Introduction — Cancer and Ancient Chinese Medicine

Although not documented as cancer in the ancient days, this pathological condition should have been in existence for as long as the human race exists. The word “tumor” (瘤) in Chinese, started to appear in prehistoric cave carvings in North-West China, as far back as 1000BC. The word “tumor” probably referred to the appearance of a lump over some parts of the human body. Another word (癌), which carried the same literal meaning, appeared around 1200AD. This medical term referred to ulcerative lumps, which were often described together with

Chinese Medicine and Cancer Treatment in Hong Kong
A General Review

Cancer

is a pathological condition. Removal of the cancer is a necessity in the treatment process. However, removal has reached its limitations as the cancer could, in the first place, be too extensive, or, in spite of the removal, recurrence still occurs. When the pathological process is not stopped, no matter how effective is the cancer removal, the formation of cancer is going to be repeated. Cancer treatment has therefore gone beyond the stage of cancer removal and other approaches such as controlling the blood supply, initiating apoptosis, and regulating the responsible genes, are considered important. The treatment approach needs to be modified from a single target, eliminative direction towards a multiple target, holistic direction. Chinese medicine lacks a perfect understanding of the causative pathology, hence it follows a multi-target holistic approach. As new systems of cancer treatment are not yet mature, using Chinese medicine as an adjuvant therapy could be an innovative and practical investment, to bring about better results of cancer control.
deformities in the limbs, kyphosis in the spine and occurrences of sinuses and fistulae somewhere in the human body. Descriptions of treatment related to such tumorous conditions have been scattered, neither systematic nor specialized. When the causative pathology was unclear or not known, clinical presentations described would be mixed, and with regards to treatment, the local appearances would invite policies like those used for infection and inflammation, while the general physiological state of the individual sufferer would provide other basis of treatment. Cancerous conditions were likely to initiate general states of anemia or debilitation, and clues relevant to cancer therapy might also be found under the treatment schemes of these clinical states.

The ancient Chinese healers, therefore, formed three main principles of treatment approach to cancerous conditions. The pathological background was thought to be related to:

(i) toxic internal derangement;
(ii) circulatory stagnation; or
(iii) collapse of defence.

Treatment policy therefore followed the alleged pathological background, so that

(i) toxic derangement was balanced with detoxication through the cooling down of heat;
(ii) circulatory stagnation was removed with the activation of blood movements and resolution of bruises; and
(iii) collapse of defence was rebuilt with the promotion of internal strength.

In addition, the clever ancient healers have observed that toxic material could have controlling effects on cancer growth, hence a system of treatment relying on the use of toxic preparations to counteract toxic derangements was also developed.

**Interest Over the Use of Herbs Against Cancer**

Since cytotoxic agents after extensive research, appeared on the market as powerful drugs to control cancer growth, the search for new cell-killing items has never stopped. Successful examples demonstrated that powerful cytotoxic material could exist within herbs; like flowers, leaves and tree barks are well shown in the examples of vincristine from periwinkle flower, artemisinin from qinghao leaves and taxol from yew tree barks.

As cytotoxic agents were known to be useful but not ideal because of generalized toxic effects and the readiness of developing drug resistance for some items, research on other mechanisms of cancer control flourished. The prevention of drug resistance, the induction of apoptosis, the blockage of cancer cell messages, the restriction of angiogenesis, and the promotion of immunological defence ability, have all gained extensive attention, and explorations for herbal components with specific cancer control abilities were started. *Rhizome chuanxiang, radix stephaniae tetrandrae* and *mylabris phalerate pallus* have been identified for the prevention of cytotoxic drug resistance. For apoptosis, the ancient formula using arsenic trioxide brought on a breakthrough in childhood leukemia; after that, other herbs, viz. *Radix miltiorrhiza* and *Radix Trichosanthis* were found to induce apoptosis of cancer in all cell lines in the laboratory. A number of herbs were found capable of slowing down cancer cell division by blocking cytokine messages; these were: *Radix Astragalus*, *Radix Angelica sinuses*, *Solani Nigri* and *Radix Puerariae*. Angiogenesis is an important facilitating factor for cancer growth. Pharmacological agents on anti-angiogenesis have already been developed and are being sold on the market. Herbs like *Herba Scutellariae Barbatae* (七葉一枝花，重樓) and *Rhizoma Paridis* (白及根) were known to possess anti-angiogenetic properties. A lot of work had already been done on the broad front of immunological defence, both in the laboratory and biochemically, on preparations of fungal origin. One of the most popular fungal product being used in South China as an adjuvant agent during and after cancer treatment, is *Coriolus versicolor*. Frameworks on the study of cytotoxicity, anti-angiogenesis and immunomodulation are represented schematically in Figs. 1 to 3.
A number of herbs were found capable of slowing down cancer cell division by blocking cytokine messages.

