MITSUDA'S SKIN REACTION (LEPROMIN TEST) IN CHILDREN OF LEPROUS PARENTS

II. OBSERVATIONS ON NEWLY-BORN TO EIGHTEEN-MONTH-OLD CHILDREN[1]

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Though few and of limited scope, the published observations on the lepromin test in young children have nevertheless given rise to certain definite conclusions which have an important bearing on the transmission and development of leprosy. Thus Chiyuto's finding (1) of a negative reaction in all children under one year of age—whether of leprous or nonleprous parentage—was considered by him to indicate lack of resistance, hence their susceptibility to leprosy; and the uniformly positive results in healthy, unexposed children above three years of age and in healthy (nonleprous) adults, were believed to explain why such persons are less susceptible to the disease. Manalang (3) accepted these findings and interpretations of Chiyuto in conjunction with those of other workers as further support of his own theory of the susceptibility of infants and young children and the nonsusceptibility of the adult. He further suggested that a positive lepromin reaction should be induced in a group of exposed infants, they to be followed carefully for evidences of early lesions.

Bargehr (cited by Pereira), and Pereira (5)—both exponents of the view assigning to the test a specific immunologic significance in leprosy—have in fact attempted to induce a positive reaction in children of nonleprous as well as leprous parentage, but without success in those under three years of age. However, they succeeded with older children and with healthy or leprous adult subjects. These authors also attribute the consistently negative reaction in the younger children to their susceptibility to the disease.

De Souza Campos (7) has also studied the lepromin reaction in children and found that all those isolated at birth from their leprous parents reacted negatively, while the more strongly positive reactions were in relation to longer periods of life with their parents. Unfortunately, no age groups are mentioned.

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More recently Lara (2) has employed the test repeatedly on a group of Culion children of ages ranging from fourteen months to five years, who had been exposed to infection for periods of from seven to seventeen months. Besides confirming the previously observed influence of age, he found that with the repeated testing the reaction showed a tendency to become positive if originally negative, or to become intensified if originally positive, regardless of whether the individuals were free from lesions throughout the entire observation period, or had previously had lesions which had cleared up, or were to show manifestations of the disease during the period of test or subsequently. The impression was gained that the lepromin test has no value either as an index of the resistance of such children to the development of the manifest disease, or as an effective prophylactic measure for them.

PRESENT WORK

The present study is of similar scope and procedure to the one just mentioned, the main object being to correlate the results of the lepromin test with the onset and later development of leprosy in children.[2] The children in this study were, however, younger than those in the previous one, ranging in age from about one week to eighteen months at the beginning of the testing. There were 110 of them, 48 boys and 62 girls. No attempt at selection was made. They represented one-half of the total number of available children, the other half, of comparable age and sex distribution, being used as the control group. Three children were isolated from their parents by removal from the colony to the nursery in the nonleprous area after the first test, at the age of 20 months. The rest, except those who died or were released earlier, remained continuously with their parents through the period of the three tests. All appeared to be nonleprous at the beginning of the study.

The tests were made at intervals of four months, instead of three months as in the previous study. The clinical observations were made regularly every two months. The readings of the reactions made after the first and second weeks were disregarded; thereafter the maximum average diameter—i.e. average of the longest and shortest diameters at the center—was taken as the basis for

[2]The lepromin used was, as before, prepared by Dr. J. O. Nolasco, and checked for adequacy of bacillary content. The bacteriological examinations of suspected lesions and the histological examinations of the sections that were taken were made, respectively, by Drs. J. Manalang and Nolasco, both of the Pathological Section, who are making separate studies of this material. Dr. J. Tiong, of the Medical Section, removed the biopsy specimens.

rating. In this connection Rotberg (6) has very recently urged the adoption of more strict criteria than those used heretofore, with a view to eliminating from the positive reactions those of doubtful significance, chiefly those not larger than 5 mm. and of uncharacteristic appearance. In the main this precaution seems justified. Nolasco (4) of this colony, working independently, has shown histological evidence supporting Rotberg's contention. Nevertheless, there sometimes occur clinically characteristic positive reactions that do not exceed 5 mm. in diameter. For this reason, and while the question awaits final determination, it was felt that the continued use of the older method of reading and rating the reaction, with the added precaution of disregarding the first two weeks' readings as stated above, would avoid needless confusion and at the same time permit appreciation in conformity with Rotberg's and Nolasco's more substantial criteria.

