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CLIMATE CHANGE, AEROALLERGENS AND PEDIATRIC ALLERGIC DISEASE

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Abstract

The degree to which aeroallergens are contributing to the global increase in pediatric allergic disease is incompletely understood. We review the evidence that links climate change to changes in aeroallergens such as pollen and outdoor mold concentrations and subsequently, aeroallergen association with pediatric allergic disease. We specifically explore the evidence on both the exacerbation and the development of allergic disease in children related to outdoor pollen and mold concentrations. Pediatric allergic diseases include atopic dermatitis or eczema, allergic rhinitis or hay fever, and some types of asthma in children, typically defined as less than 18 years of age. We discuss how the timing of aeroallergen exposure both *in utero* and in childhood could be associated with allergies. We conclude that the magnitude and type of health impacts due to climate change will depend on improved understanding of the relationship between climatic variables, multiple allergen factors, and allergic disease. Improved public health strategies such as adequate humidity control, optimum air filtration and ventilation, and improved anticipatory public health messaging will be critical to adaptation.

Keywords

aeroallergen; allergic rhinitis; ambient air; atopy; fungal spore; global warming; greenhouse gas; sensitization

Pediatric allergic disease is on the rise globally, particularly in industrialized countries (1). This rise is generally attributed to demographic transitions in both developed and developing countries but is not completely understood (2). Allergic disease can manifest with skin or respiratory symptoms including atopic dermatitis, commonly known as eczema; allergic rhinitis, commonly known as hay fever; and some types of asthma. While the etiology of allergic disease is both genetic and environmental, the specific attributable risk from various environmental exposures is a topic of much research (3). The effect of allergen exposure in childhood on the development and symptoms of allergic disease is an important area of research for understanding the recent and future trends in disease burden from climate change and developing possible public health interventions.

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[Callout] The effect of allergen exposure in childhood on the development and symptoms of allergic disease is an important area of research for understanding the recent and future trends in disease burden from climate change and developing possible public health interventions.

The windows of potential susceptibility range from *in utero* through adolescence. Indoor allergen exposure is an area of intensive ongoing research while outdoor, or ambient, pollen and mold exposure has been less explored. As aeroallergens are sensitive to meteorological conditions like temperature and humidity, a better understanding of the relationship of these aeroallergens to allergic disease is relevant due to expected changes in outdoor climatic conditions globally in coming years. Since indoor mold has been extensively reviewed, we focus on outdoor allergen studies. In this review, we exclude indoor allergen studies – specifically indoor mold. Our objective is to review the research on the association between these three elements: climate change, aeroallergens, and pediatric allergic disease.

CLIMATE CHANGE AND AEROALLERGENS

Certain gaseous components of the atmosphere help keep the Earth warm enough to support human life and are thus called greenhouse gases. Anthropogenic emissions of greenhouse gases, which include carbon dioxide and methane, augment this process, and, increasing the amount of energy in our planet's system. The additional energy in the form of heat drives changes in the hydrologic cycle around the globe (4), resulting in subsequent changes in long term patterns of rainfall and other weather patterns. The effects of these changes vary by region of the world (5), with implications for many ecosystems (6) as well as for human health (7).

Many studies have indicated that the pollen season – typically indicated by regionally specific tree pollen – is beginning earlier in the year for a number of species in various parts of the world (8–12). These changes have been described most thoroughly in Europe, although evidence of an earlier start to the pollen season has also been documented in the United States and Asia. However, it is not clear whether earlier start dates lead to a lengthening of the pollen season (13). Additionally, while there is evidence of a trend towards increasing annual pollen production in some European species over the last 30 years (11,14), research to date for the most part has not revealed any major trends in pollen production in the United States (13,15). The absence of long-term, consistently collected pollen records in the United States presents a significant challenge for determining trends over recent decades (13) and for linking such trends to clinical sequelae.

Despite the mixed evidence regarding past trends, it is thought that future climate change could affect the timing and severity of the pollen season. Numerous studies have shown that higher temperature and greater precipitation prior to the pollen season lead to increased production of many types of tree and grass pollen (13,16–18). Furthermore, ragweed pollen production has been observed to increase in response to increased temperatures and concentrations of atmospheric carbon dioxide (19–21). More studies are needed to examine the effect of carbon dioxide concentrations on woody plants such as trees.

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While a number of pollen types have been examined in relation to meteorological variables, only a few clinically-relevant outdoor fungal species, such as *Alternaria* and *Cladosporidium*, have been similarly investigated (13). Several studies have found that increased atmospheric concentrations of some mold spore types are associated with

increased temperature and humidity (22–24). Furthermore, one study found that maximum mold concentrations occurred earlier than normal in the year following the warm, wet conditions of the 1997–1998 El Niño event (22), indicating that the timing of mold counts could also be affected by climate change.

