AIRWAY DYSFUNCTION IN ELITE ATHLETES – AN OCCUPATIONAL LUNG DISEASE?

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ABSTRACT

Airway dysfunction is prevalent in elite endurance athletes and when left untreated may impact upon both health and performance. There is now concern that the intensity of hyperpnoea necessitated by exercise at an elite level may be detrimental for an athlete's respiratory health. This article addresses the evidence of causality in this context with the aim of specifically addressing whether airway dysfunction in elite athletes should be classified as an occupational lung disease. The approach used highlights a number of concerns and facilitates recommendations to ensure airway health is maintained and optimised in this population. We conclude that elite athletes should receive the same considerations for their airway health as others with potential and relevant occupational exposures.

INTRODUCTION

Airway dysfunction is common in elite athletes with studies consistently demonstrating a prevalence of between 25-75%, depending on the group of athletes studied and the diagnostic criteria employed (1, 2). Thus whilst it is accepted that regular physical activity promotes wellbeing, there is legitimate concern that the frequent, prolonged periods of hyperpnoea, characteristic of certain high-level sports, may be detrimental to respiratory health (3). Indeed it has been argued that exercise hyperpnoea may actually cause 'injury' to the airways, promoting the development of airway dysfunction and respiratory symptoms (4). This concern is substantiated by evidence that transient airway hyper-responsiveness (AHR) is temporally associated with exposure to regular athletic training (5, 6).

The negative consequences of exercise 'injuring' the airways are probably most acutely borne by elite endurance athletes, a group of individuals whose 'occupation' demands frequent episodes of prolonged hyperpnoea, often whilst exposed to potentially noxious stimuli (e.g. sport-specific environmental exposures). It has therefore been suggested that the development of airway dysfunction in this population could be considered akin to an occupational lung disease (7). While intense exposures to respiratory irritants such as chlorine, usually in the context of an accident, can induce an asthma-like disease (8), whether repeated workplace exposures at lower intensities have the same potential is far less clear (9).

Applying a label of occupational disease in this setting raises implications for the care and treatment afforded to elite athletes. Indeed it is a key mandate of the International Olympic Committee – Medical Commission (IOC-MC) that no athlete is harmed by exposure to sport and that all care is taken to ensure their health is maintained.

A number of articles have recently outlined the pathophysiological basis for airway injury in athletes (3, 10), however despite, or perhaps because of, the potential ramifications there has been no discussion as to whether airway dysfunction in elite athletes should be classified as

'occupational lung disease'. Moreover there is no specific guidance in the relevant Respiratory Society statements (11-13).

The aim of this review is therefore to specifically appraise whether the literature in this field substantiates classifying airway dysfunction in athletes as an occupational lung disease, with the purpose of improving clinical care and providing direction for future research. Publications in the peer-reviewed literature until May 2013 were reviewed using search terms such as 'exercise-induced asthma or bronchoconstriction', 'airway hyper-responsiveness', 'asthma' in combination with 'athletes'.

APPROACH TO EVALUATING AN OCCUPATIONAL LUNG DISEASE

The Occupational Safety and Health Administration describe occupational disease states as "any abnormal condition or disorder, other than one resulting from an occupational injury, caused by exposure to factors associated with employment". More specifically, an occupational lung disease is a respiratory disorder 'related to the inhalation of natural occurring or manmade agents of various chemical and physical compositions' in the workplace (14). Occupational asthma specifically refers to *new development* of asthma in relation to a causative exposure within the workplace, whilst work-exacerbated asthma describes pre-existing or concurrent asthma that is *worsened* by agents within the workplace (15). The development of occupational asthma spans a broad spectrum including IgE-mediated allergen hypersensitivities, acute exposure to high concentration irritants and chronic exposure to low level agents (16). As the respective prognosis following exposure in these groups is poor, individuals with a confirmation of occupational asthma are advised to avoid further exposure following diagnosis of their disease to provide the greatest chance of recovery (16, 17).