A Practical Approach to the Clinical Use of Chinese Herbs for Cancer Patients

While it is realistic to look forward to the production of effective anti-cancer drugs developed from herbs, which may follow new innovative pathways of cancer control, one could choose to start clinical research using herbs of expected promise immediately. The need to look for innovative supplement to the conventional cancer therapy is obvious because of its disappointing limitations and the cytotoxic complications. The current fashion on pharmacological research is aiming at molecular targets with an eventual aim towards drug production.

However, on the practical side, in Hong Kong’s Chinese community, over 90% of cancer patients are receiving supplementary treatments of various natures in an attempt to gain better chances of cancer control and survival. It is therefore justified to explore the effectiveness of the adjuvant use of the popular herbs through clinical trials. Such efforts should not be viewed as proper endorsement of popular beliefs. But rather, they are practical, responsible plans of clinical study, if well designed according to the modern concepts of good clinical practice, could have a lot to offer in the holistic care of cancer treatment. After all, developing an innovative drug is expensive and time-consuming. The
use of herbal supplements could be readily administered and safety is not difficult to ensure.

Of all the possible pathways of action offered by different herbs, since their active components and chemistry are still unknown, the most logical selection would be those that aim at holistic support through nutritional or immunological modulations. Innovative new pharmaceuticals offer specific, immediate effects. Holistic support offers non-specific, slow influences that could be defined as supplementary, palliative or preventive.

A reasonable aim of cancer treatment is not only to remove the tumor mass and the harmful cells, but also to stop the dynamic process that has led to the development of the cancer. The logical expectation is: the holistic support works through complicated, yet unknown indirect pathways, whereby the cancer development process is kept at bay. In the following paragraphs, examples of clinical trials using herbal preparations as adjuvants will be given.

**A Clinical Trial Using Herbal Preparation as Supplements to Chemotherapy for Cancer**

A Phase II, randomized, placebo-controlled trial using herbal preparations was done at the Prince of Wales Hospital of Hong Kong in 2002–2004, whereby 60 + 60 patients suffering from advanced cancer of the breast or colon were being treated with cytotoxic chemotherapy. The use of herbal preparations as supplementary support to control pain and other symptoms, tumor size and survival were checked. A qualified, experienced Chinese medicine expert served as the partner of the oncologist in charge. The expert was responsible for the prescription of the herbal preparations given according to the symptom complexes and their individualized indications. The results of this study indicated that symptom control over pain, appetite and diarrhea were improved more with the herbal medicine group compared with the placebo group. The most remarkable improvement was observed with the control of nausea. The important parameters of survival, tumor size and chemotherapy-induced hematological toxicity were not improved in both groups.

**In Hong Kong’s Chinese community, over 90% of cancer patients are receiving supplementary treatments of various natures in an attempt to gain better chances of cancer control and survival.**

This randomized controlled trial was carefully planned to objectively measure the efficacy of herbal supplements in attempts to make chemotherapy more comfortable. Thousands of cancer patients have been relying on the support from traditional Chinese medicine healers who prescribe individualized treatment. This form of individualized treatment was fully respected in the trial. The results might have supported the popular supplementary use of herbal medicine because it did no harm and was alleviating symptoms like nausea. However, the results failed to improve survival and other vital parameters like cytotoxic complications affecting the hematological state.

