Clinical reviews in allergy and immunology

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Climate change and allergic disease

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Activity Objectives

1. To understand the links between global climate change and anticipated increases in prevalence and severity of asthma and related diseases.

2. To review the airway effects of various ambient air pollutants (including nitrogen oxides, ozone, particulate matter, and carbon or volatile organic compounds).

3. To understand how specific environmental triggers such as temperature cues, photo cues, or CO_2 levels affect pollen production and allergenicity.

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Climate change is potentially the largest global threat to human health ever encountered. The earth is warming, the warming is accelerating, and human actions are largely responsible. If current emissions and land use trends continue unchecked, the next generations will face more injury, disease, and death related to natural disasters and heat waves, higher rates of climate-related infections, and wide-spread malnutrition, as well as more allergic and air pollution–related morbidity and mortality. This review highlights links between global climate change and anticipated increases in prevalence and severity of asthma and related allergic disease mediated through worsening ambient air pollution and altered local and regional pollen production. The pattern of change will vary regionally depending on latitude, altitude, rainfall and storms, land-use patterns, urbanization, transportation, and energy production. The magnitude of climate change and related increases in allergic disease will be affected by how aggressively greenhouse gas mitigation strategies are pursued, but at best an average warming of 1 to 2°C is certain this century. Thus, anticipation of a higher allergic disease burden will affect clinical practice as well as public health planning. A number of practical primary and secondary prevention strategies are suggested at the end of the review to assist in meeting this unprecedented public health challenge. (J Allergy Clin Immunol 2008;122:443-53.)

Key words: *Climate change, global warming, pollen, air pollution, ozone, allergic rhinitis, asthma, mitigation, adaptation, prevention*

The burden of disease from asthma and allergies is significant. The World Health Organization estimates that globally 300 million people currently have asthma, and approximately a quarter of a million people die of asthma annually.[1] In the United States, 20 million people, 6.2 million children younger than 18 years and 13.8 million adults, have active asthma.[2] Respiratory allergies are even more prevalent, affecting the quality of life of many millions of individuals in the United States and worldwide,

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Abbreviations used
CAP: Criteria air pollutant
DEP: Diesel exhaust particle
EPA: Environmental Protection Agency
GHG: Greenhouse gas
NMVOC: Nonmethane volatile organic carbon
NOx: Nitrous oxides
PM: Particulate matter
IPCC: Intergovernmental Panel on Climate Change
VOC: Volatile organic compound

and often serving as triggers exacerbating asthma. In this clinical review, we explore the ways allergic disease and asthma may be affected by changes in the climate system. Our intent is not to produce a comprehensive review of the literature, but to begin with the conclusions drawn by the most recent reports from the Intergovernmental Panel on Climate Change (IPCC). These experts have extensively and systematically analyzed data from contemporary direct observations, the historical record, and paleoclimatologic studies; evaluated the quality of evidence from thousands of reports and data sets; discussed issues of uncertainty; and devised a systematic, weight-of-evidence approach that resulted in an international consensus attributing current climate change substantially to human activity and describing anticipated effects on human health and other biological systems.[3] We do not attempt to reproduce this effort, but begin from it, going on to highlight just 1 aspect of how climate change is likely to affect human health. We use a number of specific examples from the scientific peer-reviewed literature to illustrate our main points, but there are many other studies that could also be cited to make the same points. We hope that this review will raise awareness of the threat climate change poses to individuals with allergy and asthma and stimulate action on the part of health care providers to become involved in adaptation and mitigation strategies to help minimize the ultimate disease burden related to climate change.

EFFECT OF THE AMBIENT AIR QUALITY ON INCIDENCE, PREVALENCE, AND SEVERITY OF ASTHMA AND ALLERGIC DISEASE

Ambient air pollutants such as nitrogen dioxide (NO_2), ozone, particulate matter (PM), and components of PM including organic carbon and volatile organic compounds (VOCs) have been linked with increased allergic disease and asthma.[4-7] Studies from around the world have shown hospitalization for asthma increases after increases in levels of airborne PM.[8-14] Ozone exposure also exacerbates asthma, as shown in increased emergency department visits, hospitalizations, and rescue medication use.[4,15] Increased emergency department visits for children with asthma have been reported in Atlanta, Mexico City, and Los Angeles after exposures to ozone above 0.12 ppm ozone for 1 hour.[4,16-19] A 2003 report by Gent et al[20] involving 271 children in southern New England demonstrated that levels of ozone below 0.12 ppm, the 1-hour standard, and 0.085 ppm, then the 8-hour standard, were also associated with exacerbation of asthma. (In March 2008, the 8-hour ozone standard was revised downward to 0.075 ppm.) Ozone also demonstrates an adjuvant effect, because individuals exposed to ozone at levels of 0.16 to 0.25 ppm demonstrate an increased level of response to inhaled allergen.[21-24] Ozone exposure may also cause new-onset asthma. A study of a cohort of 3535 Southern California school children with no history of asthma revealed new asthma cases in 265 of these children over a period of 5 years that were linked to outdoor aerobic activity in areas with increased ozone levels.[6] In another study of a cohort of 3091 adult nonsmokers conducted over a period of 15 years, new diagnoses of asthma occurred in 3.2% of men and 4.3% of women, with increased annual ozone exposure a risk factor for increased asthma in the men.[25]

