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Factors by which Global Warming Worsens Allergic Disease

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Abstract

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 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 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 use of fossil fuels and increase biodiversity and green space to enable a healthier and more sustainable future.

Keywords

Allergy; asthma; mitigation; adaptation; climate change; pollen; particulate matter; thunderstorms; sandstorms; ozone; wildfires

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Introduction

Allergic diseases have continued to increase in prevalence during the last 50 years with sensitization rates to one or more common allergens for school aged children approaching 40–50%.[1, 2] A study by the CDC found that 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] Additionally, allergic rhinitis (AR) and atopic dermatitis (AD) are estimated to affect approximately 29.4% and 26.1% of adults globally.[5] According to the CDC 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 socio-economic burden.[7]

Air pollution caused by global warming and climate change events are implicated in the increasing prevalence and severity of allergic disease.[8] Anthropogenic use of fossil fuels have increased global temperatures and air pollution through 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 (IPCC) has reported that global warming is now approximately 1°C higher than pre-industrial times and is continuing to increase.[10] Global warming has increased the frequency and intensity of wildfires and sand and dust storms 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. Further, epidemiological 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 was estimated to be 57.9 billion dollars[7]; between 252 – 314 million dollars for atopic dermatitis[7], > 4.6 billion for allergic rhinitis,[14] and 24.8 billion for childhood FA.[15] Indirect costs include absenteeism and presentism and a lower quality of life.[7]

Here, we review the climate change events, 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 in order 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 shown 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. Epidemiological 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 (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, sand and dust storms, thunderstorms, and flooding (Figure 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 due to climate change also affect allergic diseases.

Air Pollution

Air pollution, both indoor and outdoor, increase risk and severity of allergic diseases. The World Health Organization (WHO) estimates that 99% of the global population live 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 from molds).[36] Outdoor pollution sources include industrial and vehicular emissions (GHGs, PM, and other toxins) as well as from wildfires and sand and dust storms. Another natural source of air pollutants that affect allergic diseases is pollen, which is affected by increasing heat, CO_2 levels, and climate events such as thunderstorms. Air pollutants are thought to increase risk for and exacerbate respiratory disease by four main mechanisms: oxidative stress and epithelial damage, airway remodeling, inflammatory pathways and immunological responses, and enhancement of respiratory sensitization.[37] In AD, air pollutants have been shown to cause epidermal injury[38] leading to water loss and changes in microflora.[39]

Particulate Matter

PM is a major air pollutant that adversely affects allergic disease. PM concentrations tend to be higher in winter months, due to increased car traffic and domestic heating.[40] A meta-analysis of 35 studies across 12 countries (453,470 participants) showed a positive association between air pollution and the prevalence of AR.[41] PM 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 due to 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 μg/m^3 increase in exposure PM_{10} and $PM_{2.5}$ and risk of AR was 1.13 and 1.12, respectively.[44] In another meta-analysis and systematic review, increased longitudinal childhood exposure to $PM_{2.5}$ was associated with increasing risk of subsequent asthma in childhood with an odds ratio of 1.14.[45] In response to the health risks associated with PM exposure, the WHO changed its guidelines for $PM_{2.5}$ from 10 ug/m^3 to 5ug/m^3.[46]

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 while weed pollen is more common in the fall.[47] Climate change in North America has been estimated to contribute to about 50% of the lengthening pollen season.[48] Studies have shown that pollen concentrations are on the rise and estimated to increase by 200% by the end of the century.[49] Higher temperatures and elevated CO_2 levels stimulate photosynthesis, plant growth, and pollen production.[49, 50] Further, pollen season is starting earlier and lasting longer, exacerbating the problem.[49, 51] The increases in pollen concentration has 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.[52] Pollen exposure is associated with increased rates of asthma and allergies, specifically AR.[49] It is estimated that 30% of people globally have been affected by AR, with the prevalence projected to increase in the coming years.[53]

Ozone

O_3 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.[54] Ground level O_3 is a GHG and a potent oxidant. It is one of the six criteria air pollutants established by the EPA. In the United States, the current National Ambient Air Quality Standards (NAAQS) for O_3 is 70ppb (8-h maximum within a day).[55] In the US, in 2016, 90% of non-compliance to NAAQS was due to O_3.[56]

The Global Burden of Disease estimated that in 2019, 365,000 people died from exposure to ambient O_3 pollution.[57] 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.[58] It is thought to cause an inflammatory cascade in the airways through an increase in proinflammatory mediators, chemokines, and neutrophils.[59] A study used national and regional emergency room visit rates among people with asthma using published survey data and estimated that in 2015, 9–23 million (8–20% of total) asthma-related emergency room visits globally were attributable to O_3.[60] A systematic review found that increases in

long-term exposure to O_3 exposure in children was associated with a decrease in forced expiratory volume in one second (FEV1).[61]

