Published by Oxford University Press on behalf of the International Epidemiological Association *International Journal of Epidemiology* 2006;**35:**1447–1454

doi:10.1093/ije/dyl213

Is tuberculin skin testing useful to diagnose latent tuberculosis in BCG-vaccinated children?

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Accepted 30 August 2006

Background The tuberculin skin test (TST) is the most commonly used tool to detect infection with *Mycobacterium tuberculosis*. We sought to determine whether tuberculin skin testing is useful to detect latent infection by *M. tuberculosis* in a population that was vaccinated with the Bacille Calmette Guérin (BCG) vaccine.

Methods We performed a cross-sectional study during October 2000–February 2001, enrolling first and sixth graders from a random, stratified sample of public elementary schools in Orizaba, Veracruz, Mexico. We assessed the relationship between sociodemographic and epidemiological information, BCG scars, and TST reactivity.

Results There were 858 children enrolled in the study with a completed questionnaire and TST result. The prevalence of a positive TST result (≥10 mm) was 12.4%. Controlling for BCG scar, age, and other characteristics, close contact with pulmonary tuberculosis patients (odds ratio 6.56, 95% confidence interval 2.05–21.07, $P = 0.001$) was independently associated with TST reactivity.

Conclusions TST results helped identify children in a BCG-vaccinated population who had recent exposure to persons with pulmonary tuberculosis, were probably infected with *M. tuberculosis*, and could benefit from treatment for their latent tuberculosis infection.

Keywords *Mycobacterium tuberculosis*, latent infection, tuberculin skin test, Bacille Calmette Guérin (BCG) vaccine

The tuberculin skin test (TST) is the most commonly used tool available to detect infection with *Mycobacterium tuberculosis* for public health purposes among children.[1,2] The contacts of pulmonary tuberculosis patients are a population at high risk for tuberculosis infection and disease, and treating contacts with a latent tuberculosis infection (LTBI) can significantly reduce their risk of progressing to active disease. However, interpretation of TST results must take into account the sensitivity and specificity of test; the prevalence of tuberculosis in the population being studied; and the likelihood of cross-reactivity with another species of mycobacteria. Detecting infection with *M. tuberculosis* is problematic in areas where the Bacille Calmette Guérin (BCG) vaccine is included in childhood vaccination programmes because BCG-vaccinated children may be reactive to purified protein derivative (PPD) several years after their vaccination.[3,4]

In Mexico, a single BCG vaccination is recommended at birth. The current guidelines recommend treatment of LTBI among contacts of pulmonary tuberculosis patients, younger than 14 years old (all children under 5 years of age and children 6–14 years of age who were not BCG-vaccinated, regardless of the TST result).[5] This recommendation is based on the perception that it is difficult to interpret a TST result in older BCG-vaccinated children. The purpose of the present

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study was to determine whether the TST can be used to identify infection with *M. tuberculosis* among children of different age groups in an area of southern Mexico with endemic tuberculosis and a high BCG vaccine coverage rate.

Methods

Study population and enrolment

We performed a cross-sectional study of TST reactivity among school children in the municipality of Orizaba, state of Veracruz, southern Mexico.[6] The incidence rate of tuberculosis in Veracruz state during 2000 (28.0 per 100 000 inhabitants) was higher than the national incidence rate in Mexico (15.9 per 100 000 inhabitants).[7] Nationwide BCG vaccination began in 1973 and by 2001, the coverage was 99.7% among children younger than 4 years old. The vaccine is administered at birth in hospitals or during the child's first contact with health services.[8]

We randomly selected schools from among public elementary schools teaching the first through the sixth grades in the municipality of Orizaba. The study was conducted in 26 of the 57 public elementary schools in the municipality of Orizaba and subjects were recruited and enrolled between October 2000 and February 2001. All first and sixth graders of selected schools were invited to participate. The study was designed to enrol 750 participants and had a power of 80% to detect an odds ratio (OR) of 2.0 for the association between children exposed to an active case of tuberculosis and non-exposed children (two-sided, α level 0.05) and the outcome variable of a TST result $\geqslant$10 mm. Based on previous studies, the prevalence of TST reactivity $\geqslant$10 mm among school-age children was estimated to be 11%.

