Tuberculosis in the Transkei

AN EPIDEMIOLOGICAL SURVEY

SOUTH AFRICAN TUBERCULOSIS STUDY GROUP*

SUMMARY

An epidemiological survey to estimate the prevalence of infection by *Mycobacterium tuberculosis* and other mycobacteria, was conducted in the Transkei; 3 155 persons from 9 sites were randomly selected. Tuberculin tests were performed on 1 487 children over the age of 3 months. The multiple-puncture method and 2 simultaneous Mantoux tests were employed, using 2 units of human tuberculin PPD and avian tuberculin PPD. Chest radiographs were made of 1 506 out of 1 570 eligible adults.

In the age group 0 - 4 years 15,8% of the children were positive to the Mantoux test using 2 units and 10 mm induration as lower limits. A low prevalence of avian tuberculin reactors was demonstrated in 8 of the 9 sites. Double infection by *M. tuberculosis* and other mycobacteria appears to be widespread.

Due to the poor quality of radiographic films taken under difficult field conditions, the great variability of results did not permit an exact estimation of the incidence of tuberculosis-like lung abnormalities. The incidence was 8% if agreement between the 2 readers was taken as the criterion. Correlation between multiple-puncture and intradermal tests, and between radiographic findings and tuberculin status, is discussed.

S. Afr. Med. J., **48**, 149 (1974).

The Transkei is a Black homeland with a population of 1 751 000, according to the 1970 census; only 56 000 inhabitants, or 3%, are urban. The Xhosas, numbering 1 650 000, constitute the main tribe, and there are 20 000 Zulus and 61 000 Seshoeshoe. Most of the active male population work in the mines and industrial centres of South Africa and spend the bulk of their income outside the Transkei. The land is hilly, mostly uncultivated grassland, with a semitropical climate, cool winters and hot summers. Health services are hampered by poor roads and mountainous terrain. The predominant health problem, apart from tuberculosis, is malnutrition. Poor sanitation and lack of domestic water supplies prevail. Most people live in small, badly lit huts as subsistence farmers. Wages earned by the men are usually invested in livestock which is a sign of wealth and prestige.

For many years tuberculosis was regarded as the major health problem. Statistics from the Health Department and the mining industries[1] show the Transkei to be the region in South Africa most affected by tuberculosis infection. As no reliable and comprehensive figures were available as a basis for a control programme, an epidemiological survey was planned by the Regional Director of Health Services, Umtata, the local branch of the South African National Tuberculosis Association, and the Tuberculosis Research Unit of the South African Medical Research Council.

The survey, undertaken on a random sample of the population, was aimed at estimating the prevalence of infection by means of tuberculin tests and radiological lesions detected by means of a 70 mm mobile photofluorography unit. The project commenced at the end of 1971 and ended in April 1972.

MATERIAL AND METHODS

For practical reasons the survey was restricted to about 3 000 people. In a multistage sampling procedure a complete census of the population of 9 selected sites was carried out and contacts were established with the local Black authorities. Every permanent resident of a hut was registered and his card kept in a central file. A team of Black health educators and nurses of the State Health Services and SANTA was sent ahead of the investigating teams to motivate the inhabitants. This was largely responsible for the excellent attendance and co-operation of the populace.

Sampling Methods

A stratified, multistage, cluster sampling technique was used. The Transkei is subdivided into 26 districts, with populations ranging from 35 000 to 127 000 inhabitants. Each district is in turn subdivided into several locations. The existence of a regional factor in the prevalence of tuberculosis was expected. A distinct pattern of disease was thought to be related to 3 physiographical regions,

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Date received: 28 June 1973.

i.e. highveld, hinterland, and coast. They were regarded as suitable strata and 9 locations were selected at random. The actual number to be surveyed was determined by the following procedure: The population distribution in the 3 strata was determined according to the 1970 census, i.e. 37% in the coastal area, 40% in the central area, and 23% in the north-western area or highveld. The total was arbitrarily fixed at 3 000 people, and 1 110, 1 200 and 690, respectively, were allocated to each stratum (in round figures). The actual size of each cluster was strictly proportional to the population of the selected districts. Where the population in any one location exceeded the number required, the location was subdivided into clusters approximating those required for survey and a random selection was made. Population figures for each location were not available at that time and had to be obtained from the local authorities.

A hut-to-hut census was carried out by the Black staff of the regional branch of SANTA. Visitors were not recorded and, to the best of our knowledge, all permanent residents absent on the days of the census, were registered. Much effort and time were devoted to the reduction of the number of non-responding people, and the satisfactory level of only 3,5% was achieved. All professional staff members were highly conscious of the relative importance of sampling the absentees, 2 or 3 of whom sometimes require as much time as the whole cluster.[2]

A total of 3 150 people was registered and 96,6% completed the tests. Of the 1 570 adults registered, 1 506 were X-rayed (96,5%), and of the 1 585 children eligible for the tuberculin test, 1 539 (97,1%) were tested. Twenty-six persons failed to report to have the test read, but 17 were traced to their huts and their tests were read. In 26 of 101 cases, an explanation was given for non-attendance. The 70-mm X-ray plates of 96 adults were unreadable or blank, but 86 of these adults were traced and re-examined.

TABLE I. DISTRIBUTION OF SAMPLE POPULATION BY AGE AND SEX

Age group (in years)	Percentage of total sample (both sexes)	Ratio female : male
<1	3,8	1,10
1	2,9	1,12
2	3,4	0,98
3	3,8	0,95
4	3,7	0,90
5	3,7	1,07
6	3,7	0,96
7 - 10	13,4	0,98
11 - 14	12,1	1,10
15 - 25	14,7	2,78
26 - 49	19,2	4,38
50 + over	15,7	1,72
Total	100,0	1,62

Table I shows the age and sex distribution of the population in the survey. Up to the age of 15 years, the numbers of males and females are almost the same, thereafter there is a large preponderance of women at all 9 locations. In the 15 - 25-year-old age group the female: male ratio is 2,78, while in the 26 - 49-year-old age group, it is 4,38. The difference in the rates is highly significant ($P<0,001$) and reflects the effect of the migration of men from the tribal lands to towns and industrialised centres in search of work. A study was made in locations IV - IX, in the households of adults who were permanently away from home. Out of 591 absentees recorded, 491 were male (83,1%) of whom 148 (30,1%) were working in the Transkei, 198 (40,3%) in the Transvaal, and 166 (33,8%) in Natal.

Tuberculin Tests

Every child from 3 months to 14 years old was tuberculin-tested by the multiple-puncture method of Heaf and by a comparative Mantoux test. Human and avian PPD tuberculin prepared by the Tuberculosis Research Unit at Onderstepoort were used. The Heaf test was performed on the flexor surface of the proximal part of the left forearm. The East multiple-puncture apparatus Mark VI model was used, and human PPD tuberculin containing 100 000 tuberculin units (TU) per ml.

