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Nutritional Support to Maintain Proper Immune Status during Intense Training

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Abstract

Prolonged exercise and heavy training are associated with depressed immune function which can increase the risk of picking up minor infections. To maintain robust immunity, athletes should eat a well-balanced diet sufficient to meet their energy, carbohydrate, protein, and micronutrient requirements. Dietary deficiencies of protein and specific micronutrients have long been associated with immune dysfunction and an adequate intake of iron, zinc, and vitamins A, D, E, B_6 and B_{12} is particularly important in the maintenance of immune function. Consuming carbohydrate during prolonged strenuous exercise attenuates rises in stress hormones and appears to limit the degree of exercise-induced immune depression. Similar effects can be seen with daily ingestion of high-dose antioxidant vitamin supplements, though concerns have been expressed that excessive antioxidant intake may impair exercise training adaptations. It is safe to say with reasonable confidence that individual amino acids, colostrum, Echinacea, and zinc are unlikely to boost immunity or reduce infection risk in athletes. The ingestion of carbohydrate during exercise and daily consumption of probiotic and plant polyphenol (e.g. quercetin)-containing supplements or foodstuffs (e.g. non-alcoholic beer) currently offer the best chance of success. This approach is likely to be most effective for individuals who are particularly prone to illness.

Introduction

Athletes who engage in intense training or who have recently competed in endurance race events appear to be at increased risk of developing symptoms of minor respiratory illness [1]. The most common illnesses in athletes are viral infections of the upper respiratory tract (i.e. the common cold), but athletes can also develop similar symptoms (e.g. sore throat) due to allergy or

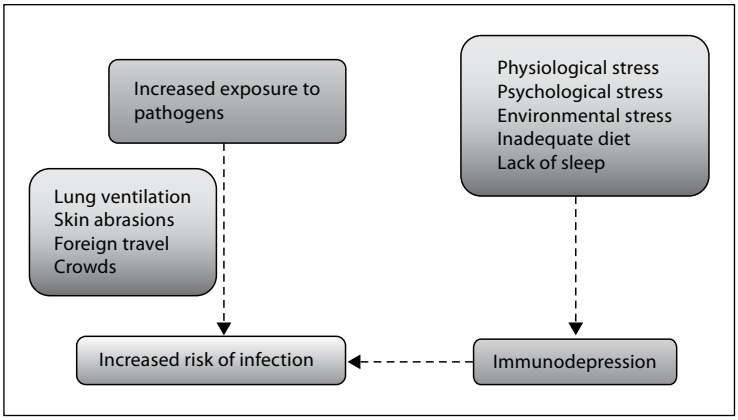

Fig. 1. Causes of increased infection risk in athletes.

inflammation caused by inhalation of cold, dry or polluted air [2]. 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, underperform or even miss an important competition. Prolonged bouts of strenuous exercise have been shown to result in transient depression of white blood cell functions, and it is suggested that such changes create an 'open window' of decreased host protection, during which viruses and bacteria can gain a foothold, increasing the risk of developing an infection [3]. Other factors such as psychological stress, lack of sleep and malnutrition can also depress immunity [4] and lead to increased risk of infection (fig. 1). There are also some situations in which an athlete's exposure to infectious agents may be increased, which is the other important determinant of infection risk. During exercise, exposure to airborne bacteria and viruses increases because of the higher rate and depth of breathing. An increase in gut permeability may also allow entry of gut bacterial endotoxins into the circulation, particularly during prolonged exercise in the heat. In contact sports skin abrasions may occur increasing the risk of transdermal infections. In some sports, the competitors may be in close proximity to large crowds. Air travel to foreign countries may be involved. Hence, the cause of the increased incidence of infection in athletes is most likely multifactorial (fig. 1). A variety of stressors (physical, psychological, environmental, and nutritional) suppress immune function, and these effects, together with increased exposure to potentially disease-causing pathogens, make the athlete more susceptible to infection.