OBSERVATIONS

The observations reported in this paper concern only the lepromin-tested group, and cover a period of twenty months. A comparative study with the control group, with special reference to leprosy incidence, onset, and early course of the disease will form the basis for further reports.

In Table 1 are listed the main observations on the 110 children studied, giving for each of them the sex, age at the first test, maximum average diameter of the reaction for each test, and pertinent remarks. In two instances the parents refused retesting after the first test, but the children continued under observation until the end of the period of testing. One child was transferred with the mother to another station after the first test; one died after the first test and another about the middle of the period of reading the second test; and one was released and another died after the second test. Only 103 children received the three tests. In Table 2 are summarized the results of the three tests, expressed as lepromin reaction ratings by age-group and sex.

Influence of sex.—A glance at Table 2 suffices to show that the reactions to the lepromin test were not influenced by the sex, though my previous study there was found a greater proportion of positive reactors among the boys than the girls.

Age.—The children in this study were grouped into three age-ranges: 12 to 18 months, twenty-five cases; 6 to 12 months, thirty-three cases; and up to 6 months, fifty-two cases, the youngest children being only one to two weeks old when first tested. Those

TABLE 1. *Lepromin reactions, repeated tests, in 110 children.*

Case Number, name and sex	Age at first test (months)	Reactions (Maximum average diameter in millimeters)			Remarks[a]
		First test	Second test	Third test	
1. M. Al., M.....	18	4	10	12	Released after 1 month.
2. R. No., F.....	18	6	16	18[b]	Released after 1 month.
3. O. Bi., M.....	18	7	22*	24*[b]	(*) Leprotic lesion present.
4. A. Al., F.....	17	4	9	10*	(*) Leprotic lesion present.
5. A. Ma., F.....	17	5	22	22*[b]	(*) Leprotic lesion present.
6. D. Ca., M.....	17	6	5	7	Released immediately.
7. F. Bi., M.....	16	4	10	11	Leprosy 2 months later.
8. L. Cr., F.....	16	7	5	5	Released after 1 month.
9. A. Pa., M.....	16	5	6	10	Still nonleprous.
10. A. Ab., F.....	16	3	8	6	Still nonleprous.
11. A. Is., M.....	16	7	8	27	Leprosy 3 months later.
12. A. Ab., F.....	15	7	15	11[b]	Released after 4 months.
13. M. Pa., F.....	15	4	5	6	Leprosy 8 months later.
14. F. Se., M.....	15	5	10	17	Still nonleprous.
15. I. Da., F.....	14	4	6	6	Still nonleprous.
16. P. Vi., M.....	14	5	8	8*	(*) Leprotic lesion present.
17. V. Ta., F.....	14	5	10*	21*	(*) Leprotic lesion present.
18. F. Pa., F.....	13	8	9	10	Released after 4 months.
19. D. Cu., F.....	13	10	20	16[b]	Leprosy 6 months later.
20. C. Fl., F.....	13	4	5*	6*	(*) Leprotic lesion present.
21. G. Ma., F.....	13	3	4	5*	(*) Leprotic lesion present.
22. B. Vi., M.....	13	3	5	6	Leprosy 5 months later.
23. F. En., M.....	13	5	6	6	Still nonleprous.
24. C. Ba., F.....	13	3	6	25	Released immediately.
25. A. Pe., F.....	13	5	7*	7*	(*) Leprotic lesion present.
26. P. Hi., F.....	12	5	6	7	Still nonleprous.
27. B. Ba., F.....	12	3	6	5	Released near end of test.
28. E. Ba., M.....	12	4	8	20	Still nonleprous.
29. S. La., F.....	12	5	5	7	Still nonleprous.
30. M. Ab., M.....	12	4	8	25	Still nonleprous.
31. B. Oc., M.....	11	7	21	20[b]	Still nonleprous.
32. F. Ma., F.....	11	6	7	6	Still nonleprous.
33. P. Ca., F.....	11	3	5	8	Still nonleprous.
34. R. Ba., M.....	11	4	5	7	Leprosy 2 months later.
35. L. Sa., M.....	11	6	9	10	Still nonleprous.
36. F. De., M.....	11	4	7	7	Leprosy 2 months later.
37. A. Ra., F.....	11	2	7	12*	(*) Leprotic lesion present.
38. J. De., F.....	10	0	12	22	Still nonleprous.
39. F. Um., F.....	10	6	14	7[b]	Still nonleprous.
40. A. Ri., M.....	10	3	13	18*[b]	(*) Leprotic lesion present.
41. M. Ka., F.....	10	4	—	—	Retest refused; released.
42. P. Pe., F.....	10	3	10	6	Still nonleprous.
43. E. Ab., F.....	10	7	11	9[b]	Still nonleprous.
44. I. Pa., M.....	9	0	5	12	Leprosy 2 months later.
45. L. Ba., F.....	9	7	13	20	Died; tuberculosis.
46. M. Fe., M.....	9	0	7	7	Leprosy 3 months later.
47. D. Ca., F.....	9	5	6	6	Leprosy 10 months later.
48. C. Pr., M.....	9	5	8	9	Still nonleprous.
49. D. Al., M.....	8	3	7	12	Still nonleprous.
50. V. Ta., M.....	8	0	11	18	Leprosy 7 months later.
51. L. Bu., F.....	8	5	17	8[b]	Leprosy 8 months later.
52. Mo., M.....	8	2	6	13	Released after 8 months.
53. M. Ga., M.....	8	3	5	9	Still nonleprous.
54. C. Pl., M.....	8	0	6	8	Still nonleprous.
55. P. Ud., F.....	8	0	7	7	Released after 9 months.

