UNIVERSITE DE LAUSANNE – FACULTE DE BIOLOGIE ET DE MEDECINE
DEPARTEMENT MEDICO-CHIRUGICAL DE PEDIATRIE
HÔPITAL DE L'ENFANCE
Directeur médical : Prof. Sergio Fanconi
Médecin chef : Docteur Mario Gehri, PD et MER

Risk factors for positive tuberculin skin tests among migrant and resident children in Lausanne, Switzerland

THESE

préparée sous la direction du Dr Jean-Pierre Zellweger,
chargé de cours, médecin adjoint

et présentée à la Faculté de biologie et de médecine de l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

Elsa COLLET

Médecin diplômée de la Confédération Suisse
Originaire de Penthéréaz/Suchy (Vaud)

Lausanne
2006

Résumé en français

Cadre : Policlinique pédiatrique à Lausanne en Suisse, pays rencontrant une proportion importante de tuberculose au sein de la population de migrants.

But : Déterminer les facteurs de risque associés à un test tuberculinique positif (ou test de Mantoux), notamment l'influence du BCG (Bacille Calmette Guérin) et d'un contact avec un personne ayant une tuberculose active. Les patients concernés étaient des enfants examinés dans le cadre d'un contrôle de santé ou dans le cadre d'une étude d'entourage d'un cas déclaré de tuberculose.

Méthode : Etude descriptive comprenant des enfants ayant eu un test tuberculinique (2 unités RT23) entre novembre 2002 et avril 2004. L'âge, le sexe, l'anamnèse de contact avec une personne ayant une tuberculose active, la vaccination par le BCG, le pays d'origine et le lieu de naissance (en Suisse ou hors de la Suisse) étaient répertoriés.

Résultats : Parmi les 234 enfants de l'étude, 176 (75%) avaient une réaction tuberculinique égal à zéro et 31 (13%) avaient une réaction positive (> 10mm). Dans le modèle de régression linéaire, la taille de la réaction tuberculinique variait significativement selon l'anamnèse de contact avec une personne ayant une tuberculose active, l'âge, l'incidence de la tuberculose dans le pays d'origine et la vaccination par le BCG. Le sexe ou le lieu de naissance n'influençait pas la taille de la réaction.
Dans le modèle de régression logistique incluant toutes les valeurs répertoriées, les paramètres significativement associés avec un Mantoux positif étaient l'âge (Odds Ratio = 1.21, 95% CI 1.08 ; 1.35), l'anamnèse de contact avec une personne ayant une tuberculose active (OR = 7.31, 95% CI 2.23 ; 24) et l'incidence de la tuberculose dans le pays d'origine (OR = 1.01, 95% CI 1.00 ; 1.02). Le sexe (OR = 1.18, 95% CI 0.50 ; 2.78) et la vaccination par le BCG (OR = 2.97, 95% CI 0.91 ; 9.72) n'étaient pas associés avec une réaction tuberculinique positive.

Conclusions : L'incidence de la tuberculose dans le pays d'origine, la vaccination par le BCG et l'âge influencent le test de Mantoux (taille ou proportion de réaction > 10mm). Toutefois, le facteur de risque le plus important d'avoir une réaction tuberculinique positive est l'anamnèse de contact avec une personne ayant une tuberculose active.

Risk factors for positive tuberculin skin tests among migrant and resident children in Lausanne, Switzerland

E. Collet[a], *J.-D. Krahenbuhl*[b], *Mario Gehri*[a], *A. Bissery*[b], *Jean-Pierre Zellweger*[c]

[a] University Children's Hospital, Lausanne, Switzerland
[b] University Institute of Social and Preventive Medicine, Lausanne, Switzerland
[c] University Medical Polyclinic, Lausanne, Switzerland

Summary

Setting: Ambulatory paediatric clinic in Lausanne, Switzerland, a country with a significant proportion of tuberculosis (TB) among immigrants.

Aim: To assess the factors associated with positive tuberculin skin tests (TST) among children examined during a health check-up or during TB contact tracing, notably the influence of BCG vaccination (Bacille Calmette Guérin) and history of TB contact.

