

Preventable Childhood Tuberculosis in Alabama: Implications and Opportunity

Michael E. Kimerling, MD, MPH*||; Jill T. Barker, MS‡; Frank Bruce, BS||; Nancy L. Brook, MPH||; and Nancy E. Dunlap, MD, PhD§||

ABSTRACT. Childhood tuberculosis (TB) cases indicate recent community transmission and thus reflect the effectiveness of TB control efforts, particularly the contact investigation.

Objective. To evaluate all preventable childhood TB cases and implications in the context of TB morbidity trends.

Design. Statewide morbidity trends are presented from 1983 to 1997. Since 1992, each child TB case is classified as either preventable or not preventable, based on a standard definition.

Main Outcome Measures. Case characteristics (preventable and not preventable), TB disease rates over time, and reasons for preventable case classification.

Setting. Alabama TB control program, from January 1, 1983 through December 31, 1997.

Results. For the period 1983–1997, nonwhite children had a higher disease rate (rate ratio: 5.7; 95% confidence interval: 4.3,7.6) than white children. Since 1990, the overall child rate has increased significantly despite a decline in the adult rate. Among 120 child cases diagnosed from 1992 to 1997, 25 (21%) were classified as preventable. The causes were contact investigation interview failure (12/25 = 48%), delay to evaluation (16%), source case non-compliance with previously prescribed preventive therapy (16%), and source case diagnosed out of state (16%) with no initial investigation performed in Alabama. All preventable cases identified were black children; the proportion of preventable cases did not vary by age group or sex. During 1996, the case rate for nonwhite children exceeded that of adult whites.

Conclusions. Childhood TB in Alabama for nonwhites is rising despite a national downward trend. TB is clearly a disproportionate disease burden for the state's African American population, and the median case age is falling. Additional research and improved training in contact investigation are required to assess this situation and effectively intervene. *Pediatrics* 2000;105(4). URL: <http://www.pediatrics.org/cgi/content/full/105/4/e53>; children, tuberculosis, preventability, contact investigation.

ABBREVIATIONS. TB, tuberculosis; PPD, purified protein derivative.

From the *Division of General Internal Medicine, ‡Comprehensive Cancer Center Biostatistics Unit, and §Division of Pulmonary and Critical Care Medicine, Birmingham, Alabama; Department of Medicine, University of Alabama at Birmingham, and the ||Tuberculosis Control Unit of the Alabama Department of Public Health, Montgomery, Alabama. Received for publication Sep 28, 1999; accepted Nov 29, 1999. Reprint requests to (M.E.K.) RPHB 217, 1530 3rd Ave S, Birmingham, AL 35294-0022. E-mail: kimerlin@uab.edu PEDIATRICS (ISSN 0031 4005). Copyright © 2000 by the American Academy of Pediatrics.

Childhood tuberculosis (TB) cases are a key indicator and measure of recent community transmission. Because transmission normally occurs from adult to child, each child case provides a window by which to observe the effectiveness of the contact investigation surrounding an index or source case. As such, evaluation of childhood TB rates provides the opportunity to assess a core component of any TB control program.

In a previous study, we evaluated the epidemiology of childhood TB in Alabama over an 11-year period (1983–1993).¹ Although the overall statewide case rate fell consistently from year to year, the childhood rate did not. We concluded that the reason for this discrepancy was related to microepidemics or clustering of childhood cases that were scattered and unpredictable over time and place. After developing a preventable child case definition in recognition that such cases are occurring, we classified 19% of cases as preventable over the 2-year period (1992–1993). Subsequently, the Alabama State Department of Public Health has been applying a standard definition of preventable versus not preventable for every child case. We present the findings over the 6-year period, 1992–1997, in the context of changing morbidity patterns. The implications for the statewide TB control program are discussed and call attention to efforts needed to improve program performance with the goal of eliminating childhood TB.

