

Jogging, Physical Exercise and Nutrition Over Time of COVID-19

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Abbreviations: QoL: Quality of Life; SCFA: Short Chain Fat Acid; GABA: Gamma Amino Butyric Acid; NPY: Neuropeptide; SAM: Sympathetic-Adrenal-Medullary System; LPS: Lipopolysaccharides; ROS: Reactive Oxygen Species; GI: Gastrointestinal; TLR: Toll Like Receptors; URTI: Upper Respiratory Tract Infections; HR: Heart Rate; MHC2: Histocompatibility Molecules; NK: Natural Killer

ABSTRACT

Introduction: The first Italian patient diagnosed with Covid-19 infection was a 38-year-old marathon runner. He was hospitalized for complicated bilateral pneumonia in intensive care. Physical activity and viral infection may not seem related. However, overtraining could induce a transient reduction of the immune defenses and allow the establishment of infectious pathological conditions.

Evidence Acquisition: Physical activity is recognized as a preventive tool for diseases such as obesity, diabetes, hypertension and cancer.

Evidence Synthesis: At now there are no vaccination or treatments to treat or prevent SARS-Covid 19 infection, therefore the strengthening of the immune system and the improvement of comorbidities are of primary interest. Even in the context of social isolation, the modulation of physical activity and diet can be the one true weapon of prevention, valid and applicable by everyone.

Conclusion: In this article we discuss the mechanisms that link overtraining and immunosuppression. In contrast, we suggest that the combination of a moderate physical activity and a supplemented diet can lead to the reduction of comorbidities and to the strengthening of the immune system. Behavioral modifications in order to prevent both acute viral pathologies and chronic ones such as cancer.

Keywords: Immunity; Covid-19; Overtraining; Physical Exercise; Cancer

Introduction

Exercise extends life expectancy and is recommended as a tool of prevention and even of treatment of different pathologies, including cancer. It is therefore not to be considered only a "good habit" for a healthy lifestyle, but it is even counted among the support therapies for cancer patients and several studies have shown its effectiveness both in terms of mortality and risk reduction of recidivism [1]. The current COVID-19 pandemic severely limits the individual's ability to maintain constant physical activity due to forced quarantine at home. It also seems to contradict the initial assumption; Mattia, the first Italian patient who was diagnosed with a Covid-19 infection, was hospitalized in intensive care for pneumonia. He was 38 years

old and was an endurance athlete, in particular a marathon runner. How could a young, healthy and trained man has manifested the symptoms of the infection so heavily? May have exercise influenced his ability to respond to the virus? Some days before the hospitalization, while the infection was incubating, unaware of what was happening in his body, Mattia intensified physical activity by participating in two half-marathons (21km) and in a soccer match, within 12 days [2]. These events, in addition to having potentially caused the infection of family members, teammates and colleagues, may have affected Mattia's immune status, causing the infection to take root with so much virulence.

Excessive physical stress can temporarily alter the athlete's immune status increasing the risk of infections and their clinical manifestations, in particular affecting the upper respiratory tract and gastrointestinal tract. The aim of this work is to show the physiological pathways through which stress, induced by physical exercise, causes transient immunodepression and the behavior that can strengthen individual defenses and improve the quality of life (QoL). Adequate physical activity and a balanced diet could promote a better outcome in case of infection, in particular from COVID-19 and even in cancer patient. We hope to sensitize the population to maintain a correct lifestyle in order to strengthen their immune system.

