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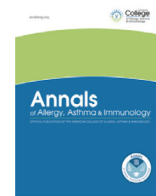

CME Review

Factors by which global warming worsens allergic disease

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Key Messages

- The prevalence of allergic diseases including asthma, allergic rhinitis, atopic dermatitis, and food allergy have continued to rise for more than 50 years.
- Climate change and global warming have been implicated in the recent increase in the prevalence and severity of allergic disease and further increases are expected.
- Pollutants, such as particulate matter, pollen, ozone, and heavy metals have varying adverse effects on human health, affecting the respiratory tract, epithelial barriers, and the immune system leading to increases in allergy and asthma.
- The number, frequency, and severity of climate change events, such as wildfires, and sand and dust storms have increased with global warming. These events increase pollutant levels and adversely impact allergic disease.
- Biodiversity (including microbiome diversity) and access to green space have an important role in promoting gut and lung health and preventing allergy, asthma, and allergic disease.
- Physicians play an important and critical role in communicating the implications of climate change on patient health outcomes and need to be key advocates for mitigation and adoption measures to combat climate change.

A R T I C L E I N F O

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A B S T R A C T

Increased use of fossil fuels has led to global warming with concomitant increases in the severity and frequency of extreme weather events such as wildfires and sand and dust storms. These changes have led to increases in air pollutants such as particulate matter and greenhouse gases. Global warming is also associated with increases in pollen season length and pollen concentration. Particulate matter, greenhouse gases, and pollen synergistically increase the incidence and severity of allergic diseases. Other indirect factors such as droughts, flooding, thunderstorms, heat waves, water pollution, human migration, deforestation, loss of green space, and decreasing biodiversity (including microbial diversity) also affect the incidence and severity of allergic disease.
Global warming and extreme weather events are expected to increase in the coming decades, and further increases in allergic diseases are expected, exacerbating the already high health care burden associated with these diseases. There is an urgent need to mitigate and adapt to the effects of climate change to improve human health. Human health and planetary health are connected and the concept of One Health, which is an integrated, unifying approach to balance and optimize the health of people, animals, and the environment needs to be emphasized. Clinicians are trusted members of the community, and they need to take a strong leadership role in educating patients on climate change and its adverse effects on human health. They also need to advocate for policy changes that decrease the use of fossil fuels and increase biodiversity and green space to enable a healthier and more sustainable future.

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Introduction

Allergic diseases have continued to increase in prevalence during the past 50 years with sensitization rates to 1 or more common allergens for school-aged children approaching 40% to 50%.[1,2] A study by the US Centers for Disease Control and Prevention found that

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Overall Purpose

Participants will be able to demonstrate increased knowledge of the clinical treatment of allergy/asthma/immunology and be able to apply new information to their own practices.

Learning Objectives

At the conclusion of this activity, participants should be able to:

- Specify the environmental factors influenced by climate change and how they impact prevalence of allergy, asthma, and other allergic diseases.
- Summarize the important role physicians play in understanding and addressing the impact of climate change on patients' health outcomes, specifically allergy and asthma.

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Target Audience

Physicians involved in providing patient care in the field of allergy/asthma/immunology.

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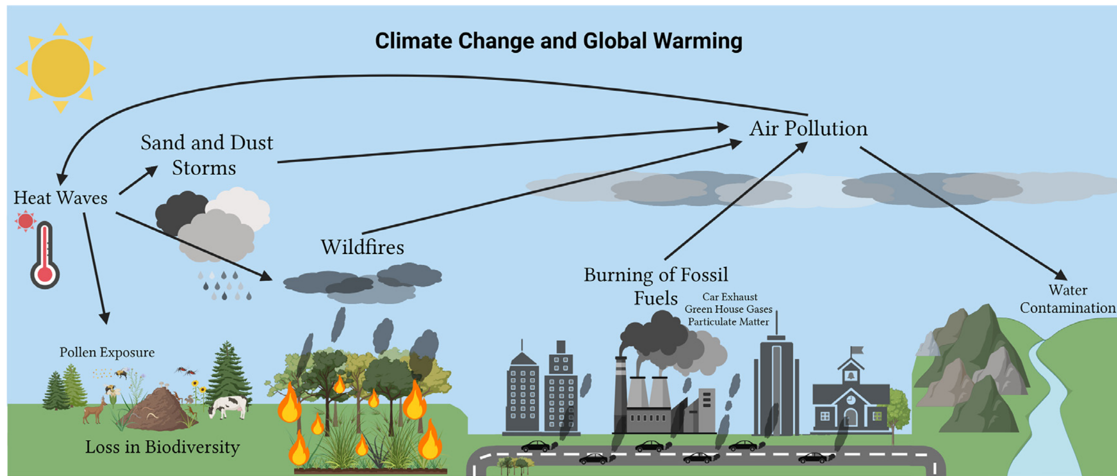