We informed the parents' and teachers' associations, municipal authorities, and local health services of the study's purpose and activities prior to initiating recruitment and enrolment. We invited children enrolled in the first and sixth grades in the selected schools to participate but excluded any children who were symptomatic for tuberculosis or had been vaccinated with measles, poliomyelitis or BCG vaccines, or ill with measles during the previous 2 months. The study's purpose, activities, risks, and benefits were explained in person to the parent or guardian of each eligible child. If the parent or guardian provided informed, written consent, the child was enrolled. The parents and guardians of participating children were individually interviewed in person using a standardized, structured questionnaire. We collected information about sociodemographic characteristics such as age, sex, school grade, household characteristics, mother's ethnicity (as being a member of an 'indigenous' population is associated to a higher rate of TB), and place of residence. We also assessed epidemiological characteristics such as household crowding (defined as three or more people sleeping in the same room), previous vaccinations, contact and the degree of contact with pulmonary tuberculosis patients or people with chronic cough, the consumption of raw milk products, and domestic animals within the living quarters (as an indicator of socioeconomic level). Attendance at a pre-school was also investigated since it represents a higher probability of interacting with other adults outside the household and, therefore, greater probability of exposure to tuberculosis cases. We collected clinical information such as the time since the last BCG vaccination, history of a prior diagnosis of tuberculosis, associated diseases, and symptoms suggestive of tuberculosis (cough, fever, weight loss, anorexia, night sweats, and haemoptysis) to ensure that children did not have active tuberculosis. The child's weight, height, and the number and location of each child's BCG scars were recorded. BCG vaccination status was also noted based on the official document used in Mexico, a vaccination card.

This study was approved by the appropriate institutional review boards at Instituto Nacional de Salud Pública (INSP), the Instituto Nacional de Ciencias Médicas y Nutrición 'Salvador Zubirán' (INCMNSZ) in Mexico, and Stanford University, USA.

Tuberculin skin testing

The clinical personnel responsible for the administration, reading, and interpretation of the TST were required to take a standardized course on how to administer and evaluate the TST. We performed TST on each enrolled child using two tuberculin units (TU) of PPD, (PPD RT-23 Staten Serum Institut, Copenhagen, Denmark), applied with the Mantoux method. Subjects received an intradermal injection of 0.1 ml of PPD-tuberculin in the volar aspect of the forearm. Opened vials of PPD were used within 24 h, and unused vials were discarded 6 months after preparation. The TST result was read at 48–72 h by measuring the transversal axis of the induration at the site of PPD application with a flexible ruler. The exact size of the induration was measured and recorded in millimetres.

For 10% of the children enrolled in the study, the intraobserver and interobserver measurements of the TST results were evaluated by the kappa coefficient for up to four different readings for a TST result.[9] All comparisons were performed with each reader blinded to the results of the other reader or to his or her own previous readings as recommended by international guidelines.[2] For the remaining 90% of children, readings were done by a single trained health care worker.

Follow-up of children

Children whose TST result measured $\geqslant$10 mm were considered TST positive, based on the recommendation of the Mexican Official Norm for tuberculosis.[5] Children whose TST result measured $\geqslant$10 mm were considered positive and were evaluated by a paediatrician who followed a specific protocol (history, symptom screening, and physical exam). In the case of abnormalities (fever, weight loss, cough, and other symptoms), chest radiograph and cultures were performed. Children with a positive TST result were contacted by trained local health care workers a year later to ascertain health status and to determine whether the child had developed tuberculosis. We also compared the list of all study participants with the local registry of tuberculosis cases 1 year after the cross-sectional study to identify children who were treated for tuberculosis.

Information of the local registry for children whose TST result measured $<$10 mm was confirmed by a household visit by trained local health care workers 5 years later to determine if the child had developed tuberculosis after the administration of the TST. We also investigated whether any of the other household members had been diagnosed or treated for active tuberculosis and, if so, the dates of diagnosis and treatment.

