

TUBERCULIN AND LEPROMIN REACTIONS IN NIGERIA

AN ANALYSIS OF THE DATA OF LOWE AND McNULTY¹

THE LATE JOHN LOWE AND T. F. DAVEY
Nigeria Leprosy Service Research Unit
Uzuakoli, Eastern Nigeria

Eastern Nigeria presents today a situation of great interest as concerns the relationship of leprosy to tuberculosis. Leprosy is declining rapidly while tuberculosis is increasing, and if there is any truth in the hypothesis that the retreat of one disease is induced by the advance of the other, circumstances are now unfolding in which it should be possible to demonstrate the facts.

Against this background the immunological studies of Lowe and McNulty (1, 2) are of particular interest and importance. Among 278 healthy adults there were found very high proportions of positive reactors to both the tuberculin and lepromin tests, and a very close degree of correspondence between the results of the two tests. Among 81 healthy children the tuberculin positivity rate was also relatively high, and although it was decidedly higher than the rate of positive lepromin reactions, a relationship between the results of the two tests was established.

Tuberculin was used in two strengths in this work: (a) the von Pirquet test was made in all cases, the dose equivalent to approximately 10 TU, and (b) all negative reactors to this test then received a Mantoux test of a strength of 50 TU. The results of these two tests were combined in the published findings.

At that time it was not known that nonspecific positive reactions to tuberculin are common in Nigeria. That type of reactivity is unlikely to have produced positive results with the von Pirquet test, but it is more than likely that such reactions were induced in some individuals by the 50 TU tuberculin dose.²

Results in healthy adults.—Combining the results of both tuberculin tests, it was found that of the 278 healthy adults, 223 gave positive reac-

¹ This is a re-examination of the data of work reported by the late Dr. Lowe and his nurse associate Miss McNulty. It was originally submitted, in response to an inquiry, as a Letter to the Editor, but because it was preferred that it should appear as an article, Dr. Davey specified that it should be accredited as it appears here.—EDITOR.

² Knowledge of nonspecific reactions to large doses of tuberculin had not emerged at the time this study was made, but Dr. Lowe became aware of it shortly afterward and, with Dr. J. A. McFadzean, he made a further investigation the results of which have appeared since this present note was written (⁶). When Lowe retired from the Nigeria service, a few months before his death, he personally handed his records of this earlier work over to me, and believing it would be his wish I have acceded to the suggestion that the findings be presented in further detail.—T. F. D.

tions to tuberculin and 224 were positive to lepromin. These findings may be distributed between the two strengths of tuberculin used, as follows:

<i>Low dose tuberculin (von Pirquet)</i>	{	Positive 79	{ Lepromin positive 76
			{ Lepromin negative 3
	{	Negative 199	{ Lepromin positive 148
			{ Lepromin negative 51

The 199 negative reactors who then received the 50 TU dose gave the following results:

<i>High dose tuberculin (50 TU)</i>	{	Positive 144	{ Lepromin positive 121
			{ Lepromin negative 23
	{	Negative 55	{ Lepromin positive 27
			{ Lepromin negative 28

Analysed in this way, the findings show two things very clearly, apart from the high rates of positive reactions (81%). In the first place, there is a very close association in these persons between the high degree of sensitivity to tuberculin indicated by a positive von Pirquet reaction and reactivity to lepromin, 79 in one case corresponding to 76 in the other. It is also probably significant that, although this number represents only one-third of the total lepromin positives, it includes one-half of those giving strongly positive reactions.

In the second place, it is clear that a very large number of positive lepromin reactions were associated with only mild degrees of tuberculin sensitivity, and that a significant number of lepromin positives occurred in persons unable to show any definite reaction to tuberculin. Here it may be said that the figures for the persons recorded as reacting positively to lepromin are conservative. All reactions that failed to exceed the 1+ level were excluded, even when that degree of positivity was maintained during the significant weeks of the test. Knowing the care taken in making readings, and the fact that refined lepromin free from tissue protein was used throughout this work, one would personally incline to the view that some of these were significant. Had such positives been included, the lepromin positivity rate would have been decidedly higher.³

Results in healthy children.—It is also profitable to examine the results in the 81 children tested. Of these, 47 were found positive in the two