Figure 1. Factors contributing to an increase in air pollution and its effect on the environment. One-way arrows indicate a causal relationship. Created with BioRender.com.

between 1997 and 2011, food allergy (FA) among children (0-17 years old) increased from 3.4% to 5.1% and skin allergies increased from 7.4% to 12.5%.[3] More recently, it has been estimated that 8% of children and 11% of adults have FA.[4] In addition, allergic rhinitis (AR) and atopic dermatitis (AD) are estimated to affect approximately 29.4% and 26.1% of adults globally.[5] According to the Centers for Disease Control and Prevention the prevalence of asthma is 5.8% in children and 8.4% in adults.[6] Allergic diseases affect millions of people worldwide and pose a huge global health and socioeconomic burden.[7]

Air pollution caused by global warming and climate change events is implicated in the increasing prevalence and severity of allergic diseases.[8] Anthropogenic use of fossil fuels has increased global temperatures and air pollution through the emission of heat-trapping greenhouse gases (GHGs) such as carbon dioxide (CO_2), methane (CH_4), nitrous oxide (N_2O), ozone (O_3), and fluorinated gases.[9] The Intergovernmental Panel on Climate Change has reported that global warming is now approximately 1°C higher than preindustrial times and is continuing to increase.[10] Global warming has increased the frequency and intensity of wildfires and sand and dust storms (SDS) leading to further increases in air pollutants, primarily in the form of particulate matter (PM). Pollen is also an air pollutant of concern for allergic diseases. There is now evidence that pollen season length and pollen concentration are increased with global warming and increased levels of GHGs.[11] Other indirect factors that adversely affect allergic diseases include droughts, flooding, thunderstorms, heat waves, water pollution, human migration, deforestation, and decreasing biodiversity.

The increasing prevalence of allergic diseases is a cause for concern. They pose a significant health burden, both in direct and indirect health care costs. They are often chronic, needing long-term treatment. Furthermore, epidemiologic studies have shown that individuals who develop one atopic condition are more likely to develop other atopic diseases over time. Individuals often develop AD in early infancy or childhood and later develop food allergies, AR, and asthma.[12] This phenomenon has been termed the allergic or atopic march.[13] In the United States, the direct costs of treating asthma were estimated to be 57.9 billion dollars[7]; between 252 and 314 million dollars for AD,[7] greater than 4.6 billion for AR,[14] and 24.8 billion for childhood FA.[15] Indirect costs include absenteeism, presentism, and a lower quality of life.[7]

Here, we review the climate change events and environmental and other factors that directly and indirectly impact allergic diseases. We also explore One Health, which is an integrated, unifying approach to balance and optimize the health of people, animals, and the environment.[16,17] As trusted members of the community, clinicians should take a lead role in educating their patients and advocating for policies to better adapt and mitigate the effects of climate change to reduce the incidence and prevalence of allergic disease and enable a healthier and more sustainable future.[18]

Climate Change Events and Associated Factors Affecting Prevalence of Allergic Diseases

Although genetics has been found to play a role in the etiology of allergic diseases, the rate of increase in allergic diseases is too rapid to be explained by genetics alone. Epidemiologic studies suggest that environmental and lifestyle factors aid in the development and exacerbation of these diseases. The main factors that have been implicated in the global increases in allergic diseases include the following: (1) changes in lifestyle (increased hygiene and decreased exposure to biodiverse plants, animals, and microbes) leading to decreases in the development of immune tolerance and increases in microbial dysbiosis; and (2) increased exposure to environmental pollutants leading to epithelial barrier disruption and immune dysregulation. These include both natural and synthetic pollutants. Natural air pollutants include GHGs, PM, pollen, and mold, which have increased with climate change events such as wildfires, SDS, thunderstorms, and flooding (Fig 1). A recent study of chemical inventories from around the world found that around 350,000 chemicals and mixtures of chemicals are registered for production and use.[19] In addition, secondary effects such as water pollution and migration because of climate change also affect allergic diseases.

