ORIGINAL ARTICLE

Clinical and epidemiological characteristics of contagious adult of tuberculosis in children*

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Background: Tuberculosis in children generally occurs as a direct result of cohabitation with a contagious adult.

Objective: To create a profile of a typical adult with contagious tuberculosis (as identified through the public health system) living with a child who has been diagnosed with tuberculosis.

Method: Case study. Children younger than 14 years of age who were diagnosed with tuberculosis were included. Parents were interviewed using structured questionnaires. Means and standard deviations were analyzed using the Student's *t*-test. Fisher's exact test or the Ç² test was used for comparisons.

Results: Fifty children, representing 96% of those diagnosed with tuberculosis in the Porto Alegre health care system between July 20, 2001 and August 10, 2002, were included. The mean age was 76 months, and 60% were girls. The classic forms of pulmonary presentation (consolidation or cavitation) were seen in 38%. The majority of the children were diagnosed in the hospital and came from homes in which there were (a mean of) 6 cohabitants and a total family income less than 2 times the local minimum wage. Using ELISA, HIV co-infection was identified in 25% (although not all were tested). The children regularly visited places other than their homes. In 78% of cases, the contagious adult was identified. These contagious adults were mostly males (56%), and the mean age was 32. In most cases (79%), the contagious adult was a relative, usually a parent. Within this group of adults with contagious tuberculosis, HIV co-infection was identified in 43% of those tested.

Conclusions: Adults with contagious tuberculosis living in the home continue to be the most likely source of tuberculosis infection in children. Co-infection with HIV in these pediatric patients, as well as in the cohabiting adults with contagious tuberculosis, is a significant finding. It must be emphasized that the possibility of contact with contagious individuals in the home should be explored in every diagnosed case of pediatric tuberculosis.

Key words: Tuberculosis/epidemiology. Children. Communicable diseases/etiology.

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Abbreviations used in this paper:

TB	– Tuberculosis
ELISA	– Enzyme-linked immunosorbent assay
HIV	– Human immunodeficiency virus
WHO	– World Health Organization
BCG	– Bacillus Calmette-Guérin
TT	– Tuberculin Test

INTRODUCTION

Tuberculosis (TB) remains a serious public health problem. There is a significant prevalence of the disease in Brazil, which is one in a group of 23 countries that have the highest TB rates in the world and ranks thirteenth in absolute numbers[1]. Since Brazil is of continental dimensions, the prevalence of TB varies by region. Higher numbers are found in the southeast and northeast, and the lowest prevalence is in the south[2]. In 2001, 1700 cases were reported in the city of Porto Alegre (in the state of Rio Grande do Sul), representing an incidence of approximately 90/100,000 inhabitants[3]. It is notable that, according to Ruffino-Neto, only two-thirds of all adult cases are reported[4]. Therefore, these numbers may represent only a portion of the actual total. This estimate is controversial and other Brazilian authors[2] have questioned it, stating that, despite diagnostic problems and underreporting, the absence of a precise model has made it difficult to more accurately estimate the number of cases.

The actual situation of TB in children is unknown[1,5]. In 1998, studies carried out by the WHO showed that the percentage of TB in children younger than 14 years of age ranged from 0.6% to 5.2% of the total number of reported cases[5]. Although TB is less common in children, it has a higher impact due to higher morbidity and mortality in this age group[6].

Contraction of TB by children is strongly correlated with recent transmission. The difficulty in isolating *Mycobacterium tuberculosis* in children frequently obligates the diagnosing physician to base the diagnosis on indirect indications such as epidemiological, radiographic, and clinical criteria as well as tuberculin test (TT) results. The diagnosis of TB in children usually involves identification of adults with contagious TB ("index cases") [8]. Reviews of the literature have shown that a contagious adult is identified in 25% to 80% of cases of childhood TB[10]. The characteristics of contagious adults vary considerably among the different studies, but parents are more frequently implicated[10,11,13]. Since these studies have not been designed to assess the characteristics of the contagious vectors, data have frequently been considered incomplete.

