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Effect of Physical Training on Immunity in Adults

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KEYWORDS

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ABSTRACT:

Introduction: Chronic disorders like obesity, type 2 diabetes, and cardiovascular disease have increased in recent years due to a rise in sedentary behaviour, especially among adults. Frequent exercise has been identified as a critical component in enhancing general health by favourably impacting immunological and metabolic processes, which may lower the chance of developing chronic illnesses.

Objective: The purpose of this review is to investigate how physical activity affects immune function in adults, with an emphasis on the signal transduction pathways that are involved and how exercise duration and intensity affect immunological responses.

Methods: The SciELO and PubMed databases were used to do a thorough literature review. Studies that focused on how exercise affects immune cell populations, cytokine profiles, and molecular signalling in adults were chosen.

Results: According to the reviewed research, the intensity and duration of physical activity have an impact on the immune cell subpopulations that are significantly altered by exercise. While high-intensity exercise tends to promote an anti-inflammatory response, which aims to reduce inflammation and muscle damage, moderate-intensity exercise is typically linked to a balanced pro-inflammatory response. Numerous immune cells, including as neutrophils, natural killer (NK) cells, dendritic cells, and macrophages, as well as surface receptors such major histocompatibility complex class II and Toll-like receptors (TLRs), exhibit these immunological alterations. Furthermore, exercise modulates cytokine release, further impacting immune regulation.

Conclusion: Based on the findings, exercise characteristics like duration and intensity have a significant impact on how the immune system reacts to physical activity in adults. Complex cell signalling pathways involving phosphorylation events mediate these immunological responses, activating transcription factors, protein synthesis, and cell proliferation. Knowing these mechanisms helps us better understand how exercise can boost immunity and lower the risk of chronic illnesses in adulthood.

Introduction

Over the past few decades, physical inactivity has gained international attention as a major factor in the development of a number of chronic illnesses, including as metabolic syndrome, obesity, type 2 diabetes, and cardiovascular diseases (CVD). Studies have clearly linked low levels of physical activity to higher rates of morbidity and death,

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making sedentary behaviour a significant risk factor for the development of these illnesses (Lee et al., 2012; Pearson et al., 2014). These illnesses are predicted to rise as the world's population ages, underscoring the critical need for preventative measures that can slow their development. One of the best and most accessible ways to prevent chronic diseases, improve general health, and increase quality of life—especially for adults—is to engage in regular physical activity (Warburton et al., 2006; WHO, 2020).

Influencing the immune system is one of the main ways that physical activity improves health. The immune system is essential for preventing infections, controlling inflammatory reactions, and identifying aberrant or malignant cells in the body. Understanding how various forms and intensities of exercise impact immune function has become a growing area of research. It has long been known that exercise, especially moderate-intensity physical activity, can improve immune function in a number of ways by influencing the production of cytokines and promoting the activity of immune cells such as neutrophils, macrophages, and natural killer (NK) cells (Gleeson, 2007; Nieman, 2000). Conversely, too little or too much exercise, especially high-intensity physical activity, can negatively impact the immune system, resulting in temporary immunosuppression, elevated inflammation, and heightened vulnerability to infections. (Nieman & Wentz, 2019).

Immune System and Physical Exercise

The innate immune system, which offers a quick, general defence against infections, and the adaptive immune system, which produces targeted immune responses to infections and sustains immunity over time, are the two main branches of the immune system. Both of these immunological branches are influenced by physical exercise. Exercise, for instance, has been demonstrated to improve the body's response to infections by increasing the circulation of leukocytes, such as neutrophils, NK cells, and T lymphocytes (Simpson & Kunz, 2016). Additionally, a balanced cytokine profile, which aids in immune response regulation and the avoidance of excessive inflammation, has been associated with exercise. Signalling molecules called cytokines are essential for immune cell communication and have an impact on apoptosis, inflammation, and cell division (Pedersen & Saltin, 2015).

Particularly positive impacts on immunological function have been linked to moderate-intensity exercise. According to studies, a short-term pro-inflammatory response—a component of the body's normal immune activation process—can be triggered by moderate exercise. However, the generation of anti-inflammatory cytokines usually counteracts this pro-inflammatory response, reducing inflammation and averting tissue damage (Pedersen, 2019). However, prolonged or high-intensity physical activity can cause immunosuppression and excessive inflammation, especially if recovery time is inadequate. According to this phenomena, which is frequently called the "open window" hypothesis, the body temporarily suppresses the immune system during vigorous exercise, making the body more vulnerable to infections, particularly respiratory tract infections (Nieman, 2000; Gleeson et al., 2011).

