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REVIEW

Risk Factors for Respiratory Viral Infections: A Spotlight on Climate Change and Air Pollution

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Abstract: Climate change has both direct and indirect effects on human health, and some populations are more vulnerable to these effects than others. Viral respiratory infections are most common illnesses in humans, with estimated 17 billion incident infections globally in 2019. Anthropogenic drivers of climate change, chiefly the emission of greenhouse gases and toxic pollutants from burning of fossil fuels, and the consequential changes in temperature, precipitation, and frequency of extreme weather events have been linked with increased susceptibility to viral respiratory infections. Air pollutants like nitrogen dioxide, particulate matter, diesel exhaust particles, and ozone have been shown to impact susceptibility and immune responses to viral infections through various mechanisms, including exaggerated or impaired innate and adaptive immune responses, disruption of the airway epithelial barrier, altered cell surface receptor expression, and impaired cytotoxic function. An estimated 90% of the world's population is exposed to air pollution, making this a topic with high relevance to human health. This review summarizes the available epidemiologic and experimental evidence for an association between climate change, air pollution, and viral respiratory infection.

Keywords: viral respiratory infection, climate change, air pollution, influenza, respiratory syncytial virus, rhinovirus, nitrogen dioxide, ozone, diesel exhaust particles, particulate matter

Introduction

Climate change is perhaps the greatest threat humans face today, with far-reaching implications for food supply chains, migration patterns, shifting habitats, extreme weather events, and human health. The average global surface temperature in July 2022 was the sixth warmest for July since 1880 when record keeping began,[1] and global temperatures are expected to continue rising over the next several decades.[2] As of 2016, global atmospheric CO2 concentrations have permanently crossed above 400 ppm, an important threshold with implications for further rising global temperatures and other climate impacts. According to the World Health Organization, climate change has both direct and indirect effects on health and disproportionately impacts vulnerable groups like children, the elderly, racial and ethnic minority groups, low-income populations, and citizens of developing nations.[3] Some of the many climate-sensitive health risks include injury or death from extreme weather events, heat-related illnesses, increase in waterborne and vector-borne diseases, malnutrition, and respiratory illnesses. Similar effects of rising global temperatures on survival have been described in animals.[4]

Earth's changing climate is primarily the result of human activity, namely the production of greenhouse gases due to our reliance on burning of fossil fuels for energy.[5] Toxic pollutants like black carbon, sulfur dioxide (SO_2), nitrogen oxides (NOx), volatile organic compounds (VOC), particulate matter (PM), and polyaromatic hydrocarbons emitted as a result of burning of fossil fuels worsen air quality and increase absorption of solar radiation that further increases temperatures.[6] Higher temperatures accelerate formation of ground-level ozone (O_3) from NOx and VOC precursors that increase risk of cardiopulmonary morbidity and mortality. Drought conditions leading to wildland fires and desertification effects increase air particulates that exacerbate respiratory conditions like asthma and COPD and increase the risk for emergency department (ED) visits and hospitalizations.[7]

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Viral respiratory tract infections are most common illnesses in humans,[8,9] with estimated 17 billion incident cases globally in 2019[10]. Common viruses causing respiratory tract infection include influenza, respiratory syncytial virus (RSV), rhinovirus (RV), and SARS-CoV-2. Viral respiratory infection imposes a substantial burden on populations and health systems.[11] Non-influenza viral respiratory infections were estimated to cost the US economy $40 billion annually.[11] Viruses are also the primary trigger for acute asthma exacerbations[12] and a major cause of COPD exacerbations.[13] While most viral respiratory infections are mild and self-limited,[11] they can lead to severe complications in susceptible patients, including pneumonia and even respiratory failure.[14,15] The SARS-CoV-2 pandemic in particular has contributed to over 3 million deaths worldwide.[16]

More than 90% of the world's population is exposed to polluted air.[17] Convincing epidemiologic data has linked air pollution exposure with increased incidence of viral respiratory infections like upper respiratory tract (URI) infections,[18,19] bronchitis,[20] and lower respiratory tract infections (LTRI)[21,22] such as pneumonia[23,24] and bronchiolitis.[25,26] Similarly, temperature,[27,28] humidity,[29] and extreme weather events[30–32] have also been directly and indirectly associated with respiratory infections.

