Climate Change and Respiratory Infections

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Abstract

The rate of global warming has accelerated over the past 50 years. Increasing surface temperature is melting glaciers and raising the sea level. More flooding, droughts, hurricanes, and heat waves are being reported. Accelerated changes in climate are already affecting human health, in part by altering the epidemiology of climate-sensitive pathogens. In particular, climate change may alter the incidence and severity of respiratory infections by affecting vectors and host immune responses. Certain respiratory infections, such as avian influenza and coccidioidomycosis, are occurring in locations previously unaffected, apparently because of global warming. Young children and older adults appear to be particularly vulnerable to rapid fluctuations in ambient temperature. For example, an increase in the incidence in childhood pneumonia in Australia has been associated with sharp temperature drops from one day to the next. Extreme weather events, such as heat waves, floods, major storms, drought, and wildfires, are also believed to change the incidence of respiratory infections. An outbreak of aspergillosis among Japanese survivors of the 2011 tsunami is one such well-documented example. Changes in temperature, precipitation, relative humidity, and air pollution influence viral activity and transmission. For example, in early 2000, an outbreak of Hantavirus respiratory disease was linked to a local increase in the rodent population, which in turn was attributed to a two- to threefold increase in rainfall before the outbreak. Climate-sensitive respiratory pathogens present challenges to respiratory health that may be far greater in the foreseeable future.

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The rate of global warming has accelerated over the past 50 years, with 2014 and 2015 being the earth's warmest years on record. The prevailing scientific view is that increased ambient temperatures are changing rainfall patterns and cause extreme weather conditions. These warming trends may have profound effects not only on the environment but also on human health directly and indirectly. In fact, climate change has been considered the biggest threat to global health in the 21st century (1).

With the accelerating pace of industrialization in the world, the need for energy has greatly increased. Energy production has relied heavily on burning fossil fuels that emit carbon dioxide and other greenhouse gases. These gases trap heat within the atmosphere and upset the balance between incoming energy from the sun and its reflection back into the space. This causes an elevation of the average earth surface temperature (2, 3). Further alterations of the earth's carbon cycle occur with thawing permafrost and vegetation changes. The terrestrial carbon storage changes may extend and amplify warming. There has been a progressive increase in monthly average temperatures in the last 200 years, which has recently dramatically increased. Figure 1 shows a global warming in the period of 1951 to 1980. Rising sea levels from polar ice cap melting and altered precipitation patterns may also contribute to the climate change and weather-related events (4, 5).

Global warming affects dissimilar climates differently. Polar regions may not be affected by changes in tropical flora, and so on. The Spatial Synoptic Classification system uses principal component analyses and other complex statistics to categorize different types of climate by moisture, temperature, and temporal trends (6). For example, humans and animals living in dry, moist, tropical, temperate, and polar regions may each face different health challenges. However, common and overlapping threats also occur. Therefore,

