*TUBERCULIN AND LEPROMIN SENSITIVITY IN E. NIGERIA

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Introduction

Outside the sphere of chemotherapy, the most important contribution to leprosy control in recent years has probably been the discovery of an immunological relationship between leprosy and tuberculosis. The existence of this relationship is not seriously in doubt. It has repeatedly been shown that in suitable circumstances BCG inoculation can induce sensitivity to lepromin as well as to tuberculin, and evidence is beginning to develop that children rendered lepromin sensitive by this method have in fact some protection against clinical leprosy. The nature of this relationship and the circumstances in which it is manifested are, however, not so clear. Increasing knowledge of the tuberculin and lepromin reactions has revealed new complexities not only in their relationship, but in the character of the reactions themselves. While it is generally agreed that high grade sensitivity to tuberculin is induced specifically by *M. tuberculosis*, the tuberculin reaction is subject to a variety of influences which have been discussed by Pepys (1954), and it is possible that low grade sensitivity may be induced by local and non-specific factors, of which one may indeed be *M. leprae* itself (Fernandez and Cabanillas 1955). Recent work on the lepromin reaction, notably that of Kooij and Gerritsen (1956) and Floch (1956) has drawn attention to non-specific elements in it. These matters would be mainly of academic interest were it not for the possibility that under field conditions the relationship between the two infections can be much more distant than it appears when stimulated by BCG. Thus Guinto, Doull and Mabalay (1956) in the Phillippines found a significant minority in whom no relationship between the two sensitivities could be detected. Kuper (1955) could detect no simple direct relationship between them in 110 South Africans. There is also the unresolved anomaly in the findings of Lowe and McNulty (1953a) that a relationship evident among healthy persons was not found among leprosy patients. It is clearly desirable to clarify the circumstances governing the operation of the relationship between the two infections and more extensive study of the subject is called for.

E. Nigeria is a very interesting field for this study at the present time. In many localities the incidence of leprosy is declining. Along trade routes tuberculosis is becoming a major problem. If the two diseases are antagonistic to one another by virtue of an immunological relationship, a demonstration of the form of that relationship

may be taking place before our eyes. Lowe and McNulty (1953a, b,) working in this area found a significant correlation between tuberculin and lepromin sensitivity in 357 healthy persons, mostly secondary school boys and the staff of the Uzuakoli leprosarium. In this work tuberculin was used in both high and low dosage. Further analysis by Lowe and Davey (1956) indicated that there was still significant agreement if the results from a low dosage of tuberculin (10 TU) were alone considered. In a further group of 621 schoolchildren Lowe and McFadzean (1956) again found significant correlation between the two reactions, but it was less marked, and could have been produced by the simultaneous exposure of those concerned to tuberculosis and leprosy. As these children came from a country town on the railway in close proximity to a large leprosarium, this is at least possible.

The extension of this study to larger groups and a wider range of age and locality is here described. It was hoped thereby not only to broaden the basis on which conclusions were reached, but also to explore the very important dynamic aspects of any relationship found between the two sensitivities. In a country where tuberculosis is spreading, tuberculin sensitivity should show considerable variation between one locality and another, high in townships and along main routes of communication, low in localities distant from them. If tuberculin sensitivity induces lepromin sensitivity, this too should vary in harmony with the tuberculin findings regardless of its basic level in the communities concerned. Part I of this paper reports the results of simultaneous tuberculin and lepromin tests undertaken in schoolchildren in six different localities. There is also much to be gained by extending such a study to complete communities in the form of a tuberculin and lepromin survey. Thereby not only could the progress of each sensitivity be observed, but the relations between the two could be followed through succeeding age groups over the whole span of life.

Facilities for mass radiography are not yet available, but a survey would also make some estimate of the amount of clinical tuberculosis in the community. Part II of this paper gives the results of such a survey. Each part covers approximately 2,500 individuals.

Material and Technique

TUBERCULIN. The tuberculin used in this work was standard PPD manufactured at Weybridge, England. Undiluted, it keeps well in tropical conditions, but once diluted was used immediately, Mantoux tests being undertaken throughout in a strength of 10 TU per 0.1 cc. dose. Reactions were measured after 48 hours, and those 6 mm. in diameter or over regarded as positive, with 12 mm. and

18 mm. indicating high grades of sensitivity.

LEPROMIN. Lepromin prepared by the modified Dharmendra technique used by Lowe, and identical with that employed in previous studies in Nigeria, was used in this work. The technique of its preparation and reading has been described by Lowe and McNulty (1953b). The early (Fernandez) reaction was recorded after 48 hours, the late (Mitsuda) reaction after 21 days.

The three attendances necessary for obtaining the basic information sought were all that could be expected in the circumstances. It would have been valuable if tuberculin could have been used in both low and high dosage, but this would have involved another attendance on the part of those involved, and wastage would have been considerable. We were concerned primarily with sensitivity induced specifically by *M. tuberculosis*, and selected a 10 TU dose as a generally accepted standard for this, with little likelihood of non-specific reactions being obtained.

While referring where necessary to the findings in the early lepromin reactions, we have followed other workers in Nigeria in laying greater emphasis on the Mitsuda reaction, as more easily read and of greater practical significance. As Lowe pointed out (1955) the Mitsuda reaction is a reaction to the whole bacillus, and indicates resistance to it, and it is the development of this resistance that we are seeking to examine.

The team engaged in this work was kept as small as possible Lepromin reactions were read by two of us (T.F.D. or S.E.D.) together with Mr. G. O. Okezie, Senior Technician at the Uzuakoli Research Unit. Tuberculin reactions were measured by two of us (S.E.D. or C.S.). Assistance in the inoculations was also given by Mr. A. Eden and Dr. G. Moneta. Estimations of age were frequently necessary, and were the responsibility of one person (T.F.D.).

