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Foreign-Born Status and Geographic Patterns of Tuberculosis Genotypes in Tarrant County, Texas

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Abstract

Regardless of destination, immigrants arrive with health profiles typical of people in their previous surroundings. Thus, immigrants change the epidemiological profile of destination communities, and immigrant neighborhoods may represent islands of infectious disease. Genotyping has emerged as a useful surveillance tool to track the spread of disease at the molecular level. Yet the spatial distribution of infectious disease at the molecular level associated with migration and immigrant neighborhoods has received little attention. Using molecular genotyping to characterize *M. tuberculosis* isolated from tuberculosis cases, this article analyzes spatial variations of unique molecular *M. tuberculosis* strains by zip code in Tarrant County, Texas. The results suggest that immigrant neighborhoods have higher rates of unique isolates of tuberculosis (suggestive of remote transmission) compared to neighborhoods occupied by the native-born. Neighborhoods dominated by the native-born have higher rates of clustered isolates (suggestive of recent transmission). Therefore, in addition to being culturally distinct, immigrant neighborhoods may also be pathogenically distinct from surrounding neighborhoods.

Keywords

disease clusters; genotypes; migration; tuberculosis

It has long been apparent that immigrant populations change the cultural landscape of the places they migrate to. Immigrants often settle in well-defined communities that form ethnic islands with pronounced and sharply defined social geography. Typically these ethnic

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islands closely resemble the original cultural landscape and are well known as “Chinatowns” or “Little Koreas.” Ethnic islands persist and thrive because they serve important needs of the immigrants; they provide defense, support, cultural preservation, and political representation (Fellman, Getis, and Getis 2007). Less well appreciated than the cultural aspects of these ethnic islands is that they are also islands of illness related to ethnicity. Populations in these ethnic islands develop distinct illness patterns that reflect the host-environment relationship both from the immigrant’s country of origin and from the country of residence. The health characteristics of migrant cohorts are influenced by the health environments and situations at their place of original residence, the environments through which they made the transition, and their new destination (Gushulak and MacPherson 2004). Thus, the population of Little Korea, besides resembling Korea culturally, comprises individuals with genetic, environmental, and communicable diseases that resemble Korea more than the geographic areas surrounding the Little Korea. Knowledge of these geographical trends is important for individual healthcare, the public health, and national infectious disease control or elimination programs.

Mapping of communicable diseases in ethnic islands is particularly important as these illnesses can thrive, spread, and therefore persist within the ethnic island and also spread into the surrounding area. In fact, there is increasing likelihood that infections that are now very well controlled in the native-born community will persist in the migrant population of the ethnic island. As a result, in a manner similar to relocation effects on the geography of cultural diffusion and cultural landscapes, ethnic islands may also contribute to explaining the emergence, spread, and geographical clustering of communicable diseases (Gushulak and Mac-Pherson 2004). The epidemiology of illness in ethnic islands is clinically important to physicians evaluating patients because different illnesses have similar presentations. Initial diagnostic testing, presumptive diagnoses, and treatment are often influenced by the physician’s knowledge of expected patterns of disease in the general area. Managing diseases that originated beyond national borders requires an international public health perspective and insight into morbidity patterns over a much larger area.

Disease mapping has provided important insights into geographic patterns of disease, risk, and mode of spread dating back to the pioneering work of John Snow on cholera. These insights were subsequently used in the first scientifically based epidemic control (Snow 1855). Since then, significant advances have emerged in microbiology that can make disease mapping even more powerful as a tool for disease analysis and control. Particularly relevant for this article and medical geography is the tool of molecular genotyping.

Each species of organisms has an individual phenotype (e.g., tuberculosis or not-tuberculosis) and the species members have a more unique genotype. There are now a variety of techniques that make it possible to separate and categorize organisms with these more unique genotypes into groups based on their genetic structure (Versalovic and Lupski 2002). The broad variability of these unique genotypes allows researchers to map out not just the spatial pattern of illness but also the spatial distribution of different genotypic strains of the illness. Consequently, medical geographers with access to these methods are no longer restricted to the spatial patterns of disease species (phenotype) and location, but can actually map the different genetic strains of the disease. Analysis of the tuberculosis

genotype distribution of bacterial isolates provides a method to identify areas of high tuberculosis incidence as well as areas with ongoing transmission of specific bacterial strains. High rates of clustered genotypes in an area suggests that ongoing tuberculosis transmission among patients in that community is likely (Moonan et al. 2004). Areas with increased unique isolates suggest that the infections were acquired elsewhere—that is, they are imported (Barnes and Cave 2003).

