

Missed Opportunities for Preventing Tuberculosis Among Children Younger Than Five Years of Age

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ABSTRACT. *Objectives.* Childhood tuberculosis (TB) is an important indicator of public health success in interrupting and preventing TB transmission. To determine the frequency and types of missed opportunities for preventing TB among children <5 years of age.

Methods. We collected data from the public health records of child TB cases and their adult source cases. These children were from health jurisdictions where TB case rates in children were higher than the California average for this age group.

Results. We reviewed the records for 165 children reported with TB (20% confirmed by culture). These children were evaluated for TB because of signs or symptoms of illness (32%), a contact investigation (26%), screening (22%), a source case investigation (4%), and unknown reasons (16%). Excluding 4 children infected by *Mycobacterium bovis*, only 59 of 161 children (37%) had a source case found. Children found in a contact investigation, born in the United States, <1 year of age, or who were black were more likely to have a source case found than children who did not have one of these characteristics. Of 43 children found in a contact investigation, improvements in contact investigations may have prevented TB in 17 of these children (40%). Among the 43 adult source cases, factors that may have facilitated transmission include delayed reporting in 23%, a delayed contact investigation in 21%, and delayed or nondocumented bacteriologic sputum conversion in 42% of culture-positive cases.

Conclusions. Important missed opportunities to prevent TB in children include the failure to find and appropriately manage adult source cases and failure to completely evaluate and properly treat children exposed to TB. Improvements in case detection, case management, and contact investigations are necessary to eliminate TB in children. *Pediatrics* 2000;106(6). URL: <http://www.pediatrics.org/cgi/content/full/106/6/e75>; *tuberculosis, children, prevention, missed opportunities.*

ABBREVIATIONS. TB, tuberculosis; TST, tuberculin skin test; RR, relative risk; CI, confidence interval; INH, isoniazid.

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Despite recent declines in the incidence of tuberculosis (TB) in the United States, TB continues to be an important health problem in specific social and racial groups. As public health agencies increasingly focus on strategies to eliminate TB in the United States,¹ childhood TB becomes an important indicator of program success in interrupting and preventing recent TB transmission. TB cases among children indicate recent transmission of *Mycobacterium tuberculosis* usually from an infectious adult, often a family or household member,^{2,3} and are a sensitive indicator of deficiencies in efforts to prevent TB transmission. The mainstays of TB prevention in children are the timely diagnosis, reporting, and curative treatment of adults with TB disease so that the transmission of *M tuberculosis* is interrupted.^{4,5} In addition, children exposed to infectious cases need a thorough medical evaluation and, if TB disease is excluded, prompt initiation of treatment for TB infection.

California reports approximately one fourth of incident TB cases among children <5 years of age in the United States.⁶ Incident TB cases in children <5 years of age increased 39% from 205 in 1985 to 285 in 1994, although cases have subsequently decreased.⁷ The case rate in California children <5 years of age was 9.6/100 000 in 1994 and 5.9/100 000 in 1998, nearly twice the national average of 5.2/100 000 and 3.4/100 000, respectively, for this age group.^{6,8} The high rate of childhood TB suggests that opportunities for preventing TB are being missed.

The purpose of this investigation was to determine for children with TB and <5 years of age the frequency and types of missed opportunities for interventions that might prevent TB exposure or, once exposure had occurred, interrupt infection or the progression of infection to disease. For this study we assessed the use of currently recommended public health interventions for preventing TB, including prompt reporting of adult cases, timely and thorough evaluation of child contacts to TB cases, use of prophylaxis for exposed children, and ensuring the completion of therapy for children with latent TB infection.

METHODS

Definitions

For this investigation, a case of TB met the surveillance–case definition of the Centers for Disease Control and Prevention⁹ or was assessed to be active TB by a local TB controller. A source case was pulmonary TB in an adult who had close contact with a child before the onset of that child's TB symptoms or before the child's

positive tuberculin skin test (TST) was read. A source case is considered known to the health department before the child's report if the source case was reported before TB therapy was started in the child. Date of report is the date the case was first known by the local health jurisdiction, as indicated by the first entry on a health department's record or log. Mode of child presentation is the reason that the child came to medical attention at the time TB was diagnosed. Initiation of a contact investigation is the date that the health department opened an investigation of exposed persons by interviewing the patient source case or any contact of the source case. Nonadherence to TB therapy is any notation in the health records of failure to keep appointments, to have prescriptions filled, to take medications, or to administer medications to a child. For children who had multiple disease sites, the site of disease was ranked in the order of disseminated (miliary), extrapulmonary other than lymphatic (eg, meningitis, bone), pulmonary, intrathoracic lymphatic, other lymphatic.

