Immigration and Tuberculosis Among Children on the United States–Mexico Border, County of San Diego, California

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ABSTRACT. *Objective.* **To identify factors contributing to a 400% increase in tuberculosis among children in San Diego County, California, from 1985 to 1993.**

Design. **Review of medical records of reported cases in 1989, 1991, and 1993 and their source case.**

Results. **Of 192 children with tuberculosis, the largest increase was observed in children younger than 5 years old, of whom 77.4% were born in the United States, 67.8% had a foreign-born parent, 73.1% came from a non-English-speaking household, and 46.2% were known to visit Mexico. Of 28 source cases, 82.1% were born outside the United States, primarily in Mexico (67.9%). Resistance to at least one first-line antituberculous drug was identified in 27.5% of isolates from children and in 33.3% of isolates from source cases.**

Conclusions. **The increase in tuberculosis and high level of drug-resistance among children born in the United States may be attributed to transmission outside of the United States or within the United States from household contacts born in countries in which tuberculosis is highly endemic. *Pediatrics* 1999;104(1). URL: http://www.pediatrics.org/cgi/content/full/104/1/e8; *tuberculosis, children, border health, drug-resistant tuberculosis, immigration.***

ABBREVIATIONS. AFB, acid-fast bacilli; TST, tuberculin skin test.

After a steady decline from 1953 through 1988, reported cases of tuberculosis in children younger than 15 years in the United States increased by 51% from 1133 cases in 1988 to 1708 cases in 1992.[1] After increased public health efforts, tuberculosis cases in children declined by 26% from 1708 cases in 1992 to 1265 cases in 1997, similar to the 26% decline among adults.[2–7] Coinciding with these declines has been a steady increase in the proportion of tuberculosis cases in the US who were foreign-born, from 22% in 1986 to 39% in 1997, of whom the largest group (43.9%) were from Latin America.[1,7,8] The trend for tuberculosis among children in the United States has been characterized by greater increases in case rates for minority children compared with that of white, non-Hispanic children and a relative risk of 8.5 to 12.7 among foreign-born children compared with that of children born in the United States.[1]

From 1985 through 1993, the state of California reported 29% of all cases of tuberculosis in children in the United States, ranking them first among the 50 states and the District of Columbia.[1] During this period, tuberculosis cases in children and adolescents younger than 20 years old reported by the County of San Diego, California increased by 400% from 15 cases in 1985 to 75 cases in 1993. Reported cases were reviewed to provide possible explanations for this increase to better describe the epidemiology of tuberculosis among children and adolescents younger than 20 years old and to identify missed opportunities for prevention of tuberculosis in children.

METHODS

Identification of Cases of Tuberculosis in Children

All suspected and confirmed cases of tuberculosis in children and adolescents younger than 20 years old reported to the County of San Diego Department of Health Services Tuberculosis Control Program during 1989 (preincrease), 1991 (during increase), and 1993 (postincrease) were identified from the local tuberculosis registry. Suspected tuberculosis cases were reported to, but not confirmed by, the health department as meeting the case definition. Suspected and confirmed tuberculosis cases were reclassified as meeting the case definition of a tuberculosis case using the following criteria: meeting the published Centers for Disease Control and Prevention (Atlanta, GA) case definition,[9] ie, 1) a positive culture for *Mycobacterium tuberculosis*; 2) a positive smear for acid-fast bacilli (AFB) but no culture performed; or 3) meeting the clinical case criteria, including a positive tuberculin skin test (TST), signs and symptoms compatible with tuberculosis, (such as an abnormal, unstable chest radiograph), treatment with two or more antituberculous drugs, and a completed diagnostic evaluation. Children who did not meet the above criteria but who had signs and symptoms compatible with tuberculosis were treated for tuberculosis, reported by their provider, and confirmed by the health department as a tuberculosis case were also analyzed as a provider-diagnosed tuberculosis case. Children with tuberculous infection alone (positive TST and no sign of active disease) and children with no evidence of tuberculous infection or active tuberculosis were excluded from analysis.

Data were abstracted from birth certificates, health department records, and medical records at hospitals and clinics. Data collected included demographic characteristics of the child and parents, household language, travel and immigration history, clinical information, and culture and drug susceptibility results. All positive cultures for *M tuberculosis* complex were screened routinely for *Mycobacterium bovis* by the Department of Health Tuberculosis laboratory.

