Targeting Tuberculosis Testing: The Yield of Source Case Investigations for Young Children with Reactive Tuberculin Skin Tests

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SYNOPSIS

Objective. This study was designed to determine the yield of investigations whose aim is to identify a source case for tuberculosis infection among tuberculin reactors 3 years of age or younger.

Methods. The authors describe the results of associate investigations conducted for child tuberculin reactors reported from January 1, 1996, through June 30, 1998. Associates were defined as individuals who live with or spend significant time with a child reactor. An associate investigation was defined as evaluation of at least one associate. A source case was an associate older than 10 years of age who had culture-positive, pulmonary tuberculosis during a period when the child could have been exposed.

Results. Two hundred seven children had an associate investigation performed with a median of four associates investigated per child (range 1–21). Birthplace was known for 187 (90%); 128 were U.S.-born. Of 1,222 associates identified, 980 (80%) were evaluated. Among 452 (46%) associates for whom birthplace was known, 250 (55%) were non-U.S.-born. Of 980 associates, 668 were household contacts; 198 (30%) were infected, three had prior tuberculosis disease, and three had active tuberculosis. Two active cases met source case criteria; the yield was 0.9 (2 of 207) source cases per 100 children investigated. Of 312 non-household contacts, 57 (18%) were infected and none had the disease.

Conclusions. Although few source cases were identified for young tuberculin skin test reactors in New York City, investigations identified a proportion of cases and infection in associates similar to that identified among contacts to pulmonary tuberculosis cases. Such investigations may be identifying a high-risk group and should be considered, depending on program resources.

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INTRODUCTION

New guidelines for tuberculin testing have been published, calling for targeted testing that identifies individuals at high risk for tuberculosis (TB) disease and discouraging testing among individuals at low risk.[1] In light of these recommendations, health departments need to reevaluate current tuberculin testing activities to determine whether these efforts identify individuals who meet the new guidelines for treatment of latent infection.

One such activity is tuberculin testing of associates of children with a positive tuberculin skin test (TST). The premise for conducting associate investigations is that young children with a positive TST are, by definition, recently infected; therefore, testing of their close associates may lead to finding and treating infectious individuals. The yield of identifying source cases from such activity, however, has been disappointing. Although associate investigations are conducted in many TB control programs, relatively few reports have been published on the effectiveness of this measure. Most of the published reports have studied the yield of source case investigations for children with *active* TB disease showing widely varying success—between 2% and 68%—depending on the age of the child and geographic locations studied.[2-4] Only two reports describing the yield of associate investigations for tuberculin reactors who do *not* have active disease have been published in the medical literature.[5,6] One of these reported the results of investigations performed by a TB control program in a group of children who were primarily non-U.S.-born (87% of children in that study were non-U.S.-born).[5]

In New York City, the health code requires the reporting of tuberculin reactors younger than 5 years of age to the health department. The Tuberculosis Control Program conducts investigations to find a source case for TST reactors 3 years of age or younger. To assess the utility of associate investigations performed in the New York City Department of Health Tuberculosis Control Program, we evaluated the yield of these investigations for identifying source cases.

METHODS

This is a descriptive study of an extant database of associate investigations conducted for all children who were reported to the health department as tuberculin test reactors. The outcome of interest was whether a source case was identified among the associates examined at the time of the investigation. The study sample included children who were: (*a*) reported to the health department between January 1, 1996 and June 30, 1998; (*b*) known as TST-positive (≥10 mm) and had a normal chest radiograph with no signs or symptoms of TB disease; (*c*) identified as 3 years of age or younger; and (*d*) identified by means other than a contact investigation of an adult with infectious TB or an associate investigation for another TST-positive child. These children are hereafter referred to as *child TST reactors.*

Associates were defined as individuals who live with or spend significant periods of time with a child TST reactor. An *associate investigation* was defined as the evaluation of at least one associate, including a TST and a chest radiograph if the associate had a positive tuberculin test result. The investigation, conducted by Tuberculosis Control Program field workers, consisted of an interview with a parent or guardian to identify persons who shared airspace with the child. For each child TST reactor and associates, demographic characteristics, address of residence, reporting source, proximity of contact, prior TST results, current tuberculin status, results of chest radiograph, and treatment were recorded. Associates received a Mantoux TST performed by outreach workers in the home, in a health department chest clinic, or through private providers in the community. Associates who had symptoms of TB, a positive tuberculin test, or a prior history of a positive tuberculin test received a chest radiograph and medical evaluation for active TB disease.