In the present study, the characteristics of contagious adults and children diagnosed with TB between July 2001 and August 2002 in the city of Porto Alegre are described.

METHOD

All children living in the city of Porto Alegre who were younger than 15 years of age and diagnosed with TB (presumptive, confirmed, or reported) between July 2001 and August 2002 were included. Patients were selected based on reporting of cases from the city epidemiological control group. Patients being treated in reference clinics, whether or not they represented reported cases, were also included.

Parents and legal guardians were interviewed using a two-part structured questionnaire. The first part of the questionnaire focused on the child, including questions regarding previous diseases, TB diagnostic data and places frequently visited, as well as socioeconomic status of the family. The second part of the questionnaire was designed to collect data regarding the contagious adult (demographics, socioeconomic data, and TB diagnostic data). The original diagnostic criteria used for both children and adults were based on guidelines established by the *I Consenso Brasileiro de Tuberculose* (First Brazilian Consensus Statement on Tuberculosis) in 1997[12].

The Sant'Anna[12] score was used for children diagnosed with pulmonary TB when no *M. tuberculosis* was identified by direct sputum smear microscopy. This scoring system considers clinical and radiographic status, contact history, TT results and nutritional state, and each category is scored. A score of more than 40 points indicates "extremely likely" TB, a score between 30 and 35 indicates "probable" TB, and a score of less than 25 indicates that a diagnosis of TB is "unlikely".

Radiographic records were obtained from the medical charts of the children included in the study. If a child was hospitalized, the hospital radiologist prepared the report. The pulmonology group responsible for the follow-up treatment of outpatients in the various reference centers prepared the chest X-ray reports. The authors of the present study had no direct access to the X-rays.

The presence of consolidation or cavitation in chest X-rays were considered forms of pulmonary presentation, whereas isolated mediastinal lymph node findings, as well as pleurisy, miliary pattern, and extrathoracic forms were considered forms of extrapulmonary presentation.

Children were routinely weighed from the first post-diagnosis visit on, and the results were analyzed using EPINUTE – EPIINFO 6.04b[14] software to determine the respective percentiles.

Database and statistical analysis were carried out through EPIINFO 6.04b[14]. Frequencies and confidence intervals as well as comparisons between variables were calculated using 2 x 2 tables and the chi-square test or Fisher's exact test, when appropriate. Variables with

means and standard deviations were compared using Student's *t*-test. Statistical significance was set at $p < 0.05$.

Characteristics of children who had had confirmed contact with contagious adults were compared with those of children who had not, and differences between the two groups were calculated. Specific characteristics such as place of diagnosis, nutritional state, and results of ELISA for human immunodeficiency virus (HIV) were also compared. The temporal relationship between the time of diagnosis of the child and that of the corresponding contagious adult was visually evaluated through graphics generated by Sigmaplot v 2.0 software.

The study was defined as "minimal risk". Verbal informed consent was obtained and the Research Ethics Committee of the *Secretaria de Saúde do Município de Porto Alegre* (Porto Alegre Municipal Department of Health) approved the study.

RESULTS

Between July 21, 2001 and August 10, 2002, 60 children were diagnosed with TB in the city of Porto Alegre. Of these reported cases, 14 patients were excluded: 6 because they did not live in the city, 7 because they were older than 15 years of age (typographical error), and 1 because atypical mycobacteriosis was identified (the patient was diagnosed with cystic fibrosis). Therefore, 46 children were eligible for inclusion in the study. Of these, 44 (88%) were included, together with 6 children who were being treated in reference clinics and who had not yet been included in the official database of the local epidemiological control group, resulting in a total of 50 children included in the study (Figure 1).

Pulmonary TB was detected in 38% of the patients. In the cases of extrapulmonary presentation, the most common types were isolated mediastinal adenopathy (16%), and cervical adenopathy. There were no significant differences between the presentation forms of the disease in when the BCG vaccine was taken, presence of vaccine scar, age less than 4 and place of diagnosis (Table 1).

