Tuberculin Conversion in Leprous Families in Northern Nigeria

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The high incidence of leprosy in certain families in endemic areas was first demonstrated by Danielssen and Boeck in Norway in 1848. The discovery of *Mycobacterium leprae* by Hansen in 1872 diverted attention from hereditary theories of the etiology of leprosy, and *M. leprae* was generally accepted as the causative organism. However, it became obvious to many leprologists that not everyone who came in contact with *M. leprae* developed leprosy, nor was it possible to predict who would be susceptible.

A large number of factors have been invoked to explain this variation in susceptibility. Aycock (1), working in North America, revived the concept that genetic factors determined susceptibility to leprosy, and Kinnear Brown (2) in 1955 reached similar conclusions in Uganda. The whole question of the possible influence of genetic factors in the pathogenesis of leprosy has been reviewed by Spickett (1964). Many other authorities have supported the concept that leprosy may occur only in people who are genetically susceptible, but this hypothesis is not held generally. There is still no means of determining the susceptibility of a particular healthy subject to leprosy, nor of determining the form of leprosy to which he might be liable.

In this investigation we vaccinated children with lyophilized vole-bacillus vaccine and compared the tuberculin responses of those with an established family history of leprosy with the responses of normal children with no family history of the disease. The investigation was carried out in Katsina Province, Northern Nigeria, where outpatient leprosy treatment with dapsone was well established and I had already studied the incidence and form of leprosy (3).

Six hundred eighty-one children, aged 4-14 years, were chosen from two districts of Katsina Province. Of these, 474 came from families with no history of leprosy, and 207 from families with an established history of leprosy (one or both parents attending a leprosy outpatient treatment center). All the children were tested with lepromin and with tuberculin.

Four hundred sixty-three failed to respond to tuberculin and, of these, 306 were given single intradermal injections of lyophilized vole-tuberculosis vaccine (0.1 mgm.) and were retested with tuberculin six months later.

The tuberculin tests were made with P.P.D. Weybridge, 2 mgm. per ml., given by the Heaf method, and the results were graded by the Heaf method for tropical countries (Heaf 1959). For the lepromin test we used a material prepared from tissue from an untreated case of lepromatous leprosy in Katsina Province.

The lepromin was made by the Mitsuda method as modified by Wade (4) and was given in a dose of 0.1 ml. intradermally. The delayed reaction was read 28 days later and recorded by the criteria recommended by the committee on immunology of the Madrid International Leprosy Congress (1953).

Table 1 shows the results of the lepromin and first tuberculin tests:

TABLE 1.

	No.	%
Tuberculin-negative, lepromin-negative	245	35.9
Tuberculin-negative, lepromin-positive	218	32.0
Tuberculin-positive, lepromin-negative	62	9.1
Tuberculin-positive, lepromin-positive	156	23.0
Total	681	

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TABLE 2.

	With family history (a)		No family history (b)	
	No.	%	No.	%
Tuberculin-negative, lepromin-negative	79	38.0	166	35.0
Tuberculin-negative, lepromin-positive	87	42.1	131	27.6
Tuberculin-positive, lepromin-negative	9	4.3	53	11.2
Tuberculin-positive, lepromin-positive	32	15.5	124	26.2
Total	207		474	

Table 2 shows the responses of children with a family history of leprosy (a) compared with those of the children with no family history of the disease (b):

Of the 463 tuberculin-negative children 306 were vaccinated and after six months were tuberculin-tested for a second time. Table 3 shows the conversion rates in the two groups.

Table 4 shows a summary of the total conversion rates in the two groups following vaccination, together with the natural conversion rates in six months of a small group of children who were originally tuberculin-negative, had no family history of leprosy, and were not vaccinated.

The overall lepromin-positive rate among the 207 children with family histories of leprosy was 57.6 per cent, compared with 53.5 per cent in those with no family history of the disease. These rates of lepromin-positive responses are compatible with the incidence of leprosy (between 1.5% and 2%) of the population of Katsina Province. The lepromatous rate among the leprosy patients under treatment was in the region of 30 per cent.

The total lepromin-positive rates in the

TABLE 3.

Results of initial tests	(a) or (b)	No. vaccinated	No. converted	% converted
Tuberculin-negative and lepromin-negative	(a)	54	8	14.8
	(b)	93	84	90.5
Tuberculin-negative and lepromin-positive	(a)	76	15	19.7
	(b)	83	73	88.0

(a)—Family history; (b)—No Family history.

TABLE 4.

	No.	No. converted	% converted
Family history of leprosy and vaccinated	130	23	17.7
No family history of leprosy and vaccinated	176	157	89.3
No family history of leprosy and not vaccinated	35	9	25.7

two Nigerian groups are comparable, but the incidence of positive responses to tuberculin among the children of parents with leprosy (20%) is much lower than that among the children of normal parents (37%).

Many authorities believe that tuberculosis in a community gradually displaces leprosy. The implication is that cell-mediated immunity to tuberculosis carries with it some degree of immunity to leprosy. It is upon this hypothesis that widescale vaccination campaigns using BCG have been carried out. The low incidence of tuberculin-positive responses among the children of parents with leprosy could mean that they had not the same opportunity of coming into contact with *M. tuberculosis* as those children whose parents have no leprosy, or that, given an equal opportunity of contact with *M. tuberculosis*, they have not the same ability to respond.

The results of vaccination with vole-bacillus vaccine suggest that it is the inability to respond to *M. tuberculosis* which is the characteristic of the children of parents with leprosy. The conversion rate to tuberculin-positive after vaccination (89.3%) was similar in the children with no family history of leprosy to the figure obtained in the Medical Research Council trial in Britain in 1959. The children of parents with leprosy had a conversion rate of only 17.7 per cent. The natural conversion rate over the period of the investigation was 25.7 per cent. It appears that the ability to respond to lepromin in no way affects these conversion rates.

The failure of a high proportion of children of parents with leprosy to convert from tuberculin-negative to tuberculin-positive after vaccination may be an indication of an increased susceptibility to mycobacterial infection. This could be genetically determined.

It is to be hoped that these investigations will be repeated in other tropical territories where leprosy is endemic, and where there are facilities for regular follow-up studies.

SUMMARY

The effect of a single injection of lyophilized vole bacillus vaccine on tuberculin-negative children one or both of whose parents were suffering from lepromatous or borderline leprosy, has been studied by re-examining the tuberculin responses of these children six months after the initial injection of vaccine.

The effect of vaccination in this group of children has been compared with the results obtained from a group of children from the same racial and social background whose parents had had no family history of leprosy in any form.

In the first group [leprosy parents] the conversion rate from tuberculin-negative to tuberculin-positive was 17.7 per cent six months after vaccination while in the second group the conversion rate was 89.3 per cent [normal parents].

The possible reasons for this disparity in response to lyophilized vole bacillus vaccine between these two groups of children in a community where lepromatous leprosy exists are discussed.

REFERENCES

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