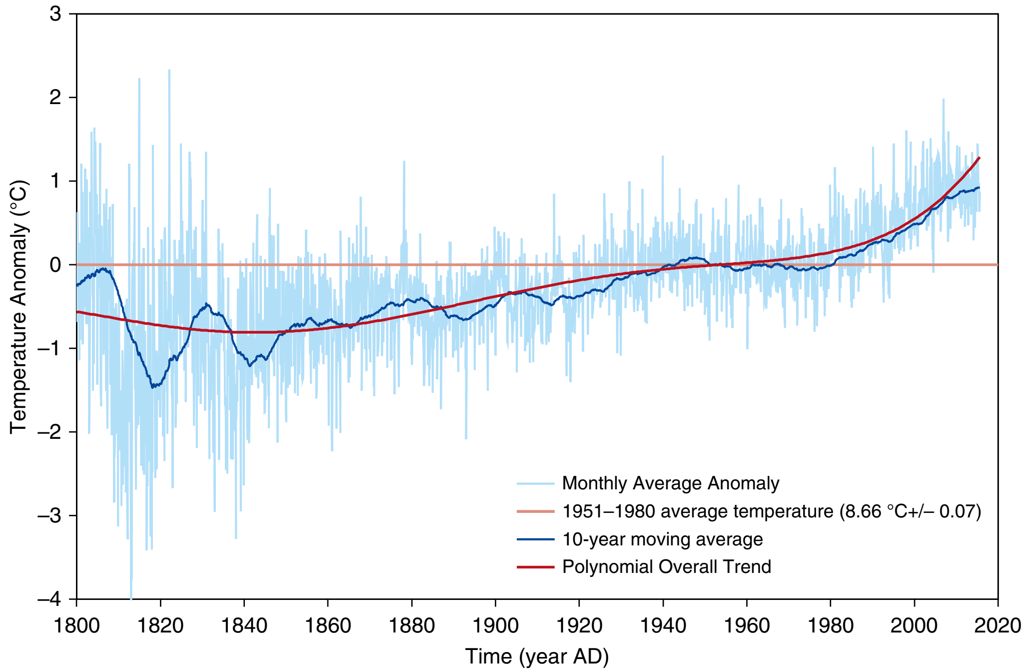


Figure 1. The estimated global land-surface monthly average temperature anomaly (*light blue*) relative to the January 1951 to December 1980 average (*orange line*). The decadal average anomaly (10-yr moving average) is shown in *dark blue*. The *red line* denotes the overall temperature anomaly since 1800. The land-surface average results produced by the Berkeley Averaging method and temperatures are reported as anomalies in °C relative to 1951 to 1980 average (absolute temperature = 8.66°C ± 0.07°C). The figure was generated with Microsoft Excel 2013 using data from Reference 86.

we did not break down the potential for respiratory infections into each of these climate systems.

Environmental effects of climate change include extreme weather events, such as heat waves, floods, and storms, and drought and dry conditions, including wildfires. Figure 2 shows a summary of events related to climate change and their effects on human health. For humans, these events lead to freshwater scarcity, reduced food yields, and higher food cost, which affect health directly and indirectly through altered patterns of infections, lack of nutrition, forced migration, and mental health problems (7, 8). Warming temperatures also affect air quality. Increase in atmospheric ozone and other reactive oxides can augment deleterious health effects on humans (9). Air pollutants are a direct contributor to hospital admissions and mortality from chronic conditions, such as asthma, chronic obstructive pulmonary disease, and cardiovascular diseases (10–14).

Climate change raises the risk of a variety of infectious diseases, including those transmitted by water, food, and vectors such as malaria and dengue (15). Several reports have linked infection outbreaks directly or indirectly to climate change. The tularemia outbreak in Turkey between 2010 and 2012 (16), the Hantavirus outbreak in Panama between 1999 and 2000 (17), the windborne coccidioidomycosis outbreak in California in 1977 (18), and aspergillosis among the survivors of the tsunami in Japan in 2011 (2) are examples. These events could be considered warning indicators of changing climate patterns and be a call to adapt and increase preventive efforts and resources to ameliorate further climate-related adverse health effects. Prominent among the health threats of climate change are infectious respiratory disease risks.

Climate Change and Bacterial Respiratory Infections

The distribution of several infectious diseases, including malaria, tick-borne diseases, and food- and water-borne diseases, is directly related to local environmental conditions. Climate alterations may directly or indirectly affect the incidence and severity of respiratory infections by affecting the vectors and the host immune responses (19). Changing weather patterns already affect some respiratory infections.

Climate change may affect the prevalence and geographic distribution of seasonal conditions but often not in a predictable fashion. Pneumonia and influenza together are the eighth leading cause of death in the United States (20). In 2013, 53,282 people died from pneumonia. Both influenza and streptococcal pneumonia have higher incidence during winter months (21, 22). Although the exact cause of pneumonia seasonality is unclear, indoor crowding (resulting in closer contacts), lower relative humidity, seasonal variation in the human immune system, association with other common seasonal respiratory pathogens (such as respiratory viruses), indoor air pollution, and low ultraviolet radiation might all contribute to this phenomenon (23–25).

