Case Characteristics and Trends in Pediatric Tuberculosis, Maryland, 1986–1993

C. Patrick Chaulk, MD MPH
Lynn Khoo, MD MPH
Diane L. Matuszak, MD MPH
Ebenezar Israel, MD MPH

Dr. Chaulk is the Senior Associate for Health with the Annie E. Casey Foundation; an Assistant Professor in the Division of Infectious Diseases, Johns Hopkins School of Medicine; Associate Faculty in the Department of Health Policy and Management, Johns Hopkins School of Public Health; and a Clinical Pediatrician with the Baltimore City Health Department Chest Clinic. Dr. Khoo, Dr. Matuszak, and Dr. Israel are with the Division of Tuberculosis Control, Maryland Department of Health and Mental Hygiene; Dr. Khoo is an Epidemiologist, Dr. Matuszak is the Deputy Director of Community Health Surveillance, and Dr. Israel is the Director of the Epidemiology and Disease Control Program.

Address correspondence to Dr. Chaulk, Annie E. Casey Foundation, 701 St. Paul St., Baltimore MD 21202; tel. 410-223-2980; fax 410-223-2983; e-mail <patc@aecf.org>.

SYNOPSIS

Objective. To identify case characteristics and trends in the incidence of pediatric tuberculosis (TB) in Maryland during the national resurgence of the disease.

Methods. The authors conducted a retrospective review of the 248 cases of TB in children ages 19 and younger reported to the state registry between 1986 and 1993.

Results. The incidence of pediatric TB in Maryland, while showing a downward trend between 1986 and 1993, was characterized by a bimodal pattern, with one peak in children younger than age 5 and another peak in adolescents. Certain case characteristics differed significantly according to age: adolescents with TB were more likely to have positive AFB smears, positive cultures, and cavitary X-rays than children in the 0–4 age group. On the other hand, PPD results did not differ significantly by age. Children with TB came from households in zip code areas for which the median family income was lower and the rate of unemployment was higher than comparable statewide figures.

Conclusions. Study findings indicate that *(a)* the general decline in adult TB in Maryland was accompanied by a decline among children; *(b)* age-specific case characteristics continue to be useful in clinical decision making for children with suspected TB; and *(c)* a state TB registry may prove useful not only in tracking disease trends and monitoring statewide control efforts but also in confirming case characteristics, all of which are important disease control issues in a time of fiscal downsizing.

The United States has experienced a resurgence of tuberculosis (TB) not only among adults but also among children and adolescents. After declining nearly 6% a year between 1962 and 1985, the number of reported TB cases in people ages 19 and younger increased 32.9% nationwide between 1985 and 1992.[1–4] In recent years, only a few large case studies of pediatric TB in the United States have been published. Their generalizability, however, may be limited because they were based on data collected prior to the national TB resurgence.[1,5,6] In addition, these studies did not look at comparable populations: one excluded adolescents older than age 15,[1] and one excluded young children.[6]

Pediatric TB presents unique challenges in terms of diagnosis, taxonomy, and therapeutic options.[7] The difficulty of obtaining timely and adequate specimens for bacteriologic confirmation, especially from infants and young children, is well documented.[8] Thus the diagnosis of pediatric TB, in contrast to that of adult TB, continues to rely on epidemiology and case characteristics.[9] For example, among all TB cases diagnosed in patients younger than age 15 and reported to the Centers for Disease Control and Prevention in 1985, only 25% were diagnosed through positive cultures and only 3% through positive smears, while diagnoses were established in 67% of the cases through a combination of case characteristics such as positive tuberculin skin test, abnormal chest X-ray, and history of exposure to an infected person. In the remaining cases the diagnosis was established through other tissue histology. Conversely, among adults a diagnosis is typically established bacteriologically based on sputum specimens.

