

# CHINESE MEDICINE AND CANCER CARE

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Activity is closer to the essence of life than structure, since structure exists for the sake of activity. The key to the living thing is the excellence of its agency. An organism can change itself.

—Robert Augros and George Stanciu  
In *The New Biology*

Every medicine emerges out of the interaction between biology and culture. Medical practices are the product of a social, political, and economic milieu, shaped by customary habits and traditions, many having little to do with science, evidence, or even medicine itself.<sup>1</sup> Chinese traditional medicine has been shaped through continuous use by what is now one-quarter of the world's population. For more than 23 centuries, the people of China have used it to diagnose, treat, and prevent disease as well as to foster health.

In modern Western medicine, the mechanistic, quantitative constructs of science prevail, whereas in the traditional medicine of China, organismic,<sup>2</sup> qualitative schemata describe individuals as resilient, dynamic ecosystems. Whereas the focus of medical science is upon the pathologic entity, Chinese traditional medicine draws upon a nature-centered cosmology that emphasizes the relationship between the seed and the soil: what is it about the terrain that permits cancer, or any disease, to take root?

Since the time of its origins 3,000 years ago, Chinese medicine (*Zhong Yi*) has been used for the treatment of tumors, identified in antiquity as *liu yan*, meaning *lumps as hard as a rock*, or as *zhong yang*, meaning *inflamed ulcers*. Over the course of these millennia, various strategies have developed, ranging from:

- Reducing pain, swelling, inflammation, and tumor mass;
- Improving host resistance through the use of *Fuzheng Gu Ben* therapy, meaning to *strengthen what is correct and secure the root*, which in modern language means to preserve immune competence and enhance the function of the internal organs to counter chemotherapy-induced immune or myelosuppression;
- Potentiating the effects of conventional radiation and chemotherapies;
- Preventing, controlling, and treating the adverse effects of conventional treatment, including fatigue, weakness, gastrointestinal distress, loss of appetite, nausea, emesis, and leukopenia.

In 1999, a San Francisco population-based study indicated that 72% of women with breast cancer used at least 1 form of complementary or alternative medicine (CAM).<sup>3</sup> While few abandoned conventional treatment, only half reported the use of CAM to their physicians.<sup>4</sup> An understanding and appreciation of Chinese medicine may lead to greater comfort on the part of providers ill at ease with the use of therapies about which they have neither training nor experience. This in turn may lead to improved doctor-patient communication and cooperation.

Because Chinese medicine appears to protect against the damaging effects of chemotherapy and radiation, it increases the likelihood that patients will suffer less during, and recover their health after completing these therapies, enhancing quality of life. Chinese medicine treats the patient as well as the disease.

There are various approaches to the subject of how Chinese medicine treats cancer, and an equivalent number of languages—one expresses how Chinese medicine understands the body and thinks about what we call cancer, using its own traditional vocabulary that has endured over centuries; another is scientific, reporting research findings on the use of acupuncture and Chinese herbal medicine, describing them in modern neurophysiological and biochemical terms.

## CHINESE MEDICINE AND CANCER: ANCIENT AND MODERN CONCEPTS

Derived from the word *malign*, meaning harmful or malevolent, *malignant* means that which may cause mortal damage. In Chinese medicine, mortal damage is a consequence of the disorganization and separation of *yin-yang* (*jing-shen*, *blood-qi*)—a threshold beyond which the organism is unable to sustain harmony and

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integrity. Cancerous masses, lumps, and tumors are the consequence of unmitigated accumulations of *qi*, *moisture*, and *blood* that have become *toxic*, transforming what is healthy into morbid tissue, simultaneously obstructing and usurping normal circulation. Prolonged stagnation eventually leads to depletion of *qi* and *blood*, and ultimately *essence*. Because *essence* governs growth and maturation, loss of or damage to it can result in a dysregulation of growth typical of cancer, a process of uncontrolled proliferation of immature, undifferentiated, malformed cells. Therefore, treatment that supplements *qi*, *moisture*, and *blood*; restores circulation and eliminates stasis; removes *toxins*; replenishes *essence*; and dissolves masses is critical in the treatment of cancer.

As early as the 11th century BCE, descriptions of tumors were inscribed on oracle bones and turtle shells. Certain doctors specialized in the treatment of these lesions, referred to as *liu*, meaning tumor, derived from a word meaning *stuck*. Around 200 BCE, during the Han Dynasty, tumors became known as hard lumps or ulcerated lesions. Both benign and malignant masses were further differentiated anatomically as ulcers or abscesses that arise between the muscle and bone (*yen*, *ai*, *chu*); carbuncles (*yung*) that appear on the surface of muscles and skin; and hard obstructions (*cheng chia*) that arise in the internal organs. In the 12th century, the term *ai*, another expression for inflamed ulcers, became synonymous with that for cancer. Comparable to identifying contemporary *early warning signs*, traditional doctors noted the severity of swellings, lumps, and masses, their depth (skin, muscle, bone, viscera), density and firmness, mobility, color, heat, presence of fluid or pus, and the severity, quality and variability of pain and other sensations such as itching and burning in formulating the diagnosis of malignancy.<sup>5</sup>

Classical and modern writings regard the etiology of most serious disorders, including benign and malignant tumors, as stemming from internal injuries, emotional trauma, invasion of pathogenic factors such as *heat*, *cold*, *dampness*, *dryness*, or the accumulation of *toxins*, often due to improper digestion and poor elimination of metabolic wastes. Jia Kun, a Chinese traditional medicine oncologist writing in 1980, says that whatever upsets normal body function can lead to tumor formation, causing cancer. Tumors are the end result of a prolonged process of accumulation and densification of tissue due to the persistent stagnation of *qi* and *blood*, which, if unrelieved, becomes *toxic*, critically damaging the healthy function of the organ systems.<sup>6</sup>

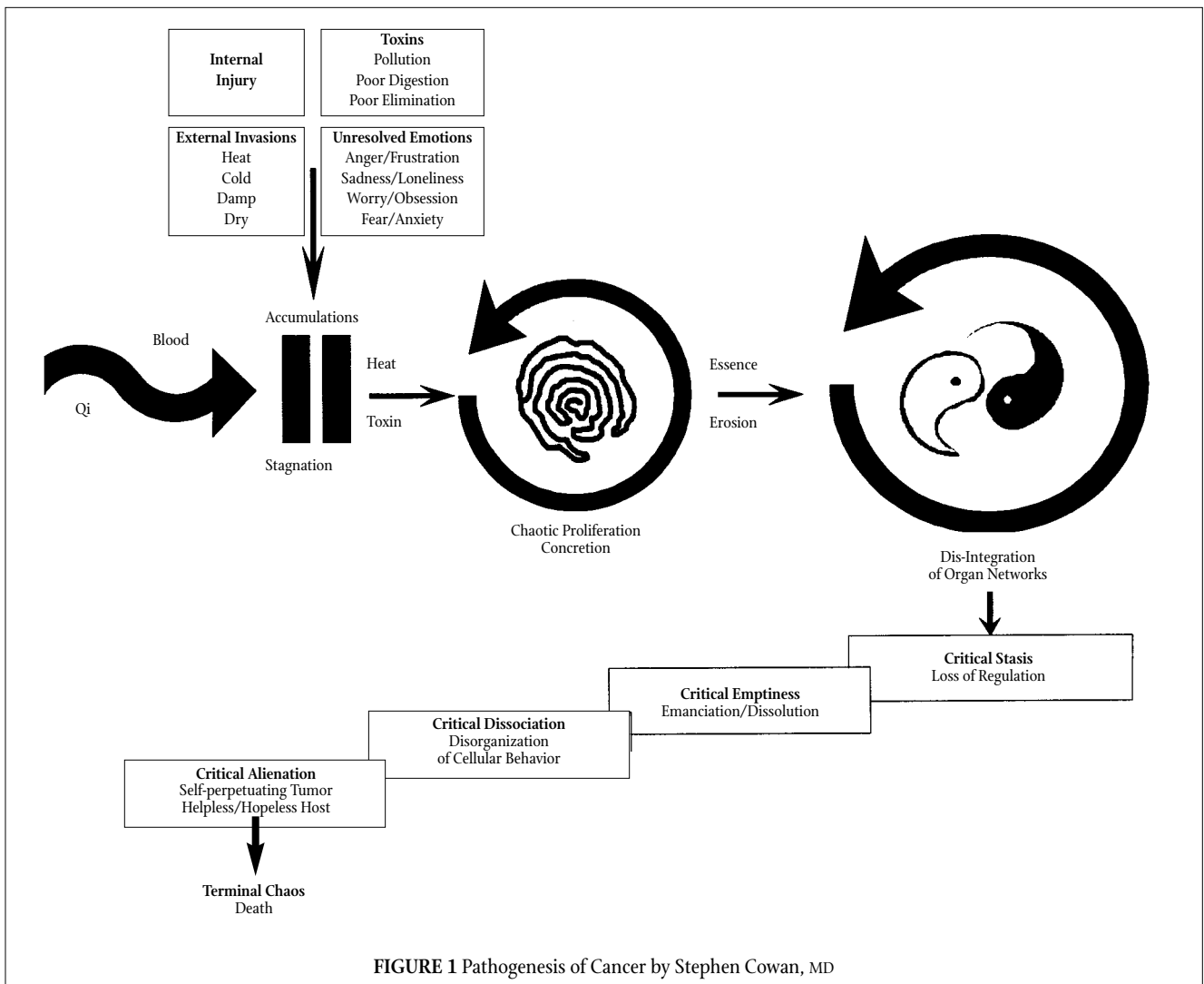
C.S. Cheung explains the relationship between generating *blood* and circulating it, preventing both deficiency and stagnation: “The essence of fluid and grain [nourishment from food and drink] infuses into the meridians and forms *ying qi*. It then circulates to the *heart* and enters the *blood*. The *blood* flows to every part of the body and moistens and lubricates all the tissues. When there is insufficiency of *ying qi*, the distribution of *qi* is endangered. Thus, the *blood* does not flow smoothly, encouraging the formation of *blood* stasis and ecchymosis [*blood* that congeals outside the vessels]. New *blood* is unable to be generated when obstructed by stasis and ecchymosis. Consequently, therapeutic measures are

taken to remove the obstruction and generate new *blood*.” Cheung recommends that herbs such as angelica, salvia, and millettia be used, explaining that the herb millettia treats both deficiency and stasis because it both engenders and circulates *blood*.<sup>7</sup>

