

Enhanced Transfer Factor

**Dietary Supplement Containing
Biologically Active Substances
For Improved Immune Function**

THIRD EDITION

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Introduction

Before we begin let us look at our current situation. Today we face many health challenges; among these are:

- New and Emerging Diseases
- Increasing Antibiotic Resistance
- Return of Old Germs (Tuberculosis, etc.)
- World Travel (leading to the rapid spread of new diseases)
- Multiple Areas of Stress
- Aging Population

Because of this we are facing a major medical services crisis. Costs of medical care are skyrocketing, malpractice suits are driving doctors out of practice and by 2020 it is projected that there will be a shortage of 200,000 doctors and 700,000 nurses in the United States alone. Under current US law Medicare's hospital insurance trust fund, which pays for inpatient hospital care, will be exhausted in 2019, seven years earlier than previously forecast.¹ The United States is not alone in this dilemma. Every country will be forced to face the problem of rising needs and expectations against a background of limited resources and the threat of limiting available health care. This gloomy reality is coldly put forth by David Dranove in his provocative book *What's Your Life Worth? Health Care Rationing . . . Who Lives? Who Dies? And Who Decides?*²

In this setting we will be forced to rethink our overall approach to health care. Since the 1940s, western health care has been operated under a dominant military/technologic crisis model in which the disease attacks a patient and the physician counterattacks the disease.³ The patient is the battlefield. Perhaps this is why even properly prescribed medications are rated as the sixth leading cause of death in the United States.⁴ Interestingly studies have also shown that only 25 percent of medical complaints can be treated; the remaining 75 percent depend upon the body's own response.⁵ Many physicians have come to a position similar to the following, "As a practicing physician for over forty years, I hereby make an admission: physicians do not cure patients. All a physician can do is to provide a good healing environment."⁶ Where are we left to turn? In a real sense we must return to where we began; we must return to our immune systems.

Millennia ago Hippocrates stated "Let thy medicines be thy foods and

thy foods be thy medicines." Recently Professor John D. Potter expressed the same sentiment "Cancer may be the result of reducing the level of intake of foods that are metabolically necessary." Using this broader definition of nutrients we can construct the following "Nutrient versus Time" chart:

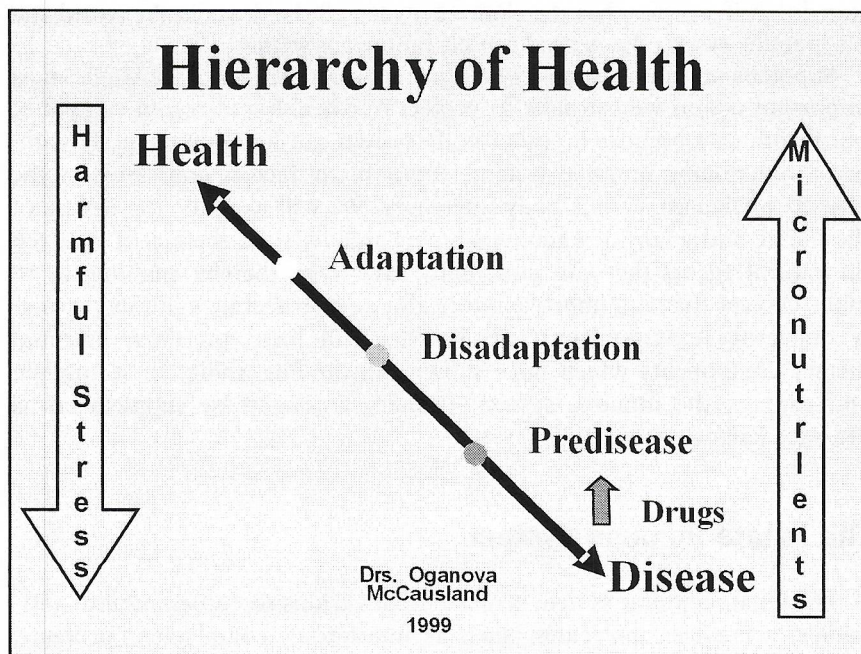
NUTRIENT	TIME TO DEFICIENCY DISEASE	DISEASE CONDITION
Oxygen	Minutes	Suffocation
Water	Hours	Dehydration
Calories	Days	Starvation
Protein	Weeks	Kwashiorkor
Essential Fatty Acids	Weeks	Inflammatory and Autoimmune Diseases
Vitamins	Months	Scurvy, Beri Beri, etc
Minerals	Years	Osteoporosis, Immune Deficiency, Oxidative Stress, etc.
Phytonutrients and other essential dietary components	Decades	Cancer, Heart Disease, Strokes, Chronic Infections and Inflammation

What is becoming increasingly obvious is that the time delays in presentation of overt disease have limited our recognition of the importance of specific supplementation. In the DSHEA congress defined a dietary supplement as a substance that strengthens and supports a natural body function. After a ground swell of public support Congress passed the Dietary Supplement Health and Education Act of 1994. Among the Congressional findings were the following:

- improving health is a national priority
- the benefits of dietary supplements have been documented in scientific studies
- dietary supplements safety problems are rare
- consumers should have data from scientific studies of dietary supplements

An enlightening presentation of the proper roles and functions of nutrients and drugs is graphically represented by Drs. Oganova and McCausland in their Hierarchy of Health Chart.⁸ In the Hierarchy of Health the distance between health and disease is divided into three stages: Adaptation, Disadaptation and Predisease. Adaptation is the condition when the body successfully adjusts to the physical, emotional, and microbial stresses of life. Disadaptation occurs when the stress is excessive or when our ability to adapt is diminished. Some examples of disadaptation would include the deposition of plaque in the arteries as an adaptation to chronic inflammatory stress. This type of adaptation can be likened to buying on credit. It gets us through today but results in a bigger bill with interest in the future. Predisease is when we are not sick, but we are very susceptible to illness.

Drugs are placed between disease and predisease. Drugs replace or sup-



press a body function but do not strengthen a body function. Drugs may restore us to a state of predisease but not to a state of health. For example, a person with a weak immune system may use an antibiotic to replace their inadequate immune response but this does not make them any more capable of fending off the next exposure. There are times when drugs are immediately essential and in each case the reason can be found in a failure of the normal body functions. There is no such thing as a drug deficiency. Put another way, a headache is not a deficiency of Tylenol®! On the other hand there are many deficiency diseases which, when the person is adequately supplemented, disappear completely and the person is able to regain full health and not just a weak, predisease status. What should be clear is that, contrary to our current use of drugs as a first option in fighting disease, drugs should be a last option.

Strengthening the body systems through intelligent dietary supplementation should be our first action to maintain and improve our health. One of the most important of our systems is the immune system. Our immune system is an intricate, interrelated defensive force made up of a trillion cells.^{9,10} Our health, quality of life, and indeed our very survival, depend on the effectiveness of our immune response. Our immune system protects us by recognizing germs and cancerous cells, reacting and destroying these intruders, and finally by remembering these pathogens and cancers as a defense against future invasions. In addressing the importance of the immune system Prof. Paul Ewald, the author of *Plague Time: The New Germ Theory of Disease*, stated that if a person has the choice between all the drugs in the world and his immune system, he better keep his immune system.¹¹

Supplementation in support of our immune function is the single most important action we can take to protect our health and regain control of our health care because no other body system can function properly without a functioning immune system. Today many factors contribute to the general weakening of our body's defenses. We will examine the nature of the innate and adaptive immune systems and consider the recent research on natural agents that can potentially save lives, thereby enabling us to make choices that can improve our health and protect us in an increasingly dangerous environment. This booklet will focus on those essential dietary components which have shown outstanding ability to strengthen and support the immune system. Primary among these supplements is Transfer Factor.

The Innate Immune System

The innate immune system is made up of various receptors, natural antibodies, messenger molecules (such as interferon), complement proteins,

and natural killer (NK) cells. The innate immune system is our first-line of defense against cancer and infectious disease.¹² The innate response works by recognizing distinct patterns in microorganisms and reacting to them.^{13,14} This pattern recognition is innately coded into our immune system DNA and does not require us to have prior exposure to the microbial agent.¹⁵ In the past, the innate immunity of vertebrates has been considered archaic and obsolete, but today the innate immune system is regarded as essential to the function of adaptive immunity and survival.^{16,17}

NATURAL ANTIBODIES

Natural antibodies are always present and do not require outside stimulus to appear. The main reason for their continual presence is their ability to target dangerous agents that are very common in the environment. These antibodies are not only produced by an effective immune system, but are also able to promote a more effective immune response. After the initial identification of the microbial invader, other antibody types are elicited as a part of the adaptive immune response.

THE COMPLEMENT SYSTEM¹⁸

The identification or tagging of the infected or malignant cell by an antibody is part of what's called the complement tagging process. The complement process is part of the innate immune system, and it provides the initial, if incomplete, antimicrobial defense. The complement system serves three main functions:

1. **Opsonization.** This involves tagging damaged or infected cells that need to be destroyed and cleared from the system.
2. **Chemotactic response.** The complement system sends out signals that mobilize immune cells and draw them to the site of infection.
3. **Membrane attack complex (MAC).** MAC is formed to destroy tagged cells. Essentially, MAC is an assembly of complement proteins that punch a hole in the lipid (fat) membrane of the invader, allowing water to rush in and burst the membrane like an over inflated balloon. Some bacteria and cancer cells have an ability to destroy MAC if its formation is slow, so MAC speed is essential.¹⁹

It is important to note that the cell membranes of animals are made up of two layers of lipids. Animal cells appear as a minute drop of water inside

a bubble made up of two layers of fat. Because of this, many viruses wrap themselves in a portion of the host's lipid membrane when they bud out from the infected host cell. By wrapping themselves in a portion of host membrane, viruses protect their fragile RNA or DNA fragments within the lipid envelope. The envelope also acts as a cloak, allowing the virus particle to evade the host immune system by masquerading as a normal, albeit small, cell. Viruses that wrap themselves in host membrane are called enveloped viruses. A partial list of enveloped and non-enveloped viruses is shown below. As you can see, the list of enveloped viruses reads like a "who's who" of the most notorious viruses emerging today.

ENVELOPED AND NONENVELOPED VIRUSES²⁰

Enveloped

- | | | |
|-----------------|------------------|--------------------|
| • Hepatitis B | • Herpes simplex | • Varicella zoster |
| • Epstein-Barr | • Smallpox | • Hepatitis C |
| • HIV | • Rubella | • Yellow Fever |
| • Ebola | • Hanta | • Influenza |
| • Parainfluenza | • Mumps | • Measles |
| • Rabies | | |

Nonenveloped

- Human papillomavirus
- Hepatitis A

Enveloped viruses, unlike cells, do not contain membrane repair machinery. This weakness can be exploited by the complement system. Even a tiny MAC prick will burst the viral bubble and destroy its infectivity.²¹ Clearly then, the complement component of the innate immune system is critical in our ability to fight viral infections.