Seasonal variation in the human immune system may relate to lower vitamin D levels during the winter months (26). In addition, ultraviolet light is bactericidal (27). In a study of 11,614 cases over a

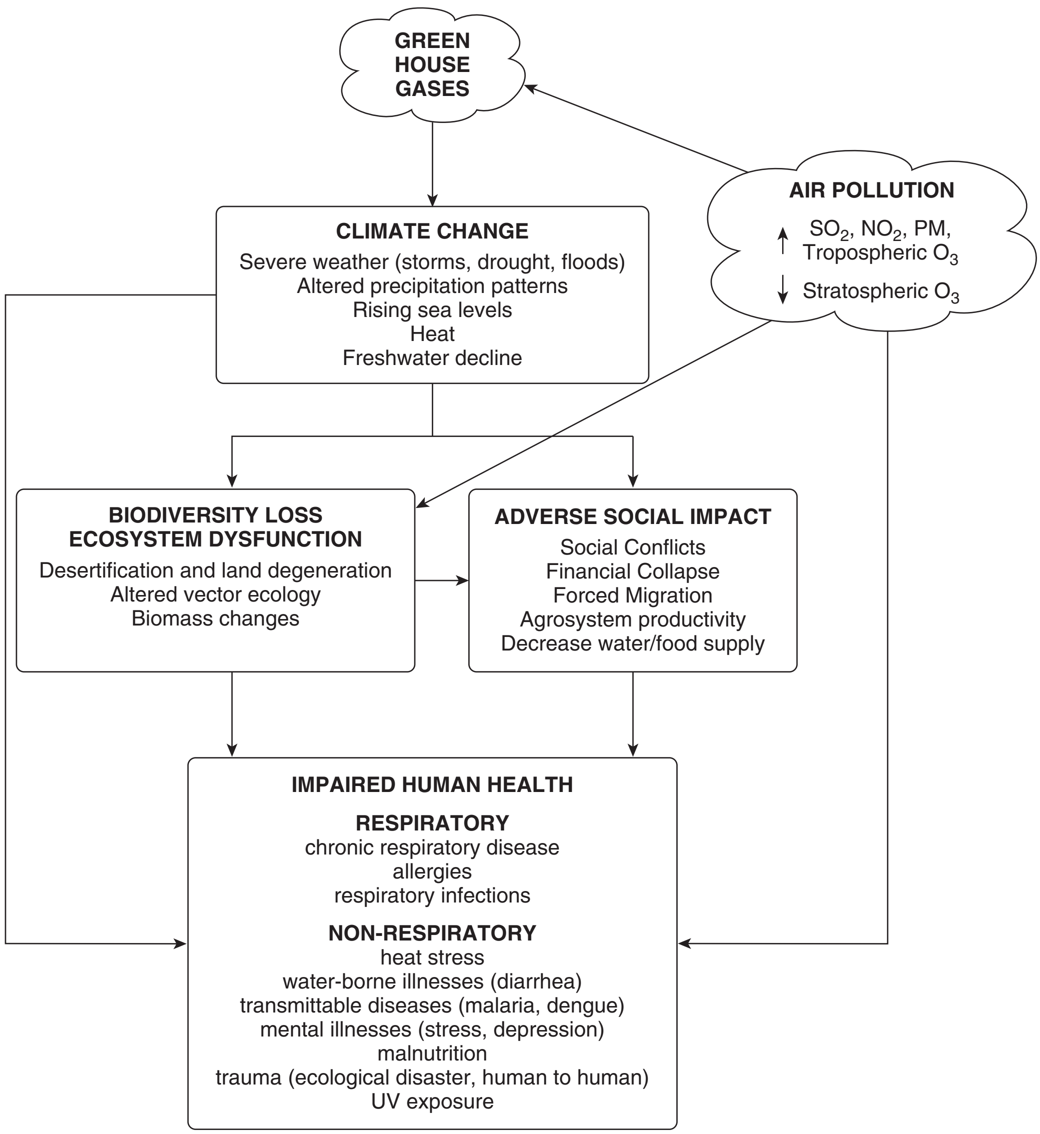


Figure 2. Illustration of the impact of climate change on respiratory infections. NO_2 = nitrogen oxide; O_3 = ozone; PM = particulate matter; SO_2 = sulfur dioxide; UV = ultraviolet.

period of 3 years, the seasonal pattern of invasive pneumococcal disease was inversely correlated with ambient temperature (28). Several other studies have shown an increased incidence of pneumonia during the winter and spring that could be attributed to close contact and greater virus transmission (29, 30). In the tropical and subtropical areas of Asia and Africa, the prevalence and mortality from pneumonia are higher during the rainy season, again showing the association of temperature and precipitation with pneumonia patterns (31).