Research Objective

This article examines the spatial distribution of specific *M. tuberculosis* strains in the foreign-born and native-born populations of Tarrant County, Texas. Genotyping is used to characterize *M. tuberculosis* isolated from tuberculosis cases. The spatial pattern of bacterial isolates is mapped at the zip-code level to provide insight into tuberculosis transmission among the foreign-born and native-born populations. We begin with a brief literature review that summarizes the spatial epidemiology of tuberculosis, introduces genotyping methods, and shows recent applications of genotyping in tuberculosis research. A brief description of our methodology and data sources is then followed by our results, findings, and conclusions.

Literature Review

Spatial Epidemiology of Tuberculosis

Tuberculosis is a communicable, airborne respiratory disease caused by *Mycobacterium tuberculosis*. Tuberculosis bacilli are propelled into the air when people with pulmonary tuberculosis (tuberculosis in their lungs), which is contagious, cough, sneeze, or talk, or even during normal breathing. Inhaling even a small number of these airborne bacilli is enough to cause infection. Thus, duration of time spent in close proximity to an infected person is an important determinant of risk. Most persons who are infected with *M. tuberculosis* develop a latent tuberculosis infection and never become ill (CDC 2005). An important minority (5–10 percent) progress from latent tuberculosis infection to what is referred to as active tuberculosis where the affected individual has progressive illness due to growth of *M. tuberculosis* within a bodily organ (CDC 2005). Active tuberculosis can affect any or multiple organs. However, when it involves the lung, as it does in 90 percent of cases, it can result in further transmission of the infection. Left untreated, each person with active tuberculosis disease will infect between ten and fifteen people every year (World Health Organization 2006; Society for General Microbiology 2003). The progression from latent to active tuberculosis occurs most often in the first few years after the initial infection but can occur at anytime during life (Daley et al. 1992; CDC 2005; Taylor, Nolan, and Blumberg 2005). Many situations can increase the probability of a person with latent infection progressing to active disease. The most important of these are immunosuppression from co-infection with the human immunodeficiency virus (HIV; Markowitz et al. 1997; Havlir and Barnes 1999; CDC 2005). Other less powerful risk factors for progression of latent tuberculosis to active disease include diabetes mellitus, chronic renal failure, silicosis, and the use of immunosuppressive medications (CDC 2005).

Despite the availability of specific diagnostic tests, chemotherapy, and vaccination, tuberculosis remains an uncontrolled communicable disease worldwide (Brudey et al. 2006).

An estimated 9 million persons are diagnosed and 2 million die yearly from tuberculosis (Brudey et al. 2006). The incidence of tuberculosis is quite variable and while tuberculosis persists and is aggressively spreading in the developing world it is declining in the developed world. Currently more than 90 percent of the global tuberculosis burden occurs within developing countries (World Health Organization 2005). Reasons for this differential impact of tuberculosis include widespread malnutrition, crowding, medication shortages, inaccessible healthcare, and inadequate public health infrastructure. The most important reason however is the syndemic effect of HIV and tuberculosis. The combination of these infections serves to amplify the spread of tuberculosis.

Increasingly, in developed countries newly diagnosed tuberculosis occurs among foreign-born immigrants. For example, in Denmark, the proportion of tuberculosis cases in foreign-born persons rose from 18 percent in 1986 to 60 percent in 1996 (Carballo and Nerukar 2001). Similarly, in England and Wales, approximately 49 percent of all reported tuberculosis cases occur in people from the Indian subcontinent (Health Protection Agency Centre for Infections 2005). In Germany and France the profile is similar—migrants in those countries are three times and six times, respectively, more likely to be diagnosed with tuberculosis than are native-born persons (Carballo and Nerukar 2001).