Throughout this review 'airway dysfunction' is used as a term to encompass the entities of exercise-induced bronchoconstriction (EIB), exercise-induced asthma (EIA), AHR and/or

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asthma. However we recognise that the nomenclature in this area remains controversial (11) and therefore we have highlighted when findings apply specifically to EIB, AHR or asthma. Moreover, where relevant, we focus on differences between physiological phenomena and clinical disease characteristics.

IS THERE AN INCREASED FREQUENCY OF AIRWAY DYSFUNCTION IN ATHLETES?

There is now a plethora of data showing that the prevalence of airway dysfunction is significantly greater in athletes than in the general population (1). This higher prevalence is observed predominately in endurance athletes (i.e. those performing sustained intense exercise at sub-maximal level), most notably those participating in pool-based or winter sports (3), with a reported prevalence of up to 70% and 50% respectively (18-23). However, and of concern, it also appears that the prevalence of airway dysfunction is high in athletes undertaking sports that have mass participation (e.g. football and rugby) (24, 25).

There is strong evidence for an interaction between the duration and characteristics of ventilatory demand in a given sport and the environmental irritant load, in leading to the development of airway dysfunction. In this respect, there is evidence to suggest that athletes who undertake endurance training have a greater prevalence of airway dysfunction (26). For example, the prevalence of EIB in cross-country skiers is typically four-fold greater than ski-jump orientated athletes (3); both groups compete in winter conditions but there is a marked difference in their total ventilatory load (26). A similar relationship is evident in pool-based sports, in which at least >17% of Olympic swimmers are reported to have airway dysfunction (26), while indoor competition divers have a prevalence of ~4% (IOC Independent Asthma Panel, 2002-2011) (3).

As the ventilation rate during swimming determines the quantity of inhaled chlorine derivatives, elite swimmers training for many hours per week are potentially at a greater risk

of developing airway dysfunction (27). In addition, a high prevalence of airway dysfunction has been observed in synchronised swimmers (26) and this may relate to the prolonged periods of time spent in apnoea following the inhalation of contaminated air.

This acknowledged, the development of respiratory symptoms in pool-based (non–athletic) workers (28) supports the theory that environmental exposure is important in the development of airway dysfunction in competitive swimmers. Dickinson et al. (29) reported that the prevalence of airway dysfunction in the British Olympic Team was 21.2% and 20.7% respectively at the 2000 and 2004 Olympic Games; with highest prevalence in endurance athletes exposed to potentially noxious environments (e.g. chlorine derivatives in swimmers and carbon monoxide in cyclists). In contrast, sports that are neither characterised by a sustained elevation in ventilatory requirement, nor performed in allergy or irritant-laden environments (e.g. badminton or weight lifting) had a prevalence of EIB similar to that in the general population (26, 29) .

DOES EXERCISE INDUCE AIRWAY DYSFUNCTION?

A number of prospective studies of elite athletes have set out to examine the temporal relationship between exercise and development of airway dysfunction (Table 1).

A deterioration in the lung function of winter-sport athletes over the course of their careers has been anecdotally recognised for some time (30). However others have failed to find a similar relationship in summer sport athletes (31).

This acknowledged, in the context of airway function, it is more logical to examine changes in bronchial hyper-reactivity rather than progressive changes in static lung function. Accordingly, Knöpfli et al. (5) prospectively assessed bronchial reactivity on three occasions over a two-year period in the Swiss national triathlon team. Participants (n=7) were free from respiratory disease at study entry but over the course of the study all developed evidence of

increased bronchial reactivity (defined as a propensity to reduced lung function following exercise challenge) and almost half developed EIB. Based on predictive modelling of changes in lung function over the study period, the authors proposed that all members of the group would develop EIB within five years of starting to compete.