Table 1 Comparison of school-aged children who completed and did not complete the evaluation (standardized interview and TST result), Orizaba, Mexico

	Complete evaluation		Incomplete evaluation		
Characteristics	n = 858	(%)	n = 49	(%)	***P***
Age (years), median, (IQR)	6	(6–11)	7	(6–15)	0.02
Age group (years)					
5–7	437/858	(50.93)	33/49	(67.35)	0.16
8–10	50/858	(5.83)	2/49	(4.08)	
11–13	355/858	(41.38)	13/49	(26.53)	
14–16	16/858	(1.86)	1/49	(2.04)	
BCG vaccination scar present	743/857	(86.7)	37/49	(75.5)	0.03
Consumed raw milk products	73/847	(8.6)	8/49	(16.3)	0.07
Person with TB within household	27/856	(3.0)	3/49	(6.1)	0.23
Household lacked public services (indoor plumbing, electricity)	278/857	(32.4)	24/49	(49.0)	0.02

IQR = Interquartile range; BCG = Bacille Calmette Guérin; TB = tuberculosis; P = P-value, based on χ^2 test of proportions or the Mann–Whitney test.

Statistical analysis

Bivariate analyses were used to identify the factors associated with tuberculin reactivity at three different levels: ⩾5 mm, ⩾10 mm, and ⩾15 mm. We estimated the association between each of the potential risk factors and tuberculin reactivity using the OR and 95% confidence intervals (CI). Individual observations were weighted by the reciprocals of the sampling probabilities. Sample weights for each participant were included in multivariate analysis to evaluate factors associated with a positive TST result (⩾10 mm). In our analyses, we considered design effects, the ratio of the variance from a cluster sample to the variance from a simple random sample of the same size.[10,11] Nutritional status was evaluated using a height for age indicator (Anthro 1.0, World Health Organization) based on the 'z' distribution.[12] We included variables in the multivariate logistic regression models if their respective bivariate analysis yielded $P < 0.20$ or if they were deemed biologically relevant. SUDAAN 7.5.6: Software for Survey Data Analysis was used for analysis.[13]

Results

Of a total of 3631 first and sixth grade children, a parent or guardian of 907 children provided informed written consent. Of these, 858 (94.6%) had a completed questionnaire and a TST result. The most frequent reason given for not providing consent was that the parent considered the test unnecessary since it was not included within the established activities of the local tuberculosis control programme's prevention and control activities. We compared the characteristics of the 858 children who did have and the 49 children who did not have a completed questionnaire and a TST result (Table 1). Children who did not have a complete questionnaire and a TST result were younger, of a lower socioeconomic level as indicated by household characteristics, and were less likely to have a BCG scar relative to children who had a completed questionnaire and TST result. A higher proportion of children whose evaluation was incomplete had lived with a pulmonary tuberculosis patient, although the difference was not statistically significant (P = 0.23) (Table 1).

Of the 858 children who completed the evaluation, 86.7% (743/857) had a BCG scar on the right arm; 32.4% (278/857) lived in a household that lacked public services such as running water or electricity; 3.0% (27/856) reported contact with a person diagnosed with pulmonary tuberculosis within the household (Table 1); 3.1% (27/848) were severely malnourished; 22.2% (189/852) referred non-immunosuppresive chronic conditions such as tonsillitis, bronchitis, or dermatitis; and 4.3% (37/858) belonged to an indigenous ethnic group (Table 2). Of the 858 children, 477 (55.6%) were first graders and 381 (44.4%) were sixth graders. The proportion of children having a TST result above each of the cut-off levels (⩾5, ⩾10, and ⩾15 mm) was 23.78% (204/858); 12.4% (106/858), and 3.03% (26/858), respectively. Table 2 shows TST positivity at ⩾10 by age group. The proportion of children with a positive TST increased with age, $P < 0.0001$ (χ^2 trend). The mean size of the transversal diameter of the induration at the site where PPD was applied for each age group (5–7, 8–10, 11–13, and 14–16 years) were 1.75 [standard deviation (SD) 3.82 mm], 1.54 (SD 3.31 mm), 3.61 (SD 5.18 mm), and 4.87 (SD 6.26 mm), respectively, ($P < 0.0001$). Kappa coefficients for interobserver and intraobserver variability were above 0.90 (0.90, 0.97, 0.98, and 0.99), for four different persons reading the TST result or four different readings of the same TST result.

