The Immune System, Cancer and Thymus Extracts

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You are doing as well as your immune system is doing. This sweeping statement is as true for a child dealing with a cold as it is for someone dealing with advanced cancer. The immune system is one of the most complex biological systems in the body whose sole function is to keep us healthy from foreign invaders.

In the case of cancer and other chronic diseases and infections, a compromised immune system lies at the leading edge of the ensuing biological chaos. As a doctor who gets to work regularly with immune compromised patients, I am reminded everyday of the severe lack of knowledge that often lies on the other side of emergent chronic diseases. Worse yet, the lack of knowledge compromises the individual's ability to overcome their health challenge.

The main goal of this article is to focus on a much-neglected and misunderstood component of the immune system: the thymus gland. The thymus is an endocrine gland that releases hormones that activate the immune system. Clinical studies have shown that patients with cancer benefit greatly from the use of thymus extracts.

But before we go into all that, let us start by first addressing a more fundamental question: "what do I need to know about the immune system?"

Demystifying the Immune System

The immune system is a large collection of cells and proteins. We can think of the immune system to consist of the following components: the *complement system*, the *phagocytes* and the *lymphocytes*.

The complement system is a group of proteins found in blood that specialize in their ability to interact with *antigens* – biological molecules that are recognized as "foreign" to the body. The complement system reaches the site of invasion or infection and can do things such as trigger inflammation, attract phagocytes (see below), make the pathogen more recognizable to the phagocytes.

Phagocytes are cells that can literally engulf pathogens, toxins and other foreign bodies. *Granulocytes* are first responder phagocytes that "eat until they die". The pus in wound areas are made of mainly dead granulocytes. *Macrophages* are a type of white blood cell (monocyte) that convert to macrophages as they get recruited to areas of immune activity. They are slower in response than granulocytes, but have much greater capacities and last longer. They also assist in activating the rest of the immune system. The *dendritic cells* are similar in action as macrophages and granulocytes, but they also play a crucial role in "immunological memory". They

capture and present foreign antigens to T lymphocyte cells, thus activating them (see below).

The Lymphocytes form the majority of the white blood cells. There are two main types of lymphocytes – B cells and T cells. Lymphocytes are produced in large quantities in the bone marrow and are distributed throughout the body through the extensive lymphatic system. The lymph nodes, spleen and thymus are important components of the lymphatic system.

From a functional perspective, lymphocytes elicit two types of immunity: *humoral* and *cellular*.

Humoral immunity is connected to what we commonly refer to as antigen-antibody reactions and involves the B lymphocytes. These include hypersensitivity reactions, hemolytic disease of newborns, anaphylaxis etc. B Lymphocytes engineer antibodies specific to an invading antigen. Once the antibodies are formed in sufficient quantities, they can clump around antigens and weaken or destroy them. They also activate the complement system and phagocytes, stimulating them into action against the invader. B Lymphocytes become a crucial component of immunological memory – once the antibodies are made, they are stored away and recalled immediately in the event of a repeat infection. As a result, the invader is disposed of well before the presentation of symptoms, and the body is said to have developed *immunity*. B Lymphocytes do not require cell-to-cell contact between the lymphocyte and the antigen for its action, an important difference between its action and that of T cells that exhibit cellular immunity, discussed next.

Cellular Immunity is mediated by T lymphocytes and involves cell-to-cell contact between the lymphocytes and the invading pathogens. There are many types of T lymphocytes: T helper, T suppressor, T cytotoxic, Killer (K) and Natural Killer (NK) cells. These cells also help in macrophage and monocyte recruitment, cells that are constantly involved in constant direct combat against pathogens. Cellular immunity is the key defense method against viruses, fungi, some bacterial and parasitic infections, as well as neoplastic (cancerous) and aging cells.

Compromised T Lymphocyte Function and Cancer

The T lymphocytes are the crucial connection between the immune system and cancer. Their ability to identify and battle abnormally forming cells ensures that any cancer foci that form in the body get eliminated even before they result in the manifestation of disease.

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Isn't it then understandable that the suppression of the cellular immune system can become the cause of entrenchment and growth of cancer? In fact, impaired cellular immunity involving T cells is involved not only with the growth, but also with spread of cancer.[1] Many studies have also shown that treatments such as chemotherapy and radiation actually decrease the ability of the cellular immune system to respond adequately, a process that is required for any sustained recovery from cancer.