Air Pollution

Air pollution, both indoor and outdoor, increases the risk, and severity of allergic diseases. The World Health Organization (WHO) estimates that 99% of the global population lives in areas with air that exceeds the WHO guideline limits for air pollutants, especially in low-, and middle-income communities.[20] Many studies, including meta-analyses, have found associations between air pollutants and atopic diseases[21] such as asthma,[22–28] AD,[29–31] FA,[32] and AR.[33–35]

Indoor air pollution sources include open fires or stoves for cooking fueled by biomass or coal, tobacco smoke, and consumer products such as cleaning supplies. Pollutants found in indoor air pollution include PM, various chemicals (including volatile organic compounds from cleaning supplies and building materials), and allergens (from pet and insect dander and molds).[36] Outdoor pollution sources include industrial and vehicular emissions (GHGs, PM, and other toxins) and from wildfires and SDS. Another natural source of air pollutants that affect allergic diseases is pollen, which is affected by

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increasing heat, CO_2 levels, and climate events such as thunderstorms. Air pollutants are thought to increase the risk for and exacerbate respiratory disease by 4 main mechanisms: oxidative stress and epithelial damage, airway remodeling, inflammatory pathways and immunologic responses, and enhancement of respiratory sensitization.[37] In AD, air pollutants have been found to cause epidermal injury[38] leading to water loss and changes in microflora.[39]

Particulate Matter

Particulate matter is a major air pollutant that adversely affects allergic disease. Particulate matter concentrations tend to be higher in winter months because of increased car traffic and domestic heating.[40] A meta-analysis of 35 studies across 12 countries (453,470 participants) found a positive association between air pollution and the prevalence of AR.[41] Particulate matter consists of a mixture of solid particles and liquid droplets with varying chemical composition depending on the source. Those that are smaller than 10 microns (PM_{10}) can enter the lungs, which, on deposition on the lung surface, can induce tissue damage and lung inflammation. Those that are smaller than 2.5 microns ($PM_{2.5}$) are considered the most harmful because of their ability to travel deep into the bronchioles and alveoli of the lungs and enter the bloodstream.[42,43] A systematic review and meta-analysis found that the odds ratio associated with a 10 $\mu g/m^3$ increase in exposure to PM_{10} and $PM_{2.5}$ and risk of AR was 1.13 and 1.12, respectively.[41] In another meta-analysis and systematic review, increased longitudinal childhood exposure to $PM_{2.5}$ was associated with an increasing risk of subsequent asthma in childhood with an odds ratio of 1.14.[44] In response to the health risks associated with PM exposure, the WHO changed its guidelines for $PM_{2.5}$ from 10 $\mu g/m^3$ to 5 $\mu g/m^3$.[45]

Pollen

Climate change and global warming are increasing pollen concentrations. Pollen season varies depending on the source. For example, tree pollen is more common in the spring whereas weed pollen is more common in the fall.[46] Climate change in North America has been estimated to contribute to approximately 50% of the lengthening pollen season.[47] Studies have found that pollen concentrations are on the rise and are estimated to increase by 200% by the end of the century.[48] Higher temperatures and elevated CO_2 levels stimulate photosynthesis, plant growth, and pollen production.[48,49] Furthermore, pollen season is starting earlier and lasting longer, exacerbating the problem.[48,50] The increases in pollen concentration have significant consequences for public health outcomes, especially for atopic diseases such as allergy and asthma. A systemic review and meta-analysis found a statistically significant increase in the number of asthma emergency department visits with increases of 10 grass pollen grains per cubic meter of exposure.[51] Pollen exposure is associated with increased rates of asthma and allergies, specifically AR.[48] It is estimated that 30% of people globally have been affected by AR, with the prevalence projected to increase in the coming years.[52]

Ozone

Ozone is a major constituent of smog and is formed when volatile organic compounds and oxides of nitrogen react in sunlight. Ozone is more readily formed in warmer climates and, thus, tends to be higher during the summer months.[53] Ground-level O_3 is a GHG and a potent oxidant. It is one of the 6 criteria air pollutants established by the US Environmental Protection Agency. In the United States, the current National Ambient Air Quality Standard for O_3 is 70 parts per billion (8-hour maximum within a day).[54] In the United States, in 2016, 90% of noncompliance to the National Ambient Air Quality Standard was because of O_3.[55]