Although it would appear that winter respiratory infections should decrease with increasing global temperature, the relationships are more complex. Fluctuating temperatures affect the incidence and mortality of respiratory infections. This is especially true among older adults and children, who are both more vulnerable to daily temperature oscillations (32). It appears that the metabolism of children does not adapt as well as adults to heat stress and temperature variations (33). An Australian study showed a correlation between sharp temperature drops from one day to the next and increased emergency visits for childhood pneumonia. The most important variable associated with childhood pneumonia was "temperature change between two neighboring days" (termed TCN), which is measured as the mean temperature difference from one day to the next. This health effect lasted for up to 3 weeks (34). The diurnal temperature range (termed DTR), which is the maximum daily temperature minus the minimum daily temperature, is another measure of global climate change (35). Both measures are expected to grow in the future and to be associated with increased incidence of bacterial pneumonia in many parts of the world.

Alterations in climate can also affect human exposure to vectors. For example, *Yersinia pestis* is usually found in temperate to tropical climates (36). A recent report highlighted the importance of climate change and exposure to prairie dogs, a common reservoir for *Y. pestis*, as the source of a pulmonary plague outbreak in Colorado (37). Increasing temperature in Colorado may have led to an increase in prairie dog colonies. The relation between climate change and vectors of other bacterial diseases, such as leptospirosis, has been modeled to predict future epidemics (38).

Climate Change and Viral Respiratory Infections

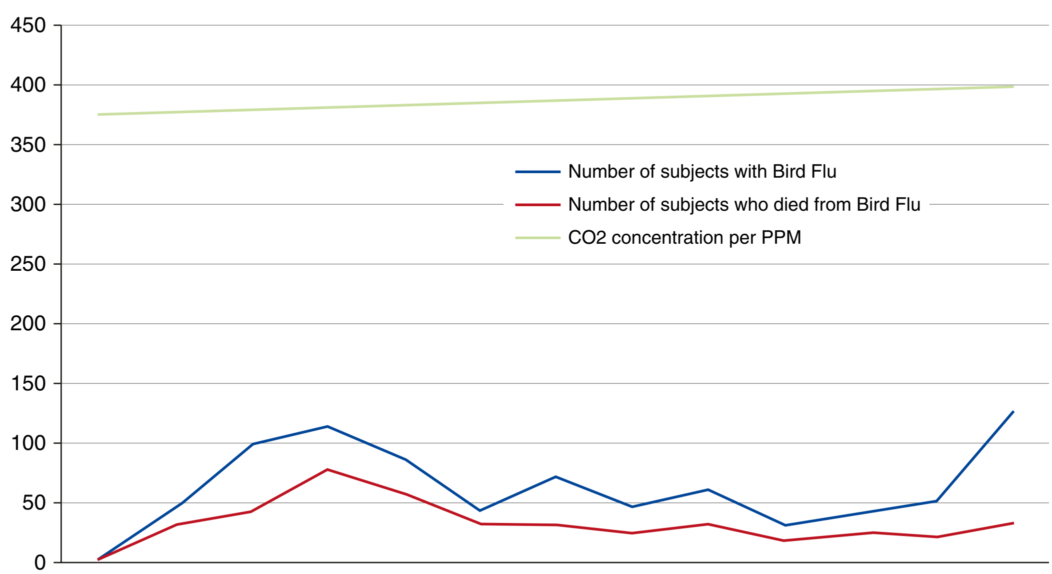
The global outbreaks of viral diseases in recent decades have taught us how fast viruses can mutate and spread (39). Human-to-human, vector-borne, and zoonotic viral transmission have resulted in the rapid spread of disease. Each of these transmission forms is highly influenced by climate, ecology, and geography. The unanticipated and emergent nature of these outbreaks requires careful study of their spread and relationship to environmental factors. Influenza, Ebola, West Nile, and dengue viruses caused unanticipated epidemics that cost millions of lives throughout history.

Changes in temperature, precipitation, relative humidity, and air pollution influence viral activity and transmission and may contribute to the size and severity of the epidemics. For example, in late 1999 and early 2000, a respiratory disease outbreak caused by *Hantavirus* was reported in Los Santos, Panama. *Hantavirus* is found in the saliva, urine, and feces of certain rodents. It appears that a two- to threefold increase in rainfall before the outbreak was responsible for increasing the rodent population, which resulted in more human contact with infected animals (17).