It is important to highlight that in some cases an athlete may have pre-existing asthma that is exacerbated by their 'occupation'. Indeed, an explanation often cited to explain the high prevalence of airway dysfunction in swimmers relates to a selection bias; whereby individuals with asthma are encouraged to take up swimming under the assumption that a warm humid pool environment is less asthmogenic (32).

There is conflicting data in this area with some authors reporting that the vast majority of swimmers develop respiratory symptoms subsequent to commencing their swimming career (33), whilst others report evidence of equal rates of childhood asthma in both pool and non-pool based athletes (22).

IS THERE AN EXPOSURE-RESPONSE RELATIONSHIP?

In this context a 'biological gradient' can be evaluated by examining exposure time in a sport or cumulative hours training and how these modify the risk of airway dysfunction. Heir and Larson (34) reported that airway sensitivity to methacholine in cross-country skiers correlated negatively with changes in the volume of exercise performed. In addition, Stensrud et al. (35) observed increased AHR to methacholine in elite athletes with increasing age and training volume.

Bougault et al. (20) and Bonsignore et al. (36) each reported a correlation between sputum neutrophilia and training load. In young competitive rowers the cellularity of induced sputum obtained shortly after 'all-out' tests correlates directly with minute ventilation during the bout (37).

More recently Pedersen and colleagues (38) reported that although adolescent swimmers do not have evidence of airway damage following the first few years of training, they develop respiratory symptoms, airway inflammation and AHR over the course of their careers.

Overall, these studies support the notion that AHR and airway inflammation are heightened in some athletes exposed to repeated bouts of heavy endurance training performed in noxious environments.

IS THE ASSOCIATION BIOLOGICALLY PLAUSIBLE?

Plausibility related to exercise hyperpnoea

Elite-level athletes often train up to three times a day at an intensity requiring ventilation levels to rise to 20-30 times those at rest (i.e. from 5 L/min to over 150 L/min). Ventilation rates in excess of 30 L/min result in a shift in breathing pattern from almost exclusive nasal airflow to combined oral and nasal airflow (39). As a result the lower airways are exposed to a greater quantity of unconditioned air and potential deposition of airborne allergens and other inhaled particles (e.g. pollutants).

It is thought that exercise hyperpnoea precipitates EIB by inducing osmotic changes at the distal airway surface (40). This precipitates inflammatory mediator release and cellular ion shifts which ultimately results in airway smooth muscle contraction.

Recent findings indicate that acute exercise hyperpnoea transiently disrupts the airway epithelium in both healthy and asthmatic athletes (41). In the chronic setting, repeated, prolonged periods of exercise hyperpnoea are associated with the development of airway change that is analogous to the pathological pattern seen in response to injury or insult; indicated by an increase in endobronchial debris, pro-inflammatory cells, cellular inflammatory mediators and airway remodelling (42, 43).

In a canine model, Freed and colleagues (44) demonstrated that a model mimicking exercise hyperpnoea, with insufflation of dry air, resulted in airway epithelial cell damage. In addition, repeated exposure to dry air hyperpnoea results in eosinophilic airway inflammation (45).

Moreover, repeated airway cooling and desiccation through peripheral airway hyperpnoea, performed in dogs, resulted in airway inflammation and remodelling; supporting the hypothesis that asthma-like symptoms in elite winter sport athletes may be the result of repeated hyperpnoea with dry cold air (46). The inhalation of warm moist air has been recently identified to limit this airway epithelial cell perturbation and injury (41).

In humans, the association between exercise hyperpnoea and airway dysfunction has perhaps been most extensively evaluated in winter sport athletes (47). In this highly specialised population, where athletes train and compete in sub-zero temperatures for several hours daily, cross-sectional studies have indicated a high prevalence of both respiratory symptoms and airway dysfunction (47). Moreover, endobronchial samples taken from elite cross-country skiers demonstrate increased epithelial basement membrane thickness and deposition of tenascin supporting the presence of chronic airway remodelling (42). Other studies reveal an increased presence of airway pro-inflammatory mediators (e.g. tumour necrosis factor-alpha) and airway neutrophilia in this population of athletes (19).

