Cancer and Traditional Chinese Medicine

Treating the Side Effects of Chemotherapy and Radiation with Traditional Chinese Herbs

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Introduction

A significant body of research has been conducted in China on the ability of Chinese herbal medicines to support the immune system of cancer patients and reduce the toxic side effects of conventional Western cancer therapies. This review details some of these studies, in hopes that cancer patients and oncologists outside of China can begin to consider Chinese herbs as a viable, safe adjunct to the conventional Western medical interventions of chemotherapy, radiation therapy, and surgery.

Research conducted on Chinese herbal medicines has frequently been criticized for its lack of scientific rigor. Much of this criticism is justified. Of the large number of reports reviewed in the preparation of this and a related forthcoming article, at least two thirds were rejected either for incomplete reporting of data or for obvious flaws in research design that may have significantly biased the results. While the studies included in this review are of relatively higher quality, some also suffer from unclear or incomplete reporting, or potentially significant design flaws. Where these flaws appear I have attempted to point them out, so that the reader may take them into consideration in evaluating the results.

Despite these shortcomings, this review is being presented to help cancer patients and their doctors make informed choices about their medical care. It may also serve as a signpost for researchers of this topic, by directing them to study some of the herbal protocols that appear to show good potential. It is hoped that over time more scientifically sound research can be conducted on Chinese herbs as complementary cancer treatment, so that a larger number of patients can reap their purported benefits.

The potential benefits of Chinese herbal treatments presented in this review include improved immunologic function as measured by levels of T lymphocytes, the monoclonal antibody T_1 (which has been shown to induce proliferation of T cells), the T_4 to T_8 (helper to suppressor) T cell ratio, soluble interleukin-2 receptors, natural killer cells, lymphokine activated killer cells, leukocytes, platelets, and immunoglobulin M. Other immunologic parameters that show improvement with herbal treatment include the lymphocyte proliferative response, interleukin-2 induction response, and macrophage activity. Some indications that Chinese herbal treatment improves organ function are also noted, as well as apparent alleviation of clinical side effects ranging from gastrointestinal symptoms and oral ulcers to skin rashes. In addition, research on possible herbal amelioration of chemotherapy-induced nephrotoxicity is presented, as well as research suggesting that Chinese herbs can effectively treat pain related to both Western anticancer interventions and the cancer disease process itself.

Cancer patients unfamiliar with scientific medicine and medical statistics may find some of this material technically challenging. To help facilitate lay comprehension of this technical data, I have included basic explanations of important terms and concepts.[1] Also, at the end of each section I have attempted to summarize research results in the broadest of terms, so that readers not able to distinguish every tree

in the forest can at least conclude that the forest is, indeed, green. In these cases, readers may wish to share this review with their doctors, using it as a point of departure for discussion and exploration of possible "alternative medicine" adjuncts to any conventional cancer treatments they are considering.

This article is by no means an exhaustive review of all works on treating side effects of chemotherapy and radiation with Chinese herbal medicines, rather it is a sampling of some of the *relatively* high quality work that has been published (primarily in Chinese) on this topic in the 1990s. Research for this project began on the Medline Plus biomedical database, but also branched into libraries of private individuals and of institutions offering professional training in traditional Chinese medicine in the United States. In addition to quality of research design and reporting, one further criterion for selecting articles for this review was the availability of herbal medicines in North America and Europe.

From the research and empirical evidence, it appears that Chinese herbal medicines are capable of enhancing the immune system and ameliorating the side effects of chemotherapy and radiation. Anecdotal reports of this nature have already led many cancer patients in the West to seek conjunctive Chinese herbal therapy. Chinese herbal medicines are available in the West, however it should be noted that the practice of Chinese medicine is highly complex and treatment recommendations should be given only by those with the proper education and training. Readers should not use the information in this article as a guide to self-treatment. Assistance locating a practitioner of traditional Chinese medicine is available from many sources, including the following:

- National Acupuncture and Oriental Medicine Alliance (NAOMA), Washington: (253) 851-6896; www.acuall.org
- American Association of Oriental Medicine (AAOM), Pennsylvania: (610) 266-1433; www.aaom.org
- California Association of Acupuncture and Oriental Medicine (CAAOM): 800-477-4564 or 888-432-5669; caaom.org

Assistance may also be available from state government offices regulating acupuncture and/or Oriental medical practice, though as of 1998 some states still lack such regulatory bodies. Readers are advised to inquire about the educational and clinical background of practitioners to whom they are referred.

The following summarized studies are organized according to their foci, beginning with research on the effects of Chinese herbal medicine on immunologic function of cancer patients, then proceeding to studies evaluating both immune function and clinical side effects, and concluding with research on nephrotoxicity and pain.

Immunologic Function

T Lymphocytes, T_1, T_4 / T_8, Soluble Interleukin-2 Receptors, Natural Killer Cells, and Lympokine-Activated Killer Cells

Lin et al.[2] randomly assigned patients with pathology confirmed stage III or IV stomach cancer to a treatment or a control group. Both groups included patients who had received varying numbers of chemotherapy courses previous to entry into this study. In this as well as all other parameters, there was no statistically significant difference between the treatment and control groups. Both groups received an FAP chemotherapy regimen [5-fluorouracil (5-Fu), epirubicin (E-ADM), and cisplatin (DDP)]. For patients with poor heart function the regimen was altered from FAP to FMP by substituting mitomycin C (MMC) for epirubicin (E-ADM). In addition, patients in the treatment group received injections of a glucose solution containing the Chinese herbs Panax Ginseng C.A. Mey *(ren shen)* and Ophiopogon japonicus Ker-Gawl. *(mai men dong)*. This is based on the traditional formula Generate the Pulse Decoction *(sheng mai san)* which, as we will see below, is commonly used in China to help patients undergoing cancer treatments.

Lin et al. observed the effects of these treatments on T lymphocyte levels. A T lymphocyte is a type of white blood cell that is crucial to the immune system. There are three main types of T lymphocytes: cytotoxic or killer cells, suppressor cells, and helper cells. Killer T cells recognize, attach to, and destroy abnormal cells within the body. Suppressor T cells appear to regulate the immune response to tumor antigens. Helper T cells enhance the activities of killer T cells and control other aspects of immune response. T lymphocytes play a critical role in the body's ability to fight infectious diseases and possibly cancer. In this study, after treatment the treatment group's T lymphocyte count showed a statistically significant *increase* from 47.63 ± 7.20% to 52.51 ± 7.13% ($p < 0.05$). In comparison, after treatment the control group's T lymphocyte count showed a statistically significant *decrease* from 48.46 ± 9.01% to 44.23 ± 7.45% ($p < 0.05$). Before treatment there was no significant difference between the T lymphocyte count of the two groups ($p > 0.05$), but after treatment the increase in T lymphocyte count of the treatment group was significant when com-

pared to the decrease that occurred in the control group ($p < 0.05$).