Exercise and Immune Health in Adults

Given the aging population and the rising incidence of chronic diseases, the effect of exercise on adult immunological function is especially pertinent. Frequent exercise is linked to better immunological responses in older persons, such as more balanced cytokine levels, greater antigen presentation, and increased NK cell activity (Loffredo et al., 2013; Woods et al., 2009). Additionally, it has been demonstrated that physical activity enhances immune cell circulation, decreases inflammation, and boosts the overall effectiveness of immune responses—all of which may help reduce the risk of age-related disorders like cardiovascular disease and cancer (Kohut et al., 2004). But the precise ways that exercise affects immunological responses are complicated and include a number of signalling pathways, such as the activation of transcription factors including AP-1, NF-κB, AP-1, and MAPKs, which regulate immune cell functions (Pedersen & Saltin, 2015).

Understanding how various forms of physical activity, especially moderate and high-intensity

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exercise, impact immune function is essential given the growing interest in exercise immunology and its potential to improve adult health outcomes. This information is crucial for creating exercise recommendations that support healthy aging, lower the risk of chronic illnesses, and strengthen the immune system. Gaining knowledge of the molecular pathways behind these processes can help one better understand how physical activity affects immune cells as well as systemic health effects, such as metabolic and inflammatory reactions.

Objectives of the Study

With an emphasis on the immunological responses brought on by moderate and high-intensity exercise, this study attempts to examine the body of research on the effects of physical activity on immune function in adults. This review will emphasize the possible advantages and disadvantages of exercise on immune health and provide light on the signalling pathways behind these effects by looking at changes in immunological indicators such cytokine profiles, leukocyte populations, and NK cell activity.

Approach: Research Design

This study analyses and synthesizes the body of information on how physical activity affects adult immune function using a systematic literature review methodology.

Sources of Data

The main resources for finding pertinent peer-reviewed research were the SciELO and PubMed databases. A variety of terms were used in the search, including: Exercise Immune function and exercise Response of cytokines Immunity-related signal transduction Immune response and exercise intensity.

Including the following criteria were satisfied by the studies that were part of this review: Adult populations (those aged 18 and up) were the main focus examined how exercise affected cytokine patterns, immune cell populations, or molecular signalling pathways. Included information on the effects of exercise duration and intensity on immunological responses published in peer-reviewed journals in English.

Table-1 summarizing the effects of physical exercise on different cells of the immune system, including the immune cell types, the exercise intensity, and the physiological effects:

Immune Cell Type	Effect of Physical Exercise	Exercise Intensity	Physiological Effect
Leukocytes (White Blood Cells)	Increase in circulation and mobilization of various leukocytes.	Moderate to High (M-H)	Exercise increases the quantity of leukocytes in the blood, which enhances immunological surveillance and pathogen-defense systems.
Neutrophils	Acute increase in neutrophil count during exercise, followed by a decrease after exercise.	(M-H)	In the early stages of the immunological response to infection, neutrophils are essential. A higher neutrophil count aids in the removal of pathogens, but it returns to normal upon recovery (Simpson & Kunz, 2016).
Natural Killer (NK) Cells	Increased NK cell activity, particularly following moderate exercise.	Moderate (M)	NK cells are essential for the innate immune response, especially when it comes to combating tumor cells and viral infections. Their cytotoxic activity is increased by exercise (Loffredo et al., 2013).
T Lymphocytes (T Cells)	Exercise may increase T cell proliferation, especially in younger individuals.	(M-H)	An important part of adaptive immunity is played by T cells. While excessive exercise may inhibit T cell activity, moderate exercise promotes T cell proliferation (Gleeson, 2007).