PART I.
TUBERCULIN AND LEPROMIN REACTIONS IN SCHOOLCHILDREN

In order to investigate the variations in tuberculin sensitivity between one locality and another, and its relation to variations in lepromin sensitivity, six schools were chosen, the first in a rapidly developing township, the others in rural areas of varying distance from main lines of communication. Tuberculin and lepromin tests were carried out on all the children attending these schools, a total of 3,052. Absentees on one or other of the days when tests were read accounted for a wastage of approximately 16%. Schools concerned, with numbers completing the tests are as follows, the school in an urban area heading the list, with rural schools listed in order of increasing remoteness from main roads, rail and river communications.

School	Status	Numbers completing test
C.M.S. School, Umuahia	Urban	455
C.M.S. School, Akwete	Rural 1	341
C.M.S. School, Ife	Rural 2	448
C.S.M. School, Abiriba ...	Rural 3	661
C.S.M. School, Nkporo ...	Rural 4	516
C.S.M. School, Ndi Oji ...	Rural 5	180
	Total	2,601

Results

(A) TUBERCULIN SENSITIVITY

In Figure I tuberculin positive rates at each school are presented graphically as a percentage of the total examined in each three year age group. The figures are analysed in Table I. At Umuahia, the urban school, the tuberculin positive rate is high, decidedly higher than was found for corresponding age groups in rural England in the M.R.C. Tuberculin survey (1953), as is evident from the following comparison.

	Age Groups			
	5	6—8	9—11	12—14
Umuahia, Nigeria	11.8	23.0	45.2	50.0
Rural England	15.0	19.1	27.6	34.6

For a fair comparison, the M.R.C. figures are here adjusted to cover a 10 TU dose only. In that survey a reaction of 5 mm. diameter was regarded as positive. The Umuahia figures are based on a minimum reading of 6 mm., so the difference is a little larger than the figures indicate. It is larger still if the Umuahia findings are compared with those in urban England.

In rural areas in Nigeria tuberculin sensitivity is at a lower level, and in general becomes lower as contact with townships decreases. We are here not concerned with bovine tuberculosis. Cattle are very scarce, and no fresh milk whatever is drunk, the very idea being abhorrent to the people. The tuberculin positive levels found appear to give a fair indication of the degree to which human tuberculosis has penetrated into the localities concerned, and do in fact reflect not only the geographical position of each locality but also the mode of life of the people. Ife, Ndi Oji and Abiriba are predominantly agricultural communities. Akwete is located on an important river, and has many contacts with the outside world. Nkporo is a very interesting case. Here the people, traditionally farmers, have progressively abandoned agriculture for trade since a road to the area was opened 10 years ago, and now have many contacts with Umuahia, where tuberculosis is known to be rife. In all cases the incidence of positive reactions in the two sexes was closely parallel.

These findings form a pattern which is reasonable and in line with local conditions. In comparison with the M.R.C. figures the level of sensitivity is rather higher than was expected. It is, however, in line with the findings of earlier workers, Lowe and McFadzean with a 5 TU dose obtaining at Uzuakoli figures rather lower than those found here at Umahia, while Lowe and McNulty's findings were well within the limits recorded here.

(B) LEPROMIN SENSITIVITY

(a) *Mitsuda Reaction*

Positive rates for the Mitsuda reaction are presented for each school and age group in Figure 2. They are analysed in Table I. It is evident that in these localities sensitivity to the late lepromin reaction varies widely, high in the urban area and one rural area, and lower in other rural areas. The findings of Lowe and McNulty and Lowe and McFadzean all fall within the range seen here.

(b) *Fernandez Reaction*

In all cases sensitivity to the early (Fernandez) reaction was much less than that shown to the Mitsuda reaction. The lepromin used is itself less sensitive to the early reaction than it is to the late, but this does not account for the findings in this work. A review of considerable numbers of leprosy patients shows that with this lepromin, among adults who are Mitsuda positive, 55% may be expected to give a positive Fernandez reaction. Among children the corresponding figure is 25%. In the healthy schoolchildren examined in this work, the level was much less than this, so low in fact that its presentation in the form of a graph is impracticable. The percentage of children giving positive Fernandez reactions at each school is compared with the corresponding Mitsuda figure as follows:—

School	Positive Mitsuda %	Positive Fernandez %
Urban	58	3·7
Rural 1	29	4.0
Rural 2	25	3.0
Rural 3	78	2.4
Rural 4	29	0.8
Rural 5	40	nil

This contrast between the findings in the two reactions among healthy children has also been found by Guinto and his colleagues (1955) in the Philippines.

The question arises how far these findings are related to the incidence of leprosy in the localities concerned. A considerable amount of information is available on this point. Leprosy was formerly exceedingly rife in three of these localities, but has declined very markedly during recent years. At Nkporo three leprosy surveys

have been undertaken, and indicated an incidence of 60 per mille in 1937, 57 per mille in 1939, and 9 per mille in 1956. At Ndi Oji, an incidence of 121 per mille in 1941 had become 76 per mille by 1947, and in 1955 had fallen to 17 per mille. In both these localities vigorous anti-leprosy measures have been in operation throughout the period of these surveys with excellent co-operation from the people, and for at least 10 years no open case of leprosy has been known to be living in the community. Abiriba comes under the same category. Although no repeated survey results are available, the locality was surveyed for leprosy purposes in 1943-4, all leprosy cases found enrolled for treatment, and open cases isolated at a segregation village three miles away. The virtual disappearance of fresh cases of clinical leprosy during recent years in all three localities is sufficient evidence of the effectiveness of the control measures being maintained there. It is difficult to see how infection with *M. leprae* can be held responsible for the Mitsuda positive levels found among young children in these localities, 69% at Abiriba, 41% at Ndi Oji and 39% at Nkporo in the 6—8 age group.