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Maintaining an Effective Immune System

Adequate nutrition and in particular appropriate intakes of energy, protein, vitamins and minerals are essential to maintain the body's natural defenses against disease-causing viruses and bacteria. Athletes are best advised to consume a sound diet that meets their energy needs and contains a variety of foods as the key to maintaining an effective immune system is to avoid deficiencies of the nutrients that play an essential role in immune cell functions [5]. Inadequate protein-energy intake or deficiencies of certain micronutrients (e.g. iron, zinc, magnesium, manganese, selenium, copper and vitamins A, C, D, E, B_6, B_{12} and folic acid) decrease immune defenses against invading pathogens and make the individual more susceptible to infection [5]. Even short-term dieting in athletes who continue to train hard that results in a loss of a few kilograms body mass over the course of a few weeks can result in significant falls in several aspects of immune function. Thus, care should be taken to ensure adequate protein (and micronutrient) intakes during periods of intentional weight loss, and it should be recognized that athletes undergoing weight reduction are likely to be more prone to infection. In general, a broad-range multivitamin/mineral supplement is the best choice to support a restricted food intake, and this may also be suitable for the travelling athlete in situations where food choices and quality may be limited. It has only recently been recognized that vitamin D plays an important role in upregulating immunity [6], and this is a concern as vitamin D insufficiency is common in athletes [7], especially if exposure to natural sunlight is limited (e.g. when training in the winter months or when training mostly indoors). An increasing number of studies in athletes and the general population have provided evidence that sufficient vitamin D status optimizes immune function and helps defend against the common cold. Hence, athletes who are deficient or insufficient in vitamin D (this can be established with a blood test to measure the circulating concentration of 25-hydroxy-vitamin D) are likely to benefit from vitamin D supplementation. For further details see the chapter on 'vitamin D supplementation in athletes' by Enette Larson-Meyer [pp. 109–121].

Nutrition Strategies to Limit Exercise-Induced Immune Depression

Certain supplements may boost immune function and reduce infection risk in individuals who are subjected to stress [5]. While there are many nutritional supplements on the market that are claimed to boost immunity (table 1), such claims are often based on selective evidence of efficacy in animals, in vitro experiments,

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Table 1. Immune-boosting supplements – claims and the scientific evidence for efficacy in humans

Arginine	yyyyy	Nonessential amino acid that is a precursor in the synthesis of nitric oxide which is a cytotoxic molecule capable of destroying microorganisms and virus-infected cells. Claimed to enhance immune response and increase resistance to infection. There is no evidence that arginine has any effect on immunity in healthy humans.
β-Glucan	IIyyy	A polysaccharide derived from the cell wall of yeast, fungi, algae, and oats that stimulates immunity. Oral feedings of oat β-glucan can offset exercise-induced immune suppression and decrease susceptibility to URTI in mice exercising heavily for 3 days. No evidence yet of a similar benefit for human athletes.
Bovine colostrum	Iyyyy	First milk of the cow that contains antibodies, growth factors and cytokines. Claimed to boost mucosal immunity and increase resistance to infection. One study suggests an effect in elevating salivary IgA in human endurance runners but no evidence that this modifies infection risk.
Carbohydrate	IIIyy	Ingestion of carbohydrate (30–60 g/h) attenuates stress hormone and (some) immune perturbations during exercise but only very limited evidence that this modifies infection risk in human athletes.
Curcumin	yyyyy	A component of the Indian spice turmeric and has potent anti-inflammatory activity. There is no evidence that curcumin has any effect on immunity in healthy humans.
Echinacea	yyyyy	Herbal extract that is a popular supplement among athletes. Claimed to boost immunity via stimulatory effects on macrophages. 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.
Ginseng (Asian or Panax)	yyyyy	Asian ginseng (*Panax ginseng*) has been a part of Chinese medicine for over 2,000 years and was traditionally used to improve mental and physical vitality. Evidence for immune-modulating effects in humans is lacking.
Probiotics	IIIyy	Probiotics are live microorganisms which when administered orally for several weeks, can increase the numbers of beneficial bacteria in the gut and modulate systemic immune function. Some placebo-controlled studies in athletes have indicated that daily probiotic ingestion results in fewer days of respiratory illness and lower severity of symptoms but larger scale studies are needed.
Plant polyphenols	IIyyy	Quercetin is a flavonol (polyphenol) compound found in onions, apples, red wine, broccoli, tea, and Ginkgo biloba. It has antioxidant activities, inhibits protein kinases and regulates gene expression. Some limited evidence of reduced infection risk in human athletes with quercetin but mechanism of action unclear. A study with a NAB polyphenol beverage showed reduced inflammation and respiratory infection incidence after a marathon.
Vitamin C	IIyyy	An essential water-soluble antioxidant vitamin taken in megadoses by many athletes. Some evidence from some (but not all) human studies that high-dose vitamin C (>200 mg/day) can be effective in reducing infection risk in stress situations and following ultramarathon races. May work by reducing stress hormone and anti-inflammatory cytokine responses to exercise.

