Air Pollution and Respiratory Infections: Reviewing the Science

Review Summary

- Tissue and animal studies indicate that exposure to air pollution may directly increase susceptibility to infectious lung diseases by interfering with host immune defenses in the lungs.

- Human population studies indicate that when air pollution spikes, more people go to the hospital with a respiratory infection, like pneumonia or bronchitis, the following week.

- Long-term exposure to air pollution contributes to the development of a number of chronic cardiac and respiratory illnesses, like coronary heart disease, lung cancer, COPD, and asthma, which increase the severity and risk of dying from respiratory infections. The World Health Organization attributes 26% of global respiratory infection deaths to air pollution (WHO, 2016).

- In epidemic or pandemic situations, where there is no level of immunity present in the population, the main driver of disease occurrence and therefore mortality is the level of social interaction occurring, not air pollution. While several studies have observed associations between air pollution and respiratory epidemic deaths (Spanish flu, SARS, COVID-19), and this association is scientifically plausible, all of these studies used grouped data, not individual data, and therefore should be interpreted with caution.

- However, the science is clear that air pollution (like particulate matter, nitrogen dioxide, and ozone) is a strong driver of disease, both infectious and non-infectious. Individuals should take steps, now and always, to protect themselves from harmful air pollution, and policymakers should prioritize protecting residents by cleaning up the air.

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Lab studies examining the relationship between air pollution and respiratory infections

A variety of research points to the conclusion that exposure to air pollution, both long and short term, may increase susceptibility to infectious lung diseases. Experiments on lab animals demonstrate that exposure to air pollutants – including particulate matter (PM) (Zhao et al., 2014, Zelikoff et al., 2003), nitrogen dioxide (NO_2)(Chauhan et al., 2003, Rose et al., 1989), and ozone (O_3)(Olivieri et al., 2005, Schlesinger et al., 1987) – increased susceptibility to both bacterial and viral lung infections by interference with immune defenses. Three specific pathophysiologic mechanisms, as demonstrated through lab studies, appear to be at play: inhibition of bronchial ciliary function, impaired alveolar macrophage response, and altered cytokine release.

One of the first lines of defense the body has against respiratory pathogens are cilia, which are the tiny hair-like structures that line the tubes of the respiratory tract. They move together in a wave-like pattern to transport mucus, which traps small particles like dust, pollen, and germs, up and out of the lungs. Cilia, however, can become overwhelmed by the toxicity or the volume of pollutants like nitrogen dioxide or particulate matter, thereby slowing or even stopping the transport of unwanted inhaled material out of the body (Cao et al., 2020, Bayram et al., 1998, Helleday et al., 1995). The longer a pathogen is sitting next to the cells lining the inside of the lungs, called the epithelium, the better chance it has of invading and colonizing, causing infection.

Alveoli are the tiny air sacs within the lungs at the end of the bronchioles (the smallest branches of the airway tubes). The alveoli perform the critically important job of absorbing oxygen into and removing carbon dioxide from the blood steam. They also contain one of the next line of defense of the immune system: the alveolar macrophages. A macrophage is a type of white blood cell that is responsible for detecting, consuming, and destroying invaders like bacteria and viruses, but also microscopic pollutants like particulate matter. Studies show us that when macrophages are working actively to clear the lungs of particulate matter, they are less efficient at removing pathogens that cause infectious diseases (Becker et al., 2003, Selgrade et al., 1994, Frampton et al., 1989, Kumae et al., 2006).

Cytokines are proteins that help regulate the immune system by acting as messengers between cells. They are responsible for many important functions of the immune system, like helping the alveolar macrophages recruit other immune cells to aid in eliminating pathogens. But too much cytokine production can lead to sustained inflammation, which may lead to worse outcomes in an infected individual. Studies indicate that exposure to air pollution both decreases the helpful production of cytokines in response to a pathogen and increases the overproduction of inflammation-causing cytokines (Michael et al., 2013, Sawyer et al., 2010, Devalia et al., 1993). Through these mechanisms, individuals exposed to air pollution may be more susceptible to infections and also fare worse once they have acquired them.

Human population studies examining the impact of air pollution on healthcare utilization for respiratory infections

Many epidemiologic studies have found positive relationships between exposure to air pollution and healthcare utilization for infectious lung diseases. Effects were seen across the human lifespan, with the strongest associations seen in young children and the elderly. Healthcare utilization data helps us understand patterns of specific diseases. Doctor's office and ER visits tell us more (but not all) about incidence of the disease than hospitalizations, since only severe cases are hospitalized. Hospitalizations can give us an idea about incidence but are a better indicator that more severe disease is occurring.

A meta-analysis of seventeen studies reviewed the relationship between daily levels of ambient air pollution and hospital visits (ER visits and hospital admissions) for pneumonia in children under 18 (Nguyen et al., 2017). Their analysis showed positive associations between short-term exposure to all pollutants considered ($PM_{2.5}$, PM_{10}, SO_2, NO_2, and 0_3) and pediatric hospital visits due to pneumonia. That is, a few days after an area experienced poor air quality, more children went to the hospital with pneumonia. The associations were observed even in countries with low mean levels of pollution, such as in New Zealand, where the 24-hour average for $PM_{2.5}$ is ≤ 11 $\mu g/m^3$.

