Environmental aeroallergens and allergic rhino-conjunctivitis

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Purpose of review
The rising prevalence of allergy and of allergic rhino-conjunctivitis is associated with changes in modern lifestyle. The current period of rapid development and consequent urbanization and migration, coupled with changes in climate, is facilitating a growth in rates of allergy.

Recent findings
Alterations to indoor and outdoor environments resulting from urbanization, industrialization, and climate change have significant implications for the prevalence and management of allergic rhino-conjunctivitis. Rising temperatures, precipitation and more extreme weather enable longer pollen seasons and greater viability of indoor and outdoor moulds and result in increased exposure to (and allergenic potential of) these aeroallergens. Outdoor air pollution is a major risk factor for rhino-conjunctivitis; key contributors are fuel combustion and dust storms because of changes in land-use and development. Further studies are needed to recognize and understand sources of indoor pollution including phthalates.

Summary
A better understanding of the role of environmental aeroallergens in allergic rhino-conjunctivitis is important to aid future management of allergic conjunctivitis. Strategies such as region-specific modelling of aeroallergens (pollens, air pollution) are required to predict and thus prevent exposure and to better inform appropriate childhood exposure and minimize lifelong effects.

Keywords
aeroallergens, allergic conjunctivitis, allergic rhino-conjunctivitis, climate change, hay fever

INTRODUCTION

Allergic rhino-conjunctivitis or hay fever is caused by exposure to allergens and characterized by inflammation of the nasal and/or ocular mucosa (conjunctiva) manifesting as redness and swelling, a runny or blocked nose and/or sneezing and watery eyes (Fig. 1). Often accompanied by symptoms of burning and itching, these signs are triggered by an allergic reaction that can be either seasonal or occur throughout the year. Symptoms of allergic conjunctivitis are easily confused with those of dry eye and the distinction between these two conditions is not always clear, especially in milder forms where clinical presentation is not diagnostic [1]. There is significant overlap between allergic conjunctivitis and hay fever and both conditions typically co-exist in some form [2,3]. In this report, evidence pertaining to any of the forms of the disease (allergic rhinitis, allergic conjunctivitis or allergic rhino-conjunctivitis/hay fever) is reviewed for possible associations with environmental factors. Findings associated with any of these conditions will be extrapolated as likely to apply to all conditions for the purpose of this review. All of these conditions have a high comorbidity with asthma and we likewise draw on the available evidence for this increasingly common allergic disease.

The prevalence of allergic rhino-conjunctivitis has markedly increased globally over the past 50 years [2,4–6]. In the International Study of Asthma and Allergies in Childhood multiphase study, the prevalence of allergic rhinoconjunctivitis symptoms in children 6 to 7 years old increased in 67% of centres sampled over a 7-year period [4]. A longitudinal study of Australian adults demonstrated a doubling of

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KEY POINTS

- Prevalence of allergic rhino-conjunctivitis is increasing in line with that of allergic disease and is associated with changes in lifestyle which occur alongside changes to indoor and outdoor environments.
- Alterations to indoor and outdoor environments resulting from urbanization, industrialization and climate change have significant implications for prevalence and management of allergic rhino-conjunctivitis.
- Rising temperatures, precipitation and more extreme weather enable longer pollen seasons and greater viability of indoor and outdoor moulds and result increased exposure to, and allergenicity of, these aeroallergens.
- A major risk factor for rhino-conjunctivitis is outdoor air pollution, to which fuel combustion and changes in land-use patterns are key contributors; further studies are needed to recognize and understand sources of indoor pollution including phthalates.
- Current and future management of allergic conjunctivitis should involve strategies to predict and thus prevent exposure, including region-specific modelling of aeroallergens, such as pollens and air pollution.

prevalence of hay fever from 19% in 1968 to 41% in the early 1990's [4]. Worldwide prevalence data and data on wholesale sales and pharmacist supply of common drugs used for the management of allergic rhino-conjunctivitis support the view that the prevalence of the disease is increasing over time [2,5–7]. Between 2001 and 2010, the total wholesale cost to community pharmacies of drugs for the treatment of allergic rhino-conjunctivitis in Australia more than doubled going from $108 million to more than $226 million [2]. The 'hygiene hypothesis' proposes that exposure to 'more hygienic' environments in infancy/early childhood increases an individual's susceptibility to allergic diseases [8]. Urbanization and reduced exposure to biodiverse and microbe-rich environments are likely to play a key role in the upward trend in allergy occurrence [7,8].

