The impact of exercise on immunity and the role of nutritional supplements in it

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Keywords: Immune, nutrition, exercise, diet.

Abstract: As an important guarantee for the human body to survive in the world, immunity is very important and will be affected by exercise and nutrition. Studies have pointed out that moderate exercise is beneficial to the immune system. At the same time, prolonged strenuous exercise is related to the decline of immune cell function. In addition, adequate and appropriate nutritional supply has a positive effect on enhancing the immune response. The antioxidants and anti-inflammatory agents in the diet can scavenge free radicals in cells in the body and reduce the damage caused by oxidation. At the same time, it can improve the inflammatory factors increase caused by exercise and other reasons. In order to maintain a good immune system, a balanced diet is required to meet the body's energy and metabolism needs.

1. Introduction

Humans and other animals live in a surrounding that is teeming with both pathogenic and non-pathogenic microbes, from bacterium to viruses and parasitic worms, and contains a vast array of toxic or allergenic substances, which can imperil normal human homeostasis. Except pathogen, the community of microbe also have beneficial commensal organisms, which the host must tolerate and hold in check to support tissue and organ function. At the same time, a huge range of pathogenic microbes and toxic substances that challenge the host through a very broad selection of pathogenic mechanisms. Therefore, it is not surprising that the immune system uses a complex array of protective mechanisms to control and eliminate these organisms and toxins for protecting the body.

The benefits of exercise for the body have been deeply rooted in popular science work over the years. However, we still hear about athletes' injuries from time to time. The difference in exercise intensity between ordinary people and athletes leads to different changes in their immune systems, which is a question worthy of discussion.

As an important support for human energy supply and metabolism, dietary nutrition has always been a research direction that medical researchers attach importance to. With the progress of scientific research, the concept of nutrients has long been not limited to carbohydrates, proteins, fats and minerals, but has been extended to a series of edible exogenous ingredients, such as dietary fiber, polysaccharides, and polyphenols. The research on these new nutrients has greatly expanded the understanding of the human body's operating mechanism.

This article briefly describes the mechanism of the immune system and the impact of exercise intensity on the immune system, as well as the effect of dietary nutrition on the immune system, in order to inspire researchers in related fields.

2. Immune system

The immune system is a network of biological processes that protects an organism from diseases. Broadly, the immune system can be classified into two types: innate and adaptive immune response. Innate (natural) responses occur to the same extent however many times the infectious agent is encountered, whereas acquired (adaptive) responses improve on repeated exposure to a given infection. The innate responses use phagocytic cells (neutrophils, monocytes, and macrophages), cells that release inflammatory mediators (basophils, mast cells, and eosinophils), and natural killer cells.

  DOI: 10.25236/gemfe.2022.015

The adaptive immune system provides a tailored response to each stimulus by learning to recognize molecules it has previously encountered. The adaptive immune system manifests exquisite specificity for its target antigens which entails the proliferation of antigen-specific B and T lymphocytes, which happens when the surface receptors of these cells attach to antigen. The host uses both innate and adaptive mechanisms to detect and eliminate pathogenic microbes. To establish an infection, the pathogen must first overcome numerous surface barriers, such as enzymes and mucus, that either are directly antimicrobial or inhibit attachment of the microbe. Because neither the keratinized surface of skin nor the mucus-lined body cavities are ideal habitats for most organisms, microbes must breach the ectoderm. Any organism that breaks through this first barrier encounters the two further levels of defense, the innate and acquired immune responses.

The immune system is an extremely efficient system that is specific, inducible, and adaptive. However, the immune system can also be dysfunctional in some cases, which are mainly divided into three categories: immunodeficiency, autoimmunity, and hypersensitivity.