Immunity and Microbiota

Immunity is the ability to defend against infections and diseases. The immune system is made up of several cells, tissues, molecules and systems [3]; among them human intestine plays a role of primary importance in the maintenance and development of the immune system. The human intestine contains about one trillion microbes, bacteria, fungi and viruses, the amount of these microorganisms is called intestinal microbiota [4,5]. The microbiota offers many benefits to the host through the maintenance of the integrity of the intestinal barrier, the production of nutrients such as vitamins, the remodeling of the epithelium and the protection against pathogens [4]. However, infections, antibiotic treatments and diet changes can change the microbiota's composition [6] with direct effects on the individual health. Diet plays a major role on the microbiota: the bacteria present in the colon have the ability to ferment complex carbohydrates, generating different metabolites, including short chain fat acid (SCFA). SCFAs such as propionate, N-butyrate and acetate are rapidly absorbed by enteral cells and are involved in the regulation of cellular processes such as gene expression, chemotaxis, differentiation, cell proliferation and apoptosis [7]. Butyrate has been shown to have anti-inflammatory and anti-tumor properties and it is an important energy source for intestinal colon cells. Butyrate reduces bacterial translocation and enhances the barrier function of the intestinal mucosa, promoting the assemblage of tight-junctions and the synthesis of mucin. SCFAs also regulate lipid and glucidic homeostasis in the liver [7,8] and influence the regulation of appetite through a mediated receptor mechanism; in fact, propionate acts on beta cells, enhancing the sense of satiety [7]. SCFAs regulate immune system and inflammatory response, influencing the production of cytokines; for example, they stimulate the production of interleukin 18 (IL-18), involved in the epithelium maintenance and repair. Furthermore, the presence of the microbiota in the intestine influences the colonization by pathogenic microorganisms, competing for adhesion sites and for nutritional resources and producing anti-microbial substances such as catelicidines, lectins C and prodefensins, as well as

stimulating the production of IgA [4]. The intestinal microbiota is involved in the synthesis of de novo essential vitamins (vitamin B 12, folate, vitamin K, riboflavin, biotin, nicotinic acid, pantothenic acid, pyridoxine and thiamine). All these factors can influence the guest health. For example, an alteration in the levels of bile acids, branched fatty acids, choline, vitamins and purine and phenolic compounds is associated with the development of obesity and type 2 diabetes [9,10].

Microbiota Response to Stress Induced by Physical Activity

Physical activity stimulates several neurohormonal systems common to stress answer. A recent review showed two different systems of correlation between stress and exercise: the sympathetic-adrenal-medullary system (SAM) and the hypothalamic-pituitary-adrenal axis [7]. The activation of these axes leads to the release of catecholamines and glucocorticoids in the circulatory stream and the autonomic nervous system activation, with the release of neurotransmitters directed to the peripheral tissues, the gastrointestinal tract and the cardiovascular system. The brain-intestine axis through the activity of the vagus nerve connect the autonomic and the enteric nervous system which releases gamma amino butyric acid (GABA), neuropeptide (NPY), dopamine and SCFA and Tryptophan, molecules produced by the intestinal microbiota [7]. The physical and emotional stress, after hours of training, causes an alteration of the physiological homeostasis of the SAM and of the hypothalamic-pituitary-adrenal axis [11]. Recent studies have shown how the brain-intestine axis is linked to the development of the microbiota. Studies with germ-free mice show that minimal stress can induce an over-production of corticosteroids and ACTH (Figure 1); therefore, the composition and maintenance of the microbiota is of primary importance in the development of an appropriate response to stress [12].

During strenuous exercise, the body temperature rises and blood flows from the gastrointestinal tract to muscles and peripheral organs such as the heart and lungs. A redistribution of blood flow and thermal damage can cause a lack of integrity in the gastrointestinal barrier and the activation of an inflammatory response. Furthermore, prolonged intense exercise increases stress hormones and the translocation of lipopolysaccharides (LPS) in the gastrointestinal tract, with an increase in the production of pro-inflammatory cytokines and intestinal permeability. Hypoxia can also increase intestinal permeability due to reactive oxygen species (ROS) production and the alteration to the microbiota composition [13]. The gastrointestinal tract responds by releasing GABA, NPY and dopamine, which cause gastrointestinal (GI) disorders, anxiety, depression and reduced appetite. The production of butyrate and propionate can increase transepithelial resistance and can improve the function of the gastrointestinal barrier, reducing inflammation

[7]. Approximately 20-50% of athletes suffer from gastro intestinal symptoms [13] linked to the type of exercise, intensity and age. In a study the incidence of GI disorders during a triathlon competition was of 93% [14] and 2 out of 29 athletes stopped the competition due to vomiting and diarrhea. Another study [15] showed that physical exercise conducted at 70% of Vo2Max leads to a 60-70% reduction in splanchnic blood flow. This hypoperfusion, together with the increase in the gastro intestinal barrier permeability, leads to ischemic intestinal damage. Stress also induces an increase in the

translocation of LPS with a recall of pro-inflammatory cytokines. In fact, very high blood LPS values were recorded in marathon runners, triathletes and ultra endurance athletes and 90% of them developed digestive disorders [16]. It has also been observed that glucocorticoids, released during intense exercise, cause a reduction in the expression of the Toll Like Receptors (TLR), therefore the ability to produce anti-inflammatory cytokines and defense against unwanted bacteria is reduced [17] (Figure 2).