KILLER CELLS

The main function of immune killer cells like cytotoxic T-lymphocytes (CTLs) and natural killer (NK) cells is destroying damaged, cancerous or infected cells. CTLs will be discussed later. NK cells target cells that are missing the self-marker that identifies a cell as one of our own.²² Foreign cells and cancer cells that have lost their self-markers are the main targets of NK cells. Normal cells with high levels of self-markers are intentionally spared from NK cell attack.²³ One could say that CTLs and NK cells are like National Guard battalions—they have roles in both defending against

foreign invaders and maintaining domestic order against seditious cells in the body politic.

A number of conditions are associated with low NK cell activity—cancer, acquired or congenital immunodeficiencies, chronic illnesses and infections, autoimmune diseases and several genetic and behavioral disorders.²⁴ The young, the old and the stressed are more susceptible to immunological breakdown. Augmenting NK cell activity may be critical in strengthening immunity in members of these groups. Laboratory findings indicate that the young may have a reduced resistance toward cancer because of their diminished NK activity.²⁵ NK cells from elderly people show a decreased ability to multiply when stimulated and demonstrate an impaired killing capacity.²⁶

Stress such as poor nutrition, infectious assault, or cancer, weaken the immune system's ability to learn new healing strategies. Inappropriate psychological reactions to stress, fatigue associated with chronic stress, and physical injury can also lead to a disruption of immunity and suppressed NK cell activity^{27,28,29} and allow tumors to grow faster.³⁰ Individuals with low NK cell activity also tend to experience more frequent and severe forms of chronic fatigue immune dysfunction syndrome (CFIDS).³¹ In addition without functionally efficient NK cells, other cells of the immune system are not optimally activated.³² Dietary supplements that enhance NK cell activity may therefore be critically important.

The Acquired Immune System

Many times our innate immune ability is insufficient to address the variety of microbes we encounter daily. In these cases, our immune system has the ability to learn new skills and construct new tools to deal with these microbial invaders. These immune responses are called adaptive or acquired responses.

"T cells" and "antibodies" are components of the immune system that are involved in adaptive responses. Once we are exposed to an infectious agent, our bodies identify, react to and hopefully destroy that agent. This process takes about ten to fourteen days. After we have successfully dealt with an infection, our immune system retains a memory of what it has learned. Typically, we are not even aware of subsequent exposures to the same microbe because our immune system responds so rapidly and with overwhelming force giving the microbe no opportunity to grow effectively. This adaptive response is the result of acquired immunity. This immune response is slow but normally very effective. Four critical components of acquired immune response are essential to its proper function. They are (1) the thymus gland and T cell development, (2) antibodies, (3) cytokines and (4) transfer factor.

THE THYMUS AND T-CELL DEVELOPMENT

The education of immune cells can be compared to a school system having grammar school, prep school, college and graduate level training. The thymus gland is the grammar and prep school for three groups of immune cells. Because of the involvement of the thymus, these cells are called T-cells. They include T-helper cells, T-regulator cells and cytotoxic T-cells (most often called cytotoxic T-lymphocytes, or CTLs).

Each type of T-cell has its own particular function. T-helper cells assist the other immune system cells in performing their important functions. T-regulator cells control immune response and keep the immune system from overreacting. Both helper and regulator T-cells perform their function by working indirectly through other immune cells. Cytotoxic T-lymphocytes, however, act directly on offending cells. CTLs are programmed in the thymus to look for self-markers *and* foreign markers. This combination of markers on the same cell identifies it as one of the body's own cells that has been damaged.

The immune training functions of the thymus gland are weak in infants and increase in strength until puberty. After puberty, the thymus gland begins to shrink and continues to diminish in size and effectiveness throughout the rest of our lives. The reduced training of T cells by the aging thymus is thought to be responsible for the immune deficiencies that develop during aging.³³ It is the job of the thymus to help us react against foreign cells and not against our own normal cells. As the thymus shrinks, the body's normal immune response to foreign cells weakens, while the autoimmune attacks on our own tissues becomes stronger. This situation is called the *aging paradox*.³⁴

Incompetent thymic training produces T-cells that are unable to adequately interpret the immunological messages they receive from their environment. Dietary supplementation that supports the thymus and improves T-cell function results in a cascading improvement in the overall immune response.

ANTIBODIES

Antibodies are protein molecules produced by B-cells. Natural antibodies react against the most common features of the most common pathogens. Natural antibodies are so important that they are coded into our DNA and are part of our innate immune system. This is only a small portion of our total antibody repertoire. We acquire most of our antibodies as a result of a process of immune recognition and reaction. This process usually takes 10 to 14 days to mature. Structurally, antibodies have claw-like features that allow the antibody to seize onto foreign microbes or damaged cells. Once the antibody has attached itself to an offending cell,

the rest of the immune system reacts by attacking the tagged cell and destroying it.

MACROPHAGES: “BIG EATERS”

Macrophages (which means “big eaters”) are large immune cells that engulf and degrade foreign, dead or damaged cells. If the engulfed cell is infected or malignant, the macrophage retains intact any new foreign sequences that can be used as antigens. Antigens serve as recognition markers used by the immune system—to stimulate antibody production. Macrophages then act as antigen-presenting cells, which means that the macrophages present the newly discovered antigens in a form that T-cells can recognize. Once this has occurred, the immune system can then initiate an adaptive immune response to eliminate any other foreign or cancerous cells.

Memory T-cells and B-cells are produced by the immune system as a means of storing the immunological information that has been gained by the host. Because of its memory capacity, the response of the immune system during the second exposure is usually so effective that we are not even aware that we have been re-exposed.

CYTOKINES

In addition to producing cells, the immune system produces a host of messenger and control molecules known as cytokines. Cytokines play important roles in all phases of immune response. Some cytokines act as mediators of innate immunity, while others are involved mainly in acquired immunity. In the latter case, cytokines control the activation, growth and differentiation of cells. Transfer factors may be among the most important cytokines.

Transfer Factor (TF)

INTRODUCTION: WHAT IS TRANSFER FACTOR?

While studying tuberculosis in the late 1940s, Dr. H. Sherwood Lawrence discovered that the immune competence of a donor could be transferred to a naïve recipient by using low molecular weight extracts obtained from white blood cells.³⁵ Dr. Lawrence called these small molecule extracts transfer factor (TF). If the thymus gland can be compared to grammar school and prep school, transfer factor can be compared to collegiate and graduate level training for the immune system. Scientists later found

transfer factors to be universally effective, regardless of the differences between the species of the donor and recipient. This aspect of transfer factors is partly explained by this core scientific belief: *the more essential a material or structure is to living organisms, the more common it is to see this material or structure throughout living systems*. Transfer factors are essential components of even the most primitive immune systems.³⁶

One basic principle of the immune system is that it must be able to respond quickly and specifically, while not exhausting itself by over responding and attacking normal tissue. Transfer factor preparations consist of three identifiable fractions named by their discovered effects on the immune system. They are inducer, antigen specific and suppressor fractions.³⁷ More recent understanding of immune function would rename the suppressor fraction as the regulator factor. The TF inducer fraction triggers a general state of readiness in the immune system. The antigen-specific fraction is an array of critical tags used by the immune system to identify a host of enemy microbes. Meanwhile, the regulator fraction keeps the immune system from focusing all its strength on a defeated infection and ignoring new microbial threats; it is responsible for controlling immune overreactions that can cause autoimmune disorders. Each fraction (inducer, antigen specific, and regulator) improves one or more aspects of the adaptive ability of the immune system.

As the product of a competent immune system, transfer factor can teach a less competent immune system how to better respond. Mammalian mothers provide transfer factors to their offspring via their colostrum.³⁸ Hens and other egg laying species deposit transfer factors inside the egg as a means of providing their young a descriptive library of immune system instructions and microbial identifiers.³⁹

Unlike antibodies that are large molecules, transfer factors are quite small.⁴⁰ In fact, their small size helps to make them nonallergenic.⁴¹ And while antibodies are used up when they attach themselves to the offending cell or protein, transfer factors perform a different role. They are immune messenger molecules that educate and alert naïve immune cells to an impending danger. In this regard, transfer factors perform a catalytic role in the immune system—triggering the effect without being consumed.⁴²

Originally, transfer factor preparations were administered by injection.⁴³ However, later studies showed that transfer factors were equally effective when taken orally.⁴⁴ The nonspecific inducer and regulator fractions of transfer factors are fully compatible between different species. The antigen-specific transfer factors are each specific to a particular pathogen and these pathogens vary from species to species. An example might help illustrate the potential benefit of antigen specific transfer factors in recipients of a different species than the donor.

Although the highly contagious and often fatal disease of smallpox dev-

astated many European and American communities in the 1700s, one subset of individuals seemed to survive the epidemics—milkmaids. Milkmaids often contracted cowpox from infected animals during milking (through a cut or break in the skin.) Milkmaids infected with cowpox usually followed a mild course of the disease that was resolved without much difficulty. It was then found that milkmaids who had contracted cowpox were immune to smallpox. In a classic, early inoculation experiment, Edward Jenner vaccinated a young boy with cowpox and then demonstrated that the child was protected from contracting smallpox. The relationship between smallpox and cowpox is a case of antigen crossover where the immune system recognizes two different pathogens after being exposed to either one. Antigen crossover between human and bovine pathogens is highly likely. The antigen-specific, bovine transfer factors should therefore provide protection to humans against the corresponding human pathogens, resulting in a milder course of disease. Appendix 1 contains a more complete list of human pathogens and their related bovine pathogens.

Similarly man and chickens have also shared the same environment for tens of thousands of years. Appendix 2 contains a partial list of human pathogens (or diseases) and their potential cross-reactivity with related avian pathogens.

BENEFITS OF TRANSFER FACTOR

The exciting benefits of transfer factors, the essence of the immunological message, could spark a revolution in medicine. The need for such a new weapon in our immune defense arsenal is clear. "Transfer factor [has] an important role to play in modern medicine which, from AIDS to Ebola, faces the emergence of new viruses or the resurfacing of old pathologies such as tuberculosis."⁴⁵ Nevertheless, there are always many who resist new ideas, regardless of their benefits. In a recent international symposium on transfer factors, Dr. D. Viza summarized this conventional resistance:

At the end of the 20th century, the triumph of biology is indisputable. However, the triumph of biological science is far from being complete. The toll of several diseases, such as cancer, continues to rise and the pathogenesis of AIDS remains elusive.

