## **Respiratory tract symptoms in endurance athletes – a review of causes and consequences**

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#### ABSTRACT

It is well established that medical conditions can be associated with endurance physical activities and that respiratory tract symptoms (RTS) is one of the more common medical conditions that is encountered in these athletes. RTS are particularly during intense training and immediately after competition. There are many studies documenting that alterations in immune parameters occur in athletes undergoing intense training and competition. It is a common assumption that RTS in endurance athletes are as a result of infections during periods where there are known alterations in immune parameters. However, there are no studies directly linking alterations in immune parameters in response to training and documented evidence of infections in athletes. Allergic conditions, in particular allergic rhinitis, are also common in endurance athletes, and there is some overlap in the symptomatology of upper respiratory tract infection (URTI) and allergic rhinitis. Chronic allergic rhinitis may also predispose to the development of URTI. The infective hypothesis, the allergic hypothesis and alternate hypotheses to explain the high prevalence of RTS in endurance athletes require further investigation. Current clinical guidelines for the management of RTS in athletes are mainly based on the assumption that RTS in athletes are only as a result of an infective cause. If other causes for RTS in athletes are documented, these guidelines may require modification.

#### INTRODUCTION

It is well established that regular exercise training is beneficial in the primary and secondary prevention of chronic diseases of lifestyle.<sup>1-3</sup> There is therefore a perception that athletes are generally healthy individuals, and that exercise training also protects against the risk of acquiring acute medical illnesses, including infections.<sup>4,5</sup> However, epidemiological evidence shows that increased exercise training (volume and intensity), particularly in endurance athletes, can be associated with an increased risk of developing respiratory tract symptoms (RTS) that may be associated with infections.<sup>6-14</sup>

This review paper focuses on the medical conditions that affect the respiratory system in endurance athletes, and more specifically the possible mechanisms that may lead to the development of RTS. These symptoms can occur at various stages of training and competition: the pre-competition period (during the preparation training period), during the competition (intra-competition), or the post-competition recovery period (from immediately after the finish up to 2-6 weeks later).

### Terminology and definitions

Endurance athletes can present with RTS ranging from 'blocked nose', 'runny nose', sore throat, swollen glands, cough, wheeze to chest pain. These symptoms may be accompanied by additional systemic symptoms such as fever, headache, muscle aches, joint pains and general fatigue. In some instances the term 'flu-like' illness has been used for RTS which are accompanied by systemic symptoms. In most studies where these RTS, or more specifically upper respiratory tract symptoms (URTS), have been documented, these were self-reported by athletes, without any evidence of ac-tual infection.<sup>15</sup> We are aware of only a few studies in which attempts have been made to obtain actual evidence of an infective agent in athletes presenting with RTS.<sup>14,16-18</sup> Therefore, the general use of the term upper respiratory tract infections (URTI), as has been used in many reports, without documenting actual evidence that these symptoms are due to an infection, may well be incorrect.

At present, it is well recognised that an athlete presenting with RTS that are localised to the upper airways (nose and orophraynx) is given different medical advice about exercise and training, when compared with an athlete presenting with RTS below the orophraynx (cough, wheeze, chest pain), or athletes presenting with accompanying systemic symptoms such as fever, myalgia, arthralgia and general fatigue.<sup>7</sup> This clinical test has also been referred to as the 'neck check'.<sup>19-21</sup> The use of the terms upper respiratory tract symptoms (URTS) ('blocked nose', 'runny nose', sore throat, swollen glands), lower respiratory tract symptoms (LRTS) (cough, wheeze, chest pain) and systemic symptoms (SS) (fever, myalgia, arthralgia, general fatigue) to describe these clinical presentations is therefore more appropriate.

For the purposes of this paper, the following terminology is used:

- Upper respiratory tract symptoms (URTS) refer to the presence of respiratory symptoms that are localised to the nose and pharynx ('blocked nose', 'runny nose', sore throat)
- Lower respiratory tract symptoms (LRTS) refer to the presence of respiratory symptoms below the level of the phraynx (cough, wheeze, chest pain)
- **Systemic symptoms (SS)** of infection refer to symptoms such as fever, myalgia, arthralgia and general fatigue that may accompany infections.

It should be pointed out that we are fully aware of the fact that RTS in athletes could also be due to many other cardiorespiratory conditions. In particular, we recognise that asthma is a very common respiratory condi-

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tion in athletes that could give rise to RTS. However, in this paper we wish to confine the discussions to RTS that have been related to infections, and the main focus is on URTS. We also acknowledge that the SS listed above can also occur as a result of many other infections (not only those affecting the respiratory tract) and other systemic conditions.

