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Characterization of Air Pollution Exposures as Risk Factors for Tuberculosis Infection

Tuberculosis is a leading cause of death owing to infectious disease worldwide, accounting for 1.4 million deaths of the 10 million persons with active tuberculosis disease in 2019 (1). Although improvements in the diagnosis and management of tuberculosis have led to declines in mortality over the past two decades, annual incidence remains unchanged. With the rapid growth in the world's population, which currently includes approximately 1.7 billion persons with prevalent latent tuberculosis infection (2), a higher absolute number of incident tuberculosis cases progressing from latent infection threatens to offset gains from improved case detection and treatment success. At the first-ever United Nations High Level Meeting on Tuberculosis in 2018, new commitments were made to scaling up prevention measures. However, low rates of uptake and completion of tuberculosis preventive therapy and lack of highly effective vaccines highlight the need for new public health approaches to tuberculosis prevention (1).

One area of tuberculosis epidemiology that offers opportunities for improving prevention is enhancing our understanding of how exposure to environmental air pollutants may influence the risks of transmission and progression from latent infection to active disease (3). For example, occupational exposure to dust and smoke, including silica, are well-recognized risk factors for active tuberculosis disease (4, 5). Second-hand exposure to tobacco smoke is also associated with a moderately higher risk of latent tuberculosis infection and a dose-dependent risk of active tuberculosis disease, especially among children (6). Exposure to solid fuel smoke and kerosene for heating and cooking are other potential factors that may increase the risk of active tuberculosis disease; however, results from epidemiological studies remain mixed (7–10), and better studies are needed to understand if these are important risk factors. Even less is known about ambient air pollution. At least one analysis of data from Beijing and Hong Kong has shown an association between seasonal concentrations of particulate matter $\leqslant$2.5 μm in aerodynamic diameter ($PM_{2.5}$) and active tuberculosis case notifications (11).

In this issue of the *Journal*, Blount and colleagues (pp. 1211–1221) present the results of a cross-sectional study examining associations between multiple urban environmental exposures and latent tuberculosis infection among 109 child household contacts of 72 patients with active tuberculosis in Hanoi, Vietnam (12). Key indoor air pollution exposure variables were assessed by questionnaire and were complemented by measurement of personal exposures to $PM_{2.5}$ over 48–72 hours. The authors constructed a multiple variable logistic regression model to explore the associations between these exposures and the outcome of latent tuberculosis infection, as defined by a positive tuberculin skin test.

This study makes some important observations. First, it confirms findings of a positive association between secondhand tobacco smoke exposure and latent tuberculosis infection. Second, the authors found that living on the ground floor was associated with a higher risk of latent tuberculosis infection when compared with floors above ground level. The authors conclude that indoor air pollution

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increases the risk of latent tuberculosis infection and suggest that mitigating these exposures may lead to better tuberculosis control.

There are some limitations to this study. Although the assessment of personal exposures to $PM_{2.5}$ was an important addition, the lack of an association with either questionnaire-based measurement of environmental risk factors or latent tuberculosis infection points to the complexity of air pollution assessment in epidemiological studies. First, air pollution assessment of urban exposures may require measurement of more than one pollutant ($PM_{2.5}$, black and elemental carbons, nitrogen oxides, carbon monoxide, sulfur dioxide, and ozone) to understand how air pollution exposures are associated with tuberculosis infection. Second, direct assessment of personal exposures over longer periods of time combined with historical reconstruction of air pollution exposures over 2–5 years may be required to improve our understanding of the relationship between air pollution and tuberculosis risk.

If air pollution increases transmission of tuberculosis, then what further actions are in order? First, there is a need for additional research to further characterize the sources, exposure intensities, and attributable tuberculosis risks associated with air pollution. Second, the causal mechanisms between the environment and the host response to tuberculosis are not well defined, and the findings in this study likely also generalize to other lung infections, including nonmycobacterial tuberculosis. Finally, these findings are a reminder to nonpulmonologists that tuberculosis is predominantly a pulmonary disease. Accordingly, assessing environmental exposures is an important part of both clinical history-taking and disease control and should inform both individual counseling and population messaging about tuberculosis risk and prevention. ■

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