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CLINICAL PERSPECTIVES

Climate change: allergens and allergic diseases

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Abstract

Climate change has been described as the biggest global health threat of the 21st century. The atmospheric concentrations of greenhouse gases, such as carbon dioxide, methane and nitrous oxide, have increased significantly since the start of the Industrial Era around 1750, with much of this increase occurring over just the last 50 years or so. This is resulting in warming of the climate system as well as changes in precipitation and weather and climate extremes. These changes in climate are having wide-ranging impacts on the Earth's physical, biological and human systems, including human health. It is these impacts of climate change on human health that are the focus of this paper, particularly the impacts on allergens and allergic diseases. Such impacts are particularly significant in many countries where the prevalence of such diseases is high and/or increasing. There is now compelling evidence that rising air temperatures and carbon dioxide concentrations are, in some plant species, resulting in increased pollen production and allergenicity and advancement and lengthening of the pollen season. Changes in extreme events, such as thunderstorms and tropical cyclones, will also have impacts on allergic diseases, with, for example, the flooding associated with tropical cyclones leading to proliferation of mould growth in damp homes. The article also considers a range of responses to these health threats, including greenhouse gas mitigation, and adaptation strategies, such as enhanced environmental monitoring and health surveillance and adequate planning for the future medical workforce.

Introduction

The *Lancet* recently stated that 'Climate change is the biggest global health threat of the 21st century',[1] and with this in mind, it is particularly significant that 2016 was the warmest year on record – warmer than 2015, which was much warmer than 2014, which was warmer than all previous years in the modern global temperature record. The year 2016 was, of course, significant for many reasons, but is also of particular significance to this article; 21 and 22 November 2016 witnessed by far the most severe thunderstorm asthma[2] event ever recorded, overwhelming emergency services and hospitals in Melbourne, Australia, with an estimated 3365 more public hospital emergency department respiratory-related presentations than expected and as many as nine deaths.[3]

This review explores the implications of climate change for human health, particularly for allergens and allergic diseases, and how this might be managed in clinical practice. We first outline the nature of climate change, particularly those aspects of it most relevant to allergens and allergic diseases. This is followed by a brief overview of the impacts of climate change on human health. We then describe the impacts of climate change on allergens and allergic diseases, focusing on allergic respiratory diseases and food allergy. We then outline several responses to these health threats.

What is climate change?

While climate change is perhaps most commonly considered to involve warming of the climate, and this is

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indeed a fundamental aspect of it, climate change actually involves what is referred to as the climate system, a highly complex system consisting of the atmosphere, the hydrosphere (oceans, seas, rivers, fresh water lakes, underground water, *etc.*), the cryosphere (sea ice, snow cover, glaciers and ice sheets, frozen ground, *etc.*), the land surface and the biosphere (all living organisms). Human influence on the climate system is clear, and warming of the climate system is unequivocal.[4]

The largest driver of climate change is the increase in the atmospheric carbon dioxide (CO_2) concentration since the start of the Industrial Era around 1750. The annual mean atmospheric CO_2 concentration in 2016 was 404.21 ppm, measured at the Mauna Loa Observatory in Hawaii.[5] This is an increase of well over 100 ppm from the pre-industrial concentration of just 280 ppm. The increase in atmospheric CO_2 concentration from 1750 to the present has not been gradual, with two thirds of the increase occurring over just the last 50 years (since 1967). CO_2 is not the only greenhouse gas to have increased since 1750 due to human activity. The atmospheric concentrations of methane and nitrous oxide have also increased significantly, by about 150 and 20% respectively.[4]

These increases in greenhouse gases have resulted in an uptake of energy by the climate system, which has led to warming. The average temperature of the Earth's surface is about 14 °C and has increased by almost 1 °C over the past 100 years or so. Importantly, the extent of warming varies over the surface of the Earth, with some places warming less than this global average and others warming more. Projections of future climate change indicate that the global mean surface temperature will increase by a further 0.3–4.8 °C by the end of this century relative to the period 1986–2005, depending on the greenhouse gas emissions scenario. Again, these future temperature increases will vary spatially, with mean warming over land being higher than over the ocean.[4]

Many other aspects of climate have also changed and will continue to do so into the future. The changes in precipitation have been more complex than those in temperature, in that some regions have observed an increase in precipitation while some have observed a decrease in precipitation and yet others have experienced no change at all. Projections for the future indicate that the contrast in precipitation between wet and dry regions and between wet and dry seasons will increase.[4]

Climate change also involves changes in extreme weather and climate events. Hot days and nights will be warmer and/or more frequent, and heat waves will be more frequent and/or longer lasting over most land areas.[4] There will be increases in the frequency, intensity and/or amount of heavy precipitation in some regions.[4] There is also evidence that thunderstorms and intense tropical cyclone activity may increase into the future.