Method: A descriptive study of children who had a TST (2 Units RT23) between November 2002 and April 2004. Age, sex, history of TB contact, BCG vaccination status, country of origin and birth outside Switzerland were recorded.

Results: Of 234 children, 176 (75%) had a reaction equal to zero and 31 (13%) tested positive (>10 mm). In a linear regression model, the size of the TST varied significantly according to the history of TB contact, age, TB incidence in the country of origin and BCG vaccination status but not according to sex or birth in or outside Switzerland. In a logistic regression model including all the recorded variables, age (Odds Ratio = 1.21, 95% CI 1.08; 1.35), a history of TB contact (OR = 7.31, 95% CI 2.23; 24) and the incidence of TB in the country of origin (OR = 1.01, 95% CI 1.00; 1.02) were significantly associated with a positive TST but sex (OR = 1.18, 95% CI 0.50; 2.78) and BCG vaccination status (OR = 2.97, 95% CI 0.91; 9.72) were not associated.

Conclusions: TB incidence in the country of origin, BCG vaccination and age influence the TST reaction (size or proportion of TST ≥10 mm). However the most obvious risk factor for a positive TST is a history of contact with TB.

Key words: tuberculosis; children; immigrants; Switzerland; tuberculin skin test

Introduction

In Switzerland, during the year 2004, 601 new cases of TB were declared to the Swiss Federal Office of Public Health, representing an incidence rate of approximately 8/100,000 inhabitants. The majority of TB cases were found among foreign-born persons, including recent immigrants. Among those, an important proportion of cases involved young adults and children. 47 (8%) patients were less than 20 years old and 11 (2%) less than 4 years old [1]. To date, 132,000 recent legal immigrants are living in Switzerland [2]. Approximately 70,000–180,000 estimated illegal immigrants from moderate to high TB incidence countries can be added to this number [3]. Consequently, our country is directly involved in TB control, especially in the paediatric age group.

Among children infected with *Mycobacterium tuberculosis*, 95% will not present active infection (i.e. pulmonary or miliary disease, meningitis or osteomyelitis) but a latent disease called Latent Tuberculosis Infection (LTBI). 5–10% of these children in apparent good health will go on to develop active disease, half of them in the following two years. The identification of these patients with LTBI, representing a reservoir of *M. tuberculosis*,

Glossary

TB	Tuberculosis
LTBI	Latent Tuberculosis Infection
TST	Tuberculin Skin Test
BCG	Bacillus Calmette-Guérin
HEL	Hôpital de l'Enfance de Lausanne, University Children's Hospital
WHO	World Health Organization

No financial support declared.

has been regarded as an essential part of the global control programme in countries with a low TB incidence [4] and for almost 100 years has been largely dependent on the Tuberculin Skin Test (TST). Appropriate interpretation of TST is therefore crucial. The major factors, described as influencing the TST, are *M. tuberculosis* infection (acquired by a contact with a person suffering from active TB), BCG (Bacille Calmette Guérin) immunization and cross reaction with other non-tuberculous environmental mycobacteria.

A recent case-control study was performed in several primary care clinics among Hispanic children in New York City. Contact with an adult with a positive TST (≥10 mm) or with active TB was the most significant predictor of a positive TST in children. Previous BCG vaccination itself was not a risk factor [5]. However, BCG immunization has been described as a confounding factor in many articles and is considered to represent a constant problem in the interpretation of a TST reaction. The proportion of positive TST after BCG vaccination has been reported to vary from 0% [6] to 90% [7].

Cross reaction with non-tuberculous mycobacteria depends on the environment and consequently differs from one population to another [8–11].

Most of these studies were carried out among schoolchildren and young adults living in countries with a low TB incidence. However, since the positive predictive value of the TST depends on the prevalence pre-test, it is affected by the country of origin. When screening a Canadian-born population, it may range from 17% to 78% among recent immigrants from TB endemic regions [12].