Climate change, air pollution, and viral respiratory infection are highly interconnected, and without interventions to halt global warming, we can expect the burden of viral respiratory disease to increase worldwide. This review will summarize the epidemiologic and experimental evidence for a relationship between climate change/air pollution and susceptibility to viral respiratory disease as well as future research priorities (Table 1).

Methods

We conducted a search for peer-reviewed studies pertinent to climate change, air pollution, and viral respiratory infection using PubMed and Google Scholar databases. We applied the keywords: climate change, air pollution, particulate matter (PM), nitrogen dioxide (NO_2), O3, RSV, RV, influenza, SARS-CoV-2, COVID-19, asthma, COPD, viral respiratory infection. Studies were included if they were 1) relevant to the aims of this review, 2) published in peer-reviewed journals, and 3) written in English.

Climate Change and Respiratory Viral Infection

Temperature, humidity, and extreme weather events are linked with respiratory infection incidence (reviewed by[33]). In temperate climates, lower temperature was usually associated with higher infection incidence. A study conducted in

Table 1 Summary Points and Knowledge Gaps

What is known about climate change, air pollution and their relationship with viral respiratory infection?
Climate change is creating increased frequency of extreme weather events such as wildfires, floods, and heat waves that are linked with increased incidence of respiratory infections, through direct and indirect mechanisms.
Earth's changing climate is the result of human activities, including burning of fossil fuels that emits harmful air pollutants. Air pollution exposure has been extensively linked with increased incidence of viral respiratory infections, including SARS-CoV-2.
Evidence suggests that air pollutant exposure may increase the severity of viral respiratory infections, with increased hospitalizations for respiratory infections particularly among children.
Laboratory studies have shown several mechanisms by which air pollutants may increase viral respiratory infection susceptibility and severity, including impaired anti-viral immune responses, altered epithelial barrier functions and augmented cell surface receptor expression that promote viral entry into cells.
What are the gaps in knowledge on this topic that should be addressed in future research?
More mechanistic work is needed to understand the causal pathway between air pollutant exposure and viral respiratory infections. Whether this a function of increased host susceptibility, enhanced viral transmission, increased severity of infection, or all of these remains to be determined.
The relationship between viral respiratory infection and pollutant exposure may differ based on length of exposure. More studies of the effects of short- and long-term exposure to air pollutants on viral respiratory infection incidence and severity are needed.
The effects of climate change and air pollution on COVID-19 incidence, morbidity and mortality require further study.

Sweden observed that lower temperature and larger weekly drop in temperature were associated with higher influenza incidence the following week.[34] Lower temperature was associated with higher incidence of influenza A, respiratory syncytial virus (RSV), human metapneumovirus, bocavirus, and adenovirus, while no association with temperature was observed for human rhinovirus and enterovirus infection incidence.[34] A US study found that warmer winters were associated with more severe epidemics of influenza A and B during the following winter season.[27] Specifically, a mild winter was followed by a more severe than average influenza epidemic 72% of the time, and this epidemic had a growth rate 40% higher and peaking 11 days earlier than average.[27] A study of RSV seasons over 8 years in the Netherlands reported a negative correlation between minimum temperature and RSV incidence (r=−0.338),[28] with others reporting similar findings.[35] For RSV specifically, some experts have proposed that climate change and resulting warmer winters may be beneficial in terms of shortening RSV seasons.[36] In contrast, Zoran et al observed a positive correlation between COVID-19 cases and air temperature (r=0.67), indicating high transmission during warmer temperatures, which may partially explain continued high levels of transmission of the SARS-CoV-2 virus observed even during the summer months.[37]

In tropical climates, increased temperature was associated with higher rates of respiratory infections. Phung et al reported that among urban children <5 years of age in the Mekong Delta region of Vietnam, rates of hospital admissions for respiratory infections increased by 3.8% (95% CI 0.4, 7.2) for every 1°C increase in 2-day moving average temperature.[38] Temperature variability was also linked to viral respiratory infection incidence. Greater temperature variability, day-to-day and within the same day, was positively associated with greater frequency of healthcare visits for acute bronchitis[39] and pneumonia in children.[40,41] However, most analyses did not account for air pollution, socioeconomic status, or behavior factors, which could have influenced infection frequency.

