TUBERCULOSIS COMMENTARY

Overseas Screening for Tuberculosis in Immigrants and Refugees to the United States: Current Status

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For many individuals from developing countries, infection with Mycobacterium tuberculosis is almost inevitable. In recent years, there has been an increase in the number of immigrants and refugees from some of these countries, and thus the proportion of these individuals among newly diagnosed cases of tuberculosis has increased. The identification of these patients and the proper management of their cases are important public health priorities. Dr. Nancy Binkin and her colleagues review the data on the epidemiology of tuberculosis in immigrants and refugees and describe the available screening and evaluation programs overseas and in this country. They also highlight the importance of maintaining and expanding health care services in this country that are appropriate and welcoming to foreign-born persons. They clearly demonstrate that the control of tuberculosis in the United States will require a coordinated effort that transcends its borders.

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The number of reported cases of tuberculosis (TB) in foreign-born persons in the United States during 1995 was 8,042, 36% of the national total. The overseas screening of immigrants and refugee visa applicants, which relies on a chest radiograph and smear microscopy, is designed to identify future U.S. residents who have active TB or who are at high risk for TB. In this commentary, we summarize current policies and review retrospective evaluations of the screening system currently in place. The system appears to detect most persons who have active TB at the time of screening. However, active TB is actually diagnosed in <15% of persons who are identified by screening as having suspected TB and who are evaluated in the United States. To improve the system, more sensitive and specific techniques as well as improved means of data transmission to state and local health departments are needed.

In the United States both the number of cases of tuberculosis (TB) in foreign-born persons and the percentage of total cases in foreign-born persons have increased substantially since 1986, when the Centers for Disease Control and Prevention (CDC) began collecting data on place of birth. In 1986, 4,925 cases in foreign-born persons were reported, thus accounting for 22% of total TB cases. By 1995, 7,930 (35%) of the 22,860 TB cases in the United States occurred in foreign-born persons, which represented a 63% increase in the absolute number of cases in foreign-born persons. Furthermore, cases in foreign-born persons increased 10.6% between 1992 and 1995, in contrast to the 24% decline in cases in U.S.-born persons observed during this time (CDC, unpublished observations).

At least three factors have been associated with the increase in cases of TB in foreign-born persons over the past decade [1]. First, the number of immigrants has increased, as has the percentage of immigrants arriving from countries where the incidence rates of TB are high. Most immigrants come from countries with rates that are three to 25 times higher than that in the United States [2, 3]. Second, foreign communities may be difficult to reach because of cultural and linguistic barriers [4–6], thus resulting in delays in diagnosis and treatment and in limited efforts at screening and preventive therapy. Third, there is a relative lack of priority placed on the follow-up of foreign-born persons by TB prevention and control programs in some parts of the United States.

Active TB may be present at the time of immigration in foreign-born persons, may subsequently develop in those infected with Mycobacterium tuberculosis before immigration,
or, in some instances, may result from infection acquired in the United States. Understanding the epidemiology of TB in foreign-born persons in the United States is essential in formulating epidemiologically based interventions to decrease the incidence of TB in this group. Currently, one of these interventions is the overseas screening of candidates applying for long-term residence in the United States. In this commentary, we will review the epidemiology of TB in foreign-born persons in the United States and the current overseas efforts to screen new arrivals, present the results of these screening efforts, and discuss possible future improvements in U.S. screening activities.

**Epidemiology of TB in Foreign-Born Persons**

National surveillance data demonstrate that TB in foreign-born persons is concentrated geographically, in terms of both the country of origin and the state of residence [7]. In 1995, nearly two-thirds (66%) of the foreign-born persons with TB were from seven countries, Mexico (22%), the Philippines (13%), Vietnam (12%), China (5%), India (5%), Haiti (5%), and Korea (4%). The remaining one-third were from >100 different countries. Although the proportion of TB cases in foreign-born persons in many states is substantial (e.g., 69% in Hawaii and 64% in Rhode Island), nearly 70% of the foreign-born persons with TB cases that were reported in 1995 resided in four states: California (3,071 cases), New York (3,071), Texas (1,259), and Florida (597).

