Environmental factors associated with non-infective acute respiratory illness in athletes: A systematic review by a subgroup of the IOC consensus group on "acute respiratory illness in the athlete"

Valérie Bougault [a,*], Paolo Emilio Adami [b], Nicola Sewry [c,d], Ken Fitch [e], Christopher Carlsten [f], Beat Villiger [g], Martin Schwellnus [c,d], Wolfgang Schobersberger [h]

[a] Université Côte d'Azur, LAMHESS, France

[b] World Athletics, Health and Science Department, Monaco

[c] Sport, Exercise Medicine and Lifestyle Institute (SEMLI), Faculty of Health Sciences, University of Pretoria, South Africa

[d] International Olympic Committee (IOC) Research Centre, South Africa

[e] School of Human Science, Sports, Exercise and Health, University of Western Australia, Australia

[f] Air Pollution Exposure Lab, Department of Medicine, University of British Columbia, Canada

[g] Swiss Research Institute for Sports Medicine SRISM Davos, Medical Center & Clinic Grand Resort Bad Ragaz, Switzerland

[h] Institute for Sports Medicine, Alpine Medicine & Health Tourism (ISAG), University Hospital – Tirol Kliniken Innsbruck and Private University UMIT Tirol, Austria

* Corresponding author.

E-mail address: valerie.bougault@univ-cotedazur.fr (V. Bougault).

Abstract

Objectives: The aim of this study is to review the evidence available suggesting that environmental conditions represent a risk factor associated with non-infective acute respiratory illness in athletes.

Design: Systematic review.

Method: PubMed, EBSCOhost and Web of Science (1st January 1990-31 July 2020) were searched systematically using keywords related to male and female athletes (i.e. from physically active individuals to elite athletes), aged 15-65 years and a combination of the terms (non-infective acute respiratory illness AND [pollution OR allergies OR climate] AND athletes AND prevalence/incidence/risk factors).

Results: A total of seven papers (n=1567 athletes) addressed our question. Among these, one focused on indoor air pollution, four on chlorinated swimming pool exposure and two on cold air conditions. None was selected for allergies, outdoor air pollution or other climatic conditions. Except rhinitis induced by swimming in chlorinated pools (n=1), no respiratory disease due to the environment was identified specifically in athletes. The levels of chloramines in swimming pools (n=2) and air pollutant in arenas (n=1) were identified as risk factors for rhinitis and respiratory symptoms when exercising.

Discussion: There is a paucity of data on the prevalence, incidence and risk factors of being acutely exposed to chlorine by-products, air pollution, cold air or altitude on the development of respiratory disease specifically in athletes. Noting the lack of a clear definition of environmentally induced lung disease in athletes, distinct from that of the general population, we addressed the few published management plans to protect athletes' airways for each specific environment.

PROSPERO registration: CRD42020168170

Keywords

Allergens, Pollution, Chlorine, Cold air, Altitude, Athletes

Abbreviations

EIB - Exercise-induced bronchoconstriction
O_3 - Ozone
NO_2 - Azote dioxide
SO_2 - Sulfur dioxide
CO - Carbon monoxide
PM - Particulate matter
AHR - Airway hyperresponsiveness
EILO - Exercise-induced laryngeal obstruction
FEV_1 - Forced expiratory volume in 1 s
SP - Swimming pool
IOC - International Olympic Committee
ARill - Non-infective airway respiratory illness
ISAAC - International Study of Asthma and Allergies in Childhood
RQLQ - Rhinitis Quality of Life Questionnaire
RH - Relative Humidity
VO_2max - Maximum oxygen uptake
PD - Physician-diagnosed
PRISMA - Preferred Reporting Items for Systematic Review and Meta-Analyses
OCEBM - Oxford Centre for Evidence Based Medicine
HRmax - Maximum heart rate
FVC - Forced vital capacity

Practical implication: Real-world setting of sport and exercise

- The clinical history of respiratory symptoms during exercise should systematically involve an investigation of the environmental conditions in which they occur,
- For cold air and air pollution the pathophysiology of symptoms may be different from classical EIB/asthma. Therapeutic approach including medication should thus be adapted accordingly,
- Suggested strategies to avoid harmful environment may be:
    - Wearing a facemask to decrease particles or cold air inhalation,
    - Wearing a nose-clip when swimming in a chlorinated pool,
    - To decrease personal exposure either, for example by using a website or individual applications to follow pollens or air pollutants concentrations during peak hours or in 'hostspot' locations.

INTRODUCTION

Athletes, including individuals that regularly participate in exercise, are constantly exposed to various environmental conditions. During moderate to high intensity exercise, there is not only a higher rate of ventilation, but also a shift from nasal to oral breathing [1], thereby bypassing the nasal functions of filtering, heating, and humidifying inhaled air [2]. Environmental conditions, and thus the composition of the inhaled air during exercise, can vary substantially not only in temperature and humidity, but inhaled air can also contain varying concentrations and types of allergens, air pollutants [Ozone (O_3), particulate matter (PM), nitrogen dioxide (NO_2), Sulphur dioxide (SO_2), Carbon monoxide (CO)], or chemicals such as chlorine by-products [3]. Athletes may also compete at various altitudes (above mean sea level), ranging from intermediate (1500-2500m), high (2500-3500m) or very high (3500-5800m) where relative hypoxia may also be of particular concern [4].

There is a high prevalence of upper and lower airway dysfunction, including rhinitis (allergic and non-allergic) [5], exercise induced laryngeal obstruction (EILO), airway hyperresponsiveness (AHR), exercise induced bronchoconstriction (EIB), and asthma [6,7] in specific groups of competitive athletes. There is evidence that outdoor endurance sports, water sports in chlorinated pools, and winter sports are types of sports activity associated with a higher prevalence of airway dysfunction [3,8,9]. Recognising that endurance athletes, such as those with greater total weekly training time (>30 hours per week), may have an inherent increased risk of airway dysfunction, these athletes may also be at even higher risk because of exposure to environmental conditions compared to recreational athletes with lower weekly training volume.

There is evidence that specific and combined environmental factors increase morbidity and mortality in people with respiratory diseases, especially asthmatics exercising in cold air in northern hemisphere countries [10]. Events that affect patterns of pollen production could also favour the development of allergies or respiratory illness in healthy individuals. Being regularly physically active could further expose healthy individuals to the negative effects of a changing climate and pollution, thus favouring the development of respiratory illness. In the current context of global climate change, with rising environmental temperatures, increased pollution and allergenic peaks [10], environmental factors that may be associated with acute respiratory illness in athletes, require further attention.