Study Population

We studied TB in children <5 years of age because TB disease in young children indicates recent exposure and is often possible to prevent through timely interventions. To concentrate on areas with likely TB transmission, we selected the 8 California health jurisdictions that in 1994 reported >10 TB cases among children <5 years of age and had an annual TB rate of >9.6/100 000 (the state average) for this age group. These jurisdictions reported 73% of TB cases among children <5 years of age in California. From 7 of these jurisdictions, we included all reported cases of TB in children <5 years of age. From the eighth and largest jurisdiction, we included all cases of TB in children from health districts that reported >5 such cases. This sample included 54.1% of that jurisdiction's cases among children <5 years of age. The 165 children in this study accounted for 57.9% of all TB cases (165/285) among children in California <5 years of age reported in 1994.

Data Collection and Analysis

To determine the types and frequency of missed opportunities for preventing TB in children, we reviewed all available health department records and contact investigation logs for children with TB and their source cases. We defined missed opportunities for preventing TB in children as delayed or nonuse of standard TB control interventions, which otherwise may have prevented a child's exposure to *M tuberculosis*, reduced exposure time once exposed, or halted progression from TB infection to active disease. We assessed 4 types of missed opportunities based on prevention guidelines published by the Centers for Disease Control and Prevention and variably reiterated in the local protocols for conducting TB investigations.^{4,10,11} We categorized missed opportunities as: 1) failure to identify an infectious adult, 2) failure or delay to report an adult case within 7 days of obtaining a sputum for acid fast bacilli, 3) inadequate or delayed contact investigation of the source case, and 4) inappropriate or delayed follow-up of contacts named. In the review of contact investigations, we compared health department records with the following standards: patients suspected of having TB should be interviewed within 3 days after the health department receives the case report, and the close contacts should be examined within 7 days after the report. For this study, we ascertained whether the child was named as a contact and received a TST within 14 days of the report of the source case. National standards also recommend that tuberculin-negative children who have had recent close contact with an infectious TB case receive preventive therapy until a repeat TST is performed 12 weeks after last contact with the infectious case. For children not found in contact investigations, we reviewed health department records to see whether an attempt was made to find a potential source case for the child's infection.

In addition, we determined the reason that the child was assessed for TB: because of TB-related symptoms, routine screening, a contact investigation, or a source-case investigation. Information collected about the source case included the family relationship between the TB patient and the child and whether the adult source case lived in the same household as the child. For children without culture results who had a source case found, we assumed the child's *M tuberculosis* had the same susceptibilities as the source case.¹² Parents were classified as foreign-born if they were born outside of the United States or if the birthplace was not

known and the parent's dominant language was other than English.

Differences in proportions were assessed by the χ^2 test (Yates corrected statistic). Continuous variables were compared by Student's *t* test. Where appropriate, relative risk (RR) and 95% confidence intervals (CIs) were computed. For all statistical tests, differences were considered statistically significant at *P* < .05 (2-tailed).

RESULTS

Demographic and Clinical Characteristics of Children With TB

The demographic and clinical characteristics of the 165 children with TB did not differ significantly from those of the 120 children who were not included in this study, except more children in the study were male (Table 1). Of the 129 children with TB who were born in the United States, 97 (76%) had at least 1 parent born outside of the United States, including all of the Hispanic and Asian children. Of the 36 foreign-born children, 29 (83%) were born in Mexico; 64% entered the United States within 18 months before their TB diagnosis.

A specimen for culture was collected from 46% of the 165 children; of these children, 42% had an isolate that grew *Mycobacterium* complex. Four children had cultures which grew *M bovis*; 1 child drank unpasteurized milk, 1 ate goat cheese in Mexico, and 2 had unknown sources.¹³ Sixty-five children had drug susceptibility testing of either their own isolate (32 children) or an isolate from their source cases (33 children). Excluding the 4 children who had *M bovis* isolated, 10 of the 61 children (16%) who had culture-proven *M tuberculosis* had resistant strains (3 to isoniazid [INH] and 7 to streptomycin). All of the children who had resistant strains isolated were Hispanic; 9 were born in the United States and 1 was born in Mexico.

