Title

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Journal

Pediatrics, 115(6)

ISSN

0031-4005

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Publication Date

2005-06-01

DOI

10.1542/peds.2004-1685

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Pediatrics 2005;115;647-653
DOI: 10.1542/peds.2004-1685

Risk Factors Associated With Latent Tuberculosis Infection in Mexican American Children

Janine Young, MD, and Mary E. O'Connor, MD, MPH

ABSTRACT. *Objectives.* **To determine risk factors that are associated with the presence of latent tuberculosis infection (LTBI) in Mexican American children.**

Methods. **In this prospective cohort study, we administered tuberculin skin tests (TSTs) and a tuberculosis (TB) risk factor questionnaire to children who were aged 1 to 18 years in immigrant families at a Denver inner-city community health center and elementary school–based health center. Information requested on the questionnaire included child demographics, child and parent birth location, Bacille Calmette-Guérin (BCG) vaccination, and a history and the duration of child and family travel to and visitors from countries where TB is endemic. TST results were read at 48 to 72 hours and were interpreted as positive at 5- and 10-mm induration, depending on risk factor history. All participants received $5 coupons on return for TST reading.**

Results. **Of 584 children enrolled, 96% returned for TST evaluation, median age was 4 years, 48.6% were male, 98.5% were Latino, 66.3% were born in the United States, and 33% were born in Mexico. Overall, 12.4% of children had positive TSTs. For all children in the study, a positive TST was associated with birth in Mexico and no BCG received (adjusted odds ratio [OR]: 15.7; 95% confidence interval [CI]: 1.5–165.2), birth in Mexico and received BCG (adjusted OR: 29; 95% CI: 12.7–66.1), birth in the United States and received BCG (adjusted OR: 9.1; 95% CI: 2.4–34.1), and child travel to Mexico (adjusted OR: 2.8;95% CI: 1.5–5.4). Risk factors for having a positive TST in the 387 children who were born in the United States were travel to Mexico (unable to calculate the OR because all had traveled to Mexico), older age (median: 6 years; adjusted OR: 1.2/year; 95% CI: 1.02–1.40), and a history of BCG vaccination (adjusted OR: 8.2; 95% CI: 2.0–34.0). For the 195 children who were born in Mexico, logistic regression of the following variables showed that none of the variables remained in the model: child age, gender, BCG status, family travel to Mexico, visitors to the United States, child travel to Mexico, years lived in Mexico, and years since BCG.**

Conclusions. **In a population of primarily Mexican American children, those who were born in the United States had an increased risk for developing LTBI when they had a history of BCG vaccination or had traveled to Mexico. For children who were born in Mexico, we were unable to identify additional risk factors for the presence of LTBI, besides their birth in Mexico. Incentives for return for TST reading, such as grocery coupons, are highly effective.** *Pediatrics* **2005;115:e647–e653. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-1685;** ***tuberculin skin test, latent tuberculosis infection, immigrants, tuberculosis screening.***

ABBREVIATIONS. TB, tuberculosis; LTBI, latent tuberculosis infection; TST, tuberculin skin test; AAP, American Academy of Pediatrics; BCG, Bacille Calmette-Guérin; WFHC, Westside Family Health Center; VSBHC, Valdez School-Based Health Center; CI, confidence interval; CSA, Central and South America; OR, odds ratio.

Although the prevalence of active tuberculosis (TB) in the United States has continually declined since its resurgence and peak in 1992, this trend has not been mirrored among immigrants to the United States. The decrease in active TB cases in people who were born in the United States has been largely attributable to public health investigation of active TB cases, contacts, and treatment of active cases via direct observed therapy. The Centers for Disease Control and Prevention reported in 2003 that the overall active TB case rate dropped by 50% from 1992 to 2002. In 2002, for the first time, immigrants to the United States made up the majority (51%) of active TB cases in the United States. The rate increased in 2003 to 53.3%.[1,2] Consequently, there is a need to improve identification and treatment of active TB in immigrants from high-risk countries.