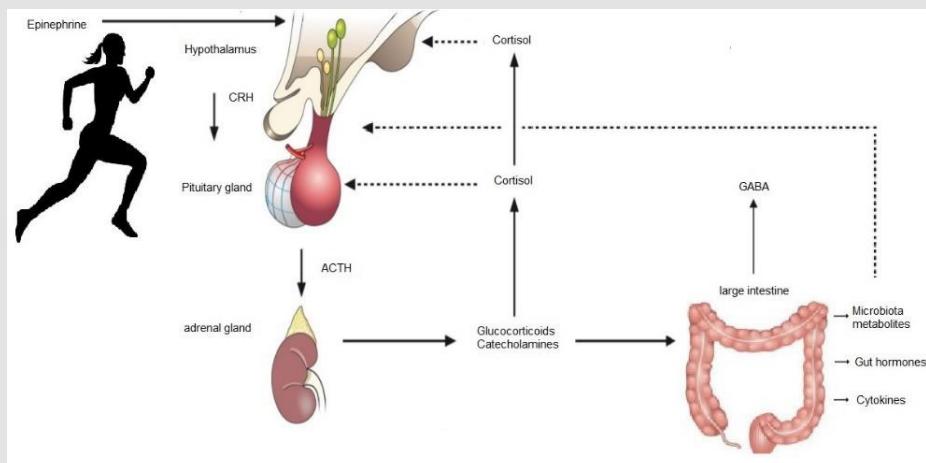


Figure 1: SAM releases epinephrine from the adrenal medullary which facilitates rapid mobilization of metabolic resources and regulation of stress response. Epinephrine increases circulating adrenaline and norepinephrine levels, heart rate, strength, peripheral vasoconstriction and energy mobilization. Stress activates the paraventricular nucleus of the hypothalamus that produces corticotropin (CRH) and vasopressin. CRH stimulate, at the level of the adenohypophysis, the release of adenocorticotropin (ACTH) into the circulatory system. ACTH binds to the receptors of the adrenal cortex and enhances the production of glucocorticoids, they, for a negative feedback system, bind to their brain receptors by inhibiting further secretion of CRH [82]. Intense physical exercise, above 60% of the maximum volume of oxygen consumed per minute (Vo2Max), stimulates the hypothalamic-pituitary-adrenal axis and the release of catabolic hormones; the release of cortisol is not stimulated below this threshold, while above 80% of Vo2Max a significant increase in ACTH is obtained [83]. Some studies have shown high levels of CRH in 60-80% of endurance athletes in the early stages of chronic stress, demonstrating the correlation between exercise-induced stress and hormone stress levels in athletes [84].

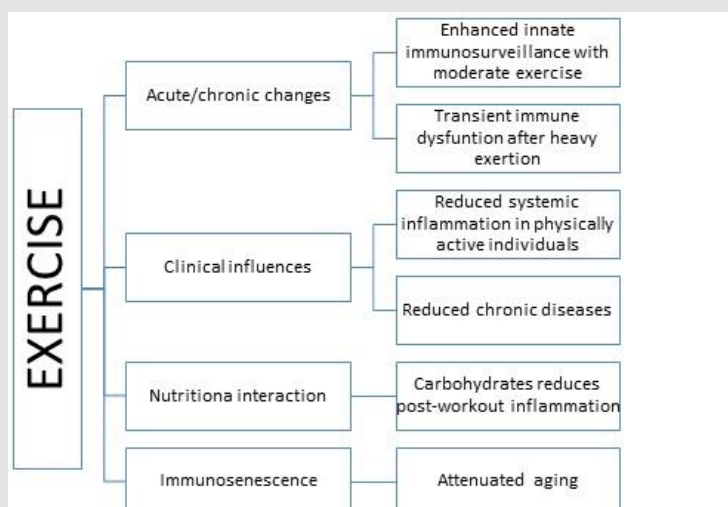


Figure 2: Correlation between exercise and immunity.

