Annual risk of tuberculous infection in the northern zone of India

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Objective To estimate the annual risk of infection with tubercle bacilli in the northern zone of India.

Methods A community-based cross-sectional tuberculin survey was conducted among children aged 1–9 years who lived in a sample of villages and urban blocks of six selected districts in a defined north zone of India. A two-stage cluster sampling method was used to select rural and urban clusters. A total of 48 624 children in 598 clusters were subjected to tuberculin testing with one tuberculin unit (1 TU) of PPD RT23 stabilized with Tween 80. The maximum transverse diameter of induration was measured about 72 hours after the test.

Findings Among the 48 624 test-read children, 22 064 (45.4%) had a bacille Calmette-Guérin (BCG) scar. On the basis of the frequency distribution of tuberculin reaction size among 25 816 children without a BCG scar, the prevalence of infection with tubercle bacilli was estimated as 10.3%. The annual risk of infection was computed as 1.9%. The proportion of infected children was significantly higher in urban than rural areas.

Conclusion The high rate of tuberculous infection in the north zone of India suggests the need for further intensification of tuberculosis control efforts on a sustained and long-term basis.

Keywords Tuberculosis, Pulmonary/epidemiology; Mycobacterium tuberculosis/pathogenicity; Tuberculin test; BCG vaccine; Periodicity; Epidemiologic factors; Cross-sectional studies; Cluster analysis; India (*source: MeSH, NLM*).

Mots clés Tuberculose pulmonaire/épidémiologie; Mycobacterium tuberculosis/pathogénicité; Réaction tuberculinique; Vaccin BCG; Périodicité; Facteurs épidémiologiques; Etude section efficace; Sondage en grappes; Inde (*source: MeSH, INSERM*).

Palabras clave Tuberculosis pulmonar/epidemiología; Mycobacterium tuberculosis/patogenicidad; Test de tuberculina; Vacuna BCG; Periodicidad; Factores epidemiológicos; Estudios transversales; Análisis por conglomerados; India (*fuente: DeCS, BIREME*).

انظر صفحة ٥٧٩ للاطلاع على الكلمات المفتاحية
والملخص باللغة العربية.

Introduction

The annual risk of infection is the preferred indicator of the epidemiological status of tuberculosis, especially in developing countries, because disease surveys are expensive and time consuming. The annual risk of infection is defined as the probability of acquiring new tuberculous infection or reinfection over a period of one year. It expresses the overall impact of various factors influencing the transmission of tubercle bacilli, specifically the load of infectious cases in the community and the efficiency of case finding and treatment programmes. The study of tuberculosis status in a large country such as India always has been a challenge. Although the importance of tuberculosis to public health has long been recognized, only in 1955–58 did a nationwide disease survey first reveal the magnitude of the problem (*1*). Most of the subsequent epidemiological studies to estimate the prevalence of disease or annual risk of infection have been confined to limited geographical areas of south India, close to two national tuberculosis institutes. Thus, information on the prevailing epidemiological status of tuberculosis has been largely unknown for most parts of the country.

The National Tuberculosis Program (NTP) has been implemented in India since 1962; however, its performance in terms of case finding and treatment has been below expectation (*2,3*). The Government of India therefore resolved to intensify efforts to control tuberculosis and to adopt the Direct Observation Treatment Strategy (DOTS) for the programme, which was renamed as the Revised National Tuberculosis Control Program (RNTCP). The RNTCP started to be introduced across the country in a phased manner in 1998, and it has shown promise, especially in terms of the cure rate for cases with sputum smears positive for tubercle bacilli (*4*). While efforts to control tuberculosis were being revitalized, it was decided to study the prevalent epidemiological situation of tuberculosis by conducting a nationwide tuberculin survey to estimate the annual risk of infection in different parts of the country. We stratified the country into four zones, each with about one quarter of the country's population (Fig. 1). The survey was designed to obtain estimates of the average annual risk of tuberculous infection in each of the four zones. This paper presents the results from the north zone.