³ The lepromin used was a refined product consisting of nondefatted bacilli that had been extracted from the lepromatous tissue with chloroform and then suspended in carbol-saline (1). This lepromin has the virtue that it is practically free from tissue elements. The 1+ Mitsuda reaction referred to is a small but definite nodule 2-4 mm. in diameter. In eliminating such reactions from the positive findings the recommended reading of the WHO Expert Committee on Leprosy (5) was followed in essence.

tuberculin tests, but only 31 positive to lepromin. These findings are analysed as follows:

<i>Low dose tuberculin (von Pirquet)</i>	{	Positive 10	}	Lepromin positive 9
				Lepromin negative 1
		Negative 71		Lepromin positive 22
				Lepromin negative 49

On further analysis the 71 negative reactors gave the following findings after a dose of 50 TU tuberculin:

<i>High dose tuberculin (50 TU)</i>	{	Positive 37	}	Lepromin positive 22
				Lepromin negative 15
		Negative 34		Lepromin positive 0
				Lepromin negative 34

This group is instructive. In the first place, whereas strongly positive reactors to tuberculin among adults constituted over one-quarter of those tested, among children they were only one-eighth; but among these the close correspondence with lepromin positivity is again seen.

In the second place, there is among these children strong presumptive evidence for the existence of nonspecific positive reactions to tuberculin. The total number recorded as tuberculin positive, 47 out of 81, or 58 per cent, represents a proportion actually higher than that found recently in the industrial area of Stoke-on-Trent in England (4). (This result was not available when the paper under discussion was written.) Furthermore, whereas the Stoke-on-Trent figures relate only to children of school age, the Nigeria figures include 28 children of less than school age.

Of even greater significance is the fact that these children came from the households of members of staff of the Uzuakoli Settlement, and both they and their parents received an unusual degree of medical supervision. No case of tuberculosis has ever arisen in this community, and there are no known circumstances in which these children as a group could have had intimate contact with *M. tuberculosis*. Contact with *M. leprae* is much more probable. It is very difficult in these conditions to explain the high positive tuberculin rate on the basis of authentic infections with tuberculosis.

The low proportion of positive lepromin reactors among these children (38%) is noteworthy. As in the case of adults it would have been decidedly higher if the 1+ responses had been included, but as it stands it corresponds with figures now being obtained elsewhere in the area.

DISCUSSION

The main facts which emerge from this analysis are as follows:

1. A high degree of sensitivity to tuberculin, as evidenced by a positive von Pirquet reaction, was found in only a minority of those tested,

29 per cent of the adults and 12 per cent of the children. In almost every case it was associated with a positive reaction to lepromin.

2. A low degree of sensitivity to tuberculin, positive to a dose of 50 TU, was found in a further 52 per cent of adults and 47 per cent of children. It is possible, and indeed probable with respect to the children, that some of these reactions were nonspecific in nature. Correspondence with lepromin positivity remained fairly close, both among adults and among children.

There is interest in the fact that, whereas among the adults who were negative to the higher tuberculin dose one-half nevertheless reacted positively to lepromin, all of the children who were entirely tuberculin negative also failed to react to lepromin.

A further point needs to be made. In this experiment the concern was solely the relationship between the two tests, both in adults and in children, and it was not intended that the figures should be taken as a definite indication of the tuberculin and lepromin positivity rates which may be expected in this part of Nigeria. The groups studied were in fact highly selected, consisting of (a) the members of the staff of the Uzuakoli Settlement and their families, and (b) the staff and students of the Methodist College, Uzuakoli. The former of these groups was living and working in close proximity to leprosy patients. The latter consisted almost exclusively of educated people, many of them accustomed to travel, and who had spent longer or shorter periods in cities and towns where tuberculosis is rife. It must not, therefore, be assumed that results of the order found among these groups are typical of the rural areas which make up the greater part of Eastern Nigeria. There is obvious interest in undertaking similar experiments among the settled population in localities where the extent of leprosy infection has been known and followed over a period of years. Such work is now in progress.

When studying patients with leprosy, Lowe and McNulty found that, in contrast to healthy people, a positive tuberculin reaction was often accompanied by a negative result with lepromin. In lepromatous cases, whereas BCG converted a negative tuberculin reactor to a positive reactor as is usual in the healthy population, lepromin conversion occurred only in a small minority, it was temporary only when it did occur and had no detectable influence on prognosis (3).

