UNDERSTANDING YOUR IMMUNE SYSTEM
IMMUNE FACTORS, WHITE BLOOD CELLS, ANTIBODIES AND INFLAMMATION –
YOUR IMMUNE SYSTEM'S ONLY DEFENSE AND HEALING MECHANISMS.

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When one is in immune balance (homeostasis), bodily defenses and healing processes are optimized and the body is at its peak of performance and wellness. i26 provides a buffet of antibodies and immune factors (*none* of which are found in vitamins, minerals, or herbs) that help your body achieve its natural immunological homeostasis.

Background

Our physical and emotional health is governed by our immune systems. The immune system is a complex network of white blood cells, immune factors, and antibodies that heal us when we are hurt, and protect our bodies from cancers, and infection by bacteria, viruses, fungi, and other foreign agents.

In the healthy person there is a delicately balanced immune system. In balance, the right amount of fire power of the immune response is triggered to repel an infection or heal a wound, and then the system must decrease, or stop a response when intervention is no longer needed. A properly balanced immune response, does not "over respond" or "under respond" (Curr Drug Targets Immune Endocr Metabol Disord 2005 5:413); it is "just right". When properly functioning, the right number and types of white blood cells and immune factors are involved to meet and resolve the challenge.

Imbalances of our white blood cells and immune factors result in immune disorders such as autoimmunity and allergies (over activity) or susceptibility to infection and cancer (under activity).

i26 holds two patents related to immune balance. US Patent 6,420,337 Cytokine Activating Factor (helps the immune system to turn on) and US Patent 7,083,809 Cytokine Inhibitory Factor (helps the body to determine when to turn off or decrease an immune response) .

Immunity **As long ago as the fifth century B. C., Greek doctors knew that people who recovered from the plague would never get the disease again. This is because they had acquired immunity against it (NIH Publication). The white blood cells of the immune system have "memory"; they "remember" having been exposed previously to a specific organism. When the body is exposed again to the same pathogen the memory cells are**

ready to release the right sorts of immune factors to destroy the pathogen preventing re-infection of the body ("immunity").

Self vs. Non-Self **The key to a well-functioning immune system is its ability to tell the difference between self- and non-self. Every living organism and cell has a unique set of surface molecules called antigens ("barcodes") that identify them.**

The "barcodes" are recognized by our immune cells and help the body identify a cell as *self*, or as *non-self*. Normally the body will not attack its own cells ("self") , but is programmed to attack those with "non-self" or foreign antigens. When the white cells of our immune system recognize these non-self, foreign, "barcodes" they can trigger other types of white blood cells to produce large proteins (antibodies) that lock onto these antigens, to mark the cells for destruction. Other cells will produce small bioactive molecules (immune factors) that stimulate other types of immune responses that will help heal or defend the body.

i26 has been shown to deliver concentrated bioactive molecules that help the body's immune system work efficiently and rapidly.

Proper Functioning of the Immune System **When balanced and stable, the immune system will destroy non-self cells such as mutated cells that multiply causing cancer, or foreign invaders (such as fungi, bacteria, and parasites) that may lead to infection if left to replicate. When it is working "properly", the immune system heals the body (wound healing), fights off infections, and kills cancer cells.**

Underactive Immune Responses **An underactive immune system may be caused by one's heredity, chemo- or radiation therapy, excessive exercise, aging, stress, etc. and may lead to being vulnerable to many illnesses.**

An underactive immune system, often leads to opportunistic infections. These sorts of infections are caused by organisms that do not bother us when we are healthy, but when our "guard is down" (meaning the immune system is working at its appropriate level) result in severe infections.

Individuals with acquired immunodeficiency syndrome (HIV/AIDS) are at risk for getting opportunistic infections. Their disease is characterized by an immune disorder or a breakdown of their immune system that leaves them susceptible to parasitic, bacterial, viral, and fungal diseases. In a person with a properly functioning immune system, these organisms would be less likely to cause disease.

People with cancers and other severe diseases may also experience lowered immune responses as a result of anticancer therapies. Also

emotional stress, malnutrition, surgery, and blood transfusions may result in depressed or altered immune responses.

