

2 NUTRITION, HEALTH AND IMMUNE FUNCTION

A LOOK AT THE INFLUENCE OF NUTRIENTS ON IMMUNE FUNCTION AND INFECTION RISK **BY MICHAEL GLEESON**

Nutrition, Health and Immune Function

Michael Gleeson

Practical Implications

- The immune system protects the body against potentially damaging microorganisms
- Athletes engaged in heavy endurance training programmes often have depressed immune function and suffer from an increased incidence of respiratory infections
- Lowered immunity in athletes may occur due to a combination of stressors including not only intensive training but also psychological stress, environmental stress, poor sleep and nutrient deficiencies
- Acute infective or allergic illness can cause a reduction in exercise performance •
- The poor nutritional status of some athletes may predispose them to immunodepression. For example, dietary deficiencies of protein and specific minerals (e.g. iron, selenium, zinc) or vitamins (e.g. A, D, E, B6, B12, folic acid) are associated with immune dysfunction and increased risk of infection An adequate intake of protein, iron, zinc, and B vitamins is particularly important for robust immunity

Consuming mega-doses of individual vitamins is generally not recommended but vitamin D

- supplementation is an exception since many athletes do not exhibit adequate vitamin D status during the winter months
- Some supplements, including probiotics, plant polyphenols, vitamin C, vitamin D3 and bovine colostrum may benefit immunity and reduce risks of infection if taken regularly in sufficient doses
- ۲ By adopting sound nutritional practice, reducing life stresses, maintaining good hygiene, obtaining adequate rest, and spacing prolonged training sessions and competitions as far apart as possible, athletes can reduce their risk of infection

Background

Nobody wants to get ill. It can often mean feeling unwell and having to take time off work. For athletes it can mean missing training or being unable to perform in competition. According to UK Sport, a third of missed training sessions are caused by illness. Around 40-60% of athletes' illnesses involve the respiratory tract, 10-20% the digestive system, 10-15% the skin, and 5-10% the urogenital system. The immune system protects us against infections but its function can be compromised by stress both physiological and psychological - as well as by a lack of sleep and poor nutrition.

A serious concern in 2020 is the risk of becoming infected with COVID-19 which is a strain of coronavirus that infects the lungs with potentially serious and life-threatening health consequences. This is in addition to the more usual concern of picking up other respiratory tract infections such as influenza and the common cold which are also caused by viruses. In fact, several other strains of coronavirus cause cold-like symptoms (although not as severe as the 2019-2020 COVID-19 pandemic) such as rhinovirus and adenovirus. The symptoms of these respiratory illnesses have some similarities but also some differences: Infection with COVID-19 is characterized by having a fever and developing a dry



tickly cough but having a sore throat and a runny nose are less common. Influenza also causes a fever, aching joints and has other symptoms similar to (but usually more severe than) the common cold which include a runny nose, sore throat and sneezing. We generally do not get a fever with the common cold. Most people who get these infections will recover within one to two weeks but they make you feel weaker, tired and generally unwell while symptoms are present. For athletes impairment of performance occurs, and is one of the most common reasons for missing training or competition. As COVID-19 infects the lungs rather than just the upper airways it can cause breathing difficulties in some people and particularly those with existing respiratory conditions such as asthma, bronchitis and chronic obstructive pulmonary disease. Among the elderly and the obese, the infection can be more debilitating, and they have an increased risk of developing more serious complications such as severe chest (lung) infections, including viral pneumonia which cannot be treated with antibiotics and can be fatal particularly in people with underlying medical conditions such as hypertension, heart disease, lung disease and diabetes.



Immune function - Our immune system protects us against the viruses (or other pathogens such as bacteria, parasites and fungi) that cause these infections, but because there is a genetic influence on the efficacy of our immune systems, some people are more prone to infections than others. However, our susceptibility to common infectious diseases is also influenced by our age, what we eat (Maggini et al., 2018), how much exercise we do, and how well we sleep (Walsh, 2018). In addition, other lifestyle behaviors such as good personal hygiene practices and social distancing (i.e. staying clear of people suffering from infection) can help to reduce our risk of picking up infections. These issues are covered in my healthy lifestyle guidebook "Eat, Move, Sleep, Repeat" (Gleeson, 2020) and in this article the focus is on the potential role of nutrition in preventing or speeding our recovery from infection.