The primary aim of this systematic review was to provide contemporary evidence that environmental conditions (air temperature, chemical exposure, pollution and altitude) are risk factors associated with non-infective acute respiratory illness (ARill) in athletes.

METHODS

Protocol and registration

This systematic review was performed in accordance to the 2020 Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines [11]. The review was prospectively registered with the PROSPERO database (registration number: CRD42020168170). In September 2019, an International Olympic Committee (IOC) consensus statement core panel on 'acute respiratory illness in athletes' was convened on behalf of the IOC medical and scientific commission and chaired by MS. A sub-group (number 3 out of 7 sub-groups) of this core panel, consisting of 8 members (VB, PEA, NS, KF, CC, BV, MS, WS), focused on non-infective ARill caused by environmental factors in athletes and was chaired by VB and WS. The members of subgroup 3 conducted this systematic review. The term "athletes" includes the range of people, from regularly physically active to high-elite competitive level.

Study selection and eligibility criteria

The electronic databases PubMed, EBSCOhost and Web of Science (core collection) were used to search for articles published between 1st January 1990 and 31 July 2020, to capture relevant contemporary literature concerning the role of the environment in the development of ARill in athletes. A combination of search terms was used to identify studies focusing on the prevalence and risk factors of ARill due to environment (e.g., non-infective acute respiratory illness/pollution/allergies/climate AND athletes AND prevalence/incidence/risk factors) and relevant exclusions (for full search string see Supplementary Appendix 1). The results of these searches were combined, and duplicate articles removed. Additionally, any further articles the authors were aware of relating to the topic were added. All article screening and selection was undertaken using the online tool CADIMA [12].

Inclusion and exclusion criteria

Studies were required to meet the following criteria for inclusion: (1) study participants were male or female athletes/physically active individuals/military personnel, aged 15-65 years, non-smokers and not pregnant; (2) original full-text studies (i.e., not research correspondence or case studies) of observational, prospective, retrospective, cross-sectional, longitudinal or intervention design, written in English; (3) non-infective ARill were self-reported or clinically-diagnosed and were the result of environmental factors (air temperature, chemical exposure, pollution, or altitude). Animal or non-human studies were excluded. Articles were also excluded if (1) the study was a conference abstract, book chapters or thesis, single case-report, review article, expert opinion or consensus position statement, (2) if full text was not available, (3) if asthma or a chronic disease was a primary condition, (4) if the study involved the provision of medication or immunomodulatory therapy, (5) if the respiratory disease was occupational, (6) if it was related to diving or hypercapnia and (6) if there was no measurement of environmental condition or a control condition allowing to identify the effects of environment. The articles were screened independently by two reviewers (VB, WS) first by title/abstract and then full text, and any conflicts resolved through discussion or via a third researcher (NS).

Data Extraction

The data extracted from the studies were clustered into three groups: (1) quality assessment of the studies (modified Downs and Black score, and Oxford Level of Evidence, 2009) [13,14]; (2) descriptive characteristics of the studies (study design, length of surveillance period (days), cohort number, sex, age (years), characteristics of the participants, sport, and level of participation, how was the diagnosis made, the environmental cause of the non-infective acute respiratory illness and measured environmental conditions), and (3) study outcome measures i.e. prevalence (or incidence), risk factor/s for ARill, and p-value (and any other statistical measures of value in the paper, e.g. risk ratios). No direct contact was made with authors to determine if further analysis was available.

Quality Assessment and Risk of Bias

A modified Downs and Black tool was used to determine the quality of the article including a 13 point scale that was adapted to remove domains specifically pertaining to randomised controlled trials. (Supplementary Appendix 2 contains the full checklist with relevant domains) [14]. Up to 7 points could be awarded for how the study reported findings, up to 2 for external validity and up to 4 for internal validity (bias and confounding). The quality assessment score of each article was determined against the following criteria: 11-13: Excellent; 9-10: Good; 7-8: Fair; ≤6: Poor. The level of evidence was also determined using the Oxford Centre for Evidence Based Medicine (OCEBM, 2009) [13]. The OCEBM is a hierarchical system, grading studies on a scale of 1 (highest level of evidence) to 5 (lowest level of evidence), including subsections for level 1, 2, and 3. Both reviewers (VB and WS) independently scored the articles and after discussions reached consensus on the final score for each article.

RESULTS

Overview and quality of the studies

A total of 23 potential articles were retrieved and the full texts were evaluated for inclusion. The final selection of articles for inclusion in the review was 7 (n=1567 athletes) (Figure 1). Data quality and quantity was not appropriate for a meta-analysis. Five studies included children (< 15 years old) and these were kept in the selection as they also included adults.

The relevant characteristics and findings of the selected articles are reported in Table S1. Study designs included three cross-sectional studies (n = 3), one observational study with an intervention (n = 1) and three quasi-experimental non-controlled studies (n = 3). The Oxford Level of Evidence ranged from 2c to 4b and Downs & Black Quality Assessment Scores ranged from 4 to 9. Respective studies were rated as poor (n = 1); fair (n = 3); good (n = 3) (Tables S2 and S3).