The relationship of humidity to viral respiratory disease incidence is inconsistent and may vary depending on the specific respiratory virus. Chowell et al reported a strong negative correlation (r=−0.70) between relative humidity and peak incidence of H1N1 influenza during the 2009 pandemic.[29] Similarly, an inverse relationship was observed between COVID-19 cases and relative humidity levels in the Lombardy region of Italy during early 2020 (r=−0.47), suggesting that dry air favors virus transmission.[37] In contrast, RSV incidence was positively correlated with relative humidity,[28,35] suggesting that higher humidity was associated with higher RSV activity.

Extreme weather events such as wildfires, heavy rainfall with flooding, and heat waves have been linked with respiratory infection risk as well. In addition to direct effects, these events can also have indirect effects on risk of respiratory infections, such as displacement of large groups of people from their homes, indoor crowding and increased time spent indoors, and inadequate food supply with malnutrition that enhance susceptibility to and transmission of disease. Increased time spent indoors may also increase exposure to indoor pollution sources such as burning biomass that contribute to respiratory symptoms.

A systematic review of air pollution exposure during natural disasters including wildland fires and volcanic eruptions concluded that PM generated by these events was associated with increased rates of acute respiratory infection, pneumonia, bronchitis, and bronchiolitis.[30] A consistent association across multiple studies was observed between exposure to wildfire-related particulate matter less than 2.5 μm in diameter ($PM_{2.5}$) and increased ED visits and hospitalizations for acute respiratory infection.[31,42–47] Delfino et al found that during wildfires in Southern California, the number of hospital admissions for pneumonia increased by 1.3x (95% CI 1.17, 1.48) and admissions for acute bronchitis/bronchiolitis increased by 1.6x (95% CI 1.09, 2.29) among area residents.[46] Rappold et al reported similar findings following wildfires in North Carolina, with residents from exposed counties experiencing an increased risk of ED visits for bronchitis and pneumonia (cRR 1.59, 95% CI 1.07, 2.34).[43]

Extreme rainfall and flooding were linked with acute respiratory infections as well. Phung et al reported a significant relationship between extreme river water levels in the Mekong Delta region and daily pediatric hospitalizations for respiratory infection (cRR 1.66, 95% CI 1.57, 1.74).[32] A retrospective study from the Netherlands reported that exposure to floodwater and performing clean-up after flooding were associated with higher odds of acute respiratory infection (aOR 3.3, 95% CI 2.0, 5.4).[48]

Heat waves may also contribute to increased respiratory infections. In California, more ED visits for respiratory infections were observed among all age groups during the July–August 2006 heat wave compared to reference periods immediately before and after the heat wave.[49] Similarly, a time-stratified case–crossover study conducted in China over

a 2-year period observed that heatwaves increased the risk of outpatient visits for respiratory infection among all ages (RR 1.31, 95% CI 1.18, 1.45), with children (1.74, 95% CI 1.52, 1.99) and the elderly (1.41, 95% CI 1.11, 1.79) at particularly elevated risk.[50] The contribution of unmeasured factors such as increased time spent indoors during periods of extreme heat is unknown. A mechanism by which extreme heat may directly contribute to increased risk of infection is unclear, though heat stress has been shown to impair airway innate immune responses in animal studies.[51] Chronic heat stress in mice was associated with a reduced production of inflammatory cytokines IL-6 and IFN-β, increased viral load and increased mortality rate following avian influenza H5N1 infection.