We examined the initial therapy for the child cases. Because some authorities treat hilar adenopathy using 2 drugs,¹⁴ we excluded 11 children who had hilar adenopathy as their site of disease and who were treated using INH and rifampin alone. Initial therapy using fewer than 3 drugs was started on 33 of the remaining 154 child cases (21%); 15 received INH monotherapy. The median interval of treatment until

TABLE 1. Characteristics of Study and Other Children Less Than Five Years of Age With TB: California, 1994

Characteristic	Study Population <i>n</i> = 165 (%)	Other Children <i>n</i> = 120 (%)
Median age, mo	26	24
Male	96 (58)*	51 (43)
Race/ethnicity†		
Hispanic	114 (69)	78 (65)
Asian	22 (13)	25 (21)
Black	17 (10)	6 (5)
White	12 (8)	11 (9)
Foreign-born	36 (22)	30 (25)
Primary site of disease		
Pulmonary	107 (65)	95 (79)
Hilar adenopathy	30 (18)	11 (9)
Cervical adenopathy	14 (8)	10 (8)
Other	14 (8)	4 (3)

* *P* = .01.

† Exclusive categories.

the start of adequate, 3- or 4-drug therapy was 25 days.

Seven children (1 with meningitis) had a positive TST 10 months or more before their TB diagnosis. At the time of their previous TST, 3 children had normal chest radiographs and INH treatment for latent TB infection was initiated, 2 had abnormal chest radiographs and INH alone was inappropriately initiated, 1 child had a normal chest radiograph but INH was not documented, and 1 had no record of a chest radiograph or treatment. Four of the 5 children who started on treatment for latent TB infection received <6 months of INH, and a fifth child was nonadherent but did not receive directly observed therapy for latent TB infection.

Child Cases' Modes of Presentation

Fifty-nine of the 161 children (37%) with non-*M bovis* TB had an adult source case found by local health departments (Table 2). Children found in a contact investigation, born in the United States, were <1 year of age, or who were black were more likely to have a source case found than were children who did not have one of these characteristics (Table 3).

Nearly one third of the 165 children (32%) with TB came to medical attention because of signs or symptoms of illness (Table 2); 116 children (70%) had signs and symptoms recorded. Thirty percent of children were evaluated during public health investigations (26% in a contact investigation and 4% in a source case investigation). Twenty-two percent were found as part of routine screening (14 through the Child Health and Disability Program, 8 through preschool or school entry, and 14 for unknown reasons).

Missed Opportunities in Preventing TB Transmission From Source Cases

Health departments identified 43 source cases for 59 of the child cases; most source cases (91%) were either smear- or culture-positive (Table 4). The adult source cases were family members, lived in the same household as the child, or cared for the child; they were 15 mothers, 14 aunts or uncles, 13 grandparents, 9 fathers, 6 family friends, and 2 child-care providers (1 in-home and 1 institutional). Thirty-six of the adult TB patients (84%) lived in the same house. At least 19 source cases (44%) had social or occupational risk factors for TB including alcohol

TABLE 2. Principal Reasons for Assessment of Children With TB and the Number of Children With Adult Source Cases Found in Each Group: California

Reason for Assessment	Child Cases n (%)	Source Case Identified n (%)
Symptoms*	52 (32)	7 (12)
Contact investigation	43 (26)	42† (71)
Screening	36 (22)	4 (7)
Source case investigation	7 (4)	4 (7)
Unknown	27 (16)	2 (3)
All reasons	165 (100)	59 (100)

* Includes 4 children infected with *M bovis*.

† One presumptive source case was reclassified as TB class 2 (infection without disease) after the contact investigation was performed.

TABLE 3. Factors Associated With Finding a Source Case for Children With TB in California*

Factor	% Source Found	RR	95% CI	P Value
Child found in a contact investigation	98	6.8	4.4–10.6	<.001
Child not found in a contact investigation	15			
Born in the United States	43	4.0	1.5–10.2	.001
Foreign-born	11			
Age <1 y	55	1.7	1.1–2.6	.04
Age ≥1 y	40			
Black	69	1.7	1.2–2.6	.05
Other racial or ethnic group	39			
At least 1 parent born in the United States†	59	1.5	1.0–2.3	.10
Neither parent born in the United States	40			

* Excludes 4 children infected with *M bovis*.

† Excludes 10 children whose parents' birthplaces were unknown.