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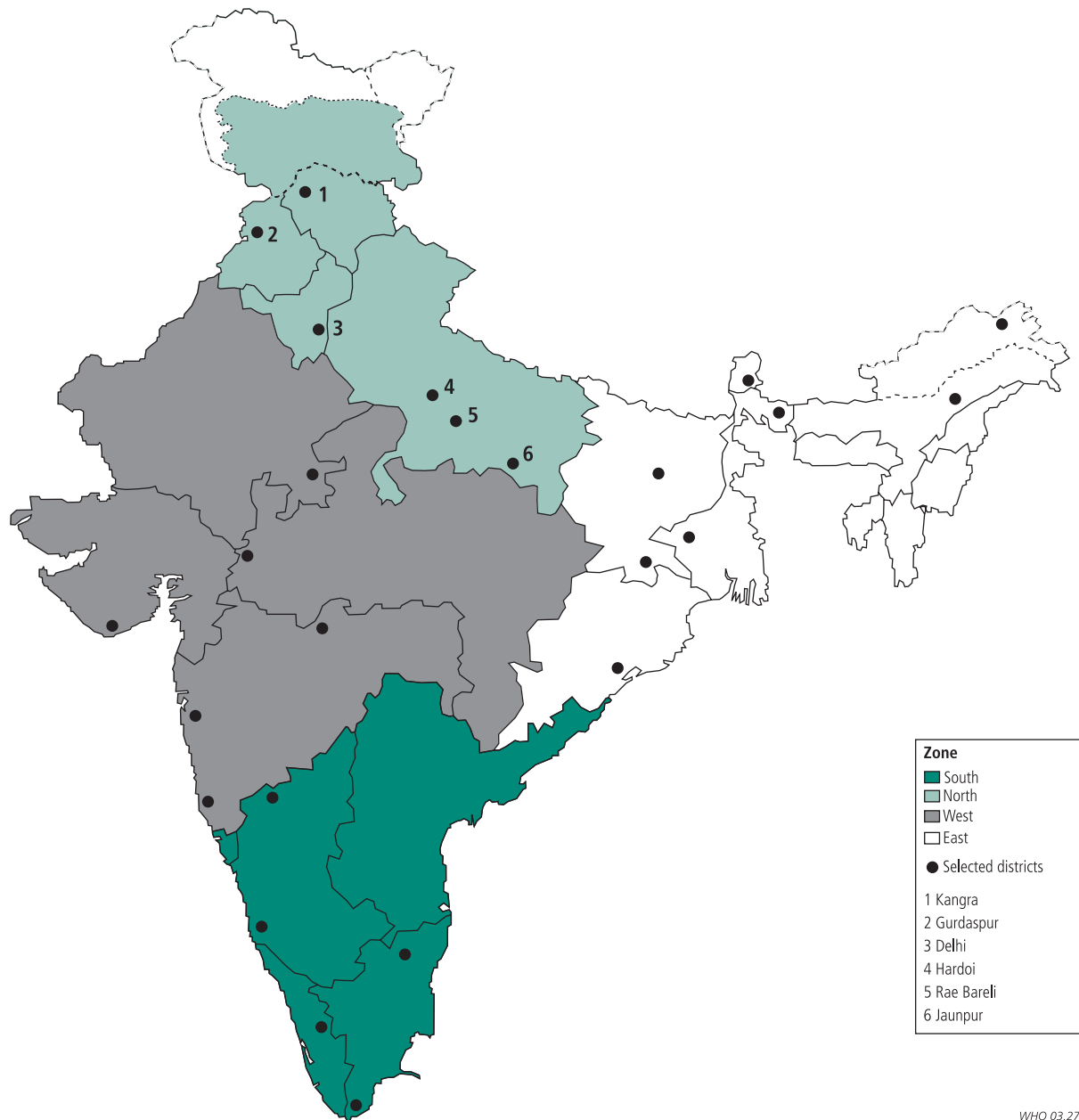[2] Senior Medical Officer, National Tuberculosis Institute, Bangalore, India.

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Fig. 1. **Zonewise location of selected districts in India**

Zone
- ■ South
- ■ North
- ■ West
- □ East
- ● Selected districts

1 Kangra
2 Gurdaspur
3 Delhi
4 Hardoi
5 Rae Bareli
6 Jaunpur

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Methods

Study population and sampling

The study population comprised children aged 1–9 years without a scar from bacille Calmette–Guérin (BCG) vaccination. Older children were not included, as they were more likely to harbour infection with environmental mycobacteria that could interfere with interpretation of study results (5, 6). Children with a scar from BCG vaccination were excluded because BCG–induced tuberculin sensitivity could interfere with interpretation of the study results (6).

The states of Himachal Pradesh, Jammu and Kashmir, Punjab, Haryana, Uttar Pradesh, and Delhi made up the north zone. The sample size was estimated on the basis of an assumed minimum prevalence of infection of 8%, which

was itself based on results obtained during earlier surveys in different parts of India (7–17). Other parameters considered for estimation of sample size are given in Table A (web version only, available from: http://www.who.int/bulletin/). The sample size needed was estimated as 12 000 children without BCG scar, to be investigated in 600 clusters. For the purpose of the survey, a village was considered as a rural cluster and an urban census enumeration block as an urban cluster. The clusters in the zone were distributed among two strata — rural (*n* = 453) and urban (*n* = 147) — in proportion to the rural and urban population.

A two-stage sampling procedure was used to select clusters within a stratum. In the first stage, six districts were selected by systematic sampling: Rae Bareli, Hardoi, and Jaunpur (all from Uttar Pradesh — the most populous state

Table 1. **Estimated prevalence of infection and annual risk of infection**

Variable	Estimate			
	Cut-off point[a]			By mirror image technique
	12 mm	14 mm	16 mm	
Prevalence (%)	11.8 (10.0–13.5)[b]	10.3 (8.4–12.2)	9.2 (7.3–11.0)	10.5 (7.4–13.5)
Annual risk of infection (%)	2.1 (1.8–2.5)	1.9 (1.5–2.2)	1.6 (1.3–2.0)	1.9 (1.3–2.5)

[a] Cut-off point for reaction size after tuberculin test.
[b] Values in parentheses are 95% confidence intervals.

in India), Gurdaspur (Punjab), Kangra (Himachal Pradesh), and Delhi (Fig. 1). Within a stratum, the number of clusters assigned to districts was in proportion to the population.

At the next level of selection, clusters in each district were selected with the population proportional-to-size method. In each cluster, 85 children with or without the BCG scar were to be registered. This number was chosen to obtain at least 20 test-read children without a BCG scar, with the assumption that 70% of children would have a BCG scar and that the drop-out rate between registration and reading of tuberculin reactions would be 20%.

Field procedures

Fieldwork was conducted by the National Tuberculosis Institute (NTI), Bangalore, with the support of district health authorities, from April 2000 to August 2001. Three visits were made to each cluster for planning, registration and testing, and reading. During the planning visit, important community leaders were apprised of the purpose of the survey. A sketch of the cluster, including hamlets and lanes, was made, and a lane in which fieldwork could be started was selected at random.

