Module 4. Immune system

Unit 4.1 Exercise and the immune system

One of the most important factors for a team in football is to make sure that the team collectively stays healthy. Preventing injury and illnesses is key to success. However, especially at the highest level, where 2 and sometimes 3 matches are played in one week, with a lot of travel, crowded spaces and so on, this can be challenging. Unfortunately, hard exercise and limited recovery will compromise immune system and therefore it is common for upper respiratory tract infections to occur during the winter periods (in European season) when there is a congested fixture schedule.

It is important to make sure the immune system is prepared to fight potentially damaging (pathogenic) microorganisms such as bacteria, viruses, and fungi. Although many factors influence exercise-induced immune depression (e.g., physical, environmental, and psychological stresses), nutrition plays a critical role. Inadequate nutrition can result in deficiencies and suboptimal function of the immune system. With adequate nutrition strategies it is possible to optimize recovery and in this section we will explore the evidence that nutritional interventions can help prevent immunosuppression. First we will study the immune system and the effects of exercise on the immune system.

4.1.1 The immune system

> The immune system is involved in tissue repair after injury and in the protection of the body against potentially damaging (pathogenic) microorganisms such as bacteria, viruses, and fungi. In some circumstances, the immune system can become functionally depressed (known as immunodepression), which may result in an increased susceptibility to infection. Several forms of stress, including a heavy schedule of training and competition, can lead to immunodepression in athletes, which places them at greater risk for opportunistic infections, particularly upper respiratory tract infections (URTIs). (Jeukendrup & Gleeson, 2018, p. 365).

Nutritional deficiencies can impair immune function and will increase the risk of infection. It is also evident that “even medically harmless infections may significantly impair athletic performance” (Jeukendrup & Gleeson, 2018, p. 365).

Simply put, the immune system recognizes, attacks, and destroys things that are foreign to the body. In actuality, the functions of this homeostatic system are far more complex, involving the precise coordination of many cell types and molecular messengers. Yet, like any other homeostatic system, the immune system is composed of redundant mechanisms to ensure that essential processes are carried out.

The immune system has two broad functions, **innate** (natural, or nonspecific) immunity and **adaptive** (acquired, or specific) immunity, which work synergistically. The attempt of an infectious agent to enter the body immediately activates the innate system. This so-called first-line of defence comprises three general mechanisms that have the common goal of restricting microorganism entry into the body:

- Physical or structural barriers (skin, epithelial linings, and mucosal secretions).
- Chemical barriers (pH of bodily fluids and soluble factors).
- Phagocytic cells (e.g., neutrophils and macrophages or monocytes).

Failure of the innate system and the resulting infection activates the adaptive system, which aids recovery from infection. Adaptive immunity is helped greatly by T-lymphocyte and B-lymphocyte acquisition of receptors that recognize the foreign molecules (called antigens), engendering specificity and “memory” that enable the immune system to mount an augmented response when the host is reinfected by the same pathogen.

The components of the immune system comprise both cellular and soluble elements. The white blood cells (leukocytes) have diverse functions, despite their common origin from the stem cells of the bone marrow. Leukocytes consist of the granulocytes (60% to 70%), monocytes (10% to 15%), and lymphocytes (20% to 25%). Various subsets of the latter can be identified through specific proteins (clusters of differentiation or cluster designators [CD]) that are expressed on the cell surface of a particular cell type. For example, all T-lymphocytes express the protein CD3 on the cell surface. B-lymphocytes do not express CD3 but express CD19, CD20, and CD22. A particular subset of T-lymphocytes called helper T-cells specifically express the CD4 protein, whereas the cytotoxic T-cells express CD8. T-cells recognize short peptide sequences from antigens only if they are held on the surface of the cell and complexed with a major histocompatibility complex (MHC) molecule. The ability of the immune system to distinguish self from nonself depends largely on the MHC, a group of protein markers

> that is present on the surface of every cell and is slightly different in each person. (Jeukendrup & Gleeson, 2018, p. 366).

4.1.2 Effect of exercise on immune function

“Athletes engaged in heavy training programs, particularly endurance events, appear to be more susceptible to infection than the general population. For example, sore throats and flulike symptoms are more common in athletes.” (Calder & Yaqoob, 2013, p. 653). Nowadays, many athletes who participate in elite sports “are exposed to high training loads and an increasingly saturated competition calendars” (Soligard et al., 2016, p. 1030). Emerging evidence indicates that inappropriate load management is a significant risk factor for both acute episodes of illness and the overtraining syndrome.

> The International Olympic Committee (IOC) [recently] convened an expert group to review the scientific evidence for the relationship of load ([including] rapid changes in training and competition load, competition calendar congestion, psychological load and travel) and health outcomes in sport. (Soligard et al., 2016, p. 1030).

They concluded that there is evidence that changes in external load (increased volume and intensity of training) and internal training load (the physiological and psychological responses to external load in each individual) are associated with an increased risk of illness and that participation in competitions (single or multiple) is associated with an increased risk of illness. However, they also recognized that it is not yet possible to quantify the magnitude of the training load increase that is related to increased risk of a specific illness in any given sport. Also that the factors responsible for increased illness risk as a result of intensive training and competition are likely to be multifactorial and need to be further explored in future studies. (Schwellnus et al., 2016)

However, “some convincing evidence suggests that this increased susceptibility to infection arises because of a depression of immune system function” (Calder & Yaqoob, 2013, p. 653). (For detailed reviews, see: Gleeson, February, 2016; Gleeson & Walsh, 2012; Gleeson & Williams, 2013; Walsh et al., 2011).

The main component of the immune system consists of the white blood cells, or leukocytes.

> The circulating numbers and functional capacities of leukocytes may be decreased by repeated bouts of intense, prolonged exercise… The cause may be increased levels of stress hormones (e.g. epinephrine and cortisol) and anti-inflammatory cytokines [e.g. IL-6 and IL-10] during exercise and

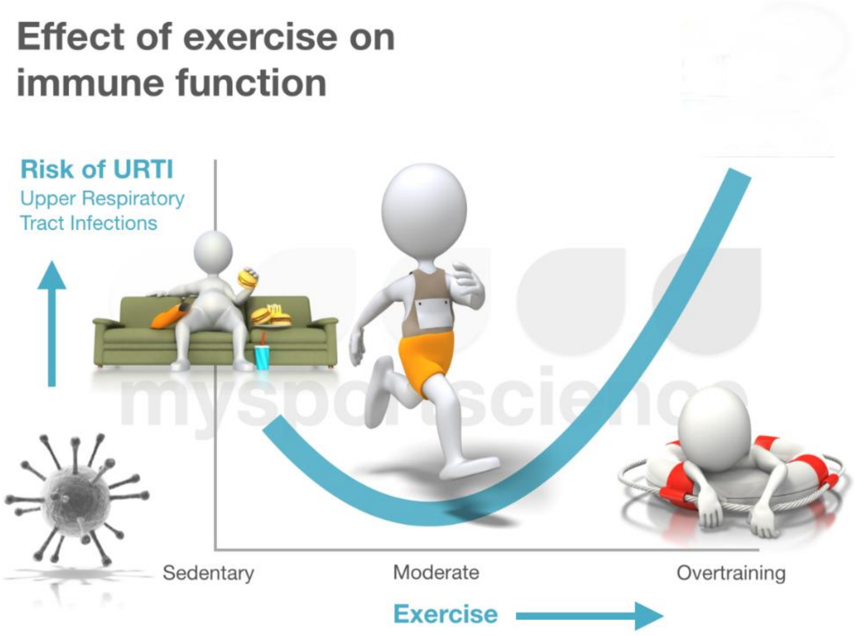
> entry into the circulation of less mature leukocytes from the bone marrow. (Calder & Yaqoob, 2013, p. 653).

Increased free radical production during exercise is another potential Inhibitor of several immune cell functions. “Drops in the blood concentration of glutamine have also been suggested as a possible cause of the immunodepression associated with heavy training, although the evidence for this is less compelling.” (Calder & Yaqoob, 2013, p. 653). Inflammation caused by muscle damage may be another factor.

> The relationship between exercise and susceptibility to infection has been modeled in the form of a J-curve (Nieman, 1994)... This model suggests that, whereas engaging in moderate activity may enhance immune function above sedentary levels..., excessive amounts of prolonged, high-intensity exercise [may] induce detrimental effects on immune function. Although the literature provides strong evidence in support of the latter point, relatively little evidence is available to suggest any clinically significant difference in immune function between sedentary and moderately active people. (Calder & Yaqoob, 2013, p. 653).

Thus, the portion of the J-curve representing this part of the relationship should perhaps be flattened out, as shown in Figure 1.

Figure 1: The J-curve model implies that risk of upper respiratory tract infection (URTI) is reduced by moderate activity but progressively elevated by heavier training loads



Source: Jeukendrup, September 26, 2016, https://goo.gl/o1XtLy

> [C. E.] Matthews et al. (2002) reported that the regular performance of about 2 hours of moderate exercise a day was associated with a 29% reduction in risk of URTI compared with a sedentary lifestyle. Similarly, in a study ofover 1,000 participants, Nieman et al. [Nieman, Henson, Austin and Sha] (2011) observed that doing moderate exercise on 5 or more days per week was associated with a 30% lower risk of URTI than doing 1 day or fewer days of exercise per week. This finding emphasizes that the benefit of regular, moderate exercise in improving resistance to infection is quite small [although there are, of course, substantial benefits to cardiovascular and metabolic health with a more active lifestyle]. (Jeukendrup & Gleeson, 2018, p. 381).

Congested competition schedules in combination with lots of travel, press events, large crowds, etc. increase the susceptibility to infection and need to be managed carefully. The factors that increase the chances of illness are discussed below.

4.1.3 Causes of illness in players

> The most common illnesses in athletes (and in the general population) are viral infections of the upper respiratory tract (i.e. the common cold and influenza), which are more common in the winter months. Adults typically experience between two and four episodes of respiratory illness per year. Athletes can also develop similar symptoms (e.g. sore throat [runny nose, dry cough]) due to allergy or inflammation [affecting the mucosal lining of the upper respiratory tract] caused by the inhalation of cold, dry or polluted air… [In themselves,] these symptoms are generally trivial, but no matter whether the cause is infectious or allergic inflammation, they can cause an athlete to interrupt training, under-perform or even miss an important competition. (Gleeson, 2015, p. 1).