TABLE 4. Demographic and Clinical Characteristics of the 43 TB Source Cases

Characteristics	No. (%)
Median age and range, y	29 (16–66)
Male	21 (49)
Race/ethnicity	
Hispanic	26 (61)
Black	9 (21)
Asian	5 (12)
White	3 (7)
Birth in United States	10 (23)
Sputum smear/culture results	
Positive/positive	33 (77)
Positive/negative	1 (2)
Negative/positive	5 (12)
Negative/negative	4 (9)

abuse (12), unemployment (12), crack cocaine use (4), migrant work (5), homelessness in the 12 months before their TB diagnosis (3), and health care work (1).

Several opportunities were missed that may have decreased the likelihood of transmission of *M tuberculosis* for all 43 source (Table 5). Ten source cases (23%) were reported to the health department >7 days after sputum for acid fast bacilli was obtained. For 9 source cases (21%) the contact investigation was delayed 14 days or more after the source was reported. In addition, at least 6 source cases had a

TABLE 5. Missed Opportunities to Prevent Transmission From 43 Source Cases

Missed Opportunities in Source Cases	Frequency* (%)
Report of source case >7 d after sputum collected	10/43 (23)
Directly observed therapy not used†	11/15 (73)
Contact investigation delayed >14 d after case report or not performed	9/43 (21)
Bacteriologic conversion delayed or not documented‡	16/38 (42)

* Total sums to >43 because each source case is categorized under every opportunity that was missed.

† Among source cases who were nonadherent with therapy.

‡ Among source cases who had a positive sputum culture.

previously positive TST and were candidates for treatment of latent TB but were not started on INH; thus, disease in these source cases was preventable.

Failure to document bacteriologic culture conversion in 42% of the culture-positive source cases may also have lengthened the infectious period and increased the likelihood of transmission. In addition, 11 of 15 source cases nonadherent to treatment did not receive directly observed therapy.

Missed Opportunities in Contact Investigations

Because contact investigations are an important means to halt TB transmission, we focused on the 43 child cases found in contact investigations to see what opportunities may have been missed. These children's TB exposure was not detected in time to prevent infection and disease. Most children (91%) found to have TB in the course of contact investigations already had disease when first assessed.

Once source cases were reported, delays in contact investigations may have contributed to the failure to halt disease progression in child contacts. Contact investigations were delayed >14 days for 10 child cases. Tuberculin skin testing for 9 children (21%) was delayed >14 days (median: 33 days) from when they were named to the health department. Seven of the 43 children were incompletely evaluated initially. The missed opportunities were 1 child who had no evaluation performed; 3 children who were TST-negative, did not have a chest radiograph, and were not started on treatment for latent TB infection; and 3 children who were TST-positive, did not have a chest radiograph, and did not start therapy. If we consider each child with at least one of the above missed opportunities as being a potentially preventable case, then improvements in contact investigations may have prevented TB in at least 17 of these 43 children (40%). In addition, 5 children were not named as contacts in 4 contact investigations; 3 of whom lived in the same household as the source cases who were relatives. Eleven of the 115 children (10%) who were evaluated other than in a contact or source case investigation had no record of any investigation.

DISCUSSION

This review of young children with TB is an important gauge of public health practices. Childhood TB is a consequential indicator of public health program performance and all child cases can be considered to represent a missed opportunity. We found several missed opportunities to prevent TB in this study of 165 children <5 years of age with TB. The most important missed opportunities were the failure to detect source cases, delayed reporting of source cases, failure to identify child contacts, delayed or incomplete evaluation of children exposed to TB, and inadequate treatment of latent TB infection. The fact that most children had disease at their initial medical evaluation suggests that interventions to prevent TB need strengthening.

The failure to find all source cases, nearly two thirds of the children did not have the source of their TB found, was an important missed opportunity for

preventing TB. In young children, because of the small number of potential sources of TB and the limited time infection could have taken place, a source case should be identified relatively frequently. Because most of the children in our study were born in the United States and because TB in young children is often transmitted from a family or household member,¹⁵ the proportion of children who had a source case found was lower than anticipated. Studies of TB cases in children <15 years of age, the majority of whom were black, found source cases for 68% to 80% of the children.¹⁶⁻¹⁸ In our study, black children had a comparable rate of source-case identification (69%). Among children born in the United States, those who had parents born in the United States were more likely than those who had parents born outside the United States to have a source case identified (59% vs 39%). The factors that make the source cases for Hispanic and Asian children (all of whom had parents born outside the United States) difficult to find need to be determined, including travel to or visitors from countries that have a high prevalence of TB, to reduce TB in children in immigrant communities.¹⁹