Gauderman et al[26] studied 1759 ten-year-old children from various Southern California cities through age 18 years and examined the effect of exposure to a number of products of vehicle fuel combustion (ozone, NO_2, acid vapor, PM <10 μm, PM <2.5 μm, and elemental carbon) on lung function. Of these, NO_2, acid vapor, PM <2.5 μm, and elemental carbon exposure were significantly correlated to diminished lung function. The percentage of children with a FEV_1 of <80% of the predicted value for age, height, and sex was 1.6% after low-level PM exposure to 5 $\mu g/m^3$ air, versus 7.9% of children exposed to more than 20 $\mu g/m^3$, a level of impairment similar to that found in children routinely exposed to secondhand tobacco smoke. NO_2 exposure is associated with chronic and acute changes in lung function, including bronchial neutrophilic infiltration, increased proinflammatory cytokine production, and enhanced response to inhaled allergens in subjects with asthma, both alone and when in the presence of sulfur dioxide.[27-35]

A British study[36] found that children admitted to the hospital for asthma were more likely to reside in a high–traffic exposure area (>24,000 vehicles/24 h at the nearest segment of main road) than those admitted to the hospital for nonrespiratory reasons ($P < .02$) or children without chronic disease ($P < .002$). There was a significant trend for traffic flow (vehicles/24 h) for those living <500 meters from a road ($P < .006$), but not beyond 500 meters. Children admitted for nonrespiratory reasons were more likely to be admitted than children from the community if they lived within 200 meters of a main road ($P < .02$). A German study[37] of a group of 7509 school children found that increased exposure to traffic correlated with active asthma, cough, and wheeze, and in children exposed to second-hand tobacco smoke, a positive allergen skin test. Measures of exposure to specific pollutants also correlated with cough, wheeze, and asthma in this study. A case-control study in Erie County, New York of children age 0 to 14 years (417 cases, 461 controls) indicated that exposure to high truck volume within a 200-meter distance was associated with increased risk for hospitalization because of asthma.[38] Diesel exhaust particles (DEP), an omnipresent type of traffic-related PM, contain varying amounts of polyaromatic hydrocarbons and are metabolized to quinones and other oxidant species, which cause pronounced airway inflammation.[39,40] In individuals with allergy, challenge studies have found an adjuvant effect of DEP exposure and pollen exposure.[41,42]

Taken together, these studies demonstrate that exposure to increased levels of ambient air pollutants and pollens exacerbate asthma and respiratory allergic responses, and some may be factors in developing disease.

CLIMATE CHANGE AND HUMAN HEALTH

According to the Fourth Assessment Report by the IPCC released in 2007, warming of the global climate system is unequivocal, and there is a >95% certainty that the cause is

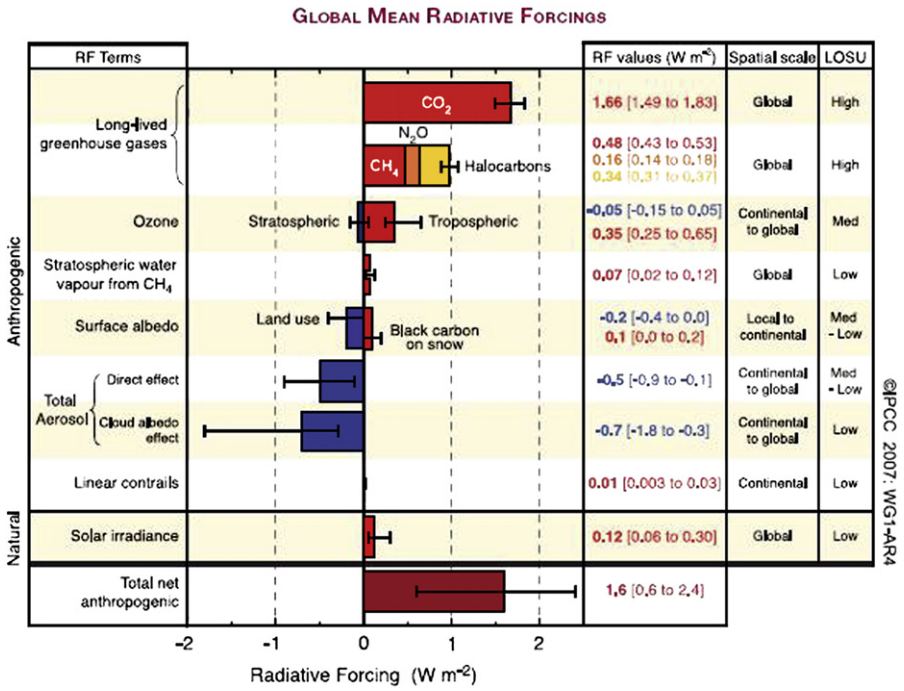

FIG 1. Average global radiative forcings *(RF)* in 2005 for anthropogenic carbon dioxide, methane, nitrous oxide, and other important agents and mechanisms, together with the typical geographical extent *(spatial scale)* of the forcings and the assessed level of scientific understanding *(LOSU)*.

