Tuberculin Skin Testing of Physicians at a Midwestern Teaching Hospital: A 6-Year Prospective Study

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The epidemiology of tuberculin reactivity among physicians practicing in regions of moderate tuberculosis prevalence is unknown. We prospectively assessed the epidemiology of tuberculin skin test (TST) reactivity among physicians in training in St. Louis between 1992 and 1998. Of 1574 physicians who were tested, 267 (17%) had positive TST results. Older age, birth outside of the United States, prior bacille Calmette-Guérin (BCG) vaccination, and practice in the fields of medicine, anesthesiology, or psychiatry were associated with a positive TST result. Among physicians born in the United States, 63 (5.7%) had positive TST results. Among physicians with ≥2 documented TSTs, 12 had conversion to a positive TST (1.6%; 1.03 conversions per 100 person-years). Physicians in this study had a high rate of tuberculin reactivity, despite a low conversion rate. The relationship between TST conversion and birth outside of the United States and BCG vaccination suggests a booster phenomenon rather than true new TST conversions.

Physicians have long been known to be at risk for occupational exposure to tuberculosis, with the potential for subsequent development of infection and active disease. In the early 1900s, nearly three-quarters of all incoming medical students were already infected with tuberculosis. Of those who were not, almost all became infected during training, and 4%–14% of these individuals subsequently developed active tuberculosis [1–3]. In retrospective surveys of physicians who graduated from medical school between 1930 and 1981, 42%–47% reported a history of positive tuberculin skin tests (TSTs) [4, 5]. In addition, 66% of cases of active tuberculosis in physicians occurred within 6 years of graduation [6]. The resurgence of tuberculosis between 1985 and 1992 brought reports of nosocomial outbreaks of infection among patients and health care providers [7–13]. Many of these nosocomial outbreaks occurred in the eastern United States and involved HIV-infected individuals [12].

These reports of nosocomial tuberculosis renewed concerns about occupational exposure among physicians. Recent studies of positive TST results among physicians showed a rate of 13%–25% [14–16], which is lower than that historically reported for physicians but still higher than that for the general population. These studies have been limited by small sample sizes [15, 16] or a retrospective survey format [15]. In the largest of these studies, investigators prospectively followed housestaff physicians in a public inner-city hospital. It showed an overall rate of positive TST results (also known as TST positivity) of 15.5% and 11.6% among medical school graduates from the United States.
States. The hospital at which these physicians were trained, however, served a large, indigent population with a high rate of tuberculosis infection [14], and an outbreak of nosocomial tuberculosis had occurred among hospital staff just prior to the beginning of the study [17].

The purpose of our study was to prospectively evaluate the prevalence of positive TST results among physicians in training and to identify epidemiological risk factors for TST reactivity. We also sought to assess the incidence of TST conversion among housestaff and fellows in a region with a moderate prevalence of tuberculosis, in comparison with that in the general population of the United States.

MATERIALS AND METHODS

Barnes-Jewish Hospital (BJH) is a 1200-bed tertiary care center in St. Louis. During the 6-year study period, 127 cases of culture-positive tuberculosis were identified at the hospital. Data available from 1988–1994 showed that 58% of patients (89% of smear-positive cases) were placed in negative-pressure rooms during their hospital stay and that the median time from admission to isolation for presumed tuberculosis was 24 h (5th and 95th percentiles, 0 and 16 days) [18, 19]. Random testing of negative-pressure rooms in 1994 revealed 59% had effective negative pressure [20]. The annual incidence of active tuberculosis during 1991–1995 in the St. Louis metropolitan area, as reported by the Missouri Department of Health, was 10.6 cases per 100,000 persons in St. Louis City and 3.6 cases per 100,000 persons in St. Louis County, versus 9.8 cases per 100,000 persons in the United States during the same time period [21].