In the absence of bacteriologic confirmation, a working diagnosis of pediatric TB requires at least two of the following: a positive tuberculin skin test, suggestive chest X-ray findings, clinical symptoms, history of exposure to an active case, and clinical improvement following initiation of recommended anti-TB therapy. Variations of this definition are widely used in developing countries where limited resources do not permit more technologically based diagnostic evaluations.[10–14]

We reviewed 248 cases of pediatric TB reported in Maryland between 1986 and 1993 to examine incidence trends and age-related TB case characteristics among children and adolescents during the nationwide TB resurgence.

Methods

The authors reviewed the records of all TB cases reported by providers, hospitals, and diagnostic laboratories to the Maryland Department of Health and Mental Hygiene's Division of Tuberculosis Control (DTC) for the years 1986 through 1993. Each case was reviewed and verified by DTC through telephone contact with the reporting source.

We extracted from the DTC's case registry all TB records for Maryland children ages 19 and younger for 1986–1993, yielding a total of 248 verified pediatric cases (6.5% of all TB cases reported in Maryland during this period). Each case record was reviewed for the following characteristics: demographic data (age, ethnicity, gender, and patient's zip code); bacteriologic and other diagnostic findings (smear, culture, tuberculin skin test, and chest X-ray results); reported type of infection; and drug treatment regimen. The TB registry does not contain verified information on household investigations for additional cases or history of prior treatment for TB.

Patients were stratified into four roughly equal age bands—preschool (ages 0–4), primary school (ages 5–9), junior high school (ages 10–14) and senior high school (ages 15–19), and case characteristics were compared across groups. In addition, we used 1990 U.S. Census figures for median family income and unemployment rate by zip code as a proxy measure of socioeconomic status. Dichotomous variables were analyzed using chi-square and trend analyses.[15]

Results

Between 1986 and 1993, the number of pediatric TB cases in Maryland declined by 2%. Approximately two-thirds of reported cases were from three predominately metropolitan areas, Montgomery and Prince Georges counties (45.3%) and Baltimore City (21.5%).

The age distribution reveals a bimodal pattern, with the highest case rate (3.7 per 100,000 population) occurring among children in the 0–4 age group and the next highest rate in the 15–19 group (1.9 per 100,000) (Table 1). Overall, the median age was five years.

Fifty-two percent of the cases were identified as males, 48% as females. In each successive age group, females constituted a progressively larger proportion of all cases ($P<0.01$).

Most patients were non-white (66.9%), with non-white children comprising a progressively larger proportion of cases in each successive age band ($P<0.001$) (Table 1).

For cases, the overall average of median family incomes by zip code area was $17,225, and the average unemployment rate was 5.2%. Comparable statewide figures for Maryland in 1990 were $17,730 for income and 4.3% for unemployment. The youngest patients (0–4 age group) were most likely to reside in zip code areas reporting the lowest average median family incomes ($16,493) and highest unemployment rates (5.5%) (see Figure).

The vast majority of children underwent tuberculin skin testing, with 78.2% reporting tuberculin reactions of 11 mm in diameter or greater. There were no statistically significant differences in tuberculin reactivity by age group (Table 2).

In 69.9% of all cases, chest X-rays were interpreted as abnormal; in 9.3% they were reported as cavitary (Table 2). Older age groups were progressively more likely to have their chest X-rays interpreted with cavitary findings ($P<0.0001$).

The two most common reported types of infection were pulmonary (75%) and lymphatic (18.1%) (Table 2). Six cases of miliary TB were reported in the 0–4 group; 13 were reported in the 15–19 group.

Smear or culture results were reported for approximately half of all cases (Table 3). The median age of patients with cultures was 12.2 years; for patients without cultures, the median age was 2.5 years. There were fewer positive smear results than positive culture results. Trend analysis revealed that the older the child, the more likely she or he was to have smears, to have culture studies performed, and to have positive results.

