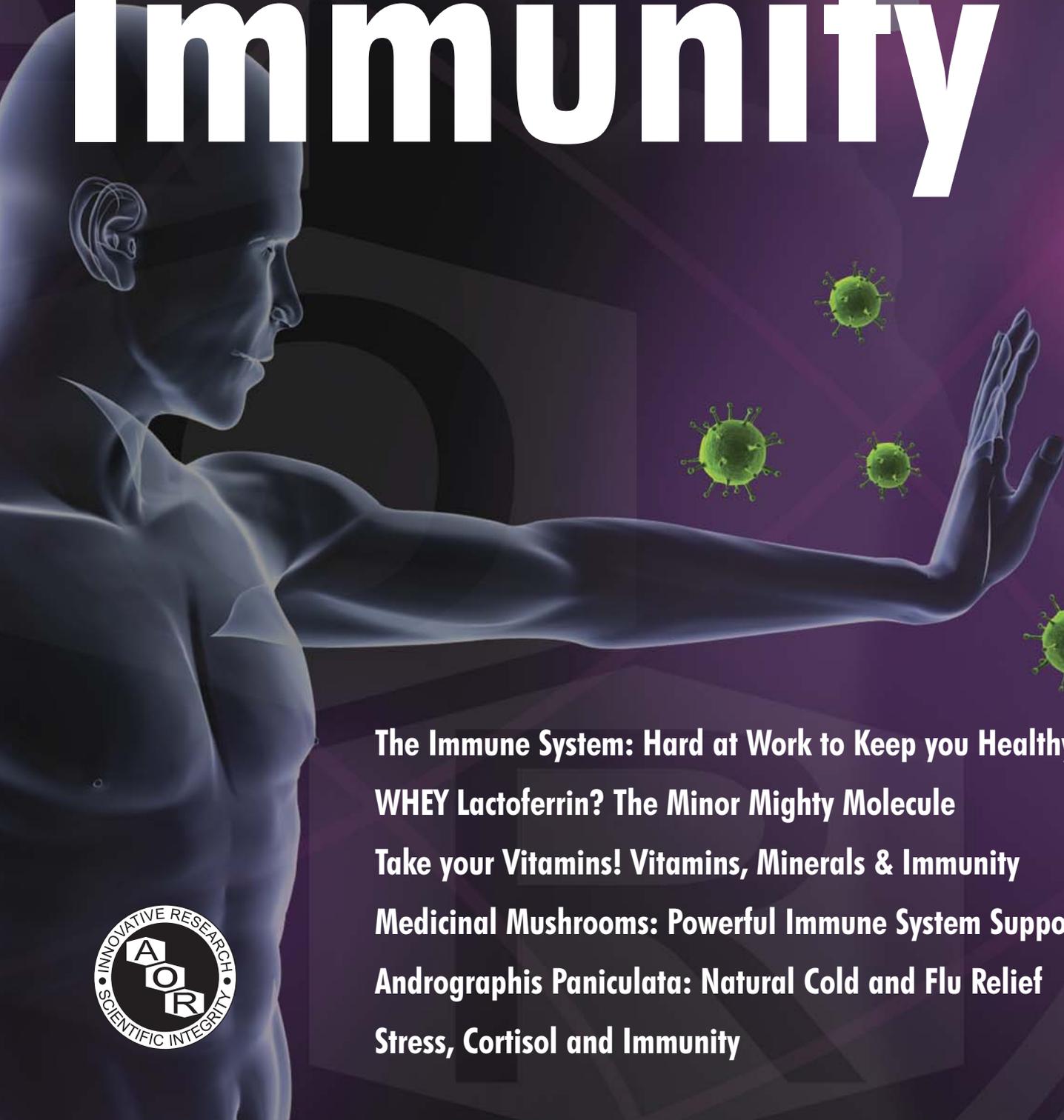


ADVANCES

IN ORTHOMOLECULAR RESEARCH

Immunity



The Immune System: Hard at Work to Keep you Healthy
WHEY Lactoferrin? The Minor Mighty Molecule
Take your Vitamins! Vitamins, Minerals & Immunity
Medicinal Mushrooms: Powerful Immune System Support
Andrographis Paniculata: Natural Cold and Flu Relief
Stress, Cortisol and Immunity



research-driven

botanical

integrative

orthomolecular

innovative

ADVANCES

IN ORTHOMOLECULAR RESEARCH

- 1. The Immune System: Hard at Work to Keep you Healthy
- 8. WHEY Lactoferrin? The Minor Mighty Molecule
- 12. Take your Vitamins! Vitamins, Minerals & Immunity
- 17. Medicinal Mushrooms: Powerful Immune System Support
- 20. Andrographis Paniculata: Natural Cold and Flu Relief
- 23. Stress, Cortisol and Immunity



1



12



20



8



17



23

ADVANCES

IN ORTHOMOLECULAR RESEARCH

Published in Canada by
Advanced Orthomolecular
Research Inc.

Publisher/Editor-in-Chief
Megan Tracey, MSc

Research & Writing
Megan Tracey, MSc
Dr. Mary Chou, PhD
Justine Florence, BSc, C.H.E.K. HLC-1

Graphic Design/Art Production
Neil Bromley
Neil@aor.ca
Kyle David Boudreau
Kyle@aor.ca

Advances in Orthomolecular Research

is published and distributed through integrative physicians, health care practitioners, and progressive health food retailers.

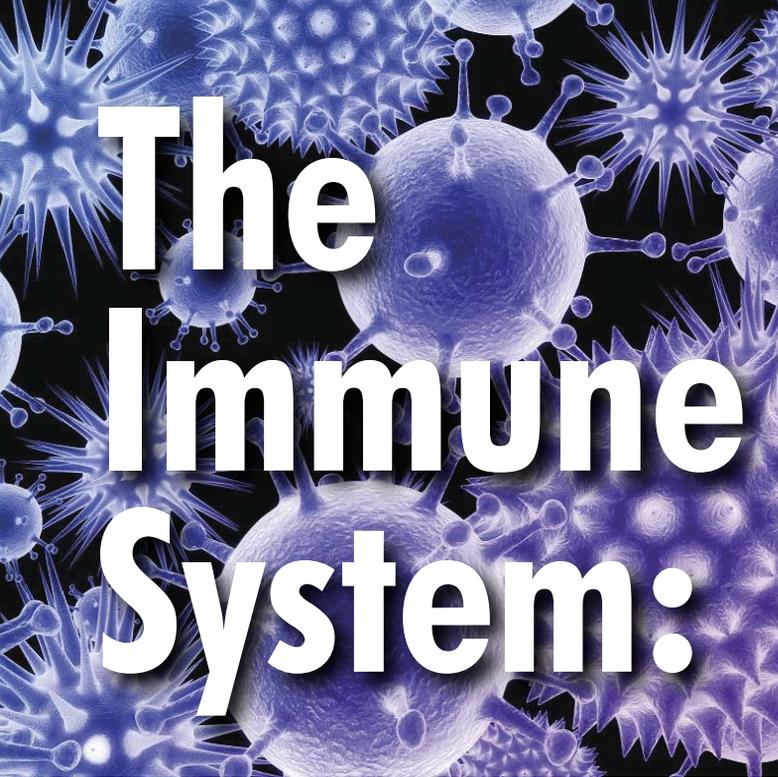
The content of this magazine is provided for informational purposes only, and is not intended as medical advice for individuals, which can only be provided by a healthcare professional. Contents and design © 2010 AOR. Any reproduction in whole or part and in print or electronic form without express permission is strictly forbidden. Permission to reproduce selected material may be granted by contacting the publisher.

Questions? Comments?

Contact us at:

AOR Inc.
3900-12 St NE
Calgary, Alberta
Canada T2E 8H9
e-mail orders@aor.ca or tech@aor.ca

www.aor.ca



The Immune System:

Hard at Work to Keep you Healthy

Every day your immune system is at work, defending you from harmful bacteria, viruses and infections. This complex system is made up of a variety of cells and signalling molecules that work together to help keep you healthy. Most of the time you don't even notice that your immune system is at work; it is only when the system fails, and you get sick that you begin to see some of its actions. In fact, many of the uncomfortable symptoms you experience like fevers and sneezing are actually your immune system's strategies for fighting infection.

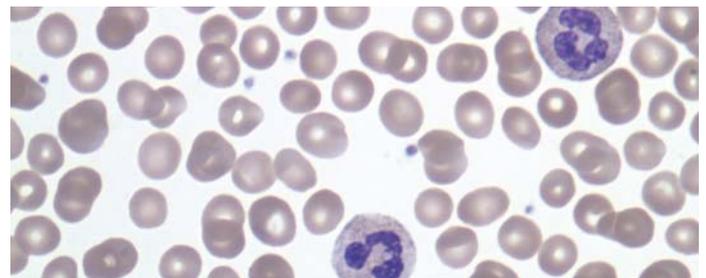
Non-Specific Defences

The body's system of defences includes non-specific defences, which provide general barriers to infection as well as specific defence mechanisms, which include all the various cells of the immune system (see Table 1). The body's first line of defence is the skin. This massive organ covers your body and protects it from invading pathogens. It provides a physical barrier against pathogens; however, cuts and tiny abrasions may still allow them to enter.¹

Table 1: An Overview of the Body's Defences¹

Non-Specific Defense Mechanisms		Specific Defense Mechanisms
First Line of Defense	Second Line of Defense	Third Line of Defense
Skin Mucous Membranes	Phagocytic white blood cells Antimicrobial proteins Inflammatory response	The Immune System Lymphocytes Antibodies

This is where the second line of defence comes into play. This mechanism includes white blood cells that non-specifically attack and destroy microbes and infected cells throughout the body. One type of cell that accomplishes this is the phagocyte. Phagocytes are cells that consume other cells. The human body has two types of phagocytic cells: neutrophils and macrophages. Neutrophils make up 60-70% of all white blood cells, and are attracted to areas of infection where they consume bacteria. Macrophages are large and very effective phagocytes.¹ The body also has a special kind of cells called Natural Killer Cells, which act to destroy the body's own infected cells, helping to prevent the spread of viruses, as well as abnormal cells that could form tumours.¹



Normal human blood showing red blood cells (pink) and white blood cells or immune system cells (purple)

The inflammatory response and antimicrobial proteins are also part of the body's non-specific defences. One antimicrobial protein that may sound familiar is interferon. Interferons are actually a group of three proteins that can help protect cells from infection by viruses.¹ Interferons are produced commercially through recombinant DNA technology, and can be used for the treatment of various diseases. For example, certain types of interferons are used to help treat various forms of cancer, viruses, multiple sclerosis and more.²

Specific Defences

Specific defences act to target and destroy particular viruses and microbes. This level of the body's defences is what is typically termed the immune system. There are four key features that characterize the immune system: Specificity, Diversity, Memory and Self/Non-self recognition (see Table 2)

Table 2: The Four Key Characteristics of the Immune System

Specificity	The immune system can recognize and eliminate specific viruses or microbes This is accomplished through antibodies
Diversity	The immune system can recognize and respond to millions of different kinds of invaders
Memory	The immune system can remember invaders it has encountered before, and respond faster This is called acquired immunity
Self/Nonself Recognition	The immune system can distinguish its own molecules from foreign ones When this fails, auto-immune diseases can result

The specific/adaptive immune system is made up of two main kinds of white blood cells, T cells and B cells. These cells are involved in the body's specific attacks on pathogens. This generally occurs through two different routes. The first is called cell-mediated immunity. This is generally carried out by T cells which act to identify cells of the body that have been infected by bacteria or viruses. They also act against fungi, protozoa or worms that invade the body.¹ The second is called humoral immunity, and involves the production of antibodies that bind to specific invaders, marking them for destruction. The humoral response involves mostly B cells, and is also unique in the regard that special B cells called memory cells "remember" pathogens they have seen before. It is for this reason that having chicken pox as a child generally results in life-long immunity. The body's immune system remembers this virus and is therefore able to react quickly and effectively if you are ever exposed again, eliminating the virus before you get sick.¹

Cold and Flu

We have all suffered from colds or the flu and would prefer not to ever have them again. However, each year brings a new round of cold and flu season. On average, adults have 2-5 colds each year and children have 7-10 cold each year.³ Colds and the flu are both caused by viruses. The most common cold viruses include rhinoviruses (30-50%), coronaviruses (10-15%) and the respiratory syncytial virus (5%). The flu on the other hand is caused by the influenza A or influenza B viruses.^{3,4} There are a variety of subtypes of all of these virus types; for example, over 100 different subtypes of Rhinovirus have been identified. Another example is "swine flu" or H1N1 flu virus, which is a subtype of influenza A. Because they are caused by viruses, antibiotics are useless against colds and the flu.



Symptoms and Duration

Cold and flu are spread through direct person-to-person contact or through the inhalation of virus-containing droplets released into the air when infected individuals cough or sneeze. Symptoms of the common cold include a sore throat, runny nose, nasal congestion, sneezing, coughing, headache and fever. The flu is generally more severe than a cold, with symptoms including chills, high fever, muscle and joint pain, malaise, headache and respiratory symptoms.⁷ Colds generally have a gradual onset of symptoms, beginning 1-3 days after infection and lasting approximately 7 days. Flu symptoms appear more abruptly, about 1-2 days after infection, usually improving after 1-2 days although coughing and general weakness may last for several more days.⁴

Box 1. The Flu by the Numbers

- Every year the flu infects 5-15% of the global population
- Every year, young, healthy people are hospitalized due to influenza
- The flu causes severe illness in 3-5 million people and leads to 250,000 to 500,000 deaths worldwide
- Most deaths occur in infants, the elderly and the chronically ill
- The flu is the 7th leading cause of death in the US and the CDC estimates that, on average, 36,000 people die of seasonal-flu related causes each year
- In Canada, the average flu claims between 2000 and 8000 lives each year
- In comparison, cancer and cardiovascular diseases each claim over 68,000 deaths in Canada each year
- Certain groups such as pregnant women, diabetics, obese individuals, immune-compromised individuals and cardiac patients are more likely to have severe illness when infected with the influenza virus

Complications

Although colds and the flu are generally self-limited illnesses of short duration, they can be associated with other complications. Colds can sometimes lead to secondary infections including ear infections, sinusitis or pneumonia. In children approximately 20% of secondary ear infections are associated with upper respiratory tract infection.⁵ Influenza viruses can have serious complications, and approximately 1% of all individuals who get the flu will require hospitalization (see Box 1).