When one or more components of the immune system are inactive, it can cause immunocompromise or immunodeficiency. Immunodeficiency occurs when the immune system is less active than normal, resulting in recurring and life-threatening infections. Generally speaking, the body's immunity works enough to give birth to the next generation, the immune system will reach its peak during the period of fertility, the end of the reproductive cycle will decline [1]. The body's immunity is after the age of 50 began to decline, the emergence of immune aging, will cause cancer and a series of diseases, after middle age people is prone to cancer, this is one of the reasons [1]. Excluding age factors, obesity, alcoholism, and drug abuse are all factors contributing to immunodeficiency in developed countries. In addition, early in development, loss of the thymus gland due to genetic mutations or surgery can cause severe immune deficiency and susceptibility to disease [2]. Immunodeficiency is heritable or "acquired" in many cases. For example, patients with chronic granulomatous disease have a reduced ability of phagocytes to attack pathogens, which is a primary immunodeficiency that can be inherited. And cancers like AIDS and some can lead to acquired immunodeficiency [3, 4].

And the other extreme corresponding to low immune function is excessive immune response, which can also damage human health and cause autoimmunity disorders [5]. For example, swelling and deformation of the joints of the hand can induced by rheumatoid arthritis, which is an autoimmunity disease. When the immune system is unable to correctly distinguish between autologous and allogeneic antigens, it attacks parts of its body. Normally, lymphocytes that recognize their own antigens disappear early in the body's development. Specialized cells located in the thymus and bone marrow present autoantigens to new-born lymphocytes and destroy cells capable of recognizing autogens, thus preventing autoimmunity [6].

Corresponding to immunodeficiency is an excessively high immune response, that is, an allergic reaction. Hypersensitivity is an immune response belong to allergic reaction that deeply damages the body. According to the hypersensitivity reaction mechanism and time course, it can be divided into four categories (Type I-IV) [7]. Type I hypersensitivity is an immediate, acute reaction that is usually associated with allergies and has symptoms ranging from mild discomfort to death. Type I hypersensitivity reactions are mediated by the immunoglobulin IgE, which, when attached to an antibody, can trigger degranulation of mast cells and basophils. When antibodies bind to antigens in a patient's own cells, they cause a type II hypersensitivity reaction that destroys these cells. Therefore, such reactions, also known as antibody-dependent (or cytotoxic) hypersensitivity reactions, are mainly mediated by IgG and IgM. Immune complexes, including antigen aggregates, complement proteins, IgG, and IgM antibodies, may precipitate type III hypersensitivity reactions if not cleared in time. Type IV hypersensitivity reactions, also known as cell-dependent or delayed hypersensitivity reactions, usually develop symptoms after 2 to 3 days. Type IV hypersensitivity is more common in autoimmunity and infectious diseases, but also in contact dermatitis. Such reactions are mediated by T cells, monocytes, and macrophages [7].

In general, immunity is the ability of multicellular organisms to resist harmful external influences. For many years, immunology focused on dissecting the molecular mechanisms that control our physiological response to infections based on the assumption that this response does not differ among individuals. However, this premise has been challenged by recent studies suggesting that we are not all equally equipped to deal with pathogens [8]. One of the most frequent differences described in the immune response is its vigor and activity in females compared to males, leading to the consequent increase in autoimmunity conditions seen in the female population as well as differences in the immune response to pathogens and viruses [8]. The hormonal and genetic effects that have been proposed as explanatory mechanisms. Sexual hormones, mostly estrogen but also progesterone and testosterone, affect immune cells quantitatively and qualitatively. Our diet, age, gender, gene and even sleep can affect our immune system and make us more prone to disease. To comprehend these factors that regulate our immune system can greatly help to build a precise medical model or treatment tailored to individual needs.

3. Exercise and immunity

Although there have been hundreds of studies in humans and animals have demonstrated that various types of exercise may have significant positive and negative effects on the immune system, there is no concrete evidence linking it to illness [9]. Moderate exercise appears to be advantageous to the human immune system, according to epidemiological studies. The relationship between infection risk and exercise training load has long been described as a J-shaped curved (Figure 1), with high training loads believed to increase the risk of opportunistic infections, particularly of the upper respiratory tract [10].