None of the children was diagnosed with active tuberculosis during the initial TST. All children with a TST result ⩾10 mm were referred to primary care providers and were evaluated for possible preventive therapy according to official recommendations. The households of children with a TST result ⩾10 mm were visited to seek and detect active tuberculosis cases. We identified 14 adults with active tuberculosis among household members; all had been previously diagnosed and treated by the local tuberculosis control programme. The 14 household pulmonary tuberculosis cases were included among those 27 tuberculosis cases that were identified by the initial screening questionnaire.

In the bivariate analyses, reporting any contact with a tuberculosis patient was associated with TST positivity at each of the cut-off levels (⩾5, ⩾10, and ⩾15 mm) with

Table 2 Characteristics of the study population of school children, Orizaba, Mexico

Characteristic	Frequency *n*	(%)
Characteristics of the household		
Household lacked public services (indoor plumbing, electricity)	278/857	(32.4)
Window absent in the room where the child sleeps	76/858	(8.9)
Household keeps animals inside living quarters	211/858	(24.6)
Child's mother of indigenous ethnic origin	37/858	(4.3)
Number of subjects in the household (median, range)	5.0	(1–30)
Characteristics of the child		
Median age of child (years), (IQR) (First graders)	6	(6-7)
Median age of child (years), (IQR) (Sixth graders)	11	(11-12)
Median age of child (years), (IQR) (All participants)	7	(6-11)
Female	430/858	(50.1)
Child attended a pre-school programme	776/857	(90.5)
Child consumed unpasteurized milk	73/847	(8.6)
Child consumed unpasteurized cheese	480/847	(56.7)
Child consumed unpasteurized cream	382/848	(45.0)
Malnourished (based on height for age)	27/848	(3.1)
Previous diagnosis of TB	14/850	(1.6)
Child had a chronic illness[a]	189/852	(22.2)
BCG vaccinated, per vaccination card	373/398	(93.7)
Less than 4 years since most recent BCG vaccination, per vaccination card	25/398	(6.3)
Total number of BCG scars present on child's arm(s)		
None	115/858	(13.4)
One	674/858	(78.6)
Two or more	69/858	(8.0)
Contact with a pulmonary TB patient in the household		
No	831/858	(96.9)
Yes	27/858	(3.1)
TST ⩾ 10 mm by age group[b]		
5–7	35/437	(8.0)
8–10	4/50	(8.0)
11–13	64/355	(18.0)
14–16	3/16	(18.7)
Total	106/858	(12.4)

BCG = Bacille Calmette Guérin vaccine; TST = tuberculin skin test; TB = tuberculosis; IQR= Interquartile range.

[a] Chronic infectious diseases such as chronic tonsillitis, bronchitis, and infectious dermatitis.

[b] $P < 0.0001$ (χ^2 test for trends).

OR = 1.82, 95% CI (1.14–2.88), $P = 0.006$; OR = 1.96 (95% CI 1.12–3.43), $P = 0.01$; and OR = 4.06 (95% CI 1.62–9.96), $P = 0.002$, respectively. Having a BCG scar (independently of the time elapsed since vaccination) was associated with a TST result of ⩾5 and ⩾10 mm (OR = 4.40 (95% CI 1.47–14.76), $P = 0.002$ and OR = 8.57 (95% CI 1.23–170.70), $P = 0.01$). Lack of windows in the room where the child slept and attending a pre-school programme were associated with a TST result ⩾10 mm. Other variables such as nutritional status based on height for age, consumption of raw milk products, crowding within the household and several other socio-demographic, epidemiological, and clinical variables were not associated with tuberculin reactivity (Table 3). The proportion of children with a positive TST result increased according to the degree of exposure to pulmonary tuberculosis cases [no contact with a tuberculosis case, 11.33% (85/750); contact with a tuberculosis case outside the household , 16.67% (13/78); contact within the household but without sharing the bedroom, 18.18% (2/11); and sharing the bed 54.55% (6/11) ($P = 0.0003$, χ^2 trend)]. In the multivariate logistic regression analysis, close contact with a tuberculosis patient, the presence of a BCG scar, lack of windows in the room where the child slept, and increasing age of the child were significantly associated with a positive TST result (⩾10 mm), controlling by the variable for attendance to a pre-school programme (Table 4). Changing the cut-off level to ⩾5 or ⩾15 mm did not modify the association between the TST result and close contact with a tuberculosis patient.