BJH employs resident physicians and some fellows (the remainder are employed by Washington University School of Medicine). The number of residents and fellows in training at BJH during the study period was ∼1600. Housestaff and fellows received the majority of their training at BJH but rotated to John Cochran Veterans Administration Hospital (500 beds) and St. Louis Regional Medical Center (a 250-bed public hospital) for 1–3 months of the year. Psychiatric residents also worked at St. Louis Metropolitan Psychiatric Center, a 130-bed psychiatric hospital.

BJH provides tuberculosis screening for all employees at the time of hire. Residents and hospital-employed fellows are skin-tested by the occupational health department when they attend orientation or if they voluntarily come to the occupational health department at the time of hire. Two-step initial skin testing started in 1998, after the study was completed. Employed physicians are given annual skin tests and postexposure testing if they have cared for nonisolated patients with documented tuberculosis. The hospital does not require routine tuberculosis skin testing for fellows who are employed directly through Washington University. Washington University School of Medicine provides voluntary annual TSTs for fellows employed by the school.

The investigators attended departmental and subspecialty conferences (clinical, research, and grand rounds) from 1 May 1992 through 14 November 1998 to solicit information and offer tuberculosis screening to physicians. The most well-attended conferences were selected, and department chairs and housestaff directors were notified of the study prior to each conference. Conferences were then attended 2–3 times over several weeks to maximize participation. The same conferences were then returned to annually, usually twice during a 3–4 week period every year. Data also were collected from BJH Occupational Health, including test results following known tuberculosis exposures.

Participants filled out a demographic survey that collected data on age, sex, place of birth, ethnicity, specialty, position, results of prior TSTs, and history of BCG vaccination. Ethnic categories were defined as white (non-Hispanic), African-American, Indian subcontinent, Middle Eastern, Asian (non–Indian subcontinent), and other (including Hispanic). Those with a history of a reactive TST filled out an additional questionnaire about chest radiography results, any previously diagnosed tuberculosis, and any therapy received for infection or active disease. All subjects who reported having a positive TST result in the past were seen by a study physician to verify results. If the history was unclear, the TST was repeated at the study site. TSTs were performed on all physicians who had a history of negative skin test results or had no prior TST results.

For the TST, 0.1 cc (5 TU) of a solution of purified protein derivative (Aplisol, Parke-Davis [1992]; Tubersol, Connaught Laboratories [1993–1998]) was injected intradermally on the volar surface of the forearm by means of the Mantoux method, and the reaction was read 48–72 h later by one of the investigators or a trained occupational health nurse. A positive reaction was defined as ≥10 mm of induration. A skin test converter was defined as a participant with a ≥10 mm increase in induration within the past 2 years, as documented at the study site. All participants with a positive TST result underwent chest radiography and were examined and counseled by one of the study physicians (V. J. F.). Recommendations for treatment of tuberculosis infection and active disease were made according to the Centers for Disease Control and Prevention and the American Thoracic Society guidelines [22–24].

Statistical analysis. Data were analyzed by use of SPSS, version 9.0 (SPSS). Univariate comparisons of categorical variables were made by use of χ² or Fisher’s exact test. Continuous variables were assessed by use of the Wilcoxon rank-sum test. A P value of ≤.05 was considered significant on 2-tailed testing. Multivariate analysis was performed by use of logistic regres-
RESULTS

Of the 1574 residents and fellows seen during the study period, 267 (17%) had positive TST results. Of those, 218 (82%) reported a prior positive test result, and 49 (18%) had an initial or follow-up positive test result at the study site. The characteristics of the study participants are shown in table 1. Available demographic data showed that the study group was predominately born in the United States (1119 subjects [71%]), male (1159 [74%]), and white (1120 [71%]). Of physicians who reported a previous positive TST result, only 66 (30%) reported ever receiving isoniazid prophylaxis. Prior BCG vaccination (P < .001), birth outside of the United States (P = 0.04), and older mean age (34.9 vs. 29.7; P = 0.008) were associated with not having received isoniazid.