The most common serious complication of the flu is pneumonia, which can be caused either by the virus itself or by a secondary bacterial infection. Elderly individuals, children and individuals with chronic illnesses are most likely to be affected by complications of the flu virus. Children under one year of age have an increased risk of not only pneumonia, but also other serious infections like meningitis and encephalitis. It is recommended that individuals with an increased risk of complications get an annual influenza vaccination or flu shot. In fact, the CDC recommends flu shots to all individuals over the age of 6 months, although individuals with a severe egg allergy, a previous allergic reaction to a flu shot, or a history of GBS after receiving a flu shot should consult a physician before getting a flu shot.

A Note of Flu Shots

The flu shot is an inactivated vaccine containing weakened versions of three seasonal flu strains. New flu shots are created every year to keep up with the constant mutation of influenza viruses. The flu shot is generally given with a needle in the arm. The flu shot is approved for all individuals older than 6 months of age.



Pros of the Flu Shot

- Most vaccinated individuals produce the antibodies required to fight the flu within 10 days of being vaccinated
- Once vaccinated, the immune system is ready to target the flu virus and offers protection against all viruses included in the vaccine
- The vaccine has been shown to prevent influenza in about 70%-90% of healthy persons younger than age 65 years old⁶
- Among elderly persons living outside chronic-care facilities (such as nursing homes) and those persons with long-term (chronic) medical conditions (such as asthma, diabetes, or heart disease), the flu shot has been shown to be between 30% and 70% effective in preventing hospitalization for pneumonia and influenza⁶
- Among elderly nursing home residents, the shot has been shown to be between 50% and 60% effective in preventing hospitalization or pneumonia and 80% effective in preventing death from the flu

Cons of the Flu Shot

- Even if you get the flu shot, you may still get the flu. Viruses evolve rapidly, so vaccines do not always cover all strains that you may encounter.
- Research has shown that in animals, infection with influenza A viruses can induce protective immunity against other unrelated subtypes. Immunizations, on the other hand, do not increase immunity to other flu subtypes. This means that if you have been immunized, but become infected with another strain of the flu, the severity of the infection could be more severe.
- The flu shot may have some side effects or cause allergic reactions in rare cases. Generally side-effects are mild and include soreness at the injection site or headaches.
- Flu vaccines may be associated with an increased risk of a rare side effect called Guillain-Barre Syndrome (GBS), a rare and serious illness in which individuals experience inflammation of the peripheral nervous system causing progressive paralysis. This paralysis may be temporary or permanent, and in some cases leads to death. In 1976, 40 million Americans were inoculated against H1N1; the program was halted due to 500 reported cases of GBS. This represents 0.00125% of immunized individuals (far less than the lethal rate for the seasonal flu).

Supporting your Immune System

Exercise and the Immune System

Studies have shown that regular, moderate exercise can help boost your immune system. One study found that recreational runners reported fewer colds after starting the exercise and another showed that individuals who walked for 40 minutes per day had half as many sick days due to colds or sore throat compared to individuals who did not exercise.⁷ Research suggests that regular, moderate exercise increases the body's production of macrophages and also increases the circulation of immune cells throughout the body, thereby improving the body's immune response.⁸

However, it is important to note that too much intense exercise can actually reduce immunity, with research showing that athletes engaging in more than 90 minutes of high-intensity endurance exercise are more susceptible to illness for up to 72 hours after the exercise session.⁹ When you are sick you should be careful not to exercise too intensely, as this could prolong your illness.

Stress and the Immune System

Psychological stress has also been associated with an increased incidence of cold and flu infection. For example, individuals experiencing the stress of caring for a loved one with Alzheimer's disease and found that they experienced twice as many colds as non-caregivers.¹⁰ A large meta-analysis found that psychological stress was associated with a significant decrease in various measures of immune system function, including natural killer cell activity and the number of circulating white blood cells.¹¹ Therefore, taking steps to reduce stress could also help to reduce your frequency of illness.

Diet and the Immune System

Proper nutrition is essential for the support of a healthy immune response. Malnutrition, anorexia and obesity have all been linked to a suppressed immune system. Many minerals and vitamins play important roles in metabolic pathways and immune cell functions, and marginal deficiencies in these nutrients can therefore have a negative impact on immune system function.



Some of these key nutrients include vitamin A, beta-carotene, folic acid, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, riboflavin, iron, zinc, and selenium.¹² If you are not obtaining adequate amounts of these nutrients in your daily diet, it may be a good idea to consider a nutritional supplement.

Antioxidants, like vitamin C and vitamin E, for example, play a very important role in immunity, by helping to prevent oxidative stress in immune cells.¹² In fact; studies have shown that high doses of vitamin C can help to significantly reduce the severity of cold symptoms.¹³ Other nutrients, including essential fatty acids, certain mushroom extracts and probiotics, have also been shown to have a positive effect of the immune system.

Staying Healthy

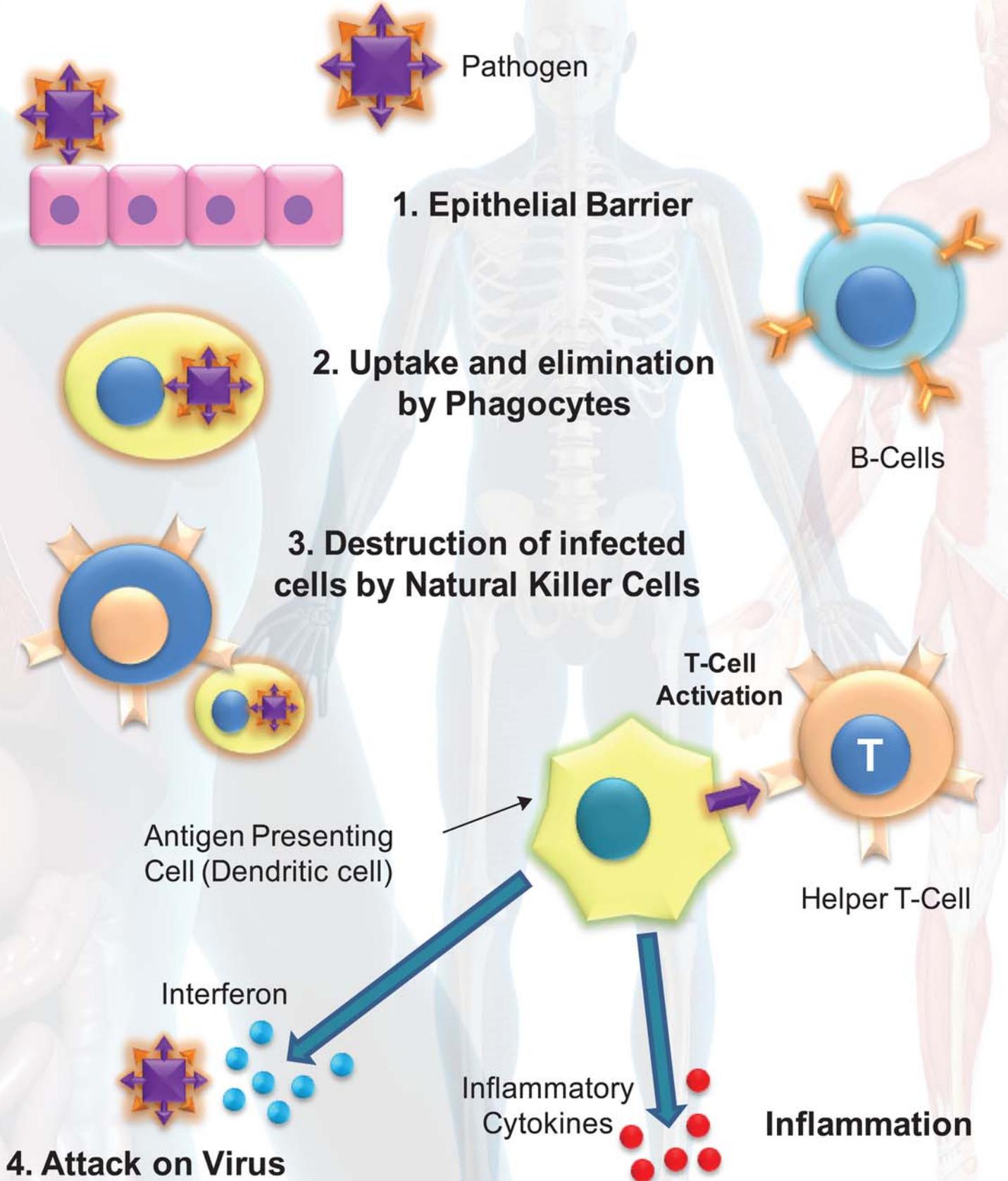
Your body's defenses are highly complex, and work every day to help keep you healthy. While it is impossible to avoid getting the occasional cold or flu, there are ways you can help to keep yourself and others healthy. For example, certain common sense actions should be taken, including washing your hands frequently and thoroughly, avoiding touching your face, coughing and sneezing into your sleeve or in a tissue rather than your hand and cover both your nose and mouth, staying home if you are sick and avoiding close contact with sick individuals. Furthermore, by maintaining a healthy lifestyle and reducing the stress in your life you can help to make sure your immune system is healthy and reduce your risk of getting infected with a cold or flu virus.

References

1. Campbell NA. *Biology* 4th edition. 1996. The Benjamin/Cummings Publishing Company. Menlo Park, California.
2. Ogburu O. Interferons. 2010. Medicine Net.com. Accessed October 25, 2010.
3. Eccles R. Understanding the symptoms of the common cold and influenza. *Lancet Infect Dis* 2005; 5: 718–725
4. Souter J. Cold or Flu? SA Pharmacist's Assistant. Winter 2007. 16-20.
5. Heikkinen T and Järvinen A. The common cold. *Lancet* 2003; 361: 51–59.
6. Centres for Disease Control and Infection. Seasonal Flu Shot. 2010. Accessed Nov 9, 2010. <http://www.cdc.gov/flu/about/qa/flushot.htm>
7. Nieman DC, Henson DA, Austin MD, Brown VA. The immune response to a 30-minute walk. *Med Sci Sports Exerc* 37:57-62, 2005. David Nieman, of Appalachian State University.
8. Acute exercise stimulates macrophage function: possible role of NF-kappaB pathways. *Cell Biochemistry and Function*. 2006 Aug 14.
9. Nieman DC. Risk of Upper Respiratory Tract Infection in Athletes: An Epidemiologic and Immunologic Perspective. *Journal of Athletic Training* 1997 Oct.
10. Kiecolt-Glaser JK. Chronic Stress and Immunity in Family Caregivers of Alzheimer's Disease Victims. *Psychosomatic Medicine*. 1987; 49: 523-535.
11. Herbert TB and Cohen S. Stress and Immunity in Humans: A meta-analytic review. *Psychosomatic Medicine*. 1993; 55: 364-379.
12. Marcos A et al. Changes in the immune system are conditioned by nutrition. *European Journal of Clinical Nutrition* (2003) 57, Suppl 1, S66–S69.
13. Gorton HC and Jarvis K. The effectiveness of vitamin C in preventing and relieving the symptoms of virus-induced respiratory infections. *Journal of Manipulative & Physiological Therapeutics*. 1999; 22(8): 530-537.