The patterns described in Europe are similar to those observed in the United States and Canada where, after decades of steady decline, a period of tuberculosis resurgence emerged in the late 1980s. In Canada, tuberculosis increased by 8.3 percent between 1987 and 1993. Even more striking was the occurrence of tuberculosis cases among the foreign-born population. Although in 2000 the foreign-born comprised only 18 percent of the Canadian population, they accounted for 65 percent of all reported tuberculosis cases in Canada. In fact, tuberculosis reported among the foreign-born population increased from 18 percent in 1970 to 65 percent in 2000 (Health Canada 2003). The trends are similar in the United States where 14,093 cases (4.8 cases per 100,000) were reported in 2005, the lowest recorded since national reporting of tuberculosis cases began in 1953 (CDC 2006). Of this number, 7,656 cases (54.3 percent) were in foreign-born persons, resulting in an incidence 8.7 times that of U.S.-born persons (CDC 2006). Although the foreign-born population contributes disproportionately to overall tuberculosis morbidity in the United States, the number of persons with tuberculosis reported in this population declined by 36 percent from 34.0 cases per 100,000 in 1993 to 21.8 cases per 100,000 in 2005 (CDC 2006).

Many immigrants and refugees entering the United States and Canada originate from countries with high tuberculosis incidence and therefore have a higher risk of having latent or active tuberculosis when they arrive (Enarson, Ashley, and Grzybowski 1997; Zuber et al. 1997). Consequently, tuberculosis is not evenly distributed throughout the United States and Canada, but tends to be disproportionately high in areas with high immigrant populations. In 2003, the three Canadian provinces that attract the vast majority of new immigrants (British Columbia, Ontario, and Quebec) accounted for 87 percent of foreign-born tuberculosis cases (Health Canada 2003). Within these provinces, tuberculosis was also not evenly distributed. A disproportionate number of the cases were reported from areas that can be considered ethnic islands in large cities such as Toronto, Montreal, and Vancouver (Long, Njoo, and Hershfield 1998). In the United States, five states (California, New York, Florida, Texas,

and Illinois) account for 66 percent of the foreign-born tuberculosis cases reported in the United States (Schneider, Moore, and Castro 2005). Similar to the Canadian pattern, major U.S. cities, including New York, Los Angeles, San Francisco, San Diego, Miami, Atlanta, and Houston, all report disproportionately high numbers of cases from ethnic islands.

Additionally, the demography of tuberculosis cases among the foreign-born from each of these states remains largely homogenous, as cases from certain countries were concentrated in specific states, revealing established migration fields (Fellman, Getis, and Getis 2007). In 2003, New York reported approximately 64 percent of the national total of tuberculosis cases among those born in the Dominican Republic; Florida reported 60 percent of the national total of cases among those born in Cuba; Texas and California accounted for 60 percent of the national total of cases among those born in Mexico; and Minnesota reported 55 percent of cases among the Somali-born (CDC 2003). These patterns probably reflect channelized migration patterns and deserve further study.

To summarize then, immigrants change the epidemiological profile in the destination communities in differing ways. For example, migrants moving because of poverty arrive with health profiles typical of those in their previous surroundings. Poverty is associated with similar diseases of poverty no matter where or when it exists (Carballo and Nerukar 2001). Similarly, immigrants from areas with low rates of degenerative diseases such as hypertension, obesity, or cancer may arrive healthier compared to the people in their destination. Auto selection is also a factor—that is, the healthy, more educated are more likely to migrate (Singh and Siahpush 2002). Immigrant neighborhoods may therefore be epidemiologically different and may potentially constitute islands of infectious disease or different strains of existing infectious diseases. Consequently, proper focus and surveillance of disease in immigrant neighborhoods is necessary to identify and then control disease spread within the ethnic island and into the wider community. To date, medical geography research has focused on the spatial distribution of phenotype disease, but the spatial distribution of disease strains associated with migration and immigrant neighborhoods has received little attention.

Medical Geography and Molecular Epidemiology of Tuberculosis

Genotyping of *Mycobacterium tuberculosis*, frequently called fingerprinting, has developed into a powerful epidemiologic tool that has expanded concepts of transmission and changed the understanding of the natural history of tuberculosis infection (van Embden et al. 1993; Barnes and Cave 2003). Genotyping is based on an analysis of chromosomal deoxyribose nucleic acid (DNA). *Mycobacteria*, the genus for tuberculosis, reproduce by binary fission, which means that under stable reproductive conditions nearly all bacilli produced will have identical DNA. However, changes in the DNA do occur spontaneously, but at low frequency. Over time, these changes, known as DNA mutations, have accumulated to produce the diversity of *M. tuberculosis* strains currently circulating in the world. Thus, there is a stable relationship between the geographic origin of the human host and the strain of tuberculosis being carried (Hirsh et al. 2004). The ability to distinguish between strains of *Mycobacterium tuberculosis* offers the potential to track individual strains and as they spread between persons and between places. Through analysis of these types of data it is

possible to identify the locations and behavioral situations associated with tuberculosis transmission and, consequently, to design and implement control measures.

