

# Assessing the Performance of Overseas Tuberculosis Screening Programs

## A Study Among US-Bound Immigrants in Vietnam

Susan A. Maloney, MD, MHSc; Katherine L. Fielding, PhD; Kayla F. Laserson, ScD; Warren Jones, BS; Nguyen Thi Ngoc Yen, MD; Dang Quy An, MD; Nguyen Huu Phuoc, MD; Nguyen An Trinh, MD; Duong Thi Cam Nhung, MD; Vo Thi Chi Mai, MD; M. Frank Seawright, BA; Thomas O'Rourke, MD; Truong Xuan Lien, MD; Nguyen Thi Ngoc Lan, MD; Nancy Binkin, MD, MPH; Martin S. Cetron, MD

**Background:** Tuberculosis cases in foreign-born persons account for more than 50% of all tuberculosis cases in the United States. The Institute of Medicine has recommended enhancing overseas screening as one measure to support tuberculosis elimination efforts. We assessed the ability of overseas tuberculosis screening (chest radiograph followed by 3 acid-fast bacilli sputum smears for persons with abnormal chest radiographs [suggestive of active tuberculosis]) to detect pulmonary tuberculosis disease among US-bound immigrants with abnormal chest radiographs.

**Methods:** During October 1998 to October 1999, 14 098 US immigrant visa applicants were screened overseas in Vietnam. Adult applicants with abnormal chest radiographs were enrolled to assess screening test characteristics among this group using mycobacterial culture as the gold standard for pulmonary tuberculosis disease diagnosis. Risk factors for pulmonary tuberculosis disease were also evaluated.

**Results:** Among 1179 adult applicants with abnormal

chest radiographs, 82 (7.0%) had positive acid-fast bacilli smear results, and 183 (15.5%) had positive *Mycobacterium tuberculosis* culture results (pulmonary tuberculosis disease). The sensitivity, specificity, and positive and negative predictive values of serial acid-fast bacilli screening among this group were 34.4% (63/183), 98.1% (977/996), 76.8% (63/82), and 89.1% (977/1097), respectively. Risk factors for pulmonary tuberculosis disease included younger age (18-34 years), no history of tuberculosis or treatment, reported symptoms, and cavitation or consolidation on chest radiograph.

**Conclusions:** The ability of current overseas screening to detect tuberculosis among immigrants with abnormal chest radiographs is low. Improved diagnostic methods, enhanced screening measures, and postmigration follow-up are essential to control tuberculosis among immigrants and support US and global tuberculosis elimination.

*Arch Intern Med.* 2006;166:234-240

**Author Affiliations:** Divisions of Global Migration and Quarantine (Drs Maloney and Cetron and Mr Seawright) and Tuberculosis Elimination (Dr Laserson), Centers for Disease Control and Prevention, Atlanta, Ga; London School of Hygiene and Tropical Medicine, London, England (Dr Fielding); International Organization of Migration, Geneva, Switzerland (Mr Jones and Dr O'Rourke); Cho Ray Hospital (Drs Yen, An, Phuoc, Trinh, Nhung, and Mai), Institute Pasteur (Dr Lien), and Pham Ngoc Thach National Tuberculosis and Lung Disease Center (Dr Lan), Ho Chi Minh City, Vietnam; and Superioe di Sanità, Rome, Italy (Dr Binkin).