The duration of U.S. residence before diagnosis of TB in foreign-born persons that was reported in 1995 varied: <1 year, 30%; between 1 and 5 years, 23%; and >5 years, 47% (CDC, unpublished observations). These values are influenced considerably by location in the United States and by country of origin; in Los Angeles, for example, most TB cases in Mexican-born persons occur in long-term residents, while most TB cases in the Filipino and Vietnamese populations occur in persons who have been in the United States <5 years [8]. In general, the risk of active disease declines as the duration of residence in the United States increases. However, on the basis of age-adjusted rates of TB, foreign-born persons from developing countries remain at higher risk for TB than do their U.S.-born counterparts [1].

**Current Policy for the Identification and Treatment of TB in Immigrants and Refugees**

U.S. immigration law, which is established by Congress, states that overseas medical screening of immigrants and refugees must be carried out, with the general goal of excluding persons with communicable diseases of public health significance, persons with physical or mental disorders associated with harmful behavior, persons who abuse drugs or are addicted to drugs, or persons who are likely to become a ward of the state [9]. According to this law, details concerning specific excludable diseases, requirements for who needs to be screened, and the examination and studies to be performed are prescribed by the U.S. Public Health Service, Department of Health and Human Services, with oversight provided by the Division of Quarantine at the CDC. The current list of infectious diseases of public health significance that are grounds for exclusion include infectious TB, HIV infection, leprosy, and certain sexually transmitted diseases [10].

The overseas medical examination, which is valid for 12 months, is carried out by panel physicians, who are local physicians appointed by the U.S. consulate. In some cases, clinics or hospitals are designated as "panel physicians," as is the case in two of the highest-volume screening sites, Vietnam and the Philippines. Panel physicians are provided with a book of technical instructions concerning the examination process, which, in addition to TB screening, consists of obtaining a history, physical examination, and screening for physical and mental disorders, substance abuse, sexually transmitted diseases, leprosy, and HIV infection [11]. There is no formal certification process. Each panel physician is expected to make local arrangements for the radiological and laboratory examinations required as part of the evaluation.

At present, none of the countries have on-site supervision beyond the local U.S. consular official. Panel physicians do, however, receive periodic supervisory visits by two CDC staff based in Frankfurt, Germany, and Bangkok, Thailand, respectively. The participating physicians are directly reimbursed by immigrant applicants on the basis of a fee scale set locally; in the case of refugees, the U.S. government reimburses the panel physician for the screening services. There are ~800 panel physicians worldwide.

The TB portion of the screening process consists of chest radiography for all persons 15 years of age or older. If the radiograph is read by the panel physician as being compatible with active TB, three consecutive early morning sputum specimens are obtained for acid-fast staining and microscopic examination. Procedures for sputum examination vary between screening sites. However, smears are usually made from uncentrifuged sputum; slides are stained by means of the Ziehl-Neelsen procedure and are examined by using light microscopy. In some locations, however, specimens are centrifuged before examination, and fluorescence microscopy is used.

Persons whose smears are found to be positive for acid-fast bacilli (AFB) are designated as having class A TB, which is an excludable condition for entry into the United States [10]. These individuals have two options: (1) they may choose to successfully complete a course of therapy for TB with documented smear negativity at the end of treatment, after which they are reclassified as having class B2 TB (see below), or (2) they may elect to be treated until their smears become negative and apply for a waiver. To receive a waiver, a document must be signed by a U.S. health care provider and countersigned by the local health department (or signed only by the local health department if they are to be the provider) in the individual’s
intended U.S. destination, thus guaranteeing that the provider will assume responsibility for the completion of TB treatment after arrival. Immigrants must seek and pay for their own TB treatment overseas; in the case of refugees treated overseas, the costs are assumed by the U.S. Department of State.

Applicants whose chest radiograph is compatible with active TB but whose three consecutive sputum smears are AFB-negative are designated as having class B1 (clinically active, not infectious) TB [10]. If the initial chest radiograph is deemed by the panel physician to be compatible with inactive TB, no specimens for smears are obtained, and the candidate is designated as having class B2 (not clinically active, not infectious) TB. The class B conditions are considered significant but not excludable for immigration purposes.