As discussed, the circulation of *qi* and *blood* can be impeded by physical or psychological disturbances. Just as thermal *cold* constricts blood vessels, causing inhibition of movement and depressed metabolism, so can prolonged sadness. *Heat* dries the *blood*, and emotions like anxiety, anger, and anguish that produce *heat* can be as harmful as prolonged exposure to intense summer sun. Congestion of *blood* and *moisture* can generate emotional discomfort, and unresolved suffering can cause *qi* and *blood* stasis. An osteoma could be the outcome of accumulated *heat* (regardless of its source) in the *kidney* (the *kidney* governs bone and marrow) that dries and erodes the moist, spongy substances in bone, causing the formation of a hard and immobile mass. Additional factors like the effects of environmental pollution, chemical contamination of food, fungi, viruses, and bacteria can also produce stagnation of *qi* and *blood*. The traditional view does not give greater emphasis to either the poisonous effects of entrenched negative emotions or spoiled food: *toxins*, regardless of their origin, are identified by their pernicious effects. Tumors in the breast may result from toxic accumulation and stagnation of *qi* and *blood* in the channels that pass through the breast, eventually producing a lump.

The following sequence outlines a likely etiology of malignancy: adverse pathogenic factors initiate the stagnation and depletion of *qi*, *moisture*, and *blood*; the persistence of deficiency and stasis impairs the coordinated function of the organ networks, which leads to further weakness, obstruction, and attrition of *essence*, the original source (*yuan*) of *qi* and *blood*. The malignant process is characterized by extreme disorder. When *qi*, *blood*, and *essence* become depleted enough, *yin-yang* begins to disintegrate or separate, and chaos ensues. Disorganization of cellular behavior is a manifestation of the loss of coherence—failure of the body to govern differentiation and proliferation.

The development of cancer is a progression from extreme stagnation to emptiness, to dissociation, to alienation, and finally, anarchy and death. Critical stasis means that a region of tissue is no longer governable by the ordinary circulatory and regulatory mechanisms of *qi*, leading eventually to a degeneration of coordinated activity. Critical emptiness means that the region sequestered by the malignant process consumes the physiological resources of the organism, but contributes nothing in return, engendering an accelerating process of attrition. And critical alienation is manifested in the attitude of hopelessness and helplessness that a person experiences when a non-responsive and insensate entity—the cancer—arising from the organism’s own sacred terrain, expropriates its vital resources while ceasing to be subject to its ontological influence. Cancer is a condition of functional chaos, representing one of the most advanced stages of disorganization—*wild qi*—requiring intensive and aggressive strategies to restore integrity. This



condition known as *wild qi* prefigures the fatal *separation of yin-yang*.<sup>8,9</sup> (See Figures 1 and 2.)

### CANCER TYPES: DIAGNOSTIC PATTERNS

Cancer patterns typically involve *phlegm*, *toxins*, deficient *qi* and *blood*, and *blood* stagnation. The same cancer, eg, stomach cancer may result from a variety of patterns, such as liver *qi* invading the *stomach*, *stomach yang deficiency*, phlegm stagnation and food retention, blood stagnation due to *qi* stagnation, *stomach yin* deficiency due to *stomach heat*, or *qi* and *blood* deficiency. For colon cancer, the patterns may be damp heat in the large intestine, toxins, spleen and *kidney yang* deficiency, *liver* and *kidney yin* deficiency, and *qi* and *blood* deficiency. Breast cancer patterns include *liver qi* stagnation, *blood* stagnation and accumulation of toxins, *qi* and *blood* deficiency, and *spleen qi* deficiency with phlegm accumulation. Brain tumors may result from *phlegm* accumulation, and *kidney qi* or *yin* deficiency.<sup>10</sup>

There are 2 diagnostic categories that interact: one is called

*bian zheng*, meaning the constitutional pattern of the person, and the other is *bian bing*, meaning the pattern of the disease. Depending on these patterns, acupuncture treatment and herbal therapy are tailored to fit—individualized according to the pathological pattern and the nature of the patient. Acupuncture relieves stagnation and deficiency by mobilizing the *qi* of particular organ networks. Herbal formulas relieve stagnation by using *qi* and *blood* activating herbs, clear heat via cooling herbs, dispel dampness with drying herbs, and antidote toxins or dissolve phlegm with herbs that remove or dissolve these pathogenic entities. *Cold* is relieved through the use of warming herbs, and overall strength is restored with tonic herbs. Some patterns may serve as markers for enhanced survival as well. For example, in a study of 254 women with cervical cancer treated with radiotherapy and followed for 3 years, those diagnosed with *qi* stagnation exhibited a significantly reduced survival compared to those diagnosed with *liver* and *kidney yin* deficiency.<sup>11</sup>

There are many treatment protocols that combine acupunc-

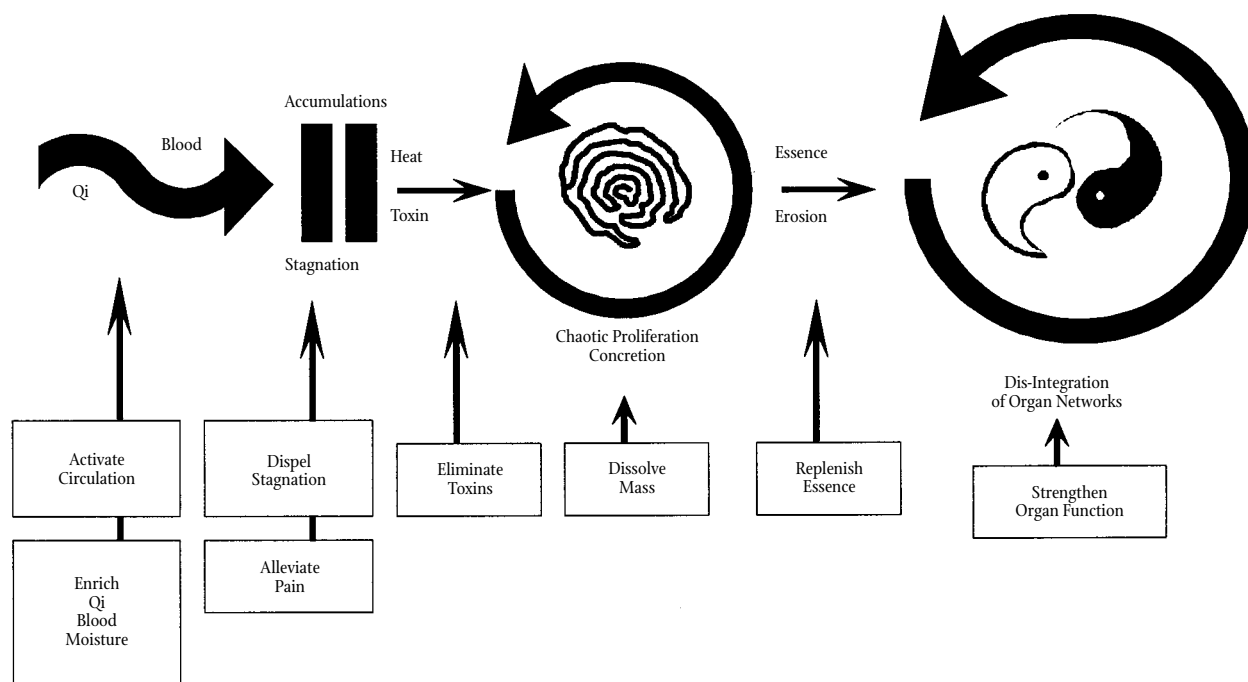


FIGURE 2 Treatment of Cancer by Stephen Cowan, MD

ture and medicinal herbs to reduce swelling and eliminate the pain caused by tumors as well as the adverse effects of surgery, radiation, and chemotherapy. In particular, herbal prescriptions that invigorate the *qi*, nourish the *blood*, clear *heat* and *toxins*, and eliminate *blood* stasis can strengthen the body, enhance adaptation to stress, increase host resistance to infection, inflammation, and proliferation of tissue, and retard the progression of tumors, promoting long-term survival. These are primary therapeutic strategies for shrinking tumors that have been applied since the 17th century.<sup>12</sup> While surgery, radiation, and chemotherapy are welcomed as viable treatments for cancer in modern China, Japan and other Asian countries, acupuncture and Chinese herbal medicine represent complementary or adjunctive therapies that sometimes improve the capacity of conventional Western medicine to achieve desired outcomes.<sup>13</sup>

#### CHEMOTHERAPY AND RADIATION: A YIN-YANG PERSPECTIVE<sup>14</sup>

Radiation is a form of extreme *yang* that produces heat and inflammation, *cooking* the *yin*, damaging the *blood* and *moisture*. The drying of *blood* and moisture leads to coagulation (static *blood*) and congelation (*phlegm*). Stagnant *blood* and *phlegm* further impair the circulation of *qi*, *moisture*, and *blood*, resulting in more deficiency and weakening of the organ networks. Radiation often penetrates deep into the bones, drying the marrow and eroding *essence*.