"Prolonged bouts of strenuous exercise [usually in excess of 90 minutes and of a continuous rather than Intermittent nature; like a fairly typical training session in football] have been shown to result in transient depression of white blood cell (leukocyte) functions" (Gleeson, 2015, p. 2), which consequently can impair defense against infectious pathogens including both, viruses and bacteria. It has been suggested "that such changes create an 'open window' of decreased host protection" (Gleeson, 2015, p. 2), during which time pathogens "can gain a foothold, increasing the risk of developing an infection" (Walsh et al., 2011, as cited in Gleeson, 2015, p. 2). Other factors including "psychological stress, lack of sleep and inadequate nutrition (particularly deficiencies of protein and essential micronutrients) can also depress immunity" (Walsh et al., 2011, as cited in Gleeson, 2015, p. 2) and lead to increased risk of infection.

There are also some situations, such as proximity to large crowds, coming into close contact with people suffering from infections and being exposed to environments with poor hygiene, in which an athlete’s exposure to infectious agents may be increased. Thus, the degree of exposure to pathogens in the athlete's environment and the status of the athlete's immune system are the two important determinants of infection risk. Various strategies, including behavioral and nutritional ones, can be employed to reduce these risk factors. Of course, in many professional sports that attract large numbers of spectators, the competitors' exposure to large crowds is unavoidable. Air travel to foreign countries may also increase the risk of picking up infections. Recently, international travel was shown to be associated with significantly more upper respiratory illness symptoms (URS) in professional rugby players travelling across multiple time zones (Fowler, Duffield, and Lu 2016; Schwellnus et al., 2012). International travel was an independent risk factor for illness in another prospective study among elite cross-country skiers (Svendsen et al. [Svendsen, Taylor, Tonnessen, Bahr, & Gleeson] 2016).

During dynamic exercise, exposure of the lungs to airborne bacteria and viruses increases because of the higher rate and depth of breathing. However, URS can also arise due to allergy and inflammation of the airways caused by breathing cold, dry or polluted air; the URS which result from this are indistinguishable from the URS that result from a respiratory infection. Hence, the cause of the increased incidence of respiratory illness symptoms in athletes is most likely multifactorial. (Jeukendrup & Gleeson, 2018)

Acute illness can cause a reduction in exercise performance, an interruption to training, and even result in missing an important competition. Acute infective illness can affect a number of the body's organ systems causing a reduction in exercise performance through a number of mechanisms including: impaired motor coordination, decreased muscle strength and power, decreased aerobic capacity, and alterations in metabolic function. Furthermore, the presence of fever causes a decrease in the body’s ability to regulate body temperature and increases fluid losses through sweating, thereby impairing endurance performance. It has also been documented that a decrease in exercise performance after full recovery from a respiratory illness can last for 2 to 4 days and data from one study indicates that runners who start an endurance race with systemic symptoms of an acute illness are 2-3 times less likely to complete the race. It has also been reported, that in 33% of cases, an infection (most commonly of the respiratory tract) was the reason why elite Great Britain athletes from 30 different Olympic sports miss training sessions. Perhaps more importantly, an acute infective illness can also increase the risk of serious medical complications and even sudden death during strenuous exercise. (Gleeson, August 19, 2016, https://goo.gl/BGyJik).

Other common illnesses in athletes are those affecting the skin, digestive tract and genitourinary system. Ear infections are more common in aquatic sports. In contact sports, skin abrasions may occur... increasing the risk of transdermal infections. In some situations, food hygiene can be a problem, which increases the risk of gastrointestinal infections.

Forms of illness that are quite common in athletes but are non-infectious include dehydration and heat illness. An increase in gut permeability may allow entry of gut bacterial endotoxins into the circulation, particularly during prolonged exercise in the heat and this can increase the risk of heat illness. Other forms of non-infectious illness include allergies that involve the respiratory tract, skin or digestive system and are caused by a hypersensitivity of the immune system to certain molecules (often proteins) that are inhaled (e.g. pollen), come into contact with the skin (e.g. latex) or are eaten (e.g. wheat gluten). All of these involve the inappropriate activation of the immune system against a compound that is normally tolerated well by the majority of people. The inflammation caused by this hypersensitivity is the major cause of the illness symptoms. Similar symptoms may arise with intolerance to certain food items, although this does not directly involve immune system activation [as explained below]. (Jeukendrup & Gleeson, 2018, p. 377).

4.1.4 Nutrition to minimise immunodepression in players

Poor nutritional practices may contribute to impaired immunity in athletes. Some athletes adopt diets that are extremely high in carbohydrate content at the expense of protein and fat. By avoiding foods high in animal fat, athletes are reducing their intake of fat-soluble vitamins and essential FAs. (Jeukendrup & Gleeson, 2018)

On the other hand, extreme low carb diets will increase the stress response to exercise, which may also increase immunosuppression.

Anecdotal and media reports promote the supposed performance benefits of certain vitamins and minerals, but most athletes do not realize that micronutrient supplementation is only beneficial when correcting a deficiency and that excessive intake of individual micronutrients can be toxic or can limit the absorption of other essential trace elements. Deficiencies or excesses of various dietary components have a substantial effect on immune function and may exacerbate the immunodepression associated with heavy training loads. (Jeukendrup & Gleeson, 2018)

How does nutrition influences immune function?

> Nutrient availability potentially affects almost all aspects of the immune system because many nutrients are involved in energy metabolism and protein synthesis. Most immune responses involve cell replication and the production of proteins with specific functions (e.g., cytokines, antibodies, and acute phase proteins). Immune system functions that may be compromised include the humoral and secretory antibody production, cell-mediated immunity, bactericidal capacity of phagocytes, complement formation, and T-lymphocyte proliferative response to mitogens.
>
> A nutritional deficiency is said to have a direct effect when the nutritional factor has primary activity within the lymphoid system and an indirect effect when the primary activity affects all cellular material or an organ system that functions as an immune regulator. (Jeukendrup & Gleeson, 2018).

For example, carbohydrate availability directly affects a number of leukocyte functions but also indirectly affects the lymphoid system through its influence on circulating levels of the catecholamines, adrenocorticotrophic hormone (ACTH), and cortisol. Changes in plasma levels of these stress hormones are probably mostly responsible for the observed changes in immune function after an acute bout of exercise.

The effect of a nutrient deficiency on the immune system depends on the duration of the deficiency as well as on the athlete's nutritional status as a whole. The severity of the deficiency is also a factor, although even a mild deficiency of a single nutrient can alter the immune response. Because the availability of one nutrient may enhance or impair the action of another, and nutrient deficiencies often occur together, nutrient–nutrient interactions on immune function are also an important consideration. Athletes who are training hard eat to satisfy their energy demands, consuming more macronutrients (carbohydrate, protein, and fat) and micronutrients (vitamins and minerals) than their sedentary counterparts. Therefore, they may ingest excessive amounts of some nutrients. Excessive amounts of specific nutrients (e.g., omega-3 polyunsaturated FAs, iron, and zinc) can have detrimental effects on immune function.

Athletes are generally advised to eat a well-balanced diet consisting of a variety of foods in sufficient quantity to cover their energy expenditures. But many athletes alter their diets. They may use diets high in protein or carbohydrate or fat, very low-energy diets, fasting, or megadoses of vitamins and minerals. Such dietary extremes may in fact compromise immune function. For example, diets that are excessively high in carbohydrate, favored by many athletes to keep glycogen stores high, are generally low in meat products and thus are low in protein (an important nutrient for immune function) and vitamin B_{12} (essential for DNA synthesis). Many athletes avoid dairy produce to minimize intake of saturated fat, but by doing so they are omitting from their diet major sources of vitamin D, B-group vitamins, and calcium, all of which play roles of varying importance in maintaining immune function. "If fat intake is a concern, then athletes should select nonfat or low-fat dairy products that provide the same (or higher) levels of calcium, vitamin D, and vitamin B_{12} as full-fat dairy products do" (Jeukendrup & Gleeson, 2018, p. 396). Only milk (regardless of fat content) is likely to be fortified with vitamin D.

Unit 4.2 Macronutrients and immune function

4.2.1 Macronutrients

Carbohydrate

The importance of adequate carbohydrate availability for maintenance of heavy training schedules and successful athletic performance is unquestionable. During periods of heavy training, athletes should consume sufficient carbohydrate. In football: 5-8 g/kg bw/day of carbohydrate. These recommendations are principally aimed at restoring muscle andliver glycogen stores to ensure sufficient carbohydrate availability for skeletal muscle contraction for training on successive days." (Gleeson, 2006b, p. 165).

> Glucose is also an important fuel… for cells of the immune system, including lymphocytes, neutrophils, and macrophages… Phagocytes utilize glucose at a rate 10-fold greater than they utilize glutamine when these substrates are both present in the culture medium at normal physiological concentrations… The importance of glucose for the proper functioning of lymphocytes and macrophages is further emphasized in a study showing that [mitogen-stimulated] proliferation of these cells in vitro depends on a glucose concentration over the physiological range. (Gleeson, 2006b, p. 165).

Cells of the immune system have extremely high metabolic rates, and this finding highlights the importance of adequate nutrition for the provision of fuels to maintain immunocompetence.

Because elevated levels of stress hormones seem to cause many aspects of exercise-induced immune function impairment,

> nutritional strategies that effectively reduce the stress hormone response to exercise would be expected to limit the degree of exercise-induced immune dysfunction. The size of the glycogen stores in muscle and liver at the onset of exercise influence the hormonal and immune response to exercise. The amount of glycogen stored in the body is limited (usually less than 500 g) and is affected by recent physical activity and the amount of dietary carbohydrate intake. (Calder & Yaqoob, 2013, p. 662).

When people perform prolonged exercise during several days on very low-carbohydrate diets (typically <50 g of carbohydrate per day), "the magnitude of the stress hormone (e.g., adrenaline and cortisol) and cytokine (e.g. IL-6, interleukin-1 receptor antagonist (IL-1 ra), and IL-10) response is markedly higher than on normal or high carbohydrate diets" (Gleeson, Blannin, Walsh, Bishop, & Clark, 1998, as cited in Gleeson, Nieman & Pedersen, 2004, p. 119). "Furthermore, the postexercise fall in plasma glutamine concentration is greater than it is on normal and high-carbohydrate diets" (Jeukendrup & Gleeson, 2018).

