THE EFFECT OF BCG IN LEPROMATOUS CASES OF LEPROSY

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As we have recently reported (2), in cases of lepromatous leprosy, which almost by definition are lepromin negative, the administration of BCG causes in some cases an increase in the reactivity to lepromin as well as the usual tuberculin conversions. The following are the data there reported, now slightly revised:

One hundred and four lepromatous cases, negative to both tuberculin and lepromin, were given one intradermal injection of 0.1 gm. of BCG, and the tuberculin and lepromin tests were repeated after two months. The results were as follows:

Tuberculin test.—Of the 104 previously negative cases, 88 showed positive reactions, 10 showed doubtful reactions, and 6 remained negative.

Lepromin test.—Of the 104 previously negative cases, 12 became definitely positive, 18 showed very slight (1+) late reactions, 15 showed slight early reactions only, and 59 showed no reaction whatever.

The two tests together.—Of the 88 becoming tuberculin positive, 11 also became lepromin positive.

Of 16 remaining tuberculin negative, 1 became lepromin positive.

Of 25 becoming strongly positive to tuberculin, 8 also became lepromin positive.

Of 79 not becoming strongly positive to tuberculin (cuti), 4 became lepromin positive.

Of 12 who became lepromin positive, 11 also became tuberculin positive.

Of 92 who did not become lepromin positive, 59 became tuberculin positive.

In brief, the definite tuberculin conversions were 88 out of 104, or 84.6 per cent. The definite lepromin conversions were 12 out of 104, or 11.5 per cent, although there were 34 others (32.7%) who showed slight reactions, early or late, but not

enough to be classed as definitely positive. In general, lepromin conversions were seen only in those patients who showed tuberculin conversions, and were seen mainly in those with the strongest tuberculin response.

These results show: (1) That lepromatous cases of leprosy show no appreciable inability to be made allergic to the tubercle bacillus by BCG. (2) That although lepromatous cases are usually not made allergic to the leprosy bacillus by BCG, 11.5 per cent were so affected and another 32.7 per cent showed a slight tendency in that direction. (3) The anergy of the lepromatous cases is specific for the leprosy bacillus; further, it is not absolute, no less than 44.2 per cent showing some reaction, early or late, after BCG.

What is the significance of this increase in response to lepromin seen in these lepromatous cases, after the administration of BCG? Several questions arise. What are the factors influencing the conversion from lepromin negativity to lepromin positivity by the administraton of BCG? Are the conversions confined to the milder cases, or to those cases which have had long treatment or have been rendered clinically inactive and bacteriologically negative by chemotherapy? If the conver-

TABLE 1.—*Findings in 12 lepromatous cases made lepromin positive by BCG.*

Patient	Treatment before BCG		Bacteriological findings			Lepromin reactions/*a*					
						Before BCG		Two months after BCG		One year after BCG	
	Drug	Time (mos.)	Before treatment	When BCG given	One year later	Early	Late	Early	Late	Early	Late
M. O.	Dapsone	22	3+	1+	1+	—	—	+	2+	+	2+
A.	Dapsone	44	2+	1+	1+	—	—	+	2+	—	1+
G.	Sulfones	50	2+	—	—	—	—	+	3+	+	3+
N.	Sulfones	52	1+	—	—	—	—	+	2+	....	....
M. N.	Sulfones	27	2+	1+	—	—	—	—	2+	—	—
T. O.	Sulfones	21	1+	1+	—	—	—	?	2+	....	....
O. O.	TB-1	2	3+	2+	2+	—	—	+	2+	—	1+
I. O.	TB-1	15	2+	1+	1+	—	—	?	4+	—	—
Ab.	TB-1	2	1+	1+	1+	—	—	+	2+	+	1+
R.	TB-1	19	4+	3+	2+	—	—	—	2+	—	—
S. E.	TB-1	15	4+	3+	3+	—	—	+	2+	—	—
L. O.	TB-1	1	2+	2+	1+	—	—	?	3+	+	2+

a The early or 40-hour reactions were recorded as positive (+), doubtful (?) or negative (—.)

The late reactions, read after 2 to 4 weeks, were recorded as negative (—), or 1+, 2+, 3+ or 4+. Less than 2+ is generally considered of doubtful significance.

sions are due to treatment, are they seen more often after any one form of treatment than others? If conversion is seen in clinically active and bacteriologically positive cases, is it followed by clinical and bacteriological improvement? Finally, does the converson last, or is it only temporary?

Our studies give us some information on all of these points. Some of the data bearing on these matters are given in Table 1.