**T**UBERCULOSIS CASES IN FOREIGN-BORN persons account for more than 50% of all tuberculosis cases in the United States.<sup>1</sup> Furthermore, tuberculosis rates among foreign-born persons are 8 times higher than those among US-born persons, and rates are highest among recently arrived migrants.<sup>1-3</sup> The Institute of Medicine has recommended enhancing overseas screening as one measure to support tuberculosis elimination.<sup>4</sup>

Overseas tuberculosis screening is required for immigrants and refugees applying to reside permanently in the United States; more than 400 000 applicants are screened annually.<sup>5-7</sup> Screening includes a chest radiograph (CXR) for applicants 15 years or older; those with a CXR suggestive of active tuberculosis must sub-

mit 3 sputum specimens on separate consecutive days for acid-fast bacilli (AFB) examination.<sup>8</sup> Guidelines also recommend that persons who report tuberculosis symptoms submit sputum specimens. This strategy is designed to prevent entry of persons who have infectious (defined as AFB sputum smear-positive) pulmonary tuberculosis disease (PTB) while referring others with suspected tuberculosis for US evaluation, where mycobacterial culture capability is more readily available and treatment supervision is easier. Applicants are classified as having (1) class A tuberculosis (infectious, active tuberculosis) based on a CXR suggestive of active tuberculosis and 1 or more sputum smears positive for AFB; (2) class B1 tuberculosis (noninfectious, active tuberculosis) based on a CXR suggestive of active tuberculosis and 3 negative sputum

smears for AFB; (3) class B2 tuberculosis (inactive tuberculosis) based on a CXR suggestive of inactive tuberculosis; or (4) no tuberculosis. Applicants with AFB smear-positive results undergo treatment overseas until they have AFB smear-negative results and then are allowed to migrate. Applicants with AFB smear-negative results and applicants with CXRs suggestive of inactive tuberculosis are allowed to migrate; the Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine notifies state and local health departments of arriving migrants with suspected tuberculosis to facilitate follow-up evaluation after arrival in the United States. In 2003, this division notified health departments of more than 8000 arriving immigrants and refugees with suspected active or inactive tuberculosis.

Early identification and treatment of tuberculosis is essential because delays can result in more severe disease for the patient and disease transmission in both host and receiving countries. However, data suggest that some tuberculosis cases in foreign-born persons could be identified earlier by enhancing overseas screening. During US follow-up, PTB has been diagnosed in 3.3% to 14.0% of immigrants and refugees classified overseas as having suspected active tuberculosis (class B1 tuberculosis) and 0.4% to 3.8% of those classified as having inactive tuberculosis (class B2 tuberculosis).<sup>9-17</sup> Most of these persons were diagnosed based on *Mycobacterium tuberculosis* cultures; the remainder met clinical tuberculosis case definitions. Because overseas tuberculosis screening is based on AFB smears, persons with AFB smear-negative, *M tuberculosis* culture-positive PTB would be missed; the magnitude of this population during overseas screening has not been assessed. Such persons can be infectious (albeit less so than AFB smear-positive tuberculosis cases); it has been estimated that AFB smear-negative PTB is responsible for approximately 17% of transmission in the United States.<sup>18</sup> In addition, although studies have shown that overseas screening is successful at preventing entry of most migrants with AFB smear-positive PTB, a recent report<sup>19,20</sup> documented relatively high rates among recently arrived US refugees despite previous screening overseas. The objectives of this study were (1) to assess the ability of overseas screening to detect PTB among immigrants with abnormal CXRs suggestive of active tuberculosis, (2) to determine risk factors associated with PTB, and (3) to identify potential modifications to overseas screening that could improve PTB case finding and management. The study was conducted in Vietnam, which has a national tuberculosis incidence of 114 per 100 000 and is the third leading country contributing to foreign-born tuberculosis cases in the United States.<sup>1,21</sup>

## METHODS

### STUDY DESIGN

US immigrant visa applicants are screened for tuberculosis at Cho Ray Hospital in Ho Chi Minh City, Vietnam, where AFB smear microscopy is available but mycobacterial cultures are not routinely performed. A directly observed tuberculosis treatment program is available through Cho Ray Hospital and the International Organization for Migration. From October 4, 1998,

through October 5, 1999, a prospective study of adult applicants was conducted to assess the ability of screening to detect PTB among migrants with abnormal CXRs, using mycobacterial culture as the gold standard for diagnosing PTB.