Chemotherapy is a form of extreme *yin*, a poison that

damages the *yang*, the ability of *qi* to move the *blood* and moisture, warm the body, and transform food into *qi* and *blood*. When the *qi* fails to move *blood* and fluids, *blood* stagnation and *dampness* arise. When circulation is retarded, it becomes difficult for the body to stay warm. Internal *cold* can transform *dampness* into *phlegm* and cause *blood* to coagulate. When digestion is impaired, the *stomach* and *spleen* fail to generate adequate *qi* and *blood*, and deficiency ensues. When *qi* is depleted, *blood* and fluids easily leak from the blood vessels and body membranes. Prolonged deficiency leads to the attrition of marrow and *essence*.

The adverse effects of radiation and chemotherapy parallel the signs and symptoms of severe deficiencies of *qi*, *moisture*, *blood*, and *essence*: weakness, fatigue, pallor, susceptibility to infection, edema, dehydration, hair loss, restlessness, irritability, depression, hot flashes, night sweats, thirst, dry skin, infertility, lack of libido, amenorrhea, indigestion, anorexia, weight loss, diarrhea, ulcerations, bruising, bleeding, flaccidity, joint and muscle pain, anemia, leukopenia, shortness of breath, congestive heart failure, inability to concentrate, memory loss, heartburn and headache.

Just when there is a demand for adequate *qi* and *blood*, the capacity to generate these resources is undermined. The conditions that produce cancer, namely stagnation, deficiency, and disharmony, are further aggravated by radiation and chemotherapy, neither of which discriminates between healthy and abnormal tissue. The vicious cycle of attrition caused by the disease is

paralleled by the treatment. While Western medicine aggressively attacks the cancer, Chinese traditional medicine supports and restores the healthy function that enables patients to tolerate and recover from conventional therapies, surviving with an improved quality of life.

## ACUPUNCTURE

The National Institutes of Health Consensus Development Conference in 1997 declared that there is clear evidence that acupuncture is an effective modality, particularly for nausea and vomiting induced by chemotherapy, and for the relief of pain. The American Cancer Society informs consumers that, "Acupuncture is simple, and often works. It has few side effects or complications, and the cost is low. For these reasons, it can be a good choice for some problems."

Acupuncture is based on the assumption that *qi* courses through a network of channels (*jing luo*), just as streams and rivers flow under and across the surface of the earth. This lattice of channels forms a *web of qi* that unites all parts of the organism. Within the Chinese traditional model, acupuncture works by regulating the movement of *qi*. By restoring healthy circulation of *qi* and *blood*, stagnation resolves. By optimizing the function of the 5 organ networks, vulnerability to disease is reduced. In modern language, acupuncture modulates fundamental homeodynamic mechanisms that govern hematopoiesis, cellular and humoral immunity, temperature and pressure, respiration, metabolism, hormonal secretion and sensitivity, neuromuscular coordination, and diurnal rhythms. Microcirculation in the capillary beds that surround internal organs is encouraged, thereby supporting processes of healthy nutrition and detoxification. Acupuncture also stimulates the central nervous system, activating mechanisms of repair and regeneration. In traditional language, acupuncture harmonizes *yin-yang* and the organ networks responsible for regulating growth, proliferation, and dynamic harmony.

Pain signals the stagnation of *qi*, *blood* and *phlegm* within the channels. Slender stainless steel needles inserted in particular points located along these channels near the surface of the skin (acupoints), can clear stagnation, reinvigorating the function of the internal organs. Within the modern scientific model, the mechanism of action of acupuncture has only been partially described, mostly in the area of pain relief. Through the use of functional magnetic resonance imaging (fMRI), descriptive studies have documented that sensory-related acupoints have brain cortical correspondences that may point toward an explanation of how acupuncture has effects beyond analgesia, namely upon homeostatic regulatory mechanisms not yet understood by Western physiology or medicine.<sup>15</sup> Normalizing of the physiological processes of the cardiovascular,<sup>16</sup> immunological,<sup>17</sup> and gastrointestinal<sup>18</sup> systems, as well as an anti-inflammatory<sup>19</sup> modulatory effect have been also documented in preliminary studies.

## Acupuncture Analgesia

Since the early 1970s, neurophysiologist Bruce Pomeranz

has studied the effectiveness of acupuncture on pain, nerve regeneration, and cutaneous wound healing. In 1976 Pomeranz used naloxone, an endorphin antagonist, to successfully block acupuncture analgesia, suggesting a physiological mechanism of action. He showed that acupuncture relieved chronic pain in 55% to 85% of patients, compared to a 30% relief of pain by placebo, demonstrating that acupuncture is as effective as many potent drugs.<sup>20</sup> Pomeranz comments, "It should be apparent that we know more about acupuncture analgesia than about many chemical drugs in routine use. For example, we know very little about the mechanisms of most anesthetic gases but still use them regularly." Acupuncture analgesia is initiated by the stimulation of small afferent sensory nerve fibers embedded in musculature that send impulses to the spinal cord to affect the three centers: spinal cord, midbrain, and hypothalamic-pituitary. When these centers are activated, neurotransmitters release endorphins, enkephalins, monoamines, and cortisol to block the pain messages.<sup>21</sup> Increases in serum  $\beta$ -endorphin, met-enkephalin and leu-enkephalin with acupuncture have also been documented.<sup>22</sup>

Needles placed near the pain site, either on an acupoint or at a tender spot (trigger point), activate segmental circuits to the spinal cord as well as all three centers. Local needling usually provides a more intensive analgesic effect than distal needling which activates the midbrain and pituitary without benefit to the local segmental circuit to the spinal cord. In practice, both local and distal needling enhances the overall analgesic effect. The Chinese experience with the use of acupuncture analgesia as an adjunct or alternative to chemical anesthesia during surgery reveals that, in addition to effectively inhibiting the pain response, acupuncture also maintains normalized blood pressure, visceral reflexes (prevents collapse of the mediastinum and diaphragm and preserves gut motility), body temperature, while markedly reducing the risk of hemorrhage, accelerating wound repair, and shortening post-operative recovery time.<sup>23</sup>

Because pain medications can cause nausea, constipation, and fatigue, as well as require escalating doses that place patients at risk for cardiopulmonary depression, hepatic or renal toxicity, acupuncture pain relief may prove to be of significant benefit.<sup>24,25</sup> In a study of 286 patients experiencing metastatic bone pain, use of an electroacupuncture apparatus resulted in 74% significant pain relief in addition to a much lower need for long-term narcotic analgesics.<sup>26</sup> In a randomized study of 48 gastric carcinoma patients receiving chemotherapy, acupuncture was compared to pharmacological pain management with narcotics and nonsteroidal anti-inflammatory agents. Although immediate (12 hour) control was better with pharmacological therapy, after 2 months, long-term pain control was similar. Only in the acupuncture group was plasma leucine-enkephalin increased at 2 months, along with improvement in other side effects of chemotherapy and overall quality of life measures.<sup>27</sup> Acupuncture has also been reported to relieve the pain of herpes zoster, a typical chemotherapeutic side effect,<sup>28</sup> as well as aid in the regeneration of nerve tissue as evidenced by improved nerve conduction in patients suffering from peripheral neuropathy.<sup>29</sup>

Both pain and edema were reduced in a study of 122 patients with late-onset edema due to radiation therapy.<sup>30</sup>

### Acupuncture for Nausea and Vomiting

There is reliable, compelling data for the effectiveness of acupuncture in relieving nausea and vomiting. The NIH Consensus Panel on Acupuncture in 1997 concluded, "there is clear evidence that needle acupuncture is efficacious for adult postoperative and chemotherapy nausea and vomiting."<sup>31</sup> A systematic review of randomized controlled trials showed consistent, positive results.<sup>32</sup> Of 29 trials in which acupuncture was used when patients were awake, and not under anesthesia, 27 supported acupuncture. More than 2000 patients showed positive results in a review of the trials that were of the best methodological quality. A 1989 study by J.W. Dundee from Queen's University in Belfast showed acupuncture to significantly relieve post-operative nausea and vomiting: 78% of patients treated with acupuncture were free of sickness compared to 32% of the non-treated control group.<sup>33</sup> Dundee's initial comparative studies examined the anti-emetic effect of the acupoint known as Pericardium 6 (Pc6 is located on the medial aspect of the arm above the wrist) in 105 patients with a history of nausea and vomiting in a previous round of chemotherapy. This study reported a 63% anti-emetic benefit from the acupuncture.<sup>34,37</sup> From 30-40% of women with early stage breast cancer still experience nausea and vomiting within 1 week of chemotherapy administration, even with the use of serotonin receptor antagonists.<sup>38</sup> Subsequent well-controlled studies have similarly shown acupressure or acupuncture applied to Pc6 provides a treatment benefit in 60-70% of patients compared to a 30% benefit with sham treatment.<sup>39</sup>

### Acupuncture Effects on Myelosuppression and Hormonal Markers

In a study of 386 patients with medium and advanced-stage cancer with chemotherapy-induced leukocytopenia, acupuncture and moxibustion (heat produced by burning the herb *Artemisia vulgaris* on acupoints) increased the leukocyte count in 38% of the patients.<sup>40</sup> Among 48 patients with persistent leukopenia, stimulation of the acupoint known as Stomach 36, located laterally below the knee, led to an increased white blood cell count in more than 90% of those treated.<sup>41</sup> In another study of 121 patients with leukopenia during radiation and chemotherapy, after 5 daily acupuncture and moxibustion treatments, white blood cell counts markedly increased.<sup>42</sup>

