

Molecular epidemiology and the dynamics of tuberculosis transmission among foreign-born people

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As incidence rates of tuberculosis fall in wealthy countries and rise in at least some poorer countries, it is not surprising that much of tuberculosis in Canada and the United States occurs in foreign-born people. The high risk of tuberculosis in immigrants to Europe, Australia, the United States and Canada has been well documented.¹⁻⁷ Although several studies have shown that the risk of tuberculosis is greatest in the first 3-5 years after arrival in the host country,^{3,8} others have shown that it persists for an extended period and increases with age.⁹ These findings are consistent with the widely accepted hypothesis that foreign-born people are infected in their country of origin and then either primary disease develops shortly after immigration or the people remain at risk for reactivated disease for the rest of their lives.

Until recently it was not possible to distinguish definitively between primary tuberculosis and reactivated disease, nor was it possible for epidemiologists to determine the proportion of cases due to recent infection and the proportion due to reactivation of remotely acquired infection. The use of DNA fingerprinting to distinguish between epidemiologically related and unrelated strains of *Mycobacterium tuberculosis* offers a new method of solving this problem and has led to the emergence of the field of molecular epidemiology of tuberculosis.

Since the advent of these molecular techniques 10 years ago, numerous community-based studies have been conducted to estimate the incidence of recently transmitted disease and to identify risk factors for recent transmission. These studies typically enroll patients with active tuberculosis, "fingerprint" their isolates and then classify them as having shared (clustered) isolates or having unique (non-clustered) isolates. People with clustered isolates are assumed to belong to a transmission chain, and those with unique isolates are assumed to have reactivated disease. Risk factors for clustering are estimated by comparing the frequency of a characteristic among the clustered cases with that among unique cases.

To some extent these studies have helped clarify the epidemiology of tuberculosis among foreign-born people in countries with low prevalence rates of the disease. Multiple molecular epidemiologic studies in these settings have shown that foreign-born people are more likely to have

unique isolates than clustered ones and that there is little evidence that tuberculosis has spread from foreign-born people to those born in the host country.¹⁰⁻¹² These findings have helped to quell the fear that immigrants are a source of rampant infectious disease transmission and have focused attention on the unexpected transmission among non-immigrants in developed countries.¹³

Despite these reassuring findings, some caution in the interpretation of the results may be warranted. When molecular epidemiologic studies give estimates of the risk of clustering among foreign-born people, they are not assessing the incidence of recently transmitted disease in the population at risk for the disease. Rather, they are comparing the number of cases of recently transmitted disease with the number of cases of reactivated disease. Since foreign-born people are far more likely to have been infected in the past, they are also more likely to have reactivated tuberculosis than are people born in countries with low prevalence rates. This does not necessarily mean that foreign-born people are at low risk of recently transmitted disease, only that they are at greater risk of reactivated disease.

Consider, for example, 2 recently published studies of tuberculosis transmission among foreign-born people in New York City¹⁴ and Denmark.¹⁵ In the New York study Geng and coauthors fingerprinted 546 isolates of *M. tuberculosis*, of which about half belonged to a cluster (thus likely transmitted) and the remainder were unique (interpreted as reactivated disease).¹⁴ Analysis showed that people born outside the United States were much less likely to be in the clustered group (odds ratio 0.47, 95% confidence interval 0.33-0.67). Nonetheless, this study showed that, among the tuberculosis patients who had been in the United States for less than 10 years and who were not HIV positive, almost half had clustered isolates, which suggested recent transmission. Similarly, in the Denmark study of tuberculosis transmission among Somali immigrants, 55% of the tuberculosis cases were clustered.¹⁵ Although it is indeed possible that some of these clustered cases were acquired in Somalia, as the authors suggested, it is perhaps equally plausible that tuberculosis is being transmitted within immigrant communities in the host country. This may be especially likely among very recent immigrants, possibly because the socioeconomic conditions in which they find themselves

lead to transmission of airborne infectious diseases.

The 2 studies of tuberculosis transmission reported in this issue (pages 349 and 353) highlight some of these issues. In the first article, Eduardo Hernández-Garduño and coauthors¹⁶ used molecular fingerprinting to classify all *M. tuberculosis* isolates available in Greater Vancouver over a 3-year period. Although they found that birth outside Canada was strongly associated with the probability of having a unique isolate, they also found that half of the clustered cases involved foreign-born people. Because it is unlikely that half the population of Greater Vancouver was born outside Canada, it follows that, in Vancouver, the risk of recently transmitted tuberculosis must be higher among immigrants than among people born in Canada. Similarly, although the odds ratio for belonging to a cluster was high among Aboriginal patients, there were half as many patients with recently transmitted disease who were Aboriginal as there were who were foreign born. In the second article, Sophie Kulaga and coauthors¹⁷ report on a similar study over a 2-year period in Montreal. Unlike the Vancouver investigators, this group found that Haitian birth was the only risk factor for being in a cluster.

Despite their differences, both of these studies show that 80% of the tuberculosis cases reported in these cities occurred in foreign-born people. Clearly, this group remains at risk for tuberculosis and should be the target of future control strategies.

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