On average, the children evaluated lived in homes in which there were 6 inhabitants. More than 87% of the families of these children had a total family income less than 3 times the minimum wage. Most (65%) of the children regularly visited places other than their homes, especially school (57%), and 23% of the children were looked after by relatives or friends in other homes. In 31 of the homes, there were other children younger than 15, and less than half of these other children had been examined.

The majority of the children (82%) were diagnosed in the hospital, especially those presenting extrapulmonary TB. In children diagnosed with pulmonary TB without confirmation through direct microscopy, the mean Sant'Anna score was 45, and 94% of these children scored above 30. Therefore, they were classified as possible or very likely cases of TB[32].

Chest X-rays were taken of 49 children, and 40 presented alterations, mainly mediastinal adenopathy and consolidation (Table 2).

Forty-three children were submitted to TT. Indurations were equal to or greater than 15 mm in half of the patients and larger than 10 mm in 67%. All the patients who had not taken BCG vaccine presented induration larger than 10 mm. Of the 32 patients tested for HIV using ELISA, 25% were positive. There were no significant differences between positive HIV results and the presentation forms of the disease or TT reactivity. This finding may be related to the small number of cases with positive results. Sputum smear microscopy showed good efficiency. Children older than 6 whose X-rays revealed consolidation or cavitation were submitted to the test, and it was positive in 29% of the cases. Other complementary tests were either rarely used or showed poor efficiency. Acid-fast bacilli testing in gastric lavage – performed in 21 patients – was positive in only one case. Polymerase chain reaction, BCG test and fiber bronchoscopy were used in few patients. Children with pleural involvement were diagnosed in the hospital. Diagnosis was achieved

through pleural biopsy and identification of granuloma in the anatomopathological examination of the sample.

In the analysis of weight characteristics (Table 3), evaluated in consideration of standard weight by age group, 13 (32%) children were below the 10th percentile in relation to their age, and almost half were below the 25th percentile. Children who were HIV positive weighed significantly less than HIV-negative children.

Contact with a contagious adult was confirmed in 78% of the cases (39 contagious adults). Comparisons were made between children who had such contact and those who did not (Table 4). Significant differences between the two groups were found in relation to earlier vaccination and TT induration larger than 10 mm. Children younger than 4 had more confirmed contacts, but the difference was not statistically significant.

At the time of diagnosis, sputum samples were obtained from 75% of the contagious adults. Testing of those samples revealed 1+ in 10%, 2+ in 32% and 3+ in 52%.

Analysis of the contagious adults showed that, in 41% of cases, parents were responsible for the TB contact, followed by nonrelatives at 20%, uncles and aunts at 15%, siblings at 13% and grandparents at 10%. In 7 cases, contact with more than one contagious adult was confirmed. There was a trend for children younger than 4 to have had a higher percentage of parental TB contact than had older children (53% and 23% respectively, $p = 0.054$; Table 5).

It is important to note that one-third of the adults were diagnosed with TB after the children had been diagnosed. This proportion was greater in relation to the 86% of children who were diagnosed in the hospital (Figure 2).

Half of the identified contagious adults reported having no profession, being unemployed or working only sporadically. Mean monthly wages, which were less than 2 times the minimum wage, reflected this reality.

DISCUSSION

In children, TB is an indicator of the quality of the health care system, showing that adults with contagious TB have not been identified soon enough to prevent the dissemination of the disease. The difficulty in diagnosing TB in children makes the identification of contagious adults essential for presumptive diagnosis and therapeutic management of TB in children.

In the present study, through an active search, we identified contagious adults in 78% of the cases. This number is higher than in other recent studies in which researchers were able to identify index cases in only 36% to 61% of cases[9-11,15-17]. However, this number is still low if we consider that contagious adults were not identified in one-fifth of the children younger than 4, virtually all of whom live with their parents.

