Abstract

Regular moderate exercise reduces the risk of infection compared with a sedentary lifestyle, but very prolonged bouts of exercise and periods of intensified training are associated with increased infection risk. In athletes, a common observation is that symptoms of respiratory infection cluster around competitions, and even minor illnesses such as colds can impair exercise performance. There are several behavioral, nutritional and training strategies that can be adopted to limit exercise-induced immunodepression and minimize the risk of infection. Athletes and support staff can avoid transmitting infections by avoiding close contact with those showing symptoms of infection, by practicing good hand, oral and food hygiene and by avoiding sharing drinks bottles and cutlery. Medical staff should consider appropriate immunization for their athletes particularly when travelling to international competitions. The impact of intensive training stress on immune function can be minimized by getting adequate sleep, minimizing psychological stress, avoiding periods of dietary energy restriction, consuming a well-balanced diet that meets energy and protein needs, avoiding deficiencies of micronutrients (particularly iron, zinc, and vitamins A, D, E, B₆ and B₁₂), ingesting carbohydrate during prolonged training sessions, and consuming – on a daily basis – plant polyphenol containing supplements or foodstuffs and Lactobacillus probiotics.

Introduction

A person’s level of physical activity influences his/her risk of infection, most likely by affecting immune function. Regular moderate exercise reduces the risk of infection compared with a sedentary lifestyle [1, 2], but very prolonged bouts of exercise and periods of intensified training are associated with increased infection risk. Acute bouts of exercise cause a temporary depression of various
aspects of immune function that will usually last for up to 24 h after exercise, depending on the intensity and duration of the exercise bout [3]. Several studies indicate that the incidence of symptoms of upper respiratory tract illness (URTI) is increased in the days after prolonged strenuous endurance events [4, 5], and it has been generally assumed that this reflects the temporary depression of immune function induced by prolonged exercise. More recently, it has been proposed that at least some of the symptoms of URTI in athletes are attributable to upper airway inflammation rather than to infectious episodes [6]. Periods of intensified training lasting a week or more have been shown to depress immune function [7], and although elite athletes are not clinically immune deficient, it is possible that the combined effects of small changes in several immune factors may compromise resistance to common minor illnesses, particularly during periods of prolonged heavy training and at times of major competitions.

**Causes of Illness in Athletes**

The most common illnesses in athletes (and in the general population) are viral infections of the upper respiratory tract (i.e. the common cold) which are more common in the winter months, and adults typically experience 2–4 URTI episodes per year. Athletes can also develop similar symptoms (e.g. sore throat) due to allergy or inflammation caused by inhalation of cold, dry or polluted air [7]. 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. A recent survey of hundreds of elite GB athletes in 30 different Olympic sports reported that among the reasons for athletes having to miss training sessions in 33% of cases, it was because of infection (most commonly URTI). Recent analysis of the 126 reported illnesses in athletes competing in the 2011 World Athletics Championships in Daegu, South Korea, revealed that 40% of illnesses affected the upper respiratory tract with confirmed infection in about 20% of cases [8]. Other main causes of sickness were associated with exercise-induced dehydration (12% of cases) and gastroenteritis/diarrhea (10% of cases).

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 [9] 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,
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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) may suppress immune function, and these effects, together with increased exposure to potentially disease-causing pathogens, can make the athlete more susceptible to infection. There appears to be no influence of the sex of an athlete on susceptibility to URTI [10] but some athletes are more illness-prone than others.