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.[62, 63] A study, which analyzed how climate change affects the transport of heavy metals, found enhanced cadmium and zinc contamination in lowland catchments (groundwater) in the Netherlands due to enhanced runoff and accelerated leaching.[62] In some areas, heavy metals such as arsenic and cadmium are found in drinking water,[64–66] 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 cord blood of infants, suggesting these exposures might contribute to altered immune function of infants.[67] Another study has shown that exposure to arsenic is associated with high levels of Th2 mediators, IL-4, IL-6 and IL-13, which in turn results in increased susceptibility to allergic asthma.[68]

Detergents, allergens, and other pollutants have also been shown to have adverse effects on the immune system by disruption of the epithelium barrier and promoting inflammation. This has been termed the epithelial barrier hypothesis.[38, 69] Multiple studies have been published linking detergents to disrupted epithelium barriers.[70–72] A study demonstrated that laundry detergents, even at a very high dilution (1:25,000) show significant cell toxicity by disrupting barrier integrity of human bronchial epithelial cells.[70] Detergents have been shown to disrupt epithelial barrier integrity through their effects on tight junction or adhesion molecules and promote inflammation through epithelial alarmin release.[73] Epithelial barrier dysfunction and increased permeability can trigger an immune response and contribute to the development of allergies and other immune-related disorders.[74]

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.[75, 76] 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 approximately 220%, 20% and 151%, respectively.[77] By increasing GHGs, wildfires accelerate climate change leading to a positive feedback loop.[78] Wildfire smoke has been associated with increased rates of asthma[79] and increased levels of proinflammatory markers such as C-reactive protein (CRP) and IL-1B, which can worsen asthma and allergy symptoms.[80] A study by Aguilera et al. found that $PM_{2.5}$ emissions from wildfire smoke was about 10 times more harmful on children's respiratory

health than from $PM_{2.5}$ emissions from vehicles, particularly for children aged 0 to 5 years.[81] After the 2016 Fort McMurray fire in Alberta, Canada, there was an increase in asthma consultations among firefighters involved in fighting the fire. FEV1 and FVC were positively associated with increasing exposure. A fifth of the firefighters also had a positive methacholine challenge test and bronchial wall thickening.[82] 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 (SDS) have become more frequent and severe in recent years due to increased temperatures, droughts, and deforestation.[83] 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.[84] Studies have shown that SDS can exacerbate air pollution levels, including higher levels of PM, CO_2, and O_3.[85] In addition, SDS is known to include pathogens and microorganisms such as bacteria, fungi and spores.[86] Research has shown how particles in dust storms can travel long distances leading to respiratory infections, asthma and allergies.[87] For example, in California, an increase in Coccidiomycosis infection, caused by the fungi *Coccidioides immitis*, was associated with dust exposure and dust storms.[88] A study found that over a five-year period, on days with dust storms, same day asthma and respiratory admission at hospitals increased significantly.[89]

Thunderstorms and flooding

Thunderstorm asthma (TA) refers to an observed increases in asthma incidence following the occurrence of thunderstorms when pollen counts are high, generally in late spring and early summer.[90] TA can result in significant morbidity and mortality.[91] 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 to the past three years. This incident resulted in the death of 10 individuals.[92] During thunderstorms, the high humidity causes pollen grains to rupture into sub pollen allergenic particles by osmotic shock resulting in each grain releasing hundreds of small (<5μm) allergenic granules, which are capable of reaching the lower airways.[93]

Flooding is also associated with increased asthma and other respiratory systems. After major floods, there is proliferation of mold spores due to increased dampness exposing residents to indoor aeroallergen exposure[93, 94]. 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.[95]

Extreme temperatures

Heat waves are becoming more frequent and severe due to 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.[96, 97]The National Weather Service published a heat index chart categorizing heat ranges as “Caution”, “Extreme Caution”, “Danger” and “Extreme Danger”.[98]For example, any temperature above 105°F (41°C) is considered “Dangerous” to human health. According to the United States Environmental Protection Agency, heat waves have increased in frequency, duration, and intensity.[99] Studies suggests that exposure to extreme temperatures may be a risk for asthma. A meta-analysis of 111 studies found that the pooled relative risks for asthma attacks in extreme heat was 1.07.[100]

Analysis of data from asthma hospital visits at all medical facilities in Shenzhen, China between 2016–2020 found that during extreme temperature events the cumulative relative risk of asthma during heat waves compared to other days was 1.06.[101] Further, a study by Jin et al, 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}.[102]

Biodiversity and Green Space

The biodiversity hypothesis suggests that contact with natural and a biodiverse environment enriches the human microbiome, promotes immune balance and protects from allergic disease.[103] Human activities such as deforestation and urbanization has 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.[104] 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 richness of bacteria by 9.6%, fungi by 14.5% and protists by 7.5%.[105] Increased hygiene, more time spent indoors and decreased exposure to green space and to farm animals and pets has been shown to have adverse effects on immune health and increase risk of atopic diseases including allergy and inflammatory disorders.[103]

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.[106] 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.[107] Another study found that lower microbial richness and imbalances in specific gut bacteria were significantly associated with atopic sensitization.[108] Additionally, research has shown that individuals with allergies have significantly lower fecal microbial richness.[109] A recent case study found that fecal microbiota transplantation was a successful treatment for a patient with FA and chronic urticaria.[110] The lung microbiome also acts as an important layer of biodiversity and affects health outcomes of patients. For example, one study found that children living on farms and experiencing greater microbial diversity, were significantly less likely to develop asthma compared to children not on farms.[111]