The comparison of physicians with negative versus positive TST results is shown in table 2. Nonwhite physicians accounted for 58% of the positive TST results but only 28% of the total number of physicians tested. A total of 124 (83%) of 149 TST-positive, nonwhite physicians were either of Asian or Indian origin. Likewise, physicians who were not born in the United States accounted for 26% of the total group but 66% of those with a positive TST (175 of 267). A total of 149 (60%) of 248 physicians with a history of BCG vaccination were TST-positive, compared with only 7% of participants who had never been vaccinated (88 of 1263). The multivariate model was 87.9% correct at assigning physicians into the appropriate groups. BCG vaccination and birth outside of the United States were highly correlated (96% of vaccinated physicians were foreign-born); however, both variables were included in the model because of their significance on univariate analysis. Older age, birth outside of the United States, prior BCG vaccination, and practice of internal medicine, anesthesiology, or psychiatry were all associated with having a positive TST result.

Univariate and multivariate analysis findings and characteristics of the 1108 BCG-negative physicians who were born in the United States are shown in table 3. Sixty-three (5.7%) of the individuals in this subgroup had a history of positive TST results or were positive upon testing during the study. TST-positive physicians were older than TST-negative physicians in this group (mean age, 34.4 years vs. 29.9 years; P = .03). On multivariate analysis of the subset of physicians born in the United States, older age and practice in anesthesiology, internal medicine, and psychiatry were associated with having positive TST results, findings similar to those for all physicians in the study.

A total of 731 of the participants underwent >1 TST during the study period; 12 (1.6%) of these physicians subsequently converted to TST positivity, with an overall conversion rate of 1.03 per 100 person-years. Among the TST converters, 9 converted on the second skin test and 3 converted on the third...
Table 2. Univariate and multivariate analysis of physicians with negative and positive tuberculin skin test (TST) results.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) of physicians with TST result</th>
<th>P</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative (prior or new)</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>All physicians</td>
<td>1307 (83)</td>
<td>267 (17)</td>
<td>NA</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>30.0</td>
<td>31.5</td>
<td>.10</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>971 (75)</td>
<td>188 (71)</td>
<td>.24</td>
</tr>
<tr>
<td>Female</td>
<td>325 (25)</td>
<td>75 (29)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whitea</td>
<td>1013 (78)</td>
<td>107 (42)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nonwhite</td>
<td>288 (22)</td>
<td>149 (58)</td>
<td>.39 (0.91–2.13)</td>
</tr>
<tr>
<td>Place of birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United Statesa</td>
<td>1048 (81)</td>
<td>71 (29)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other</td>
<td>241 (19)</td>
<td>175 (71)</td>
<td>2.69 (1.59–4.56)</td>
</tr>
<tr>
<td>BCG vaccinated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noa</td>
<td>1175 (92)</td>
<td>88 (37)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Yes</td>
<td>99 (8)</td>
<td>149 (63)</td>
<td>8.30 (5.08–13.6)</td>
</tr>
<tr>
<td>Specialty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal medicine</td>
<td>556 (43)</td>
<td>123 (46)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Surgery</td>
<td>337 (26)</td>
<td>53 (20)</td>
<td>2.04 (0.98–4.26)</td>
</tr>
<tr>
<td>Radiologya</td>
<td>168 (13)</td>
<td>16 (6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Anesthesiology</td>
<td>84 (6)</td>
<td>28 (10)</td>
<td>3.61 (1.55–8.39)</td>
</tr>
<tr>
<td>Pathology</td>
<td>87 (7)</td>
<td>21 (8)</td>
<td>1.80 (0.76–4.29)</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>73 (6)</td>
<td>26 (10)</td>
<td>3.69 (1.53–8.88)</td>
</tr>
</tbody>
</table>

NOTE. We used a multivariate logistic regression model including age, race, BCG status, specialty, and place of birth as variables. NA, not applicable.

a Reference group for logistic regression model.

skin test at the study site. Compared to all physicians undergoing >1 skin test, converters were more likely to have been born outside of the United States (P < .001) and to have previously received BCG vaccination (P < .001), findings suggestive of booster reactions rather than new or recent infections in most cases.