# EPIDEMIOLOGY OF RTS IN ENDURANCE ATHLETES

Respiratory tract infections (RTI), in particular URTI, are very common in the general population,<sup>22</sup> and are more likely to affect individuals in the extremes of age and the immune-compromised individual.<sup>23</sup> It has been reported that 75-80% of all acute morbidities in the population of the USA are due to respiratory disease, 80% of which are due to viral infections of the respiratory tract, with an average of 3-6 respiratory tract illnesses per person per year.<sup>22,24</sup> URTI are the most common types of infection, and are mainly caused by viruses.<sup>22</sup>

In athletes, it has also been reported that URTI (commonly caused by viruses) are by far the leading cause of infectious diseases in the training room.<sup>22</sup> A number of studies have documented URTS in endurance athletes, including runners, <sup>25-29</sup> cyclists, <sup>14</sup> cross-country skiers,<sup>30</sup> swimmers, <sup>12,31,32</sup> rowers,<sup>33</sup> and in participants of other sports such as tennis players,<sup>34</sup>, gymnasts,<sup>35</sup> wheelchair athletes,<sup>36</sup> and even in those undergoing military training.<sup>37</sup> It is very important to note that in all these studies, there is no verification that the symptoms are due to an infection. Hence, in all these studies it is correct to describe these as *symptoms of URTI* rather than actually documented URTI. The term URTS is therefore used consistently in this paper, when referring to these studies.

The risk of developing URTS in athletes has been reviewed.<sup>6,13,38</sup> In one of the first studies to document the relationship between URTS and endurance exercise, Peters and Bateman<sup>25</sup> in 1983 found that the incidence of URTS was twice as high in ultradistance runners in the first 10-14 days following an endurance race, when compared with suitable sedentary controls followed up in the same time period. These researchers also reported that the incidence of URTS was higher among the faster runners.

Following that first report, there have been a number of retrospective, <sup>11,39,40</sup> and prospective, <sup>14,17,18,26,27,36,41-43</sup> studies documenting URTS in different groups of athletes. An in-depth discussion of the findings of all these studies is beyond the scope of this review. However, a summary of the main findings from these studies is as follows:

- Following endurance events (mainly ultramarathon running) athletes experience an increased incidence of URTS compared with sedentary controls.<sup>25,27,39</sup>
- Prospective studies and retrospective surveys in endurance athletes over months show that increased training is associated with an increased risk of URTS.<sup>11,14,26,41</sup>
- Some studies report other factors that increase an athlete's risk of developing URTS including female gender,<sup>11,26</sup> decreased vitamin C intake,<sup>27</sup> perceived stress,<sup>11</sup> sleep deprivation,<sup>11</sup> and lack of awareness about nutrition.<sup>11</sup>
- In two prospective studies, moderate intensity training resulted in increased natural-killer-cell function, increased T-cell function and reduced incidence of URTS.<sup>42,43</sup>

Over the past decade, the results of studies in athletes and other populations have led to the commonly accepted hypothesis that the relationship between exercise training and risk of URTS is a 'J'-shaped curve.<sup>11,19,44,45</sup> It appears that physical inactivity is associated with an increased risk of URTS,<sup>46</sup> while moderate intensity and duration of physical activity has been shown to be protective in some<sup>10,47-50</sup> but not in all studies.<sup>51,52</sup> However, high-intensity, prolonged exercise, such as during endurance training and competition, may increase the risk of developing URTS.<sup>11,26,41,53</sup>

# AETIOLOGY AND PATHOPHYSIOLOGY OF RTS IN ENDURANCE ATHLETES

Until recently, it was generally assumed that RTS in athletes were due to an infective cause, and that this increased risk of infection was because prolonged, intense training or competition has been associated with a 'suppression' of a variety of parameters in the immune system. The 'suppression' of immune parameters in the 3-72 hours following intense and prolonged training has been termed the 'open window' period. During this period, it is hypothesised that infective agents entering the URT would cause URTI. Additional factors that may increase the risk of infection are the large volumes of air entering the respiratory tract particularly when mouth breathing is used by athletes during high-intensity exercise<sup>54</sup> and nutritional deficiencies, in particular carbohydrate<sup>55</sup> and vitamin C deficiency.<sup>28,29,56-58</sup>

However, it is also well established that RTS are not always due to an infection and that there may be other causes for these symptoms such as allergies or inflammation caused by other physical or chemical irritants.<sup>12,17,18,59</sup> It is only more recently that other possible causes of URTS in athletes during training or competition have been proposed. The possible hypotheses for the cause of RTS in endurance athletes are discussed under the following headings: infective hypothesis, allergic hypothesis, and other causes. Scientific evidence for each of these is briefly reviewed.

### Infective hypothesis for RTS in athletes

Since 1990, the relationship between an acute exercise bout and immune parameters, as well as the relationship between exercise training and changes in the immune parameters, has received more and more attention. Over the past 10-15 years, the number of publications in this field have increased by more than . 10-fold.<sup>60</sup> There is now an extensive body of knowledge documenting the relationship between exercise and the immune system and this has been reviewed in a number of publications.<sup>5,8,15,60-65</sup> The main focus of this review is not on exercise immunology, and hence an in-depth review of the interaction between exercise and the immune system is beyond the scope of this review. However, the main current findings relating to changes in the immune system as a result of exercise, and how these may relate to RTS in athletes are briefly reviewed.