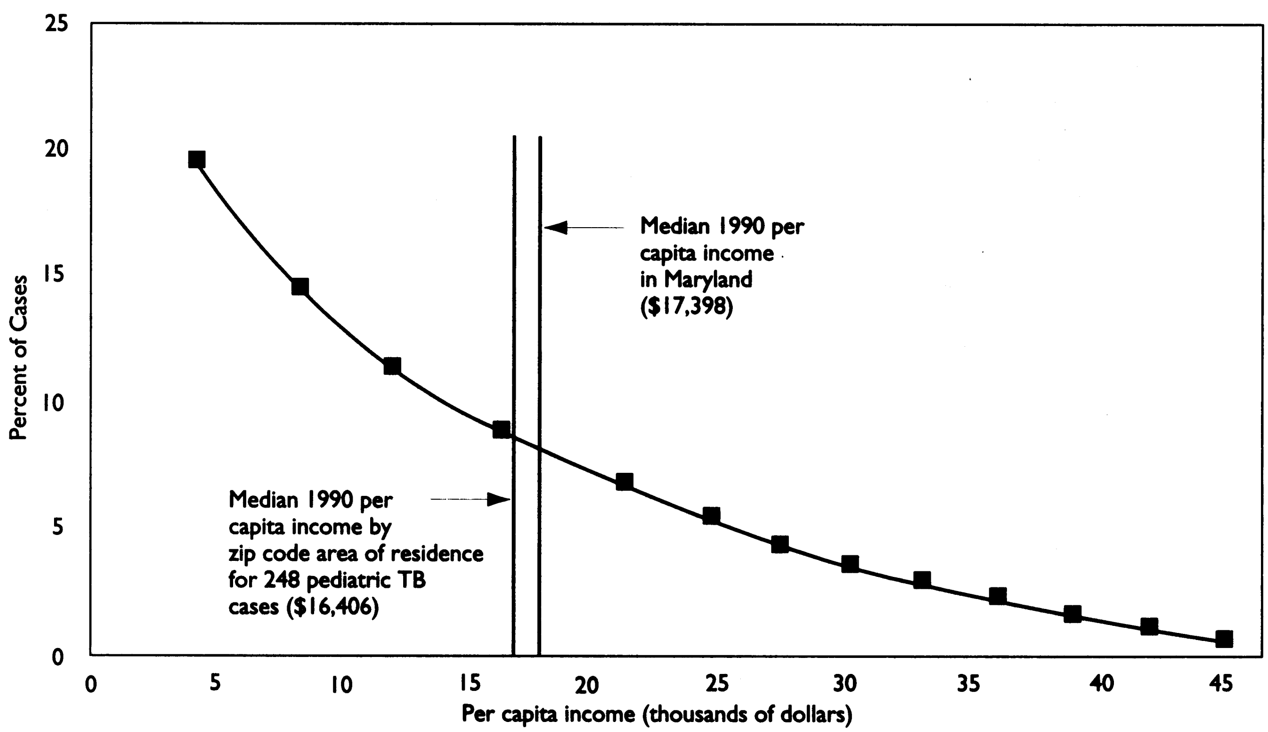
We compared the 59 culture-positive cases with the 69 culture-negative cases (Table 4). Patients with positive cultures included a higher proportion of girls than patients with negative cultures and on average were older (median

Table 1. Demographic characteristics of children and adolescents with tuberculosis, by age group, in Maryland, 1986–1993 (*N*=248)

	Age (years)							
	0–4 (n=107)		*5–9 (n=52)*		*10–14 (n=33)*		*15–19 (n=56)*	
Characteristic	*Number*	*Percent*	*Number*	*Percent*	*Number*	*Percent*	*Number*	*Percent*
Gender[a]								
Male	62	57.9	29	55.8	18	54.5	20	35.7
Female	45	42.1	23	44.2	15	45.5	36	64.3
Ethnicity[b]								
White	39	36.4	17	32.7	12	36.4	6	10.7
Black	44	41.1	12	23.1	10	30.3	20	35.7
Hispanic	8	7.5	9	17.3	2	6.1	15	26.7
Asian	9	8.4	6	11.5	5	15.2	10	17.8
Other	5	4.7	8	15.4	4	12.1	5	8.9
Missing	2	1.9	0	...	0	...	0	...
Group mean age (years)	2.3		6.6		12.2		17.3	