Air Pollution and Respiratory Infection: Epidemiologic Evidence

Short- and long-term exposure to air pollution has been extensively linked with increased susceptibility to respiratory infection. Short-term exposure to increased PM was associated with increased susceptibility to respiratory infections including influenza[24,52] and influenza-like illness,[53–55] RSV bronchiolitis,[25,26,56] and acute lower respiratory tract infections (LTRI)[22] including pneumonia.[23,24,57] Chen et al observed that across 47 Chinese cities, a 10 μg/m^3 increase in $PM_{2.5}$ was associated with an increased risk of influenza (RR 1.020, 95% CI 1.006, 1.034) at lag days 2–3, after controlling for seasonality and weather conditions.[52] Croft et al examined data from 500,000 ED visits and hospitalizations from New York state and found that IQR increases in $PM_{2.5}$ during the prior week were significantly associated with higher rates of ED visits for influenza (3.9%, 95% CI 2.105.6%; at 7 days) and culture-negative pneumonia (2.5%, 95% CI 1.4–3.6%; at 6 days).[24] Similarly, in two studies in Italy, RSV infection incidence and risk of hospitalization for RSV bronchiolitis in infants were positively associated with concentrations of PM less than 10 μm in diameter (PM_{10}) during the prior 1–2 weeks.[25,26] Using both single and multipollutant exposure models to estimate the association between air pollutants and respiratory infection in preschool-aged children, Zhang et al observed a significant association between $PM_{2.5}$ levels and respiratory infections in children 6 months of age and under (single pollutant model: OR 1.012, 95% CI 1.008–1.018) (multipollutant model: 1.019, 95 CI 1.012–1.026).[58] Similar associations with viral respiratory infections were seen with O_3 (1.025, 95% CI 1.018–1.033) in children ≤6 months of age, with smaller but significant associations in 7–12 month old and 1–3-year-old children. PM_{10} levels were associated with viral respiratory infections as well (1.025, 95% CI 1.008–1.042) but only among 3-6-year-old children.

NO_2 exposure was also implicated to increase susceptibility to viral respiratory infections. Elevated NO_2 concentrations were associated with increased hospital admissions for acute respiratory infections,[19] including croup[20,59] and viral infection-induced asthma exacerbation,[60] pneumonia,[21] and influenza.[21] Exposure to increased O_3 was also associated with hospital admission for pneumonia[21,61] and influenza[21] infection.

Further, in a systematic review and meta-analysis of ambient air pollution and pneumonia in children, Nhung et al reported an overall positive association between pediatric hospitalization for pneumonia and exposure to air pollutants, including $PM_{2.5}$, PM_{10}, SO_2, O_3, and NO_2. The largest association observed was for SO_2, with ER visits increasing by 2.9% (95% CI 0.4–5.3%) per 10 ppb increase. The authors noted significant effect modification by study location, with stronger associations observed in low- and middle-income countries compared to high-income countries.[23] The same authors later reported that higher O_3 and PM_{10} concentrations were associated with an increased length of hospital stay among children 5 years and under admitted for lower respiratory infection, with no relationship between $PM_{2.5}$, SO_2, or NOx and length of stay.[62] Specifically, per IQR increase in O_3, there was a 5% (95% CI 2–8%) decrease in odds of hospital discharge, and for PM10, there was a 6% decrease in odds of hospital discharge in the 2–5-year-old group only.

There is also convincing evidence suggesting that long-term exposure to air pollutants predisposes to respiratory infection, though it is unclear whether this susceptibility is a function of exposure during the prenatal period, postnatal period, or both. Within the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort, Brauer et al observed that long-term exposure to traffic-related pollutants ($PM_{2.5}$, NO_2, soot) was associated with higher odds of ear, nose, and throat infections at 2 years of age[63] as well as influenza and serious cold infections at 4 years of age.[64] A meta-analysis of over 16,000 children from 10 birth cohorts from the ESCAPE project found that physician-diagnosed pneumonia during the first 2 years of life was significantly associated with annual average air pollution levels of PM_{10} (OR 1.76, 95% CI 1.00, 3.09 per 10 μg/m^3) and NO_2 (1.30, 95% CI 1.02, 1.65 per 10 μg/m^3), but not $PM_{2.5}$ (2.58, 95% CI 0.91, 7.27).[65]