DISCUSSION

This prospective study shows that among physicians who are training in a region where the incidence of active tuberculosis is moderate in comparison with that in the entire United States, the overall prevalence of infection with tuberculosis, as measured by TSTs, remains high. Risk factors associated with having a positive skin test result included older age, birth outside of the United States, prior BCG vaccination, and practice in internal medicine, anesthesiology, and psychiatry. Race was not found to be a statistically significant independent risk factor. To our knowledge, this study is the only reported large-scale, prospective analysis of tuberculosis risk factors for physicians who are training in a region of the United States with a moderate incidence of tuberculosis.

There are several limitations to our study. First, although annual testing of physicians is the current policy of BJH as per guidelines of the Occupational Safety and Health Administration [25], this policy was not actively enforced during the study period. Therefore, only a proportion of the total number of physicians could be tested during each year of the study by attending conferences. This study design was chosen because it would allow for the most physicians to be tested at one time and it targeted physicians in training, a group that has been shown to be at high risk for recent infection and subsequent disease [6, 26–28].

In addition, 2-step TSTs were not performed. The association seen between birth outside of the United States, prior BCG vaccination, and conversion to a positive TST result suggests that a booster effect resulted in a number of individuals with a remote history of tuberculosis infection or BCG vaccination being misclassified as new converters. In one large-scale study, 30% of Asian refugees with an initially negative skin test result...
were positive on subsequent (second and third) tests 7 and/or 90 days later [29]. A booster effect that resulted in artificially elevated conversion rates among health care workers has been reported elsewhere [30]. Past reports have also noted a relationship between BCG vaccination and apparent TST conversion among hospital employees, which is similar to that seen in our study [31]. If the conversions of BCG-vaccinated and foreign-born physicians were all considered secondary to a booster effect and excluded, then the true conversion rate would be .26 per 100 person-years, which is dramatically lower than the 5.98–1.09 per 100 person-year rate noted by Blumberg et al. [14]. However, despite inclusion of physicians with apparent booster effects in the group of new converters, the overall conversion rate in this cohort remains low. Our findings further support the use of 2-step testing for new health care workers, if it is necessary to determine the true conversion rate. However, in an area of low transmission, such as our study site, it is unclear whether the benefit of 2-step testing outweighs the cost and additional workload.

Over half of the foreign-born physicians who practice medicine at BJH come from Asia, where the rates of endemic tuberculosis are high. Previous studies have noted positive TST rates of 35%–55% in Asia [29, 32] and 54% among international students at one university in the United States [27]. Our positive skin test rate of 42% among foreign-born physicians is consistent with these rates and would suggest that most of these physicians’ reactions were due to infection with tuberculosis or BCG vaccination prior to immigration to the United States. Recent studies in which investigators have attempted to determine the relationship between positive TST results and prior BCG vaccination have been retrospective or performed in areas with high rates of tuberculosis [33–35], but their findings suggest that past BCG vaccination may contribute to increased TST reactivity.

The association between older age and higher likelihood of a positive TST result has been well described in reports on previous studies of physicians and other health care workers [4, 36, 37]. The difference in mean age between TST-positive and TST-negative physicians is only 1.5 years in this cohort, and the mean age is 30 years. Given the young age of this group, the cohort effect seen in older populations seems less likely, but this study does suggest that physicians further along in their training have more cumulative opportunities for exposure.

Our study showed a relationship between the practice of internal medicine, anesthesiology, or psychiatry and having a positive TST result for all physicians and for those born in the United States. Internists have been previously noted to be at increased risk for infection, most likely as a result of caring for a high-risk population [4, 14]. However, there is no clear explanation for the increased number of positive TST results among the other 2 specialties. Psychiatrists have been shown in one previous study to be at lower risk for tuberculosis infection [4], but in our study they had the highest rate of positive skin test results of any specialty in multivariate analysis. Although psychiatric patients have been previously noted to have high rates of TST positivity [38], none of the patients with