TABLE 1. *Lepromin reactions, repeated tests, in 110 children (cont).*

56.	L. Pa., M.....	7	4	5	8	Still nonleprous.
57.	E. Di., M.....	7	4	21	15[b]	Leprosy 6 months later.
58.	E. An., F.....	7	0	6	6	Still nonleprous.
59.	F. Gu., M.....	6	3	6	5	Leprosy 7 months later.
60.	F. Wa., M.....	6	3	4	5	Still nonleprous.
61.	M. Is., F.....	6	3	—	—	Died: tuberculosis.
62.	R. Pa., M.....	5	3	12	21[b]	Released immediately.
63.	A. Se., M.....	5	3	3	6	Still nonleprous.
64.	L. Go., F.....	5	3	6	6	Still nonleprous.
65.	F. Ab., F.....	5	3	8	7	Still nonleprous.
66.	R. Ad., M.....	5	4	15	13[b]	Still nonleprous.
67.	L. Ar., F.....	5	3	4	5	Still nonleprous.
68.	C. Es., M.....	4	2	5	3	Died: anemia, etc.
69.	A. Ac., F.....	4	3	—	—	Retest refused; released.
70.	L. Ma., M.....	4	3	5	4	Still nonleprous.
71.	F. La., M.....	4	2	7	7	Still nonleprous.
72.	R. So., F.....	4	3	20	19[b]	Still nonleprous.
73.	P. Gr., F.....	3	2	4	6	Leprosy 3 months later.
74.	G. Ma., M.....	3	2	17	8[b]	Still nonleprous.
75.	L. Ar., M.....	3	2	4	5	Still nonleprous.
76.	M. Ta., F.....	3	0	5	5	Still nonleprous.
77.	A. Al., F.....	3	6	24	22[b]	Still nonleprous.
78.	R. Re., M.....	2	5	14	8[b]	Still nonleprous.
79.	C. Fl., M.....	2	4	16	7[b]	Released after 2 months.
80.	V. Pa., F.....	2	3	7	8	Still nonleprous.
81.	J. Ji., F.....	2	4	3	4	Still nonleprous.
82.	F. Qu., M.....	2	0	7	5	Anemia, still nonleprous.
83.	S. Sa., M.....	2	2	6	5	Still nonleprous.
84.	J. Ce., F.....	2	3	7	8	Still nonleprous.
85.	C. Ro., F.....	2	3	6	9	Still nonleprous.
86.	F. Di., F.....	1	4	12	6[b]	Still nonleprous.
87.	J. Ca., F.....	1	3	11	15	Still nonleprous.
88.	R. Fr., M.....	1	2	6	7	Leprosy 10 months later.
89.	C. Su., F.....	1	2	4	3	Still nonleprous.
90.	Z. Al., F.....	5	0	3	—	Died; tuberculosis.
91.	R. Ba., F.....	4	3	0	5	Eczema at 2nd test; nonleprous.
92.	R. Ca., M.....	4	3	5	6	Still nonleprous.
93.	E. Ma., F.....	4	3	4	6	Still nonleprous.
94.	P. Be., M.....	4	3	4	7	Still nonleprous.
95.	A. At., F.....	4	3	7	11	Still nonleprous.
96.	S. Jo., F.....	4	0	5	9	Still nonleprous.
97.	S. Ob., F.....	4	1	4	—	Released after 2nd test.