Determinants of infection risk - There are two main factors that influence our chance of picking up a respiratory tract infection: one is the degree of exposure to pathogens like COVID-19 and influenza virus and the other is the status of our immune



system. Among athletes several factors have been identified that can increase infection risk (Walsh, 2018). These include very prolonged continuous bouts of strenuous exercise and intensified training (Schwellnus et al., 2016), life stress causing worry, anxiety or depression I.e. psychological stress), poor sleep quantity (i.e. less than 7 hours) or quality (i.e. frequent awakenings), exercise in environmental extremes (e.g. altitude), long haul travel across multiple time zones, and nutritional deficits (Gleeson, 2016; Bermon et al., 2017; Walsh, 2018) (Figure 1). The effectiveness of our immune systems is also influenced by our genetics and some people are more prone to illness than others. Being overweight or obese is associated with more frequent infections and in some illnesses (e.g. infection with COVID-19) can result in more severe health outcomes. We can reduce our risk of infection by doing various things that limit the transmission of infections and there are several behavioral and nutritional strategies that we can do to help make our immune systems more robust (figure 2).

Nutritional strategies to maintain robust immune function

Several things that people can do to limit their risk of infection are to adhere to some practical guidelines to maintain robust immunity and limit the impact of stress which is known to impair the functioning of our immune system and increase susceptibility to respiratory infections. These guidelines are summarised in figure 2 and relate mostly to nutritional, behavioural, and lifestyle strategies and are based on the findings of numerous research studies. The most effective nutritional strategies to maintain robust immune function are to avoid deficiencies of energy, protein and essential micronutrients.

In general, unless there is a desire to lose excess weight, an athlete's daily energy intake should match their daily energy expenditure with at least 50% coming from dietary carbohydrate. The latter is important for restoring muscle and liver glycogen which become depleted after prolonged exercise and carbohydrate is also an important fuel for the cells of the immune system. Ingesting about 40 g of carbohydrate per hour of exercise helps maintain blood sugar levels and reduces stress hormones to limit depression of immune function. Athletes also need 1.2-1.6 g of protein per kilogram of body mass per day, as opposed to the 0.8-1.2 g recommended for the general population. For optimal immune function, athletes need a higher level of protein and if you do get infected your immune system will need more protein to produce antibodies and multiply the cell lines that will defend you against the pathogen.

Various micronutrients are essential for normal functioning of the immune system, particularly vitamins A, C, D, E, B2, B6, B12, folic acid, and minerals including iron, magnesium, selenium, and zinc (Maggini et al., 2018). The ingestion of Lactobacillus or Bifidobacterium probiotics on a daily basis (Gleeson et al., 2011; Hao et al., 2015; Jäger et al., 2019; Pyne et al., 2015), and eating plenty of fruit and vegetables are other dietary practices that can help to reduce infection risk. Probiotics are live bacteria which when ingested in adequate amounts, modify the bacterial population (known as the microbiota) that inhabits our gut and modulate immune function by their interaction with the gut-

Resis	tance = ability to kill mi	crobes
Reversal of mechanism that is currently inhibiting immune function EXAMPLES: Carbohydrate during exercise to inhibit cortisol rise Glutamine to counter post-exercise fall Antioxidants to counter oxidative stress Supplements to improve poor sleep	Correct a deficiency of nutrient(s) needed for optimal immune function EXAMPLES: Energy Protein Vitamin D Vitamin E Iron Magnesium Selenium Zinc	Stimulation of aspect of barr immune funct inflammatory EXAMPLES: Colostrum to mucosal barri Vit D to increa antimicrobial production Probiotics to i NK cell or pha cell activity Zinc to increa interferon-y
▼ INF	ECTION INCIDE	NCE
	Fewer infections	

associated lymphoid tissue, leading to positive effects on the systemic immune system and other mucosal barriers including the respiratory tract (Jäger et al., 2019). Some well-controlled studies in children, adults, endurance athletes, and the elderly have indicated that daily probiotic ingestion results in fewer days of respiratory illness and lower severity or duration of infection symptoms.