Air Pollution and SARS-CoV-2

Many have hypothesized that air pollution contributed to the initial spread of SARS-CoV-2 during the early days of the pandemic[66–68] and may also increase the risk of mortality.[69,70] Air particulates from indoor[71] and outdoor samples were shown to contain SARS-CoV-2 viral particles.[72,73] In addition to having high levels of air pollution, densely populated urban centers like Wuhan and New York City were also hot spots for SARS-CoV-2 transmission and COVID-19-related mortality. Concentrations of $PM_{2.5}$, PM_{10}, NO_2, and O_3 in the prior 2 weeks were significantly associated with daily confirmed COVID-19 cases in an analysis of data from 120 cities in China between January and February 2020, with the largest association observed with per 10 $\mu g/m^3$ increase in NO2 (6.94%, 95% CI 2.38%, 11.51%).[74] Higher SO_2 concentrations were associated with a decrease in new COVID-19 cases. Moderate correlations were observed between air pollutants and COVID-19 cases (Pearson's r ranging from 0.41 for PM_{10} to 0.58 for $PM_{2.5}$) in hard-hit regions of Italy.[75] In China's Hubei province, a significant correlation was observed between NO_2 levels and SARS-CoV-2 transmission rate in 11 cities ($r > 0.5$), indicating that SARS-CoV-2 transmission was higher in regions with higher NO_2 exposure.[76] The same group reported a significant association between higher COVID-19 case fatality rates and higher levels of $PM_{2.5}$ and PM_{10} in Wuhan, China.[77] Ogen observed that over 80% of COVID-19-related fatalities in Europe during the first 2 months of the SARS-CoV-2 pandemic occurred in places with the highest NO_2 concentrations, particularly the Lombardy region of Italy.[69] In the majority of studies, potentially confounding health variables such as age and pre-existing disease could not be accounted for, limiting the ability to accurately estimate the impact of pollutant exposure on outcomes. Another uncertainty is the effect of length of exposure and whether short- or long-term exposure is more important in terms of risk of contracting SARS-CoV-2 infection, disease severity, and mortality risk. A recently published prospective study of residents in Varese, Italy, found that long-term exposure to airborne pollutants PM2.5, PM10, NO2, and NO increased the incidence of COVID-19.[78] The largest effect was seen in single and bi-pollutant models of PM2.5, which was associated with a 5% increase in COVID-19 incidence (95% CI 2.7%, 7.5%). Further studies are needed to answer remaining questions about the relationship between air pollution and SARS-CoV-2 infection.

Summary of Epidemiologic Studies

The totality of the epidemiological evidence supports a link between air pollution exposure and increased susceptibility to viral respiratory infection. However, our review of the literature has several limitations. Population-level studies are limited in their ability to accurately estimate an individual's pollutant exposure. Additionally, under real-world conditions, populations are exposed to a mixture of air pollutants. Differences in study outcomes were influenced by differences in study design, exposure assessment, and adjustment for potential confounders. Further work is needed to address important research questions about the causal pathway between air pollution exposure and viral respiratory infection, particularly for SARS-CoV-2 virus. It is currently unclear whether air pollutants predominantly influence transmission and susceptibility to viral infection or if they significantly impact disease severity and mortality risk. The impact of short- versus long-term exposure to pollutants on infection risk is another poorly understood area in need of high-quality research.

Air Pollution and Increased Susceptibility to Viral Respiratory Infection: Mechanistic Evidence

Since it is not possible to separate out the health effects of individual pollutants in epidemiologic studies, in vitro studies, animal model studies, and human controlled exposure studies have been performed to help establish the mechanisms of the apparent synergistic relationships between exposure to air pollutants and viral respiratory infection (Figure 1).

Altered Immune Response to Viral Infection

Exposure to air pollutants augments airway inflammatory responses to viral infection, through exaggeration or impairment of the innate and adaptive immune responses and/or skewing of the response from predominantly antiviral to an allergic, Th2-predominant response. In human bronchial epithelial cells exposed to urban PM, enhanced activation of the