The immune modulatory effects of acupuncture upon patients undergoing chemotherapy and radiation are summarized in a review article that shows an increase in peripheral blood counts of CD<sub>3</sub>+, CD<sub>4</sub>+ and natural killer (NK) cells, as well as an elevation in the CD<sub>4</sub>+ / CD<sub>8</sub>+ ratio. Macrophage activity is also increased by both acupuncture and moxibustion.<sup>43</sup> In a study of premenopausal women that compared normal subjects to those with benign mammary hyperplasia, measuring immune and hormonal markers, levels of CD<sub>8</sub>+ cells rose significantly after acupuncture, and the CD<sub>4</sub>+ / CD<sub>8</sub>+ ratio was reduced to match the control group. Serum E<sub>2</sub> and Prolactin levels declined

following acupuncture, while levels of follicle-stimulating hormone (FSH) increased. More than 50% of the women with hyperplasia had complete resolution of their nodules, while the others had a significant reduction.<sup>44</sup> Women with climacteric symptoms due to chemotherapy-induced menopause or treatment with agents like tamoxifen experience hot flashes, night sweats, dry skin and vaginal dryness, and insomnia. Studies have indicated that acupuncture can help to control these symptoms in over 90% of the women treated.<sup>45,46</sup>

### MODERN CHINESE HERBAL RESEARCH

With the renaissance of traditional Chinese medicine in the 1950s, clinical researchers in China and Japan began searching for ways to improve outcomes for cancer patients undergoing chemotherapy and radiation. Over the last decades, this approach has become known as *Fuzheng Gu Ben* therapy, meaning to strengthen what is correct and secure the root. *Fuzheng* herbs support non-specific resistance and are known as biological response modifiers or adaptogens. In a monograph in 1981 on the use of *fuzheng* herbs with cancer patients, Tu Gouri commented, "the treatment of malignant tumors with combined methods of traditional Chinese medicine and western medicine has made much progress...patients with advanced malignant tumors usually have the symptoms of deficiency in *qi* and *blood*, deficiency of *liver* and *kidney*, and dysfunction of *spleen* and *stomach*. Tonics may improve the general condition and the immune function of the patients, enhance resistance against disease, and prolong their survival period. Furthermore, tonics also have protective effects against immune suppression, lowering of leukocyte count, suppression of bone marrow, and decrease of plasma cortisol levels induced by radiotherapy and chemotherapy. All this benefits the treatment of malignant tumors."<sup>47</sup>

Researchers from the University of California at San Francisco comment that *Fuzheng* therapy produces possible diverse biologic effects that include: "reduce the tumor load; prevent recurrence or formation of a new primary cancer; bolster the immune system; enhance the regulatory function of the endocrine system; protect the structure and function of internal organs and glands; strengthen the digestive system by improving absorption and metabolism; protect bone marrow and hematopoietic function; and prevent, control, and treat adverse side effects caused by conventional treatments for cancer."<sup>48</sup> Excellent sources covering the role of Chinese herbs in cancer care may be found in *Cancer and Natural Medicine* and *Natural Compounds in Cancer Therapy* by John Boik<sup>49</sup> and the relevant monographs written by Subhuti Dharmananda, PhD, of the Institute for Traditional Medicine in Portland, Oregon.<sup>50</sup>

### Treatment Strategies

Clinically, Chinese herbs are usually administered not as single agents, but in multi-ingredient formulas. Formulas are designed to address various aspects of the disease pattern, as well as the constitutional needs of the individual patient. For example, a given formula might use herbs that supplement *qi*, *blood*,

and essence combined with other ingredients to eliminate stagnation, toxins, and reduce tumor mass. Crude herbs are decocted in teas; ingested as powders: compressed into tablets; extracted in alcohol, water, or both; and in China they may be prepared for injection or intravenous administration.

Five principles organize the formulation of many herbal prescriptions for the treatment of cancer: supplement the *qi* and *blood* to strengthen host resistance; activate circulation to dispel *blood* stasis and ecchymosis; relieve pain; eliminate *heat* and eliminate *toxins*; and soften lumps and dissolve masses.<sup>51</sup>

Herbal formulas may contain anywhere from 6-20 ingredients and emphasize 1 or all of the 5 therapeutic principles. The clinical application of these principles might best be illustrated by describing both the known pharmacological properties and actions as well as the traditional characteristics, indications, and effects of several individual herbs and multi-ingredient formulas that are currently being investigated and used clinically in China, Japan, and the United States.

### Individual Herbs

The preponderance of herbs used for cancer has been an integral part of traditional practice for centuries. Although recently identified as adaptogenic, immune enhancing, anticoagulant and fibrinolytic, detoxifying, and tumor-resolving, agents such as *Astragalus membranaceus* (*huang qi*), *Panax ginseng* (*ren shen*), *Atractylodes macrocephala* (*bai zhu*), *Glycyrrhiza uralensis* (*gan cao*), *Poria cocos* (*fu ling*), *Ganoderma lucidum* (*ling zhi cao*), *Polyporus umbellatus* (*zhu ling*), *Cordyceps sinensis* (*dong chong xia cao*), *Coix lachrymi-jobi* (*yi yi ren*), *Angelica sinensis* (*dang gui*), *Salvia miltiorrhiza* (*dan shen*), *Rheum palmatum* (*da huang*), *Coptis chinensis* (*huang lian*), *Scutellaria baicalensis* (*huang qin*), *Isatis tinctoria* (*ban lan gen*), *Chrysanthemum morifolium* (*ju hua*), *Bupleurum chinense* (*chai hu*), *Artemisia capillaries* (*yin chen hao*), *Sophora subprostrata* (*shan dou gen*), and *Oldenlandia diffusa* (*bai hua she she cao*) have 1,800 years of clinical use.

In addition to these venerable medicines, new herbs have been discovered and old ones have been put to new uses. *Eleutherococcus senticosus* (*ci wu jia*) and *Gynostemma pentaphyllum* (*jiao gu lan*) were discovered, through modern research, to contain saponin glycosides similar to those found in *Panax ginseng* (*ren shen*) and to exert similar adaptogenic and anti-cancer effects with the added advantage of being easier to cultivate and therefore cheaper and easier to supply. *Astragalus membranaceus* (*huang qi*), *Eleutherococcus senticosus* (*ci wu jia*), and *Angelica sinensis* (*dang gui*) were also found to contain immune modulating polysaccharides similar to those occurring in *Ganoderma lucidum* (*ling zhi cao*), *Polyporus umbellatus* (*zhu ling*), *Poria cocos* (*fu ling*), *Cordyceps sinensis* (*dong chong xia cao*), and *Lentinus edodes* (*xiang gu*). *Salvia miltiorrhiza* (*dan shen*), *Angelica sinensis* (*dang gui*), and *Rheum palmatum* (*da huang*) have demonstrated effects on microcirculation including normalization of fibrin, platelet adhesion, and significant anti-angiogenic properties. *Coptis chinensis* (*huang lian*), *Scutellaria baicalensis* (*huang qin*), *Isatis tinctoria* (*ban lan gen*), *Chrysanthemum morifolium* (*ju hua*),

*Glycyrrhiza uralensis* (*gan cao*), *Bupleurum chinense* (*chai hu*), *Artemisia capillaris* (*qing hao*), *Sophora subprostrata* (*shan dou gen*), and *Oldenlandia diffusa* (*bai hua she she cao*), traditionally used to treat poisoning, infection, inflammation, and ulceration, have proven to have a broad range of actions including anti-tumor, anti-histamine, anti-thrombotic, anti-proliferative, anti-angiogenic, cytotoxic, and immune stimulating activity.

Because modern investigators are in the habit of analyzing single agents and identifying active compounds, considerable research has focused on celebrity herbs such as: *Astragalus membranaceus* (*huang qi*-*astragalus polysaccharides*), *Panax ginseng* (*ren shen*-*saponin ginsenosides*), *Glycyrrhiza uralensis* (*gan cao*-*saponin glycyrrhizin*), *Eleutherococcus senticosus* (*ci wu jia*-*polysaccharides and saponin eleutherosides*), *Angelica sinensis* (*polysaccharides*), *Curcuma zedoaria* (*e zhu-curcumin*), *Ganoderma lucidum* (*ling zhi cao*-*beta glucan polysaccharides*), *Lentinus* (*xiang gu*-*beta glucan polysaccharides*), *Coriolus versicolor* (*PSK and PSP*-*beta glucan polysaccharides*), *Sophora subprostrata* (*shan dou gen*-*matrine and oxymatrine alkaloids*), and *Isatis tinctoria* (*ban lan gen*-*indirubin alkaloid*). A single herb is biologically more complex than an isolated organic compound, and in traditional thinking confers a better result due to the natural synergism of all the constituents. Similarly, a multi-herb formula is exponentially more complex than a single herb, delivering even more therapeutic benefits than one herb alone. (See Table 1.)

### Herbal Formulas

Many of the herbal formulas used in modern cancer therapy and research in China are part of the traditional pharmacopoeia. *Shi Quan Da Bu Tang* (All Inclusive Great Tonifying Decoction), *Jian Pi Tang* (Decoction For Tonifying The Spleen and Stomach), *Si Jun Zi Tang* (Four Gentleman Decoction), *Bu Zhong Yi Qi Tang* (Decoction For Tonifying The Middle and Augmenting The Qi), *Ren Shen Yang Rong Tang* (Ginseng Decoction To Nourish The Nutritive Qi), *Xiao Chai Hu Tang* (Minor Bupleurum Decoction) are classical (pre-19th century) prescriptions that belong to the category of tonifying and harmonizing formulas that generally improve health, strengthen resistance to stress and disease, and facilitate recovery from the debilitating effects of chronic illness. Since the adverse effects of modern cancer treatments mimic the consequences of chronic illness—weakness, fatigue, decreased resistance, reduced appetite, weight loss, diminished libido, cognitive decline, musculo-skeletal stiffness and soreness—tonic prescriptions treat these conditions and maintain healthy function. Such formulas share many of the promising anti-cancer agents mentioned above.