Improved immune function in the treatment group was also observed in the level of T_1 cells and in the helper/suppressor (T_4 / T_8) ratio. T_1 cells are a type of monoclonal antibody that has been shown to induce proliferation of T cells.[3] T_4 cells are T helper cells, while T_8 cells are T suppressor cells. In this study, in addition to a significantly improved T lymphocyte count, patients in the treatment group also showed significant increases in T_1 value and the helper/suppressor (T_4 / T_8) ratio. Prior to treatment the T_1 level in the control group was significantly higher than in the treatment group ($p < 0.05$). One week after treatment the T_1 value for both groups dropped. However, in the second and third weeks after treatment the T_1 value for the treatment group stabilized and began increasing. By the fourth week after treatment, the T_1 value for the treatment group was significantly higher than it had been before treatment (65.72 ± 6.81% compared to 61.73 ± 6.98%) ($p < 0.05$). For patients in the control group, the pattern was essentially opposite. In the second and third weeks after treatment, the T_1 values for the control group continued to decline, and though they began to increase in the fourth week, by this time they were significantly lower than before treatment (62.61 ± 6.44% compared with 66.64 ± 4.93%) ($p < 0.05$). After the fourth week, the T_1 values of the treatment group were significantly higher than those of the control group ($p < 0.05$). Similar results were observed for the helper/suppressor (T_4 / T_8) ratio. Prior to treatment there was no statistical significance between the treatment group (1.36 ± 0.54) and the control group (1.37 ± 0.25). Four weeks after treatment the helper/suppressor (T_4 / T_8) ratio for the treatment group was significantly higher (1.46 ± 0.18) than in the control group (1.26 ± 0.28) ($p < 0.05$).

Lin et al. also evaluated the effect of Panax Ginseng C.A. Mey *(ren shen)* and Ophiopogon japonicus Ker-Gawl. *(mai men dong)* on other aspects of the immune system important in cancer therapy, such as soluble interleukin-2 receptors (sIL-2R), natural killer cells (NK), and lymphokine-activated killer cells (LAK). Interleukin-2 (IL-2) is a major growth factor for and activator of T cells. "When natural killer (NK) cells are stimulated by high concentrations of IL-2 in vitro or in vivo, they take on a broader spectrum of killing against tumor cells, and are then called lymphokine-activated killer (LAK) cells."[4] Soluble IL-2 receptors can dampen this effect by binding with the IL-2, thus preventing it from turning T cells into LAK cells. Prior to treatment Lin et al. found no statistically significant difference ($p > 0.05$) between the treatment and control groups in levels of soluble interleukin-2 receptors (sIL-2R), natural killer cells (NK), and lymphokine-activated killer cells (LAK). After treatment the soluble interleukin-2 receptor level dropped significantly in the treatment group from 972 ± 19 u/ml to 591 ± 50 u/ml ($p < 0.05$), while there was no statistically significant drop in interleukin-2 receptors in the control group. After treatment, the soluble interleukin-2 receptor level was significantly lower in the treatment group than in the control group (591 ± 50 u/ml compared with 899 ± 40 u/ml) ($p < 0.05$), indicating that there was more chance in treatment group patients for T cells to be activated by IL-2 and thus perform their tumor killing activity. At the same time the natural killer cell and lymphokine-activated killer cell levels increased significantly in the treatment group. Natural killer cell levels in the treatment group increased from 32.27 ± 10.31% to 54.63 ± 7.24% ($p < 0.05$), while they decreased in the control group from 33.42 ± 11.41% to 25.82 ± 13.14% ($p < 0.05$). Lymphokine-activated killer cell levels in the treatment group increased from 50.24 ± 10.39% to 64.57 ± 9.42% ($p < 0.05$), while they decreased in the control group from 52.64 ± 9.93% to 45.61 ± 13.47% ($p < 0.05$). The treatment group's post-treatment increase in both natural killer cell and lymphokine-activated killer cell levels was statistically significant ($p < 0.05$). There was no statistically significant difference between the two groups' pre- and post-treatment levels of immunoglobulin A, M, or G.

Leukocytes (White Blood Cells)

'Support the normal' *(fu zheng)* is a type of Chinese herbal therapy designed to support and enhance the body's natural defenses in order to treat disease and restore health. In Chinese medical cancer therapies the *support the normal* approach is often used to support the body during chemotherapy and radiation therapy. Chen[5] compared the effects of a *support the normal* herbal prescription on leukocyte counts of 31 gastric cancer patients undergoing chemotherapy, with the effects of Western immune-enhancing drugs, and with another herbal prescription designed to disperse masses. Twenty-seven of the 31 patients had stage II or III disease, staging data of the remaining 4 is not provided in the original article. Prior to treatment there was no significant difference between the leukocyte counts of the three groups ($p > 0.1$), the average for all three groups being above 5.0 x 10^9/L. One weakness of this study is that Chen does not report by what criteria group assignments were made, or if there were any significant differences among the three groups in age, gender, disease stage or previous treatment received.

All patients in the study received chemotherapy. The primary regimens used were: 1) mitomycin C (MMC), 5-fluorouracil (5-Fu), and arabinosylcytosine (Ara-C); and 2) 5-fluorouracil (5-Fu), Adriamycin (ADM), and mitomycin C

(MMC). Based on drug availability a small number of patients used either 3) 5-fluorouracil (5-Fu) and mitomycin C (MMC); or 4) mitomycin C (MMC) exclusively. In addition the *support the normal* therapy group received a prescription of the following herbs:

- Astragalus membranaceus (Fisch.) Bge. *(huang qi)*
- Codonopsis pilosula (Franch.) Nannf. *(dang shen)*
- Dioscorea opposita Thunb. *(shan yao)*
- Rhizoma Atractylodis Macrocephalae *(bai zhu)*
- Rehmannia glutinosa (Gaertn.) Libosch. *(di huang)*
- Cornus officinalis Sieb. et Zucc. *(shan zhu yu)*
- Ligustrum lucidum Ait. *(nü zhen zi)*
- Lycium barbarum L. *(gou qi zi)*
- Cuscuta chinensis Lam. *(tu si zi)*
- Psoralea corylifolia L. *(bu gu zhi)*
- Pinellia ternata (Thunb.) Breit. *(ban xia)*
- Salvia miltiorrhiza Bge. *(dan shen)*
- Aucklandia lappa Dence *(mu xiang)*
- Alpinia katsumadai Hayata *(cao dou kou)*

Concurrent with chemotherapy patients in the Western medicine control group received 2 to 3 of the following Western drugs to boost leukocyte counts and/or enhance the immune system: essential amino acids,[6] batyl-alcohol, vitamin B_4, Neupogen[7], inosine, transfer factor, and interferon. Concurrent with chemotherapy patients in the disperse masses Chinese herb control group received a prescription containing:

- Trichosanthes kirilowii Maxim. *(gua lou)*
- Pinellia ternata (Thunb.) Breit. *(ban xia)*
- Allium macrostemon Bge. *(xie bai)*
- Bupleurum chinense D.C. *(chai hu)*
- Citrus aurantium L. *(zhi shi)*
- Ligusticum chuanxiong Hort. *(chuan xiong)*
- Cyperus rotundus L. *(xiang fu)*
- Paeonia lactiflora Pall. *(bai shao)*
- Sparganium stoloniferum Buch.-Ham *(san leng)*
- Curcuma zedoaria (Berg.) Roscoe *(e zhu)*
- Eupolyphaga sinensis Walker *(zhe chong)*
- Buthus martensi Karsch *(quan xie)*

In keeping with convention, when any patient's leukocyte count dropped below 3.5 x 10^9/L they were given blood products such as "leukocyte suspension," whole blood, or blood plasma, etc.[8] When leukocyte levels dropped below 3.0 x 10^9/L chemotherapy treatments were postponed until levels had increased to at least 4.0 x 10^9/L.