Human and avian tuberculin for the Mantoux tests had been standardised to have similar potencies by biological assay. A fresh dilution in isotonic buffer with Tween 80 was prepared each morning in the field to obtain a strength of 20 TU per ml. Biological assays on guinea pigs were performed to check the stability of the final solutions after various intervals. After 4 days under field conditions the potency was 85,9% compared with a fresh dilution (lower fiducial limit at P = 0,05 : 60,1%) and after 12 days 24,8% potency remained (lower fiducial limit: 15,9%) when tested according to the *British Pharmacopoeia*, 1968, using a Latin square design. No significant loss of potency by adsorption to glass could have taken place during the few hours' use of the PPD solution.[3-5]

Comparative tests of our human PPD (batch 203) used in this survey and the Copenhagen product RT23, were done several times on guinea pigs and on tuberculous patients. Rather contradictory results were obtained. In each of the repeated trials on guinea pigs, batch 203 was stronger than RT23 (potency ratio about 140%), but in humans the mean induration with batch 203 was 2 mm smaller than with RT23.[6] This problem of divergence between clinical and biological assay was mentioned by Guld and Bentoom.[7] According to the comparative tests in the same population, 2 TU of our batch 203 was approximately equal to 1 TU of RT23.

One-tenth millilitre of PPD solution was injected intradermally in the upper third of the flexor surface of each forearm. Disposable plastic syringes with needles fitted, and discarded after 10 injections, were used. Two medical officers gave the injections, each handling both tuberculins to prevent any bias, possibly due to unequal techniques. The arm in which human tuberculin was to be injected was chosen by using a list of random binary digits giving 0 or 1. To provide for a comparative analysis of injectors, children with even registration numbers were allocated to one injector, and those with odd numbers to the other. If an injection was unsatisfactory another injection was made on a site at least 3 cm away. In order to identify a child should his card be lost, the registration number was painted on his arm, with gentian violet. The dye was not durable, however, and very few numbers were legible on the day of reading.

On the day of injection the presence or absence of a BCG scar in children was recorded. For both children and adults, any previous or current tuberculosis therapy was also recorded. Children were examined for 3 different signs of kwashiorkor, but no record was kept of the moderate stages of malnutrition. Twenty-six BCG scars and 23 cases of kwashiorkor, i.e. 1,5% of the children, were thus reported. Sixty-one persons (2%) admitted to having been under treatment, but the true figure is likely to be higher. There were 28 children among the 61 so-called known TB cases.

Both Heaf and Mantoux tests were read by the 2 medical officers independently after 72 hours. The Heaf test was read in 4 grades as proposed by Heaf.[8]

The reactions to the intradermal injections were measured by the transverse diameter of the induration, erythema being ignored. High-precision calipers with dials were used. The margin of induration is often ill-defined, and the rounding-off of readings to the nearest millimetre was found to be permissible.

The readers had no knowledge of the PPD which had been injected into the right or left forearm. Moreover, one doctor measured the induration in inches, while the other measured in millimetres. The reactions on the left forearm (Mantoux and Heaf tests) were read by one reader, A, and reactions on the right forearm (Mantoux only) by the other reader, B. After a number of children had been read in this way the reactions on the right forearm were read by reader A. By this procedure independent readings were assured, in spite of the 2 readers working together.

X-Ray Examination of Adults

All persons 15 years and over were eligible for a 70 mm chest photofluorogram. Some younger children were X-rayed whenever circumstances permitted. All films were read by 2 readers independently, another classified the findings as follows: 0 = clear; 1 = minimal, equivalent of unilateral apical lesion; 2 = moderate, up to and including involvement of the whole right upper lobe (unilateral); 3 = extensive, in excess of 2 above, or bilateral disease; 4 = pleural and pericardial effusions; 5 = fibrotic and apparently inactive disease; 6 = primary tuberculosis. No reader had knowledge of the history of the individual concerned. Because of the poor quality of some films, 96 adults had to be transported to the nearest hospital where large plates were used.

RESULTS

The preliminary tests for standardising the tuberculin, and the 2 readers, will be discussed first. The multiple-puncture method is used as a routine in South Africa for the scanning of reactors in tuberculosis control programmes. The results of a few surveys using 10 TU PPD intradermally, have been published. The change to a lower dose was made in order to be in line with modern trends in tuberculosis research.[9] A preliminary test with 2 and 5 units of Onderstepoort batch 197 (SA) and International Standard PPD-S was carried out in 1971 on 148 patients with bacteriologically confirmed pulmonary tuberculosis. The 2 observers read the reaction after 72 and 96 hours.

TABLE II. MEAN INDURATION: TWO READERS, TWO READINGS, TWO TUBERCULINS

	3rd day SA PPD		4th day SA PPD		3rd day PPD S		4th day PPD S	
Reader	A	B	A	B	A	B	A	B
Mean induration (mm)	**15,1**	**13,6**	**13,2**	**12,8**	**16,9**	**14,8**	**16,0**	**13,8**
Standard error of the mean	**0,46**	**0,32**	**0,49**	**0,39**	**0,52**	**0,42**	**0,53**	**0,45**

Table II shows the mean induration after 3 and 4 days (2 TU human PPD, batch 197, SA) for each reader. The coefficients are as follows: between readers 0,72; between days of reading 0,73 for reader A, 0,68 for reader B. The reading on the fourth day compared with the routine reading after 72 hours, slightly underestimated the reaction.

Several authors have attached great emphasis to the standardisation between 2 readers. Teruel and Netto[10] and Carruthers[11] determined the percentage agreement within certain limits of the recorded diameters of induration of the same reaction. It is essential to analyse the patterns of the 2 readers and exclude any bias. Furthermore, analysis of the results can be easily performed separately for each reader for the mean of the 2 readings, giving better insight into possibly divergent conclusions.

Heaf Tests — Agreement Between and Within Readers

Complete agreement between readers was achieved in 1 236 of 1 456 readings (84,9%). If a difference of one grade is disregarded (except between grades II and III) agreement was 96,5%. The cut-off point between negative and positive reaction was between grades II and III in this survey. Disagreement was most frequent between negative and grade I. Cross-tabulation of the 2 readings shows a fairly symmetrical and balanced pattern, confirmed by perfect concordance of the conclusions drawn from the separate analysis performed on each set of results.

The blind, double reading of the reactions by the same readers showed a fairly good agreement (97,3% reader A, 94,6% reader B). Variation between results obtained by the 2 readers was greater than variation between results obtained by an individual reader.

Epidemiological Pattern

A highly significant difference in the sensitivity to human tuberculin, between the 9 sampling sites, was shown (χ^2-test, $P<0{,}001$). Fig. 1 shows the histograms of reactions in each location as read by reader A. Figures for reader B are similar.