NOTE: Percentages may not total 100 due to rounding errors.
[a]Significantly more likely to be female with increasing age ($P<0.01$).
[b]Significantly more likely to be non-white with increasing age ($P<0.001$).
SOURCE: Maryland Department of Health and Mental Health, Division of Disease Control, 1994

Regression of percent of pediatric tuberculosis cases on per capita income by zip code area of residence, Maryland, 1986–1993 (*N*=248)



SOURCES: Epidemiology and Disease Control Program, Maryland Department of Health and Mental Hygiene, and U.S. Census data

Table 2. Clinical characteristics of pediatric tuberculosis cases, by patient age group, Maryland, 1986–1993 (*N*=248)

	Age (years)							
	0–4		5–9		10–14		15–19	
Characteristic	*Number*	*Percent*	*Number*	*Percent*	*Number*	*Percent*	*Number*	*Percent*
Purified protein derivative (mm)								
0–5	10	9.3	4	7.7	2	6.1	4	7.1
6–10	3	2.9	3	5.8	0	0	0	0
11 or more	89	83.2	38	73.1	24	72.7	43	76.8
Not done	5	4.7	3	5.8	3	9.1	7	12.5
Missing	0	0	4	7.7	4	12.1	2	3.6
Chest X-ray[a]								
Normal	19	17.8	8	15.4	7	21.2	7	12.5
Abnormal non-cavitary	77	71.9	41	78.8	22	66.7	33	58.9
Abnormal cavitary	6	5.6	1	1.9	3	9.0	13	23.2
Not done	1	1.0	0	0	0	0	1	1.8
Missing	4	3.7	2	3.8	1	3.0	2	3.6
Infection type								
Pulmonary	78	72.9	38	73.8	22	66.7	48	85.7
Lymphatic	23	21.4	9	16.7	7	21.2	6	10.7
Bone	1	0.9	1	2.4	3	9.1	0	0
Miliary	3	2.8	1	2.4	0	0	0	0
Central nervous system	0	0	1	2.4	0	0	1	1.8
Lymph node	1	0.9	1	2.4	0	0	0	0
Genito-urinary	0	0	0	0	1	3.1	1	1.8
Missing	1	0.9	1	2.4	0	0	0	0

NOTE: Percentages may not total 100 due to rounding errors.
[a]Chest X-ray significantly more likely to be cavitary with increasing age ($P<0.0001$).
SOURCE: Maryland Department of Health and Mental Hygiene, Division of Disease Control, 1994

age 15 years versus 7 years). Those with positive cultures were more likely to have cavitary radiographs and significantly more likely to be smear-positive ($P<0.0001$ for each).

Considerably more than half of all those for whom treatment regimens were reported received treatment with either three or four drugs, and patients with positive cultures were most likely to receive three or four drugs (Tables 3 and 4). Only two patients received single drug therapy (isoniazid).

Discussion

Although the incidence of pediatric TB has increased dramatically nationwide since 1985, the incidence in Maryland declined 2% between 1986 and 1993, parallelling a decline among Maryland adults (Unpublished data, DTC, 1993). For example, in Baltimore, the state's largest city, the incidence of TB declined 29.5%, which contrasts with an average increase of 33.3% among the 20 largest U.S. cities in that same period.[16,17] This reaffirms the long-held assumption that controlling adult TB is an effective strategy to reduce the incidence of TB among children.

This bimodal age distribution, with a rising tail in late adolescence, confirms the need to continue TB surveillance of children up to age 19. Recent annual TB reports from the U.S. Centers for Disease Control (CDC) combine adolescents with young adults in a 15-to-24-year-old category.[18,19] Since adolescent health status is increasingly associated with a variety of significant health risks complicated by high rates of uninsurance,[20] low rates of access to primary care providers,[21,22] and high risk of HIV infection,[22,23] it will be important to continue TB surveillance of this age group.