It is well established that an acute bout of exercise as well as exercise training can alter a variety of immune parameters. Changes in systemic immunity,<sup>5</sup> mucosal immunity, and cytokines<sup>62</sup> in response to exercise have been reviewed.<sup>66</sup> To date, there have been numerous studies that were conducted to relate these changes in immune parameters to URTS in athletes. However, in most of these studies, no direct relationship between changes in immune parameters and the presence of URTS could be documented. This lack of association between measures of immune function and URTS was first pointed out by Shephard in 2000, <sup>15</sup> and again more recently.<sup>60,63</sup> The evidence for a direct link between observed changes in immune parameters, and the development of URTS can be summarised as follows:

- An acute bout of exercise as well as regular exercise training can alter systemic <sup>8,33,42,43,67-72</sup> and mucosal immunity<sup>34,35,37,47,73-81</sup> by enhancing some parameters and suppressing others.
- The biological significance of these alterations in the immune system is not well established, and requires further investigation.
- The association between changes in immune parameters and the development of RTS in athletes has been examined,<sup>31,34,35,37,70,74,75,79,82</sup> but to date, no consistent cause-effect relationship has been documented.
- Nutritional interventions to change immune system parameters and decrease the risk of URTS in athletes have been reviewed.<sup>83,84</sup>
- Although the effect of nutritional supplements such as carbohydrates,<sup>55</sup> glutamine,<sup>85</sup> and vitamin C<sup>28,29,56-58</sup> on immune parameters have been studied,<sup>86-89</sup> with the exception of vitamin C supplementation,<sup>27</sup> none of the other supplements has been shown to decrease URTS in athletes.<sup>55,87</sup>
- There is early experimental evidence from one study<sup>90</sup> to suggest that the use of probiotics may be of value in reducing the duration and severity of RTS in endurance athletes, perhaps by modulating the immune response to exercise training.<sup>91</sup>

It is therefore clear that the relationship between exercise-induced changes in immune parameters and the development of RTS in athletes is not well established. Furthermore, there are no studies confirming the diagnosis of an infection in athletes presenting with URTS where either serological criteria have been used, or where actual pathogens have been cultured. In conclusion, scientific evidence supporting the infective hypothesis as the cause of URTS in athletes undergoing training or competition is lacking. Alternative hypotheses, perhaps linking changes in the immune system parameters during intense exercise, and the development of RTS have to be considered. It has been suggested that allergic disorders, which are also mediated through the immune system, may account for the development of at least some RTS in athletes. This hypothesis will now be explored.

### Allergic hypothesis for RTS in athletes

It is well established that allergies are very common worldwide and that the prevalence of allergies has increased over the last few decades.<sup>92,93</sup> The prevalence of allergic diseases in the population of industrialised countries has been estimated at 10-25%. As mentioned, allergies have increased significantly over the last 50 years in developed countries, probably as a result of air pollution.<sup>94</sup> There is a very wide spectrum of clinical presentations of allergic conditions, ranging from a benign rash to exercise-induced anaphylaxis.<sup>95</sup> Allergic conditions of the respiratory tract in athletes can vary from allergic sinusitis, allergic rhinitis, allergic rhinoconjunctivitis to allergic asthma, and these conditions have been reviewed in other papers in this issue of the journal.<sup>93,96-99</sup> In summary, there is evidence that allergies are common in elite athletes with the prevalence of any allergy varying between 16% and 32%.

For the purposes of this review paper, it is important to note that the clinical presentation of allergic conditions that affect the respiratory tract may mimic those of URTI. Common URTS that could be due to either infections or allergies are 'blocked nose' and 'runny nose', while more systemic symptoms, such as headache, malaise and fatigue, can also occur as a result of allergies.<sup>93</sup> Associated symptoms, such as itchy nose, sneezing and itchy runny eyes, are more likely due to allergic than infective causes.<sup>54,98,100</sup> However, chronic allergies can, similarly to infections, also result in impaired sports performance; the mechanisms underlying this effect have been described in this edition of the journal.<sup>93,101</sup> It can be therefore be hypothesised that URTS in endurance athletes may be related to allergies rather than being infective in nature, or there may be an interaction between these two mechanisms. There may well be a continuum of URT disease with an overlap between respiratory tract allergies and infections, which has to date not been explored.

# Other hypotheses for RTS in athletes (physical factors)

Any discussion of the possible causes of RTS in athletes will not be complete unless it is mentioned that many other irritants can also cause an inflammatory response in the respiratory tract. A non-allergic, noninfective rhinitis can be caused by physical factors. Physical factors that may cause RTS in athletes include high ventilatory rate, cold, dry air, increased air turbulence, mouth-breathing, and inhaled irritants (physical, chemical and allergens).<sup>12,17</sup> When the ventilatory rate exceeds 30 l/min there is a tendency towards both mouth breathing and nasal breathing and this causes deposition of airborne allergens and irritants in the upper and lower respiratory tracts.<sup>54</sup> Pollutant irritants are classified as primary or secondary. Primary pollutants are directly from the source such as inorganic gases. Secondary pollutants result from chemical reactions of emitted and natural precursors. Pollutants of major concern to respiratory health are sulphur dioxide (SO<sub>2</sub>), photochemical smog (ozone and nitrogen dioxide, NO<sub>2</sub>) and airborne particulates.<sup>94</sup> Recently, it has been documented that there is an increase in airway inflammatory cells, possibly related to increased ventilation of cold and dry air.<sup>102,103</sup> The precise relationship between these observed inflammatory cells and respiratory tract pathology in athletes requires further investigation.<sup>102</sup> It is important to point out that other hypotheses relating physical and chemical factors to RTS in athletes may require further study.