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Table 1. Continued

Vitamin D	IIIyy	An essential fat-soluble vitamin that is known to have immunomodulatory effects. An increasing number of studies in athletes and the general population indicate that sufficient vitamin D status optimizes immune function and defends against respiratory infections. Thus, athletes who have deficient or insufficient vitamin D status are likely to benefit from supplementation.
Vitamin E	Iyyyy	An essential fat-soluble antioxidant vitamin that is another popular supplement taken in megadoses by athletes. Good evidence for some immune-boosting effects in the frail elderly, but no evidence of similar benefit for younger healthy humans or athletes.
Zinc	Iyyyy	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.

The scientific evidence is indicated with IIIII meaning very strong evidence and yyyyy meaning limited to no evidence.

children, the elderly or clinical patients in severe catabolic states, and direct evidence for their efficacy for preventing exercise-induced immune depression or improving immune system status in athletes is usually lacking. The bulk of this short review focuses on describing the limited number of nutritional strategies and supplements for which there is some supportive scientific evidence base for efficacy in reducing immune perturbations during exercise and/or in decreasing infection incidence.

Carbohydrate Beverages

Carbohydrate ingestion during exercise limits metabolic stress by helping to maintain the blood glucose concentration. The use of a high-carbohydrate diet and carbohydrate ingestion (about 30–60 g/h) during prolonged workouts lowers circulating stress hormone (e.g. adrenaline and cortisol) and anti-inflammatory cytokine (e.g. interleukins 6 and 10) responses to exercise and delays the appearance of symptoms of overreaching during intensive training periods [8]. This reduces the impact of prolonged exercise on several, but not all, aspects of immune function, although evidence is currently lacking to demonstrate that this translates to a reduced incidence of illness symptoms following competitive events. When training sessions are performed in a fasting or low-glycogen state and without carbohydrate ingestion during exercise, it is likely that a more substantial degree of immune depression will develop (especially if this is not the first training session of the day).

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If this train-low (glycogen) concept is to be applied to maximize training adaptation [9], it should not be done for more than a few days per week or immune function will be compromised.

The consumption of beverages during exercise not only helps prevent dehydration (which is associated with an increased stress hormone response) but also helps to maintain saliva flow rate during exercise. Saliva contains several proteins with antimicrobial properties including immunoglobulin A, lysozyme and α-amylase. Saliva secretion usually falls during exercise, but regular fluid intake during exercise can prevent this.

Antioxidant Vitamins

Although it is not known whether hard training increases the need for dietary antioxidants – as the body naturally develops an effective defense with a balanced diet and endogenous antioxidant defenses actually improve with exercise training – some recent evidence suggests that regular intake of relatively high doses of antioxidant vitamins can also reduce the stress response to prolonged exercise [10, 11]. These studies have used combinations of vitamin C and E, or vitamin C alone, and provide a possible mechanism to explain earlier findings of a benefit of vitamin C supplementation in reducing the incidence of respiratory illness symptoms in individuals who took part in ultramarathon races [12].

