The prevalence of symptoms associated with pulmonary tuberculosis in randomly selected children from a high burden community

B J Marais, R P Gie, H S Schaaf, A C Hesseling, N Beyers.
Centre for TB Research and Education (CENTRE), Faculty of Health Sciences, Stellenbosch University, Cape Town, South Africa
C C Obihara.
Wilhelmina Children's Hospital, University Medical Center, Utrecht, The Netherlands
C Lombard.
Medical Research Council of South Africa, Cape Town, South Africa
D Enarson.
International Union against Tuberculosis and Lung Disease (IUATLD), Paris, France
E Bateman.
Division of Pulmonology, Department of Medicine, University of Cape Town, Cape Town, South Africa

Correspondence to: Dr B J Marais, Department of Paediatrics and Child Health, Centre for TB Research and Education (CENTRE), Faculty of Health Sciences, Stellenbosch University, PO Box 19063, Tygerberg, 7505, South Africa; bjmarais@sun.ac.za

Published: Archives of Disease in Children, November 2005, 90(11):1166-1170, doi:10.1136/adc.2004.060640.

Abstract

Background: Diagnosis of childhood tuberculosis is problematic and symptom based diagnostic approaches are often promoted in high burden settings. This study aimed (i) to document the prevalence of symptoms associated with tuberculosis among randomly selected children living in a high burden community, and (ii) to compare the prevalence of these symptoms in children without tuberculosis to those in children with newly diagnosed tuberculosis.

Methods: A cross sectional, community based survey was performed on a 15% random sample of residential addresses. A symptom based questionnaire and tuberculin skin test (TST) were completed in all children. Chest radiographs were performed according to South African National Tuberculosis Control Program guidelines.

Results: Results were available in 1415 children of whom 451 (31.9%) were TST positive. Tuberculosis was diagnosed in 18 (1.3%) children. Of the 1397 children without tuberculosis, 253 (26.4%) reported a cough during the preceding 3 months. Comparison of individual symptoms (cough, dyspnoea, chest pain, haemoptysis, anorexia, weight loss, fatigue, fever, night sweats) in children with and without tuberculosis revealed that only weight loss differed significantly (OR = 4.5, 95% CI 1.5 to 12.3), while the combination of cough and weight loss was most significant (OR = 5.4, 95% CI 1.7 to 16.9). Children with newly diagnosed tuberculosis reported no symptoms in 50% of cases.

Conclusion: Children from this high burden community frequently reported symptoms associated with tuberculosis. These symptoms had limited value to differentiate children diagnosed with tuberculosis from those without tuberculosis. Improved case definitions and symptom characterisation are required when evaluating the diagnostic value of symptoms.

What is already known about this topic

- No previous community based report has described the prevalence of symptoms traditionally associated with tuberculosis in randomly selected children from a high burden community; hospital based reports are limited by selection bias.
- There is a need to reassess the value of symptom based approaches for the diagnosis of childhood pulmonary tuberculosis, especially in high burden settings with limited resources; current symptom based diagnostic algorithms are poorly validated.

What this study adds

- This is the first report describing the prevalence of symptoms traditionally associated with tuberculosis in the average child from a high burden community.
- This study indicates that poorly defined symptoms, traditionally associated with tuberculosis, are too common in children from these communities to be of real diagnostic value.

In areas with a high prevalence of tuberculosis, children contribute a significant proportion of the disease burden and experience considerable morbidity and mortality related to tuberculosis.[1,2] This is demonstrated by the fact that pulmonary tuberculosis rivals bacterial pneumonia as a respiratory cause of death in African children older than 6 months of age.[3] The diagnosis of tuberculosis in children is difficult because bacteriological confirmation is rarely achieved and is often not even attempted.[4–8] Chest radiography is regarded as a valuable diagnostic tool, but it is often impossible to identify hilar adenopathy, considered to be the most consistent sign of primary pulmonary tuberculosis, with certainty.[9] In addition, the distinction between recent primary infection and active disease is highly problematic.[10] Most diagnostic algorithms are partly symptom based, but these algorithms are poorly validated and lack standard symptom definitions.[11]

To our knowledge, no previous study has documented the prevalence of symptoms associated with tuberculosis in randomly selected children living in a high burden community. In these communities a large number of individuals become infected with *Mycobacterium tuberculosis* (*M tuberculosis*) during childhood,[12] and symptom based diagnostic approaches are often promoted to screen children for active tuberculosis. The literature on tuberculosis related symptomatology in children is almost exclusively hospital based, which does not reflect the prevalence of symptoms in the general population.