Overactive Immune Responses **Overactive immune systems may lead to conditions such as allergies, or autoimmune conditions. Allergies are the result of an "over reaction" of the immune system to non-threatening substances such as pollen or animal dander.**

Autoimmune responses are also the result of overactivity of immune components and occur when the immune system confuses self with non-self and attacks its own tissues and cells. Autoimmune conditions, such as arthritis, multiple sclerosis, lupus, diabetes, psoriasis, inflammatory bowel diseases, *etc*., are typically treated with drugs that suppress one's immune responses.

Imbalances of immune factors, such as cytokines, play a central role in the development of autoimmune disease (*Nature Reviews Immunology* 2002 2:37).

i26 helps the body modulate cytokine ratios as evidenced by pre-clinical and clinical trials, and patents (e.g., US Patents 6,420,337 and 7,083,809).

The Body's Defenses **The natural defenses of the immune system consist of an extremely elaborate and complex network of a billions of lymphocytes (white blood cells). Releasing small bioactive molecules, these cells pass information back and forth to each other like bees going out in search for pollen. Just as bees in their colonies have different jobs, the white blood cells in the body have their specific tasks and responsibilities. "The result is a sensitive system of checks and balances that produces an immune response that is prompt, appropriate, effective, and [in a properly functioning immune system] self-limiting" (NIH Publication).**

The Organs of the Immune System **Since the immune system influences almost every physical and mental aspect of the body, it is not surprising to find pockets of white blood cells throughout the body. Tonsils, lymph nodes, spleen, bone marrow, and thymus are some of the concentrations of lymphocytes where cells grow and develop.**

White Blood Cells (Lymphocytes) **Lymphocytes recognize foreign invaders and coordinate the natural defenses of the body. There are many different types of lymphocytes, each with its own specialized functions. Some of these cells are:**

Regulatory T cells (Tregs)	**Control and coordinate white blood cell traffic.**
B cells	**Produce antibodies specific to the antigen that stimulated them.**
Killer Cells	**Kill cancer cells and cells carrying viruses**
Macrophages	**Present "barcode" information (antigens) about the invader so that other white blood cells can recognize invaders. Produce cytokines. Start immune responses. Scavenge dead organisms and cells.**
Phagocytes	**"PAC-Men"; gobble up infected cells**
Dendritic cells (DC)	**Like macrophages, dendritic cells are key regulators of the immune system activating other immune cells.**
Eosinophils	**Kill parasites bacteria, cancer cells; associated with allergies.**
Mast Cells	**Involved in allergic and inflammatory responses. Releases chemicals that trigger other cells.**

Many white blood cells (lymphocytes) recognize and react to specific antigens which starts a *specific immune response* against an individual class of invaders. Other types of cells respond in a *nonspecific* manner killing any and all invaders.

Lymphocytes are involved in: 1) inflammatory reactions, 2) increasing the numbers of cells for a strong defense of the body, and 3) the destruction of cancer, and infected cells.

When immune cells recognize that an infection has occurred, they release different classes of immune factors, or bioactive molecules such as cytokines. These immune factors activate B cells to produce antibodies and other immune cells to release immune factors that help the body recruit cells for a battle against pathogens or for the healing process.

Regulatory T Cells The traffic cops of the immune system, these cells play an essential role in maintaining immune balance, homeostasis. They direct the circulation of other immune cells that all together form the immune network. They may call in reinforcements, or "tell" cells to stop an immune response.

There are primarily two classes of regulatory T cells. 1) Helper cells - "turn-on" other cells like B cells, other T cells, killer cells and macrophages and 2) Suppressor cells that "turn" immune responses down or even off.

B-Cells (Plasma cells) Each B cell is a self-contained factory that

manufactures one specific type of antibody (immunoglobulin). Antibodies are "smart" bullets designed to identify invaders, and cancer cells, by their antigen and attach to them. This "flags" the cell for destruction by other inflammatory immune cells.