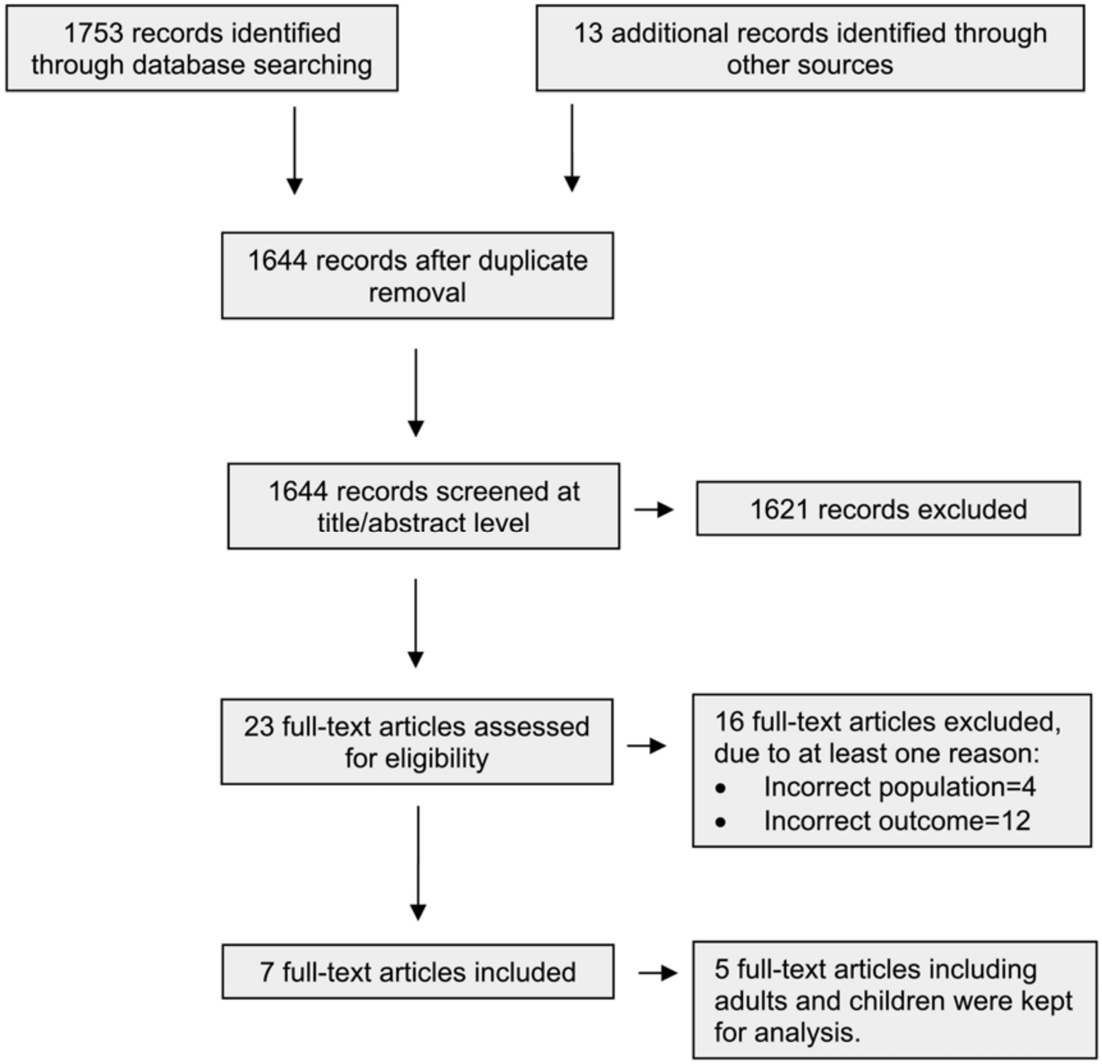

Figure 1: Process of study selection, from initial identification as potentially relevant to inclusion (Prisma flow diagram)

Level of play and environmental exposure

Studies included competitive athletes (n = 6) and recreational athletes (n = 3) (Table S1). Environmental exposure consisted of cold air conditions (n = 2), chlorinated swimming pool exposure (n = 4) and air pollution in a sporting arena (nitrogen dioxide, NO_2) (n = 1). There were no articles on allergies, outdoor air pollution or other climatic conditions (heat, hypoxia) that fulfilled the inclusion and exclusion criteria.

Table 1. **Description and main findings of the studies**

First author (ref)	Characteristics of the subjects	Study design	Sporting history/Physical capacities	Type of environment	Main outcome
Air temperature (cold)					
Carey et al. [15]	12 subjects apparently healthy without EIB	Two randomized visits: 8-min run at 85-95% of maximum Heart rate with warm or cold air	**Running history**: 25.9± 4.9 miles/week **Years running**: 10.2±6.2 years. **VO_2max men**: 60±8 ml/kg/min **VO_2max women:** 53±6 ml/kg/min	Warm air (22±0.4°C and RH: 55%) *vs* Cold air (-10 ±11°C and RH: 63±11%)	No effect of cold air on symptoms or disease. 0/12 had respiratory symptoms in any condition (coughing or wheezing). One subject had a fall in FEV1≥10% for at least 2-time points post-run in cold air *vs* 0 in warm air.
Kennedy et al. [16]	17 aerobically fit women. Apparently healthy without heightened symptoms of cough or EIB during exercise in cold.	Five randomized visits. The same exercise (15min warm-up and 8 min at last stage speed of graded exercise test) at five cold temperatures.	VO_2max> 40 ml/kg/min (49.6±6.6 ml/kg/min)	Cold air: 0°C, -5°C, -10°C, -15°C and -20°C (RH: 40%)	**Significant difference in the frequency of symptoms:** ↑ Frequency of cough with ↓ in temperature (P=0.00 across the temperature : 0°c *vs* -15°C (p=0.04) and -5°C *vs* -15°C (p=0.005) ↑ Frequency of chest tightness with ↓ in temperature (P=0.01 across the temperature **Subjects with EIB** (FEV1≥10%): 0°C to -10°C: n=2 (mild EIB); -15°C and -20°C: n=3 (one had moderate EIB at -20°C, i.e. -25.3% fall in FEV1)

Chemical exposure (chlorine)					
Surda et al. [19]	101 elite swimmers, 107 non-elite swimmers, 38 non-swimmer athletes and 50 controls [Allergic rhinitis: 12/101 elite swimmers; 10/107 non-elite swimmers; 7/38 non-swimmer athletes; 6/50 controls]	General, ISAAC and Mini RQLQ questionnaire given in Fall and Winter 2016	**Elite athletes**: > 8 hours/week during at least one year (field and track clubs or swimmers in chlorinated pools). **Non-elite swimmers**: 2 to less than 8 hours/week during at least one-year **Controls**: <90 min/week in the last 6 months	Chlorinated SP (not measured)	Significant correlation between time spent in pool and total RQLQ score in swimmers (mixing elite and non-elite). *But the dose of exposure, i.e. through training ventilation, duration and chloramine concentration is not taken into account (note of the current review authors).*
Gelardi et al. [17]	54 competitive swimmers with symptoms of rhinitis clearly due to sport activity (within 1h after swimming and persisting for at least 12h). 15 had asthma and 24 had allergic rhinitis (SPT+ and eosinophils).	Two visits: before and after 30 days wearing a nose-clip during training	Competitive training since at least 2 years and swimming 3 to 5 times per week	Chlorinated SP (not measured)	Risk factor: Chlorinated water exposure during training In the group with neutrophilic rhinitis only: significant ↓ in neutrophilic infiltration (p=0.04) and in nasal resistance (p=0.03). In all rhinitis types, except the group with non-allergic rhinitis with eosinophils and mast cells, ↓ in perceived severity of rhinitis.
Levesque et al. [20]	72 competitive swimmers divided into less exposed *vs* more exposed to chloramines (threshold of (1) air chloramines: 0.37 mg/m^3 and (2) water chloramines: 0.63 mg/l)	5 training sessions. 7 swimming pools included in the study.	Local competitive swimmers listed in regional associations. Training > 3 times/week, 1.5 to 3h/session	Chlorinated SP: Chloramines in 7 swimming pools: Mean [range] (1) In the water: 0.54 mg/l [0.45-1.03]; (2) In the air: 0.34 mg/m^3 [0,26-0,41]	**Risk factor:** Chloramines in the water (above or below 0,63 mg/l) and air (above or below 0,37 mg/m^3) **Upper respiratory symptoms:** adjusted OR [95%CI]: 2.2 [1.0-4.8] when exposed to chloramines in the air above the threshold **Lower respiratory symptoms:** 2.3 [1.0-5.2]