All adult immigrant visa applicants ( $\geq 18$  years of age) with a CXR suggestive of active tuberculosis were asked to participate in the study. Demographic, clinical, and laboratory data on consenting applicants were collected on standardized forms, including date of birth, sex, medical history and physical findings, human immunodeficiency virus (HIV) test results, CXR findings, history of tuberculosis or treatment, tuberculosis exposure, tuberculosis symptoms, and AFB sputum smear and mycobacterial culture results. Institutional review board approval was obtained from the CDC and the Human Subjects Protection Committee for Cho Ray Hospital, Pasteur Institute, and Pham Ngoc Thach National Tuberculosis and Lung Disease Center.

### AFB SMEAR MICROSCOPY AND SPUTUM SPECIMEN PROCESSING

The AFB smear examination was performed on uncentrifuged specimens using auramine O fluorescent staining and fluorescent microscopy, and positive smears were graded as recommended by the CDC.<sup>22</sup> After direct smear examination, the remainder of the sputum specimen was transferred to the Pasteur Institute, where culture facilities were available, and was digested using oxalic acid processing,<sup>22</sup> and then mycobacterial culture was performed.

### MYCOBACTERIAL CULTURE MEDIA FOR SPUTUM SPECIMENS

The BACTEC 460 tuberculosis liquid system (Becton, Dickinson and Company, Franklin Lakes, NJ) was used as the primary culture method. The BACTEC 12B bottles were prepared with PANTA Plus (Becton Dickinson, Sparks, Md), then inoculated with 500  $\mu\text{L}$  of oxalic acid-processed sediments. Bottles were incubated at 35°C to 37°C for 6 weeks or until the growth index was 30 or higher. The 12B bottles that produced positive results underwent Ziehl-Neelsen staining to confirm the presence of AFB. Three Lowenstein-Jensen (LJ) slants were also prepared for each specimen, incubated at 35°C to 37°C for 2 months, and inspected weekly for growth. A specimen was considered *M tuberculosis* culture-positive if 1 or more of the culture media (BACTEC 12B or LJ slants) grew *M tuberculosis*; *Mycobacterium avium-intracellulare* complex culture-positive if 1 or more of the culture media grew *M avium-intracellulare* complex and none grew *M tuberculosis*; negative if at least 1 culture media indicated no growth and none grew *M tuberculosis* or *M avium-intracellulare* complex; and contaminated if at least 3 of the 4 culture media grew organisms other than *M tuberculosis* or *M avium-intracellulare* complex.

### IDENTIFICATION AND SUSCEPTIBILITY TESTING OF MYCOBACTERIAL ISOLATES

Mycobacterial isolates were identified by standard procedures<sup>22,23</sup> and by DNA probes for *M tuberculosis* or *M avium-intracellulare* complex (AccuProbe; Gen-Probe Inc, San Diego, Calif).<sup>24</sup> The *M tuberculosis* isolates were tested at Pham Ngoc Thach Hospital for susceptibility to antituberculosis drugs using the following minimum critical concentrations: isoniazid, 0.2  $\mu\text{g}/\text{mL}$ ; rifampin, 40.0  $\mu\text{g}/\text{mL}$ ; ethambutol hydrochloride, 2.0  $\mu\text{g}/\text{mL}$ ; and streptomycin sulfate, 4.0  $\mu\text{g}/\text{mL}$ . A multidrug-resistant (MDR) isolate was defined as one resistant to at least isoniazid and rifampin.

**Table 1. Acid-Fast Bacilli (AFB) Smear and Mycobacterial Culture Results at the Specimen Level, US-Bound Immigrants, Ho Chi Minh City, Vietnam, October 1998-October 1999\***

	<i>Mycobacterium tuberculosis</i> Culture Positive	Negative Culture	<i>Mycobacterium avium-intracellulare</i> Complex Culture Positive	Contaminated Culture	Total
AFB smear positive	119	35	0	3	157
AFB smear negative	245	3284	14	95	3638
<b>Total</b>	<b>364</b>	<b>3319</b>	<b>14</b>	<b>98</b>	<b>3795†</b>

\*Includes 3 specimens each from 1265 study eligible participants. AFB smear sensitivity at the specimen level was 32.7% (119/364) (95% confidence interval, 27.9%-37.8%).