# *Summary: Hypotheses for the aetiology of RTS in athletes*

In summary, the precise aetiology and pathogenesis of RTS in athletes during training, and immediately after intense competition is not clear. Until recently, the prevailing hypothesis for the high incidence of mainly URTS in endurance athletes following competition was that alterations in the immune system postexercise cause infections. However, actual infection has never been documented either clinically, by serological means, or through culture of organisms. Furthermore, despite numerous attempts, no clear relationship between altered immune parameters and URTS has been documented. Therefore, the infective hypothesis for RTS in athletes requires further study, or alternative hypotheses have to be considered.

Concomitantly, it has been documented that respiratory tract allergies, in particular allergic rhinitis, are common in athletes, especially in endurance athletes. The symptoms of allergic conditions of the URT and the symptoms of URTI overlap, and the possibility that RTS in endurance athletes is related to allergies has to be considered. Finally, other physical factors causing RTS in athletes must not be disregarded.

### EFFECTS OF RTS ON TRAINING AND COM-PETITION IN ENDURANCE ATHLETES

The effect of RTS on training and performance has not been well investigated. This is probably because the aetiology of RTS in athletes is not established. The effects of both RTI and allergic conditions of the respiratory tract on training and athletic performance will now be discussed.

There are only a few studies where the effects of RTI on training and performance have been examined. The main reason for this is that although very rare, some infective agents can cause an associated myocarditis.<sup>22,104-106</sup> Viral myocarditis has been the cause of sudden death in athletes.<sup>105,106</sup> Therefore, the current guideline for athletes with documented RTS is to avoid training if there are any symptoms of possible concomitant myocarditis, such as chest pain, shortness of breath at rest, resting tachycardia, or systemic symptoms, such as fever, myalgia or joint pain. If any of these symptoms are present, athletes are advised not to train at all based on clinical evidence.<sup>22</sup> For obvious ethical reasons the validity of this advice has not been studied systematically.<sup>7</sup> If symptoms are localised to the URT, athletes frequently do not seek medical assistance and, according to anecdotal evidence, many continue training. However, the effects of these localised URTS on training and performance have not been well investigated.

The effects of febrile illness on muscle function in humans have been investigated in a few studies. In one study where a fever was induced in seven volunteers by inoculation with the sandfly fever virus, it was documented that there is a transient decrease in muscle function which correlated with myalgia, rather than the presence of fever.<sup>107</sup> In this study, it was not possible to distinguish between inactivity (bed rest) or the febrile illness as the main cause of loss of muscle strength. In another study by the same investigators, isometric muscle strength and isometric muscle endurance were recorded serially (during fever, after fever, at 1 and 4 months after the infection) at the time of an acute infectious disease of viral or mycoplasmal aetiology in over 30 young men. In this study, the febrile illness resulted in a 5-15% decrease in isometric muscle strength and a 13-18% decrease in isometric muscle endurance as compared with control subjects undergoing bed rest for the same time period as the infected subjects.<sup>108,109</sup> It is important to point out that in these studies the infection was clearly documented, and that it was associated with SS (fever). The effects of a localised URTI on exercise performance and training have to our knowledge not been studied, other than in a report where URTI was the main medical reason for absence from training in elite skiers.<sup>30</sup>

## CLINICAL ADVICE TO ATHLETES PRE-SENTING WITH RTS

The clinical advice that is currently given to athletes presenting with RTS is largely based on whether the RTS are confined to the upper airways (above the neck), or whether there are LRTS or SS (below the neck). This clinical test has been termed the 'neck check'.<sup>19-22</sup> The main reasons for adopting this clinical approach are twofold. Firstly, LRTS or SS may indicate a generalised (systemic) infection, and systemic viral or bacterial infections may be associated with myocarditis, and this is a potential cause of sudden death in an exercising athlete.<sup>22,104,105</sup> Secondly, as has been discussed, there are indications that exercise performance is impaired significantly when LRTS or SS are present. Therefore the current clinical approach when athletes present with RTS is to document localised ('runny nose', 'blocked nose', sore throat) or additional LRTS (cough, chest pain, wheeze) or SS (muscle aches, joint pain, fever, fatigue). If only localised symptoms are present, moderate intensity exercise is allowed for a short duration, and depending on how the athlete feels, this can be continued. In the presence of any LRTS or SS exercise is not allowed and follow-up clinical assessment is advocated.<sup>19-22</sup>

However, in this current clinical approach, the presence or absence of allergic symptoms and their management, which is different to that of URTI,<sup>93,98,100</sup> are largely ignored. If a closer association between RTS in athletes undergoing intense training and allergies is documented, this current clinical approach may have to be reconsidered.