As stated above, before treatment all patients' leukocyte counts were above 5.0 x 10^9/L ($p > 0.1$). After treatment, counts for all three groups dropped significantly compared with pretreatment levels, however there were significant differences in the rate of decrease between the three groups. Counts in the combined *support the normal* and chemotherapy treatment group dropped from 5.6 ± 1.4 x 10^9/L before treatment to 4.4 ± 1.03 x 10^9/L after treatment, while counts in the Western drug control group dropped significantly more from 6.3 ± 1.19 x 10^9/L to 3.47 ± 0.98 x 10^9/L ($p < 0.05$). The same pattern occurred in the combined *support the normal* and chemotherapy treatment group versus the combined herbal disperse mass and chemotherapy control group: *support the normal* and chemotherapy treatment group counts dropped from 5.6 ± 1.4 x 10^9/L before treatment to 4.4 ± 1.03 x 10^9/L after treatment, while counts in the combined herbal disperse mass and chemotherapy control group dropped significantly more from 6.4 ± 1.66 x 10^9/L to 2.4 ± 0.84 x 10^9/L ($p < 0.001$). These results suggest that in the short term, at least, the *support the normal* approach of supporting the body is more appropriate in combination with chemotherapy than an herbal anti-tumor approach, though assessment of the advantages of the *support the normal* over the herbal anti-tumor approach would need to take into consideration total results and survival.

In the combined *support the normal* and chemotherapy treatment group leukocyte counts for 100% (all 11 patients) remained above 3.0 x 10^9/L, so all were able to maintain a regular chemotherapy schedule. In contrast a significant number (35.7% or 5 of 14) of Western drug control patients had leukocyte levels drop below this mark ($p < 0.05$). This greater level of immune suppression in the Western drug control group mandated the postponement of chemotherapy treatments. The same pattern held true when comparing the combined *support the normal* and chemotherapy treatment patients with the combined herbal disperse mass and chemotherapy control patients: 66.7% (4 of 6) of whom had leukocyte levels drop below the 3.0 x 10^9/L mark ($p < 0.05$), and therefore could not maintain a regular chemotherapy schedule.

In addition to these results, Chen reports that patients in the combined *support the normal* and chemotherapy treatment group also experienced fewer gastrointestinal and general toxicities than patients in the two control groups, but does not provide data to illustrate this. This study suggests that patients taking *support the normal* therapy experienced significantly less leukocyte decrease than those taking Western immune supporting drugs, and those taking a non-*support the normal* Chinese herbal formula.

In another study, Zhang et al.[9] observed the effect of another *support the normal* prescription on leukocyte levels of 82 patients with mid- to late-stage malignant tumors. All malignancies were confirmed via pathology report, CT or

ultrasound. The treatment group consisted of 59 patients with cancers of the lung, breast, stomach, colon, ovary, esophagus, kidney, and urinary bladder. The control group consisted of 23 patients with mid- to late-stage malignancies of unspecified types. One weakness of this study is that the researchers do not state if there were statistically significant differences in the composition of the two groups, and that the treatment and control groups do not appear to be randomly assigned.

All patients were treated with chemotherapy or radiation therapy. Chemotherapy regimens were selected for appropriateness to each patient's condition, and consisted primarily of cyclophosphamide, cisplatin, 5-fluorouracil, and Adriamycin. Radiation therapy was delivered using a cobalt 60 source or a linear accelerator. In addition the treatment group took an herbal formula consisting primarily of the following botanicals:

- Raw Astragalus membranaceus *(sheng huang qi)*
- Cuscuta chinensis Lam. *(tu si zi)*
- Psoralea corylifolia *(bu gu zhi)*
- Codonopsis pilosula (Franch.) Nannf. *(dang shen)*
- Ligustrum lucidum Ait. *(nü zhen zi)*
- Drynaria fortunei (Kunze) J. Sm. *(gu sui bu)*
- Rehmannia glutinosa (Gaertn.) Libosch. *(xi sheng di)*
- Cornus officinalis Sieb. et Zucc. *(shan yu rou)*
- Lycium barbarum L. *(gou qi zi)*

Leukocyte levels were tested 8 days after treatment, and improvement was defined in two ways: for patients whose leukocyte count was below normal prior to treatment, a post-treatment return to normal levels was considered improvement, while for patients whose leukocyte counts were normal before treatment, a post-treatment level that remained normal was considered improvement. Forty-one of 59 patients in the treatment group had low leukocyte counts prior to treatment. Of these, 37 had leukocyte counts that exceeded 4.0×10^9 /L after treatment. The other patients in the treatment group also appeared to respond well to the treatment, but the researchers neglect to compare overall improvements in leukocyte levels of the treatment and control groups. However, they do compare the rates at which leukocyte count improved in the two groups. The leukocyte recovery rate was 8 days for the 37 treatment group patients whose counts increased from below normal before treatment to 4.0×10^9 /L after treatment, compared with 20.6 ± 1.8 days in the control group. This treatment sub-group's rapid increase in leukocyte count was statistically significant when compared with the control group ($p < 0.01$).

Soluble Interleukin-2 Receptors, Natural Killer Cells, Lymphokine-Activated Killer Cells

Feng et al.[10] studied the effects of *Shenmai* injection on the serum soluble interleukin-2 receptor (sIL-2R), natural killer cell (NK), and lymphokine-activated killer cell (LAK) levels of patients with late-stage cancers of the stomach, colon, and lung. Another protocol based on the traditional herbal formula Generate the Pulse Decoction *(sheng mai san)*, *Shenmai* injection consists of Panax Ginseng C.A. Mey *(ren shen)* and Ophiopogon japonicus Ker-Gawl. *(mai men dong)* in a glucose solution, As this was essentially an uncontrolled study the results must be considered preliminary. However, the patients did show significant improvement after treatment, indicating that a controlled study on this treatment might yield results beneficial to the field of cancer therapy.

The treatment group consisted of 20 patients with adenocarcinoma of the stomach, 20 patients with adenocarcinoma of the colon, 12 patients with adenocarcinoma of the lung, and 8 patients with squamous carcinoma of the lung. All patients were classifiable as being in the late-stage of their illnesses, with metastases to lymph nodes, bones, or other organs. Due to overall debility and the extent of metastases, the patients were considered untreatable with chemotherapy and radiation therapy. At least 1 month prior to commencing treatment with Shenmai injections, all patients ceased using medications known to affect immune system function. During the *Shenmai* injection treatment period patients did not receive any other Western drugs or Chinese herbal treatments that affect the immune system.