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Identification of Potential Source Cases and Potential Missed Opportunities to Prevent Tuberculosis in Children

To identify potential source cases, health department investigation records and medical records for each child with tuberculosis were reviewed. The health department routinely conducts an investigation of all children diagnosed with tuberculosis. Investigation includes household interviews to identify contacts and possible source cases, screening contacts for signs and symptoms of tuberculosis, and tuberculin skin testing. For children younger than 7 years, the emphasis is on source case finding. Health department records of potential source cases who matched the county tuberculosis registry were reviewed to determine whether they were reportedly in contact with the child when the source case had infectious pulmonary tuberculosis.

Potential missed opportunities to prevent tuberculosis in cases among children were identified by matching children with tuberculosis to the list of children younger than 6 years reported to the health department with a positive TST, a reportable condition in San Diego County, and by a review of the contact investigations of source cases. Missed opportunities were classified as 1) no evidence of preventive therapy for a child reported with a positive TST, 2) no evidence of preventive therapy for a child 5 years of age or younger pending determination of tuberculous infection status after exposure to an adult with pulmonary tuberculosis,[10,11] 3) not identifying a child as a contact during contact investigation of an adult with pulmonary tuberculosis, and 4) not screening a child routinely for tuberculous infection according to recommended guidelines.[11] Categorical variables among tuberculosis cases were compared using the χ^2 test, and trends between age-groups and over time were assessed with the χ^2 test for trend using Epi Info Version 6 (Centers for Disease Control and Prevention, Atlanta, GA).[12]

RESULTS

Demographic Characteristics of Cases

Of 255 suspect and confirmed cases reviewed, 63 were excluded from analysis, including 33 with tuberculous infection only, 13 who met the case definition but resided in the jurisdiction of another health department in the state, and 17 with no evidence of tuberculosis or tuberculous infection. Among the 192 cases analyzed, 32 were reported in 1989, 85 were reported in 1991, and 75 were reported in 1993. Demographic characteristics of cases are summarized in Table 1. Some significant trends across age groups were identified. With increasing age of children, there was a decrease in the number who were born in the United States but an increase in the number who were born in Southeast Asia ($P <$ .01 for both). Among the children who were born in the United States, 62.3% had at least one parent who was born in a country in which tuberculosis is highly endemic (Mexico, Phillippines, Vietnam, Somalia, Laos, Ethiopia, and Guatemala), 39.1% were known to visit family in Mexico before the diagnosis of tuberculosis, and 87/105 (82.8%) came from households in which the primary spoken language was not English. The greatest increase in cases was observed among children who were born in the United States and who were younger than 5 years; most (86.1%) of these children were of Hispanic ethnicity and among foreign-born adolescents (Fig 1).

Among children born in the United States (Fig 2), the proportion who were Hispanic increased significantly from 70% in 1989 to 80.4% in 1991 and to 95.3% in 1993 (P = .006). Although children of Hispanic ethnicity accounted for most of the increase among foreign-born children, children from Asia and Africa were also important contributing factors (Fig 2). Among the 77 foreign-born cases with known arrival dates in the United States, 37 (48.1%) were diagnosed with tuberculosis within 1 year of arrival,

TABLE 1. Characteristics of 192 Tuberculosis Cases Among Children by Age Group, County of San Diego, 1989, 1991, and 1993

	Age Group (Years)				
	<5 Years N = 93	5–9 Years N = 22	10–14 Years N = 24	15–19 Years N = 53	Total N = 192
Characteristic	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Female	59 (63)	8 (36)	10 (42)	26 (49)	103 (53)
Child's birthplace					
US-born*	72 (78)	11 (50)	14 (58)	13 (24.5)	110 (57)
Mexico	17 (18)	6 (27)	3 (13)	25 (47)	51 (27)
Southeast Asia*†	1 (1)	2 (9)	6 (25)	13 (24.5)	22 (11)
Africa/Central America†	3 (3)	3 (14)	1 (4)	2 (4)	9 (5)
Ethnicity					
Hispanic	80 (86)	15 (68)	16 (67)	35 (66)	146 (76)
Asian	3 (3)	2 (9)	6 (25)	14 (26)	25 (13)
Black	7 (8)	2 (9)	0 (0)	3 (6)	12 (6)
Native American	2 (2)	2 (9)	1 (4)	0 (0)	5 (3)
White, non-Hispanic	1 (1)	1 (5)	1 (4)	1 (2)	4 (2)
Parent foreign-born					
Unknown	30 (32)	11 (50)	10 (42)	42 (79)	93 (48)
Mexico	57 (62)	9 (41)	9 (37)	6 (11)	81 (42)
Southeast Asia†	3 (3)	0 (0)	5 (21)	5 (9)	13 (7)
Africa/Central America†	3 (3)	2 (9)	0 (0)	0 (0)	5 (3)
Household language non-English‡	68 (73)	16 (73)	9 (37)	22 (42)	115 (59)
Child known to have visited Mexico	43 (46)	4 (18)	4 (17)	14 (26)	65 (34)
Culture-positive*§	31/69 (45)	5/16 (31)	10/19 (53)	46/53 (87)	92/157 (59)