Climate change may shift habitats and bring wildlife, crops, livestock, and humans into contact with pathogens to which they have had less exposure and immunity (39). This could mean that climate change will foster the spread of infectious diseases into new regions and new hosts. Influenza H1N1 infects pigs, birds, and humans, but humans are vulnerable species. Climate change affecting one animal or plant may affect other species even outside of the immediate ecosystem.

Influenza is greatly affected by temperature change. Towers and coworkers analyzed influenza seasons and temperature changes and found that warm winters tend to be followed by severe and early-onset influenza incidence the following season (40). Modeling studies have shown that influenza outbreaks have a positive association with geographical differences in minimum temperature and specific humidity. This relationship has a lag period of several months, depending on other factors (41). Climate change occurs, in part, from increases in carbon dioxide concentration (42). Figure 3 shows the association between the incidence of confirmed human cases of avian influenza and changes in the concentration of carbon dioxide in atmosphere from 2003 to 2015.

Respiratory syncytial virus (RSV) is another highly contagious seasonal virus that can lead to symptoms similar to the common cold. It is the most common cause of lower respiratory tract infections among young children worldwide. According to a report by the Centers for Disease Control and Prevention, each year RSV leads to 2.1 million outpatient visits and 57,527 hospitalizations among children younger



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Number of subjects with Bird Flu	4	46	98	115	88	44	73	48	62	32	39	52	125
Number of subjects who died from Bird Flu	4	32	43	79	59	33	32	24	34	20	25	22	33
CO2 concentration per PPM	374.96	376.77	378.8	380.93	382.68	384.78	386.29	388.58	390.45	392.48	395.25	397.16	399.45

Figure 3. Graph showing the associations between incidences of confirmed human cases of avian influenza and changes in concentration of CO_2 in atmosphere from 2003 to 2015. CO_2 expressed as a mole fraction in dry air, μmol/mol. The figure was generated from data reported by U.S. Department of Commerce (87) and the World Health Organization (88).

than 5 years of age in the United States. It causes 177,000 hospitalizations and 14,000 deaths among adults older than 65 years annually (43). In contrast to influenza, warmer winters may decrease the RSV seasonality pattern (44). In England, Donaldson found that for each 1°C increase in annual temperature between 1981 and 2004, the RSV season (as determined by laboratory isolation and related emergency department admissions) terminated between 2.5 and 3.1 weeks earlier (44). In China, Zhang and colleagues studied 42,664 nasopharyngeal secretions from hospitalized children with acute respiratory infection and showed an inverse correlation between monthly RSV detection rates and mean monthly air temperature, total monthly sunshine duration, monthly rainfall, monthly relative humidity, and mean monthly wind velocity (45).

Climate-Sensitive Viral Infections with Main Effects outside the Respiratory System

Dengue is a debilitating mosquito-borne disease caused by the dengue virus. The numbers of dengue cases are underreported and often misclassified. One recent study estimated 390 million dengue infections occurred per year, with a range of 284 to 528 million (46). The wide range results from the variation in presentation and reporting, but even with the low estimate, the incidence of dengue poses an enormous burden on world health. Today, dengue is the most important mosquito-borne viral disease in the world, and the incidence of the disease appears to have increased 30-fold in the past 50 years. If global warming increases wetland area, it may facilitate mosquito population expansion and augment the transmission of dengue (47).

West Nile virus is another mosquito-borne agent that infects humans, birds, horses, and other animals. Mild forms of West Nile disease cause flu-like symptoms and may be confused with other influenza-like illnesses. Symptoms include headache, fever, myalgia, lymphadenopathy, nausea, vomiting, and rash. Between 1999 and 2014, the Centers for Disease Control and Prevention reported 41,752 cases of West Nile viral disease and 1,765 deaths (48). Climatic factors, such as temperature, precipitation, relative humidity, and wind velocity, are main determinants of its epidemiology. These weather conditions affect the vector's ability to acquire, maintain, and transmit the virus. Viral replication within the mosquito is also affected by the weather (49). Using a model to predict climate change in North America, Harrigan and colleagues found an expansion of conditions favoring West Nile disease between 2050 and 2080 (50). Because mosquitos develop in water, one would expect that wet conditions would favor expansion of the mosquito population. However, in a study of 82 counties of Mississippi, Wang and colleagues showed an inverse relationship between human West Nile virus disease incidence and total annual rainfall during the previous year (51). Accordingly, Shaman and colleagues found that a drought in spring followed by a rainy summer greatly increased the risk of West Nile disease in southern Florida (52). These findings emphasize the eccentricity of environmental conditions contributing to human disease.