**Intensive Training Effects on Immune Function**

Prolonged bouts of strenuous exercise have a temporary negative impact on immune function. Post-exercise immune function depression is most pronounced when the exercise is continuous, prolonged (>1.5 h), of moderate to high intensity (55–75% of aerobic capacity), and performed without food intake [11]. Both aspects of innate immunity (e.g. neutrophil chemotaxis, phagocytosis, degranulation and oxidative burst activity, monocyte toll-like receptor expression and natural killer cell cytotoxic activity) and acquired immunity (e.g. antigen presentation by monocytes/macrophages, T lymphocyte cytokine production and proliferation, immunoglobulin production by B lymphocytes) are depressed by

![Fig. 1. Causes of increased infection risk in athletes.](image-url)
prolonged exercise. The salivary secretory immunoglobulin A (SIgA) response to acute exercise is variable, though very prolonged bouts of exercise are commonly reported to result in decreased SIgA secretion [12]. The causes of immune depression after prolonged exercise are thought to be related to increases in circulating stress hormones (e.g. adrenaline and cortisol), alterations in the pro-/anti-inflammatory cytokine balance and increased oxidative stress.

Markers of immune function in athletes in the true resting state (i.e. at least 24 h after the last exercise bout) are generally not very different from their sedentary counterparts, except when athletes are engaged in periods of intensified training. In this situation, immune function might not fully recover from successive training sessions and some functions can become chronically depressed [7]. Both T and B lymphocyte functions appear to be sensitive to increases in training load in well-trained athletes undertaking a period of intensified training, with decreases in circulating numbers of type 1 T cells, inhibition of type 1 T cell cytokine production, reduced T cell proliferative responses and falls in stimulated B cell immunoglobulin synthesis and SIgA reported. However, to date, the only immune variable that has been consistently associated with increased infection incidence is SIgA. Low concentrations of SIgA in athletes or substantial transient falls in SIgA are associated with increased risk of URTI [13]. In contrast, increases in SIgA can occur after a period of regular moderate exercise training in previously sedentary individuals and could, at least in part, contribute to the apparent reduced susceptibility to URTI associated with regular moderate exercise compared with a sedentary lifestyle [3].

The prevention of infection is vitally important research area both in terms of the health of the population at large and particularly for athletes undertaking prolonged periods of heavy training. In terms of negative impact on training, repeated periods of infection are akin to recurrent physical injuries which can be catastrophic when they occur as athletes approach major competitions. Therefore, the study by Neville et al. [13] is particularly encouraging because it showed on retrospective analyses of the salivary samples of 38 Americas Cup athletes taken over 50 weeks that when their relative IgA values fell by 40% or more they were likely to experience infections within a week or two. With the impending availability of rapid ‘in the field’ salivary analysis using hand-held devices, these measurements may offer a way of informing coaches when athletes are most vulnerable to infection and so infection problems associated with increased training loads might be avoided.

The available, albeit limited, evidence does not support the contention that athletes training and competing in cold conditions experience a greater reduction in immune function compared with thermoneutral conditions [3]. The inhalation of cold dry air can reduce upper airway ciliary movement and decrease
mucous flow, but it remains unknown if athletes who regularly train and compete in cold conditions report more frequent, severe or longer-lasting infections. Other environmental extremes (e.g. heat and altitude) or dehydration do not seem to have a marked impact on immune responses to exercise [3].

Infections can occur following exposure to new pathogens, but can also be caused by reactivation of a latent virus. For example, it has been shown that symptoms of URTI in swimmers were positively associated with previous infection with Epstein-Barr virus and partially with viral shedding [14]. Prior infection with cytomegalovirus may also have a similar effect. Both these viruses produce a homologue of interleukin-10, a potent anti-inflammatory cytokine which impairs the body’s ability to mount an effective immune response to pathogenic challenges.

Recently, in a collaboration with researchers from the Anthony Nolan Research Institute (London), we have compared the levels of T cell receptor excision circles (TREC), a marker of recent thymic emigrants, as well as the levels of circulating lymphocyte subsets in a group of elite triathletes and in age-matched controls [15]. This analysis revealed that the concentration of TREC molecules in the athletes was significantly lower than in age-matched controls, and the athletes also had far fewer naïve T cells. Thymus function declines with age, and while the output of both TREC and naïve T cells is relatively constant in the first 3 decades after birth, there is a significant decline observable from the late 20s to 30 years of age. Values as low as those seen in the athletes are not normally observed in normal individuals until they reach at least 60 years of age. Athletes prolonging their careers into their 30s (or beyond) may run the risk of passing from an exercise-induced thymic deficiency to an age-dependent one, creating a permanent distortion, in effect a premature ageing, in their peripheral T cell repertoire that leaves them at reduced capacity to respond to new infectious challenges. Such changes could also increase autoimmunity, as is seen in ageing. The extent to which these effects on the immune system persist on cessation of exercise training is not known, and is clearly of importance to establish if the long-term health of athletes is to be protected.