Elite winter sport athletes, exposed to extreme cold and thus 'noxious' conditions, are not necessarily representative of the general elite athletic population. This acknowledged, a similar if somewhat less exaggerated pattern of chronic airway pathology is apparent in non-winter sport athletes, including rowers (37) and swimmers (6, 48). In these athletes, studies also reveal evidence of epithelial damage and shedding after both acute and repeated exercise bouts (37, 49).

Others have reported increased serum and urine biomarker signals of active airway injury-repair cycling, e.g. Clara cell protein – CC16, following dry air hyperpnoea (50). Importantly, changes in CC16 levels are attenuated with inhaled warm humid air, suggesting that dry air hyperpnoea in humans directly insults the airway. This insult may be transient and it is important to note that many of the pro-inflammatory changes apparent within the airway lumen following hyperpnoea are resolved over a short period (<24 hours) (50).

Variable degrees of both neutrophilic and eosinophilic airway inflammation have been identified in summer sports athletes (51). The process driving cellular infiltration into the airway lumen in the context of exercise is complex (40, 44); it has been proposed that airway eosinophilia may relate to certain environmental exposures (e.g. indoor swimming pool toxins) (52). This supposition was supported by recent work revealing eosinophilia in the bronchial biopsies of swimmers (48).

A further possible mechanism linking airway dysfunction and exercise hyperpnoea relates to the consequence of exercise hyperpnoea causing mechanical stress (53). Although somewhat controversial, repeated episodes of bronchoconstriction are now recognised to promote the development of structural changes within the airway wall and predispose to bronchoconstriction (54, 55) . In addition, airway shear stress may also promote release of chemo-attractants promoting a pro-inflammatory milieu (56).

Despite this, it is important to acknowledge that murine studies have failed to demonstrate the development of airway injury or dysfunction in response to exercise training (57, 58). Moreover, in contrast to elite athletes, a reduction in airway reactivity has been observed in non-elite runners following a prolonged bout of exercise (59). In addition, whilst an accelerated decline in FEV_1 has been observed in occupational asthmatics, following repeated exposure to the causative agent (60), the long-term implications of structural airway remodelling on lung function (i.e. FEV_1) in athletes has yet to be established.

Plausibility related to training environment

A number of environmental pollutants or irritants have been implicated in the development and progression of airway dysfunction in elite athletes (21) (Table 2). A comprehensive review of the literature in this area is beyond the scope of this article but it is worth highlighting the evidence in two groups of well-studied athletes with a high prevalence of airway dysfunction (20, 61), namely swimmers and ice-arena athletes.

Elite level swimmers may train up to 30 hours per week (49), inhaling air from just above the water surface where the mean chlorine concentration can be 0.4 mg/m^3. Although below the threshold limited value of 1.45 mg/m^3, this value could be reached and even exceeded when considering the total amount of chlorine that a swimmer inhales during a training session (62).

Chlorine derivatives, used to disinfect swimming pools, interact with other chemicals in the water to form chloramines. Ambient chloramine levels have been linked with the development of upper respiratory symptoms and atopy in lifeguards and swimming pool workers (28). The mechanisms underlying the association between airway dysfunction and chloramine exposure remain unclear but it is recognised that chloramine exposure induces structural change in the airway epithelium and is associated with rapid increases in circulating proteins indicative of altered lung permeability (63). This is relevant for elite swimmers, who over a two-hour training session may be exposed to chlorine levels that exceed the recommended levels for a pool worker during an eight-hour exposure and over the course of a week will be exposed to 100 times more chlorine compounds than a recreational swimmer (64).