The same is true of Umuahia. This growing township is located near to the area of former high leprosy incidence, though in nearby villages an incidence of only 14 per mille was encountered in 1938. Although 61 patients are still attending a nearby leprosy clinic, very few come from the township itself, none of them an apen case. It is difficult to see how 47% of children by the age of 5 can have had sufficient contact with *M. leprae* to have been sensitised to it.

At Akwete and Ife the incidence of leprosy has never been high.

In comparing the levels of sensitivity between one locality and another, the possibility of variations induced by season and states of nutrition must not be ignored. The school at Abiriba was studied in the cool wet season (June), the other schools in the hot dry season. Diet is least satisfactory during the wet season, particularly where the vitamon B complex is concerned. Seasonal influences on the lepromin reaction were studied by Dharmendra, Lowe and Mukherji (1942), who noticed in leprosy patients an enhancement of the reaction in summer. We think such influences cannot explain the difference in level found between different localities in this work.

Thus although higher levels of sensitivity to the Mitsuda reaction are found in localities where leprosy has been rife in the past, it is very unlikely that here or elsewhere infection with *M. leprae* is alone responsible for the actual levels found among children at the present time. Neither can it be said that comparing results in one locality with those in another, the Fernandez positive rates reflect the known incidence of leprosy.

A curious finding in three localities is a tendency for the levels of lepromin sensitivity actually to fall in the years around puberty. No explanation can be offered for this. In the second part of this work also, large groups at these ages displayed a tendency for a slowing down in the progress of lepromin sensitivity.

(C) THE INFLUENCE OF TUBERCULIN SENSITIVITY ON LEPROMIN SENSITIVITY

The tuberculin and Mitsuda findings are brought together in Table I, which shows for each school the percentage of children in each age group giving positive or negative reactions to the two tests. Actual numbers examined in each age group are also given.

TABLE I

Tuberculin and lepromin positive rates

To—Tuberculin negative % age group. Lo—Lepromin negative % age group. T+—Tuberculin positive % age group. L+—Lepromin positive % age group.

Place		Age Groups 5		6—8		9—11		12—14		15—16	
		To	T+	To	T+	To	T+	To	T+	To	T+
Urban	Lo	47	6	43	5	31	9	19	15		
	L+	41	6	34	18	24	36	31	35		
Numbers tested		17		248		135		55			
Rural 1	Lo			60	10	69	10	57	17	35	31
(Akwete)	L+			18	12	12	19	11	15	19	15
Numbers tested				169		58		88		26	
Rural 2	Lo	82	9	65	7	60	11	60	15	39	35
(Ife)	L+	15	3	22	6	22	7	14	11	23	3
Numbers tested		39		106		46		126		31	
Rural 3	Lo			31	1	17	1	11	0	11	11
(Abiriba)	L+			59	9	71	11	76	13	64	14
Numbers tested				277		188		168		28	
Rural 4	Lo			56	6	54	12	51	29	27	47
(Nkporo)	L+			21	17	18	16	9	11	3	23
Numbers tested				68		304		114		30	
Rural 5	Lo			77	3	65	0	40	10	40	3
(Ndi Oji)	L+			17	3	18	17	39	11	33	24
Numbers tested				49		47		54		30	
Total tested		56		917		878		605		145	

At every school these findings indicate the existence of a relationship between tuberculin and lepromin sensitivity. If individual age groups are examined it is found that with two exceptions, both in the 15—16 age group, the proportion of lepromin positive reactors is higher among tuberculin positive reactors than it is in the age group as a whole. The converse is also true, that tuberculin positive reactors are relatively more numerous among lepromin positive reactors than they are in the age group as a whole. This association does indeed extend further than is indicated here. The proportion of strongly positive lepromin reactors is higher among strongly positive tuberculin reactors than it is among weak reactors. The converse also applies.

That is as far as the examination of individual age groups can take us. It demonstrates the existence of a relationship between the two sensitivities, but gives no clue to its significance. There are at least three possibilities here. Both leprosy and tuberculosis flourish in the same conditions of overcrowding. It is possible therefore that both infections have a bias towards the same groups in the community, and this could explain their association. There is also the familiar possibility that tuberculosis is inducing lepromin positivity. There still remains the possibility that other sensitising agents are entering into the picture and confusing it. Some light on these questions begins to appear when we compare the relationship between the two sensitivities in different localities, and follow their changes through succeeding age groups. If one is influencing the other, there should appear a constant element in their relationship which such a study should reveal.

We may begin by observing that in the urban area the proportion of children exhibiting sensitivity both to tuberculin and lepromin is decidedly higher than elsewhere, 36% between the ages of 9 and 11 and 35% between the ages of 12 and 14. Any relationship that exists between the two sensitivities is neverthless very far from perfect. Even if we could assume that tuberculosis infection was responsible for all the lepromin positive reactors in this group, there would still remain important minorities among positive tuberculin reactors in whom no lepromin conversion had occurred, 20% of them in the 1—11 age group and 30% in the 12—14 age group. At its best, therefore, the relationship is defective and tends to grow less as the level of tuberculin sensitivity rises with age.

In rural areas the proportion of children positive to both tests is decidedly lower, and varies between 7% and 19%. The influence of tuberculosis on the lepromin reaction is best examined by considering the proportion of tuberculin positive reactors who are also lepromin positive. In Table II this proportion is given as a percentage of tuberculin positive reactors in each age group. Consideration is given only to age groups between the extremes of 6 and 14 years, including thereby in the analysis only age groups containing considerable numbers of children. The average tuberculin and lepromin levels over the same period are also given.