Children were registered on the day of testing, starting with those from the first house of the selected lane. Contiguous houses were visited in a clockwise direction until 85 children aged 1–9 years (completed one year and <10 completed years) were registered. An individual card was opened for each child, and identification particulars were noted. Tuberculin tests were performed at a temporary centre. Each child was injected intradermally on the volar aspect of the left forearm with 0.1 ml of tuberculin containing 1 TU of PPD RT23 stabilized with Tween 80 (WHO standard tuberculin test (18)). Tests were recorded as "satisfactory" when they raised a flat pale wheal with clearly visible pits and well demarcated borders, and "unsatisfactory" in case of leakage or subcutaneous injection. The presence or absence of a BCG scar was recorded after both of the child's shoulders were examined. If a scar was present but did not possess the characteristics of a BCG scar, it was recorded as "doubtful". Children with fever, history of skin rash, or anti-tuberculosis treatment during the previous six months were excluded from testing. Informed written consent was obtained from the parent or guardian before the test was performed. The fieldwork could not be carried out in two of 600 clusters, because of inaccessibility in one and refusal in the other.

The reactions were read approximately 72 hours after the test. The reader identified the margins of induration on careful palpation, and the maximum transverse diameter of induration was measured in millimetres. The presence of any vesicles, bullae, or necrosis also was recorded. The data were

entered into the computer twice with FoxPro software and validated.

In addition, 493 cases of pulmonary tuberculosis were subjected to tuberculin testing within one week of being found positive for acid-fast bacilli on smear microscopy. This was intended to corroborate the criteria used to estimate prevalence of infection.

The tuberculin dilutions used in the survey were prepared by the BCG Laboratory, Guindy, Chennai, from the original seed lot of PPD RT23 stabilized with Tween 80 sent by the Statens Serum Institut, Copenhagen.

Statistical methods

Analysis was restricted to children without a BCG scar. The frequency distribution of tuberculin reaction sizes was plotted, and reactions equal to or greater than the identified cut-off point were considered attributable to "infection with tubercle bacilli" (19). Since the number of test-read children without a BCG scar varied from cluster to cluster, the proportion of children infected in each cluster was calculated first. After weights equal to the inverse of the initial probability of a cluster being selected were assigned, the proportions were pooled to estimate the proportion of infected children in the rural and urban areas of each district.

The proportions of infected children in the rural and urban strata of the entire zone were estimated further, by combining the estimates for the districts and by using the proportion of district population (rural/urban) in the zone as the weight. The zonal estimate of prevalence of infection was obtained similarly by pooling the rural and urban estimates. The formulae used for the above estimations are given in Table A (web version only, available from: http://www.who.int/bulletin/).

The annual risk of infection (ARI) was calculated from the estimated prevalence of infection (P) by using the following equation, where A = mean age of test-read children (20).

$$ARI = 1 - (1-P)^{1/A}$$

The χ^2 test with continuity correction was used to test the significance of differences between proportions. The calculated values of the test criteria were compared with the tabular value at the 95% level to ascertain the significance of the test. The data were analysed with SPSS software.

Results

A total of 55 433 children were registered; 48 624 (87.7%) of these were test-read. Overall, 22 064 (45.4%) of the 48 624 test-read children had a BCG scar. In rural areas, 15 142

Fig. 2. **Frequency distribution of tuberculin reaction size among 25 816 children without a scar from bacille Calmette–Guérin vaccination**
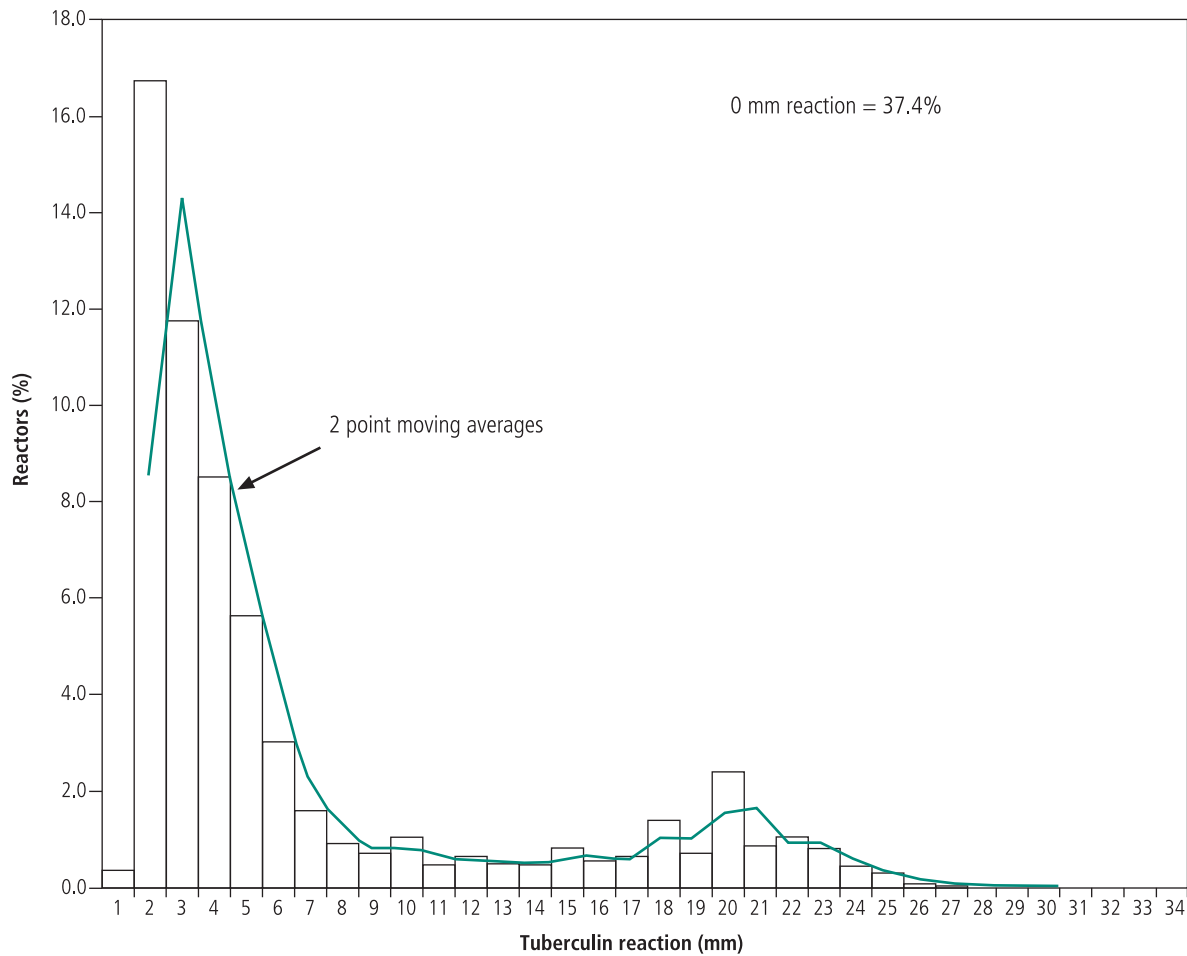
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(40.5%) of the 37 391 test-read children had a BCG scar and 6922 (61.6%) of the 11 233 test-read children in urban areas had a BCG scar. This difference in the proportion of children with a BCG scar between rural and urban area was statistically significant (*P* = 0.000).