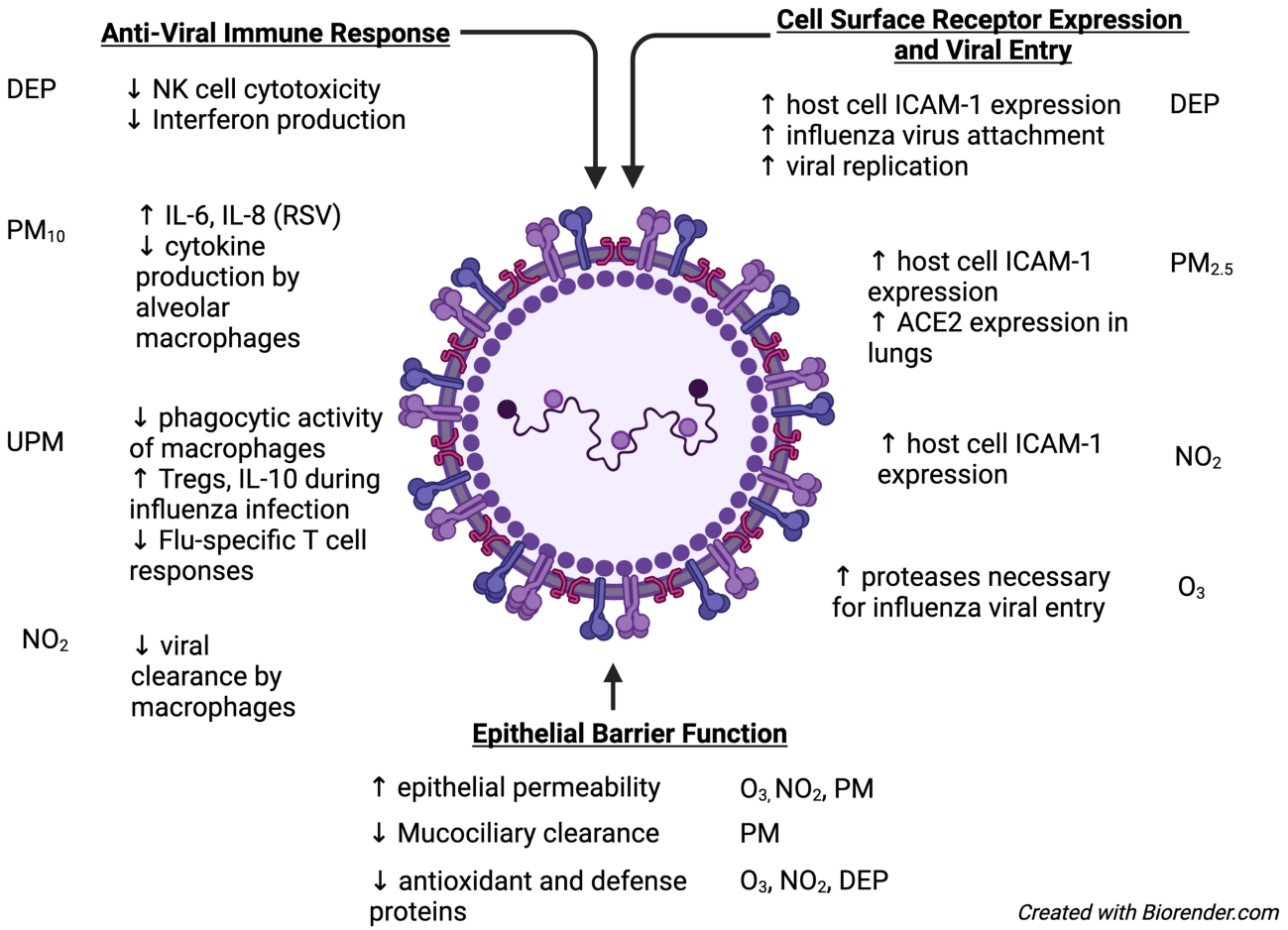

Figure 1 Proposed mechanisms by which air pollutants contribute to viral respiratory infection susceptibility and severity.

NLRP3 inflammasome was observed with increased production of interleukin (IL)-1β following influenza A infection, but not RSV infection, suggesting an exaggerated inflammatory response.[79] Similar to PM, DEP exposure was associated with enhanced susceptibility and inflammatory response to influenza infection in primary human bronchial epithelial cells[80,81] and mouse models.[82]

Primary human nasal epithelial cells infected with RV and exposed to NO_2 or O_3 showed enhanced release of the inflammatory cytokine IL-8 compared to RV infection alone or pollutant exposure alone, suggesting that epithelial-derived inflammation from viral respiratory infection is enhanced by exposure to air pollutants.[83] However, other groups observed a reduction in virus-induced lung injury[84] and mortality[85] when mice were exposed to O_3 during influenza infection, potentially owing to *dampening* of the immune response to infection.[84] Similarly, alveolar macrophages exposed to O_3 showed diminished cytokine production after infection with RSV.[86] The effects of O_3 exposure on respiratory viral infection may be virus-specific.