The Global Burden of Disease estimated that in 2019, 365,000 people died from exposure to ambient O_3 pollution.[56] Ambient O_3 has been linked to respiratory tract irritation, inflammation, oxidative stress, decreased function, and increased epithelial barrier permeability. Using crowd-sourced allergy symptom data in addition to pollen, weather, and air quality data, a study found that O_3 affects symptom severity of pollen allergy.[57] It is thought to cause an inflammatory cascade in the airways through an increase in proinflammatory mediators, chemokines, and neutrophils.[58] A study used national and regional emergency department visit rates among people with asthma using published survey data and estimated that in 2015, 9 to 23 million (8%-20% of total) asthma-related emergency department visits globally were attributable to O_3.[59] A systematic review found that increases in long-term exposure to O_3 exposure in children were associated with a decrease in forced expiratory volume in 1 second.[60]

Water Pollution

Since the start of the Industrial Revolution, many potentially harmful metals, such as cadmium, chromium, copper, nickel, zinc, lead, and mercury have been introduced into our waterways.[61,62] A study that analyzed how climate change affects the transport of heavy metals, found enhanced cadmium and zinc contamination in lowland catchments (groundwater) in the Netherlands because of enhanced runoff and accelerated leaching.[61] In some areas, heavy metals such as arsenic and cadmium are found in drinking water,[63–65] which can cause adverse effects on the epithelial barrier and immune function. A study found that maternal arsenic and cadmium exposure was associated with alterations in the T-cell population in the cord blood of infants, suggesting these exposures might contribute to the altered immune function of infants.[66] Another study has found that exposure to arsenic is associated with high levels of T helper 2 cells mediators, interleukin (IL)-4, IL-6, and IL-13, which in turn results in increased susceptibility to allergic asthma.[67]

Detergents, allergens, and other pollutants have also been found to have adverse effects on the immune system by disrupting the epithelium barrier and promoting inflammation. This has been termed the epithelial barrier hypothesis.[38,68] Multiple studies have been published linking detergents to disrupted epithelium barriers.[69–71] A study found that laundry detergents, even at a very high dilution (1:25,000) exhibit significant cell toxicity by disrupting the barrier integrity of human bronchial epithelial cells.[69] Detergents have been reported to disrupt epithelial barrier integrity through their effects on tight junction or adhesion molecules and promote inflammation through epithelial alarmin release.[72] Epithelial barrier dysfunction and increased permeability can trigger an immune response and contribute to the development of allergies and other immune-related disorders.[73]

Climate Change Events

As the number, frequency, and severity of climatic events have increased with climate change, they adversely impact human health, including allergies, and asthma. Some of the major climate change events that impact allergies are wildfires, sand, and dust storms, thunderstorms, heat waves, and flooding. These are discussed below.

Wildfires

Wildfires have become more frequent and severe with global warming, releasing large amounts of PM, O_3, and carbon monoxide.[74,75] Although summer months have historically been considered wildfire season, global warming is causing wildfires to be a year-round problem. In California, after the onset of a wildfire in 2020, $PM_{2.5}$, O_3, and carbon monoxide concentrations increased by

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approximately 220%, 20%, and 151%, respectively.[76] By increasing GHGs, wildfires accelerate climate change leading to a positive feedback loop.[77] Wildfire smoke has been associated with increased rates of asthma[78] and increased levels of proinflammatory markers such as C-reactive protein and IL-1B, which can worsen asthma and allergy symptoms.[79] A study by Aguilera et al[80] found that $PM_{2.5}$ emissions from wildfire smoke were approximately 10 times more harmful to children's respiratory health than $PM_{2.5}$ emissions from vehicles, particularly for children aged 0 to 5 years. After the 2016 Fort McMurray fire in Alberta, Canada, there was an increase in asthma consultations among firefighters involved in fighting the fire. The forced expiratory volume in 1 second and forced vital capacity were positively associated with increasing exposure. A fifth of the firefighters also had a positive methacholine challenge test and bronchial wall thickening.[81] These findings highlight the need for measures to prevent wildfires and protect individuals from their harmful effects.

