Editorial

Mycobacterium tuberculosis Transmission in Healthcare Settings: Is It Influenced by Coinfection with Human Immunodeficiency Virus?

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Infection with Mycobacterium tuberculosis is a recognized occupational risk in healthcare environments, and guidelines exist for preventing its transmission in these settings.[1] In the United States, several recent outbreaks of tuberculosis, including outbreaks of multidrug-resistant strains of *M tuberculosis*, have heightened concerns about nosocomial transmission and served as a reminder of the need to fully implement measures to minimize the risk of tuberculosis infection within healthcare facilities.[2-7] In each instance, coinfection with human immunodeficiency virus (HIV) and *M tuberculosis* contributed to the spread of the outbreak by accelerating the progression from tuberculosis infection to active disease. However, in none of the outbreaks did the investigators find evidence suggesting that HIV-infected patients with tuberculosis are more likely to transmit tuberculosis than non-HIV-infected tuberculosis patients.

In this issue, Di Perri and colleagues report that the rate of clinically active tuberculosis in healthcare workers caring for HIV-infected patients with tuberculosis was significantly higher than the rate in healthcare workers caring for non-HIV-infected patients with tuberculosis.[8] At first glance, the data appear to support the authors' argument. However, under more careful scrutiny, at least five factors potentially confound the scientific argument presented by Di Perri and colleagues.

First, no information is provided about the HIV infection status or other medical conditions of the healthcare workers who developed active tuberculosis. In the United States, HIV-infected healthcare workers commonly volunteer to care for HIV-infected patients. These healthcare workers would be at greatly increased risk of developing active tuberculosis if exposed to and infected *with M tuberculosis*. Thus, the apparent difference could be due to host factors causing an increased risk of progression to active disease, rather than to an increased risk of becoming infected.

Second, the best measure of recent infection with tuberculosis in immunocompetent healthcare workers is documentation of tuberculin skin-test conversions following exposure to patients with infectious tuberculosis. Di Perri and colleagues state that, because of routine BCG vaccination of healthcare workers at employment, tuberculin skin-test evaluations in the five hospitals are unreliable. However, no clinical data are presented to clearly demonstrate that the tuberculosis diagnosed in the nine healthcare workers represented primary tuberculosis after recent infection versus reactivation of latent tuberculosis. Therefore, reactivation of latent tuberculosis remains a possibility, especially for healthcare workers originating from areas with high rates of tuberculosis.

Third, no laboratory data are presented to suggest that both patients and healthcare workers were infected with *the same* strain of *M tuberculosis*. Recent epidemiologic observations of possible nosocomial tuberculosis transmission have been confirmed by matching patterns of DNA-fingerprints (restriction fragment-length polymorphism) of *M tuberculosis* strains obtained from patients and healthcare workers.[4,5,7]

Fourth, since the acid-fast bacilli isolation precaution procedures and facilities are not described in detail, it cannot be determined whether differences in these could account for the observed differences in the incidence of active tuberculosis among healthcare workers in the three infectious diseases wards and the two pneumology wards. When describing the settings where HIV-infected tuberculosis patients are hospitalized, the authors state that "facial masks are routinely worn by members of hospital staff." However, these facial masks were either "usually" or "rarely" worn in the pulmonary and tuberculosis wards housing non-HIV-infected tuberculosis patients. Ventilation control precautions for acid-fast bacilli isolation are considered much more important than masks (ie, particulate respirators) in preventing tuberculosis transmission.[1] In many of the

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recent nosocomial tuberculosis outbreaks, lack of early identification of tuberculosis and the resulting delayed initiation of appropriate therapy and acid-fast bacilli isolation are thought to have substantially contributed to the spread of tuberculosis. Environmental evaluations of acid-fast bacilli isolation rooms during outbreak investigations also demonstrated that the airflow systems often did not have negative pressure relative to adjacent hallways and rooms, as expected.[5,7]

Fifth, in this report the rate of active tuberculosis is calculated based on the cumulative number of tuberculosis patients in each ward rather than on the total number of healthcare workers. When the rate of active tuberculosis is calculated based on the total number of healthcare workers among those caring for HIV infected patients (7/135) versus non-HIV-infected patients (2/186), the difference is not statistically significant (relative risk = 2.75; 95% confidence interval = *0.58* to 12.96).

Recent correspondence with the authors of this report have served to clarify some but not all of these potentially confounding variables.[9,10] It will be important to ultimately control for these variables in analyses before we can conclude that caring for HIV-infected patients with tuberculosis carries an increased risk of occupational exposure to tuberculosis.

Why would HIV-infected patients be expected to be more infectious than non-HIV-infected patients? The infectiousness of a person with tuberculosis correlates with the number of organisms that are expelled into the air, which, in turn correlates with the anatomic site of disease, the presence of cough or other forceful expirational maneuvers, the presence and quantity of acid-fast bacilli in the sputum smear, and the presence of cavitary pulmonary disease. Compared to non-HIV-infected patients with tuberculosis, HIV-infected tuberculosis patients are more likely to have extrapulmonary disease, may be less likely to have positive sputum acid-fast bacilli smears, and are less likely to have cavitary pulmonary disease. There is no reason to suspect that they are more likely to cough, or to cough more forcefully. Thus, there are no intrinsic differences between HIV-infected and non-HIV-infected tuberculosis patients that should lead to greater infectivity among HIV-infected patients. In fact, three studies have demonstrated that contacts of HIV-infected tuberculosis patients are no more likely to be infected with *M tuberculosis* than contacts of non-HIV-infected tuberculosis patients.[11-13]

There are several extrinsic factors that may lead to a higher risk of transmission of *M tuberculosis* and that might be misinterpreted as evidence for greater infectivity. Factors common to recent nosocomial tuberculosis outbreaks have included patients with unrecognized tuberculosis, patients with untreated tuberculosis (or in the case of drug-resistant disease, ineffectively treated tuberculosis), and patients undergoing procedures that enhance aerosol generation (eg, bronchoscopy, endotracheal intubation, sputum induction). These factors are common to both HIV-infected and non-HIV-infected patients with tuberculosis.

There is no question about the possibility of tuberculosis transmission in healthcare facilities. However, it is unlikely that there is any substantial intrinsic difference in the infectiousness of HIV-infected and non-HIV-infected tuberculosis patients. Factors that enhance transmission are the same for both groups of patients. The challenge to health providers is to rapidly identify patients who may have infectious tuberculosis, promptly initiate effective acid-fast bacilli isolation precautions, and initiate effective antituberculosis therapy rapidly. The report by Di Perri and colleagues should serve to heighten awareness about the need to quickly implement existing guidelines to prevent tuberculosis transmission and acquisition in all healthcare settings.

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