A potential source case was defined as an associate older than age 10 who had culture-positive, pulmonary TB during a period when the child could have been exposed. Potential source cases were further classified as *probable* or *possible* source cases. A *probable* source case was defined as an associate older than age 10 years who had culture-positive pulmonary TB, in which the positive culture occurred during a period when the TST reactive child could have been exposed to that associate. A *possible* source case was defined as an associate older than age 10 who did not have bacteriologic confirmation of active disease, but was considered a verified case of TB because of clinical improvement in response to TB treatment. Individuals who were not born in the United States were classified into one of two groups, according to TB incidence in the country of birth: *high-incidence countries* were those with ≥20 smear-positive incident cases per 100,000 individuals per year; and *low-incidence countries* were those with <20 smear-positive cases per 100,000 individuals per year.[7] Any associate classified as having current, suspected, or prior TB disease was considered a potential source case, and the health department records were reviewed to determine if they met the epidemiologic criteria for being a source case.

Data were obtained from the computerized registry, which includes suspected and confirmed TB cases as well as contacts of cases and child TST reactors. The demographic, treatment, and bacteriologic characteristics of child TST reactors and their associates were reviewed, and the reporting source for the child TST reactors. The characteristics of children who had an associate investigation performed were compared with those of children for whom associates were not investigated. The characteristics of the associates who were examined were also reviewed. Household and non-household associates were compared according to these characteristics. Proportions were compared with the Pearson chi-square or Fisher's exact test using Epi Info.[8] Continuous data were compared with Student's *t*-test or, if not normally distributed, with the Wilcoxon Rank-Sum test. A two-tailed *p*-value of <0.05 was considered statistically significant for all comparisons.

RESULTS

Child TST reactors

Three hundred sixty-nine children met the study criteria; 39 (10%) were ≤1 year old. Child TST reactors were reported primarily by health department chest clinic [n = 93 (24%)] and public hospital outpatient providers [n = 147 (38%)]. The remaining 36% of children were reported by providers in nonprofit hospital outpatient departments and other clinics serving low-income communities. The vast amount of children (72%) resided in neighborhoods with active TB incidence rates that exceeded the citywide average of 21 per 100,000 people. Only 7% of the study children lived in neighborhoods with a TB incidence rate lower than 10 per 100,000 people. Associate investigations were completed for 207 (56%) children, with a median of four associates evaluated per child (range 1–21); the remaining 162 (44%) associates were not examined.

The characteristics of children with and without associate investigations are shown in Table 1. Children with associate investigations were less likely than children without associate investigations to be ≤1 year old ($p<0.01$), to be non-Hispanic whites ($p=0.01$), and to have unknown human immunodeficiency virus (HIV) serostatus or unknown birthplace. Among those for whom birthplace was known, the groups did not differ by birthplace. Of the 207 child TST reactors with associate investigations, 8% were ≤1 year old. Nearly half of the children were black, and 37% were Hispanic. HIV serostatus was known for 30%, and 5 (3%) of the children were HIV-infected. Birthplace was known for more than 90% of children. Seventy percent were born in the United States. Among the U.S.-born children, nearly one-third had an associate that was not U.S.-born. Nearly 70% of the children born outside the United States were from a country of high TB incidence. Although information relating to history of vaccination with Bacille Calmette-Guerin (BCG) was not available for children in our study, one-third were born in countries that administer BCG as part of their national vaccination programs.[9]

Associates

A total of 1,222 associates were identified; 980 (80%) were evaluated. The median age of associates was 25 years (range <1–99 years); 441 (45%) associates were non-Hispanic black, and 353 (36%) were Hispanic. Treatment of latent TB infection was initiated in 108 (42%) of the 258 associates who were infected without TB disease; 54 (50%) completed treatment.