extrinsic.[43] Human activities have a net warming effect (>90% confidence) that is dominated by greenhouse gas (GHG) emissions[44] (Fig 1). The most important GHG is carbon dioxide (CO_2) released by the burning of fossil fuels and to a lesser extent land use practices, followed by nitrous oxide and methane. Over the past 10 years, CO_2 emissions have accelerated globally, driving faster temperature rise. Because of the inertia in the climate system and the long residence time of CO_2 in the atmosphere, even if emissions were abruptly reduced to zero, global warming would continue throughout the 21st century and likely persist for hundreds of years.[44,45] Using climate models validated with paleoclimatologic evidence and historical data, the IPCC has developed a suite of future scenarios based on various levels of GHG mitigation, economic development, and population growth. Under the most ambitious reduction scenario, global temperatures are predicted to rise by 1.8°C (90% CI, 1.1-2.9) by 2099 compared with a 4.0°C (90% CI, 2.4-6.4) rise under "business-as-usual," the scenario that assumes current accelerating emissions and land use trends.[44] The rate and magnitude of anthropogenic GHG emissions are unprecedented in human history and may be pushing the climate system toward critical thresholds or "tipping points" at which a very small additional change can qualitatively and permanently (on the human time scale) alter the state of major earth systems (eg, altered ocean circulation, loss of Arctic summer sea-ice, exaggeration of El Nino–Southern Oscillation). Several independent analyses suggest that tipping points in some systems could occur with temperature increases of anywhere from +0.5 to +6°C, a range of change that is possible this century.[44,46,47] The impact of crossing a tipping point is unknown, but significant sea level rise, massive species extinctions, changes in storm and drought cycles, altered ocean circulation, and redistribution of vegetation including crops are all feasible.

Regardless of whether the world experiences gradual warming or abrupt change, human health will likely be affected adversely by accelerating climate change. Public health officials anticipate more injury, disease, and death related to natural disasters and heat waves; higher rates of food-borne, water-borne, and vector-borne infections; widespread malnutrition from drought and crop failure; and more air pollution–related morbidity and mortality.[48] Health effects will not be distributed uniformly but will vary according to geographic region, latitude, altitude, population characteristics, the built environment, level of development, and public health infrastructure.[44] Climate change–related increased burden of disease, specifically from allergy and asthma, is anticipated because of changes in the distribution, quantity, and quality of pollens, and changes in the timing and duration (lengthening) of pollen season. Asthma and allergic disease will also likely be worsened because of interaction between heavier pollen loads and increased air pollution; thunderstorms and extreme precipitation events; worsening heat-related ground-level ozone pollution; increased ambient air pollution from natural and anthropogenic sources; and air pollution related to wildfires. These are reviewed in the following sections.

POLLEN AND CLIMATE CHANGE

The correlation between climate and pollen distribution is well described. Investigation of abrupt climate change has used a number of techniques including ice core and sediment sampling for isotope shifts, pollen changes, and beetle and midge larval responses.[49,50] Vegetation changes have proven to be very sensitive indicators of climate change, easily showing responses within a century; and when transitional zones are examined, vegetational responses can occur within a decade of climate change.[49] Paleopalynology, the study of fossil pollens, spores, and algae, provides

information about how climate affects the distribution and variety of vegetation from the distant past to the most recent decades.[50-52] This has been shown in the North Atlantic fossil pollen record, with southern encroachment of boreal trees such as fir, larch, and alder with cooling, and replacement with oak and white pine with subsequent warming.[49] Records of aeroallergen sampling give insight into ongoing responses to changing conditions from the more immediate past into the present.[53,54]

Floristic zones define the type of native vegetation found in a region, and are in turn defined by several factors including high and low temperatures and average precipitation.[55] A major factor is the hardiness zone, which is characterized by the average annual minimum temperature. Recent shifts in global temperatures have resulted in migration of these zones northward, requiring a revision in 2006 of the US Department of Agriculture hardiness zone map for North America[56] (Fig 2). This demonstrates that current warming has already had an impact on the type of trees and other vegetation likely to survive and thrive at any latitude in a given region. In fact, the IPCC Fourth Assessment Report documents hundreds of studies on tens of thousands of data series that report statistically significant recent changes in climate sensitive traits of biological systems, 90% of which are consistent with warming.[57]