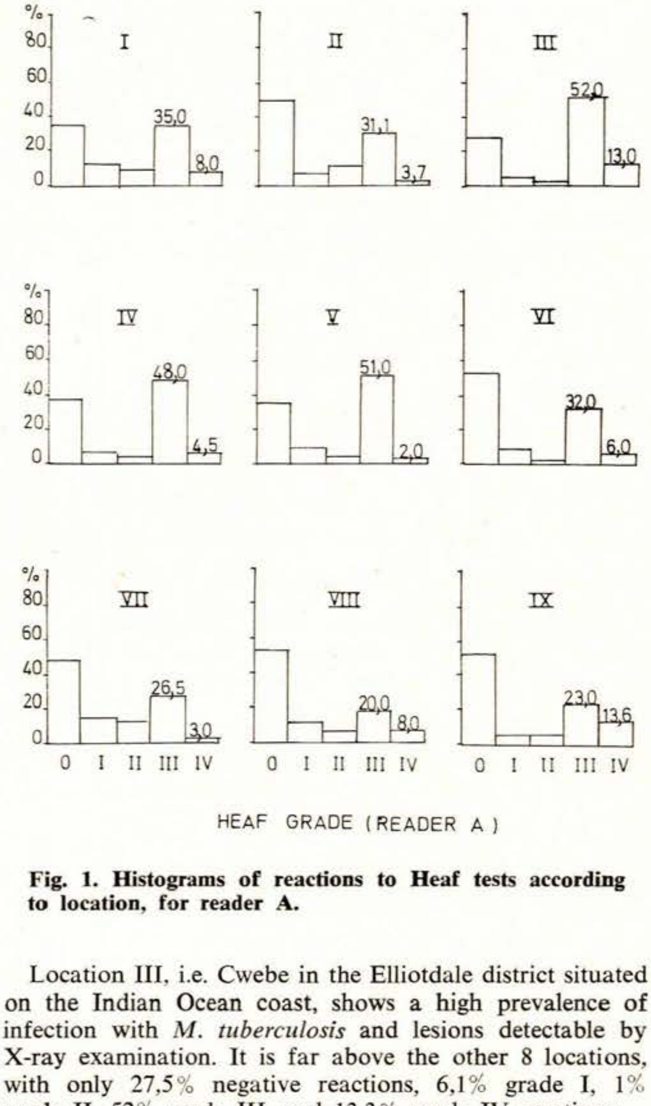

Fig. 1. Histograms of reactions to Heaf tests according to location, for reader A.

Location III, i.e. Cwebe in the Elliotdale district situated on the Indian Ocean coast, shows a high prevalence of infection with *M. tuberculosis* and lesions detectable by X-ray examination. It is far above the other 8 locations, with only 27,5% negative reactions, 6,1% grade I, 1% grade II, 52% grade III, and 13,3% grade IV reactions.

If this site is excluded the difference between the other sites is still highly significant ($P<0{,}001$), varying between 28% and 53% for grades III and IV reactors. This lack of agreement between sites occurred for all measurements and made any analysis more complex.[2]

The sample sites were drawn from different geographic regions of the Transkei on the assumption that they would show different patterns of tuberculosis, but no significant difference could be linked to this subdivision. The usefulness of such geographical stratification is made rather doubtful by the findings of this survey.

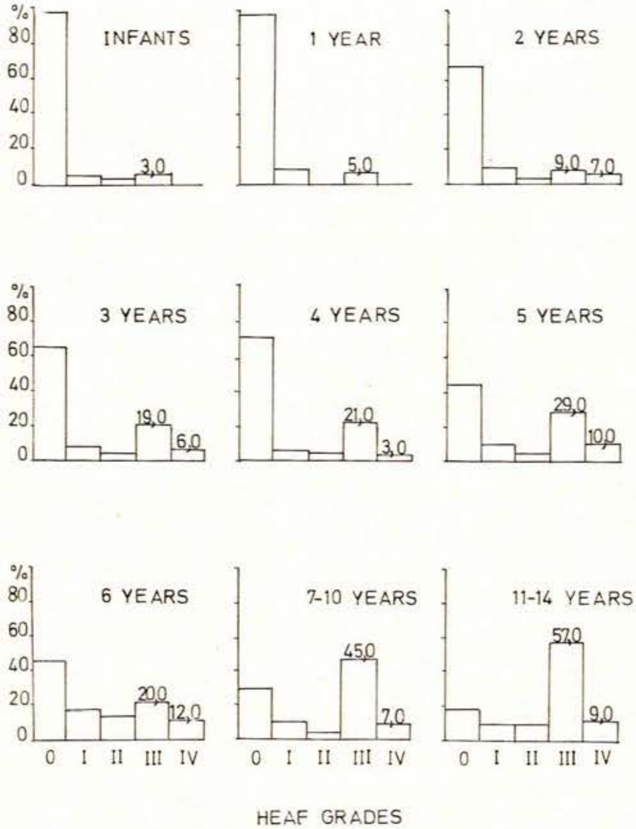

Fig. 2. Tuberculin reactions for all groups up to 14 years.

Fig. 2 illustrates the tuberculin sensitivity for all age groups up to 14 years. The rate of infection as indicated by grades III and IV reactions is nearly nil below 2 years, and it reaches 66% in the age group 11 - 14 years. No statistically significant differences were demonstrated by the χ^2-test between the sexes, although the males showed a slightly higher percentage of positives in most groups and for both readers (sign test significant).

Mantoux Tests — Agreement Between and Within Readers

If the 2 readers and the human PPD reactions are compared, 72,3% of the readings were within 2 mm of each other, 73,6% within 3 mm, and 86,7% within 4 mm. Like Carruthers,[11] we regard a difference of 3 mm or less as not being significant.

Fig. 3 shows the plotted diagram of the 1 456 double readings of the reactions to 2 TU of human PPD. There was a trend of reader B to over-read the larger reactions of

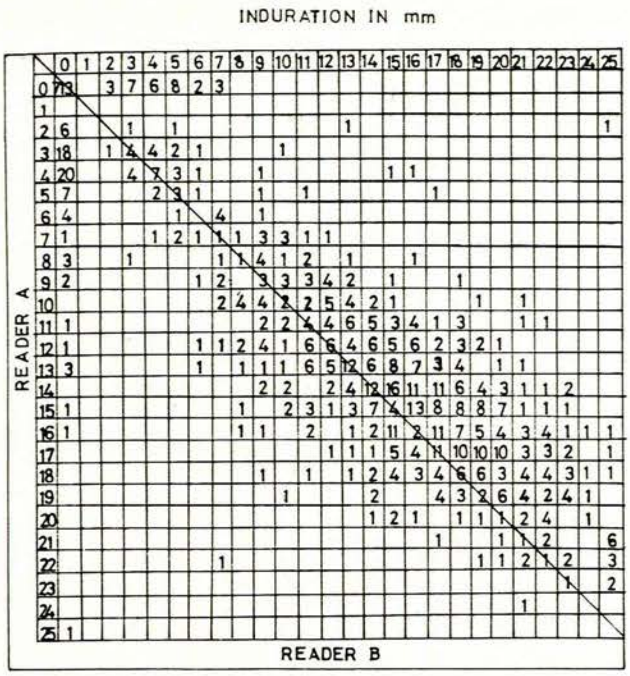

Fig. 3. Scattergram or plotted diagram of double readings of 1 456 Mantoux reactions.