Allergens for rhino-conjunctivitis are airborne and include indoor allergens such as mould spores, mammalian dander (small scales from the skin or hair), secreta (e.g. saliva) and excreta (e.g. faeces) of insects, pets and mites (including house dust mites), and outdoor allergens such as pollen grains, fungal spores and chemical air pollution. Seasonal allergic rhino-conjunctivitis is triggered primarily by outdoor aeroallergens, whereas perennial rhino-conjunctivitis is felt to be associated primarily with indoor aeroallergens. Rapidly occurring changes to both the indoor and outdoor environment resulting from urbanization, industrialization and climate change have significant implications for prevalence and management of allergic disease, including conjunctivitis.

NATURAL ALLERGENS: POLLENS AND MOULDS

There are considerable geographical, seasonal, and year to year variations in the composition of outdoor aeroallergens [9,10▪▪]. Pollen is produced by plants during their life cycle. The microscopic pollen grains come in a variety of shape and sizes (Fig. 2). Grasses are the major clinically important outdoor aeroallergen source in Australia [9]. Grass pollens are also the most likely cause of hay fever in

FIGURE 1. Mild allergic conjunctivitis. Courtesy Mr Sailesh Kolanu, UNSW, Australia.

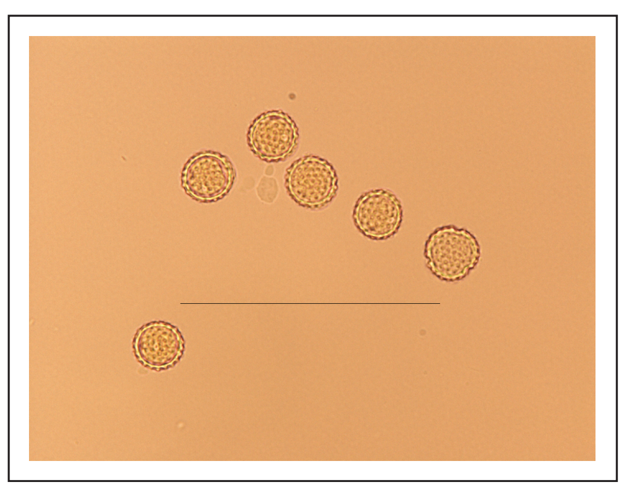

FIGURE 2. Ambrosia pollen, light microscopy. Courtesy Dr Lukasz Grewling, Adam Mickiewicz University, Poland.

Europe (large amounts, high allergen content) [11]. In Australia, indigenous vegetation (e.g. Eucalyptus, Acacia, Sorthum grass), introduced Northern Hemisphere species (e.g. ragweed, birch), and exotic invasive species can all potentially contribute. The pattern of the flowering/pollen season is dependent on species and geographical location. The characteristics of airborne pollen have been shown to change in response to changes in climate, weather, and land use (e.g. urbanization) [9,10▪▪,11]. Interestingly, a key source of allergenic pollen in the Mediterranean region, *Parietaria judaica*, has been found to be more viable in areas with heavy metal pollution [12].