It will be seen that the period of treatment in these converted cases varied widely, from 1 to 52 months; that the severity of the cases as reflected in the bacteriological findings before treatment, and later before BCG was given, also varied widely; that the conversions were seen in patients receiving either of the main treatments used here, sulfones and thiosemicarbazone; that the conversions were not followed by marked or rapid bacteriological improvement; and that in most cases the conversion was temporary, for one year later only 3 of the 10 cases retested remained definitely positive (2+ or more), while 7 had become doubtful (1+) or negative.

Thus it appears that conversions produced by BCG in lepromatous cases do not depend entirely upon the mildness of the disease before or after the preceding treatment, on the length or the form of that treatment, or on the clinical inactivity or bacteriological negativity of the patients produced by that treatment before BCG is given. There is, moreover, no evidence that the bacteriological status of the patient at the time that BCG was given—and this was of course influenced by the severity of the original disease and the duration of the preceding treatment—had any influence on the conversion rate. The data on this matter are recorded in Table 2.

TABLE 2.—*Relation of the bacteriological status and lepromin conversions in 104 lepromin-negative lepromatous cases given BCG.*

Bacteriological status when BCG was given	Number of cases	Number of conversions
4+	3	0
3+	11	2
2+	20	2
1+	51	6
—	19	2
Total	104	12

DISCUSSION

We have made the unexpected finding that, in 12 of 104 lepromatous cases, a single intradermal injection of BCG converted the response to the lepromin test from negative to positive. This study was made in patients under treatment, most of them still bacteriologically positive. There was no proof that in those few that had already become bacteriologically negative under treatment, BCG made the lepromin reaction positive more readily than in the many that were still bacteriologically positive.

The significance of these lepromin conversions needs further investigation. Our present study indicates, (*a*) that the change is often temporary, and (*b*) that it does not appear to improve the prognosis. These findings suggest that BCG is not likely to be of value in the actual treatment of leprosy. It may, however, be worth while to study the value of repeated administration of BCG in an attempt to make and keep the reaction to lepromin positive. The BCG would have to be given orally, for with repeated injections the Koch phenomenon would be serious.

Convit *et al.* (1) have made a similar study of 113 lepromatous patients who, however, had been rendered bacteriologically negative by sulfone treatment. Of 51 previously negative to both the lepromin and tuberculin tests, 25.4 per cent showed lepromin conversions. Of 62 previously negative to lepromin but positive (1+) to tuberculin, 53.2 per cent showed lepromin conversions. Further, of 40 patients with leprosy of the indeterminate type, negative to both the lepromin and tuberculin tests, 35 (87.5%) showed lepromin conversion after BCG.

These workers concluded that BCG vaccination should be of value "in solving the problem of discharge from the leprosaria," presumably by reducing the danger of relapse, "and that it should help to reduce the high incidence of transformation of cases of the 'indeterminate' form, negative to lepromin, to the lepromatous type." In other words, they think that BCG vaccination should improve the prognosis of lepromatous or potentially lepromatous cases, particularly in those in which sulfone treatment had arrested the disease.

This may be so, but our own findings so far do not give much support to this idea, although it must be admitted that our work was not planned to provide evidence on this point. We shall study the matter further.

ADDENDUM.—Since this paper was written we have more and rather curious data. We have now retested the lepromatous cases that did not show lepromin conversion before and some of them show it now. The total showing conversion, either early (i.e., after two months) late (i.e., after one year), is quite high. Conversions, however, are often temporary, and we are now trying to see if we can keep them positive by oral administration of BCG.

RESÚMEN

De un total de 104 casos lepromatosos negativos tanto a lepromina como a la tuberculina, quienes fueron inoculados con BCG por vía intracutánea y de nuevo sometidos a las pruebas de la lepromina y la tuberculina dos meses después, el 84.6% (88 casos) reaccionaron positivamente a la tuberculina y el 11.5% (12 casos) reaccionaron positivamente a la lepromina (2+ o más), mientras que el 32.7% (34 casos) demostraron reacciones menores, precoces o tardías, pero que no se pudieron clasifacar como definitivamente positivas. Se discute en el reporte el significado de éste inesperado hallazgo.

La conversión positiva a la lepromina no pareció depender del estado de la enfermedad o del tratamiento administrado, segun indicios bacteriológicos. La conversión positiva no fué seguida por mejoriá bacteriológica. En la mayoría la conversión fué temporera, pues cuando 10 de los 12 casos fueron sometidos a nueva prueba un año más tarde, solamente 3 reaccionaron definitivamente positivos. Es necesario ampliar las investigaciones pues es necesario determinar si vacunas repetidas, por vía oral necesariamente, influenciarián el prognóstico de la enfermedad.

REFERENCES

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