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Exercise and immunity

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Abstract
During the aging process, a decrease in the ability of the immune system to control infection, known as immuno senescence, takes place. Paradoxically, aging also results in chronic low-level inflammation and exaggerated inflammatory responses. A number of studies have investigated the effects of a variety of exercise training interventions on the immune system both in humans and using animal models of aging. Cross-sectional studies that compared masters athletes to untrained, age-matched controls found that the athletes had significantly better immune function, but these studies suffered because of the difficulty in generalizing results from highly trained athletes to a general population of physically active older adults. Prospective studies in humans have attempted to address this, but these studies have resulted in sometimes equivocal findings, possibly as a result of the differences in exercise training programs used. Finally, animal studies, both observational and mechanistic, have almost universally supported the exercise effect on enhancing immune status in the aged. More research is needed to determine the mechanism by which exercise influences immunity in the aged and to identify exercise training programs for use in this population. It is clear, however, that exercise is likely to be effective at boosting immunity in the older people when undertaken regularly.

Keywords: Exercise, immune system, immunology

Introduction
Exercise or training has many benefits. Active individuals claim they feel better and also are healthier than their sedentary friends. We are constantly exposed to bacteria, viruses and parasites capable of causing mild to serious disease. The relationship between exercise and immune function has important implications for public health and for athletes. The immune system is a complex and precisely ordered system of cells, hormones and chemicals that regulate susceptibility to severity of, and recovery from infection and illness. Immune system operates with nervous system and endocrine system to maintain homeostasis.

Over the past 15 years a variety of studies have demonstrated that exercise induces considerable physiological change in the immune system. The interactions between exercise stress and the immune system provide a unique opportunity to link basic and clinical physiology and to evaluate the role of underlying stress and immuno physiological mechanisms. It has been suggested that exercise represents a quantifiable model of physical stress. Many clinical physical stressors (e.g., surgery, trauma, burn, and sepsis) induce a pattern of hormonal and immunological responses that have similarities to that of exercise. Whereas neural-endocrine-immune interactions have been investigated using a variety of psychological models, the exercise model provides a further opportunity to establish these links using a physical stress paradigm. This review extends earlier work on exercise immunology and focuses on underlying endocrine and cytokine mechanisms

Immune System
*Cells:
Leucocytes Lymphocytes – B. Cell, T. Cells, Natural killer
Phagocytes : 1. Monocytes 2. Neutrophils 3. Eosinophils
Auxiliary cells : 1. Basophil 2. Mast cells3. Platelets
*Soluble mediators
*Processes

