Risk Factors for Tuberculosis Infection in Children in Contact With Infectious Tuberculosis Cases in The Gambia, West Africa

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ABSTRACT. *Objective.* **Tuberculosis (TB) infection is highly prevalent in developing countries. As infected children represent a large proportion of the pool from which TB cases will arise, knowledge of the factors that influence TB infection in children are of importance to evaluate transmission of infection in the community and adapt TB control activities. There are limited data on the risk of infection in child populations in developing countries.**

Methods. **We performed a household contact study in The Gambia (West Africa), in which children who were living in contact with individuals who had proven smear-positive pulmonary TB cases were investigated. A questionnaire was addressed to the mother or caregiver of the child to investigate the presence of various risk factors and assess the degree of exposure of the child to the individual with TB within the household. A tuberculin skin test (TST) was performed on each child. TST sizes ≥5 and 10 mm, respectively, were considered positive.**

Results. **Households of 206 TB cases were visited, and 384 children aged <5 years were examined. The median age was 2, and 48% were girls. The distribution of TST responses followed a bimodal pattern, with 135 (35%) children presenting a palpable induration. Random effects logistic regression analysis demonstrated that the risk of positive TST response in the child increased with the geographic proximity of the child to the individual with TB within the household and with the degree of activities shared with the individual with TB. It was also associated with the clinical severity of the disease in the index case. Nutritional status and presence of a bacille Calmette-Guérin (BCG) scar were not independent risk factors for TST positivity in this population. On multivariate analysis, the effect of geographic proximity to the individual with TB, household size, and duration of cough in the index case persisted for TST responses ≥5 mm.**

Conclusions. **In a highly endemic country with high BCG vaccination coverage in Africa, TB infection in children who were in contact with individual with infectious TB was directly related to the intensity of exposure of the child to the individual with TB. Our data suggest that a positive TST in a child reflects most probably TB infection rather than previous BCG vaccination. Contact tracing can play a major role in the control of TB in developing countries.** *Pediatrics* **2003;111:e608–e614. URL: http://www.pediatrics.org/cgi/content/full/111/5/e608;** ***tuberculosis infection, child, tuberculin skin test, Mantoux test.***

ABBREVIATIONS. TB, tuberculosis; TST, tuberculin skin test; BCG, bacille Calmette-Guérin; MUAC, middle-upper arm circumference; CI, confidence interval; SD, standard deviation; OR, odds ratio.

In 1995, the World Health Organization estimated that at least 180 million children under the age of 15 years were infected with *Mycobacterium tuberculosis* worldwide and that nearly 170 000 children died of tuberculosis (TB).[1,2] TB infection and disease among children are much more prevalent in developing countries, where resources for TB control are scarce, than in industrialized countries.[3] However, despite the public health importance of the disease, TB is rarely investigated in children, as the diagnosis is difficult in the young age groups and children are usually not infectious.[4] In addition, contact tracing is rarely done in nonindustrialized countries because of lack of resources, and Isoniazid prophylaxis is not systematically provided to children who are in contact with individuals who have infectious TB.

Most children acquire infection from adults with whom they come in contact in their environment, so the epidemiology of TB in children usually follows that in adults. As infected children represent a large proportion of the pool from which cases will arise in the future, the distribution of TB infection in children can be considered a marker of recent ongoing transmission in the community. This concept has been used in the calculation of the annual risk of TB infection, which is based on the measurement of TB infection in cohorts of school-aged children through repeated tuberculin skin test (TST) surveys.[5] Although of limited specificity, especially because of exposure to environmental mycobacteria[6,7] or previous bacille Calmette-Guérin (BCG) vaccination,[8,9] the TST has been the classic method used to measure the prevalence of *M tuberculosis* infection in populations and identification of infected individuals.[10] As such, it has been the most widely used immunologic test in the world.[11] Thus, the knowledge of the distribution of TB infection and of the factors that influence it in children are of importance to evaluate the level of ongoing transmission of infection and to help adapt activities within national TB control programs.

