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Finding and Closing the Gaps in the Tuberculosis Elimination Campaign

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One of the major barriers to the global plan to eliminate tuberculosis (TB) by 2050 is that 30% of individuals with active TB do not receive a diagnosis and are not treated, according to estimates by the World Health Organization (1). This estimate is based in part on national prevalence surveys conducted in higher-burden countries in which all adults selected to participate are interviewed for symptoms and undergo chest radiography, regardless of the presence of symptoms. Sputum specimens are collected for acid-fast bacilli smear and culture for *Mycobacterium tuberculosis* complex, if individuals are symptomatic or if almost any radiologic abnormality is detected (2). Using this highly sensitive radiologic criteria, the majority of prevalent TB cases detected in many high-burden countries are asymptomatic (3), identified early in the TB disease course, or subclinical (4).

The U.S. guidelines for the panel clinics (clinics that conduct predeparture TB screening of adult immigrants and refugees during overseas visa application) involve a very similar strategy of universal

chest radiography followed by sputum examination for those with abnormalities detected using highly sensitive interpretation criteria. For U.S. visa applicants, however, an additional TB evaluation is recommended within 6–12 months of arriving in the United States. This postarrival case-detection process is recommended by the U.S. Centers for Disease Control and Prevention and is performed by state and/or local health departments of the U.S. destination of the new arriver. A major diagnostic gap was closed when the predeparture guidelines for sputum testing with an acid-fast bacilli smear were revised in 2007 to require cultures and assure treatment of applicants with culture-confirmed TB before departure (5). The impact of the culture-based TB screening process in reducing the TB burden among immigrant and refugee populations entering the United States has been well documented. Among Filipino immigrants to California, the postarrival detection of TB dropped by 75% with the addition of cultures to acid-fast bacilli smear testing (6). The benefit of adding sputum culture testing was also apparent nationally, with a reduction of approximately 1,500 TB cases among non–U.S.-born persons from 2007 to 2012 (7).

In this issue of *AnnalsATS*, Liu and colleagues (pp. 1401–1412) provide the first comprehensive evaluation of local and state health department efforts to provide the postarrival evaluation recommended for the immigrants and refugees at increased risk for TB after panel-clinic testing (8). The postarrival evaluations that were completed resulted in 667 TB diagnoses (277 positive culture results), providing a 15.8% increase in cases detected beyond the 4,225 diagnoses resulting from positive culture results in the panel clinics. For state and local health departments, this analysis shows opportunities to improve the completion of postarrival evaluations, and the authors provide an estimate that up to 344 pulmonary TB cases, including 142 with positive culture results, were missed among

the individuals arriving in the United States who were not evaluated. The proportion evaluated among those treated for TB by the panel clinic was 71%, but the low yield of active TB in this treated population raises questions about whether postarrival follow-up is warranted at all or should be targeted for a subset of individuals. The proportion evaluated was only 66% for new arrivers with radiographic evidence of TB who had not received treatment by the panel clinic. The 60% evaluation rate for those with latent TB infection (LTBI) diagnosed overseas, almost all under 15 years of age, is concerning, but the impact is less clear because most immigrants and refugees during those years were not tested with an interferon-γ release assay. Using these data to provide ongoing feedback to local health departments is the first step toward improvement in the evaluation rate.

If adequate resources are provided, a number of TB prevention gaps could be addressed. First, there are potential gaps in the accuracy of the predeparture TB classification that warrant evaluation and improvement. The 36,492 individuals with abnormal predeparture chest radiographs who had negative sputum culture results in the panel clinic and completed the evaluation in the United States would appear to be prime candidates for LTBI treatment if both definite radiographic evidence of TB and positive LTBI test results were obtained. The reasons for LTBI treatment being recommended for only 35% will require further study of radiologic interpretations, LTBI test results, public health funding, and other factors. The use of highly sensitive radiologic criteria has identified a high-risk population, but the expected lower specificity may result in some individuals being required to undergo unnecessary evaluation before departure and after arrival. One potential gap-closing option for improving the accuracy and efficiency of identifying TB cases that could be evaluated is the use of artificial-intelligence interpretation of chest radiographic screening findings (9). Perhaps
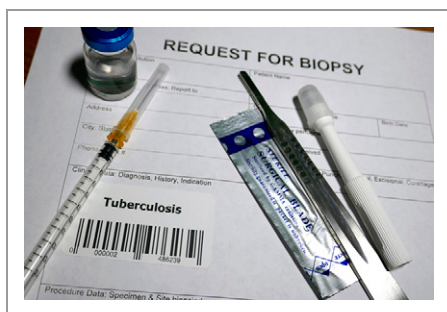
the TB risk prediction among those with abnormal chest radiographs could be improved by the addition of predeparture interferon-γ release assay testing or other predictive tests under evaluation.

Despite these gaps, radiologic and culture-based screening of adults with initial LTBI testing of children as instituted in the U.S. TB screening process for immigrants and refugees is highly effective in preventing the arrival of infectious TB and has resulted in recommended follow-up for only 4.3% of 2.1 million entrants over 4 years. Immigrant populations arriving in the United States experience a 4.9-fold reduction in TB rates in Years 1 through 9 after arrival and experience a 10-fold reduction in later years (10) when compared with the population remaining in their country of origin. In contrast, this reduction in TB disease after arrival was not observed in the United Kingdom when immigrants were not screened (11).

Although reducing the risk that immigrants and refugees have TB on arrival in the United States is the major focus of the predeparture screening and postarrival follow-up, this process does not prevent

infectious TB that later develops from untreated LTBI. Unlike cases during the year of arrival, most TB cases (76%) among Filipino immigrants to California were among those with normal predeparture chest radiographs (6). Domestic strategies to encourage and achieve high rates of LTBI identification and treatment in new arrivers will make an important difference on our road to TB elimination. Efforts to optimize pre- and postdeparture TB screening represent one step we can take to move a bit closer to the goal of TB elimination.

How can this be accomplished? Without a requirement for the immigrant or refugee to access care or without a systematic care linkage in each U.S. municipality, once health departments receive notification of a newly arrived immigrant or refugee, they must conduct outreach and make efforts to retain those in care so that these individuals can complete a multistep evaluation and, if needed, undergo multiple weeks or months of treatment. Specifically, an ideal process might provide an automatic linkage to care and incentives for

engaging and completing care steps, including treatment. Mandatory evaluation adds a burden to newcomers who have many stressors, but evaluation coupled with incentives with value for the new arriver could help improve outcomes.

TB, like coronavirus disease (COVID-19), is an infectious life-threatening respiratory disease that is found throughout the world. Although hard-won successes have driven the disease downward, *M. tuberculosis* remains the leading killer among infectious pathogens. Among high-impact interventions, screening and testing those who have recently migrated into a country creates an important opportunity for TB detection and treatment for the individual and a method to prevent spread. Providing more opportunities for TB detection and prevention to migrating and nonmigrating persons is a critical step to help us achieve the ambitious goal of TB elimination. ∎

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