Practical Guidelines to Maintain Immune Health and Limit the Risk of Infection

It is generally agreed that prevention is always preferable to treatment, and although there is no single method that completely eliminates the risk of contracting an infection, there are several effective behavioral, nutritional and training strategies that can reduce the extent of exercise-induced immunodepression and lower the risk of infection [9], and these are summarized in figure 2.
Some practical guidelines to limit transmission of infections among athletes are shown in table 1. The most important of these are good hand hygiene and avoiding contact with persons that are infected. Hand washing (with the correct technique to ensure all parts of hands are cleaned effectively) with soap and water is effective against most pathogens but does not provide continuous protection. Hand gels containing >60% alcohol disinfect effectively but the protection they provide does not last long (only a few minutes), so they need to be applied frequently and this can cause skin drying and irritation. Other sanitization methods include the use of non-alcohol based antimicrobial hand foams (e.g. Byotrol products which contain a mixture of cationic biocides and hydrophobic polymers) that are claimed to disinfect hands for up to 6 h. However, individuals need to be aware that these products are removed by hand washing and excessive sweating and so really need to be reapplied every few hours.

The other things that athletes can do to limit their risk of infection are to adhere to some practical guidelines to maintain robust immunity and limit the impact of training stress. These guidelines (table 2) relate mostly to nutritional,
Training and recovery strategies and are based on the findings of numerous research studies; only some of the more important ones are cited as examples in table 2. The most effective nutritional strategies to maintain robust immune function during intensive training are to avoid deficiencies of essential micro-nutrients, ingest carbohydrate during exercise and ingest *Lactobacillus* probiotics on a daily basis. While not all probiotics have been shown to help maintain healthy levels of salivary IgA, prolonged ingestion of some *Lactobacillus* strains has provided encouraging results [16]. Therefore, athletes should be advised on how best to fortify their diets with the appropriate type of probiotic.

In addition to obeying the rules of good personal hygiene, the composition of the diet and timing of food intake may also help provide protection against infections. Recognizing that after heavy training and competition immune function is compromised and that carbohydrate, protein and fluid ingestion helps restore function [17–19], it is even more important that athletes are encouraged to develop feeding strategies that focus on the post-exercise period as part of their overall nutritional plans.

When cold symptoms begin, there is some evidence that taking zinc lozenges at this time (>75 mg zinc/day; high ionic zinc content) can reduce the number of days that illness symptoms last for. Ensuring that the individual has adequate

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Table 1. Guidelines to limit transmission of infections among athletes

- Individuals should be updated on all vaccines needed at home and for foreign travel. Influenza vaccines take 5–7 weeks to take effect; intramuscular vaccines may have a few small side effects, so it is advisable to vaccinate out of season. Don’t vaccinate just before competitions or if symptoms of illness are present.
- Minimize contact with infected people, young children, animals and contagious objects.
- Keep at distance to people who are coughing, sneezing or have a ‘runny nose’, and when appropriate wear (or ask them to wear) a disposable mask.
- Quickly isolate an individual with infection symptoms from others.
- Protect airways from being directly exposed to very cold (<–10°C) and dry air during strenuous exercise by using a facial mask.
- Wash hands regularly, before meals, and after direct contact with potentially contagious people, animals, blood, secretions, public places and bathrooms.
- Use disposable paper towels and limit hand to mouth/nose contact when suffering from respiratory or gastrointestinal infection symptoms (putting hands to eyes and nose is a major route of viral self-inoculation).
- Carry alcohol-based hand-washing gel with you.
- Do not share drinking bottles, cups, cutlery, towels etc. with other people.
- While competing or training abroad, choose cold beverages from sealed bottles, avoid raw vegetables and undercooked meat. Wash and peel fruit before eating.
Table 2. Guidelines to help maintain robust immunity and limit training stress

- Ensure adequate dietary energy, protein and essential micronutrient intake. It has only recently been recognized that vitamin D plays an important role in upregulating immunity [22], and this is a concern as vitamin D insufficiency is common in athletes [20], 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 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 and monitoring of circulating 25-hydroxy vitamin D concentration in athletes at risk of insufficiency is warranted.