Winter sport athletes (e.g. ice hockey players) can be subjected to high levels of pollutants emitted from internal combustion fossil-fuelled ice resurfacing machines such as carbon monoxide, nitrogen dioxide, sulphur dioxide and particulate matter (PM) (65). In particular,

ultra-fine particles (<0.1 μm) ($PM_{0.1}$) have been identified as an important stimulus driving airway dysfunction (23, 66). The exact mechanism by which $PM_{0.1}$ exposure induces airway dysfunction remains to be fully determined; however, systemic oxidative stress as a result of a release of inflammatory mediators from airway cells entering the circulatory system may be implicated (66).

Plausibility related to allergen exposure

Outdoor endurance athletes can be exposed to a very heavy aeroallergen load in the spring and summer seasons with the change in pattern of ventilation necessitated by hyperpnoea (to predominately mouth breathing) diminishing the nasal filtering of pollen particles. Moreover, exposures to common aeroallergens in indoor training arenas often exceed the threshold for sensitisation (67).

In addition, a high proportion of young athletes are atopic in comparison to the general population (61, 68) with over 80% of allergic athletes poly-sensitised (69). One study reported that the risk of an athlete developing asthma was strongly associated with atopic disposition (70); the relative risk of developing asthma increasing ~25 fold in atopic speed and power athletes and ~75 fold in atopic endurance athletes in comparison to controls (71). Moreover, the likelihood of an athlete having increased bronchial responsiveness increases in relation to the number of positive skin responses to aeroallergen (72).

It is possible that prolonged repeated exposure to pollen in sensitised athletes may induce mild persistent bronchial inflammation sensitising airway mast cells (73). In addition, epithelial damage mediated by exogenous factors such as allergen exposure has been postulated to be a key mechanism resulting in airway remodelling in asthmatics (74).

Finally, it has been proposed that circulating levels of IgE in atopic athletes may result in the airway smooth muscle becoming 'passively sensitised' through transient yet repeated

exposure to bulk plasma (40). This sensitisation may alter contractile properties of the airway smooth muscle, resulting in a heightened sensitivity to inflammatory mediators (4, 40).

DOES REDUCING EXERCISE OR RELATED EXPOSURES IMPROVE AIRWAY DYSFUNCTION?

Helenius et al. (33) undertook a comprehensive five-year prospective evaluation of the effect of discontinuing high level exercise on airway inflammation, bronchial responsiveness and asthma in highly trained elite swimmers from the Finnish national team. In swimmers who stopped high-level training there was a reduction in eosinophilic airway inflammation and an attenuation or disappearance of AHR. In contrast, in the control group who continued intensive training on a regular basis, there was no such change.

The findings are supported by those from a further study of elite level swimmers indicating that alterations in airway inflammation and AHR over a one-year period related to training load (6). More specifically, training load contributed to the development of AHR and the latter was reversed in the majority of athletes following a two-week recovery period.

It would be reasonable to assume that reducing exposure to noxious agents would offer protection and result in a similar improvement in lung function. Devices such as face masks and heat and moisture exchange (HME) devices have been identified as novel strategies to increase the water content of inspired air - thereby reducing the rate of water loss from the airway. Furthermore, they possess the potential to increase inspired air temperature from -10°C to at least 19°C, thus reducing the potential for airway injury (3). Such devices have been reported to block a cold exercise-induced decline in lung function at least as effectively as pre-treatment with salbutamol (75).

SUMMARY – SHOULD AIRWAY DYSFUNCTION IN ATHLETES BE CLASSIFIED AS AN OCCUPATIONAL LUNG DISEASE?

Airway dysfunction has now been consistently reported in athletes training and competing across a range of both summer and winter endurance sports. Whilst we acknowledge that further work is required, the current best available evidence suggests the explanation for this association lies in the provocative nature of repeated exercise hyperpnoea performed in irritant laden environments.

Injury or disease?