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Numerous studies have been conducted both in industrialized and in nonindustrialized countries to compare TST-positive and TST-negative children to identify factors that influence the risk of TB infection. Few studies were conducted, however, within the households of the infectious TB cases with the view to assess the factors that influence infection given exposure. Within the frame of a prospective household study to investigate the role of environmental and host-related risk factors in susceptibility to TB, a TST was systematically administered to all members of the households of individuals with TB.[12] This test was performed to determine the level of *M tuberculosis* infection in the high-risk population of contacts of individuals with TB and to estimate the incidence of TB after infection. This study took place from 1999 to 2001 in 3 countries in West Africa. We report here the results obtained at baseline in children who lived in the households of individuals with infectious TB in The Gambia, West Africa, a country where BCG is given as a single dose at birth to >90% of children.

METHODS

The study was approved by the Medical Research Council/Gambian Government Ethics Committee. The detailed design of the study has been described elsewhere.[12] Patients with TB were recruited at 3 major urban health centers in The Gambia. All patients who had newly detected smear-positive pulmonary TB and were older than 15 years and had been living at the same address for >3 months were eligible for the study. Pulmonary TB was confirmed by 2 consecutive sputum smears positive for acid-fast bacilli and/or positive culture. Informed consent was obtained before enrollment. Households of individuals who had TB were visited at the time of recruitment, and consent was sought from the head of the household to undertake the study. Information was collected using standardized questionnaires on various variables, including household size, house structure, hygiene, water supply, sanitation, presence of animals, and socioeconomic status. Detailed demographic information was collected from each member of the household, including duration of residence in the compound, relatedness to the index case, exposure to the index case, medical history, and presence of symptoms of TB. Field workers checked the presence of a BCG scar on the left or right deltoid region and measured the weight, the height, and the middle-upper arm circumference (MUAC) in children younger than 5 years. A TST was performed on the volar surface of the left forearm of each household member aged >3 months, using 2 TU of RT 23 (Statens Serum Institut, Copenhagen, Denmark). Induration diameters were measured along and across the arm within 48 to 72 hours by trained field workers. For ensuring validity of the TST reading and to reduce intraobserver and interobserver variability, TST reading by each field worker was tested regularly during the course of the study against the same reference reader. Those who departed from standard reference reading were retrained. For analysis purposes, the average of width and length diameters was considered. Various criteria for skin test positivity were explored, and cutoff points of 5 and 10 mm were chosen.[13,14]

As part of the main study,[12] control households were selected at random in the neighborhood of the TB cases. The study was explained to the members of the household, and after agreement, the household was recruited in the study. Members of the household were then investigated in a similar way as for the household of the case, including tuberculin skin testing.

Data were double-entered and checked for data-entry errors. A random effects logistic regression model, which takes into account the clustering of contacts within households, was used to assess the relationship between the tuberculin response of the contact and risk factors. Results are reported as unadjusted and adjusted odds ratios and their 95% confidence intervals (CIs). The likelihood ratio test was used to assess the overall significance of risk factors, tests for trend, and tests for interaction. All statistical analyses were conducted using Stata software (version 7; Stata Corp, College Station, TX).

The nutritional status of children was assessed through the use of the weight-for-age and weight-for-height indices. These are expressed as z scores, which represent the distribution in a reference population standardized to a mean of 0 and a standard deviation (SD) of 1. The World Health Organization recommends that 2 SD below the reference median ($z = -2$) is the cutoff point for defining abnormally low values.[15]

Household contacts were followed-up for 2 years to detect any incident TB case among contacts of individuals with TB and controls and to determine progression to disease. We report here the results of the TST responses among children who were household contacts of patients with TB at the time of inclusion in the study.