Data pertaining to 25 816 children without a BCG scar were analysed after 22 808 test-read children were excluded because of the presence of a BCG scar (*n* = 22 064), the presence of a doubtful BCG scar (*n* = 648), and the absence of a BCG scar, but an unsatisfactory tuberculin test (*n* = 96).

The frequency distribution of tuberculin reaction size among children without a BCG scar was bimodal, with the mode of reactions attributable to infection with tubercle bacilli at 20 mm and an antimode apparent at 14 mm (Fig. 2). Similar distributions were obtained when tuberculin reaction sizes were plotted separately for rural and urban strata. All reactions ≥14 mm therefore were considered to be attributable to infection with tubercle bacilli for the purpose of estimating the prevalence of infection.

On the basis of the above criterion, the prevalence of infection in the zone was estimated as 10.3% (95% confidence interval, 8.4–12.2). The annual risk of infection computed from the estimated prevalence was 1.9% (1.5–2.2).

Estimates of prevalence of infection and annual risk of infection in the zone were also made by varying the cut-off

points by 2 mm on either side — that is to 12 mm and 16 mm. Finally, estimates made with the mirror image technique, with the mode considered to be at 20 mm, were found to be similar to estimates based on the cut-off point at 14 mm (Table 1).

Table 2 gives the proportion of infected children and computed annual risk of infection by stratum, sex, and age group, when 14 mm was used as the cut-off point. In rural areas, 2 115 (9.1%) of 21 816 children were infected compared with 675 (14.1%) out of 4000 in urban areas. The computed annual risks of infection were 1.6% and 2.6%, respectively (*P* = 0.000). No significant difference was seen between boys and girls in the proportion infected. In total, 525 (4.6%) out of 10 196 children aged 1–4 years and 2 265 (14.1%) out of 15 620 children aged 5–9 years were infected. The annual risk of infection computed from the prevalence of infection estimates for these age groups were 1.5% and 2.0%, respectively. A small proportion (207, 0.8%) of the children presented with additional features, including vesicles and bullae at the test site.

Fig. 3 shows the frequency distribution of tuberculin reaction size among 493 test-read cases who were smear positive for pulmonary tuberculosis. The mode of reactions was at 20 mm, and 438 (88.8%) of cases elicited tuberculin reactions ≥14 mm.