Modern herbal protocols often use classical formulas as a foundation, while adding additional ingredients with anti-cancer effects. For example, the formula *Fu Zheng Shengjin Tang* for treating the side effects of radiotherapy is based on *Si Jun Zi Tang* (Four Gentleman Decoction) with the addition of ingredients to supplement *yin* (*blood and moisture*) and eliminate heat (*yang*) and toxins: *Codonopsis pilolusa* (*dang shen*) (a substitute for *Panax*

TABLE 1 Debu Tripathy Herbal Examples Diagram

Pinyin transliteration	Botanical name and family	Traditional indications	Biological Effects	Chemical Constituents
<b>Prevention</b>				
Chai hu	Radix <i>Bupleurum chinensis</i> DC. (Umbelliferae)	Reducing fever, soothing the liver and upper GI, cures organ ptosis.	CNS effects (Antipyretic effect, sedative effect, analgesic and antitussive effect.) Anti-inflammatory effect. GI effect (hepatoprotective and choleric effect, prevents gastric ulcer. Hypolipemic effect, antimicrobial effect, protects from renal damage.	Triterpene saponins: saikosaponins a, b <sub>1</sub> -b <sub>4</sub> , c, d, e and f. Essential oil: bupleurmol, spinasterol, stigmasterol
Dang kui	Radix <i>Angelica sinensis</i> (Oliv.) Diels (Umbelliferae)	Enriching the blood and activating blood circulation. Regulating menstruation and relieving menstrual pain. Used for constipation.	Different fractions can both inhibit and stimulate uterine contractions. Endometrial proliferation without direct estrogenic effect was found. Decrease contraction magnitude and frequency of heart muscle. Significantly dilates and increases coronary flow. Decreases artery pressure while reducing arterial resistance and increasing arterial flow. Inhibits platelet aggregation and serotonin release. Decreases blood lipids and reduces arteriosclerosis. Analgesic effect. Antiasthmatic effect.	Essential oil: ligustilide, ferulic acid, n-butylidenephthalide, n-valerophenone-O-carboxylic acid. Novolatile: brefeldin A, sitosterol, stigmasterol, sitosterol-D-glucoside, vitamin A, B <sub>12</sub> and E.
Bai shao	Radix <i>Paeonia lactiflora</i> Pall. (Ranunculaceae)	Supplements blood, controls pain, alleviates sudden onset of disease, subdues hyperactive liver, controls excessive sweating.	Antispasmodic and analgesic effect by lowering muscle tonicity. Sedative effect, inhibits gastric secretions and inhibits gastric ulceration. Antibacterial effect. Protects from myocardial ischemia and from platelet aggregation. Causes coronary and peripheral vasodilatation.	Paeoniflorin, paeonol, paeonin, albiflorin, oxypaeoniflorin, benzoylpaeoniflorin and paeoniflorigenone. Benzoic acid, sitosterol, gallotannin, pedunculagin. Polysaccharide: peonan SA. Acidic polysaccharide: peonan SB, peonan PA and Triterpenoids.
Chen pi	Pericarpium <i>Citrus reticulata</i> blanco (Rutaceae)	Regulating the flow of qi and invigorating digestive function. Eliminating damp and resolving phlegm.	Inhibits GI smooth muscle movement. Inhibits gastric ulceration without inhibition of gastric secretions. Expectorant and antitussive effect. Anti-inflammatory and antiallergic effect. Relaxes uterine muscle contraction.	Essential oil: d-limonene, citrol. Monoterpenes: pinene, piniene, camphene, myrcene, 3-carene, phellandrene, phellandrene, terpinene, terpinene. Flavones, alkaloids, synephrine and N-methyltyramine.
Wang bu liu xing	Semen <i>Vaccariae pyramidata</i> Medic. (Caryophyllaceae)	Moves blood, regulates menses, increases lactation, disperses swelling carbuncles, promotes healing of incised wounds.	Stimulates uterine contraction.	Saponins: vacasegoside, isosaponarin. Starch, fat, alkaloids, cyclic peptides.
<b>Commonly prescribed herbs with chemotherapy</b>				
Huang qi	Radix <i>Astragalus membranaceus</i> (Fisch.) Bge. (Leguminosae)	Supplements qi, increases yang, consolidates surface, increases resistance to diseases, controls sweating, delivers fluids, disperses swelling, discharges pus.	Increased CD <sub>4</sub> /CD <sub>8</sub> ratio and phagocytic activity in patients with gastric cancer undergoing chemotherapy Stimulation of lymphocyte IL-2, IL-3, IL-6, TNF $\alpha$ and IFN- $\gamma$ . Diuretic effect and antinephrotic effect. Anti-inflammatory effect. Hepatoprotective effect.	Saponins: astragalosides I-VIII, acetylastragaloside I. Flavones: kaempferol, quercetin, isorhamnetin, rhamnocitin, formononetin, calycosin. Polysaccharides: astragalans I,II,III. Glucans: AG-1 and AG-2.
Bai zhu	Rhizoma <i>Atractylodis macrocephalae</i> Koidz. (Compositae)	Replenishing qi and reinforcing the spleen. Harmonizes spleen and stomach, relieves fatigue. Induces diuresis and eliminate damp. Arresting excessive perspiration and spontaneous sweating.	Increased phagocytosis, lymphocyte transformation, rosette formation, and serum IgG post chemotherapy. Increases body weight and endurance. Potentiates reticuloendothelial system. Diuretic effect, antitussive effect, hypoglycemic effect. Anticouagulant effect. Hepatoprotective effect. Lowers blood pressure and dilates blood vessels.	Essential oil: atractylon. Lactones: atractylenolides II,III. Vitamin A. Sesquiterpene and fufural.

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TABLE 1 (continued) Debu Tripathy Herbal Examples Diagram)

Pinyin transliteration	Botanical name and family	Traditional indications	Biological Effects	Chemical Constituents
Ling zhi	<i>Ganoderma lucidum</i> (Leys. Ex Fr.) Karst. (Basidiomycetes)	Nourishes, tonifies, supplements qi and blood. Removes toxin, astringes essence and disperses accumulations. Relieves fatigue and subdues deficiency insomnia.	Antitussive effect. Expectorant effect. Hypotensive effect. Hepatoprotective effect. Antibacterial effect. Sensitizes radiation effect. Protects from radiation damage. Immune stimulating effect.	Ergosterol, coumarin, mannitol, polysaccharides, organic acids, resins.
Dang shen	Radix <i>Codonopsis pilosula</i> (Franch.) Nannf. (Campanulaceae)	Tonify qi, increases body resistance, promotes digestion, absorption of nutrients. Increases secretion of body fluids.	Promotes digestion and metabolism. Stimulates the CNS: decrease monoamine oxidase-B (MAO-B) activity in the brain. Hematopoietic. Hypotensive effect. Significantly decrease erythrocyte electrophoretic time and fibrinogen. Enhance cardiac function and increases tolerance to cold without increasing body weight and it elevates activity of superoxide dismutase (SOD). Increases phagocytosis. Promotes leukocyte production. Increases hemoglobin levels antagonizes insulin induced hypoglycemia, but was ineffective with phagocytosis and the transformation of lymphocytes. It also inhibited type II allergic reactions and stimulated the adrenal cortex. Inhibits transplanted sarcoma 180 in mice.	Phytosterols and triterpenes: spinasterol and D-glucopyranoside, 7-stigmasterol, 5,22-stigmasterol, taraxerol, taraxeryl acetate and friedelin. Phenols: syringaldehyde, vanillic acid, syringin, tangshenoside I. Essential oil: methyl palmitate, octadecane, nonadecane, heptadecane, carboxylic acid <sup>3</sup> .
Fu ling	Sclerotium <i>Poria cocos</i> (Schw.) Wolf (Polyporaceae)	Induces diuresis and excreting dampness. Invigorating the spleen function. Tranquilizing the mind.	Increased monocyte GM-CSF production. Enhanced recovery of myelosuppression in mice after radiation. Increased spontaneous rosette formation, lymphocyte transformation, and serum IgG. Diuretic effect. Sedative effect. Antitumor promotion effect. Increases cardiac contractility.	Polysaccharide: -pachyman. Triterpene: pachymic acid, tumulosic acid, eburicoic acid, pinicolic acid.
<b>Antineoplastic agents</b>				
Pu gong ying	Herba <i>Taraxacum mongolicum</i> Hand.-Mazz. (Compositae)	Removes toxic heat. Removes swelling and nodulation. Relieves dysuria.	Antimicrobial effect. Immune stimulating effect: increases peripheral lymphoblast transformation rate. Choloretic effect and hepatoprotective effect.	Taraxasterol, taraxacerin, taraxicin, choline, inulin and pectins.
Jin yin hua	Flos <i>Lonicera japonica</i> Thunb. (Caprifoliaceae)	Removes toxic heat. Dispels wind heat.	Antimicrobial effect. Anti-inflammatory effect, antilipemic effect. Decreases pregnancy rate after mating. Antispasmodic effect. Diuretic effect.	Chlorogenic acid. Inositol and flavonone. Essential oil: 2,6,6-trimethyl-2-vinyl-5-hydroxytetrahydropyran and linalool.
Shan ci gu	Bulbus <i>Crematista variabilis</i> (Blume) Nakai (Orchidaceae)	Reduces heat. Removes toxin, disperses accumulation, dissipates swelling.	Antineoplastic effect. Cardiotonic effect. Antiviral effect.	Tulipine, colchicines.
Huang yao zi	Rhizoma <i>Dioscorea bulbifera</i> L. (Dioscoreaceae)	Resolves phlegm. Controls cough. Disperses goiter and controls bleeding.	Antibacterial effect. Antifungal effect. Increases uterine contraction.	Terpenoids: diosbulbin A,B,C,D. 2,4,6,7-tetrahydroxy-9,10-dihydrophenanthrene, 2,4,5,6-tetrahydroxy-phenanthrene. Tannin.
Bai hua she she cao	Herba <i>Oldenlandia diffusa</i> (Willd.) Roxb. (Rubiaceae)	Removes toxic damp heat, clears abscesses, infections with fever.	Increases phagocytosis, lowers fever, arrests growth of spermatogonia and empties convoluted seminiferous tubules.	Iridoid glycosides: oldenlandosides A and B. hentriacontane, stigmasterol, ursolic acid, oleanolic acid, $\beta$ sitosterol, sitosterol-D-glucoside, p-coumaric acid and flavonoid glycosides.

