EXTENSIVE TRANSMISSION OF *MYCOBACTERIUM TUBERCULOSIS* FROM A CHILD

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ABSTRACT

Background and Methods Young children rarely transmit tuberculosis. In July 1998, infectious tuberculosis was identified in a nine-year-old boy in North Dakota who was screened because extrapulmonary tuberculosis had been diagnosed in his female guardian. The child, who had come from the Republic of the Marshall Islands in 1996, had bilateral cavitary tuberculosis. Because he was the only known possible source for his female guardian's tuberculosis, an investigation of the child's contacts was undertaken. We identified family, school, day-care, and other social contacts and notified these people of their exposure. We asked the contacts to complete a questionnaire and performed tuberculin skin tests.

Results Of the 276 contacts of the child whom we tested, 56 (20 percent) had a positive tuberculin skin test (induration of at least 10 mm), including 3 of the child's 4 household members, 16 of his 24 classroom contacts, 10 of 32 school-bus riders, and 9 of 61 day-care contacts. A total of 118 persons received preventive therapy, including 56 young children who were prescribed preventive therapy until skin tests performed at least 12 weeks after exposure were negative. The one additional case identified was in the twin brother of the nine-year-old patient. The twin was not considered infectious on the basis of a sputum smear that was negative on microscopical examination.

Conclusions This investigation shows that a young child can transmit *Mycobacterium tuberculosis* to a large number of contacts. Children with tuberculosis, especially cavitary or laryngeal tuberculosis, should be considered potentially infectious, and screening of their contacts for infection with *M. tuberculosis* or active tuberculosis may be required. (N Engl J Med 1999;341:1491-5.)

YOUNG children rarely transmit tuberculosis.[1,2] In five recently published reports of school-based outbreaks, all source patients were adults or adolescents.[3-7] Tuberculosis in young children is rarely infectious, because young children are less likely than adults to have a productive cough, to generate the force needed to aerosolize organisms into droplet nuclei, or to have cavitary lesions on chest radiography.[1,2] In July 1998, infectious tuberculosis was identified in a nine-year-old child residing in North Dakota. The child was screened because extrapulmonary tuberculosis had been diagnosed in his female guardian. Bilateral cavitary tuberculosis was diagnosed in the child. Because the child was the only known possible source of his female guardian's tuberculosis, an investigation of the child's contacts was undertaken.

METHODS

Case Review and Laboratory Investigation

We reviewed the medical records of the child and his female guardian and interviewed the family. A patient was considered infectious if he or she had pulmonary tuberculosis with sputum specimens that were positive for acid-fast bacilli on microscopical examination and had a culture that grew *Mycobacterium tuberculosis*. We determined infectious periods by reviewing histories of symptoms, chest radiographs, and medical records. We performed drug-susceptibility testing and DNA-fingerprint analysis, using the IS*6110* insertion sequence on isolates from patients with tuberculosis.[8]

Investigation of Contacts

We conducted an investigation of the child's contacts because he was considered a likely source of transmission (i.e., the source patient). Although the female guardian was the first patient in whom the infection was identified (i.e., the index patient), she was not infectious and therefore was not considered a possible source of transmission. The investigation involved identifying persons exposed to the child while he was infectious and testing them for tuberculosis infection and active tuberculosis. A list of close contacts of the child was compiled. The list included nonhousehold social contacts such as extended family members, friends, and neighbors as well as children attending the source patient's first-grade class and day-care center and their staff members. Because English was their second language, the nine-year-old source patient and his twin brother were only in the first grade. We screened the contacts in mid-July with tuberculin skin tests, chest radiography, and assessments of symptoms of and risk factors for tuberculosis. Because of evidence of transmission from the source patient to classmates and children and staff at the day-care center, we performed a second screening in late July for all children enrolled in and all staff working in the school system in 1998 and for concerned community members who requested testing. At each screening, five or six trained nurses from local health departments and one nurse from the Division of Tuberculosis Elimination, Centers for Disease Control and Prevention (CDC), administered and read skin tests. All skin tests were administered with the Mantoux method.