The serum interleukin-2 receptor, natural killer cell, and lymphokine-activated killer cell levels of all patients were tested before and after treatment and compared with those of 40 healthy individuals. The differences in these parameters between the pretreatment patients and the healthy individuals was significant ($p < 0.05$), suggesting that the cancer patients had soluble interleukin-2 receptor levels that were abnormally high (894.00 ± 30.83 u/ml) compared with those of the healthy group (260.00 ± 50.20 u/ml). These comparisons also suggested that natural killer cell levels in the pretreatment cancer patients were abnormally low (36.10 ± 9.32%) compared with 60.40 ± 10.60% in the healthy group. Likewise, the cancer patients' lymphokine-activated killer cell levels appeared abnormally low (47.38 ± 1.32%) compared with the healthy group (71.20 ± 11.20%). The differences in all these parameters were statistically significant ($p < 0.05$). The researchers do not explicitly state if these abnormal immune measures were due to past chemotherapy

and radiation or due to cancer-induced malnutrition and immune suppression. Regardless, the abnormal measures appear consistent with the chemotherapy and radiation induced immune suppression of other cancer patients.

The differences in these parameters within the treatment group before and after treatment were also significant ($p < 0.05$), suggesting that *Shenmai* injection improved the immune response. For example, the soluble interleukin-2 receptor level of the cancer patients dropped from 894.00 ± 30.83 u/ml before treatment to 560.00 ± 32.21 u/ml after treatment, thereby bringing it much closer to the 260.00 ± 50.20 u/ml of the healthy group. While the soluble interleukin-2 receptor levels dropped with treatment, the natural killer and lymphokine-activated killer cell levels increased. The natural killer cell level increased from 36.10 ± 9.43% before treatment to 55.23 ± 6.20% after treatment, approaching the 60.40 ± 10.60 % of the healthy group. Likewise, lymphokine-activated killer cells increased from 47.38 ± 1.32% before treatment to 62.53 ± 9.43% after treatment, also approaching the 71.20 ± 11.20 % of the healthy group.

For all of the parameters reported above, there were no significant differences between the patients with stomach, colon, and lung cancer ($p > 0.05$), suggesting the possibility that the immune enhancing properties of Shenmai injections are not specific to patients with any one particular cancer.

Immunologic Function and Clinical Symptoms

Leukocytes, Platelets, Organ Function, Gastrointestinal Symptoms, Oral Ulcers, and Skin Rashes

Liu et al.[11] studied the ability of Chinese herbs to treat the side effects of chemotherapy in 58 patients with osteogenic sarcoma. Patients were assigned to either a combined Chinese herbal medicine and chemotherapy group, or a chemotherapy control group. In addition, all patients underwent surgery appropriate for their specific presentation. While the researchers do not state if there were any statistically significant differences between the two groups, they do note that the two groups were "essentially matched" in clinical presentation, pathological examination, type of surgery, gender, and age. Before and after each chemotherapy treatment routine tests of each patients' blood and urine as well as heart, liver, and kidney functions were checked. In addition, throughout each chemotherapy course general and gastrointestinal toxicities were observed. The researchers do not state how or by whom these toxicities were evaluated.

Two chemotherapy regimens were used in the study: 1) cisplatin and dexamethasone, with the addition of sedative, anti-emetic, diuretic, and unspecified hepato-protective[12] drugs, and 2) methotrexate and vincristine, with hydration and alkalinization therapy, high dose methotrexate with calcium leucovorin rescue (HD-MTX-CFR), and sedative, anti-emetic, and unspecified hepato-protective drugs.

Chinese herbal treatment also consisted of two decoctions, one used with each of the two different chemotherapy regimens. Because cisplatin tends to cause severe nausea and vomiting, the herbal decoction administered with cisplatin drew heavily from the traditional category of herbs used to "harmonize the stomach and stop vomiting." Also used were herbs to improve the appetite and digestion, as well as herbs thought to supplement the blood and protect the liver. The decoction used as an adjunct to cisplatin consisted of:

- Citrus reticulata Blanco *(chen pi)*
- Bamboo breviflora Munro *(zhu ru)*
- Pinellia ternata (Thunb.) Breit. *(jiang ban xia)* treated with ginger
- Amomum kravanh Pierre ex Gagnep. *(bai dou kou)*
- Raw Astragalus membranaceus (Fisch.) Bge. *(sheng huang qi)*
- Pseudostellaria heterophylla (Miq.) Pax ex Pax et Hoffm. *(tai zi shen)*
- Ligustrum lucidum Ait. *(nü zhen zi)*
- Lycium barbarum L. *(gou qi zi)*
- Cuscuta chinensis Lam. *(tu si zi)*
- Artemisia capillaris Thunb. *(yin chen hao)*

For severe vomiting, the following was added:

- Aquilaria agallocha Roxb. *(chen xiang)*

Because methotrexate has a tendency to cause skin rashes, oral ulcers, and other symptoms traditionally attributed to pathological "heat in the blood,"[13] the decoction used adjunctly with the methotrexate-vincristine chemotherapy regimen drew from the traditional "clear heat and cool the blood" category of herbs. It also included herbs thought to supplement the blood and protect the liver. The decoction used with the methotrexate-vincristine regimen consisted of:

- Raw Calcium Sulfate *(sheng shi gao)*
- Anemarrhena asphodeloides Bge. *(zhi mu)*
- Scrophularia ningpoensis Hemsl. *(yuan shen* a.k.a. *xuan shen)*

- Rehmannia glutinosa (Gaertn.) Libosch. *(sheng di huang)*
- Ophiopogon japonicus Ker-Gawl *(mai men dong)*
- Paeonia veitchii Lynch *(chi shao)*
- Paeonia suffruticosa Andr. *(mu dan pi)*
- Raw Astragalus membranaceus (Fisch.) Bge. *(sheng huang qi)*
- Pseudostellaria heterophylla (Miq.) Pax ex Pax et Hoffm. *(tai zi shen)*
- Lycium barbarum L. *(gou qi zi)*
- Ligustrum lucidum Ait. *(nü zhen zi)*
- Eclipta prostrata L. *(han lian cao)*
- Untreated Pinellia ternata (Thunb.) Breit. *(qing ban xia)*
- Artemisia capillaris Thunb. *(yin chen hao)*

For severe skin rashes, the following was added:

- Powdered Bubalus bubalis L. *(shui niu jiao fen)*

Statistically significant reductions in several of the side effects of chemotherapy were observed in the combined Chinese herbal medicine and chemotherapy treatment group. Patients in this group exhibited smaller decreases in blood counts than patients in the control group. With use of the cisplatin regimen decrease in platelet count was significantly less in the combined treatment group ($c^2 = 3.97$, $p < 0.05$), while with the methotrexate-vincristine regimen decreases in both leukocyte and platelet counts were significantly smaller than in the control group ($c^2 = 7.96$, $p < 0.01$ and $c^2 = 18.8$, $p < 0.001$, respectively).

In addition, patients in the combined treatment group also showed fewer signs of organ toxicity when compared with the control group. Serum glutamic-pyruvic transaminase (SGPT), also known as alanine transaminase (ALT), is a measure of liver function that often increases in disease or as a side effect of chemotherapy and other drugs. In this study, with the methotrexate-vincristine regimen a significantly smaller percentage of patients in the combined treatment group showed serum glutamic-pyruvic transaminase (SGPT) levels higher than 130 u ($c^2 = 27.9$, $p < 0.001$), suggesting less liver toxicity. Though a similar pattern was observed in the combined treatment group with the cisplatin regimen, the difference was not significant ($c^2 = 3.48$, $p > 0.05$). Bilirubin levels after use of both chemotherapy regimens showed no evidence of jaundice in either the treatment or control group. Significant difference was also observed in heart function as measured by electrocardiogram (ECG). Irregularities observed via ECG were an elevated or fallen ST segment, and a flattening or inversion of the T wave. With both the cisplatin and methotrexate-vincristine regimens these irregularities occurred significantly less frequently in the treatment group ($c^2 = 8.2$, $p < 0.01$ and $c^2 = 9.24$, $p < 0.01$, respectively), though changes in ECG are not known side effects of either of these chemotherapy regimens. Some tests of kidney function were also performed, though not with enough consistency to yield any statistically useful data.