In the realm of inductive science, the dominant paradigm can seldom be challenged in a frontal attack, especially when it is apparently successful, and only what Kuhn calls 'scientific revolutions' can overthrow it. Thus, it is hardly surprising that the concept of transfer factor is considered with contempt, [since] its putative mode of action contravenes dogmas of both immunology and molecular biology. And when facts challenge established dogmas, be [it] in religion, philosophy or science, they must be suppressed . . . because they

challenge the prevalent paradigm. However, when observations pertain to lethal disorders, their suppression in the name of dogmas may become criminal. Because of the failure of medical science to manage the AIDS pandemic, transfer factor, which has been successfully used for treating or preventing viral infections, may today overcome a priori prejudice and rejection more swiftly.⁴⁶

The benefits of transfer factor have been reviewed and the proceedings of the Tenth International Symposium on Transfer Factor have been published.^{47,48,49} These reports cover the successful use of transfer factor in addressing viral, parasitic, fungal, malignant, neurological and autoimmune diseases. Transfer factor has been shown to be beneficial to all age groups, from children to the elderly. The benefits from human use of animal-derived transfer factors have been repeatedly illustrated. In like manner the efficacy of the oral administration of transfer factor has been demonstrated. In most of the published research on the use of transfer factor, disease and malaise were present, but the real power of transfer factor is actually in prevention. *The use of transfer factor in the prevention of illness and the maintenance of health is its greatest potential benefit, and its safety when used chronically has been well established.* The future financial burden of medical care could be curbed significantly by the general use of transfer factor.

SOURCES AND SAFETY OF TRANSFER FACTOR

Transfer factor was first discovered inside human white blood cells. Two patents currently govern the commercial production of transfer factor from colostrum⁵⁰ and eggs.⁵¹

Transfer factor has an excellent safety record, and no adverse side effects have been reported. This has been shown even when transfer factor was administered in extreme excess or over several years.⁵² Infants and the elderly are two groups most at risk for infection. The naturally high levels of transfer factor in colostrum clearly indicate its intended use and safety for infants. In particular, oral administration of transfer factor is convenient and easily accepted by all age groups.⁵³

In addition, over 3,000 papers have been written on transfer factor since it was first reported in 1949. Studies on the human use of transfer factor have shown how it can relieve unnecessary suffering simply and safely. For a more complete examination of transfer factor and its benefits to human health, interested readers are referred to the booklet *Transfer Factor: Natural Immune Booster*.

Innate and Adaptive Immunity Working Together

Recent research has significantly advanced our understanding of the interplay between the innate and adaptive immune systems.⁵⁴ We now know that the innate immune system initiates and improves the slower, but more specific, acquired immune response.²² The complement system is where the early innate immune reaction and the later acquired immune reaction merge, providing a continuous immune response.⁵⁵ Natural killer (NK) cells are normally considered part of the innate immune system. Nevertheless, NK cells produce a number of cytokines (messenger molecules) that are potent immune regulators of the adaptive immune response.⁵⁶

Microbial and Malignant Immune Evasion

Most pathogens invading the human body are actively attacked by the immune system. In order to protect themselves, some pathogens have developed “cloak and dagger” immune evasion techniques. “Cloaking” strategies include a continuous changing of surface antigens in a process called antigenic drift or interfering with antigen presentation. This strategy makes the infected cell invisible to certain parts of the immune system.⁵⁷ “Dagger” strategies include the infection and destruction of immune cells themselves, as in the case of the Human Immunodeficiency Virus (HIV).

Other evasive techniques used by pathogens involve tactics such as shedding antigenic markers. These antigenic markers are the handles the immune system uses to grab onto infected cells. By putting out numerous unattached handles, the immune cells have their hands so full that they are unable to effectively attach themselves to real pathogens. Meanwhile, other pathogens disrupt the complement system in order to evade detection. For instance, an elegant pathogenic technique involves the production of imitation complement inhibitory proteins (molecular mimicry) that block complement activation.⁵⁸ Another evasive technique used by pathogens involves disruption of cytokine production, which creates a false sense of security in the immune system.⁵⁹

The evasion of the immune system by cancer cells is an instructive example of how invaders can circumvent immunity. Cancer cells are derived from our own cells. This complicates the immune surveillance process since they look so much like our normal cells.⁶⁰ Initially, cells that become transformed into cancer cells retain all of the normal self-markers that define them as our own cells. However, these cancer cells also display markers that should not be present on our own cells. These markers indicate that the cell is damaged, and their presence signals the Cytotoxic T-lymphocytes

(CTLs) to destroy the cell before it has a chance to multiply. But if immune response is slow, for whatever reason, the cancer cell has a chance to multiply. When the immune system does respond, those cells that are most susceptible to CTL attack will be selectively killed.

Occasionally a cancer cell will mutate further and yield offspring without self-markers. This situation is critical for two reasons. First, the loss of a self-marker increases the ability of the cancer to metastasize. Second, the CTLs can no longer recognize the cancer cell and destroy it. At this point, the NK cells that target foreign cells take over. In fact, both natural and elicited antibodies are commonly present in the serum of cancer patients. Unfortunately, the responses of these antibodies toward many cancers are ineffective in stopping tumor growth.⁶¹

This weak antibody response however, is often sufficient to launch the complement system. Antibody involvement restricts deposition of the complement-generated iC3b tag to tumor cells, and normal tissue surrounding the malignant cells should be spared. Activation of the membrane attack complex (MAC) is often blocked by inhibitory/regulatory proteins that are normally present on our cells. These same inhibitory/regulatory proteins are also present on cancer cells. Because of this cancer cells are also able to reject the developing MAC if its formation is slow.⁶² Tumors seem to be able to develop several other immune-escape mechanisms that either inactivate specific immune cells or prevent the activation of anti-tumor mechanisms.⁶³

Dietary Supplements

If an infection or cell abnormality is too complex, the inadequately trained immune cells may not be able to develop skills fast enough to contain the infection, resulting in us "getting sick." When this happens, additional outside support may be needed. Conventionally, we have employed drugs such as antibiotics when we are sick. The function of most drugs is to replace rather than strengthen the immune system. Oftentimes the toxicity of a drug toward its target microbe or cancer cell will also have a negative effect on other cells or systems of the body.⁶⁴ On the other hand, the role of a supplement is to strengthen the body from within by working with the body rather than circumventing its natural functions. This approach reduces the risk of toxic side effects. Before recorded history, man used dietary supplements to improve his health. Most of these supplements were derived from plants containing peculiar healing properties. Two of the oldest recorded medicinal supplementation codes are the Chinese codex from the Shang dynasty (ca. 1766-1122 B.C.) and the Indian medical system Ayurveda, first recorded in the seventh century B.C. In ancient America, echinacea was used from Texas to Saskatchewan. The whole discipline of

ethno-pharmacology developed in order to capture and substantiate the folk medicine of cultures throughout the world.

Many of the oldest and most revered supplements have been found to strengthen the immune system. Interestingly plants may not be the most ancient source of immune system supplements used by man. The oldest immunological supplement may in fact be transfer factor found in colostrum and eggs.

IMMUNOLOGICAL AGENTS FOUND IN COLOSTRUM

Transfer Factor. The first milk of every mammalian mother naturally contains transfer factors that reflect her rich immunological experience.⁶⁵ This source makes it obvious that nature intended colostrum transfer factors to be taken orally. If the baby is allowed to nurse, initial immunity is rapidly established. This is nature's way of quickly educating a naïve infant in the hazards of a microbe-infested world.⁶⁶ On the other hand, infants who are not breast-fed show a greater susceptibility to infections, allergies and childhood cancer.⁶⁷

The nature of the modern dairy cow is such that she is in intimate microbial contact with her environment and produces far more colostrum—and therefore more transfer factor—than her calf needs. Since transfer factors are universally effective regardless of the differences between the species of the donor and the recipient, harvesting the excess colostrum and isolating the transfer factor provides a commercial source of transfer factor for human consumption.

Transfer factor, as an extract of colostrum, is generally recognized as safe (GRAS) and is considered to have a safety profile similar to milk. Although lactose intolerance due to milk ingestion is present to a degree in many populations, even persons who are clinically lactose sensitive can tolerate between two and six grams of lactose, as a result of colonic bacterial degradation of lactose.⁶⁸ Unlike large-molecule antibodies, transfer factors are quite small.⁶⁹ As stated earlier the small size of transfer factors helps to make them non-allergenic. In fact, it is actually the immunoglobulins (antibodies) found in bovine colostrum that are the source of most cow-milk allergies in humans.⁷⁰

Antibody (Immunoglobulin) Supplements. Absorption of maternal immunoglobulins ceases after the first 30 hours of life for a human.⁷¹ Beyond the first 30 hours of life, no absorption of intact antibodies has been shown in humans.⁷² Oral administration of antibodies to adults leads to rapid degradation of the antibodies both due to the acidity of the stomach and the action of intestinal enzymes. This led to the recommendation that both stomach acid and intestinal enzymes be neutralized to obtain maximum benefit from orally administered antibodies.⁷³

Rapid transit and incomplete digestion are the hallmarks of diarrhea. It is in just such a condition that oral ingestion of antibodies is most effective.⁷⁴ No absorption of the intact antibodies is required since the troublesome agent is in the intestines.

Antibodies from one species are not effective in other species. No positive systemic effects can be expected after oral administration of foreign antibodies to humans.⁷⁵

Lactoferrin. Lactoferrin is a protein that binds iron.⁷⁶ Because of its iron-binding properties, lactoferrin has been proposed to act as a bacteriostatic agent by withholding iron from iron-requiring bacteria. Lactoferrin is found in high concentrations in human colostrum, but the level of lactoferrin in bovine colostrum is very low. Thus, consuming bovine colostrum as a lactoferrin source is not effective.

IMMUNOLOGICAL AGENTS FOUND IN EGGS

Transfer Factor. Hens and other egg laying species deposit transfer factors inside the egg as a means of providing their young a descriptive library of immune system instructions and microbial identifiers.⁷⁷ Unlike mammals, birds and other egg laying species have only one opportunity to convey the immunological experience of the mother to their offspring; that is during the time the egg is forming.

Birds even more than grazing animals are in intimate contact with their environment since they often feed on insects and worms. In addition birds must swallow small rocks to enable their gizzards to grind seeds. This process insures exposure to the viruses, bacteria and parasites found abundantly in the soil.