98.	N. Di., F.....	3	3	3	7	Still nonleprous.
99.	D. Du., F.....	3	5	7	11	Still nonleprous.
100.	B. Vi., F.....	3	0	12	15	Still nonleprous.
101.	R. Ta., M.....	2	0	4	8	Still nonleprous.
102.	G. Bu., F.....	2	0	0	0[c]	Still nonleprous.
103.	M. Ca., F.....	2	2	4	5	Still nonleprous.
104.	J. Vi., F.....	1	0	6	10	Still nonleprous.
105.	B. La., M.....	1	0	0	9	Released after 2 months.
106.	E. Ki., F.....	1	4	4	8	Still nonleprous.
107.	J. Lo., M.....	1	3	6	10	Still nonleprous.
108.	R. Al., M.....	1	3	—	—	Died; cholera infantum.
109.	A. Bu., F.....	1	2	—	—	Released after 1st test.
110.	V. Di., F.....	1	0	8	17	Still nonleprous.

[a] Time periods mentioned in this column are after the third test. Children released from the colony were nonleprous at the time.

[b] One-half of the usual dose used (0.05 cc.).

[c] In this case the third test became distinctly positive six weeks after the usual time of reading.

TABLE 2. *Analysis of results of tests, by age groups and sex.*

Case group	Degree of reaction	Sex	Results of tests					
			First		Second		Third	
			No.	Pct.	No.	Pct.	No.	Pct.
GROUP 1 12 to 18 months (25 cases)	Neg.	M.	0	0.0	0	0.0	0	0.0
		F.	0		0		0	
	±	M.	0	0.0	0	0.0	0	0.0
		F.	0		0		0	
	1+	M.	7	68.0	2	24.0	0	8.0
		F.	10		4		2	
	2+	M.	3	32.0	7	56.0	5	48.0
		F.	5		7		7	
	3+	M.	0	0.0	1	20.0	5	44.0
		F.	0		4		6	
GROUP 2 6 to 12 months (33 cases)	Neg.	M.	4	21.2	0	0.0	0	0.0
		F.	3		0		0	
	±	M.	1	6.0	0	0.0	0	0.0
		F.	1		0		0	
	1+	M.	10	54.5	4	18.7	0	3.1
		F.	8		2		1	
	2+	M.	2	18.2	9	53.1	8	59.4
		F.	4		8		11	
	3+	M.	0	0.0	4	28.2	9	37.5
		F.	0		5		3	
	0[a]				1 case		1 case	
GROUP 3 To 6 months (52 cases)	Neg.	M.	3	19.2	1	6.2	0	2.1
		F.	7		2		1	
	±	M.	6	21.1	0	0.0	0	0.0
		F.	5		0		0	
	1+	M.	12	57.7	8	41.7	7	28.3
		F.	18		12		6	
	2+	M.	0	1.9	6	31.2	11	50.0
		F.	1		9		12	
	3+	M.	0	0.0	5	20.8	2	19.6
		F.	0		5		7	
	0[a]				4 cases		6 cases	
TOTAL (110 cases)	Neg.	M.	7	15.4	1	2.8	0	0.9
		F.	10		2		1	
	±	M.	7	11.8	0	0.0	0	0.0
		F.	6		0		0	
	1+	M.	29	59.1	14	30.5	7	15.5
		F.	36		18		9	
	2+	M.	5	13.6	22	43.8	24	52.5
		F.	10		24		30	
	3+	M.	0	0.0	10	22.8	16	31.0
		F.	0		14		16	
	0[a]				5 cases		7 cases	