Exposure to airborne pollen above a threshold level can trigger allergy symptoms in sensitized individuals and early-life exposure is also an important factor. A recent Australian study [13] showed that persistent exposure to pollen up to 3 months in infancy was associated with higher risk of hay fever (adjusted odds ratio = 1.14, 95% confidence interval, 1.01–1.29). Similarly, a study [14] of 508 preschool children in Hong Kong found exposure to moisture and mould in the first year of life increased risk of rhino-conjunctivitis (adjusted odds ratio = 2.09; 95% confidence interval, 1.15–3.80). These studies reflect the findings of an earlier systematic review of environmental exposure, which highlighted early childhood exposure to indoor mould and outdoor allergens (pollen, fungal spores) as consistently associated with increased risk for development of asthma [15]. Sensitization to mould occurs as a result of inhalation of airborne fungal spores or allergens in fungal dust. Relevant moulds associated with allergic rhino-conjunctivitis have not as yet been determined. However, a U.S.-based study [16] showed that asthma in 7-year-old children was significantly associated with the presence of three mould species, *Aspergillus ochraceus*, *Aspergillus unguis* and *Penicillium variabile*, collected from their home in infancy. Exposure to moulds, both indoor and outdoor, is likely to be affected by increases in precipitation and temperature resulting from climate change.

FIGURE 3. Air pollution, Hong Kong. Courtesy Dr Melissa Hart, ARC Centre of Excellence for Climate System Science, NSW, Australia.

CHEMICAL AIR POLLUTION

Indoor and outdoor air pollution has now been well established as a major environmental risk factor for allergic rhino-conjunctivitis. Many studies [17▪▪, 18▪,19,20,21▪] suggest an association between air pollution and rhino-conjunctivitis. Relevant air pollutants for the setting of rhino-conjunctivitis include tobacco smoke, pollutants derived from fuel combustion [17▪▪,20], Asian dust (Fig. 3) [18▪,19] and phthalates [21▪]. It is thought that these air pollutants may be allergenic, irritant or a combination of both.

Polluted air is air that contains gases, dusts or fumes in amounts that are considered harmful to the health or comfort of humans. Sources of pollution can be natural (e.g. dust storms) or man-made (e.g. tobacco smoke or residue of fossil fuel consumption). Common pollutants include nitrogen dioxide, carbon monoxide, ozone, sulphur dioxide and particulate matter. Particles comprise a complex mixture of acids, organic chemicals, metals, and soil. Particulate matter is primarily caused by combustion of coal or fossil fuels associated with power generation or motor vehicle fuels, agricultural burning practices and emissions from domestic solid fuel heaters and woodstoves. They are classified based on size as ultrafine if particles are smaller than 0.1 μm, fine (PM2.5) if they are between 0.1 and 2.5 μm and coarse if particles are between 2.5 and 10 μm in size. A significant association between the number of outpatient visits for allergic conjunctivitis and levels of airborne particulate matter (PM2.5) ($r = 0.62$, $P = 0.018$) was found in Tokyo hospital outpatients in autumn but not in spring, where presumably levels of pollens override any responses to airborne pollutants [17▪▪]. In the same study [17▪▪], PM2.5 levels were a significant predictor of the number of outpatient visits from May to July (odds ratio = 9.05, $P = 0.046$) and PM2.5 levels were exacerbated by low humidity.

Asian dust is a meteorological phenomenon that affects much of East Asia during spring where dust blown from the deserts of Mongolia, China and Kazakhstan is carried eastwards to Korea, Japan, Russia and even the United States. Over the last decade, the severity and impact of the dust storms have been seen to increase, in part because of the increasing amount of industrial pollutants contained in the dust and the intensified desertification – a process of land-degradation by which a region becomes progressively drier, eventually becoming desert – in China associated with major development projects. The number of clinical visits for allergic rhinitis in Taiwanese appeared to increase in the days following an occurrence of an Asian dust storm [19]. Exposure to Asian dust induced worsening of respiratory symptoms in 184 Japanese adult outpatients with asthma, 31 of which suffered from allergic rhinitis or chronic sinusitis [22]. In a case–control study [18▪] involving 10 patient with allergic rhino-conjunctivitis, multivariate analysis showed a significant association of subjects' responses to Asian dust on skin prick testing with their responses to pollen and fungi. These suggest a potential role for Asian dust in the development of allergic conjunctivitis.