Bud set and flowering are intimately linked to accumulated warmth for many herbaceous and woody plants. Anthropogenic global warming, which includes both higher temperatures and higher ambient CO_2 levels, speeds flower development, resulting in earlier blooming. A 2002 study of 385 British plant species found that the average first flowering had advanced by 4.5 days during the previous decade.[58] One sixth of species had a marked advancement of 15 days, whereas 10 species (3%) had delayed flowering. Spring-flowering plants were the most affected and were sensitive to temperature in the preceding month. Entomophilous (insect-pollinated) plants were more affected than anemophilous (wind-pollinated) ones, although many anemophilous aeroallergenic pollens have demonstrated altered seasons. European pollen monitoring has shown increases over the past 30 years in hazel, birch, and grass counts in Switzerland and Denmark.[59-61] Birch anthesis (flower opening) across Europe is occurring earlier in London, Brussels, Zurich, and Vienna; has a variable onset in Turku; and is later in Kevo.[62] Observations from 1982 to 2001 show earlier onset of pollination of European olive in Spain.[63] The onset of olive flower opening and pollen release is expected to advance by 1 to 3 weeks over the coming century. Earlier flowering of oak (*Quercus*) associated with increased temperatures in the preflowering periods has been demonstrated over the past 50 years,[53] with higher oak pollen counts found in warmer Mediterranean sites. Assuming temperature increases associated with a doubling of CO_2 levels by the end of the 21st century, pollen season for oaks will start a month earlier, and concentrations will be 50% higher.[53] Similar trends have already been demonstrated, linking climate change with longer pollen seasons, greater exposure, and increased disease burden for late summer weeds such as *Artemisia* (mugwort) and *Ambrosia* (ragweed).[54,64]

Earlier-onset pollination with warmer temperature is not a universal finding. Japanese cedar counts in Japan from 1987 to 1998 showed a longer season because of increased pollination in the autumn, but no increase in count amplitude or earlier spring onset.[65] Boreal hardwoods require a fixed cumulative amount of chilling temperatures to break dormancy, followed by subsequent accumulation of heat to initiate flowering. Warmer winters may result in a delay in achieving the necessary length of chill.[66] These sorts of changes may result in later allergen exposures in some locations and under some circumstances.

There are several studies evaluating the effects of increased CO_2 and temperature on the allergenicity of plants. A 6-year study of the impact of increased CO_2 on poison ivy in loblolly pine stands showed increased photosynthesis, water use efficiency, and biomass.[67] In Addition, the CO_2-enriched plants produced a greater percentage of unsaturated urushiol, which is more antigenic. Other investigators have reported increased short ragweed (*Ambrosia artemisiifolia*) biomass and an increase in pollen production of 61% to 90% with increased ambient CO_2.[68,69] In an experiment manipulating both temperature and CO_2, increasing temperature to simulate early spring resulted in increased inflorescences and pollen production in earlier blooming ragweed compared with later blooming plants.[70] Increasing CO_2 also resulted in greater biomass and pollen production, but had a greater impact on later growing cohorts. Because content of the ragweed major allergen Amb a 1 will vary in plants from site to site and even from year to year at the same site, the question was raised whether increased pollen production necessarily implies an increase in airborne allergenic load.[71,72] This issue was addressed partially by a study of ragweed pollen along an urban transect, using the urban environment as a surrogate for climate change.[73] There was a gradient of both air temperature and CO_2 level through 4 sites: urban, suburban, semirural, and rural. The urban site averaged 2°C warmer and a 30% higher CO_2 level than the rural site. As expected, the urban ragweed grew faster with a greater above-ground biomass, flowered earlier, and produced more pollen than the rural site. Although there was an almost 2-fold greater concentration of Amb a 1 per microgram of protein in the rural versus the other sites, there was a greater than 7-fold increase in pollen production from the urban sites, supporting an increased airborne allergenic burden in the urban model for climate change.

There is now a wealth of evidence that climate change has had and will have further impact on a variety of allergenic plants.[74] Increased CO_2 increases plant biomass and pollen production. Increased temperature stimulates earlier flowering and longer pollen seasons for some plants. Increased ambient CO_2 may cause some plant products to become more allergenic. It is conceivable that increases in airborne pollen numbers will increase the efficiency of wind-borne pollination, thereby increasing propagation of such plants.[72] The extent to which these climate-related ecological changes are coupled with worsening air pollution will further add to the burden of allergic disease in exposed populations[75] (Table I). The expectation then is that there will be increasing amounts of robust allergenic plants and an increasing aeroallergen burden for patients with inhalant allergy.