Identifying active TB in immigrants is not always straightforward. Many immigrants from high-risk countries, particularly children, do not immigrate with symptomatic TB disease. Instead, they come to the United States with latent TB infection (LTBI), having no symptoms of active TB disease but harboring the risk for activating and becoming infectious at some time in their lives. LTBI is diagnosed when a child or an adult has a positive tuberculin skin test (TST) and a normal chest radiograph and are asymptomatic.[3] Children with a positive TST most likely have an equivalent lifetime risk for developing active disease compared with most adults.[4] Risks for a child with LTBI for developing active TB include stressors such as going through an adolescent growth spurt and the development of chronic diseases such as diabetes.[3] TB infection in children represents more recent exposure than in many adults and therefore is indicative of recent TB transmission.[5] A multisite evaluation of primarily US-born

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Accepted for publication Dec 16, 2004.
doi:10.1542/peds.2004-1685
No conflict of interest declared.
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children who were younger than 5 years and had active TB found that for the children in whom a source could be identified by genotyping and public health investigation, 51% of the identified source cases were foreign born.[6] In adult immigrants, the first 5 years after immigration carries the highest risk for developing active TB. This probably reflects that acquisition of TB infection most often occurs before immigration.[7,8] This has been supported by several molecular epidemiologic studies that have shown that isolates of active TB in immigrants were not associated with any known US cases.[9,10]

It is arguably the reservoir of immigrants with LTBI—patients without symptomatic infectious TB disease but with the potential to develop active TB later—that has served as a continued source of active TB cases. Although legal immigrants are required to have a TST placed to be considered for residency or citizenship in the United States, a large number of undocumented immigrants are never screened. Given that there is no mandated screening, treatment, or reporting of cases of LTBI, this may explain why current public health measures have done little to decrease rates of active TB in immigrants.

The American Academy of Pediatrics (AAP) guidelines for screening children for TB recommend screening only children who are at "higher risk" for contracting TB. "Higher risk" variables include child or parent birth in a foreign country; history of foreign visitors in a child's home; travel to a high-risk country; and exposure to people with active TB or people who have HIV, are homeless, are institutionalized, are users of illicit drugs, or are migrant farm workers.[11] On immigration, it is recommended that children be screened with a TST if they are from a high-risk country.

Given the ambiguity in the current AAP guidelines, the continued increase in the percentage of active TB cases in immigrants, and the wide variability in LTBI screening practices applied by practitioners,[12–14] we designed a questionnaire to be used in a Mexican immigrant population to attempt to identify risk factors for a positive TST. Previously, questionnaire studies have been done to assess risk factors for a positive TST in pediatric populations consisting of the middle-class insured and those of low-income, mixed ethnicity.[15–18] The main goals of our study were to (1) identify factors that are associated with a positive TST in a Mexican immigrant population; (2) evaluate Bacille Calmette-Guérin (BCG) vaccine history affect on TST results; and (3) determine whether a history of foreign visitors to the child's home, family or child travel to Mexico, and cumulative length of time of these exposures to potential active TB cases increases risks for a positive TST.

METHODS

Study Subjects

Children who were 1 to 18 years of age were enrolled 2 to 3 days per week, depending on availability of a research assistant. The research assistant was present on Mondays, Wednesdays, and Fridays and enrolled all children who had a TST placed. Criterion for inclusion was the provider decision to place a TST. This decision was based on high-risk criteria, most commonly the child's or parent's being born in a high-risk country. Parental birth in a high-risk country was usually assumed when English was not the parents' preferred language. Exclusion criteria were previous TST placement in the last year, history of positive TST with treatment, or sibling in the study. When the research assistant was present, an attempt was made to enroll all children who had a TST placed. When the research assistant was not available when the TST was placed, the child was referred to the research assistant when he or she returned for the TST reading. No data were obtained regarding children who were not enrolled when the research assistant was unavailable. Children were enrolled primarily at well-child care visits by pediatric providers at an inner-city community health center (Westside Family Health Center [WFHC]) and secondarily at an elementary school–based health center (Valdez School-Based Health Center [VSBHC]). No parents refused enrollment in the study. Parents of children at VSBHC were enrolled while attending an educational session about eligibility for discount insurance programs where TB was also discussed.