Innate (non specific) Immunity

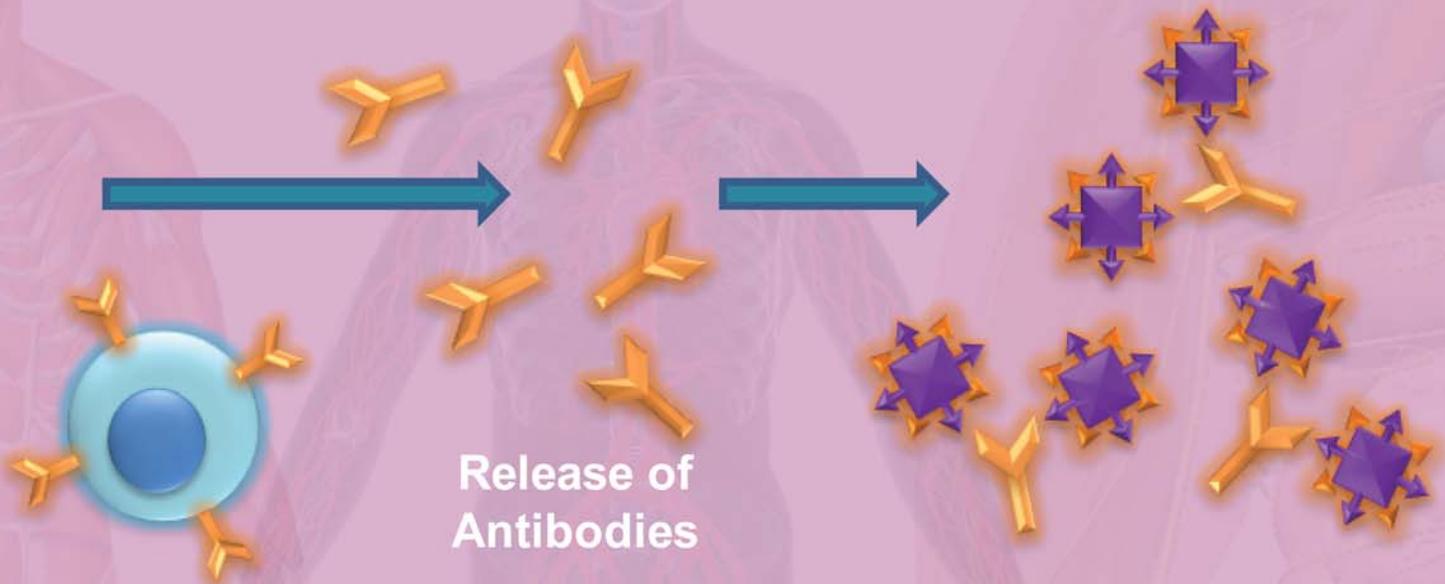


0 - 12 HOURS AFTER INFECTION

Adaptive (specific) Immunity

Humoral Immunity

Neutralization and Destruction of Pathogens

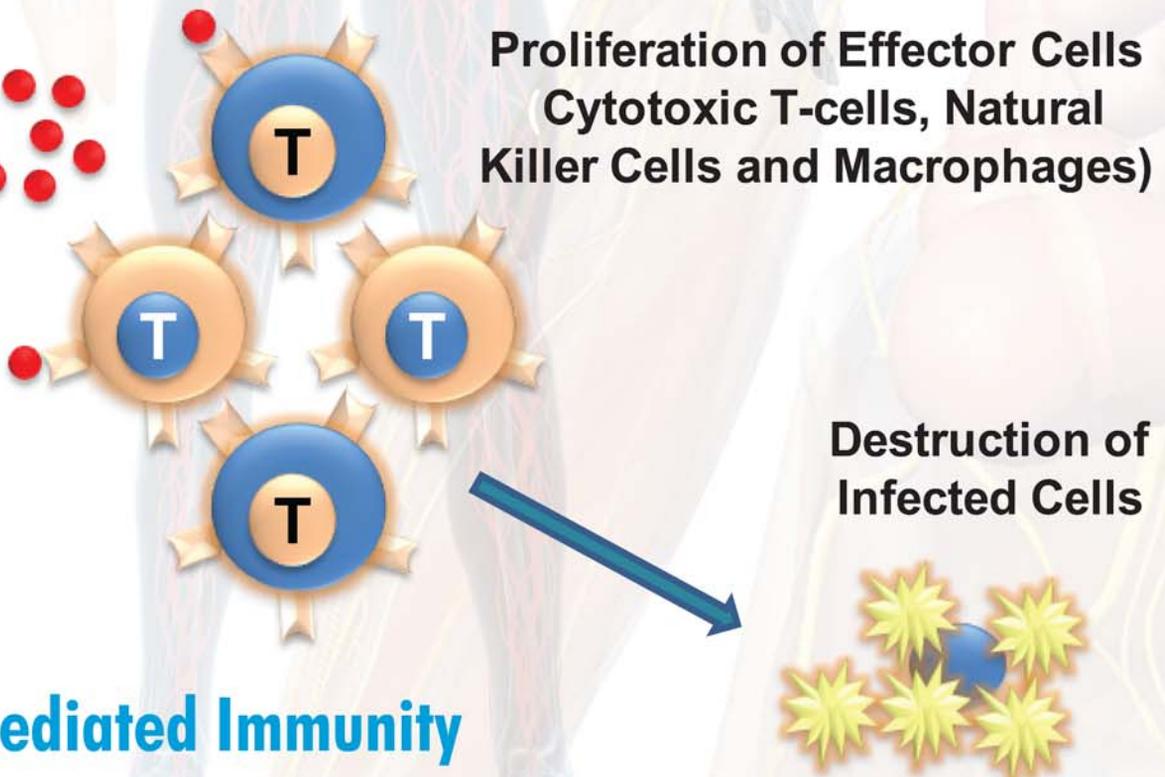


Release of Cytokines

Proliferation of Effector Cells
(Cytotoxic T-cells, Natural
Killer Cells and Macrophages)

Cell-Mediated Immunity

Destruction of Infected Cells



1 - 5 DAYS AFTER INFECTION

WHEY LACTOFERRIN:

The Minor Mighty Molecule

Whey Protein & Lactoferrin

Whey protein has long been recognized as a reputable source of protein for human health and fitness. Indeed, whey protein is one of the highest quality proteins and is digested and absorbed at many locations throughout the intestine.¹ Whey protein is often used as an additional protein source for those whose diets may not contain enough or for those wanting to build more lean muscle mass. The benefits of whey protein are attributed to the diverse types of proteins which comprise it, each with unique functions lending benefits far greater than simply maintaining muscle mass.

Table 1. The Impact of Processing on Bioactive Proteins and Peptides (adapted from Korhonen et al. 1998. Trends in Food Science and Tech. 9: 307-319.)

Protein	Concentration g/L	Biological Activity
Caseins	28	Transport of ions (Ca, P ₀₄ , Fe, Zn, Cu) Precursor of bioactive peptides
B - lactoglobulin	1.3	Retinol carrier Binding of fatty acids Antioxidant
A - lactalbumin	1.2	Lactose synthesis Ca carrier Immunomodulation Anticarcinogenic
Immunoglobulins	0.7	Immune protection
Glycomacropeptide	1.2	Bifidobacteria growth Immunomodulation Antiviral
Lactoferrin	0.1	Antimicrobial, wound healing Antiviral Antioxidant Anticarcinogenic Antitoxin Antiinflammatory Antithrombotic Immunomodulation Fe absorption
Lactoperoxidase	0.03	Antimicrobial, wound healing
Lysozyme	0.0004	Antimicrobial, wound healing Synergistic effect with lactoferrin Synergistic effect with immunoglobulins

Of the approximately 32.43g of protein that are found in one liter of bovine milk, there is a minor protein present in the measly amount of 0.1 g/L, which has more recognized roles than any other milk protein¹, and may well be the most biomedically valuable.² This protein is called Lactoferrin (Lf). Lactoferrin's roles in the body exceed double that of other milk proteins, although they are all intertwined into the realm of immunity. Studies have noted lactoferrin's function as an antimicrobial, antiviral, antioxidant, anticarcinogenic, antitoxin, anti-inflammatory, and an antithrombotic¹. A plethora of studies have also documented its involvement in immunomodulation, iron sequestering and transport as well as wound healing¹. Lactoferrin is touted to be a faithful warrior as it influences the effective destruction of harmful pathogens while protecting the body against damage from excessive immune responses.^{2,3} In other words, Lf both up-regulates and suppresses immunity to protect the body from dangers, including danger from the body itself!

The Role of Lactoferrin in Immunity and Inflammation

Lactoferrin plays a vital role in the body's first line of defense and innate immunity since it is present in various secretions such as tears, nasal secretions, saliva, genital fluids, mucus, intestinal mucosa, bile and pancreatic juice.^{1,2} Innate immunity is the first, rapid, and non-specific immune defense; it includes cells such as macrophages, neutrophils, basophils, eosinophils, mastocytes and natural killer cells. Lactoferrin also plays an important role in adaptive immunity, however, its influences are indirect. Adaptive immunity is a slower yet highly specific immune defense; it may either mobilize B cells or T cells depending on the type of threat encountered.

Lactoferrin, a digested form of lactoferrin, has been noted to stimulate phagocytosis, a mechanism to remove pathogens and cell debris, by both neutrophils and macrophages in response to injury or infection.² The expression of pro-inflammatory cytokines (such as IL-1, IL-6, IL-8, TNF- α and IL-23) has been shown to be modulated by Lf.³ Cytokines, which are signaling molecules, are necessary to initiate tissue healing, however an overactive immune response created by an unregulated expression of cytokines can destroy the same tissue. One study even found that Lf attenuated the severity of an influenza-induced pneumonia response by minimizing immunity-mediated cellular infiltration and thus fluid volume.³ In another study, Lf attenuated asthma-induced airway obstruction due to

its anti-inflammatory modulation.³ Conversely, supplementation of Lf in a study done in healthy male volunteers improved immunity as measured by increased T-cell activation and hydrophilic antioxidant capacity.⁸ Using similar immune measures, another study found that in mice with both healthy and compromised immune systems, toxic infection by *T. gondii*, a single-celled parasite, was weakened.⁹

Box 1: Lactoferrin & the Immune System

Enhances Innate Immunity (Non-specific Immune Response)

- Present in mucous, tears and other body fluids where it has direct antimicrobial and antiviral effects
- Increases Neutrophil activity
- Increases Macrophage activity
- Direct antimicrobial and antiviral action in the body by depriving pathogens of iron, which they need to survive
- Prevents oxidative damage to body tissues and cells

Enhances Adaptive Immunity (Specific Immune Response)

- Increases dendritic cell activity leading to T-cell proliferation
- Increases and modulates T-cell activation and activity
- Moderates cytokine release helping to prevent the occurrence of a "cytokine storm", which results from overstimulation of the immune system

In any case, inflammation is the manifesto of immunity; hence a brief discussion on it follows. Neutrophils are often the first to respond to an assault. As they arrive on scene with increased plasma flow, they then release signals attracting other immune cells to the site; both the signaling molecules and cells further contribute to inflammation. During inflammation, neutrophils scavenge lactoferrin from the plasma and bring it to the affected tissues where Lf binds iron and inhibits iron-catalyzed oxidative damage⁷. This is evident in post-surgical patients where elevated Lactoferrin levels have been found. In fact, an investigative study found that topical talactoferrin, a human recombinant form of lactoferrin, improved the healing of neuropathic ulcers, or skin wounds, of diabetic origin.² With a less

detrimental but more common problem, researchers found that fermented milk supplemented with additional lactoferrin decreased the inflammation underlying acne vulgaris.⁶ This shows that Lf is both medically and cosmetically valuable.

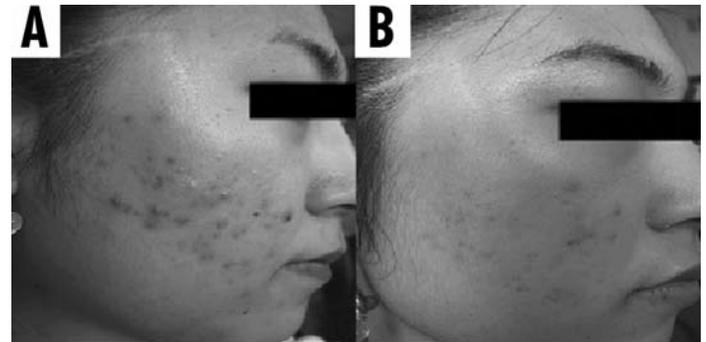


Figure 1. Decreased acne as a result of lactoferrin supplementation (from Kim et al. 2010. *Nutrition* 26: 902-909.)

Antimicrobial Actions of Lactoferrin

Lactoferrin was initially known for its ability to bind metals, or more specifically, iron. Copper, manganese, aluminum and zinc can also be bound by Lf but in smaller amounts as compared to iron.^{1,7} This could be an essential delivery system of vital minerals to a breastfeeding infant from the mother. The capacity to bind iron confers antimicrobial properties to Lf as many bacteria, parasites, and other pathogens require iron to function, so its deprivation becomes detrimental to the intruders.^{1,3}

Lactoferrin has been documented to inhibit many kinds of pathogenic microorganisms including bacteria, yeast, fungi, parasitic protozoa, and antibiotic-resistant pathogens¹. Interestingly, when digested by peptides, lactoferrin yields the bioactive component lactoferricin, perhaps a more potent antimicrobial.^{2,3} It has also been recently shown that lactoferrin contains two distinct peptide domains through which it exerts antimicrobial effects⁷; an iron-binding domain and a lipopolysaccharide (LPS) binding domain³. When Lf binds to the LPS, which is a vital component of the bacterial cell wall, it destabilizes its membrane causing the bacterium to burst.^{1,7} Another way that Lf disturbs the bacterial membrane of *E. coli* in particular, causing cell death, is by blocking porins; this inhibits the exchange of nutrients between the bacteria and its environment⁷.

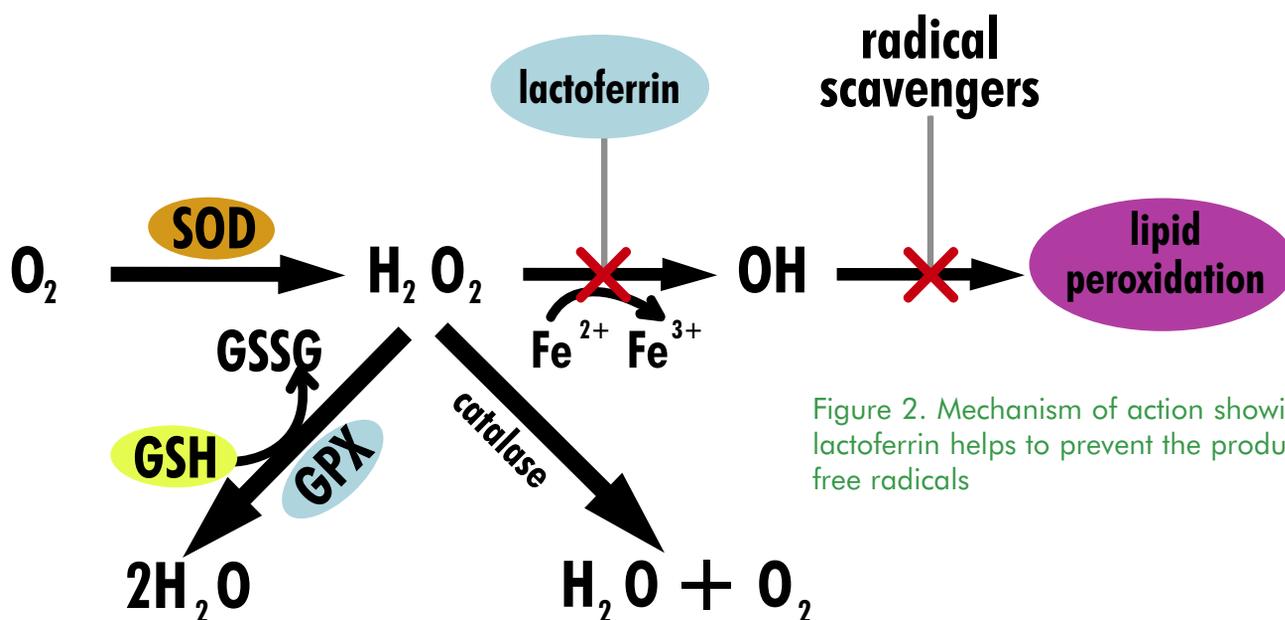


Figure 2. Mechanism of action showing how lactoferrin helps to prevent the production of free radicals

Other research has shown that Lf can also inhibit the growth of 3 types of candida fungi, including the well-known pathogen *Candida albicans*, which alternative medicine often refers to as yeast overgrowth, by depriving the yeast of iron¹⁰. Furthermore, increased interest in Lf's role in the prevention of late-onset sepsis in neonates (infection by any pathogen within the first 48 hours of life) has found Lf helpful in reducing infection of many sources and it may even assist in killing antibiotic resistant microbes that have developed due to overuse of antibiotics.^{1,4,5} In cases of helicobacter pylori (the bacteria that is a main cause of acid reflux) infection, for example, where antibiotics alone did not work, the addition of Lf to the treatment helped eradicate *H. pylori*.²

Lactoferrin may also protect the host against viruses such as HIV-1, hepatitis C and herpes in any stage of infection. In the case of HIV, not only is the replication of the virus in T-cells inhibited by Lf, but even its transmission via dendritic cells². Its mechanism of inhibition appears to be by blocking cellular receptors or by binding to the viral cell itself¹, helping prevent both viral replication and transport to other sites in the body².

On a microbe-friendly note, lactoferrin promotes the growth of certain strains of Bifidobacteria (probiotics) which act as biological barriers in the intestines against pathogenic bacteria.¹

Lactoferrin as an Antitoxin

As mentioned earlier, Lf binds to bacterial lipopolysaccharides (LPS), which is one of two antitoxin mechanisms exerted by Lf.³ Lipopolysaccharides are the part of the bacteria's cell wall, which are responsible for illness, thus classified as endotoxins.