Twelve months after the cross-sectional study was performed, 97 of the 106 TST-positive children were revisited. Three TST-positive children (3.1%, 3/97) who had not previously reported contact with tuberculosis patients had been treated for pulmonary tuberculosis and were reported as cured.

Review of the local registry of tuberculosis cases revealed that none of the TST negative children had been diagnosed with tuberculosis. This was confirmed by the household visit that was performed 5 years after the TST study. Sixty-seven per cent (502/752) of households of children with negative TST results were revisited to determine whether any of the children had developed active tuberculosis or whether any of the other household members had been diagnosed with the disease. None of the children who was initially TST negative and whose household was visited had been diagnosed with tuberculosis. We found that three children had been exposed to a pulmonary tuberculosis case (as compared with 14 cases in the households of the 106 children with a positive TST). All these pulmonary tuberculosis cases had been diagnosed and treated by the local tuberculosis programme.

Discussion

In this study, we show that the TST used together with a standardized questionnaire eliciting information about risk factors for exposure to infectious tuberculosis can identify children who have been exposed to an active pulmonary tuberculosis case in an area with high BCG vaccination coverage. The risk of infection by *M. tuberculosis* was higher the closer the contact, e.g. sharing the bed with a tuberculosis patient. None of the TST positive children in the study who reported contact with a tuberculosis patient and who received treatment for a LTBI developed active disease. Three children

Table 3 Results of bivariate analyses to determine the factors associated with a positive TST result (⩾10 mm) among schoolchildren in Orizaba, Mexico

	TST result ⩾10 mm		
Potential risk factor	*n*/total (%)	OR (95% CI)	***P***
Contact with a pulmonary TB patient in the household			
Yes	8/27 (29.6)	3.13 (1.34–7.36)	0.009
No	98/828 (11.8)	1.0	
Total	106/855		
BCG-vaccinated*			
Yes	47/343 (13.7)	8.57 (1.23–170.70)	0.01
No	1/55 (1.8)	1.0	
Total	48/398 (12.1)		
BCG scar present			
Yes	102/743 (13.7)	4.38 (1.51–14.26)	0.002
No	4/114 (3.5)	1.0	
Total	106/857 (12.4)		
Time since last vaccination			
BCG vaccination within past 4 years[a]	12/25 (48.0)	8.60 (3.30–22.0)	<0.0001
BCG vaccination >4 years ago[a]	36/373 (9.7)	1.0	
Total	48/398 (12.1)		
Number of BCG scars present			
None	4/115 (3.5)	1.0	
One	81/674 (12.0)	3.79 (1.30–12.41)	0.006
Two or more	21/69 (30.4)	12.14 (3.67–44.36)	<0.0001
Total	106/858 (12.5)		
Window present in the room where child slept			
No	15/76 (19.7)	1.87 (0.97–3.54)	0.04
Yes	91/782 (11.6)	1.0	
Total	106/858 (12.5)		
Household kept animals within living quarters			
Yes	35/211 (16.6)	1.61 (1.01–2.55)	0.03
No	71/646 (11.0)	1.0	
Total	106/857 (12.4)		
Child attended a pre-school programme			
Yes	102/776 (13.1)	2.91 (1.00–9.57)	0.03
No	4/81 (4.9)	1.0	
Total	106/857 (12.4)		
Household lacked public services (indoor plumbing, electricity)			
Yes	33/278 (11.9)	0.93 (0.59–1.48)	0.75
No	73/579 (12.6)	1.0	
Total	106/857 (12.4)		

OR = odds ratio; CI = confidence interval.