Fresh eggs have been a human food staple for many millennia. Transfer factors are universally effective regardless of the differences between the species of the donor and the recipient. Therefore harvesting eggs and isolating the transfer factor provides a commercial source of transfer factor for human consumption. As stated earlier the small size of transfer factors helps to make them non-allergenic. The use of whole uncooked egg powder as opposed to carefully pasteurized yolk extracts exposes the consumer to undenatured egg whites which is the source of most of the egg allergens.⁷⁸

EGG ANTIBODY (IMMUNOGLOBULIN) SUPPLEMENTS

Chicken antibodies offer many advantages in the laboratory over the traditional mammalian antibodies due to the evolutionary differences between mammalian IgG and chicken IgY. The main source of these advantages is that the chicken antibodies do not activate the human complement

system or the human Fc-receptors both of which are critical components of an effective human immune response.⁷⁹ What is beneficial in the sterile environment of the laboratory is in this case detrimental in the body. A recent and very hopeful review stated "there is still controversy regarding the stability of IgY through the GI tract. Finding an effective way to protect the antibodies from degradation in the GI tract would open the door for significant advances in IgY technology and nutraceutical applications."⁸⁰ It is a well known fact that antibodies from one species are not effective in other species (except in the treatment of diarrhea as stated previously). No positive systemic effects can be expected after oral administration of chicken antibodies to humans.⁸¹

ZINC AND THYMUS SUPPORT

Zinc. Zinc is an essential element for growth, nervous system function and especially the immune system response. The relevance of zinc for immune efficiency has been well established.⁸² Zinc-deficient persons experience increased susceptibility to a variety of pathogens.⁸³ The regulation of innate immunity, as well as the function and maturation of lymphocytes and monocytes, is critically dependent on zinc concentration.⁸⁴ Zinc deficiency causes an imbalance in T-helper cell functions as well as a deficiency in natural killer (NK) cell activity.⁸⁵ Indeed the activities of many immunostimulants are influenced by zinc concentration.⁸⁶

With advancing age, humans undergo a progressive reduction in their zinc levels. Studies suggest that the age-related thymic involution (regression) and peripheral, immunological dysfunctions are not intrinsic and irreversible events but are largely dependent on the altered zinc pool.⁸⁷ Interestingly, melatonin helps restore zinc balance from negative to positive values which further demonstrates the interdependence of the neuroendocrine, digestive and immune systems.⁸⁸ As little as ten milligrams of supplemental zinc improved cell-mediated immune response in an older population.⁸⁹ Similarly, only five milligrams of zinc per day reduced morbidity and improved immune function, as well as growth, in low birth weight, full-term infants.⁹⁰ Two studies have shown zinc supplementation to decrease child mortality by more than 50 percent among deficient populations.⁹¹

Thymulin. Thymulin is a thymus hormone. Diminished levels of thymulin occur in immunodeficiency and autoimmune diseases. It has been demonstrated that thymulin plays a role in immune and neuroendocrine system interactions.⁹² Thymulin has also been shown to reduce inflammatory pain.⁹³ Thymulin is not active by itself. Thymulin requires an equal amount of zinc for it to be biologically active.⁹⁴ In one set of tests, the highest degree of vaccine effectiveness was achieved when a mixture of thy-

mulin and zinc was administered concurrently.⁹⁵ In the case of AIDS, levels of total thymulin are not diminished, but the amounts of active thymulin are reduced to nearly undetectable levels. By adding zinc, all of the missing thymulin activity was recovered.⁹⁶ In addition the recurrence of *Candida aesophagea* or *Pneumocystis carinii* in persons with AIDS ceases after supplementation with zinc.⁹⁷

Plasma levels of active thymulin are also reduced in cervical cancer due to low zinc bioavailability. Thus, zinc supplementation may restore impaired central and peripheral immune efficiency in cervical carcinoma.⁹⁸ A recent examination of the importance of zinc indicated that it "significantly determines development of diseases."⁹⁹

CARBOHYDRATE ADJUVANTS

Agaricus Blazei (Sen Su Take). *Agaricus blazei* is considered by many to be the king of medicinal mushrooms. Reported health benefits of *Agaricus blazei* span millennia and application of modern scientific methods have validated the traditional use and benefits of *Agaricus blazei*. Dr. Fujimiya and his colleagues have studied the effects of *Agaricus blazei* extracts on solid tumors. They found that when a solid tumor is injected with *Agaricus blazei* extracts, the tumor begins to shrink. Most interestingly other tumors present in the host also shrink. Such a distant response is a clear indication of an immune system reaction.¹⁰⁰ Dr. Fujimiya was able to show that the body's natural killer (NK) cells were able to recognize and actively attack the local and distant tumors.¹⁰¹ Dr. Fujimiya found the cytotoxicity or cell killing activity of *Agaricus blazei* was selective for the tumor cells.

Dr. Mizuno, et al. clearly demonstrated that both the helper T-cell (CD4+) and cytotoxic T-cell (CD8+) populations were significantly increased after oral administration of *Agaricus blazei* extract.¹⁰² 5-Fluorouracil, a common anticancer drug, is known to suppress the immune system.¹⁰³ By including *Agaricus blazei* polysaccharide extracts in a 5-Fluorouracil drug program, the antitumor effects of 5-Fluorouracil were enhanced.¹⁰⁴ These results, along with the work of Dr. Ito, clearly indicate that *Agaricus blazei*'s antitumor effect occurs through strengthening the host's immune system.¹⁰⁵

Cordyceps Sinensis. *Cordyceps sinensis* is a fungus that is highly valued in China as a tonic food and herbal medicine. Its use in Chinese medicine is now centuries old though originally it was available only to the imperial family. In ancient China, *Cordyceps sinensis* was used to hasten recovery from exhaustion, an effect that has recently been scientifically validated. *Cordyceps sinensis* has been tested in trials involving over two thousand patients. Researchers were unable to establish a toxic dosing level, which

shows that it is very safe. The only side effects of chronic ingestion of *Cordyceps sinensis* have been an increase in sperm count and testes weight. A recent exhaustive two-part review of the Chinese and English literature provides a wealth of historical and scientific validation for the safety and benefits of *Cordyceps sinensis*.¹⁰⁶

Cordyceps sinensis extract greatly increased the very low levels of interferon-gamma, tumor necrosis factor-alpha, and interleukin-1 in cell cultures of leukemia cells. *Cordyceps sinensis* also increased the production of interleukin 2 and its absorbency by immune cells. Each of these cytokines is associated with increased antiviral and/or antitumor activity as well as overall immune responsiveness.

A preparation of cordyceps caused significant elevation in the number of T-helper cells and increased the helper to regulator T-cell ratio. Cordyceps augments the NK cell activity. The importance of these effects should not be underestimated (for example see previous discussion on natural killer cells).

As discussed earlier, tumors use a myriad of methods to escape immune surveillance. Two of these techniques are down-regulation of self-markers on tumor cell surfaces and reduction of the macrophage migration toward and engulfment of tumor cells. This latter technique is often dramatically seen in lymphoid tumors.

The antitumor effect of *Cordyceps sinensis* is mediated through its immunomodulating action rather than through any direct toxicity toward the cancer cells. *Cordyceps sinensis* extracts caused an increased appearance of self-markers, making the host immune surveillance more effective against those tumor cells which down-regulated self-markers as a means of immune evasion. Oral administration of cordyceps sinensis also induced an above normal level of macrophage activity, resulting in reduced lymphoma tumor size and increasing the survival rate in mice.

Cordyceps sinensis has been tested against other cancer cell lines as well. Extracts of *Cordyceps sinensis* increased the median survival time of mice bearing either Ehrlich ascites carcinoma or Meth-A fibrosarcoma by over 300 percent. *Cordyceps sinensis* extract, in combination with blood mononuclear cells, inhibited the proliferation of human leukemia U937 cells by 78 to 83 percent. Cancer cells are often immature cells, and maturation of the cancer cells diminishes their cancerous characteristics. Examination of the U937 cells after treatment with *Cordyceps sinensis* extract showed that about 50 percent of the leukemia cells had become mature monocytes and macrophages. *Cordyceps sinensis* also reduced colony formation of B16 melanoma and helped to maintain NK cell activity in spite of the presence of the immunosuppressive drug cyclophosphamide, suggesting its potential usefulness in treating cancer in immunodeficient patients. Helper T cells were also protected from the deleterious

effects of the immunosuppressive drug prednisolone acetate. These results further substantiate the potential utility of cordyceps in immunodeficient or immunosuppressed patients.

Cordyceps sinensis appears to evoke a balanced immune response. In experimental transplants, high doses of *Cordyceps sinensis* (4 g/kg/day) significantly prolonged the survival time of unmatched skin grafts. It has also been suggested that cordyceps may have great potential for the management of human systemic lupus erythematosus (SLE), which is a serious autoimmune disease with multiple organ system involvement. The immunosuppressive ingredients contained in *Cordyceps sinensis* are not cytotoxic to human mononuclear cells.

Oral administration of *Cordyceps sinensis* was tested against systemic infection by salmonella. The protective effects were probably due to the observed increase in antibody response. *Cordyceps sinensis* also improves liver function and positively adjusts body immunocompetence in chronic hepatitis B patients.

Cordyceps sinensis has both immunostimulating and immunosuppressive effects. Cordyceps stimulates significant protective effects in both the liver and kidney, and it has a very safe profile even during chronic ingestion of large doses.

Glucans. Defense against fungi such as yeast is one of the most primitive functions of the immune system. This is accomplished through recognition of molecular patterns found only in the cell walls of microorganisms. One of the main molecular recognition patterns is poly-1,3-beta-glucose or beta-glucan. Hundreds of papers have been published on various aspects of beta-glucan's ability to modify biological responses.¹⁰⁷

The natural killer cells require dual signals before they unleash their violence. When a cancer cell is tagged with complement system proteins, the natural killer (NK) cells can attach themselves to the cancer cell. If a second confirmatory signal molecule is present on the cancer cell, the NK cells are activated and the cancer cell is destroyed. If the second signal is absent or if the cancer cell has developed a blocking protein, the tumor cell will survive.