We conducted follow-up screenings in August and September (12 weeks after the last exposure to the source patient). We considered screened persons with no known, direct exposure to the source patient to be noncontacts. For clinical purposes, we considered

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contacts with induration of at least 5 mm on a tuberculin skin test to be infected.[9] To compare contacts with noncontacts in epidemiologic analyses, we considered a skin test that produced induration of at least 10 mm to be positive. We defined a tuberculin skin-test conversion as an increase of at least 10 mm in a skin-test result within two years after a previously negative result.

Preventive Therapy

We developed an algorithm for use in making recommendations about preventive therapy. All persons with positive tuberculin skin tests (induration of at least 5 mm) but without active tuberculosis were eligible for preventive therapy with isoniazid.[10] After we found a high rate of tuberculin skin-test positivity among first-graders at the initial screening, we recommended preventive therapy and chest radiography for first-graders and other exposed children who were six years of age or younger, regardless of the result of the first tuberculin skin test, because tuberculosis can develop rapidly in young children. Preventive therapy was discontinued for children whose skin tests remained negative at a screening at least 12 weeks after the last exposure to the source patient. Before initiating preventive therapy, we assessed all eligible contacts for active tuberculosis; the assessment included a review of symptoms and chest radiography. For school-age children, we recommended that preventive therapy be directly observed, which included trained personnel watching the patients swallow their antituberculous medications. Directly observed therapy was implemented at the school when school began again in August 1998. We encouraged parents to have their children participate in the school-based preventive-therapy program if the children were eligible. Before school began, from mid-July until mid-August, the parent or guardian in the household administered the preventive therapy to the child.

RESULTS

Tuberculosis in North Dakota

North Dakota has a very low incidence of tuberculosis: 1.9 cases per 100,000 per year, with 12 cases of tuberculosis reported in 1997.[11] Since 1992, only one case of tuberculosis has been reported in a child younger than 15 years of age in North Dakota; in the two-county area around the source patient's residence, there were two cases of tuberculosis in the 5 years before this investigation, neither of them in a child (CDC: unpublished data).

Cases in Family Members

The index patient was the 36-year-old female guardian of the source patient. She had no record of having a prior tuberculin skin test. Apart from visiting Montana, she had never left North Dakota and had no known exposure to anyone with tuberculosis or symptoms suggestive of tuberculosis. She reported pain in her left hip in December 1997, after an injury at work. She was seen by several physicians during three office visits between January and May 1998. Plain-film radiographs taken in January and May 1998 showed only progressive narrowing of the left hip-joint space. In May 1998, a computed tomographic scan showed fluid in the left hip joint. Specimens obtained by aspiration were smear-positive for acid-fast bacilli and culture-positive for *M. tuberculosis.* Consultants in orthopedics and infectious diseases diagnosed tuberculous arthritis, early osteomyelitis of the left femur head and proximal femur, left obturator myositis, and a pelvic abscess. Because there was no indication of infection on the plain-film radiographs and there was no history of osteomyelitis or any hip problems, it is unlikely that the infection in the index patient was long-standing. She had induration of 10 mm on a tuberculin skin test and a normal chest radiograph, and because there was no evidence of pulmonary disease, she was not considered to be infectious. She began antituberculous therapy in June 1998.

The source patient and his identical twin brother arrived in North Dakota from the Republic of the Marshall Islands in 1996 and resided together with the index patient and her husband. The index patient did not meet the twins until their arrival in North Dakota. Shortly after arrival in the United States, the twins underwent a tine test, which was not read; no other testing for tuberculosis was performed. The source patient had a tuberculin skin test with induration of 22 mm in July 1998, when he was screened after the diagnosis of his female guardian's tuberculosis. His only symptom reported by his guardian was a dry cough that had started in March 1998. However, his teacher reported that he had repeatedly fallen asleep in class since the previous winter.

At the time of his diagnosis of tuberculosis, the source patient was 5 cm (2 in.) shorter and 5 kg (11 lb) lighter than his twin brother. A chest radiograph obtained in July 1998 revealed extensive bilateral cavitary disease (Fig. 1). Sputum specimens were 4+ smear-positive for acid-fast bacilli and culture-positive for *M. tuberculosis.* The child began antituberculous therapy in July 1998 and completed a six-month course of therapy in January 1999. On the basis of a review of medical records, the natural history of bone and joint tuberculosis, and the onset of symptoms in the female guardian, the source patient was considered to have been infectious as of September 1997.