[a] Not tested.

in the oldest group all showed 1+ or 2+ reactions in the first test; of the next group about 73 percent and of the youngest one only about 60 percent showed similar reactions. There was not a single 3+ reaction in the first test, but 32 percent of the oldest

group gave 2+ reactions, as compared with only 18 percent and 2 percent, respectively, for the two younger groups. These results once more confirm some of the previous observations regarding the influence of age on the lepromin reaction in children. They further show, contrary to some other previous observations, that a considerable proportion of the children of leprous parents under one year of age give positive lepromin reactions, although not many of these are more than 1+ in the first test.

Effect of further ageing and retesting.—In the second and third tests there were progressive increases in the total proportions of positive reactors and of more strongly positive reactions (i.e., 2+ to 3+) in all three groups. Thus in the oldest group the proportion of such stronger reactions rose to 76 percent in the second test and to 92 percent in the third test. The corresponding figures for the next group were 81.3 percent and 96.9 percent, and for the youngest group, 52 percent and 69.6 percent. While these increases might have been and probably were in part the effect of further ageing, the influence of the retests can also be demonstrated. Thus from the same table (Table 2) the results in the first test with the first and second groups show, respectively, a distinctly smaller proportion of 2+ to 3+ reactions than do those with the second and third groups in the second test, despite the fact that the retested groups were somewhat younger than those receiving the first test. Finally, there were eighty-five children who were only one year old or younger at the first test; of these, seven (8.2 percent) gave a 2+ reaction in that test. In the second and third tests there were, respectively, fifty-eight and thirty-eight children of corresponding upper age-range but with an increasing lower age-range. The proportions of 2+ to 3+ reactions in these last two groups were 57 percent and 71 percent, respectively—even much higher than the 32 percent corresponding to the 12 to 18 months group in the first test—thus showing clearly the intensifying effect of retesting. These findings corroborate my earlier observations regarding the effect of retesting, but are definitely in contrast to those of other observers with respect to children under one year of age.

Another observation of interest was the occasional reactivation, apparently due to retesting, of previous positive or even doubtful reactions which had already subsided partially or completely before the retest.

Effect of reducing the dose of lepromin.—In some of the children the lepromin reaction was so marked in the second test that it was felt advisable to halve the dose (to 0.05 cc.) in the third test in the

hope of minimizing the swelling and the period of ulceration and healing, which in some instances lasted more than two months and caused dissatisfaction among the parents. A number of these strongly positive reactors were, however, again given the usual dose, for comparison. In addition, the strongly positive reactors of another, smaller group of children, all of whom except one had been included in my first study and had previously received from one to three tests, were dealt with in a similar manner. The resulting reactions are shown in Tables 3 and 4.

TABLE 3. *Results with originally S-plus reactors on retesting; usual dose of lepromin used.*

Patient and series number	Maximum reaction (mm.)		Remarks
	Original	Retest	
L. E., Old 8	11	23	Released after 5 months.
A. T., " 17	19*	27*	(*) With active leprosy.
F. C., " 62	14	7	Released after 1 month.
V. P., " 53	12*	21*	(*) With active leprosy.
E. B., " 41	18*	20*	(*) With active leprosy.
R. V., " 45	17	20	Released after 5 months.
C. B., " 50	20	23	Leprosy 12 months later.
J. D., New 38	12	22	Still nonleprous.
L. B., " 45	13	20	Died; tuberculosis.
V. T., " 50	11	18	Leprosy 7 months later.
J. C., " 87	11	15	Still nonleprous.
B. V., " 100	12	15	Still nonleprous.