To date much of the work evaluating elite athletes has examined surrogate markers of airway disease (i.e. presence of airway inflammatory change and/or hyper-reactivity) for which there may be a poor relationship with symptom burden. This has important implications for the classification of an athlete's condition as an occupational 'disease'. The latter can be defined as an 'abnormal condition that affects the body of an organism' (76), however it is generally accepted to describe a condition with specific symptoms and signs (77); with 'injury' being specifically excluded.

In this respect, whilst there is an evolving literature indicating that pathophysiological airway change is more prevalent in elite level athletes (3, 43), there currently remains a paucity of detail relating this to manifestations classically associated with airway disease (e.g. exacerbations). Moreover, there is no current evidence to suggest long-term morbidity or mortality arising from the development of airway dysfunction in athletes (78).

Implications for athletes

The re-classification of airway dysfunction as an occupational lung disease would have a number of important implications. Firstly we speculate it is likely that few affected athletes would wish to stop performing their sport prematurely even if they were advised that this would probably lead to an improvement in their airway function.

Secondly, classifying airway dysfunction in athletes as an occupational disease would have implications if an athlete is considered 'employed'. Specifically it raises considerations for insurance, remuneration and potentially dictates a requirement for sporting bodies and organisations to cover litigation arising from an athlete developing airway dysfunction. The 'employment' status of elite athletes varies according to the sport and level of participation of an individual; premiership level professional footballers for example are often employed by their club whilst elite track athletes are usually supported by a grant but not officially 'employed'. By extension, it is also potentially relevant to consider occupations in which individuals (such as those in certain military roles) are required to exercise to a similar extent to endurance athletes.

Thirdly, it raises issues for the way in which the airway health of athletes is monitored. In order to prevent airway dysfunction developing in elite athletes it first needs to be accurately detected. The screening of athletes for underlying disease has precedent in the field of cardiology. In some European countries, any individual wishing to compete in an official organised sporting event is required by law to undergo an annual electrocardiogram exercise test. Identification of an underlying cardiac abnormality results in immediate disqualification from participation. Although proponents of this approach point to a fall in cardiac-related deaths during exercise as a sign of its success (79), the relative merits of this process have been debated and some authors have argued that the cost implications preclude the introduction of a widespread cardiac screening programme (80, 81). Similar considerations need to be taken into account prior to the introduction of screening athletes for airway dysfunction.

We have previously argued (2) that population screening of athletes for airway dysfunction is not substantiated when appraised against the WHO screening criteria; there remains too little clarity over diagnostic methodology and the natural course of the disease to support this

recommendation. Moreover, in any widespread screening programme the cost of implementation needs to be considered prior to initiation. Despite this, medical surveillance however is commonplace in certain high-risk occupations (e.g. air-force pilots and firefighters) and it may be that a similar programme would be appropriate in certain high-risk athletic groups, e.g. competitive swimmers.

Protecting airway health in athletes

Strategies aimed at a reduction in the factors driving airway dysfunction in athletes are paramount (Table 2). Both pharmacological and non-pharmacological strategies are likely to be relevant (3) and further research in this area is urgently needed. Beta-2 agonists are the most commonly used medication to treat EIB in athletes, yet although disputed, evidence of chronic, frequent use of beta-2 agonists has been reported to be associated with tachyphylaxis (82). More specifically, evidence exists to suggest excessive use of short-acting bronchodilators result in adverse changes in lung function when inhaled corticosteroid (ICS) therapy is neglected (83). Inhaled corticosteroids (ICS) administered on a daily basis have been identified to reduce the severity of EIB (84) and are considered the most effective anti-inflammatory agent for EIB management (85). While the work of Sue-Chu and colleagues provides the only longitudinal data available in relation to daily treatment with ICS, indicating no beneficial effect on AHR to methacholine provocation (86), a wide body of literature is in opposition to these findings. Recent recommendations suggest patients who continue to experience symptoms despite frequent use of short-acting bronchodilators or administration before exercise to initiate daily ICS therapy (13). Likewise, while dietary modification (e.g. fish oil supplementation) may attenuate EIB (87) there are no data yet to support a long-term beneficial impact on airway integrity in athletes.