The impacts of these many and varied changes in climate have been observed for some time now. Glaciers are shrinking, Arctic sea ice is thinning, the sea level is rising and oceans are becoming more acidic as they absorb some of the excess CO_2 from the atmosphere. Many plant and animal species have shifted their geographic ranges, seasonal activities, migration patterns, abundances and species interactions in response to climate change.[6] Impacts are also occurring on what are referred to as human systems, of which human health is one. The following section outlines these impacts.

Health impacts of climate change

The health impacts of global climate change will be widespread and will have variable effects depending on geographic region, socioeconomic status of a population and pre-existing population vulnerabilities. There are many consequences, mostly negative, for public health, and these have been summarised in global terms by the World Health Organisation (WHO) as threats to safe drinking water, adequate shelter, stable food source and clean air.[7]

Threats to public health result from the major consequences of climate change:

- **a** increases in natural, weather-related disasters or major weather events that create havoc, with destruction of housing, dislocation of populations and threat of spreading disease;
- **b** changes in rainfall – in some areas excessive, leading to flooding, and in others a striking lack, resulting in prolonged drought and crop failure;
- **c** heat waves are associated with documented excess mortality.[1] Increasing heat will also have important impacts on air quality and pollutant levels, and these are particularly threatening to children, the elderly and those with cardiovascular and respiratory disorders;
- **d** warmer temperatures and increased CO_2 have impacts on allergens and allergic diseases, such as asthma and allergic rhinosinusitis. These will be among the most important climate change influences on human health and are the focus of the remainder of this article.

Aeroallergens and allergic diseases

A comprehensive review of the impacts of climate change on allergens and allergic diseases has been published recently.[8] Through the effects of key climate change factors, we expect significant changes in exposure patterns to plants, pollen and fungi. In addition,

Internal Medicine Journal **48** (2018) 129–134

complex interactions between pollutants, dust storm material, thunderstorm events and allergens may be expected to impact respiratory health negatively as well. Respiratory allergic diseases, such as asthma and allergic rhinoconjunctivitis, have become very prevalent in many parts of the world over the last few decades. Therefore, there is a very large population at risk of significant allergic disease with any increase in pollen exposure and allergenicity. Furthermore, pollen allergy is also implicated in certain forms of food-allergic disorders, so changes in pollen distribution and allergenicity may be expected to impact these conditions as well.

Clinical evidence of the importance of pollen exposure in causation of allergic respiratory diseases comes from a variety of approaches, ranging from exploring the patterns of sensitisation to various pollen allergens to examining correlations between the pollen count and asthma exacerbations, usually measured by hospital attendances or admissions.[9,10] Asthma exacerbations are an important parameter as they carry significant economic implications.

Pollen production and allergenicity

There is now compelling evidence that rising temperatures and CO_2 levels impact plant and pollen production. For many plants, rising CO_2 levels represent an increase in a vital resource, and they respond accordingly with increased growth and reproduction and greater pollen yields.[11,12] Singer *et al.*,[13] have shown that with increasing CO_2 levels, the major allergen from ragweed, Amb a 1, increases, although there is no change in total pollen protein level.

Ragweed, a native of North America, has been invading large areas of South America and Europe for the last few decades. It is a major cause of respiratory allergy. Hamaoui-Laguel *et al.*,[14] have used modelling frameworks that account for various factors under high-end and moderate climate and land-use change scenarios to predict airborne ragweed pollen concentrations in Europe in the future. Their modelling shows that, by 2050, airborne ragweed pollen concentrations will be about four times higher than they are now, almost certainly increasing the incidence and prevalence of ragweed allergy. Indeed, in subsequent work,[15] it has been found that sensitisation to ragweed will more than double in Europe, from 33 to 77 million people, by 2041–2060; that the greatest proportional increases will occur where sensitisation is uncommon (e.g. Germany, Poland, France) and that higher pollen concentrations and a longer pollen season may also increase the severity of symptoms.[15] While ragweed is not an important allergen in Australia at present, it has been introduced and is likely to spread and become a problem if effective eradication measures are not in place.