### SUMMARY AND CONCLUSIONS

- Medical conditions associated with endurance physical activities are common.
- RTS is one of the more common medical conditions that is encountered in endurance athletes, particularly during intense training and immediately after races.
- There are many studies documenting alterations in immune parameters in athletes undergoing intense training and competition.
- It is a common assumption that RTS in endurance athletes are as a result of infections during periods where there are known alterations in immune parameters.
- There are no studies directly linking alterations in immune parameters in response to training and documented evidence of infections in athletes.
- Allergic conditions, in particular allergic rhinitis, are common in endurance athletes.
- There is some overlap in the symptomatology of URTI and allergic rhinitis.
- Chronic allergic rhinitis may predispose to the development of URT infections.
- The infective hypothesis, the allergic hypothesis and alternative hypotheses to explain the high prevalence of RTS in endurance athletes require further investigation.
- Current clinical guidelines for the management of RTS in athletes are mainly based on the assumption that RTS in athletes are only as a result of an infective cause.
- If other causes for RTS in athletes are documented, these guidelines may require modification.

### Declaration of conflict of interest

The authors declare no conflict of interest.

#### REFERENCES

- Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. CMAJ 2006; 174: 801-809.
- Karacabey K. Effect of regular exercise on health and disease. Neuro Endocrinol Lett 2005; 26: 617-623.
- Kohl HW, III. Physical activity and cardiovascular disease: evidence for a dose response. *Med Sci Sports Exerc* 2001; 33(6 Suppl): S472-S483.
- Brenner IK, Shek PN, Shephard RJ. Infection in athletes. Sports Med 1994; 17: 86-107.
- Nieman DC. Special feature for the Olympics: effects of exercise on the immune system: exercise effects on systemic immunity. *Immunol Cell Biol* 2000; 78: 496-501.
- Schumacher YO, Pottgiesser T, Koenig D. The risk of upper respiratory tract infections (URTI) in athletes. *International Sportmed Journal* 2003; 4: 1-12.

- Friman G, Wesslen L. Special feature for the Olympics: effects of exercise on the immune system: infections and exercise in highperformance athletes. *Immunol Cell Biol* 2000; 78: 510-522.
- Lakier SL. Overtraining, excessive exercise, and altered immunity: is this a T helper-1 versus T helper-2 lymphocyte response? *Sports Med* 2003; 33: 347-364.
- Nieman DC. Is infection risk linked to exercise workload? Med Sci Sports Exerc 2000; 32(7 Suppl):S406-S411.
- 10. Calabrese LH, Nieman DC. Exercise, immunity, and infection. J Am Osteopath Assoc 1996; 96: 166-176.
- Konig D, Grathwohl D, Weinstock C, Northoff H, Berg A. Upper respiratory tract infection in athletes: influence of lifestyle, type of sport, training effort, and immunostimulant intake. *Exerc Immunol Rev* 2000; 6: 102-120.
- 12. Bougault V, Turmel J, Levesque B, Boulet LP. The respiratory health of swimmers. *Sports Med* 2009; 39: 295-312.
- Moreira A, Delgado L, Moreira P, Haahtela T. Does exercise increase the risk of upper respiratory tract infections? *Br Med Bull* 2009; 90: 111-131.
- Spence L, Brown WJ, Pyne DB, et al. Incidence, etiology, and symptomatology of upper respiratory illness in elite athletes. Med Sci Sports Exerc 2007; 39: 577-586.
- Shephard RJ. Special feature for the Olympics: effects of exercise on the immune system: overview of the epidemiology of exercise immunology. *Immunol Cell Biol* 2000; 78: 485-495.
- Schwellnus M P, Kiessig M, Derman W, Noakes T D. Fusafungine reduces symptoms of upper respiratory tract infections (URTI) in runners after a 56km race. *Med Sci Sports Exerc* 1997; 29(5 (Suppl)):S296.
- Cox AJ, Gleeson M, Pyne DB, Callister R, Hopkins WG, Fricker PA. Clinical and laboratory evaluation of upper respiratory symptoms in elite athletes. *Clin J Sport Med* 2008; 18: 438-445.
- Bermon S. Airway inflammation and upper respiratory tract infection in athletes: is there a link? *Exerc Immunol Rev* 2007; 13: 6-14.
- Nieman DC. Current perspective on exercise immunology. Curr Sports Med Rep 2003; 2: 239-242.
- Metz JP. Upper respiratory tract infections: who plays, who sits? Curr Sports Med Rep 2003; 2: 84-90.
- 21. Eichner E R. Infection, immunity, and exercise: what to tell patients. *Phys Sports Med* 1993; 21: 125-135.
- Hosey RG, Rodenberg RE. Training room management of medical conditions: infectious diseases. *Clin Sports Med* 2005; 24: 477-506, vii.
- Kostka T, Berthouze SE, Lacour J, Bonnefoy M. The symptomatology of upper respiratory tract infections and exercise in elderly people. *Med Sci Sports Exerc* 2000; 32: 46-51.
- 24. Ray CG. Influenza. Respiratory syncytial virus, adenovirus, and other respiratory viruses. In: Ryan KJ, ed. *Sherris Medical Microbiology An Introduction to Infectious Diseases*. 3rd ed. Upper Saddle River: Prentice Hall, 1994: 451-466.
- Peters EM, Bateman ED. Ultramarathon running and upper respiratory tract infections. An epidemiological survey. S Afr Med J 1983; 64: 582-584.
- Heath GW, Ford ES, Craven TE, Macera CA, Jackson KL, Pate RR. Exercise and the incidence of upper respiratory tract infections. *Med Sci Sports Exerc* 1991; 23: 152-157.
- Peters EM, Goetzsche JM, Grobbelaar B, Noakes TD. Vitamin C supplementation reduces the incidence of postrace symptoms of upper-respiratory-tract infection in ultramarathon runners. *Am J Clin Nutr* 1993; 57: 170-174.
- Peters EM, Anderson R, Nieman DC, Fickl H, Jogessar V. Vitamin C supplementation attenuates the increases in circulating cortisol, adrenaline and anti-inflammatory polypeptides following ultramarathon running. *Int J Sports Med* 2001; 22: 537-543.
- Peters EM, Anderson R, Theron AJ. Attenuation of increase in circulating cortisol and enhancement of the acute phase protein response in vitamin C-supplemented ultramarathoners. *Int J Sports Med* 2001; 22: 120-126.
- Berglund B, Hemmingsson P. Infectious disease in the elite crosscountry skiers: a one-year incidence study. *Clinical Sports Medicine* 1990; 2: 19-23.
- Gleeson M, McDonald WA, Pyne DB, et al. Immune status and respiratory illness for elite swimmers during a 12- week training cycle. Int J Sports Med 2000; 21: 302-307.
- Gleeson M, Pyne DB, Austin JP, et al. Epstein-Barr virus reactivation and upper-respiratory illness in elite swimmers. *Med Sci Sports Exerc* 2002; 34: 411-417.
- Nieman DC, Nehlsen-Cannarella SL, Fagoaga OR, et al. Immune function in female elite rowers and non-athletes. Br J Sports Med 2000; 34: 181-187.
- Novas AM, Rowbottom DG, Jenkins DG. Tennis, incidence of URTI and salivary IgA. Int J Sports Med 2003; 24: 223-229.