Twelve cases, including three already with leprotic lesions at the preceding test, were given the usual dose of 0.1 cc. in the retest (Table 3). Of these cases only one, which has remained nonleprous, showed a diminution of reaction which reduced the rating to 2+; the rest showed a further intensification of reaction. The increase occurred regardless of the presence or absence of active leprotic manifestations, or the later development of the disease.

Twenty-seven cases, including seven already with manifest lesions at the time of the preceding test, were given the half dose (Table 4). Of these seven, four showed less marked reactions than before, but in only one of them was the rating reduced to 2+; one case showed the same intensity of reaction as in the preceding test, while two cases showed an increased reaction. Two other cases developed leprosy before the retest; one of these showed no change in intensity of reaction, while the other gave a more marked reaction to the half dose of lepromin. Of the eighteen cases which have remained nonleprous, sixteen showed a less intense reaction, which led to a reduced rating of 2+ in seven of them, while two cases showed an increased reaction.

The number of children studied is not sufficiently large to permit drawing any definite conclusion. However, there seems to be some indication that, among strongly positive reactors, retesting with a markedly reduced dose of lepromin may result in either decreased, increased, or unchanged reaction in the presence of early manifest leprosy, but is more apt to result in a decreased reaction when there is as yet no recognizable disease.

TABLE 4. *Results with originally S-plus reactors on retesting; one-half of usual dose of lepromin used.*

Patient and series number	Maximum reaction (mm.)		Remarks
	Original	Retest	
A. R., New —	15*	8†	(*) With active leprosy. (†) Lesion almost healed.
N. V., Old 61	16	14	Released after 1 month.
M.D.P., " 63	12*	17*	(*) With active leprosy.
C. R., " 64	21	14	Released after 1 month.
B. M., " 55	17*	17†	(*) With active leprosy. (†) Lesion subsiding.
E. G., " 54	27*	21*	(*) With active leprosy.
V. Z., " 56	20*	18†	(*) With active leprosy. (†) Lesion subsiding.
P. P., " 57	25*	17*	(*) With active leprosy.
R. N., New 2	16	18	Released after 1 month.
O. B., " 3	22*	24*	(*) With active leprosy.
A. M., " 5	22	22*	(*) With active leprosy.
A. A., " 12	15	11	Released after 4 months.
D. C., " 19	20	16	Leprosy 6 months later.
B. O., " 31	21	20	Still nonleprous.
F. U., " 39	14	7	Still nonleprous.
A. R., " 40	13	18*	(*) With active leprosy.
E. A., " 43	11	9	Still nonleprous.
L. B., New 51	17	8	Leprosy 8 months later.
E. D., " 57	21	15	Leprosy 6 months later.
R. P., " 62	12	21	Released, immediately.
R. A., " 66	15	13	Still nonleprous.
R. S., " 72	20	19	Still nonleprous.
G. M., " 74	17	8	Still nonleprous.
A. A., " 77	24	22	Still nonleprous.
R. R., " 78	14	8	Still nonleprous.
C. F., " 79	16	7	Released after 2 months.
F. D., " 86	12	6	Still nonleprous.

Lepromin reaction and onset of manifest leprosy.—Only ten children in the present series developed definite lesions during the actual period in which the three tests were made. In four of them this event occurred shortly before or coincidently with the second test, while in six it happened just before or during the third testing. Of these ten cases only two showed no change in intensity of reaction after the appearance of manifest lesions; the rest, paradoxically from the prevailing idea of the matter, showed an increased reaction. Further retesting in four cases resulted in further

intensification of the reaction in three and no change in one.

One hundred children showed no definite manifestations of leprosy up to the end of the third test, but sixteen of them developed such manifestations after intervals of from two to ten months (average five months) thereafter. In nine of these cases the reaction had been greater in the third than in the second test; in four of them the reaction was less, but three of these four children were given only one-half of the usual dose of lepromin in the third test.

