Air Pollution and Inflammatory Skin Disease—Can Clinicians Make Recommendations to Reduce Risk?

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The Global Burden of Disease Study estimated that exposure to air pollution resulted in 103.1 million lost years of healthy life in 2015, primarily due to the impact of fine particulate matter with a diameter less than 2.5 μm (PM_{2.5}) on cardiovascular and respiratory disease. While these impacts are well established, additional research on other health effects remains important to inform regulatory thresholds by governing bodies. The study examining air pollution and psoriasis elsewhere in JAMA Network Open by Wu et al adds to a growing body of literature on the association of air pollution with inflammatory skin disease. The study leveraged data from the UK Biobank, a population-based cohort of nearly 500,000 adults residing in the UK, that included robust estimates of annual average near-surface air pollutants at a 1 × 1-km resolution between 2006 and 2021. The authors found that long-term exposure to air pollutants, including PM_{2.5}, particulate matter with a diameter less than 10 μm (PM_{10}), nitrogen dioxide (NO_{2}), and nitrogen oxides (NO_{x}), was associated with a 34% to 121% increased risk of incident psoriasis when comparing individuals in the highest quartile of exposure with those in the the lowest quartile of exposure. Even in areas where air pollutant levels were lower than the 2005 World Health Organization (WHO) global guidelines, 3 of the 4 pollutants (PM_{2.5}, PM_{10}, and NO_{2}) were found to be associated with 60% to 103% increased risk of incident psoriasis for those in the highest quartile compared with those in the lowest quartile of exposures.

The updated 2021 WHO air quality guidelines reduced the recommended acceptable levels from 10 to 5 μg/m^3 for PM_{2.5}, 20 to 15 μg/m^3 for PM_{10}, and 40 to 10 μg/m^3 for NO_{2}, highlighting how regulatory recommendations have evolved over time. However, these recommendations are variably implemented. Lower-income countries, especially in East and South Asia, currently have the highest levels of air pollution globally, and the gap between higher- and lower-income countries appears to be widening. Between 1990 and 2015, the proportion of PM_{2.5}-attributable deaths in lower- and middle-income countries increased from 15.9% to 16.5% but decreased from 10.0% to 8.1% in higher-income countries, partially due to clear air policies. Furthermore, even within higher-income countries such as the US, there remain disparities. For example, racial and ethnic minoritized populations are disproportionately exposed to PM_{2.5} and other pollutants across states, urban and rural areas, and income levels.

It is also important to consider the differential impacts of pollutants on other vulnerable populations. For example, older adults may experience greater exposure to PM_{2.5} due to skin barrier decline that occurs with age. The mean age of the population studied by Wu et al was 57 years, and the authors found in another study in China that the association between PM_{2.5} and psoriasis outpatient visits was largest among older adults. Future work should examine whether exposure to air pollution could help to explain why there is a second peak of psoriasis incidence in older adulthood.

Psoriasis is a chronic systemic inflammatory condition driven by T-helper (Th) 17 immune pathways triggered by a combination of genetic, lifestyle, social, and environmental factors. In the study by Wu et al, the authors found an interaction with genetic risk of psoriasis: there was a 144% to 329% increased risk of incident psoriasis among those with the high genetic risk living in areas with higher air pollution levels in comparison with those with low genetic risk living in areas with lower air pollution levels. Although the exact mechanisms by which air pollutants exacerbate or cause psoriasis have yet to be elucidated, research to date points to the alteration of the skin microbiome.
oxidative stress, and inflammatory pathways. Future work examining specific gene-by-environment associations may help to elucidate mechanisms and preventive measures for patients.

For example, there is evidence of an interaction between genetic variants in the gene for the aryl hydrocarbon receptor (AhR) and atopic dermatitis, an inflammatory skin disease that is distinct from psoriasis but does have some overlapping pathways. Basic research has shown that after exposure to air pollution, AhR acts as a transcription factor and can cause an atopic dermatitis–like phenotype in mouse models. A population-based study found that minor allele carriers of the AhR variant rs2066853 had an elevated risk of atopic dermatitis with exposure to air pollution. Notably, topical tapinarof, an AhR agonist, has shown efficacy in phase 3 clinical trials for atopic dermatitis and is already US Food and Drug Administration–approved for the treatment of psoriasis. These seeming paradoxical effects of worsening atopic dermatitis from AhR activation by air pollution, but improvement of inflammation with AhR activation by topical tapinarof may be explained by the presence of ligand-specific interactions that produce different downstream effects from the AhR receptor. A better understanding of the different mechanisms by which AhR activation can stimulate gene expression could help to elucidate the potential impact of treatments targeting AhR or downstream pathways in polluted regions. More generally, future research is needed on gene-environment interactions with air pollution and the potential role of treatments on the interaction between air pollution and inflammatory skin disease.

Despite accumulating evidence on the interactions between air pollutants and inflammatory skin disease, data to support practical clinical recommendations are lacking. It is unclear whether topical moisturizers and treatments are likely to protect high-risk individuals or whether they may increase the penetration of air pollutants. While it may seem intuitive to counsel patients to use protective clothing, there are little data to support the efficacy of such a recommendation. Potential benefits could be outweighed by reduced exposure to ultraviolet radiation, which can have beneficial effects on inflammatory skin disease. Furthermore, it remains unclear whether the impact of air pollution on skin disease is fully mediated through cutaneous pathways; inhalation and ingestion of air pollutants can also result in systemic effects. As climate change induces worldwide alterations in air quality, additional research to inform clinical recommendations on how best to protect patients from and treat pollution-sensitive inflammatory skin disease is urgently needed.
REFERENCES