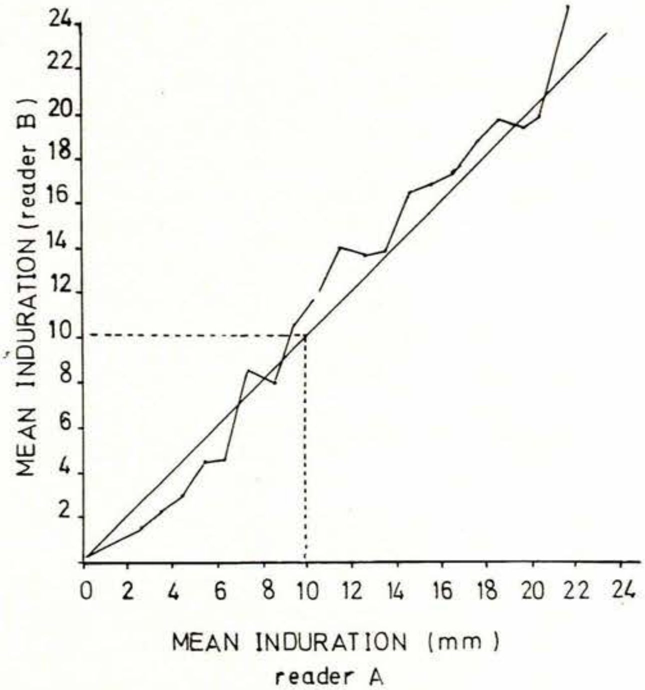

Fig. 4. Illustration of the agreement between readers on the Mantoux reactions.

more than 10 mm, and to underrate the small ones of 2 - 6 mm. Arbitrary convention would allow us to regard reader A as standard in any comparison (Fig. 4). The reactions were divided in groups of 1-mm units according to the reading of reader A, and the mean of the corresponding readings of reader B was calculated for each group. Superimposed is the regression line of reader B on reader A ($Y = -0,05 + 1,07\ X$). The complete analysis of the results of both readers showed little divergence. We accept the average of the 2 readings of each reaction as final for all figures and graphs displayed. Agreement within readers has been proved very satisfactory, especially for reader A. (Coefficient of correlation = 0,96 for reader A, 0,92 for reader B.) The regression line did not show any bias. Agreement within readers and between readers was similar.

Prevalence Rates Based on Tuberculin Sensitivity

We used 2 units of our batch 203 human tuberculin, and this corresponded to about 1 unit of the Danish RT23. This low dose of human PPD had not been used before on a large scale in South Africa, therefore no preconceived size of the reaction was laid down for estimating the prevalence of tuberculous infection. Fig. 5 gives the distribution of all reactions to the human tuberculin.

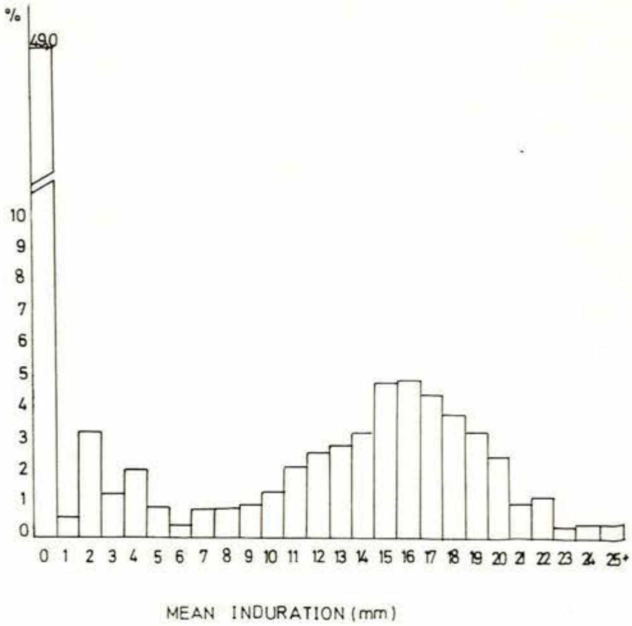

Fig. 5. Histogram on the distribution of all reactions of the children to human PPD (Mantoux).

In Tables III and IV, the prevalence rates of infection for each group and for each site were computed to fit 5 possible definitions of a positive reactor, namely, a person reacting with an induration of 8 mm or more, 9 mm or more, 10 mm or more, 10 mm or more and a smaller avian reaction, and finally 10 mm or more and an avian reaction which is at least 2 mm smaller than the human reaction. Classification of a reaction of 8 mm or larger

TABLE III. PREVALENCE RATES OF TUBERCULOSIS INFECTION BY AGE ACCORDING TO 5 CRITERIA FOR 'POSITIVE REACTION'

	Age group									
Criteria	3 - 12 mo. (%)	1 yr (%)	2 yrs (%)	3 yrs (%)	4 yrs (%)	5 yrs (%)	6 yrs (%)	7 - 10 yrs (%)	11 - 14 yrs (%)	All ages (%)
8 mm or more	4,5	4,0	16,1	26,3	23,9	40,0	32,0	52,0	65,2	41,2
9 mm or more	4,5	4,0	15,1	26,0	23,3	40,0	31,0	51,0	63,1	40,2
10 mm or more	4,5	4,0	15,1	23,4	23,3	38,1	31,0	48,9	61,0	38,8
10 mm or more and larger than avian reaction	4,5	2,7	14,1	20,0	21,4	30,9	26,2	39,8	49,7	32,0
10 mm or more and at least 2 mm larger than avian reaction	1,5	2,7	12,1	19,1	15,8	28,1	23,3	33,5	44,9	27,8

TABLE IV. PREVALENCE RATES OF TUBERCULOSIS INFECTION BY SITE ACCORDING TO 5 CRITERIA FOR 'POSITIVE REACTION'

	Site (location)								
Criteria	1 (%)	II (%)	III (%)	IV (%)	V (%)	VI (%)	VII (%)	VIII (%)	IX (%)
8 mm or more	54,3	36,2	65,3	50,5	50,3	56,3	25,8	29,4	40,3
9 mm or more	53,3	34,8	64,2	50,0	49,6	35,1	24,5	28,2	39,7
10 mm or more	52,6	34,8	64,2	48,8	48,9	32,7	20,6	26,5	38,5
10 mm or more and larger than avian reaction	50,8	28,1	25,5	40,9	44,9	29,7	19,3	22,5	33,1
10 mm or more and at least 2 mm larger than avian reaction	45,6	25,9	12,2	34,6	40,9	27,9	18,7	18,2	30,1