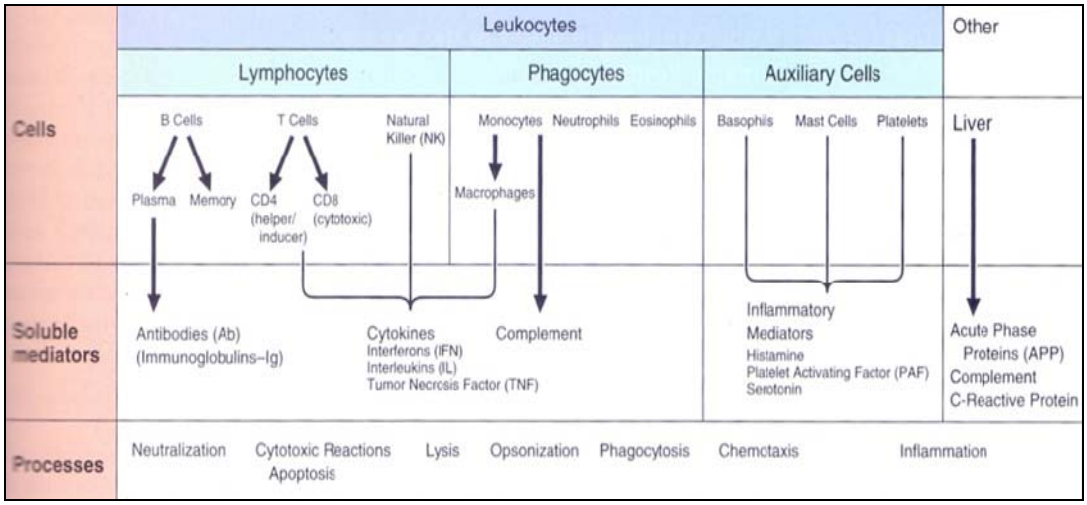

Fig 1: Components of the Immune System

Cells

Lymphocytes: Both B cells and T cells are derived from bone marrow cells. Each B-cell and T-cell is generally programmed to recognize only one particular antigen. Plasma cells produce an antibody to act immediately. Memory cells provide lasting immunity. Natural killer cells are large granular lymphocytes and act spontaneously against any target. Phagocytes are leucocytes bind to pathogenic microorganisms and antigens and then kill them. Auxillary cells release mediators to produce inflammation.

Soluble Mediators

Soluble Mediators are intervening agents dissolved in a solution. Antibodies produced by B plasma cells are known as Immunoglobin (Ig). Cytokines are proteins or peptides, released from immune cells, skeletal muscles and adipose tissue. Cytokines are involved in communication between immune cells and other cells of the body.

Processes

The immune system can destroy or inactivate a pathogen in numerous system:

Apoptosis: A target cell may be signaled to self-destruction.

Neutralization: It occurs when antibodies block the binding site on antigens to prevent tissue damage.

Opsonization: It is the coating of the membrane of an antigen to make it easier for phagocytes to engulf the antigen.

Phagocytosis: It is the engulfing and digesting of a pathogen.

Lysis: It is a form of cystotoxic reaction in which a cell is killed by the destruction of its cell membrane.

Immune Response to Exercise

Immune response to exercise depends largely on the intensity and duration of the exercise. Exercise may alter immune system in the following ways. Directly stimulating immune function. Stimulating the sympathetic nervous system, altering hormones (especially epinephrine, norepinephrine, cortisol, growth hormone, prolactin and thyroxine). Increasing body temperature. Exercise-induced cell damage, increasing oxidative stress.