RESULTS

Data were collected in the households of 206 individuals with infectious TB in the greater Banjul area in The Gambia between March 1999 and December 2000. The number of contacts in the households was 2870 (median household size: 8; minimum: 2; maximum: 43), 384 (13.4%) being under the age of 5. Among them, 45 (11.7%) were aged <1 year. The median age of children was 2 years, and 48% were girls. To assess the background situation, we first compared the distribution of TST responses in households of individuals with TB with control households ($n = 202$). For both chosen cutoff points,

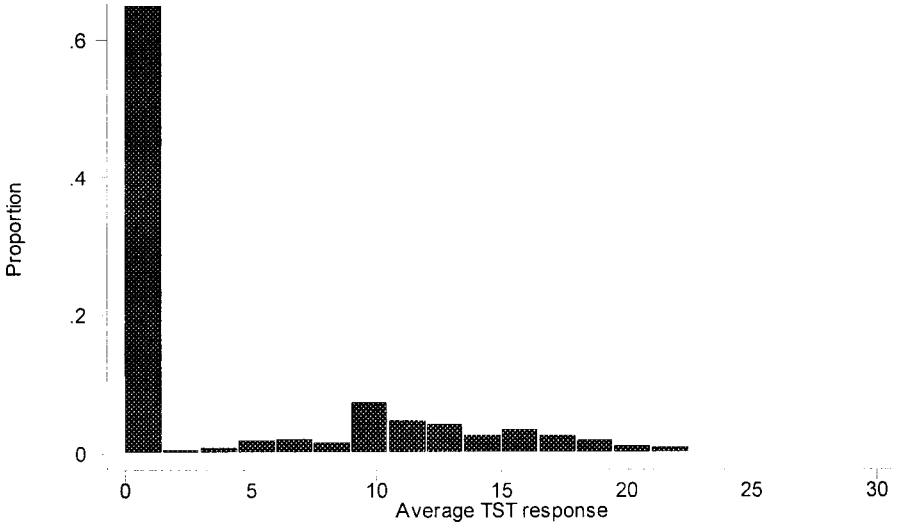

Fig 1. Distribution of TST responses in 384 children who were in contact with individuals with infectious TB in The Gambia (in mm).

the risk of being TST-positive was found to be higher in children who were in contact with individuals with infectious TB than in those who were in contact with community controls (odds ratio [OR]: 9.43; 95% CI: 4.96–17.8; $P < .001$; and OR: 22.21; 95% CI: 8.03–61.39; $P < .001$, for TST positivity defined as ≥5 and ≥10 mm, respectively).

We then focused on the distribution of the TST responses in the 384 children who were younger than 5 years and living in the household of individuals with TB. As can be seen in Fig 1, it follows a bimodal pattern, with 249 (65%) children presenting no induration at all and 135 (35%) presenting a palpable induration (TST response >0 mm). Among the latter, the mean induration size was 11.9 mm (SD: 4.3 mm) and the median size was 11.5 mm. Using the set criteria for TST positivity, 33.6% children had a TST response ≥5 mm and 25.8% had a TST response ≥10 mm.

On univariate analysis, the risk of being TST-positive (defined as ≥5 mm and ≥10 mm, respectively) within the households of the individuals with TB seemed to be higher after 1 year of age and in girls (Tables 1 and 2). The risk of TST positivity was associated with the total number of people living in the household of the individual with TB, the risk being higher in smaller than in larger households (test for trend, $P < .001$). It was not associated, however, with the average number of people per room in the household (OR for 2 or 3 people per room as compared with <2: 1.03; 95% CI: 0.51–2.12 for TST positivity ≥5 mm and OR: 1.31; 95% CI: 0.56–3.07 for TST positivity ≥10 mm).

To evaluate the degree of exposure to the individual with TB, we recorded the geographic proximity of the children to the individual with TB within the household at nighttime and the extent of activities shared with the individual with TB during the day. As can be seen, the risk of positive TST response increased with the geographic proximity of the child to the individual with TB (test for trend, $P < .001$) and with the importance of activities shared with the individual with TB (test for trend $P = .007$ for cutoff

TABLE 1. Risk Factors Associated With TST Positivity (Positive TST Defined as ≥5 mm) in Children in Contact With Individuals With TB: Univariate Analysis ($n = 384$)