When the LPS are bound by Lf, the bacteria can no longer replicate or cause endotoxic shock and illness. Such binding disturbs the bacterial membrane, causing cell lysis or death. The second antitoxin mechanism is by inhibiting the production of toxic free radicals.

Lactoferrin as an Antioxidant

This means that Lf can act as an antioxidant. Upon tissue injury or infection, reactive oxygen species, which are a form of free radicals that can be produced by free iron, are released from digested tissues or from the overactivation of immune cells.^{2,3,7,11} In addition, cytokines can be released in massive quantities due to oxidative stress, hence causing the production of more oxidants. Fortunately, neutrophils pick up Lf and bring it to the site of insult, where it binds iron, limiting oxidative species formation and thus further damage.^{1,11} Whey proteins have also been found to enhance the body's own production of natural antioxidants such as glutathione as investigated in cases of HIV, cancer and high oxidative stress.^{1,2}

The terms antioxidant and anticarcinogenic could almost be synonymous as it is well known that free radicals are associated with cancer development. Many studies have shown Lf to inhibit tumor growth and metastasis. One proposed mechanism of action is that Lf, or other whey components, may inhibit the production of GSH (growth-stimulating hormone) in cancer cells. Lactoferrin may cause selective apoptosis (cell death) of certain human cancerous cells, and when combined with chemotherapy, may completely eliminate tumors.² Other forms of cancer therapy are also enhanced when combined with Lf, such as

improving the efficiency of immunotherapy (such as dendritic cell therapy) or enhancing drug cytotoxicity to cancer cells. Supplementation with Lf has also been shown to quickly restore immunity after chemotherapy for cancer.²

Conclusion

Evidently, lactoferrin has many health benefits and has high biomedical value. It is potentially a future adjunct to treatments for cancer, autoimmune disorders, and antibiotic or antimicrobial therapy where drugs alone have failed to safely and effectively reduce the risks. The exciting part for general consumers is that lactoferrin is already a natural component in the human body, and bovine Lf is two thirds to three quarters similar in protein and DNA sequences to human lactoferrin⁷, and in some cases more efficacious. As if Lf was lacking in might on its own, other components of whey have additional powerful health benefits towards bone growth, lipid balance, blood pressure control, insulin activity, mood and cognition, to name a few.² From the origins of dairy products being nutritional staples to our current and evolving understanding of its numerous health benefits, we sure have come a long “whey”.

References

1. Yalçın, A.S. (2006). Emerging therapeutic potential of whey proteins and peptides. *Current Pharmaceutical Design*, 12: 1637-1643.
2. Krissansen, G.W. (2007). Emerging health properties of whey proteins and their clinical implications. *Journal of the American College of Nutrition*, 26(6): 713S-723S.
3. Legrand, D. & Mazurier, J. (2010). A critical review of the roles of host lactoferrin in immunity. *Biometals*, 23: 365-376.
4. Gordon, A., Jeffery, H.A. (2005). Antibiotic regimens for suspected late onset sepsis in newborn infants. *The Cochrane Library*, 3.
5. Manzoni, P., Decembrino, L., Stolfi, I., Pugni, L., Rinaldi, M., Cattani, S., Romeo, M.G., Messner, H., Laforgia, N., Vagnarelli, F., Memo, L., Bordignon, L., Saia, O.S., Maule, M., Gallo, E., Mostert, M., Magnani, C., Quercia, M., Bollani, L., Pedicino, R., Renzullo, L., Betta, P., Ferrari, F., Magaldi, R., Mosca, F., Stronati, M., Farina, D. (2010). Lactoferrin and prevention of late-onset sepsis in the pre-term neonates. *Early Human Development*, 86: S59-S61.
6. Kim, J., Ko, Y., Park, Y., Kim, N., Ha, W., Cho, Y. (2010). Dietary effect of lactoferrin-enriched fermented milk on skin surface lipid and clinical improvement of acne vulgaris. *Nutrition*, 26: 902-909.
7. Lönnerdal, B. & Iyer, S. (1995). Lactoferrin: molecular structure and biological function. *Annual Review of Nutrition*, 15: 93-110.
8. Mulder, A.M., Connellan, P.A., Oliver, C.J., Morris, C.A., Stevenson, L.M. (2008). Bovine lactoferrin supplementation supports immune and antioxidant status in healthy human males. *Nutrition Research*, 28: 583-589.
9. Mossallam, S.F. (2009). Prophylactic effect of bovine lactoferrin against acute toxoplasmosis in immunocompetent and immunosuppressed mice. *Journal of the Egyptian Society of Parasitology*, 39(3): 1033-1047.
10. Al-Sheikh, H. (2009). Effect of lactoferrin and iron on the growth of human pathogenic *Candida* species. *Pakistan Journal of Biological Sciences*, 12(1): 91-94.
11. Butterfield, T.A., Best, T.M., Merrick, M.A. (2006). The Dual Roles of Neutrophils and Macrophages in Inflammation: A Critical Balance Between Tissue Damage and Repair. *Journal of Athletic Training*, 41(4): 457-465.

Advanced Whey



- Contains 3 powerful immune system boosters
- Anti-inflammatory
- Lowers cholesterol
- Guaranteed free of hormones and antibiotics

Take your Vitamins

Vitamins, Minerals & Immunity



Everyone has heard that you should take more vitamin C if you have a cold, but why is that? Vitamins are important for maintaining good health, but how do they help you out when you are suffering from a cold? Vitamin C is certainly the most widely recognized vitamin for supporting the immune system; however, many other vitamins play a critically important role in keeping your immune system running at an optimal level.

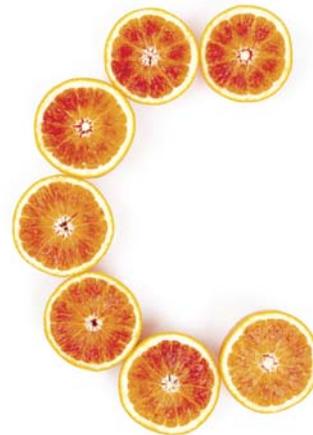
Vitamins can act on your immune system in a variety of ways. Many vitamins act as antioxidants, and can help to improve and protect immune function as a result of their antioxidant actions. Vitamins which support the immune system primarily through their role as antioxidants include vitamins C and E as well as some of the B vitamins. Other vitamins play a much more specific role in immunity, targeting very specific aspects of the immune response. These vitamins include vitamin A and vitamin D, which are unique from other vitamins in that they have hormone-like properties, which are highly related to their role in immune system functioning. Minerals are also essential for proper immune function, and can act as

antioxidants or play fundamental roles in regulating cell function. While all vitamins and minerals are essential for good health, including immune system support, some of them play a stronger role than others.

Vitamin C – The Immunity Superstar

Vitamin C is probably the most widely known vitamin for supporting the immune system and for combating colds and the flu. This reputation is not without reason! In the body, white blood cells contain up to 80 times more vitamin C than the plasma. These important immune cells actively store this vitamin and deliver it to infection sites. At these sites the antioxidant actions of vitamin C come into play, eliminating free radical stress and oxidizing toxins.¹ A wide variety of studies have attested to the benefits of vitamin C for supporting the immune system.

The recommended dietary intake (RDI) of vitamin C is 45 mg per day, however this represents the amount required to avoid an all-out deficiency in the vitamin, leading to scurvy. The renowned researcher Linus Pauling has suggested that higher doses of 240-4000 mg of vitamin C per day are required in order to reduce cold and flu severity and duration.² This was based on a study performed by Pauling involving 272 students at a ski camp in Switzerland. Although Pauling's results have come under scrutiny, growing evidence still supports a beneficial role for vitamin C in immune system support.³



Overall; the results of numerous studies show that increased vitamin C intake can reduce the duration and severity of cold symptoms. For example, in one study involving over 800 individuals, a daily supplement of 4000 mg of vitamin C was associated with a 21% decrease in disability associated with illness, as defined as days confined to their house. This was also associated with reduced duration of symptoms, fewer days of work missed and fewer

Table 1. Key Functions of Vitamins. Daily doses are for adults and are those recommended by Health Canada.²⁶ Minimum doses represent requirements to avoid a state of outright deficiency. Higher doses provide more therapeutic benefits.

Vitamin	Daily Dose	Function	Natural Sources
Vitamin A	Minimum: 65 mcg Maximum: 3000 mcg	Promotes skeletal growth, normal tooth structure, healthy immune function, healthy mucous membranes, healthy skin, eyes and hair; essential for night vision.	Fish liver oils, liver, carrots, green and yellow vegetables, dairy products
Vitamin C	Minimum: 6 mg Maximum: 2000 mg	Essential for the formation of collagen; prevents oxidation of other vitamins; aids in metabolism of amino acids and calcium; stops internal bleeding; strengthens blood vessels maintains hard bones and teeth; prevents infections, colds, fatigue and stress; reduces allergies; heals wounds and burns.	Citrus fruits, berries, green and leafy vegetables, tomatoes, cauliflower, potatoes, sweet potatoes
Vitamin E	Minimum: 1 mg Maximum: 179 mg	Protects body from destructive oxidation; strengthens capillary walls; prevents loss of other vitamins; aids blood flow to heart; lowers blood cholesterol and fatty acids; vital to cell health and immune function.	Soybeans, vegetable oils, broccoli, Brussels sprouts, leafy greens, enriched flour, whole wheat, wheat germ, whole grain cereals, eggs
Vitamin D	Minimum: 30 IU Maximum: 1000 IU	Promotes bone and tooth development and normal growth; aids utilization of phosphorus and calcium; maintains nervous system and heart action; prevents rickets; modulates the immune system.	Exposure to UVB light, not present in significant amounts in food.
Vitamin B1 (Thiamin)	Minimum: 0.07 mg Maximum: 100 mg	Helps convert sugar and starches into energy; promotes digestion, strong heart muscle, child growth; prevents fatigue and fat deposits in arteries	Liver, lean meat, whole wheat, brewer's yeast, wheat germ, fish, eggs, roasted peanuts, poultry, sesame seeds, nuts
Vitamin B2 (Riboflavin)	Minimum: 0.07 mg Maximum: 100 mg	Aids in releasing energy to body cells; enables utilization of fats, proteins and sugars	Dairy products, liver, kidney, yeast, leafy greens, fish, eggs
Vitamin B3 (Niacin)	Minimum: 1 mg Maximum: 500 mg	Aids normal functioning of tissues, particularly skin, gastrointestinal tract and nervous system; used with other vitamins in converting carbohydrates to energy	Liver, lean meat, whole wheat, brewer's yeast, wheat germ, fish, eggs, roasted peanuts, poultry, sesame seeds, nuts
Vitamin B5 (Pantothenic Acid)	Minimum: 0.4 mg Maximum: 500 mg	Needed for many chemical processes in the body; Helps modulate stress response; energy production and metabolism; antioxidant; fights infections and accelerates wound healing	Liver, lean meat, whole grain cereals and legumes
Vitamin B6	Minimum: 0.1 mg Maximum: 100 mg	Aids metabolism of protein carbohydrates and fats; controls cholesterol level; builds hemoglobin; Improves energy production	Wheat bran, wheat germ, organ meats, beef, avocados, bananas, milk, eggs
Vitamin B12	Minimum: 0.14 mcg Maximum: 1 mg	Promotes utilization of protein, fats and carbohydrates; essential for formation of red blood cells; builds nucleic acid; prevents pernicious anemia; helps nervous system	Liver, beef, pork, eggs, dairy products, shellfish
Folic Acid	Minimum: 30 mcg Maximum: 1 mg	Crucial for proper brain function and plays an important role in mental and emotional health, especially important during pregnancy	Green, leafy vegetables, orange juice, organ meats, sprouts
Vitamin K	Minimum: 6 mcg Maximum: 120 mcg	Essential for normal blood clotting, supports skeletal health	Green leafy vegetables like swiss chard, spinach and kale

doctor visits.³ A more recent study from 2002 including 167 individuals found that supplementation with 1000mg of vitamin C daily for 60 days resulted in a significant decrease in number of colds as well as the duration of symptoms when infected.⁴

While there is substantial support for vitamin C's ability to reduce symptom duration, the evidence regarding its ability to prevent infection in the first place is mixed. Generally, it seems that vitamin C is most likely to provide protection against infection under harsh circumstances.³ For example, several studies have shown that vitamin C supplementation can help to reduce cold incidence in individuals under heavy physical stress, like athletes and military troops.⁵ In these higher risk groups, supplementation can help to reduce infection incidence by up to 50%.⁵

Vitamin E – Another Antioxidant Vitamin

Vitamin E is another well-known antioxidant vitamin which has also been shown to have positive effects on the immune system. Like vitamin C, this vitamin is highly concentrated in the white blood cells, helping to protect them from oxidative damage, thereby supporting immune function.⁶ Immune system benefits from vitamin E supplementation seem to be particularly pronounced in elderly individuals. As we age T-cell function naturally begins to decline, however, research on both mice and humans has shown that supplementation with vitamin E can help to restore T-cell function.⁷ In one study, supplementation with 200 mg of vitamin E in elderly individuals for 235 days significantly improved various indices of immune function. The results of this trial suggested that vitamin E can help to improve T-cell-mediated immunity in healthy elderly individuals.⁸ Vitamin E supplementation has also been shown to have similar effects in younger individuals, helping to modulate cell-mediated immunity and reduce oxidative stress.⁶

Other research has suggested that these improvements do translate into tangible results. For example, a study examining the effects of vitamin E supplementation (200IU per day) for one year in an elderly population showed that supplementation had a protective effect, reducing the chance of acquiring an upper respiratory tract infection.

To date, most studies of vitamin E and immune function have focused on only the alpha-tocopherol fraction of vitamin E. However, preliminary studies are suggesting that the tocotrienol fraction of vitamin E may also have a profound effect on immune function. Tocotrienol supplementation in old mice was found to

significantly reduce the age-related decline in white blood cell proliferation that was seen in the control mice.¹⁰ In humans, women who supplemented with 400 mg of palm-sourced tocotrienols for one month prior to receiving a tetanus vaccination showed an improved immune response, including increased antibody and interferon levels.¹¹



Vitamin D – Immune System Modulator

More and more research is starting to show the importance of vitamin D for supporting a healthy immune system. This vitamin is synthesized in the skin in response to UVB radiation, and is difficult to obtain from dietary sources.¹² Many individuals, especially those living at northern latitudes, are deficient in this very important vitamin.