There is also evidence that several nutritional supplements including vitamins C and D, zinc, plant polyphenols (Somerville et al., 2016), and bovine colostrum (Jones et al., 2019) may also support immunity and defend against respiratory infections. Such supplements may exert their effects via different mechanisms that either strengthen immunity and reduce infection incidence or make the body more tolerant to microbes (Walsh, 2019) by dampening immune responsiveness resulting in less severe or shorter periods of infection (Figure 3). Some studies suggest that regular consumption of fruits and plant polyphenol supplements or beverages that contain high amounts of polyphenols (e.g. non-alcoholic beer and green tea) can also reduce common cold incidence (Scherr et al., 2012).



The importance of vitamin D

Ensuring that the individual has adequate vitamin D may also be helpful, and supplementation with vitamin D3 (1,000-2,000 IU/day or 25-50 micrograms (μ g)/day) may be warranted for some people, especially in the winter months for those living at latitudes of 35°North and above (equivalent to Southern Spain and Washington DC in the USA) since the skin is unable to form vitamin D between the months of October through to March because the sunlight is not strong enough (Figure 4). In the summer months we get about 80% of our vitamin D from sunlight exposure (only 15-20 minutes per day is needed) but it is obvious that this cannot

be sustained in winter meaning that vitamin D status falls. Low vitamin D status is commonly reported in athletes and predisposes to increased infection incidence (He et al., 2016). Daily vitamin D3 supplementation has been shown to improve immune function and reduce respiratory infection incidence or severity in several large scale studies in both athletes and the general population with the biggest benefits being observed in those with low vitamin D status. For further information on the importance of vitamin D for athletes readers are directed to the article by Graeme Close and Daniel Owens in this series.



but this may be compromised in the winter months leading to deficient or inadequate vitamin D status

Other supplements to support immune function

Several studies have reported that taking 600 mg of vitamin C daily can reduce susceptibility to infection in the week following participation in an ultramarathon event (Peters et al., 1993) and in those with physically stressful occupations (Douglas et al.,

2007). Many other nutrition supplements, including β -glucan, ginseng, glutamine, and others, are on sale with claims that they can boost the immune system, but the scientific evidence that any of these are effective in preventing infections is not compelling. When respiratory illness symptoms begin, there is some evidence that taking zinc or certain herbal

supplements (e.g. echinacea, kaloba) can reduce the number of days that illness symptoms last for (Sholto and Cunningham, 2019). The case is probably strongest for zinc with one meta-analysis concluding that taking zinc acetate lozenges (containing 75 mg of elemental zinc) daily from the onset of respiratory illness symptoms reduces infection episode duration by a third (Hemilä, 2017). Zinc is involved in several aspects of immune cell functions and in sufficient amounts can reduce viral replication by inhibiting the enzyme (viral RNA-dependent RNA polymerase) that allows the virus to proliferate in infected host cells. It should be noted that for all supplements there is an optimal dose and exceeding this amount can result in impaired immunity and/or toxic effects so athletes contemplating taking such supplements should take careful note of the recommended amount. As with taking any supplement there is a risk of a doping violation due to contamination of some supplements with banned substances and therefore any supplement should be independently batch tested before being considered by athletes.

Guidelines to maintain robust immunity

- If you participate in regular exercise, avoid very prolonged training sessions (longer than 2 hours) and excessive periods of intensified training as this can depress your immunity (Schwellnus et al., 2016).
- Wear appropriate outdoor clothing in inclement weather, and avoid getting cold and wet after exercise.
- Get adequate sleep (at least 7 hours per night is recommended). Missing a single night of sleep has little effect on immune function at rest or after exercise, but respiratory illness episodes are more prevalent in those who regularly experience low sleep quantity (less than 7 hours per night) and poor sleep quality (frequent awakenings).
- Keep other life stresses to a minimum.