Methodological considerations / Focus for future research

The structure of this review has been largely narrative given the brevity of literature examined and heterogeneous nature of the issues covered, i.e. the article draws together diverse manuscripts ranging from an examination of the effectiveness of screening to papers evaluating the biological evidence in support of airway injury in athletes.

This approach limits the ability to systematically appraise the strength of the literature in this field. However as high quality data in this field continues to accumulate then it will be desirable to perform a formal systematic appraisal of the literature evaluating the key components of causality in the context of the relative strength of the data available (i.e. is the association biologically plausible). Until this time, readers are referred to up to date guideline documents by Parsons et al. that have employed a systematic and objectively graded process of manuscript appraisal (13).

A further methodological consideration concerns the paucity of longitudinal studies in the field. Further prospective studies are required to truly evaluate the causal relationship in the development of airway dysfunction in athletes. As discussed previously, further research is also required to describe and distinguish the features of injury versus disease. This is central to permit focus on interventions that may protect athletes from developing airway dysfunction.

Finally, the impact of undetected airway dysfunction on athletic performance is yet to be established. This should be a key focus for future research given that the ability to compete optimally is essential to an athlete's 'occupation'.

Conclusion

The available literature indicates that participation in high intensity exercise in certain environmental situations is implicated in the development of airway pathophysiology. Thus,

whilst the benefit of regular physical activity for health and well-being is widely recognised, there is legitimate concern that the intensity of hyperpnoea necessitated by elite level exercise may be detrimental for respiratory health. It remains to be determined how the development of airway dysfunction translates into classic 'disease' manifestations and further work is needed in this area. In the meantime it is our opinion that the evidence is currently sufficient to afford elite athletes the same considerations for their airway health as other individuals with potential and relevant occupational exposures.

TABLE FOOTNOTES

Table 1. Longitudinal studies evaluating airway function in athletes.

Definition of abbreviations: **AHR**, airway hyper-responsiveness; $PM_{0.1}$, particulate matter (ultra-fine particles).

Table 2. Sport-specific environmental exposures and their role and potential prevention. Definition of abbreviations: NO_X, Nitrogen oxide; $PM_{0.1}$, particulate matter (ultra-fine particles); **AHR**, airway hyper-responsiveness.

Table 1.

First Author	Design / Follow-up	Cohort	Outcome measures	Key findings
Helenius (33)	5 year prospective	Elite competitive swimmers ($n = 42$)	Histamine challenge Sputum cytology	Eosinophilic airway inflammation increased in swimmers who continued to train regularly. AHR attenuated in athletes who stopped training.
Verges (30)	10 year prospective	Elite cross country skiers ($n = 3$)	Methacholine challenge	Airflow limitation present in all case studies following 9-12 years.
Rundell (23)	4 year prospective	Female ice-hockey players ($n = 14$) Nordic skiers ($n = 9$) (control)	Exercise challenge	Controls showed no decline in lung function over 4 years, however ice hockey player's lung function deteriorated over the same time period. $PM_{0.1}$ related to airway function decay in ice rink athletes.
Kippelen (31)	1 year prospective	Cyclists ($n = 6$) and triathletes ($n = 7$) Physically inactive (<2 hrs/week) ($n = 6$)	Exercise challenge Symptom questionnaire	No evidence of lung function deterioration in healthy Mediterranean endurance trained athletes.
Knöpfli (5)	2 year prospective	Swiss national triathlon team; healthy and non-asthmatic ($n = 7$)	Exercise challenge	AHR present in 43% of athletes. Athletes developed AHR over a short follow-up period.
Bougault (6)	1 year prospective	Competitive swimmers ($n = 19$) training >10 hr/week Control group ($n = 16$) non-asthmatic; not involved in competitive sport and did not swim regularly	Exhaled nitric oxide Eucapnic voluntary hyperpnoea Methacholine challenge Sputum cytology	Training may contribute to the development of AHR in elite swimmers, but this appears reversible after 2 weeks training cessation.