					when exposed to chloramines in the water above the threshold
Goma et al. [18]	320 recreational and 53 competitive swimmers frequenting the same SP. **Recreational swimmers**: 5.8% asthma and 14.6% allergic disease. **Competitive swimmers**: 8% asthma and 24.7% allergic disease. Water polo players did not use goggles or nose clip, but some swimmers had goggles or nose clip.	Change of water disinfection in a swimming pool to reduce chloramines in the air. One training sessions before the change and one after. Questionnaire on health fulfilled immediately after each swimming session.	Competitive swimmers: 19 swimmers and 34 water polo players.	Chlorinated SP: Trichloramines in the air: 0.62±0.34 mg/m^3 (before) and 0.38±0.19 mg/m^3 (8 weeks after change in disinfection)	Risk factors: **Type of practice**: competitive vs recreational **SP disinfection** Significant changes from before to after disinfection change: None for competitive athletes and for recreational swimmers less nose symptoms ($p=0.001$) and cough ($p=0.04$) after change in disinfection method.
Pollution					
Salonen et al. [21]	793 men ice hockey players: 40% had allergy; 18% allergic rhinitis; 4.4% asthma	Health questionnaire distributed to 57 registered teams with a total of 1082 players in Finnish A, B and C junior leagues at the end of training season	Indoor arena Hockey players national A, B and C junior league Years training: 7.3±2,8 Training h/week: 7.8±3.2	NO_2 in 31 home arenas: 31 to 1176 ug NO_2 in the air of 31 arenas	Risk factor: OR [95%CI] of respiratory symptoms per ↑ of 100ug/m^3 in weekly average NO_2 concentration in arenas: Rhinitis: 1.54 [1.05-2.26] ($p=0.0028$) Cough: 1.62 [1.06-2.47] ($p=0.0025$)

CI: confidence interval; EIB: Exercise-induced bronchoconstriction; FEV_1; Forced expiratory volume in one second; NO_2: nitrogen dioxide; RH: relative humidity; SP: swimming pool: VO_2max: maximal uptake measured during an incremental maximal test
Need to define ISAAC and RQLQ

Environmental conditions (air temperature, chemical exposure, pollution) as risk factors associated with non-infective acute respiratory illness (ARill) in athletes

The characteristics and main results of the studies are shown in Table 1. Main outcome variables were self-reported upper and lower airway respiratory symptoms (nasal symptoms, cough, wheezing, chest tightness, mucus production, difficulty to breathe), questionnaire scores (ISAAC and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)) or exercise-induced bronchoconstriction (EIB) defined as a fall in $FEV_1 \geq 10\%$ after exercise. Main outcome variables differed between all the studies and therefore results could not be pooled and are reported for individual studies.

Air temperature (cold air)

The effect of cold air exposure as a risk factor for non-infective ARill was reported in 2 studies. In the first study among 10 apparently healthy physically active young adults with no history of EIB, the frequency of respiratory symptoms after running for 8 min at 85-95% HRmax did not differ when exposed to warm air (22±0.4°C; RH=55%) vs. cold air (-10 ±11°C; RH: 63±11%) [15]. One participant (1/10 = 10%) developed "EIB" in the cold air condition [15]. In the second study, 17 apparently healthy female participants performed graded treadmill exercise tests (at least 8 min) while exposed to five randomly assigned cold temperatures (0°C, -5°C, -10°C, -15°C and -20°C; RH=40%) [16]. The frequency of cough and chest tightness significantly ($p<0.05$) increased with colder temperature exposures, while "EIB" was diagnosed in 3 participants (18%) at exposure to temperatures below -10ºC [16].

Chemical exposure (chlorine)

The effect of exposure to chlorine as a risk factor for non-infective ARill in swimmers was evaluated in 4 studies [17–20]. In the first study, the total RQLQ score was significantly correlated to the time swimmers spent in a chlorinated pool [19]. In the second study among 54 competitive swimmers with swimming-induced rhinitis, the neutrophilic aetiology of rhinitis and its symptoms, decreased significantly after wearing a nose clip for 30 days during training in chlorinated pools, suggesting that chlorinated swimming pool water induced the rhinitis [17]. In a third study among 72 competitive swimmers, higher concentrations of water and air chloramines (above the threshold) increased the risk of upper (OR=2.2;

95% CI=1.0-4.8) and lower respiratory tract symptoms (OR=2.3; 95% CI=1.0-5.2) [20]. In a large study among 320 recreational and 53 competitive swimmers, a reduction in air trichloramine concentrations from 0.62±0.34 mg/m^3 to 0.38±0.19 mg/m^3 (8 weeks after change in disinfection) reduced nasal symptoms and cough in the recreational swimmers [18].

Pollution

The effect of pollution as a risk factor for non-infective ARill was evaluated in 1 study [21]. In a study on 793 junior ice hockey players, the chances of developing rhinitis (1.54; 95% CI=1.05-2.26) and cough (1.62; 95% CI=1.06-2.47) increased significantly for each 100ug/m^3 increment in the weekly average of NO_2 concentration in the sports arena [21].

DISCUSSION

Athletes are constantly exposed to various environmental conditions when they perform moderate to high intensity exercise, which is associated with higher rates of ventilation and a shift from nasal to oral breathing. The aim of this study was to review evidence that environmental conditions (air temperature, chemical exposure, pollution) are factors associated with non-infective acute respiratory illness (ARill) specifically in athletes. The basic motivation herein was to inform consideration of risk in this population, given that the large volume of literature does not target athletes specifically. The main finding is that very few studies investigated the association between environmental conditions (air temperature, chemical exposure, pollution) and non-infective ARill in this specific population. The heterogeneous nature of the data from a limited number of studies, made it challenging to formulate firm conclusions. The acute effects of air temperature, chemical exposure or pollution on respiratory health in athletes remains poorly documented.