METHODS

Data Collection

Statewide data collection methods, calculation of case rates, and definition of a positive Mantoux skin test (purified protein derivative [PPD]) have been previously described.¹ Case rates per 100 000 population were calculated for the 15-year period (1983–1997). Statewide case data were obtained from the Alabama State TB Control Unit. Population estimates were provided by the Alabama State Data Center at the University of Alabama with revised Bureau of the Census estimates for 1983–1989. Projected population figures were used for 1991–1997, based on the corrected 1990 modified age, race, and sex census data.

A child case <15 years old is determined by either clinical (positive PPD, abnormal chest radiograph, or response to multiple drug anti-TB therapy) or laboratory criteria (isolation of *Mycobacterium tuberculosis* from a clinical specimen or demonstration of acid-fast bacilli when culture cannot be performed).² Once a TB suspect or case is identified, a list of close contacts is developed by the public health staff and investigated for infection with or without disease. A chief goal of this investigation is to determine the source case, which represents the source of infection to a new child case. These efforts, performed within 30 days of case notification, identified 67% of the source cases during the study. Preventive therapy is given to all child contacts with an initial positive skin

test result (5 mm or more); it is also given to those with an initial negative skin test result until a second PPD test is placed and evaluated 10 to 12 weeks later. A state-contracted TB physician reads all chest radiographs and conducts periodic reviews to determine response to multidrug therapy.

Definition of a Preventable Childhood TB Case

The following definitions were approved by the Alabama State TB Medical Advisory Council: preventable case—a child who develops disease in the context of 1) an interview failure (evaluated 30 days or more after the initial interview of the source case), or 2) inadequate preventive therapy given to the child, or 3) contact with a known infected person who had been offered and refused preventive therapy who subsequently develops disease within 2 years. Additionally, an interview failure is further categorized as either a) a child who was never named as a contact by a previously investigated source case, or b) a delay of 30 days or more occurred before evaluation of a child contact was made. Not preventable case—a child with no known previous exposure to TB who 1) is found to be infected with disease on the initial contact investigation of an index case, or 2) becomes ill and is found to be infected with disease. Each classification is initially determined by the Public Health Area TB control manager and reviewed by the central program office in Montgomery. A final review is made by the study staff, including consultation with the Public Health Area manager if there is conflicting or missing information.

Data Analysis

All data entered into computer were analyzed using the software packages EpiInfo 6.0 (Centers for Disease Control and Prevention, public domain) and SAS (SAS Institute, Cary, NC). The relationships between TB classification (preventable vs not preventable) and independent predictors (age group, race, sex, and time period) were examined by Fisher's exact test (2-tailed) and multiple logistic regression. Trend lines for TB case rates from 1983 to 1997 were fit using Poisson regression with time in years as the independent predictor and the log (rate) as the dependent variable. Using 1990 as the midpoint, additional trend lines for the latter period (1990–1997) were determined to evaluate more recent

program data. Associations between variables and child TB rates were tested with Poisson regression for all years. All statistical analyses were performed with Proc Logistic and Proc Genmod in SAS 6.12. An $\alpha < .05$ was considered statistically significant. Two-sided 95% confidence intervals were calculated for all odds ratio and rate ratio estimates.

RESULTS

Morbidity Trends Over Time, 1983–1997

Since 1983, the statewide TB case rates (per 100 000 population) for adults and children show different trends. Although the adult rate shows a significant decline from 17.0 to 11.25 ($P = .0001$), the child rate shows a nonsignificant increase (.77–1.7; $P = .15$). However, since 1990, the upward trend among children shows less variation by year and is significantly increased ($P = .003$) despite continued downward trends in the overall (all ages) and adult rates ($P = .0001$). There was no change in the proportion of culture-determined cases during this time frame for either adults or children. Figure 1 presents Alabama case rates by race for both adults and children. Despite significant rate declines for adults since 1983 ($P = .0001$), the wide difference in case rates for adult nonwhites and adult whites is evident. Of note, the case rate for nonwhite children exceeded that of adult whites during 1996. Since 1990, there has been a significant increase in the case rate for nonwhite children, accounting for the overall child rate increase noted above.