In a historic study performed in the USA in the 1950s involving a group of 400 children diagnosed with TB, contagious adults were identified in 81% of the cases[18]. This study reflected the concern, even at that time, with a extremely prevalent disease of high morbidity and mortality. A recent study carried out in the same country revealed a much lower number of contagious adults[15].

In Spain, a two-phase study with an interval of 20 years between phases revealed a decrease of 9% (from 67% to 58%) in the number of adult index cases identified[10]. This finding could be explained by factors similar to those responsible for the increase of the incidence of TB in developed countries within the past decade. Lack of awareness on the part of health professionals, reductions in resources allocated, demobilization of TB control groups and illegal immigration from poorer countries have all made TB control more problematic and the identification of contacts more difficult[19,20].

In Brazil, there have been few studies on contact with contagious TB patients. A study conducted in the city of Rio de Janeiro evaluated diagnostic and bacteriological criteria in children and identified contagious adults in 61% of cases[16]. In another study carried out in Porto Alegre among hospitalized children, such contact was only confirmed in a little more than half of the cases[21].

The epidemiological characteristics of the children in the present study are very similar to those evaluated in other studies we reviewed. Minor differences in relation to gender, age group and race are probably attributable to variations in the number of patients included in each study[8-10,16,22]. The number of people per home and the low socioeconomic level of the families involved caught our attention. These data are similar not only to those from other poor countries, but also to those from areas with large populations of immigrants in industrialized countries or within immigrant groups (coming from countries where there is a high prevalence of the disease) living in such countries[23].

In contrast to the findings by Sanchez-Albisua[10], we found no direct relation between lower age and extrapulmonary presentation, malnutrition or higher frequency of contact identification. This can be explained by the small number of patients in this group, in which only 21 children were younger than 4 (type II error). We must also consider that the children included in the study were weighed during visits to the reference clinics and the scales were not calibrated prior to each weighing, although the same medical staff took the measurements in every reference clinic. The results of a study conducted in South Africa also showed no relationship between lower age and malnutrition[24]. In addition, the authors identified older children among those diagnosed with extrapulmonary TB. In the 1980s, a Brazilian study that evaluated children in contact with sick adults showed an inverse relationship between age and TB. However, the types of TB were not described, nor were any correlations drawn between these factors and the nutritional status of the children[25].

Data on co-infection with HIV are always relevant. In the present study, 25% positivity among the children tested is alarming, especially because the risk of rapid evolution of TB is higher among these patients, as well as the fact that they are more likely to become infected by more resistant strains. We did not evaluate bacterial resistance in our study since it has low incidence in Brazil (about 1%), and culture is not a routine procedure. In another study conducted in South Africa, the authors reported that adult patients co-infected with HIV are more likely to present resistant strains isolated in cultures, and that children living in close quarters with these adults may be contaminated with germs having the same sensitivity profile[17]. In poor countries or in countries where prevalence is high, every ill patient must be submitted to serological tests for HIV[1]. In the present study, only two-thirds of the children evaluated were submitted to this test.

Among the complementary tests, the TT proved to be useful since more than two-thirds of the children submitted to the test had reactions of larger than 10-mm induration. The data from the present study reinforce the usefulness of strong TT reaction as an adjunctive diagnostic indicator in children whose received the BCG vaccination more than 24 months prior to the test. However, this practice is not recommended by either the *Secretaria da Saúde do Estado do Rio Grande do Sul* (Rio Grande do Sul State Department of Health) or the national *Ministério da Saúde* (Ministry of Health). Some studies carried out in countries with limited resources have shown that the TT is useful for the investigation of children suspected of having TB, without regard for their vaccination status. Some authors have recommended raising the cutoff point to 15 mm when defining positive results in vaccinated children[9,24]. Even using this higher cutoff point, half of the children in the present study would be considered positive.