The source patient's twin had a skin test with induration of 20 mm in July 1998, a normal chest radiograph, and no symptoms of tuberculosis. Three sputum specimens from July 1998 were smear-negative, but one grew *M. tuberculosis.* He was not considered infectious. His physician prescribed a six-month course of antituberculous therapy, which the boy completed. Isolates from the female guardian and twins had an identical 20-band DNA-fingerprint pattern and were susceptible to all first-line drugs.

Household Contacts

The male guardian had conversion on tuberculin skin testing from 0 mm of induration on the first screening to 17 mm at the postexposure screening. His chest radiograph was normal, and he had no symptoms. He received six months of preventive therapy. In late June 1998, a six-year-old biologic cousin of the boys arrived from the Marshall Islands and resided in the same household. Induration on her first

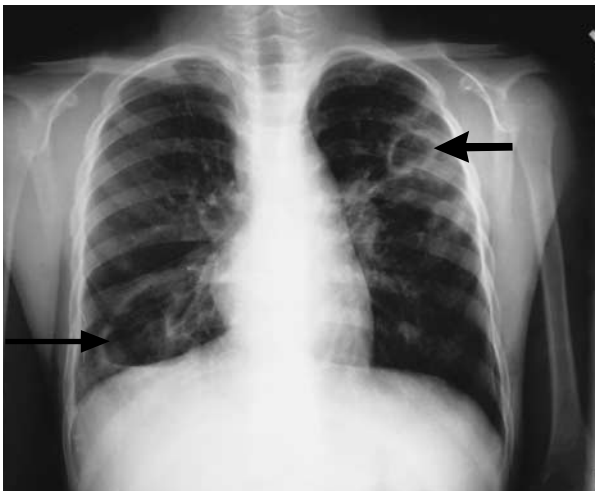

Figure 1. Chest Radiograph of the Source Patient, Showing Cavitary Lesions in the Right Base (Long Arrow) and the Left Upper Lobe (Short Arrow).

These findings are associated with interstitial and some nodular infiltrates in the left mid-lung field and in the right perihilar and infrahilar regions. An air–fluid level can be seen in the inferior portion of the right lung. The heart, lungs, bones, and mediastinum are otherwise unremarkable.

tuberculin skin test was 0 mm; she had no symptoms, and she had a normal chest radiograph. She received preventive therapy until she was found to have a second negative skin test (0 mm) 12 weeks after exposure.

Nonhousehold Contacts

The area in which the outbreak occurred is a rural farming community. The town where the source patient attended school has a population of fewer than 1000, and most of the residents are U.S.-born whites. Of the contacts, one was Asian American, and all were U.S.-born.

The school system has two buildings, which together house classrooms for prekindergarten through 12th grade. The elementary-school building houses prekindergarten through 6th grade, and the second building, the high school, is for grades 7 through 12. All students eat lunch in the elementary-school cafeteria, but children in grades 7 through 12 eat at a different time from the elementary-school children. Children in grades 7 through 12 were screened, but as a group they were not considered to be contacts.

The source patient's first-grade classroom measures 9.8 by 9.1 m (32 by 30 ft) and has a ceiling height of 3.0 m (10 ft). During instruction, the children often sat together on a small set of bleachers in the front of the classroom. The children used their desks while completing schoolwork, but seating assignments changed throughout the school year. The source patient rode a school bus each weekday morning for 1 hour and 15 minutes. Other passengers' exposures to him ranged from 35 minutes to 1 hour and 15 minutes daily. The source patient did not ride the bus home but attended a day-care center for 30 minutes to 1 hour after school and for 6 to 8 hours every weekday after school finished at the end of May. At the day-care center, no more than 19 children were present at once, and they often played outdoors.