†No specimens grew both *Mycobacterium tuberculosis* and *Mycobacterium avium-intracellulare* complex.

### AFB SMEAR AND MYCOBACTERIAL CULTURE RESULTS AT THE SPECIMEN AND PARTICIPANT LEVELS

Study participants were evaluated if 3 sputum specimens for AFB smear and mycobacterial cultures were obtained. Specimens were categorized by AFB smear result and mycobacterial growth on culture media. In addition to specimen-level analysis, participants were also categorized based on the combined results of their 3 sputum specimens to assess the overall performance of serial screening. Participants with 1 or more AFB-positive smear results were designated as AFB smear positive, and those with 3 AFB-negative smear results were designated as AFB smear negative. Any participant with at least 1 *M tuberculosis*-positive culture result was designated as *M tuberculosis* culture positive and was therefore determined to have PTB. Participants with no *M tuberculosis*-positive culture results were divided into 4 separate categories: (1) those with 3 negative culture results were designated as being *M tuberculosis* culture negative; (2) those with 3 contaminated culture results were designated as having contaminated cultures; (3) those with 3 *M avium-intracellulare* complex-positive results were designated as being *M avium-intracellulare* complex culture positive; and (4) those with at least 1 but fewer than 3 negative culture results were designated as being *M tuberculosis* culture indeterminate (ie, the 2 additional culture results were some combination of negative, contaminated, or *M avium-intracellulare* complex).

### STATISTICAL ANALYSES

Statistical comparisons were 2-sided and performed using the  $\chi^2$  test and Fisher exact tests, where appropriate. Odds ratios and 95% confidence intervals were calculated to assess factors associated with PTB, using the logistic regression model. Any records with missing data were excluded from the analysis based on that risk factor only.

All risk factors with  $P < .20$  on the univariate analysis were considered for the multivariate analysis, and only risk factors that had  $P < .05$  were retained in the final model. No interactions between risk factors were considered to be of a priori interest. Analysis was performed using SAS statistical software (version 6.14; SAS Institute Inc, Cary, NC) and Stata statistical software (version 8.1; Stata Corporation, College Station, Tex) at the specimen and participant levels.

## RESULTS

From October 4, 1998, through October 5, 1999, 14 098 immigrants were screened for tuberculosis; less than 0.1% of immigrants screened had positive HIV serologic test results. Of 1331 applicants eligible for the study (adults

with CXRs suggestive of active tuberculosis), 1269 (95.3%) agreed to participate. A total of 1265 participants were evaluated because 4 were unable to provide the required 3 sputum specimens and were therefore excluded from analysis.

### MYCOBACTERIAL CULTURE MEDIA RESULTS

Among the 1265 study participants, 3795 specimens were collected, and 15 178 culture media were inoculated (3795 BACTEC 12B and 11 383 LJ slants). The contamination rate for all culture media was 7.8% (1186/15 178), the rate for BACTEC 12B was 3.3% (124/3795), and the rate for LJ slants was 9.3% (1062/11 383).

### AFB SMEAR AND MYCOBACTERIAL CULTURE RESULTS AT THE SPECIMEN AND PARTICIPANT LEVELS

The AFB smear and culture results for the 3795 specimens (associated with the 15 178 culture media) are presented in **Table 1**. The AFB smear sensitivity among specimens was 32.7% (119/364). For participant-level analysis, among the 1265 study participants, 4 (0.3%) participants were designated as having contaminated culture status and were excluded, as were 82 participants (6.5%) who were designated as having indeterminate *M tuberculosis* cultures. Therefore, the participant-level analysis was limited to the 1179 study participants designated as being *M tuberculosis* culture positive or negative. Characteristics of these 1179 study participants are presented in **Table 2**. A total of 183 participants (15.5%) were designated as being *M tuberculosis* culture positive (ie, had PTB), of which 63 participants (34%) were also designated as being AFB smear positive.