The number of immigrant children is increasing in all European countries but, to our knowledge, there are no systematic european studies of the risk factors for positive TST reaction in children. The aim of our study was to evaluate the effect of age, sex, foreign origin, birth outside of Switzerland, contact with an adult suffering from TB and BCG immunization status on TST reaction in such a population. The determination of these parameters could help clinical staff to interpret the TST reaction and guide them through the treatment decision process.

Participants and methods

Study design

A descriptive study of all children who received a TST at the outpatient clinic of the Hôpital de l'Enfance de Lausanne (HEL) was conducted between November 2002 and April 2004. During the study period, a complete dataset was obtained for each child who had a TST.

Study site

The outpatient clinic of the Hôpital de l'Enfance de Lausanne (HEL). In 2001, the outpatient clinic of the HEL received 35'000 patients of whom 70% were immigrant children. Approximately 200 TST per year were performed among them.

Indications to TST

In accordance with the national guidelines of the Swiss Lung Association, TST is currently only used for detection of LTBI in immigrant children, in children of foreign workers (at least one foreign-born parent) and for TB contact tracing [13].

Exclusion criteria

Immunodeficient patients and patients known to have an exaggerated TST reaction were excluded.

TST methodology

Patients underwent an intradermal injection of 2 TU of RT23 Copenhagen (bioequivalent to 5 TU of PPD-S). The transverse diameter of the induration (and not the erythema) was measured 48–72 hours later by the clinic physician. Reactions were considered to be positive with an induration of ≥10 mm [13].

Data collection

During the visit, the physician completed a standardised questionnaire on demographic characteristics, foreign birth or origin, previous TST, BCG vaccination and contact with a person suffering from TB.

The history of contact with a TB case was reported as "yes", "no" or "unknown", if the patient did not remember. For our analysis, we considered only two categories: "known" and "not known" ("no" and "unknown"). The notification of the BCG status was based on the presence of a BCG scar or according to the vaccination booklet [14–16]. It was reported as "yes", "no" or "several" if the child had more than one documented BCG vaccination. The children were distributed into five age categories (0–2, 3–5, 6–8, 9–11, 12–16 years). We classified the countries of origin into nine categories according to the classification of the Global TB Control WHO Report 2004. For each country of origin, the TB incidence rate (case notification rates) was extracted from the above report [17].

Follow-up of the patients

Following the guidelines of the Swiss Lung Association, children with a TST ≥10 mm underwent a chest X-ray. Gastric fluid was obtained on three separate mornings for culture and PCR, if the standard chest X-ray was abnormal. The detailed history of a TB contact was further investigated. Children with a TST ≥10 mm and normal chest x-rays were considered to have LTBI and were treated with isoniazid 10 mg/kg/day for nine months, with monthly follow-up. Equivocal cases were discussed with a specialist for respiratory medicine.

Data analysis

Data were entered and managed in a FileMaker Pro 4.1 database and analysed using Stata 8.0. Firstly, we performed a descriptive analysis of the demographic characteristics. The results for quantitative variables are given as mean (standard deviation) unless stated otherwise. Secondly, we considered two different analyses to identify independent factors associated with TST size and positivity.

The first model was a multivariate linear regression with TST size as a linear response and the second was a multivariate logistic regression with TST as a binary re-

sponse variable: TST size inferior, superior, or equal to 10 mm. Both these models were useful. The first one was more powerful and the second one was more convenient, as this 10 mm cut-off is commonly used by physicians to establish a diagnosis. The potentially confounding factors were set as predictor variables in both models: age (in years), sex, history of contact (known versus no or unknown), BCG vaccination, TB incidence rate in country of origin and native country (Switzerland versus other) and an interaction term between BCG and history of contact.

BCG vaccination was a three categorical variable: one, several or no vaccination. Since there were few children with several vaccinations, we did a sensitivity analysis to decide on the most appropriate coding of BCG. We then compared the model using BCG as a three categorical variable with the one using BCG as a binary variable. As the second model was nested in the first one, we used a likelihood ratio test to compare these models. These sensitivity analyses helped us to decide on the most appropriate coding of BCG.

Ethical consent

The study was reviewed and approved by the local Ethical Committee (Comité d'éthique de la recherche clinique, Faculté de médecine de Lausanne).