Questionnaire

The questionnaire was designed by the authors on the basis of review of the literature, other questionnaires, and consultation with the Denver Department of Health TB Clinic staff and experts in pediatric infectious disease. The study questionnaire was piloted on families who presented to WFHC during a 2-week period. It was available in Spanish and English. At WFHC, the questionnaire was administered orally by 1 bilingual research assistant, and at VSBHC, the questionnaire was administered orally by a bilingual nurse practitioner.

The questionnaire requested information on child age, gender, and race/ethnicity; child and parent birth location; and length of time the child and parents had lived in the United States. Parental report of previous TST placement and results was obtained. History of BCG vaccine and date (per parent report or from vaccine records) was recorded. Parents were asked about history and duration of family travel to high-risk countries and of foreign visitors to the child's home in the past year. They were also asked about the child's travel to a high-risk country since birth and duration of the visits. A "high-risk country" was defined by increased active TB case rates as reported by the World Health Organization.[19] Parents were also asked about other TB risk factors, including exposure to people who had active TB, worked or were in jail, had HIV/AIDS, were homeless, and were abusing drugs or alcohol. When parents reported TB exposure history, they were asked whether a chest radiograph was obtained, results of the radiograph, type of treatment, and length of treatment.

Study Protocol

At WFHC, either before or after the research assistant administered the oral questionnaire, the children received an intradermal injection of 5 tuberculin units of the tuberculin TST by a nurse or a medical assistant who was trained at the TB Clinic of the Denver Department of Public Health. When the research assistant was unavailable on the day when the TST was placed but was available when the child returned for the reading, the research assistant administered the questionnaire at this time. TST results were interpreted at 48 to 72 hours by a group of 5 nurses and the research assistant, who were trained to read TSTs at the Public Health Department. Children who had TSTs placed on Thursdays had their TST evaluated on Monday. There was no testing of intra- or interobserver reliability in TST placement or reading. When possible, participants received a reminder telephone call to return for TST reading, and all participants received a $5 coupon for groceries on their return. Millimeters of induration were reported for all positive TST results.

Study participants at the VSBHC were recruited while their parents were attending an educational session about eligibility for discount insurance programs with added discussion about TB. Five-dollar coupons were given to parents at the time of obtaining parental consent. The questionnaire was administered and the TSTs were placed on Mondays and Wednesdays. TSTs were read while the child was at school, at 48 to 72 hours by 1 nurse practitioner (also trained at the TB Clinic of the Denver Department of Public Health).

TSTs were read as positive when there was ≥10-mm indura-

tion. TSTs were read as positive at ≥5-mm induration when children had close contact with someone with active or suspected active TB, had clinical symptoms of active TB, or were immunosuppressed.[3] All participants with positive TSTs had a chest radiograph taken and were given appointments at the TB clinic for follow-up and initiation of treatment.

Approval for the study was obtained from the Colorado Multiple Institutional Review Board at the University of Colorado Health Sciences Center. Written informed consent for study enrollment was obtained from all parents.

Sample Size

On the basis of an estimate that 30% of the sample would be lower risk (born in the United States to immigrant families or having been in the United States >5 years) and that the rate of positive TSTs in the higher risk 70% of the sample would be 5% compared with 1% in the low-risk group, with a power of 80% and 95% confidence intervals (CIs), a sample size of 850 was calculated. This was increased to 1000 to account for an estimated 15% of the children who did not return for reading of their TST. However, when study monitoring showed a very high rate of return for TST reading (>95%) and a higher-than-expected rate of TST positivity (>10%), the sample size was decreased to 600.