### RISK FACTORS FOR PTB

In univariate analysis, demographic and clinical risk factors significantly associated with an increased odds of PTB included younger age (18-34 years), no history of tuberculosis disease or treatment, and reported tuberculosis symptoms (**Table 3**). The CXR findings associated with an increased odds of PTB were cavitation or consolidation, whereas fibrosis or calcification was found to be protective for PTB (**Table 4**). When the CXR analysis was stratified by AFB status, only calcification was found to be negatively associated with PTB among those who had

AFB smear–positive results. The multivariate logistic regression model indicated that younger age (18–34 years), no history of tuberculosis or treatment, reported symptoms, and cavitation or consolidation were independent risk factors for PTB (**Table 5**).

### TEST CHARACTERISTICS OF SCREENING AMONG IMMIGRANTS WITH ABNORMAL CXRs SUGGESTIVE OF ACTIVE TUBERCULOSIS

Among study participants, the sensitivity, specificity, and positive and negative predictive values of serial AFB screening for identifying PTB were 34.4% (63/183), 98.1% (977/996), 76.8% (63/82), and 89.1% (977/1097), re-

spectively (**Figure**). Sixty-three (77%) of 82 participants with abnormal CXRs and AFB-positive smear results (class A tuberculosis) had PTB, and 120 (11%) of 1097 participants with abnormal CXRs and AFB-negative smear results (class B1 tuberculosis) had PTB. Because tuberculosis symptoms were a risk factor for PTB, we also assessed screening among participants who reported tuberculosis symptoms (103/1179 [8.7%]); in this subgroup, the sensitivity increased to 45.5% (15/33), with a 95% confidence interval of 28.1% to 63.6%.

### ANTITUBERCULOSIS DRUG SUSCEPTIBILITY RESULTS

Antituberculosis drug susceptibilities for 151 *M tuberculosis* isolates were available from the 183 study participants with PTB. Fifty-two (34%) of 151 were resistant to 1 or more drugs; 5 (3%) were MDR.

**Table 2. Characteristics of Study Participants, US-Bound Immigrants, Ho Chi Minh City, Vietnam**

Characteristic	No. (%) of Study Participants (N = 1179)*
Age, mean (SD) [range], y	48.6 (16.2) [18-95]
Female	606 (51.4)
History of previous tuberculosis disease or treatment†	181 (15.4)
Positive HIV status‡	2 (0.2)
Positive AFB sputum smear status	82 (7.0)
Positive <i>Mycobacterium tuberculosis</i> culture status	183 (15.5)
Positive AFB sputum smear and positive <i>M tuberculosis</i> culture status	63 (5.3)
Positive AFB sputum smear and negative <i>M tuberculosis</i> culture status	19 (1.7)
Negative AFB sputum smear and positive <i>M tuberculosis</i> culture status	120 (10.2)
Negative AFB sputum smear and negative <i>M tuberculosis</i> culture status	977 (82.8)

Abbreviations: AFB, acid-fast bacilli; HIV, human immunodeficiency virus.  
 \*Data are number (percentage) of participants unless otherwise indicated.  
 †Five participants were missing.  
 ‡Three participants were missing.

### COMMENT

This study is the first, to our knowledge, to assess the performance of overseas tuberculosis screening (serial AFB sputum smears) for detecting PTB among US-bound immigrants with abnormal CXRs. We demonstrated that the rate of PTB among US-bound immigrants from Vietnam is high and that current overseas screening has limited ability to detect PTB among persons with abnormal CXRs; nearly two thirds of participants with PTB did not have their conditions diagnosed and were not given treatment overseas, although all were referred for follow-up in the United States. Overall, the rate of PTB found among all Vietnamese immigrants screened (183/14 098 or 1298 per 100 000 persons) was remarkably higher than the reported tuberculosis incidence rate in Vietnam. Furthermore, among study participants (immigrants with abnormal CXRs), we documented that almost 16% had PTB.