* χ^2 for trend; $P < .05$.
† Southeast Asia = Phillippines, Vietnam, Laos; Africa = Ethiopia, Somalia; and Central America = El Salvador, Guatemala.
‡ "Non-English" refers to instances in which the health department record (for purposes of whether an interpreter was required) included only languages other than English because the household language was non-English only. Households that were bilingual and included English were considered English-speaking.
§ Of children for whom a specimen was collected, positive specimens include 14/38 (37%) gastric aspirates and 17/31 (55%) lymph nodes.

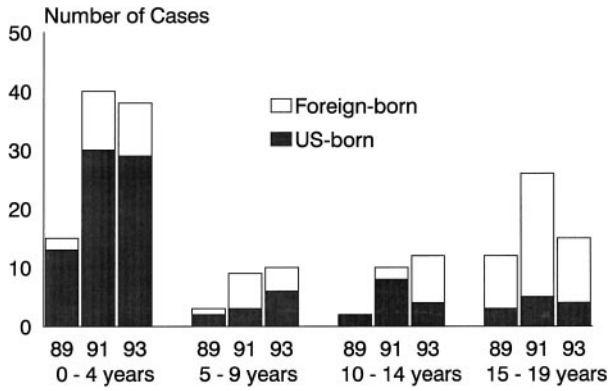

Fig 1. Age group and birthplace for 192 cases of tuberculosis in children, County of San Diego, California in 1989, 1991, and 1993.

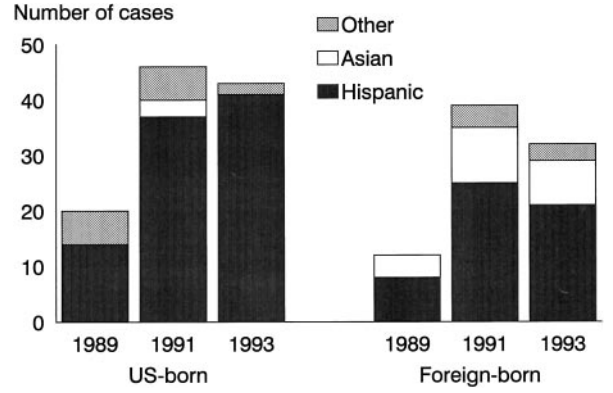

Fig 2. Ethnicity and birthplace of 192 cases of tuberculosis in children, San Diego County, California in 1989, 1991, and 1993.

and 45 (58.4%) were diagnosed with tuberculosis within 2 years of arrival, including 16/19 (84.2%) children younger than 5 years.

Clinical Characteristics

Overall, 87 (45.3%) cases had a positive culture for *M tuberculosis* complex, 4 (2.1%) cases had positive AFB smears and no culture done, 85 (44.3%) cases met the clinical criteria for a case, and the remaining 16 (8.3%) cases were diagnosed by a provider. A specimen was collected for laboratory testing from 81.8% of the cases. The proportion of positive gastric aspirate specimens in children younger than 5 years was 14/38 (36.8%). The proportion of culture-positive cases declined from 50.0% in 1989 to 45.9% in 1991 and to 33.3% in 1993 ($P = .07$). In contrast, the proportion of cases confirmed based on clinical criteria increased from 34.4% in 1989 to 36.4% in 1991 and to 57.3% in 1993 ($P = .008$). Most cases were detected as a result of seeking care for symptoms of tuberculosis (58.8%), followed by screening at well-child examination (13.0%), contact investigation (8.8%), refugee/immigrant screening (6.3%), screening of adolescents for employment, pregnancy, or incarceration (3.1%); for 9.9%, the reason for detection was unknown. Of cases detected during well-child examinations, 84.0% of the children or their parents were from a country in which tuberculosis is highly endemic. Only 1/21 (4.8%) children with test results was known to be HIV-positive.