Macrophages	Activation of macrophages and increased phagocytic activity post-exercise.	(M-H)	Both innate and adaptive immunity are mediated by macrophages. According to Kohut et al. (2004), exercise increases their activation and improves their capacity to present antigens and eliminate infections.
Dendritic Cells	Increased antigen presentation and cytokine production.	(M-H)	Dendritic cells are essential for presenting antigens and triggering adaptive immune reactions. Immune surveillance is enhanced and these cells are stimulated by exercise (Pedersen & Saltin, 2015).
B Lymphocytes (B Cells)	Moderate exercise promotes an increase in B cell activity and antibody production.	(M)	Antibody production is carried out by B cells. Exercise may improve B cell activity and antibody production, especially at moderate intensities (Pedersen, 2019).
Cytokines	Alteration in cytokine levels, with a shift toward anti-inflammatory cytokines after moderate exercise.	(M-H)	An anti-inflammatory cytokine response follows a brief rise in pro-inflammatory cytokines brought on by exercise. This aids in lowering inflammation and regulating immunological responses (Pedersen & Saltin, 2015).
Toll-like Receptors (TLRs)	Exercise can alter the expression of TLRs, enhancing pathogen detection.	(M-H)	TLRs have a role in identifying molecular patterns linked to pathogens. Exercise improves immune cells' capacity to identify pathogens by increasing TLR expression (Simpson & Kunz, 2016).
Basophils	Moderate exercise can increase basophil degranulation and cytokine release.	(M)	Basophils play a role in immune response regulation and allergic reactions. Their capacity to release cytokines can be improved by exercise, which helps to regulate the immune system (Gleeson, 2007).

Key Findings:
Moderate-intensity exercise generally improves immune cell function, enhancing both innate and adaptive immunity. High-intensity exercise may suppress immune function temporarily, increasing susceptibility to infections due to inflammation and immune suppression. Immune modulation through exercise is complex and depends on exercise intensity, duration, and individual factors like age and fitness level.

Cytokines
Small signalling proteins called cytokines are essential for controlling inflammation, tissue healing, and immunological responses. They can affect the function of immune cells like neutrophils, natural killer (NK) cells, and lymphocytes and are important mediators in the communication between immune system cells. Numerous ways have been demonstrated for exercise to influence cytokine production, and the impact of physical activity on cytokine levels is mostly determined by the intensity and length of the exercise.

Pro-inflammatory cytokines such as interleukin (IL)-6 and tumour necrosis factor-alpha (TNF-α) temporarily rise after moderate-intensity exercise. But following the workout, anti-inflammatory cytokines including IL-10 and IL-1 receptor antagonist (IL-1ra) are upregulated, which results in leading to a balanced immune response (Pedersen, 2019). High-intensity exercise or prolonged endurance exercise may induce a more pronounced increase in pro-inflammatory cytokines, potentially leading to muscle damage and inflammation, although this is generally followed by an anti-inflammatory response (Nieman, 2000). It is believed that a number of cell signalling pathways, such as the NF-κB pathway, which is implicated in inflammation, and the MAPK (mitogen-activated protein kinase) pathway, which is involved in immune cell activation and cytokine production, regulate the cytokine response to exercise (Pedersen & Saltin, 2015).

Neutrophils

White blood cells, especially neutrophils, are the most prevalent type and are essential for the body's first line of defence against infections. The quantity of neutrophils in the blood rises dramatically during and after exercise. The primary cause of this increase is the mobilization of neutrophils from the spleen and bone marrow, which enhances the body's ability to fight against any infections (Simpson & Kunz, 2016). It has been demonstrated that moderate-intensity exercise improves neutrophil function by boosting their capacity to phagocytose infections and emit reactive oxygen species (ROS), both of which are essential for the removal of pathogens (Pedersen & Saltin, 2015).

High-intensity exercise may cause neutrophil function to be temporarily suppressed. As a result, the body may be more vulnerable to infections during the "open window" a brief period of immune suppression that occurs right after vigorous physical activity (Nieman, 2000).

Accordingly, excessive or severe exercise may momentarily limit neutrophil function, increasing the likelihood of post-exercise infections, but moderate exercise increases neutrophil activity (Gleeson, 2007).

Antigen-Presenting Cells (APCs)

Through their ability to capture, process, and present antigens to T lymphocytes, antigen-presenting cells such as dendritic cells and macrophages are crucial for triggering adaptive immune responses. Additionally, these cells generate cytokines that control inflammation and immunological responses. It has been demonstrated that exercise affects APC activity and function. The ability of macrophages and dendritic cells to deliver antigens is improved by moderate-intensity exercise, which strengthens the adaptive immune response. The presentation of antigens to T helper cells depends on the overexpression of surface components like major histocompatibility complex (MHC) class II (Loffredo et al., 2013).