Of the associates with TB disease, two met the source case criteria, one was probable, and one was possible. The yield of source cases per 100 children investigated was 0.9. One probable source case, a 28-year-old father, had culture-positive pulmonary disease and was diagnosed three months after the child was found to be TST-positive. One possible source case, a 2-year-old's mother, had culture-negative pulmonary disease. She was 21 years old and had an abnormal chest radiograph and symptoms associated with TB two weeks after the child's diagnosis. Although not considered a source case because of his age, active TB disease was also diagnosed in a 9-year-old boy; he had culture-negative, clinically confirmed disease. Both he and the index child reactor were exposed to a common unidentified source case with active TB. The three associates with prior TB disease were not considered source cases because they completed treatment, on average, seven months before the index child was born, and all were reevaluated and found to be free of active disease after the child was reported.

Of the 980 associates that were evaluated, 668 (68%) lived in the same household as the child, and 312 (32%) were non-household associates. The characteristics of household and non-household associates are shown in Table 2. A greater proportion of household associates had missing information on country of origin, compared with non-household associates; 404 (61%) of 668, compared with 124 (40%) of 312 ($p<0.01$). A greater proportion of household associates were TST-positive, compared with non-household contacts [198/668 (30%) vs. 57/312 (18%); $p<0.01$]. All the potential source cases were identified among household contacts.

Table 1. Selected characteristics of child TST reactors ≤3 years, New York City, January 1, 1996–June 30 1998 (*n* = 369)

Characteristic	With associate investigation (n = 207)		Without associate investigation (n = 162)	
	Number	Percent	Number	Percent
Age at reporting (years)				
≤1	16	8	28	17[a]
>1	191	92	134	83
Sex				
Male	92	44	80	49
Female	115	55	82	51
Race/ethnicity				
White, non-Hispanic	11	5	20	12[a]
Black, non-Hispanic	96	47	63	39
Hispanic	76	37	54	33
Asian/Pacific Islander	21	10	25	16
American Indian	3	1	0	0
HIV status				
Positive	5	3	0	0
Negative	56	27	7	4
Unknown	146	70	155	96
Birthplace				
United States	128	62	25	16
Non-United States				
Low TB incidence countries	18	8	7	4
High TB incidence countries	41	20	15	9
Unknown	20	10	115	71[a]

[a]*p*-value ≤0.01

HIV = human immunodeficiency virus

TB = tuberculosis

TST = tuberculin skin test

DISCUSSION

The yield of source cases identified in our associate investigations is consistent with the results of other published reports. A report of a comparable age group of TST reactors found 2.9 new TB cases per 100 children investigated, and 1.24 cases per 100 associates evaluated.[5] More recently, Soren et al. found no new cases of active TB among associates of 187 TST reactors.[6] That study included TST reactors whose age ranged from 1 to 21 years; only 31 children were younger than 6 years of age. TST reactors in our study were all 3 years of age or younger. Younger children are presumed to have more limited exposures to individuals outside the household and are therefore more likely to have a source case identified.

There are several possible reasons for a low yield of source cases identified. Nearly half (46%) of the children were either born in or had an associate who was born in a country where TB is endemic. Travel to or having visitors from a country of high TB prevalence has been reported as a factor associated with an increased risk of TB infection in young children.[10] There may have been visitors from these countries who were not identified as associates of the children, or the children may have traveled and been exposed to TB cases abroad, thus precluding identification of a source case among the associates investigated in New York City. Because country of birth was unknown for more than half of the associates, we likely underestimated the proportion of children who could have had exposure to a visitor or TB abroad.

Another possible reason for the low yield in this group is that the reaction to tuberculin may have been

Table 2. Characteristics of associates of child TST reactors (n = 980)

Characteristic	Household (n = 668)		Non-household (n = 312)	
	Median	Range	Median	Range
Age at reporting (years)	25	0.1–98	26	0.1–98
	Number	Percent	Number	Percent
Sex				
Male	279	42	133	43
Female	389	58	179	57
Race/ethnicity				
White, non-Hispanic	54	8	33	10
Black, non-Hispanic	320	48	121	39
Hispanic	226	34	127	41
Asian/Pacific Islander	68	10	31	10
Birthplace				
United States	89	13	113	36[b]
Non-United States				
Low TB incidence countries	32	5	6	2
High TB incidence countries	143	21	69	22
Unknown	404	61	124	40[b]
Associate TB status				
TST-negative (not infected)	464	69	255	82
TST-positive				
Infected without disease	198	30	57	18[b]
Current TB disease	3[a]	0.5	0	0
Old TB disease	3	0.5	0	0
Source cases identified	2	0.3	0	0