Overall, 51.6% of cases had pulmonary disease, 33.3% had extrapulmonary disease, and 15.1% had both pulmonary and extrapulmonary disease. Of the 93 cases with extrapulmonary disease, types or sites of disease included cervical adenopathy (26.9%), hilar adenopathy (26.9%), other lymphadenopathy (12.9%), pleura (12.9%), meninges (12.9%), peritoneal involvement (8.6%), bone (6.4%), miliary tuberculosis (2.2%), and other sites (2.2%).

Of the 87 children with a positive culture for *M tuberculosis* complex, 14 (16.1%) had a culture positive for *M bovis* and all were of Hispanic ethnicity with extrapulmonary disease; 78.6% were younger than 5 years, and 71.4% were born in the United States. Excluding those children with *M bovis*, drug susceptibility results were available for 94.5% of culture-positive cases and are summarized in Table 2. Most children with drug-resistant tuberculosis were Hispanic (47.4%) or Asian (31.6%), and 89.4% of children or their parents were from a country in which tuberculosis is highly endemic (Mexico, Phillippines, Vietnam, or Ethiopia).

Results of Contact Investigation and Potential Missed Opportunities to Prevent Tuberculosis in Children

Health department investigations were conducted for 90.6% of tuberculosis cases in children. Of 1244 contacts identified, results were available for 80.7%. Of these, 38.0% had at least a 10-mm induration response to tuberculin skin testing and a normal chest radiograph, 10.6% had at least a 10-mm induration but no chest radiograph result on the contact sheet, 10.8% had a previous positive TST, 12.9% refused testing, 4.1% were new cases of tuberculosis identified during household investigation, 4.0% of contacts (including children and adults) had already known current or previous tuberculosis, and 19.3% had either a negative test or a test that was not read. Cases identified as a result of health department investigation included 17 new cases in children and 7 adults who were the source cases. A significantly higher proportion of contacts with evidence of tuberculous infection was observed when the index child, parent, or source case was foreign-born, compared with when all were known to be born in the United

TABLE 2. Drug Susceptibility Results From 69 Children With Tuberculosis and 21 Potential Source Cases, County of San Diego, 1989, 1991, and 1993

	Children With TB ($N = 69$)	Source Cases ($N = 21$)
Drug resistance pattern	*n* (%)	*n* (%)
Any resistance	19 (28)	7 (33)
Resistant to:		
Only isoniazid	5 (7)	0 (0)
Only streptomycin	8 (12)	4 (57)
Only ethambutol	1 (1)	1 (5)
Isoniazid and streptomycin	4 (6)	1 (5)
Isoniazid and ethambutol	1 (1)	0 (0)
Streptomycin and ethambutol	0 (0)	1 (5)

Table excludes 14 children with *M bovis* disease (none had resistance to any drug other than pyrazinamide) and 4 children and 7 source cases with positive cultures but no drug susceptibility test results.

States (mean 39.8% of contacts compared with 26.2% of contacts; $P = .03$).

Of the 192 cases in children, 67 had potential source cases identified. Of these, 32 had potential source cases but no additional information was available, including 18 cases whose potential source case resided outside of the United States. For the remaining 35 children, 27 of whom were younger than 5 years, a total of 28 source cases were confirmed. Characteristics of the source cases are summarized in Table 3. Of the 14 source cases with both known date of arrival in the United States and date of the first positive sputum smear for AFB, 35.7% arrived in the United States <2 years before being diagnosed with tuberculosis. Drug susceptibility results for source cases are summarized in Table 2. The majority of source cases with drug-resistant tuberculosis (71.4%) were from a country in which tuberculosis is highly endemic (Mexico or Ethiopia). Both secondary cases in children with positive cultures had matching drug susceptibility patterns, but the remaining 5 children had negative cultures or cultures were not performed.