Although positivity from direct sputum smear microscopy is low in children, we identified *M. tuberculosis* in 26% of the children who were submitted to this test. Sputum could be collected only from children older than 6. Their X-rays also revealed mainly cavitations or consolidations. These findings are important and we recommend sputum testing when children over the age of 6 are suspected of having TB, bearing in mind that patients presenting positive results from sputum smear microscopy can contaminate other individuals.

The traditional diagnostic imprecision in the detection of pulmonary TB in children, due to the absence of positive results from sputum smear microscopy, may call into question several cases included in the present study. However, those patients, when submitted to Sant'Anna[13] scoring, scored more than 30 points, indicating a very likely, or at least

possible, diagnosis of TB. This leads us to believe that those cases did, in fact, represent children with pulmonary TB.

An interesting finding of our study was that there were few positive results in the testing of gastric aspirate. This procedure was performed in 20 children younger than 24 months of age, and there was only one positive result. This can be explained by technical failures in the performance of the test. Specific guidelines, which have not yet been defined, for the use of this test as a routine procedure in hospitals, are needed in order to increase its efficiency. Azambuja, in a study carried out in Porto Alegre in the 1980s, directed the collection of specimens and achieved a more than 50% rate of positivity. When the author became disassociated from supervising the collection of samples and the test came to be routinely used in the hospital, the number of positive results progressively decreased, sinking to as low as 10% in recent years[21].

Parents and other relatives living in the home with children are still the most common vectors of contagious diseases. Various studies conducted since the 1950s have confirmed this[10,11,18,25]. However, some recent studies using genotypic identification of mycobacteria showed that, in highly populated areas, contact with adults in the home is not always the true TB vector[22,26]. Most of the children evaluated in the present study regularly visited places outside of their homes. Considering that their neighborhoods were the most highly populated as well as being those where the prevalence of TB was the highest in Porto Alegre, we cannot rule out the possibility that adults other than those identified could have infected these children. We highlight the fact that, in 7 cases, we identified more than one contagious adult with whom the child may been in contact. Contact with parents was found to be the most common source of contamination in children younger than 4. This is compatible with the fact that virtually all of those children live with their parents. This was also the finding of a national study conducted in the 1980s and involving a large number of cases of children in contact with adults diagnosed with TB. The higher the incidence of TB was, the younger the children were and the closer the family relationship was (father or mother)[25].

As expected, we found a high prevalence of TB/HIV co-infection (43%) in the evaluation of the infected adults. This value is similar to those obtained in other studies conducted in Brazil and other countries[3,27-29]. High incidence of alcoholism and drug addiction was also of interest. All drug addicts but one tested positive for HIV in the ELISA. There were no significant differences in gender, age or schooling between HIV-positive and HIV-negative groups. In contrast, a national study conducted in the 1980s and 1990s that showed a higher prevalence of HIV positivity in males younger than 30 with less than 8 years of schooling[30]. This discrepancy may be attributable to the small number of cases evaluated in our study.

A higher incidence of TB among young males of low socioeconomic status has also been reported in other studies[23,27,31]. Infection of these individuals in their productive prime is worrisome and justifies the mobilization of health organizations to control the disease.

The high incidence of children diagnosed prior to the diagnosis of the corresponding adult who was the probable source of infection is alarming. Those adults were diagnosed during, and as a result of, the investigation of the children. Therefore, a significant number of adults had been symptomatic for a long time and had infected the children, allowing the disease to spread. This indicates an inversion of the standard protocol of TB control programs, which is to prioritize the identification of symptomatic adults. In 1999, Ruffino-Neto shed light on this issue by reporting that, over the preceding five years, the estimated number of TB cases identified in Brazil had decreased significantly – to less than 65%[4]. Although other authors have claimed that this value was underestimated[2], we are still concerned about the significant number of adult TB cases that go undiagnosed.

Sant'Anna highlighted the fact that the investigation of TB in children in contact with contagious adults is one of the most easily executed strategies used in TB control[13]. In the present study, most of the contagious adults identified had been sick for more than 3 months, and there was high incidence of positive results (75%) from sputum smear microscopy, showing that they were highly contagious. Although there was more than one

child living in most (78%) of the homes, less than half of the cohabiting children were examined, providing evidence that this strategy is not being applied.