Variables	TST-Negative	TST-Positive (n [%])	OR	95% CI	P Value
Gender					
Female	115	71 (38)	1.74	1.02–2.99	.04
Male	140	58 (29)	1		
Age (y)					
<1	39	6 (13)	0.28	0.009–0.91	.007
1	43	28 (39)	1.84	0.80–4.23	
2	50	29 (37)	1.50	0.66–3.42	
3	63	40 (39)	1.63	0.78–3.68	
≥4	60	26 (30)	1		
Household size (no. of people in household)					
1–5	16	27 (63)	6.92	2.63–18.25	<.001
6–10	57	36 (39)	1.81	0.92–3.59	$p_t < .001$
>10	182	66 (27)	1		
Geographic proximity to the case*					
1	85	21 (20)	1		
2	113	53 (32)	2.44	1.14–5.21	<.001
3	21	17 (45)	4.15	1.46–11.84	$p_t < .001$
4	36	38 (51)	5.74	2.40–13.72	
Activities shared with the case					
Occasional	76	21 (22)	1		
Part of day	64	35 (35)	1.98	0.90–1.49	.03
Most part of day	115	73 (39)	2.77	1.09–1.76	$p_t = .007$
Genetic proximity to case					
First degree	72	67 (48)	3.15	1.03–9.60	<.001
Second degree	104	33 (24)	0.76	0.24–2.37	
Third–fifth degree	34	12 (26)	1		
Own house					
No	51	38 (43)	1.90	0.95–3.81	.07
Yes	204	91 (31)	1		
BCG scar					
Yes	120	56 (32)	0.91	0.55–1.55	.7
No	135	73 (35)	1		
Duration of cough (wk)					
1–4	123	46 (27)	1		
5–10	70	29 (29)	1.02	0.48–2.16	.01
>10	57	51 (47)	2.72	1.33–5.55	$p_t = .007$
No. of zones involved on chest radiograph					
1–3	86	24 (22)	1		
4–5	94	50 (35)	2.11	1.01–4.43	.01
6	44	34 (44)	3.33	1.40–7.90	$p_t = .004$

p_t indicates test for linear trend.
* 1, sleeps in a different compound or in a different house in the same compound; 2, sleeps in same house, not same room; 3, same room, not same bed; 4, same room, same bed.

TABLE 2. Risk Factors Associated With TST Positivity (Positive TST Defined as ≥10 mm) in Children in Contact With Individuals With TB: Univariate Analysis (n = 384)

Variables	TST-Negative	TST-Positive (n [%])	OR	95% CI	P Value
Gender					
Female	130	56 (30)	2.17	1.12, 4.18	.02
male	155	43 (22)	1		
Age (y)					
<1	42	3 (7)	0.12	0.02–0.60	
1	48	23 (32)	1.50	0.59–3.79	.03
2	59	20(25)	0.94	0.36–2.44	
3	72	31 (30)	1.36	0.56–3.29	
≥4	64	22 (26)	1		
Household size (no. of people in household)					
1–5	21	22 (51)	6.89	2.35–20.25	.002
6–10	66	27 (29)	1.71	0.76–3.88	(p_t < .001)
>10	198	50 (20)	1		
Geographic proximity to the case*					
1	89	17 (16)	1		
2	125	41 (25)	2.30	0.95–5.54	.02
3	27	11 (29)	2.72	0.80–9.24	
4	44	30 (41)	4.96	1.84–13.33	
Activities shared with the case					
Occasional	80	17 (17)	1		
Part of day	70	29 (29)	2.08	0.76–5.67	.17
Most part of day	135	53 (28)	2.38	0.96–5.86	(p_t = .08)
Genetic proximity to case					
First degree	82	57 (41)	4.71	1.26–17.61	.003
Second degree	112	25 (18)	1.26	0.33–4.82	
Third–fifth degree	39	7 (15)	1		
BCG scar					
Yes	139	37 (21)	0.60	0.32–1.11	.10
No	146	62 (30)	1		
Own house					
No	64	25 (28)	1.43	0.68–3.19	.42
Yes	226	69 (23)	1		
Duration of cough (wk)					
1–4	132	37 (22)	1		
5–10	78	21 (21)	0.80	0.31–2.04	.10
>10	70	38 (35)	2.13	0.90–5.01	(p_t = .007)
No. of zones involved on chest radiograph					
1–3	91	19 (17)	1		
4–5	108	36 (25)	1.77	0.74–4.20	.09
6	52	26 (33)	3.03	1.12–8.21	(p_t = .02)

* 1, sleeps in a different compound or in a different house in the same compound; 2, sleeps in same house, not same room; 3, same room; not same bed; 4, same room, same bed.

point of 5 mm). It also increased with the genetic proximity of the child to the individual with TB, the first-degree relatives (son/daughter of individual with TB) being more likely to be TST-positive than the more genetically remote contacts.