The most recent Cochrane meta-analysis examined the evidence that daily doses of more than 200 mg vitamin C were more effective in preventing or treating the common cold than placebo [13]. 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: 0.92–1.00). A subgroup of six trials that involved physically active subjects (a total of 642 marathon runners, skiers, and soldiers on sub-arctic exercises) reported a pooled RR of 0.50 (95% CI: 0.38–0.66). 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: 3–13%) for adult participants. Fifteen trial comparisons that involved 7,045 respiratory episodes contributed to the meta-analysis of severity of episodes, 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. The authors concluded that the failure of vitamin C supplementation to reduce the incidence of colds in the normal population indicates that routine ingestion of mega-doses of vitamin C is not generally justified but that individuals subjected to periods of severe physical exercise and/or cold environments may well gain some benefit. However, even if some protective effect of high-dose antioxidant supplementa-

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tion on infection risk is indeed a reality, athletes need to consider the risks that may include the blunting of some of the adaptations to training with a high intake of antioxidants [14], though whether or not this is likely to affect adaptations in already well-trained athletes performing intensive training has recently been questioned [15]. Excessive supplementation with other antioxidant vitamins cannot be recommended because there is little evidence of benefit, while it is known that oversupplementation can actually diminish the body's natural antioxidant defense system. Ensuring that the diet contains plenty of fresh fruits and vegetables is probably the wisest option.

Immunonutrition Support for Athletes

Various other nutritional supplements have been tested for their capacity to reduce immune changes following prolonged strenuous exercise and thus lower infection risk. This strategy is similar to the immunonutrition support provided to patients recovering from trauma and surgery, and to the frail elderly. Supplements studied thus far in human athletes include zinc, omega-3 polyunsaturated fatty acids, herbal extracts (e.g. Echinacea), plant sterols, polyphenols (e.g. quercetin) and polysaccharides (e.g. β-glucan), glutamine, branched-chain amino acids, and bovine colostrum. Although some supplements (e.g. zinc [16] and some herbals such as Kaloba [17]) may reduce severity or duration of illness if taken close to the onset of symptoms, thus far results have been generally disappointing with regard to reducing infection incidence (see table 1), and focus has shifted to examining the effects of probiotics and plant polyphenols.

Plant Polyphenols

Plant polyphenols are potent antioxidant compounds. One of these, quercetin, has received a lot of attention in recent years in relation to its possible effects on exercise performance, training adaptation and immune function. Quercetin is classified as a flavonoid, a phytonutrient found in a variety of fruits and vegetables. The physiologic effects of these compounds are of great current interest due to their antioxidant, anti-inflammatory, antipathogenic, cardioprotective, and anticarcinogenic activities. Animal studies indicate that 7 days of quercetin feeding improves survival from influenza virus inoculation. A recent human study [18] showed that 1,000 mg of a quercetin supplement ingested daily for 3 weeks significantly increased plasma quercetin levels and reduced respiratory illness during the 2 weeks following a 3-day period of exhaustive exercise in cyclists. Immune dysfunction, inflammation, and oxidative stress, however, were not altered, suggesting that quercetin may have exerted direct antiviral effects. Another study

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reported a lower incidence of respiratory infections among physically active middle-aged people with daily quercetin supplementation [19], but larger scale, double-blind, placebo-controlled studies are needed to confirm an effect of quercetin in reducing infection incidence in athletes who are training hard. 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 recent study investigated whether regular ingestion of non-alcoholic beer (NAB) polyphenols prior to and after a marathon would attenuate post-race inflammation and decrease the incidence of respiratory illness symptoms [20]. Healthy middle-aged male runners (n = 277) were randomly assigned to drink 1–1.5 l per day of a NAB or placebo beverage for 3 weeks before and 2 weeks after a marathon race. Blood markers of inflammation were significantly reduced in NAB compared to placebo immediately after the race and 24 h later and the incidence of respiratory illness was 3.25-fold lower in the NAB group compared with the placebo group during the 2-week post-marathon period. Another recent study that examined the effects of regular ingestion of dark chocolate (cocoa is another source of polyphenols) prior to an exhausting bout of cycling reported reduced oxidative stress markers but no effects on hormonal or immune responses to the exercise [21], so the type and dose of polyphenols may be important.