Data Analysis

Data were entered into the computer using Microsoft Access, and analysis was performed using SPSS for Windows, version 10.00, and Epi Info 2000. Data on all children who were born in the United States and Central and South America (CSA) were analyzed together and then as separate groups. Univariate odds ratios (ORs) were calculated for demographic factors and the presence of any family member's travel in the past year, family visitors to the United States in the past year, and child travel to country of origin during the child's lifetime. For children who had traveled, parents were asked the number of trips that the child had made during their lifetime and to estimate the duration of each trip. These data were collected in months and added for all of the trips to yield total number of months spent in the country of child or parental origin.

Logistic regression analysis was performed with the outcome variable being TST results. Variables that were significantly associated with positive TST results on univariate analysis were included in the logistic regression. The total number of months of child travel (0 to maximum number of months) was entered into the logistic regression equations when child travel was an associated factor.

RESULTS

Study Population

A total of 613 children were enrolled. Five patients were excluded because they were screened at <1 year of age. Of the remaining 608 children, 24 (4%) patients did not return for evaluation of their TST and were also excluded. The 24 children with unread TSTs had an older mean age compared with the children who returned for TST reading (6.83 vs 4.76 years; $P \leq .004$). More of the children who had their TSTs read had a history of family travel ($P \leq .001$).

Data were analyzed for 584 children who had a median age of 4 years. A total of 283 (48.6%) children were male; 575 (98.5%) were Latino; 387 (66.3%) were born in the United States; 195 (33%) were born in Mexico; and 1 child each was born in Honduras, Peru, Algeria, and Ethiopia. Mexico, Honduras, and Peru were defined as CSA. The 2 children who were born in Algeria and Ethiopia were excluded from final data analysis. The majority of mothers (91%) and fathers (92%) were born in Mexico, and 33 (5.7%) of mothers and 26 (4.5%) of fathers were born in the United States. A total of 2% of parents were born in Honduras, Guatemala, El Salvador, Peru, Thailand, Algeria, Ethiopia, or Vietnam.

TST Results

Results of the univariate and multivariate analysis of risk factors for having a positive TST for all children who were born in the United States or CSA are listed in Table 1. All 72 (12.4%) of the 584 subjects with a positive TST were born in the United States or CSA. Twelve (2%) were born in the United States, and 60 (10%) were born in CSA. Of this group of children with a positive TST, 1 was identified as having asymptomatic active TB (diagnosed by the presence of hilar adenopathy on chest radiography). This case, a 6-year-old boy who was born in Mexico, had a TST induration of 13 mm, had received BCG at birth, and had been living in the United States for 1.5 years. He had no history of a prior TST and no travel to Mexico by him or his family. Since immigration, he had 2 relatives who cumulatively visited for 2 weeks over the past year. He had no known contact with anyone with active TB. The 71 remaining children received a diagnosis of LTBI. One child had a positive TST at 7 mm as a result of exposure to a

TABLE 1. Univariate and Multivariate Analysis of Risk Factors for LTBI in Children Who Were Born in the United States and CSA ($N = 582$)

Variable	TST+ ($N = 72$)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Female	34/299 (11%)	Reference	—
Male	38/283 (13%)	0.83 (0.49–1.39)	—
Median age	6 y*	—	†
Born in US, no BCG	8/363 (2%)	Reference	—
Born in US, received BCG	4/20 (20%)	11.1 (2.5–47.1)	9.1 (2.4–34.1)
Born in CSA, no BCG	1/5 (20%)‡	11.1 (0.0–131.9)	15.7 (1.5–165.2)
Born in CSA, received BCG	58/187 (31%)‡	19.9 (8.9–46.5)	29.0 (12.7–66.1
No family travel	50/412 (12%)	Reference	—
Family travel	22/170 (13%)	1.08 (0.61–1.9)	†
No visitors to US	46/374 (12%)	Reference	—
Visitors to US	26/208 (12%)	1.02 (0.59–1.75)	†
No child travel	43/359 (12%)	Reference	—
Child travel	29/223 (13%)	1.10 (0.64–1.87)	2.8 (1.5–5.4)

— indicates analysis not performed.
* $P < .001$, Mann-Whitney U test compared to median age of 4 years in the TST$^-$ group.
† Did not remain in model.
‡ The parents of 1 child who was born in Mexico with a positive TST reported "don't know" to the question regarding receipt of BCG.

grandfather with possible active TB in the past. Figure 1 shows the frequency of TST sizes.