CLIMATE CHANGE AND TROPOSPHERIC OZONE

Ground level ozone is created by a heat dependent photochemical oxidation of VOCs, nitrogen oxides (NOx), and atmospheric hydroxyl radicals. Higher temperatures favor greater ozone production even without increases in precursor molecules.[76,77] The most abundant atmospheric VOC is methane, but in suburban and urban areas, anthropogenic nonmethane VOC (NMVOC) compounds from combustion of fossil fuels including vehicle exhaust, industrial emissions, and chemical solvents are primary sources contributing to ozone production.[78] Apportionment studies of anthropogenic NMVOC have demonstrated that gasoline vehicle exhaust, liquid gasoline, and gasoline evaporation contribute 50%

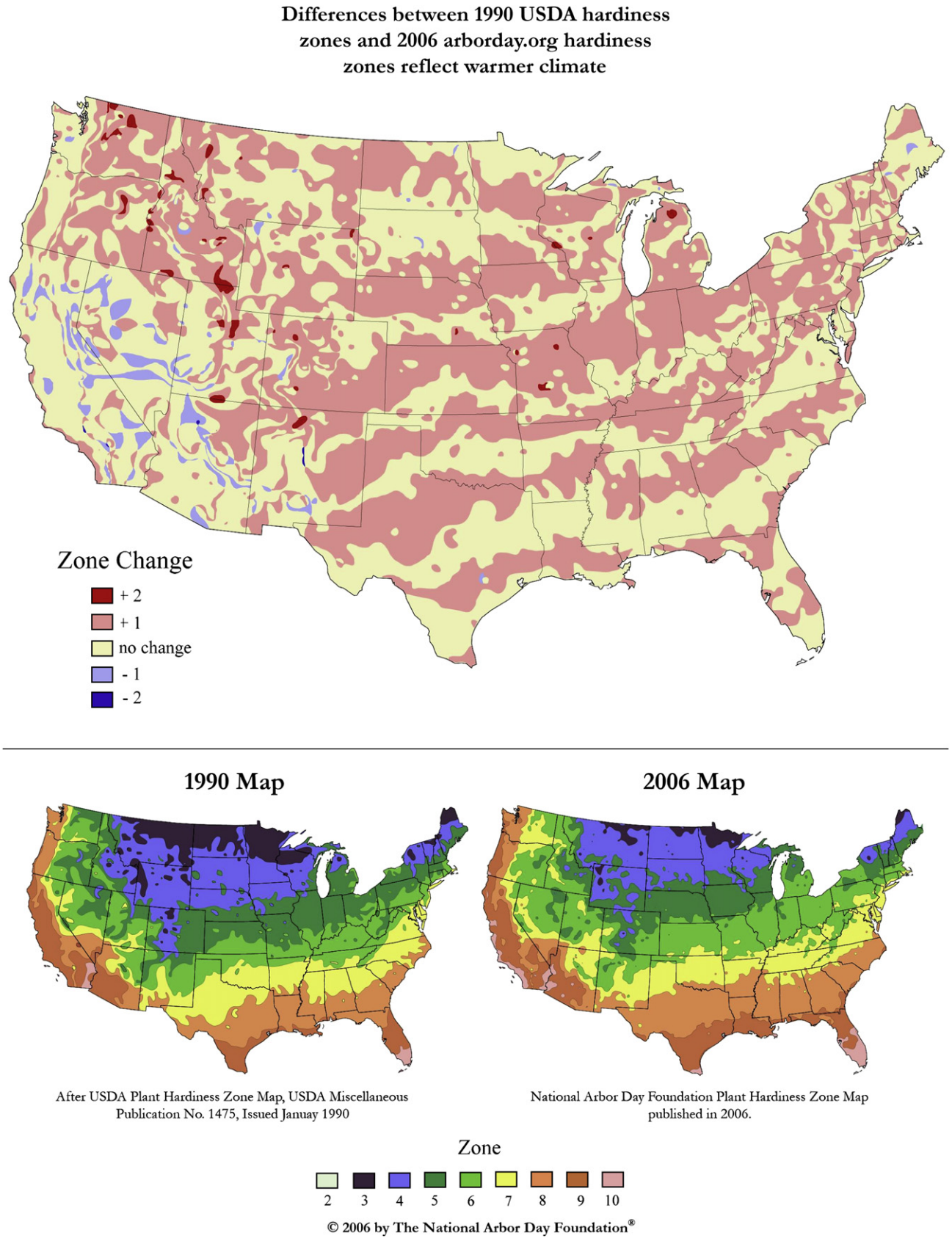

FIG 2. Changes in the United States Department of Agriculture (*USDA*) hardiness zones from 1990 to 2006 due to warming climate.