**Table 3. Characteristics of 1108 BCG-negative physicians who were born in the United States.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) of physicians with TST result</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative (prior or new)</td>
<td>Positive</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>29.9</td>
<td>34.4</td>
</tr>
<tr>
<td>Sex</td>
<td>793 (76)</td>
<td>47 (71)</td>
</tr>
<tr>
<td>Male</td>
<td>244 (24)</td>
<td>19 (24)</td>
</tr>
<tr>
<td>Female</td>
<td>904 (87)</td>
<td>59 (92)</td>
</tr>
<tr>
<td>Race</td>
<td>137 (13)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>White</td>
<td>438 (42)</td>
<td>37 (56)</td>
</tr>
<tr>
<td>Nonwhite</td>
<td>273 (26)</td>
<td>12 (18)</td>
</tr>
<tr>
<td>Specialty</td>
<td>64 (6)</td>
<td>8 (12)</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>65 (6)</td>
<td>1 (&lt;2)</td>
</tr>
<tr>
<td>Surgery</td>
<td>59 (6)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>Radiology</td>
<td>66 (6)</td>
<td>1 (&lt;2)</td>
</tr>
</tbody>
</table>

**NOTE.** TST, tuberculin skin test.
tuberculosis admitted to BJH during 1988–1998 were admitted to the psychiatry service. Among psychiatric nursing staff members, the rate of TST positivity was similar to that among other nurses during this period. In addition, no patients with tuberculosis were known to have been admitted to the other hospital in which the psychiatrists worked.

Anesthesiologists also had a higher-than-expected rate of TST positivity, independent of place of birth or vaccination status. Similar to the findings concerning psychiatrists, none of these physicians were exposed to the culture-proven cases of tuberculosis at the hospital during 1988–1998.

Non–BCG-vaccinated physicians born in the United States had a rate of skin test positivity that was much lower than in the foreign-born group. However, when compared to that for the United States population in general, the TST positivity rate among physicians born in the United States is much higher than the 0.97% rate noted among active military personnel [39] and comparable to the 5.6%–11% rate reported among economically disadvantaged youths and prison inmates [40–43]. One possible explanation is that physicians born in the United States may have attended medical schools in regions with higher rates of tuberculosis and thus been exposed to tuberculosis earlier in their training. Data on past medical school training was not obtained in the original study. However, 100 housestaff and fellows were randomly sampled from the cohort, and the city in which they attended medical school was determined. The 7 TST-positive physicians in the sample had studied in cities with a mean tuberculosis case rate of 4.4 cases per 100,000 persons; in comparison, the 93 negative subjects had studied in cities with a mean case rate of 9.3 cases per 100,000 persons (P = .09). This analysis, of course, does not take into account the individual rates of the training hospitals in each city, which may be greater than the metropolitan rates.

Forty-eight percent of physicians in our study who were <35 years of age and who had a history of TST positivity reported having received isoniazid therapy at some time. This study did not address whether these physicians were ever offered or ever completed an appropriate course of treatment. The efficacy of isoniazid at reducing the risk of reactivation of latent tuberculosis infection is well known: isoniazid chemotherapy prevented 75%–90% of cases of reactivated disease in 28,000 tuberculin-positive individuals with previously untreated fibrotic pulmonary lesions [44].

A disappointingly low rate of treatment compliance among physicians has been noted in past studies [4, 15], including a smaller study done previously at our institution [16]. There are many potential reasons for this low rate of compliance, including denial of illness, neglect of illness due to stress and overwork, and the belief that childhood BCG vaccination will cause lifelong TST positivity. This last point conflicts with guidelines of the Centers for Disease Control and Prevention (CDC), which state that a positive TST result for an individual who underwent BCG vaccination >10 years previously is evidence of Mycobacterium tuberculosis infection [45]. The results of this study support the recommendations of the CDC that all physicians be periodically screened for tuberculosis infection, even those who are from regions with a moderate incidence of tuberculosis, and that increased efforts should be focused on effectively providing treatment for those with evidence of latent tuberculosis infection.

Acknowledgment

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References