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DOES HIGH-INTENSITY RESISTANCE TRAINING AFFECT AN ATHLETE'S IMMUNE FUNCTIONS?

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A B S T R A C T

This research aims to comprehensively examine the latest literature on the effects of high-intensity resistance training on the immune system's long-term performance. Many athletes and active individuals believe that moderate physical activity can enhance resistance to minor illnesses like upper respiratory tract infections (URTI), while intense exercise may have the opposite effect. The study involved 90 athletes who regularly train at Ahly Sporting Club and were divided into three groups: Group 1 included 30 athletes at rest, Group 2 comprised 30 athletes after normal training, and Group 3 had 30 athletes after intense training. Athletes who undergo intense training have lower total white blood cell counts than those who train at normal or resting levels. However, their neutrophil numbers slightly increase after heavy training, while lymphocyte and natural killer cell levels decrease. Additionally, those who undergo heavy training have higher PHA-induced proliferation levels but show a decline in serum immunoglobulin levels, mucosal immunoglobulin concentrations, and plasma glutamine levels. To prevent upper respiratory tract infections in athletes, it is essential to avoid over training and provide sufficient rest and recovery during and after training and competition. It is currently uncertain whether moderate exercise training can prevent infectious illness among the general population.

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1. INTRODUCTION

Physical education is not merely a play-time or leisure activity that brings satisfaction and comfort to individuals. It is the face of education and shares the same objectives as education in general. It aims to develop student's physical competence and knowledge of movement and safety, to use these to perform in a wide range of activities associated with the development of an active and healthy lifestyle (Södergren, Sundquist, & Johansson 2008). Physical education should be considered one of the most important parts of the school curriculum as well as for the total life of individuals. It has several contributions, and one of the major contributions is the promotion of the level of health and physical fitness among individuals. To ensure full benefit from physical education and its activities, they must be well taught and organized through an effective physical education program for schools, and athletes. There is a strong relation between physical education and health, and they are two aspects of the same element. Physical education and sports activities are a way to promote high levels of health, and accordingly health is considering integral part of physical education. A study conducted in 1985, stated Physical activity is defined as any physical movement produced by skeletal muscles thatresult in energy expenditure (Södergren, Sundquist, & Johansson 2008). Physical activity has immediate and long-term health benefits. Just 60 minutes a week can make a difference (Azar 2018). Exercise training is not only a necessary means to

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improve the level of exercise, but also an important means to improve the body's immunity (HIRT 2022).
High-intensity resistance training (HIRT) is a form of physical fitness training that involves performing exercises of strength-training with an all-out effort and then taking short rest periods before returning training again (HIRT 2022). A study conducted in 2020 indicated that regular moderate-intensity exercise can make positive of improvement of immunity function. Moreover, regular moderate-intensity exercise has been shown to benefit cardiovascular health and reduce overall disease mortality (Gleeson 2015). Millard et al. suggested that short-term high-intensity exercise training may increase the number of NK cells but can reduce the toxicity of the cells (Bai, et al. 2023). Another study conducted in (2014) indicated that Long-term high-intensity exercises training affects the function of innate immune cells, reduces the ability of immune cells to cope with acute exercise, and increases the risk of infection (Meacham 2022).
Vitamin C significantly decreased after exercise in the highest-intensity group in comparison with initial values, whereas vitamin E levels significantly increased in the medium and high-intensity groups (Nieman et al. 1999, Nieman 2000, Nieman & Pence 2020). It is clear that high-intensity exercise training has bad effect on most epidemic cells; especially the damage of long-term high-intensity exercise training to cells is very obvious, while the effect of short-term high-intensity exercise training on NK cells is more obvious (Nieman& Wentz2019).
A number of studies indicated above mentioned that regular moderate exercise training reduces the risk of infection compared to a sedentary lifestyle, but very long bouts of exercise and periods of intense training are associated with an increased risk of infection. A common observation among athletes is that symptoms of respiratory illness cluster around competition and can impair exercise performance (Gleeson 2015).