Results

Between November 2002 and April 2004, we recorded 241 TST in 241 children. We excluded seven children because we were unable to determine their BCG vaccination status and therefore 234 children remained in the sample. There were 198 (85%) immigrant children (foreign born). Among the children born in Switzerland, 28 (12%) were children of foreign-born parents, 6 (2%) were included in a contact tracing and 2 (1%) had recurrent symptoms. No children presented exclusion criteria.

Demographic characteristics of the study population.

Results are given as means (standard deviation) unless stated otherwise.

The study population was composed of 113 (48%) males and 121 (52%) females. The mean age of the children was 8 (4) years. Males were 9 (4) years old and females 7 (4) years old.

157 (67%) children had been vaccinated with BCG, of which 9 (4%) had been vaccinated several times. The children with several BCG were 12 (3) years old, which is older than the children who had been vaccinated only once or not at all, respectively 8 (4) and 8 (5) years old. The proportion of subjects with several BCG vaccinations was greater among males (8 males for 1 female).

21 (9%) children had a history of contact.

Although most of the children came from Established Market Economy countries and Latin America, there were children from all main regions in the world.

Chest X-ray were performed in 40 patients (indications for children with a TST <10 mm were symptoms suggesting another pulmonary disease). One gastric fluid culture was performed and was negative.

Descriptive analysis of the factors associated with TST

Results of sex distribution, age, BCG vaccination status, history of contact, country of origin and native country for all children are reported in table 1. The table also shows the size of TST and the proportion of TST <10 mm and TST ≥10 mm according to these factors. The size of the TST was inhomogeneous with 176 (75%) TST equal to 0 mm, 28 (12%) between 0 and 10 mm and 30 (13%) equal to or greater than 10 mm. The mean size of TST in the children with a TST ≠ 0 was 11 (7) mm.

Linear and logisitic regression analysis of risk factors.

Table 2 and 3 present both final models.

In the sensitivity analysis, no differences between parameter estimates were detected using models with or without the 9 children with several BCG vaccinations, for both linear and logistic models. Furthermore, the likelihood ratio test was not statistically significant for both models. Finally, a binary coding was chosen for BCG.

In the linear regression model, the history of contact (coefficient 7.06, 95% CI 3.81; 10.3), age (0.33, 95% CI 0.16; 0.50), incidence rate in the native country (0.025, 95% CI 0.01; 0.04) and BCG vaccination (1.74, 95% CI 0.02; 3.46) were independent risk factors associated with larger TST reactions. We added an interaction term between BCG and history of contact, which was significant in this analysis (–5.95, 95% CI –10.7; –1.16), and calculated the coefficient of mean increase of the TST reaction with contact and vaccination (7.06 + 1.74 – 5.95 = 2.85).

In the logistic regression model, the factors significantly associated with a positive TST were history of contact (Odds Ratio = 7.31, 95% CI 2.23; 24), age (OR = 1.21, 95% CI 1.08; 1.35) and incidence rate in the country of origin (OR = 1.01, 95% CI 1.00; 1.02). BCG vaccination was not an independent factor (OR = 2.97, 95% CI 0.91; 9.72). The interaction term between BCG and history of contact was not significant.

We added a second interaction term between BCG and age, which was not significant in either model. We compared the models with and without interaction term using a likelihood ratio test. The nested models with the interaction term were not better than the other models.

Table 1

Descriptive analysis of the study population.