A recent review of studies from the pre-chemotherapy era documented the natural history of tuberculosis in childhood.[10] It confirmed that immune competent children, older than 2 years of age, are at low risk of disease progression following primary infection.[10] The presence of symptoms associated with tuberculosis had definite diagnostic value in these low risk children, in whom the principal diagnostic challenge was to distinguish self-contained infection from progressive disease.[10]

The aims of this community based study were (i) to document the prevalence of symptoms associated with tuberculosis among randomly selected children living in a high burden community, and (ii) to compare the prevalence of these symptoms in children without tuberculosis to those in children with newly diagnosed tuberculosis.

METHODS

A cross sectional community based survey was carried out between July and December 2002. A questionnaire was completed and a tuberculin skin test (TST) administered to each child (<15 years of age). Chest radiographs (CXR) were performed according to the South African National Tuberculosis Control Program (NTCP) guidelines.

Study setting

The study area is an established epidemiological field site in Cape Town, South Africa, comprising two suburbs with a population of 38 656 (census 1996) and a high burden of tuberculosis (average notification rate of new bacteriologically confirmed cases 320/100 000 per year).[13] Childhood tuberculosis constitutes a high percentage (39%) of the total caseload.[14] The proportion of the population infected with human immunodeficiency virus (HIV) is relatively low, less than the average of 8.8% (95% CI 4.9 to 12.7%) calculated for the Cape Town/Metropole region in 2001.[15]

Sample selection

A 15% sample of residential addresses was randomly selected, based on a geographical information system of the area. Trained field workers enumerated the people at each of the 839 residential addresses selected. Written informed consent was obtained from the parent or legal guardian. The 218 addresses (26%) that refused consent were systematically replaced by neighbouring addresses. A CXR was performed in children less than 5 years of age who had been in household contact with a sputum smear positive source case or had a positive TST (induration $\geqslant$15 mm in diameter), and in all children with suspect symptoms according to World Health Organisation guidelines (loss of weight, cough >3 weeks, fever >1 week, or haemoptysis).[16]

Questionnaire

A standard questionnaire recorded symptoms that are commonly associated with tuberculosis, experienced during the preceding 3 months (table 1). The duration of each symptom (other than haemoptysis) was categorised as less than 1 week, 1–2 weeks, 2–3 weeks, or more than 3 weeks. Questionnaires were completed by the parent under supervision of a trained field worker. Parents were requested (but put under no obligation) to confidentially report previous HIV tests and results.

Tuberculin skin test

Trained field nurses performed TST by intra-dermal injection of 2 tuberculin units (TU) of *M tuberculosis* PPD RT 23 (Statens Serum Institut, Copenhagen, Denmark) on the volar aspect of the left forearm. The largest transverse diameter of induration was measured after 48–72 h.

Chest radiograph

Standard antero-posterior (AP) and lateral views were taken, using the same *x* ray machine in all children. A single expert screened all CXR. A second independent expert was used to confirm that the radiographical signs were suggestive of tuberculosis in all children identified with possible tuberculosis during the initial screening. Children with confirmed radiographical signs suggestive of tuberculosis had sputum or gastric aspirate samples taken for culture.

A probable tuberculosis case was defined as a child with a "diagnostic" CXR, confirmed by two independent observers (modified WHO guidelines).[17] A confirmed tuberculosis case was defined as a child with bacteriological proof of tuberculosis. All children with probable or confirmed tuberculosis were referred to a local clinic for treatment, in accordance with the NTCP guidelines. Children aged less than 5 years, in household contact with a sputum smear positive source case or with a positive TST, were referred for chemoprophylaxis or treatment of latent infection after active tuberculosis was excluded. The study was approved by the Ethics Review Board of Stellenbosch University and by the Department of Health, City of Cape Town.

Statistical analysis

Data analyses were carried out with SPSS for Windows version 11.0. The frequencies of symptoms and specific symptom durations were compared between age groups, and TST positive and TST negative children, as well as between those with newly diagnosed tuberculosis and those without. Comparisons were performed by using the Mantel-Haenszel χ^2 test. The two sided Fisher's exact test was used to determine the p values.