One of our main objectives was to assess the test characteristics of serial AFB smear screening among im-

**Table 3. Selected Demographic and Clinical Risk Factors for PTB, US-Bound Immigrants, Ho Chi Minh City, Vietnam**

Risk Factor	PTB, No. (%) (n = 183)*	No PTB, No. (%) (n = 996)†	Odds Ratio (95% CI)	P Value
Male sex	93 (51)	480 (48)	1.11 (0.81-1.52)	.51
Age group, y				
<18-34	68 (37)	195 (20)	1.00 (Referent)	<.001
35-44	34 (19)	225 (23)	0.44 (0.28-0.70)	
45-54	21 (11)	194 (19)	0.32 (0.19-0.54)	
55-64	22 (12)	160 (16)	0.60 (0.38-0.96)	
≥65	27 (15)	218 (22)	0.36 (0.22-0.59)	
History of previous tuberculosis disease or treatment‡	22 (12)	346 (35)	0.26 (0.16-0.41)	<.001
Recent tuberculosis exposure§	8 (4)	27 (3)	1.64 (0.73-3.68)	.22
Any reported tuberculosis symptoms	33 (18)	70 (7)	2.91 (1.86-4.56)	<.001
HIV status¶	1 (0.5)	1 (0.1)	5.45 (0.34-87.53)	.29**

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; PTB, pulmonary tuberculosis disease.  
 \**Mycobacterium tuberculosis* culture positive (at least 1 of 3 cultures positive).  
 †*M tuberculosis* culture negative (3 cultures with no growth).  
 ‡Five participants were missing.  
 §Twelve participants were missing.  
 ||Tuberculosis symptoms included fever, cough, night sweats, and blood-tinged sputum.  
 ¶Three participants were missing.  
 \*\*Fisher exact test (2-sided).



**Table 4. Chest Radiograph Risk Factors for PTB, US-Bound Immigrants, Ho Chi Minh City, Vietnam**

Risk Factor	PTB, No. (%) (n = 183)*	No PTB, No. (%) (n = 996)†	Odds Ratio (95% CI)	P Value
Cavitation	7 (4)	9 (1)	4.36 (1.60-11.86)	.006‡
Consolidation	79 (43)	322 (32)	1.59 (1.15-2.19)	.004
Adenopathy	5 (3)	22 (0.2)	1.24 (0.46-3.23)	.66
Fibrosis	135 (74)	830 (83)	0.56 (0.39-0.81)	.002
Calcification	29 (16)	241 (24)	0.59 (0.39-0.90)	.01
Nodules	0 (0)	3 (0.3)	NA	>.99‡
Effusion	0 (0)	2 (0.2)	NA	>.99‡
Volume loss	0 (0)	2 (0.2)	NA	>.99‡

Abbreviations: CI, confidence interval; NA, not applicable; PTB, pulmonary tuberculosis disease.

\**Mycobacterium tuberculosis* culture positive (at least 1 of 3 cultures positive).

†*M tuberculosis* culture negative (3 cultures with no growth).

‡Fisher exact test (2-sided).