Of the remaining eighty-four children, only seventy-seven received the three tests. Of the latter number, forty-seven showed a greater reaction in the third than in the second test, in spite of a reduced lepromin dose in two of them; twenty-one showed a less intense reaction in the third test, with eleven of them receiving the smaller dose of lepromin; and nine showed equally intense reactions in the second and third tests.

It would seem from the above analysis that the children in whom leprosy developed after the third test reacted essentially like those who have not as yet developed any manifestation of the disease, while the children in whom the disease appeared earlier, during the period of testing, showed an apparently greater tendency to react positively to the test.

Exposure to infection and isolation.—A study was also made of the possible influence of these factors, in view of the recent findings of de Souza Campos cited earlier in this paper. A comparison of the results of the first lepromin test in some of the groups in the first and the present series of children is shown in Table 5.

The average total period of exposure for the older-series children was 15.7 months for the 18 to 24 months age-group, and 14.1 months for the 12 to 18 months age-group. The test was first given to most of these children after they had been isolated for a period averaging 4.1 months for the older group and 1.5 months for the younger group.

The children of the present series had been with their parents continuously up to the time of the first test and only three were isolated thereafter, the rest remaining with their parents through the entire test period. Therefore the average age of the 12 to 18 months group of the present series, 15 months, also represents the average time of exposure, without an intervening period of isolation, before the first test. However, the average total time of exposure for this group was about 23 months, up to the time

of the third test, or more than 7 months and 8 months, respectively, longer than that of the 18 to 24 months group and the 12 to 18 months group of the old series. The average age—and period of exposure—of the 6 to 12 months group of the present series was 9.6 months at the time of the first test, and their total period of exposure up to that of the third test was 17.6 months.

TABLE 5. *Result of first lepromin tests in the old and new series.*

Result	Old series				New series			
	Age 18 to 24 months		Age 12 to 18 months		Age 12 to 18 months		Age 6 to 12 months	
	Cases	Pct.	Cases	Pct.	Cases	Pct.	Cases	Pct.
Neg.	3	13.0	7	20.0	0	0.0	7	21.2
±	4	17.4	17	48.6	0	0.0	2	6.0
1+	11	47.8	8	22.8	17	68.0	18	54.5
2+	3	13.0	3	8.6	8	32.0	6	18.2
3+	2	8.7	0	0.0	0	0.0	0	0.0
TOTAL	23	99.9	35	100.0	25	100.0	33	99.9

Table 5 shows that the children of the present series were comparatively better reactors to the first test than those of the old series of similar or even greater ages. Further analysis, not shown in the table, revealed that the 18 to 24 months group of the old series gave in the second test a total of 88.8 percent positive reactions, with 33.2 percent of 2+ to 3+ intensity, among eighteen children tested; while in the third test the corresponding figures for fifteen tested children were 93.3 percent and 73.3 percent. Among the 12- to 18-months group of the old series the corresponding figures for the second and third tests were 75.7 percent and 21.2 percent for thirty-three children tested and 82.6 percent and 69.6 percent for twenty-three tested children. Table 2 shows that all of the twenty-five children in the 12 to 18 months group of the present series gave positive reactions in the retests, and that in the second and third tests there were 76 percent and 92 percent, respectively, of 2+ to 3+ intensity. In the 6- to 12-months group, likewise, all of the thirty-two retested children gave positive reactions, with 81.3 percent and 96.9 percent, respectively, 2+ to 3+ reactions in the second and third tests. In fact, even the youngest age group (up to 6 months) of the present series gave at least as high a proportion of definitely positive reactions in the retests as did the 12- to 18-months group of the old series.