In terms of its effects on the immune system, the active metabolite of vitamin D, 1,25(OH)2D3, is a very important immune modulator. Vitamin D acts to inhibit the formation of dendritic cells, which are important for activating the rest of the immune system, and are specialized in antigen presentation. This means that they will engulf invaders and then display markers of the invader, or antigens, which in turn activate other cells of the immune system, such as helper T-cells. By inhibiting dendritic cells, vitamin D reduces the activation of T-cells, and the T-cell mediated immune response.^{13,14} In addition to the regulation of T-cells, vitamin D also has an effect on the actions of B-cells. It seems to act on them in two primary ways; first, it stimulates increased production of interleukin (IL)-10, which inhibits antigen presentation by dendritic cells and prevents T-cell activation, and second, it inhibits the production of IgE antibodies, the primary antibody associated with the allergic response.¹⁵ Overall, the immunomodulatory actions of vitamin D play a very important role in preventing the activation of an inappropriate immune response, and is very important for maintaining self-tolerance and preventing auto-immunity.

Beyond its role in immune system modulation, vitamin D is also critically involved in the body's innate immune response. Specifically, vitamin D has been shown to activate important antibacterial proteins, called defensin and cathelicidin.¹³ Researchers have related these actions to numerous beneficial effects, including a reduction in the risk of skin infection in individuals with atopic dermatitis¹⁶, a reduced risk of placental infections during pregnancy¹⁷, and even a reduction in the occurrence of the common cold.¹⁸

For example, an examination of the results of the Third National Health and Nutrition Examination Survey found that serum vitamin D levels were inversely associated with the incidence of upper respiratory tract infections.¹⁸ The study examined vitamin D levels and recent URTI in over 18,000 individuals, and found that recent infections were reported in 24% of individuals with the lowest serum levels (<10ng/mL) as compared to only 17% of individuals with the highest serum levels (>30ng/mL).¹⁸

Scientists have also speculated that vitamin D may be important for helping to reduce the severity of influenza infections. During an influenza infection macrophages release a large amount of pro-inflammatory cytokines, and in many cases the severity of infection is associated with the virus's ability to stimulate cytokine release.¹⁹ For example, highly dangerous flu epidemics such as the 1918 Spanish flu have been associated with high levels of cytokine release, or a cytokine "storm". This innate cytokine immune response can be overwhelming, and levels of such cytokines are significantly higher in those with a fatal outcome.¹⁹ This response also explains how some flu strains are highly virulent even in young, healthy individuals. Research suggests that vitamin D may play a role in regulating the response of monocytes, preventing them from releasing too many pro-inflammatory cytokines.¹⁹ Furthermore, the antimicrobial proteins that are activated by vitamin D have also been shown to help inactivate the influenza virus directly.¹⁹

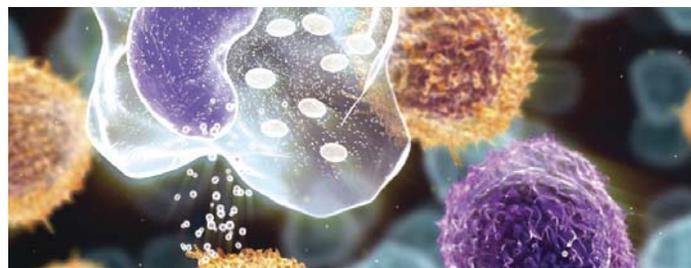


Figure 1. Cytokines released by macrophages in response to influenza infection

These hypotheses have been supported by a recent clinical trial examining whether vitamin D supplementation could help to reduce influenza A incidence in school children.²⁰ The study occurred over 4 months and involved 334 Japanese school children. The authors found that supplementation with 1200IU of vitamin D3 daily had a protective effect, significantly reducing the incidence of influenza A infection over the study period. Only 10% of children receiving vitamin D suffered from flu infection, as compared to 18% in the placebo group.²⁰

Key Minerals to help keep you Healthy

A large number of minerals also play an important role in maintaining and supporting the immune system. For example zinc, copper, iron and selenium are some of the important mineral players involved in immunity. Individuals with zinc deficiency are more susceptible to infection.²¹ Zinc plays an essential role in RNA and DNA replication, and is therefore essential for normal immune cell development and proliferation. Zinc deficiency also results in damage to epidermal cells, preventing the skin from acting as an effective barrier to infection.²¹ The importance of zinc for proper immune function was shown in one study which found that zinc supplementation can reduce the incidence of acute lower respiratory infections by 45%.²² However, supplementation with zinc can lead to copper deficiency, which can also depress the immune system, so it is important to balance supplementation of these two minerals.

Another essential element for proper immune function is selenium. Selenium has been shown to have an enormous number of effects on the immune system, and has been implicated in both helping to prevent infection as well as showing potential for helping to prevent certain cancers.²³ Selenium is a powerful antioxidant, and exerts many of its beneficial effects by preventing oxidative stress and damage in the body. Selenium has also been shown to help boost immunity by improving T-cell response and enhancing neutrophil function.^{23,24} Selenium deficiency has been found to be associated with the progression of a number of viral infections including HIV, and in AIDS patients selenium levels have been correlated to survival times.²³ In terms of cold and flu infection, new research in mice has shown that selenium deficiency may actually be a driving force contributing to the evolution of more virulent influenza strains!^{23,25} Studies have shown that when selenium deficient mice are infected with the influenza virus, the strain emerges from the mice with far more mutations, which can drive the evolution of more virulent strains of the flu.²⁵

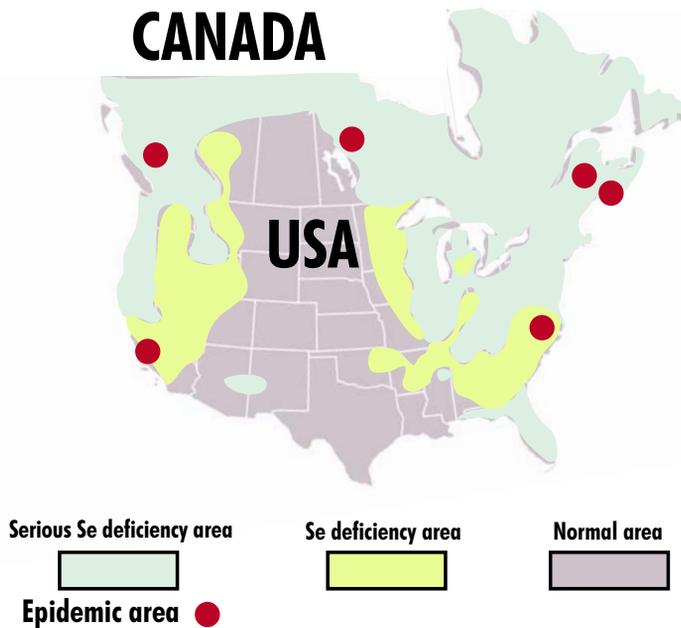


Figure 2. The relationship between selenium levels and the 2005 avian flu epidemic in North America

Conclusion

It is obvious that an adequate intake of vitamins and minerals is important for keeping your immune system functioning and, therefore, for keeping you healthy. A deficiency in any vitamin or mineral, not just those mentioned above, can result in impaired immune function and other serious health complications. A healthy diet can go a long way towards keeping vitamin and mineral levels up; however, many of us do not eat well all of the time. Furthermore, some nutrients, like vitamin D, cannot be obtained in high enough amounts even from the healthiest of diets. In these cases supplementation is a great solution for getting the nutrients that you need. A good multi-vitamin or individual vitamin or mineral supplements can be used to complement your diet and support your immune system. Not every cold or flu can be prevented, but with vitamins and minerals on your side, your body will be better equipped to face the challenge.

References

- Ottoboni F and Ottoboni A. 2005. Ascorbic Acid and the Immune System. *Journal of Orthomolecular Medicine*; 20(3): 179-183.
- Cook JD and Monsen ER. 1977. Vitamin C, the Common Cold and Iron Absorption. *The American Journal of Clinical Nutrition*; 30: 235-241.
- Hemilä H. 1997. Vitamin C Supplementation and the Common Cold, was Linus Pauling right or wrong? *Internat J Vit Nutr Res*; 67: 329-335.
- Van Straten M and Josling P. 2002. Preventing the Common Cold with a Vitamin C Supplement: A Double-Blind, Placebo-Controlled Survey. *Advances in Natural Therapy*; 19(3): 151-159.
- Hemilä H. 1996. Vitamin C and Common Cold Incidence: A Review of Studies with Subjects under Heavy Physical Stress. *Int. J. Sports Med.*; 17(5): 379-383.

- Lee CYJ and Wan F. 2000. Vitamin E Supplementation Improves Cell-Mediated Immunity and Oxidative Stress of Asian Men and Women. *Journal of Nutrition*; 130: 2932-2937.
- Galli F and Azzi A. 2010. Present trend in vitamin E research. *Biofactors*; 36(1): 33-42.
- Meydani SN, Meydani M, Blumberg JB, Leka LS, Siber G, Loszewski R, Thompson C, Pedrosa MC, Diamond RD and Stollar BD. 1997. *JAMA*; 277(17): 1380-1386.
- Meydani SN, Leka LS, Fine BC, Dallal GE, Keusch GT, Singh MF and Hamer DH. 2004. *JAMA*; 292(7): 828-836.
- Ren Z, Pae M, Dao MC, Smith D, Meydani SN and Wu D. 2010. Dietary Supplementation with Tocotrienols Enhances Immune Function in C57BL/6 Mice. *Journal of Nutrition*; 140(7): 1335-1341.
- Mahalingam D, Radhakrishnan AK, Amom Z, Ibrahim N and Nesaretnam K. 2010. Effects of supplementation with tocotrienol-rich fraction on immune response to tetanus toxoid immunization in normal healthy volunteers. *Journal of Clinical Nutrition*. Published online ahead of print, doi:10.1038/ejcn.2010.184
- Mora JR, Iwata M and von Andrian UH. Vitamin effects on the immune system: vitamins A and D take centre stage. *Nat Rev Immunol*. 2008; 8(9): 685-698.
- Hyppönen E, Berry DJ, Wjst M and Power C. Serum 25-hydroxyvitamin D and IgE – a significant but non-linear relationship. 2009. *Allergy*. 64: 613-620.
- Cantorna MT and Mahon BD. Mounting evidence for vitamin D as an environmental factor affecting autoimmune disease prevalence. *Exp Biol Med*. 2004. 229: 1136-1142.
- Heine G, Niesner U, Chang H, Steinmeyer A, Zügel U, Zuberbier T, Radbruch A, Worm M. 1,25-dihydroxyvitamin D promotes IL-10 production in human B-cells. *Eur J Immunol*. 2008. 38: 2210-2218.
- Hata TR et al. Administration of oral vitamin D induces cathelicidin production in atopic individuals. *J Allergy Clin Immunol*; 122(4): 829-831.
- Liu N, Kaplan AT, Low J, Nguyen L, Liu GY, Equils O and Hewison M. Vitamin D induces innate antibacterial responses in human trophoblasts via an intracrine pathway. *Biology of Reproduction*. Published online November 12, 2008.
- Ginde AA, Mansbach JM, Camargo CA. Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the third national health and nutrition examination survey. *Arch Intern Med*. 2009; 169(4): 384-390.
- Cannell JJ, Vieth R, Umhau JC, Holick MF, Grant WB, Madroncic S, Garland CF and Giovannucci E. Epidemic influenza and vitamin D. *Epidemiol. Infect.* (2006), 134, 1129-1140.
- Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y and Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. *Am J Clin Nutr*. 2009. doi: 10.3945/ajcn.2009.29094
- Shankar AH and Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. *Am J Clin Nutr* 1998;68(suppl):447S-63S.
- Sazawal S, Black R, Jalla S, Mazumdar S, Sinha A, Bhan MK. Zinc Supplementation reduces the incidence of acute lower respiratory infections in infants and preschool children: a double-blind controlled trial. *Pediatrics*. 1998; 102: 1-5.
- McKenzie RC, Rafferty TS and Beckett GJ. Selenium: an essential element for immune function. *Trends Immunology Today*. 1998; 19(8): 342-345.
- Arthur JR, McKenzie RC and Beckett GJ. Selenium in the Immune System. *J. Nutr*. 2003; 133: 1457S-1459S.
- Beck MA, Nelson HK, Shi Q, Van Dael P, Schiffrin EJ, Blum S, Barcaly D and Levander OA. Selenium deficiency increases the pathology of an influenza virus infection. *The FASEB Journal*. 2001 Jun; 15(8): 1481-3.
- National Health Products Directorate of Health Canada. Multivitamin/Mineral Supplements Monograph. October 27, 2007. Available at: http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/licenprod/monograph/multi_vitmin_suppl-eng.php

Medicinal Mushrooms:

Powerful Immune System Support

The healing effects of mushrooms have been recognized for thousands of years. Maitake, shiitake, reishi and brazilian mushrooms, for example, have long histories of medicinal use. Only more recently have scientists begun to understand what components of mushrooms are responsible for their beneficial properties. Several major substances with immunomodulatory and/or antitumor activity have been isolated from mushrooms. These include mainly polysaccharides; in particular β -glucans, polysaccharopeptides (PSP), polysaccharide proteins, and proteins. Furthermore, other bioactive substances, including triterpenes, lipids, and phenols, have been identified and characterized in mushrooms and have been shown to have proven medicinal properties.

The various glucans, and especially β -glucans, have become the focus of a great deal of research into immune system modulation, infection prevention and cancer. β -glucans are large polysaccharides, which means that they are formed from a large number of sugar molecules (glucose) linked together in specific patterns. Research has shown that the most active types of β -glucans are insoluble and have a very specific type of linkage between their individual molecules called a β 1,3/ β 1,6 linkage¹ (see Figure 1).

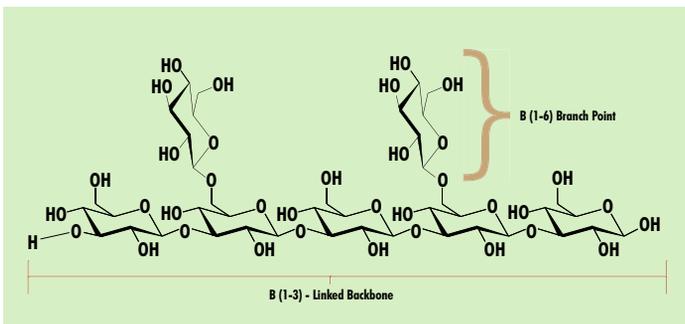


Figure 1. The Typical Structure of immunomodulatory β -glucans from mushrooms

Immune System Modulation and Enhancement

Studies have shown that the active substances in mushrooms can act to modulate and enhance both the innate and adaptive immune response.¹ Overall, the major immunomodulating effects of these active substances is their ability to stimulate the proliferation and enhanced functioning of important immune system cells. The therapeutic effects of mushrooms, such as protection against infection, anticancer activity and the suppression of autoimmune diseases and allergies have been associated in many cases with these immunomodulating effects.