Intensity of exposure is also related to the infectivity of the case. All 206 index TB cases were sputum positive, 193 (94%) of them being confirmed on culture. Of those, 9 presented atypical mycobacteria on culture, but no difference was noted in the distribution of TST responses in their contact children compared with the others (data not shown). The risk of TST positivity in contacts was not influenced by the density of acid-fast bacilli in the sputum of the individual with TB but increased with the duration of cough and with the number of lung zones affected on the chest radiograph of the individual with TB. It was not associated with the age or gender of the individual with TB and was not modified by the human immunodeficiency virus status of the individual with TB (OR: 1.17; 95% CI: 0.33–4.10 for TST ≥5 mm and OR: 1.01; 95% CI: 0.23–4.48 for TST ≥10 mm).

We also investigated the effect of potential child-related risk factors. The risk of TST positivity in child contacts was not associated with the presence of a BCG scar, for either chosen cutoff points (OR: 0.91, 95% CI: 0.55–1.55 for TST positivity ≥5 mm and OR: 0.60; 95% CI: 0.32–1.11 for TST positivity ≥10 mm). Positive TST responses were not associated with the nutritional status of the child, although this analysis was performed on a reduced number of children, of whom only 10 (3%) of 295 were undernourished (MUAC <12.5 cm). A nonsignificant trend was observed, the risk of TST positivity being higher in the few undernourished children compared with the others (MUAC ≥12.5 cm; OR: 2.93; 95% CI: 0.56–15.42 for the cutoff point of 5 mm and OR: 3.09; 95% CI: 0.45–21.32 for the cutoff point of 10 mm). The OR for weight-for-age z score <−2 was 1.42 (95% CI: 0.80–2.53) for TST positivity ≥5 mm and 1.42 (95% CI: 0.73–2.77) for TST positivity ≥10 mm.

Last, information was collected on several variables reflecting the socioeconomic status and the structure of the house. In this population, the risk of TST positivity seemed to be inversely associated with

ownership of the house ($P < .07$). It was not related, however, to other markers of socioeconomic status (employment and income of the household head, ownership of items) or with the structure of the house and general hygiene conditions (water supply, sanitation, refuse disposal, etc; data not shown).

A multivariate model was constructed to control for confounders. The effect of geographic proximity to the case, household size, and duration of cough in the individual with TB remained when TST responses ≥5 mm were considered positive (Table 3). Other variables, including age and gender, were no longer significant. However, when the cutoff point of ≥10 mm was chosen, the effect of household size only remained significant (Table 4). Geographical proximity of the contact to the individual with TB seemed to be confounded by household size, the ORs for proximity being reduced once household size was controlled for. Genetic proximity and geographic proximity are, as expected, strongly related variables (collinearity). Genetic proximity also seemed to be confounded by household size (children in "remote" genetic contact are more likely to come from larger households) and therefore lost statistical significance in multivariate analysis (data not shown).

DISCUSSION

This large tuberculin data set provides a unique opportunity to assess the distribution of responses to TST among children who have been recently exposed to an individual with smear-positive TB and to examine the influence of various factors on this distribution, given exposure, in a developing country with high BCG vaccination coverage. Within the frame of the main study, we showed earlier that the risk of TST positivity in contacts of individuals with infectious TB was higher than in contacts of healthy community controls (OR: 3.46; 95% CI: 2.80–4.27) and that the distribution of positive TST responses varied with age, gender, household size, family history of TB, and socioeconomic status.[16] We found also that, when positive, the TST responses were larger in size in the households of individual with TB than in the households of controls. In the present study, after confirming that recent exposure to an individual with infectious TB was a major factor for TST positivity in children by comparing with control households, we focused on the distribution of TST responses in children within the households of the individuals with TB.