Of 582 children who were born in the United States or CSA, only 88 (15%) reported a history of a negative TST. Of these 88, 23 (26%) were born in CSA. Nine (40%) of these children who were born in CSA and had a history of a negative TST now had a positive TST and received a diagnosis of LTBI. Four (6%) of 65 children who were born in the United States and had a previous negative TST now had a positive TST ($P < .001$, Fisher exact test). These 13 children seem to be TST converters, indicating TB exposure since their previous TST. Because of the small number of children in this category, we could not determine which types of exposures were significant. Of the 195 children who were born in CSA, 172 (88%) had no reported previous TST. Of the 60 (31%) children in this group with positive TSTs, 24 (40%) had been living in the United States for >2 years before their first TST.

BCG

Twenty (5%) of the children who were born in the United States received BCG compared with 187 (96%) of the children who were born in CSA. Of 20 children who were born in the United States and received BCG vaccine while visiting Mexico, 4 (20%) were TST positive. These 4 children received BCG within the first year of life when they traveled to Mexico. Of 187 children who were born in CSA and received BCG vaccine, 58 (31%) were TST positive and 129 (69%) were TST negative. For all children in the study, receipt of BCG vaccine was associated with a positive TST (see Table 1).

The diameter of induration of positive TST was not correlated to months since receipt of BCG. For both those who did and did not receive BCG vaccine, median size of positive TSTs was 14 mm. Of the 60 subjects who had received BCG vaccine and were TST positive, the older the subject, the larger the induration of the TST (age 1–5 years, median TST induration: 12 mm; 6–12 years, median TST induration: 14 mm; >12 years, median TST size: 19.5 mm; $P = .01$ by Kruskal Wallis test).

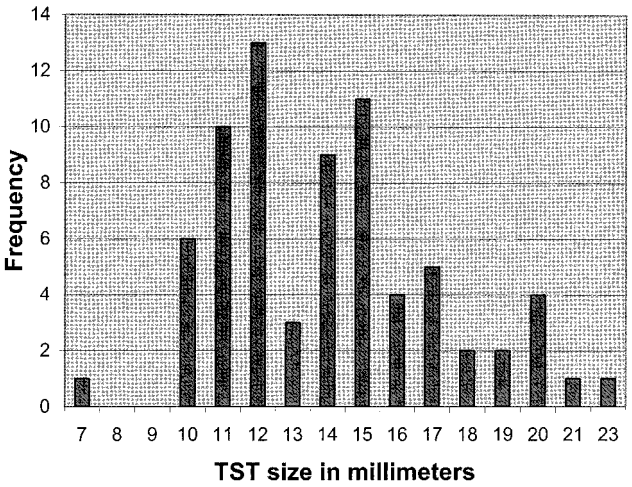

Fig 1. Frequency of size in millimeters of positive TST ($N = 72$).

Child Birth Location

Birth in CSA was a significant risk factor for developing LTBI, irrespective of receipt of BCG vaccine (see Table 1).

Travel/Visitors

Travel by the children to CSA during their lifetime was also a significant risk factor for developing LTBI; however, duration of child travel was not significant (see Table 1). There was no significant correlation between visitors to the United States in the past year with child travel to CSA in the child's lifetime. Visitors from high-risk countries did not increase the risk for children's having a positive TST.

Exposure to High-Risk People

There was 1 exposure of a child to a person with active TB. Exposure of this population to other high-risk people (eg, HIV-positive patients, alcohol/drug users) was <2% for all categories. Of this group, only the child who was exposed to a person with active TB had a positive TST of 7 mm and received a diagnosis of LTBI.