Table 1 gives child patient characteristics with associated risks of TB disease since 1983. During the study, no Hispanic child was diagnosed and only 7

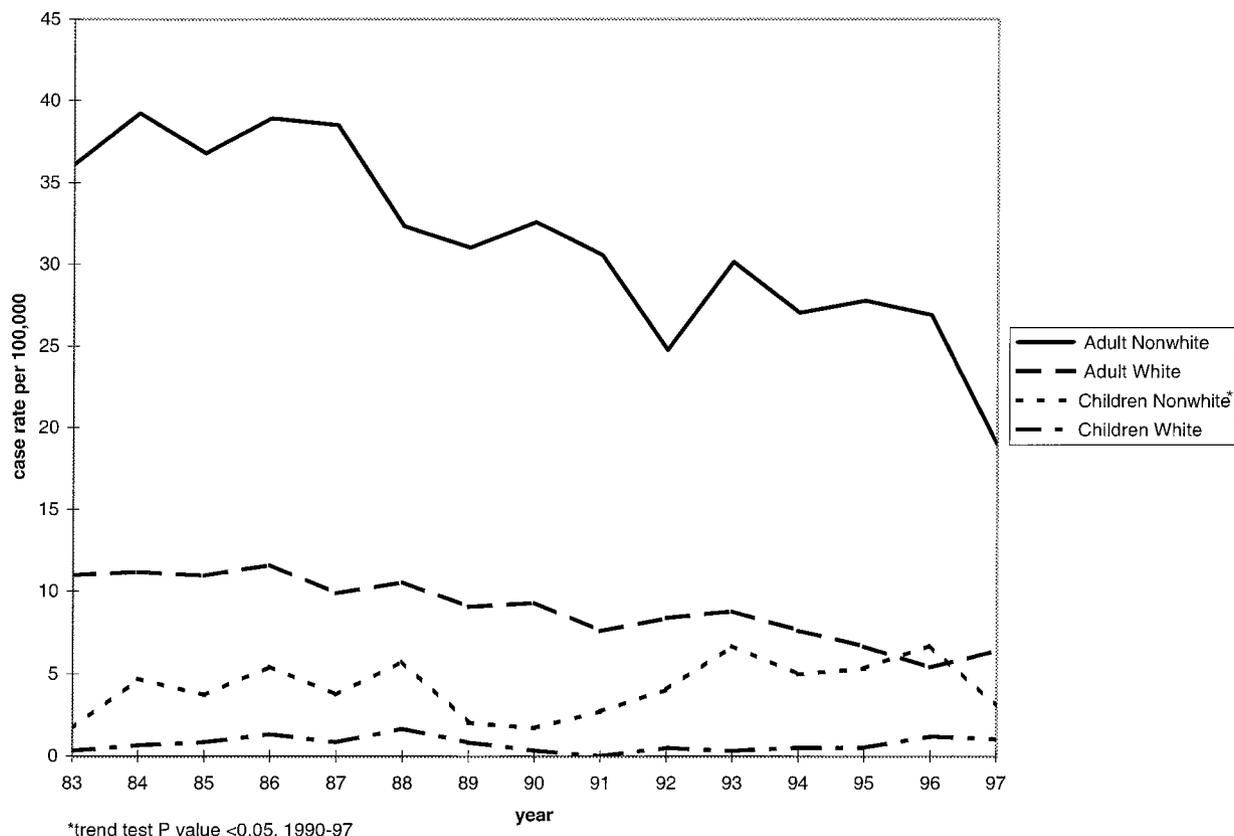


Fig 1. Alabama TB case rates for adults and children according to race, 1983–1997.

TABLE 1. Patient Characteristics and Associated Risk of TB Disease, 1983–1997 (*n* = 250)

Factor	Number of Cases	Case Rate*	Rate Ratio†	95% Confidence Interval	<i>P</i> Value
Age‡					
0–4 y	149 (60)	3.4	3.01	2.3, 3.9	<.001
5–14 y	101 (40)	1.1	1.0		
Race					
White	65 (26)	.7	1.0		
Black	178 (71)	4.2	5.7	4.3, 7.6	<.001
Asian-Pacific Islander	7 (03)				
Sex					
Male	124 (50)	1.8	1.0		
Female	126 (50)	1.9	1.0	.8, 1.3	.7

* Case rates per 100 000 population.