Given that the drop in T cell-derived immunity is not only a factor preceding cancer, but also a consequence of some of the most popular treatment, merits a clear understanding of methods that can be use to boost T lymphocyte activity, in particular, and cellular immune response, in general.

The Factors Underlying a Compromised Immune System

So, what is it that causes a breakdown of this exquisitely intricate defense system? Each body's immune system has a threshold beyond which it cannot overcome the disease influence – this threshold determines the adequacy of the body's immune response. Even in the worst of epidemics, not everybody dies, becomes ill or even gets infected. Cancer should not be able to grow in an immune-fortified body environment. However, when the immune response is low, the susceptibility to the growth of the disease is inevitably high.

Clinical studies have shown that the following factors can individually suppress immune response:[2]

Inadequate nutrition, excess or lack of exercise, physical trauma, inadequate sleep, excess fatigue, starvation, smoking, excessive intake of alcohol, most recreational drugs including barbiturates, cocaine, marijuana, chemotherapy, surgery, radiation, some antibiotics, extremes of weather and chronic diseases.

The Thymus Gland and T Lymphocytes

The thymus gland is intricately intertwined into the lymphatic system. The thymus gland is located under the breastbone and reaches maximum size and activity

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[1] Berkow, R. and Fletcher, A.J. The Merck Manual of Diagnosis and Therapy, 16th Edition. Merck Research Laboratories, Rahway, NJ, 1992, 308.
[2] Wilson, J. Thymus Extracts, An International Literature Review of Clinical Studies. 1999 Foundation for Immunology and Nutrition, Development, Education and Research.

during early childhood years and puberty. While T lymphocytes develop on the bone marrow, they mature in the thymus gland. That is why they are also called *thymocytes*. Some of them migrate to the thymus during the peak growth years or early childhood and puberty. During those years, the majority of the body's thymocyte population is created. Following the puberty years, the thymus shrinks in size, folding over itself (involution). The marked decrease in activity that follows leads many to believe that they thymus stops playing an important role following the growth period. This is true for the most part – however, as aging and chronic disease set in, the need for a renewal of T lymphocyte production and maturation starts becoming an essential need to overcome the growing challenges.

The cell surface markers of the thymocytes change as they mature. Immature thymocytes carry a T1 marker (also known as CD1). As they leave the bone marrow, the thymocytes lose the T1 marker, that is replaced by a T3 marker (CD3), making this cell a helper/inducer cell. Other T cells are indentified by their markers, for example, cytotoxic and suppressor T cells carry the CD8 marker.

Once thymocytes are committed to an antigen, they remain vigilant and committed to it for the rest of their life, but they do depend on hormones derived from the thymus for normal activity.

The Need for the Thymus in Overcoming Disease

How do we know that the thymus is still important in later years, especially during the onset of chronic disease? Maybe the best evidence comes from documented impact from the use of thymus extracts.

Thymus extracts are mostly reported from bovine origin and have been available for over 75 years. The hormones thymulin, thymopoietin and thymosin are typical constituents of these extracts. Some of the extracts also contain shortened peptides that have a similar biological activity profile as the parent hormones.

Thymus extracts have been demonstrated to have the following biological activities:

1. Evidence of improvement in B lymphocyte function.[3]
2. Modulate the production, maturation and activation of T lymphocytes.[4]

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[3] Twomey, J.J. and Kouttab, N.N.L. Selected phenotypic induction of null lymphocytes from mice with thymic and nonthymic agents. *Cell Immun.* **1982**, 72:186.
[4] a. Skotnicki, A.B. Therapeutic application of calf thymus extract TFX. *Medical Oncol. & Tumor Pharmacother.* **1989**, 6:31. b. Kouttab, N.M.;Prada, M.; Cazzola, P.

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3. Effectively increase the number and function of T helper/inducer lymphocytes (T4 cells)[5] and suppressor cells (T8 cells)[4b].
4. Ability to produce immune response even in significantly immune compromised patients who were previously unresponsive.[6]
5. Restoration of skin test responsiveness to delayed-type hypersensitivity (DTH) skin test, implying the increase in production and maturation of T lymphocytes and macrophages in previously unresponsive patients.