Our study confirms that pediatric TB case characteristics differ by age, especially when children are compared with adolescents. We found that specimen cultures and AFB smears were significantly less likely to be positive among infants and children. Since AFB staining of specimens is the standard screening tool for TB control, the low number of positive smears among young children may compromise early case detection. Moreover, among all cases, smears when available were nearly twice as likely as cultures to be negative, again complicating early case identification.

Overall, cavitary lesions were rare (9.3%), especially among infants and young children, with most chest X-rays reported as abnormal (noncavitary). The vast majority of patients had tuberculin reactions of at least 11 mm.

Our findings are consistent with those of the CDC study conducted nearly 10 years ago.[1] The median age of

Table 3. Diagnosis and treatment of children and adolescents with pediatric tuberculosis, by age group, Maryland, 1986–1993 (*N*=248)

	Age (years)							
	0–4		*5–9*		*10–14*		*15–19*	
Characteristic	*Number*	*Percent*	*Number*	*Percent*	*Number*	*Percent*	*Number*	*Percent*
Smear[a]								
Positive	8	7.5	8	15.4	1	3.0	23	41.1
Negative	27	25.2	18	34.6	24	72.7	20	35.7
Not done	36	33.6	12	23.1	4	12.1	5	8.9
Unknown	36	33.6	14	26.9	4	12.1	5	8.9
Missing	0	0	0	0	0	0	1	5.4
Culture[b]								
Positive	11	10.3	9	17.3	13	39.4	27	48.2
Negative	26	24.3	13	25.0	14	42.4	16	28.6
Not done	34	31.8	10	19.2	1	3.0	6	10.7
Unknown	36	33.6	20	38.5	5	15.2	7	12.5
Missing	0	0	0	0	0	0	0	0
Drug therapy[c]								
IR plus 2 other drugs	4	3.7	4	7.7	3	9.0	16	28.6
IR plus 1 other drug	48	44.8	28	53.8	15	45.5	16	28.6
IR only	50	46.7	20	38.5	14	42.4	14	25.0
I only	1	0.9	0	0	0	0	1	1.8
Missing	4	3.7	0	0	1	3.0	9	16.1

NOTE: Percentages may not total 100 due to rounding errors.
[a]Smear significantly more likely to be positive with increasing age ($P<0.015$.
[b]Culture significantly more likely to be positive with increasing age ($P<0.001$).
[c]Treatment significantly more likely to involve three or four drugs with increasing age ($P<0.02$).
IR = Isoniazid with rifampin
I = Isoniazid
SOURCE: Maryland Department of Health and Mental Hygiene, Division of Disease Control, 1994

TB patients in that study was 3 years old. If the CDC study's upper cut-off of 15 years were applied to our data, the median age for our population would be 3.5 years. The distribution of types of infection in our study population closely parallels that of the population in the CDC study (pulmonary 75%, lymphatic 16.7%, meningeal 3.3%, pleural 1.4%, miliary 1.3%, bone/joint 1.0%).[1] The proportion of culture-positive cases in that study (25%) is also consistent with our findings (23.8%). Our proportion of smear-positive cases (16.1%), however, was some fivefold higher than in the CDC study (3%).

The use of case characteristics in diagnosing TB in children may be particularly important since, in addition to the other diagnostic challenges already described, the standard recommendation of serial morning gastric aspirations can be cumbersome, uncomfortable for the patient, and still result in poor yields. (Studies have reported proportions of culture-positive specimens ranging from 30% to 40%.)[24,25] Moreover, flexible bronchoscopy appears to produce results no better than gastric aspiration.[26] Nonetheless, establishing a bacteriologic diagnosis remains important since the highest proportion of pediatric cases is found among infants and very young children, who are particularly susceptible to aggressive TB and greater mortality.[27]

Our findings also serve as a reminder of the value of public disease surveillance registries for tracking disease trends and for identifying populations at risk and case characteristics. Other public health functions of particular significance to the control of pediatric TB include associate investigations to identify the adult source case (who can then undergo culture and sensitivity studies to rule out drug resistance) and household contact investigation of other children exposed to an adult case (to institute timely preventive therapy).