- 35. Filaire E, Bonis J, Lac G. Relationships between physiological and psychological stress and salivary immunoglobulin A among young female gymnasts. *Percept Mot Skills* 2004; 99: 605-617.
- Furusawa K, Tajima F, Okawa H, Takahashi M, Ogata H. The incidence of post-race symptoms of upper respiratory tract infection in wheelchair marathon racers. *Spinal Cord* 2007; 45: 513-517.
- Tiollier E, Gomez-Merino D, Burnat P, et al. Intense training: mucosal immunity and incidence of respiratory infections. Eur J Appl Physiol 2005; 93: 421-428.
- Page CL, Diehl JJ. Upper respiratory tract infections in athletes. *Clinical Sports Medicine* 2007; 26: 345-359.
- Nieman DC, Johanssen L M, Lee J W. Infectious episodes in runners before and after a roadrace. J Sports Med Phys Fitness 1989; 29: 289-296.
- Fricker PA, Gleeson M, Flanagan A, *et al.* Do elite swimmers experience more upper respiratory tract illness than nonathletes? *Clin Exerc Physiol* 2000; 2: 155-158.
- Linde F. Running and upper respiratory tract infections. Scan J Sports Sci 1987; 9: 21-23
- Nieman DC, Nehlsen-Cannarella SL, Markoff PA, et al. The effects of moderate exercise training on natural killer cells and acute upper respiratory tract infections. Int J Sports Med 1990; 11: 467-473.
- Nieman DC, Henson DA, Gusewitch G, et al. Physical activity and immune function in elderly women. *Med Sci Sports Exerc* 1993; 25: 823-831.
- 44. Baum M, Liesen H. [Sports and the immune system]. Orthopade 1997; 26: 976-980.
- 45. Nieman DC. Exercise, infection, and immunity. Int J Sports Med 1994; 15 Suppl 3: S131-S141.
- Jedrychowski W, Maugeri U, Flak E, Mroz E, Bianchi I. Cohort study on low physical activity level and recurrent acute respiratory infections in schoolchildren. *Cent Eur J Public Health* 2001; 9: 126-129.
- Klentrou P, Cieslak T, MacNeil M, Vintinner A, Plyley M. Effect of moderate exercise on salivary immunoglobulin A and infection risk in humans. *Eur J Appl Physiol* 2002; 87: 153-158.
- Klentrou P, Hay J, Plyley M. Habitual physical activity levels and health outcomes of Ontario youth. *Eur J Appl Physiol* 2003; 89: 460-465.
- Kotaniemi-Syrjanen A, Reijonen TM, Korhonen K, Korppi M. Wheezing requiring hospitalization in early childhood: predictive factors for asthma in a six-year follow-up. *Pediatr Allergy Immunol* 2002; 13: 418-425.
- Matthews CE, Ockene IS, Freedson PS, Rosal MC, Merriam PA, Hebert JR. Moderate to vigorous physical activity and risk of upperrespiratory tract infection. *Med Sci Sports Exerc* 2002; 34: 1242-1248.
- Hemila H, Virtamo J, Albanes D, Kaprio J. Physical activity and the common cold in men administered vitamin E and beta-carotene. *Med Sci Sports Exerc* 2003; 35: 1815-1820.
- Schouten WJ, Verschuur R, Kemper HC. Physical activity and upper respiratory tract infections in a normal population of young men and women: the Amsterdam Growth and Health Study. *Int J Sports Med* 1988; 9: 451-455.
- Nieman DC. Upper respiratory tract infections and exercise. *Thorax* 1995; 50: 1229-1231.
- Alaranta A, Alaranta H, Heliovaara M, Alha P, Palmu P, Helenius I. Allergic rhinitis and pharmacological management in elite athletes. *Med Sci Sports Exerc* 2005; 37: 707-711.
- 55. Nieman DC, Pedersen BK. Exercise and immune function. Recent developments. *Sports Med* 1999; 27: 73-80.
- Krause R, Patruta S, Daxbock F, Fladerer P, Biegelmayer C, Wenisch C. Effect of vitamin C on neutrophil function after high-intensity exercise. *Eur J Clin Invest* 2001; 31: 258-263.
- Nieman DC, Peters EM, Henson DA, Nevines EI, Thompson MM. Influence of vitamin C supplementation on cytokine changes following an ultramarathon. J Interferon Cytokine Res 2000; 20: 1029-1035.
- Peters-Futre EM. Vitamin C, neutrophil function, and upper respiratory tract infection risk in distance runners: the missing link. *Exerc Immunol Rev* 1997; 3: 32-52.
- Pyne DB, Gleeson M. Effects of intensive exercise training on immunity in athletes. Int J Sports Med 1998; 19 Suppl 3: S183-S191.
- Malm C. Exercise immunology: the current state of man and mouse. Sports Med 2004; 34: 555-566.
- MacKinnon LT. Special feature for the Olympics: effects of exercise on the immune system: overtraining effects on immunity and performance in athletes. *Immunol Cell Biol* 2000; 78: 502-509.
- Pedersen BK. Special feature for the Olympics: effects of exercise on the immune system: exercise and cytokines. *Immunol Cell Biol* 2000; 78: 532-535.
- Gleeson M, Pyne DB, Callister R. The missing links in exercise effects on mucosal immunity. *Exerc Immunol Rev* 2004; 10: 107-128.