Probiotics

In recent years, several studies have examined the efficacy of oral probiotics in athletes, and some of these, particularly those containing *Lactobacillus* strains, have shown some promise. Often called the friendly bacteria, probiotics are live microorganisms which when administered in adequate amounts, modify the bacterial population that inhabits our gut and modulate immune function by their interaction with the gut-associated lymphoid tissue, leading to positive effects on the systemic immune system. Some well-controlled studies in athletes have indicated that daily probiotic ingestion results in fewer days of respiratory illness and lower severity of upper respiratory tract infection (URTI) symptoms [22–25], and a recent meta-analysis using data from both athlete and non-athlete studies involving 3,451 subjects concluded that there is a likely benefit in reducing URTI incidence [26]. Thus, probiotic supplements may convey some benefit to immunity and reduce URTI incidence as well as reduce gastrointestinal problems (a common complaint of endurance runners). Another potential benefit of probiotics could be a reduced risk of gastrointestinal infections – a particular concern when travelling abroad. Further large-scale studies are needed to confirm that taking probiotics can reduce the number of training days lost to infection and to determine the most effective probiotics as their effects are strain spe-

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cific. The studies to date that have shown reduced URTI incidence in athletes have been mostly limited to *Lactobacillus* 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.

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 h. 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. The gangliosides in colostrum may modify the gut microbial flora and act as decoy targets for bacterial adhesion as well as having some direct immunostimulatory properties. A few studies suggest that several weeks of bovine colostrum supplementation can elevate levels of antibodies in the circulation and saliva, prevent exercise-induced falls in salivary lysozyme and speed the recovery of neutrophil function after strenuous exercise [27, 28]. 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.

Conclusions

It is difficult to make firm judgments about which nutritional supplements are really effective in boosting immunity or reducing infection risk in athletes. It is safe to say with reasonable confidence that individual amino acids, colostrum, Echinacea, vitamin E and zinc are unlikely to be of benefit. The ingestion of adequate amounts of protein and micronutrients in the diet (vitamin D status may be of particular concern), intake of carbohydrate during exercise and daily consumption of probiotic and plant polyphenol (e.g. quercetin) supplements currently offer the best chance of success. This approach is likely to be most effective in those individuals who are particularly prone to illness. Athletes might consider taking zinc and Kaloba supplements in the days leading up to an important competition just in case they do come down with a cold at that important time. It is important to remember that nutrition is only one factor with regard to infection risk, and there are several other strategies listed below that can minimize the risk

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of developing immune function depression or reduce the degree of exposure to pathogens and thus limit infection risk.

Minimize the chances of developing immunodepression:

- Avoid very prolonged training sessions (>2 h), overtraining and chronic fatigue
- Keep other life stresses to a minimum
- Get adequate sleep quantity (at least 7 h) and quality
- Avoid rapid weight loss
- Vaccinate against influenza if competing in the winter

Minimize the potential for transmission of infectious agents:

- Avoid sick people and large crowds in enclosed spaces if possible
- Good personal skin and oral hygiene (wash hands and use antimicrobial gels on hands; brush teeth regularly and use an antibacterial mouth rinse)
- Never share drink bottles, cutlery, towels, etc.
- Avoid putting hands to eyes and nose (a major route of viral self-inoculation)

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Questions and Answers

Question 1: Vitamins are important to maintain proper immune function, and many athletes are taking vitamin supplements. Would you recommend using vitamin supplements?