† Adjusted rate ratio and 95% confidence interval estimates are from multiple Poisson regression analysis (black race and Asian-Pacific Islander are combined as nonwhite race for rate calculation).

‡ Numbers in parentheses are percentages.

Asian children were found. Young age (0–4 years old) and black race were associated with disease ($P < .001$), whereas sex was not ($P = .7$). Figure 2 shows the Alabama median case age by race and sex starting from 1990. The median age for blacks, male and female, is less than that for whites.

Preventable Versus Not Preventable Cases, 1992–1997

There were 120 child cases 0 to 14 years old diagnosed from 1992 to 1997. Among these, 25 (21%) were classified as preventable. Table 2 presents case characteristics according to their preventable status.

All preventable cases found were black children. Neither sex nor age group was a significant factor.

The reason a case was considered preventable is given in Table 3 and compares it with other published reports. In the current study, interview failures were the most important reason identified (12/25 = 48%) followed by delay to evaluation of a child contact (16%), noncompliance of the source case with previously prescribed preventive therapy (16%), and source case diagnosed out of state (16%), ie, no contact investigation was conducted in Alabama.

DISCUSSION

National TB morbidity data show a 25% decline in reported childhood cases (age group: 0–14 years) from 1992 to 1997 for children born in the United States and a 29% decline for those born outside the country.⁶ This contrasts with a 20% increase in childhood TB over the same period in Alabama and comes despite a corresponding 4% decrease in reported adult cases. The recent rise in the childhood case rate since 1990 is highlighted by a longstanding gap in rates according to race (Table 1). Statewide, there has been a decline in disease rates for both the white and nonwhite populations (Fig 1), which reflects the impact of current disease control measures. Of greater significance, however, the case rate for nonwhite children surpassed that of white adults during 1996, a clear reflection of the substantially higher case rate for nonwhite adults (27.5/100 000 vs 6/100 000 for white adults). Thus, TB transmission to nonwhite children continues at a substantial rate,