Mice exposed to ultrafine carbon black prior to RSV infection showed skewing of the immune response away from an antiviral Th1 milieu (IFN-gamma, IL-12, and IP-10) towards an allergic, Th2-predominant inflammatory milieu (RANTES, eotaxin, MCP-1, MIP-1a, MIP-1b, and IL-13).[87,88] Ultrafine PM exposure in neonatal mice resulted in increased amounts of immunosuppressive T-regulatory (Treg) cells and IL-10 following influenza infection and showed decreased influenza-specific T-cell responses.[89] Exposure to carbon black particles was associated with increased morbidity from RSV in these mice, including increased airway hyperresponsiveness.[90] Similar Th2 skewed airway inflammation was observed after exposure of primary respiratory epithelial cells to diesel exhaust particles (DEP), a type of PM,[80] which may increase susceptibility to viral infection. Chronic exposure to DEP was associated with decreased interferon production in response to influenza infection in mice; infection-specific antibody titers were also reduced compared to controls.[91]

Altered Epithelial Barrier Function

The epithelial barrier represents the first line of defense against inhaled pathogens. Integrity of epithelial junctions, mucociliary clearance, and antioxidant and antimicrobial protein composition of airway lining fluid are key defenses. Exposure to O_3,[92,93] NO_2,[94,95] and PM[96] has been shown to alter airway epithelial permeability.[66] Rats exposed to O_3 and injected with an IV tracer showed increased presence of tracer in bronchoalveolar lavage fluid (BAL) compared to rats exposed to clean air, suggesting disruption of the airway epithelium induced by O_3.[93] Short-term exposure of hamsters to NO_2 showed significant but transient disruption of bronchiole tight junctions (TJ) with as little as 6 hours of exposure.[97] Experiments testing the effect of long-term NO_2 exposure in hamsters showed significant, non-reversible TJ disruption.[94] Liu et al showed that PM exposure of primary human bronchial epithelial cells infected with *Pseudomonas aeruginosa* resulted in oxidative injury with degradation of TJs and increased intracellular bacteria.[96] PM was also shown to impair airway mucociliary clearance,[98] and increase production of the pathogenic glycoprotein mucin MUC5AC.[99] Exposure to O_3[100] in vivo and NO_2[101] ex vivo were associated with depletion of antioxidant proteins from lung lining fluid. Epithelial cell-derived defense proteins like surfactants SP-A and SP-D are important in the defense against respiratory viral infection.[102,103] Ciencewicki et al observed that DEP exposure of mice increased susceptibility to infection with influenza virus by reducing expression of SP-A and SP-D.[82] Interestingly, SP-D was previously shown to bind SARS-CoV-1 spike protein, which could suggest a defensive role against SARS-CoV-2.[66,104]

Altered Cell Surface Receptor Expression and Viral Entry

Pollutants may enhance susceptibility to viral infection by altering viral entry into respiratory epithelial cells. Exposure of rat lung epithelial cells to DEP resulted in upregulated expression of intercellular adhesion molecule 1 (ICAM-1), the receptor used by RV to gain entry into the cell, in a concentration-dependent manner, increasing opportunities for viral entry;[105] similar effects were observed with NO2 exposure in vitro.[83] Human nasal and bronchial epithelial cells exposed to DEP showed increased influenza virus attachment to epithelial cells and increased numbers of influenza-infected cells 24 hours after application of virus.[80] Similarly, mice exposed to DEP had more severe influenza infection assessed by the presence of lung consolidation, increased viral replication and decreased antiviral interferon production compared to controls.[91] Mice exposed to $PM_{2.5}$ showed upregulation of ACE2 expression in the lungs,[106] and it was suggested that PM-induced overexpression of ACE2 may impact susceptibility to SARS-CoV-2 infection and infection severity.[107] The effects of O_3 exposure on viral respiratory infection are less consistent. O_3 exposure of human nasal epithelial cells resulted in increased expression of proteases that cleave influenza HA surface protein, an essential step in viral entry into the cell, thus promoting viral entry and enhancing viral replication.[108] However, primary human bronchial epithelial cells exposed to O_3 prior to RSV infection showed decreased viral production.[109] Mice exposed to O_3 and infected with influenza showed reduced severity of lung injury and reduced immune response to infection with fewer T and B cells recovered from the lungs and reduced influenza-specific antibody titers in serum.[84]