RESULTS

In total, 1593 children were enumerated at the selected addresses. Questionnaire and TST results, available in 1415 (88.9%) children, were included in the analysis. Table 2 summarises the demographic characteristics of the whole group. A positive TST was recorded in 451 (31.9%) children. Seventy five children reported previous HIV testing, with only one reporting a positive test result. CXR were performed in 239 (16.9%) children, applying current NTCP guidelines. The main reasons for performing the CXR were as follows: (i) 177 (74.1%) <5 years of age with household contact ever, (ii) 33 (13.8%) <5 years of age and with TST $\geqslant$15 mm, and (iii) 29 (12.1%) with suspect symptoms. Eighteen (1.3%) children were newly diagnosed with probable or confirmed tuberculosis. Table 3 summarises the disease characteristics (type of disease) in these 18 children. Bacteriological confirmation (a positive *M tuberculosis* culture) was achieved in two cases (11.1%). None of the children with newly diagnosed tuberculosis had clinical signs suggestive of HIV disease.

Table 4 describes the demographics of the 1397 children without tuberculosis, compared to the 18 children with newly diagnosed tuberculosis. Most children with newly diagnosed tuberculosis (14; 77.8%) were less than 5 years of age. Household contact with a recent sputum smear positive source case was reported in three (16.7%) children with newly diagnosed tuberculosis, compared to 50 (3.6%) children without

tuberculosis (OR = 5.4; 95% CI 1.5 to 19.2). The TST result was equal to or greater than 15 mm (median 17 mm; range 0–31 mm) in all but one child with newly diagnosed tuberculosis.

Table 5 compares the symptoms reported in children without tuberculosis to those in children with newly diagnosed tuberculosis. Of the 1397 children without tuberculosis, 253 (26.4%) reported a cough during the preceding 3 months. Prolonged symptoms were not uncommon, and 66 (6.9%) reported coughing of more than 3 weeks duration. No significant differences in symptom prevalence or symptom duration existed between age groups (<2 years, 2–4 years, 5–9 years, 10–14 years) or between those with and without TST proof of tuberculosis infection. Significantly more children with newly diagnosed tuberculosis reported weight loss in the preceding 3 months (OR = 4.5, 95% CI 1.5 to 12.3). None of the other symptoms showed statistically significant differences between the two groups, even when the reported duration of symptoms was taken into account. When children less than 5 years of age were analysed separately, to correct for possible selection bias in the older children, the results were similar.

The presence of more than one symptom increased the odds for tuberculosis, but this reached significance only with the inclusion of weight loss. The combination of cough and weight loss was most significant (OR = 5.4, 95% CI 1.7 to 16.9). Nine (50%) children with newly diagnosed tuberculosis reported no symptoms at all, compared to 910 (65.2%) of those without tuberculosis (OR = 1.9, 95% CI 0.7 to 4.7).

DISCUSSION

This community based survey documents the prevalence of symptoms associated with pulmonary tuberculosis in the average child living in a high burden community. The results demonstrate that within this setting, these symptoms are common in the general paediatric population. Only weight loss, alone or in combination with other symptoms, was significantly more common in children with newly diagnosed tuberculosis. Combinations of symptoms (symptom complexes) were more likely to be associated with tuberculosis than individual symptoms, but the small number of tuberculosis cases limited the analysis. This is an inevitable limitation of community based surveys that document relatively rare events.[18] The detection of 18 new tuberculosis cases during this survey demonstrate a high prevalence of undiagnosed childhood tuberculosis within this community (1272/100 000 of the child population).

The observation that nearly a third of children coughed in the preceding 3 months may be explained by the fact that both viral and bacterial infections are common in this community, especially during the winter months (May to September). It is also common practice for children to share a bed with their parents, which may increase parental awareness of night time symptoms such as cough, fever, or sweating. Similar to previous observations, some (exactly 50%) of the children with newly diagnosed tuberculosis reported no symptoms.[19–21] Although significant differences were found between the symptoms reported in children with tuberculosis and those without, these differences are of limited diagnostic value and only relevant from an epidemiological perspective. This is illustrated by the fact that the symptom complex with the highest significance, cough and weight loss, had a positive predictive value of only 5%.