> It has been speculated that athletes deficient in carbohydrate are placing themselves at risk from the immunosuppressive effects of cortisol and reduced glutamine availability, including the suppression of antibody production, lymphocyte proliferation, and NK cell cytotoxic activity.In the study by Mitchell et al. (1998) it was observed that exercising (for 1 hour at 75% of VO$_2$max) in a glycogen-depleted state (induced by prior exercise and 2 days on a low-carbohydrate diet) resulted in a greater fall in circulating lymphocyte numbers at 2 hours postexercise compared with the same exercise performed after 2 days on a high-carbohydrate diet.
>
> Consumption of carbohydrate during prolonged exercise attenuates rises in plasma epinephrine, cortisol, and cytokines (Nehlsen-Cannarella et al., 1997); attenuates the trafficking of most leukocyte and lymphocyte subsets, including the rise in the neutrophil: lymphocyte ratio; prevents the exercise-induced fall in neutrophil function; and reduces the extent of the diminution of mitogen-stimulated T-lymphocyte proliferation (on a per cell basis) after prolonged exercise. It was shown that consuming 30 to 60 g of carbohydrate per hour during 2.5 hours of strenuous cycling prevented both the decrease in the number and percentage of interferon-gamma (IFN-γ) positive T lymphocytes and the suppression of IFN-γ production from stimulated T-lymphocytes observed on the placebo control trial. IFN-γ production is critical to antiviral defence and it has been suggested that the suppression of IFN-γ production may be an important mechanism leading to increased risk of infection after prolonged exercise bouts.
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> The consumption of carbohydrate in beverages during exercise may have the additional benefit of helping to maintain saliva flow rate during exercise. Saliva contains several proteins with antimicrobial properties, including immunoglobulin A (IgA), lysozyme, and β-amylase. During periods of heavy training, athletes have lower levels of IgA in their saliva and this condition may contribute to their increased incidence of URTI. Saliva secretion is under neural control. The sympathetic nervous system stimulation that occurs during exercise causes vasoconstriction of the blood vessels to the salivary glands and results in a reduction in saliva secretion. Regular fluid intake during exercise prevents this effect, and a study (Bishop, Blannin, Armstrong, Rickman, & Gleeson, 2000) has confirmed that regular consumption of carbohydrate-containing drinks

> helps maintain saliva flow rate and, hence, saliva IgA secretion rate during prolonged exercise. (Jeukendrup & Gleeson, 2018).

It is important to note that changes in these indicators of immune function do not necessarily mean compromised immune function or increased infections.

> Evidence that any beneficial effect of carbohydrate feeding on immune responses to exercise translates to reduced incidence of URTI after prolonged exercise is currently lacking. Although a trend for a beneficial effect of carbohydrate ingestion on postrace URTI was reported in a study of 98 marathon runners [Nieman et al., 2002], this finding did not achieve statistical significance. Larger-scale studies are needed to investigate this possibility. (Jeukendrup & Gleeson, 2018).

Fat

Fat intake is commonly 20-35% of dietary energy but this itself is not actually a recommendation. The type of dietary fat, however, is important.

> Two groups of polyunsaturated FAs (PUFAs) are essential to the body: the omega-6 (n-6) series, derived from linoleic acid, and the omega-3 (n-3) series, derived from linolenic acid. Adequate intakes of these FAs for adult men and women are 17 and 12 g/day, respectively, for n-6 FAs, and 1.6 and 1.1 g/day, respectively, for n-3 FAs. These FAs cannot be synthesized in the body and therefore must be derived from the diet. Diets rich in either of these PUFAs improve the conditions of patients suffering from diseases characterized by an overactive immune system, such as rheumatoid arthritis and there is also evidence that fish oil n-3 FA supplements can help minimize respiratory symptoms in individuals who are susceptible to exercise-induced bronchoconstriction (Mickleborough, Head, & Lindley, 2011). These PUFAs thus have immunomodulatory functions.
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> Although FAs are utilized as fuels by lymphocytes, their oxidation does not appear to be crucial for lymphocyte function, because the inhibition of FA oxidation does not affect the ability of lymphocytes to proliferate in response to mitogens. FAs exert either direct effects (by altering cell membrane fluidity) or indirect effects (as precursors of cell-signaling molecules called eicosanoids) on immune function, generally resulting in reduced IL-2 production and suppressed mitogen-induced lymphocyte proliferation. But supplementation with vitamin E or vitamin C appears to provide partial protection against some of these immunosuppressive effects.

Relatively little is known about the potential contribution of FAs to the regulation of exercise-induced modification of immune function. Although no study has been done in athletes, excessive intake of PUFA could possibly further potentiate the exercise-induced suppression of IL-2 production and lymphocyte proliferation. High intakes of arachidonic acid relative to intakes of FA of the n-3 group may also exert an undesirable influence on inflammation and immune function during and after exercise. Alteration of essential FA distribution through dietary changes or nutritional supplementation is already being applied in the treatment of chronic inflammatory diseases. More research is needed on the effects of altering essential FA intake on immune function after exercise and during periods of heavy training. A study that investigated the effects of endurance training for 7 weeks on carbohydrate-rich (65% of dietary energy) or fat-rich (62% of dietary energy) diets concluded that diet during training may influence natural immunity because NK cell activity increased on the carbohydrate-rich diet compared with the fat-rich diet (Pedersen, Helge, Richter, Rohde, & Kiens, 2000). The results of this study suggest that a fat-rich diet is detrimental to immune function compared with a carbohydrate-rich diet but do not clarify whether this effect is the result of a lack of dietary carbohydrate or an excess of a specific dietary fat component. (Jeukendrup & Gleeson, 2018).

Protein and Amino Acids

“Inadequate intake of protein impairs host immunity, with particularly detrimental effects on the T-cell system, resulting in increased incidence of opportunistic infections... Some impairment of host-defense mechanisms is observed even in moderate protein deficiency.” (Calder & Yaqoob, 2013, p. 656).

Excessive dietary protein could also be harmful to immune function. A diet rich in protein (24% protein, 72% fat, and 3% carbohydrate) consumed for 4 days caused a 25% lowering of muscle and plasma glutamine levels (D. E. Matthews & Campbell, 1992). This decline was attributed to increased renal uptake of glutamine to reestablish normal acid–base balance because a high intake of protein combined with a low intake of carbohydrate induces chronic metabolic acidosis. Furthermore, falls in the plasma glutamine concentration after prolonged strenuous exercise are greater when consuming a low-carbohydrate diet compared with a normal diet. Ingesting carbohydrate during exercise, however, does not prevent the postexercise fall in plasma glutamine. (Jeukendrup & Gleeson, 2018).

The ingestion of protein stimulates protein synthesis and this may be particularly important in the postexercise period to promote muscle repair and adaptation to training. It has also been shown that postexercise ingestion of about 20 g protein (0.3 g/kg bw) can help to restore some aspects of immune function during the recovery period (Witard, Jackman, Kies, Jeukendrup, & Tipton, 2011) and reduce respiratory infection incidence in overreaching athletes, emphasizing the importance of encouraging athletes to develop feeding strategies that focus on the postexercise period as part of their overall nutritional plans.

4.2.2 Vitamins

Vitamins are essential organic molecules that cannot be synthesized in the body and therefore must be obtained from food… Several vitamins are essential for normal immune function: fat-soluble vitamins A and E and water-soluble vitamins B_{12} and C… Other vitamins (e.g., B_6 and folic acid) also play important roles in immune function, but dietary deficiencies of these vitamins in humans are extremely rare. (Gleeson, 2006b, p. 184).

“There are no indications in the literature to suggest that vitamin intake among athletes in general is insufficient” (Gleeson, 2006b, p. 184), with the exception of vitamin D. Athletes tend to ingest above-average quantities of most micronutrients, and as with dietary protein requirements, increased dietary intake may satisfy any increase in need apart from vitamin D which is mostly derived from endogenous synthesis requiring the action of sunlight on the skin with only a small proportion of daily requirements coming from dietary sources. The requirement for most vitamins is not thought to be increased in athletes compared with the general population. “For example, vitamin loss through sweat during exercise is negligible and vitamin metabolism is largely unaffected by exercise.” (Jeukendrup & Gleeson, 2018).

Antioxidant Vitamins

> Vitamins with antioxidant properties, including vitamins C, E, and beta-carotene (provitamin A), may be required in increased quantities in athletes to inactivate the products of exercise-induced lipid peroxidation. Oxygen free-radical formation that accompanies the dramatic increase in oxidative metabolism during exercise… could potentially inhibit immune responses. (Jeukendrup & Gleeson, 2018).
>
> Reactive oxygen species [ROS] inhibit locomotory and bactericidal activity of neutrophils, reduce the proliferation of T-lymphocytes and B-lymphocytes, and inhibit NK cell activity. Sustained endurance training

> appears to be associated with an adaptive upregulation of the antioxidant defense system...
>
> Vitamin C (ascorbic acid) is found in high concentration in leukocytes and is implicated in a variety of anti-infective functions, including promotion of T-lymphocyte proliferation, prevention of corticosteroid-induced suppression of neutrophil activity, production of interferon, and inhibition of virus replication. (Gleeson et al., 2004, pp. 117-118).

Studies report that daily supplementation of large doses of vitamin C reduced the incidence of symptoms of URTI in athletes after they participated in extreme exercise (ultramarathon races). The results of one of these studies also show that the supplementation of additional dietary antioxidants (vitamin E and b-carotene) does not confer any additional beneficial effect.

The doses of vitamin C used in these studies (600 to 1,000 mg/day) were very high.