Beta-glucans were first reported to stimulate tumor rejection in 1963.¹⁰⁸ Beta-glucan appears to supply the second signal that completes the activation of NK cells. Having received both recognition and activation signals, the NK cells are authorized to destroy their malignant target.¹⁰⁹ This may be the same mechanism that is responsible for the frequently observed tumor regression that follows an infection.¹¹⁰ Orally administered beta-D-glucan greatly enhances the anti-tumor effects of monoclonal anti-tumor antibodies (mAb) irrespective of antigen, human tumor type or tumor site.^{111,112}

Bacteria like *Escherichia coli* and *Staphylococcus aureus* can produce lethal septic infections in animals. Treating the animals with beta-glucan prior to bacterial infection prevented death.^{113,114} Purified water-soluble beta-glucan stimulated the macrophage function sufficiently to enable it to be used as an intravenous injection for sepsis.¹¹⁵ In humans, preoperative administration of glucan reduced serious postoperative infections and death by 39 percent after high-risk operations.¹¹⁶ The threat of bioterrorism has prompted a widespread search for defenses against this peril. Beta-glucan administered orally for 1 week prior to lung exposure to anthrax increased survival in mice from 50 percent to 100 percent; therapeutic administration of oral beta glucan for 10 days post-infection increased survival from 30 percent up to 90 percent.¹¹⁷

Eimeria is a genus of parasitic protozoa of immense medical and veterinary importance.¹¹⁸ *Eimeria* cause coccidiosis, a major pathogenic disease of pigs, sheep, goats, rabbits and poultry worldwide. Multiple administrations of oat beta-glucan by intragastric or subcutaneous routes reduced fecal oocyst shedding compared to the non-treated control group. Oat beta glucan appeared to up-regulate immune mechanisms and provide enhanced resistance against eimerian coccidiosis in mice.¹¹⁹

The effects of beta-glucan are also beneficial in strengthening the immune response to viral infections. Oat beta-glucan strengthened macrophage antiviral resistance and NK cytotoxicity sufficiently to counteract the increased herpes simplex virus-1 (HSV-1) respiratory infection brought on by exhaustive exercise induced stress.¹²⁰ Orally administered yeast beta-glucan was found to reduce the lung lesions and viral replication rate of swine influenza virus (SIV).¹²¹ The effectiveness of oral HIV vaccines was enhanced when they were coadministered with oral beta-glucan preparations.¹²²

Beta-glucan has been administered by intramuscular and intravenous injection, and is also bioactive when administered orally.¹²³ Sources of beta-glucan include yeast, mushrooms,¹²⁴ including Shiitake¹²⁵ and the Maitake D-fraction,¹²⁶ and certain higher plants.¹²⁷

Mannans. Acemannan is the major carbohydrate fraction obtained from the gel of the Aloe vera leaf.¹²⁸ Most if not all of the immunological benefits of aloe gel appear to come from the acemannan fraction of the gel.

The use of aloe vera gel as a skin treatment is centuries old. Recently acemannan was shown to reduce the effects of radiation damage to skin if applied immediately and continuously for two weeks after radiation exposure.¹²⁹ Radiation is also extremely damaging to immune cells. Acemannan appears to be an effective adjunct to surgery and radiation.¹³⁰ The benefit of acemannan is probably due to its support of the immune cell populations during and after irradiation.¹³¹

At least three immune cell types can be strongly affected by acemannan. The adjuvant activity of acemannan is at least in part due to its capacity to promote differentiation of immature dendritic cells.¹³² Acemannan enhanced the number and killing capacity of cytotoxic T-lymphocytes (CTLs) by almost 50 percent.¹³³ Macrophages incubated with acemannan for ten minutes demonstrated a ten-fold increase in their ability to kill the yeast *Candida albicans*. After sixty minutes of exposure to acemannan, the ability of macrophages to kill candida raised another three-fold, resulting in a nearly complete destruction of all the fungi.¹³⁴ This occurs in spite of the fact that no dose of acemannan was found to be cytotoxic to the target pathogens.¹⁹³ Clearly acemannan operates through the immune system rather than independent of this system. The antitumor activity of acemannan in tumors is believed to result from macrophage activation and the release of antitumor cytokines.^{135,136,137,138}

Viruses use a variety of mechanisms to avoid destruction by the immune system. One of these mechanisms is the inhibition of T-cells. Pretreatment with acemannan reduced the virus-induced inhibition of T-cells,¹³⁹ and acemannan therapy was significantly beneficial for cats exhibiting clinical signs of feline immunodeficiency virus (FIV) infection.¹⁴⁰ Acemannan is one of only a very few plant-derived, anti-HIV products that have been used in a limited number of patients suffering from AIDS.¹⁴¹ To date, the benefit of acemannan on HIV patient health has been limited in cases of advanced HIV.¹⁴²

Acemannan has shown benefit in other areas as well. Acemannan inhibited adherence of the bacteria *Pseudomonas aeruginosa* to lung cells.¹⁴³ In addition its use as a vaccine adjuvant was shown to be beneficial either in raising or sustaining the immune response.¹⁴⁴ Acemannan increased the primary response to the heartworm antigen ten-fold over control levels.¹⁴⁵ A combination of melatonin and aloe extract has been reported to arrest, though not reverse, brain carcinoma.¹⁴⁶ The safety of acemannan at high dosages has been clearly demonstrated.¹⁴⁷ Further, acemannan does not potentiate HIV-1 or HSV-1 replication.¹⁴⁸

Phytic Acid, Inositol Hexaphosphate, or IP6. Inositol hexaphosphate, also known as phytic acid (IP6), its lower phosphorylated forms (IP 1-5), and inositol are important in regulating vital cellular functions.^{149,150,151,152} IP6 is found in cereal bran and legumes, and it has been shown to be the agent responsible for much of the anticancer activity of high fiber diets.¹⁵³ The anticancer action of IP6 has been demonstrated both in vivo and in vitro against cancers of the liver, breast, prostate, large intestine and colon. The effectiveness of IP6 against human mammary cancers is independent of the estrogen receptor status of the cells.

IP6 is rapidly absorbed and metabolized by human malignant cells in

vitro. IP6 up-regulates the expression of tumor suppressor genes and also blocks incitement of tumor activator proteins. These discoveries help in part to explain the decreased tumor aggression and diminished tumor size prompted by IP6.

OLIVES AND OLIVE LEAF EXTRACTS

Oleuropein, Hydroxytyrosol and Elenolic Acid. Studies of oleuropein provide a new link between the Mediterranean diet and prevention of coronary heart disease (CHD) and cancer.¹⁵⁴ Indeed many of the beneficial effects of the Mediterranean diet may be derived from oleuropein and its hydrolysis products hydroxytyrosol and elenoic acid.

Oxidatively modified low-density lipoproteins (LDL) contribute to the onset of the atherosclerotic disease. Natural antioxidants abound in the Mediterranean diet and may contribute to the observed protection from CHD by retarding the formation of the atherosclerotic plaque. Not only is LDL oxidation inhibited by oleuropein¹⁵⁵ and hydroxytyrosol¹⁵⁶ but also the blood levels of both total and free cholesterol are significantly reduced.¹⁵⁷

The olive tree, *Olea europaea*, is a potential source of promising antimicrobial agents for treatment of intestinal or respiratory tract infections in man.¹⁵⁸ The recent discovery that microbial infection and heart disease are correlated¹⁵⁹ provides an additional dimension to the protective features of olive and olive leaf extract consumption in CHD.¹⁶⁰ The addition of oleuropein significantly and immediately decreased outgrowth of *Bacillus cereus* T spores.¹⁶¹ Low concentrations of oleuropein also delayed the growth of *Staphylococcus aureus*.¹⁶² In addition oleuropein improves the macrophage-mediated response during endotoxin challenge leading to an increased cellular and organism protection.¹⁶³

Elenoic acid has been repeatedly demonstrated to exert antiviral activity. Calcium elenolate reduced influenza viral infectivity and was also demonstrated to be both preventive and therapeutic in the case of parainfluenza-3 virus.¹⁶⁴ More than ten years before HIV was identified, calcium elenolate was shown to inhibit a viral reverse transcriptase enzyme.¹⁶⁵ In the case of myxoviruses, calcium elenolate was found to be as effective as the anti-viral drug Virazole against influenza virus.¹⁶⁶ The safety of oral ingestion was demonstrated in rabbits, rats, mice, dogs and humans in both acute and chronic toxicity models.¹⁶⁷

Olive and olive leaf extracts provide an array of anti-inflammatory benefits. Hydroxytyrosol was the best anti-inflammatory component found in olives.¹⁶⁸ Inhibition of inflammation may reduce damage to arterial linings. Hydroxytyrosol was also highly protective against DNA damage which is involved in the pathology of several chronic diseases.¹⁶⁹ There is growing evidence that reactive oxygen species are involved in the etiology of fat-related neoplasms such as cancer of the breast and colorectum.

Hydroxytyrosol is a potent inhibitor of free radical generation in the feces providing a clear mechanism for prevention of colorectal carcinogenesis.¹⁷⁰

The bioavailability and safety of oleuropein and hydroxytyrosol are excellent. Kinetic data demonstrate that hydroxytyrosol can be quantitatively absorbed at the intestinal level with the majority of the absorbed material excreted in the urine.¹⁷¹ Neither oleuropein nor hydroxytyrosol were toxic to leukocytes at the concentrations tested.¹⁷²

PHYTOSTEROLS

Phytosterols are important constituents of healthful diets.¹⁷³ Legumes, long known for their healthful properties, are one of the best sources of phytosterols.¹⁷⁴ Peanuts have also been found to be an excellent source of phytosterols.¹⁷⁵ Beta-sitosterol is the major phytosterol in higher plants. Western processed diets contain only 20-25 percent of the beta-sitosterol present in vegetarian and Asian diets.¹⁷⁶ Like vitamin C, humans do not produce any beta-sitosterol. In nature beta-sitosterol is bound to plant fiber, making it difficult to absorb. Concentration procedures break down much of the plant fiber matrix, which should improve the bioavailability of beta-sitosterol.