- Jeurissen A, Bossuyt X, Ceuppens JL, Hespel P. [The effects of physical exercise on the immune system]. Ned Tijdschr Geneeskd 2003; 147: 1347-1351.
- MacKinnon LT. Chronic exercise training effects on immune function. Med Sci Sports Exerc 2000; 32(7 Suppl): S369-S376.
- Gleeson M. Immune function in sport and exercise. J Appl Physiol 2007; 103: 693-699.
- Green KJ. Improving understanding of exercise effects on in vitro T-lymphocyte function - the role of fluorescent cell division tracking. *Exerc Immunol Rev* 2002; 8: 101-115.
- McKune AJ, Smith LL, Semple SJ, Wadee AA. Influence of ultraendurance exercise on immunoglobulin isotypes and subclasses. *Br J Sports Med* 2005; 39: 665-670.
- Muns G. Effect of long-distance running on polymorphonuclear neutrophil phagocytic function of the upper airways. *Int J Sports Med* 1994; 15: 96-99.
- Pedersen BK, Toft AD. Effects of exercise on lymphocytes and cytokines. Br J Sports Med 2000; 34: 246-251.
- Shephard RJ. Cytokine responses to physical activity, with particular reference to IL-6: sources, actions, and clinical implications. *Crit Rev Immunol* 2002; 22: 165-182.
- Shinkai S, Kurokawa Y, Hino S, et al. Triathlon competition induced a transient immunosuppressive change in the peripheral blood of athletes. J Sports Med Phys Fitness 1993; 33: 70-78.
- Akimoto T, Kumai Y, Akama T, et al. Effects of 12 months of exercise training on salivary secretory IgA levels in elderly subjects. Br J Sports Med 2003; 37: 76-79.
- 74. Ciloglu F. The effect of exercise on salivary IgA levels and the incidence of upper respiratory tract infections in postmenopausal women. *Kulak Burun Bogaz Ihtis Derg* 2005; 15(5-6): 112-116.
- Fahlman MM, Engels HJ, Morgan AL, Kolokouri I. Mucosal IgA response to repeated wingate tests in females. *Int J Sports Med* 2001; 22: 127-131.
- Gleeson M. Mucosal immune responses and risk of respiratory illness in elite athletes. *Exerc Immunol Rev* 2000; 6: 5-42.
- Libicz S, Mercier B, Bigou N, Le Gallais D, Castex F. Salivary IgA response of triathletes participating in the French Iron Tour. *Int J* Sports Med 2006; 27: 389-394.
- Muns G, Singer P, Wolf F, Rubinstein I. Impaired nasal mucociliary clearance in long-distance runners. *Int J Sports Med* 1995; 16: 209-213.
- Nehlsen-Cannarella SL, Nieman DC, Fagoaga OR, et al. Saliva immunoglobulins in elite women rowers. Eur J Appl Physiol 2000; 81: 222-228.
- Reid MR, Drummond PD, MacKinnon LT. The effect of moderate aerobic exercise and relaxation on secretory immunoglobulin A. Int J Sports Med 2001; 22: 132-137.
- Sari-Sarraf V, Reilly T, Doran DA. Salivary IgA Response to Intermittent and Continuous Exercise. Int J Sports Med 2006; 27:849-855.
- Dressendorfer RH, Petersen SR, Moss Lovshin SE, Hannon JL, Lee SF, Bell GJ. Performance enhancement with maintenance of resting immune status after intensified cycle training. *Clin J Sport Med* 2002; 12: 301-307.
- Moreira A, Kekkonen RA, Delgado L, Fonseca J, Korpela R, Haahtela T. Nutritional modulation of exercise-induced immunodepression in athletes: a systematic review and meta-analysis. *Eur J Clin Nutr* 2007; 61: 443-460.
- Nieman DC. Immunonutrition support for athletes. Nutr Rev 2008; 66: 310-320.
- Krieger JW, Crowe M, Blank SE. Chronic glutamine supplementation increases nasal but not salivary IgA during 9 days of interval training. J Appl Physiol 2004; 97: 585-591.
- Nieman DC. Exercise immunology: nutritional countermeasures. Can J Appl Physiol 2001; 26 Suppl: S45-S55.