2. DOES REGULAR EXERCISE HELP ATHLETE'S IMMUNE FUNCTION?

The answer is yes. Exercise benefits athletes body in many ways, and boosting their immunity is just one of them. A study which conducted in 2023 concluded that intense exercise improved the physical function of participants to a greater extent than either regular exercise or no exercise (Bai et al. 2023). But there is one important caveat: The frequency, duration, and intensity of athlete's workouts matter (Meacham 2022).Periods of intense training with insufficient recovery may lead to a temporary state of immunosuppression which should resolve with a few days of relative rest (Bai et al. 2023). This is an important consideration if the athlete is training for endurance events such as a marathon. In these cases, athlete should take extra care to give his body enough time to recover (Meacham 2022).There is a general perception among a number oftop athletes, coaches, and sports physicians that athletes are at increased risk of developing upper respiratory tract infections during periods of their intense training and their major competition (Nieman& Pence2020). Several studies have confirmed that intense training causes oligomenorrhea and amenorrhea in athletes (Nieman& Wentz 2019). In this paper, the focus will be on the authors' preliminary data as well as a review of the published literature on the acute and chronic effects of prolonged and intense training on systemic immunity.

3. MATERIAL AND METHODS

Data were collected on a total of 90 athletes who trained at the Ahly Sporting Club in Benghazi – LIBYA during our working stay there. Those athletes were scattered into 3 groups:

1- Group 1 includes 30 athletes at rest
2- Group 2 includes 30 athletes after normal training
3- Group 3 includes 30 athletes after intense training

Immune parameters:
The immune functions consist of the following:
1- Total and differential count of peripheral white blood cells using the automated hematology analyzer (Sysmex corporation, America)...
2- Natural killer cell (NKC) counting using detection of the CD-16 receptor by direct immunofluorescence technique(Markey& MacDonald1989).
3- Neutrophil function test tested by the method reported in Nelson, Quie and Simmons(1975).
4- Testing of lymphocyte proliferation in the laboratory through the use of phytohemagglutinin (PHA) mitogen activation test performed on whole blood samples (Zhang, Feng & Liu 2022).
5- Immunoglobulin concentration in the blood using the radial immune-diffusion technique test (Biomed, Egypt).
6- Mucosal immunoglobulin levels were tested using (RID) Low kits on nasal and saliva samples (Biomed, Egypt).
7- Plasma glutamine level tested byGlutamine Colometric Kit-WST (Dojindo)
Statistical analysis was performed by the computerized SPSS-17 package.

4. RESULTS

Data allocated in Table 1 demonstrated that total leucocyte count was suppressed in athletes trained heavily compared to those performed normal or at rest athletes.In Table-2, neutrophil numbers increased slightly after heavy training, whereas lymphocyte count. In Table-3, natural killer cell level, decreased in people who accomplished heavy exercise .
With respect to the Phytohemagglutinin (PHA)-induced proliferation, the investigation showed higher levels in those trained heavily (Table-3).

Concerning serum immunoglobulin level, mucosal immunoglobulin concentration, and plasma glutamine levels, all of these parameters were declined by the heavy training (Tables-3 and4).

Table 1. Chronic changes in leucocyte, Neutrophil and Lymphocyte numbers during exercise training

Immune parameter	Resting values in athletes (No.=30)	After normal or moderate training (No.=30)	After intense training (No.=30)	P value
Leucocyte number	7.25 ± 2.5× 10^9/L)	7.25 ± 2.5× 10^9/L)	4.0± 2 × 10^9/L)	<0.05
Neutrophil number	2,500 and 7,000 neutrophils/mm^3 5.000 ± 2.5 /mm^3	4.5 ± 2.5 /mm^3	7.0 ± 3.25/ mm^3	<0.05
Lymphocyte number	3.0 ± 2.0/mm^3	3.0 ± 2.0/mm^3	1.25± 1.0/ mm^3	<0.05