> In a more recent randomized, double-blind, placebo-controlled study, intake of 1,500 mg/day of vitamin C for 7 days before an ultramarathon race and consumption of vitamin C in a carbohydrate beverage during the race (subjects in the placebo group consumed the same carbohydrate beverage without added vitamin C) did not affect oxidative stress, cytokine, or immune function measures during and after the race. (Nieman et al., 2002, as cited in Gleeson, Bishop, & Walsh, 2013, p. 227).
>
> The most recent Cochrane meta-analysis examined the evidence that daily doses of more than 200 mg vitamin C were more effective than placebo in preventing or treating the common cold (Douglas *et al.*, 2007). Twenty-nine trial comparisons involving 11,077 study participants contributed to this meta-analysis on the relative risk (RR) of developing a cold while taking prophylactic vitamin C. The pooled RR was 0.96 (95% CI 0.92 to 1.00). A subgroup of six trials that involved physically active subjects (a total of 642 marathon runners, skiers, and soldiers on subarctic exercises) reported a pooled RR of 0.50 (95% CI 0.38 to 0.66). Thirty comparisons that involved 9,676 respiratory episodes contributed to the meta-analysis on common cold duration during vitamin C or placebo supplementation. A consistent benefit of vitamin C was observed, representing a reduction in cold duration of 8% (95% CI 3% to 13%) for adult participants and 13.5% (95% CI 5% to 21%) for child participants. Fifteen trial comparisons that involved 7,045 respiratory episodes contributed to the meta-analysis of severity of episodes experienced while on prophylaxis and the results revealed a benefit of vitamin C when days confined to home and off work or school

> were taken as a measure of severity. A limited number of trials had examined cold duration and severity during therapy with vitamin C that was initiated after the onset of cold symptoms and no significant differences from placebo were found. The authors concluded that the failure of vitamin C supplementation to reduce the incidence of colds in the normal population indicates that routine mega-dose prophylaxis is not generally justified but that individuals subjected to brief periods of severe physical exercise or cold environments may well gain some benefit. (Gleeson et al., 2013, p. 228-229).

"Thus, although some inconsistencies are seen in the literature regarding antioxidant supplementation and immune responses to exercise, there is some basis for believing that such supplementation could have beneficial effects in alleviating exercise-induced immunodepression." (Gleeson, 2006a, p. 125). But even if high-dose antioxidant supplementation offers some protective effect of infection risk, "athletes need to consider the risks, which may include the blunting of some of the adaptations to training" (Gleeson et al., 2013, p. 229).

For vitamin A, β -carotene, and vitamin E there may be less evidence but the potential negative effects are still present.

As there is little evidence of any immune benefit from excessive supplementation with antioxidant vitamins (with the possible exception of vitamin C) this practice cannot be recommended. "Indeed, over-supplementation can diminish the body's natural antioxidant defense system and may attenuate some endurance training adaptations such as mitochondrial biogenesis" (Gomez-Cabrera, Ristow, & Vina, 2012; Merry & Ristow, 2016; Ristow et al., 2009; as cited in Jeunkendrup & Gleeson, 2018, p. 396). Thus, probably the wisest option is to ensure that the diet contains plenty of fresh fruit and vegetables.

Vitamin B_{12} and Folic Acid

Vitamin B_{12} and folic-acid deficiencies have profound effects on immune function. Both of these vitamins are essential for the synthesis of nucleic acids and hence are required for the normal production of red and white blood cells in the bone marrow. Vitamin B_{12} can be absorbed from the gut only in the presence of the glycoprotein intrinsic factor. Lack of this factor or deficiency of vitamin B_{12} causes pernicious anemia, which has detrimental effects on immune function. For example, impaired lymphocyte proliferative responses to mitogens, and a modest reduction in the phagocytic and bactericidal capacity of neutrophils have been reported in people with primary pernicious anemia. The only natural sources of vitamin B_{12} are of animal origin. As such, vegetarian athletes and athletes who are avoiding dairy produce to minimize saturated fat intake are at high risk of deficiency of this vitamin. If fat intake is a concern, then athletes should select non-fat or low-fat dairy products that provide the same (or higher) level of B_{12} as full-fat dairy products (Jeukendrup & Gleeson, 2018).

Vitamin D

While most athletes who consume a varied diet sufficient to meet their energy needs should meet their micronutrient requirements, one exception can be the failure to achieve adequate vitamin D status (He et al., 2013). In recent years it has been established that vitamin D is not only important for calcium homeostasis and bone health but also for the optimal function of skeletal muscle and immune function as well as some other health outcomes.

“Vitamin D is not actually a vitamin but a secosteroid hormone [that is mostly] produced in the skin from 7-dehydrocholesterol after exposure to sunlight ultraviolet-B radiation” (Gleeson et al., 2013, p. 229). Two forms of vitamin D can be obtained from dietary sources: vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol). The endogenously synthesised vitamin D3 and diet-derived D2 and D3 must first be hydroxylated in the liver into 25-hydroxy vitamin D (25(OH)D), the main storage form (Jeukendrup & Gleeson, 2018). In the second hydroxylation, 25(OH)D is converted to the biologically active form, 1,25-dihydroxy vitamin D (1, $25(OH)_2D$), by 1-α-hydroxylase in the kidney or some cells in non-renal compartments, including several immune system cells including T cells, B cells, macrophages and dendritic cells (Aranow, 2011).

Vitamin D status is determined by measuring the serum concentration of the major circulating form of the prohormone, 25-hydroxyvitamin D (25(OH)D) which is formed in the liver. Vitamin D deficiency (serum 25(OH)D < 40 nmol/L) is not uncommon and reaches epidemic levels among adults with limited sunlight exposure (Calder & Yaqoob, 2013, p. 668**.**

“A recent study in university athletes reported a higher level of plasma cathelicidin and salivary secretory immunoglobulin A (SIgA) secretion in those who had plasma 25(OH)D greater than 120 nmol/L compared with those who had lower vitamin D status” (He et al., 2013).

> Furthermore, low vitamin D status (25(OH)D <30 nmol/L) was associated with substantially lower in vitro antigen-stimulated production of the pro-inflammatory cytokines (IL-6, IFN-g and TNF-α) by whole blood culture than in athletes with high vitamin D status (25(OH)D >90 nmol/L). (Jeukendrup & Gleeson, 2018, 398).

“A higher pro-inflammatory cytokine production in response to an antigen challenge with better vitamin D status could be seen as being beneficial to host defense against pathogenic microorganisms” (He et al., 2013), and indeed, in the He et al. (2013) study, those athletes with relatively high vitamin D status had fewer upper respiratory tract illness (URI) episodes during 4 winter months than those with inadequate levels of vitamin D. Moreover, in those who experienced at least one URI episode, both the severity and duration of symptoms were negatively associated with vitamin D status.

Under most circumstances the major source of vitamin D (~80-90%) comes from skin sunlight exposure, thus dietary vitamin D typically accounts for a small component (~10-20%). “The main dietary sources of vitamin D are found in food from animal origin, such as egg yolk, cod-liver oil, and salmon (most of this as vitamin D3), and vitamin D2 is present in some plants and fungi” (Jeukendrup & Gleeson, 2018). Also some breakfast cereals, dairy products and margarines may be fortified with vitamin D. Diet and supplements become a very important source of vitamin D in northerly latitudes during the wintertime because the limited sunlight exposure and weak strength of the sunlight at this time of year is known to be inadequate for inducing endogenous vitamin D production. Adequate skin sunlight exposure to avoid vitamin D deficiency is about 15 minutes in the middle of the day several times each week.

“Vitamin D insufficiency has been reported to be common in athletes in the United Kingdom especially when training in the winter months (Close et al., 2013; He et al., 2013; Morton et al. 2012)” (Jeukendrup & Gleeson, 2018). A study that assessed the vitamin D status of UK-based professional athletes (latitude 53°N) reported that 62% of athletes (38/61) including “professional rugby players, soccer players and jockeys had inadequate serum total 25(OH)D concentrations (< 50 nmol/L) in the winter months (Close et al., 2013)” (Jeukendrup & Gleeson, 2018). In a study of elite soccer players in the English Premier League, 65% (13/20) of players presented serum total 25(OH)D concentrations <50 nmol/L in December (Morton et al., 2012)

In summary, the overwhelming evidence points to the benefits of avoiding vitamin D deficiency to maintain immunity and prevent respiratory infection in athletes and military personnel (see review by He et al., 2016 “Recent work in athletes shows beneficial effects of optimising vitamin D status on innate and mucosal immunity” Although the Institute of Medicine describes vitamin D sufficiency (for bone health) as a circulating 25(OH)D level > 50 nmol/L, recent evidence tentatively supports an optimal circulating 25(OH)D level of 75 nmol/L for the prevention of upper respiratory infections (He et al., 2016).

This is difficult to achieve in winter from dietary sources of vitamin D alone but very high doses of oral vitamin D supplements (e.g. → 250 µg or 10,000 IU per day) do not appear necessary to reach this proposed optimal vitamin D status for immune health; in addition, consuming very high doses of oral vitamin D supplements raises the risk of toxicity.

Practical recommendations are, firstly, to get adequate but safe summer sunlight exposure. At latitudes of 30-60 °N vitamin D sufficiency (circulating 25(OH)D level > 50 nmol/L) can be achieved in most people by spending as little as 15 minutes in the summer sun between 10am and 3pm, on most days each week wearing T-shirt and shorts. Secondly, a daily supplement of 50-100 µg or 2,000-4,000 IU vitamin D3 can help to maintain vitamin D status during the winter months.

Vitamin supplements and megadoses

"In general, supplementation with individual vitamins or consumption of large doses of simple antioxidant mixtures is not recommended" (Jeukendrup & Gleeson, 2018, p. 290). "Athletes should obtain complex mixtures of antioxidant compounds from increased consumption of fruits and vegetables" (Gleeson, 2006b, p. 258).

> Consuming megadoses of individual vitamins is likely to do more harm than good. Because most vitamins function mainly as coenzymes in the body, after the enzyme systems are saturated, the vitamins in free form can have toxic effects. For example, 300 mg of vitamin E (as α-tocopherol acetate), given daily to 18 men for 3 weeks, produced a significant depression in the bactericidal activity of peripheral blood leukocytes and mitogen-induced lymphocyte proliferation. (Gleeson & Jeukendrup, 2018)

Consuming "megadoses of vitamin A may impair the inflammatory response and complement formation as well as having other pathological effects, including causing... fetal abnormalities when consumed by pregnant women" (Gleeson, 2006b, p. 186) and reducing bone mineral density. "Vitamin D3 in doses of up to 100 µg or 4,000 IU/ day is known to be safe, but toxicity becomes a risk (e.g.hypercalcemia, kidney stones) at daily doses In excess of 250 µg or 10,000 IU/ day" (Gleeson & Jeukendrup, 2018).

4.2.3 Minerals

> Minerals are classified as macrominerals or microminerals (trace elements), based on the extent of their occurrence in the body. Of particular importance here are the trace elements that each compose less than 0.01% of total body mass of which 14 have been identified as essential for maintenance of health. (Nieman & Pedersen, 2000, p. 150).