Specific Antibodies **Just as one key fits one lock, each antibody produced can only "fit" (attach to) one specific antigen ("barcode") on bacteria, virus, parasite, or cancer cell. A specific antibody is directed against an individual antigen.**

Cell Interactions **Many cells are involved in triggering the B cell to produce antibodies. Dendritic cells and macrophages, using immune factors, "tell" T cells about the architecture of the invaders. Then the T cells release other factors that program the B cell to "design" the right antibody for the job. Once the B cell "knows" what sort of antibody it needs to produce, it will manufacture millions of antibody-producing plasma cells, each which manufactures millions of identical antibody proteins directed against that one specific antigen.**

Immune Factors (Bioactive Messages) **During the process of generating antibodies, the immune cells of the body produce different types and amounts of immune factors, including cytokines. These molecules signal inflammatory immune cells to direct the body's immune system in its natural defenses.**

Delicately Balanced Immune Systems **A great deal of effort and energy goes on in the body to maintain its exquisite balance of white blood cells and immune cofactors. Too much activity may result in an immune response that gets "carried away" (such as an inflamed finger); a response that doesn't stop for days. If however, the immune response ends too quickly, then the infection may not be resolved completely or healing may be incomplete.**

One combination of immune inflammatory factors, for example cytokines, may start an immune response, and another combination of these factors may "down-regulate" an immune response, either slowing it down or stopping it entirely. A proper ratio of immune factors is absolutely necessary for an appropriate immune response.

The Balance between Foreign Cells and Our Own Cells **The digestive system is the major entryway for bacteria and other organisms to enter the body.**

The digestive system is home to a very complex bacterial ecosystem, a huge community (PLoS ONE 4(6): 2009) of more than 100 trillion bacteria (they outnumber our own human cells 10:1!) (Nature 2007 449: 804). According to recent gene studies, there are over 40,000 different species

of bacteria, the majority of which have not yet been studied (Curr Opin Gastroenterol 2008 24:4).

Immunity and the Gut **It is often not recognized, even among scientists and clinicians, that the largest immunological organ of the body is the intestine; 75-80% of the immune system is represented in the gut. The gut-associated lymphoid tissue (GALT) has an enormous number of immune cells, some of which are in clusters of B and T cells called Peyer's patches (Proc Nutr Soc. 2010 69:644) embedded in the intestinal wall. These cells help protect the intestine from contaminated food or drink.**

There are many interactions between the bacteria and the immune cells in the gut (Annu Gastroenterol 2009 22:239). The immune cells, using for example IgA antibodies (Adv Immunol. 2010 107:153) produced by the B cells, play a key role in regulating the types and numbers of intestinal bacteria that populate the intestine.

Invasion of the Gut **Let's say we've eaten a picnic sandwich that sat too long in the heat. If this meat had been contaminated with *Salmonella,* a type of bacteria that causes problems in human guts, the warm temperature would have encouraged rapid growth of the numbers of the *Salmonella* organisms. Therefore we might be eating a sandwich contaminated with millions of bacteria. When large numbers of infectious organisms enter the gut, a number of events occur:**

—Specific antibodies continuously produced by the immune cells in the gut in response to previous exposure, bind to the bugs, stopping them from attaching to the gut where they might start to multiply and cause illness.

B cells, for example from the intestine's Peyer's patches, will be stimulated by white blood cell immune factors to produce new "lock and key" antibodies and mount a specific immune defense against the bacteria.

The specific antibodies lock onto the *Salmonella* marking them for death by other immune cells and preventing their attachment and replication in the gut. If the infection is overcome, suppressor cells will release immune cofactors to stop other cells from being triggered and the immune process will be "down regulated".

Simultaneously with the antibody defense strategy, the *Salmonella* may be targeted by lymphocytes and killed with their potent chemicals. Different types of white blood cells will be triggered by immune cofactors to try to physically destroy and then gobble up the

Salmonella. They in turn will release immune cofactor signals to recruit other cells.

Active vs. Passive Production of Antibodies There are two ways that we can obtain antibodies to defend our bodies from harmful pathogens, and cancer cells. These are by: 1) active production (having our own immune systems make antibody) and 2) getting "ready-made" antibodies, from foods such as eggs or milk, or as a pharmaceutical product.