TABLE II

Percentage of positive tuberculin reactors who are positive to lepromin

	AGE GROUP				Average rate %	
	6—8	9—11	12—14	Average	Tuberculin	Lepromin
Urban	78	80	70	77	33	56
Rural 1	55	60	47	53	37	41
Rural 2	47	39	42	42	19	27
Rural 3	90	92	100	97	11	79
Rural 4	74	57	28	50	31	31
Rural 5	50	100	52	71	15	42

The wide variation in these figures between one place and another, and the irregularity of their movement through succeeding age groups make it hard to believe that a common influence is at work in their production. We may very well ask how tuberculosis could induce 97% lepromin conversions in one place and only 42% in another. Furthermore, the percentage of positive tuberculin reactors who are positive to lepromin does not bear any direct relation to the level of tuberculin sensitivity itself. The differences in level from place to place are indeed related not to the tuberculin positive rate but to the lepromin positive rate. Where the lepromin rate is high, a high proportion of positive tuberculin reactors are lepromin positive. When it is low, the proportion is low. It is also noticeable that in four of the six localities, as the number of positive tuberculin reactors increases with age, the proportion of them who are lepromin positive actually falls. It is impossible to reconcile these findings with the theory that tuberculosis is inducing lepromin postivity to any significant degree. The same result is obtained if the findings are examined from other angles.

f the lepromin positive levels in rural areas lack any significant component contributed by tuberculosis, their further examination is of interest. It has already been stated that infection with *M. leprae* is not likely to be responsible for the high levels found among young children in certain localities. What then is responsible? It is impossible at present to answer this question. It is discussed further later.

Summarising the findings so far it may be said that in both urban and rural areas tuberculin and lepromin sensitivity tend to be associated in the same individuals. In the urban areas it is possible that tuberculosis infection is responsible for this to a small extent, but in rural areas where tuberculosis is at a lower level it is impossible to find any evidence that it is having any appreciable influence on lepromin sensitivity. In some localities it is very doubtful that *M. leprae* could itself be responsible for the level of lepromin sensitivity seen in young children and here at least it is probable that geographical and constitutional factors are influencing the situation.

In view of the findings so far in this study it was considered desirable to expand the investigation in one of the localities concerned to cover as many of the population as possible, and follow the levels of tuberculin and lepromin sensitivity through successive age groups over the whole span of life. Such an investigation is described in Part 2 of this paper.

PART II
TUBERCULIN AND LEPROMIN REACTIONS IN ENTIRE COMMUNITIES

For the second part of this work a group of four associated villages was chosen, having a combined population of almost exactly 2,500. It was from these villages that the children attending Ndi Oji school were mainly drawn. Leprosy was formerly very rife in this locality, and as repeated leprosy surveys have been undertaken during the past 15 years, the people could be relied upon to co-operate in the rather strenuous demands made upon them in the present work. There would also be the important advantage that lepromin and tuberculin sensitivity could be considered against a background of accurate knowledge of the incidence and trend of leprosy during recent years.

Tuberculin and lepromin tests were carried out on the entire resident population of these villages, from infants in arms to the oldest inhabitant, and although some wastage was inevitable, 2,221 out of a total of 2,491 inoculated, were actually present and examined on both the occasions when the reactions were read.

Results

The percentage of tuberculin and lepromin positive reactors in each age group is shown in Figure 3, which is based on the following figures.

	AGE GROUP							
	5-9	10-14	15-19	20-29	30-39	40-49	50-59	60+
Tuberculin positive %	7.1	16.0	28.1	34.2	51.6	64.9	62.0	64.3	65.8
Lepromin positive %								
(a) Mitsuda	13.2	28.0	43.2	44.4	49.9	62.0	65.6	59.4	68.4
(b) Fernandez	1.1	1.5	2.5	0.9	4.0	7.8	4.8	5.6	8.9
Number tested	450	482	248	108	327	204	163	160	79

Differences in the development of tuberculin and lepromin sensitivity noticed among schoolchildren are again evident in the large groups tested in these villages. Signs of sensitivity to lepromin began to be evident in the first year of life and developed rapidly up to the age of twelve. Sensitivity to tuberculin tended to appear later and develop more slowly, but more steadily. From the age of twelve onwards there was a noticeable slowing down in the rate of increase of lepromin sensitivity, with the result that the difference between the two sensitivities diminished during adolescence, and early in adult life both levels met. From the age of about 35, when approximately 64% of the population had become sensitised to both reactions the level of each remained remarkably steady and in close approximation to the other.

The extremely low level of sensitivity to the Fernandez

reaction is again noticeable. It tends slowly to increase with age, and is not considered further.

During childhood there were no appreciable differences between the two sexes in sensitivity to either reaction. During adult life distinct differences became perceptible. The respective levels are given below and drawn in Figure 4.

	AGE GROUPS								
	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	60+
Tuberculin positive rate %									
Males	9	16	26	52	67	80	74	72	72
Females	9	16	33	32	48	57	53	48	61
Lepromin positive rate % (Mitsuda)									
Males	12	33	40	70	60	77	74	74	74
Females	11	26	49	35	48	56	60	50	67

The influence of tuberculin sensitivity on lepromin sensitivity

A quite remarkable similarity between the two sensitivities is evident in this community. Although the actual level of tuberculin sensitivity is related to the 10 TU dose used, and higher levels would doubtless have resulted from the use of a larger dose, it is impossible to deny the existence of a relationship between the two sensitivities so plain in their behaviour through succeeding age groups and between the sexes. When analysed in detail, however, the picture is once again confused, and it is impossible to find real evidence that the lepromin level is in any way dependent on the tuberculin level. The percentage of each age group giving negative, weak or strong reactions to each of the two tests is as follows:—

TABLE III

AGE GROUP

	0-4			5-9			10-14			15-19		
	To	Tw	Ts	To	Tw	Ts	To	Tw	Ts	To	Tw	Ts
Lo	81.6	3.5	1.7	64.9	4.3	2.8	47.2	6.5	3.1	41.7	7.4	6.5
Lw	9.7	0.4	0.9	15.9	2.9	3.9	20.6	8.1	4.1	15.8	7.4	0.9
Ls	1.6	0.4	0.2	3.2	1.0	1.1	4.1	3.2	3.1	8.3	6.5	5.5
Numbers tested		450			482			248			108	