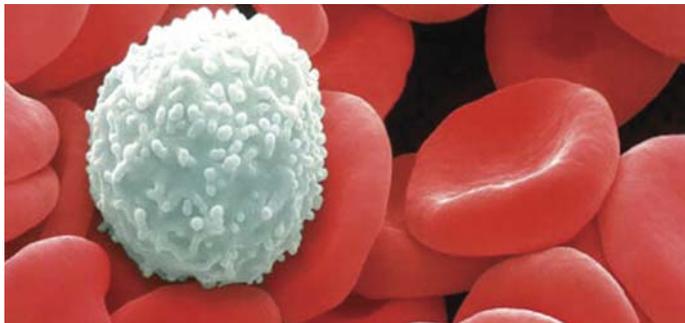


Figure 2. Human immune cell (white blood cell or lymphocyte) surrounded by red blood cells.

For example, some mushroom metabolites like the D-fraction from the maitake mushroom represent important biological response modifiers due to their ability to enhance the activity of natural killer cells in cancer patients.² Mushroom polysaccharides also induce the maturation and function of cells called dendritic cells, causing them to stimulate the proliferation of T-cells, thereby enhancing the immune response. B cells and antibody production have also been shown to be activated by mushroom polysaccharides.² Overall, glucans and other mushroom molecules have wide ranging effects on the immune system, and are able to enhance its function, whether it is for preventing infection with the common cold or flu or for improving the health of cancer patients.

Anti-Cancer Effects

The most studied use for medicinal mushroom extracts is their potential in the treatment and prevention of cancer. Progression to malignant cancer occurs when the tight controls that normally govern cellular division break down, resulting in the uncontrolled proliferation of cancerous cells. It also involves the ability of these cells to spread and invade into surrounding tissue. The modulation of the host immune system attributed to mushrooms, particularly mushroom glucans, is likely

to affect primarily the promotion and progression stages of cancer. When mushroom glucans stimulate macrophages this results in the production of various signaling molecules called cytokines which induce anti-tumor activity by the macrophages.²

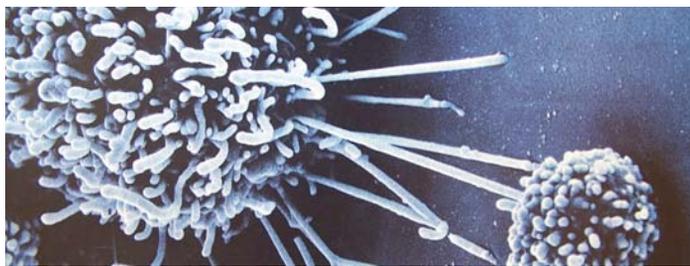


Figure 3. A Tiny Natural Killer Cell attacking a huger Cancer Cell

A highly specific extract from Basidiomycetes mushrooms called Active Hexose Correlated Compound (AHCC) has been shown to have very promising anti-cancer effects. Arguably the most active nutrient in AHCC is acetylated α -glucan, a component known to enhance the immune system.³ A prospective cohort study with AHCC involving 269 patients with liver cancer showed positive results.⁴ 113 of these patients were given AHCC following surgery and the remainder was not. The survival rate of the AHCC group was 79% compared to 51% for the control group. Furthermore, the recurrence rate among the AHCC group was 49% compared to 67% for the control group.⁴ Other studies have shown that AHCC can work synergistically with chemotherapy, helping to improve outcome and reducing side-effects.⁵

Other substances contained in mushrooms may be able to interfere with tumor initiation through a variety of mechanisms, such as enhancing the host's antioxidant capacity, or up-regulating enzymes involved in the detoxification of cancer causing compounds. For example, extracts of *Agaricus blazei* (brazilian mushroom) and *Grifola frondosa* (maitake mushroom) have been found to contain a compound with antitumor activity called ergosterol. Ergosterol has been shown to exhibit antioxidant activity and anti-inflammatory actions through the suppression of inflammation inducing molecules like COX-2. Oxidative damage is strongly implicated in the development of many chronic diseases, including cancer. COX-2 also appears to play an important role in certain cancers. Thus, its inhibition can result in the inhibition of tumor development, and it appears to be beneficial even in some established tumors.

Mushrooms for Everyday Immune Support

The immune system enhancing effects of mushroom extracts and glucans have benefits for everyday support as well. By increasing the proliferation of and activity of the cells of the immune system they can boost the body's defenses against all kinds of infections. This was demonstrated in a study examining the effects of AHCC on the body's response to influenza infection. In the study, 29 individuals were immunized with an influenza vaccine. Half of them were supplemented with 3000 mg/day of AHCC on the day of vaccination and for two weeks following the inoculation, the other half were given a placebo.⁶ It was found that individuals taking AHCC had significantly higher levels cytotoxic T-cells and Natural Killer cells, suggesting an improved immune response. In studies with mice, AHCC has been shown to improve survival and viral clearance in mice infected with influenza.⁷

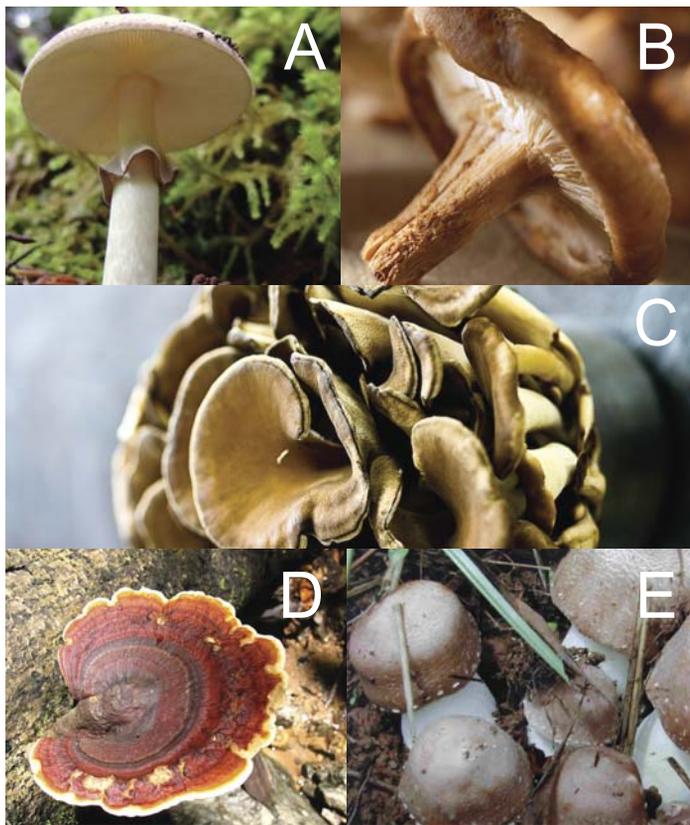


Figure 4. Various types of mushrooms with immune enhancing effects. A) Basidiomycetes; B) Shitake; C) Maitake; D) Reishi and E) Brazilian.

Other types of mushroom extracts have also been shown to improve resistance to infection. For example, a patented blend of four mushroom species (maitake, shiitake, reishi and brazilian mushrooms) called Immunutrin™ has been clinically shown to enhance

immune function and to help prevent infection. In one open-label study involving 18 subjects, supplementation with 1000 mg per day of Immunutrin™ for two months resulted in a 10% increase in levels of natural killer cells, helper T cells, cytotoxic T cells, and B cells and an 18% increase in total lymphocytes.⁸ During the study, 16 of 18 subjects reported no symptoms of viral or bacterial infection, indicating that the heightened immune response was associated with prevention of sickness. In a follow-up study, five subjects were given 3000 mg of Immunutrin™ per day for 2 weeks to assess the supplements' effect on natural killer cell cytotoxicity, which is their ability to attack and destroy infected cells.⁸ It was found that the number of natural killer cells increased by 19% compared to baseline after two weeks of supplementation, and natural killer cell cytotoxicity increased by 17%. These results confirm that the increased natural killer cell numbers generated by taking Immunutrin™ are associated with greater immune activity in the body.

Conclusion

Cumulatively, the studies on mushroom extracts suggest that they contain compounds that may support immunity, help prevent infection and modulate tumorigenesis and carcinogenesis at different stages. Overall, the compounds contained in mushrooms could potentially provide additive, or even synergistic, effects in supporting immunity and in the prevention

and treatment of cancer. Furthermore, evidence suggests that these substances also have benefits for everyday immune support by enhancing immune system activity, thereby helping the body to stave off infection.

References

1. Borchers, A.T., Keen, C.L. & Gershwin, M.E. Mushrooms, tumors, and immunity: an update. *Exp. Biol. Med.* (Maywood.) 229, 393-406 (2004).
2. Bao, X., Fang, J. & Li, X. Structural characterization and immunomodulating activity of a complex glucan from spores of *Ganoderma lucidum*. *Biosci. Biotechnol. Biochem.* 65, 2384-2391 (2001).
3. Kenner D. AHCC: The Japanese Medicinal Mushroom Immune Enhancer. Woodland Publishing.; ISBN: 1-58054-340-5: P. 7
4. Matsui Y., Uhara J., Sato S., Kaibori M., Yamada H., Kitade H., Imamura A., Takai S., Kawaguchi Y., Kwon A., Kamiyama Y. Improved Prognosis of Postoperative Hepatocellular Carcinoma Patients When Treated With Functional Foods: A Prospective Cohort Study. *Journal of Hepatology*, vol. 37/1, pp 78-86, July 2002.
5. Uno K., et al. Active Hexose Correlated Compound (AHCC) Improves Immunological Parameters And Performance Status of Patients with Solid Tumors. *Biotherapy* 2000 14(3) 303-309.
6. Gardner EM, Beli E, Kempf LP, Lifton D and Fujii H. Active Hexose Correlated Compound (AHCC) improves immune cell populations after influenza vaccination of healthy subjects. *FASEB J.* April 2010 24 (Meeting Abstract Supplement) 1b327.
7. Ritz BW, Nogusa S, Ackerman EA and Garder EM. Supplementation with Active Hexose Correlated Compound Increases the Innate Immune Response of Young Mice to Primary Influenza Infection. 2006. *J. Nutr.* 136:2868-2873.
8. Immunutrin™ Product Summary. 2008. NutraGenesis LLC. Brattleboro, VT



Andrographis paniculata:

Natural Cold and Flu Relief

There are a vast number of natural products available on the market for the relief of cold symptoms. For example, Echinacea has become extremely popular over the past several years. Andrographis paniculata, which is also known as Chiretta, King of Bitters or Kalmegh, is another plant that has shown potential for cold and flu relief.¹ Andrographis is relative new comer on the immune support scene in North America, but it has a long history of use in Scandinavia as a cold and flu remedy as well as in traditional Ayurvedic and Chinese medicine as a fever reducer.² Pharmacological studies have shown that this herb has antiviral, antipyretic, anti-inflammatory and immune enhancing properties. Studies in humans are beginning to show impressive effects as well, suggesting that this herb could be the “new Echinacea.”



Symptom Relief from Andrographis

In one study evaluating the effectiveness of Andrographis 223 patients were treated with either 200mg of Andrographis or a placebo for five days during an upper respiratory tract infection.¹ Symptoms including cough, expectoration, nasal discharge (running nose), headache, fever, sore throat, earache, malaise/fatigue and sleep disturbance were assessed on days 1, 3 and 5 of treatment. The results of the study showed that from days 3 to 5 the majority of symptoms measured remained unchanged or were worse in the placebo group; whereas symptom severity decreased significantly in the Andrographis group.¹ Overall the results showed that Andrographis was 57% more effective than the placebo for reducing the severity and duration of symptoms.¹



These results are further supported in a systematic review of the use of Andrographis.² The Review evaluated seven clinical trials using this herb for the treatment of cold symptoms and concluded that it is a safe and promising treatment for the symptoms of uncomplicated upper respiratory tract infections.² In another study comparing the effectiveness of Andrographis against acetaminophen (Tylenol™) for the relief of sore throat and fever, a dose of 6g per day of Andrographis was found to be as effective as the acetaminophen for controlling symptoms.³ Research has shown that Andrographis can also help to prevent infection altogether. In one three month long study involving 107 eighteen year old students, participants were given either a placebo or 200 mg of Andrographis daily. At the end of the three months twice as many individuals in the placebo group had reported having a cold as compared to individuals taking Andrographis!⁴ These results suggest a strong protective effect for Andrographis, likely due to its immune system enhancing properties.

What about Echinacea: Does it Work?

Echinacea is currently one of the most popular supplements on the market and is generally taken to help prevent the common cold. A number of studies have shown that this supplement can help to reduce cold symptoms, duration and frequency. There remains some debate, however, as to whether or not this herbal remedy is truly effective.



Recently, several large-scale trials have put the herb to the test without significant results. One study involving nearly 400 college students found that supplementation with the equivalent of 900mg of dried Echinacea root daily had no significant effect on the duration or severity of cold symptoms.³ In another trial, a dose of 6 g of unrefined Echinacea or Echinacea root on the first day of infection, and 3g per day for each subsequent day of the illness also had no effect on cold symptoms in 150 students.⁴ Another very large trial including 524 children between the ages of 2 and 11 supplemented with Echinacea syrup or a placebo did find a slight reduction in the frequency of upper respiratory tract infections (URI's) in children taking Echinacea. They found that those taking the Echinacea supplement

experienced 337 cases of URI's compared to 370 cases in children taking the placebo over a four-month period. However, once again, no benefit for reducing infection duration or severity was observed. Furthermore, the researchers involved in the study pointed out that taking Echinacea also increased the risk of developing a rash in the children taking it, and therefore did not recommend Echinacea supplements in children under the age of 11.⁵

In the end there is still a great deal of uncertainty regarding this herb's effectiveness. Adding to this issue is the fact that the Echinacea preparations available on the market vary widely in terms of their standardization, method of preparation and even the species they contain! Currently, the exact benefits of Echinacea remain uncertain. While it may provide some measure of immune system support, it certainly does not live up to the conception that it is a "cure for the common cold".

Which is Better?

