟地 山萸肉 山药 茯苓 丹皮 泽泻
Anemarrhena asphodeloides, cortex *Phellodendri chinensis*, radix Rehmanniae preparata, Fructus Corni, *Dioscorea opposita*, *Poria cocos* Wolf, cortex Moutan, *Alisma plantago-aquatica*.
左归饮（《景岳全书》）
Zuogui Decoction (*Jingyue Quanshu* [*Complete Works of Zhang Jingyue*])
熟地 山萸肉 杞子 山药 茯苓 甘草
Radix Rehmanniae preparata, Fructus Corni, *Lycium barbarum* L., *Dioscorea opposita*, *Poria cocos* Wolf, *Glycyrrhiza uralensis* Fisch.
竹叶石膏汤（《伤寒论》）
Zhuye Shigao Decoction (*Shanghan Lun* [*Treatise on Febrile Diseases*])
人参 麦冬 石膏 竹叶 甘草 半夏 粳米
Radix ginseng, *Ophiopogon japonicus*, calcium sulfate dihydrate, folia *Bambusae*, *Glycyrrhiza uralensis* Fisch., *Pinellia* tuber, polished round-grained rice.

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