[a] BCG = Bacille Calmette-Guerin vaccination status based on the vaccination card.

with initial positive TST test results who did not report prior contact with tuberculosis patients developed disease during the follow-up period vs none of the children who were TST negative. Consistent with previous studies, there was a strong association between contact with a tuberculosis patient and a positive TST result,[14–17] and TST-positive children with no other risk factor were at greater risk of developing disease than children who were TST negative.[18] Our results demonstrate that the TST can be used to identify BCG-vaccinated children who are probably infected with *M. tuberculosis* and could benefit from treatment for an LTBI.

Previously published risk factors for TST reactivity among paediatric populations include household size, geographical proximity to the active tuberculosis case, and the number of bedrooms within the household.[16] In our study, we found that increased ventilation decreases the likelihood of an infection and a positive TST result after exposure to an active tuberculosis case.[19,20]

The interpretation of TST results in BCG vaccinated populations has been controversial. TST reactivity in school-age children has been associated with neonatal BCG vaccination[21–25] and wanes after several years.[26,27] Other studies failed to confirm this association.[15,28–31] Several factors such as the child's age at vaccination, interval between vaccination and TST, the strain of BCG vaccine used, skin testing reagents used, the method of TST application,[32,33] and the geographic location of the study population[34] probably contribute to the discrepancies in results.

Increasing the cut-off level that defines a positive TST result increased the specificity of the TST in our study population. While exposure to a tuberculosis case was positively associated with TST reactivity at all three cut-off levels (⩾5, ⩾10, and ⩾15 mm), having a BCG scar was associated with TST reactivity at only ⩾5 and ⩾10 mm. Additional information from the standardized questionnaire about potential exposures and contact with tuberculosis patients allowed us to identify BCG-vaccinated children with positive TST results who were probably infected with *M. tuberculosis* and could benefit from treatment of LTBI. Our results confirm the usefulness of tuberculin skin testing to detect infection with *M. tuberculosis* in a BCG-vaccinated population using a cut-off level of at least 10 mm.

A large proportion of children with a BCG scar had a TST result <10 mm. Of 743 children with a BCG scar, 641 (86%) had a TST result <10 mm. Several other recent studies also reported that the proportion of subjects with negative tuberculin reactivity is high despite prior BCG vaccination.[4,32] Because we excluded children who had recently been vaccinated with viral vaccines and 3.2% of children in the study population were malnourished, we do not consider that the high proportion of negative TST results among BCG vaccinated children can be attributed to these factors. Moreover, although we did not test participants for HIV infection, HIV infection among general population in Mexico is estimated to be 1%[35] and we consider that HIV infection among study participants was infrequent. Because the proportion of BCG-vaccinated children who were TST negative was high, those who did have a positive TST result were probably exposed to an infectious pulmonary tuberculosis patient and became infected with *M. tuberculosis*.

Our study has several limitations. Owing to its cross-sectional design, we measured cumulative tuberculosis infection, reflected as the prevalence of TST positivity. However, the exposures took place within the short lifetime of the children in the study

Table 4 Results of adjusted multivariate logistic regression analysis to identify the factors independently associated with a positive TST result (≥10 mm)

Characteristic	TST + / total (%)	Adjusted OR (95% CI)	*P*
Contact with pulmonary tuberculosis cases within the household			
No contact with a tuberculosis case	85/750 (11.3)	1.0	
Contact with a tuberculosis case outside the household	13/78 (16.7)	1.70 (0.82–3.51)	0.15
Contact within the household but without sharing the bedroom	2/11 (18.2)	3.30 (0.29–36.98)	0.33
Sharing the bed	6/11 (54.5)	6.56 (2.05–21.07)	0.001
BCG scar			
None	3/76 (3.9)	1.0	
One	79/700 (11.3)	1.59 (0.56–4.51)	0.38
Two or more	24/82 (29.3)	4.99 (1.53–16.29)	0.007
Child attended a pre-school programme			
No	4/81 (4.9)	1.0	
Yes	102/776 (13.1)	1.75 (0.66–4.61)	0.25
Window present in room where child slept			
Yes	91/782 (11.6)	1.0	
No	15/76 (19.7)	2.14 (1.01–4.56)	0.04
Age (years), (median, IQR)	7 (6–11)	1.18 (1.07–1.29)	0.0005