Exercise and Immunity Function

Moderate regular physical activity is more beneficial in terms of preventing infections than the sedentary lifestyle or intense training of elite athletes. This has been demonstrated in both observational and experimental studies conducted on animals and humans; in particular, many studies have focused on the prevention of upper respiratory tract infections (URTI) [13]. Mice which run 20-30 minutes per day compared to sedentary mice showed less mortality and reduced morbidity after pathogen inoculation [18]. In a study in elderly or obese individuals, it was shown that 30-

45min of physical activity at 60-70% of heart rate (HR), 5 times a week, for 12-15 weeks, led to a lower incidence of URTI and a shorter duration of symptoms compared to sedentary individuals [19,20]. The immunosurveillance is linked to physical activity in relation to the duration, intensity and type of physical activity. For example, an hour of cycling seems to enhance the dependent and independent receptor recognition of neutrophils [13,21]. A moderate and constant aerobic activity guarantees the homeostasis of IgA production (Figure 3), an important factor in URTI prevention [22].

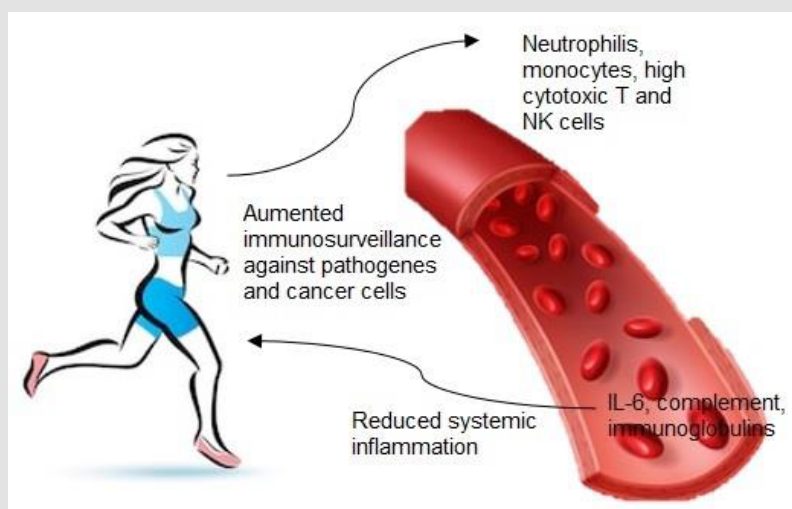


Figure 3: Exercise stimulates the innate immune response and enhances immunosurveillance. Moderate physical activity enhances the type 1 immune response, mainly mediated by helper and cytotoxic T lymphocytes (for example during a viral infection), enhances the switch to TH2 lymphocytes and stimulates the anti-inflammatory response.

Endurance sports increase the concentration of neutrophils and monocytes in the blood during the activity and last about two hours, this process allows the infiltration, repair and regeneration of muscle tissue [22]. However, excessive workload, such as during a competition, and associated stress are linked to immune system dysfunction, increased oxidative stress and muscle damage. The concentration of NK lymphocytes, neutrophils, T and B lymphocytes, salivary IgA is modified after an intense training for more than two hours and the expression of class 2 histocompatibility molecules (MHC2) in macrophages [23], increases the serum content of various lipid compounds (including oxidolipids) and triggers an inflammatory process [7,18]. Oxidolipids are involved in promoting, regulating and turning off this inflammatory process. This inflammatory process induces an infiltration of inflammatory cells and cytokines and impairs the inflammation circulating pool with a weakening systemic defenses [7].

Increased risk of URTI has been shown in marathon runners and ultra-endurance athletes [13]. From 2311 runners of the

Los Angeles Marathon, about 13% of the runners reported respiratory infection during the week following the competition, compared to 2.2% of the similarly experienced runners who did not participate (Odds Ratio = 5.9) [24]. In an under analysis, 40% of runners had experienced at least one infectious episode during the two winter months preceding the marathon; this percentage represented athletes who had run more than 96 km per week [24]. In a retrospective study endurance athletes who had a high load of stress and sleep deprivation showed a higher incidence of URTI [25]. Epidemiological data recorded during international competitions [26] have shown that 2 to 18% of athletes experience an episode of infection, with a higher percentage in women and athletes in endurance sports. About half of the infections involve the respiratory tract, while the other half involves the gastrointestinal tract, the skin and the genitourinary tract [26]. Regular physical activity has an anti-inflammatory effect, different pathways control the inflammatory signals (such as the interaction with toll like receptors) and induce the release of muscle myokines, the production of interleukins, the decrement of dysfunctional fat, and

stimulate the tissue oxygenation. In this way the function of innate immunity and the homeostasis of the oxidolipins are stimulated [27,28].