Table 2.

First Author	Potential irritant	Key findings / authors study conclusions	Preventative strategies to be considered
Pool-based sport (e.g. swimming, water polo, triathlon)			
Bougault (6) Bougault (88) Helenius (33) Helenius (64) Carbonelle (89)	Chlorine derivatives - sodium hypochlorite and chlorinated isocyanuric acids Trihalomethanes – chloroform Haloacetic acids - trichloroacetic acid Chloramines	Chronic long-term and repeated exposure to chlorine compounds in swimming pools during training and competition implicated in the increased prevalence of bronchial hyper-responsiveness, airway inflammation and structural remodelling processes in swimmers.	• Train in outdoor pools when possible to achieve optimum ambient ventilation. • Athletes without access to outdoor facilities should choose to train in well-ventilated indoor pools (i.e. a flow rate of fresh air of at least 60 m^3/h). Staff should monitor training environment. • Swimming pools should implement good sanitary practice, e.g. wearing a swim cap, removing cosmetics prior to entering the pool area. Athletes should be instructed to shower before entering the pool to reduce chloramine formation. • Use of non-chemical pools (e.g. Ozone) need further investigation however impractical and may increase infection.

Winter sport

Indoor (e.g. speed skating, ice hockey)

Rundell (23) Rundell (18) Lumme (61) Levy (65) Brauer and Spengler (90)	Carbon monoxide Nitrogen dioxide Sulphur dioxide Diesel fuel Particulate matter	Daily high ventilation rates with cold dry air and ice re-surfacing pollutants implicated in development of airway dysfunction.	• Indoor air quality should be monitored, with particular attention regarding the levels of NO_X and $PM_{0.1}$. • Incorporate 'fresh air' recovery periods into training sessions. • Utilise electric-powered ice resurfaces to ensure acceptable air quality.
Outdoor (e.g. cross-country skiing, biathlon)			
Sue-Chu (91) Verges (30) Karjalainen (42)	Cold / dry air	Environmental stress to the proximal and distal airway Results in the development of respiratory symptoms, airway inflammation, AHR, epithelial injury and structural remodelling.	• Warm up prior to exercise. • Nasal breathing during low intensity training. • Face masks/heat and moisture exchange devices to reduce respiratory water and heat loss. • Athletes should adhere to the Federation Internationale de Ski's medical recommendations. • Skiers performing their own 'hot waxing' should carry this out as quickly as possible in well-ventilated conditions.

Summer sport

Knöpfli (5) Helenius and Haahtela (49) Helenius (67) Helenius (70) Weiler (92)	Humid / dry air Aeroallergens	Aeroallergens (dog, cat and mite) identified within indoor arenas exceeding the threshold for allergic symptoms and/or sensitisation.	• Ensure good ventilation of indoor facilities. • Warm up prior to exercise. • Incorporate 'fresh air' recovery periods into training sessions.
Helenius and Haahtela (49) Helenius (70) Helenius (93) Helenius (72)	Primary agents Carbon monoxide Carbon dioxide Sulphur dioxide Nitric oxide Aeroallergens Pollen Secondary agents Ozone Nitric acid Sulphuric acid Nitrate peroxyacetyl Inorganic compounds	Exposure to high levels of environmental pollutants / irritants / allergens when combined with prolonged exercise hyperpnoea may provoke nose and throat infection, lung function deterioration including airway inflammation.	• Warm-up prior to exercise. • Avoid areas of high pollution (PM levels above Environmental Protection authority levels). • Incorporate buffer zone away from traffics areas. • Monitor training environment and organise training time to minimise exposure – i.e. early morning. • Atopic athletes should assess pollen counts prior to training.

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