Regular bouts of short-duration (up to 45 minutes) moderate-intensity exercise are thought to be good for host immunological response, especially in older persons and people with chronic conditions [11]. Infection burden, on the other hand, is high among high-performance athletes, coming in second only to injury in terms of the number of training days missed during the build-up to major sporting events. This has shaped the popular belief that strenuous exercise (i.e., activities performed by high-performance athletes or military personnel that much exceed prescribed physical activity guidelines) might lower immunity and increase infection risk.

Inflammation markers in the blood have been linked to chronic disease in the elderly, and inflammation has been related to the pathophysiology of a number of cardiovascular and metabolic diseases. According to latest research, exercise appears to have anti-inflammatory properties, the levels of biomarkers used to detect systemic inflammation are lower in those who are physically active on a regular basis [12]. Higher levels of habitual physical activity, for example, are linked to reduced levels of mitogen-stimulated inflammatory cytokine production, skeletal muscle inflammatory protein content, adipokine production, and C-reactive protein (CRP) serum levels [12]. Thus, while acute exercise stress may impede immune function and increase susceptibility to infection, this may not be completely harmful to the host, and may be one of the ways via which moderate exercise enhances long-term health by reducing immune activation and subsequent inflammation. One of the explanations for this anti-inflammatory impact could be the immune system depression that occurs after intense bouts of exercise [11].

Immune cell functions are impaired following acute sessions of prolonged, high-intensity exercise, and some studies have found that athletes are at a higher risk for infections. Studies have shown that strenuous stress for long duration, such as training for a marathon, can suppress the immune system by decreasing the concentration of lymphocytes. The immune systems of athletes and nonathletes are generally similar. Athletes may have a slightly elevated natural killer cell count and cytolytic action, but these are unlikely to be clinically significant. Studies of marathon runners indicated that their extended high-intensity exercise was connected with an increased risk of infection occurrence, moderate exercise has been linked to a 29 percent lower incidence of upper respiratory tract infections (URTI) [11]. According to David Nieman' assays, who showed that individuals engaged in regular exercise of a moderate intensity reported fewer symptoms associated with upper URTI compared to sedentary peers, while, conversely, those engaged in frequent high-volume exercise training appeared to be at a greater risk of infection than those who remained sedentary [13]. In a study of HIV, beneficial immune effects of exercise in HIV subjects are likely to occur early after infection before CD-4 counts are not greatly compromised compared to sedentary HIV subjects [9]. In individuals with heart disease, exercise interventions lower blood levels of fibrinogen and CRP, an important cardiovascular risk marker [14]. In a review of nine studies that examined the effects of acute exercise on vaccine responses that a single bout of moderate intensity exercise mostly enhances immune responses to vaccination [15].

Acute bouts of exercise elicit a temporary reduction in immune activity (e.g., neutrophil respiratory burst, lymphocyte proliferation, monocyte TLR, and major histocompatibility complex class II protein expression) that lasts 3–24 hours depending on the intensity and duration of the workout [11]. When the exercise is continuous, long (>1.5 h), moderate to high intensity (55–75 percent maximum O_2 uptake), and performed without food, the post-exercise immune function decrease is the most apparent [11]. Periods of intense training (overreaching) lasting a week or longer can result in immunological dysfunction that lasts longer. Although great athletes are not immune deficient clinically, it's plausible that the cumulative effects of tiny alterations in multiple immunological markers weaken resistance to common mild infections like URTI.

Exercise has obvious influence on the immune system's normal functioning, these effects are likely to compound over time, forming immunological responses to persistent exercise training. In terms of exercise "dosage," it's widely assumed that lengthy periods of intense exercise training will lower immunity, whereas frequent moderate-intensity exercise is good (figure 2) [16]. Exercise is a potent behavioral intervention that is being utilized to help the aged and obese, as well as individuals with cancer and chronic viral infections like HIV, enhance their immunological and health outcomes.