Environmental factors and non-infective acute respiratory illness (ARill) during exercise

There are no relevant data on non-infective ARill development in athletes due to the inhaled air at rest. Therefore, only exposure to environmental factors during exercise will be discussed. Several environmental conditions are regarded as possible extrinsic factors that may acutely exacerbate existing airway pathology or trigger acute respiratory symptoms in healthy, but predisposed, individuals. The results of this review were limited to a few papers, but the main findings were: 1) frequency of cough and chest tightness during exercise significantly increased with exposure to colder environmental temperatures, 2) Exercise-induced bronchoconstriction (decrease in FEV_1 > 10%) occurred in 6-8% of athletes (without EIB above 0°C) when exercising in very cold (< -10ºC) environments [15,16], 3) swimmers exposed to higher concentrations of water and air chloramines during exercise had a significantly increased risk of upper and lower respiratory tract symptoms [20], and the use of nose clips while swimming in chlorinated pools decreased nasal symptoms [17], 4) in swimmers, upper and lower respiratory tract symptoms decreased when the concentration of trichloramines was reduced in the pool water [18], and 5) rhinitis and cough increased significantly when the average NO_2 concentration in the sports arena increased [21].

If we add to our results, older publications and those from literature reviews (before 1990), there are three common aspects in the exposure to different pollutants during exercise in healthy subjects. Firstly, acute effects such as respiratory symptoms, airway responsiveness, decreases in lung function and/or airway inflammation are documented in healthy individuals after exercise when exposed to various air pollutants [CO, NO_2, O_3, PM, SO_2, chlorine by-products] or cold air [3,16,18,20,22]. Secondly, the airways response generally depends on the magnitude of the stimulus, and the acute effects on respiratory health will generally be greater in colder air (-15°C or lower) or at higher concentrations of chlorine (air and water), or pollutants [3,16,18,20,23]. The level of ventilation (intensity of exercise) and the time spent exercising also play a significant role [3,16,19,23]. Thirdly, there is also evidence of individual variation in the susceptibility to these stimuli, as some individuals do not appear to show any respiratory symptom or airway change despite exposure to very cold temperatures or very high concentrations of chemicals or pollutants [3,16,24]. However, currently no intrinsic or extrinsic risk factors to identify this individual susceptibility have been identified. The exception is for allergic or atopic athletes at risk of allergic disease in the case of allergen exposure and cold-air induced exercise bronchoconstriction [25,26]. Finally, it is important to note that when apparently healthy individuals are exposed to adverse environmental conditions or pollution and develop respiratory symptoms, they are often incorrectly diagnosed with EIB or asthma. In the case of exposure to cold or polluted air, symptoms and documented bronchoconstriction are often dissociated [27–31].

Therefore, these data show that various unfavourable environmental conditions may be responsible for abnormal airway responses during exercise in apparently healthy athletes, without any respiratory disease. Interestingly, a fall in FEV_1 greater than 10% post-exercise in cold or polluted air, is termed EIB, despite the fact that the reason for this may be cold air exposure and not exercise itself [3,15,16]. In these cases, whether the 10% fall in lung FEV_1 or FVC should be considered as a threshold for abnormal airway response or due to an environmental stimulus, is yet to be determined. The clinical implications are that although the characteristics of upper or lower airway response to cold air or polluted air may be similar to EIB, asthma or rhinitis, the pathophysiological mechanisms and management of environmental-induced respiratory symptoms may differ from that of EIB, asthma or rhinitis [27,30].

Clinical relevance: Prevention and treatment of environmentally induced non-infective acute respiratory illness (ARill)

The clinical relevance of this review is that the main findings can guide prevention and treatment of non-infective ARill in athletes. In the case of symptoms related to the practice of sports in a specific environment (polluted, cold, allergens or chlorinated), a first prevention strategy is to avoid potentially harmful environments or reduce exposure. The attendance and choice to train in indoor chlorinated pools, sports halls, arenas or gyms, with appropriate ventilation for the removal of pollutants and where hygiene measures are respected, is within the reach of most athletes to reduce their personal exposure [40,41]. For example, moving away from the source of particles can reduce the inhaled dose [32], whereas for O_3, this is not necessarily possible. Swimmers may prefer a pool disinfected with a product other than chlorine, which is outdoor and/or with appropriate ventilation, which does not have too strong a "chlorine" smell. During swimming, wearing a nose clip may also be very effective for non-allergic rhinitis related to the chlorinated environment [17]. The efficiency of non-pharmacological treatment such as rinsing the nose with saline before or after swimming may help some swimmers suffering from chlorine-induced rhinitis, but scientific evidence has yet to be provided. For winter sport athletes living in cold countries, it is a bit more difficult to avoid unfavourable climatic conditions. However, some athletes of such sports may choose their training location according to expected forecast. Allergic athletes should avoid locations exposed to concerned allergen or pollen during training and take measures to reduce its exposure also in their daily life. Allergic athletes may also choose to train in allergen-free zones (altitude), during pollen outbreaks. Alpine regions above 1600 m generally show significantly reduced exposures to pollens, moulds and mites, which may have a positive impact on the lung function of asthmatic subjects [42]. It is thus possible that athletes with allergic disease or asthma benefit from such conditions when exposure to pollens is high at lower altitudes. Climate change, however, increases the intensity and duration of the pollen seasons, and in mountainous regions shifts in treelines and upper limits of plants and moulds to higher elevations, is observed [43]. Therefore, allergic athletes may now be negatively affected by climate change when exposed in low to intermediate altitude during the pollen season, but probably still less than in the lowlands. Finally, various official websites to assess climatic conditions, allergen levels in ambient air and the concentration of pollutants are already available [33,34]. In future, dedicated websites/applications and individual sensors, may become a valuable resource for athletes, coaches, and medical staff to guide decisions before exercising in different environments.