Active Antibody Production Active antibody production is the result of our B cells producing their own antibodies in response to an infectious agent or its antigens.

Depending on where they are produced, antibodies may be found in our gut or circulating in our blood stream. Because antibodies are large molecules, antibodies produced in the gut do not cross the digestive tract walls and those found in the blood cannot get into our digestive tracts. (Often the gut is referred to as being "outside" of our bodies since food is digested and then the remainder is excreted. That material that is excreted is always kept "outside" of our inner bodies.)

Since we always consume food that is contaminated with pathogens, and are exposed to organisms through the air we breathe, we are always actively producing our own antibodies in response to foreign organisms.

Passive Immunity Passive immunity is the transfer of "ready-made" antibodies produced in another person or animal, or obtained from food. The recipient does not "make the antibodies". The individual receives the benefit of protective antibodies without having *actively* produced them.

There are two ways that antibodies are passively passed onto an individual. These are by 1) injection into the blood stream or body tissues and 2) orally consuming the product. (If an antibody is able to be injected into the body, it is a drug manufactured by a pharmaceutical company.)

When a mother nurses her offspring, she is *passing on, passively* transferring, immunity. Her offspring will have this "ready-made" immunity to protect it from harmful pathogens in the environment. Since both the offspring and the mother are exposed to the same environmental pathogens, mother's antibodies (and lymphocytes and immune factors) will be directly used by the offspring to help defend itself from infection and disease. Eventually the offspring's own immune system will develop to the point that it can a*ctively* produce its own immunity, and is longer needs mom’s immune factors.

Antibodies vs. Antibiotics When our body's immune cells recognize an

invader, they may produce antibodies that were biologically programmed to defend against the harmful pathogen (bacteria, viruses, fungi, molds, *etc*.). Each antibody neutralizes only one specific bacteria, virus, or foreign cells. Each antibody is "custom-designed" to attach to a single appropriate pathogen.

Antibiotics, on the other hand, are medications that are prescribed to kill bacteria. Unfortunately in too many cases, antibiotics may harm the body by killing our friendly bacteria, causing harmful side effects. Sometimes, if the dose of antibiotic is not enough to kill all the bacterial invaders, these bacteria can then multiply, and often mutate to a more potent form of bacteria. They may become resistant to being killed by medication and are termed antibiotic-resistant bacteria.

MRSA (Methicillin-resistant *Staphylococcus aureus)* is a bacteria that is resistant to many common types of antibiotics and can lead to severe or life-threatening infections of the skin, surgical sites, bloodstream, or lungs (Centers for Disease Control).

Antibiotics can only kill bacteria by stopping them from multiplying. Antibiotics cannot kill viruses. Viruses are a different type of pathogen in that they seize control of a cell in the body and use it as a factory to produce copies of itself. Anti-viral medications are specifically designed to interfere with the ability of viruses to replicate themselves.

Inflammation Inflammation is the tool that the immune system uses in response to an infectious agent or tissue injury. Inflammation is accompanied by a feeling of warmth in the area, redness and swelling. Warmth and redness occur when immune cofactors dilate blood vessels to carry more blood and white blood cells. Swelling occurs with the formation of "pus" which occurs when the immune cells migrate into an area attracted by immune factors, such as antibodies, and inflammatory cytokines, released by lymphocytes.

Long-term (chronic) inflammation is a major contributor, if not the major cause of diseases and conditions including autoimmune conditions, obesity, cardiovascular disease, osteoporosis, Alzheimer's, muscle wasting, and old age (Scand J Immunol. 2010 72:173; Ann N Y Acad Sci. 2010 1207S 1:E94-102; National Institute on Aging, 2004).

Immune Inflammatory Balance Immune inflammatory homeostasis, the ability to balance both increased and decreased inflammation, is essential for optimized immune responses and is controlled by immune factors such as cytokines.

Cytokines are bioactive molecules produced by immune cells to communicate with one another; they are also known as signaling molecules. They signal the rest of the immune system when to turn on, when to turn off an immune response like inflammation.