The study had several limitations; of most importance is the fact that CXR were performed on a selective subgroup of children. Only children under 5 years of age were radiologically screened following household exposure or a positive TST and as a result older children with asymptomatic primary infection may not have been diagnosed. Although this could have biased the results, the statistical findings in children less than 5 years of age and in the group as a whole were similar when comparing symptoms in those with and without tuberculosis. This potential bias seems

unavoidable as both the WHO and NTCP guidelines recommend that a CXR should only be performed in older children if they are symptomatic. It may even be argued that it is unethical to perform a CXR in an asymptomatic child older than 5 years of age, as the risk of developing disease following primary infection is less than 1%.[10] The group diagnosed with tuberculosis during this survey represents a true reflection of children who would have been diagnosed with tuberculosis in a "real life" setting, where resources permit active contact tracing and adequate investigation.

The majority of children diagnosed with tuberculosis had signs indicative of recent primary infection only (positive TST and elements of the Ghon complex on CXR). The natural history of tuberculosis in children illustrates that following primary pulmonary infection, transient visibility of the Ghon complex is common and does not necessarily indicate disease.[10,22,23] The fact that current, internationally accepted definitions of disease often reflect recent primary infection, especially in children who are diagnosed after active contact tracing, does hamper the interpretation. Therefore, it is important to point out that, although the study indicates that symptoms have limited diagnostic value, their value for differentiating active disease from recent primary infection requires further investigation.

Questionnaire driven surveys are inherently limited by recall bias and subjectivity. Bias was reduced by the use of standardised questionnaires and the fact that the diagnostic tests (TST and CXR) were performed after completion of the questionnaire. Reported weight loss reflected a subjective impression and objective weight measurements were not taken into account, as these were not routinely done in all children. In addition, the questions used may have been too imprecise, as the pre-chemotherapy literature identifies important symptom characteristics, associated with progressive tuberculosis, that were not elucidated in the present study. These characteristics include persistent, non-remitting symptoms of recent onset.[10] Careful symptom characterisation may be essential to improve their diagnostic value.

Nearly a third (5, 27.8%) of children with newly diagnosed tuberculosis reported previous household contact with a sputum smear positive source case. This is in agreement with a study from the same community that employed restriction fragment length polymorphism (RFLP) analysis, providing proof that 34% of children acquired disease following infection from a source case within the household.[24] In high burden settings, most infection, particularly in children older than 2 years of age, is contracted outside the household within the community.[9,13,24]

In conclusion, this study illustrates the importance of community based research. It describes symptomatology within the general community and highlights the danger of extrapolating findings from hospital based studies to the community level. It is essential to know the prevalence of symptoms within the general community in order to evaluate the value of any particular symptom based diagnostic approach. Comparing the symptoms reported in children without tuberculosis to those in children with newly diagnosed tuberculosis demonstrates why current symptom based scoring systems perform poorly in clinical practice. Most importantly, the study emphasises the need for improved symptom characterisation and accurate outcome definitions which will adequately differentiate *M tuberculosis* infection from active disease.

Tables

Table 1
Questionnaire

1) Did your child experience a daily cough in the preceding 3 months?
What was the duration of daily cough?
2) Did your child experience any breathing difficulty in the preceding
3 months?
What was the duration of difficult breathing?
3) Did your child experience any chest pain in the preceding 3 months?
What was the duration of chest pain?
4) Did your child cough up any blood in the preceding 3 months?
5) Did your child experience any deterioration in appetite in the
preceeding 3 months?
What was the duration of appetite loss?
6) Did your child lose any weight in the preceding 3 months?
What was the duration of weight loss?
7) Did your child experience any abnormal lethargy/fatigue in the
preceeding 3 months?
What was the duration of abnormal fatigue/lethargy?
8) Did your child experience daily or recurrent fever in the preceding
3 months?
What was the duration of daily or recurrent fever?
9) Did your child experience night sweats in the preceding 3 months?
What was the duration of night sweats?
Once a specific symptom was reported the duration was specified as: a) less than 1 week; b) 1–2 weeks; c) 2–3 weeks; or d) more than 3 weeks.

Table 2
Demographics of all children enrolled (n = 1415)

	Total number (%)
Gender	
Male	709 (50.1)
Female	706 (49.9)
Age distribution in years	
<2	188 (13.2)
2–4	243 (17.2)
5–9	508 (35.9)
10–14	476 (33.7)
TST positive (⩾15 mm in diameter)	451 (31.9)
Age distribution of TST positive children in years	
<2	35 (2.5)
2–5	42 (3.0)
5–10	164 (11.6)
10–14	210 (14.8)
HH contact with an adult source case ever	201 (14.2)
Recent HH contact with an adult source case	53 (3.7)
CXR done	239 (16.9)
CXR suggestive of tuberculosis	18 (1.3)
The total number of children enumerated was 1593 of whom 1415 (88.8%) were enrolled. CXR, chest radiograph; HH, household; Recent HH contact, household contact with a sputum smear positive source case, currently on treatment; TST, tuberculin skin test.	