	n (%)	TST size = 0 mm n (%)	TST size ≠ mm n (%)	TST size ≠ (mm) TST size (mm) Mean (SD)	TST size ≠ (mm) TST <10 mm n (%)	TST size ≠ (mm) TST ≥10 mm n (%)
All children	234 (100)	176 (75)	58 (25)	11 (7)	27 (47)	31 (53)
Sex						
Female	121 (52)	95 (79)	26 (21)	11 (7)	11 (42)	15 (58)
Male	113 (48)	81 (72)	32 (28)	10 (7)	16 (50)	16 (50)
Age groups, years						
0–2	32 (14)	23 (72)	9 (28)	5 (5)	7 (78)	2 (22)
3–5	49 (21)	43 (88)	6 (12)	9 (3)	3 (50)	3 (50)
6–8	61 (26)	49 (80)	12 (20)	11 (7)	5 (42)	7 (58)
9–11	44 (19)	36 (82)	8 (18)	10 (7)	5 (63)	3 (37)
12–16	48 (20)	25 (52)	23 (48)	14 (7)	7 (30)	16 (70)
BCG vaccination						
No	77 (33)	62 (80)	15 (20)	14 (10)	5 (33)	10 (67)
One	148 (63)	109 (74)	39 (26)	10 (6)	21 (54)	18 (46)
Several	9 (4)	5 (56)	4 (44)	11 (4)	1 (25)	3 (75)
History of contact						
No or unknown	213 (91)	163 (77)	50 (23)	10 (6)	27 (54)	23 (46)
Known	21 (9)	13 (62)	8 (38)	18 (7)	0	8 (100)
Country of origin (incidence rates per 100000: median[range]))						
Africa (228 [32;250])	27 (12)	13 (48)	14 (52)	14 (8)	5 (36)	9 (64)
Central Europe (40 [19;41])	24 (10)	19 (79)	5 (21)	8 (7)	3 (60)	2 (40)
Eastern Europe (86 [82;89])	4 (2)	3 (75)	1 (25)	14	0	1 (100)
Eastern Mediterranean (27 [16;77])	12 (5)	9 (75)	3 (25)	19 (9)	0	3 (100)
Established Market Economy * (8 [8;44])	50 (21)	46 (92)	4 (8)	13 (8)	1 (25)	3 (75)
Latin America (46 [16;135])	110 (47)	81 (74)	29 (26)	9 (5)	16 (55)	13 (45)
South East Asia (101 [80;101])	5 (2)	4 (80)	1 (20)	4	1 (100)	0
Western Pacific (78 [36;119])	2 (1)	1 (50)	1 (50)	7	1 (100)	0
Native country						
Switzerland	36 (15)	34 (94)	2 (6)	20 (3)	0	2 (100)
Other	198 (85)	142 (72)	56 (28)	11 (7)	27 (48)	29 (52)

* Australia, Austria, Belgium, Canada, Czech Rep, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Japan, Luxembourg, Netherlands, New Zealand, Norway, Portugal, Singapore, Spain, Sweden, Switzerland, United Kingdom, United States.

Table 2

Linear regression analysis of risk factors for Tuberculin Skin Test size.

Variable	Coefficient	CI 95%
Age (years)	0.33	[0.16; 0.50]
Sex (male/female)	0.24	[–1.12; 1.61]
Contact (yes/no or unknown)	7.06	[3.81; 10.3]
BCG vaccination (yes/no)	1.74	[0.02; 3.46]
TB incidence rate in country of origin (per 100000)	0.025	[0.01; 0.04]
Native country (Switzerland/other)	0.63	[–1.60; 2.85]
BCG*contact *	–5.95	[–10.7; –1.16]

BCG = Bacille Calmette Guérin, TB = Tuberculosis

* Interaction term between BCG vaccination and history of contact

Table 3
Logistic regression analysis of risk factors for positive Tuberculin Skin Test.

Variable	Odds ratio	CI 95%
Age (years)	1.21	[1.08; 1.35]
Sex (male/female)	1.18	[0.50; 2.78]
Contact (yes/no or unknown)	7.31	[2.23; 24]
BCG vaccination (yes/no)	2.97	[0.91; 9.72]
TB incidence rate in country of origin (per 100000)	1.01	[1.00; 1.02]
Native country (Switzerland/other)	0.92	[0.17; 5.07]

BCG = Bacille Calmette Guérin, TB = Tuberculosis

Discussion

According to the Global TB Control Program WHO, targeting screening of LTBI on the high-endemic paediatric population is essential. Infected children are an important source of future active TB and the youngest are at higher risk of serious disseminated disease. In Switzerland, it is known that in a population of 15 year-old children, the foreign borns have a prevalence of positive TST approximately twofold higher than indigenous children [18]. However, to our knowledge, our study is the only study in Switzerland, or even in Europe, of the major factors associated with positive TST in children.