TABLE I. The rationale for the interrelationship between agents of air pollution and pollen allergens in inducing respiratory allergy

Air pollution can interact with pollen grains, leading to an increased release of antigens characterized by modified allergenicity.
Air pollution can interact with allergen-carrying paucimicronic particles derived from plants. The paucimicronic particles, pollen-originated or not, are able to reach peripheral airways with inhaled air, inducing asthma in sensitized subjects.
Air pollution—in particular ozone, PM, and sulfur dioxide—have been shown to have an inflammatory effect on the airways of susceptible subjects, causing increased permeability, easier penetration of pollen allergens in the mucus membranes, and easier interaction with cells of the immune system.
There is also evidence that predisposed subjects have increased airway reactivity induced by air pollution and increased bronchial responsiveness to inhaled pollen allergens.
Some components of air pollution seem to have an adjuvant immunologic effect on IgE synthesis in atopic subjects—in particular, DEPs, which can interact in atmosphere with pollens or paucimicronic particles.

From D'Amato GD, Cecchi L, Bonini S, Nunes C, Annesi-Maesano I, Behrendt H, et al. Allergenic pollen and pollen allergy in Europe. Allergy 2007;62:976-90.[75]

or more of total measured NMVOC.[79] Many types of trees produce biogenic VOCs, mostly in the form of isoprene, and during extended warm periods in heavily treed terrain, biogenic emissions of NMVOCs may dominate anthropogenic sources.[80] Biogenic NMVOCs react with atmospheric NOx and contribute to tropospheric ozone production.[81] Because of dependence on heat and sunlight, ozone levels are highest during summer, although some urban areas exhibit decreased seasonal variability.[82]

The urban heat island effect, a combination of anthropogenic and climatologic heat, can increase urban temperatures as much as 5°C compared with rural locations and further drive the formation of ozone.[83] Some recent studies are using the urban heat island as a model for the ecologic consequences of global warming.[73] Bell et al[84] modeled temperature-dependent ozone pollution to 2050 for 50 US cities assuming constant anthropogenic emissions and found a 2.1% (95% CI, 0.6-3.6) increase in asthma hospitalizations across all cities, with the largest city-specific effect of 4.7% (95% CI, 1.4-8.1) from ozone exposure alone. Most increases in ozone-related morbidity and mortality occurred in cities already experiencing excess ozone pollution. In the United States, at least 48% (144 million people) of the population lives in Environmental Protection Agency (EPA) ozone 8-hour nonattainment areas, and concentrations of ground level ozone are increasing in most regions of the world. (An area is designated as a nonattainment zone if the 3-year average of the annual fourth-highest daily maximum 8-hour average at every ozone monitor is greater than the level of the standard.)[85,86] Intercontinental and long-range continental transport of ozone has been documented,[87] and models suggest increasing emissions from Asia over the next 2 decades will measurably increase the monthly mean ozone concentration in North America.[88]

Given sustained growth in the size and population of urban areas worldwide, continued use of fossils fuels will lead to exposure of more people to higher levels of ozone in the future. Rural areas will experience an increase in ozone via long-range atmospheric transport of urban ozone, higher temperatures, biogenic VOC release, and agricultural fuel use. Future predictions of ozone production are most closely linked with levels of atmospheric NOx, which is increasing worldwide, and business-as-usual emissions are forecast to more than double from the current amounts by 2100.[89]

CLIMATE CHANGE AND AIR POLLUTION

As required by the 1970 Clean Air Act (CAA), the EPA identified 6 criteria air pollutants (CAPs) and set standards to protect human health and the environment. The 1990 amendments to the CAA defined 188 hazardous air pollutants, and the EPA has issued national emission standards for hazardous air pollutants to limit emissions from specific industrial sectors. Future ambient atmospheric concentration of CAPs and hazardous air pollutants are difficult to predict, but current worldwide trends suggest both continued reliance on and increased use of energy sources and industrial processes that produce these pollutants. Disease burden related to allergy and asthma, among other endpoints, will increase as these pollutants increase.

NOx is produced when nitrogen reacts with oxygen at high temperatures, usually from fuel burning. In the United States, motor vehicles account for nearly half of all NOx emissions.[90] Although NOx has an atmospheric lifetime of only hours to days, exposure is associated with chronic and acute changes in lung function, including bronchial neutrophilic infiltration, increased proinflammatory cytokine production, and, as mentioned, enhanced response to inhaled allergens.[27-35] The currently forecast business-as-usual levels of NOx emissions will lead to continued increases in ground level ozone, increases in levels of pulmonary proinflammatory mediators (both directly and through ozone production), and increased allergen sensitivity, especially in individuals with asthma.

More than 65% of sulfur oxides released to air in the United States comes from coal-burning electric utilities.[91] Inhalation of SO_2 has significant bronchospastic effects with rapid onset of symptoms after exposure. Most individuals with asthma will experience bronchospasm at levels of 0.5 ppm, and sensitive individuals can experience a decrease of FEV_1 as much as 60% at exposures of 0.25 ppm.[27-29] Epidemiologic studies have shown decreased lung function in children with increased ambient exposure to SO_2 and to SO_2 mixed with other CAPs.[92] Coal is the most abundant worldwide energy source, much of it with high sulfur content, and worldwide coal use under a business-as-usual scenario is projected to increase by 74% over current levels by 2030.[93] Coal burning is currently the second largest fuel source of CO_2 emissions worldwide and is projected to become the largest source by 2010. Thus, coal burning will contribute substantial amounts of atmospheric sulfur oxides well into the future, exacerbating human disease and forcing additional climate change.