**A Clinical Trial Using a Herbal Formula as Supplement to Radiotherapy for Cancer Patients**

The second trial was done in the same hospital on nasopharyngeal cancer patients receiving radiotherapy, which was the standard curative treatment for this cancer, common for the male population of South China. It was designed as a small pilot, randomized, placebo-control and double-blinded trial. Apart from general fatigue, the head and neck symptoms related to irradiation were well-known and included local skin irritations, muscle tightness and spasm, mouth stiffness, loss of taste, mouth stiffness, loss of taste, loss of salivation, dry eyes, etc.

For this study, a uniform herbal formula consisting of two herbs was used and the principle of generalization was observed rather than individualization of treatment. This preparation contained a fungal component, *Coriolus*, which had the reputation of immuno-boosting property. For this reason, the immunological state of the 20 + 20 clients was assessed before and after four months of treatment.

Results of the pilot study revealed that fatigue was significantly relieved in the treatment group compared with placebo ($p \leq 0.05$), but the general trend of decline in the quality of life score in both groups after irradiation showed no difference between the two groups. In the immunological assessment, T-lymphocytes suppression was obvious in both groups but the decline was significantly less in the herbal supplement group.

The objectives on the use of herbal supplement in this study were not confined to the control
of symptoms arising from the radiotherapy. Instead, possible positive effects of the herbal preparation in the promotion of immunological defense were explored. Moreover, this cancer is unique in that it possesses a serological marker, the DNA of Epstein-Barr Virus (EBV-DNA), which offers a direct indication of cancer activity. A significant decline indicates a positive control of cancer growth. After radiotherapy, EBV-DNA dropped dramatically. The herbal study tried to look for possible supplementary effects of the *Coriolus* preparation, which might initiate further drops of EBV-DNA. No difference, however, was seen between the herbal and control groups, both of which showed limited changes of the DNA. This observation might indicate that the *Coriolus* preparation did not work through a direct control of the cancer growth, but rather indirectly via the immuno-supportive pathway.

A Clinical Trial Using Herbal Preparation as a Palliative Agent in the Treatment of Multiple Bone Metastases

This was a clinical trial done in the same hospital in Hong Kong on 46 + 46 patients known to be suffering from multiple bone metastases arising from various types of cancer. It was a randomized, comparative trial using a herbal formula and a bisphosphonate. The assessments included bone mineral density (BMD), control of secondaries, biochemical bone markers, quality of life and adverse effects.

The design was based on observations on the use of bisphosphonates for bone secondaries. Bisphosphonates suppress the bone resorption initiated by osteoclasts without affecting the osteoblasts. The newer bisphosphonate preparations were first used for bone metastases when they were found to be effective in the control of pain arising from bone destruction. Later, it was observed that bisphosphonate also lessened the destruction of bone, hence it might even prevent more secondary deposits. It was therefore deduced that if there were herbal agents which supported bone mineral density, the same agents should have protective effects on bone metastases like bisphosphonates. A herbal preparation active for the support of osteoporosis was therefore compared with a bisphosphonate (clondronate), and the parameters of assessment followed closely those of BMD studies.

A total of 46 + 46 patients were recruited randomly into the clondronate and herbal groups. Six months of respective treatment was given, followed by six months of further assessment.

The study was not totally successful because too many (45%) recruited patients died before the completion of treatment. Analyzing the fully treated patients, the herbal group showed some trend of superiority over the bisphosphonate group in pain control and the average quality of life scores.

As some modern drugs non-specific for cancer treatment have started to be used in cancer patients to achieve secondary benefits, such as the control of angiogenesis and the relief of bone pain, many herbal preparations could be studied and developed for similar effects in an attempt to look for practical solutions of symptom control for cancer patients.