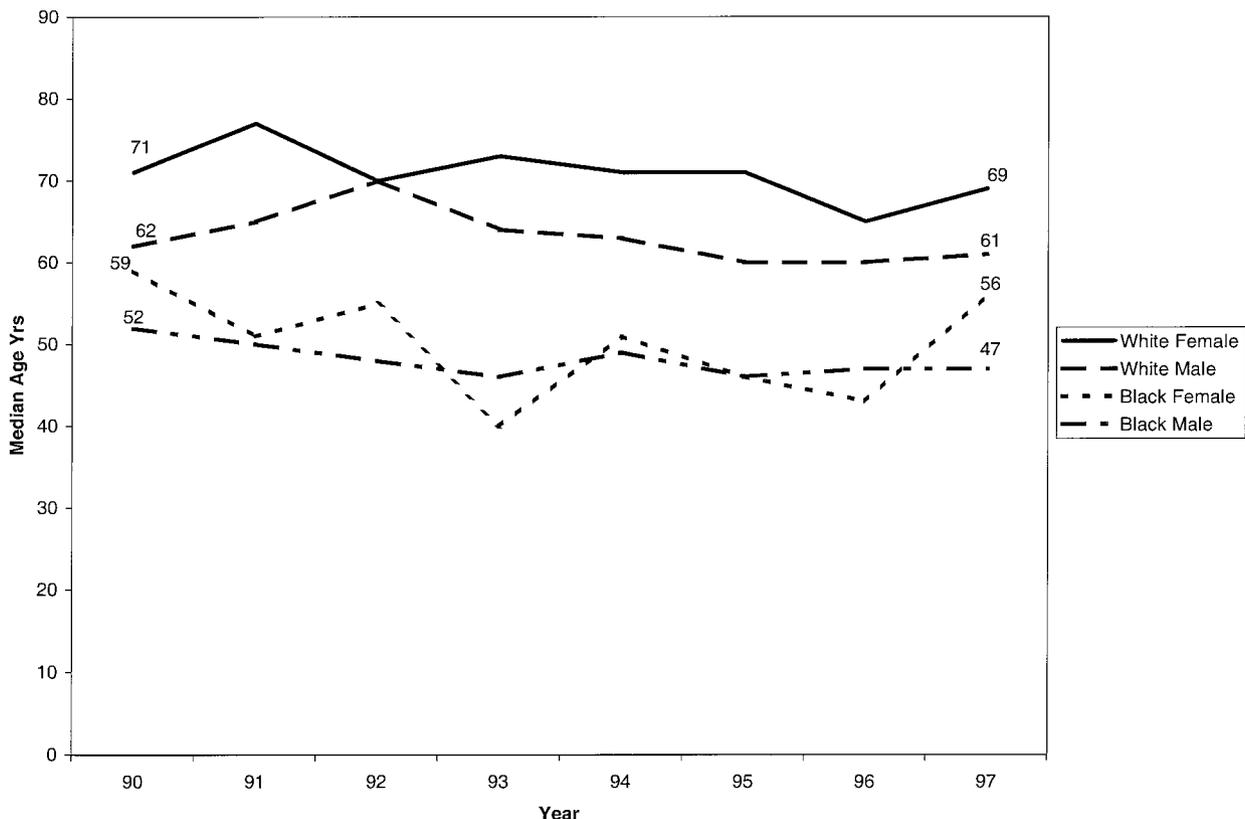


Fig 2. Median case age (in years) according to sex and race: Alabama, 1990–1997.

TABLE 2. Patient Characteristics and Associated Risk of Preventable Disease, 1992–1997 (*n* = 120)

Factor	Number of Cases Preventable	Number of Cases Not Preventable	Odds Ratio†	95% Confidence Interval	<i>P</i> Value
Age					
0–4 y	14	55	2.01	.50, 8.00	.32
5–9 y	8	19	3.37	.77, 15.1	.11
10–14 y	3	21	1.0		
Sex					
Male	13	54	1.0		
Females	12	41	1.4	.5, 3.6	.44
Race					
White	0	25	1.0		
Black	25	65	*		
Asian	0	5	*		

* Odds ratio could not be computed because of zero cells.

† Adjusted odds ratio and 95% confidence intervals estimates are from multiple logistic regression analysis (black race and Asian-Pacific Islander are combined as nonwhite race).

TABLE 3. Preventable Childhood TB Cases by Reason for Designation in Four Sites: Alabama, Tennessee, Houston (Texas), and North Carolina^{3–5}

Study Site (Years and Total Number of TB Cases)	Preventable TB Cases <i>n</i> (%)	Interview Failure (Not Named)	Delay (≥30 Days)	Inadequate or No PT Given	SC Noncompliant With PT	SC Out-of-State	Other
1. Alabama (1992–1997; <i>n</i> = 120)	25 (21)	12	4	1	4	4	
2. Tennessee (1981–1988; <i>n</i> = 109)	23 (21)	3	7	11			2
3. Houston* (1985–1987; <i>n</i> = 139)	35 (25)		24	3	9†		6
4. North Carolina (1977–1981; <i>n</i> = 99)	26 (26)			15			11‡

PT indicates preventive therapy; SC, source case.

* More than 1 factor was recorded for some cases.

† Represents previous SC treatment (multidrug) failure with disease relapse. Directly observed therapy was not used.

‡ According to the study's authors, this finding most likely represents failure by children to comply with PT as directly observed PT for a PPD-positive child contact was not practiced.

and the control of TB disease in this group is less effective.

One issue in the undiminished child TB rates, despite overall declines among adults, is the decreasing median age among adult cases in Alabama. These age declines are more pronounced among African American adults, who also show an overall lower median age compared with whites (Fig 2). The increasing concentration of TB among younger adult groups and other caregivers of children may well impact transmission of TB to children.