Class A and class B designations are placed on the visa forms that all immigrants and refugees carry with them to the United States. Visa forms carried by individuals with class A and class B TB are collected by the Immigration and Naturalization Service (INS) at one of 295 international airports, border posts, or ports within the United States. In turn, the information is transferred to one of eight quarantine stations operated by the CDC's Division of Quarantine, where a form is completed and sent to the state or local health jurisdiction at the intended destination of the arriving immigrant or refugee. A copy is sent to the CDC headquarters and to the arrivals themselves, notifying them to report to their local health department within 30 days. Health departments are expected to return the forms to the CDC, thus reporting on the outcome of the evaluation.

Those persons designated as having class A TB are required to visit the health department or risk deportation if they do not meet the condition of their waiver. For persons designated as having class B1 and class B2 TB, the health department visit is considered voluntary. However, some health departments perform active follow-up of arrivals designated as having class B1 or B2 TB, on the basis of the notification provided by the CDC.

The procedures for the overseas screening of arrivals detailed above are based on three important precepts [4, 9–11]: (1) concentrating on immigrants and refugees, who are the groups most likely to become long-term residents of the United States; (2) reducing the importation of active infectious TB that poses an acute public health risk by denying visas to persons whose smears are AFB-positive; and (3) allowing those individuals who have radiographic abnormalities but whose smears are AFB-negative to enter the United States, where a more complete medical evaluation can be performed and appropriate treatment can be administered under supervision.

Past experience has demonstrated that adequate evaluation and treatment of individuals overseas who do not represent an immediate public health threat are logistically difficult because many countries lack the technical capacity to perform mycobacterial cultures and chest radiographs alone cannot be relied upon for the definitive diagnosis of TB. In addition, because anti-TB treatment for immigrants is at their own expense and often unsupervised, there is an increased risk of partially treated, drug-resistant TB developing.

**Contribution of Immigrants and Refugees to Diagnosed TB Cases in Foreign-Born Persons Who Have Recently Arrived in the United States**

Not all foreign-born persons for whom TB is diagnosed within 1 year of arrival entered as immigrants or refugees. To evaluate the percentage of cases occurring in recently arrived foreign-born persons who had entered as immigrants and refugees and were therefore subject to the requirements of overseas screening, studies were conducted in conjunction with the health departments of Hawaii and Seattle and the INS.

In Hawaii and Seattle, a substantial fraction of persons for whom TB was diagnosed within the first year after arrival in the United States had entered as immigrants and refugees. In Hawaii, after excluding Filipino World War II veterans, who were allowed to apply for U.S. citizenship during a window of time between 1992 and 1995 without undergoing a medical examination [12], a total of 78% of the remaining 124 foreign-born persons with TB had been immigrants or refugees; the remainder were students (4%), tourists (4%), and individuals of indeterminate status (14%). In Seattle, 28 (58.3%) of the 48 persons who had been in the United States <1 year at the time of diagnosis were immigrants and refugees, and the remainder were persons of indeterminate status; there were no tourists or students (data for Hawaii and Seattle are unpublished).

Similar data were not available for other parts of the country. However, it is likely that the percentage of cases occurring in immigrants and refugees varies considerably from state to state, depending on the local mix of categories of legal entrants as well as the number of persons who enter illegally.

**U.S. Follow-up of Immigrants and Refugees Designated as Having Class B1 and Class B2 TB**

In recent years, it has been estimated that an average of 50 individuals with class A TB and 18,000 individuals with class B TB arrive annually in the United States (CDC, Division of Quarantine, unpublished data). Although national data are not available, it appears that one-third of the persons classified as having class B TB have class B1 TB, and the remainder have class B2 TB (table 1). However, the ratio of persons classified as having class B1 or B2 TB varies between countries of origin.