Investigation of Contacts

During the tuberculin skin-test screenings held in July, August, and September 1998, we obtained results of skin tests of 277 of 284 contacts (98 percent). One contact had had a positive skin test in the past and was excluded from further analysis; of the other 276 contacts we tested, 56 (20 percent) had induration of at least 10 mm. Of these 56 contacts, 49 were positive at the first screening, and 7 had documented skin-test conversions (from 0 mm to at least 10 mm of induration): the male guardian, a first-grader, two school-bus riders, two children from the day-care center, and an additional elementary-school student. We also tested 156 people who were not contacts of the source patient (107 high-school students and 49 concerned community members), 5 of whom (3 percent) had a positive tuberculin skin test.

The 432 persons screened were classified in mutually exclusive and hierarchical groups according to their level of contact with the source patient (Table 1). Each contact group had a significantly elevated risk of a positive tuberculin skin test as compared with noncontacts. The household and classroom contact groups had the highest proportion of infected persons; 75 percent and 67 percent, respectively, had positive skin tests (at least 10 mm of induration) in these two groups. Overall, contacts were 6.3 times as likely as noncontacts to have a positive tuberculin skin test. We also calculated results using a 5-mm cutoff point for a positive tuberculin skin test. The results did not differ significantly when we used this cutoff point (Table 1).

Preventive Therapy

After the initial screening, 120 contacts were eligible for preventive therapy. Of these contacts, 56 were young children with an initial negative skin test in whom preventive therapy was discontinued after their postexposure tuberculin skin test remained negative. Of the remaining 64 contacts with a tuberculin skin test with induration of 5 mm or more, 2 discontinued preventive therapy (1 because of elevated levels of serum hepatic aminotransferases and another because of other medical problems); 10 contacts moved, and no follow-up information on them is available; 26 completed preventive therapy; 24 continue to receive preventive therapy; and 2 declined preventive therapy. Most children who were eligible for preventive therapy received it under direct obser-

TABLE 1. TUBERCULIN SKIN-TEST RESULTS FOR CONTACTS AND NONCONTACTS OF THE NINE-YEAR-OLD SOURCE PATIENT.*

PERSONS TESTED	NO. TESTED	INDURATION OF ≥5 mm	RELATIVE RISK (95% CI)	INDURATION OF ≥10 mm	RELATIVE RISK (95% CI)
		no. (%)		no. (%)	
Noncontacts†	156	6 (4)		5 (3)	
All contacts‡	276	64 (23)	7.2 (3.0–17.6)	56 (20)	6.3 (2.6–15.5)
Household	4	3 (75)	19.5 (7.4–51.3)	3 (75)	23.4 (8.3–65.6)
Classroom	24	19 (79)	20.6 (9.2–46.3)	16 (67)	20.8 (8.4–51.6)
School bus	32	11 (34)	8.9 (3.6–22.4)	10 (31)	9.8 (3.6–26.6)
Day care	61	10 (16)	4.3 (1.6–11.2)	9 (15)	4.3 (1.6–13.2)
Other social contacts	23	5 (22)	5.7 (1.9–17.0)	3 (13)	4.1 (1.0–15.9)
Other elementary-school contacts	132	16 (12)	3.2 (1.3–7.8)	15 (11)	3.6 (1.3–9.5)

*The noncontacts are the reference group. CI denotes confidence interval.

†Noncontacts include high-school students and staff and other community members who had no exposure to the source patient.

‡Categories of contacts are mutually exclusive and hierarchical in the (descending) order shown.

vation. At the beginning of school, 91 percent of the eligible children (48 of 53) received directly observed preventive therapy.

DISCUSSION

This investigation documents the transmission of *M. tuberculosis* from a nine-year-old child with extensive bilateral cavitary pulmonary disease to 20 percent of his contacts in rural North Dakota. It is highly probable that the children with positive tuberculin skin tests were infected through exposure to this child, because this geographic area has a low incidence of tuberculosis and because no other potentially infectious patient was identified.

There are three possible explanations for the unusual presentation of the source patient's twin, who had a sputum specimen that was culture-positive but had a negative chest radiograph. We cannot rule out the possibility that the twin brother's positive culture was the result of cross-contamination. The twin brother gave three sputum specimens on three consecutive days in July 1998; only one grew *M. tuberculosis.* This specimen was collected at the same time as a specimen from the source patient, and the two specimens were processed at the same time in the laboratory. However, there are published reports that specimens obtained at the time of skin-test conversion from asymptomatic infected persons can be culture-positive for *M. tuberculosis.*[12-14] Moreover, the twin may have had mild disease that was not seen on the plain film, and no computed tomographic scan or other imaging study was performed. The attending physician elected to treat the child as having active tuberculosis, so the child received a six-month course of therapy.