ginseng), *Atractylodes macrocephala* (*bai zhu*), *Poria cocos* (*fu ling*), *Glycyrrhiza uralensis* (*gan cao*) are the base formula for supplementing *qi* to which are added *Ophiopogon japonicus* (*mai men dong*), *Asparagus cochinchinensis* (*tian men dong*), *Glehnia littoralis* (*sha shen*), *Rehmannia glutinosa* (*di huang*), *Anemarrhena asphodeloides* (*zhi mu*), and *Polygonatum odoratum* (*yu zhu*) for supplementing yin, *Scrophularia ningpoensis* (*xuan shen*), *Imperata imperitae* (*bai mao gen*), *Lonicera japonica* (*jin yin hua*), *Solanum lyratum* (*shu yuan quan*), and *Oldenlandia diffusa* (*bai hua she she cao*) for eliminating heat and toxins, and, finally, *Salvia miltiorrhiza* (*dan shen*) for activating *blood* and removing stagnation. The objectives of the formula are not only to relieve the *blood* deficiency (anemia), *moisture* deficiency (dehydration), *heat* (due to radiation), and *toxins* (waste products and dead tissue due to tumor necrosis), but also to enhance the anti-cancer effects of the radiation via the anti-tumor activity of *Salvia miltiorrhiza* (*dan shen*), *Oldenlandia diffusa* (*bai hua she she cao*), *Glycyrrhiza uralensis* (*gan cao*), and *Solanum lyratum* (*shu yuan quan*).<sup>52</sup>

The same formula, *Si Jun Zi Tang* (Four Gentleman Decoction), can be used as the core of a prescription to treat the side effects of chemotherapy. Chemotherapy damages the *qi* and weakens the *spleen* and *stomach*, ultimately depleting the *essence* and undermining the *kidney*. Adding *Astragalus membranaceus* (*huang qi*), *Polygonatum odoratum* (*yu zhu*), *Pseudostellaria heterophylla* (*tai zi shen*), *Euryale ferox* (*qian shi*), *Nelumbo nucifera* (*lian zi*), and *Dioscorea opposita* (*shan yao*) augment the *qi* supplementing and *stomach* and *spleen* strengthening properties of the formula. Three more herbs *Ligustrum lucidi* (*nu zhen zi*), *Rehmannia glutinosa* (*shu di huang*), and *Lycium barbarum* (*gou qi zi*) replenish *essence* and strengthen the *kidney*. This formula called *Bu Shen Jian Pi Tang* alleviates fatigue, weakness, chilliness, anorexia, anemia, leukopenia, hair loss, and increases resistance to infection.<sup>53</sup>

In 1983, Jia Kun created a formula called *Ping Xiao Dan*, containing *Citrus aurantium* (*zhi ke*), *Curcuma longa* (*yu jin*), *Niter* (*xiao shi*), *Lacca sinica exsiccata* (*gan qi*), *Alumen* (*ming fan*), *Strychnos nux-vomica* (*ma qian zi*), *Trogoxterus xanthipes* (*wu ling zhi*), and *Agrimonia pilosa* (*xian he cao*). Dr Kun recommends *Ping Xiao Dan* as a general formula for the prevention and treatment of cancer, to be combined with additional formulas that are specific for particular types of cancer. *Ping Xiao Dan* has multiple effects: *Lacca sinica exsiccata* (*gan qi*), *Trogoxterus xanthipes* (*wu ling zhi*), *Curcuma longa* (*yu jin*), *Citrus aurantium* (*zhi ke*), *Strychnos nux-vomica* (*ma qian zi*), and *Agrimonia pilosa* (*xian he cao*) eliminate stagnation of *qi* and *blood*, promote the normal function of the liver and intestines, relieve pain, promote tissue regeneration, and dissolve lumps and masses. *Niter* (*xiao shi*) and *Alumen* (*ming fan*) neutralize toxins and reduce fever and inflammation. And even though the major thrust of the formula appears to be anti-pathogenic, the *Curcuma longa* (*yu jin*), *Agrimonia pilosa* (*xian he cao*), and *Citrus aurantium* (*zhi ke*) also have a tonic effect on the body as a whole: "The combination of all these ingredients...controls and palliates solid neoplasms and manages the corrosion. It also has the function of a tonic, antidote, analgesic and appetizer, revives vigor, nourishes the

nerves, encourages recovery, increases the capacity of organs to resist disease, nourishes *qi*, and causes cancer cells to degenerate, change shape, reduce in size, and melt."<sup>54</sup>

### Research Investigations

A literature review performed in 1998 by the University of Texas Center for Alternative Medicine Research in Cancer summarized many Chinese studies, including controlled trials with human subjects, animal, and *in vitro* laboratory experiments.<sup>55</sup> The studies showed the impact of medicinal herbs on: disease response, survival outcome, immune response, reduction in adverse effects from chemotherapy and radiation, improved recovery from surgery, better quality of life, and alleviation of pain. This review indicated that some patients who received Chinese herbal medicine combined with conventional Western treatment demonstrated significantly better survival and/or disease response than patients receiving Western treatment alone. But often research design has involved inadequate methodology, including the absence of randomized, placebo or blinded controls. While the examples that follow hardly constitute proof of efficacy, they are suggestive of benefit, indicating that further research is desirable and necessary.

For example, in a study of 76 patients with second-stage primary liver cancer there were no 5-year survivors in the groups treated with chemotherapy or radiation alone, whereas there was a 10% survival in the group treated with a combination of *Fu Zheng* herbs and radiation, and a 16.7% survival in those treated with both herbs and chemotherapy.<sup>56</sup> Five-year survival rates in another study of patients with liver cancer who received chemotherapy alone were 6%, whereas when combined with the herb formula *Si Jun Zi Tang* (*Panax ginseng*, *Atractylodes macrocephala*, *Poria cocos*, *Glycyrrhiza uralensis*), 5-year survival rose to 43%.<sup>57</sup>

Herbs that are *qi* and *yang* tonifying, that warm and strengthen the *spleen* and *kidney*, are thought to ameliorate the adverse effects of chemotherapy and radiation. Zhang Xinqi comments, "The leukopenia caused by chemotherapy or radiotherapy is classified as a deficiency type of illness which is referred to as the morbid condition showing deficiency of genuine *qi*, lowered body resistance, and declining of function. Then, supplementing *qi* and nourishing the *blood*, warming and invigorating the *spleen* and *kidney* are the essential therapeutic principles for remitting toxic side effects."<sup>58</sup>

Two of the important toxin-removing herbs used in cancer therapy are *Sophora flavescens* (*ku shen*, meaning bitter root of miraculous effect) and *Sophora subprostrata* (*shan dou gen*), containing matrine and oxymatrine series alkaloids that show cytotoxic activity *in vitro* and antitumor activity *in vivo*, (inhibit the growth of sarcoma-180 in laboratory mice). Oxymatrine itself is 7.8 times stronger than the chemotherapeutic agent mitomycin C in its tumor inhibiting effects, without suppressing the immune system.<sup>59</sup> *Sophora flavescens* (or *subprostrata*) also increases leukocytes and promotes peripheral immune responses. *Scutellaria baicalensis* (*huang qin*) is another potent *heat* and toxin-clearing herb with anti-tumor and immune-stimulating

properties in vivo and, in vitro, that inhibits platelet aggregation and induces apoptosis.<sup>60</sup> And another herb, *Isatis tinctoria* (*ban lan gen*) contains the compound indirubin, observed by Chinese scientists to exert an effect against chronic myelocytic leukemia (CML). It inhibits DNA synthesis in neoplastic cells, particularly immature leukemic cells in bone marrow, while simultaneously stimulating immune response.<sup>61</sup>

*Angelica sinensis* (*dang gui*) is a blood supplementing and activating herb with anti-tumor, immune stimulating, and anti-angiogenic properties that reduces vascular permeability *in vitro*.<sup>62</sup> Other potent herbs in the blood activating category with direct cancer-inhibiting properties are *Curcuma zedoaria* (*e zhu*), *Salvia miltiorrhiza* (*dan shen*), and *Panax pseudoginseng* (*tian qi*). These herbs are fibrinolytic, antithrombic, and anti-inflammatory. People with cancer often have elevated fibrinogen levels, increasing the stickiness of the blood so that it is more likely to coagulate. Because the "sticky" factors in blood facilitate the adherence of metastatic cells to healthy tissue, and because tumors are often encapsulated within a tough fibrin coating difficult for anti-neoplastic drugs or immune cells to penetrate, herbs that increase microcirculation, make the blood less viscous, the fibrin coating more permeable, and soften and disperse masses. When extracts of curcuma are injected in mice with tumors, the tumors shrink.<sup>63</sup>

### Enhancing Conventional Protocols

To overcome the adverse effects while at the same time potentiating the desired effects of conventional treatment, a popular biological response modifying formula called All Inclusive Great Tonifying Decoction (*Shi Quan Da Bu Tang*) is often used. It appears to restore hematopoietic function to improve peripheral blood counts, and increases interleukin production along with NK cells. This formula contains *Panax ginseng* (*ren shen*), *Angelica sinensis* (*dang gui*), *Poria cocos* (*fu ling*), *Atractylodes macrocephala* (*bai zhu*), *Astragalus membranaceus* (*huang qi*), *Ligusticum wallichii* (*chuan xiong*), *Peonia lactiflora* (*bai shao*), prepared *Rehmannia glutinosa* (*shu di huang*), *Cinnamomum cassia* (*rou gui*), and prepared *Glycyrrhiza uralensis* (*zhi gan cao*). It was found to potentiate the therapeutic activity of chemotherapy (Mitomycin, Cisplatin, Cyclophosphamide, Fluorouracil) and radiotherapy, inhibit recurrence, prolong survival, and prevent or ameliorate adverse treatment effects such as: anorexia, nausea, vomiting, hematotoxicity, immuno-suppression, leukopenia, thrombocytopenia, anemia, and nephropathy.