The percentage of immigrants and refugees with class B TB who were successfully evaluated in the United States and the delay between arrival and reexamination are presented in table 1. Rates of follow-up of persons with class B1 and class B2 TB exceeded 82% in all but one of the areas. Most examinations were performed within 3–9 weeks of arrival. All of the sites with high rates of follow-up have active outreach policies, consisting of home visits, mailings, or telephone calls to the
Table 1. Evaluation of immigrants and refugees to the United States who were designated as having class B1 or B2 tuberculosis in the overseas examination.

<table>
<thead>
<tr>
<th>Location, period (mo/y)</th>
<th>Class B1 tuberculosis</th>
<th></th>
<th>Class B2 tuberculosis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of persons</td>
<td>No. (%)</td>
<td>Median time to first U.S. evaluation*</td>
<td>No. of persons</td>
</tr>
<tr>
<td></td>
<td>evaluated</td>
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<td></td>
<td>evaluated</td>
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<tr>
<td>Hawaii, 10/1991 to 12/1993</td>
<td>598</td>
<td>590 (99)</td>
<td>6 d</td>
<td>940</td>
</tr>
<tr>
<td>Los Angeles, 10/1992 to 9/1993</td>
<td>690</td>
<td>608 (88)</td>
<td>9 w</td>
<td>1,221</td>
</tr>
<tr>
<td>Seattle, 1/1992 to 9/1994</td>
<td>465</td>
<td>409 (88)</td>
<td>4 w</td>
<td>632</td>
</tr>
<tr>
<td>New York City, 1/1995 to 6/1995</td>
<td>100</td>
<td>95 (95)</td>
<td>3 w</td>
<td>367</td>
</tr>
<tr>
<td>New York State, 1/1994 to 12/1994</td>
<td>67</td>
<td>42 (63)</td>
<td>NA</td>
<td>150</td>
</tr>
<tr>
<td>Portland, Oregon, 1/1994 to 12/1994</td>
<td>111</td>
<td>106 (95)</td>
<td>4 w</td>
<td>82</td>
</tr>
</tbody>
</table>

NOTE. NA = not available.
* Time from arrival in the United States to follow-up.

immigrant or refugee’s intended residence; such active outreach is not practiced, however, in many parts of the United States.

Sensitivity of Screening for the Diagnosis of TB in Newly Arrived Immigrants and Refugees

To examine the sensitivity of the screening process in establishing a diagnosis of active TB, we used data from the previously mentioned studies in Hawaii and Seattle, where information was available on the immigration classification of most cases that had been diagnosed within 1 year of arrival. For purposes of this evaluation, we included only those TB cases in immigrants and refugees that were diagnosed within 12 months of arrival in the United States.

In Hawaii, 95 (77%) of 124 immigrants for whom active TB was diagnosed within 1 year of arrival had been classified overseas as having class B1 or B2 TB. In Seattle, the corresponding number was 19 (68%) of 28. Because of the short median time between arrival and evaluation, the failure of the screening system to detect all cases probably represents problems in the overseas classification of radiographs of persons not identified as having class B1 or B2 TB rather than the development of TB after the medical screening. Unfortunately, however, the chest radiographs of persons not classified as having class A or B TB overseas are rarely available for review.

Discrepant TB Status

According to the current screening system, cultures of specimens from some individuals with class B1 TB might be expected to be positive, but smears of specimens from these persons should be AFB-negative. Similarly, individuals with class B2 TB should have only inactive TB, and both smears and cultures of specimens from these persons would be expected to be negative. Relatively few discrepancies were observed between the overseas examination and the examination conducted in the United States. In Hawaii, Los Angeles, and Seattle, of 1,679 individuals with class B1 TB who were evaluated within 30 days of U.S. arrival, 30 (1.8%) had positive smears. Of 2,432 persons with class B2 TB, 17 (0.7%) and 20 (0.8%) had positive smears and positive cultures, respectively (unpublished findings).

Predictive Value of a Positive Overseas Screening Classification

In the United States, TB was diagnosed for between 3.3% and 14.0% of persons designated as having class B1 TB and between 0.4% and 3.8% of those designated as having class B2 TB (table 2). The differences in yield within the categories were in part explained by differences in criteria used to define a TB case. In Seattle, where the lowest proportion of cases was found among individuals designated as having class B1 or B2 TB, most cases (89%) were bacteriologically confirmed. In Hawaii, by contrast, 56% of the cases were culture-confirmed; the remainder were diagnosed on the basis of the CDC’s clinical definition, which does not require bacteriologic confirmation [13].