	20-29			30-39			40-49			50-59			60+		
	To	Tw	Ts	To	Tw	Ts	To	Tw	Ts	To	Tw	Ts	To	Tw	Ts
Lo	31.5	12.8	5.8	19.7	10.9	7.4	16.6	9.8	8.0	19.4	13.1	8.1	12.7	8.8	10.1
Lw	12.6	11.9	8.6	8.8	11.2	9.8	12.2	9.8	10.4	9.4	6.2	12.5	15.2	8.8	19.0
Ls	4.3	5.2	7.3	6.6	12.8	12.8	9.2	7.4	16.6	6.9	8.8	15.6	6.3	7.8	11.3
Numbers tested		327			204			163			160			79	

To. Tuberculin negative %

Tw. Tuberculin positive weak %

Ts. Tuberculin positive strong %

Lo. Lepromin negative %

Lw. Lepromin positive weak %

Ls. Lepromin positive strong %

These findings have been examined statistically for us by Mrs. A. Foster who has also prepared the accompanying histograms which show the relation of each sensitivity to the other at negative, weak and strong levels of response. They illustrate the conclusion, that neither reaction is directly dependent upon the other to any significant extent.

Applying the method of analysis followed in Part I of this paper, the percentage of those positive to one test who are also positive to the other is as follows:—

	AGE GROUPS								
	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	60+
% of T plus who are also L plus	27	56	66	59	62	72	71	67	71
% of L plus who are also T plus	14	32	43	46	66	75	67	73	69

In both cases we notice that these figures are dependent on the actual level of the other sensitivity in the age group concerned. When in adult life a stable situation is attained, the proportion of tuberculin positive reactors who are lepromin positive is only slightly larger than it is in the general population. The same is true of the proportion of lepromin positive reactors who are tuberculin positive. Both sensitivities behave in a manner independent of the other, but both are related in some way.

There remains one line of inquiry open to us. During recent years leprosy has declined very markedly at Ndi Oji, from an incidence of 120 per mille in 1941 to 17 per mille in 1955. It is of interest to compare the tuberculin and lepromin levels among present and past patients with those encountered in the general population. The population tested in this work include 144 patients and ex-patients, most of whom are distributed fairly evenly among the adult age groups. Among them the tuberculin and lepromin positive rates are as follows:—

	AGE GROUPS				
	20-29	30-39	40-49	50-59	60+
T+% ...	56	69	60	57	61
L+%	50	69	41	61	79

The tuberculin levels in every case fall between the levels for the two sexes in the general population. Of the lepromin levels, three fall between the limits found in the general population, one below them, and one above them. There is thus no evidence that clinical leprosy has been associated with a lower level of tuberculin sensitivity than prevails in the general population.

Discussion

The findings obtained in this work may be summarised as follows. Among large groups of children in urban and rural areas in Nigeria and in equally large groups of adults in one rural area, sensitivity to lepromin and to tuberculin tends to be associated in the same individuals, and each occurs more frequently among those

sensitive to the other than among those insensitive to it. In the urban area the possibility cannot be ruled out that tuberculosis is exerting some influence on lepromin sensitivity. There is, however, no real evidence that in rural areas sensitivity to tuberculin has any capacity to induce sensitivity to lepromin to any appreciable extent. There is certainly no simple direct relationship between them.

The low level of sensitivity to the Fernandez reaction encountered in both schoolchildren and adults is of interest. Tuberculosis infection has clearly had no tangible influence on this. In this work healthy people exhibited decidedly less sensitivity to the Fernandez reaction than is encountered among leprosy patients.

These findings immediately present an important problem. It is an established fact that BCG inoculation can and usually does produce lepromin conversion in healthy negative reactors. There is strong evidence that in many parts of the world infection with tuberculosis can do the same. Here in rural Nigeria it is failing to do so, in spite of the existence of an obvious relationship between the two sensitivities. It is impossible at present to offer any satisfactory explanation for this phenomenon. A few observations can, however, be made.

In the first place, although tuberculosis is certainly rife in Umuahia township, all the indications are that in rural areas it is as yet a minor problem. No case of clinical tuberculosis was encountered at Ndi Oji among the 2,500 people seen, and although in the absence of radiography accurate information is lacking, it can at least be said that tuberculosis is not an important public health problem in that locality. With active tuberculosis at a low level exposure to *M. tuberculosis* is likely to be casual and infrequent. BCG inoculation administers a dose of antigen of a totally different order from that likely to be encountered in these circumstances.

A most interesting finding at Ndi Oji was the steady level at about 65% maintained by both sensitivities from the age of about 30 onwards. Continuing contact with the sensitising agents concerned must be assumed at all ages, but in later decades was not associated with any increase in sensitivity to either. This finding can only suggest that saturation point had been reached in the capacity of that community to react positively in the conditions which applied, and that geographical and constitutional factors were therefore exerting a significant influence upon both sensitivities.

What are these factors One geographical factor may very well relate to the frequency and extent of exposure to the sensitising agents concerned. The habits of the people should be noted here. It is a general custom for youths to leave home and see the world, seeking a living for a number of years in one or other of the towns

or cosmopolitan areas favoured by them. Here, living often in overcrowded conditions, contact with *M. tuberculosis* is almost inevitable. At around the age of 30, they tend to return home and settle down, subsequently having only occasional contacts with townships. Women do not travel in this way, their movements being mainly confined to frequent visits to markets in nearby villages. These facts doubtless have some bearing on the levels of tuberculin sensitivity in various age groups. Once tuberculin sensitivity has been produced, exposure appears to be sufficient to maintain it at a relatively steady level during adult life, but the reinforcement needed to raise it is lacking. It is not surprising that the stimulus needed to produce lepromin conversion is also lacking.