Chronic high levels of inflammation biomarkers are linked to multiple pathologies, such as obesity, arthritis, atherosclerosis, renal failure, metabolic syndrome, insulin resistance, type 2 diabetes mellitus, sarcopenia, osteoporosis, dementia, depression and different types of cancer [26]. For example, obesity induces a constant state of inflammation, characterized by a pro-inflammatory infiltration with macrophages and granulocytes, an altered production of acute phase proteins, reactive oxygen species, metal-proteases, oxidolipins, adipokines and cytokines pro-inflammatory. After intense and prolonged exercise, the biomarkers of inflammation transiently increase, while they are chronically expressed at low levels in obese individuals [26]. In a study on the

incidence of influenza A, Warren, et al. [29] have shown that exercise can restore the normal protective capacity of the immune system in obese patients. In fact, in the obese patient the immune response is often delayed or completely inhibited. Exercise balances energy expenditure, leptin response, INF production and increases specific IgG2c levels in response to influenza A infection and enhances the percentage of circulating CD8 T lymphocytes [29]. Epidemiological studies have shown reduced levels of leukocytes, C-reactive protein, interleukin 6 (IL-6), interleukin 18 (IL-18), TNF α , in fit adults (i.e. who do constant physical activity 3 times per week); however, many trials have failed to demonstrate wane of inflammatory processes due to physical activity, in the absence of weight loss [30]. In fact, the evidence shows a reduction in chronic inflammation only in subjects who train more than 300 minutes a week only when physical activity is associated with a weight loss [30].

How Nutrition Influence Exercise Immune Response

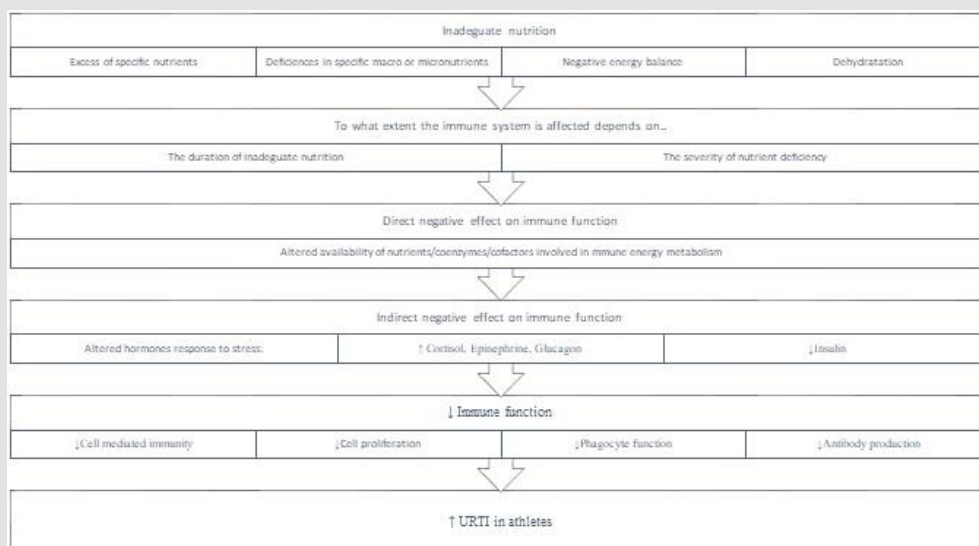


Figure 4: Effects of inadequate nutrition on the immune system.

Diet can have a direct and indirect effect on the immune system. The availability of some nutrients in athletes under stress can affect energy metabolism, protein synthesis and endocrine-nervous and immune systems. In general, many athletes consume a high load of carbohydrates and proteins and a low load of fibers and fats to have fast energy resources, but this nutritional behavior can cause an alteration of the intestinal function due to the low fiber load in the diet [7]. Furthermore, the athletes' diet contains some metals, calcium, amino acids and essential fatty acids and antioxidants. We are aware that the microbiota composition may affect the stress and performance (Figure 4). Carbohydrates supply the hepatic and muscle reserves of glycogen, during prolonged periods of intense exercise, reducing stress hormones such as cortisol and

the immunosuppression associated with high physical activity [7,31]. However, post-workout is characterized by the so-called "Open Window", that is, a temporary drop in the immune system due to the energy and metabolites consumption during exercise [31]. A carbohydrate intake of about 8-10g/kg of body weight per day is indicated to restore the pre-workout glycogen values in 24 hours [31]. At the same time, it is also important to restore body fluids, in fact during exercise there is a consumption of about 150% of fluids based on body weight [31]. Adequate availability of all amino acids is necessary to maintain immunocompetence. In the last decade, particular attention has been paid to some categories of amino acids. In particular, glutamine is the most abundant circulating amino acid, and it alone represents about