Role of Overseas Screening in Identifying Candidates for Preventive Therapy

Most persons classified as having class B1 and class B2 TB are confirmed to have radiological abnormalities when their radiographs are reexamined in the United States. If they are also found to have positive tuberculin tests, then they are candidates for preventive therapy [14]. The studies performed in San Francisco and Seattle evaluated the percentage of persons who were classified as having either class B1 or B2 TB and were not found to have active TB but were candidates for preventive therapy.

In San Francisco, 62% of persons designated as having class B1 or B2 TB who did not have active TB were considered eligible for preventive therapy [15]. This proportion was 43%
in Portland, Oregon [16]. In Seattle, 56% of persons classified as having class B1 TB and 27% of those classified as having class B2 TB received preventive therapy; therapy for the remainder was not started because they had negative tuberculin tests, were older than 35 years of age with unremarkable chest radiographs, or had already received treatment for tuberculosis [17].

Future Directions

Overseas Screening

The overseas screening process for identifying and treating TB in immigrants and refugees is responsible for the identification of substantial numbers of persons arriving in the United States who have active TB. However, not all cases in newly arrived immigrants and refugees were identified by the screening as having suspect TB, which is in part a result of limitations of the screening process. Of those persons identified overseas as having suspect TB, not all are followed up in the United States; this fact represents an important missed opportunity for timely treatment of TB and reduction of TB transmission in the community.

Although chest radiography is a reasonably sensitive screening tool, it is not highly specific. Since active TB is not diagnosed after arrival for most persons identified overseas as having class B1 and class B2 TB, it would be unreasonable to suggest that all such individuals receive a course of anti-TB therapy overseas without further diagnostic confirmation.

A number of efforts are under way to improve the overseas screening process, the satisfactory transmission of information about suspect TB cases to U.S. health departments, and the follow-up of those persons identified overseas as having class B1 and class B2 TB after arrival in the United States. Studies exploring means of improving the sensitivity of the current screening system are being conducted, as are analyses of sputum concentration through centrifugation or cytocentrifugation.

Plans are under way to evaluate the feasibility of using some rapid diagnostic tests for TB, such as amplification of mycobacterial DNA by PCR.

A second improvement in the system that is being explored is strengthening the training of the panel physicians and improving the oversight and standardization of the medical examination process. At present, the training given to the physicians and to radiology and laboratory technicians is limited, and supervision is infrequent because of their large numbers. An assessment of training needs, the development of evaluation instruments and of a certification and recertification process, and the development and implementation of training materials are likely to improve the quality of the examinations.

A third means of improving the current process is to expedite transmission of data for persons who are identified as having class A or B TB so that follow-up can be performed in a timely fashion. It is unclear whether the paperwork for all immigrants with class A and class B TB reaches the state and local health departments at their intended destination. In addition, one can expect increasing difficulty in finding those immigrants and refugees who do not present spontaneously for evaluation when there are delays in notification of health departments. Electronic transmission of information from overseas sites is being explored, such that the current chain of paperwork that involves overseas consulates, the INS at the numerous U.S. ports of entry, the domestic quarantine stations, and various state and local health departments can be kept to a minimum.

A fourth area likely to improve the timely identification of TB is working in consultation with state and local health departments to develop guidelines for investigation and follow-up of immigrants with class A and class B TB. The current system of classifying TB as A, B1, and B2 was developed in 1991, and, although no studies have been done to assess the understanding of this classification system, it appears that considerable confusion remains about the meaning of these categories. Efforts are needed to inform health departments of the high rates of TB in these populations and the urgency of providing adequate follow-up.