Our determination of 21% preventable childhood TB cases over a 6-year period is consistent with our previous finding of 19% from 1992 to 1993.¹ This percentage is also similar to the available data reported by programs in North Carolina, Tennessee, and Houston, Texas.^{3–5} With the exception of the Houston data, however, results from the other programs largely predate the national upsurge of TB cases during the late 1980s and early 1990s. Furthermore, many of those cases deemed preventable resulted from not giving preventive therapy to exposed children as jointly recommended by the Centers for Disease Control and Prevention, American Thoracic Society, and American Academy of Pediatrics.⁷ In contrast, the Houston data underscore the problem of delay in initiating a contact investigation (median delay: 3 months). Although this problem accounted for 16% of preventable cases in Alabama, the overwhelming majority (48%) of preventable cases in our setting resulted from interview failures where child contacts were not named by

index cases and consequently not investigated. If children are not named, then preventive therapy cannot be given.

The failure of the interview process is a primary concern that clearly demands additional study and improved training of TB field staff to obtain the names of all potential child contacts to active cases. However, the finding that all preventable cases occurred in African American children raises important questions. Are contact interview failures attributable to natural limits of the investigative approach or to barriers of race or social and economic situation? Although all state TB field workers are similarly trained and follow standard contact interview procedures, the willingness of an index case to reveal names can be affected by a desire to keep personal relationships and interactions private. We have linked several preventable child cases to such situations previously.¹ Interview failure may also reflect an unwillingness to acknowledge the social complexity within certain households to representatives of a state health bureaucracy. In other instances, it may truly result from insufficient understanding on the part of a household that a very young child can be a significant contact to a case, even if direct contact is limited or irregular. It is unlikely, however, that the observed interview failures represent a simple issue of concordance/discordance between investigator and index case race, because field workers are well mixed racially. Social and economic differences are a likely barrier in the naming of contacts, reflective of the difficulties encountered regarding adherence to

referral and preventive therapy despite the use of peer counselors or community workers to improve communication.⁸⁻¹⁰

Our findings raise additional issues for consideration that move beyond the contact investigation process, reflecting weaknesses in the operational system of TB control. One such systems issue that we found involves inadequate communication between state health departments so that contact investigations around index/source cases diagnosed and treated in other states can be readily initiated in all appropriate locations. This problem accounted for an additional 16% of preventable cases, involved 3 states, and represents a second type of delay. It may well represent a primary interview failure in the other location.

The failure of infected adults to take previously prescribed preventive therapy is also associated with childhood cases. Such a failure by an adult contact to an active case, who subsequently develops disease and passes it to a child, was found in 16% of preventable cases. This operational problem is more difficult to address. Specifically, it raises the issue of providing directly observed preventive therapy to high-risk adults with recognized exposure to young children. The targeting of such adult contacts and the resources required would present a challenge to health departments, especially in the current period of fiscal pressures and competing priorities.

Active childhood TB cases represent only a fraction of all children infected with the *M tuberculosis* organism, the latter representing an important reservoir for future cases. To resolve the program inefficiencies documented by others and us requires attention on a broad scale. Through enhanced identification of child contacts coupled with a significant reduction in preventable child cases, the epidemiology of TB in Alabama would be positively impacted over time. Nationally, however, childhood cases overlap with certain factors that increasingly define the national TB morbidity picture, such as immigration⁶ (39% of all new cases diagnosed in the United States during 1997 were in foreign-born persons) and risk groups with ongoing transmission. Among the latter are the homeless, intravenous drug abusers, persons with human immunodeficiency disease, and those from a lower socioeconomic status population.¹¹⁻¹⁶

Unique to our present study is its continued collection, evaluation, and use by the Alabama State Department of Public Health as well as its expanded time frame and assessment by demographic characteristics. Because the absolute numbers of child TB cases and preventable cases remain relatively small in Alabama, it is not surprising that a correlation between the 2 was not found when analyzed by year.

However, the finding of significant differences according to race is important and reflects the disproportionate burden of disease in the state's African American population. Additional investigation is necessary to untangle the involved issues and probable reasons. Nonetheless, future progress toward realizing the goal of TB elimination will ultimately depend on the efficiency and effectiveness of the contact investigation process with careful targeting of high-risk groups.

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As it is for all our tuberculosis-related studies, we are deeply indebted to the Alabama TB control field staff and area managers for maintaining a statewide program with the single goal of improving its effectiveness. The open and frequent interactions involved are truly a driving force in this process.

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