Fig. 3. **Frequency distribution of tuberculin reaction size among 493 cases with sputum smears positive for tuberculosis**
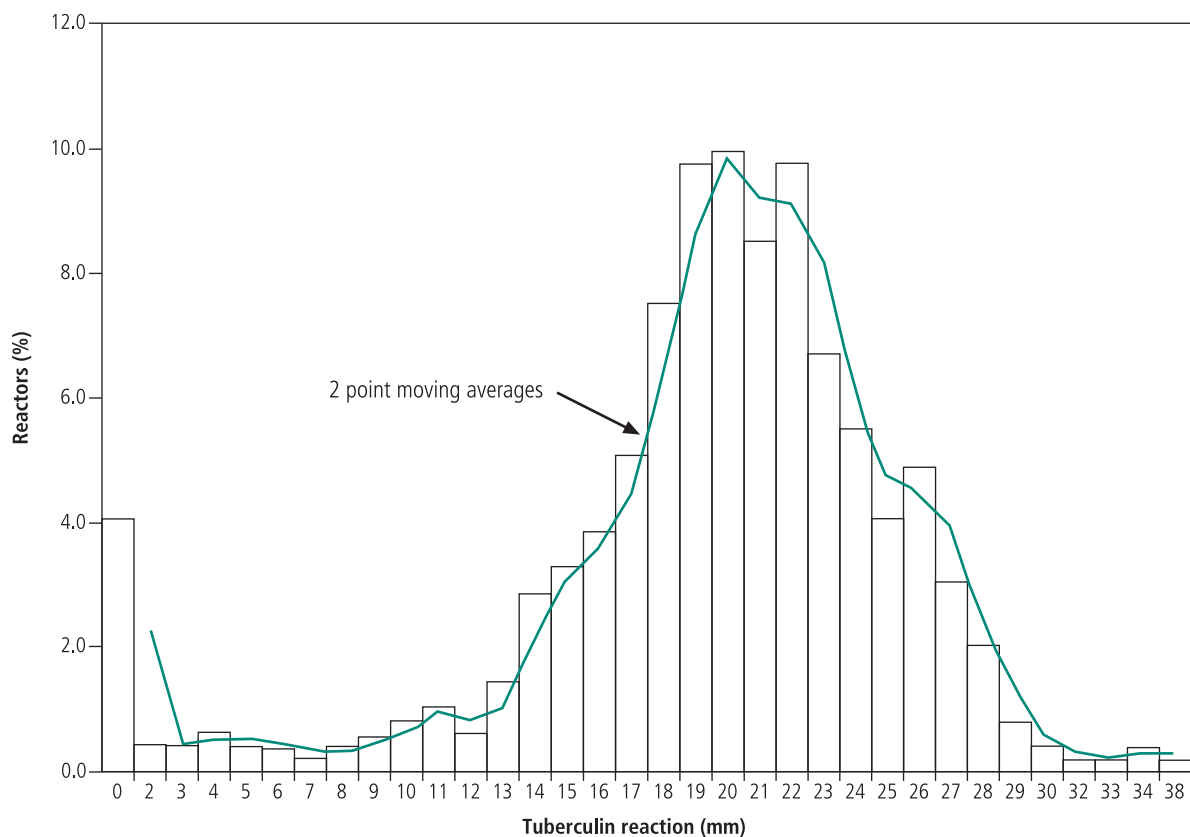
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Discussion

The results of the survey provide useful information on the prevailing epidemiological status of tuberculosis in the north zone of India. They could be used as baseline data to evaluate the impact of disease control measures and epidemiological trends in the future.

The number of test-read children without a BCG scar was higher than the estimated sample size, because the proportion of children without a BCG scar was larger than expected and the drop-out rate was lower. The frequency distribution of tuberculin reactions among children without a BCG scar was bimodal, and the observed mode of reactions attributable to infection with tubercle bacilli was similar to the mode of reactions among smear-positive cases.

The annual risk of infection in the north zone of India was estimated as 1.9%. A higher rate of transmission of infection was observed in urban areas, which implied that such areas have a worse status of disease than rural areas. Our results differed from the findings obtained during the nationwide disease survey from 1955–58, when the prevalence of pulmonary tuberculosis was similar in urban and rural areas (*1*). The living conditions in urban areas have deteriorated in the intervening period, with about one quarter of the population now living in slums (*21*). Moreover, the delivery of anti-tuberculosis services has been more unsatisfactory in urban areas than in rural areas, with a multiplicity of services, most of which do not adopt standardized methods of case finding and treatment (*22*).

We cannot comment on any change from the previous epidemiological status of tuberculosis, because no previous data on risk of infection have been available from any part of north India. The relatively lower risk of infection in those aged 1–4 years compared with those aged 5–9 years might be attributable to a decline in the rates of transmission of infection, in addition to differences in the risk of exposure. Age dependency in the risk of infection has been reported from some other countries (*23, 24*). We also cannot comment on the possible contribution of the HIV epidemic, which is still at a relatively low level in the states of the north zone compared with the other zones. Sentinel surveillance data in these states in 2001 showed that the prevalence of HIV infection was <1% among antenatal women and 0.3–4.6% among those suffering from other sexually transmitted diseases (*25*).

The estimated annual risk of infection was higher than most recent estimates from many other developing countries: Algeria, Egypt, the Republic of Korea, Kenya, and the United Republic of Tanzania (*26–30*). A higher rate of 2.3% was observed only in the Philippines (*31*). Annual risks of infection in most developed countries are <0.1% (*32*).

Most of the above-mentioned countries used 2 TU doses of PPD RT23 stabilized with Tween 80 dilutions prepared at Statens Serum Institut (except the Republic of Korea, where 1 TU of the same product was used). A series of comparative studies conducted earlier at the NTI suggested, however, that 1 TU dilution of PPD RT23 stabilized with Tween 80 prepared at the BCG Lab, Guindy, could be used for tuberculin surveys in India (*33*).

Most of the earlier tuberculin surveys in India were conducted in South India, with the exception of one conducted in a subdivision in Rajasthan and another in a tribal area of

Table 2. **Proportion of infected children and annual risk of infection by stratum, age group, and sex**

Variable	Children		
	No. analysed	% Infected	Annual risk of infection (%)
Stratum			
Rural	21 816	9.1 (7.1–11.0)	1.6 (1.3–2.0)
Urban	4 000	14.1 (12.6–15.7)	2.6 (2.3–2.9)
Sex			
Female	12 769	10.5 (8.3–12.8)	1.9 (1.5–2.3)
Male	13 047	10.1 (8.4–11.8)	1.8 (1.5–2.1)
Age group (years)			
1–4	10 196	4.6 (3.6–5.6)	1.5 (1.2–1.8)
5–9	15 620	14.1 (11.7–16.5)	2.0 (1.6–2.4)
Total	25 816	10.3 (8.4–12.2)	1.9 (1.5–2.2)

Madhya Pradesh. Estimates of the annual risk of infection from most of these surveys ranged from 1–2% to higher in the tribal area mentioned above and a congested area of Madras city (now called Chennai) (7–17).