However, because inflammatory cytokines released during vigorous activity can change the expression of antigen-presenting molecules and prevent effective antigen presentation, high-intensity or prolonged exercise can cause a transient reduction in APC function (Pedersen & Saltin, 2015). Therefore, while excessive activity may impede the body's ability to generate an adaptive immune response, frequent moderate exercise can assist sustain the function of APCs.

Natural Killer (NK) Cells

One subset of innate lymphoid cells called natural killer cells is essential for protecting the body from malignancies and cells infected by viruses. The immune system's quick reaction to infections is largely dependent on NK cell activity. Exercise has been demonstrated to affect NK cell activity and numbers in both acute and long-term contexts. According to Loffredo et al. (2013), moderate-intensity exercise boosts NK cell activity, which improves the body's capacity to eliminate malignant or contaminated cells. This is especially crucial for strengthening the body's defences against viral infections and the advancement of cancer.

A brief decrease in NK cell activity may result after high-intensity exercise, especially prolonged or intense physical activity. It is believed that the increased levels of cortisol and other stress hormones released after vigorous exercise are responsible for this suppression, which is frequently seen during the recovery phase (Nieman & Wentz, 2019).

Increased production of activation markers such NKG2D and CD69, which improve their cytotoxic potential, may also be linked to the NK cells' increased activity after moderate exercise (Simpson & Kunz, 2016).

Subpopulations of Lymphocytes

In both innate and adaptive immunity, lymphocytes such as B cells, T cells, and NK cells are essential. Exercise significantly alters the quantity and function of lymphocyte subpopulations. T helper lymphocytes (Th): By producing cytokines and assisting in the activation of cytotoxic T cells and B cells, T helper cells play a crucial role in coordinating the immune response. It has been demonstrated that exercise, particularly moderate-intensity exercise, increases Th cell activation and proliferation (Gleeson, 2007). High-intensity exercise, however, may temporarily inhibit T cell activity and proliferation (Pedersen, 2019).

Cytotoxic T lymphocytes (CTLs): Exercise boosts the quantity of CTLs in the blood, which are in charge of destroying malignant or contaminated cells. While high-intensity exercise can decrease CTL function, moderate activity improves their effectiveness temporarily (Simpson & Kunz, 2016). The regulation of these lymphocyte subpopulations is influenced by exercise-induced changes in cytokine profiles and cell signalling pathways.

T Helper Lymphocytes (Th)

A subset of CD4+ T cells known as T helper lymphocytes (Th) play a crucial role in orchestrating immunological responses by generating cytokines that stimulate B cells, cytotoxic T cells, and macrophages, among other immune cells. Based on the cytokines they generate, Th cells are divided into several subsets, such as Th1, Th2, Th17, and regulatory T cells (Tregs).

A Th1 response, which is linked to pro-inflammatory cytokines including interferon-gamma (IFN-γ), is induced by moderate-intensity exercise. This aids in the immunological surveillance of malignancies and the defence against intracellular infections such viruses (Pedersen & Saltin, 2015).

According to Simpson and Kunz (2016), high-intensity exercise may suppress the Th1 response and promote a Th2 shift, which is linked to the synthesis of cytokines that reduce inflammation, such as IL-4 and IL-10. This change could be a part of the body's strategy to mitigate inflammation and prevent excessive tissue damage after intense exertion.

Effect of Physical Exercise on Cytokine Production

Changes in cytokine production brought on by exercise are complicated and rely on the kind, level of intensity, and length of exercise. In general, moderate-intensity exercise encourages a balanced cytokine response, which is marked by an increase in pro-inflammatory cytokines (like IL-6) while exercising and an anti-inflammatory response with higher levels of IL-10 and IL-1ra thereafter (Pedersen, 2019). This equilibrium encourages tissue healing while reducing excessive inflammation.

However, prolonged or high-intensity exercise might cause an overabundance of pro-inflammatory cytokines, which can lead to immunological suppression, muscle injury, and an increased risk of infection (Nieman & Wentz, 2019).

Impact of Exercise on Signalling Routes Associated with Immune Response

Through intricate signalling networks, the immune system's reaction to exercise is controlled. Important routes consist of:

• NF-κB pathway: This route is essential for controlling immunological responses and inflammation. Pro-inflammatory cytokines are produced when exercise activates NF-κB. To combat excessive inflammation, the body also triggers anti-inflammatory pathways after moderate-intensity exercise (Pedersen, 2019).