Analysis of Children Who Were Born in the United States

For the 387 children who were born in the United States to immigrant families, all 12 children with a positive TST had traveled to CSA. Using logistic regression for all other risk factors, receipt of BCG had an OR of 8.2 (95% CI: 2.0–34.0). For each additional year of the child's life, the probability of having a positive TST increased by a factor of 1.2 (see Table 2).

Analysis of Children Who Were Born in CSA

For the 195 children who were born in CSA, logistic regression of the following variables showed that none of the variables remained in a model to predict a positive TST: child age, gender, BCG status, family travel to CSA, visitors to the United States, child travel to CSA, years lived in CSA, and years since BCG (see Table 3).

DISCUSSION

Currently, neither the Centers for Disease Control and Prevention nor public health departments maintain a national registry of reported cases of LTBI. In addition, treatment of LTBI is not required because patients with LTBI are not infectious and therefore are not considered an immediate public health risk.

Although there are no absolute numbers available to quantify total US cases of LTBI and those represented by subpopulations, several studies, including ours, have studied LTBI in children from different regions of the country.[15–18,20] Our study looked at a predominantly Mexican American immigrant population in inner-city Denver (32% of Denver County's population is Hispanic[21]). Our sites for recruitment occurred at a community health clinic (WFHC), where 89% of the pediatric population is Hispanic, 56% receive Medicaid, 13% have commercial insurance, and 24% are uninsured (7% described as

TABLE 2. Univariate and Multivariate Analysis of Risk Factors for LTBI in Children Who Were Born in the United States ($N = 387$)

Variable	TST+ ($N = 12$)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Female	8/201 (4%)	Reference	—
Male	4/186 (2%)	0.53 (0.13–1.98)	†
Median age	6 y*	—	1.2/y (1.02–1.4)
No BCG	8/363 (2%)	Reference	—
Received BCG	4/20 (20%)	11.1 (2.5–47.1)	8.2 (2.0–34.0)
No family travel	6/254 (2%)	Reference	—
Family travel	6/133 (5%)	1.95 (0.55–7.0)	†
No visitors to US	7/239 (3%)	Reference	—
Visitors to US	5/148 (3%)	1.16 (0.31–4.16)	†
No child travel	0/203 (0%)	Reference	—
Child travel	12/184 (7%)	Unable to calculate	0.00 (0.00–1.19 × 10^{22})
Median mo of child travel	5‡	—	†

— indicates analysis not performed.
* $P = .03$, Mann Whitney U test compared with 3 years in the TST− group.
† Did not remain in model.
‡ $P = .18$, Mann Whitney U test compared with 0 months in the TST− group.

TABLE 3. Univariate and Multivariate Analysis of Risk Factors for LTBI in Children Who Were Born in Mexico ($N = 195$)

Variable	TST+ ($N = 60$)	Unadjusted OR (95% CI)
Female	26/98 (27%)	Reference
Male	34/97 (35%)	1.5 (0.78–2.89)
Median age	6 y*	—
No BCG	1/5 (20%)†	Reference
Received BCG	58/187 (31%)†	1.8 (0.18–43.2)
No family travel	44/158 (28%)	Reference
Family travel	16/37 (43%)	1.97 (0.89–4.4)
No visitors to US	39/135 (29%)	Reference
Visitors to US	21/60 (35%)	1.33 (0.66–2.7)
No child travel	43/156 (27%)	Reference
Child travel	17/39 (44%)	2.03 (0.93–4.45)
Median years since BCG	7‡	—
Median years lived in Mexico	3.75§	—

— indicates analysis not performed.
* $P > .05$, Mann Whitney U test compared with median age of 6 years in the TST− group.
† The parents of 1 child who was born in Mexico with a positive TST reported "don't know" to the question regarding receipt of BCG.
‡ $P > .05$, Mann Whitney U test compared with median years since BCG of 5 in the TST− group.
§ $P > .05$, Mann Whitney U test compared with median years lived in Mexico of 3.75 in the TST− group.