Phytosterols have been shown to modulate the immune system, inhibit colon cancer development, and normalize cholesterol levels.¹⁷⁷ Beta-sitosterol as an immune-modulator is involved in normalizing T-cell function, dampening overactive antibody responses, and rebalancing DHEA-to-cortisol ratios.¹⁷⁸ Proliferation of T-cells, increased secretion of IL-2 and gamma interferon, and increased NK-cell activity are some of the immune parameters that are enhanced during immune challenge when phytosterols are present.¹⁷⁹

Epidemiologic and experimental studies suggest that dietary phytosterols may offer protection from the most common cancers in Western societies, such as colon, breast and prostate cancer.¹⁸⁰ Early work demonstrated that phytosterols including beta sitosterol were protective against chemically induced colon cancers.¹⁸¹ Rao and Janezic have proposed that the interaction of phytosterols with gut micro-flora protects the colon from toxic metabolites of cholesterol.¹⁸² High intakes of phytosterols also explained most of the gastric and esophageal cancer protection that results from high vegetable and fruit intakes.¹⁸³ Mechanistic studies by Awad, et al. are elucidating the mechanisms whereby phytosterols inhibit prostate cancer cell growth.¹⁸⁴

Awad et al. demonstrated that dietary phytosterols retard the growth and spread of breast cancer cells.¹⁸⁵ Further studies by Awad's group revealed the mechanisms by which phytosterols may be functioning including the activation of "executioner" enzymes in cancerous cells.^{186,187,188} Phytosterols stimulated isolated mammary tumor cells studied outside of

the body (in vitro studies). Nevertheless, in vivo (live animal) studies by the same researchers, reported in the same paper, demonstrated a 30-40 percent reduction in tumor growth.¹⁸⁹ This contrast in results illustrates the importance of critically examining the experimental conditions used before drawing any conclusions about the safety and efficacy of dietary supplements. Further evidence for both the safety and efficacy of phytosterols is found in the work of Park, et al. who have shown that the anticancer properties of the Korean traditional food, kimchi, are largely due to the presence of the phytosterol beta-sitosterol.¹⁹⁰

Beta-sitosterol has also been identified as the antimicrobial and antifungal constituent of many medicinal plants.¹⁹¹ When pulmonary tuberculosis patients added sitosterol to their diet, in addition to an efficacious anti-tuberculosis regimen, their immune parameters and overall quality of life improved.¹⁹²

Phytosterols including beta-sitosterol have been identified as the active anti-inflammatory principles in cactus and other medicinal plants.¹⁹³ Beta-sitosterol was found to be nearly as potent as indomethacin in inhibiting ear inflammation.¹⁹⁴ A decrease in the cortisol to DHEAs ratio may in part explain this diminished inflammation.¹⁹⁵

Benign Prostate Hypertrophy (BPH) is a non-cancerous enlargement of the prostate that affects the quality of life for most men as they enter their fifth and subsequent decades of life. In a rigorous and matched study, the efficacy of phytosterols was validated as an effective approach to BPH.¹⁹⁶ Beta-sitosterol improves urological symptoms and flow measures in BPH.¹⁹⁷ A German multi-center study of 177 BPH patients showed that beta-sitosterol is an effective option in the treatment of BPH.¹⁹⁸ These results were supported by the results of a three month Japanese study employing a low dose of phytosterol containing 180 mg of sitosterol per day. Significant improvement in the patients' International Prostate Symptom Scores (IPSS) and their quality-of-life (QOL) scores were recorded.¹⁹⁹ In a critical review of sitosterol effectiveness in controlling BPH, Lowe and Ku noted that it was sitosterol, not its glycoside, that has shown the greatest benefit in relieving BPH.²⁰⁰ Four placebo-controlled studies involving 519 men support this conclusion that the non-glucosidic beta-sitosterols improve urinary symptoms and flow measures.²⁰¹ The beneficial effects of beta-sitosterol treatment for BPH were maintained for 18 months.²⁰²

Lowering total and especially LDL cholesterol levels is strongly recommended for the prevention of coronary heart disease. Dietary phytosterols are beneficial in regulating cholesterol levels.²⁰³ Phytosterols have been shown to lower serum cholesterol in approximately 88 percent of mildly hypercholesterolemic subjects.²⁰⁴ Physicians and researchers have stated that the addition of sitosterol and the other phytosterols to the diet may be the preferred method for controlling hypercholesterolemia in both adults

alpha (INF α) to awaken the immune response. These signaling molecules do not inhibit the replication of the virus. The first cells to respond to the virus infection are the NK cells. As shown in the graph it takes 24 to 48 hours for the NK cells to activate sufficiently to control the viral expansion. After three to six days the T-killer cells and the antibody responses develop and finish off the residual viral infection. Inadequate basal activation of the NK cells is associated with many disease conditions. Conversely those persons with alert and responsive NK cells enjoy greater overall health.²¹⁶

The initial testing of transfer factor products was conducted in 1999 using a drug protocol.²¹⁷ In this procedure a 50-to-1 ratio of NK cells to target cancer cells was used. Comparing the results from this study to the previously reported enhancements of NK cell activity showed that colostrum transfer factor more than doubled the enhancement of any previously tested natural product.²¹⁸

The high (50:1) NK to cancer cell ratio, the short preconditioning time, as well as the short reaction time used in the previous tests, reflect the optimal conditions for testing a drug for direct NK cell activation. Recent testing at the Oncology Research Center of the Russian Academy of Medical

Table 1. Percent Increase in Natural Killer (NK) Cell Activity Induced by Selected Nutritional Supplements.

	Product	% Increase in Natural Killer Activity	Testing protocol
1	Colostrum Transfer Factor	103	a
2	Enhanced Colostrum Transfer Factor ^d	232 ^c	a
3	Colostrum Transfer Factor	204	b
4	Colostrum/Egg Transfer Factor	283	b
5	Enhanced Colostrum/Egg Transfer Factor ^d	437 ^e	b

- a) High (50:1) NK:Cancer cell ratio; 4 hr preconditioning time; 4 hr reaction time
- b) Low (2:1) NK:Cancer cell ratio; 48 hr preconditioning time; 18 hr reaction time
- c) The reported value of 232% increased NK cell activity for this preparation of an Enhanced Transfer Factor formulation can be compared to the previously reported 248% increase for a similar Enhanced Transfer Factor formulation that differed slightly in the inclusion of thymus components and the exclusion of beta-sitosterol and oleuropein. **Within experimental accuracy the values 232% and 248% are equivalent.**
- d) Enhanced Transfer Factor formulations contain 25% transfer factor and 69% plant extracts supplying, among other components: beta-glucans, alpha-mannans, beta-sitosterol, oleuropein, and inositol hexaphosphate (IP6); and 0.84% zinc.
- e) The K562 cancer cell kill rate was 97%. The reported value may represent a minimal effect since essentially no cancer cells were left intact.

Sciences employed a protocol more reflective of the natural conditions that would occur internally after oral supplementation (Low [2:1] NK-to-cancer cell ratio; 48 hour preconditioning time; 18 hour reaction time).²¹⁹ Some of the results of these two studies are contained in Table 1.

Correlating the drug protocol to the more naturally modeled protocol is difficult. Nevertheless, by comparing lines one and three of Table 1 which correspond to the testing of the same product, one can get a sense of their relative value. A rise such as that seen between the drug and natural protocols for the colostrum transfer factor would not be predicted on the basis of direct drug interactions with the natural killer cells.

Recent discoveries have led to the conclusion that natural killer cells are made, not born, indicating that certain conditions need to be present for the natural killer cell response to be initiated and properly developed.²²⁰ On the other hand, transfer factors are commonly believed to be produced by T-cells.²²¹ These two facts can be brought together because of the recent discoveries of cell-to-cell interactions involving natural killer cells, T-cells and other cells of the immune system. One must be aware that the procedures used to obtain NK cells do not remove T-cells. It appears therefore that the extended preconditioning time allows the added transfer factors to interact with the T-cells and T-cells to interact with the NK cells resulting ultimately in a more effective recognition and destruction of cancerous cells.

It is much more difficult however to justify this rise in effectiveness between the two experiments when only 4 percent of the natural killer cells were present in the naturally modeled protocol. Even given the extended reaction time (eighteen hours) one still cannot adequately justify this improvement based on a direct drug interaction. Whether this increased effectiveness is due solely to increased NK cell efficiency or if there is an expansion of the Cytotoxic T-cells (CTLs or T-killer cells) is yet to be unraveled. What does seem reasonable is that a cell-to-cell amplification cascade has been greatly improved.

Drs. Kisilevsky and Khalturina at the Oncology Research Center of the Russian Academy of Medical Sciences studied the enhancement of the natural killer cell effectiveness using colostrum- and egg-derived transfer factor. When the egg derived transfer factor is mixed with the colostrum-derived transfer factor, keeping the total amount of transfer factor constant, the studies demonstrated a significant synergy. The basis for the synergistic improvement is still under investigation and probably lies in the differences that exist in the immune systems of cows and chickens. In cattle the young are born dependent upon the mother for nourishment and immunological education. The hatchlings of many birds are also dependent upon their parents for nourishment. All however are immunologically detached from their parents. In the case of common poultry such as chickens and ducks the young are independent at birth. A chicken matures quickly and repro-

duces prolifically compared to a cow. These differences may lead to differences in the fine-tuning of the immune responses of chickens and cows.²²² The relatively long life of cattle results in exposure to a broad range of pathogens over an extended period of time but in a relatively limited geographical area. Migratory birds on the other hand must have the ability to rapidly adapt to new pathogens from widely separated areas.²²³ The chicken likely shares some of this rapid immunological response ability even though it is not migratory. The combination of the two transfer factor profiles may then lead to both a broad and a rapid responsiveness.

Finally, the augmentation of the combined colostrum-egg transfer factor mixture with additional plant extracts and zinc further enhances the NK cell efficiency (see Table 1 line 5). In this case the measured 437 percent increase corresponds to 97 percent of the K562 cancer cells being destroyed. The reported value may represent a minimal effect since essentially no cancer cells were left intact. By comparison the controls were treated with interleukin 2 (IL2) which acted as an upper level standard in these tests and resulted in an 88 percent kill rate.

It must be cautioned that the natural killer cell effects of transfer factor are only a fraction of the overall impact of transfer factor on the immune system. Nevertheless the interconnections between the adaptive immune response and the innate immune response are extensive and reveal that natural killer cells play a prominent role in host defense.²²⁴

Summaries of Recent Clinical and Laboratory Reports

Immune system functioning is at the heart of the increasing infectious and immunologic disorders seen in clinical practices. Through its unique properties and activities, Transfer Factor is an extremely useful, relatively risk-free alternative and adjunctive therapy for treatment of cell-mediated or TH1-deficient conditions.²²⁵

The following summaries of recent clinical reports will focus on materials published since 1998. For previously published works the reader is referred to the extensive 1994 reviews by Fudenberg and Pizza^{226,227} and to the abstracts and published reports of the 1995 and 1999 International Transfer Factor Symposia.^{228,229} In addition three recent reviews have been published; two in Spanish^{230,231} and one in Ukrainian.²³²

ATOPIC DERMATITIS

In a series of significant papers Dr. Estrada-Parra and his colleagues studied the effects of transfer factor treatments on patients with atopic dermatitis. High doses of transfer factor were demonstrated to improve the clinical manifestations of atopic dermatitis,²³³ a condition that was further

improved with the addition of psychological support.²³⁴ In these later cases it may be that the visible improvement in physical appearance enabled the psychological component to be more effective. Transfer factor treatments were shown to be as effective as certain drug treatments in decreasing the intensity of the atopic symptoms.^{235,236} The effects of transfer factor were also studied in refractory cases of atopic dermatitis. In these studies Cyclosporin A (CyA, 4 mg/kg/day dosage) was used as the control treatment. Transfer factor was administered in a regimen of decreasing frequency over six months. Both the CyA and the transfer factor groups showed clinical improvement but they displayed opposite T-cell effects. CyA reduced the CD4 levels, while the transfer factor increased the levels of CD8 cells.²³⁷ Effectively CyA weakened the immune response while transfer factor strengthened the immune response. In addition patients taking CyA must be monitored for liver and kidney function while no such problems are associated with transfer factor treatments. In a related study involving patients with moderate atopic dermatitis, the excessive eosinophil levels were significantly reduced.²³⁸