- Avoid crash dieting and rapid weight loss. 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.

- Ensure adequate carbohydrate intake before and during strenuous prolonged exercise in order to limit the extent and severity of exercise-induced immunodepression. 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 [23]. 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.

- Avoid very prolonged training sessions (>2 h) and excessive periods of intensified training. Adequate recovery is important to avoid overtraining and chronic fatigue. Periodization of training will help to avoid becoming stale. Avoid training monotony by ensuring variation in the day-to-day training load: ensure that a hard training day is followed by a day of lighter training. Monitoring of symptoms of overreaching (mood, feelings of fatigue and muscle soreness) may be helpful [24].

- 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 [23], especially if this is not the first training session of the day. If this train-low (glycogen) concept is to be applied to maximize training adaptation [25], 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.

- The efficacy of most so-called dietary immunostimulants has not been confirmed. However, there is limited evidence that some flavonoids (e.g. quercetin) or flavonoid-containing beverages (e.g. non-alcoholic beer) can reduce URTI incidence in highly physically active people [26–28]. Some well-controlled studies in athletes have indicated that daily probiotic ingestion results in fewer days of respiratory illness and lower severity of URTI symptoms [29–31], and a recent meta-analysis using data from both athlete and non-athlete studies concluded that there is a likely benefit in reducing URTI incidence [32]. Another potential benefit of probiotics could be a reduced risk of gastrointestinal infections – a particular concern when travelling abroad. 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.

- High daily doses (up to 1,000 mg) of vitamin C are not generally justified, but individuals engaged in intensive training and/or cold environments may gain some benefit according to the latest Cochrane systematic review on vitamin C for preventing the common cold [33].
vitamin D status may also be helpful [20], and this can be assessed using blood tests to measure the plasma concentration of 25-hydroxy vitamin D.

The strategies described in tables 1 and 2 are designed to limit pathogen transmission and maintain immune competence, respectively, assuming that these symptoms all have an infectious cause. While it is certainly true that symptoms of respiratory illness are commonly reported in athletes and are generally associated with impaired athletic performance, an infectious cause of these symptoms has not always been confirmed. A study that examined the causes of symptoms of respiratory illness in both elite and recreational triathletes and a control group of age-matched sedentary subjects over a 5-month period found that only 11 out of 37 illness episodes had an identifiable infectious cause [6], with rhinovirus being the most commonly identified pathogen. There is now a consensus that airway inflammation may be at least partly responsible for some of the respiratory illness symptoms reported by athletes and probably occurs following airway damage caused by high lung ventilation rates during intensive exercise, particularly when breathing cold, dry or polluted air. Allergy can also trigger an inflammatory response, and subsequent symptoms of respiratory illness are very similar to those caused by infections. A recent study on over 200 runners who participated in the 2010 London marathon found a strong correlation between the prevalence of allergy and post-race reporting of symptoms of upper respiratory illness [21]. Allergy is both treatable and manageable if correctly diagnosed, but until recently has not generally been considered as a cause of respiratory illness by sport physicians. This suggests that screening for common allergens could be a useful addition to the recommended strategies to help minimize respiratory illness episodes in athletes.

Should infection occur, athletes can follow some basic guidelines for exercise during infectious episodes [30] before being referred to a doctor (table 3). These guidelines relate to the illness symptoms that are evident in the athlete and whether these symptoms persist, improve or worsen.