"other"). Recruitment also occurred at a Denver elementary school clinic (VSBHC), where ~65% of children come from Spanish-speaking households and where 98% are from low-income families (based on eligibility for free meal program). Of the studies that have examined LTBI in children, ours had the highest LTBI prevalence rate of 12.5% (other studies ranged from 0.4% to 7.6%).[15–18,20] These disparate prevalence rates most likely reflect the varying regions studied and makeup of the population, including differences in race, ethnicity, country of origin, and age ranges of enrollees in each study.

Colorado is a state with a low incidence of active TB (2.4 cases per 100 000 population in 2003).[2] However, 70.2% of active TB cases in Colorado in 2003 occurred in the foreign born.[22] Our 12.5% LTBI prevalence rate reflects a subpopulation with a known higher incidence of active TB: the Mexican American immigrant population. With Mexico's rate of active TB reported as 12 per 100 000 population and Mexican immigrants having the highest reported rate of active TB (25.6%) of all immigrants in the United States in 2003, outranking immigrants from Vietnam (8.4%) and from the Philippines (11.6%), it is not surprising that an urban area such as Denver, with a high concentration of Mexican American immigrants, would have a relatively high prevalence of LTBI.[2,16]

In our study, 96% of screened children returned for evaluation of their TSTs. Other studies have noted difficulty in having patients return for reading of TSTs, with return rates ranging from 40% to 45%.[23,24] Our very high return rate may have been attributable to the $5 coupons given when the TST was read and/or the greater fear of TB infection in our Mexican immigrant population. This improved return rate was noted in another study that used telephone call or postcard reminders with a return rate of 91%.[25] The children who were tested for TB infection at our school-based health center were available for follow-up of their TST on site. This group had a 100% rate of follow-up. Given the low number of no-shows for evaluation of TSTs in our study, the results of our project should be representative of our clinic population.

Analysis of all of the children with a positive TST in our study showed that birth location, receipt of BCG, and a history of child travel to Mexico were associated with a positive TST. These factors are similar to those found in other studies.[15–18] However, when we analyzed the children who were born in Mexico separately from those who were born in the United States to immigrant families, our results were different in the 2 groups. In our children who were born in the United States, the risk factors that were independently associated with having a positive TST were older age at presentation, a history of BCG, and child travel to Mexico. Duration of child travel was not associated with an increased risk for developing a positive TST.

In the children who were born in CSA, other than their birth in a high-risk country, we could not de-

termine other factors that were associated with a positive TST. For children who were born in CSA, there is a clear need to test for TB at immigration. Perhaps previous exposure to active TB in Mexico is such an overwhelming risk factor compared with other factors that these other factors cannot be measured. In our study, only 23% of children who were born in CSA had a history of a reported negative TST, and 9 of these converted to positive TSTs. We therefore were unable to determine risk factors for development of LTBI once members of this population were living in the United States. Of children who were born in CSA and received a diagnosis of LTBI in our study, 31% had been in the United States for >2 years before their diagnosis. Additional study needs to evaluate ways of effectively educating health care providers so that high-risk children are screened appropriately.

It is known that the specificity of the TST is decreased by cross-reactivity from BCG vaccination and from infection with atypical mycobacterial disease.[6,26] It is also known that the closer temporally TST testing is to BCG vaccination, the more likely a patient will have a reactive TST[27] and that the larger the size of TST, the less likely it is assumed to be attributable to BCG.[28–30] As such, there is some concern that vigorous TB screening in immigrant children, particularly young children, may identify cross-reactors to BCG vaccine and not cases of LTBI. In our study, the size of a positive TST was not associated with time since BCG vaccination. The median size of positive TSTs was equal for those who did and did not receive BCG vaccination. Of the children who were born in CSA, 69% received BCG and were TST negative. The median age of all children in our study with a positive TST was older than the median age of the children with a negative TST. Older children were more likely to have larger induration of their positive TSTs than younger children. The majority of these older children had BCG placement at birth. One interpretation of these findings is that older children with larger TST sizes had more potential years of cumulative exposure to cases of active TB and therefore were more likely to be truly positive than the younger children who had smaller TST sizes.