A second prevention strategy may be to consider facemasks when exposed to some pollutants or cold air. Facemasks are also available to protect the airways, even if the protection is sometimes not complete, they reduce the level of exposure [35,36]. Facemasks differ in their role, as they either humidify and heat the inhaled air (cold air) [36] or filter particles, but not gases (air pollution) [35]. The efficiency of facemasks to fight against allergens has not been adequately studied, but may be partly efficient, depending on the wind conditions [37]. Athletes however, may find it difficult to exercise at high intensities whilst wearing a facemask [38,39], and experience has demonstrated winter endurance athletes refrain from using them in competition. There is still insufficient evidence of the absence of undesirable physiological effects or of their efficiency over time.

Finally, the supplementation of anti-oxidant and anti-inflammatory nutrients (mainly vitamins A, B, C, D, E, carotenoids or long-chain polyunsaturated fatty acids) has been proposed in the case of air pollution as well as respiratory disease [44–46]. There is no clear evidence in favour of these supplements on respiratory health when exercising in cold or polluted air, either in the short or long term.

Pharmacological treatment may also be prescribed in prevention when athletes suffer from symptoms during or after an effort practised in a specific environment. For allergic disease or exacerbation of asthma due to the environment, the reader should refer to the international guidelines dedicated to allergies and asthma [47,48]. For cold air and air pollution especially, care should be taken as to the pathophysiology of symptoms due to exercising in various environments, as it may be different from classical EIB/asthma. Medication should thus be adapted accordingly. As the mechanisms of cold air-provoked respiratory symptoms vary considerably and are dependent on the individual`s susceptibility, symptoms should be managed accordingly [9,49]. In the absence of evidence towards the efficiency of various inhaled anti-inflammatories (either glucocorticosteroids or Cysteine-leukotriene receptor antagonists (LTRAs)), anticholinergic or β2-agonists, when exercising in polluted environments, symptom control may require testing several medications, acting on inflammatory mediators, including neurogenic, before finding the most effective one for everyone. A particularly worrisome point is the possible reduced effectiveness or ineffectiveness of pre-treatment with short-acting β_2-agonists [50], anticholinergic [51,52], daily budesonide [53,54] or daily beclomethasone dipropionate combined with a long-acting β2-agonist [55], or cyclooxygenase inhibitors [56], in cases of some pollutant-induced EIB, either in healthy subjects or in well-controlled asthmatics. It is not known whether the treatment is equally effective depending on the type of pollutants (type of PM, O_3, chlorine by products, cold air etc.), or whether interplay with pollens may have an impact on the pharmacological control of the disease [57]. As it has been hypothesized that regular inhaled corticosteroid intake may increase vulnerability to pollutants in children [58,59] and that pollution exposure may induce a resistance to inhaled corticosteroids [60], much research needs to be undertaken on the management of environment-related diseases in athletes.

STUDY LIMITATIONS

This review had several limitations. Firstly, as for all systematic reviews, a selection bias cannot be excluded. It is possible that we did not identify all relevant studies with respect to the topic, mainly due to a possible publication bias (negative studies often being left unpublished), but also because there may be studies with athletes embedded within a larger less specific population but in a manner difficult to extract from. However, by systematically searching different databases as well as hand-searching reference lists and grey literature, we believe that this bias was minimized. In addition, a language bias might also have led to the fact that not all available data regarding the topic was included as only publications in English were included. A significant limitation of this review is related to the small number of studies that could be included in this review and the low quality of studies. The evidence level is poor overall, and therefore the conclusions should be interpreted with caution. In addition, because we excluded articles published before 1990, this may have led to the exclusion of some additional papers. However, the authors are familiar with the literature in this area as the physical activity status of the healthy subjects included in older studies was mostly not specified. These articles would have been excluded from this review, therefore the exclusion of older articles does not change the outcome of this review. There is a clear need that further studies of higher quality and evidence level should be conducted to make statements regarding risk for ARill in athletes. Finally, we used a very general definition of “athlete” and it is possible that specific subgroups of athletes are at risk in ways not yet revealed in this very limited database.

CONCLUSION

In this review, our research aim was to investigate the influence of air temperature, chemical exposure, pollution and altitude as risk factors associated with ARill in healthy adult athletes. Very few studies that examined this association could be included in this review, and therefore concrete answers for our study questions were not possible. However, from data derived from individual studies we did show that: 1) during exercise upper and lower respiratory tract respiratory symptoms and bronchoconstriction may occur or increase with exposure to colder environmental temperatures, 2) higher concentrations of water and air chloramines during swimming was associated with increased risk of upper and lower respiratory tract conditions including rhinitis, which could be reduced by wearing nose clips while swimming in chlorinated pools or by reducing the concentration of trichloramines in the pool water, and 3) that upper and lower respiratory tract symptoms increased as the level of pollution (increased average NO_2 concentration) increased in a sports arena. However, no specific ARill was clearly associated with environmental exposure or pollution in athletes. In the current context of climate change, further studies are needed to address our main question, especially in endurance sport where athletes are exposed to specific potentially adverse environmental conditions.

Confirmation of ethical compliance

Not applicable

Acknowledgements

None.

References

1 Chadha TS, Birch S, Sackner MA. Oronasal distribution of ventilation during exercise in normal subjects and patients with asthma and rhinitis. *Chest* 1987; 92(6):1037–1041. Doi: 10.1378/chest.92.6.1037.

2 Daviskas E, Gonda I, Anderson SD. Local airway heat and water vapour losses. *Respir Physiol* 1991; 84(1):115–132. Doi: 10.1016/0034-5687(91)90023-c.

3 Rundell KW, Smoliga JM, Bougault V. Exercise-Induced Bronchoconstriction and the Air We Breathe. *Immunol Allergy Clin North Am* 2018; 38(2):183–204. Doi: 10.1016/j.iac.2018.01.009.

4 Schommer K, Menold E, Subudhi AW, et al. Health risk for athletes at moderate altitude and normobaric hypoxia. *Br J Sports Med* 2012; 46(11):828–832. Doi: 10.1136/bjsports-2012-091270.

5 McIntosh C, Clemm HH, Sewry N, et al. Diagnosis and management of nasal obstruction in the athlete: a narrative review by subgroup 6 of the IOC Consensus Group on "Acute Respiratory Illness in the Athlete." *J Sports Med Phys Fitness* 2021. Doi: 10.23736/S0022-4707.21.12821-X.

6 Price O, Sewry N, Schwellnus M, et al. Prevalence of lower airway dysfunction in athletes: a systematic review and meta-analysis by sub-group 4 of the IOC consensus group on "acute respiratory illness in the athlete." *Br J Sports Med* 2021; (Accepted for submission).