Pollen seasons

Phenology is the study of the influence of climate on periodic plant and animal life-cycle events. There are some long-term phenological records in many European countries, and these demonstrate measurable changes occurring in recent decades. Flowering is particularly sensitive to temperature over the preceding month. Fitter and Fitter[16] have demonstrated an average 4.5-day advancement in the first flowering date for nearly 400 British plant species over the 1990s compared with the previous four decades. Menzel[17] has examined data from a Europe-wide network, the International Phenological Gardens, and reports that the average annual growing season has lengthened by approximately 11 days since the 1960s.

In countries where there are long-term aerobiological survey data, it is possible to examine trends in airborne pollen and fungal spore counts. The trends are by no means uniform but vary with geographical location and plant type. Analysis of these data makes it possible not only to track changes in the pollen season but also to examine changing patterns in flowering phenology, one of the most valuable indicators of climate change impact.[18]

Ariano *et al.*,[19] had a unique opportunity to study variations in pollen levels and allergic sensitisation in Western Liguria, Italy, because of the existence of almost three decades of pollen monitoring and meteorological variable data and skin test and clinical data from residents in the region. They describe a progressive increase in the duration of the pollen season for *Parietaria* (+85 days), olive (+18 days) and cypress (+18 days). All pollen monitored, except for grasses, showed an increase in total counts. They report an increase in the percentages of patients sensitised to pollen over these years, whereas sensitisation rates to the house dust mite remained stable.

Consistent with the findings of Ariano *et al.*,[19] a 30-year (1982–2011) olive pollen record from Spain has shown a trend towards increasing pollen production, most likely caused by longer flowering periods as a result of higher temperatures.[20]

Fungal exposure and allergy

Fungi are a large and diverse group of eukaryotic organisms that have complex metabolisms, secreting numerous enzymes into their surroundings. Many of these are well-described allergens.[21] Other chemicals include ergosterol, which can be used as a measure of fungal biomass; constituents of cell walls, such as β-glucans that have been shown to cause respiratory symptoms, itching and fatigue in a dose-dependent manner and mycotoxins, which are low molecular weight organic compounds important in agriculture (e.g. aflatoxin). The role of the latter in producing human disease in domestic environments is far more contentious. Volatile fungal metabolites are responsible for the musty smell associated with fungal growth.[22]

Adverse health effects from fungal exposure can occur by a variety of mechanisms, including infection, allergy, irritation and toxicity, depending on the nature and dose of the exposure. Infection may be seen in normal and immune-compromised patients. Fungal components, such as β-glucan, may produce effects through activation of the innate immune system or through T cell and other mechanisms. Allergic sensitisation to fungi is an important risk factor for allergic asthma, and fungal exposure has been linked to asthma exacerbations and hospital presentations[23] as well as a described association with asthma mortality.[24] In addition to allergic rhinitis and asthma, fungal exposure has been linked to conditions like allergic broncho-pulmonary aspergillosis, hypersensitivity pneumonitis, allergic fungal sinusitis and atopic dermatitis.

Increased flooding in many areas of the world is seen as a consequence of climate change. Flooding leading to long-term dampness in residential dwellings promotes fungal growth. In the aftermath of Hurricane Katrina in New Orleans, USA, high indoor and outdoor fungal counts were noted.[25] Increased moisture along with higher temperatures and CO_2 levels encourage fungal growth.

Food allergy

Food allergy has become a very significant public health concern as 4–8% of children and 3–4% of adults in Westernised countries have a food allergy.[26,27] Aeroallergens, and sensitisation to them, are important in some expressions of food allergy.

IgE-mediated food allergy to common foods, such as cow's milk, egg, soy, nuts, wheat and seafood (known as Class 1 food allergens), may result from sensitisation through the gastrointestinal tract. A less well-recognised form of food allergy may occur as a result of primary sensitisation to homologous pollen allergens through the respiratory tract, causing reactivity to cross-reactive food allergens (Class II allergens).[18] Global differences in food sensitisation patterns have been particularly observed for these plant food allergens, whereby differences in allergenic plant distribution, agriculture and dietary patterns determine the predominant pattern of pollen and food allergy.[18] For instance, in Europe, prevalence of plant food allergy is significantly influenced by sensitisation to particular proteins in birch pollen, such as Bet v 1 and Bet v 2, while in the Mediterranean region, there is a higher sensitisation rate to profilins and non-specific lipid transfer proteins.[28] A recent study has shown differences in the pattern of allergen reactivity causing peanut sensitisation across different geographic regions, and these differences are largely determined by aeroallergen exposure.[29] Thus, it is likely that changes in climate that result in altered distribution of various allergenic plants may, in time, bring about a change in the pattern of food allergy, especially that caused by plant food allergens.[18] Furthermore, there is now limited experimental evidence that increasing CO_2 concentrations may directly alter the allergenicity of some plant-derived foods, with a recent study showing increased allergen concentration in peanut when grown under such conditions.[30]