The current polices of TB control programs – both state and federal – focus on the evaluation and treatment of symptomatic adults. There is little concern about TB in children. When children younger than 15 are infected, the Rio Grande do Sul State Department of Health recommends the investigation of only those contacts that are symptomatic[32]. However, the First Brazilian Consensus Statement on Tuberculosis[12] and the national Ministry of Health[33] recommend the investigation of all contacts, even if they are asymptomatic, using chest X-rays if possible. Use of the TT is not recommended in the case of vaccinated adults, since it delays diagnosis and may explain why most of our cases (82%) were diagnosed while hospitalized. These patients, when symptomatic, already presented more severe symptoms. Studies in countries where all contacts are investigated have shown that children are predominantly diagnosed early and as outpatients[10,31,34].

··We propose a new design for the investigation of children in contact with contagious adults. In children who received the BCG vaccine less than 2 years prior, TT response should be considered positive if larger than 15 mm, and if larger than 10 mm in those who were vaccinated more than 2 years prior (Figure 3).

We conclude that individuals in frequent contact with children in the home, especially parents, are still the most likely vectors of infection. We recommend the investigation of all contagious adults in contact with children in the home, without regard for their vaccination status, and the active investigation of all possible contamination foci associated with those children who are diagnosed with TB. We also recommend frequent evaluation of co-infection with HIV. The TT is very useful, even in vaccinated children, and direct sputum smear microscopy is efficient in children over the age of 6. It is important to reassess protocols for the investigation and treatment of latent infection in children because many of them have been diagnosed with TB prior to identification of the corresponding contagious adults, especially since most of those children were diagnosed only after being hospitalized. We propose that a new protocol, involving systematic use of TT and chest X-ray, be created for the assessment of asymptomatic children in contact with contagious adults.

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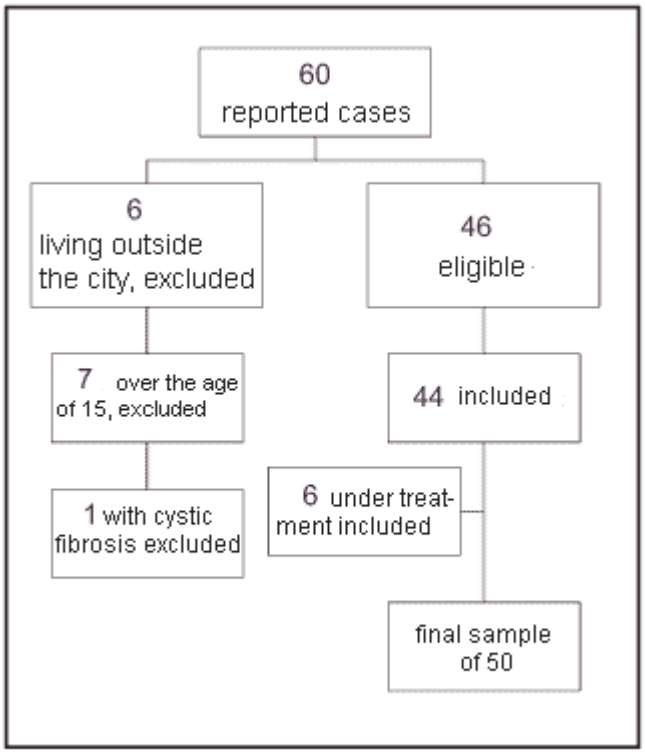