The estimated annual risk of infection of 1.9% indicates a high number of infectious cases in the community. This confirms the unsatisfactory performance of the NTI implemented throughout the country since 1962, which has poor efficiency of case finding, unsupervised chemotherapy, and irregular drug supplies that have resulted in low rates of treatment completion (2, 3). Fortunately, the DOTS strategy being phased in across the country as the RNTCP has achieved cure rates >80% among new cases with smear-positive sputum in almost all areas in the country in which it has been implemented (4, 34–37). The detection rate of new cases with smear-positive sputum in areas covered by the RNTCP in the north zone improved from 45 per 100 000 population in 2000 to 57 per 100 000 in 2001 and to 80 per 100 000 (annualized) by the second quarter of 2002 (34–37). Only about one quarter of the population in the north zone was covered by the RNTCP by the end of June 2002 (37). In areas where RNTCP had not been introduced, the detection rate of new smear-positive cases remained at about 35 per 100 000 population, and no reliable informa-tion on the cure rates of infectious cases is available (38–40). The incidence of new cases with smear-positive sputum in the north zone estimated on the basis of our results would be about 95 per 100 000 population (based on the parametric relationship derived by Styblo (41)).

Conclusion

The three-quarters of the population in the north zone of India for which access to DOTS is unavailable should be given access. Private sector and nongovernmental organiza-tions should be obliged to follow national guidelines in case finding and treatment practices. The estimated annual risk of infection implies that the incidence of new cases will remain high in the future and that any reductions in inci-dence as a result of the programme cannot be expected to occur quickly. The intensification of tuberculosis control measures will have to be undertaken, therefore, on a sus-tained and long-term basis. ■

Résumé

Risque annuel d'infection tuberculeuse dans le nord de l'Inde

Objectif Estimer le risque annuel d'infection par le bacille tubercu-leux dans la partie nord de l'Inde.

Méthodes Une enquête tuberculinique transversale a été réalisée au niveau communautaire sur des enfants de 1 à 9 ans résidant dans un échantillon de villages et de quartiers urbains de six districts choi-sis dans une zone définie du nord de l'Inde. Les grappes rurales et urbaines ont été sélectionnées selon une méthode de sondage à deux niveaux. Au total, 48 624 enfants appartenant à 598 grappes ont été soumis à un test tuberculinique avec une unité tuberculi-nique de PPD RT23 stabilisé par le Tween 80. Le plus grand diamè-tre de l'induration a été mesuré 72 heures après le test.

Résultats Parmi les 48 624 enfants dont le test a été lu, 22 064 (45,4 %) avaient une cicatrice de vaccin BCG (bacille Calmette-Guérin). D'après la distribution de fréquence du diamètre de la réac-tion tuberculinique chez les 25 816 enfants n'ayant pas de cicatrice de vaccin BCG, la prévalence de l'infection par le bacille tuberculeux a été estimée à 10,3 %. Le risque annuel d'infection calculé était de 1,9 %. La proportion d'enfants infectés était significativement plus élevée dans les zones urbaines que dans les zones rurales.

Conclusion Le taux élevé d'infection tuberculeuse dans la partie nord de l'Inde indique la nécessité d'intensifier encore davantage les efforts de lutte contre la tuberculose, de façon soutenue et prolongée.

Resumen

Riesgo anual de infección tuberculosa en el norte de la India

Objetivo Calcular el riesgo anual de infección por el bacilo de la tuberculosis en el norte de la India.

Métodos Se realizó una encuesta tuberculínica transversal de ámbito comunitario entre niños de 1–9 años que vivían en una muestra de aldeas y edificios urbanos de seis distritos seleccionados en una determinada zona del norte de la India. Se utilizó un método de muestreo por conglomerados en dos etapas para seleccionar conglomerados rurales y urbanos. Un total de 48 624 niños de 598 conglomerados fueron sometidos a la prueba tuberculínica con una unidad de tuberculina (1 UT) en forma de PPD RT23 estabilizado con Tween 80. Unas 72 horas después de la prueba se midió el diámetro transversal máximo de la induración.

Resultados Entre los 48 624 niños sometidos a la prueba, 22 064 (45,4%) presentaban una cicatriz de bacilo de Calmette-Guérin (BCG). Teniendo en cuenta la distribución de frecuencias del tamaño de la respuesta a la tuberculina entre 25 816 niños sin cicatriz de la BCG, se estimó que la prevalencia de la infección por el bacilo de la tuberculosis era del 10,3%. Se calculó así que el riesgo anual de infección era del 1,9%. La proporción de niños infectados fue significativamente mayor en las zonas urbanas que en las rurales.

Conclusión La alta tasa de infección tuberculosa detectada en el norte de la India muestra la necesidad de intensificar aún más los esfuerzos de control de la tuberculosis de forma sostenida y a largo plazo.

ملخص

الاختطار السنوي للعدوى بالسل في المنطقة الشمالية من الهند

الغرض: تقييم الاختطار السنوي للعدوى بالعصيات السلية في المنطقة الشمالية من الهند.