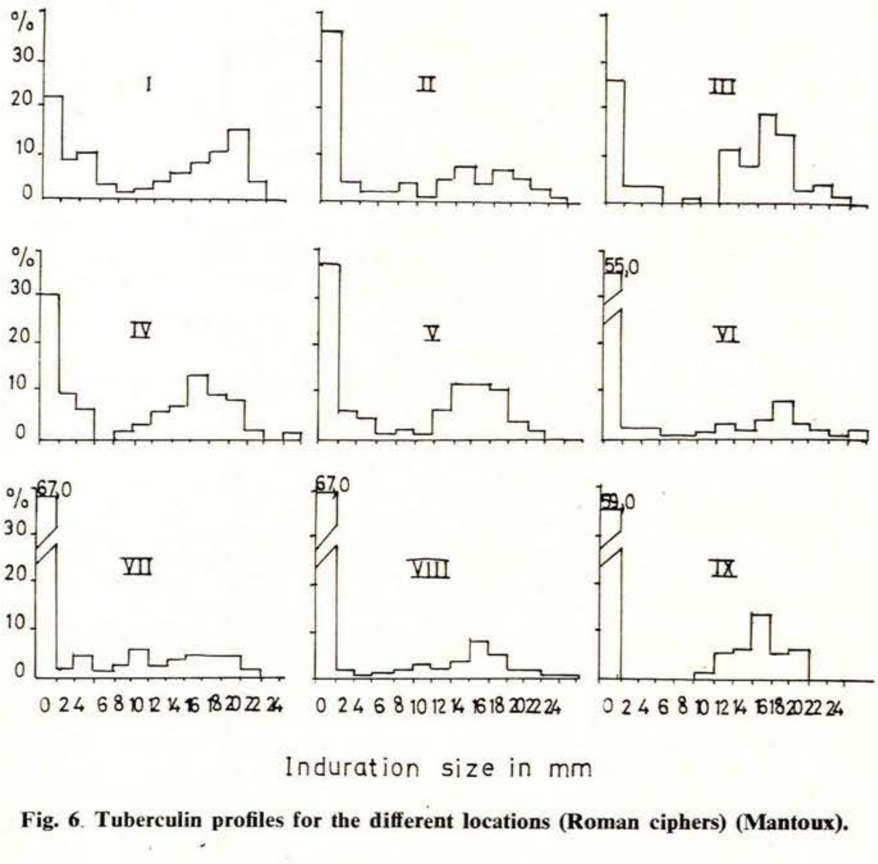

Fig. 6. Tuberculin profiles for the different locations (Roman ciphers) (Mantoux).

:op line) as a positive sign of *M. tuberculosis* infection in ontrast to the adoption of the internationally accepted mit of 10 mm (third line) would not alter the prevalence ates significantly. With regard to the last column of 'able III, 38,8% of the children tested were positive eactors in the 10-mm or more limit, compared with 41,2% eactors in the 8-mm or more limit. Such a difference is of o significance in any mass campaign or tuberculosis con- ·ol programme. For the sake of standardisation and iternational comparison, the criterion of 10-mm indura- on is used in this article.

A highly significant difference in infection rates was btained between the 9 sites as shown in Table IV and lustrated in Fig. 6. The rank order of the rates is very milar to that obtained by multiple puncture. In Fig. A the mean induration of each site is displayed and the ormal reference distribution of the mean, centred to the eneral mean induration, is drawn (scaling factor

$$\frac{s^2}{n} = 0{,}51 \text{ mm, confidence interval } \pm 1{,}2 \text{ mm}).$$

ecause the reference distribution (the bell-shaped curve) ay shift to any horizontal position, it is clear that the ean indurations are not necessarily members of a single stribution. Clearly, there is a regional factor, but again e geographical subdivision of the Transkei into 3 regions as not shown to be of any epidemiological value. The evalence of tuberculous infection was similar for both xes, and ranged from 15,8% for the age group 0 - 4 ears to 62,6% in the age group 11 - 14 years. Mean in-

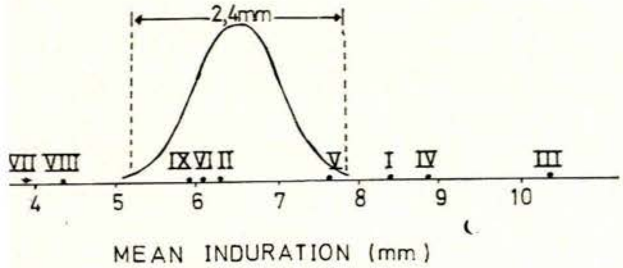

Fig 7A. Reference normal distribution curve of mean reaction to 2 TU human PPD per location (I - IX).

durations are strictly parallel to the prevalence rate of positive reactors (Fig. 8).

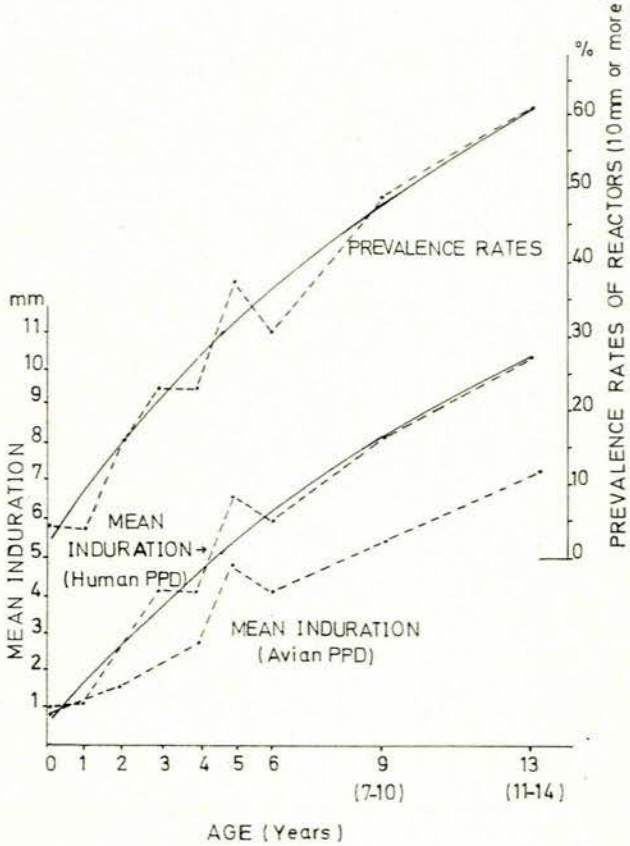

Fig. 8. Prevalence and mean induration versus age. Observed values and best fit values.

A significantly lower mean induration (human PPD = 2,1 mm instead of 6,6 mm) was found in children with severe malnutrition and showing signs of kwashiorkor. The condition occurred predominantly in younger children with an average age of 2,4 years, and comparison with reactor rates of children of the same age did not reach a significant level.

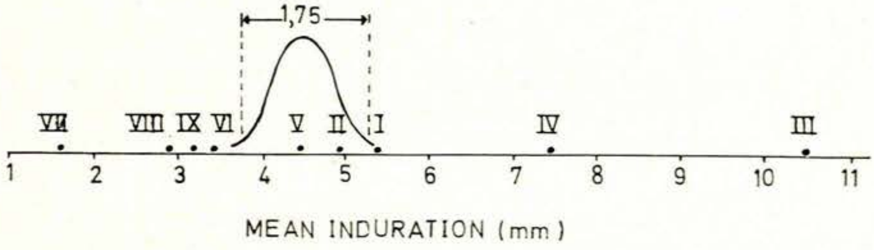

Fig. 7B. Reference normal distribution curve of mean reaction to 2 TU avian PPD per location.

Epidemiological Pattern of Sensitivity to Avian PPD

Non-specific tuberculin sensitivity has been investigated widely in the last 10 years. Survey results in Nigeria and in other countries in Africa have shown that non-specific reactions are common, although the occurrence varies from place to place.[12,13] In South Africa the Tuberculosis Research Unit at Onderstepoort studied the occurrence of atypical mycobacteria in domestic animals, in the environment, and in man.[14-16] They isolated 14 strains from the sputa of 4 000 tuberculous patients.[17] They concluded that disease due to atypical mycobacteria is very rare, but that *M. avium*-like mycobacteria occur frequently in the surroundings of man and animals. Their work confirms the generally accepted view that low-grade sensitivity to mammalian tuberculin may be due to contact and 'infection' with atypical mycobacteria. Many surveys with various skin antigens from atypicals were undertaken, but there is no agreement on the interpretation of the cross-reactions. When double infections are present or when homologous antigens are not available, the results of multiple skin tests are even less satisfactory.[18] Multiple infection may be rather frequent, judging from a bacteriological survey by the Tuberculosis Research Unit.