Table-2. Chronic changes in NK cell and Neutrophil functions during exercise training

Immune parameter	Resting values in athletes (No.=30)		After normal or moderate training (No.=30)	After intense training (No.=30)	P value
NK cell number	100±20 × 10^6/L		90±20 × 10^6/L	60±10 × 10^6/L	<0.05
Neutrophil function (neutrophil killing activity)	% Phagocytosis Number of *E. coli* per neutrophil % of killed *E. coli*	39.8 ± 14 2.9 ± 0.7 39 ± 10.5	35.0 ± 13 2.8± 0.6 38 ± 10.5	25.0 ± 5 2.0± 0.2 28 ± 7.5	<0.05

Table3. Chronic changes in lymphocyte activation and immunoglobulin concentration during exercise training

Immune parameter	Resting values in athletes (No.=30)	After normal or moderate training (No.=30)	After intense training (No.=30)	P value
Lymphocyte activation	60% viability	63%	80%	<0.05
Serum Ig. concentration	IgG 11 ± 4.0g/L IgA 2 ± 1.5g/L IgM 1.5 ±2.5g/L	IgG 11 ± 4.0g/L IgA 2 ± 1.5g/L IgM 1.5 ±2.5g/L	IgG 7 ± 2.0g/L IgA 1 ± 0.5g/L IgM 1.0 ±1.5g/L	<0.05

Table-4. Chronic changes in mucosal immunoglobulin conc. And plasma glutamine conc during exercise training

Immune parameter	Resting values in athletes (No.=30)	After normal or moderate training (No.=30)	After intense training (No.=30)	P value
Mucosal Ig conc.	In saliva, the IgG 2-3 mg/dl IgA concentration in saliva 10-20 mg/dl	In saliva, the IgG 2-3 mg/dl IgA conc. in saliva 10-20 mg/dl	In saliva, the IgG 1 mg/dl IgA conc. in saliva 5 mg/dl	<0.05
Plasma glutamine conc.	430 µmol/L	420 µmol/	340 µmol	<0.05

5. DISCUSSION

Immune function in endurance athletes and non-athletes:

There is a common perception among elite athletes and their coaches that stressful endurance racing events and overtraining reduce resistance to upper respiratory tract infection (URTI) (Furusawa et al. 2007). Several studies using epidemiological designs have demonstrated that the risk of upper respiratory tract infections (URTI) is elevated during periods of intense training and in the 1-2week period after participation in competitive endurance races (Nieman et al. 1990, Corcoran & Bird 2012, Elkhatib, Alley& Jepsen2021). A high incidence of pathology occurs when elite athletes exceed individually defined training thresholds, most of which are related to training stress (Elkhatib, Alley & Jepsen 2021). In contrast, a common belief among endurance athletes is that regular training sessions confer resistance against infection. A survey of 750 professional athletes (40 to 81 years of age) showed that 76% of them considered themselves at lower risk of contracting viral diseases than their peers who did not exercise (Reaburn& Dascombe2008).

Three randomized exercise studies have shown that near-daily exercise is associated with a significant reduction in upper respiratory tract infections (Nieman 2011, Sarin et al. 2019,Scartoni et al. 2020). Do the immune systems of endurance athletes and non-athletes function differently at rest? Although epidemiological data for URTI suggest variations, comparisons suggest that athletic endeavor is associated with some clinically important changes in immunity.

Adaptive immunity

At rest, the adaptive immune system is largely unaffected by intense and prolonged training, although results may vary depending on training status, examination method, and age. We have compared mitogen-induced lymphocyte proliferative responses in 30 normally trained males and 30 heavily male footballs during periods of both low- and high-volume training [table-1].No significant difference was measured between groups while males were participating in low-volume training; however, during a period of intense training, PHA mitogen assays increased by 35-50% in endurance athletes. However, another comparison showed no difference in mitogen-induced lymphocyte proliferative responses between controls and elite cyclists during periods of low or high training (Baker et al. 2022, Tvede et al. 1991).