[a]One case occurred in a 9-year-old child with culture-negative TB disease

[b]*p*-value <0.01

TB = tuberculosis

TST = tuberculin skin test

falsely positive because of BCG vaccination or cross-reaction with non-tuberculous mycobacteria. Cell-mediated reactions to tuberculin happened because BCG occurs most frequently in the first year after vaccination, waning in subsequent years. Because of the young age of the children in our study, the reaction to tuberculin may have been falsely positive among the nearly 30% who were non-U.S.-born because of BCG vaccination. A number of additional children may have been vaccinated with BCG during visits to the parent's country of origin. The absence of information relating to history of BCG vaccination in the study children did not permit us to explore this as a factor influencing source case identification.

The predictive value of the tuberculin test depends on the prevalence of TB infection in the group being tested and the prevalence of cross-reactions with non-tuberculous mycobacteria. The prevalence of infection in children of this age group who were not known to have been exposed to TB is less than 1%. The predictive value of the test in such a group with 95% specificity is 16%.[11] To the extent that a tuberculin test result was falsely positive among our study sample, a source case would not have been identified.

Whereas few source cases were identified for these child TST reactors, the yield was comparable with that of finding an active case among contacts to pulmonary TB cases. In 1998, 1.3% of contacts with adults having pulmonary TB had active TB (New York City Department of Health, Tuberculosis Control Program, unpublished data). The associate investigations also identified a proportion of adults with latent TB infection similar to that identified among contacts of pulmonary TB cases (31% in 1998). The prevalence of TB infection and disease in contacts of persons with infectious pulmonary TB is attributed to known re-

cent contact with infectious individuals.[1] The risk of active disease in people with recent contact is higher than in people who have not had recent contact with an infectious person.[12,13] The benefit of testing and treating associates depends on the likelihood that they also had recent contact with an infectious person. The risk of TB and potential benefit from treatment of latent TB infection in associates of young TST reactors is not known. Our experience in New York City suggests that the yield of associate investigation for identifying a source case and latent TB infection among household associates of very young TST reactors was comparable with that among contacts to pulmonary cases. If infected associates meet the criteria for treatment of latent TB infection as outlined in the 2000 American Thoracic Society guidelines for tuberculin testing,[1] such investigations would be beneficial. Among the major groups targeted in the new guidelines are individuals from high incidence countries who have been in the United States less than five years. We believe the household associates are likely to meet such criteria; however, this will need to be assessed in future research. In addition, the guidelines discourage testing of those at low risk for infection. Thus, increasingly, tuberculin testing of children will take place only among those who have risk factors for infection. For these reasons, tuberculin testing and case-finding among household associates of very young TST reactors should be considered.

Our study is limited by several factors. First, the reason for administration of the tuberculin test was not known. If the study children were at lower risk for TB infection than other New York City children, the likelihood of identifying a source would have been underestimated, compared with the expected yield if the test was applied according to screening guidelines.[14] It was not likely that the study children were at lower risk because: (*a*) the children resided primarily in neighborhoods with the highest TB incidence in the city; and (*b*) the reporting sources were primarily public health care providers or not-for-profit providers in low-income communities serving children whose risk for TB infection would be as high as the risk for other New York City children. A second potential limitation is that tuberculin tests were done by many different providers and, therefore, the reading of the results may not have been performed uniformly among all reactors. A third limitation is that a sizeable number of TST-positive children reported did not have a source case investigation performed. Children who did not have source case investigations performed did not differ from children who did have source case investigations, according to the factors that were most likely to influence likelihood of identifying a source case (i.e., country of birth and area of residence in New York City).

In conclusion, although few source cases were identified for these child TST reactors, the yield was comparable with that of finding an active case among contacts of pulmonary TB cases. Associate investigations also identified a proportion of household associates with latent TB infection similar to the proportion identified among contacts to pulmonary TB cases (30%); a significantly lower proportion of non-household associates were infected (17%). No source cases were found among non-household associates. Source case investigations may be identifying a high-risk group and, therefore, should be considered among household associates of very young TST reactors.

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