The general distribution of TST responses observed in this population follows the classic bimodal pattern found in households elsewhere in Africa[6] and other places,[17] with a large proportion of children being TST-negative. Those results are similar to those from an earlier tuberculin survey conducted in 1984 in The Gambia among children aged 0–9, using intradermal injection of 10 TU of purified protein derivative.[18]

The prevalence of positive responses to TST in the general population is commonly reported to increase with age.[6,19] In our data set, the main effect of age is observed before 1 year, when the majority of children are TST-negative, after which there is little variation (overlap of CIs), especially when a cutoff point of 10 mm is considered. However, this apparent effect was not confirmed in multivariate analysis after adjusting for household size and proximity to the individual with TB. Similarly, we observed in univariate analysis that female children were more likely to be TST-positive than male children, but this was not confirmed in multivariate analysis, as the effect was probably confounded by the geographic proximity to the individual with TB.

Studies conducted in the 1960s and 1970s showed that household contacts of individual with TB had higher risk of infection than individuals in the general population.[20–22] This was confirmed in several recent studies conducted among children in New York City,[23] Botswana,[24] and Brazil,[25] in which contact with an individual with TB came out as the strongest risk factor for TB infection. In our study, we showed that the level of infection in children was directly related to the intensity of exposure to the individual with infectious TB (as assessed through both the geographic proximity to the individual with TB at nighttime and the extent of activities shared with the individual with TB during day time) as well as to the infectivity of the individual with TB (dura-

TABLE 3. Risk Factors Associated With TST Positivity (Positive TST Defined as ≥5 mm) in Children in Contact With Individuals With TB: Multivariate Analysis ($n = 376$)

Variable	Univariate		Multivariate	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Proximity to case				
Not same house	1		1	
Not same room	2.57 (1.17–5.66)	<.001	2.20 (1.01–4.77)	.04
Not same bed	3.60 (1.21–10.72)	($p_t < .001$)	2.61 (0.88–7.73)	($p_t = .009$)
Same bed	6.32 (2.54–15.73)		3.61 (0.88–7.73)	
Household size				
1–5	7.07 (2.56–19.51)	<.001	3.68 (1.29–10.43)	<.04
6–10	1.80 (0.89–3.63)	($p_t = .001$)	1.29 (0.64–2.61)	($p_t = .02$)
>10	1		1	
Duration of cough (wk)				
1–4	1		1	
5–10	1.02 (0.48–2.16)	.01	1.24 (0.58–2.65)	.05
>10	2.72 (1.33–5.55)	($p_t = .007$)	2.39 (1.16–4.94)	($p_t = .02$)

Note: duration of cough is associated with the number of zones involved on chest radiograph ($P = .001$).

TABLE 4. Risk Factors Associated With TST Positivity (Positive TST Defined as ≥10 mm) in Children in Contact With Individuals With TB: Multivariate Analysis (n = 376)

Variable	Univariate		Multivariate	
	OR (95% CI)	P Value	OR (95% CI)	P Value
Proximity to case				
Not same house	1		1	
Not same room	2.47 (0.98–6.19)	.01	2.10 (0.84–5.24)	.2
Not same bed	2.12 (0.60–7.80)	(p_t = .002)	1.50 (0.40–5.66)	(p_t = .08)
Same bed	5.63 (1.99–15.92)		3.12 (1.03–9.43)	
Household size				
1–5	6.90 (2.22–21.44)	.004	3.97 (1.20–13.17)	.06
6–10	1.72 (0.74–4.00)	(p_t = .001)	1.34 (0.56–3.16)	(p_t = .03)
>10	1		1	
Duration of cough (wk)				
1–4	1		1	
5–10	0.80 (0.31–2.04)	.10	0.98 (0.38–2.49)	.3
>10	2.13 (0.90–5.01)	(p_t = .10)	1.84 (0.78–4.36)	(p_t = .18)

Note: duration of cough is associated with the number of zones involved on chest radiograph (P = .001).

tion of cough). As TB is an airborne disease, the risk of an uninfected person's becoming infected is strongly associated with the probability of coming into contact with an individual with infectious TB and the intimacy of that contact.[26,27] We did not observe a variation in TST positivity with crowding, assessed through the average number of people per room in the household, similar to studies conducted in Botswana[24] and in New York City.[23] In this limited group of children under 5, however, we observed a clear inverse association between household size and TST positivity, as well as a positive association between the risk of TST positivity and the intensity of exposure to the individual with TB within the household. This finding has recently been substantiated in a study in India that showed that among contacts of individual with infectious TB, the immunologic response to specific mycobacterial antigens increased with the spatial proximity of the subject to the individual with TB within the household.[28] Altogether, this suggests that, more than the proportion of people per room, it is the increased occurrence and the intimacy of contact with the individual with TB that determine the transmission of infection.