Table 3
Disease characteristics in the children with newly diagnosed TB (n = 18)

Characteristics	**Number (%)**
TST ⩾15 mm in diameter	17 (94.4)
Type of disease on CXR	
Elements of the Ghon complex only	15 (83.4)
Parenchymal consolidation (apart from	1 (5.5)
the Ghon focus)	
Parenchymal cavities	2 (11.1)
Bacteriological proof (culture positive)	2 (11.1)
TB, bacteriological confirmation or definite radiological signs with proof of *Mtuberculosis* infection; TST, tuberculin skin test.	

Table 4
Demographics of children without TB (n = 1397) compared to children with newly diagnosed TB (n = 18)

Demographics	**No TB (%)**	**TB (%)**	**OR (95% CI)**	**p value**
Gender				
Male	701 (50.2)	9 (50.0)	1.00 (0.4 to 2.6)	0.998
Female	696 (49.8)	9 (50.0)	1.00 (0.4 to 2.6)	0.998
Age distribution in years				
<2	185 (13.2)	3 (16.7)		
2–4	232 (16.7)	11 (61.1)		
5–9	505 (36.1)	3 (16.7)		
10–14	475 (34.0)	1 (5.5)	$\chi^2 = 11.0$	0.001*
HH contact with adult source case ever	195 (14.0)	5 (27.8)	2.31 (0.3 to 20.0)	0.442
Recent HH contact with adult source case	50 (3.6)	3 (16.7)	5.39 (1.5 to 19.2)	0.004**
Positive TST (⩾15 mm in diameter)	434 (24.0)	17 (94.4)	37.7 (5.0 to 284.4)	0.000
*p trend; **p<0.01.				
CI, confidence interval; CXR, chest radiograph; HH, household; OR, odds ratio; Recent HH contact, household contact with a sputum smear positive source case, currently on treatment; TB, bacteriological confirmation or definite radiological signs with proof of *M tuberculosis* infection; TST, tuberculin skin test.				

Table 5
Symptoms reported in children without TB (n = 1397) during the preceding 3 months compared to symptoms reported in those with newly diagnosed TB (n = 18)

	No TB (%)	**TB (%)**	**OR (95% CI)**	**p value**
Individual symptoms				
1) Cough	365 (26.1)	8 (44.4)	2.3 (0.9 to 5.8)	0.080
2) Difficult breathing	150 (10.7)	1 (5.6)	0.5 (0.1 to 3.7)	0.478
3) Chest pain	77 (5.5)	0 (0.0)	1 (0.9 to 1.1)	0.305
4) Haemoptysis	7 (0.6)	0 (0.0)	1 (0.9 to 1.1)	0.763
5) Anorexia	123 (8.8)	4 (22.2)	2.9 (0.9 to 9)	0.052
6) Weight loss**	110 (7.8)	5 (27.8)	4.5 (1.6 to 13)	0.002
7) Fatigue	110 (7.8)	3 (16.7)	2.3 (0.7 to 8.2)	0.172
8) Fever	162 (11.6)	4 (22.2)	2.2 (0.7 to 6.7)	0.164
9) Night sweats	153 (10.8)	3 (16.7)	1.6 (0.4 to 5.7)	0.443
Combined symptoms				
Cough and weight loss**	70 (5.0)	4 (22.2)	5.4 (1.7 to 16.9)	0.001
Cough, anorexia, and weight loss**	51 (3.7)	3 (16.7)	5.3 (1.5 to 18.8)	0.004
No symptoms	911 (65.2)	9 (50.0)	1.9 (0.7 to 4.7)	0.182
**p<0.01.				
Symptoms 1) to 9): individual symptoms correlate with questions described in table 1. CI, confidence interval; OR, odds ratio; TB, bacteriological confirmation or definite radiological signs with proof of *M tuberculosis* infection.				

Acknowledgments

We thank all parents and children who participated in this study. We are indebted to Dr Ivan Toms, Director of Health for the City of Cape Town, for permission to conduct this community based study.