Since our data are drawn from a state registry, there are potential limitations to our findings. We did not have individual patient records for review; therefore, it is possible that some of the nonculture-confirmed cases may reflect overreporting. We chose the 1986–1993 time period because during this period all cases were followed up by the DTC with the reporting physician or hospital, which should have reduced this bias.

Our study is also limited from an epidemiologic standpoint since the DTC case registry does not contain complete information on other household cases to establish a more comprehensive transmission pattern to children.

Table 4. Comparison of 59 culture-positive and 69 culture-negative pediatric tuberculosis cases, Maryland, 1986–1993

Characteristic	Positive Number	Positive Percent	Negative Number	Negative Percent
Median age (years)	15		7	
Gender				
Male	24	40.7	39	56.5
Female	35	59.3	30	43.5
Ethnicity				
White	13	22.0	23	33.3
Black	20	33.9	25	36.2
Asian	12	20.3	8	11.6
Hispanic	6	10.2	5	7.2
Unknown	8	13.6	8	11.6
Chest X-ray				
Normal	8	14.3	12	17.4
Abnormal non-cavitary	38	67.9	48	69.6
Abnormal cavitary	10	17.9	5	7.2
Unknown or not done	3	...	4	5.7
Purified protein derivative size (mm)				
0–5	9	15.5	3	4.3
6–10	1	1.7	2	2.9
More than 10	31	53.4	60	87.0
Not done	16	27.6	3	4.3
Unknown	2	1.7	1	1.1
Smear results				
Positive	30	52.6	4	5.8
Negative	17	29.8	62	89.9
Not done	4	7.0	3	4.3
Unknown	8	10.5	0	0
Drug therapy				
IR plus 2 other drugs	14	23.7	11	15.9
IR plus 1 other drug	14	23.7	16	23.1
IR only	29	49.2	42	60.8
I only	2	3.4	0	0

NOTE: Percentages may not total 100 due to rounding errors.
[a]Smear was significantly more likely to be positive if culture was positive ($P<0.0001$).
IR = Isoniazid with rifampin
I = Isoniazid
SOURCE: Maryland Department of Health and Mental Hygiene, Division of Tuberculosis Control, 1994

Although new strategies to enhance the diagnosis of pediatric TB have been tested,[28,29] additional research must be directed toward more practical and effective diagnostic techniques applicable to children. This is particularly important in view of the national increase in multidrug-resistant TB; the absence of specimens for culture and drug sensitivity may jeopardize the proper management of pediatric cases.

This paper was presented in abstract form at the Pediatric Tuberculosis Conference sponsored by the Centers for Disease Control and Prevention and the American Lung Association, August 1, 1994. The authors are grateful to George Comstock, MD PhD, of the Johns Hopkins School of Hygiene and Public Health for reviewing an earlier version of the paper.

References

1. Snider DE, Rieder HL, Combs D, Bloch AB, Hayden CH, Smith MHD. Tuberculosis in children. Pediatr Infect Dis J 1988;7:271–270.
2. Starke JR, Jacobs RF, Jereb J. Resurgence of tuberculosis in children. J Pediatr 1992;120:839–855.
3. Amodio J, Abramson S, Berdon W. Primary pulmonary tuberculosis in infancy: a resurgent disease in the urban United States. Pediatr Radiol 1986;16:185–189.