20% [32]. More than 70% of the circulating glutamine derives from skeletal muscles [33] where it is released by proteolysis or synthesized *de novo* [34]. Therefore, after prolonged exercise, there was a drop in the plasma glutamine concentration of about 20%, the so-called “the glutamine hypothesis” [31,35] seemed to explain the transient immunodepression after the exercise and the increased risk of infections. However, despite the essential role of glutamine in the synthesis of cytokines, and in the macrophage and leukocyte function, no study has confirmed that supplementation in the immediate post workout balanced this immune defense dysfunction [36].

Recent epidemiological data have shown how exercise reduces the risk of all types of cancer [37]. A very recent study investigated the role of glutamine on the development of tumor cells on mouse models with triple negative lung and breast tumors [38]. The hypothesis of this study is that physical activity, by reducing the share of circulating glutamine, reduced cancer uptake of glutamine inhibiting the tumor growth. Moreover, the study demonstrated that a decrease in the tumor bioavailability of glutamine, induced by pharmacological means or by physical activity (running on the wheel), caused a decrease in tumor growth. In addition, physical activity reduced the mRNA gene expression of muscle atrophy determining the state of sarcopenia and abolished weight loss [38]. Although the athletes follow a low-fat diet (15-30% of total daily calories) [31], the fat metabolism allows the protection of glycogen reserves during prolonged exercise, improving performance. A high-fat diet reduces intestinal inflammation, bacterial translocation and intestinal damage following intestinal hypoperfusion during exercise, consequently reducing digestive disorders [7]. A dose of about 1-2 g / day of omega 3 seems to reduce the production of cytokines and reactive oxygen species (ROS) during exercise [7]. On the other hand, Pedersen, et al. [39] monitored the serum concentration of NK and cytokines in 10 sedentary individuals, who consumed a high carbohydrate diet (approximately 65% of the daily calorie intake), and 10 athletes, who consumed a high fat diet (approximately 62% of the daily calorie intake), during a training session 3-4 times a week for 7 weeks. Immune function was enhanced in the group that consumed the carbohydrate-rich diet. Furthermore, a high-fat diet can have a harmful effect on the composition of the microbiota, increasing the permeability of the GI barrier and the translocation of LPS [7]. A lack of micronutrients such as metals, zinc and vitamin A can have negative effects on the immune function; however, an excessive introduction compared to the real need does not seem to enhance its function. Although high doses of antioxidants can reduce cortisol and IL-6 levels, recent evidence has shown that healthy individuals do not benefit from preventing URTI [13]. Indeed, high doses of a single antioxidant, such as vitamin E, can be pro-oxidant and pro-inflammatory.

Instead, suboptimal serum vitamin D levels lead to impaired immune defenses and an increased risk of infections [40,41]. In particular, vitamin D helps keep tight-junctions intact, stimulates the production of antimicrobial peptides, reduces the pro-inflammatory cytokine cascade, stimulates anti-inflammatory cytokines and promotes the formation of regulatory T lymphocytes [42]. Several observational studies and clinical trials have reported that a vitamin D supplement determines a lower risk of developing flu. However, the benefit of vitamin D supplementation is evident in individuals who lack it [43-45]. Vitamin D has recently been used for the prevention of Covid-19 infection thanks to its anti-inflammatory action and low side effects [45]. It would be interesting to evaluate its use for preventive purposes, we await clinical studies confirm this hypothesis. As for vitamin C, it keeps the alveolar barrier intact and promotes the transcription of protein channels, regulating the clearance of alveolar fluids. During an infection serum vitamin C levels decrease proportionally to the severity of the infection; an intravenous infusion of high dose vitamin C seems to have a protective effect in subjects whose sepsis is related to a respiratory distress syndrome [46]. A study has recently been recorded to evaluate the efficacy of vitamin C infusions in patients with SARS-Covid 19 [47].