Impaired Cytotoxicity

Pollutant exposure may impact the ability of immune cells to engulf and/or kill viral-infected cells.[110–112] Rose et al found that mice exposed to NO_2 required 100-fold lower amounts of murine cytomegalovirus to become infected compared to mice exposed to clean air, and NO_2-exposed mice also showed signs of decreased clearance of the virus by macrophages.[112] Alveolar macrophages exposed to PM_{10} infected with RSV showed reduced activation, cytokine production, and uptake of viral particles, suggesting impairment of the antiviral response.[110] Guinea pig alveolar macrophages exposed to PM_{10} and infected with RSV showed markedly reduced viral replication and infection-induced inflammatory cytokine production.[111] Using a macrophage cell line, Renwick et al observed that exposure to ultrafine particulates significantly impaired phagocytic activity.[113] Natural killer (NK) cells stimulated with polyinosinic:polycytidylic acid (pI:C) to simulate viral infection and DEP showed reduced production of IL-1β, IL-8 and TNFα and reduced expression of granzyme B and perforin. Cell-mediated cytotoxicity functional assay showed a significant reduction in cytotoxic activity with pI:C+DEP compared to pI:C alone.[114] BAL fluid cells from volunteers with repeated exposure to NO_2 showed reduced quantities of cytotoxic T cells and NK cells but intact phagocytic activity of alveolar macrophages.[115]

Direct Viral Transmission

In addition to increasing susceptibility to viral respiratory infection, PM may serve as a carrier for viral particles. Hsiao et al detected influenza virus within samples of $PM_{2.5}$ and suggested that this could be a mode of direct transmission of virus to the airway epithelium.[116] Multiple research groups have identified SARS-CoV-2 virus within $PM_{2.5}$ from air samples supporting this conclusion, with the caveat that temperature, humidity, and other weather conditions can also affect the efficiency of viral transmission.[71,73,117] However, the World Health Organization (WHO) has concluded based on properties of the virus that ambient air pollution is not likely to contribute to SARS-CoV-2 transmission.[118]

Conclusion

There is substantial evidence supporting the relationship between natural and anthropogenic sources of climate change, namely air pollution, and increased susceptibility to respiratory infections through several proposed mechanisms. Conversely, it is possible that climate change could have some positive effects on respiratory viral infection due to shorter, warmer winters, particularly in the case of RSV. However, this comes at the expense of increased exposure to toxic air pollutants and susceptibility to respiratory viruses whose transmission is not impaired by warmer temperatures (as appears to be the case with SARS-CoV-2, for example). Another important consideration is that climate change also alters animal migration patterns and shifts habitats such that humans and domesticated animals are in closer proximity to wild animals.[119] These changes can be the catalyst for the emergence of new zoonotic viruses with potential to cause future pandemics. The need has never been greater for aggressive interventions to reduce emissions of greenhouse gases and toxic pollutants to mitigate the effects of climate change. The initial rapid fall in air pollutants around the world during the initial COVID-19 lockdowns showed us what is possible, though at a significant economic price. A report from a joint workshop between the WHO, the European Respiratory Society, and several other scientific societies noted that the COVID-19 pandemic has brought to light the vast interconnectedness between climate change and infectious disease.[118] Without significant long-term strategies for phasing out fossil fuel use in favor of green energy, we will likely see an increase in the burden of respiratory viruses in human populations, particularly in vulnerable groups such as children, the elderly, and those with chronic respiratory disease.

Disclosure

The author has no conflicts of interest in this study to disclose.

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