Figure 1. Sample selection

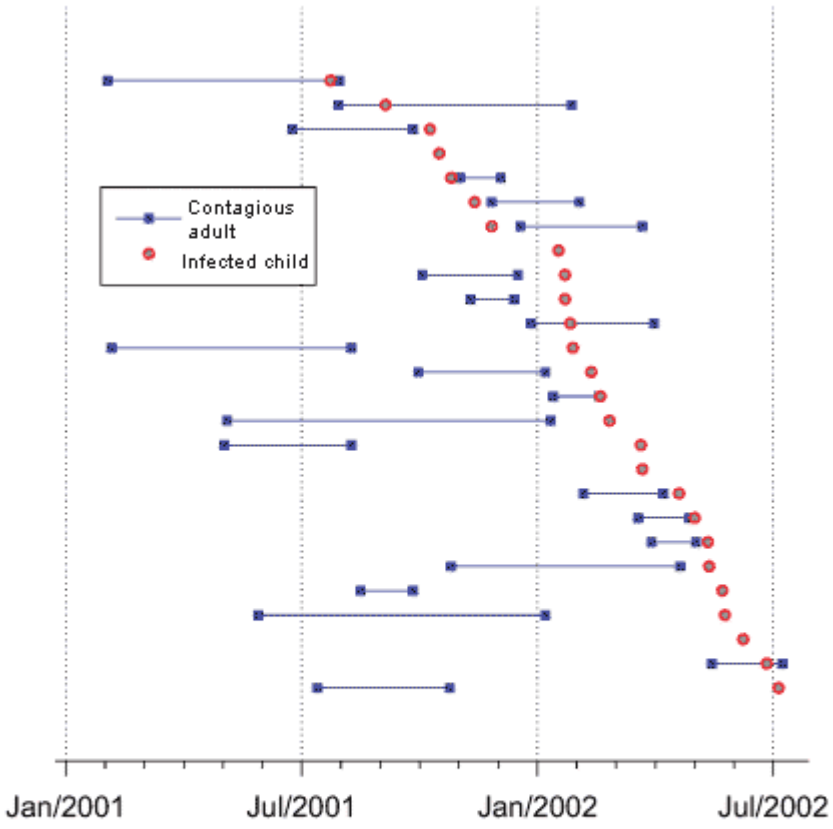

Figure 2: Temporal relationship between diagnosis of the child and that of the adult. The starting point of each line represents the onset of symptoms in the adult, and the end point represents the time of diagnosis. Each ball represents the time at which the child was diagnosed.

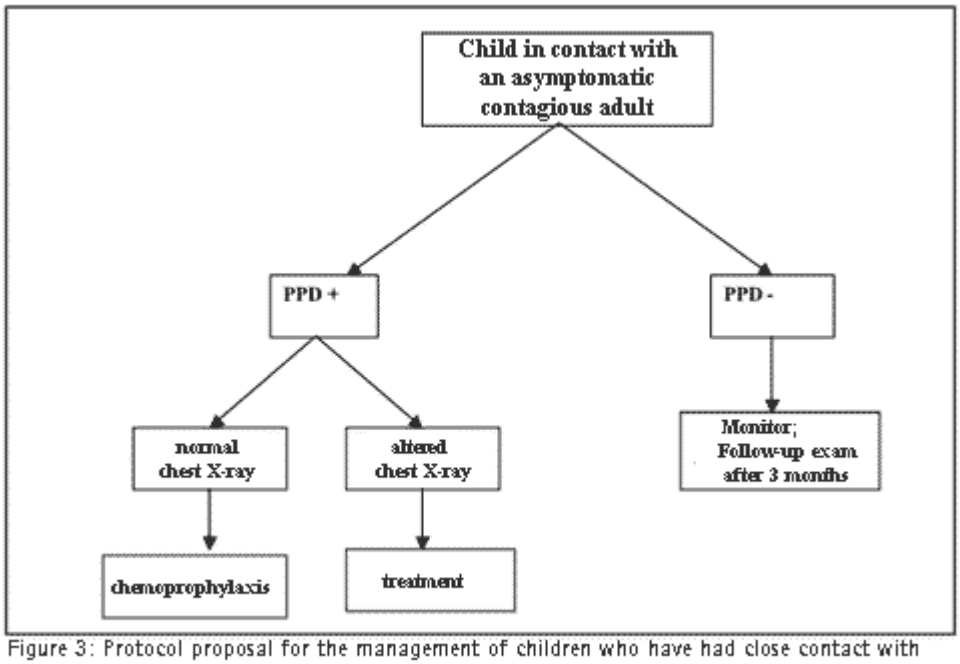

Figure 3: Protocol proposal for the management of children who have had close contact with contagious adults