Confirmed source cases were diagnosed with tuberculosis as a result of seeking medical attention for symptoms (32.1%), as a result of health department investigation 25%), during refugee/immigrant screening (17.9%), and for unknown reasons (25%). Chronologically, 57.1% of source cases were identified as having tuberculosis before the index child case was identified, 35.7% were identified after the child, and it was unclear for 7.1% of source cases who was identified first.

Overall, 92.8% of cases in children were linked to a country in which tuberculosis is highly endemic, ie, child, parent, or source was born there; or the child was known to have visited family in Mexico; or the primary household language was other than English. The proportion of cases with this linkage increased significantly from 81.2% of cases in 1989 to 90.6% of cases in 1991 and to 98.7% of cases in 1993 ($P = .002$). Among children born in the United States, the children younger than 5 years were more likely than the older age groups to be linked to a country in which tuberculosis is highly endemic (91.7% of children younger than 5 years, compared with 81.2% of children 5 to 9 years old, 85.7% of children 10 to 14 years old, and 61.5% of adolescents 15 to 19 years old; $P = .02$).

TABLE 3. Characteristics of 28 Confirmed Source Cases, County of San Diego, 1989, 1991, and 1993

Characteristic	Number (%)
Male	16 (57)
Mean age (range)	25 (12–66)
Ethnicity	
Black	5 (18)
Hispanic	20 (71)
Asian	3 (11)
Birthplace	
United States	5 (18)
Mexico	19 (68)
Ethiopia	2 (7)
Somalia	1 (3.5)
Laos	1 (3.5)
Relationships to children with tuberculosis*	
Mother	12 (43)
Father	7 (25)
Siblings/other housemates	4 (14)
Relatives	6 (21)
Unknown	6 (21)
Household non-English speaking	24 (86)
Visits family in Mexico	11 (39)
Previous tuberculosis treatment in Mexico	5 (18)

* The 28 source cases could be sources for more than one child and can be counted in more than one category.

Medical records were available for review to assess adequately potential missed opportunities to prevent tuberculosis in children in 26% of cases cases. Of these cases, 34% of children were diagnosed with tuberculosis within a few months of entering the United States and were probably not preventable by the health care system in the United States. The remainder included 26% of children who were from a high-risk group and who had not received routine TST screening during well-child care, 12% who had not been identified as a contact to a tuberculosis case, 10% who completed <1 year of preventive therapy, 10% who were younger than 5 years and a known contact to a tuberculosis case yet who were never placed on preventive therapy, 4% with a previous positive TST who did not receive preventive therapy, and 4% who were a known contact of a case but who were not screened.

DISCUSSION

The increase in tuberculosis among children on the United States–Mexico border may be largely attributable to transmission outside of the United States in countries in which tuberculosis is highly endemic, as well as within the United States from household contacts born in those countries. In contrast to the national trend of increased cases among those born in countries in which tuberculosis is highly endemic, the greatest increase in San Diego County was observed among young children born in the United States. Over 90% of tuberculosis cases among US-born children younger than 5 years had a parent or source case from a country in which tuberculosis is highly endemic, a history of foreign travel, or a primary household language other than English. These findings may help explain national trends in which only 15% of tuberculosis cases in children younger than 5 years are foreign-born, compared with 35% of cases in children 5 years or older.[1] Tuberculosis surveillance systems in the United States do not monitor routinely the birthplace of parents or source cases of children and probably are underestimating the contribution of the global tuberculosis epidemic to US-born children in this country.

The findings of this investigation in San Diego County support the recommendation that children who are from or who have parents who are from regions of the world with a high prevalence of tuberculosis are at high risk and should be screened for tuberculous infection.[11] However, the findings also indicate that screening of children in this population should occur earlier than the currently recommended 4- to 6-years of age.[11] Because most of the very young children with tuberculosis were <4-

years old when diagnosed with tuberculosis, screening at the recommended ages in this setting would not have identified the majority of young children with tuberculosis. The evidence that only 54% of source cases were known to be parents also supports the recommendation of screening children who have a circle of close contacts (eg, other relatives, caretakers, family friends, and neighbors) that includes persons from regions of the world with a high prevalence of tuberculosis regardless of their relationship to the child.