Eosinophilic oesophagitis has become a commonly recognised condition in children with dysphagia, with antigen exposure being the driving force for the eosinophilic inflammation seen in this condition.[31] While food allergens are the obvious major allergens involved in this process, there are data to suggest that aeroallergen exposure is capable of triggering eosinophilic inflammation either because of the swallowed fraction or because of ingestion of foods cross-reacting with pollen allergens. The potential role of aeroallergens in provoking paediatric eosinophilic oesophagitis has recently been studied by Fahey *et al*.[32]

Response to climate change health threats

For years, a reduction in greenhouse gases has been central to our approach to managing the effects of climate change, and for the sake of planet and human health, these efforts must continue and grow much stronger. Immediate and sustained reduction of all pollutants, coal-burning technologies and transport-related pollution must be enabled. However, there are many indicators that the rising greenhouse gases have already brought about significant changes that must be addressed and managed. This realisation has shifted the focus from purely attempting to reduce greenhouse gases to one of managing the many aspects of health impacts caused by the changing climate. The WHO has made adaptation a critical component of the United Nations Framework Convention on Climate Change (UNFCCC), with particular emphasis on planning strategies for the developing world where the impact on population health will be the greatest.[33]

Internal Medicine Journal **48** (2018) 129–134

Central to endeavours for managing climate change and associated health impacts is the establishment of precise, ongoing measurements of all those parameters demonstrated to be important for their impacts on human health. For instance, in the case of aeroallergen impact on respiratory health, the studies on influences of climate change on plant growth and distribution, and pollen production, have come predominantly from the Northern Hemisphere. In Australia, until recently, there has been no systematic aerobiological monitoring. This is beginning to be addressed, with the establishment of a national pollen monitoring service within a partnership known as the AusPollen project.[34] Long-term, longitudinal studies to map allergenic pollen and fungi distribution are necessary to help understand the patterns of respiratory allergy and to plan for times of peak exposures and likely hospital presentations. The significance and importance of this have been noted very recently in the context of the November 2016 Melbourne thunderstorm asthma event.[35]

This paper has highlighted the important role of aeroallergens in driving inflammation in many allergic conditions, so the management of aeroallergen sensitisation and allergy will be an important aspect of planning specific mitigation strategies given the exposure increases we can expect with climate change. Although allergic conditions are some of the most common afflictions in medical practice, highly trained specialists in this field are few in number. Endeavours to upskill the general medical workforce in the recognition and management of allergic disorders will be an important component in any mitigation strategy. Immunotherapy, as a treatment strategy for those expressing the clinical consequences of inhalant allergy, has been in use for a century. Improvements in allergen characterisation, methods of delivery and length of treatment programmes will enhance its utility in addressing some of the morbidity produced by aeroallergen exposure.

Conclusion

The medical community has engaged in understanding and managing risks within the health arena for many decades. As such, all members of the medical community have roles to play in managing responses to climate change, from data collection and mitigation to adaptation. We need to be advocates for rapid and sustained reductions in greenhouse gas emissions, leading by example in institutions like hospitals. Alongside these efforts must be planning and adoption of strategies for adaptation to the inevitable climate change factors that so powerfully impact many facets of health.

Adaptation strategy must incorporate improved and effective monitoring of the many variables and consequences associated with climate change factors. This includes accurate measures of particulates and pollutants; precise records of infection transmission and vector populations and accurate, long-term aerobiological monitoring to map changing patterns of pollen and mould spore distribution.

Another vital aspect is appropriate forward planning for workforce diversity that will be required to manage specific challenges, some of which have been outlined in this paper. Finally, it is imperative that the more affluent communities assist those in developing countries to achieve these same goals as they are likely to bear the consequences of climate change to an even greater extent than those in affluent communities.

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