Of these 14, "several... are known to exert modulatory effects on immune function" (Nieman & Pedersen, 2000, p. 150), including zinc, iron, selenium, and copper.

> Yet with the exception of zinc and iron, isolated deficiencies are rare. Indeed, iron deficiency is reported to be the most widespread nutrient deficiency in the world, and field studies consistently associate iron deficiency with increased morbidity from infectious disease. Furthermore, Exercise has a pronounced effect on both zinc and iron metabolism. (Bishop, Blannin, Walsh, Robson, & Gleeson, September, 1999, p. 169).

Zinc

> The role of zinc... in immune function has received increasing attention in recent years. Zinc is essential for the development of the immune system, and more than 100 metalloenzymes have been identified as zinc-dependent, including those involved in the transcription [of DNA] and synthesis of proteins. For example, zinc is a cofactor for the enzyme terminal deoxynucleotidyl transferase, which is required by immature T-cells for their replication and functioning. The effects of zinc deficiency on immune function include lymphoid atrophy, decreased delayed-hypersensitivity cutaneous responses, decreased IL-2 production, impaired mitogen-stimulated lymphocyte proliferative responses, and decreased NKCA. Furthermore, Zinc availability affects superoxide free-radical production by stimulated macrophages, although in the laboratory this effect seems to depend on the actual molecular form of zinc.
>
> Vegetarian athletes are at risk for zinc deficiency because meat and seafood are the richest zinc sources... Although nuts, legumes, and whole grains are good sources of zinc, the high levels of fiber in these foods can decrease zinc absorption. Zinc deficiency can also be a problem for athletes in sports where a low body mass is thought to confer a performance advantage. Very low-energy or starvation-type diets may induce significant zinc losses.... As zinc is lost from the body mainly in sweat and urine and these losses are increased by exercise, it is possible that a heavy schedule of exercise training could induce a zinc deficiency in athletes. Certainly, highly trained women have significantly higher urinary zinc excretion compared with untrained control individuals. (Bishop et al., September, 1999, pp. 169-170).

And in well-trained male games players an acute bout of high-intensity exercise increases daily urinary zinc excretion by 34% compared with resting values (Bishop et al., September, 1999).

Male and female athletes have lower plasma zinc concentrations than untrained people. Studies concerning the relationship between immune function, exercise, and zinc status in athletes are lacking.

> However, a study of male runners found that 6 days of zinc supplementation (25 mg of zinc and 1.5 mg of copper, twice a day) inhibited the exercise--associated increase in superoxide free-radical formation by activated neutrophils... and exaggerated the exercise-induced suppression of T-lymphocyte proliferation in response to mitogens. Such effects might temporarily predispose athletes to opportunistic infection. Megadoses of zinc have further detrimental effects on immune function. The administration of zinc (150 mg twice a day) to 11 healthy males for a 6-week period was associated with reduced T-lymphocyte proliferative responses to mitogen stimulation and impaired neutrophil phagocytic.. activity. Hence, megadoses of zinc are not recommended. Athletes should be encouraged to emphasize zinc-rich foods in the diet (e.g., poultry, meat, fish, and dairy products). Vegetarians have been recommended to take a 10 to 20 mg supplement of zinc daily [the RDA is 10 mg and 12 mg for females and males, respectively], but in view of the... findings [just discussed], supplements at the lower end of this range may be more suitable for vegetarian athletes.
>
> The efficacy of zinc supplementation as a treatment for the common cold has been investigated in at least 11 studies... published since 1984. The findings have been equivocal, and recent reviews of this topic have concluded that further research is necessary before the use of zinc supplements to treat the common cold can be recommended (Macknin, 1999; Marshall, 2000). (Gleeson, 2006b, pp. 194-195).
>
> Although only limited evidence suggests that taking zinc supplements reduces the incidence of URTI (McElroy, & Miller, 2002; Veverka et al., 2009), in the studies that have reported a beneficial effect of zinc in treating the common cold (i.e., reduction of symptom duration, severity, or both) zinc lozenges with high ionic zinc content (> 75 ·mg/day) had to be taken within 24 hours of the onset of symptoms to be of any benefit (Hemila, 2011). Potential problems with zinc supplements include nausea, bad taste reactions, lowering of HDL cholesterol, depression of some immune cell functions (e.g., neutrophil oxidative burst), and interference with the absorption of copper (Gleeson, 2000). (Jeukendrup & Gleeson, 2018).

Iron

“Iron deficiency is prevalent throughout the world and by some estimates as much as 25% of the world’s population is iron deficient” (Bishop et al., ., September, 1999, p. 170). Endurance competitors risk potential iron deficiency because of increased iron losses in sweat, urine, and feces. The incidence of iron depletion among athletes, however, “is no greater than that found for the general population. Nevertheless, exercise may contribute to an iron-depleted state; the acute-phase host response to stress (including exercise) involves the depression of circulating free iron levels” (Gleeson, 2006b, p. 195).

> Stress-induced elevation of IL-1 causes granulocyte release of the iron-binding protein lactoferrin within the circulation. Lactoferrinis then thought to bind (chelate) iron from transferrin and form lactoferrin-iron complexes, which leads to a depression of plasma iron concentration that is independent of plasma volume changes. (Jeukendrup & Gleeson, 2018).
>
> The immune system itself appears to be particularly sensitive to the availability of iron. Iron deficiency has neither completely harmful nor enhancing effects on immune function. On the one hand, free iron is necessary for bacterial growth: removal of iron with the help of chelating agents such as lactoferrin reduces bacterial multiplication, particularly in the presence of a specific antibody. (Gleeson, 2006b, p. 195).

“A study reported that iron-deficient mice had a lower mortality after infection with *Salmonella* compared with iron-replete mice” (Jeukendrup & Gleeson, 2018).

> Thus, iron deficiency may… protect an individual from infection, whereas supplementation may predispose the individual to infectious disease, particularly because iron catalyzes the production of hydroxyl free radicals, and high intake of iron can impair gastrointestinal zinc absorption. On the other hand, iron deficiency depresses various aspects of immune function, including macrophage IL-1 production, the lymphocyte proliferative response to mitogens, NKCA [neutrophil phagocytic activity] and delayed cutaneous hypersensitivity [an index of cell-mediated immune function]…
>
> A number of causes of iron deficiency in endurance athletes involved in heavy training have been suggested: exercise may cause reductions in gastrointestinal iron absorption, and iron is lost in sweat, which contains 0.3 mg/L… This could contribute to losses of up to 1.0 mg of iron per day in athletes who are training extensively. Because only about 10% of dietary iron is absorbed, [such losses] increase the dietary requirement by about 10 mg/day, which is approximately double the normal daily iron requirement [the RDA is 15 mg for females and 10 mg for males]. (Gleeson, 2006b, pp. 195-196).

In addition, some damage to red blood cells (hemolysis) may occur in runners and games players because of foot strike, and in swimmers because of body friction in moving through the water. Subsequently, loss of hemoglobin in the urine will occur, although this loss is thought to be a negligible drain on iron stores. Some athletes are also susceptible to gastrointestinal bleeding during exercise, which may increase fecal iron losses.

The bioavailability of iron is lower in vegetarian diets because of the lack of heme iron, which is more easily absorbed. The consensus is that all athletes should be aware of foods rich in heme iron such as lean red meat, poultry, and fish, and include them in the daily diet. Iron requirements in endurance athletes may double the RDA, although these requirements can be met through the diet without the need for artificial supplements. Vegetarian athletes should ensure that plant food choices are iron dense (e.g., green leafy vegetables, legumes, whole-grain breads and pasta, and iron-fortified products) (Jeukendrup & Gleeson, 2018). Some breakfast cereals, bars, and bread are fortified with iron and provide a good source, though usually in amounts less than the RDA. “Megadoses of iron are not advised, and routine oral supplements of iron should not be taken without medical advice” (Jeukendrup & Gleeson, 2018).

Selenium

> Selenium deficiency can affect all components of the immune system. Selenium is a cofactor of glutathione peroxidase and reductase and thus influences the quenching of ROS. As such, the requirement for selenium may increase in athletes involved in regular intensive training programs. But any selenium supplement should be taken with caution. (Jeukendrup & Gleeson, 2018).

“Supplements with doses up to the RDA appear nontoxic, but the safety of larger doses has not been confirmed. Intakes of 25 mg (approximately 40 times the RDA) have been associated with vomiting, abdominal pain, hair loss, and fatigue” (Jeukendrup & Gleeson, 2018).

Copper

> The effects of copper deficiency on immune function include impaired antibody formation, inflammatory response, neutrophil phagocytosis, NKCA, and lymphocyte stimulation responses. The results of changes in copper status due to exercise and training are controversial, and perhaps reflect the inadequacy of techniques used to measure copper status. (Nieman & Pedersen, 2000, p. 147).

With exercise

some redistribution of copper between body compartments may occur…, and athletes have been reported to lose copper in sweat collected after exercise. Although copper deficiency is rare in humans, athletes who take zinc supplements may compromise the gastrointestinal absorption of copper because of the similar physicochemical properties of these two minerals. (Jeukendrup & Gleeson, 2018).

Magnesium

Magnesium is an essential cofactor for many enzymes involved in biosynthetic processes and energy metabolism and is required for normal neuromuscular coordination. The total-body content of magnesium is about 25 g. The RDA for magnesium is 350 mg/day for men and 280 mg/day^{-1} for women; hence, magnesium is classified as a macromineral rather than a trace element. Most studies of dietary habits in athletes suggest that magnesium intake exceeds the RDA. But the data used to determine RDAs for micronutrients often did not include athletes, or the activity levels of the subjects were not reported. Therefore, although the RDAs may apply to the sedentary population, they may not be an accurate means of evaluating the nutritional needs of athletes. Several studies report low serum magnesium concentrations in athletes, and prolonged strenuous exercise is associated with increased losses of magnesium in urine and sweat. As with zinc and iron, a single bout of exercise is unlikely to induce substantial magnesium losses, but a state of mild magnesium deficiency may be induced during a period of heavy training, particularly in a warm environment where sweat losses are high.

Magnesium deficiency in both humans and animals is associated with neuromuscular abnormalities, including muscle weakness, cramps, and structural damage of muscle fibers and organelles. The structural damage may be caused by an impairment of calcium homeostasis secondary to an oxygen free-radical-induced alteration in the integrity of the membrane of the sarcoplasmic reticulum. A lack of magnesium may also be associated with a depletion of selenium and reduced glutathione peroxidase activity, which increases the susceptibility to damage by free radicals. Hence, magnesium deficiency may potentiate exercise-induced muscle damage and stress responses, but direct evidence for this effect is lacking (Nieman & Pedersen, 2000, pp. 146-147).