Gastrointestinal side effects were also significantly reduced in treatment group patients. Nausea and vomiting were significantly less common in the treatment group than in the control group for both the cisplatin ($c^2 = 41.47$, $p < 0.001$) and the methotrexate-vincristine ($c^2 = 47.53$, $p < 0.001$) chemotherapy regimens, though the researchers do not state if this was measured by number of episodes, intensity, or both. By the sixth day after treatment, a significantly greater number of patients in the treatment group had normal appetites; this result was observed with both the cisplatin ($c^2 = 79.9$, $p < 0.001$) and the methotrexate-vincristine ($c^2 = 79.6$, $p < 0.001$) regimens. With the methotrexate-vincristine regimen oral ulcers were an additional side effect. Here again, the combined Chinese medicinal herb and chemotherapy treatment group fared significantly better than the exclusively chemotherapy control group ($c^2 = 1.94$, $p < 0.001$). The occurrence of skin rashes was also significantly lower in the treatment group ($c^2 = 7.89$, $p < 0.01$).

Lymphocyte Proliferative Response, Interleukin-2 Induction Response, and Immunoglobulin M

Zeng et al.[14] studied 171 cancer patients undergoing radiation therapy to evaluate the effects of Codonopsis pilosula (Franch.) Nannf. *(dang shen)* on their immune systems and blood cell development. This study included 69 patients with lung cancer and 102 patients with esophageal cancer. Approximately 76% of patients had stage III disease, while the remainder had stage II disease. All diagnoses were confirmed via endoscopic, cytologic, or pathologic examination. The researchers report that the patients were assigned randomly to treatment and control groups, though an unexplained discrepancy appears in the distribution of patients between the two groups: the treatment group included 32 patients with esophageal cancer while the control group included 70. The distribution of lung cancer patients between the two groups was roughly equal. Nevertheless, the researchers report that these groups were essentially similar in gender, age range, and disease stage.

The two groups received essentially identical radiation treatments. Patients with lung cancer received approximately 6000 Gy for 7 to 8 cycles. Esophageal cancer patients

received 6500 to 7000 Gy for 6 to 7 cycles. In addition, the treatment group received oral administration of Codonopsis pilosula (Franch.) Nannf. *(dang shen)* in gel form.

The results of this study show that Codonopsis pilosula (Franch.) Nannf. *(dang shen)* improved some aspects of the treatment group's immunologic and hematopoietic (blood cell forming) functions. After treatment, the lymphocyte proliferative response decreased in both groups. However, the post-treatment drop in the treatment group was not statistically significant when compared to pretreatment rate, whereas the drop in the control group was (treatment group: 13203 ± 9433 cpm before treatment compared with 12952 ± 9513 cpm after treatment, $p > 0.05$; control group: 16687 ± 10954 cpm before treatment compared with 12639 ± 8246 cpm after treatment, $p < 0.005$). The interleukin-2 (IL-2) induction response rate showed a similar pattern. After treatment the interleukin-2 induction response rate dropped insignificantly in the treatment group from 14971 ± 10392 cpm to 13642 ± 9165 cpm ($p > 0.05$), while in the control group it dropped significantly from 16011 ± 9591 to 1226 ± 7615 ($p < 0.005$).

The treatment group also showed slightly increased levels of immunoglobulin M (part of the humoral immune system) from 159.2 ± 64.0 u/ml before treatment to 172.0 ± 66.0 u/ml after treatment. In contrast, the control group showed a significant decrease in IgM levels from 161.4 ± 62.0 u/ml before treatment to 142.6 ± 51.8 u/ml after treatment ($p < 0.05$). This result suggests that Codonopsis pilosula (Franch.) Nannf. *(dang shen)* can protect against the immunoglobulin M suppressing effects of radiation therapy. Codonopsis pilosula (Franch.) Nannf. *(dang shen)* also appeared to significantly improve immunologic function as measured by delayed hypersensitivity tests.

In contrast to other research on Chinese medicinal herbs, in this particular study Codonopsis pilosula (Franch.) Nannf. *(dang shen)* showed no ability to influence other measures of immune function such as hemoglobin, leukocytes, immunoglobulin G, immunoglobulin A, or C_3. The researchers suggest that the apparent lack of influence on hemoglobin and leukocytes in this study may be explained by the fact that patients were essentially all within normal limits for these two parameters. In contrast, the literature contains other studies showing that this herb does increase hemoglobin and leukocyte levels in patients with levels below normal limits. It is also possible that Codonopsis pilosula (Franch.) Nannf. *(dang shen)* interacts with other herbs in some treatments to produce these immune-enhancing effects, as herbs are normally used within larger prescriptions in traditional Chinese medicine, rather than as exclusive agents.

This study does suggest that Codonopsis pilosula (Franch.) Nannf. *(dang shen)* positively affects lymphocyte proliferative response, interleukin-2 induction response rate, and immunoglobulin M levels in patients receiving radiation therapy, as well as improve immunologic function as measured by delayed hypersensitivity tests.

Leukocytes, BPC, Body Weight, and Gastrointestinal Symptoms

Yu et al.[15] randomly divided 669 patients with stage III and IV gastric carcinoma into two groups. Of these 669 patients, 365 had adenocarcinoma, 189 had poorly differentiated carcinoma, 119 had muco-adenocarcinoma, and 5 had unspecified types of gastric cancer. All patients in the study received chemotherapy consisting of mitomycin, fluorouracil, and vincristine. In addition patients in the treatment group received an herbal prescription consisting primarily of the following herbs:

- Salvia miltiorrhiza Bge. *(dan shen)*
- Rhizoma Atractylodis Macrocephalae *(bai zhu)*
- Lycium barbarum L. *(gou qi zi)*
- Ligustrum lucidum Ait. *(nü zhen zi)*

Slightly more than 50% of patients in each group also received surgery. One potentially significant flaw in this study is that the authors do not provide other details on the composition of the groups, so we are left wondering if there were statistically significant differences between them in regard to age, gender, type or stage of cancer, and use or not of surgery. Results are included here nonetheless, as the rest of the trial appears to be reasonably well designed.

Yu et al. found that the herbal treatment administered in this study significantly improved the hematopoietic (blood cell forming) functions of the treatment group. After treatment only 7.49% of treatment group patients had leukocyte counts under 4000, compared with 33.33% of the control patients ($p < 0.001$). Similarly, only 3.38% of treatment patients had BPC[16] counts below 80,000, compared with 16.67% of control group patients ($p < 0.001$).