الطريقة: أجري مسح مرتكز عنها لمجمعة وعلى قطاع مستعرض منه على الأطفال ممن تتراوح أعمارهم بين سنة وتسع سنوات والذين يعيشون في عينة من القرى والأرياف في ست مقاطعات مختارة من منطقة محددة في الهند. وقد استخدمت طريقة الاعتيان (أحد ثعيات) للمجموعات على مرحلتين لاختيار مجتمعوهم الريفية والحضرية. وقد خلت الدراسة إجراء اختبار النوردين كلينا 48 624 طفلاً من 598 مجموعة، وذلك باستخدام وحدة واحدة من المشتق البروتيني المنقى للنوبركين PPD RT23 المثبت بطريقة Tween 80. وقد تم قياس أقصى قطر مستعرض للارتشاح بعد مرور 72 ساعة من إجراء الاختبار.

الموجودات: من بين 48 624 قراءة لنتائج الاختبار لدى الأطفال وجدت ندبة لعصيات كالميت وغيرات (BCG) لدى 22 064 منهم (45.4%)؛ وبناء على توزّع التواتر لمساحة التفاعل اخندى ضد النوبركين لدى 25 816 طفلاً ممن لم تتشكل لديهم ندبات لعصيات كالميت وغيران، فقد تم تقدير انتشار العدوى بالعصيات نسبية 10.3% وتم حساب الاختطار السنوي للعدوى 1.9% وقد كانت النسبة المئوية للأطفال المصابين بالعدوى أعلى في المناطق الحضرية منها في المناطق الريفية.

الاستنتاج: إن المعدل المرتفع نعدوى بالسل في المنطقة الشمالية من الهند ضوء الحاجة لزيد من التكييف للمجهود لمكافحة السل على أسس مصمونة الاستمرار لمدة طويلة.

الكلمات المفتاحية: السل، السل الرئوي، وبائيات السل، المتفطرة السلية، إمراضية المتفطرة السلية، احتيان النوبركين، نقاح بي سي جي، دورية: عوامل وبائية دراسة مستعرضة، تحليل بمجتمعوهم، الهند (المصدر: رؤوس الموضوعات الطبية، المكتب الإقليمي لشرق المتوسط)

References

1. Indian Council of Medical Research. *Tuberculosis in India — a sample survey, 1955–58. Special Report Series No. 34. New Delhi*: Indian Council of Medical Research; 1959.

2. Suryanarayana L, Vembu K, Rajalakshmi R, Satyanarayana C. Performance of National Tuberculosis Programme in 1993: an appraisal. *Indian Journal of Tuberculosis* 1995;42:101-15.

3. National Tuberculosis Institute, Bangalore. Performance of national tuberculosis programme: January to September 1999 – a report. *Indian Journal of Tuberculosis* 2001;48:25-9.

4. Khatri GR, Frieden TR. The status and prospects of tuberculosis control in India. *International Journal of Tuberculosis and Lung Disease* 2000;4:193-200.

5. Chakraborty AK, Ganapathy KT, Nair SS, Bhushan K. Prevalence of non-specific sensitivity to tuberculin in a South Indian rural population. *Indian Journal of Medical Research* 1976;64:639-51.

6. Rider HL. Methodological issues in the estimation of the tuberculosis problem from tuberculin surveys. *Tubercle and Lung Disease* 1995;76:114-20.

7. Narain R, Geser A, Jambunathan MV, Subramanian M. Tuberculosis prevalence survey in Tumkur district. *Indian Journal of Tuberculosis* 1963;10:85-116.

8. Narmada R, Narain R, Raju VB, Naganna K, Shanmuga Sundaram R. Incidence of tuberculosis among infected and non-infected children. *Indian Journal of Medical Research* 1977;65:171-83.

9. Gothi GD, Chakraborty AK, Nair SS, Ganapathy KT, Banerjee GC. Prevalence of tuberculosis in a south Indian district twelve years after initial survey. *Indian Journal of Tuberculosis* 1979;26:121-35.

10. Mayurnath S, Vallishayee RS, Radhamani MP, Prabhakar R. Prevalence study of tuberculosis infection over 15 years in a rural population in Chingleput district (South India). *Indian Journal of Medical Research* 1991;93:74-80.

11. Chakraborty AK, Chaudhuri K, Sreenivas TR, Krishna Murthy MS, Shashidhara AN, Channabasavaiah R. Tuberculous infection in a rural population of south India: 23-year trend. *Tubercle and Lung Disease* 1992;73:213-8.

12. Chakma T, Vinoy Rao P, Pall S, Kaushal LS, Manjula Datta, Tiwary RS. Survey of pulmonary tuberculosis in a primitive tribe of Madhya Pradesh. *Indian Journal of Tuberculosis* 1996;43:85-9.

13. Siddiqi D, Ghose S, Krishna Murthy MS, Shashidhara AN. Tuberculosis infection rate in a rural population of Bikaner district. *Indian Journal of Tuberculosis* 1996;43:91-7.

14. Chadha VK, Suryanarayana HV, Krishna Murthy MS, Jagannatha PS, Shashidhara AN. Prevalence of undernutrition among peri-urban children and its influence on the estimation of annual risk of tuberculosis infection. *Indian Journal of Tuberculosis* 1997;44:67-71

15. Kumari Indira KS, Sivaraman S, Joshi M, Sivanandan Pillai N. Annual risk of tuberculosis infection: an estimate from ten-year-old children in Trivandrum district. *Indian Journal of Tuberculosis* 2000;47:211-8.

16. Chadha VK, Jagannatha PS, Shashidhar Savanur J. Annual risk of tuberculosis infection in Bangalore City. *Indian Journal of Tuberculosis* 2001;48:63-71.