In the same conditions, sensitivity to lepromin is also limited during adult life, although the likelihood of contact with *M. leprae* in rural localities is greater than the likelihood of contact with *M. tuberculosis*. We note that sensitivity to lepromin tends to be very persistent, and the marked reduction in exposure to *M. leprae* which has undoubtedly taken place during the past 15 years may have a bearing on the matter. At the same time, as has already been pointed out, it is difficult to implicate *M. leprae* alone as the agent responsible for the lepromin levels observed among young children, or, when every allowance has been made for seasonal and nutritional factors, for the variation in level between one place and another. With *M. tuberculosis* largely excluded from this role we are faced with the possibility that other as yet unidentified sensitising agents may be inducing some degree of sensitivity in these cases. Lepromin sensitivity is not specific, though a lack of it may be. We have to admit the possibility that just as non-specific factors may influence tuberculin sensitivity, so they may also influence lepromin sensitivity, and may account for the association found between the two sensitivities in conditions where tuberculosis does not appear to be responsible for it.

Summary

In order to study further the relations between tuberculin and lepromin sensitivity in Eastern Nigeria, simultaneous tuberculin and lepromin tests were undertaken (a) on 3,000 schoolchildren in six localities, one urban, the others rural, (b) on the complete population of a group of four villages comprising just under 2,500 individuals. In the variations of each sensitivity between one locality and another, between the sexes and through succeeding age groups, it was hoped to obtain fresh information regarding their relationship. By choosing localities where the incidence and trend of clinical leprosy were known, the findings could also be related to this.

Tuberculin sensitivity to a 10 TU dose was high in an urban

area, lower in rural areas. Late lepromin sensitivity (Mitsuda) also showed considerable variation but during the years of childhood followed a different pattern. Although it is possible that in the urban area where tuberculosis was rife, tuberculosis infection was contributing to lepromin sensitivity, no evidence could be found in rural areas, where tuberculosis was at a lower level, that tuberculin sensitivity was having any appreciable influence on lepromin sensitivity during the years of childhood, in spite of the fact that both senstivities tended to be associated, both in their occurrence in the same individuals and in their intensity.

In the complete communities examined this association was also found, though when both sensitivities attained stable levels in adult life, it largely disappeared. The association operated in both directions and no satisfactory evidence could be found that tuberculin sensitivity was influencing lepromin sensitivity to any appreciable extent.

In all localties sensitivity to the early lepromin reaction (Fernandez) was at a very low level.

It is very doubtful that contact with *M. leprae* could alone be held responsible for the levels of lepromin sensitivity found and their variation from place to place. In this and in the steady levels maintained by lepromin sensitivity during adult life, non-specific geographical and constitutional factors appear to be operative, and the possibility arises that they are responsible for the association found between tuberculin and lepromin sensitivity in these areas.

Acknowledgments

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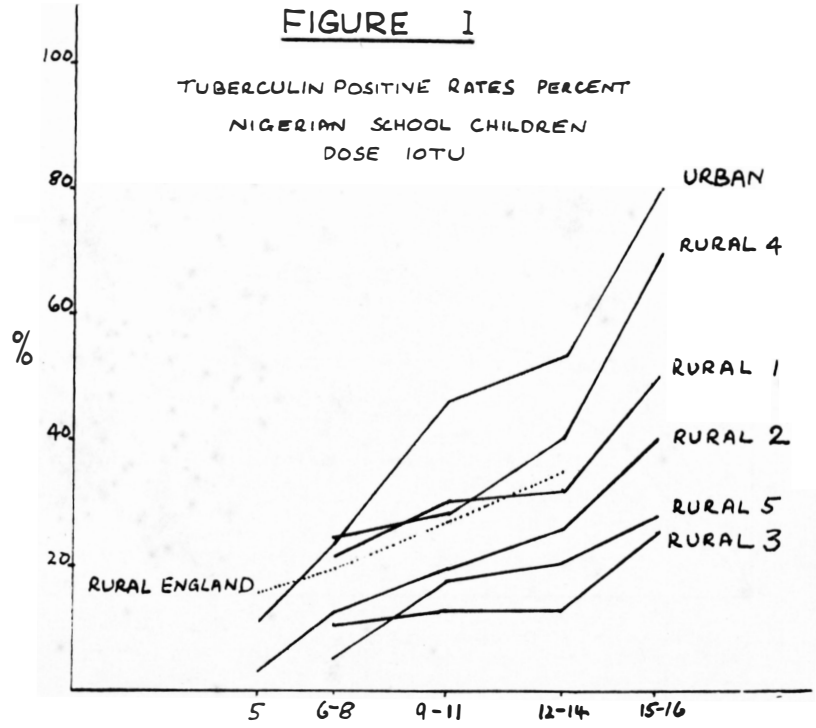
FIGURE 1