7 Hull JH, Jackson AR, Ranson C, et al. The benefits of a systematic assessment of respiratory health in illness-susceptible athletes. *Eur Respir J* 2021; 57(6):2003722. Doi: 10.1183/13993003.03722-2020.

8 Helenius IJ, Tikkanen HO, Sarna S, et al. Asthma and increased bronchial responsiveness in elite athletes: atopy and sport event as risk factors. *J Allergy Clin Immunol* 1998; 101(5):646–652. Doi: 10.1016/S0091-6749(98)70173-3.

9 Carlsen K-H. Sports in extreme conditions: the impact of exercise in cold temperatures on asthma and bronchial hyper-responsiveness in athletes. *Br J Sports Med* 2012; 46(11):796–799. Doi: 10.1136/bjsports-2012-091292.

10 D'Amato G, Holgate ST, Pawankar R, et al. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. *World Allergy Organ J* 2015; 8:25. Doi: 10.1186/s40413-015-0073-0.

11 The PRISMA 2020 statement: An updated guideline for reporting systematic reviews - PubMed. Available at: https://pubmed.ncbi.nlm.nih.gov/33780438/. Accessed September 27, 2021.

12 Kohl C, McIntosh EJ, Unger S, et al. Online tools supporting the conduct and reporting of systematic reviews and systematic maps: a case study on CADIMA and review of existing tools. *Environ Evid* 2018; 7(1):8. Doi: 10.1186/s13750-018-0115-5.

13 Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009) — Centre for Evidence-Based Medicine (CEBM), University of Oxford. Available at: https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009. Accessed June 10, 2021.

14 Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998; 52(6):377–384. Doi: 10.1136/jech.52.6.377.

15 Carey DG, Aase KA, Pliego GJ. The acute effect of cold air exercise in determination of exercise-induced bronchospasm in apparently healthy athletes. *J Strength Cond Res* 2010; 24(8):2172–2178. Doi: 10.1519/JSC.0b013e3181e34739.

16 Kennedy MD, Faulhaber M. Respiratory Function and Symptoms Post Cold Air Exercise in Female High and Low Ventilation Sport Athletes. *Allergy Asthma Immunol Res* 2018; 10(1):43–51. Doi: 10.4168/aair.2018.10.1.43.

17 Gelardi M, Ventura MT, Fiorella R, et al. Allergic and non-allergic rhinitis in swimmers: clinical and cytological aspects. *Br J Sports Med* 2012; 46(1):54–58. Doi: 10.1136/bjsm.2009.066456.

18 Gomà A, de Lluis R, Roca-Ferrer J, et al. Respiratory, ocular and skin health in recreational and competitive swimmers: Beneficial effect of a new method to reduce chlorine oxidant derivatives. *Environ Res* 2017; 152:315–321. Doi: 10.1016/j.envres.2016.10.030.

19 Surda P, Putala M, Siarnik P, et al. Rhinitis and its impact on quality of life in swimmers. *Allergy* 2018; 73(5):1022–1031. Doi: 10.1111/all.13359.

20 Lévesque B, Duchesne J-F, Gingras S, et al. The determinants of prevalence of health complaints among young competitive swimmers. *Int Arch Occup Environ Health* 2006; 80(1):32–39. Doi: 10.1007/s00420-006-0100-0.

21 Salonen RO, Pennanen AS, Vahteristo M, et al. Health risk assessment of indoor air pollution in Finnish ice arenas. *Environ Int* 2008; 34(1):51–57. Doi: 10.1016/j.envint.2007.06.012.

22 Horvath SM. Exercise in a cold environment. *Exerc Sport Sci Rev* 1981; 9:221–263.

23 Potts J. Factors associated with respiratory problems in swimmers. *Sports Med Auckl NZ* 1996; 21(4):256–261. Doi: 10.2165/00007256-199621040-00002.

24 D'Alessandro A, Kuschner W, Wong H, et al. Exaggerated responses to chlorine inhalation among persons with nonspecific airway hyperreactivity. *Chest* 1996; 109(2):331–337. Doi: 10.1378/chest.109.2.331.

25 Helenius IJ, Tikkanen HO, Haahtela T. Exercise-induced bronchospasm at low temperature in elite runners. *Thorax* 1996; 51(6):628–629. Doi: 10.1136/thx.51.6.628.

26 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(2):125–129. Doi: 10.1136/bjsm.32.2.125.

27 Banner AS, Chausow A, Green J. The tussive effect of hyperpnea with cold air. *Am Rev Respir Dis* 1985; 131(3):362–367. Doi: 10.1164/arrd.1985.131.3.362.

28 Rundell KW, Im J, Mayers LB, et al. Self-reported symptoms and exercise-induced asthma in the elite athlete. *Med Sci Sports Exerc* 2001; 33(2):208–213. Doi: 10.1097/00005768-200102000-00006.

29 Bougault V, Turmel J, Boulet L-P. Bronchial challenges and respiratory symptoms in elite swimmers and winter sport athletes: Airway hyperresponsiveness in asthma: its measurement and clinical significance. *Chest* 2010; 138(2 Suppl):31S-37S. Doi: 10.1378/chest.09-1689.

30 Adams WC. Effects of ozone exposure at ambient air pollution episode levels on exercise performance. *Sports Med Auckl NZ* 1987; 4(6):395–424. Doi: 10.2165/00007256-198704060-00002.

31 Stenfors N. Self-reported symptoms and bronchial hyperresponsiveness in elite cross-country skiers. *Respir Med* 2010; 104(11):1760–1763. Doi: 10.1016/j.rmed.2010.07.014.

32 Rundell KW, Caviston R, Hollenbach AM, et al. Vehicular air pollution, playgrounds, and youth athletic fields. *Inhal Toxicol* 2006; 18(8):541–547. Doi: 10.1080/08958370600685640.

33 project TWAQI. Air Pollution in World: Real-time Air Quality Index Visual Map. Aqicn.Org. Available at: https://aqicn.org/map/asia/. Accessed October 19, 2021.

34 Antunes A. Map of the world's pollen monitoring stations | EAACI.org. Available at: https://www.eaaci.org/19-activities/task-forces/4342-pollen-monitoring-stations-of-the-world.html. Accessed October 19, 2021.

35 Pacitto A, Amato F, Salmatonidis A, et al. Effectiveness of commercial face masks to reduce personal PM exposure. *Sci Total Environ* 2019; 650(Pt 1):1582–1590. Doi: 10.1016/j.scitotenv.2018.09.109.