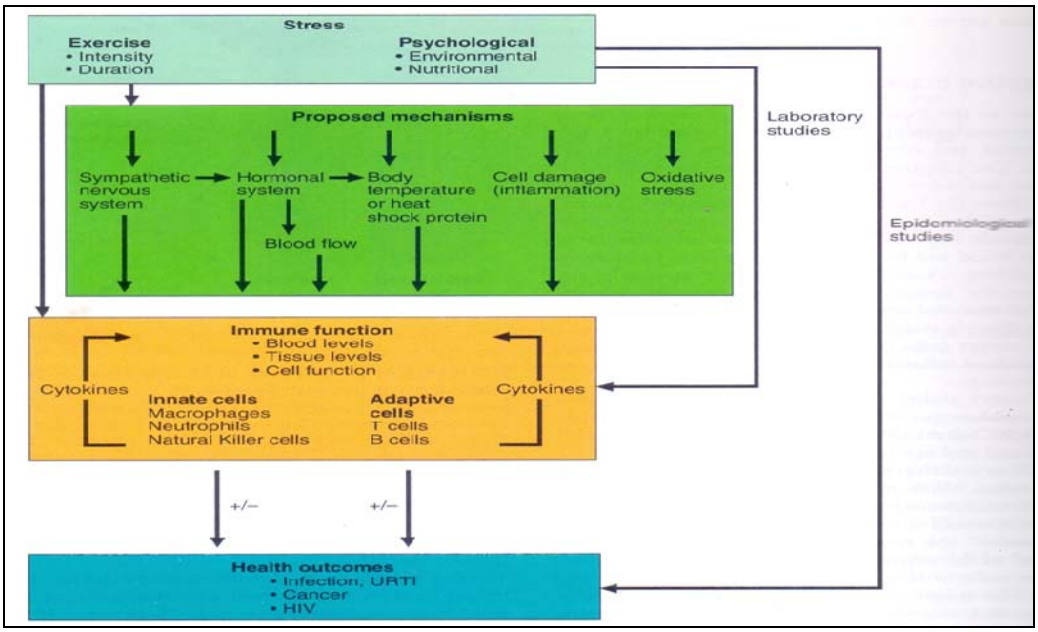

Fig 2: Relationships among Exercise, Immune Function and Health

Variable/Exercise Intensity	During or Immediately After Exercise	Recovery
Total leukocytes		
Moderate-intensity	↑ 0–40%	Unknown
High-intensity	↑ 50%	↑ 50–100% 2 hr postexercise
Innate immune system		
Neutrophils		
Moderate-intensity	↑ 30–50%	Unknown
High-intensity	↑ 30–150%	Unknown up to 2 hr postexercise 25–100% 2–4 hr postexercise
Monocytes		
Moderate-intensity	No Change	Unknown
High-intensity	↑ 0–20%	↑ 0–50% 2 hr postexercise
Natural Killer cells		
Moderate-intensity	↑ 0–50%	Normal by 1 hr postexercise
High-intensity	↑ 100–200%	↓ 40% 2–4 hr postexercise
Adaptive immune system		
T cells		
Moderate-intensity	No change	Unknown
High-intensity	↑ 100%	↓ 30% 1–2 hr postexercise
B cells		
Moderate-intensity	No change	Unknown
High-intensity	No change	↓ 0–25% 1–2 hr postexercise
Serum Ig		
Moderate-intensity	No change	No change
High-intensity	No change	No change
Salivary IgA		
Moderate-intensity	No change	No change
High-intensity	No change	No change

Source: Based on data from Mackinnon, L. T.: *Advances in Exercise Immunology*. Champaign, IL: Human Kinetics (1999).

Fig. 3: Exercise Response of Immune Cell Numbers to Medium-duration (45 min.), Moderate-, and High-intensity Aerobic Exercise

Impact of Exercise on Immunity

Prolong high intensity exercise results in the greatest leukocytosis immediately after exercise and in recovery.

Neutrophils increase in number as a result of aerobic exercise.

Prolonged moderate-exercise is associated with enhanced neutrophil function (phagocytic activity, oxidative burst activity and antimicrobial activity).

Strenuous exercise, however, causes a greater disruption of the immune system and in decrease of some cells and cellular function.

Strenuous training or overtraining is associated with a suppression of several immune variables. A decrease in neutrophil function and a reduction in lympohocytes (B cells, T cells and NK cells) have been noticed.

Prolonged strenuous exercise such as marathon running, lead to a higher incidence of URTI.

Improper nutrition can compound the negative influence of heavy exertion on the immune system.

Other life stress must be minimized.

Avoid over training and chronic fatigue. There should be proper load and recovery in training.

Physical activity is associated with lower prevalence and mortality rates for cancers involving the colon, breast, prostrate and lung.

Type	Signs and Symptoms
Performance Related	• Consistent decrement in performance • Persistent fatigue and sluggishness that leads to several days of poor training • Prolonged recovery from training sessions or competitive events • Reappearance of already corrected errors • Increased occurrence of muscular accidents/injuries
Physiological	• Decreased maximal work capacities and markers • Increased disruption of homeostasis at submaximal workloads • Headaches or stomachaches out of proportion to life events • Insomnia • Persistent low-grade stiffness and soreness of the muscles and joints • feeling of "heavy" legs • Frequent URTIs: sore throats, colds, or cold sores • Constipation or diarrhea • Loss of appetite; loss of body weight or muscle mass, or both, when no conscious attempt is being made to diet or when weight loss is undesirable • An elevation of ~10% in the morning resting heart rate taken immediately on awakening
Psychological/ behavioral	• Feelings of depression • General apathy, especially toward previously enjoyed activities • Decreased self-esteem • Emotional instability or mood changes • Difficulty in concentrating • Loss of competitive drive or desire • Perceived insufficient recovery

Fig 4: Signs and Symptoms of the Overtraining Syndrome (OTS)

Many of the health benefits of exercise have been well studied and publicized. For instance, we know that different types of exercise can promote weight maintenance and muscle growth, improve respiratory endurance and cardiovascular health and increase bone density in weight-bearing joints. However, what many people don't know (or at least fail to understand) is that exercise also can improve the immune system. Years of evidence support the claim that the right amount of certain types of physical activity can promote good health and improve symptoms in individuals with conditions of impaired immunity. Interestingly, the benefits of exercise appear to be similarly evident in persons with deficient immune systems and in persons whose systems are overly active (as is the case with autoimmune disorders). Although science still strives to better understand the exact relationship that links exercise and improved immunity, a number of theories have already been advanced.