Sand and Dust Storms

Sand and dust storms have become more frequent and severe in recent years because of increased temperatures, droughts, and deforestation.[82] According to a report by the United Nations, approximately 2 billion tons of dust are emitted into the atmosphere each year, with the Asia-Pacific region contributing 27% of those emissions.[83] Studies have found that SDS can exacerbate air pollution levels, including higher levels of PM, CO_2, and O_3.[84] In addition, SDS is known to include pathogens and microorganisms such as bacteria, fungi, and spores.[85] Research has found how particles in dust storms can travel long distances leading to respiratory infections, asthma, and allergies.[86] For example, in California, an increase in Coccidiomycosis infection, caused by the fungi *Coccidioides immitis*, was associated with dust exposure and dust storms.[87] A study reported that over a 5-year period, on days with dust storms, same-day asthma, and respiratory admission at hospitals increased significantly.[88]

Thunderstorms and Flooding

Thunderstorm asthma (TA) refers to observed increases in asthma incidence after the occurrence of thunderstorms when pollen counts are high, generally in late spring, and early summer.[89] Thunderstorm asthma can result in significant morbidity and mortality.[90] For example, on November 21, 2016, Melbourne, Australia experienced a catastrophic epidemic of TA. Grass pollen concentrations were extremely high (>100 grains/m^3) and within 30 hours, there was a 672% increase in respiratory issues at the emergency department and a 992% increase in asthma-related admissions compared with the past 3 years. This incident resulted in the death of 10 individuals.[91] During thunderstorms, the high humidity causes pollen grains to rupture into subpollen allergenic particles by osmotic shock resulting in each grain releasing hundreds of small (<5 μm) allergenic granules, which are capable of reaching the lower airways.[92]

Flooding is also associated with increased asthma and other respiratory systems. After major floods, there is a proliferation of mold spores because of increased dampness exposing residents to indoor aeroallergen exposure.[92,93] In the aftermath of hurricane Harvey, flood-exposed individuals were at increased risk of upper respiratory tract allergic symptoms with exposures to dirty water and mold associated with increased risk of multiple allergic symptoms.[94]

Extreme Temperatures

Heat waves are becoming more frequent and severe because of climate change, with many regions experiencing record-breaking temperatures. Extreme temperatures and heat waves are defined as persistent periods of ambient temperature higher than the average.[95,96] The National Weather Service published a heat index chart categorizing heat ranges as "caution", "extreme caution", "danger," and "extreme danger."[97] For example, any temperature above 105°F (41°C) is considered dangerous to human health. According to the US Environmental Protection Agency, heat waves have increased in frequency, duration, and intensity.[98] Studies suggest that exposure to extreme temperatures may be a risk for asthma. A meta-analysis of 111 studies found that the pooled relative risk for asthma attacks in extreme heat was 1.07.[99] Analysis of data from asthma hospital visits at all medical facilities in Shenzhen, People's Republic of China between 2016 and 2020 found that during extreme temperature events, the cumulative relative risk of asthma during heat waves compared with other days was 1.06.[100] Furthermore, a study by Jin et al[101] found strong evidence that temperature-related hospitalization risk increased with PM level, with the effects of $PM_{2.5}$ being stronger than that of PM_{10}.

Biodiversity and Green Space

The biodiversity hypothesis suggests that contact with natural and biodiverse environments enriches the human microbiome, promotes immune balance, and protects from allergic disease.[102] Human activities such as deforestation and urbanization have led to habitat and biodiversity loss with significant impacts on the functioning of the ecosystem and human health. Since 1970, it is estimated that within wildlife populations there has been a 69% decrease in biodiversity.[103] One study found that climate change has led to a reduction in microbial diversity in grassland soil. The researchers analyzed soil samples and found that experimental warming decreased the richness of bacteria by 9.6%, fungi by 14.5%, and protists by 7.5%.[104] Increased hygiene, more time spent indoors, and decreased exposure to green space and to farm animals and pets have been found to have adverse effects on immune health and increased risk of atopic diseases including allergy and inflammatory disorders.[102]

Studies have linked a decrease in the gut microbiome to allergic, inflammatory, and autoimmune diseases. Particularly for infants, research highlights how the gut microbiome plays an important role in the development of FA.[105] For example, a study found that higher microbial diversity at 3 months of age was associated with a resolution of milk allergy by age 8.[106] Another study found that lower microbial richness and imbalances in specific gut bacteria were significantly associated with atopic sensitization.[107] In addition, research has found that individuals with allergies have significantly lower fecal microbial richness.[108] A recent case study found that fecal microbiota transplantation was a successful treatment for a patient with FA and chronic urticaria.[109] The lung microbiome also acts as an important layer of biodiversity and affects the health outcomes of patients. For example, 1 study reported that children living on farms and experiencing greater microbial diversity were significantly less likely to develop asthma compared with children not on farms.[110]