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<th>Table 2. Continued</th>
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<tr>
<td>– Wear appropriate outdoor clothing in inclement weather and avoid getting cold and wet after exercise.</td>
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<tr>
<td>– Get adequate sleep (at least 7 h per night is recommended). Missing a single night of sleep has little effect on immune function at rest or after exercise, but recent work indicates that the common cold is more prevalent in those who regularly experience low sleep quantity (&lt;7 h per night) and poor sleep quality (frequent awakenings) [34]. Consider monitoring sleep quantity and quality using small, non-invasive movement sensors.</td>
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<tr>
<td>– Wear flip-flops or similar footwear when going to the showers, swimming pool and locker rooms in order to avoid dermatological diseases.</td>
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<tr>
<td>– Keep other life stresses to a minimum. Consulting a sport psychologist may be helpful to find ways to reduce stress and adopt suitable coping behaviors.</td>
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When recovering from a respiratory illness, it is important to closely observe the individual athlete’s symptoms and tolerance to increasing training load. The following guidelines [35] can be given (table 4), but the golden rule must always be to stop training and consult a doctor if symptoms recur.

**Table 3. Guidelines for training when suffering from URTI in athletes**

- **First day of illness:** Avoid strenuous exercise or competitions when experiencing URTI symptoms like sore throat, coughing, runny or congested nose. Avoid all exercise when experiencing symptoms like muscle/joint pain and headache, fever and generalized feeling of malaise, diarrhea or vomiting.

- **Second day:** Avoid exercise if fever, diarrhea or vomiting is present or if coughing is increased. If no fever or malaise is present and there is no worsening of ‘above the collar’ symptoms, undertake light exercise (heart rate <120 beats per min) for 30–45 min (indoors during winter) by yourself.

- **Third day:** If fever and URTI (or gastrointestinal) symptoms are still present, consult your doctor. If no fever or malaise is present and there is no worsening of initial symptoms, undertake moderate exercise (heart rate <150 beats per min) for 45–60 min, preferably indoors and by yourself.

- **Fourth day:** If there is no symptom relief, do not try to exercise and pay a visit to your doctor. If this is the first day of improved condition, wait one day without fever and with improvement of URTI or gastrointestinal symptoms before returning to exercise.

- Finally, it is important to stop training and consult your doctor if a new episode with fever occurs or if initial symptoms become worse, coughing persists or breathing problems during exercise occur.

**Table 4. Guidelines for returning to training after an episode of URTI in athletes**

- Make sure you have had at least one day without fever and with improvement of other illness symptoms before resuming exercise sessions.

- Observe your body’s reaction to your first exercise session before beginning a new session.

- Begin with light training and build gradually over several days.

- Observe your tolerance to increased exercise intensity and take a day off training if recovery is less than satisfactory.

- Stop exercise altogether and consult your doctor if there is a recurrence of fever or if initial symptoms become worse, coughing persists or breathing problems during exercise occur.

When recovering from a respiratory illness, it is important to closely observe the individual athlete’s symptoms and tolerance to increasing training load. The following guidelines [35] can be given (table 4), but the golden rule must always be to stop training and consult a doctor if symptoms recur.

**Conclusions**

There is now substantial evidence to support the notion that prolonged strenuous exercise is associated with a transient suppression of immune functions which usually recover within 24 h. However, in situations of intensive training, a lack of sufficient recovery between exercise sessions can lead to chronic depression of immune responses. It has been suggested that such effects on host
defense account for the apparent higher incidence of upper respiratory and gastrointestinal illness among highly trained athletes, leading to absence from training and impaired performance. While it is certainly true that symptoms of respiratory and gastrointestinal illness are commonly reported in athletes, an infectious cause of these symptoms, particularly with regard to respiratory illnesses, has not always been confirmed. There are various training, behavioral and nutritional strategies that can help to minimize URTI risk, and these should become part of the athlete’s normal routine. A possible concern with intensive exercise training from an early age and over many years is a premature involution of the thymus and alteration of the T cell repertoire which in later life may compromise the ability to respond to new infectious challenges.

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References