AUTISM

The use of transfer factor to help correct the broad underlying immune dysfunctions present in autism is gaining support.^{239,240,241} Other papers have reported neurotransmitter²⁴² and potentially anti-epileptic effects of immune modulation with transfer factor.²⁴³

CANCER

Historically the most active researcher in the use of transfer factor in cancer therapy has been Giancarlo Pizza.²⁴⁴ Recently an enhanced transfer factor preparation was employed as a key component in an extensive immunotherapeutic approach to cancer treatment.²⁴⁵ In a follow-up study, a group of the patients who had achieved remission using the above protocol were maintained on an enhanced transfer factor supplementation program. After five years the recurrence rate was 7.3 percent. A survey of the unsupplemented patients revealed a 5 year recurrence rate of 69.8 percent.²⁴⁶ Additional anecdotal reports involving the use of transfer factor and enhanced transfer factor preparations to strengthen and support immune function during cancer treatment have been compiled.²⁴⁷

HIV AND OTHER VIRAL DISEASES

Ojeda, et al, have demonstrated that dialyzable leukocyte extracts (one of the sources of transfer factor) is able to inhibit HIV-1 replication in MT-4 cell cultures. Ojeda and his coworkers also demonstrated that after seven days of transfer factor treatments NF-kappaB activity was completely sup-

pressed.²⁴⁸ Transfer Factor has gained the attention of the AIDS community²⁴⁹ and additional investigations into "hard-to-reach" infections have been called for.²⁵⁰

In a double-blind clinical trial of transfer factor versus acyclovir in patients with acute stage herpes zoster, the group treated with transfer factor was found to have a more favorable clinical course. Tests showed an increase in IFN-gamma levels, augmentation in the CD4+ cell population in the TF treated group but not in the acyclovir treated group which confirms the immunomodulating properties of transfer factor.²⁵¹ Similar immunomodulating properties were also demonstrated for a transfer-factor preparation specific to tick-borne encephalitis virus.²⁵²

CANDIDA

Transfer factors were prepared using soluble antigens and whole cells of *Candida albicans* were prepared. Transfer factors from both preparations provided specific and non-specific immune activation. The soluble antigen however, elicited a greater transfer factor response.²⁵³

RECOVERY OF STEM CELL FUNCTION AND BLOOD CELL POPULATIONS

Transfer factor was shown to enhance the recovery of the pools of hemopoietic stem cells (CFUs) and of granulocyte-macrophage hemopoietic progenitor cells (GM-CFC) in the bone marrow in vivo after exposed to a sublethal dose of gamma-rays. In addition the administration of transfer factor increased the numbers of mice surviving potentially lethal doses of radiation.²⁵⁴ Transfer Factor also assisted in the recovery of immune reactivity after radiation induced hypothyroidism.²⁵⁵

Transfer Factor stimulated an increase in lymphocytes and plasmocytes after antigen injection.²⁵⁶ The effectiveness and insignificant occurrence of side-effects has again been reconfirmed.²⁵⁷

COMBINATIONS OF DRUGS AND TRANSFER FACTOR

Recognizing that "Problems of logistics, compliance and drug resistance point to an urgent need for immunotherapeutic strategies capable of shortening the current six month antibiotic regimens used to treat tuberculosis," Dr. Estrada-Parra and his colleagues demonstrated that a more rapid elimination of lung bacteria occurred with the combination of transfer factor and chemotherapy than was possible with chemotherapy alone.²⁵⁸ Leprosy is another condition wherein the use of transfer factor may serve as an adjunct to chemotherapy shortening the treatment period by enhancing bacterial killing and clearance.²⁵⁹

The power of transfer factor in combination with drug therapy is illustrated by the case of a 65-year-old woman suffering from resistant ble-

pharoconjunctivitis and rosacea, which did not respond to antibiotic, steroid or antihistamine treatments. Oral ivermectin gave a good response to the underlying demodicidosis infection but within two months the infection recurred. Retreatment with a combination of ivermectin and transfer factor resulted in total remission.²⁶⁰

These results are fully consistent with a series of Russian studies on the use of transfer factor with conventional chemotherapy. In those cases where neither transfer factor nor drugs have been sufficient the combined application may be the solution.^{261,262}

CHEMICAL STRUCTURE

Charles Kirkpatrick has been able to isolate individual antigen specific transfer factors and established that the antigen specific transfer factors are polypeptides of about 44 amino acid units. Dr. Kirkpatrick was unable to sequence the entire structures of the isolated transfer factors due to a blockage of the N-terminal end. Dr. Kirkpatrick was able to identify a novel highly conserved region (LLYAQDL/VEDN) present in each of the isolated transfer factor. This novel sequence may represent the portion of Transfer Factors that binds to the "target cells."²⁶³

Clinical Studies Leading to a Governmental Recommendation of Transfer Factor

UROGENITAL CHLAMYDIOSIS

In recent years chlamydial infection has become a serious health-care problem. The use of modern antibiotics has lead to the development of such adverse effects as dysbacteriosis, toxic liver lesions, and secondary immunodeficiencies.

In a study of the use of transfer factor alone and with mineral and phytochemical enhancement revealed that treatment times and side effects could be greatly reduced without sacrificing therapeutic efficacy.^{264,265} The treatment course and registered side effects of the various treatments are tabulated in the table on the following page.

The intensity and frequency of side effects observed in the triple antibiotic sequence required the additional use of hepatoprotectors, eubiotics, enzymes and fungicides thus prolonging the course of treatment and increasing the cost. The patients employing the transfer factor-assisted, shortened mono-antibiotic regimen very rarely needed additional protective therapy. Urologists often prefer transfer factor formulations that contain zinc, because of its beneficial effects on sexual function.

H. PYLORI INDUCED DUODENAL ULCERS

Patients with duodenal ulcer disease of more than a ten-year duration associated with Hp were treated with 20 mg of Omez two times daily, 2.0 g. of Amoxycilin once a day and 1.0 g. of Klarithromycin once a day for ten days. A group of these patients were also treated with an enhanced transfer factor formulation according to the following regimen: 2 capsules three times daily for the first ten days and then 1 capsule three times daily for twenty days. Each patient received 120 capsules in one month.

The incidence of side effects in urogenital chlamydiosis patients in the course of antibacterial therapy.

Side effects	1. Claritromycin 500 mg 2 times daily (10-14 days) 2. doxycyclin 100 mg 1 time daily (10 days) 3. ofloxacin 200 mg 2 times daily (10 days) The drugs were administered in succession.	Claritromycin 500 mg 2 times daily (10-14 days) AND Transfer Factor Plus (TF+) 1 capsule 3 times daily administered simultaneously for 10 days beginning with the first day of treatment.	Claritromycin 500 mg 2 times daily (10-14 days) AND Transfer Factor 1 capsule 3 times daily administered simultaneously for 10 days beginning with the first day of treatment.
Nausea	32 %	4 %	7 %
Vomiting	12 %	-	-
Bitter taste in the mouth	56 %	4 %	4 %
Diarrhea	12 %	-	-
Epigastric Discomfort	72 %	-	-
Flatulence	63 %	-	4 %
Hepatotoxic effect	54 %	-	-
Gastrointestinal and/or genital candidosis	88 %	4 %	4 %
Headache	26 %	-	4 %

The addition of the enhanced transfer factor regimen was found to result in a 21.7 percent increase in successful Hp eradication; an earlier cessation of pain and dyspeptic syndromes; an earlier repairing of the defects in the ulcerated mucosal tissue and the elimination of the secondary immunodeficiencies.²⁶⁶

PSORIASIS

Eight patients (5 children and 3 adults) with widely distributed exudative psoriasis, which was resistant to conventional treatment, were studied. An enhanced transfer factor formulation was administered according to the following schedule: 4 capsules daily for 14 days and then 4 capsules a day twice a week for two weeks.

Seven patients demonstrated a marked improvement of skin condition by the end of the course of treatment. One patient, with a five year history of psoriasis with signs of joint involvement, required an additional two weeks of supplementation to achieve comparable results.²⁶⁷

HERPES

Recurrent genital herpes infection leads to suppression of interferon production and a weakening of T-cell responsiveness indicating a need to correct the immune dysfunctions in addition to applying specific antiviral therapy. Nine adult patients with a known history (six months to five years) of moderate to severe recurrent genital herpes were enrolled. An enhanced transfer factor preparation was given as a monotherapy to the patients during periods of genital herpes relapse according to the following schedule: 4 capsules daily for two weeks, then 4 capsules a day three times a week and in the following two weeks—4 capsules a day twice a week.

The therapeutic effectiveness of the product was evaluated against the patients' previous personal histories. Seven out of nine patients receiving the enhanced transfer factor supplementation did not suffer any herpetic relapse during the course of treatment. Two patients had a relapse on the second and the fourth weeks of the treatment, respectively, but both relapses were of short duration and had minimal impact on the patients' quality of life (less acute pain, etc.). In the six weeks following completion of the supplementation program, all patients demonstrated stable clinical remission.²⁶⁸

HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Thirty-five HIV-infected persons were enrolled in an initial trial to evaluate the effects of an enhanced transfer factor supplement on the immune parameters of HIV-infected patients. Twenty-five HIV-infected patients (twenty male and five female), who did not receive antiretroviral or

immunocorrecting therapy, received one capsule twice a day for seven days of the enhanced transfer factor supplement. Ten similarly infected HIV-patients taking cycloferon (1st, 2nd, 4th, 6th, 8th, 10th, 12th and 14th days) served as the control group. An evaluation of cell and cytokine profiles was carried out before treatment began and then seven to ten days after treatment to assess the immune status of the patient groups.

Approximately half the enhanced transfer factor supplemented patients registered a significant increase in CD3, CD4 and CD8 cells. In the supplemented group the average total lymphocyte count increased 25 percent, the CD4 levels increased 35 percent and the CD8 levels increased 21 percent. The CD4/CD8 ratio in the supplemented group increased 22 percent and the IL-1b level rose 35 percent. These are all indicators of improved immune competence in the supplemented patients. In the cycloferon control group, the above parameters declined or remained unchanged.