A spectrum of clinical evidence exists that demonstrates the usefulness of thymus extracts in many disease states, either standalone, or in combination with existing treatment protocols. Documented literature shows that thymus extracts can be useful in the following areas:[2]

a. Severe chronic allergies.
b. Severe acute and chronic infectious diseases, including immunodeficiency diseases such as AIDS.
c. Autoimmune diseases such as lupus, rheumatoid arthritis, scleroderma.
d. Decrease of damage from chemotherapy and radiation.
e. Reduction in post-surgical infections.
f. Adjunctive therapy to mainstream treatments for cancers

Some Examples of the Clinical Study of Thymus Extracts in Cancer

The examples cited below are just a few examples of how thymus extract therapy has been used against cancer in combination with other mainstream therapies, or even as a standalone, and to what effect. Most of the patients involved have been in

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Thymomodulin: biological properties and clinical applications. *Medical Oncol. & Tumor Pharmacother.*. **1989**, 6:5. c. Hadden, J.W.; Hadden, E.M. Therapy of secondary T-cell immunodeficiencies with biological substances and drugs. *Medical Oncol. & Tumor Pharmacother.* **1989**, 6:11.

[5] Stankewiez-Szymezak, W.; Moszynsld, B.; Dabrowsla, M.P.; Dabrowski Bernsztein, B.K.; Stasiak, A. The initial results of TFX-Polfa application in patients with chronic recurrent infections of the upper respiratory tract. *Pol. J. Ofolaryng.* **1986,** 2:350.

[6] a. Cangemi, V.; Volpino, P.; D'Andrea, N.; Gentili, S.; Ippoliti, F.; Piat. G. Thymostimulin effect on the immune response in neoplastic patients submitted to surgical treatment. *Panminerva Medica* **1993,** 35:218-23. b. Fagiolo, U.; Amadori, A.; Biselli, R.; Paganelli, R.; Nisini, R.; Cozzi, E.; Zamarchi, R.; D'Amelio, R. Quantitative and qualitative analysis of anti-tetanus toxoid antibody response in the elderly. Humoral immune response enhancement by thymostimulin. *Vaccine,* **1993,** 11:1336-1340.

advanced stages of disease, often non-responsive to mainstream treatments, where any alteration in the course of the disease can be viewed as a major event. The results obtained must be viewed in that perspective. These studies are detailed in an extensive review of clinical studies using thymus extracts.[2]

Lung Cancer. Lung cancer is easily one of the most difficult cancers to treat, with a very low long-term survival rate. In fact, over 90% of lung cancer patients survive less than 8 months following diagnosis.

The most popular treatment method, chemotherapy, not only suppresses the immune system but causes alterations in the airways, significantly affecting breathing in both affected and unaffected lungs. Radiotherapy reduces the total lymphocyte count and the T-cell helper/inducer to suppressor cells in the lungs. When used in combination, chemotherapy and radiation cause synergistic side effects leading to reduction in breathing capacity, reduced B, T and NK cells as well as cytotoxic and suppressor cells, compromising the cellular immune system.

In this scenario, tools are needed that can help not simply in overcoming the intrinsic immunodeficiency of the cancer patient, but also to combat the negative impact of chemotherapy and radiation.

Thymic Factor X (TFX) was given alone, twice a week for 10 weeks to 12 patients suffering from undifferentiated cell carcinoma or squamous cell carcinoma. **Ten out of the 12 patients showed subjective and objective improvements that included inhibition of local tumor growth, decreased metastatic spread to lymph nodes and other organs, partial regression of tumor mass (3 patients) and an increase in 6 month survival rate to 42% in the treated group compared to 7% in the control group receiving symptomatic treatment.[7]**

In another study involving 26 patients, the effect of thymostimulin (TP-1) on chemotherapy induced toxicity and long term survival was studied. The patients were randomly treated with 6 cycles of alternating chemotherapy regimens: cyclophosphamide, 4'-etidoxorubicin and etoposide, alternated with etoposide and cisplatin. Out of these 26 patients, 15 patients received TP-1 (1 mg/kg body weight, intramuscular injection) on days 7-14 of each treatment cycle. Once the six cycles of chemo were over, TP-1 was continued twice a week at the same dose to complete responders until the tumor relapsed.

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[7] Skotnicki, A.B. Therapeutic application of calf thymus extract TFX. *Medical Oncol. & Tumor Pharmacother.* **1989**, 6:31.