Poor nutritional status has been reported to decrease TST reactivity in children.[29,30] In these studies, severe malnutrition was shown to depress immune responsiveness to BCG, although there was some uncertainty about the effect of mild malnutrition. We did not find an association between TST induration and nutritional status, similar to what was reported previously in The Gambia[18] and in Botswana.[24] In our study, however, the proportion of undernourished children was very small among the contacts of individuals with TB, which gave low power to detect an effect.

Vaccination with BCG has been reported to induce cross-reactivity with tuberculin-purified protein derivative, but the degree of tuberculin sensitivity after BCG immunization has been shown to be highly variable, depending on the vaccine strain used, the dosage, the method of administration, the time since vaccination, the age and nutritional status at time of vaccination, and factors known to influence the reaction to TST.[9,31,32] TST reactivity in BCG-vaccinated children fades over time but can be boosted in children with repeated skin testing.[8,33] There is no reliable method to distinguish tuberculin reactions caused by vaccination with BCG from those caused by natural mycobacterial infections.[13] In a large data set collected in Malawi, the prevalence of TST positivity was consistently higher over all ages in individuals with a BCG scar than in individuals without a BCG scar.[11] Similar findings were reported among school entrants as well as among household contacts of children with latent TB infection in New York City.[34,35] In our data set, however, we did not find a difference in the prevalence of TST positivity among children with and those without a BCG scar for both cutoff points of 5 and 10 mm. Similar observations were reported among children under 5 years of age in Botswana—when TST positivity was set at 10 mm diameter[24]—and in New York City,[23] as well as among children aged 1–15 in Brazil[25] and in Northern Canada.[36]

Some discrepancy between effective BCG vaccination and presence of a scar is to be expected, as scars are not invariably present among all vaccinees.[37] Thus, in The Gambia, a scar was found in only 71% of children aged 0 to 9 years with a health-card record of a vaccination.[18] In the Canadian study, 17% of subjects with a record of past BCG vaccination showed no visible scar.[36] As BCG is given immediately after birth in The Gambia and vaccination coverage is reported to be high (>95%), the absence of association between BCG scar and TST positivity can be attributable to the waning of tuberculin sensitivity induced by BCG with time.[31,38] It was thus reported that, in Malawi, BCG rarely induces very strong tuberculin sensitivity and that the majority of vaccinated individuals lost their BCG-induced tuberculin sensitivity shortly after the vaccination.[11] In many tropical countries, postvaccination sensitivity cannot be entirely attributed to BCG in the presence of naturally acquired low-grade sensitivity caused by environmental mycobacteria.[6,20] Thus, some evidence for cross-protection from natural exposure to certain environmental mycobacteria has been associated with the geographic distributions of mycobacterial disease in Malawi.[39]

Children who are in contact with individuals with

infectious TB are at high risk of developing TB.[40] Despite the former vaccination with BCG, it has been suggested that a positive TST in a child who has close contact with an adult with infectious TB most likely represents infection with *M tuberculosis*, and treatment of this latent infection should be considered, especially if the child is younger than 5 years.[41] This finding is of importance in light of the increasing rates of TB in sub-Saharan Africa, where children who are vaccinated with BCG are exposed to adults with active TB. Tracing of the children who are in contact with individuals with infectious TB has been relatively neglected within TB control programs in developing countries, mainly because of managerial difficulties. Our data show that, in the absence of more specific markers of infection, TST can continue to be used to assess TB infection in children who live in the household of individuals with infectious TB in areas with high BCG coverage. They also support the importance of contact tracing activities in the control of TB in developing countries, associated with early case detection and treatment.

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