Although contact investigations involving children are considered a public health priority,¹⁰ only 26% of children with TB were found through contact investigations. This study finding contrasts with other studies of TB in children and adolescents that found 50% and 80% of child cases through contact investigations^{16-18,20,21} and may explain, in part, the low yield of source cases that were found. Other child cases were detected by less direct and presumably more delayed means such as presenting because of symptoms or undergoing routine tuberculin skin testing. Further study is necessary to determine how contact investigations of infectious TB cases and source case investigations of child cases can be improved, especially in immigrant communities, to prevent child and adult contacts from progressing to TB disease. Other investigative techniques, such as DNA fingerprinting, may help to identify unrecognized linkages to other adult cases that were not found in routine contact and source-case investigations.²² Also, review of other adult cases or review of cases later in time may have revealed more links between child and adult cases. Current local health department practice should be reviewed to ensure that contact investigations are conducted promptly and thoroughly and that recommendations for the evaluation of contacts and the treatment of TB infection are followed.

Delayed reporting of source cases was a missed opportunity that defers timely public health investigations that might prevent TB. We found that 23% of source cases were reported later than the 7 days from suspicion or diagnosis of TB allowed by state regulation at the time of the study. To improve the promptness of reporting, the state of California now requires that providers and laboratories notify the health department within 1 working day after a TB case is suspected or diagnosed.

This study provides worrisome data on case management of adult source cases. Delayed demonstra-

tion of bacteriologic conversion from a positive to a negative sputum culture and failure to ensure completion of therapy among source cases allow for prolonged infectiousness that may permit TB transmission.²³⁻²⁵ All 43 identified source cases were family members, caregivers, or household members. Shortening their infectious periods may have prevented transmission to children. Nearly one half of the 38 source cases (42%) who were culture-positive for *M tuberculosis* lacked documented conversion to a negative culture after 3 months of treatment and 11 of the 15 nonadherent source cases (73%) did not receive directly observed therapy. Limiting the infectious period of adults with TB by timely case detection and more effective case management is integral to the prevention of TB in children. Early case detection was the only means possible to prevent the majority of cases among the 59 children who had a source case found. We did not assess other missed opportunities such as delays in seeking medical attention and delays in starting anti-TB treatment for the source cases.²⁶⁻²⁹ Defining such delays in adult cases will better define the events that allow pediatric TB to continue unprevented.

Another important missed opportunity found in this study was the inadequate treatment of latent TB infection in children whose infection was detected before their diagnosis of TB disease. Five children who had a positive tuberculin skin test and later progressed to active disease did not start or complete INH, although INH is close to 100% efficacious in children infected with an INH-sensitive strain.^{30,31} Among children at risk for TB,³² targeted testing is cost-effective,³³ and failure to be appropriately tested may also be a marker for other missed prevention measures such as immunization.³⁴

This study is subject to several limitations. First, our interpretation that undocumented information in public health records meant that the event did not occur. We did this because TB programs cannot make decisions or assess program effectiveness if information is missing. If undocumented interventions did occur, we may have overestimated the missed opportunities. Second, we did not review medical information unless it was part of the public health record. Review of records other than those of the health department may have provided pertinent information. For example, the percentage of children found by routine screening (22%) was much higher than that found in other studies (3% to 11%).^{16-18,21} Children found by screening may have been misclassified and actually evaluated because they had unrecorded symptoms suggestive of TB. Third, most children did not have culture confirmation of their TB. It is possible that some children had infection caused by nontuberculous *Mycobacterium* or other organisms. In such cases, a source case would not be found because the source is environmental.

This study indicates that despite the close contact of child TB cases and their adult source cases, missed opportunities to prevent TB in young children are common. Prevention and, ultimately, elimination of TB in children require the early identification, reporting, and treatment of infectious source cases and

assurance that their contacts are evaluated quickly and treated when necessary. Experience demonstrates that commitment to effective interventions, such as directly observed therapy, facilitates high rates of bacteriologic cure and results in a decline in TB rates.²² Health departments and practitioners need improved communication and partnerships to expand interventions that interrupt TB transmission among children. Conversely, failure to thoroughly identify and evaluate child contacts to infectious adult TB cases in a timely manner will delay the elimination of childhood TB in the United States.

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