Yu et al. also found that clinically observable adverse reactions to the chemotherapy regimen were markedly reduced in the treatment group. For example, 18.6% of patients in the treatment group increased body weight compared with 11.4% of control patients. Only 5.6% of treatment patients showed decreased body weight, compared with 20.4% of control patients. Overall, the difference in body weight between the treatment and control groups was statistically significant ($c^2 = 37.22$; $p < 0.01$). While the authors do not state how appetite or nausea were evaluated,

treatment patients also appeared to fare significantly better in this area than control patients. 8.0% of treatment patients showed reduced appetite compared with 35.0% of control patients ($c^2 = 76.7578$; $p < 0.01$). Likewise, only 8.45% of treatment patients experienced increased nausea, compared with 32.5% of control patients ($c^2 = 63.0643$; $p < 0.01$). There was also a statistically significant difference in vomiting, with only 5.6% of treatment patients showing increased vomiting, compared with 15.3% of control patients ($c^2 = 17.7982$; $p < 0.01$). In this study the leukocyte, BPC levels, and adverse reactions to chemotherapy of treatment group patients were better than control patients and these differences were statistically significant.

Leukocytes, T Lymphocyte Proliferative Response, Macrophage Activity, and Body Weight

In a clinical trial that included 176 patients with cancers of the digestive tract, Li[17] found that injection of an herbal medicine preparation reduced the immune compromising effects of chemotherapy. Overall, the design of this study is fairly reasonable, however the researcher fails to report whether there were any significant differences between the treatment and control groups. The results of this study should therefore be considered cautiously. This clinical trial involved patients with the following types of cancers:

- Stomach cancer (80 patients)
- Colon cancer (81 patients)
- Esophageal cancer (15 patients)

Over half of the patients in the study had stage III or IV disease. All 176 patients in the study had undergone at least exploratory surgery, with many of them receiving further surgical procedures specific to their condition.

The patients were divided into three groups: a combined Chinese herbal medicine and chemotherapy treatment group, a Chinese herbal medicine control group, and a chemotherapy control group. As noted earlier, the researcher does not report whether any significant differences existed between the three groups. Patients in the combined herbal medicine and chemotherapy treatment group received a chemotherapy regimen consisting of mitomycin C, 5-fluorouracil, and vincristine. Concurrently, they received injections of a glucose saline solution containing extracts of Codonopsis pilosula (Franch.) Nannf. *(dang shen)* and Astragalus membranaceus (Fisch.) Bge. *(huang qi)*. Patients in the exclusively herbal medicine control group and the exclusively chemotherapy control group received the respective component of the regimen described for the combined therapy group.

Several measures suggested that Chinese herbs improved immunologic function of patients. During treatment, the leukocyte levels of 100% of the patients in the combined therapy group remained above 3×10^9 / L. This sustained leukocyte level enabled all combined therapy patients to complete their chemotherapy regimens. In contrast, the leukocyte level of 26.5% of patients in the chemotherapy control group dropped below 3×10^9 / L, making it impossible for these patients to complete chemotherapy. The chemotherapy completion ratio between the two groups was significant ($c^2 = 22.87$, $p < 0.01$[18]), suggesting that the herbal medicine treatments stabilized leukocyte levels so that patients could obtain maximum benefit from the chemotherapy regimen.

The researchers also found that the T lymphocyte proliferative response in the combined treatment group increased significantly after treatment ($p < 0.001$), while no significant increase was observed in the chemotherapy control group ($p > 0.05$). In the exclusively herbal medicine group the percentage of lymphocytes also increased significantly after treatment ($p < 0.005$). The researchers also note that in both the combined therapy and exclusively Chinese herbal medicine groups total blood viscosity[19] decreased significantly after treatment ($p < 0.05$), though no relevant data was provided for the chemotherapy control group. The researchers do not provide any quantitative values for viscosity. While interesting, p values comparing the treatment and control groups were not provided for the results mentioned in this paragraph.

In addition, the macrophage activity of the combined therapy treatment group and the exclusively herbal medicine control group *increased* significantly after treatment, while that of the chemotherapy control group *decreased* significantly. Macrophage activity for the combined therapy group was $32.56 \pm 1.40\%$ before treatment, and $44.46 \pm 1.67\%$ after treatment ($p < 0.001$). Similarly, macrophage activity in the exclusively herbal medicine group increased from $34.23 \pm 1.47\%$ before treatment to $46.23 \pm 1.92\%$ after treatment ($p < 0.001$). In contrast, macrophage activity in the chemotherapy control group decreased from $38.91 \pm 1.59\%$ before treatment to $32.23 \pm 1.88\%$ after treatment ($p < 0.001$). Macrophage activity in the combined therapy and exclusively Chinese herbal medicine groups increased significantly after treatment compared to the chemotherapy treatment group ($p < 0.001$).

The researchers also provide data on changes in body weight. After treatment, patients in the combined therapy group showed an average weight gain of 1.05 ± 0.25 kg, a significant *increase* over pretreatment levels. In comparison, patients in the chemotherapy control group showed a signif-

icant post-treatment *decrease* in body weight by 1.22 ± 0.26 kg. The increase in body weight observed in the combined therapy group was very significant ($p < 0.001$) compared to the decrease observed in the chemotherapy control group, suggesting that the herbal medicine decreased impairment to the digestive system caused by conventional Western medical intervention. The researchers also note that the exclusively Chinese herbal medicine group showed a significant increase in post-treatment body weight by 1.46 ± 0.24 kg ($p < 0.001$), but they do not provide a statistical comparison with the chemotherapy control group.

Nephrotoxicity

Cisplatin is a chemotherapeutic drug used in the treatment of a wide variety of cancers. High doses of cisplatin can injure the kidneys, and this nephrotoxicity is a dose-limiting factor in clinical use of cisplatin. In a non-blinded, randomized, controlled clinical trial, Cheng et al.[20] found that a Chinese herbal decoction significantly reduced some of cisplatin's nephrotoxic effects. Cheng et al. randomized 95 cancer patients into two groups, a treatment group that received chemotherapy, reduced-dosage hydration therapy, and an herbal medicine decoction called *Qi Ling Tang*, and a control group receiving chemotherapy and conventional hydration therapy. One significant flaw of this study is that the treatment and control group therapies appear to differ slightly beyond the administration of the herbal decoction to the treatment group: the researchers note that the control group also received unspecified diuretics and anti-nausea drugs, but do not report administering these drugs to the treatment group. Further, the treatment and control groups also differed in the amount of hydration therapy they received. The total sample of 95 persons in this study included patients with the following cancers:

- lung cancer (33 patients)
- nasopharyngeal cancer (32 patients)
- colon cancer (9 patients)
- esophageal cancer (7 patients)
- stomach cancer (6 patients)
- breast cancer (3 patients)
- other cancers (5 patients)

Prior to commencing treatment all patients had blood urea nitrogen (BUN) and creatinine (Cr) levels within normal limits. Blood urea nitrogen and creatinine were measured after treatment to assess degree of nephrotoxicity.