A separate meta-analysis looked at long-term exposure to particulate matter ($PM_{2.5}$) and occurrence of acute lower respiratory infections (ALRI) in young children (0-2 years old), which includes both pneumonia and bronchitis (Mehta et al., 2011). A 10 $\mu g/m^3$ increase in $PM_{2.5}$ annual average concentration was associated with a 12% increased risk of ALRI occurrence as measured by either physician diagnosis or hospitalization.

A research study done along the Wasatch Front in Utah, an area with periodic high levels of outdoor air pollution, examined 4,336 pneumonia cases across several hospitals and found positive associations between levels of $PM_{2.5}$ above 12 $\mu g/m^3$ within 6 days of presentation to the ER and instances of pneumonia, severe pneumonia, and inpatient mortality, particularly in individuals over 65 years of age (Pirozzi et al., 2017). The researchers estimated that reducing $PM_{2.5}$ daily averages below this level would prevent 76-112 cases of pneumonia in this region.

Similarly, Croft et al. (2018) found that increased ER visits and hospitalizations for pneumonia and influenza were associated with increased $PM_{2.5}$ concentrations during the previous week. Tian et al. (2019) found a similar pattern with pneumonia and both $PM_{2.5}$ and PM_{10}. Li et al. (2016) found that $PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO exposures were associated with increased outpatient visits for acute bronchitis and pneumonia.

Epidemic-specific studies

Studies on community-acquired pneumonia and influenza are helpful in understanding patterns of incidence and severity of respiratory infections in relation to air pollution.

However, when considering novel viruses against which no one has any level of immunity, we must also consider studies that specifically look at epidemic or pandemic viruses, which are limited in number and quality. It is important to remember that in epidemic situations, the main driver of disease occurrence and therefore mortality is the level of social interaction occurring, not air pollution.

A study from the National Bureau of Economic Research (Clay et al., 2018) examined historical mortality rates from the 1918 Spanish influenza pandemic, which infected one-third of the global population and killed over 50 million people. The researchers compared mortality rates between U.S. cities that primarily burned coal to generate electricity, a major source of air pollution at the time, versus those that did not. They estimate that the air pollution in those coal-powered cities was responsible for between 30,000 and 42,000 excess deaths (19-26% of the total pandemic mortality).

An ecologic study done in China (Cui et al., 2003) found a positive association with regions of worse air quality – as measured by an index of particulate matter, sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone – and mortality rates from SARS (severe acute respiratory syndrome). They found that patients from regions with the worst air quality were twice as likely to die from SARS compared to those from regions with a low air pollution index. It should be considered that this study did not control for confounding factors such as socioeconomic status, smoking, age, and gender, which may have been hidden factors influencing the observed mortality rates.

Studies on COVID-19 and air pollution

In March 2020, the Italian Society of Environmental Medicine observed in a position paper an association between the geographical distribution of daily PM_{10} exceedances (over 50 $\mu g/m^3$) and the spreading of COVID-19 prior to the shutdown imposed by the Italian government. The researchers hypothesized that the high COVID-19 mortality rates in northern Italy may be related to high particulate matter levels in the region. They also proposed that particulate matter may act as a physical "carrier" for the spread of the disease, and that more research should be done to determine if this could be true. A more conservative conclusion would be that long-term exposure to air pollution chronically impairs human health and thereby leads to worse disease outcomes for those who have acquired the disease. However, in a preliminary paper, not yet peer reviewed (Setti et al., 2020), scientists have found COVID-19 RNA on the surface of PM_{10} from samples collected near an industrial site in Bergamo, Italy. No assumptions can yet be made from this finding since we don't yet know whether the virus survives or can infect people after being inhaled while adsorbed to particulate matter.

Epidemiologists from Harvard looked at long-term $PM_{2.5}$ averages and mortality rates from COVID-19 for 3,000 U.S. counties (98% of U.S. population) up to April 22, 2020. In a not-yet-peer-reviewed paper (Xiao et al., 2020), the researchers calculate that each 1 $\mu g/m^3$ increase in the 17-year average $PM_{2.5}$ level for a given county is associated with an 8% increase in the COVID-19 death rate. This study did control for the following confounders

at the county level: population density, age, poverty level, race, education level, socioeconomic status, obesity, smoking status, number of hospital beds, average temperatures, and state level number of COVID-19 tests performed. But this was another ecologic study that did not measure exposure or outcome on the level of the individual, but rather on the county level. Such findings should be interpreted with caution. The authors hypothesize that since long-term exposure to $PM_{2.5}$ adversely affects the respiratory and cardiovascular systems, it can also worsen the severity of COVID-19 symptoms and therefore may increase the risk of death in those who have acquired the disease.

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