GURE 2

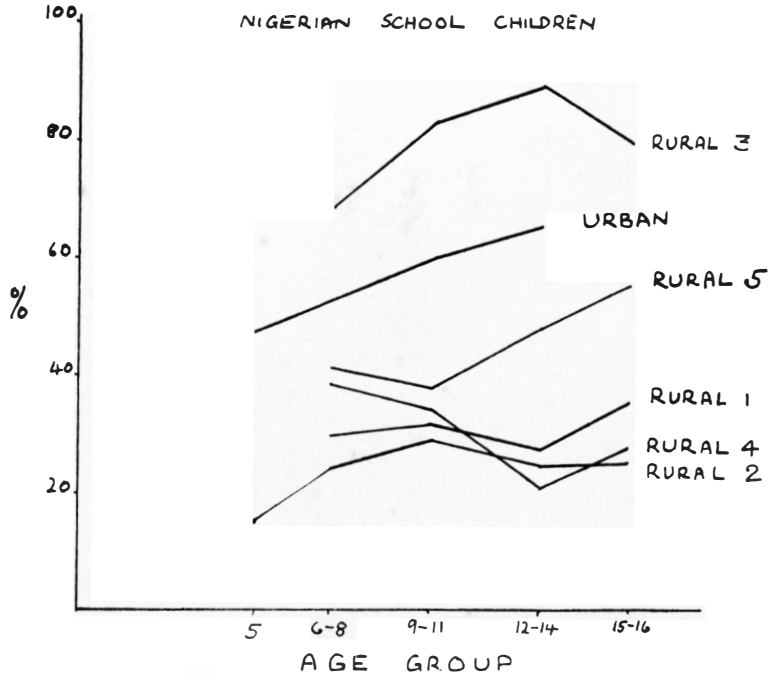


FIGURE 3

TUBERCULIN AND LEPROMIN SENSITIVITY
NDI OJI

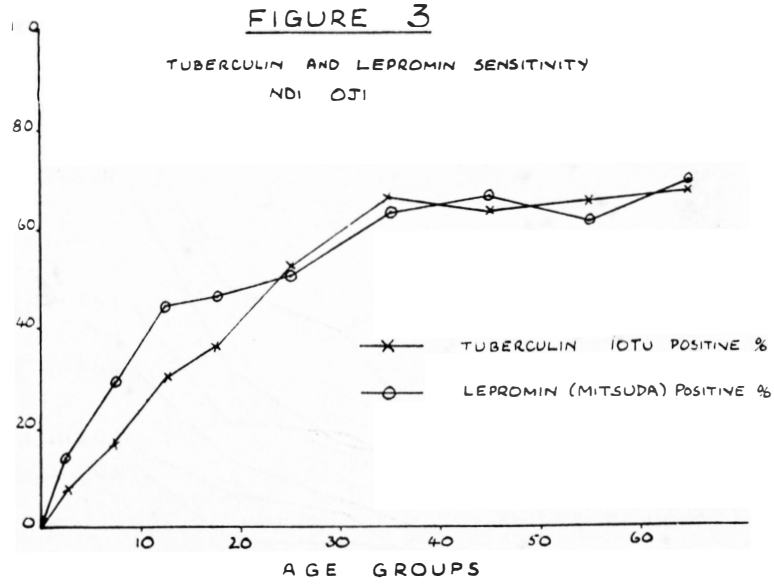
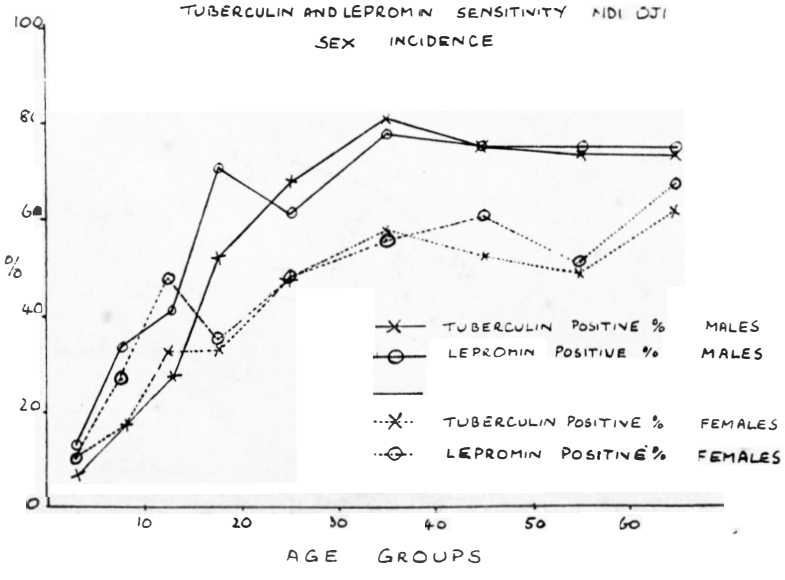


FIGURE 4

TUBERCULIN AND LEPROMIN SENSITIVITY NDI OJI
SEX INCIDENCE



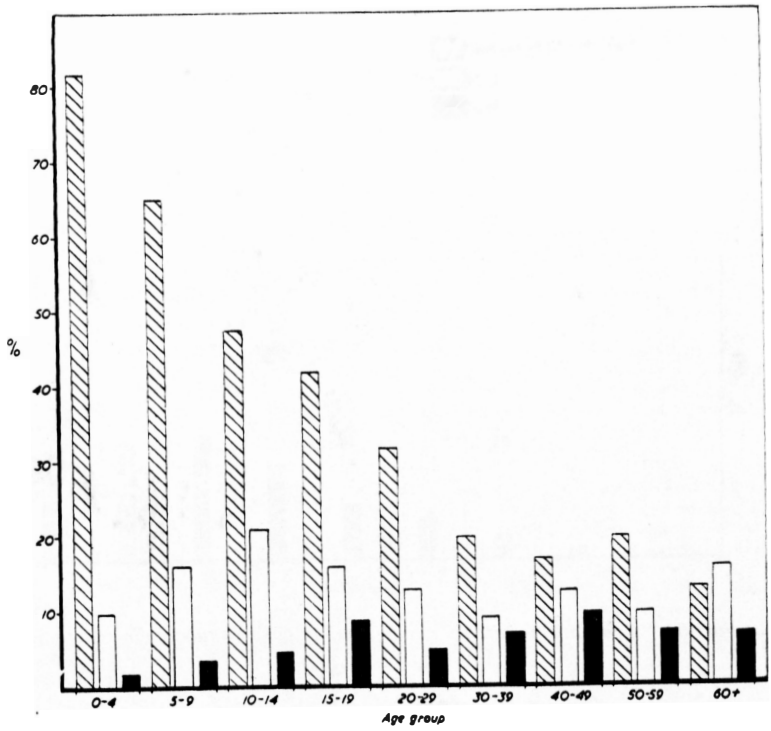


Fig. 5a. Lepromin sensitivity among negative tuburculin reactors.