Patients in both the treatment and control groups received combined chemotherapy regimens in which cisplatin was the primary drug. Concurrent with cisplatin usage, patients in the control group were given hydration therapy consisting of 3500 to 4000 ml on the first day, followed by 1500 to 2000 ml on the second and third days. As noted above, patients in the control group were also given diuretics and anti-nausea drugs. Concurrent with cisplatin usage, patients in the treatment group were given reduced-dosage hydration therapy consisting of 1000 ml on the first and second days. In addition they received *Qi Ling Tang,*an herbal medicine decoction consisting primarily of the following herbs:

- Astragalus membranaceus (Fisch.) Bge. *(huang qi)*
- Poria cocos (Schw.) Wolf *(fu ling)*
- Rhizoma Atractylodis Macrocephalae *(bai zhu)*
- Codonopsis pilosula (Franch.) Nannf. *(dang shen)*
- Glycyrrhiza uralensis Fisher *(gan cao)*

Prior to commencing treatment, and after each cisplatin cycle, nephrotoxicity was measured by several biological parameters.

After treatment, the average blood urea nitrogen (BUN) and creatinine (Cr) levels were significantly lower in the treatment group than in the control group, suggesting that use of the herbal medicine decoction lowered the degree of cisplatin nephrotoxicity. Post treatment the average blood urea nitrogen (BUN) level in the treatment group was 4.52 ± 1.10 mmol/L compared with 5.04 ± 1.37 mmol/L in the control group ($p < 0.05$). The average post-treatment creatinine (Cr) level was 109.0 ± 20.5 μmol/L in the treatment group, compared with 120.8 ± 27.6 μmol/L in the control group ($p < 0.01$). These results suggest that *Qi Ling Tang* decreased the nephrotoxic effects of the chemotherapeutic drug cisplatin, since elevated blood urea nitrogen and creatinine are correlated with nephrotoxicity. The decreased nephrotoxicity is unlikely to be due to the differences in hydration between the treatment and control groups since lower hydration in the treatment group would be expected to lead, if anything, to greater nephrotoxicity. However, as noted above, these results must be evaluated with caution as the diuretics and anti-emetics given to the control group might have played a role in the greater nephrotoxicity observed in this group.

Pain

Liu et al.[21] studied 486 patients with pain caused by cancer or cancer treatment to test the effects of Chinese herbs in a "4-step analgesic ladder" of drug administration. Though this was an uncontrolled, non-blinded study the results are

interesting nonetheless. More rigorous future studies might yield more scientifically sound data. Despite the shortcomings of this study, the results indicate that Western cancer patients may also benefit from Chinese herbal treatment of cancer-related pain. The types of cancers represented in this study were:

- primary liver cancer (285 patients)
- secondary late-stage liver cancer[22] (11 patients)
- colon cancer (108 patients)
- lymphoma: Hodgkin's disease (4 patients), non-Hodgkin's lymphoma (37 patients)
- esophageal cancer (10 patients)
- lung cancer (10 patients)
- breast cancer, post-surgery (9 patients)
- nasopharyngeal carcinoma (10 patients)
- chordocarcinoma (1 patient)
- sebaceous gland carcinoma (1 patient)

The study included 401 men and 85 women. Age range was 16 to 85 years with the average age for all cancer types between the early forties and fifties.[23]

Evaluation of pain was based on the WHO standard of cancer pain quantification introduced by Ventaffridda. The system used in this study and the percentage of patients at each level was as follows:

- Level 0: No pain. (0% of patients in this study)
- Level 1: Slight pain which does not impact patient's ability to sleep (71.6% of patients in this study)
- Level 2: Moderate pain which negatively impacts the patient's ability to sleep. (22.8% of patients in this study)
- Level 3: Severe, unbearable pain accompanied by facial pallor, sweating, and cold limbs. (5.6% of patients in this study)

The pain experienced by patients in this study was due to a variety of causes, including but not limited to increased tension on the liver capsule, bleeding below the liver capsule, rupture of the liver, gastrointestinal hemorrhage, irritation caused by secreted substances, tumors causing compression of surrounding tissues, metastases to the bones, bleeding due to extensive metastases, and pain caused by radiation therapy.

Patients were divided into six groups based on traditional Chinese medicine diagnostic categories. For example, patients diagnosed with "damp obstruction" were given herbs appropriate to that condition, while those with "blood stasis" were given a different prescription.[24] Any given patient received a small subset of the following main herbs used in this study:

- Codonopsis pilosula (Franch.) Nannf. *(dang shen)*
- Rhizoma Atractylodis Macrocephalae *(bai zhu)*
- Poria cocos (Schw.) Wolf *(fu ling)*
- Astragalus membranaceus (Fisch.) Bge. *(huang qi)*
- Immature fruit of Citrus aurantium L. *(zhi shi)*
- Bupleurum chinense D.C. *(chai hu)*
- Magnolia officinalis Rehd. et Wils *(chuan hou po)*
- Fruit of Akebia trifoliata (Thunb.) Koidz. var. australis (Diels) Rehd. *(ba yue zha)*
- Atractylodes lancea Thunb. *(cang zhu)*
- Magnolia officinalis Rehd. et Wils *(hou po)*
- Ripe fruit of Citrus aurantium L. *(zhi ke)*
- Pinellia ternata (Thunb.) Breit. *(ban xia)*
- Artemisia capillaris Thunb. *(yin chen hao)*
- Polyporus umbellatus (Pers.) Fr. *(zhu ling)*
- Alisma plantago-aquatica L. var. orientale Samuels *(ze xie)*
- Rheum palmatum L. *(da huang)*
- Adenophora tetraphylla (Thunb.) *(sha shen)*
- Ophiopogon japonicus Ker-Gawl *(mai men dong)*
- Lycium barbarum L. *(gou qi zi)*
- Rehmannia glutinosa (Gaertn.) Libosch. *(sheng di huang)*
- Typha angustifolia L. *(pu huang)*
- Trogopterus xanthipes Milne-Edwards *(wu ling zhi)*
- Corydalis yanhusuo W.T. Wang *(yan hu suo)*
- Rubia cordifolia L. *(qian cao)*
- Raw Calcium Sulfate *(sheng shi gao)*
- Anemarrhena asphodeloides Bge. *(zhi mu)*
- Oryza sativa L. *(geng mi)*
- Glycyrrhiza uralensis Fisher *(gan cao)*
- Areca catechu L. *(da fu pi)*
- Scutellaria barbata D. Don *(ban zhi lian)*
- Rhaponticum uniflorum (L.) DC. *(lou lu)*
- Massa Fermentata *(shen qu)*
- Hordeum vulgare L. *(mai ya)*
- Bamboo breviflora Munro *(zhu ru)*
- Buthus martensi Karsch *(quan xie)*
- Scolopendra subspinipes mutilans L. Koch. *(wu gong)*

The first step in the 4-step analgesic ladder to treat pain was the administration of Chinese herbal medicine. If pain continued with sudden or frequent onset other traditional Chinese medical treatments were employed. These treatments included external use of herbal plasters such as Plaster with Bufo Bufo Gargarizans Cantor *(Chan Su Gao)* or Pain Relieving Plaster with Moschus Moschiferus L. *(She Xiang Zhi Tong Gao)*. If pain still persisted or was relieved for only short periods traditional acupuncture or acupoint injection were used. Unfortunately, the researchers do not state in how many cases these additional methods were utilized, nor do

they state what substances were injected at acupoints, though normally these would be herbal substances appropriate for the patient's condition, as determined by traditional diagnostic methods. (Pain-relieving herbal plasters and acupuncture treatment are available in North America, though acupoint injection generally is not.)