Avian PPD tuberculin was standardised in *M. avium*-sensitised guinea pigs to provoke a reaction equal to that of mammalian PPD in *M. tuberculosis*-sensitised guinea pigs. It was also checked against the WHO standard. The inverted potency ratio of human PPDs RT23 and SA batch 203 in guinea pigs and humans and the fact that *M. tuberculosis* grows in man as a susceptible species, while the *M. avium* group usually does not, makes it debatable whether the results of standardisation in guinea pigs are fully applicable to human beings. It may be assumed, however, that a child who shows a bigger skin reaction to avian PPD than to human PPD is likely to be infected with mycobacteria antigenically more closely related to *M. avium* than to *M. tuberculosis*.[19]

We do not know which comparative skin reaction is indicative of single infection with mycobacteria other than the human tubercle bacillus. Therefore, the prevalence of the 'avian bigger than human reaction', is given for various differences of induration diameter (Table V and VI). Incidence rate of *M. avium*-type infection were not calculated, because of the lack of agreement on the inter-

TABLE V. PREVALENCE RATES BY AGE OF PREDOMINANTLY AVIAN REACTORS ACCORDING TO 6 CRITERIA

	Criteria	Age group: 0 - 4 yrs (%)	5 - 6 yrs (%)	7 - 10 yrs (%)	11 - 14 yrs (%)
Avian reaction 6 mm or more	At least				
	2 mm more than human reaction	1,1	7,0	8,9	12,6
	4 mm more than human reaction	0,4	4,7	4,8	6,6
	6 mm more than human reaction	0,2	3,7	2,8	5,4
Avian reaction 10 mm or more	At least				
	2 mm more than human reaction	0,6	5,6	7,1	10,2
	4 mm more than human reaction	0,2	3,3	3,3	4,5
	6 mm more than human reaction	0,0	2,8	1,8	3,9
	Number of children tested	483	220	402	353

TABLE VI. PREVALENCE RATES OF SUBJECTS REACTING PREDOMINANTLY TO AVIAN TUBERCULIN (SUBDIVIDED BY SITE, AND ASSESSED BY 6 CRITERIA)

	Criteria	Site (location): I (%)	II (%)	III (%)	IV (%)	V (%)	VI (%)	VII (%)	VIII (%)	IX (%)	Total sample (%)
Avian reaction 6 mm or more (single test)	Avian at least										
	2 mm more than human reaction	2,6	7,4	28,6	6,8	4,0	6,5	5,8	5,4	3,0	6,9
	4 mm more than human reaction	1,8	3,7	6,1	5,1	3,4	4,2	3,9	4,1	1,8	3,8
	6 mm more than human reaction	1,8	3,7	5,1	2,8	2,0	1,8	3,2	3,7	0,6	2,7
Avian reaction 10 mm or more (single test)	Avian at least										
	2 mm more than human reaction	1,8	4,4	28,6	4,5	4,0	4,2	4,5	3,3	3,0	5,5
	4 mm more than human reaction	1,8	1,5	6,1	2,8	3,4	2,4	2,6	2,1	1,8	2,6
	6 mm more than human reaction	1,8	1,5	5,1	1,7	2,0	1,2	1,9	2,1	0,6	1,9
	Number of children tested	175	137	98	175	150	166	155	241	162	1 455

pretation of avian PPD reactions. There were no significant differences between the sexes. Avian and human PPD sensitivity increased with age (Fig. 8). This indicates a permanent and general contact with, or infection from the environment by, mycobacteria related to *M. avium*. Location III, Cwebe, is once more an exception, and it would be worth a further field investigation. The prevalence rate varies greatly with the criterion adopted, from 28,6% for an acceptable difference of 2 mm to 5,1% for the 6-mm difference. It is also the only site where avian reactions (mean 10,5 mm) were bigger than human reactions (mean 10,4 mm). The scatter diagram in Fig. 9 compares location III with 2 others which are representative of the usual pattern. Avian PPD sensitivity shows a significant difference between sites, and this is illustrated in Fig. 7B, by drawing the normal reference distribution curve of the mean induration (scaling factor $\frac{s^2}{n} = 0{,}446$ mm; confidence interval +0,88 mm).

Comparison of Multiple-Puncture and Intradermal Tuberculin Testing

Similar results were obtained by both methods, but significance tests failed to show conclusive differences with the less exacting Heaf method. The multiple-puncture method is considered an efficient and easy method for field screening of positive reactors, but it is not suitable for epidemiological research.

Heaf grade II reactors should be classified as doubtful positives, and should be retested by intradermal injection of 2TU PPD. Table VII gives the correlation between the 4 grades of Heaf's classification and the mean indurations from simultaneous intradermal human and avian PPDs, as measured by reader A. It is evident that Heaf grade I reactions have no epidemiological meaning in our population (mean induration 0,8 mm). The large standard deviation in the intradermal test on Heaf grade II reactors casts some doubt on the diagnostic value of grade II reactions. The corresponding mean induration from human PPD, of 5,6 or even 6 mm, is hardly acceptable as a positive reaction in the 2 TU Mantoux test.

RESULTS OF RADIOGRAPHIC EXAMINATION OF THE CHEST

Of the 1 570 adults registered and eligible for 70-mm chest X-ray examination, 1 506 (96,5%) were examined by the mobile unit. Before presenting any diagnostic results, we must discuss the inaccuracy inherent in mass chest radiography. Much has been published about the efficiency of interpretation and observer error.[20-24] We can distinguish 2 components of observer error: (*i*) failure of the observers to see a shadow or abnormal opacity; (*ii*) failure to agree on its significance.

According to Nyboe,[25] a procedure to determine the efficiency of the interpreter to see an abnormal opacity, requires a collection of film material for which the evalua-

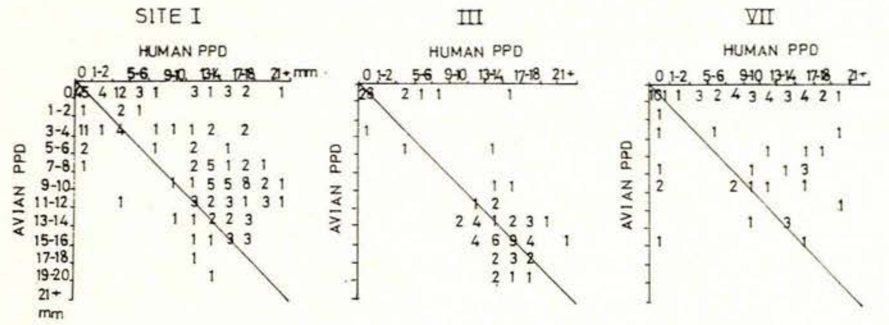

Fig. 9. Scatter diagram of 3 sites correlating human and avian Mantoux reactions. Sites I and VII show the typical pattern.