The numbers and types of cytokines tell the body how much "fuel" has to be added to get the appropriate inflammatory response. The proteins used by your body within the inflammatory response identify and neutralize foreign agents, such as bacteria and viruses.

i26 has been granted two specific United States Patents that support claims that i26 delivers immune factors that influence immune homeostasis: 1) United States Patent 6,420,337 Highly purified Cytokine Activating Factor and method of use and 2) United States Patent 7,083,809 Purified Cytokine Inhibitory Factor.

Mechanism of Disease [New Eng J of Med 1998 336:436]
Immune factors, such as cytokines control the circulation and recruitment of different types of lymphocytes throughout the body. They also control the type and length of time that an immune response such as inflammation will last.

"Over activity" of the immune system over a long period of time, may result in an inflammatory condition that results in autoimmune disease. Similar types of white blood cells and immune factors are involved in autoimmune, inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease, psoriasis, lupus, multiple sclerosis, *etc.* The inflammatory reaction occurs when a particular ratio of immune cells and immune factors exist. One category of white blood cell may increase in numbers, while another type of cell may decrease the inflammatory response.

The nature of autoimmune disease often depends on the part of the body in which inflammation is occurring. So for example, inflammation of: the joints may result in arthritis; of the digestive tract, inflammatory bowel disease; of nerve cell insulation (myelin sheath) in multiple sclerosis.

The same sort of inflammatory response associated with autoimmune diseases appears to be responsible for atherosclerosis. In such cardiovascular diseases similar categories of white blood cells and immune factors are found as are seen in other inflammatory and autoimmune conditions.

Stress, Emotional States, and the Immune System The immune system does not operate in a vacuum (J Leukoc Bio 2008 84:881). There is substantial "cross-talk" between our nervous and hormonal systems and vice versa (G Ital Dermatol Venereol. 2010 145:221-8).

All these systems are integrated as one, and together govern our emotional as well as physical feelings. Stress (Ann Acad Med Singapore. 2010 39:191), dieting, joy, distress, bereavement, fatigue-- all affect our immune systems .

Hormones are intimately involved in emotions. Certain glands release hormones into the blood in response to external and internal stress. These hormones prepare the body for "flight or fight" and in the process increase flow of blood to the intestines, decrease antibody production, and modify the numbers and types of lymphocytes.

The change in immune cell populations is controlled by immune factors, such as cytokines, that guide the traffic patterns and activities of other white blood cells. Stress and tissue and organ injury can result in changes of the numbers of circulating lymphocytes (Leukemia 2010 24:1667) and the kind of tasks they perform.

Stress also decreases natural defenses resulting in less efficient and slower healing (Psychosom Med 2007 69:597) and to greater susceptibility to infection (Brain Behav Immun. 2010 24:49). The literature is clear that constant stress affects the immune system leading to serious health consequences.

Cardiovascular Health and Immune Function. Individuals that are depressed and anxious are at greater risk of developing high blood pressure (Ethn Dis 2007 17:389; Hypertension 2001 38:798). Since the immune system is linked to various hormones and other factors that control blood pressure, it is not surprising that inflammatory immune cofactors, such as cytokines, contribute in a major way to the state of our cardiovascular health (J Leuko Biol 2005 78:805).

Age and Immune Function Aging is associated with changes in immune function (In Vivo 2010 24:471). Individuals that do not age well have greater susceptibility to infection, autoimmune conditions (Arthritis Res Ther 2003 5:223) and cancer (*Nature* 2007 448:767). Healthy aging depends on maintaining an optimum state of inflammatory immune homeostasis (Vestn Ross Akad Med Nauk 1998 1:19).

Summary The immune network of cells defends the body from cancer cells and foreign invaders, and helps the body to heal itself when injured. Immune cells communicate with each other, and recruit other white blood cells, lymphocyes, through immune cofactors (bioactive messages) such as cytokines. White blood cells, with the aid of antibodies may attach to, and destroy or eliminate bacteria, viruses, and cancer cells before they

reproduce and create harm in the body.

CONCLUSION The immune system is a complex network of white blood cells and immune factors that regulates our physical and mental status. Balance is what it's all about! An immune network with its well-balanced components is absolutely essential to good health.