A Clinical Trial Using Herbal Preparation as Preventive Agent for Immuno-Support

Many herbal items are popular among the general public of the Chinese community for use as health promotion agents. These are particularly popular among the elderly, the frail and weak after illnesses, survivors of serious accidents, and those bothered by different forms of derangement. Apart from the large choices of food rarities, well-known energizers and life-supporting herbs include the ginsengs, cordyceps, gonoderma, and other fungi.

A large scale clinical trial using healthy volunteers was designed in 2002 to examine the immuno-modulating effects of a simple preparation consisting of a fungus, *Coriolus*, and another herb. It was a randomized, placebo-controlled, cross-over trial. A group of 50 volunteers given the herbal preparation was tested against 50 others who received placebos. Four months of consumption was required for each group, followed
by a cross-over for another four months.

The results showed very convincing immuno-boostering effects of the herbal preparation on all immunological parameters—T-helper cells, T-suppressor cells, T-helper/T-suppressor ratio, B-lymphocyte levels were all increased. Quality of life also showed significant improvement when the volunteers were maintained on the herbal preparation.

System Review of Effects of Coriolus on the Survival of Cancer Patients

This review was done by E. Wong of the Institute of Chinese Medicine at the Chinese University of Hong Kong in 2005. The main outcome measures were set at the survival rate at five years and adverse effects encountered. Fifty-eight potentially eligible trials were identified, of which 12 met the criteria for inclusion in the data-analysis. One trial was split into two sets of comparisons because there were three treatment groups. Therefore, a total of 13 comparisons were included in the meta-analysis. Most trials were of poor to average quality. The overall five-year survival rate was significantly better in patients receiving Coriolus than in patients receiving the same conventional cancer treatment without Coriolus RR = 1.11 (95% CI, 1.07–1.16), but sub-group analysis showed that the significant effect was restricted to poor quality trials. Among patients randomized to receive Coriolus, there was a 6–12% absolute reduction in the five-year mortality. There was no significant difference in the risk of adverse events in the groups treated with and without Coriolus. The benefit remained after possible publication bias was corrected. It was therefore concluded that Coriolus had a beneficial effect on the survival of cancer patients. This seemed to be particularly evident when Coriolus was used in conjunction with chemotherapy.

Many other clinical trials have been done on the immuno-modulating effects of various herbs, particularly those of the fungal family. The clinical observation from volunteers further support these past reports. Nevertheless, in spite of the positive evidences of immunological boosting effects, how that translates to the direct applicative of cancer control is still not understood.

Conclusion

Cancer is a pathological condition. Removal of the cancer is a necessity in the treatment process. Removal has been achieved through surgery, radiotherapy or chemotherapy. However, removal has reached its limitations as the cancer could, in the first place, be too extensive, or, in spite of the removal, recurrence still occurs, an all too frequent occurrence.

Cancer is a pathological process in which the cells either grow too much or too rapidly; or the normal programmed cell death (apoptosis) is not functioning properly. When the pathological process is not stopped, no matter how effective is the cancer removal, the formation of cancer is going to be repeated.

Cancer treatment has therefore gone beyond the stage of cancer removal and other approaches aiming at the causations, such as controlling the blood supply, initiating apoptosis, and regulating the responsible genes have started. The treatment approach needs to be modified from a single target, eliminative direction towards a multiple targets, holistic direction. Chinese medicine lacks perfect understanding of the causative pathology, hence it has followed a multi-target holistic approach. As new systems of cancer treatment are not yet mature, using Chinese medicine as an adjuvant therapy, could be an innovative and practical investment, to bring about better results of cancer control.

Correspondence to:
Professor P C Leung
Centre for Clinical Trials on Chinese Medicine
Address: The Institute of Chinese Medicine
5/F, School of Public Health Building
The Chinese University of Hong Kong Shatin, New Territories, Hong Kong
Tel: +852 2632 2723/2252 8868
Fax: +852 2686 8463/26325441
E-mail: pingcleung@cuhk.edu.hk