This outbreak was unusual, because most children younger than 10 years who have active tuberculosis are not infectious. As compared with adults, young children more often have negative smears; they rarely have cavitary disease; they often have little or no cough; and when cough is present, it is generally not forceful enough to expel aerosolized bacilli efficiently.[1,2] From 1993 through 1997, 4 percent of 5020 children younger than 10 years of age with reported pulmonary tuberculosis had cavitary disease, as compared with 11 percent of the 939 children who were 10 to 15 years old and 24 percent of the 88,065 who were at least 16 years old (CDC: unpublished data).

Few cases of infectious pulmonary disease in other young children have been reported. In five published reports of children younger than 10 years with infectious tuberculosis, all transmission occurred in a hospital.[15-19] In four of the five reports, an infant younger than 15 months was the source.[15-18] All four infants required suctioning, and in two cases, the infants received mechanical ventilation through an endotracheal tube. Five nurses had tuberculin skin-test conversions after providing direct care, including suctioning, to these four infants. In the fifth case, 2 of 28 health care workers had skin-test conversion after exposure to a five-year-old boy with the acquired immunodeficiency syndrome and cavitary tuberculosis that was positive on sputum smear and culture.[19] In Lincoln's extensive review of 84 school-based outbreaks of tuberculosis that occurred in 12 countries during the mid-1900s, only four children younger than 10 years of age were reported as source patients.[20] We identified no other published report of infectious tuberculosis in a child younger than 10 years in the past 30 years. Infectious tuberculosis among young children remains rare.

Tuberculosis in a young child usually signifies new

transmission of *M. tuberculosis* from an infectious adult. However, in this case, the index patient was an adult with extrapulmonary disease, and the infectious source patient was a nine-year-old child with cavitary disease that was likely to have been due to endogenous reactivation. The child had no known recent contact with a patient with infectious tuberculosis, but he was born in an area with a high incidence of tuberculosis. It is likely that he acquired *M. tuberculosis* infection while in the Marshall Islands, which has a high incidence of tuberculosis; in 1996, a total of 56 cases were reported, resulting in an incidence of 104 cases per 100,000 population for that year.[21] The Republic of the Marshall Islands is a Pacific nation with close ties to the United States. Citizens are U.S. nationals, are considered U.S.-born, and do not require any screening for tuberculosis to travel to, or reside in, the United States.

When infectious tuberculosis is identified in a person in a day-care center or school, investigations should be conducted in a timely manner to identify infected contacts and active cases and to provide preventive therapy to those who are eligible. This is especially true for investigations in day-care settings that involve infants, who are at the highest risk for rapid progression to active tuberculosis as well as to serious forms of disease, including tuberculous meningitis and miliary tuberculosis.[1,9] In very young children, infection can progress to disease before the development of a positive tuberculin skin-test result.[10] It is recommended that young children with negative skin tests who are close contacts of an infectious patient receive preventive therapy until there is a documented negative skin test at 10 to 12 weeks after exposure.[9,10]

This investigation showed that young children can transmit *M. tuberculosis* to a large number of contacts. Children with tuberculosis, especially cavitary or laryngeal disease, should be evaluated on a case-by-case basis. They should be considered potentially infectious, and their cases may merit investigations of contacts as extensive as the one described here. To prevent similar outbreaks, guidelines from the CDC and the American Academy of Pediatrics recommend that children from areas with high rates of tuberculosis — both those who are U.S.-born and those who are foreign-born — be screened and given treatment or preventive therapy as indicated.[9,10,22] Screenings should include a tuberculin skin test by the Mantoux method (regardless of the history with respect to bacille Calmette–Guérin vaccination), evaluation for symptoms of tuberculosis, and chest radiography if induration after a skin test is 10 mm or greater or if symptoms are present. In this case, the source patient was from an area with a high rate of tuberculosis. Had this child been screened with a Mantoux test and given preventive therapy on his arrival in North Dakota, this outbreak might have been averted.

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