Most people accept a few things on blind faith, but knowing how and/or why something works encourages many individuals to find a way to incorporate those things into their lives (assuming it is believed to be important). Exercise is no exception. Yet, to really understand the effects of exercise on the immune system, it's useful to first have a basic knowledge of the system itself.

The Immune System "Starting Lineup" The immune system is an amazing and somewhat complex system, with the lymph vessels serving as its delivery (or highway) system. Lymph is a semi-clear liquid that carries needed water, oxygen and nutrients that have been transferred through the blood system (via the walls of the capillaries) to the cells themselves. Together, the lymph and lymph vessels transport uninvited guests and cell waste from the cells and their surroundings to the lymph nodes to be filtered, processed and drained. Lymph nodes are found throughout the body (including the sides of the neck) and frequently enlarge as they respond to new white blood cell production during an infection. For instance, when a person's glands are swollen, there's a good chance that his or her body is trying to fight something. Although any biologist would accuse us of oversimplifying the definitions, let's take a look at some of the major players of the immune system: T Cells. Most of the cells that make up the immune system are white blood cells. One type of white blood cell, the lymphocytes, includes two major groups referred to as" T cells" and" B cells." T cells have receptors on their surface that interact with molecules (i.e., small particles of a substance composed of two or more atoms) that are found on other cells of the body. By "hooking up" to the molecules, T cells can recognize the matter as something that is supposed to be in the body, or recognize it as a foreign substance or invader like a virus or bacterium. Once an invader is detected, the different types of T cells either work to directly destroy them or work to assist other immune cells in coordinating an attack. Cytokines and Chemokines. One of the responses that T cells can mount against a trespasser is to secrete cytokines and chemokines. Cytokines are molecules that can activate other immune system cells that are nearby, or signal them to grow or to die. Chemokines are small groups of cytokines that attract more immune system cells to the area of the body where they are needed. B Cells and Antibodies. Certain cytokines released by T cells will activate and direct another type of lymphocyte, the

B cells, to make specific antibodies (aka, immunoglobulin) against a foreign substance. Antibodies then seek the invaders and bind them to sites on their surface known as antigens. By binding to an antigen, an antibody can either neutralize the foreign object directly or mark it for destruction by other members of the immune system.

Phagocytes. Phagocytes are white blood cells that are either stationary or circulate through the bloodstream and ingest harmful substances and dead or dying cells. A certain class of phagocytes, known as "professional" phagocytes (e.g., macrophages, neutrophils, monocytes, dendritic cells and mast cells), also possesses receptors on their surface (somewhat like those found on T cells). Once they have successfully engulfed a foreign invader, they will display part of its remains on their receptor and then present it to other cells of the immune system (including lymphocytes in the lymph nodes) to stimulate a larger response to the infectious agent.

Benefits of Exercise Understanding how these players in the immune system work, let's look at 10 ways that exercise might benefit the immune system.

1. One of the most apparent benefits of light exercise is its ability to promote the flow of lymph and the immune. Moderate exercise improves blood flow through the cardiovascular system, thereby helping to flush toxins and germs from the body through the excretory system via urine and sweat. Cells and antibodies it carries through the body. Unlike the arterial blood vessels, lymph vessels don't have the power of a pump (i.e., the heart) behind them. Instead, they depend on normal body motion, muscle contraction and manual manipulation such as massage to move the lymph along. Deep breathing with stretching (e.g., yoga or tai chi) is another effective exercise for circulating lymph.
2. Moderate exercise improves blood flow through the cardiovascular system, thereby helping to flush toxins and germs from the body through the excretory system via urine and sweat. Increased blood flow also keeps the antibodies and white blood cells needed to fight infection circulating rapidly as a possible early defense against foreign invaders.
3. When the body is deprived of sufficient oxygen as a result of high altitude, strenuous exercise, impaired breathing or other situations (a condition known as hypoxia), the immune function is impaired. Moderate exercise increases oxygen delivery through the bloodstream, thereby potentially improving the body's resistance.
4. Exercise slightly raises the body's temperature. Although the increase is not nearly as dramatic as running a fever (one of the body's natural reactions against many types of infection), it may still help to kill and/or inhibit the growth of an unwanted aggressor.
5. Scientific studies have recorded a temporary increase in phagocyte activity and function immediately following exercise. It is believed that this increase could take some potentially harmful substances out of the bloodstream before they ever get the chance to travel further. It may also help to boost the fight against an active infection.
6. Regular exercise may help the lungs to rid themselves of airborne viruses and bacteria that are associated with respiratory tract infections.
7. A certain group of cytokines are produced as a consequence of muscle contraction during exercise. One of these cytokines, IL-6, initially promotes inflammation (an important first response of the immune system against infection), but is shortly followed by an increase in anti-inflammatory cytokines. Turning off the inflammation phase is just as important as turning it on;

otherwise, tissue and organ damage can occur.