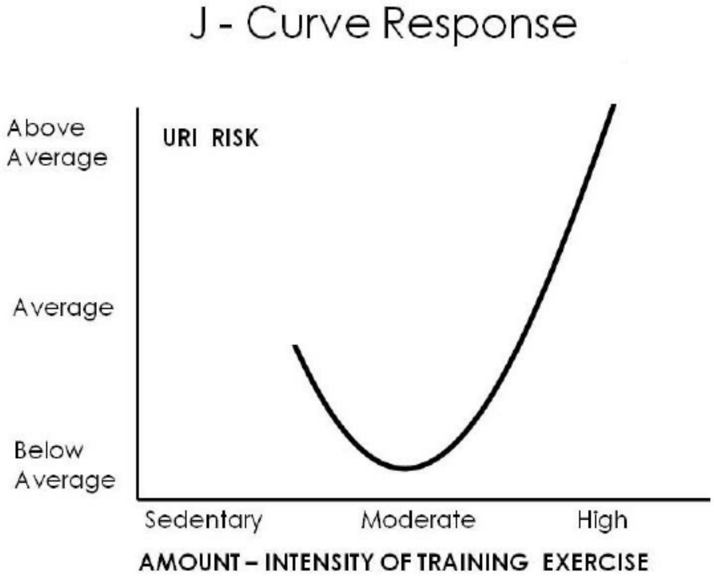

Figure 1. J-Curve Response between URI risk and intensity of training exercise [10]

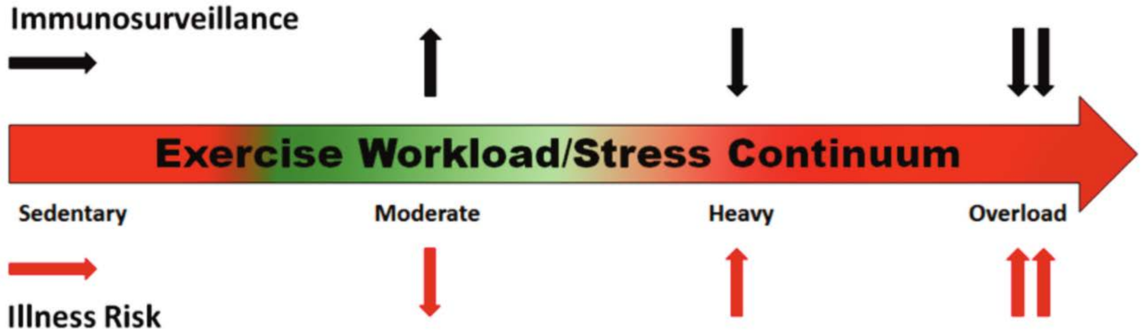

Figure 2. Schematic model of the exercise workload/stress continue and the relationship between immunosurveillance measures and risk of illness as the exercise workload is increase to moderate, heavy and overload [17]

4. Nutrition and immunity

The immune system's functioning is influenced by an individual's overall nutrition status, state of nourishment, and pattern of food intake (which includes foods, nutrients, and non-nutritive bioactive compounds) (figure 3); this impact can occur at the level of physical barriers (e.g., skin, intestinal mucous membranes), the microbiome, the innate immune system (e.g., macrophage function and polarization), and the adaptive immune system (e.g., T- and B-cell function) [18]. The immune system, on the other hand, has an impact on nutrition metabolism and requirements, as well as the physiological reaction to nutrition.

All cells, including those in the immune system, require adequate and proper nourishment to function optimally. During periods of infection, an "active" immune system boosts the need for energy even more, with higher basal energy expenditure during fever, for example. Thus, the ideal nutrition for the best immunological outcomes would be nutrition that supports immune cell functions, allowing them to initiate effective responses against pathogens while also allowing them to resolve the response quickly when necessary and avoiding any underlying chronic inflammation [19]. The immune system's energy and nutrient requirements can be satisfied through exogenous sources, such as the diet, or endogenous ones, such as body storage, if dietary sources are insufficient.