Answer: Yes, I would. Vitamins are essential for the normal functioning of the immune system. If you become deficient in virtually any of them, but particularly vitamin A, vitamin E, vitamin B_{12} or folic acid, your immune system actually goes down, and it won't function as well, and you're more

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likely to get infections. One way of protecting against that is to simply take a multivitamin tablet on a daily basis. So yes, I would recommend them.

Question 2: What actually causes infections?

Answer: Infections are caused mostly by viruses. The most common infection that athletes and the general population get is the common cold, and 90% of common colds are caused by viruses. The other 10% or so are the result of bacterial infections.

Question 3: Is it true that endurance athletes like cyclists get more infections than weightlifters, for example?

Answer: In general, yes. The endurance athletes get more infections than the power athletes and the sprinters. This is thought to be because the long hard hours of training that the endurance athletes do actually cause sufficient stress to depress their immunity, at least temporarily for several hours after exercise. In fact, there have been some studies done where people have run a marathon, and the guys who have run the marathon actually come down with more infections in the week or two afterwards compared to guys that might have trained for the marathon but didn't compete for reasons other than illness.

Question 4: Are there any nutritional strategies to minimize the risk of infections for endurance athletes?

Answer: There's only a few that we can currently recommend because the evidence isn't very clear on a lot of things. There are so many of those things in the health food shops that are claimed to boost immunity, but most of the studies that have been done in athletes have shown that they don't really work. Of the things that do work, we know, the most important is to avoid deficiencies of energy, protein and all the essential micronutrients you need. Not only vitamins, but also minerals like manganese, iron and zinc, are very important for maintaining immunity. Taking probiotics is probably a good idea. There have been a number of recent studies using the *Lactobacillus* species of probiotics that show a positive effect in reducing infection incidence and in some cases also reducing the severity or duration of infections when they do occur in endurance athletes.

Question 5: What about additional antioxidants?

Answer: That's a difficult one to answer. There were some studies done in the 1990s by Edith Peter's group in South Africa. They reported that taking high doses of vitamin C in particular for several weeks before running an ultra-marathon race decreased the incidence of infections when compared with a placebo treatment. But subsequently, in recent years the story has come about that if you take high doses of antioxidant vitamins, it might actually impair some of the adaptations to training. This is because when we do exercise, we generate some increased free radicals or reactive oxygen species, and these are thought to be

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important signals in the training adaptation process. So, taking too high levels of antioxidant vitamins might actually quench those free radicals as they're being produced and so prevent or limit the training adaptations. However, those studies have actually mostly been done either in animals or untrained humans. There are one or two more recent studies that are coming out now that have looked at already well-trained athletes. When these guys take high doses of combined vitamins C and vitamin E for several months, no performance changes, and no impairment to training adaptations has been reported in those studies. So it's not really clear whether or not they do have a negative effect. Athletes take high-dose vitamin C because they've probably heard or read something that tells them that it might reduce their risk of infection, and that was really based on the studies that were done in the 1990s. We now know that one of the mechanisms by which the antioxidants might be working actually is by suppressing cortisol release during exercise. Cortisol is a stress hormone that depresses immunity. So, if you can prevent that being secreted or reduce its secretion, you don't get as much immune depression with your exercise bout.

Question 6: Do you believe that a lot of athletes are having micronutrient deficiency?

Answer: Well, that seems to be so certainly when these nutrition surveys are done or when you test the blood of athletes to see what their vitamin status is, for example. A number of studies show that iron status is usually a little bit on the low side. So they have low levels of serum ferritin and possibly low levels of hemoglobin, which would actually impair performance. You certainly don't want that. But vitamin D is another one that has come up recently. It has been recognized in the last 3 or 4 years that vitamin D is actually very important for maintaining normal immune function. It actually stimulates the activity of some of our immune cells. Some studies indicate that vitamin D insufficiency is quite common among athletes.

Question 7: And what about vitamins C or E?

Answer: These vitamins are rarely deficient. We usually get enough of those in the diet, provided that you are eating plenty of fruit and vegetables. That's probably the best way to get the vitamins and minerals you need.

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