A study in elite female rowers and non-athletes 3 months before the World Championships found a slight increase in mitogen-induced lymphocyte proliferation when whole blood cultures were used, but not with separate mononuclear cells. Highly conditioned females have been reported to have a significantly greater reproductive response compared to their sedentary elderly peers, a finding also confirmed in comparisons between trained and untrained elderly males (Tvede et al. 1991). Together, these data suggest that T and B cell function is not consistently altered by exercise exertion, except in older adults. This interpretation is strengthened by the finding that the antibody response to vaccination is normal in endurance athletes (Brauer et al. 2021).

Innate immunity

The innate immune system appears to respond differently to chronic stress induced by intense exercise. With natural killer cell (NKC) counts tending to decrease as well as neutrophil function being inhibited (particularly during periods of high-volume training).Most cross-sectional studies have shown an enhancement of NKCA in endurance athletes compared to non-athletes (Gleeson 2007, Suzuki & Hayashida2021). A study of elite cyclists in Denmark reported higher NKCA during the summer (their intense training period) compared to the winter (their low training period) (Zhang,Feng& Liu2022). Several prospective studies using moderate endurance training regimens of 8-15 weeks have reported no significant elevation in NKCA compared to sedentary controls (either young or elderly) (Nelson, Quie& Simmons 1975, Tvede et al. 1991, Sarin et al. 2019).

These data suggest that endurance exercise may be involved in an athlete's workload before NKCA is chronically elevated. Neutrophil function (phagocytosis capacity and oxidative burst) has been reported to be normal in endurance athletes except during periods of high-intensity training, when it is suppressed (Papacosta & Gleeson 2013, Bartlett et al. 2021, Silveira et al. 2021). This is particularly evident in our studies and that of Gleeson, et al. 2007, where neutrophil function in athletes was similar to that in controls during periods of low-volume training but was significantly suppressed during the summer months of intense training. In contrast, no difference in neutrophil/monocyte phagocytosis or oxidative burst activity was measured in elite rowers and controls 3 months before the world championships.

Clinical implications

Even when significant changes in the concentration and functional activity of blood immune markers have been observed in athletes, researchers have had little success in linking these changes to a higher incidence of infection and disease (Billings 2009, Nieman& Wentz2019, Suzuki& Hayashida 2021). Elite swimmers undertaking intense training have significantly lower neutrophil oxidative activity at rest than age- and sex-matched sedentary individuals, but URTI rates do not differ between swimmers and sedentary controls. URTI rates were similar in elite and non-athlete rowers over the 2-month winter/spring period, despite higher NKCA and T-cell function (complete blood test) in the rowers.

The acute immune response: The open window theory:

Comparing resting immune functions in athletes and non- athletes may not be as meaningful from a clinical perspective as measuring the magnitude of change in immunity that occurs after each bout of prolonged exercise. During this 'open window' of altered immunity (which may last between 3 and 72 h, depending on the immune measure) viruses and bacteria may gain a foothold, increasing the risk of subclinical and clinical infection. Although this is an attractive hypothesis, researchers have made no serious attempt to prove that the athletes who show maximum immunosuppression after extreme exertion are those who develop infections within the following week or two. This connection must

be made before the "open window" theory can be fully accepted.
Many components of the immune system exhibit change after prolonged, heavy exertion(Wentz etr al. 2018). Some examples follow:

High neutrophil and low lymphocyte blood counts induced by high plasma cortisol
Aerobic exercise is associated with a widespread disruption of the white blood cell count, with prolonged, high-intensity endurance exercise producing the greatest degree of cell migration (increase in the number of granulocytes and monocytes, decrease in lymphocytes and increase in neutrophils/lymphocytes ratio) (Müns et al. 1989, Steerenberg et al. 1997, Bizjak et al. 2021). Several mechanisms appear to be involved, including exercise-induced changes in stress hormone and cytokine concentrations, changes in body temperature, increases in blood flow, lymphocyte death and dehydration. After prolonged, high-intensity running, blood cortisol concentrations rise significantly above control levels for several hours, and this has been linked to several changes in cell movement that occurred during recovery (Bizjak et al. 2021).