If the Chinese medical treatments did not result in complete resolution of pain, treatment progressed to step 2 of the analgesic ladder, consisting of Chinese treatment with the addition of the non-steroidal anti-inflammatory drug indomethacin. If complete pain resolution was not achieved at step 2, treatment proceeded to step 3: Chinese treatment with increased dosage of indomethacin and/or use of salicylates such as phenylbutazone. If after use of steps 1, 2, and 3, pain resolution was achieved for only short periods or was otherwise unsatisfactory, treatment proceeded to step 4: Chinese treatment with the addition of opioid drug administration.

All 486 patients in the study achieved some level of pain relief, though 3 died of unspecified causes before reaching step 4 of the analgesic ladder. With step 1, consisting only of Chinese herbal and other traditional therapies, 52.1% of patients in the study achieved complete resolution of pain, with the majority of these (71.6%) being patients with level 1 pain (pain that did not impact their ability to rest). Step 1 treatment also resulted in improvement for 65.8% of patients with level 2 pain (moderate pain that negatively impacted patients' ability to sleep), and for 11.1% of patients with level 3 pain (severe, unbearable pain accompanied by facial pallor, sweating, and cold limbs). With steps 2 and 3 (Chinese therapies plus non-opioid Western drugs) complete pain resolution reached 96.5%. Only 3.5% of patients in the study had to resort to use of opioids with Chinese therapies (step 4) to attain pain relief. No data is provided on the duration of the trial or the frequency of observation of each patient or each phase.

The 4-step analgesic ladder used in this study provided notable relief of pain associated with cancer and conventional Western cancer treatments. The effective rate for pain due to radiation therapy was 100%. Broken down by cancer type, the 4-step analgesic ladder was effective for 91.9% of patients with liver cancer, 62.8% of patients with malignant lymphoma, 86.1% of patients with colon cancer, 100% of patients with breast, lung, esophageal, and nasopharyngeal cancers, and 50% of patients with chordoma and sebaceous gland carcinoma.[25] The researchers note that no obvious side effects were observed with the Chinese herbal or other traditional Chinese treatments. They also suggest that these treatments reduced the side effects and addictive nature of the Western analgesic drugs, but present no data to support this.

Conclusion

The above studies suggest that when used in conjunction with conventional Western cancer interventions Chinese herbal medicines improve the immune system as measured by levels of T lymphocytes, the monoclonal antibody T_1, the T_4 to T_8 (helper to suppressor) T cell ratio, soluble interleukin-2 receptors, natural killer cells, lymphokine activated killer cells, leukocytes, platelets, BPC, and immunoglobulin M. Other immunologic parameters that showed apparent improvement included the lymphocyte proliferative response, the interleukin-2 induction response, and macrophage activity. As a caveat, it should be noted that improvements in the immune function of human cancer patients have not been clearly linked to clinically significant benefits such as fewer infections, improvement of symptoms, remission, recurrence, or survival rates, though future research may yield evidence of these effects.

Regardless, Chinese herbal treatment also appeared to improve liver and heart functions, and to moderate clinical side effects ranging from gastrointestinal symptoms and reduced body weight, to oral ulcers and skin rashes. Finally, Chinese herbal medicine showed potential for reducing chemotherapy caused nephrotoxicity, and appeared capable of effectively treating pain related to both Western anticancer interventions and pain caused by the cancer disease process itself. These studies show that a large number of Chinese herbal medicines may be useful in treating the side effects of chemotherapy and radiation therapy. The broad range of cancer types included in this review suggests that these results may be applicable to patients with many different types of cancer: from common carcinomas such as those affecting the lung, breast, and liver to rarer carcinomas such as cancers of the esophagus and nasopharynx.

None of the articles cited in this review specifically address the issue of possible side effects of the Chinese herbal treatments used. This may simply be because nothing has caused the Chinese physicians and researchers to assume or suspect that the herbs have toxic side effects. Indeed, most of the herbs cited in these trials are quite common and have been used in China for hundreds, if not thousands, of years with few to no reported side effects. While this fact does not conclusively rule out the possibility of herbal side effects, it does suggest that they may be negligible or completely absent. Nevertheless, future researchers would serve us well by exploring toxicity and possible adverse drug interactions as well as efficacy.

Also unaddressed in these studies are a few issues that may have positively influenced results. First, none of the researchers address the issue of "treatment effect," that is how

the additional attention and care received by those in the treatment groups may have impacted outcome. Second, none of the researchers explore sociological or anthropological factors—such as the impact of utilizing culturally appropriate medicine—that may have positively affected treatment group patients. Hopefully, future research performed on the use of Chinese medicinal herbs in cancer treatment will not only be more scientifically solid and inclusive of both efficacy and toxicity data, but will also address these significant issues.

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7. The correct translation for the term ¿˚—™…˝ (li xue sheng) is most likely "Neupogen", though some Chinese sources translate the term as "leucogen." Neupogen is also known as G-CSF (granulocyte colony stimulating factor), a recombinant hematopoietic growth factor usually given to boost the neutrophil (granulocyte) count, and thereby reduce the duration of neutropenia and the incidence of infection in patients receiving chemotherapy.
8. Chen does not explain the nature of "leukocyte suspension" (∞◊œ∏∞˚ªÏ–, "∫), nor explain why it and/or blood plasma were given to patients with low leukocyte counts. These are not standard treatments in the West — typically Neupogen would be the standard treatment (see note 7). This author thanks Isaac Cohen, L.Ac. for pointing out this disparity in treatment approach.
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12. Chinese researchers have derived hepato-protective drugs from herbs, such as Biphenyl Dimethyl Dicarboxylate from Schisandra chinensis (Turcz.) Baill. *(wu wei zi)*, but it is unclear whether the drugs mentioned here are of Western or Chinese origin. The author thanks Isaac Cohen, L.Ac. for providing this information.
13. "Heat" and "cold" are two frequently used traditional Chinese medical diagnostic categories. "Heat" symptoms include sensations of heat in the body, a red face, and a rapid pulse, etc. and are usually treated with herbs thought to be cooling in nature. "Cold" symptoms include sensations of cold in the body, a pale or white complexion, and a slow pulse, etc. and are usually treated with herbs thought to be warming in nature.
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18. Later in the article this p value is reported as $p < 0.001$. Regardless of which figure is accurate, the results are statistically significant.
19. In accordance with traditional Chinese medical principles and supported by some Chinese research, blood stasis and blood viscosity are important in diagnosis and cancer prognosis, as a correlation has been observed between blood viscosity and disease progression, metastasis, and survival. To date there is no correlating Western scientific data on this topic. For more information please see Yan De-Xin, *Aging and Blood Stasis: A New Traditional Chinese Medical Approach to Geriatrics,* (Boulder: Blue Poppy Press), 1995. Thanks to Isaac Cohen, L.Ac. for elucidating this point.
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22. It is unclear whether "secondary" here refers to recurring liver cancer or to liver metastases.
23. For the average ages by the major types of cancer represented, see the original text.
24. "Damp obstruction" and "blood stasis" are two of many traditional Chinese medical etiologies of pain. "Damp obstruction" describes an excess of fluids that obstruct normal blood and fluid circulation, thereby causing pain. "Blood stasis" describes a similar situation, but here the obstruction and pain are attributed to stagnated blood collecting in a particular area of the body.

25. More detailed figures are provided in the original article but could not be included here due to space limitations.

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