Phthalate esters are plasticizers for plastic products including toys, food containers, furniture and paints. They are a commonly encountered indoor pollutants. Phthalates leach out of materials and disperse into the air or settle into dust, acting as allergens for humans sensitized to them. Humans are exposed to phthalates through dust ingestion, inhalation, dermal absorption and food ingestion. It has been suggested that phthalates can also potentiate allergic reactions, increasing the potency of other allergens. Sensitization (IgE+) in Danish children with rhino-conjunctivitis was associated with phthalates levels in dust from home and childcare [21▪]. A study [23] of 156 Japanese homes found that associations between house dust phthalate levels and the prevalence of allergic rhinitis and conjunctivitis were stronger in children than adults. Further studies are needed to advance our understanding of the potential impact of phthalates on human health including ocular health.

The relative balance of indoor and outdoor allergens will vary with geographic location, season, changes in industrial pollution levels and indoor aeration and cleaning and use of phthalate-containing products. Adequate control of this multitude of factors in population studies presents a significant challenge. This may partially explain why the literature is equivocal as to whether the indoor home environment or the outdoor environment has the stronger influence on allergy development [14].

CLIMATE AND CLIMATE CHANGE

The prevalence of allergic rhino-conjunctivitis is approximately 10–15% and is modulated by sex, age and geographic location [2,24▪▪,25,26]. As for other allergic diseases, allergic conjunctivitis is perhaps most common in children [4,26]. Geographical differences in prevalence of allergic rhino-conjunctivitis may be attributed to differences in climate, housing, society and culture. Proximity to the equator and higher UV-B exposure is speculated to modulate the T_H2 immune response, and thus risk of hay fever, through consequent variations in vitamin D levels [27,28]. Within a given year, outdoor allergens are susceptible to changes in meteorological conditions associated with changing temperatures, wind speed and direction and humidity. A large U.S. study [24▪▪] merged the data from the 2007 National Survey of Children's Health and the 2006–2007 National Climate Data Center to demonstrate several associations between the prevalence of allergic rhinitis and geographic and climate factors such as relative humidity, drought index, ozone levels, temperature, precipitation and UV index.

According to the Intergovernmental Panel on Climate Change, warming of the climate system is unequivocal [29]. The Lancet Commission on Health and Climate Change labelled the impact of climate change on health as perhaps the biggest global challenge of this century [30]. Climate change has a direct impact on the aeroallergens. The characteristic of airborne pollen has been shown to change in response to changes in climate, carbon dioxide levels, weather and land use (e.g. urbanization) [9,10▪▪,11]. Over the last few decades, the increase in temperature associated with climate change has hastened the start of the pollen season in a variety of settings by as much as 22 days and is expected to keep advancing [11]. Earlier flowering and pollen release are also a consequence of higher CO_2 levels and temperature in urbanized areas [31]. The length of the pollen season is also increasing [32]. Although this has not been formally measured, earlier and longer pollen seasons are likely to also lead to an earlier start of the allergy season, including seasonal allergic conjunctivitis, and to extend its duration.

Given this, it appears likely that in the future allergens will be modulated not only by seasonal variations but also by climatic changes associated with global warming. Climate may not only drive pollination and increase the impact of pollution but also may provide good conditions for certain indoor aeroallergens to proliferate, for example moulds and dust mites. Increased sporulation and antigen production of the mould *Alternaria alternata* has been shown in elevated atmospheric carbon dioxide conditions [33]. Greater mould growth is likely with higher relative humidity and precipitation associated with global warming; increased air-conditioner use is a compounding factor.

CONCLUSION

A fundamental role for a diverse environmental microbiota being protective against inflammatory diseases is becoming increasingly evident [7]. Alterations in indigenous microbiota of the respiratory tract associated with urbanization, loss of biodiversity and an increasingly sedentary indoor life has been proposed to be at least partially responsible for altered immunological tolerance and increases in allergic diseases [7]. Industrialization and climate change may result in significantly altered exposure to air pollutants and allergens worldwide; this may profoundly influence public health.

Possible strategies to address these challenges may include better and region-specific modelling of pollen season start, peak, duration and end [10■■,34]. Studies need to be conducted locally because of different patterns of land use and region-specific species causing allergy. This is important not only for the clinical management of allergic conjunctivitis but will also enable improved prediction and thus prevention of exposure.

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Conflicts of interest

There are no conflicts of interest.

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■ of special interest
■■ of outstanding interest

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