Proteins such as immunoglobulins, cytokines, and acute-phase proteins require an appropriate number of amino acids to be produced [20]. It is believed that the low pool of available proteins also results in a decreased amount of functional active immunoglobulins and gut-associated lymphoid tissue, which play a role in gut-mucosal defense against infection [21, 22]. Protein hydrolysates have been demonstrated to enhance barrier function and IgA production in animal models, and as a result may have applications for incorporation within hypo-allergenic infant formula and clinical nutrition for those with conditions such as inflammatory bowel disease [23, 24].

Fatty acids (FAs) may significantly alter immune responses, including changes in the organization of cellular lipids and interactions with nuclear receptors [25]. FAs in particular have been shown to affect the homeostasis and immune cell functioning in mice, e.g., epithelial cells, macrophages, dendritic cells, innate lymphoid cells, neutrophils, and T- and B cells [26]. In general, increased fibrinogen and high-sensitivity C-reactive protein (hs-CRP), an acute phase protein of hepatic origin, have been linked to saturated FAs consumption, while lower hs-CRP levels have been linked with polyunsaturated FA [27].

High glycemic index-induced acute hyperglycemia and acute insulin response, due to high consumption of processed carbohydrates (white flour, refined sugar), lead to an overload of the mitochondrial capacity and an increase of the production of free radicals [28]. Fibers as non-digestible parts of fruits, vegetables and cereals are an important energy source for bacteria that, by fermentation, lead to the production of short-chain fatty acids (SCFA) as essential nutrients for humans [29]. A high-fiber diet favors microbial diversity and production of SCFA and prevents the fermentation of less favorable substrates such as proteins and amino acids, leading to a reduced risk for colorectal cancer and Crohn’s disease [30].

Micronutrients play important roles in nucleotide and nucleic acid synthesis (e.g., iron, zinc and magnesium). Antioxidants are compounds that inhibit oxidation, a chemical reaction that can produce free radicals and chain reactions that may damage the cells of organisms which inhibit these reaction [31]. The commonly used dietary antioxidants are vitamins A, C, and E. Antioxidant availability (e.g., vitamin C) may be particularly important during heavy exertion or infection when oxidative stress increases [31]. Vitamin C supplementation has been associated with a lower incidence of URTI in marathon runners [11, 32]. Vitamin D can directly influence immune cell functions by regulating gene expression [33, 34]. Although certain levels of antioxidant vitamins in the diet are required for good health, there is still considerable debate on whether antioxidant-rich foods or supplements have anti-disease activity [32, 34-36]. Moreover, if they are actually beneficial, it is unknown which antioxidants are health-promoting in the diet and in what amounts beyond typical dietary intake [36].

Dietary constituents with especially high anti-inflammatory and anti-oxidant capacity include vitamin C, vitamin E, and phytochemicals such as carotenoids and polyphenols. Several of these can interact with transcription factors such as NF-kB and Nrf-2, related to anti-inflammatory and antioxidant effects, respectively [21]. Omega-3 fatty acids have been shown to disrupt inflammation cell signaling pathways by binding to the GPR120 receptor [37]. This benefit, however, can be inhibited or even reversed if the ratio of omega-6/omega-3 is too high, as omega-6 serves as a precursor to inflammatory chemicals (prostaglandin and leukotriene eicosanoids) in the body [38]. Trans-fatty acid intake, especially from processed foods such as fries and chips, has also been described as pro-inflammatory, being associated with increased TNF-α, IL-6, and hs-CRP levels [39].

Under-nutrition impairs immune defense at all stages of the life cycle. A well functioned immune system is key to providing good defense against pathogenic organisms and to providing tolerance to non-threatening organisms, to food components and to self. Having a balance and enrich diet is extremely important for human kind. Special populations such as elite athletes and people "at risk" such as elderly, pregnant women and infant, should alter their diet to fit their demand under instruction.