Although assuring the treatment of individuals with known active TB should remain the number one priority of health departments with respect to TB, follow-up of immigrants with class B1 and class B2 TB may even exceed the yield of contact tracing and justify its undertaking as a health department priority.
Contact tracing identifies a large number of infected persons who are ideal candidates for preventive therapy because of the likelihood of recent infection, but of those persons evaluated, only 0.7% will have active TB (CDC, unpublished data). By contrast, from 3% to 14% of immigrants and refugees with class B1 TB and 0.4% to almost 4% of immigrants and refugees with class B2 TB are subsequently found to have active disease. Of the remaining persons, many are high-priority candidates for preventive therapy regardless of age because they have positive tuberculin tests and abnormal chest radiographs; studies suggest that individuals with such characteristics have a 0.3% risk of active TB per year [18].

A number of states have developed successful and innovative approaches for following up their immigrant and refugee populations (e.g., mailing out letters of welcome to newly arriving individuals with class B TB and informing local health jurisdictions of the steps to follow in evaluating these individuals), and these experiences may prove useful in other jurisdictions as well.

Screening of Other New Arrivals Not Coming Through Overseas Channels

The studies conducted in Hawaii and Seattle suggest that many new TB cases in foreign-born individuals occur in immigrants and refugees who undergo overseas screening. However, findings from sites such as Los Angeles demonstrate that very few of the Central American persons with cases diagnosed within 1 year of arrival in the United States had been identified as having class A or B TB, thus suggesting that many persons are not entering as either immigrants or refugees [8].

Some new arrivals may be detected by a second screening mechanism that was developed for certain categories of foreign-born persons already within the United States who wish to adjust their status and become permanent legal residents without returning to their country of origin. This mechanism was widely used for applicants of the Immigration Reform and Control Act; these persons were given the opportunity between 1989 and 1994 to legalize their residency status.

There are no data on the number of active TB cases detected through this second screening mechanism. However, the Denver Health Department, which served as a “civil surgeon” to examine foreign-born persons who applied to adjust their status, reported identifying some cases of TB in a large population of predominantly Mexican applicants in the early 1990s [19]. In addition, however, they identified large numbers of candidates for preventive therapy. The individuals who started receiving preventive therapy reportedly were more adherent than other members of the foreign-born population, presumably because they perceived that noncompletion of treatment could adversely affect the immigration process.

Efforts are currently under way to explore a greater role for the CDC and state and local health departments in the training of physicians designated to provide follow-up examinations of foreign-born persons; this role would assure adequate understanding and skills for those performing the examinations and facilitate referrals to state and local health departments for further evaluation and treatment.

For those persons who enter the United States under other categories, the CDC and INS are also exploring whether screening is feasible. Two groups of concern are students and asylum seekers. Neither group is currently screened on a routine basis. Students are not screened because the risk of active disease in these persons is believed to be relatively low compared with the risk in other categories of entrants and because their duration of residence in the United States is relatively short. Asylum seekers are not screened because of the logistic difficulties of providing screening to persons who often come without money to defray the costs of screening and who are not detained long enough to undergo adequate evaluation.

Studies are under way to document the incidence of disease in students before taking further action. For the asylum seekers (of whom there are currently >400,000 awaiting hearings regarding their status), consideration is being given to establishing mechanisms for screening those who come from countries with a high prevalence of TB. However, the mechanism for funding this latter process, as well as the logistics, will require considerable planning.

For those persons who come into the United States as seasonal workers or as undocumented aliens or for those persons who do undergo overseas screening but whose TB is not identified, screening is more challenging. Programs have been put in place in migrant clinics to screen agricultural workers [20]. Some states have successfully identified TB in new arrivals by conducting screening of hotel and restaurant workers (a job category that contains large numbers of new arrivals in certain states) and through targeting programs teaching English as a second language.

Additional innovative mechanisms will need to be explored to identify other persons with TB who are not currently being detected to provide them with timely treatment and limit further spread to their contacts within the United States.

Controlling and preventing the importation of infectious diseases into the United States will remain a challenge in the foreseeable future. Efforts to limit the access to care for illegal aliens are likely to be counterproductive barriers to effective interventions [21]. Ultimately, the adequacy of TB prevention and control efforts in the United States, and the eventual elimination of TB, will depend on our collective ability to successfully address TB in foreign-born populations.

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