4. Centers for Disease Control and Prevention [US]. Tuberculosis statistics in the United States. Atlanta: CDC; 1985–1992.
5. Smith ND. Tuberculosis in children and adolescents. Clin Chest Med 1989;10:381–395.
6. Nemir RC. Perspectives in adolescent tuberculosis: three decades of experience. Pediatrics 1986;78: 399–405.
7. Starke JR, Taylor-Watts KT. Tuberculosis in the pediatric population of Houston, Texas. Pediatrics 1989; 84:28–35.
8. Kibel MA. Problems in the diagnosis of childhood tuberculosis. S Afr Med J 1990;70:379–380.
9. Starke JR. Modern approach to the diagnosis and management of tuberculosis in children. Pediatr Clin North Am 1988;35:441–464.
10. Stegen G, Jones K, Kaplan P. Criteria for guidance in the diagnosis of tuberculosis. Pediatrics 1969;43: 260–263.
11. Ghidey Y, Habte D. Tuberculosis in childhood: an analysis of 412 cases. Ethiop Med J 1983;21:161–167.
12. Cundall DB. The diagnosis of pulmonary tuberculosis in malnourished Kenyan children. Trop Paediatr 1986; 6:249–255.
13. Stoltz DB, Donald PR, Strebel PM, Talent JMT. Criteria for the notification of childhood tuberculosis in a high-incidence areas of the Western Cape Province. S Afr Med J 1990;77:385–386.
14. Migliori GB, Rossanigo P, Adriko C, Neri M, Santini S, Bartoloni A, Paradisi F, Acocella G. Proposal of an improved score method for the diagnosis of pulmonary tuberculosis in childhood in developing countries. Tuber Lung Dis 1992;73:145–149.
15. Dean AG, Dean JR, Burton AH, Dicker RC. Epi-Info, Version 5: a word processing, database, and statistics program for epidemiology on microcomputers. Stone Mountain (GA): USD, Inc., 1990.
16. Chaulk CP, Chaisson R, Lewis JN, Rizzo RT. Treating multi-drug resistant tuberculosis: compliance and side effects. JAMA 1994;271:103–104.
17. Chaulk CP, Moore-Rice C, Rizzo T, Chaisson R. Eleven years of community-based directly observed therapy for tuberculosis. JAMA 1995;274:945–951.
18. Centers for Disease Control and Prevention [US]. Tuberculosis case rates by state: United States, 1993. Atlanta: CDC; 1994.
19. Centers for Disease Control and Prevention [US]. Tuberculosis case rates by state: United States, 1994. Atlanta: CDC; 1995.
20. Fossett J, Perloff J, Kletke P, Peterson J. Medicaid and access to child health care in Chicago. J Health Polit Policy Law 1992;17:273–298.
21. Starfield B. Primary care and health. JAMA 1991;266:2268–2271.
22. St. Louis ME, Conway GA, Hayman CR, Miller C, Petersen LR, Dondero TJ. Human immunodeficiency virus infection in disadvantaged adolescents: findings from the U.S. Job Corps. JAMA 1991;266:2387–2391.
23. D'Angelo LJ, Getson PR, Luban NLC, Gayle ND. Human immunodeficiency virus infection in urban adolescents: can we predict who is at risk? Pediatrics 1991;88:982–986.
24. Pierre C, Olivier C, Lecossier D, Boussougant Y, Yeni P, Hance AJ. Diagnosis of primary tuberculosis in children by amplification and detection of mycobacterial DNA. Rev Respir Dis 1993;147:420–424.
25. Lincoln EM, Harris LC, Bovornkitti S, Carretero RW. Endobronchial tuberculosis in children: a study of 156 patients. Rev Tub 1958;77:39–61.
26. deBlic J, Azevedo I, Burren CP, Le Bourgeois M, Lallemend D, Scheinmann P. The value of flexible bronchoscopy in childhood pulmonary tuberculosis. Chest 1991;100:688–692.
27. Tuberculosis in children: guidelines for diagnosis, prevention and treatment (a statement of the scientific committees of the IUATLD). Bull Int Union Tub Lung Dis 1991;66:61–67.
28. Bhaskar A, Pradhan P, Chaturvedi P, Basak A, Lodam A, Narang P, Harinath BC. Immunodiagnosis of childhood pulmonary and extrapulmonary tuberculosis using *Mycobacterium tuberculosis* ES antigen by penicillinase ELISA. Ann Trop Paediatr 1994;14:25–30.
29. Delacourt C, Gobin Jr Gaillard J-L, de Blic J, Veron M, Scheinmann P. Value of ELISA using antigen 60 for the diagnosis of tuberculosis in children. Chest 1993;104:393–398.