Several methods have been used alone and in combination to genotype *Mycobacterium tuberculosis* isolates. The first widely used method of fingerprinting, restriction–fragment–length–polymorphism (RFLP), digests the genomic DNA with specific restriction enzymes. After separation of the DNA fragments on agarose gel into distinct bands the pattern created by the generated bands can be compared (van Embden et al. 1993). Repetitive elements and insertion sequences are frequently used as target sequences to differentiate between mycobacterial strains. The most widely used epidemiologic application of tuberculosis, RFLP analysis, uses an insertion sequence (IS) known as IS6110. IS6110-RFLP is a stable molecular marker for strain identity and has been used in many epidemiologic investigations. One disadvantage of IS6110-RFLP fingerprinting is that it requires culturing the isolates for several weeks to obtain sufficient DNA (Barnes and Cave 2003).

Spacer oligonucleotide typing (spoligotyping), another method for genotyping, detects direct-repeat locus within the *Mycobacterium tuberculosis* genome that are separated from one another by spacers that have different sequences. Strains that are similar or different can be distinguished by their spoligotype patterns, characterized by the number and identity of spacers (van Soolingen et al. 1995). Spoligotyping simultaneously allows accurate detection of tuberculosis bacteria and distinguishes between strains of *M. tuberculosis* complex bacteria (van Soolingen et al. 1991; Kamerbeek et al. 1997). It provides rapid and accurate results within one day, compared to several weeks using methods such as IS6110-RFLP. One disadvantage is that when used alone it has less power to discriminate between strains than does IS6110-RFLP (Kremer et al. 1999).

Tuberculosis genotyping identifies genetic links between *Mycobacterium tuberculosis* isolates from different tuberculosis patients. It helps to determine whether two clinical isolates of *Mycobacterium tuberculosis* are identical or different. Epidemiologically, individuals identified with the same strain of *Mycobacterium tuberculosis* (i.e., the same fingerprint) are likely to have shared a common chain of transmission within the local environment (Castro and Jaffe 2002). This often means that one person transmitted tuberculosis to the other, or both became infected by a third person, but other more complex or unknown transmission scenarios are also possible (National TB Controllers Association/CDC Advisory Group on Tuberculosis Genotyping 2004). In such cases, additional investigation is required to probe shared epidemiologic links that can explain where and how transmission occurred. Patients who have isolates with matching genotypes are said to belong to the same genotyping cluster. Patients in the same genotyping cluster who share known epidemiologic links—have been in the same place when one of them was infectious—are said to belong to an epidemiologically confirmed genotyping cluster. If two tuberculosis patients have isolates with nonmatching genotypes, this generally indicates remote transmission or reactivation of strains acquired in the distant past (Burgos and Pym 2002). If two patients have isolates with matching genotypes but have no known epidemiologic links (i.e., they live and work in different locations, at different jobs, share no risk factors, and have not spent time at any common location), it is possible that, despite belonging to the same genotyping cluster, the two patients are not involved in the same

chain of recent transmission. In contrast, persons who are infected by strains with unique fingerprints were infected by means of a different exposure, typically outside the local environment.

Population-based investigations typically assume a prevalent tuberculosis strain represents widespread uncontrolled person-to-person transmission. This ultimately gives rise to strain variants that are distinguished by subtle genetic changes. A collection of closely related strains derived from a common ancestor is classified as a group. Over time, progenies derived from a group may disseminate in new populations and produce a second group of related strains.

Applications of Genotyping in Tuberculosis Research

Tuberculosis genotyping has been used to estimate the fraction of cases attributable to recent transmission of *Mycobacterium tuberculosis* (Alland et al. 1994), to document in a single person reinfection with a new strain (Small, Schafer, and Hopewell 1993), and to study patterns of drug resistance (Davies et al. 1999). New York City implemented universal tuberculosis genotyping in 2001 and was able to “identify previously unknown links among genotypically clustered patients, unidentified sites of transmission, and potential false positive cultures” (Clark et al. 2006, 719). From a study conducted in Baltimore, Bishai et al. (1998) found that of the 182 patients who had isolates of *M. tuberculosis* available, 84 (46 percent) showed molecular clustering with 58 (32 percent) defined as being recently transmitted. Only twenty (24 percent) of eighty-four cases with clustered DNA fingerprints had epidemiologic evidence of recent contact. Geographic analysis revealed significant spatial aggregation of the clustered cases with epidemiologic links occurring in areas of low socioeconomic status and high drug use. The study concluded that recently transmitted tuberculosis accounts for a high proportion of tuberculosis cases in Baltimore; such cases occur in geographically distinct areas of the city, and location-based control efforts may be more effective than contact tracing for the early identification of cases.