17. Tuberculosis Research Centre. Trends in the prevalence and incidence of tuberculosis in South India. *International Journal of Tuberculosis and Lung Disease* 2001;5:142-57.

18. *The WHO standard tuberculin test. Geneva*: World Health Organization; 1963. WHO/TB/Technical Guide No.3.

19. Bleiker MA, Sutherland I, Styblo K, Ten Dam HG, Misljenovic O. Guidelines for estimating the risk of tuberculous infection from tuberculin test results in a representative sample of children. *Bulletin of the International Union Against Tuberculosis and Lung Disease* 1989;64:7-12.

20. Cauthen GM, Pio A, ten Dam HG. *Annual risk of tuberculous infection*. Geneva: World Health Organization; 1988. WHO document WHO/TB/88.154.

21. Office of the Registrar General, India. *Slum population in states/UTs*. New Delhi: Office of the Registrar General; 2001. Available from: URL: http://www.censusindia.net/results/slum1.html

22. Upelkar MW, Rangan S. Private doctors and tuberculosis control in India. *Tubercle and Lung Disease* 1993;74:332-7.

23. Waaler H, Galtung O, Mordal K. The risk of tuberculous infection in Norway. *Bulletin of the International Union against Tuberculosis and Lung Disease* 1975;50:5-61.

24. Nagelkerke NJD, Heisterkamp S, Borgdorff MW, Broekmans J, Houwelingen H Van. Semi-parametric estimation of age-time specific infection incidence from serial prevalence data. *Statistics in Medicine* 1999;18:307-20.

25. National AIDS Control Organization. *Estimation of HIV infection among adult population; HIV estimates for year 2001*. New Delhi: National AIDS Control Organization; 2002. Available from: URL: http://www.naco.nic.in/indianscene/esthiv.htm

26. Liard R, Tazir M, Boulahbal F, Perdrizet. Use of two methods of analysis to estimate the annual rate of tuberculosis infection in Southern Algeria. *Tubercle and Lung Disease* 1996;77:207-14.

27. Hong YP, Kim SJ, Lew WJ, Lee EK, Han YC. The seventh nationwide tuberculosis prevalence survey in Korea, 1995. *International Journal of Tuberculosis and Lung Disease* 1998;2:27-36.

28. Bosman MCJ, Swai OB, Kwamanga DO, Agwanda R, Idukitta G, Misljenovic O. National Tuberculin Survey of Kenya, 1986–1990. *International Journal of Tuberculosis and Lung Disease* 1998;2:272-80.

29. El lbiary S, De Coster EJM, Tolba FM, Van Maaren P, Wasily L, Van Cleeff M, et al. Trend in the annual risk of tuberculous infection in Egypt, 1950–1996. *International Journal of Tuberculosis and Lung Disease* 1999;3:294-9.

30. Tanzania Tuberculin Survey Collaboration. Tuberculosis control in the era of the HIV epidemic: risk of tuberculosis infection in Tanzania, 1983–1998. *International Journal of Tuberculosis and Lung Disease* 2000;5:103-12.

31. Tupasi TE, Radhakrishna S, Pascual ML, Quelapio MID, Villa ML, Co VM, et al. BCG coverage and the annual risk of tuberculosis infection over a 14-year period in the Philippines assessed from the nationwide prevalence surveys. *International Journal of Tuberculosis and Lung Disease* 2000;4:216-22.

32. Murray CJL, Styblo K, Rouillon A. Tuberculosis in developing countries: burden, intervention and cost. Bulletin of the International *Union against Tuberculosis and Lung Disease* 1990;65:6.

33. Chadha VK, Jagannatha PS, Vaidyanathan P, Jagota P. PPD RT23 for tuberculin surveys in India. *International Journal of Tuberculosis and Lung Disease* 2003;7:172-9.

34. *TB India 2001, RNTCP Status Report*. New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare; 2001.

35. *TB India 2002, RNTCP Status Report*. New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare; 2002.

36. *RNTCP performance quarterly reports–First Quarter 2002*. New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare; 2002. Available from: URL: http://www.tbcindia.org

37. *RNTCP performance quarterly reports–Second Quarter 2002*. New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare; 2002. Available from: URL: http://www.tbcindia.org

38. Report on performance of National Tuberculosis programme. *DTP Quarterly reports; 24/4 January-December 2000*. Bangalore: National Tuberculosis Institute; 2001.

39. Report on performance of National Tuberculosis programme. *DTP Quarterly reports; 25/4 January-December 2001*. Bangalore: National Tuberculosis Institute; 2002.

40. Report on performance of National Tuberculosis programme. *DTP Quarterly reports; 26/2 January- June 2002*. Bangalore: National Tuberculosis Institute; 2002.

41. Styblo K. The relationship between the risk of tuberculous infection and the risk of developing infectious tuberculosis. *Bulletin of the International Union Against Tuberculosis and Lung Disease* 1985;60:117-99.

42. Lwanga SK, Lemeshaw S. Sample size determination in health studies — a practical manual. Geneva: World Health Organization; 1991.

43. Nagelkerke NJD, Borgdorff MW, Kalisvaart NA, Broekmans JF. The design of multi-stage tuberculin surveys: some suggestions for sampling. *International Journal of Tuberculosis and Lung Disease* 2000;4:314-20.

44. Bennett S, Woods T, Winitha Liyanage M, Duana Smith LA. Simplified general method for cluster-sample surveys of health in developing countries. *World Health Statistics Quarterly* 1991;44:98-106.