Atmospheric PM sources are of both natural and anthropogenic origin, but in suburban and urban areas, diesel and fuel-burning vehicles are the major source.[94] PM can remained suspended in the atmosphere for long periods and can be transported thousands of miles before deposition.[95-97] Evidence for the health effects of PM is stronger than that for ozone, and multiple studies have demonstrated that increased exposure to PM worsens asthma and is associated with decreased lung function in both children and adults.[98-101]

Anthropogenic PM is a complex mixture of components around a carbonaceous core. Components include sulfates, VOCs (such as toluene and xylene), metals (iron, vanadium, nickel, copper, and

TABLE II. Examples of GHG-reducing strategies with health cobenefits

Mitigation strategy	Mechanism of GHG reduction	Health benefit
Increased active transport: bicycles and walking	Reduced personal automobile exhaust	More physical activity promotes cardiopulmonary health and fights obesity
		Cleaner air promotes cardiopulmonary health and reduces premature mortality
		Reduced traffic congestion reduces accidents
Use public transport	Reduces personal vehicle exhaust	As in rows above
		Promotes community interaction, reduces commuter stress, fights social isolation and depression
Eat fresh, locally grown, when possible organic, food	Reduced emissions from transport and processing	Improved nutrition with less loss of micronutrients in processing and storage, lower exposures to residual pesticides
	Reduced emissions from petroleum-based pesticides and nitrogen fertilizers	
Eat less beef and pork, more fruits, vegetables, and whole grains	Reduced methane production from ruminant stomachs, reduced emissions related to feeding, transport, slaughter, and processing	Heart-smart diet improves cardiopulmonary health
		Low saturated fat diet prevents colon cancer, fights obesity
Energy efficiency: turn it off at the power source when not in use, use energy-efficient lighting and appliances, optimize insulation	Reduced electricity use decreases emissions from coal-fired power plants	Cleaner air promotes cardiopulmonary health and reduces premature mortality
		Saved money can be used for medicines, fresher, organic foods, stress reduction activities that promote health

zinc), polyaromatic hydrocarbons, pollen, and endotoxin.[102-104] Industrial point sources of PM have been demonstrated to induce airway inflammation, with an influx of neutrophils, monocytes, and inflammatory mediators.[105,106] DEPs cause pronounced airway inflammation.[39,40] DEP exposure studies have demonstrated increased nonspecific airway reactivity, increased bronchial neutrophil and B-lymphocyte infiltration, and increased nasal production of IgE with enhanced allergen response in sensitive individuals.[41,42] This adjuvant effect of DEPs, coupled with increased pollen production of ragweed in atmospheric conditions of increased temperature and CO_2, preference of ragweed for disrupted soils such as occur in suburban and urban areas, and increased DEP and ozone production in suburban and urban areas will create significant future risk of asthma exacerbations and allergic response among populations living in these areas.

CLIMATE CHANGE, STORMS, AND WILDFIRES

In addition to pollen redistribution, the changing climate will very likely lead to increased drought, heat waves, and wildfires in some regions, and increased storms and extreme precipitation events in other regions.[57] These changing regional patterns may exacerbate allergic disease and asthma.

Areas of the world experiencing increased heat and drought will likely experience more wildfires. In addition to the direct loss of life, geographic displacement, disruption of social networks, and economic loss, wildfire smoke contains a complex mixture of carcinogenic and respiratory irritant substances. Wildfire smoke produces large amounts CO, CO_2, NOx, ozone, PM, and VOCs.[107-109] Wildfires that impinge on human settlements contain residues of plastics, pesticides, herbicides, and fungicides in smoke.[110] Smoke plumes can travel thousand of meters upwards in the atmosphere: smoke from 1998 wildfires in Mexico and South America was visible in Florida and North Dakota.[111,112] Population-level epidemiologic studies have shown modest short-term increases in cardiorespiratory hospitalizations caused by acute exposure to wildfire smoke.[113-115] Seasonal forest fire fighters 24 hours after exposure to wildfire smoke show a statistically significant increases in inflammatory mediators (serum white blood cells, band cells, IL-6, and IL-8).[116]

The IPCC 2007 considers it very likely that heavy precipitation events will increase in most areas, and an increase in tropical cyclones is likely globally.[57] In areas where climate change causes thunderstorms and extreme precipitation events during pollen season, there is reason to expect that there will be worsening asthma caused by an increased airborne burden of respirable allergen-laden particles released from fragmented pollen grains.[117-119]