**Table 5. Multivariate Analysis of Risk Factors for PTB, 1174 US-Bound Immigrants, Ho Chi Minh City, Vietnam\***

Risk Factor	Adjusted Odds Ratio (95% CI)	P Value
Age group, y		
18-34	1.00 (Referent)	<.001
35-44	0.44 (0.27-0.71)	
45-54	0.27 (0.15-0.47)	
55-64	0.50 (0.30-0.83)	
≥65	0.25 (0.14-0.42)	
History of previous tuberculosis disease or treatment†	0.20 (0.12-0.33)	<.001
Any reported tuberculosis symptoms‡	3.14 (1.92-5.14)	<.001
Cavitation on chest radiograph	4.68 (1.44-15.17)	.01
Consolidation on chest radiograph	2.38 (1.64-3.45)	<.001

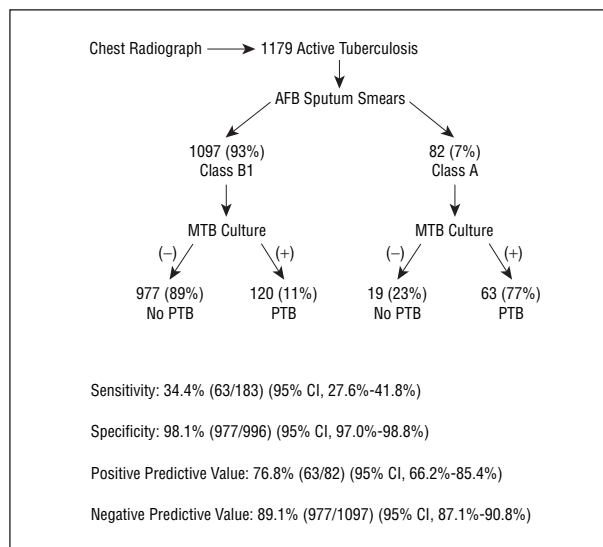
Abbreviations: CI, confidence interval; PTB, pulmonary tuberculosis disease.

\**Mycobacterium tuberculosis* culture positive (at least 1 of 3 cultures positive).

†Five participants were missing.

‡Tuberculosis symptoms included fever, cough, night sweats, and blood-tinged sputum.

migrants with abnormal CXRs. Acid-fast bacilli sputum smear staining is a highly specific test, but estimates of its sensitivity are moderate and variable, ranging from 22% to 80%. Sensitivity has been noted to vary with the staining technique used and whether direct or concentrated specimens are examined; in addition, previous estimates evaluate AFB smears in the diagnostic mode (ie, among persons with tuberculosis symptoms).<sup>25-29</sup> This study is the first, to our knowledge, to evaluate AFB smear sensitivity used in the screening mode among persons with abnormal CXRs (but most without reported symptoms). We found that screening AFB sensitivity falls in the lower range of previous estimates and is likely less sensitive than AFBs used in the diagnostic mode. We also found a lower positive predictive value for AFB smears than previously reported.<sup>28</sup> Reasons for this are likely multifactorial. First, errors in smear stain-



**Figure.** Test characteristics of the overseas tuberculosis screening algorithm. Serial acid-fast bacilli (AFB) smears among immigrants with abnormal chest radiographs, Ho Chi Minh City, Vietnam. MTB indicates *Mycobacterium tuberculosis*; PTB, pulmonary tuberculosis; plus sign, positive; minus sign, negative; and CI, confidence interval.

ing, examination, and culture preparation could have occurred; however, this is unlikely because a laboratory quality assurance program was maintained throughout the study. Second, oxalic acid processing was used to minimize *Pseudomonas* contamination caused by the high incidence of oral colonization in this population; such processing could have sterilized some *M tuberculosis*-positive specimens. Third, applicants may have taken antituberculosis medications before tuberculosis screening, causing false-negative culture results. Fourth, AFB-positive smears with *M tuberculosis*-negative cultures can occur owing to colonization or contamination with other mycobacterium. However, given the low contamination rate, this alone cannot explain our findings. Finally, we found a relatively low negative predictive value for AFB smears; approximately 11% of applicants with abnormal CXRs and AFB-negative smear results were found to have PTB. Furthermore, although 63 immigrants with PTB had AFB smear-positive results, almost twice as many (120 immigrants) with PTB had AFB smear-negative results and were not identified during standard screening.