There were several limitations to our study. First, we did not record the amount of induration of the TST in TST-negative children. This information could have helped us to improve the interpretation of the affect of BCG on TST size. Second, in foreign-born patients with a reportedly negative previous TST and a history of BCG at birth, repeat TSTs that are positive may be true positive. However, these positive results may also be attributable to boosting from previous BCG vaccination or infection with an atypical mycobacteria. To help distinguish between true positives and boosting, additional study is needed of patients with documented previous negative TSTs and history of BCG vaccine. Alternatively, development of other testing methods to improve measurement of immunity to mycobacterium TB infection needs to be pursued more vigorously. Because of the inability to separate boosting and atypical mycobacterial infection in these children, all children with a positive TST were assumed to have LTBI. Third, we did not screen household contacts of children with positive TSTs and, thus, were unable to determine whether a childhood case of LTBI in a household was associated with other cases of LTBI. Fourth, we may have created some degree of recall bias by, at times, administering the questionnaire after reading TSTs, potentially increasing the estimation of active TB exposures. However, because none of our children with a positive TST reported an exposure to active TB, this does not seem to be a significant issue. Fifth, in the majority of cases, TST history was obtained by parental report and not through medical records. This may have caused inaccuracy in TST histories. Sixth, we had multiple professionals interpreting TST results. Although all had been trained at 1 site, we did not measure inter- or intraobserver validity of TST interpretation, potentially causing some over- or underdiagnosing of positive and negative TSTs. However, the normal spread of TST sizes makes it more likely that readers had equivalent interpretations (see Fig 1). Given that our study looked at a select population of children who were primarily from Mexico and had immigrated, there may be limited applicability of our study results to Hispanic immigrants from other countries.[20]

CONCLUSIONS

In our population of primarily Mexican American children, those who were born in the United States had an increase in risk of 20% per year for developing LTBI. All children who were born in the United States and had positive TSTs had traveled to Mexico. A history of BCG vaccination was also independently associated with a positive TST. Given these results and the recommendations of the AAP for TB screening, we would recommend that children who are born in the United States to Mexican immigrant families have a TST at 12 to 15 months of age unless there are other known risk factors. Repeat TST should occur after any travel to Mexico and when there are multiple episodes of travel in a given year, 1 year after previous TST testing. If no travel has occurred, then testing should probably be repeated every 2 to 4 years.

For children who were born in Mexico, we were unable to determine adequately risks for a positive TST besides birth in Mexico. There needs to be additional study of this group, particularly focusing on immigrants to the United States with repeated trips back to Mexico. For children who are born in Mexico, initial TST testing should occur at 12 to 15 months of age or at first presentation to a health care system if the child is older than 1 year. The majority of child immigrants who had a history of BCG vaccination administered in Mexico were TST negative. Additional research on the predicting factors for TST conversion needs to take place before more specific recommendations on frequency of repeat TST testing can be made for this group. The AAP guidelines should be followed for this group. As a result of our

study, routine practice of screening for LTBI has dramatically increased at our clinic.

ACKNOWLEDGMENTS

We thank the Duncan Trust for funding this study; the Denver Department of Public Health, TB clinic, for coupons; Caroline Ponce, BS, for excellent research skills; Judy Kralewski, RN, PNP, for data collection at VSBHC; Tim Johnson for translation of the questionnaire; Drs John Ogle, Randall Reves, and Lourdes Yun for guidance and critical review; and the pediatric clinicians, nurses, medical assistants, and patients at Westside Family Health Center.

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Pediatrics 2005;115;647-653
DOI: 10.1542/peds.2004-1685