Manganese

Manganese is a co-factor of the enzyme superoxide dismutase, which aids in protection against free radicals. The RDA for manganese is 2.0 to 5.0 mg/day. Sources are whole-grain products, dried peas and beans, leafy vegetables, and bananas. The effects of exercise on manganese status are presently unknown, but training is associated with an increase in levels of antioxidant enzymes, suggesting an increased requirement for manganese during periods of increased training. As with other trace elements, losses of manganese in urine and sweat are likely higher in athletes than in nonathletes. (Nieman & Pedersen, 2000, p. 148).

Cobalt

Cobalt as a component of vitamin B_{12} promotes the development of red and white blood cells in the bone marrow. Deficiencies are associated with pernicious anemia, reduced blood leukocyte counts, impaired lymphocyte proliferation, and impaired bactericidal capacity of neutrophils. Major food sources of cobalt are meat, liver, and milk. Hence, athletes who avoid animal foods are at risk for cobalt and vitamin B_{12} deficiency. (Gleeson, 2006b, p. 198).

Fluorine

Although not directly required for normal immune function, fluorine is needed for the normal formation of healthy bones and teeth, and it protects against dental caries (tooth decay by oral bacteria). Given the relatively high intake of sugary foods and sports drinks by athletes, good oral hygiene is important in maintaining healthy teeth. Frequent intakes of soft drinks and carbohydrates, particularly sugars, depress the oral pH with a resultant net demineralization of the teeth. Sugars are metabolized to organic acids by the bacteria in the plaque on teeth and gums. Therefore, all sports people should maintain good plaque control. The RDA for fluorine is 1.5 to 4.0 mg/day, and this trace element is found in milk, egg yolk, seafood, and drinking water. Several toothpastes and mouth rinses contain fluorine (as sodium fluoride), and in some countries, including the United States, fluoride is added to drinking water. (Gleeson, 2006b, p. 198).

4.2.4 Dietary Immunostimulants

> Certain supplements may boost immune function and reduce infection risk in immunocompromised people, including athletes engaged in heavy training and competition. Many nutritional supplements are on the market besides the amino acids (e.g., glutamine), vitamins (e.g., vitamin C), and minerals (e.g., zinc) already mentioned in this chapter that are claimed to boost immunity. These include ß-glucans, bovine colostrum, probiotics, and herbals such as echinacea, kaloba, ginseng, and curcumin. The claims for many of these supplements are often based on selective evidence of efficacy in animals, in vitro experiments, children, the elderly, or clinical patients in severe catabolic states. Direct evidence for their efficacy for preventing exercise-induced immune depression or improving immune system status in athletes is usually lacking. In recent years, however, the effects of some of these supplements on immune function or infection incidence have been evaluated in physically active populations. (Jeukendrup & Gleeson, 2018, p. 402).

Table 1 provides a summary of some of the most commonly used supplements and a rating of their efficacy in enhancing immunity and/or reducing infection risk in athletes.

Table 1: Nutrition supplements (listed in alphabetical order) that are claimed to boost immunity and reduce URS incidence in athletes: proposed mechanisms of action and summary of evidence for efficacy.

Supplement	What is it, what are the effects?	Evidence
β-glucans	Polysaccharides derived from the cell walls of yeast, fungi and oats that stimulate innate immunity. Effective in mice inoculated with influenza virus but mixed results from human studies for immune modulation and URS incidence.	●●○○○
Bovine colostrum	First milk of the cow that contains antibodies, growth factors and cytokines. Claimed to boost mucosal immunity and increase resistance to infection. Several studies in athletes that indicate some immune boosting effects and reduced URS incidence and duration.	●●●○○
Carbohydrate	Maintains blood glucose during exercise, lowers stress hormone and anti-inflammatory cytokine responses, and thus counters immune dysfunction. Ingestion of carbohydrate (30-60 g/h) attenuates stress hormone and some (but not all) immune perturbations during	●●●○○

	exercise but only very limited evidence that this modifies infection risk in human athletes.	
Echinacea	Herbal extract that is a popular supplement among athletes. Claimed to boost immunity via stimulatory effects on macrophages and there is some in vitro evidence for this. Early human studies indicated possible beneficial effects but more recent, larger scale and better controlled studies indicate no effect of Echinacea on infection incidence or cold symptom severity.	●○○○○
Glutamine	Nonessential amino acid that is a precursor in the synthesis of nucleic acids and important for rapidly dividing cells. Also an important fuel for immune cells. Plasma concentration of glutamine falls during prolonged exercise. Supplementation before and after exercise does not alter immune perturbations despite maintenance of plasma glutamine.	●○○○○
Kaloba	Herbal medicine that has been shown to boost some aspects of immunity in vitro via stimulatory effects on macrophages. Evidence from human studies for reduction in severity and duration of symptoms of sinusitis and common cold but used as a treatment rather than as a preventative.	●○○○○
N-3 Polyunsaturated fatty acids	Exert anti-inflammatory effects post-exercise. No evidence in exercising humans.	○○○○○
Probiotics	Probiotics are live microorganisms which when administered orally for several weeks, can increase the numbers of beneficial bacteria in the gut. This has been associated with a range of potential benefits to gut health, as well as modulation of immune function. Human studies show improvements in some aspects of acquired immunity and reduced incidence of URS and gastrointestinal problems.	●●●○○
Quercetin	A plant flavonoid; in vitro studies show strong anti-inflammatory, anti-oxidative, and anti-pathogenic effects. Animal data indicate increase in mitochondrial biogenesis and endurance performance. Human studies show some reduction in URS incidence during short periods of intensified training and mild	●●●○○

	stimulation of mitochondrial biogenesis and endurance performance in untrained subjects.	
Quercetin with epigallocatechin gallate	Flavonoid mixture promotes anti-inflammatory and anti-oxidative effects, and immune function improvement, above that of quercetin alone. Human study showed strong anti-inflammatory effect, with modest anti-oxidative effect and improvement in innate immunity but no data on URS incidence.	●●●○○
Vitamin C	An essential water-soluble antioxidant vitamin that quenches reactive oxygen species and augments immunity. Reduces interleukin-6 and cortisol responses to exercise in humans. Relatively small effects on cortisol compared with carbohydrate; immune measures no different from placebo. Some evidence of efficacy in reducing URS incidence after ultramarathon events.	●●○○○
Vitamin D3	Fat soluble vitamin that is mostly produced via the action of sunlight in the skin. Induces production of antimicrobial proteins, enhances natural killer cell cytolytic activity, increases the generation of reactive oxygen species in phagocytic cells, augments macrophage interleukin-1β secretion and upregulates the expression of CD14, the lipopolysaccharide receptor. Low vitamin D status is associated with low saliva immunoglobulin A secretion, low pro-inflammatory cytokine production by antigen-stimulated mononuclear cells and increased respiratory infection risk with longer lasting illness symptoms. Oral vitamin D3 supplements of around 4,000 IU · day^{-1} can reduce URS incidence.	●●●●○
Vitamin E	An essential fat-soluble antioxidant vitamin that quenches exercise-induced reactive oxygen species and augments immunity. Good evidence for some immune boosting effects in the frail elderly. No evidence of similar benefit for younger healthy humans or athletes.	●○○○○
Zinc	Zinc deficiency results in impaired immunity and zinc deficiency is not uncommon in athletes. An essential mineral that is claimed to reduce incidence and duration of colds. No evidence for reduced infection incidence with zinc supplementation in adult humans.	●○○○○

	Some (but not all) human studies suggest a reduction in duration of cold symptoms if zinc gluconate lozenges are administered within 24 h of cold symptom onset. Unlikely to be of any real benefit to athletes unless they are zinc deficient.	

Source: Gleeson, 2016b, p. 16 (https://dspace.lboro.ac.uk/dspace-jspui/bitstream/2134/20675/1/ICB%E2%80%93%20ACCEPTED%20MS%20%E2%80%93GLEESON%2004-12-2015.pdf). The scientific evidence is indicated with ●●●●● meaning very strong evidence and ○○○○○ meaning limited to no evidence.

Echinacea and other herbals

Several herbal preparations are reputed to have immunostimulatory effects, and consumption of products containing *Echinacea purpurea* is widespread among athletes. In a double-blinded, placebo-controlled study, the effect of a daily oral pretreatment for 28 days with pressed juice of Echinacea purpurea was investigated in 42 triathletes before and after a sprint triathlon (Berg et al., 1998). A subgroup of athletes was also treated with magnesium as a reference for supplementation with a micronutrient important for optimal muscular function. During the 28-day pretreatment period, none of the athletes in the echinacea group became ill, compared with 3 subjects in the magnesium group and 4 subjects in the placebo group. Pretreatment with echinacea appeared to reduce the release of soluble IL-2 receptor before and after the race and increased the exercise-induced rise in lL-6.

Numerous experiments have shown that Echinacea purpurea extracts exert significant immunomodulatory effects in vitro. These effects include the activation of macrophages, neutrophils and natural killer cells and there are a few reports of changes in the numbers and activities of T-cell and B-cell leukocytes. However, evidence of positive effects on leukocyte activities *in vitro* does not mean that these effects will also be observed *in vivo*. Several dozen human experiments, including a number of blind, randomized trials, report modest health benefits, particularly those that have examined the effects of Echinacea purpurea extracts in the treatment of acute URTI. However, the majority of these trials have been limited both in size and in methodological quality. In a randomized, double-blind, placebo-controlled trial, administering unrefined echinacea at the onset of symptoms of URTI in 148 college students did not provide any detectable benefit or harm compared with placebo (Barrett et al., 2002).