IQR = Interquartile range.

population and are indicative of recent and ongoing transmission of *M. tuberculosis* in the households and the community where the study was conducted. Our results are biased by the self-selection of participants and probably underestimate the real risks of infection with *M. tuberculosis* among schoolchildren. Children who dropped out of the study after agreeing to participate had more risk factors for tuberculosis infection and several of these risk factors reached statistical significance despite fairly small numbers. Therefore, the study results probably underestimate the benefit of doing a TST among high-risk children who received a BCG vaccine. The inferences from our study may not be generalized to children who do not attend school or to children who attend private schools. Finally, we used 2 TU of PPD-RT-23, whereas, in some countries, the standard is to use 5 TU.

Mexico has achieved very high rates of BCG vaccination since it was first used in the country in 1965. Since 1993, the national BCG vaccine coverage rates have been reported to be at least 95%.[36] Existing guidelines for the treatment of tuberculosis infection among school-aged children base their recommendations on the child's prior BCG status and completely exclude children 5–14 years old who have been BCG-vaccinated from treatment for an LTBI. Our results indicate that these children would probably benefit from targeted tuberculin testing and the detection and treatment of an LTBI, regardless of their BCG status. We consider that high BCG coverage should not be an obstacle for using tuberculin skin testing to diagnose tuberculosis infection. The impact of BCG vaccination is expected to be higher in situations where the expected prevalence of true infection is low, such as in screening situations. When the expected prevalence of tuberculosis infection is high, such as among close contacts of sputum smear-positive cases, the predictive value of a positive tuberculin test is high even among BCG-vaccinated persons.[37] Mass testing of children in Mexico would lead to many false positive results, while testing children known to be in close contact with tuberculosis patients would not, demonstrating the application of the positive predictive value.

Treatment of LTBI has been recommended for contacts and other persons at high risk of progressing to active tuberculosis disease.[38,39] Mexico, as well as other Latin-American countries,[40–42] follows the recommendation of WHO and the International Union Against Tuberculosis and Lung Disease (UIATLD)[43] and recommends chemoprophylaxis for tuberculin reactive children 5–14 years old only if they have not been BCG-vaccinated.[5] However, TST-positive children would probably benefit from treatment of LTBI, regardless of prior BCG vaccination status. Mass vaccination with BCG and targeted tuberculin testing followed by treatment of LTBI are useful tuberculosis control activities and do not interfere with each other.

Acknowledgements

The authors thank the participating children, parents, teachers, school authorities, and the collaborating physicians, nurses, interviewers, and health authorities in Orizaba who supported the study's recruitment, diagnosis, treatment and follow-up of participants. Part of this information was presented at the Encuentro Nacional de Investigadores, San Juan del Río, Querétaro, Mexico, in October 2001. The study was supported by the National Institutes of Health (NIH) of the United States (AI35969 and K01-TW000001), the Wellcome Trust (176W009), the Howard Hughes Medical Institute (ID 55000632), and the Mexican Council of Science and Technology (CONACyT) (G26264M and 30987-M).

The authors declare no conflict of interest.

KEY MESSAGES

- The TST can be used to identify BCG-vaccinated children who are probably infected with *M. tuberculosis* and could benefit from treatment for an LTBI.
- Children who are at higher risk are those who have close contact (e.g. sharing the bed) with a pulmonary tuberculosis patient.
- International guidelines on treatment of LTBI in developing countries do not include recommendations for treatment of older, BCG vaccinated children who would benefit from treatment if TST positive.

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