This study has important implications because it demonstrates the limitations of current screening for identifying PTB and highlights the need to improve its performance; the consequences of delays in tuberculosis diagnosis and treatment include increased morbidity for patients and potential disease transmission to other persons in both host and migrant-receiving communities. Several avenues for improving screening performance can be considered. First, concentration methods such as centrifugation can provide some improvement in AFB sensitivity with a quality assurance program in place.<sup>29,30</sup> Adding culture and susceptibility testing should also be considered; although levels of MDR tuberculosis found among Vietnamese immigrants were low, MDR tuberculosis is increasing in many areas of

the world, and culture and susceptibility data can facilitate timely and appropriate therapy for both drug-sensitive and resistant disease. At the time of this writing, the CDC is responding to a large outbreak of tuberculosis and MDR tuberculosis among Hmong refugees in Thailand. Because cultures have not typically been required for entry into the United States, some MDR tuberculosis cases were not identified during overseas screening, causing a substantial burden on health departments in US resettlement communities and potentially facilitating tuberculosis transmission in Thailand and the United States. Including cultures in screening is challenging in that it would require regulatory and programmatic changes and resources to develop laboratory and directly observed therapy (DOT) treatment capacity, in collaboration with national tuberculosis programs. However, it is likely that this investment would be beneficial to indigenous and emigrating populations in resource-poor and developed countries alike.<sup>31</sup>

Second, it has been shown that AFB sensitivity can be enhanced by 20% to 60%, using a novel specimen-processing method that uses a zwitterion detergent, C<sub>18</sub>-carboxypropylbetaine, in conjunction with centrifugation, including in the context of overseas screening.<sup>32-36</sup> Third, studies of serodiagnostic assays and molecular testing methods to improve the sensitivity of tuberculosis diagnosis are needed, and some are already in progress.<sup>37,38</sup> Finally, applicants with identified PTB risk factors, such as tuberculosis symptoms and cavitation or consolidation on CXR, could be targeted for enhanced diagnostic testing or presumptive tuberculosis treatment. However, such a strategy would address only 16% of the 120 persons with AFB smear-negative PTB in this study.

This study demonstrated that a substantial number of immigrants with abnormal CXRs and PTB are undetected by overseas screening; however, more studies are needed. These studies include a cost-effectiveness analysis of the different proposed options for modifying current screening procedures; an assessment of screening performance among persons with normal or other CXR findings, especially among HIV- and tuberculosis-coinfected persons; determination of screening utility in other foreign-born groups<sup>4,9,39</sup>; and collection of long-term outcome data on migrants screened overseas after US resettlement. Overseas screening offers a unique opportunity to diagnose, treat, and prevent tuberculosis in migrant populations. Ultimately, investments in improved diagnostic methods, enhanced screening measures, and expanded laboratory and DOT treatment capacity in host countries will reduce tuberculosis morbidity and advance both US and global tuberculosis elimination efforts.

**Accepted for Publication:** July 26, 2005.

**Correspondence:** Susan A. Maloney, MD, MHSc, Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, 1600 Clifton Rd, MS E-03, Atlanta, GA 30333.

**Author Contributions:** Dr Maloney had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

**Financial Disclosure:** None.

**Funding/Support:** Financial support for this study was provided by the Centers for Disease Control and Prevention, Department of Health and Human Services, Atlanta, Ga.

**Acknowledgment:** We thank Truong Van Viet, MD, Hoang Hoa Hai, MD, Le Thien Huong Loan, RN, and Tran Thi Tin, RN, Cho Ray Hospital, Ho Chi Minh City, Vietnam; Mary Kamb, MD, and Patrick Chong, MS, Global AIDS Program, Hanoi, Vietnam; and Michael F. Iademarco, MD, Patricia Simone, MD, Charles Wells, MD, Beverly Metchock, MD, Thomas Shinnick, MD, and Kenneth Castro, MD, CDC, for their support and contributions.

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