Therefore, with a comparable period of exposure but with an intervening several months period of isolation before the first

test, the 18- to 24-months old children of the old series gave somewhat poorer reactions to the lepromin test than did the 12- to 18-months old, continuously exposed children of the present series. In the retests the latter group, which remained exposed to leprous environment, also gave better reactions than the former which were isolated. Furthermore, among the children in comparable age groups (i.e., 12 to 18 months), and with comparable periods of exposure before the first test, those of the older series who had a shorter total period of exposure besides an interval of 1.5 months of isolation before the first test, gave definitely poorer reactions, not only to the first test but also to the second and third tests, than did the present series children who remained exposed through the three tests. Thus it would seem that both the duration and the constancy of exposure have a direct relation to the proportion of distinctly positive lepromin reactions.

Intercurrent disease.—Practically all of the children suffered from more or less generalized and recurring scabies, and many had at least one attack of "colds" or other passing affections common to young children during the period comprised by the three tests. One child had extensive eczema at the time of the second test and then gave a negative lepromin reaction, though in the first one, before the onset of the eczema, it had been 1+ and was again of that grade in the third test, after that condition had subsided. Another child, subject to asthmatic attacks since the age of one year, gave definitely positive reactions in the second and third tests. Two children had marked anemia, concomitant with chronic malaria in one and probably of dietary origin in the other. The malaria case gave negative reactions throughout, but six weeks after the third test, when the child had recovered and was in better general condition, a definite positive reaction developed at the site of that test. The other case of anemia gave a negative reaction to the first test, a 2+ reaction to the second test at the age of less than six months, and a 1+ reaction to the third test, four months later, when the anemia was very marked. One child two months old, with a 1+ reaction to the test at the age of less than one month, died of cholera infantum before a retest could be made. Two children died of generalized tuberculosis, one in the middle of the second testing, with a ± reaction as compared to a 1+ in the first test; the other, already tuberculous, gave a 3 mm. reaction in the second test three months before death, compared with a negative reaction in the first test. A third

child, with early tuberculosis and a 3+ reaction in the third test, died eight months later.

It may be concluded from the foregoing that the usual intercurrent diseases not of serious nature do not seem to affect the lepromin reaction, but that serious illness or cachectic states may occasionally depress it or delay its appearance.

COMMENT

Previous statements in the literature that the lepromin reaction is constantly negative in children under one year of age are not borne out by the present study. Not only was a definite, positive reaction obtainable in a small, but by no means negligible, proportion of children of leprous parents in that age group, but it could be induced in a large majority of them while they were still less than one year old. Furthermore, in several cases leprosy became manifest irrespective of satisfactory positive reactions; in fact, the onset of the disease seems to have favored further intensification of the reaction, at least in some of the cases. There was a further indication that prolonged, constant exposure to the infection and repeated testing likewise acted as sensitizing factors. These more recent findings necessitate a revision of the current idea that a negative lepromin reaction indicates susceptibility to leprosy and a positive one an adequate resistance to the disease. How long lepromin-positive children will remain positive if left exposed to or removed from a leprous environment, or with respect to the later progress of the disease, cannot yet be said.

SUMMARY

One hundred and ten unisolated, nonleprous children of leprous parents, ranging in age from newly-born to eighteen months, all closely observed since birth, were given the lepromin test repeatedly at intervals of four months. These children were examined regularly every two months, with special attention to the appearance of early, recognizable lesions of leprosy, and the results of the tests were analyzed and correlated with the clinical observations.

Sex was found to have no influence on the lepromin reaction. The frequency of positive reactions was in direct relation to the age, a small but not negligible proportion of undoubtedly positive reactions occurring, in the first test, among the children less than one year old.

In the retests there was a further progressive increase in

the proportion of positive reactors which could not wholly be attributed to further ageing, but was probably in part the effect of retesting. Thus a majority of the children who were still less than one year old gave definitely positive reactions in the second or third test.

Retesting of strongly positive reactors with a markedly reduced dose of lepromin more frequently resulted in a distinctly diminished reaction in the absence of manifest leprosy than when lesions were already in evidence.

The appearance or existence of early leprotic lesions in the children was associated with an apparently undiminished, and possibly even greater tendency to react positively to the test.

Both the duration and the constancy of exposure to leprous environment seemed also to bear a direct relation to the proportion of positive reactions.

Intercurrent disease not of a serious nature showed no depressing influence on the reaction.

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