Footnotes

- The study was funded by the Stellenbosch University and the University of Cape Town Lung Institute. The research was funded by a USAID research grant awarded by the IUATLD and an Astra Zeneca research fellowship awarded by the South African Thoracic Society
- Competing interests: none declared
- This manuscript is in partial fulfilment of a PhD thesis

REFERENCES

1. ***Donald PR**. Childhood tuberculosis: out of control? Curr Opin Pulm Med2002;8:178–82.*
2. ***Walls T** , Shingadia D. Global epidemiology of paediatric tuberculosis. J Infect2004;48:13–22.*
3. ***Chintu C** , Mudenda V, Lucas S, et al. Lung diseases at necropsy in African children dying from respiratory illnesses: a descriptive necropsy study. Lancet2002;360:985–90.*
4. ***Donald PR**. Childhood tuberculosis: the hidden epidemic. Int J Tuberc Lung Dis2004;8:627–9.*
5. ***Nelson LJ**, Wells CD. Global epidemiology of childhood tuberculosis. Int J Tuberc Lung Dis2004;8:636–47.*
6. ***Eamranond P** , Jaramillo E. Tuberculosis in children: reassessing the need for improved diagnosis in global control strategies. Int J Tuberc Lung Dis2001;5:594–603.*
7. ***Starke JR**. Childhood tuberculosis: a diagnostic dilemma. Chest1993;104:329–30.*
8. ***Osborne CM**. The challenge of diagnosing childhood tuberculosis in a developing country. Arch Dis Child1995;72:369–74.*
9. ***Marais BJ**, Gie RP, Starke JR, et al. A proposed radiological classification of childhood intra-thoracic tuberculosis. Pediatr Radiol2004;34 (11) :886–94.*
10. ***Marais BJ**, Gie RP, Schaaf HS, et al. The natural history of childhood intra-thoracic tuberculosis – a critical review of the literature from the pre-chemotherapy era. Int J Tuberc Lung Dis2004;8:392–402.*
11. ***Hesseling AC**, Schaaf HS, Beyers N, et al. A critical review of diagnostic approaches used in the diagnosis of childhood tuberculosis. Int J Tuberc Lung Dis2002;6:1038–45.*
12. ***Marais BJ**, Gie RP, Schaaf HS, et al. The clinical epidemiology of childhood pulmonary tuberculosis: a critical review of literature from the pre-chemotherapy era. Int J Tuberc Lung Dis2004;8:278–85.*
13. ***Verver S** , Warren RM, Munch Z, et al. Proportion of tuberculosis transmission that takes place in households in a high-incidence area. Lancet2004;363:212–14.*
14. ***van Rie** , Beyers N, Gie R. et al Childhood tuberculosis in an urban population in South Africa: burden and risk factors. Arch Dis Child1999;80:433–7.*
15. ***Department of Health, South Africa**. 12th National HIV and syphilis seroprevalence survey of women attending public antenatal clinics in South Africa 2001. Epidemiol Comments2002;5:2–15.*
16. ***Shingadia D** , Novelli V. Diagnosis and treatment of tuberculosis in children. Lancet Infect Dis2003;3:624–32.*
17. ***Stoltz AP**, Donald PR, Strebel PM, et al. Criteria for the notification of childhood tuberculosis in a high-incidence area of the western Cape Province. S Afr Med J1990;77:385–6.*
18. ***Grimes AD**, Schults KF. An overview of clinical research: the lay of the land. Lancet2002;359:57–61.*
19. ***Schaaf HS**, Beyers N, Gie RP, et al. Respiratory tuberculosis in childhood: the diagnostic value of clinical features and special investigations. Pediatr Infect Dis J1995;14:189–94.*
20. ***Salazar GE**, Schmidtz TL, Cama R, et al. Pulmonary tuberculosis in children in a developing country. Pediatrics2001;108:448–53.*
21. ***Starke JR**, Taylor-Watts KT. Tuberculosis in the pediatric population of Houston, Texas. Pediatrics1989;84:28–35.*
22. ***Gedde-Dahl T** . Tuberculous infection in the light of tuberculin matriculation. Am J Hyg1952;56:139–214.*
23. ***Delacourt C** , Mani TM, Bonnerot V, et al. Computed tomography with normal chest radiograph in tuberculous infection. Arch Dis Child1993;69:430–2.*
24. ***Schaaf HS**, Michaelis IA, Richardson M, et al. Adult-to-child transmission of tuberculosis: household or community contact? Int J Tuberc Lung Dis2003;7:426–31.*