Tuberculosis genotyping is currently used in clinical medicine in a number of circumstances. Examples include (i) determining whether cultures may be positive as a result of laboratory contamination, (ii) providing evidence that active tuberculosis is due to re-infection with a different tuberculosis strain or if the strain from a patient with recurrent tuberculosis is the same reactivation of an inadequately treated disease, and (iii) evaluating *Mycobacterium tuberculosis* transmission, such as outbreaks (Barnes and Cave 2003).

Tuberculosis genotyping has also been used to evaluate transmission dynamics in specific populations and in defined geographical settings. A study of 623 Dutch tuberculosis cases using genotyping concluded that 17 percent of cases were attributable to recent transmission from a non-Dutch source (Borgdorff et al. 1998). The transmission index, defined as the average number of secondary cases of infectious tuberculosis caused directly or indirectly through transmission from a single potential source case, varied strongly by nationality and was highest among the Surinamese, Moroccan, and Turkish populations. Aggregation of tuberculosis cases of given nationalities within clusters was most pronounced among recent immigrants from Somalia and the former Yugoslavia. These data demonstrate that

tuberculosis transmission varies in different ethnic islands, perhaps in juxtaposition with social mixing patterns that may vary by nationality (Borgdorff et al. 1998).

In summary, incorporating genotyping into traditional tuberculosis epidemiology has been instrumental in confirming suspected outbreaks, identifying cases of unsuspected transmission, and tracking recent transmission of new strains of disease. Yet, application of genotypes in medical geography research is rare. This study combines genotyping of tuberculosis isolates with home address at diagnosis to examine the spatial pattern of molecular clusters of tuberculosis in Tarrant County Texas.

Methodology and Data Sources

This study is part of an ongoing U.S. Centers for Disease Control and Prevention (CDC) study of the molecular epidemiology of tuberculosis. Tarrant County, Texas, was chosen for this study because the ongoing CDC study had already compiled the needed data and made it available. All positive isolates obtained from persons residing in Tarrant County are sent to the Texas Department of State Health Services for DNA fingerprinting (Crawford et al. 2002). For this study the population included all persons newly diagnosed with culture positive tuberculosis at the Tarrant County Health Department between 1 January 1993 and 31 December 2002, a total of 538 cases. Each eligible patient was prospectively identified and participated in a structured interview as part of a routine initial medical evaluation. Epidemiological factors included in this study were age, country of birth, date of entry into the United States, race/ethnicity, onset of symptoms, date of diagnosis, and physical address. Tuberculosis genotyping results were incorporated into the database using unique patient identification numbers.

Mycobacterium tuberculosis culture isolation, identification, and drug susceptibility were conducted at the Texas Department of Health Bureau of Laboratories. Clinical isolate IS6110-based RFLP and PCR (Polymerase Chain Reaction)-based spoligotyping methods were utilized to identify patients infected with the same *Mycobacterium tuberculosis* strain using published methods (van Embden et al. 1993; Kamerbeek et al. 1997). In the RFLP and spoligotyping cluster frequency analysis, clusters were defined as groups of two or more patients living in Tarrant County with *Mycobacterium tuberculosis* bacterial isolates that have 100 percent identical number of band copies, IS6110-RFLP, and spoligotyping patterns (Glynn, Vynnycky, and Fine 1999). We refer to these as *clustered* strain. In contrast, unique strains with non-matching patterns were classified as *nonclustered* or *unique* strains. Tuberculosis incidence at zip-code level was computed using U.S. Census Bureau 2000 population information.

The spatial pattern of molecular clusters of tuberculosis is presented in three steps. First, the spatial pattern for all cases is presented for both unique isolates (Figure 3) and clustered isolates (Figure 4). Next, the spatial pattern for clustered native-born-only cases is presented (Figure 5), and finally, the clustered foreign-born-only cases (Figure 6). Because confidentiality precludes presentation of the exact locations (home addresses) of cases, summary data are presented at the zip-code level. For each zip code, the number of clustered cases is computed as a ratio of the total number of cases—the *clustered ratio*. The zip-code

areas with high cluster ratios have a high proportion of patients with identical isolates or related strains, and thus reveal evidence of recent, ongoing transmission. Low cluster ratios occur in areas with high frequency of unique strains and indicate remote transmission or transmission occurring outside Tarrant County. Chi-square tests of independence and Pearson's product moment correlation are used for the statistical analysis.