In a meta-analysis of trials on echinacea (Linde, Barrett, Wolkart, Bauer, & Melchart, 2006) that included 22 well-controlled trials, three trials

> investigated prevention of colds and 19 trials tested treatment of colds. A variety of different echinacea preparations were used. None of the three comparisons in the prevention trials showed any benefit of echinacea over placebo. In the trials that examined the effectiveness of echinacea versus placebo in the treatment of colds, a significant beneficial effect was reported in nine comparisons, a trend in one, and no difference in six. The authors' main conclusions were that there is some evidence that preparations based on the aerial parts of the echinacea plant might be effective for the early treatment of colds in adults but that results have not been fully consistent. In the relatively few large scale, well-controlled randomized trials that have been performed, no beneficial effects of echinacea have been shown. Hence, it is still rather uncertain whether or not echinacea has any real value in preventing or treating URTI in the general population and only a very few trials, with small numbers of subjects have attempted to examine its effectiveness for reducing URS in athletes. (Jeukendrup & Gleeson, 2018)

The active ingredients of Echinacea extracts are thought to include alkamides, chicoric acid, and polysaccharides.

> Other herbals are also claimed to have various antiviral, anti-bacterial, immune-modulating and antioxidant properties. Examples include extracts of elderberries (Sambucus nigra which contains flavonoids, anthocyanins, glycosides, viburnic acid and vitamins A and C), kaloba (the common name for an extract of the roots of Pelargonium sidoides which contains flavan-3-ols, 7-hydroxycoumarin derivatives, proteins and saccharides), ginseng (Panax quinquefolium which contains mostly poly-furanosyl-pyranosyl-saccharides), astragalus (Astragalus membranaceus which contains polysaccharides, flavonoids, multiple trace minerals and amino acids) and leaves of the olive tree (Olea europaea which contains phenolic compounds such as oleuropein and its derivative elenoic acid). Much of the evidence base for these herbal preparations is based on in vitro studies demonstrating immune cell stimulatory effects or direct anti-viral actions (preventing viral entry into host cells or viral replication). Most preparations like echinacea and others that are classed as 'herbal medicines' are used to reduce the severity and duration of cold symptoms rather than to prevent infections. (Jeukendrup & Gleeson, 2018)

Whether these are more effective than taking anti-viral medications or non-prescription cold remedies containing local anaesthetics, anti-inflammatories, decongestants, and stimulants (e.g. ephedrine, caffeine) for the treatment of URTI symptoms such as sore throat, nasal congestion and coughs is debatable. (Calder & Yaqoob, 2013)

Curcumin

Curcumin (diferuloylmethane) is an orange yellow component of turmeric, a spice that is commonly found in curry powders and sauces.

“Traditionally, curcumin has been known for its an anti-inflammatory effects, and several studies have demonstrated that curcumin is a potent immunomodulatory agent that can modulate the activation of T-cells, B-cells, NK cells, neutrophils, macrophages, and dendritic cells” (Jagetia, & Aggarwal, 2007, as cited in Jeukendrup & Gleeson, 2018)

“Curcumin can also downregulate the expression of various proinflammatory cytokines including TNF, IL-1, and IL-2… most likely through inactivation of the transcription factor NF-kappaB. Interestingly, however, curcumin at low doses can also enhance antibody responses” (Jagetia, & Aggarwal, 2007).

Polyphenols

“The plant kingdom uses tens of thousands of secondary metabolites (generally referred to as phytonutrients) including terpenes, alkaloids and phenolics for defence” (Jeukendrup & Gleeson, 2018), attraction, and protection. The phenolic compounds or polyphenols are divided into four main classes: “flavonoids (~50% of all polyphenols), phenolic acids, lignans, and stilbenes” (Jeukendrup & Gleeson, 2018)

> Flavonoids are further classified into six simple (flavan-3-ols, flavanones, flavones, isoflavones, flavonols, anthocyanins) and two complex (condensed and derived tannins) subgroups. In foods, flavonoids, lignans, and stilbenes are usually found as glycosides, and phenolic acids as esters with various polyols, and structural variations influence their absorption and bioavailability. A recent systematic review and meta-analysis showed that flavonoid supplementation (range of 0.2 to 1.2 g/day in 14 selected studies) decreased acute URS episode incidence by 33% compared with control or placebo treatments (Somerville, Braakhuis, & Hopkins, 2016). One flavonoid in particular, quercetin, has received a lot of attention in recent years in relation to its possible effects on exercise performance, training adaptation and immune function. (Jeukendrup & Gleeson, 2018, p. 404).

Quercetin is “found in variety of fruits and vegetables… [with] the richest food sources of quercetin being apples, blueberries, broccoli, curly kale, hot peppers, onions and tea” (Calder & Yaqoob, 2013)

> Total daily flavonol intake (with quercetin representing about 75%) varies from 13 to 64 mg depending on the study sample and the population

studied. Human subjects can absorb significant amounts of quercetin from food or supplements, and elimination is quite slow, with a reported half-life ranging from 11-28 hours. Animal studies indicate that 7 days of quercetin feeding improves survival from influenza virus inoculation. (Davis, Murphy, McClellan, Carmichael, & Gangemi, 2008, as cited in Gleeson, 2013).

A few human trials have now been conducted and a double-blind, placebo controlled study with 40 cyclists showed that 1,000 mg/day quercetin for 3 weeks significantly increased plasma quercetin levels and reduced URTI incidence during the 2-week period following 3 successive days of exhaustive exercise (Nieman et al., 2007). In this study a surprisingly high proportion (45%) of subjects in the placebo group reported URTI symptoms in the 2-week post-training period, yet markers of immune dysfunction, inflammation, and oxidative stress were not different from the quercetin treated group, suggesting that quercetin exerted direct anti-viral effects, at least within the context of the study design. There is increasing support for coingestion of quercetin with other flavonoids and food components to improve and extend quercetin's bioavailability and bioactive effects. These include the flavonoid epigallocatechin 3-gallate (EGCG) from tea, isoquercetin which is the glycosylated form of quercetin in onions and other foods, n- 3 PUFA such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), vitamin C and folate.

Other naturally occurring polyphenolic compounds are present in foods such green leafy vegetables, onions, apples, pears, citrus fruits and red grapes as well as some plant-based beverages such as citrus juices, green tea, red wine and beer. A large scale study in physical active individuals indicated that a high fruit intake was associated with fewer respiratory illness episodes (Nieman et al., 2011). (Calder & Yaqoob, 2013)

β-Glucans

β-Glucans are not only present as major structural components of the cell walls of yeast, fungi and some bacteria, but are also present in the diet as part the endosperm cell wall in cereals, such as barley and oat. β-Glucans are carbohydrates consisting of linked glucose molecules and differ in macromolecular structure depending on the source. β-glucans from bacteria are unbranched 1,3 β-linked glycopyranosyl residues. The cell wall β-glucans of yeast and fungi consists of 1,3 β-linked glycopyranosyl residues with small numbers of 1,6 β-linked branches, whereas oat and barley cell walls contain unbranched β-glucans with 1,3 and 1,4 β-linked

> glycopyranosyl residues. The specific characteristics of the various β-glucans may influence their immune modulating effects... This implies that the addition of β-glucans to the diet may be used to modulate immune function and so might improve the resistance against invading pathogens in humans... Therefore, it might be possible to modulate immune function by increasing the dietary β-glucan intake, for example by developing functional foods. (Calder & Yaqoob, 2013, p. 652)
>
> One trial in humans found no effect of 3 weeks of oat β-glucan supplementation on immune responses to exercise or infection incidence during the 2-week period following 3 successive days of exhaustive exercise [Nieman et al., 2008]. More recently, however, another human study reported a 37% reduction in the number of URS days following a marathon with yeast β-glucan supplementation versus placebo which the authors attributed to a post-exercise increase in salivary IgA [McFarlin, Carpenter, Davidson, & McFarlin, 2013]. (Gleeson, February, 2016)

At present, however, there is not enough evidence to recommend β-glucan supplements to improve immune function.

Probiotics

> Probiotics are food supplements that contain live microorganisms which when administered in adequate amounts confer a health benefit on the host. There is now a reasonable body of evidence that regular consumption of probiotics can modify the population of the gut dwelling bacteria (microbiota) and influence immune function..., although it should be noted that such effects are strain specific. (Gleeson et al., 2013, p. 234).

Probiotics survive transit through the acid conditions of stomach into the intestine, where they may modify the intestinal microbiota in such a way that the numbers of beneficial bacteria increase and usually numbers of species considered harmful are decreased. These effects have been associated with a range of potential benefits to the health and functioning of the digestive system, as well as modulation of immune function.

> Probiotics have many mechanisms of action. By their growth and metabolism, they help inhibit the growth and reduce any harmful effects of other bacteria, antigens, toxins and carcinogens in the gut, but in addition, probiotics are known to interact with the gut –associated lymphoid tissue, leading to positive effects on the innate and even the acquired immune system. This is possible because the gut, as the largest surface area of the body, has a significant role to play in immunity as every day it has to deal

> with three different immune challenges. First, it must differentiate and tolerate the large commensal microbiota otherwise inflammation will occur, and secondly, it must also tolerate the food antigens. On the other hand, the gut must be able to mount a defence against any potential pathogens when required. This explains why 85% of the body's lymph nodes are located in the gut, and why probiotics, as functional foods that target the gut, are able to affect the health of the whole body including parts of the body distant from the gut. Although to date there are few published studies of the effectiveness of probiotic use in athletes, interest is beginning to grow, mostly in examining their potential in helping to maintain overall general health, enhancing immune function or reduce URTI incidence and symptom severity or duration (Gleeson & Walsh, 2012). (Gleeson et al., 2013, pp. 234-235).

In a double-blind, placebo-controlled, cross-over trial in which 20 healthy elite distance runners received the probiotic Lactobacillus (L.) fermentum or placebo daily for 28 days with a 28-day washout period between the initial and the second treatment, the athletes suffered fewer days of respiratory illness and lower severity of respiratory illness symptoms when taking the daily probiotic (Cox, Pyne, Saunders, & Fricker, 2010). The probiotic treatment elicited a two-fold greater change in whole-blood culture IFN-γ production compared with placebo, which may be one mechanism underpinning the positive clinical outcomes.

In a somewhat larger scale, randomized, double-blind intervention study, 141 marathon runners received L. rhamnosus GG (LGG) or placebo daily for a 3-month training period and then participated in a marathon race with a 2-week follow-up of illness symptoms (Kekkonen et al., 2007).

> Although there were no differences in the number of respiratory infections or gastrointestinal (GI)-symptom episodes, the duration of GI-symptom episodes in the LGG group was shorter than in the placebo group during the training period (2.9 vs. 4.3 days) and during the 2 weeks after the marathon (1.0 vs. 2.3 days). (Calder & Yaqoob, 2013).