36 Hanstock HG, Ainegren M, Stenfors N. Exercise in Sub-zero Temperatures and Airway Health: Implications for Athletes With Special Focus on Heat-and-Moisture-Exchanging Breathing Devices. *Front Sports Act Living* 2020; 2:34. Doi: 10.3389/fspor.2020.00034.

37 Gotoh M, Okubo K, Okuda M. Inhibitory effects of facemasks and eyeglasses on invasion of pollen particles in the nose and eye: a clinical study. *Rhinology* 2005; 43(4):266–270.

38 Morris NB, Piil JF, Christiansen L, et al. Prolonged facemask use in the heat worsens dyspnea without compromising motor-cognitive performance. *Temp Austin Tex* 2020; 8(2):160–165. Doi: 10.1080/23328940.2020.1826840.

39 Wong AY-Y, Ling SK-K, Louie LH-T, et al. Impact of the COVID-19 pandemic on sports and exercise. *Asia-Pac J Sports Med Arthrosc Rehabil Technol* 2020; 22:39–44. Doi: 10.1016/j.asmart.2020.07.006.

40 Bougault V, Boulet L-P. Is there a potential link between indoor chlorinated pool environment and airway remodeling/inflammation in swimmers? *Expert Rev Respir Med* 2012; 6(5):469–471. Doi: 10.1586/ers.12.51.

41 Andrade A, Dominski FH. Indoor air quality of environments used for physical exercise and sports practice: Systematic review. *J Environ Manage* 2018; 206:577–586. Doi: 10.1016/j.jenvman.2017.11.001.

42 Vinnikov D, Khafagy A, Blanc PD, et al. High-altitude alpine therapy and lung function in asthma: systematic review and meta-analysis. *ERJ Open Res* 2016; 2(2). Doi: 10.1183/23120541.00097-2015.

43 Inouye DW. Effects of climate change on alpine plants and their pollinators. *Ann N Y Acad Sci* 2020; 1469(1):26–37. Doi: 10.1111/nyas.14104.

44 Whyand T, Hurst JR, Beckles M, et al. Pollution and respiratory disease: can diet or supplements help? A review. *Respir Res* 2018; 19(1):79. Doi: 10.1186/s12931-018-0785-0.

45 Dreßler M, Fussbroich D, Böhler L, et al. Oil supplementation with a special combination of n-3 and n-6 long-chain polyunsaturated fatty acids does not protect for exercise induced asthma: a double-blind placebo-controlled trial. *Lipids Health Dis* 2020; 19(1):167. Doi: 10.1186/s12944-020-01343-2.

46 Gomes EC, Allgrove JE, Florida-James G, et al. Effect of vitamin supplementation on lung injury and running performance in a hot, humid, and ozone-polluted environment. *Scand J Med Sci Sports* 2011; 21(6):e452-460. Doi: 10.1111/j.1600-0838.2011.01366.x.

47 Brożek JL, Bousquet J, Agache I, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol* 2017; 140(4):950–958. Doi: 10.1016/j.jaci.2017.03.050.

48 New: Global Initiative for Asthma 2021 Executive Summary on Asthma Management and Prevention. Global Initiative for Asthma - GINA. Available at: https://ginasthma.org/new-global-initiative-for-asthma-2021-executive-summary-on-asthma-management-and-prevention/. Accessed October 19, 2021.

49 Koskela HO. Cold air-provoked respiratory symptoms: the mechanisms and management. *Int J Circumpolar Health* 2007; 66(2):91–100. Doi: 10.3402/ijch.v66i2.18237.

50 McKenzie DC, Stirling DR, Fadl S, et al. The effects of salbutamol on pulmonary function in cyclists exposed to ozone: a pilot study. *Can J Sport Sci J Can Sci Sport* 1987; 12(1):46–48.

51 Beckett WS, McDonnell WF, Horstman DH, et al. Role of the parasympathetic nervous system in acute lung response to ozone. *J Appl Physiol Bethesda Md 1985* 1985; 59(6):1879–1885. Doi: 10.1152/jappl.1985.59.6.1879.

52 Deal EC, McFadden ER, Ingram RH, et al. Effects of atropine on potentiation of exercise-induced bronchospasm by cold air. *J Appl Physiol* 1978; 45(2):238–243. Doi: 10.1152/jappl.1978.45.2.238.

53 Nightingale JA, Rogers DF, Chung KF, et al. No effect of inhaled budesonide on the response to inhaled ozone in normal subjects. *Am J Respir Crit Care Med* 2000; 161(2 Pt 1):479–486. Doi: 10.1164/ajrccm.161.2.9905031.

54 Vagaggini B, Taccola M, Conti I, et al. Budesonide reduces neutrophilic but not functional airway response to ozone in mild asthmatics. *Am J Respir Crit Care Med* 2001; 164(12):2172–2176. Doi: 10.1164/ajrccm.164.12.2009090.

55 Vagaggini B, Carnevali S, Macchioni P, et al. Airway inflammatory response to ozone in subjects with different asthma severity. *Eur Respir J* 1999; 13(2):274–280. Doi: 10.1034/j.1399-3003.1999.13b09.x.

56 Alexis N, Urch B, Tarlo S, et al. Cyclooxygenase metabolites play a different role in ozone-induced pulmonary function decline in asthmatics compared to normals. *Inhal Toxicol* 2000; 12(12):1205–1224. Doi: 10.1080/08958370050198548.

57 Carlsten C. Synergistic Environmental Exposures and the Airways Capturing Complexity in Humans: An Underappreciated World of Complex Exposures. *Chest* 2018; 154(4):918–924. Doi: 10.1016/j.chest.2018.06.004.

58 Ierodiakonou D, Zanobetti A, Coull BA, et al. Ambient air pollution, lung function, and airway responsiveness in asthmatic children. *J Allergy Clin Immunol* 2016; 137(2):390–399. Doi: 10.1016/j.jaci.2015.05.028.

59 Lewis TC, Robins TG, Mentz GB, et al. Air pollution and respiratory symptoms among children with asthma: vulnerability by corticosteroid use and residence area. *Sci Total Environ* 2013; 448:48–55. Doi: 10.1016/j.scitotenv.2012.11.070.

60 Rider CF, Carlsten C. Air pollution and resistance to inhaled glucocorticoids: Evidence, mechanisms and gaps to fill. *Pharmacol Ther* 2019; 194:1–21. Doi: 10.1016/j.pharmthera.2018.08.005.