Centered on the City of Fort Worth, Tarrant County is located in north-central Texas, to the west of Dallas County, and is part of the Dallas–Fort Worth Metroplex (Figure 1). The U.S. Census estimated the county population in 2001 at 1,486,392, an approximately 24 percent increase since 1990. Foreign-born residents comprised about 12.7 percent of the population in 2000, compared to 13.9 percent for all of Texas. Median household income per capita in 1999 was \$46,179 and per capita income was \$22,548. The figures for Texas as whole were \$39,927 and \$19,617, respectively.

Most foreign-born residents originated from Mexico (118,576). Vietnam was the next largest source of foreign-born residents with 15,789, then India (5,562), China (4,148), and the Philippines (3,064). The European country with the highest population in Tarrant County was the United Kingdom with 3,033. Europe as a whole contributed 4,739 compared to 5,217 from Central America, 5,984 from sub-Saharan Africa, and 7,830 from South Asia.

Figure 1 shows a map of the proportion of the population that is foreign-born. The areas immediately adjacent to the city center to the north (e.g., zip codes 76106, 76111), south (76110), and east (focusing on 76010 and 76011) have much higher concentrations of foreign-born. In contrast, outer parts of the county have low concentrations of foreign-born. Zip codes with high concentrations of foreign-born had low median household and per capita incomes ($r = -0.561$, $p < 0.01$) and ($r = -0.410$, $p < 0.01$), respectively.

Results

The average incidence of tuberculosis for the entire county during the study period was 8.9 cases per 100,000 people. Zip code 76102 recorded the highest average incidence with 94.3 cases per 100,000 people, followed by, on its southern border, zip code 76104 with an average incidence of 55.2 cases per 100,000 people (Figure 2). Both of these zip-code areas are characterized by very low socioeconomic status, high unemployment rates, homelessness, drug use, and poor housing conditions. Zip codes with high percentages of foreign-born had high average incidence rates ($r = 0.260$, $p < 0.05$).

Spatial Patterns of Molecular Clusters of Tuberculosis

Simple choropleth maps are used to display the spatial pattern of these cluster ratios (Gatrell et al. 1996; Cromley and McLafferty 2002). In Figure 3, darker shades indicate higher rates of unique isolates, but in Figures 4–6, dark shades indicate higher rates of molecular clustering. Figure 3 shows the ratio of unique isolates per zip code for all tuberculosis cases in Tarrant County during the study period. This map portrays the wide presence of unique strains in the eastern part of the county, centering on zip-code areas 76010 and 76016, as well as the southeastern part focusing on 76110 and surrounding regions. Comparison of Figure 3 with Figure 1 reveals a broad similarity between the map of unique isolates and the

foreign-born population percentage. Areas with high concentrations of foreign-born appear to have high rates of unique isolates. The northern areas including zip codes 76137 and 76180 have very low average incidence of tuberculosis (Figure 2).

Figure 4 shows the cluster ratio per zip code for all tuberculosis cases in Tarrant County during the study period. A very distinct distribution of isolates can be seen graphically. For example, a high proportion of clustered strains is observed in the core area of Tarrant County. In zip code 76102, 80.4 percent of all reported cases were molecularly clustered strains. In zip code 76105, 76.6 percent of all reported cases were clustered strains. In contrast, other areas had high proportions of unique isolates. In zip code 76010, seventeen of the twenty-six reported cases (65.4 percent) had disease resulting from unique strains. In zip codes 76117 and 76112, 63.6 percent and 62.5 percent, respectively, of the cases were due to unique strains. (Notice the low ratios of clustered isolates in zip codes with high concentrations of the foreign-born, such as 76010, 76106, and 76110.) These maps are invaluable for planning interventions. Although unique strains occur in many areas of Tarrant County (Figure 3), only a few areas show evidence of ongoing transmission and merit aggressive surveillance and case finding.