The question remains, what is the best natural herb to take to help relieve the symptoms of colds and the flu? One study has actually compared the effectiveness of Andrographis and Echinacea to determine which was actually more effective.⁸ The study included 138 children between the ages of 4 and 11, who were diagnosed with an uncomplicated upper respiratory tract infection. The children were placed into one of three groups: a control group, a group receiving 510 mg of Andrographis extract daily and a group receiving 30 drops of Echinacea extract daily over the course of ten days. Overall the researchers found that the Andrographis was more effective than Echinacea for reducing the severity and duration of symptoms.⁸ Andrographis was especially effective for reducing nasal secretion and congestion, and resulted in an accelerated recovery time, whereas Echinacea did not.⁸ Overall the study concluded that Andrographis was well-tolerated and more effective than Echinacea in helping to reduce cold symptom duration and severity.⁸ There is some evidence that both Andrographis and Echinacea can help protect against infection, however when it comes to symptom relief Andrographis is the clear winner.

In the end it seems that Andrographis may be an emerging star in the area of natural cold and flu relief. Its ability to help prevent and treat viral infections makes it a great choice for both everyday immune system support as well as for short term relief of cold and flu symptoms.

References

1. Saxena RC, Singh R, Kumar P, Yadav SC, Negi MPS, Saxena VS, Joshua AJ, Vijayabalaji V, Goudar KS, Venkateshwarlu K and Amit A. A randomized double blind placebo controlled clinical evaluation of extract of *Andrographis paniculata* (KalmCold™) in patients with uncomplicated upper respiratory tract infection. *Phytomedicine*. 2010; 17: 178-185.
2. Coon JT and Ernst E. *Andrographis paniculata* in the Treatment of Upper Respiratory Infections: A Systematic Review of Safety and Efficacy. *Planta Med*. 2004; 70: 293-298.
3. Thamlikitkul V, Dechatiwongse T, Theerapong S, et al. Efficacy of *Andrographis paniculata* (Nees) for pharyngotonsillitis in adults. *J Med Assoc Thai* .1991;74:437-442.
4. Caceres DD, Hancke JL, Burgos RA, et al. Prevention of common colds with *Andrographis paniculata* dried extract: a pilot double blind trial. *Phytomedicine* 1997;4:101-104.
5. Turner RB, Bauer R, Woelkart K, Hulsey TC and Gangemi D. An Evaluation of *Echinacea angustifolia* in Experimental Rhinovirus Infections. *The New England Journal of Medicine*. 2005; 353: 341-348.
6. Barret BP, Brown RL, Locken K, Maberry R, Bobula JA and D'Alessio D. Treatment of the Common Cold with Unrefined *Echinacea*: A Randomized, Double-Blind, Placebo-Controlled Trial. *Annals of Internal Medicine*. 2002; 137(12): 939-946.
7. Taylor JA, Weber W, Standish L, Quinn H, Goesling J, McGann M and Calabrese C. Efficacy and safety of echinacea in treating upper respiratory tract infections in children: a randomized controlled trial. *JAMA*. 2003; 290(21): 2824-2830.
8. Spasov AA, Ostrovskij OV, Chernikov MV and Wikman G. Comparative Controlled Study of *Andrographis paniculata* Fixed Combination, Kan Jang® and an *Echinacea* Preparation as Adjuvant, in the Treatment of Uncomplicated Respiratory Disease in Children. *Phytotherapy Medicine*. 2004; 18: 47-53.

TOTAL E

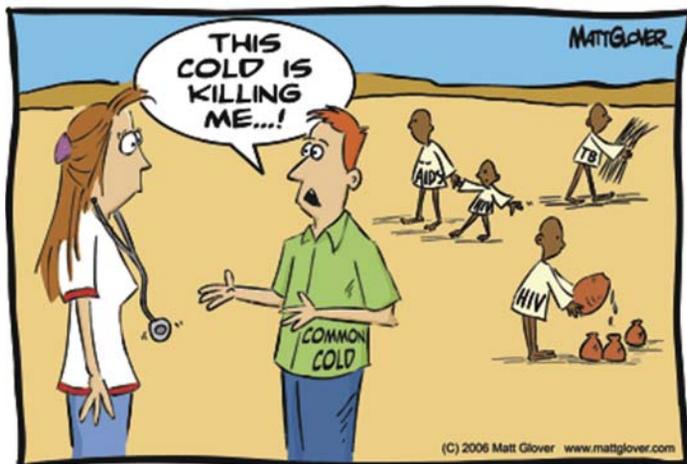
Complete, Balanced Vitamin E Supplementation

- Contains all 8 vitamin E molecules
 - Fights oxidants
 - Suppresses inflammation
- Reduces the risk of heart failure



Stress, Cortisol and Immunity

In today's lifestyle, we often hear about stress and its negative effects on the body. Disease and malfunction are widespread and rising. The proverb, "There is nothing new under the sun," tells a true tale. There has always been stress, but perhaps it shows up in different disguises today than for our ancestors. Also, the body's resources for coping with the stress may be more limited today.



MattGlover.com. Cartoon reflection: third-world sickness. Cartoons & Cartoonists, August 26th 2006. Retrieved Jan. 3rd 2010 from <http://www.mattglover.com/wordpress/wordpress/2006/08/25/cartoon-reflection-third-world-sickness/>

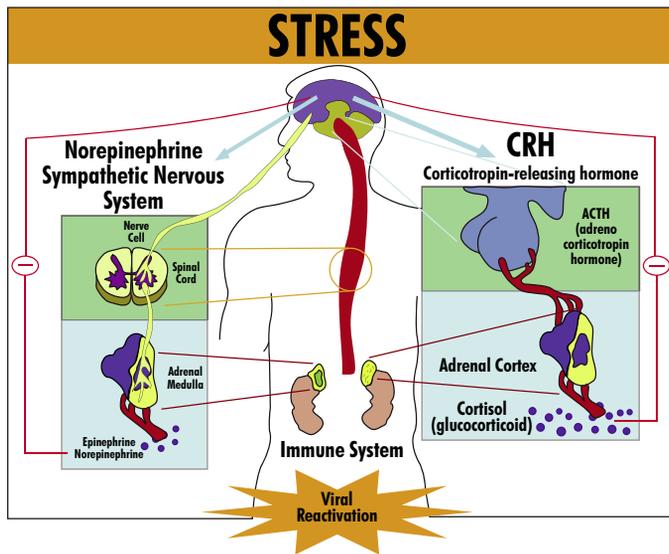
In the past century, industrialization and technology have changed our world, and we are being exposed to a greater variety of stressors daily. We may think that one type of stress is better or worse than another, but in reality, the body interprets and responds to all stress in the same manner: cortisol release. You may have heard cortisol described as the "stress hormone." When the body experiences stress, cortisol is released from the adrenal cortex which activates the "fight-or-flight" mechanism. This mechanism prepares us for self-defense and survival and is intended for short-term bursts of energy and heightened function. Cortisol

causes the release of sugar into the blood so that we have energy to deal with the stress, moves blood away from the organs to the peripheral muscles to be ready to move the body, increases blood pressure by improving the sensitivity of the vessels to adrenaline, decreases bone formation, acts as a diuretic by excreting water, and heightens awareness. Among these effects is suppressed immunity, which opens the door to infection and suppresses inflammation.



Stress and Illness: Understanding the Connection

When we get sick, the fever, stuffy nose, phlegm build-up and swollen lymph nodes are not the result of the infection itself, but rather they are the result of the immune system fighting the infection. Our immune system responds to infection with a flux of white blood cells to the infected area, and it is their activity that causes the symptoms. The inflammatory response to sickness or injury is also the result of the immune system trying to heal the tissues by bringing a flood of plasma (blood), white blood cells and nutrients to the injured area. When stress is present, cortisol is released and our body is primed to deal with the stressor. When cortisol returns to baseline levels, the suppression is removed. This is why we often seem to get sick after a stressful situation has passed, such as after exams, a stressful time at work, family events, and so on. It's not that we've gotten sick, but rather that the immune system is finally responding to the infection.



results when the adrenal cortex has been so overworked through chronic stimulation that the adrenals experience “burn-out” or fatigue, and can no longer produce enough hormones for proper stress response and function.¹⁹ This can lead to chronic fatigue, illness and inflammation, among other things. Fortunately, with proper care, this can be reversible. So how much and what kind of stress causes the release of cortisol? All of it! The body interprets and responds to all stress in the same way: cortisol release. The hypothalamus interprets each stimulus and releases hormones that result in cortisol release in response to any stimulus that an individual perceives as fearful or threatening.

The Importance of Good Nutrition

Nutritional stress includes what we eat and what we don’t eat. Today, we eat less fresh, unadulterated food and consume more processed, preserved foods than ever before. We do not only need calories from food for energy, we need also the vitamins, minerals and phytonutrients that are present in food in just the right amounts so that they can work synergistically to promote health. Food that has been enriched has been stripped of most of its nutritional value through the refining process and only some of it is replaced. Heat and chemical processing may remove or kill many of the nutritional elements that are naturally present in food.¹ When we consume food that has been heavily processed or has little nutritional value, our body may not recognize what we consume as food and will try to expel it from the body quickly. The body will also use nutrients from its own reserves or from other foodstuffs in order to digest it, since the enzymes used to digest food require nutrients, such as minerals, to catalyze reactions.¹⁶ All of this causes stress throughout the body because it is not getting what it needs to function properly. This will eventually lead to the exhaustion of non-primary bodily processes, hormonal imbalances, and disease.^{10,11,16}



Figure 3. An ear of corn contaminated with aflatoxin

Figure 1. Stress can suppress the immune system long enough to allow infections to spread. By the time the immune system can effectively respond, some damage has already been done.

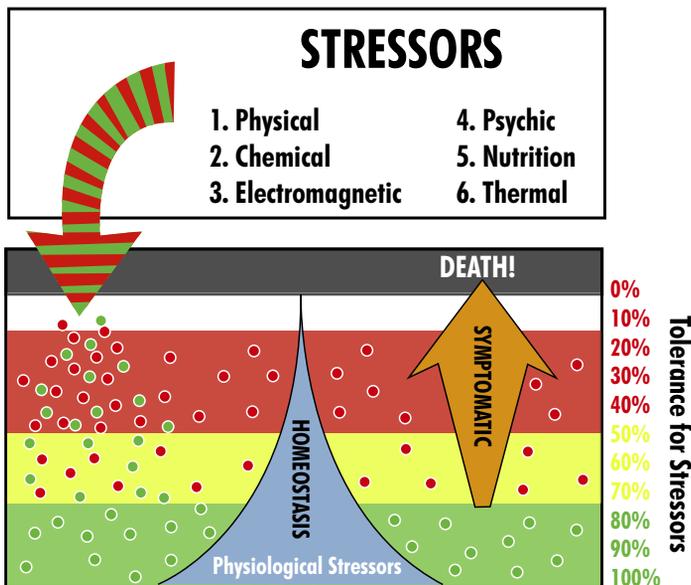


Figure 2. All stressors are funneled together within your body by the nervous system

If stress remains for a lengthy period of time, hypercortisolemia can occur, which is a higher than normal level of cortisol in the blood. This creates a longer period of time during which bone maintenance is diminished, sleep is not restful, tissue repair is slowed, and cells are less sensitive to insulin which causes high blood sugar. In fact, research has shown stress to be related to many of the illnesses that devastate our society, such as mental illness, cancer, autoimmune diseases such as arthritis and fibromyalgia, and heart disease and all its components including high blood pressure, diabetes, dyslipidemia, weight gain, and more. In cases of chronic stress a condition called adrenal insufficiency (also known as adrenal fatigue) may occur. This

The Effect of Toxins and the Environment

Nowadays, chemicals and toxins reach our body through food, drugs, our water supply, in the air, in our cleaning products, and in our merchandise.²³ Many chemicals are toxic to our bodies or they become toxic when present in higher amounts. Toxic residues from pharmaceuticals and personal care products (PPCP) end up in our water supply.¹⁷ If they are toxic in diluted amounts in our water supply, how toxic are they when we ingest, wear or use them? Studies have found that long-term exposure to water pollutants has caused an impaired cortisol response to stress in fish.¹⁹ Additives that give colour, taste and shelf-life to processed foods are poisonous to the body.¹⁶ In smaller amounts, chemicals are known to cause weight gain by altering hormonal balance, which affects immunity.²³ Chemicals such as pesticides and drug residues have also been found in human fat stores, even after cessation of exposure. If these toxins are not cleared out by appropriate detoxification systems, they just sit in fatty tissues and continue to damage cells. It is possible that this accumulation of toxins in the body contributes to the weight gain and diseases we attribute to being part of the "middle-aged metabolism crash" or "a normal part of aging". Additionally, mold and fungi can accumulate on our food supply due to pesticide use, improper storage, and processing. These can then secrete mycotoxins that are toxic to the body.¹⁴

There are several detoxification systems at work in the body. The immune system plays an important role by generating antioxidants to harness toxins and detoxify the body. The more toxins one is exposed to, the more antioxidants are used up, leaving fewer antioxidants for normal immune processes, such as protecting tissues from pathogens and from inflammation.

Although electromagnetic radiation is not a new phenomenon, the magnitude to which we are exposed to it has greatly increased recently. Electricity now surrounds us, and even if we did not use electrical devices, we would still be exposed to radio and satellite frequencies and electrical fields. Non-ionizing electromagnetic radiation comprises most of our daily exposure; however, we may be exposed to small amounts of ionizing radiation in our daily lives as well as in medical facilities. One study found that exposure to cellular telephone non-ionizing radiation caused a 12% decrease in cortisol levels during a 4-week exposure period.²¹ Another study found that both low and high levels of non-ionizing radiation from TV and radio broadcasting stations caused subjects to secrete higher levels of cortisol.²² Remember that both high and low levels of cortisol can negatively affect immunity. There continues to be controversial evidence related to the health effects of non-ionizing radiation, and its cumulative effects. Due to the multitude of sources we are exposed to daily this is certainly something to be aware of.²

The Role of Physical and Emotional Stress

Physical stress results from physical harm or insufficient repair processes. This can result from a severe injury, injury caused by weak tissues due to malnutrition or a lack of exercise, or due to tissues that have been overworked, overactive, unrested or unrepaired. An example of the latter is too much high intensity exercise, also known in athletics as overtraining (although overtraining is multifaceted), since exercise increases free radical production.¹⁵ Tissue repair processes are slower and may be incomplete when cortisol levels are too high or too low. High levels suppress immunity and repair processes.¹¹ Low levels offer no suppression, which might permit infections to fester or the immune system to become overactive, resulting in tissue damage, inflammation and pain.⁹ High levels of cortisol also diminish the quality and length of our sleep during which repair processes occur and may disturb the natural circadian hormonal balance of metabolic hormones that help maintain a healthy metabolism. In fact, a lack of adequate sleep is recognized as a factor.