A randomized, placebo controlled trial in 64 university athletes reported a lower incidence of URTI episodes during a 4-month winter training period in subjects receiving a twice daily L. casei supplement compared with placebo, and this study also reported better maintenance of salivary IgA in the probiotic group (Gleeson, Bishop, Oliveira, & Tauler, 2011). Although most studies to date have examined probiotic effects in recreationally active individuals or endurance sport athletes, a recent study on elite rugby players provides evidence that beneficial effects of probiotics in reducing URTI incidence, but not severity, may extend to team games players (Haywood et al., 2014).

From the available research, one cannot be certain of a health benefit with regular probiotic ingestion for sportspeople but there is now sufficient understanding of the mechanism of action of certain probiotic strains, and enough evidence from trials with athletes and sportspeople to signify that this is a promising area of research with mostly positive indications at present. A meta-analysis using data from both athlete and non-athlete studies involving 3,451 participants concluded that there is a likely benefit in reducing URTI incidence (Hao, Lu, Dong, Huang, & Wu, 2011).

The studies to date that have shown reduced URS incidence in athletes have been mostly limited to Lactobacillus and Bifidobacterium species and have used daily doses of ~10^{10} live bacteria. “Given that some probiotics appear to provide some benefit…, with no evidence of harm and are low cost, there is no reason why athletes should not take probiotics, especially if travelling abroad or illness-prone” (Gleeson et al., 2013, p. 236).

Table 2: Reduction in number of URS symptom days and symptom severity with a daily probiotic supplement in male runners

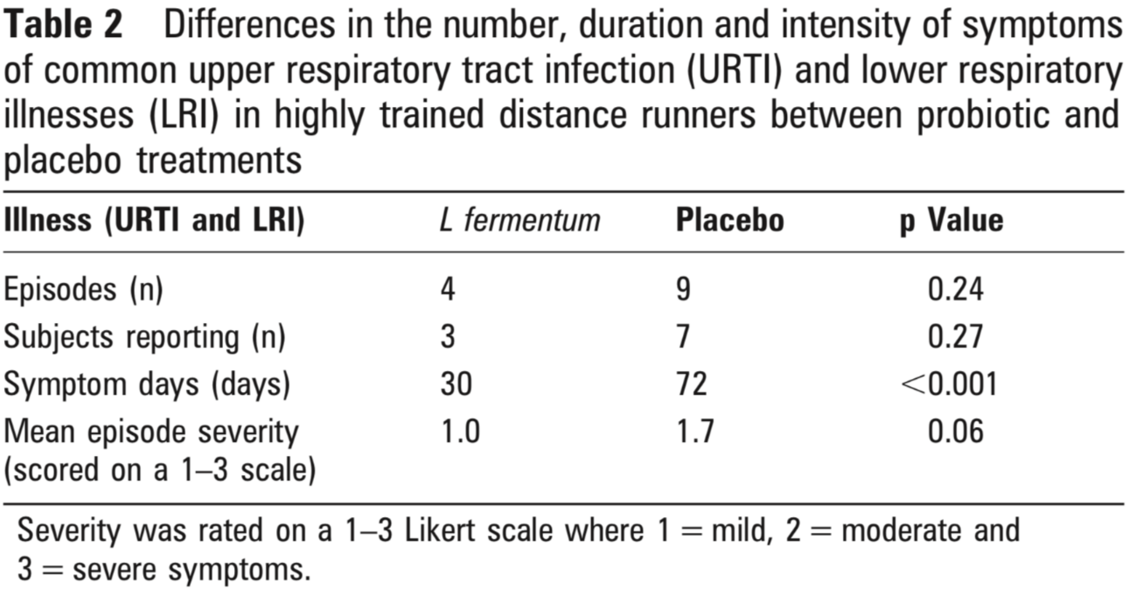

Table 2 Differences in the number, duration and intensity of symptoms of common upper respiratory tract infection (URTI) and lower respiratory illnesses (LRI) in highly trained distance runners between probiotic and placebo treatments

Illness (URTI and LRI)	*L fermentum*	Placebo	p Value
Episodes (n)	4	9	0.24
Subjects reporting (n)	3	7	0.27
Symptom days (days)	30	72	<0.001
Mean episode severity (scored on a 1–3 scale)	1.0	1.7	0.06

Severity was rated on a 1–3 Likert scale where 1 = mild, 2 = moderate and 3 = severe symptoms.

Source: Cox et al., 2010, p. 224.

Colostrum

Bovine colostrum is the first collection of a thick creamy-yellow liquid, produced by the mammary gland of a lactating cow shortly after birth of her calf (usually within the first 36 hours). Colostrum contains antibodies, growth factors, enzymes, gangliosides (acid glycosphingolipids), vitamins and minerals and is commercially available in both liquid and powder forms. Numerous health claims have been made for colostrum ranging from

> performance enhancement to preventing infections, but well-controlled studies in athletes are rare… A few studies suggest that several weeks of bovine colostrum supplementation can elevate levels of antibodies in the circulation and saliva. In a study of 35 middle-aged distance runners who consumed a supplement of either bovine colostrum or placebo for 12 weeks, median levels of salivary IgA increased by 79% in the colostrum group after the 12-week intervention, with no change in the placebo group (Crooks et al. [Crooks, Wall, Cross, & Rutherfurd-Markwick], 2006). While this result was statistically significant, its physiological interpretation must be viewed with caution due to the small numbers in this study and the large variability in salivary IgA levels. Davison and Diment (2010) reported that 4 weeks of daily bovine colostrum supplementation prevented exercise-induced falls in salivary lysozyme and speeded the recovery of neutrophil function after 2 h of strenuous cycling in healthy men compared with placebo. (Jeukendrup & Gleeson, 2018)

Several studies have also reported that daily oral bovine colostrum supplementation reduces the total number of days with self-reported URS, the incidence of URS episodes the total number of days with self-reported URS, and duration of self-reported URS episodes, in adults involved in exercise training. (Crooks et al., 2006; Jones et al., 2014). "Further studies are needed to confirm and extend these observations of effects on immune responses to exercise and to establish if bovine colostrum can reduce the incidence of URTIs in athletes" (Calder & Yaqoob, 2013).

4.2.5 Applying science to reduce illness and infections

Both heavy exercise and nutrition exert separate influences on immune function; these influences appear to be greater when exercise stress and poor nutrition act synergistically. Exercise training increases the body's requirement for most nutrients, and in many cases, these increased needs are countered by increased food consumption. But some athletes adopt an unbalanced dietary regimen, and many surveys indicate that few athletes follow the best dietary pattern for optimal sport nutrition.

> Despite an abundance of studies investigating the effects of nutrition on immune function and the effects of nutrition on physical performance, relatively few have investigated the interrelationships between nutrition, performance, and immune function concurrently. Therefore, some of the conclusions drawn in this chapter remain speculative, relying on generalizations between sedentary and athletic populations. The poor nutritional status of some athletes, however, likely predisposes them to immunodepression. Although countering the effects of all of the factors that contribute to exercise-induced immunodepression is impossible,

minimizing many of the effects is possible. Athletes can help themselves by eating well-balanced diets that include adequate carbohydrate, protein, and micronutrients.

Consumption of carbohydrate drinks during training and competition is recommended because this practice appears to attenuate some of the immunosuppressive effects of prolonged exercise. The ingestion of individual amino acids, echinacea, vitamin E and zinc are unlikely to be of significant clinical benefit in preventing common infections such as URTI. The dangers of oversupplementation of vitamins and minerals should be emphasized because many micronutrients given in quantities beyond a certain threshold reduce immune responses and may also pose a risk to health.

Current recommendations for immuno-nutrition support in athletes (Bermon et al., 2017; Gleeson, [February] 2016) include:

- Overall daily energy intake should match energy needs with >50% coming from carbohydrate
- Ingest 30-60 g of carbohydrate per hour during strenuous training sessions
- Ingest of adequate amounts of protein (1.2-1.6 g/kg bw/day) which should include ingestion of 0.3 g/kg bw/day in meals following training sessions
- Ingest adequate amounts of micronutrients (this can be ensured by taking a daily multi-vitamin/mineral tablet that meets the RDAs
- Take a daily oral vitamin D3 supplement of 25 µg or 1,000 IU at the start of autumn until early spring
- Take a daily probiotic supplement containing at least 10^{10} live bacteria
- Include a variety of fruit and vegetables as part of the normal diet (at least on 5 days per week); this can be supplemented with plant polyphenol supplements or beverages (e.g. green tea, non-alcoholic beer) or concentrated fruit/vegetable extracts
- Consider taking a daily 10-20 g bovine colostrum powder supplement
- Consider taking zinc supplements in the days leading up to an important competition in case cold symptoms should begin at that important time. (Jeukendrup & Gleeson, 2018)

This approach is likely to be of great benefit to those individuals who are particularly prone to illness.

It is important to remember that nutrition is only one factor with regard to infection risk and “there are several other strategies that can minimise the risk of developing immune function depression or reduce the degree of exposure to pathogens and thus limit infection risk” (Jeukendrup & Gleeson, 2018):

“Other factors that may lower infection risk in athletes include reducing other life stresses, maintaining good oral and skin hygiene, obtaining adequate rest, and spacing prolonged training sessions and competitions as far apart as possible” (Schwellnus et al., 2016, as cited in Calder & Yaqoob, 2013). The practices listed below are recommended.

Figure 2: 17 ways to reduce illness risk in athletes

17 ways to reduce the risk of illness in athletes

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1. Cough or sneeze on to the elbow and not on the hands
2. Minimise contact with infected people, young children, animals and contagious objects
3. Avoid shaking hands
4. Wash hands regularly and effectively with soap and water
5. Always clean the hands and nose after sneezing or coughing
6. Avoid crowded areas
7. Use disposable paper towels and limit hand to mouth/nose contact
8. Keep at distance to people who are coughing, sneezing or have a 'runny nose'
9. Wear open footwear when using public showers
10. Practice safe sex
11. Adopt strategies that facilitate good quality sleep
12. Carry insect repellent, anti-microbial foam/ cream or alcohol-based handwashing gel
13. Avoid excessive drinking of alcohol
14. Wash and peal fruit before eating
15. Choose beverages from sealed bottles,
16. Not to share drinking bottles, cups, cutlery, towels etc. with other people
17. Avoid raw vegetables and undercooked meat when abroad

by Professor Mike Gleeson

Source: Jeukendrup 2016. https://bit.ly/2y3xc1x

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