Future changes in meteorological variables and carbon dioxide concentrations associated with climate change could therefore lead to changes in atmospheric concentrations of both pollen (13) and mold. Driven by changing climate, changes in pollen and mold could lead to changing patterns of allergic disease morbidity (Figure 1) (25).

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However, more work into the specific relationships between meteorologic variables and aeroallergen timing, intensity, and allergenicity will help quantify the impacts moving forward. Furthermore, the relationship of outdoor pollen and mold to allergic disease has been incompletely explored. While there is some evidence that climate change -- through changes in humidity or extreme weather events that lead to flooding -- could affect indoor mold concentrations as well (26), indoor mold studies are excluded from this review.

PEDIATRIC ALLERGIC DISEASE AND AEROALLERGENS

A number of studies have demonstrated that aeroallergens such as pollen and mold can worsen symptoms of allergic disease in already affected individuals. A review by Schmier and Ebi (27) examining the relationship of daily ambient pollen and fungus concentrations with the severity of childhood asthma concluded that weed pollen appeared to be associated with asthma exacerbations and use of emergency and hospital services. More recently, a study based in Montreal, Canada found an association between pediatric emergency department asthma visits and daily grass pollen concentrations (28). There is also sufficient evidence to support association of damp indoor spaces and mold with respiratory symptoms and asthma symptoms in people who are already sensitized. However, there is only limited or suggestive evidence regarding the association of damp indoor spaces with respiratory illness in otherwise healthy children or the development of asthma in susceptible persons (29). Thus, while exposure to aeroallergens can exacerbate existing allergic disease, their role in the development of allergic disease is less understood (30). Additionally, as stated earlier, the literature on an association between indoor mold and allergic disease development has been recently reviewed (29) but review of the literature for outdoor mold and pollen is lacking and thus prompted this review.

For the purposes of this article, allergic disease refers to atopic types of illness which are mediated by IgE antibodies (30). We understand, both intuitively and empirically, that exposure to allergens is a risk factor to sensitization and furthermore that reduction of exposure to allergens can reduce disease symptoms (31). In research, there are a number of clinical and laboratory measures of sensitization including skin prick testing, serum IgE testing (including RAST, ImmunoCAP, and other techniques), cytokine or T cell proliferation, and Th1/Th2 ratios as well as maternal and cord blood IgE levels (32). While each of these measures provides some insight into sensitization, there is no single ideal measure. Furthermore, sensitization can only serve as a rough measure of subsequent disease burden (33,34). Diseases such as asthma are multi-factorial with only a subset being atopic and many other gene-environment interactions and external management factors affect the disease induction and course. In addition, the timing and duration of exposure to various allergens appear to also play a role in disease development and course. The development of the immune system is a lengthy and complex process and exposure to potential allergens could have various impacts at different stages of development (35). One

recent study on air pollution supports this concept of windows of vulnerability in humans by showing association of exposure by two air pollutants, particulate matter and polycyclic aromatic hydrocarbons, in early and late gestation with lymphocyte cell distribution (36).

When considering pollen and outdoor mold, previous articles and reviews have focused on childhood allergic symptoms and asthma exacerbations. Here, we examine the limited literature on sensitization patterns and development of allergic disease in relation to actual or proxies for ambient pollen and fungal types.

Season of Birth

Numerous studies have demonstrated associations of birth month or season with both allergic sensitization – such as ryegrass sensitization - and allergic rhinitis or some types of asthma (32,37–39). However, the relationship of sensitization and overt disease development are not always consistent. For example, one recent study out of Denmark showed no correlation of season of birth with any type of pollen sensitization as measured by skin prick testing or IgE antibodies but did show an association with prevalence of asthma (39). This study illustrates how positive sensitization tests and clinical allergic disease are not always well correlated. However, it does support the idea of a critical window of development impacting later life allergic disease. Additional factors with strong seasonal signals such as upper respiratory infections and moisture in homes limit birth season as a stand alone proxy for pollen or mold exposure.

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Ambient Pollen and Fungal Concentrations

Season or qualitative measures such as parental report are proxies for exposure to pollens or molds. Studies that relate quantitative measures of outdoor pollen and mold concentrations to child-specific outcomes are particularly relevant in the present context, as we review the handful of such studies in the next section.,

Sensitization—A series of studies emerged from Sweden following an anomalously high birch pollen season (40–42). These studies examined two separate cohorts, one composed of infants exposed to the high birch pollen levels during the first three months of life and the other composed of infants whose mothers were exposed to the high birch pollen levels while pregnant. The infants exposed at ages 0–3 months had higher odds of positive skin prick tests (SPT) to birch pollen between 4 and 5 years of age than did infants exposed *in utero*. However, both of these groups had higher odds (OR, 2.4; 95% CI, 1.2 – 4.6 and OR, 1.7; 95% CI, 0.7–4.1) of positive SPT to birch pollen compared to children who were exposed to the high birch pollen later in life (approximately 1 year of age) (40,41). In another study that looked at prevalence and ratio of Th1 and Th2 type cells (identified by flow cytometry by positive stains for interferon- γ and interleukin 4 respectively) in infants at age 24 months, the Th phenotype was not associated with mean pollen and outdoor mold concentrations during the first three months of life, and the authors concluded that the Th cell profile, thus, seemed unlikely to be related to atopic sensitization in this population of children under 24 months (43).