An insufficiency of a single nutrient is rare, the use of multivitamin complexes or mineral salt supplements can be a valid prevention choice. This method prevents the excessive introduction of a single nutrient, avoiding side effects. However, the benefits are obtained by correcting a slight nutrient insufficiency because of consumption during exercise. It should be considered that the association of some foods can naturally provide these micronutrients, increasing their bioavailability and having a synergistic effect [48]. In a previous study, there has been shown a reduction in the incidence of URTI in individuals who consume 3 servings of fruit per day, compared to those who consume less than two [49]. Many substances are considered potentially beneficial to the immune system, but often these benefits are only evident in *in vitro* studies which use them at high concentrations. Only a few supplements have shown some solid evidence in humans, such as bovine colostrum, echinacea, probiotics and some polyphenols. Bovine colostrum has beneficial effects on the integrity of the intestinal barrier, on the activity of phagocytes and on the production of salivary IgA [50-52]; however, these benefits are more evident in people who have a compromised immune system. Supplementation with selected families of probiotics is capable of modulating the intestinal flora and improving its homeostasis. These benefits are more evident in individuals who have a compromised immune status as a result of increased risk of gastrointestinal infections or, for example, to prevent antibiotic-induced diarrhea. Polyphenols are powerful antioxidants and *in vitro* have shown anti-microbial

and anti-viral activity [53]. Quercetin is widely used in athletes since its consumption (1000mg / day for two weeks before and two weeks after the competition) has been shown to reduce the incidence of URTI (5% of incidence compared to 45% in the placebo arm) [21]. However, this flavonoid is present in many foods such as onions, fruit and berries, green leafy vegetables and tea; therefore a correct consumption of these foods can provide a protective effect against infections.

Effect of Exercise on Immunosenescence

Aging is associated with a decreased functionality of organs and physiological systems, including the immune system. Aging causes immune dysfunction that it is called immunosenescence, it is related to a greater susceptibility to infections, autoimmune diseases, neoplasms, metabolic disorders, osteoporosis and neurological disorders [26]. Immunosenescence leads to a reduced response to vaccines, a reduced proliferative capacity and activity of T and natural killer (NK) lymphocytes, a reduced pool of circulating cytokines, a reduced phagocytic activity and an exaggerated inflammatory response to bacterial infections [54]. However, exercise and nutritional habits are important modifiable factors that can have a significant impact on strengthening the immune system in all stages of life. Recent studies have compared the immune function of elderly trained with sedentary population. In one study, 30 sedentary older women were compared to 12 women who had participated in senior running national teams [19]; in trained women there was a higher concentration of NK and an increase in the activity of T lymphocytes compared to sedentary women. In another study, the immune function of 17 senior runners who had been training for about 17 years and 19 sedentary control cases was compared. Also in this study, an increase in T lymphocyte activity was seen in runners [49]. These data show that constant physical activity can modulate the immune system, slowing down aging.

Exercise and COVID-19

The current SARS-COVID-19 pandemic began in China and since January 2020 has become the world's largest calamity both in terms of contagiousness and death and in economic terms. No drug or vaccine is currently available for the treatment and prevention of the infection [55], and if on the one hand the few sources, constantly updated, are rapidly shared by the whole world scientific community, there is still no certainty on the mechanisms of spread, transmission, incubation, contagiousness and lethality of the virus [56]. Latest news agreed that the most symptomatic and serious patients would develop tissue damage, due to a tropism of the virus for cells expressing angiotensin 2 (ACE2) receptors at high levels (present both at the alveolar and at the level macrophage and endothelial), and an out-of-control inflammatory process, with the consequent formation of clots and thrombi that