The most obvious risk factor for a positive TST in our study was a history of TB contact. Large or strongly positive TST reactions are commonly associated with exposure to a person suffering from active TB [19]. In addition, the proximity of the contact case is a known risk factor for infection [20]. We also showed that coming from countries with a high TB incidence, such as those in Africa (32–250/10000), is a risk factor for a TST ≥10 mm. These findings emphasize the importance of inquiring about previous domicile and travel and of targeting surveillance on this particular child population.

In a population of migrant children, BCG coverage is commonly high (67% in our study with 85% of migrant children) and influence of vaccination on the TST reaction is a recurrent difficulty for the medical team. The 10 mm cut-off point for positive TST that we considered in our study is an arbitrary value. This is the value used in the clinical practice and recommended for the detection of paediatric TB infection and the indication for chemopreventive treatments and follow-up [13]. Our study was not designed or powered to look for different cut-off points. BCG vaccination had some influence on the size of the reaction but was not an independent risk factor for a positive TST (i.e. TST ≥10 mm). One possible explanation of this could be that previous BCG increases the size of TST reaction but that this increase is limited to values of less than 10 mm. The corollary would be that TST reactions ≥10 mm are influenced only by the history of contact, the country of origin or the age. Several more powerful studies demonstrate that the reactivity of young subjects, who received BCG vaccination at birth, is not significantly different from unvaccinated subjects [12, 14, 15, 21]. On the other hand, subjects vaccinated after the age of one year may present a persistently positive TST [7, 12, 22]. Wang's recent meta-analysis suggests that, in subjects without active TB, previous BCG immunization (in infancy) significantly increases the likelihood of a TST ≥10 mm for as long as 15 years and that the risk factors for infection and the clinical context modify the interpretation of the TST [23]. In our study, we assume that most children had been vaccinated at birth, according to the WHO recommendations [24], very likely strengthening the findings that BCG at birth does not influence TST reaction after the first year of life. However, in the logistic regression model, the CI 95% for the OR of the BCG vaccination was wide so that another explanation could be that our study has insufficient power. With more subjects, the proportion of TST ≥10 mm in vaccinated children could well be significant.

We found a significant interaction between BCG and history of contact. The mean increase of the TST size reaction due to history of contact is smaller in vaccinated children than in non vaccinated children. This suggests that BCG could have a limited protective effect against LTBI and haematogenous dissemination from the lungs. This observation has already been reported in several animal studies such as the Fox study, which demonstrates the absence of haematogenous seeding in BCG vaccinated guinea pigs [25]. This interaction term is not significant in the logistic regression model as it is less powerful than the linear regression.

The children who received more than one BCG vaccination (i.e. the first BCG at birth, the second one at the age of 6–7 years) seem to present a larger mean size of induration of the TST and a larger proportion of TST ≥10 mm than the children vaccinated only once, but they were too few in our study (9 children) to demonstrate a significative difference. However, as confirmed by other larger studies, the effect of multiple BCG immunizations on the TST has to be kept in mind [26].

We showed that increasing age was a risk factor for TST ≥10 mm, independently of known con-

tact with a person suffering from TB. We also observed a significant increase of the TST size with increasing age. This could be due to a longer period of potential contact with TB, as demonstrated in a Canadian study of a population of non BCG vaccinated school-children, health professional students and young adult workers [27], even when the contact is unknown or undocumented. This may also be explained by cross-reaction with non tuberculous Mycobacteria, as postulated in another Canadian study in which a double injection of PPD-T and PPD-B was used to demonstrate that some positive TST reactions were due to cross-reaction with environmental mycobacterial antigens [28]. We introduced an interaction term between BCG and age. It was neither significant in the linear nor in the logistic regression, suggesting that the mean increase of the TST reaction size with age is the same in vaccinated and unvaccinated children. Indeed, the effect of BCG received at birth is known to wane rapidly with age, as demonstrated in the Lifschitz study, ranging from 50% of skin tests ≥10 mm at 6 months of age to 0% after one year [6].