Increase in blood granulocyte and monocyte phagocytosis, but a decrease in nasal neutrophil phagocytosis
After prolonged, high-intensity running, substances released from injured muscle cells initiate an inflammatory response (Steerenberg et al. 1997, Müns et al, 1989). Monocytes and neutrophils invade the inflamed area and phagocytosis debris. Thus, an increase in blood granulocytes and monocyte phagocytosis may represent part of the inflammatory response to acute muscle injury. Phagocytosis samples collected from peripheral blood react differently than those from the respiratory tract. Using nasal wash samples, Müns et al. 1989 showed that the ability of macrophages to take up Escherichia. Coli are significantly suppressed in athletes compared to controls more than 3 days after performing a 20 km road race (Müns et al 1995).

Decrease in nasal and salivary IgA concentration
We reduce the concentration of IgA in nasal secretions by approximately 70% for at least 18 hours after a 31 km race (Nieman et al. 1997) after prolonged strenuous exercise, salivary secretion rates decrease, reducing the level of IgA-mediated immune protection on the mucosal surface (Amin et al. 2021).

Decrease in nasal mucociliary clearance
Mucociliary transit time is significantly prolonged after a marathon race by several days and results in part from abnormally functioning ciliated cells (Bernecker et al. 2011). These data, combined with impaired nasal neutrophil function and nasal/salivary IgA secretion rates, suggest that host protection in the upper airway pathways is suppressed for a prolonged period after endurance racing.

Decrease in granulocyte and macrophage oxidative burst activity (killing activity)
After sustained and heavy exertion, granulocytes have a low oxidative burst capacity. The decrease in granulocyte oxidative burst may represent a decrease in the killing capacity of blood neutrophils (on a per cell basis) due to stress and overload.

Decrease in NK cell cytotoxic activity
After intense and prolonged endurance exercise, NKCA decreased by 40-60% for at least 6 hours (Cox et al,. 2010, Docherty et al. 2022).This decrease is greater and longer lasting than post-exercise for less than 1 hour and is associated with cortisol-induced redistribution of NK lymphocytes in the blood from the blood chamber to other tissues (Gleeson 1997).The decrease in NKCA closely parallels the decrease in the concentration of NKA cells in the blood, meaning that each NKA cell retains its normal function. It has not yet been determined where blood NK cells go and whether decreased NKCA in the blood compartment represents what happens in other lymphoid tissues or is associated with URTI risk.

Decrease in mitogen-induced lymphocyte proliferation
PHA-induced lymphocyte proliferation in the blood decreases by 30-40% (unadjusted for changes in T-cell numbers) over 3 hours after 2.5 hours of intense running. Others have reported greater declines after endurance racing events (Ostrowski, et al. 1999). The decline in T cell function is more prolonged than has been described after exercise of less than 1 hour. Except for the time point immediately following operation, the decrease in T-cell function parallels the decrease in T-cell concentration in the blood.

Plasma glutamine levels:
The current study indicated lower plasma glutamine levels in athletes who engage in heavy exercise. MacKinnon &Hooper (1996)showed a slight increase in plasma glutamine concentrations during a 4-week period of intense training in well-trained elite swimmers, but not in those showing symptoms of overtraining syndrome. Plasma glutamine concentration was significantly higher after 2 weeks. It is more intense training for well-trained swimmers than for over-trained swimmers. In addition, plasma glutamine concentration did not differ between athletes who had an upper respiratory tract infection over the four weeks, and those who didn't. These data suggest that although the concentration may differ between over-trained and well-trained athletes, the plasma glutamine level may not necessarily decrease during long periods of intense training, and that the onset of upper respiratory tract infection is not associated with changes in the plasma,

glutamine concentration during intense training in elite swimmers.