TABLE 1
Characteristics of children diagnosed with tuberculosis

Characteristic	number (%)
Age	
<1	5 (10)
1 to 4	16 (32)
> 4	29 (58)
Gender	
male	20 (40)
female	30 (60)
Race	
Caucasian	29 (58)
Black	18 (36)
Mixed	3 (6)
BCG Vaccination*	43 (88)
BCG Vaccination scar*	35 (71)
Pulmonary TB	19 (38)
Extrapulmonary TB	31 (52)

*Data available from 49 children
BCG: Bacillus Calmette Guérin; TB: tuberculosis

TABLE 2
Radiographic findings in children with tuberculosis

Finding	number (%)
Mediastinal adenopathy	11 (27)
Adenopathy + consolidation	9 (23)
Consolidation	7 (17)
Miliary pattern	5 (13)
Cavitation	4 (10)
Pleurisy	4 (10)

TABLE 3
Nutritional state (weight/age) of children with tuberculosis

Characteristic	Percentile < 10% (n = 13) ratio (%)	Percentile > 10% (n = 31) ratio (%)	p^*
ELISA HIV+**	4/9 (40)	2/20 (10)	0.05
Extrapulmonary presentation	2/13 (15)	8/30 (27)	0.35
Female	8/13 (62)	18/31 (58)	0.83
Caucasian	10/13 (77)	16/28 (57)	0.80
Over 4 years of age	6/13 (46)	9/31 (29)	0.13

*Fisher's exact test
**29 patients were submitted to the test

TABLE 4
Characteristics found in children in relation to the identification of contacts

Characteristic	Identified contact (n = 39)	Unidentified contact (n = 11)	p^*
	number (%)	number (%)	
Age			
< 1		4 (10)	1 (9)
1-4	13 (33)	3 (27)	0.69
> 4	22 (57)	7 (64)	0.66
Gender			
male	15 (38.5)	6 (55)	
female	24 (61.5)	5 (45)	0.34
Race			
Caucasian	24 (61.5)	5 (45)	
African-descent	13 (33)	5 (45)	0.40
BCG Vaccination**	32 (84)	11 (100)	0.20
BCG Vaccination scar**	29 (76)	6 (55)	0.15
ELISA HIV+†	7 (27)	1 (17)	0.50
Place of diagnosis			
Outpatient clinic	8 (21)	1 (17)	
Hospital	31(79)	10 (83)	0.35
Mantoux test response ⩾ 10 mm	26 (76)	3 (33)	0.02
	mean ± SD	mean ± SD	
Time since vaccination (in months)‡	45.8 ± 31.8	50.5 ± 40.6	0.02

*Student's t-test, Chi-square test or Fisher's exact test
**data available from 49 patients
†32 children submitted to the test; ± 33 children submitted to the test
‡data available from 44 children
BCG: bacillus Calmette Guérin; SD: standard deviation

TABLE 5
Characteristics of the contagious adults identified

Characteristic	
Mean age	32.2
	ratio (%)
Male gender	22/39 (56)
Caucasian	22/39 (56)
Habits	
Smoking	26/39 (67)
Alcoholism	17/39 (44)
Drug addiction	9/39 (23)
ELISA HIV+	13/30 (43)
	mean ± SD
Years of schooling*	8.5 ± 15.89
Duration of symptoms†	5 ± 4.08
	number (%)
Relationship	
father	9 (23)
mother	7 (18)
uncle/aunt	6 (15)
sibling	5 (13)
grandparent	4 (10)
not related	8 (21)

*data available from 35 patients
†data available from 33 patients
SD: standard deviation