In our population of children up to 16 years of age, sex was not an independent risk factor. This seems to be different in the adult population where the prevalence of TST ≥10 mm and of TB varies according to sex. This difference in sex ratio between children and adults is well-demonstrated in other studies and is explained by the fact that boys and girls have similar social conditions [19], whereas this is not the case for adult men and women. Cases of tuberculosis among adult women might also have been under-reported in developing regions [29]. However, in our study, the wide confidence intervals, both in the linear and logistic regression, imply that our study is not powerful enough to rule out this sex difference.

This study suffers from several limitations. The first and most important limitation is that it lacks power to detect several risk factors for a greater TST reaction size or TST positivity.

Secondly, we did not compare the results in this population of children composed of a majority of migrant children with a control group of Swiss children, as there is currently no indication to perform TST in this group except for rare contact tracing. A prior study among college students demonstrated that the prevalence of positive TST is higher among foreign-born children than among native Swiss children [18].

Thirdly, we had frequent difficulties in communicating with the foreign patients during our study. Information about TB contact was often not reliable and had, for example, to be detailed by asking about foreign travel in their country, visitors in their house or past living in a refugee camp. For this reason, we chose to consider only information given with sufficient details to be reliable. We may therefore have omitted some possible TB contacts, introducing the possibility of a recall bias. Indeed, subjects with positive TST reaction may be more prone to recall TB contact than those with negative TST. This emphasizes the fact that, in spite of language barriers, an initial precise history requires specific, culturally adjusted questions to investigate history of contact, as suggested in a recent study among Hispanic children performed in New York City [5].

Conclusion

In conclusion, our study shows that the TB incidence in the country of origin, BCG vaccination, as well as age, influence the TST reaction (size or proportion of TST ≥10 mm). However, the most obvious risk factor for a positive TST is a history of contact and this has to be kept in mind when interpreting the TST reaction. The significance of positive TST reactions should be clarified in the near future with a more reliable test, such as one of the new tests relying on the release of gamma-interferon by sensitised lymphocytes.

Acknowledgement

We kindly acknowledge Ms Françoise Gürtner for proofreading and secretarial support.

Correspondence:
Dr Mario Gehri, director
University Children's Hospital
Ch. de Montétan 16
CH-1000 Lausanne 7
Mario.Gehri@chuv.hospvd.ch

References

1 Déclaration obligatoire des maladies infectieuses. Département Fédéral de l'intérieur, Office Fédéral de la Santé Publique, Division d'épidémiologie et des maladies infectieuses 2003.
2 Statistiques en matière d'asile. Département Fédéral de justice et police, Office Fédéral des réfugiés 2003.
3 Piguet E, Cattacin S. Effectif des personnes sans autorisation de séjour en Suisse. Forum suisse pour l'étude des migrations 2001.
4 Broekmans JF, Migliori GB, Rieder HL, Lees J, Ruutu P, Loddenkemper R, et al. European framework for tuberculosis control and elimination in countries with a low incidence. Recommendations of the World Health Organization (WHO), International Union Against Tuberculosis and Lung Disease (IUATLD) and Royal Netherlands Tuberculosis Association (KNCV) Working Group. Eur Respir J 2002;19:765–75.
5 Saiman L, San Gabriel P, Schulte J, Vargas MP, Kenyon T, Onorato I. Risk factors for latent tuberculosis infection among children in New York City. Pediatrics 2001;107:999–1003.
6 Lifschitz M. The value of the tuberculin skin test as a screening test for tuberculosis among BCG-vaccinated children. Pediatrics 1965;36:624–7.
7 Horowitz O B-CK. Correlation between tuberculin sensitivity after two months and five years among vaccinated subjects. Bull WHO 1972;47:49–58.
8 Grange JM. Environmental mycobacteria and BCG vaccination. Tubercle 1986;67:1–4.