In traditional terms, the herbs *Panax ginseng* (*ren shen*), prepared *Glycyrrhiza uralensis* (*gan cao*), *Poria cocos* (*fu ling*), and *Atractylodes macrocephala* (*bai zhu*) tonify *qi*, while *Angelica sinensis* (*dang gui*), *Ligustici wallichii* (*chuan xiong*), *Peonia lactiflora* (*bai shao*), and prepared *Rehmannia glutinosa* (*shu di huang*) nourish the blood, and *Astragalus membranaceus* (*huang qi*) and *Cinnamomum cassia* (*rou gui*) further invigorate *qi* and *yang*.<sup>64</sup> In another study to determine effects of this formula on white blood cell counts, 134 patients with cancer who had previously undergone chemotherapy and radiation therapy that resulted in

leukopenia were given the formula and 113 patients experienced an increase of white blood counts to normal levels.<sup>65</sup> In a study of 58 patients with osteogenic sarcoma who were receiving either Cisplatin and Dexamethasone (CD) or high-dose Methotrexate and Vincristine (MV), patients were randomly assigned to the herbal arm or observation. Those using the herb formula in the MV group experienced improvements in white blood cell and platelet counts and there was less transaminase enzyme elevation. Both the CD and MV groups showed improvement in post-therapy cardiac function, less nausea and vomiting, and fewer rashes than those in the control group.<sup>66</sup>

Whereas tumor recurrence for post-surgical patients with bladder cancer was 65% with conventional treatment alone, this was reduced to 33% when patients added the use of the Chinese medicinal mushroom *Polyporus umbellatus* (*zhu ling* or *maitake* in Japanese).<sup>67</sup> In another study, those receiving radiation alone suffered from low white blood cell and platelet counts, but this was reversed in subjects who received Chinese herbs: 40 patients recovered from 3450/c.mm to 5425/c.mm, whereas in the control group without herbs, white blood cell counts dropped significantly.<sup>68</sup>

Five-year survival for advanced nose and throat cancer patients receiving radiation alone was 24% whereas adding the herbal formula *Yi Qi Yang Yin Tang* to the conventional protocol produced a 52% five-year survival.<sup>69</sup> In a study of 197 patients with stage III and IV nose and throat cancers, half received radiation in combination with the formula *Yi Qi Yang Yin Tang* and half received only radiotherapy. After 3 years the survival rates were 67% and 33% respectively. This formula is targeted to nourish the *qi* and fluids as well as clear *heat* and *toxins* and eliminate *blood* stagnation.<sup>70</sup> In yet another study of this formula for nasopharyngeal cancer, 272 patients were treated with radiation, half of whom received the formula. In the herb-treated group, 5-year relapse was 68% lower (12% versus 38%), and survival rates were also significantly improved (67% versus 48% at 5-years).<sup>71</sup>

In 285 patients with lymph node metastases, one group received only chemotherapy with no significant tumor shrinkage; another received only herbal medicine with only 12% showing significant shrinkage; whereas in the group that received chemo, radiation, and herbs, or radiation plus herbs, 75% showed significant tumor shrinkage.<sup>72</sup> When 70 patients with chronic gastritis and dysplasia were divided in groups according to traditional Chinese pattern diagnosis (hyperactive *liver qi*, deficiency *cold* of the *spleen* and *stomach*, deficiency of *stomach yin*, and *damp heat* in the *spleen* and *stomach*) and treated accordingly, 84% markedly improved, 4% responded partially, and 11% were unresponsive.<sup>73</sup>

A study at Drew University in Los Angeles investigated the effects of medicinal mushrooms on patients with advanced malignancies: in 2 weeks there were marked decreases in tumor associated antigens and marked increases in natural killer cell activity in 8 out of 11 subjects.<sup>74</sup> In another study, patients with primary liver carcinoma who received herbs in combination with chemotherapy had increased numbers of NK cells.<sup>75</sup>

A study of 176 patients compared half the subjects who received injections of *Astragalus membranaceus* (*huang qi*) and *Panax ginseng* (*ren shen*) while undergoing chemotherapy for colon cancer, to a control group that was not administered herbal injections. Those receiving the herbal injections had higher white blood cell counts, greater macrophage activity, and increased body weight.<sup>76</sup> A study of the herb *astragalus* at MD Anderson Hospital and Tumor Institute in Houston, Texas confirmed earlier reports by the same authors that this herb possesses immuno-potentiating activity, correcting *in vitro* T-cell function deficiency found in many cancer patients. Decades of pharmacological research have revealed that the polysaccharides and other compounds in *Astragalus membranaceus* promote cellular (intensifies phagocytosis) and humoral (increases function of B lymphocytes) immune function and have *in vitro* anti-tumor effects on cancer cell lines.<sup>77</sup> Research at MD Anderson Hospital in Houston reproduced these results in a 1983 study, demonstrating that aqueous extracts of *Astragalus membranaceus* *in vitro* and *in vivo* enhanced levels of circulating lymphocytes. A second study in 1988 confirmed and expanded the previous findings that extracts of Chinese herbs possess potent immune restorative activity. A polysaccharide fraction of *Astragalus membranaceus* (fraction 3, F-3) was isolated as most potent. The data indicated that extracts of *astragalus* could restore T-cells from immune compromised cancer patients to normal levels of function.<sup>78</sup> In a human trial, *Astragalus membranaceus* was found to potentiate IL-2 tenfold, permitting a smaller, less toxic effective dose, restoring T-cell function in 9 out of 10 cancer patients.<sup>79</sup> Whereas the common dose of *Astragalus membranaceus* is 9 to 30 grams of dried herb for non-cancerous conditions, doses as high as 60 grams per day may be administered as an immunostimulant. Although toxicity is low at high doses, occasionally symptoms of over-stimulation such as insomnia, increased heart rate, palpitations, or hypertension can occur at these high doses.<sup>80</sup>

Multiple studies on patients with stomach cancer were conducted using the formula *Pishen Fang* (*Jian Pi Yi Shen*) that supplements *qi* and *yang*, has immuno-stimulating properties, and contains: *Codonopsis pilulosa* (*dang shen*), *Atractylodes macrocephala* (*bai zhu*), *Lycium barbarum* (*gou qi zi*), *Ligustrum lucidum* (*nu zhen zi*), *Cuscuta chinensis* (*tu si zi*), and *Psoralea corylifolia* (*bu gu zhi*). One study examined 81 patients with stage III gastric cancer who received chemotherapy. Those who also took the herbal formula experienced improved digestive and bone marrow function, as well as increased survival. In the herbal group, 5-year survival was 46% compared to 20% in the chemotherapy-only group.<sup>81</sup> In another study, 669 late-stage gastric cancer patients who were receiving chemotherapy were randomly divided into the herbal arm, and the control group. Improvements in body weight, appetite, reduced nausea and vomiting, were observed in the group that received the formula. White blood cell counts were 7% in the herb-treated group compared to 33% in the control group. Macrophage activity was 21% greater in the treated group, and 5-year survival among 303 stage III and 63 stage IV patients who received follow-up were 53% and 10% respectively. After 10 years, 47% of the stage III patients remained alive.<sup>82</sup> Another study

examined 216 postoperative stomach cancer patients at stage III, and 110 patients at stage IV, showing that of the half who did not receive the herbal formula, 75% were able to finish the complete chemotherapy course, compared to 95% who received the herbs. Patients in the herb-treated group gained weight (23% vs. 8%); fewer lost weight (6% vs. 14%); fewer lost their appetite (10% vs. 32%); and fewer had vomiting (4% vs. 12%).<sup>83,84</sup>

In an animal study, Mitomycin C showed a stronger anti-tumor effect when combined with ginseng.<sup>85</sup> Similarly, when an extract of the mushroom *Polyporus umbellatus* (*zhu ling*) was combined with Mitomycin C, the life span of tumor-bearing mice was increased by 119.9%, compared to 70% in the control group treated with the drug alone.<sup>86</sup> Ginsenosides, the active saponin compounds in the ginsengs, increase phagocytosis, appetite, blood formation, accelerate the biosynthesis of DNA, and appear to induce cancer cells to change their morphology and become more like healthy cells. The polysaccharides in *Astragalus membranaceus* (*huang qi*) and *Panax ginseng* (*ren shen*) and medicinal mushrooms regulate T-cells and stimulate interferon and phagocytosis, producing both immune-restorative and cancer-inhibiting effects.

An herbal formula used to relieve signs of cardiac distress (palpitation, irregular, small and slow pulse, occasional premature systole, lower-wall myocardial ischemia) secondary to treatment with Adriamycin (doxorubicin), is called *Zhi Gan Cao Tang*, or Baked Licorice Decoction, consisting of 20 gm *Glycyrrhiza uralensis* (*gan cao*), 30 gm *Rehmannia glutinosa* (*di huang*), 30 pieces *Ziziphus jujuba* (*da zao*), 15 gm *Zingiberis officinale* (*jiang*), 15 gm *Cannabis indica* (*huo ma ren*), 10 gm *Panax ginseng* (*ren shen*), and 10 gm *Cinnamomum cassia* (*gui zhi*) administered as a decoction. When cardiac function normalized after 6 days, Adriamycin therapy resumed, and administration of the decoction was continued.<sup>87</sup>

Another prescription developed in modern times, is a formula described in 1982 by Dr Hong-Yen Hsu containing *Wisteria sinensis* (*zi teng*), *Terminalia chebula* (*he zi*), *Trapa bispinosa* (*ling jiao*), and *Coix lachryma-jobi* (*yi yi ren*).<sup>88</sup> Both *Wisteria sinensis* (*he zi*) and *Trapa bispinosa* (*ling jiao*) have a history of use in China and Japan for the treatment of tumors. *Coix lachryma-jobi* (*yi yi ren*) and *Terminalia chebula* (*he zi*) have been used traditionally to strengthen digestive and respiratory functions as well as to relieve infection and inflammation.<sup>89</sup> *Coix lachryma-jobi* is now considered a general anti-cancer agent. This prescription conforms to the principles of invigorating *qi* and strengthening resistance (improving digestive and respiratory function) and clearing *heat* and eliminating *toxins* (removing infection and inflammation).