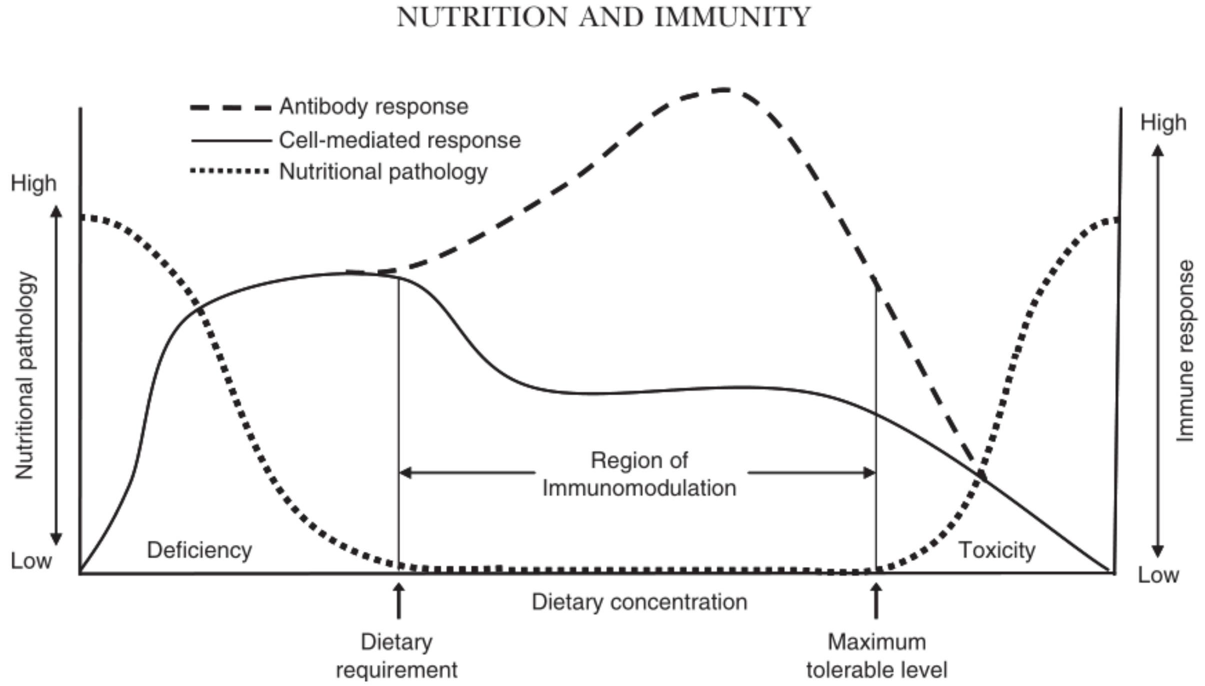

Figure 3. Tissue pathology occurs at low dietary inclusion rates (below established requirements) and at high rates (toxicity). Nutritional pathologies are absent at rates between the dietary requirement and the maximum tolerable rate. Increasing dietary nutrient concentrations at rates below the requirement typically boosts all aspects of immunity. Over and above the bare minimum, the immune system's various components are affected differently (immunomodulation) [23]

5. Conclusions

Immune system is essential for normal daily life, exercise and nutrition have both positive and negative impact on immune system in varying degrees. The trilateral relation among immune, exercise and nutrition are tightly boned together. Compared to sedentary life style, having regular exercise of a moderate intensity is thought positive to immune system. However, immune cell functions are impaired following acute sessions of prolonged, high-intensity exercise. Exercise will promote the production of free radicals and inflammatory factors, causing damage to the body.

At the same time Having balance and adequate nutrition intake (in both macronutrients and micronutrients) have positive impact on immune system. Dietary deficiencies of energy, protein and specific micronutrients are associated with depressed immune function and increased susceptibility to infection. Food contains anti-oxidants and anti-inflammatory components are beneficial which can prevent or reduce the damage caused by oxidation and inflammation.

In summary, we must not only improve immunity through proper exercise, but also maintain the immune system with reasonable nutritional supply. Reasonable nutrition will also relieve the damage caused by exercise. Immunity, exercise, and nutrition, the close connection between these three will provide guidance for population health strategies.

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