8. T1 helper cells also stimulate inflammation and other changes in the body as a first defense against infection. They are followed by T2 helper cells that produce an anti-inflammatory response. A recent study at the University of Illinois demonstrated that moderate exercise in mice appears to accelerate the change from a T1 to T2 response enough to help combat infection with the flu.
9. Another recent study conducted at Iowa State University found that mice that regularly ran on a treadmill during a period of three and a half months experienced flu symptoms that were less severe than those developed by mice that did not exercise. The study's lead researcher suggested that repeated stress from moderate exercise may improve the body's ability to respond to other types of stress, like those caused by the flu.
10. Speaking of stress, one of the greatest benefits of regular exercise is its ability to help relieve mental and emotional stress linked to suppressed immunity and increased illness. Exercise helps to provide an outlet for nervous energy, take our mind off of our greatest concerns (at least momentarily) and improve our body image. It also even relatively low levels of aerobic exercise can help to boost the immune system reduces the emission of stress-related hormones long thought to suppress the immune system.

Putting Science Into Action The 1st century Roman philosopher Marcus Cicero declared, "Never go to excess, but let moderation be your guide." These words should be applied prudently toward many aspects of our lives: eating, drinking, sleeping, working, playing — and exercising! Note that the key to the positive outcomes observed in many of the theories and research listed above is "regular and moderate exercise." In fact, many studies assert that high-intensity or strenuous exercise can actually cause a temporary decrease in the immune system's defenses, referred to as an "open window" period, which can last anywhere from three to 72 hours following the activity. Arduous exercise may also exacerbate other symptoms with autoimmune diseases. Of course, exercising too little or not at all can be just as detrimental to an individual's health. So, how much exercise is just the right amount? The answer, of course, varies somewhat among individuals, and a doctor should always be consulted first before beginning a new program or before making any major changes to a routine exercise program. However, even relatively low levels of aerobic exercise can help to boost the immune system. Generally speaking, 20 to 30 minutes of a low-impact activity (e.g., brisk walking, light jogging, swimming or biking), three to five times a week, is a great place to start. Regular moderate exercise appears to have a cumulative effect that leads to a more permanently improved immune response, and again, the benefits seem to be accessible to nearly everyone, regardless of their personal immune status or history. Several other factors can contribute considerably to the effects of exercise on the immune system and should be considered when planning activities. For example: • Exercise is discouraged in extreme heat or cold because the changes that are required to help regulate the body's temperature can be stressful to the immune response. Those who live in a cool climate during the winter months should plan more indoor activities like swimming, stationary biking, or walking or jogging on a treadmill (good sanitation techniques should be used when using public facilities). Those who live in a hot climate should try to arrange outdoor physical activities earlier in the morning or later in the evening to escape the heat of the day. •Exercising at especially high altitudes or in areas of high air pollution should be avoided, because both situations can stress the respiratory system and, in turn, the immune system due to decreased oxygen in the air.

Finally, individuals who aren't feeling well need to be honest with themselves. When ill, the immune system is already under strain from trying to fight the infection. The related stress caused by exercise may challenge recovery. However, for individuals who feel like they are just coming down with something, symptoms are mild and they don't have a fever, there is evidence to suggest that moderate exercise might actually decrease the duration and severity of a mild infection (a doctor should always be consulted for direction).

Remember that there are many benefits of exercise besides those immediately related to an improved immune system. If 20 to 30 minutes of walking is beyond an individual's current ability, there is always something that can be done (see the article, "Exercise and Immune Disease" in the December-January 2010 issue of IG Living magazine). The body's little friends are working hard to maintain well-being — and sending them a big breath of fresh oxygen can only help.

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