The US Food and Drug Administration approved the first Chinese-made anti-cancer drug for Phase II clinical human trials in 2001, to be conducted by the US biopharmaceutical company, Oncoherb. The drug, called Kanglaite injection, is an extract distilled from the seeds of the herb *Coix lachryma-jobi* (*yi yi ren*). It has demonstrated efficacy against *lung* cancer in clinical trials with over 200,000 cancer patients conducted in China.

Studies have indicated that it may also be useful in the treatment of other types of cancer, including stomach and cervical cancers, and solid tumors. The preliminary findings of research conducted in the US support the Chinese trials. The new drug significantly improves the efficacy of radiation therapy and chemotherapy treatments in late-stage, lung cancer patients. It is far less toxic than existing chemotherapeutic agents and is effective in patients for whom existing treatments did not show any improvements.<sup>90</sup>

In the November 2001 issue of *Life Sciences*, Henry Lai from the University of Washington reported on the cytotoxic activity of artemesinin, a compound from *Artemisia annua* (*qing hao*). Artemesinin kills human breast cancer cells *in vitro* by interfering with their iron metabolism. It was first discovered to be an effective anti-malarial agent in chloroquine-resistant cases. Malarial parasites depend on high iron concentrations for reproduction, as do cancer cells, and any micro-organisms. Excess iron is associated with increased cancer rates. Breast cancer cells have up to 15 times more transferrin receptors than healthy cells. Acute leukemia and pancreatic cancers have also been responsive to this agent *in vitro*, with no apparent adverse effects upon healthy tissue. The Breast Cancer Fund in San Francisco is supporting this research. Earlier studies showed that *Artemisia annua* and capillaries have direct cytotoxic effects *in vivo* without causing immunosuppression.<sup>91</sup>

While Debu Tripathy was an oncologist at the University of California at San Francisco (UCSF), he conducted an on-going placebo-controlled randomized trial for women with breast cancer, using a formula containing 21 Chinese herbs to investigate the alleviation of common side effects of chemotherapy, namely nausea, vomiting, fatigue, marrow suppression, risk of infection, and hair loss.<sup>92</sup>

### Safety and Herb-Drug Interactions

Herb safety and herb-drug interactions are complex and controversial issues. With the increasing use of herbs by Westerners has come legitimate concern for potential abuse and toxicity. The safety of a drug, herb, or food is always relative and contextual. Safety is determined by defining the conditions under which a substance is considered to be safe or dangerous, and weighing potential benefits against possible short and long-term adverse effects. Herb-drug interaction is a similar puzzle: all substances that enter the body interact with each other, ultimately affecting all body processes. The issue again is determining the benefit or detriment of such interactions.

Compared to the record of approved pharmaceutical drugs, with a few well-known exceptions such as *Aconitum carmichaelie* (*fu zi*), *Cinnabaris* (*zhu sha*), *Aristolochia fangchi* (*guang fang ji*), and *Ephedra sinica* (*ma huang*), Chinese medicinal herbs are safer.<sup>93</sup> Aconite contains aconitine, a recognized poison, that is traditionally detoxified by boiling and then combined with other herbs such as *Zingiberis officinale* (*jiang*), *Ziziphus jujuba* (*da zao*), and *Glycyrrhiza uralensis* (*gan cao*) that further mitigate its toxicity, yielding important therapeutic

benefits. For example treated *Aconite* is combined with *Panax ginseng* in the treatment of acute cardiac failure. *Cinnabaris*, a crude ore, contains mercuric oxide and although considered unsafe by American standards, is still utilized in small doses in China for the short-term treatment of acute mental agitation without negative consequences. Many *Aristolochia* species have recently been shown to exert carcinogenic effects when used continuously for longer than 6 months, yet these species continue to be used in China with good results in the treatment of cancer and nephropathy, the very conditions for which they have been considered causative agents in the West. *Ephedra sinica* (*ma huang*) has appropriately been used as an anti-asthmatic, antitussive diaphoretic and vasodilating component of numerous pulmonary and anti-arthritis formulas for centuries.

In the US over the past two decades, *Ephedra* has been inappropriately marketed over-the-counter as a natural energy and weight loss stimulant, resulting in incidences of high blood pressure, palpitations, agitation, and insomnia. It is unfortunate that abuse and misuse have caused herbs such as these to become less available to professional health care providers, and have cast a dark shadow over the credibility and safety of Chinese medicinal herbs in general.

The hundreds of herbs that are in common use in China and the West are rarely associated with adverse effects that are not easily reversible. These effects are seldom serious and include such transient reactions as: nausea, indigestion, diarrhea, headache, dizziness, hot flashes, chills, and rashes that are rapidly abated by discontinued use or dose reduction. The preponderance of evidence shows that when used as an adjunct to conventional medicine, Chinese herbs both enhance the desired effects and mitigate the harmful ones.

Sophisticated monitoring with biological testing, sterilization, and spectrographic analyses by manufacturers in the United States is insuring that herbal products are free of chemical contaminants, adulterants, pathogens, and substitutions. This heightened awareness along with stringent standards is encouraging Chinese manufacturers to adopt the good manufacturing practices (GMP) required by the Food and Drug Administration (FDA) and the Federal Trade Commission (FTC).

There is a paucity of data that describes the interactions between pharmaceutical agents, and even less between herbs and drugs. A few herbs and foods have well understood interactions with drugs. Tetracycline absorption can be impeded by milk-based foods, whereas grapefruit juice increases the blood volume of certain drugs (antidepressants, antihistamines, anti-hypertensive) by inhibiting a drug-metabolizing enzyme (cytochrome P450). *Hypericum perforatum* (St. John's Wort, *tian ji huang*) reduces blood levels of protease inhibitors by increasing their metabolism, while potentiating the effects of MAO and SSRI antidepressants by elevating serotonin levels. Green vegetables high in Vitamin K can oppose the blood-thinning action of drugs like Heparin, Coumadin, or Warfarin. Because *Ginkgo biloba* (*ying guo ye*), *Salvia miltiorrhiza* (*dan shen*) and *Angelica sinensis* (*dang gui*) promote microcirculation and inhibit platelet aggregation, they can

potentiate the effects of anti-coagulants, as can *Allium sativum* (garlic)(da suan) and *Zingiberis officinale* (ginger, jiang). *Astragalus membranaceus* (huang qi), because of its immuno-stimulating properties, may counter the immunosuppressive action of anti-rejection drugs like Cyclosporin. In high doses, *Glycyrrhiza uralensis* (licorice)(gan cao) can mimic the action of cortisol, elevating blood pressure and increasing fluid retention.<sup>94</sup> These findings are based on the use of these herbs as single agents.

When *Angelica sinensis* is incorporated into a formula such as *Shi Quan Da Bu Tang*, which supplements *qi* and *blood* and activates circulation, its hematopoietic properties are enhanced and its anti-coagulant properties are reduced by the inclusion of herbs such as *Rehmannia glutinosa* (di huang) and *Peonia lactiflora* (bai shao), making it an effective treatment for the anemia, bruising, and bleeding caused by radiation and chemotherapy. One of the side effects of standard anti-coagulant therapy is anemia. To solve this problem with Chinese medicine, the herbs *Panax pseudoginseng* (tian qi) and *Milletia reticulata* (ji xue teng) are used because of their triple hematopoietic, circulation-activating, and anti-hemorrhagic properties. *Glycyrrhiza uralensis* (licorice, gan cao) is ubiquitous, appearing in countless formulas in part because of its ability to modulate adrenal function. For example, the Decoction of *Bupleurum chinense* (chai hu) and *Poria cocos* (fu ling, Chai Ling Tang) contains many herbs, including *Glycyrrhiza uralensis* (gan cao), and is used to aid in the withdrawal from corticosteroid dependence.<sup>95</sup>

Rather than suggesting that people stop eating grapefruit or green vegetables, new information is broadening our understanding of the complexity of drug-food and drug-herb combinations, enhancing our ability to make prudent choices. Biologist Subhuti Dharmananda, PhD, suggests, "Herb-drug interactions may be minimized by having patients take the herbs and drugs at different times (one hour apart to avoid direct interaction in the digestive tract; 1.5 hours to avoid maximum blood levels of drug and herb at the same time). The dosage of herbs that are aimed therapeutically at the same function as the drugs (eg both are sedatives; both are hypoglycemics; both are anti-coagulants) should be reduced to alleviate concerns about additive or synergistic effects that are too great. A certain level of additive effects might be desired in cases where the drug therapy is not producing the desired response."<sup>96</sup>

Fundamentally, Chinese medicine is concerned with the behavior of *qi*. Consequently, all of the major modalities of Chinese medicine (acupuncture, herbal medicine, dietetics, *qi gong*) are employed to provoke the *qi* to reorder itself once a pathological process has begun and, ideally, before it has become clinically manifest. While Chinese medicine has developed its own sophisticated repertoire of treatments for specific diseases, its primary emphasis is ultimately upon restoring and preserving the healthy function of the body.

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