- Ensure adequate dietary energy, protein, and essential micronutrient intake. Daily energy intake should match daily energy expenditure with at least 50% coming from dietary carbohydrate. For active individuals a daily protein intake of 1.2-1.6 grams of protein per kilogram body mass is recommended. A daily multivitamin tablet supplying the RDA for all essential vitamins is a good insurance policy to avoid deficiencies.
- Vitamin D plays an important role in promoting immunity, and this is a concern as vitamin D insufficiency is common in people especially in situations where exposure to natural sunlight is limited (e.g. during the winter months or when living, training or working mostly indoors). A vitamin D3 supplement (1,000-2,000 IU/day or 25-50 µg/ day) may be beneficial to optimize immune function from October to March in Northern hemisphere countries.
- Avoid crash dieting and rapid weight loss. Care should be taken to ensure adequate protein (and micronutrient) intakes during periods of intentional weight loss, as individuals undergoing weight reduction are likely to be more prone to infection. In general, a broadrange multivitamin/mineral supplement is the best choice to support a restricted food intake, and this may also be suitable when travelling abroad in situations where food choices and quality may be limited.
- Eat several different fruits daily at least 5 times per week as regular fruit intake is associated with a lower incidence of the common cold.
- If you plan to do a prolonged (90 minutes or more) moderate to high intensity exercise session, ensure adequate carbohydrate intake before and during exercise in order to limit the extent and severity of exerciseinduced immune depression. Ingesting about 40 g carbohydrate per hour of exercise during prolonged workouts maintains blood sugar levels and lowers circulating stress hormones and so helps to limit immune function depression. A 500 mL bottle of a

sports drink usually contains 30-40 g of carbohydrate.

- 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, -amylase, and defensins. Saliva secretion usually falls during exercise, but regular fluid intake (water is fine) during exercise can prevent this.
- The efficacy of most so-called dietary immunostimulants has not been confirmed. However, there is limited evidence that some flavonoids (e.g. guercetin at a dose of 1 g/day) or flavonoid containing beverages such as green tea or non-alcoholic beer (Scherr et al., 2012), and Lactobacillus and/ or Bifidobacterium probiotics (daily doses of ~1010 live bacteria) can reduce respiratory infection incidence in physically active people or those under stress. Another potential benefit of probiotics could be a reduced risk of gastrointestinal infections - a particular concern when travelling abroad.
- High daily doses (500-1000 mg) of vitamin C may reduce infection incidence following marathon, ultramarathon, triathlon or other very prolonged endurance events. Individuals engaged in intensive training and/or cold environments may also gain some benefit for preventing respiratory infections.
- Avoid binge drinking of alcohol which is known to impair immune function (Afshar et al., 2015) and wound healing.
- Avoid strenuous exercise for a few days when experiencing upper respiratory symptoms like sore throat, sneezing, runny, or congested nose. Avoid all exercise other than walking when experiencing symptoms like muscle/joint pain and headache, a chesty cough, fever (indicated by a resting body temperature of 38-40∞C), and generalized feeling of malaise, diarrhea, or vomiting. Some

light exercise like walking may be beneficial to help avoid fluid accumulation in the lungs which increases the risk of developing dangerous complications like pneumonia.

In the current COVID-19 pandemic you may be asked to self-isolate for up to 14 days if you experience respiratory illness symptoms and this advice is generally for the protection of others by limiting virus transmission. After your symptoms resolve, start to do some light to moderate exercise around the home and the garden. The virus is highly contagious and it is important to realise that nothing you eat will stop you become infected if you are exposed to it. However, good immune defence is vital to combatting infections including COVID-19.

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Professor Michael Gleeson PhD. **fBASES**. **fECSS**

Michael is Emeritus Professor of Exercise Biochemistry at Loughborough University. He retired in 2016 after 40 years of research and teaching mostly related to the diet, metabolism, health and performance of athletes. He had a particular interest in the effects of diet and exercise on the function of the immune system and is a Past-President of the International Society of Exercise and Immunology (ISEI). He has provided advice on minimising risks of infection and nutritional strategies to maintain immune function to numerous sports clubs and organisations. He has co-authored several books on exercise biochemistry, sport nutrition and exercise immunology and published over 200 research papers in scientific and medical journals. In the past few years has contributed to international expert consensus reviews sponsored by the IOC (training load and illness risk), ISEI (immuno-nutrition), ISSN (probiotics) and UEFA (nutrition in elite football) as well as completing the 3rd edition of his highly popular book Sport Nutrition coauthored with Professor Asker Jeukendrup. In 2020 he has released his first solo books: Eat, Move, Sleep, Repeat, Beating Type 2 Diabetes and The Pick'n'Mix Diet. These are a series of healthy lifestyle guidebooks that have been written for the benefit of public health.

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