would cause cardiac, renal, encephalic and lung complications with possible patient is death [57]. The primary goal to date is to try to contain the infection by limiting the movement and social contacts of people. Quarantine, however, has negative consequences, such as, an increase in sedentary activities line watching television or playing video games. Low daily physical activity and reduced energy expenditure, if not balanced with a correct reduction in caloric intake, promote weight gain and worsening of pre-existing pathological conditions such as diabetes, hypertension, respiratory disorders, obesity, and the typical frailty of the elderly patient such as sarcopenia and dementia [58-60]. In obese patients, hormonal status, depression of the innate and specific immune system and sedentary lifestyle are determining factors in the manifestation of the severity of the infection. The UK's National Intensive Care Audit and Research Center (ICNARC) on COVID-19 published a report (July 17, 2020) in which 73.7% of the 10492 hospitalized COVID-19 patients were observed to be overweight or obese and that among patients with BMI > 30 who had undergone intensive care, 71.9% died [61]. While the data from Istituto Superiore di Sanità (ISS) (July 9, 2020) show that, among 3857 patients who died from COVID-19, the 61.8% presented more than 3 comorbidities, and the overall prevalence of patients who presented obesity as the only comorbidity was of 10.9% [62]. In the obese patient there is a constant inflammatory state determined by a condition of hypoxia and dysfunction of the adipocytes, which results in an exuberant secretion of pro-inflammatory cytokines (TNF- α , IL-1 β and IL-6) and the recruitment of macrophages, T and B lymphocytes, creating a self-regenerating inflammatory circuit [63]. Obesity alters the immune response by memory CD8 T lymphocytes in response to influenza virus infection, resulting in increased mortality, viral titer and worsening pulmonary clinic [64]. These adverse effects have been associated with obesity-induced failure to maintain influenza-specific CD8 + memory T cells, which are essential for ensuring vaccine efficacy [64]. Obesity is not only an individual risk but the increase in the number of obese individuals could allow the development of a more virulent viral strain and increase the mortality rate [65]. Chronic inflammation and impaired fibrinolysis contribute to increasing the risk of developing thrombosis, an event that worsens lung damage and death in patients with COVID-19 infection, which justifies the use of heparin for prophylactic and therapeutic purposes [66]. As illustrated above, physical exercise leads to significant benefits for both the healthy and the pathological individual [67,68]. Maintaining constant physical activity such as 30 minutes of moderate physical activity and 20 minutes of intense physical activity [67] per day is a fundamental way of prevention of sedentary lifestyle. Physical activity is of primary importance especially in the elderly individual to maintain physiological functions and reserves in order to fight the symptoms related to covid-19 infection [69].

Exercise and Cancer

Exercise in cancer patients improves the QoL and reduces the symptoms and side effects of treatments [1]. Physical activity and exercise can relieve side effects of antineoplastic treatments such as tiredness, nausea, vomiting and significantly improve the patient's QoL [70-73]. They can also implement strength, muscle elasticity and improve body composition with an increase in lean mass [73,74]. In fact, even in cancer patients, body composition is a determining QoL factor [75], and cancer patients should have an active lifestyle, an intense-moderate aerobic activity of at least 90 minutes per week and strength activities twice a week [76]. Several studies and reviews of the literature have shown that physical activity is safe and even beneficial in metastatic patients, for example with breast cancer [77] or with lung cancer [70,78,79]. The prospective DELCap study showed a linear correlation between intensity of physical activity and reduction of the risk of recurrence and mortality in patients treated for high-risk breast cancer [80]. Exercise lessens the endurance of symptoms, enhances the expectations and hopes, and allows the continuation of treatments. In essence, physical activity with specific and individualized exercises improves physical status and psycho-spiritual representations of the disease on daily life [56]. Other studies have focused attention on the psychosocial impact of exercise such as running for women treated for breast cancer [81], exercise is an important part to recover personal esteem, the challenge for life, the fight against the disease, the recovery of physical and aesthetic condition [82-84].

Conclusion

Moderate physical activity strengthens the immune system and improves health. However, the excessive physical effort associated with other stressful conditions can compromise the immune status, increasing the infections risk, in particular airways infections, because of dysbiosis, alteration of the permeability of the gastro intestinal barrier and immunodeficiency. Playing a moderate and constant physical activity, taking care of nutritional intake and filling any deficiencies is an essential way to maintain an efficient immune system. Sensitize the population to adopt healthier lifestyles, avoids the worsening of clinical conditions or the onset of new pathologies in the event of a COVID-19 infection is a priority. In conclusion, an excessive physical activity can worsen the individual health. It is important to modulate it, and to take care of the food intake in order to develop an efficient immune system that can fight infections, such as COVID-19 infection, and the development of tumor pathologies, as well as enhancing the response to therapies and avoiding the onset of sarcopenia.

Declarations

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Material

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contribution

All authors contributed to the study conception and design. Ester Oneda is the author who has taken care of the research of the material, the drafting of the article and its revisions, Michele Martinetti is the author who has taken care of the details related to training and dietary supplements in particular in the athlete and Alberto Zaniboni is the author who has dedicated himself to drafting the key messages and reviewing the final work. The first draft of the manuscript was written by Ester Oneda and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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