TABLE VII. CORRELATION: HEAF AND MANTOUX TEST RESULT

Heaf test (human PPD)	No.	Mantoux test (human PPD) Mean induration (mm)	Mantoux test (human PPD) Standard deviation (mm)	Mantoux test (avian PPD) Mean induration (mm)	Mantoux test (avian PPD) Standard deviation (mm)
Negative	638	0,5	1,9	0,6	1,9
Grade I	140	0,8	2,2	1,4	2,6
Grade II	86	5,6	5,9	3,9	5,5
Grade III	495	14,1	4,2	9,2	6,1
Grade IV	99	17,2	3,4	11,6	5,6

tor knows the correct result of the examination. Such a collection was not available at the time of our survey. Only a cross-comparison of recording of abnormalities could be carried out without knowledge of the 'correct interpretation'.

Agreement Between and Within Interpreters

Out of the 1 859 films read by both interpreters, 331 (17,8%) presented some abnormality according to one reader but which were clear according to the other observer. Of the 256 films recorded as clear by reader A, 153 were classified by reader B as 'fibrotic inactive' and 74 as 'primary PTB'.

In Table VIII, 186 cases are cross-tabulated, in which both observers see some abnormalities, excluding pleuricardiac effusion. It permits a crude analysis of the agreement of observers on the significance attaching to these abnormalities. Divergence on the significance of these opacities occurred in 71 cases (38,2%). Furthermore, 44 (23%) were considered as 'fibrotic inactive' by one reader, but were classified as 'active' by the other.

Agreement between observations made at different times by the same interpreter could be partly assessed. From each of 300 adults, 2 different readable X-ray films were examined by the same observer. Lack of agreement could be due to the inconsistency of interpretation as well as to differences of exposure, sharpness, contrast, or positioning of the subject. The consistency of the 2 interpreters in assessing the presence or absence of a lesion or an abnormal opacity on the 2 readings of films, was 71,4% for reader A and 79,3% for reader B. The standard error of the difference was 3,51%, thus a significant difference exists between readers A and B. The consistency in interpreting the image in the same way, i.e. to arrive at the same diagnosis, was 70,2% for reader A and 68,2% for reader B. A finding of 'fibrotic inactive' was often confused with 'extensive destruction'. A second reading of the same roll of film could have led to bias owing to the ability of some diagnosticians to recognise abnormal opacities seen previously.

The normal chest X-ray film presents a pattern which requires good judgement to decide whether a small shadow observed in a film, reflects a lung lesion or merely a variation of the normal pattern.[25] The quality of films was unsatisfactory, and mobile X-ray units taking 100-mm pictures would have been better. Laing[1] has shown that, in recruits for the mines, good, standard 100-mm films are as effective as the full-size film, in more than 90% of cases, and that the 70-mm film is not as effective for screening purposes.

Epidemiological Pattern of Radiological Lesions

The lack of agreement between and within readers as well as the poor quality of the films decrease the value of X-ray examination. The prevalence rates of shadows classified as TB lesions by one or both interpreters, are tabulated in Table IX. If agreement between readers A and B is used as the criterion, 7,9% of persons over 15 years showed some pulmonary lesion. If the number observed by the higher reader is used, 23,8% would be included. Chi-square analysis performed on all distributions, such as first X-ray film compared with a second X-ray film, interpreter A compared with interpreter B, showed a highly significant difference ($P<0,001$).

TABLE VIII. EVALUATION OF 186 X-RAY FILMS IN WHICH BOTH OBSERVERS RECORDED ABNORMALITIES

		Interpreter A					
		Minimal PTB	Moderate PTB	Extensive PTB	Fibrotic inactive lesion	Primary TB	Total
Interpreter B	Minimal PTB	—	—	—	—	—	—
	Moderate PTB	—	**11**	3	5	—	19
	Extensive PTB	—	12	**57**	17	2	88
	Fibrotic inactive lesion	4	8	10	**26**	4	52
	Primary TB	1	5	—	—	**21**	27
	Total	5	36	70	23	27	**186**

TABLE IX. PREVALENCE RATES OF RADIOLOGICAL ABNORMALITIES CLASSIFIED AS TUBERCULOUS LESIONS

	Minimal or moderate PTB (%)	Extensive destruction (%)	Fibrotic inactive lesion (%)	Primary TB (%)	Total lesions No.	Total lesions %	Total X-ray films (No.)
Interpretation by A	**3,1**	**3,9**	**4,6**	**2,6**	**271**	**14,2**	**1 899**
Interpretation by B	**1,7**	**5,4**	**11,1**	**5,6**	**452**	**23,8**	**1 887**
Complete agreement between A and B	**0,8**	**3,9**	**1,7**	**1,4**	**115**	**7,9**	**1 453**

The best, though possibly a conservative, estimation of the prevalence of radiologically discernible lesions is 7,9% (bottom row, Table IX). A regional factor was again demonstrated. For example, in Cwebe (location III), 25% of lesions were seen by reader A and 43% by reader B. The prevalence of 25% for reader A and 39,5% for reader B of primary tuberculosis in children aged 4 - 6 years is startling, but film quality was poor and the number of children tested, small (44).

CORRELATION BETWEEN RADIOLOGICAL FINDINGS AND TUBERCULIN INDURATION

Whenever operational circumstances were adequate, children under 15 years of age were X-rayed. The correlation between the tuberculin state and radiography could be studied in 386 children. The mean induration of human and avian PPD reactions, as well as the average grade for Heaf reactions, were tabulated with X-ray findings according to age; no significant relationship was found, i.e. children with X-ray shadows had no higher Mantoux positivity than other children.

The 9 locations in the survey were ranked in order of prevalence of disease measured by the Mantoux reaction to human PPD, using mean induration as an index, and by the prevalence of radiological abnormalities. Analysis of the rank correlation was performed. X-ray shadows as diagnosed by interpreter B, and Mantoux mean induration showed a very high degree of association (Spearman's rank coefficient = 0,85, $P<0,01$; Kendall's rank coefficient = 0,72). This supports the conclusion that X-ray mass surveys and tuberculin testing are to some extent assessing the same phenomenon. The first, however, is cumbersome, expensive, fraught with technical difficulties and observer errors, while the second is simpler and cheaper.

DISCUSSION

The reliability of the recorded results has been critically discussed in the previous sections. The main objective of this survey was to answer 2 important practical questions: What is the tuberculosis situation in the Transkei, and what are the prospects? Two parameters were investigated in January - February 1972. Further conclusions will be drawn from a bacteriological survey.

During 1953 and 1954, tuberculin and mass X-ray studies were undertaken in the Transkei by Wiles and Rabie.[26] The two aspects of the study were not performed concurrently and, for the most part, not done on the same communities. The study covered an area within a 65-km radius of the town Umtata. In the age group 5 - 9 years, 60,6% showed positive reactions of more than 6 mm to an intradermal dose of PPD equivalent to 10 TU. A rate of 2,3% of 'radiologically positive cases of pulmonary tuberculosis' was found. The authors said that 2,3% was a far higher figure than that found in other mass X-ray surveys of Blacks up to that time. The mobile unit worked at 57 points and 21 080 people were examined. Unfortunately no census was taken and no random sample drawn.