Chikungunya is another viral disease transmitted by mosquitoes. It was first identified in Tanzania in 1952 and limited to Central Africa, but new cases were found in Asia, Indian Ocean Islands, Italy, and recently the Caribbean and the United States. Outbreaks seem to have a periodicity and are often separated by several years (53). The pattern of humidity and precipitation influences the vector, which affects this disease (54). Chikungunya viral infection can cause pulmonary complications, including pulmonary edema (55).

The distribution of *Aedes* mosquitoes could be another element in climate-sensitive viral infections. Recently, north and eastern South America experienced their highest recorded sustained temperature in history. This remarkable climate change might also affect adult vector survival and infectivity periods. Disease caused by the Zika virus is an example of one with multiple modes of transmission, which further complicates understanding the role of climate change in its spread.

Climate Change and Fungal Respiratory Infections

Climate change increases fungal infections by increasing the inhalational exposure of soil. Increased respiratory fungal infections have been reported after storms, earthquakes, and other natural or human activity affecting the soil. Coccidioidomycosis is typically transmitted by inhalation of airborne spores and cannot be transmitted from person to person. A well-documented outbreak of coccidioidomycosis occurred in California (56); in 1977, 130 newly diagnosed cases of symptomatic coccidioidomycosis, characterized by fever, chest pain, and coughing (valley fever), developed within 2 to 4 weeks after exposure to a severe natural dust storm. In another instance, 203 new coccidioidomycosis cases and three fatalities occurred between January 24 and March 15, 1994 in Ventra County, California, after an earthquake (57). These are examples of how natural disasters can release microbes to cause an epidemic. Comrie showed a strong bimodal seasonality of coccidioidomycosis in Arizona. He found that peak exposure to this fungus occurs between June or July and late October or November when the land is dry and dusty (58). The seasonal outbreak of coccidioidomycosis was not associated with changes in human population characteristics, exposures, or comorbidities (59).

Flooding is a second climatic mechanism to increase respiratory fungal disease incidence. Flooding normally dry soil and housing materials results in fungal growth leading to fungal and polymicrobial infections. Epidemiological studies in Mozambique (60) and Bengal (61) documented increased incidence of respiratory infections after flooding. Siddique and colleagues found that respiratory infections caused 13% of all mortality rates after a Bangladesh flood in 1988. Acute respiratory tract infections were responsible for nearly half of them (62). If the climate change results in more floods, acute respiratory infections may increase.

Fungal infections caused by aspiration in flood survivors have been reported. Disseminated aspergillosis occurred in an immunocompetent victim of near drowning from the tsunami after the Japanese earthquake of 2011 (2). Despite intensive treatment, she died from multiple organ dysfunction. At autopsy, she was found to have disseminated aspergillosis. A similar case of disseminated infection was reported after the 2004 earthquake and tsunami in Indonesia in a previously healthy 17-year-old who had been engulfed by floodwater. Seven weeks after the tsunami, she was hospitalized with respiratory distress and hemiparesis and diagnosed with tsunami-related aspiration pneumonia. She had lung and brain abscesses. Although no organism was isolated from sputum, pleural effusion, or cerebrospinal fluid, she probably had polymicrobial infection (63).

Air Pollution and Respiratory Infections

Fossil fuel combustion, from coal and other sources, releases both greenhouse gases (carbon dioxide, methane, nitrous oxide, and fluorinated gases) and air pollutants. The main air pollutants are particulate matter (PM), ground level ozone (O_3), carbon monoxide (CO), sulfur oxides (SO_2 and others), nitrogen oxides (NO and others), and lead. The air pollutants exert health effects directly, whereas the greenhouse gases exert their health effects largely through climate change (64). Although greenhouse gases and air pollutants have different dynamics, they accumulate in the air by common means. Air pollution significantly affects infectious disease patterns by influencing both the infecting agent and the host. For instance, air pollution causes a proinflammatory response in the airway that may be mediated by toll-like receptor activation (65).