• MAPK pathway: Immune cell proliferation, differentiation, and cytokine generation are all regulated by MAPKs, which are activated by exercise. Exercise activates MAPKs, which in turn activates AP-1 and other transcription factors that affect the immunological response (Pedersen & Saltin, 2015).

• The JAK-STAT pathway: Cytokine signalling is significantly influenced by this route. The JAK-STAT pathway, which affects immune cell function and survival, especially in T cells and NK cells, is activated by exercise-induced cytokine production (Gleeson, 2007).

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Exercise affects immune cell activation, cytokine production, and general immunological health through a variety of mechanisms that balance pro- and anti-inflammatory reactions.

Table 2 - Summary on the effects of physical exercise on various immune cells, cytokines, and signalling pathways:

Immune Component	Effect of Physical Exercise	Exercise Intensity	Physiological Outcome
Cytokines	Modulation of pro-inflammatory and anti-inflammatory cytokines.	Moderate to High (M-H)	While high-intensity exercise raises pro-inflammatory cytokines (IL-6, TNF-α), moderate exercise increases anti-inflammatory cytokines (IL-10, IL-1ra) (Pedersen & Saltin, 2015).
Neutrophils	Increase in neutrophil count and activity.	(M-H)	While vigorous exercise may momentarily inhibit neutrophil function, increasing the risk of infection, moderate exercise improves neutrophil function (Simpson & Kunz, 2016).
Antigen-Presenting Cells (APCs)	Enhanced antigen presentation and cytokine production.	(M-H)	High-intensity exercise may reduce APC activity, but moderate exercise enhances APC function (macrophages, dendritic cells) and antigen presentation (Pedersen, 2019).
Natural Killer (NK) Cells	Increased NK cell activity and number.	(M)	High-intensity exercise may momentarily decrease NK cell activity, while moderate exercise increases NK cell cytotoxicity and improves immunological surveillance (Loffredo et al., 2013).
Lymphocytes (T & B Cells)	Increased lymphocyte proliferation, particularly Th cells.	(M-H)	While excessive exercise may impair T cell function, moderate exercise increases Th1 response and lymphocyte activation (Pedersen, 2019).
T Helper Cells (Th)	Increased Th1 cytokine production (IFN-γ).	(M-H)	While vigorous exercise may result in a Th2 shift and the reduction of inflammation, moderate exercise promotes Th1 activation (Simpson & Kunz, 2016).
Signalling Pathways	Activation of NF-κB, MAPK, JAK-STAT pathways.	(M-H)	Excessive exercise changes signalling and suppresses immune function, while moderate exercise activates NF-κB and MAPK pathways, controlling immunological response (Pedersen & Saltin, 2015).

Conclusion

To sum up, exercise has a significant and diverse effect on the immune system, affecting different immune cells, the synthesis of cytokines, and immunological signalling pathways. Exercise frequency, duration, and intensity all have a significant impact on the results. By increasing immune cell activity, especially through the activation of natural killer (NK) cells, neutrophils, and antigen-presenting cells (APCs), moderate-intensity exercise generally supports a balanced immunological response. A change toward anti-inflammatory cytokines is also encouraged by this kind of exercise, which boosts immune function and lessens the harmful effects of inflammation.

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Conversely, prolonged or high-intensity exercise may cause short-term immunological suppression. This is frequently seen as decreased neutrophil function, decreased NK cell activity, and a change in the cytokine profile toward more pro-inflammatory markers. Known as the "open window," this immune suppression raises the risk of infections and, if exercise intensity is not well controlled, may have detrimental implications on long-term immunological health.

Complex cell signalling pathways such as NF-κB, MAPK, and JAK-STAT, which are essential for regulating cytokine release and immune cell activation, control the immunological response to exercise. Comprehending these signalling pathways can assist in customizing exercise regimens to maximize immune response and reduce overtraining hazards. Balancing exercise intensity is crucial to prevent the possible immunosuppressive consequences linked to excessive exercise, even while moderate exercise is good for improving immune surveillance and fostering general health. One of the best ways to boost immunity and enhance overall health while lowering the risk of exercise-induced immune suppression is to engage in regular, moderate physical activity.

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