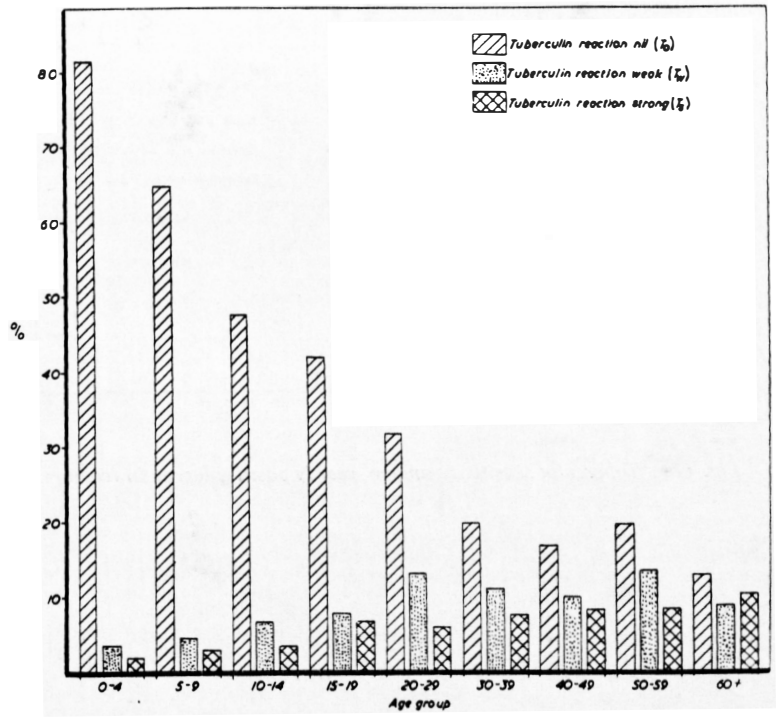


Fig. 5b. Tuberculin sensitivity among negative lepromin reactors.

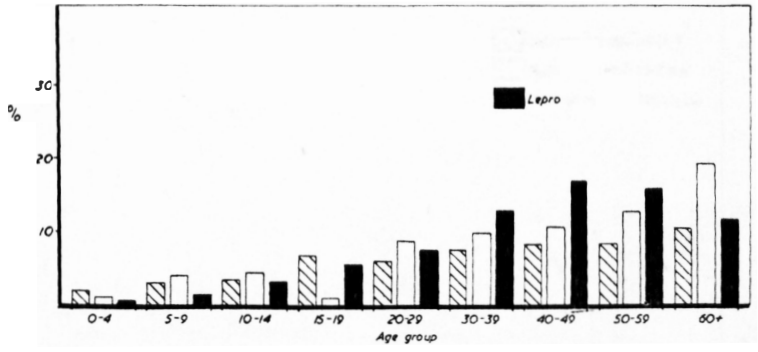


Fig. 6a. Lepromin sensitivity among weakly positive tuberculin reactors.

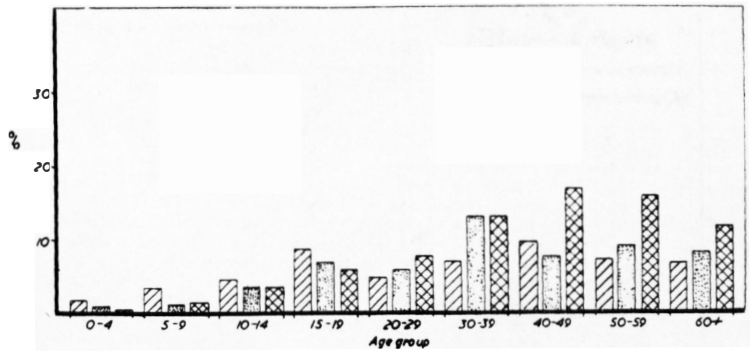


Fig. 6b. Tuberculin sensitivity among weakly positive lepromin reactors.

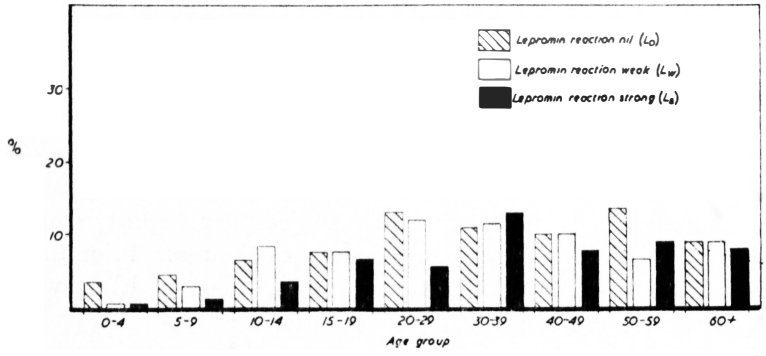


Fig. 7a. Lepromin sensitivity among strongly positive tuberculin reactors.

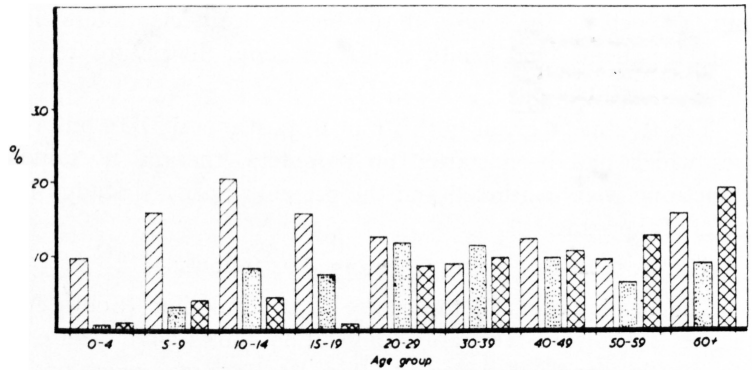


Fig. 7b. Tuberculin sensitivity among strongly positive lepromin reactors.