- Nieman DC, Bishop NC. Nutritional strategies to counter stress to the immune system in athletes, with special reference to football. *J Sports Sci* 2006; 24: 763-772.
- Peters EM. Nutritional aspects in ultra-endurance exercise. Curr Opin Clin Nutr Metab Care 2003; 6: 427-434.
- Venkatraman JT, Pendergast DR. Effect of dietary intake on immune function in athletes. Sports Med 2002; 32: 323-337.
- Cox AJ, Pyne DB, Saunders PU, Fricker PA. Oral administration of the probiotic Lactobacillus fermentum VRI-003 and mucosal immunity in endurance athletes. *Br J Sports Med* 2010; 44: 222-226.
- West NP, Pyne DB, Peake JM, Cripps AW. Probiotics, immunity and exercise: a review. Exerc Immunol Rev 2009; 15: 107-126.
- Komarow HD, Postolache TT. Seasonal allergy and seasonal decrements in athletic performance. *Clin Sports Med* 2005; 24(2): e35-50, xiii.
- MacKnight JM, Mistry DJ. Allergic disorders in the athlete. Clin Sports Med 2005; 24(3):507-viii.
- Katelaris CH. Atmospheric emissions and the allergic athlete. International Sportmed Journal 2000; 1(2):1-7.
- Terrell TT, Hough DO, Alexander R. Identifying exercise allergies, exercise-induced anaphylaxis and cholinergic urticaria. *Phys Sports Med* 1996; 24: 76-89.
- Helenius IJ, Tikkanen HO, Sarna S, Haahtela T. Asthma and increased bronchial responsiveness in elite athletes: atopy and sport event as risk factors. J Allergy Clin Immunol 1998; 101: 646-652.
- Helenius IJ, Tikkanen HO, Haahtela T. Occurrence of exercise induced bronchospasm in elite runners: dependence on atopy and exposure to cold air and pollen. *Br J Sports Med* 1998; 32: 125-129.
- Katelaris CH, Carrozzi FM, Burke TV. Allergic rhinoconjunctivitis in elite athletes: optimal management for quality of life and performance. Sports Med 2003; 33: 401-406.
- Schwartz LB, Delgado L, Craig T, et al. Exercise-induced hypersensitivity syndromes in recreational and competitive athletes: a PRACTALL consensus report (what the general practitioner should know about sports and allergy). Allergy 2008; 63: 953-961.
- Katelaris CH. Allergic rhinoconjunctivitis an overview. Acta Ophthalmol Scand Suppl 2000; 230: 66-68.
- Katelaris CH, Carrozzi FM, Burke TV, Byth K. A springtime olympics demands special consideration for allergic athletes. J Allergy Clin Immunol 2000; 106: 260-266.
- 102. Bonsignore MR, Morici G, Vignola AM, et al. Increased airway inflammatory cells in endurance athletes: what do they mean? Clin Exp Allergy 2003; 33: 14-21.
- 103. Karjalainen EM, Laitinen A, Sue-Chu M, Altraja A, Bjermer L, Laitinen LA. Evidence of airway inflammation and remodeling in ski athletes with and without bronchial hyperresponsiveness to methacholine. *Am J Respir Crit Care Med* 2000; 161: 2086-2091.
- 104. Leonard EG. Viral myocarditis. *Pediatr Infect Dis J* 2004; 23: 665-666.
- Shephard RJ, Shek PN. Infectious diseases in athletes: new interest for an old problem. J Sports Med Phys Fitness 1994; 34: 11-22.
- 106 Roberts JA. Viral illnesses and sports performance. Sports Med 1986; 3: 298-303.
- 107. Friman G, Wright JE, Ilback NG, et al. Does fever or myalgia indicate reduced physical performance capacity in viral infections? Acta Med Scand 1985; 217: 353-361.
- Friman G. Effect of acute infectious disease on isometric muscle strength. Scand J Clin Lab Invest 1977; 37: 303-308.
- Friman G. Effects of acute infectious disease on circulatory function. Acta Med Scand Suppl 1976; 592: 1-62.