Figure 5 shows the spatial pattern of molecular cluster ratios for the native-born. The higher rate of molecular clustering over a much larger spatial area contrasts sharply with the much smaller area and lower rate of molecular clustering among the foreign-born (Figure 6). For example, among the foreign-born, three major areas of concentration can be observed in the central part of Tarrant County (centering on zip codes 76102, 76119, and 76134). In contrast, the native-born have a much larger area where the patients have identical isolates. Clearly, areas with more foreign-born population (i.e., ethnic islands) have more unique strains of tuberculosis when compared to areas with native-born patients.

Statistical analysis confirms that unique strains occur more frequently in the foreign-born. A chi-square test of independence comparing the strain type for the foreign-born and the native-born found a significant association ($\chi^2 = 66.375$, $p < 0.01$). Foreign-born persons with tuberculosis were more likely to have a unique strain (71.8 percent) than a clustered strain (28.2 percent). Similarly, native-born persons with tuberculosis were more likely to have a clustered strain (64.7 percent) than a unique strain (35.3 percent). These data confirm prior observation that foreign-born persons are more likely to be infected with tuberculosis isolates with unique fingerprints than are the native-born. Therefore, the foreign-born may not necessarily be the source of recent tuberculosis transmission. Furthermore, because the majority of foreign-born persons were infected before arrival, the TB isolates probably reflect the dominant isolates in their places of origin.

Discussion

Although imported tuberculosis from high prevalence countries accounts for high rates of tuberculosis cases in developed regions such as North America, the rates at which these individuals transmit disease to the general population remain low. We found that foreign-born incident case patients carried mostly unique isolates, indicating that although an important part of transmission, immigrants were not the source of ongoing transmission of tuberculosis in Tarrant County.

Distinguishing between areas with increased incidence and higher and lower percentages of clustered strains is clinically important in tuberculosis control program decision making. Moonan et al. (2006) report an intervention using a geographically based targeted screening program in areas with high incidence and the highest percentage of clustered isolates. The study did not screen zip codes with high incidence and unique isolates because it assumed that clustered persons with disease from geographically related areas represent ongoing community transmissions that could be identified and interrupted through treatment by screening commonly shared facilities and locations in those communities. Tuberculosis screening and treatment were arranged in the high-incidence high clustered areas. Tuberculosis control activities targeted commonly used areas such as temporary labor services, churches, community services centers, an HIV congregate living facility, and other congregate living facilities sponsored by different faith-based organizations. During the twenty-eight months of screenings, the number of persons identified with tuberculosis decreased from 28.5 cases per 1,000 screenings to 2.4 cases per 1,000 screenings. The rate of developing latent tuberculosis infection fell from 14.3 to 2.2 per 100 person-years of exposure. The intervention was successful because it assumed that areas with unique isolates represented remote transmission. Thus, location-based screening in areas with high rates of unique isolates would be less likely to identify either persons with active tuberculosis or recently acquired latent tuberculosis infection (Moonan et al. 2006).

Two limitations of this study are the use of zip codes instead of more homogenous spatial units such as census tracts (Krieger et al. 2002), and the small-numbers problem (Cromley and McLafferty 2002) that may cause areas with low average incidence of tuberculosis to be unduly influenced by strain differences. These issues are important and should be addressed in future research, but they do not detract from the main point of this study or its findings.

Conclusion

The geographic distribution of tuberculosis isolates in Tarrant County suggests that immigrant neighborhoods have higher rates of unique strains of tuberculosis compared to neighborhoods occupied by the native-born. Neighborhoods dominated by the native-born tend to have higher rates of clustered isolates. Therefore, in addition to being culturally distinct, immigrant neighborhoods may also be pathogenically distinct from surrounding neighborhoods. Immigrant neighborhoods deserve special attention in surveillance efforts to track new strains of disease before they spread into the general community. Molecular-level epidemiology combined with spatially focused disease surveillance can identify ethnic islands of disease. Once these islands are identified, traditional disease control measures can be used to identify and treat individuals and thereby reduce further spread. Medical geographers need to embrace genotyping as another tool in our quest to unravel and understand the spatial patterns of disease. Genotyping-based disease mapping provides critical information for planning effective intervention and optimizing the use of limited resources.

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Figure 1.
Percentage of foreign-born residents.

Figure 2.
Average tuberculosis incidence by zip-code area.

Figure 3.
Ratio of unique isolates for all cases.

Figure 4.
Ratio of clustered cases for all cases.

Figure 5.
Ratio of clustered cases for native-born only.

Figure 6.
Ratio of clustered cases for foreign-born only.