Conclusion

Global climate change is now measurably affecting many physical and biological systems that are critical to human health.[57] Effects pertinent to allergic disease and asthma are changes in the distribution, quantity, and quality of aeroallergens; increased ground-level ozone pollution, and further deterioration in air quality. Both individuals with allergy and asthma are at risk of worsening disease, more symptomatic days, and reduced quality of life as a result of these environmental changes.[64] Further, some data suggest that the incidence of allergic disease and asthma could increase with increased environmental exposures

driven by climate change. The magnitude of the increased disease burden is directly linked to the magnitude of climate change, although additional factors are also at play. Continued warming of the climate system is certain because of the long residence time of GHG already released into the atmosphere and the slow equilibration time of the oceans and terrestrial systems, but the magnitude and rate of warming is still modifiable.[45-47] For clinicians caring for atopic patients and patients with asthma, this means that both adaptation to disease linked to inevitable climate change (secondary prevention) and mitigation of the drivers that will worsen climate change (primary prevention) are important strategies to employ to minimize disease burden.

There are a number of readily available adaptation strategies that should improve quality of life for individuals at risk for asthma and allergies. In addition to optimization of medical management, clinicians should provide guidance and education on how to locate and interpret daily air quality indices[120] and pollen counts.[121] Additional education on the synergies of mixed exposures including CAPs, pollens, weather, storms, and fires will further assist patients to understand how to minimize exposures and symptoms. Improved public health tracking of asthma and allergic disease will help public health officials understand how these illnesses are changing as climate changes and develop appropriate responses. The health sector should work with community and regional planners to design and protect landscapes that are least likely to produce large quantities of aeroallergens within the context of anticipated changes in the local and regional ecology because of accelerating climate change. Similarly, health professionals must become involved in development of local, state, and federal air pollution prevention laws and regulations to ensure that adequate health protective standards are codified and then enforced. Examples of health protective measures include enacting a transition to clean diesel buses, anti-idling laws for buses and cars, and more stringent controls on power plant emissions.

There is an even greater need for the medical sector to become fully engaged in the development and dissemination of effective GHG mitigation strategies (primary prevention) as part of the public health agenda for the 21st century. The Director General of the World Health Organization states unambiguously that "climate change will affect, in profoundly adverse ways, some of the most fundamental determinants of health: food, air, water. In the face of this challenge, we need champions throughout the world who will work to put protecting human health at the centre of the climate change agenda."[122] Successful stabilization of the climate before exceeding tipping points with unknown and potentially catastrophic consequences is the responsibility of the current generation of adults who, through action or inaction, will determine the future for generations to come. Fortunately, many of the most readily available mitigation strategies have immediate health benefits and are actions that correlate well with health promotion and primary prevention. The story of the dramatic reductions in hospitalizations and emergency department visits for asthma during the Atlanta Olympics is 1 example of rapid improvement of air quality with immediate health benefits from systematic reduction in automobile use.[17] Table II lists a number of other win-win scenarios. Although such actions alone will not be enough to stabilize the climate, they need to be implemented immediately to begin the process and help to set the stage for further innovation and technical solutions to the climate change challenge.

We hope that this review stimulates health care providers to provide quality care for patients with allergy and asthma confronting new threats from climate change, as well as to work toward mitigation of the drivers of climate change at the individual, community, and policy levels as part of a long-term commitment to protecting public health.

What do we know?

- **Ambient air pollution increases the frequency and severity of asthma attacks and the number of symptomatic days.**
- **Pollen, air pollution, and weather interact and affect the clinical expression of allergic disease.**
- **Climate change is unequivocal, accelerating, and largely anthropogenic, and will continue through at least the 21st century.**
- **Climate change is measurably affecting the timing, distribution, quantity, and quality of aeroallergens and changing the distribution and severity of allergic disease.**
- **Climate change alters local weather patterns including minimum and maximum temperature, precipitation, and storms, all of which affect the burden of allergic disease.**
- **Warming temperatures promote production of ground-level ozone, which worsens asthma.**
- **There are clinical interventions that can be used to minimize climate change–related increases in asthma and allergic disease (secondary prevention).**
- **Greenhouse gas mitigation is the current global recommendation for stabilizing the climate (primary prevention).**

What is still unknown?

- **Future air quality will be determined by energy and transportation choices, economic development, and population growth.**
- **The degree to which human intervention and planning can minimize changes in vegetation and aeroallergen exposure remains unexplored.**
- **The rate and magnitude of climate change in the future will depend on how rapidly and successfully global mitigation and adaptation strategies are deployed.**
- **The outcome of crossing climate tipping points is unknown but potentially very grave for large portions of the global population.**
- **New technologies addressing climate change and air pollution as well as new medical treatments for asthma and/or allergic disease could alter current predictions and trends.**

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