Summary and clinical implications

Together, these data suggest that the immune system is suppressed and stressed, albeit transiently, after prolonged endurance exercise. The risk of infection may increase when an endurance athlete undergoes repeated cycles of heavy exertion, is exposed to new pathogens and faces other stressors on the immune system, including lack of sleep, severe mental stress, poor nutrition or weight loss However, the immune system's ability to mount an antibody response to vaccination during the 2-4 week period after exercise is not affected. For example, male athletes when compared to sedentary controls had normal production of antibodies to pneumococcal, tetanus, and diphtheria vaccines after a competitive Ironman triathlon event.Immune changes after heavy exertion differ markedly from those following moderate exercise. For example, after brisk walking or sports and exercise, blood cortisol and cytokine levels remain close to pre-exercise levels, disruption of immune cell number and function is mild and overall immune surveillance is enhanced.

6. CONCLUSIONS

1. To counter exercise-induced alterations in immune-surveillance and host protection against pathogens, the endurance athlete should consider these guidelines:
2. Keep other life stresses to a minimum (mental stress in and of itself has been linked to increased URTI risk).
3. Eat a well-balanced diet to keep vitamin and mineral pools in the body at optimal levels.
4. Avoid overtraining and chronic fatigue.
5. Obtain adequate sleep on a regular schedule (disruption is linked to suppressed immunity).
6. Avoid rapid weight loss (linked to adverse immune changes).
7. Avoid putting your hands to the eyes and nose (a major route of viral self-inoculation).
8. Before important race events, avoid sick people and large crowds when possible.
9. For athletes competing during the winter months, influenza vaccination is recommended.

Recommendations

There are some preliminary data suggesting that various immune modulator drugs may afford athletes some protection against infection during competitive cycles, but much more research is needed before any of these can be recommended.

The influence of a growing list of nutritional supplements on the immune and infection response to intense and prolonged exercise has been measured. Supplements studied thus far include zinc, dietary fat, plant sterols, antioxidants (e.g. vitamins C and E, β-carotene, *N*-acetyl cysteine and butylated hydroxyanisole), glutamine and carbohydrate.

Vitamin and glutamine supplements have received much attention, but the data thus far do not support their use as countermeasures to exercise-induced alterations in immunity. At this point, athletes should eat a varied and balanced diet in accordance with the food guide pyramid and energy needs and should be assured that vitamin and mineral intake is adequate for both health and immune function.

Carbohydrate supplementation before, during and after intensive endurance exercise lasting longer than 90 min is recommended, however. Carbohydrate beverage ingestion has been associated with higher plasma glucose levels, an attenuated cortisol and growth hormone response, fewer perturbations in blood immune cell counts and a diminished pro- and anti-inflammatory cytokine response. Overall, these data indicate that the physiological stress to the immune system is reduced when endurance athletes use carbohydrate beverages (about 1 L/h of a 6% carbohydrate beverage). Although it is logical to assume that these favorable carbohydrate-induced effects on the endocrine and immune systems should reduce the risk of infection, well-designed studies of large groups of athletes are necessary before this link can be established.

Compliance with Ethical Standards

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Conflict of Interest

The author(s) of the manuscript hold no conflict of interest that may affect the integrity of the manuscript and the validity of the findings presented in it.

Availability of data and materials

Data are available [from the authors / at URL] with the permission of [third party]. The data that support the findings of this study are available from the corresponding author, Kamil Abidalhussain Aboshkair: dr.kamilabidalhussain@gau.edu.iq], upon reasonable request.

Ethics approval

All subjects gave their informed consent for inclusion before they participated in the study.

Author contributions

All *authors* discussed the results and *contributed* to the final results of the manuscript.

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