Psychological stress, mental stress and emotional stress can all be summarized with one word: thoughts. The nature of our thoughts affects the physical and chemical state of the body.⁷ They are intertwined and inseparable. Negative or destructive thoughts and emotions can cause physical harm to the body.³ Disharmony in the mind produces disharmony in the body, which results in illness and disease. It is said that many heart attacks happen on Monday mornings, and it is surmised that this phenomenon is related to scheduled activities and work.^{4,5} Fibromyalgia and shingles often appear after prolonged periods of stress.^{6,8} The placebo effect is a good example of how thoughts affect the body. One study's results also suggested that obese women tend to have a hyperactive cortisol response to stress.²⁰ This shows that the way in which an individual perceives and responds to stress influences their cortisol release and thus their hormonal balance and metabolism. All of this in turn influences immune factors.

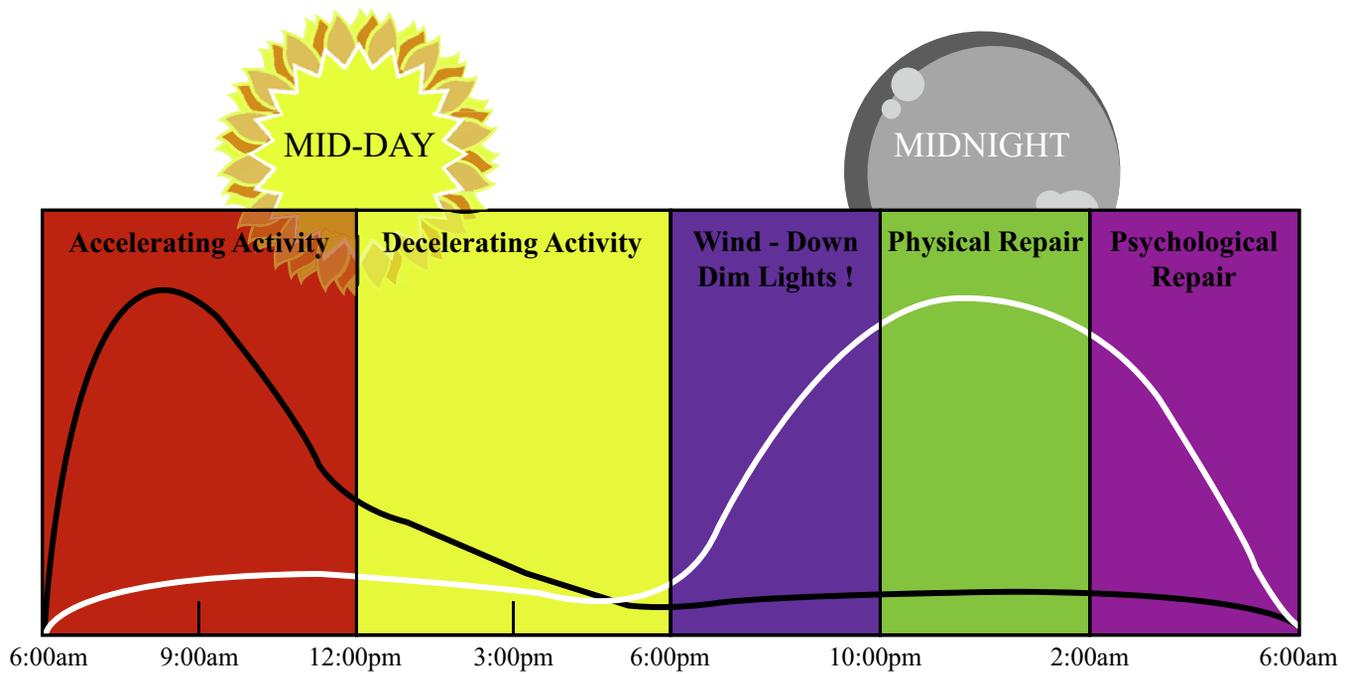


Fig 1. Healthy balance of stress (cortisol) & hormonal cycle.
May vary with seasonal daylight changes.¹⁵

BLACK LINE: cortisol & stress hormones
WHITE LINE: repair hormones

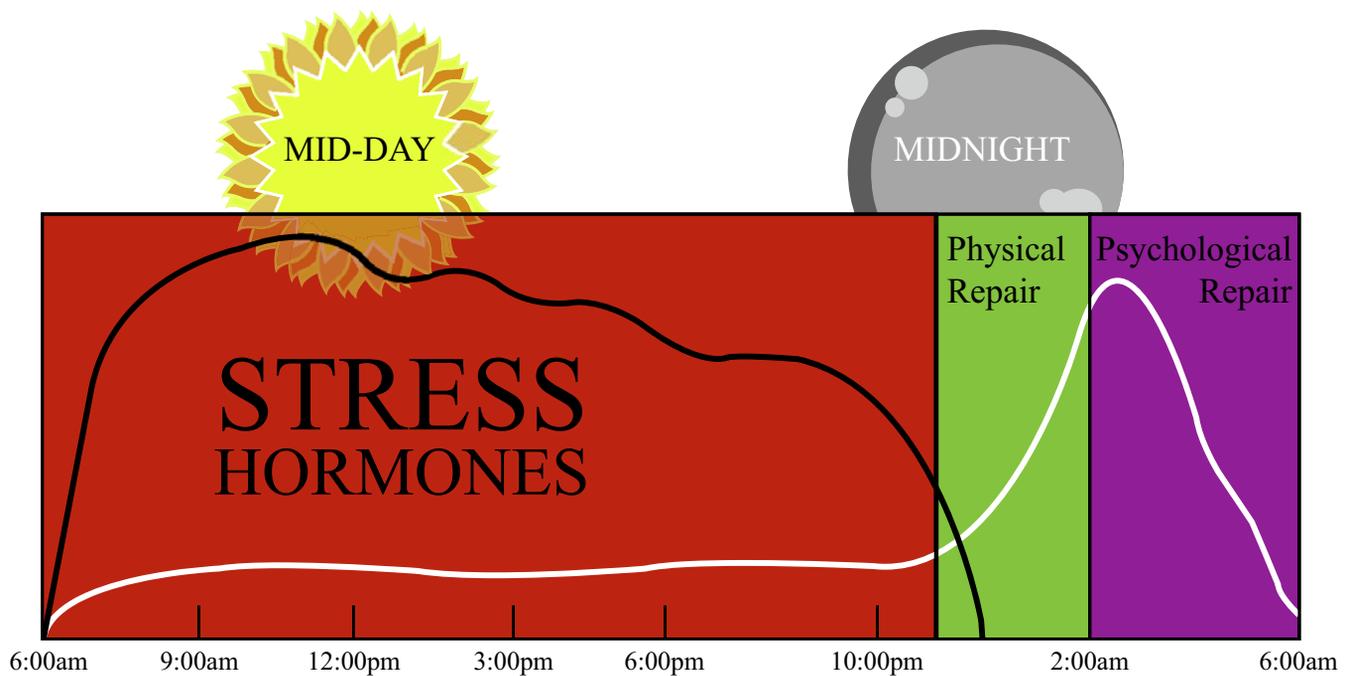


Fig 2. Imbalanced stress (cortisol) & repair hormonal cycle.
Will vary according to lifestyle.¹⁵

BLACK LINE: cortisol & stress hormones
WHITE LINE: repair hormones

Manage Stress, Stay Healthy

Evidently, we are constantly encountering forms of unavoidable stress. Of course, there are ways to reduce stress. The most effective way to reduce stress is to remove or minimize the stressor. If this is not possible, the next best thing is to learn how to manage stressful situations. Behavioural and cognitive strategies, deep breathing, positive thinking, various therapies, keeping adequately hydrated with clean water, eating nutritious foods that are as close to their natural states as possible, taking dietary supplements, getting enough good quality sleep during optimal time periods, relaxing more often, doing enjoyable activities, and getting the right amount of the right kind of exercise are some techniques to manage stress. Managing stress, and hence cortisol release, may cost money, time, or certain lifestyle changes, but does any good thing come without a cost? And the price is worth the benefit!



Take rest; a field that has rested
gives a bountiful crop

Ovid

References

1. Sánchez-Moreno C, de Ancos B, Plaza L, Elez-Martínez P, Cano MP. (2009). Nutritional approaches and health-related properties of plant foods processed by high pressure and pulsed electric fields. *Crit Rev Food Sci Nutr*. 49(6):552-76.
2. Yakymenko I, Sidorik E. (2010). Risks of carcinogenesis from electromagnetic radiation of mobile telephony devices. *Experimental Oncology*, 32(2):54-60.
3. Yamanaka G, Otsuka K, Hotta N, Murakami S, Kubo Y, Matsuoka O, ...Halberg F. (2005). Depressive mood is independently related to stroke and cardiovascular events in a community. *Biomedicine & Pharmacotherapy*, 59, Suppl 1:S31-9.
4. Gnechi-Ruscone T, Piccaluga E, Guzzetti S, Contini M, Montano N, Nicolis E. (1994). Morning and Monday: critical periods for the onset of acute myocardial infarction. The GISSI 2 Study experience. *European Heart Journal*, 15(7):882-7.
5. Manfredini R, Citro R, Previtali M, Vriza O, Ciampi Q, Pascotto M, ...Italian Network investigators (2010). Monday preference in onset of takotsubo cardiomyopathy. *American Journal of Emergency Medicine*, 28(6):715-719.
6. Montesó Curto MP, Ferré i Grau C, Martínez Quintana V.(2010). Fibromyalgia: beyond the depression. *Revista de Enfermería*, 33(9):20-6.
7. Merkes, M. (2010). Mindfulness-based stress reduction for people with chronic diseases. *Australian Journal of Primary Health*, 16(3):200-10.
8. Schmader K, Studenski S, MacMillan J, Grufferman S, & Cohen HJ. (1990). Are stressful life events risk factors for herpes zoster? *Journal of the American Geriatrics Society*, 38(11):1188-94.
9. Bauer ME, Wieck A, Lopes RP, Teixeira AL, & Grassi-Oliveira R. Interplay between neuroimmunoendocrine systems during post-traumatic stress disorder: a minireview. *Neuroimmunomodulation*, 17(3):192-5.
10. Hughes CM, Woodside JV, McGartland C, Roberts MJ, Nicholls DP, & McKeown PP. (2010). Nutritional intake and oxidative stress in chronic heart failure. *Nutrition, Metabolism & Cardiovascular Disease*. 2010 Dec 24. [Epub ahead of print].
11. Reiche EM, Morimoto HK, & Nunes SM. (2005). Stress and depression-induced immune dysfunction: implications for the development and progression of cancer. *International Review of Psychiatry*, 17(6):515-27.
12. Sesti-Costa R, Baccan GC, Chedraoui-Silva S, & Mantovani B.(2010). Effects of acute cold stress on phagocytosis of apoptotic cells: the role of corticosterone. *Neuroimmunomodulation*, 17(2):79-87.
13. Leproult R. & Van Cauter E. (2010). Role of sleep and sleep loss in hormonal release and metabolism. *Endocrine Development*, 17:11-21.
14. Hussein HS. & Brasel JM. (2001). Toxicity, metabolism, and impact of mycotoxins on humans and animals. In: *Toxicology*, 167(2):101-34.
15. Chek, Paul (2004). *How To Eat, Move and Be Healthy*. C.H.E.K. Institute, San Diego, CA.
16. Hoffer, A & Walker, M (1996). *Putting it all together: the new orthomolecular nutrition*. Keats Publishing Inc.: New Canaan, CT
17. Snyder, S.A., Westerhoff, P., Yoon, Y. & Sedlak, D.L.(2003). *Pharmaceuticals, Personal Care Products, and Endocrine Disruptors in Water: Implications for the Water Industry* Environmental Engineering Science, 20(5): 449-469.
18. Lehmann, M., Foster, C., Dickhuth, H. & Gastmann, U. (1998). Autonomic imbalance hypothesis and overtraining syndrome, 30(7): pp 1140-1145.
19. Hontela, A., Rasmussen, J.B., Audet, C. & Chevalier, G. (1992). Impaired cortisol stress response in fish from environments polluted by PAHs, PCBs, and mercury. *Archives of Environmental Contamination and Toxicology*, 22(3): pp. 278-283.
20. Pasquali. R., Anconetani, B., Rabih, C., Biscotti, M., Spinucci, G., Morselli Labate, A.M. (1996). Hypothalamic-pituitary-adrenal axis activity and its relationship to the autonomic nervous system in women with visceral and subcutaneous obesity: Effects of the corticotropin-releasing factor/arginine-vasopressin test and of stress. *Metabolism - Clinical and Experimental*, 45(3): pp. 351-356.
21. Djeridane, Y., Touitou, Y. & de Seze, R. (2008). Influence of Electromagnetic Fields Emitted by GSM-900 Cellular Telephones on the Circadian Patterns of Gonadal, Adrenal and Pituitary Hormones in Men. *Radiation Research*, 169: 337-343.
22. Israel, M., Vangelova, K. & Tschobanoff, P. (2006). Study of the secretion of melatonin and stress hormones in operators from broadcasting and TV stations exposed to radiofrequency (RF) electromagnetic radiation (EMR). *Bioelectromagnetics*, 27:1-280.
23. Baillie-Hamilton, B.F. (2002). Chemical toxins: a hypothesis to explain the global obesity epidemic. *The Journal of Alternative and Complementary Medicine*, 8(2): 185-192.

Vitamin C

An Essential Vitamin and Antioxidant



Powerful antioxidant
Helps regulate the
immune system
Helps detoxify harmful
compounds

IMMUNE ULTRA

- Enhances the immune system
- Fights cancer
- Blocks bacterial and viral growth
- Increases levels of antioxidants



AHCC

- Improves defenses against cancer
- Enhances immune cell production
- Helps control infections
- Protects the liver



LACTOFERRIN

- Inhibits pathogen growth
- Enhances the immune system
- Promotes a healthy gastrointestinal system
- Anti-inflammatory



IMMUNE SUPPORT

- Helps support healthy immune function
- Enhances the body's immune defenses
- Optimizes immune capacity to help prevent infection



TOTAL E

- Contains all 8 vitamin E molecules
- Fights oxidants
- Suppresses inflammation
- Reduces the risk of heart failure



ZINC COPPER BALANCE

- Supports the immune system
- Avoids harmful excesses of zinc
- Improves cholesterol balance
- Antioxidant



C + BIOFLAVONOIDS

Vitamin C With a Boost

- Fights oxidants
- Recharges vitamin C
- Prevents inflammation
- Maintains healthy cell division