In referring to these matters in the paper under discussion no figures were included. Since it was written the practice of making tuberculin and lepromin tests of all newly admitted patients at the Uzuakoli Research Unit has been continued. The present position is that out of 321 persons suffering from lepromatous leprosy tested during the past three years, all of whom were lepromin negative, 103 (32.2%) gave positive reactions to the von Pirquet test. Many of these were early cases of leprosy, and it is not likely that tuberculous infection occurred in any significant number subsequently to infection with leprosy. The findings indicate,

rather, that in approximately one-third of all the lepromatous cases encountered during this period a high degree of sensitivity to tuberculin was unable to induce any corresponding sensitivity to lepromin. It may be doubted whether BCG could have achieved anything different. This specific inability of lepromatous leprosy cases to become sensitized to lepromin is of great interest and importance, and is being studied further.

RESUMEN

Derivase esta comunicación del re-examen de los datos contenidos en un estudio ya presentado por Lowe y McNulty, con referencia particular a los resultados de pruebas tuberculínicas con dosis pequeñas (von Pirquet con TA) y luego en los negativos con dosis altas (50 UT de DPP, intradérmicamente). Los resultados se correlacionan con los de la reacción a la lepromina.

Entre 278 adultos sanos, 79 (29 por ciento) fueron positivos a la Pirquet. De estos positivos, 96 por ciento también reaccionaron a la lepromina; pero una gran proporción de los negativos fueron también lepromino-negativos. De los 199 individuos negativos a la primera prueba con tuberculina, no menos de 144 (73 por ciento) fueron positivos a la prueba con 50 UT. La mayor parte de estos positivos (84 por ciento) figuraban entre los reactores a la lepromina, en tanto que la mitad de los negativos a altas dosis también fueron negativos a la lepromina.

En los resultados en los 81 niños comprobados, hubo una semejanza fundamental, pero con notables diferencias cuantitativas. De ellos, sólo 10 (12 por ciento) reaccionaron a la Pirquet, pero, lo mismo que antes, casi todos (90 por ciento) fueron positivos a la lepromina. De los 71 negativos a la Pirquet, apenas una mayoría (52 por ciento) reaccionó a la dosis de 50 UT. De estos positivos, de nuevo, una mayoría indudable (59 por ciento) fueron también positivos a la lepromina, pero en este caso, todos los que no reaccionaron a las dosis grande de tuberculina fueron también negativos a la lepromina.

Apúntase que, en casi todos los individuos de alta sensibilidad a la tuberculina, este estado se asociaba con positividad a la lepromina y que hubo también una correlación bastante alta entre los que sólo fueron positivos a la dosis alta de tuberculina. Sin embargo, no hubo tal correlación entre los que fueron absolutamente negativos a la tuberculina. Considérase posible, y con respecto a los niños hasta probable, que algunas de las reacciones a la tuberculina a dosis alta fueran de naturaleza inespecífica.

Un punto del mayor interés que se estudia más a fondo es la incapacidad específica de los enfermos lepromatosos para volverse reactores a la lepromina, aun siendo hipersensibles a la tuberculina o habiendo sido vacunados con BCG.

REFERENCES

1. LOWE, J. and McNULTY, F. Tuberculosis and leprosy. Immunological studies. *Leprosy Rev.* **24** (1953) 61-90.
2. LOWE, J. and McNULTY, F. Tuberculosis and leprosy: Immunological studies in healthy persons. *British Med. J.* **2** (1953) 579-584.
3. LOWE, J. and McNULTY, F. The effect of BCG in lepromatous cases of leprosy. *Internat. J. Leprosy* **21** (1953) 173-177.
4. MILLER, J. S. A tuberculin survey in Stoke-on-Trent. *British Med. J.* **2** (1953) 917-920.
5. WORLD HEALTH ORGANIZATION. Expert Committee on Leprosy; First Report. *World Hlth. Org. Tech. Rep. Ser. No. 71*, 1953, pp. 28.
6. LOWE, J. and MCFADZEAN, J. A. Tuberculosis and leprosy—further immunological studies. *Leprosy Rev.* **27** (1956) 140-147.