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The message from the results was clear: there were 7 complete remissions in the group receiving TP-1 as compared to 1 remission in the control group. Tumor progression was seen in 4 of the TP-1 patients, and 7 of the control group. **Mean survival of the TP-1 group was 14.5 months, while the control group average was only 5.5 months.** Additionally, the severity of neutropenia was significantly lower in the TP-1 group. This group also experienced significantly fewer chemo induced side effects such as the severity and duration of myelosuppression as well as febrile and infectious episodes. All these factors combined to an improved quality of life for TP-1 patients and an improved ability to handle chemotherapy.[8]

Breast Cancer. In a study consisting of 50 women with breast cancer, significant positive outcomes in quality of life indices were recorded.[9] The patients were divided into two groups, both receiving 6 rounds of chemotherapy consisting of cyclophosphamide, methotrexate and 5-florouracil, with one of the groups concurrently receiving TP-1 (50 mg/square meter intramuscular injection) daily for 2 weeks, followed by twice weekly for a minimum of 3 months. The TP-1 group showd fewer infections (37% compared to 77%), lesser incidence of myelotoxicity (suppression of bone marrow that is a show-stopper for chemotherapy treatment, 21% vs 77%), lower incidence of viral and fungal infections.

Colorectal and Gastric Cancer. In a study consisting of 50 patients with inoperable colorectal cancer, TFX thymus extract injections were given over the course of the disease.[10] Increased production of granulocytes and lymphocytes was observed with enhancement of cellular immunity, clinical improvement and increase in survival time. Twelve of the cases had repeated histological examinations of the cancerous tissue to find that the tissue started resembling what is normally observed during spontaneous tumor regression by an intact, native immune system to a neoplastic invasion.

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[8] Macchiarini, P.; Danesi, R.; Del Tacca, M.; Angeletti, C.A. Effects of thymostimulin

[9] Pavesi, L. Florouracil (F), with and without high-dose folinic acid (HDFA) plus Epirubicin (E) and Cyclophosphamide (C): FEC versus HDFA-FEC plus or minus Thymostimulin (TS) in metastatic breast cancer: results of a multicenter study. *Eur. J. Cancer* **1993,** 29A:S77 (401).

[10] a. Turowski, G.; Cybulski, L.; Politowsid, M.; Turszwili, T.; Zubel, M. First trials of immunopotentiation by thymic extract (TFX) in surgical patients with malignant disease. *Acta Med. Pol.* **1976**, 17:18. b. Urban, A.; Turowski, G.; Cybulski, L. The histological changes of the colon and rectal cancer stroma observed in patients after immunopotentiation by thymus extract (TFX). *Pathol. Pol.* **1977,** 28.47.

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Conclusion: Bypassing the "Thymic Menopause"

The above examples were given simply to illustrate the importance of a revitalized immune system for cancer and other immune-compromised disease states. The shutdown or slow-down of thymic activity following the initial growth years can be handled well by a healthy, young body. But as people grow older, there is a steady erosion in the number and vitality of T lymphocytes leading to a "thymic menopause" and a senescence of the cellular immune system. As people grow older, their nutritional status weakens, their exercise levels decrease, their consumption of drugs with side effects directed towards the immune system increases. This correlation between aging and the erosion of the immune system results in the slow but sure rise in the incidence of infections and chronic diseases such as cancer.

At the Hope4Cancer Institute in Baja California, Mexico, in a relatively new introduction, we offer Thymus Extract Therapy as an adjunctive therapy to our cytolytic and cytostatic therapies. When used alongside Sono-Photo Dynamic Therapy, Hyperthermia and others, Thymus Extract Therapy helps with synergistic clinical improvement, especially in quality of life parameters. Reinvigorating the immune system is one of our *Seven Key Principles of Cancer Therapy*, and Thymus Extract Therapy provides us an avenue to meet that essential need for patients suffering from cancer and other immune compromised diseases. Bypassing the "thymic menopause" appears to be an important gateway towards restoring health and vitality for those who need it the most.

Dr. Antonio Jimenez, M.D. *is the Founder and Medical Director of the Hope4Cancer® Institute (established 2001) located in Baja California, Mexico. As a physician with 25 years of experience treating cancer and other chronic diseases with alternative, non-toxic methods, Dr. Jimenez is known internationally for his "Seven Key Principles for Cancer Therapy" and the clinical introduction of pioneering treatment methods such as Sono-Photo Dynamic Therapy and the BX Antitoxin Protocol. Dr. Jimenez has been an active member of ACAM in good standing since 2009.*

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