The present study appears to confirm the high prevalence in the Transkei. The proportion of children aged 0 - 4 years with a positive reaction to 2 units is a recognised index of tuberculous infection. The rate of 15,8% is high — in fact, among the highest reported in Africa. The past policies for tuberculosis control were successful in urban and developed rural areas, and a decline in tuberculosis is widely noted. The new approach of the Health Department is more likely to show an impact on the problem in the rural areas.[27] If we accept the conservative rate of 8% of chest abnormalities, about 70 000 adults out of 1,7 million inhabitants constitute a huge high-risk group. They require at least additional investigation, as other non-tuberculous lesions can also cause radiological abnormali-

TABLE X. REGIONAL SURVEYS IN SOUTH AFRICA

Tuberculin surveys of Black children	Year	No.	Age (yrs)	Technique	Criteria	Results (%)
OFS — rural	**1955**	**158**	**0 - 4**	**RT23 10 TU intradermal**	**6 mm**	**13,3**
OFS — urban	**1955**	**73**	**0 - 4**	**RT23 10 TU (ID) intradermal**	**6 mm**	**13,7**
Transkei — rural	**1955**	**548**	**5 - 9**	**PPD 10 TU (ID) intradermal**	**6 mm**	**60,6**
West Natal	**1956**	**218**	**0 - 4**	**PPD 10 TU (ID) intradermal**	**6 mm**	**11,0**
	1956	**1 465**	**5 - 9**	**PPD 10 TU (ID) intradermal**	**6 mm**	**18,2**
Transvaal	**1967**	**154**	**0 - 4**	**Multiple-puncture method**	**III, IV**	**3,8**
Ga-Ranukwa (Tvl)	**1967**	**1 638**	**5 - 9**			**10,6**
Sebokeng	**1969**	**3 280**	**0 - 4**	**Multiple-puncture method**	**III, IV**	**3,3**
Pretoria — urban	**1969**	**7 397**	**0 - 5**	**Multiple-puncture method**	**III, IV**	**2,8**
Mass miniature X-ray on Blacks						
OFS — urban	**1955**	**2 856**	**Over 5**	**70 mm film**	**Reinfection and**	**0,45**
OFS — rural	**1955**	**11 026**	**Over 5**	**70 mm film**	**progress**	
					Primary TB	**0,6**
Transkei — rural	**1955**	**21 080**	**Over 6**	—	**Active TB**	**2,3**
West Natal	**1956**		**Over 10**	**70 mm film**	**Active TB**	**1,2**
Pretoria (work seekers)	**1969**	**51 240**	**Adults**	**70 mm film**	**Active TB**	**0,4**

TABLE XI. PREVALENCE RATES OF INFECTION IN AFRICA

Country	Year	No.	Age (yrs)	Method	Criteria	(%)
Tunisia	1958 - 1961	4 779	0 - 4	RT19 - 20 - 21	10 mm	5,7
Botswana	Before 1964	619	0 - 4	RT23 5 TU	10 mm	9,5
Ghana	Before 1964	616	0 - 4	RT23 5 TU	10 mm	5,3
Nigeria	Before 1964	261	0 - 4	RT23 5 TU	10 mm	13,0
Sierra Leone	Before 1964	636	0 - 4	RT23 5 TU	10 mm	7,7
Tanzania	Before 1964	474	0 - 4	RT23 5 TU	10 mm	3,7
Uganda	Before 1964	1 117	0 - 4	RT23 5 TU	10 mm	3,5
Zambia	Before 1964	409	0 - 4	RT23 1 TU	10 mm	4,1
Kenya	Before 1964	1 842	0 - 4	RT23 1 TU	10 mm	2,8
Liberia	Before 1964	583	0 - 4	RT23 1 TU	10 mm	2,2
Zanzibar	Before 1964	714	0 - 4	RT23 1 TU	10 mm	3,1
Swaziland	1963 - 1965	1 054	0 - 4	RT23 1 TU	10 mm	5,7
Tanzania	1963 - 1966	1 174	5 - 9	RT23 1 TU	10 mm	7,2
Rhodesia	1971	138	0 - 4	Multiple puncture	Grade III, IV	6,2
Lesotho	1962 - 1967	5 376	0 - 4	RT23 1 TU	10 mm	5,6
Upper Volta	1966	136	0 - 4	RT23 1 TU	10 mm	3,5
Rwanda	1961	5 437	6 - 10	1% old tuberculin	5 mm	31,0
Rwanda	1971	778	6 - 10	1% old tuberculin	5 mm	14,4

ties. Isoniazid chemotherapy of clinically healthy but infected individuals is part of the official policy. Of schoolchildren aged 7 - 14 years in the Transkei, 58% were positive reactors (Heaf grade III and IV) to human PPD. Therefore, more than 250 000 children qualify for a course of isoniazid prophylaxis. Children with severe malnutrition should be treated regardless of the reaction. In South Africa positive tuberculin reactors under 5 years of age are notifiable as TB cases. Of this age group, 15,8% or 40 000 children are notifiable and this would add significantly to the notification figures.

If studies on selected groups, such as miners and industrial workers, are excluded, then only a few surveys have been published in the past 20 years in South Africa and neighbouring countries. These were by Fine [28] and others in South West Africa, by Dubovsky in the Orange Free State and the northern Cape,[29] by Osburn in the north-western Cape and in Natal,[30,31] and by SANTA in 1970 in the Transvaal.[32] For many reasons, such as sampling techniques, various tuberculin tests and different criteria for radiological diagnosis, these studies are not comparable with ours or with each other. In Table X a few statistics of the extent of tuberculosis in South Africa are tabulated.

Table XI serves as a partial review of available data on tuberculin surveys performed in Africa in the last 10 years, usually with guidance by the WHO. It must be remembered that the Transkei survey is far from representative of South Africa; indeed, the territory constitutes a very special problem, and previous efforts, based mainly on hospitalisation and chemotherapy, were apparently unsuccessful.

CONCLUSION

This survey provides better knowledge of the actual situation regarding tuberculosis in the Transkei. An accurate prevalence rate of infection, as assessed by the Mantoux test, is now available for reference purposes. The radiological findings might be questioned.

The accuracy of the intradermal tuberculin test which is a major tool of epidemiological research, is confirmed. The multiple-puncture method is shown to be comparable with the Mantoux test for the screening of infected children. Heaf grade II reactions should be regarded as suspicious and not necessarily positive, and should be checked by an intradermal test.

The diagnostic value of a tuberculin test in children more than 10 years old in a tuberculosis control programme in the Transkei is very limited, since the majority will have a positive reaction.

The use of mass X-ray techniques did not prove satisfactory in this survey, but the poor quality of the equipment and the difficult field conditions played a role in this failure.

Bacteriological investigations are part of a complete epidemiological survey. A positive culture or microscopical finding has far more significance in a community than a suspicious lung shadow or a positive tuberculin reaction.

We emphasise that an epidemiological survey must be based on sound statistical sampling. There must be a census of the population at the sites, the sites must be randomly selected, and one must constantly strive to keep the non-response rate at a minimum.

Surveys should be undertaken in other rural parts of the country, to provide reliable epidemiological data. The significant differences between the 9 locations suggest that the problem of tuberculosis is more involved than it was expected to be. A similar survey in the Transkei in 5 or 10 years' time with more clusters should determine the trend of the disease.

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