Over the past years, several studies have shown a link between air pollution and a wide range of diseases. The respiratory system, in the front line of toxic inhalation, is the organ facing the greatest affront. The health effects of air pollution range from allergies and acute infections to debilitating chronic lung diseases (66). Hospitalizations and mortality attributed to air pollution are greatest in persons with preexisting respiratory conditions, such as chronic obstructive pulmonary disease, asthma, and pneumonia (10, 13, 67). The risks are highest among infants (68), children (69), and the elderly (11).

Short-term exposure to air pollutants is associated with respiratory tract infections, including pneumonia or bronchiolitis. Ambient air pollution is clearly related to daily hospital admission rates for lower respiratory tract infections (70). A report from Vietnam evaluated the average daily level of air pollutants (PM_{10} [particles $\leqslant$ 10 μm in diameter], NO_2, SO_2, and O_3) and 15,717 pediatric hospital admissions for lower respiratory tract infections over 3 years. It showed a link between hospitalizations and the levels of PM_{10}, SO_2, and NO_2 between the months of November and April each year (71) but found no association in the rainy season months of May through October. Interestingly, neither of these studies found a link between the ozone levels and respiratory-related hospitalizations in the children.

It has been proposed that the germicidal effect of ozone could at least partially account for the decreased incidence of streptococcal pneumonia during the summer months (10). Tropospheric, or ground-level, ozone is not formed directly from fuel combustion. It is produced by interactions of volatile organic compounds and nitrogen oxides, reactions that are accelerated by higher temperatures (72). This accounts for the strong correlation between temperature and ground-level ozone concentrations (73). In contrast to the observations of infections in children, an association between tropospheric ozone and lung disease in adults has been established. Elevated ozone concentrations have been related to bronchial inflammation, aggravation of chronic obstructive pulmonary disease (74), decline in lung function, increased hospitalizations, and increased mortality, largely related to obstructive lung disease and pneumonia (75).

The elderly are more susceptible to the effects of ambient air pollution. Studies have correlated the levels of air pollutants (PM_{10} and O_3) with hospital admissions for pneumonia (76, 77) as well as asthma (78) in elderly patients. Another study of 345 hospitalized patients in Ontario showed an association between hospital admissions for pneumonia in patients older than 65 years with long-term exposure to the high levels of air pollution (PM $\leqslant$ 2.5 μm in diameter [$PM_{2.5}$] and NO_2) (11). In Sao Paulo, Brazil, increases in pollutants (PM_{10}, SO_2, and CO) increased the number of chronic obstructive pulmonary disease admissions especially in the elderly (79). In this study, women appeared to be susceptible to elevations in CO levels.

PM includes solid particles and liquid droplets suspended in the air for prolonged periods of time. The particles come from many sources, such as diesel exhaust, construction sites, power plants, woodstoves, wildfires, etc. Tsai and Yang observed a significant correlation between hospitalizations for pneumonia and high levels of $PM_{2.5}$ in Taiwan (80). A direct relationship between RSV seasonality with particulate matter concentrations (mean PM_{10}) and mean minimum temperature has been described in a pediatric population in Bologna, Italy (81). In Beijing, Liang and coworkers found a strong correlation of $PM_{2.5}$ level and human influenza infections over a period of 5 years (82).

Elevations in SO_2 levels have been associated with invasive pneumococcal disease in many settings (83). The levels correlate with emergency room visits for influenza and pneumonia among children (84) and adults. An elevated SO_2 concentration of 7.8 $\mu g/m^3$ is associated with a cumulative 6-day increase in hospital admissions for chronic obstructive lung disease of 16% (79).

Although many studies have emphasized the importance of a high level of pollutants, recent studies show that even low-level exposure to air pollutants has adverse health outcomes (85). Whether these low levels also affect the incidence of respiratory infections needs to be determined.

Conclusions

Climate change carries a threat to human health and health care systems in the coming decades. The occurrence of many infectious respiratory diseases is affected by climate and its corollary, air pollution. The range of influences on viral infections, disease-causing vectors, and host susceptibility with climate enhances these concerns. Knowledge of these associations is important to adapt public health policies, disaster preparedness, societal awareness, and education. Preparation for the deleterious human health effects of climate change must include measures to prevent or mitigate the occurrence and prevention of respiratory infections. Much more needs to be learned and done in this area. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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