The increase in tuberculosis among children in San Diego County coincided with similar increases in immigration into California. After the Immigration Reform and Control Act of 1986, the number of immigrants into California increased by 334% from 168 790 in 1986 to a peak of 732 735 in 1991.[13] The Immigration Reform and Control Act provided for immigration of undocumented aliens who had been resident in the United States since 1982 and for seasonal agricultural workers who had been resident during 1985 through 1986. Children younger than 15 years are not required to be screened for tuberculosis during immigration unless known to be contacts to a tuberculosis case. Each year, >3 million nonimmigrant visitors also come to California, but their contribution to transmission would be difficult to document.[13] Nearly half of children younger than 5 years were known to have traveled to visit family in Mexico, suggesting that cross-border contact may have also contributed to transmission in addition to immigration into the United States. Since 1993, tuberculosis cases in children have decreased nationwide. This is also true for San Diego County in which cases decreased from 75 cases in 1993 to 45 cases in 1997. The largest decrease occurred in those children younger than 5 years in which there was a 70% decrease in the number of cases between 1993 and 1997.

Health department investigation of children with tuberculosis in San Diego County demonstrated that they came from a household environment in which nearly 70% of contacts had evidence of tuberculous infection. This was particularly true if the child, parent, or source case was foreign-born. Identification and investigation of these tuberculosis households should be an effective strategy for case finding and identification of potential candidates for preventive therapy. However, the challenges to investigations of tuberculosis on the border by the health department were demonstrated by the relatively low proportion (8.8%) of tuberculosis cases in children identified as a result of contact investigation, the low proportion (14.5%) of cases in whom a source case was identified, and the high proportion (35.7%) of instances in which the child with tuberculosis was identified before the source case was diagnosed as having tuberculosis. To help improve tuberculosis control in the United States, cross-border cooperation and collaboration toward tuberculosis control should continue to be promoted and encouraged by public health officials in neighboring communities on both sides of the United States-Mexico border.

The level of primary drug resistance (27.5%) in the cases among children in this investigation may be the highest reported to date in children in the United States.[1] The level of drug resistance among the source cases (33.3%) is equally alarming. The children and their source cases with drug-resistant tuberculosis diagnosed in the United States were linked with countries in which tuberculosis is highly endemic and levels of drug-resistance are high, demonstrating the importance of global control of drug-resistant tuberculosis to the control of drug-resistant tuberculosis in the United States.[14] Moreover, 16% of children with a positive culture had *M bovis*, which is uniformly resistant to pyrazinamide and has different public health and clinical implications. The presence of extrapulmonary disease in the Hispanic or foreign-born child should prompt the clinician to collect appropriate specimens to recover an organism. Clinical specimens, eg, gastric aspirates or lymph node biopsy, for culture and drug susceptibility testing should be collected routinely from children, particularly when the drug susceptibility results of the isolate from the source case are unknown. Ongoing surveillance for drug resistance among young children should help define trends in recent transmission of drug-resistant organisms in a population, as well as optimizing effective therapy for the child.

This study had several limitations. The extent to which improved tuberculosis surveillance may have contributed to increased case detection cannot be determined, but this may have been a factor as evidenced by the increase in the proportion of cases lacking bacteriologic confirmation from 1989 to 1993. Also, our methodology using medical record review limited the ability to assess potential missed opportunities to prevent tuberculosis in children. The number of children who had not been screened by a TST during well-child care is probably particularly underestimated, because the location of all well-child records was often unknown and it was clear that many parents sought care for their children on both sides of the border. Nonetheless, the majority of cases of tuberculosis in children were potentially preventable through current control measures except for the cases among children who became ill or acquired tuberculosis in an endemic country and who first presented to health authorities in the United States with active disease. Our methodology also probably underestimated the magnitude of contacts between cases in the United States and foreign-born individuals because of a lack of complete information about parents' country of birth, their travel to endemic countries, and visits from individuals who live in endemic countries. Such information could help communities to understand local dynamics of transmission and to develop strategies for improvement. Finally, the role of HIV in tuberculosis in San Diego County could not be assessed because of the lack of information concerning both the children and the source cases.

Control of tuberculosis in children on the United States-Mexico border will depend on improved control within Mexico and screening of adult immigrants who may transmit *M tuberculosis* to young

children. Recommended screening of children who have immigrated recently from endemic countries and of children who have traveled to endemic countries or have household contacts from endemic countries may help increase detection of tuberculosis in children and identify potential candidates for preventive therapy in the United States.[11]

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