Disease Development—Early life exposure – defined as exposure during 0 – 3 months of age - to several types of pollen (cypress, pine and alder) and mold spores (Basidiospores and Ascospores) as well as total pollen counts were associated with early wheeze among children under 24 months in a cohort study in California that involved children of mostly

Mexican immigrants in an agricultural community (43). Furthermore, in the series of studies from Sweden with the elevated birch pollen year, the infants exposed to high pollen concentrations during the first 3 months of life had an increased prevalence of pollen- and animal dander-induced allergic asthma at age 4–5 years compared to children born other years (OR, 2.6; 95% CI, 1.2–5.6). The children whose mothers were exposed when pregnant also showed a trend (although insignificant) toward increased prevalence of bronchial asthma, allergic rhinoconjunctivitis, and atopic dermatitis (40,41). In this same series of studies, children of mothers with pollen allergy symptoms showed increased symptoms of various atopic diseases compared to other children regardless of past exposure (42) underscoring the importance of heritability or possibly microenvironment.

LINKING CLIMATE CHANGE, AEROALLERGENS, AND PEDIATRIC DISEASE

As we have seen, there is growing evidence to support an association between climate change and aeroallergens as well as pediatric allergic disease and exposure to pollen or outdoor mold and subsequent later-life allergen sensitization and allergic disease induction. These associations are supported by extensive review of indoor mold and damp indoor spaces and health effects (29). While climate change could impact indoor allergens through changes in humidity or extreme weather events that result in flooding, pollen and outdoor mold spores will be more directly affected by regional weather changes resulting from climate change (Figure 1).

[Callout] There is growing evidence to support an association between climate change and aeroallergens as well as pediatric allergic disease and exposure to pollen or outdoor mold and subsequent later-life allergen sensitization and allergic disease induction.

A general limitation of all the studies included in this review, as well as those in prior reviews (27), is that few measure pollen exposure on the level of the individual. Additionally, many of the studies identified in the latter part of this review are geographically limited and focus on children with atopic parents or who were already enrolled at an allergy clinic, which limits our ability to generalize these findings to the entire population (40–42). Furthermore, many studies examining sensitization imply a relevance of sensitization measures to disease development or clinical symptoms. While allergen sensitization is a known risk factor, some scientists argue against placing too much weight on this association (44). Allergen sensitization – as discussed above – is a well known risk factor for allergic disease development but is not an *a priori* risk factor. In other words, some non-sensitized individuals can still have allergic-type symptoms or an asthma disease phenotype called non-atopic asthma (30). Additional research to explore the question of how pollen and mold exposure *in utero* or in early life relate to the development of allergic disease and other types of asthma could benefit from collection of better ambient pollen and mold records, the measurement of pollen and mold exposure on an individual level, and further work to understand the relationship of cord blood IgE to pollen and mold exposure. In addition, continuous, long-term ambient pollen and mold records with improved geospatial resolution could better elucidate the relationship of actual exposure and allergic disease development and recent trends.

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Overall, the findings of the studies examined in this review support the idea that there are one or more critical windows of allergic and immunologic development *in utero* and during infancy (30,36,45). If climate change conditions – including higher temperatures, higher carbon dioxide concentrations, more intense periods of precipitation, and changes in humidity – lead to higher concentrations, altered timing, or increased allergenicity of ambient outdoor pollen and mold, the prevalence of sensitization or even of allergic symptoms in children could change. Understanding the magnitude and directionality of such changes require more detailed understanding of the relationship of mold and pollen exposure to allergic disease development. Addressing this gap is critical in order to be able to quantify the pediatric allergic disease burden and model future impacts under different climate change scenarios.

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Preventative measures should include mitigation of greenhouse gases to reduce the severity of potential climate change. Adaptation measures are also essential and need to involve studying and strengthening existing public health strategies and as well as encouraging multi-disciplinary collaborations between such groups as public health professionals, emergency preparedness agencies, city planners, architects and others. Planning for adequate humidity control and optimum air filtration and ventilation could benefit people who suffer from outdoor allergies as well as allergies to indoor allergens. Improved anticipatory public health messaging – such as improved pollen alerts – could help prevent exposures that increase risk of not only disease symptoms but also disease development. Ultimately, the health impacts from climate change will depend on public health adaptation strategies.

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Figure 1.
Potential mechanism by which climate change could impact pediatric allergic disease.