In addition to microbial diversity, some studies have found an inverse relationship between the amount of forest cover close to children's homes and the development of allergic diseases.[111,112] Living close to a green environment at birth was protective and decreased the risk of developing allergic diseases and asthma by age 7 years.[113] More research is emerging, highlighting how living in an environment with more biodiversity or green space can enhance immunologic resilience and prevent allergic diseases and asthma.[114] However, a recent systematic review and meta-analysis found that the relationship between greenspace exposure and asthma and AR was not significant. Further research is needed.[115]

Migration

Currently, 55% of the world lives in urban cities, but it is estimated to grow to nearly 70% by 2050.[116] The World Bank estimates that by

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2050, 143 million people in Sub-Saharan Africa, South Asia, and Latin America will become displaced because of climate change.[117] Increased urbanization results in increased exposure to air pollution and a higher risk of developing respiratory diseases such as asthma. A study conducted in Canada found that asthma rates were higher in urban environments compared with rural areas.[118] Another study in the United Kingdom found that individuals living in urban areas recorded greater hay fever symptoms than in rural environments.[119] They also found that the severity of the symptoms correlated with pollutant and pollen levels.[119] Increases in the prevalence of allergy have been observed between migrants and native-born and between second and first-generation migrants.[120]. These varying patterns offer clues regarding the mechanisms underlying allergic disorders and emphasize the role of the environment in allergic disease.

Next Steps

To improve human health, there is an urgent need to adapt to and mitigate the effects of climate change. As climate change affects the health of all human beings, a concerted effort is needed from each and every one of us from an individual, community, national, and global level. Physicians as trusted members of the community, working with vulnerable and at-risk populations on the front lines, can play a critical and important role in leading the efforts in mitigating the effects of climate change (Fig 2). Health care providers can assist in these efforts in numerous ways. They can educate patients regarding climate change-related risks and advocate for policy change.[121,122]

A study conducted in a hospital in Wisconsin found that 44% of patients in a waiting room thought climate change affected their health, with 6% expecting their physician to be the main source of information on this topic. Meanwhile, the same study found that, although 64% of physicians believed climate change was affecting their patients' health, only 17% were comfortable counseling their patients.[123] This study reported that although most physicians and a substantial number of patients believe climate change affects their health, many feel inadequately prepared to discuss it with their patients.[123] There is now a push for medical school and residency training programs to incorporate curricula on climate change and its effects on health.[124,125] This can empower physicians to advocate for climate reform policies, treat patients experiencing the effects of climate change, and educate patients to reduce their carbon footprint and their exposure to air and other pollutants.

In the United States, it is estimated that the health care sector is responsible for 8.5% of carbon emissions[126] making it imperative to develop a more environmental approach to practicing and delivering health care by developing green health care systems that reduce carbon emissions and waste production and create more sustainable practices.[126] On an individual level, physicians can reduce their own carbon footprint, for example, by biking, walking, or using public transport to commute to work when possible, rather than using a car.[121,122,127]

Further mechanistic research is warranted, especially in understanding the effect of climate change on immune responses to aller-

Figure 2. Mitigation and adaptation actions for clinicians to help address the effects of climate change and global warming. Created with BioRender.com.

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gens and pollutants. This will assist with the development of novel therapeutics for treating the increasing number of patients with allergic diseases.[128] An environmental justice focus is also necessary to ensure that vulnerable populations, including those with preexisting respiratory conditions, low-income communities, the elderly, and children are not disproportionately impacted by the impacts of climate change. Finally, a One Health approach should be considered, which recognizes the interconnectedness of human, animal, and environmental health. This approach emphasizes collaboration across sectors to address the complex challenges presented by climate change and emphasizes the importance of protecting biodiversity and the health of the planet.

Conclusion

Global warming and climate change have significant implications for the environment and human health including allergic and atopic diseases. To address these challenges, a multifaceted, environmental justice and One Health approach is necessary. Mitigation strategies, such as reducing GHG emissions and transitioning to renewable energy sources, can help to slow the rate of climate change and reduce the severity of its impacts. Adaptation strategies, including heat mitigation and disaster preparedness, can help to reduce the vulnerability of communities to the impacts of climate change. Ultimately, research to better understand the effects of climate change on human health—particularly on allergy, asthma, and atopic disease—is necessary to provide the best care for patients. Physicians as trusted members of the community should educate their patients on climate change and be role models for decreasing their and the health care sector's carbon footprint. They should also educate their patients and the community on how to mitigate and adapt to climate change. Finally, they should advocate for policies that reduce the effects of climate change.

Disclosures

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