Even short-term transfer factor supplementation, enhanced with zinc, various plant polysaccharides and phytosterols, considerably improves the immune status of HIV-infected patients. Further studies are needed to determine optimal therapy and the frequency of repeat courses of supplementation.²⁶⁹

VIRAL HEPATITIS

Patients with viral hepatitis B or C were supplemented with either transfer factor or an enhanced transfer factor preparation for fourteen days. In each group of patients the results were comparable to the effects of three 3,000,000 IU treatments per week with interferon (reaféron). Increases in liver enzyme levels were noted in one-third of the chronic hepatitis C patients treated with interferon, which was not unexpected. Patients ingesting the enhanced transfer factor preparation reported a significant improvement in their energy levels and general sense of well-being. Transfer factor preparations were recommended as an alternative treatment to recombinant interferons or as an addition to the conventional therapies for viral hepatitis.^{270,271}

OSTEOMYELITIS AND CELLULAR RECOVERY

Thirty-three patients with various forms of osteomyelitis were divided into two groups (twenty patients in the supplementation group and thirteen patients in the control group). All patients underwent surgery, aimed at the removal of purulent infection focus, followed by strong antibacterial treatment (gentamycin, ampicillin, etc.) in the postoperative period. Those persons assigned to the supplementation group received 2 capsules of transfer factor three times daily one week before and two weeks after surgery.

Blood drawn one week before surgery and one month after surgery were

evaluated chemically and biochemically to assess the changes in antioxidant status, enzyme levels, and protein and lipid oxidation levels. The physical stability of red blood cells was used as an indicator of overall cellular integrity. The results are tabulated in the table.

Measured Parameter	% change*	
	Control Group	TF Group
Reduced ascorbates	12.4	80
SH/SS ratio	0	16
Super Oxide Dismutase (SOD)	14	-36
Glutathione Peroxidase (GPO)	0	-24
Catalase (Cat)	44	30
Glutathione-S-Transferase (G-S-T)	22	171
Protein Integrity	-2.8	16.1
Lipid Integrity	-30.3	14
Cellular Integrity	-12.5	5.5

*% change refers to the % difference between the average levels measured one month after surgery to the levels measured one week prior to surgery

These data show that, in osteomyelitis, transfer factor brings about biochemical and immunological changes both of which are beneficial in deterring disease processes. "The improvement of these values in combination with the pronounced positive dynamics of the immune system leads us to conclude that even in cases of severe infection, as in osteomyelitis, TF can be recommended as an addition to the conventional treatment."^{272,273}

PARASITE—OPISTHORCHIASIS

Ninety-four patients received conventional therapy consisting of Biltricide (75 mg/kg bodyweight three times orally during one day.) Fifty of the patients also received two capsules of an enhanced transfer factor preparation (TF+) three times per day for seven days. Both regimens were successful in eliminating the parasite. Significant differences however were found in the elimination of conditions caused by and secondary to the primary infection as listed in the following tables.^{274,275}

Clinical Manifestations	After 2 Weeks		After 3 Months	
	Biltricide (Control) (n=44)	Biltricide and TF+ (n=50)	Biltricide (Control) (n=44)	Biltricide and TF+ (n=50)
	%	%	%	%
Pains - right hypochondrium	52.3	10.0	6.8	absent
Heaviness - hypochondrium	75.0	3.0	36.4	4.0
Pains - epigastrium	29.5	2.0	absent	absent
Nausea	36.4	2.0	11.4	absent
Bitter taste	18.2	absent	absent	absent
Heartburn	27.3	absent	4.5	absent
Weakness & fatigue	36.4	absent	Absent	absent
Headache	18.2	absent	4.5	absent
AP elevation and drop	2.3	absent	2.3	absent
Skin rash	6.8	absent	absent	absent
Arthralgia	29.5	20.0	29.5	14.0
Subfebrile condition	4.5	absent	2.3	absent
Cough	4.5	absent	4.5	absent
Attacks of asphyxia	15.9	absent	9.1	absent
Patients Suffering from Opisthorchiasis				
Clinical Manifestations	Biltricide and TF+		Biltricide	
	Prior to treatment	6 mo. after treatment	Prior to treatment	6 mo. after treatment
Arthralgia	12	0	13	9
Vasculitis	9	2	6	6

The inclusion of enhanced transfer factor supplements for immunorehabilitation in conjunction with standard chemotherapeutic treatment results in a more rapid and complete recovery and prevents the autoimmune effects of the disease. The clinical manifestations were corroborated by concurrent laboratory studies.

STOMACH CANCER

Fifty patients with second to third stage stomach cancer were equally divided into experimental and control groups. Both groups underwent surgical treatment consisting of gastrectomy (or proximal stomach resection) with D2 size lympho-dissection involving splenectomy. All patients also received a postoperative immunotherapeutic treatment comprised of interleukin-2 and lymphokine activated killers (or LAK-cells, which were generated by extra-corporal activation of mononuclear blood cells). In addition the experimental group received 1 capsule of an enhanced transfer factor preparation three times daily for thirty days.

Immunological evaluation revealed an improvement in the interferon and cytokine indices, an increase in the CD3+, CD4+, CD8+ subpopulations of blood lymphocytes, and a marked increase in NK-cell activity. The normalization of the levels of TNF-a and IL-1b was also observed. The IF-a concentration in blood plasma remained unchanged.

There were positive changes in clinical signs and symptoms which were expressed as decreased systemic intoxication, better appetite, less weakness and weariness and a general improvement in the patients' physical condition. In order to optimize the effect of the enhanced transfer factor supplementation the researchers recommend that an increased dose and an increase in the duration of supplementation be pursued.²⁷⁶

ACUTE RESPIRATORY DISTRESS

Transfer factor supplementation of college-age students suffering from frequent non-bacterial acute respiratory distress (ARD) resulted in a marked reduction of the number of new ARD episodes and concomitant decrease in herpes simplex outbreaks and a subjective improvement in the general state of health. There was an increase in the number of cytotoxic T-lymphocytes and NK-cells in peripheral blood flow but no statistically significant impact on the indices of immunoglobulins and NBT-test.

There was a more prolonged clinical and immunological benefit of the transfer factor supplementation when the product was taken for 30 days as opposed to 15 days. No significant side effects were registered during the course of transfer factor treatment.²⁷⁷

PEDIATRICS

The Rostov Microbiological Institute has developed a bovine colostral immunoglobulin preparation which has found wide use in treating pediatric intestinal infections. Physicians at the Rostov State Medical University have extended this work through their investigations of the use of transfer factor for systemic conditioning of the infant immune systems. The use of transfer factor in premature babies and in infants was

found to promote the development of adequate acquired immunity. They further state that transfer factor supplementation is mandatory in colostrum-deprived infants beginning with the first days of life. Supplementation with transfer factor prior to preventive vaccination was recommended to help activate a specific immune response, increase the production of specific antibodies and prevent adverse atopic reactions. The Rostov physicians also recommend the use of transfer factor in helping to correct the immune dysfunctions and chronic infections of the expectant mother as a means of protecting the child from a maternally imposed immunodeficiency.^{278,279}

Methodological Letter

The concept of immune reconstitution has gained somewhat of a following among AIDS researchers. In Russia the recognition of the critical and central position of the immune system and its frequent compromise due to environmental and infectious pressures has lead to a focus on immunorehabilitation; literally rehabilitation of the immune system. The preceding ten studies formed the basis for the application for approval of transfer factor for use in immunorehabilitation. The result was the issuance of Methodological Letter No. 14/231 by the Ministry of Health and Social Development of the Russian Federation on July 30, 2004, authorizing health care professionals to exploit "Transfer Factors Use in Immunorehabilitation After Infectious-Inflammatory and Somatic Diseases."

In his preface to the Methodological Letter, Academician Anatoly A. Vorobiev, a Doctor of Immunology and a member of the Russian Academy of Medical Sciences observed "A multitude of immune modulators are used in medical practice but their effectiveness and the other properties defining their safety, simplicity in use and economy factors differ greatly (A.A. Vorobiev, RAMS Bulletin, #4, 2002). Transfer Factor is superior to other, even well known immune modulators in being extremely effective in boosting the immune system. It possesses a broad spectrum of action, is safe, is used orally as gelatinous capsules, has no contraindications, causes no adverse reactions and is effective both in adults and children."²⁸⁰

Summary

The immune system is an elegant and sophisticated network of cells and molecules that strive constantly to maintain our health and physical integrity against an onslaught of increasingly resistant microbial invaders. These

microbes and our own cancer cells use an array of techniques to evade or subvert our immune responses. Dietary supplementation discussed in this booklet may help us attain an immunological advantage over invading microbes and invasive cancers.

Transfer factor is not a vitamin, mineral or herb. It is an elegant universal mechanism of immune communication. It is not species specific; meaning that there are no species restrictions between the donor of transfer factor and the recipient. This is similar to the universality of pictures as a form of communication as compared to the restricted utility of words which must have a common meaning between the speaker and listener.

Zinc is involved in over two hundred critical biochemical functions including immunity. Adequate zinc absorption diminishes with age. Maintenance of the body's zinc levels through dietary supplementation helps reduce or stop the age related decline in immune function. Reactivation of thymulin by dietary zinc supplementation has been used to recover immune competence in immune compromised individuals.

Rediscovery and scientific validation of the ancient benefits of Sen-su-take, Maitake, and shiitake mushrooms as well as Cordyceps sinensis provide a valuable basis for the use of these products and their extracts in strengthening the immune response. Some of the ingredients of these plants that provide the immunological benefits have been identified. Many other minor components may also play significant roles in supporting the immune system.

The beneficial effects of acemannan depend on the presence of the immune system. Beta-glucan has an extensively documented immunological benefit. Recent research has clarified much of the earlier therapeutic confusion and has led to a rational basis for the effective use of beta-glucan as a biological agent. The combination of acemannan and beta-glucan appears to provide a greater immunological impact than what occurs when either agent is used alone.

The phytosterols are important elements of healthful diets. They help modulate the immune response, inhibit cancer growth, and normalize cholesterol levels. Phytosterols are the active principles in many medicinal plants exerting antimicrobial, antifungal, and anti-inflammatory activity.

Oleuropein, hydroxytyrosol, and elenolic acid from olive leaf extracts have been shown to be antibacterial, antiviral, as well as being anti-inflammatory. All of these characteristics help protect the body and reduce the strain on the immune system. In addition these natural products are good anti-oxidants and this may in part explain their ability to protect cells from DNA damage that is associated with cancer and other chronic diseases. Inositol hexaphosphate (IP6) appears to act by a different mechanism that results in improved intracellular control of malignant cells.

The combination of these agents has demonstrated a synergistic impact on NK cell activity with no measurable toxicity, even at excessively high concentrations. These facts open up the potential for enhanced nutritional support for an optimally functioning immune system.