9 Kardjito T, Beck JS, Grange JM, Stanford JL. A comparison of the responsiveness to four new tuberculins among Indonesian patients with pulmonary tuberculosis and healthy subjects. Eur J Respir Dis 1986;69:142–5.
10 Report on the 3rd tuberculosis prevalence survey in Korea-1975. Edition 1. Ministry of Health and Social Affairs, Korean Institute of Tuberculosis, Korean National Tuberculosis Association. Seoul: The Korean Institute of Tuberculosis 1976.
11 Styblo K. Preliminary results of the 3rd round of the national tuberculin survey in 19 regions – Tanzania 1993–1997. Tuberculosis Surveillance Research Unit Progress Report 1998;2: 31–66.
12 Menzies R, Vissandjee B. Effect of bacille Calmette-Guerin vaccination on tuberculin reactivity. Am Rev Respir Dis 1992;145: 621–5.
13 Ligne directrices concernant le test tuberculinique. Association Suisse contre la Tuberculose et les maladies Pulmonaires (ATPS), Office Fédéral de la Santé publique (OFSP). Bull OFSP 1997;16:13–4.
14 al-Kassimi FA, al-Hajjaj MS, al-Orainey IO, Bamgboye EA. Does the protective effect of neonatal BCG correlate with vaccine-induced tuberculin reaction? Am J Respir Crit Care Med 1995;152:1575–8.
15 Johnson H, Lee B, Doherty E, Kelly E, McDonnell T. Tuberculin sensitivity and the BCG scar in tuberculosis contacts. Tuber Lung Dis 1995;76:122–5.
16 Smith PG. Epidemiological methods to evaluate vaccine efficacy. Br Med Bull 1988;44:679–90.
17 World Health Organisation W. Global Tuberculosis Control: Surveillance, Planning, Financing. WHO Report 2004, Geneva, Switzerland 2004.
18 Schalcher C, Brändli O, Beran J, Gaze H, de Haller R, Howald H, et al. Tuberkulintests bei Schulabgängern in den Kantonen Bern, Neuenburg und Wallis 1992/1993. Schweiz Med Wschr 1994;124(Suppl):58:18.
19 Lienhardt C, Fielding K, Sillah J, Tunkara A, Donkor S, Manneh K, et al. Risk factors for tuberculosis infection in sub-Saharan Africa: a contact study in The Gambia. Am J Respir Crit Care Med 2003;168:448–55.
20 Zangger E, Gehri M, Krahenbuhl JD, Zuberbuhler D, Zellweger JP. Epidemiological and economical impact of tuberculosis in an adolescent girl in Lausanne (Switzerland). Swiss Med Wkly 2001;131:418–21.
21 al-Kassimi FA, Abdullah AK, al-Orainey IO, Benar AB, al-Hajjaj MS, al-Majed S, et al. The significance of positive Mantoux reactions in BCG-vaccinated children. Tubercle 1991;72: 101–4.
22 Comstock GW, Edwards LB, Nabangxang H. Tuberculin sensitivity eight to fifteen years after BCG vaccination. Am Rev Respir Dis 1971;103:572–5.
23 Wang L, Turner MO, Elwood RK, Schulzer M, FitzGerald JM. A meta-analysis of the effect of Bacille Calmette Guerin vaccination on tuberculin skin test measurements. Thorax 2002; 57:804–9.
24 BCG Vaccine. Weekly epidemiological record 2004; n°4, 79: 25–40.
25 Fox J, Ho R, Arora P, Harding G, Smith D. Host-parasite relationships in experimental airborne tuberculosis. V. Lack of hematogenous dissemination of Mycobacterium tuberculosis to the lungs in animals vaccinated with Bacille Calmette-Guerin. J Infect Dis 1976;133:2.
26 Sepulveda RL, Ferrer X, Latrach C, Sorensen RU. The influence of Calmette-Guerin bacillus immunization on the booster effect of tuberculin testing in healthy young adults. Am Rev Respir Dis 1990;142:24–8.
27 Menzies D, Chan CH, Vissandjee B. Impact of immigration on tuberculosis infection among Canadian-born schdolchildren and young adults in Montreal. Am J Respir Crit Care Med 1997;156:1915–21.
28 Menzies R, Vissandjee B, Amyot D. Factors associated with tuberculin reactivity among the foreign-born in Montreal. Am Rev Respir Dis 1992;146:752–6.
29 Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis 1998; 2:96–104.