In addition to microbial diversity, some studies have found an inverse relationship between the amount of forest cover close to children’s home and the development of allergic disease.[112, 113] Living close to a green environment at birth was protective and decreased the risk of developing allergic diseases and asthma by age 7.[114] More research is emerging, highlighting how living in an environment with more biodiversity or green space can

enhance immunological resilience and prevent allergic diseases and asthma.[115] However, a recent systematic review and meta-analysis found that greenspace exposure on asthma and AR was not significant. Further research is needed.[116]

Migration

Currently 55% of the world lives in urban cities, but it is estimated to grow to nearly 70% by 2050.[117] The World Bank estimates that by 2050, 143 million people in Sub-Saharan Africa, South Asia, and Latin America will become displaced due to climate change.[118] 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 to rural areas.[119] Another study in the UK found that individuals living in urban areas recorded greater hay fever symptoms than in rural environments.[120] They also found that the severity of the symptoms correlated with pollutant and pollen levels.[120] Increases in the prevalence of allergy has been observed between migrants and native-born and between second and first generation migrants.[121]. 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 effects 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 (Figure 2). Healthcare providers can assist in these efforts in numerous ways. They can educate patients about climate change related risks and advocate for policy change.[122, 123]

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.[124] This study shows that although the majority of physicians, and a substantial number of patients believe climate change affects their health, many feel inadequately prepared to discuss it with their patients.[124] There is now a push for medical school and residency training programs to incorporate curricula on climate change and its effects on health.[125, 126] This can empower physicians to advocate for climate reform policies, treat patients experiencing the effects of climate change, educate patients to reduce their carbon footprint and their exposure to air and other pollutants.

In the United States, it is estimated that the healthcare sector is responsible for 8.5% of carbon emissions[127] making it imperative to develop a more environmental approach to practicing and delivering healthcare by developing green healthcare systems that reduce carbon emissions and waste production and create more sustainable practices.[127] 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.[122, 123, 128]

Further mechanistic research is warranted, especially in understanding the effect of climate change on immune responses to allergens and pollutants. This will assist with the development of novel therapeutics for treating the increasing number of patients with allergic disease.[129] An environmental justice focus is also necessary to ensure that vulnerable populations, including those with pre-existing 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 disease. 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 and 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. Lastly, they should advocate for policies that reduce the effects of climate change.

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Conflict of Interest

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Abbreviations/Acronyms

AD	Atopic Dermatitis

AR	Allergic Rhinitis
CH4	Methane
CO2	Carbon Dioxide
FA	Food Allergy
GHG	Green House Gases
N2O	Nitrous Oxide
O3	Ozone
PM	Particulate Matter
SDS	Sand and Dust Storm
TA	Thunderstorm Asthma

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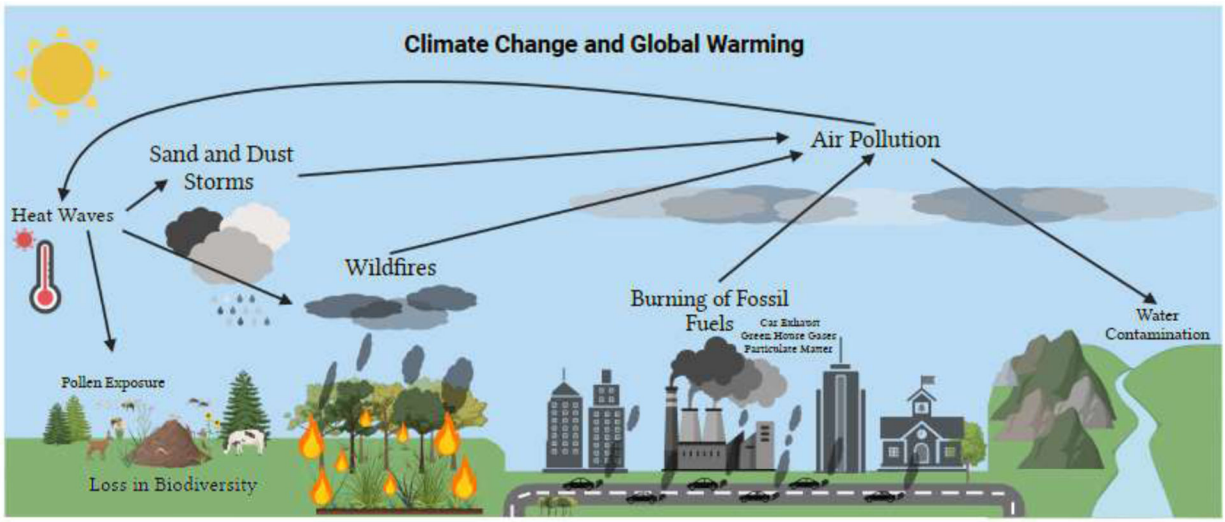

Figure 1.

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.

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