

LEPROMIN HYPERSENSITIVITY INDUCED BY INTEGRAL LEPROMIN IN PERSONS PRESUMABLY FREE FROM LEPROSY¹

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Wade (5), in a recent editorial in the *International Journal of Leprosy*, presented an interesting bibliographic digest concerning the induction of lepromin reactivity by repeated injections of integral lepromin, and related succinctly the findings of several workers in presumably healthy persons.

Fernandez and Olmos Castro, in 1942 (1), demonstrated that healthy adults can be sensitized by integral lepromin. Fernandez (2) found that a high percentage of presumably nonleprous persons be sensitized by means of intradermal injections of heat-killed *Mycobacterium leprae*.

These investigations, and our observations on the sensitization of dogs by integral lepromin which confirmed the work of Wade (4), induced us to undertake this present study, to establish the frequency of sensitization by a single injection of integral lepromin and to study the relationship between the reactions of hypersensitivity (early, or Fernandez) and of resistance (late, or Mitsuda).

PLAN OF STUDY

In our leprosy service in San Miguel de Tucumán 225 persons, residents of the city over 20 years of age, affected with various kinds of dermatoses but without known contact with leprosy, were given systematically, without discrimination, intradermal injections of 0.1 cc. of the Mitsuda-Hayashi lepromin. The lepromin was prepared by us at different times, as required. Readings were made after 48 hours (Fernandez reaction) and 21 days (Mitsuda reaction). In evaluating the results we followed the recommendations of the VI International Congress of Leprology (Madrid, 1953).

A second injection of integral lepromin was given, regardless of the results of the previous one, on the 21st day after the first injection, i.e., on the day that the Mitsuda reaction was read. Again both results were recorded for the progressively diminishing numbers of persons who appeared for the readings.

RESULTS

(a) *Results of the first injections.*—Out of the 225 persons tested 214

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returned for the early reading, but only 92 for the late reading. The results are shown in Table 1.

Out of the 214 persons whose early reactions were observed, only 25, or 11.7 per cent, were positive. A large majority of the positives (22, or 88%)

TABLE 1.—Results of the first injection of integral lepromin in adult noncontacts, Fernandez and Mitsuda reactions.

Reaction	Cases read	Total positive	Degree of positivity		
			1+	2+	3+
Fernandez	214	25 (11.7%)	22 (88.0%)	2 (8.0%)	1 (4.0%)
Mitsuda	92	89 (96.7%)	20 (22.5%)	49 (55.0%)	20 (22.5%)

were weakly so (1+), and only 1 case (4%) gave strong (3+) reactions. On the other hand, 89 of the 92 whose late reactions were seen, or 96.7 per cent, were positive. A majority of them (49, or 55.0%) were of moderately strong degree, and another 20 cases (22.4%), had reactions which became ulcerated, making a total of 69 (77.5%) who were above the weakly positive grade.

(b) *Hypersensitivity (Fernandez) reactions to the second injection.*—The early reading of the second test, out of the 92 persons who were reinjected when they returned for the first late reading, could be made in 79 of them. The results are shown in Table 2, grouped according to the results of the first test with respect to the same reaction.

Of the 79 who returned for the early reading, 57 had previously been Fernandez negative; but 32 of them, or 56.1 per cent, were now positive—a majority of them (59.4%) only weakly so, although several (18.7%)

TABLE 2.—Results of the second injection of integral lepromin in adult noncontacts; Fernandez reaction only, compared with first test.

Fernandez reaction, first test	No. of cases	Fernandez reaction, second test			
		Total positives	Degree of positivity		
			1+	2+	3+
Negative	57	32 (56.1%)	19 (59.4%)	7 (21.9%)	6 (18.7%)
Doubtful	7	6 (85.7%)	4 (66.6%)	1 (16.7%)	1 (16.7%)
Positive	15	15 (100.0%)	5 (33.3%)	8 (53.3%)	2 (13.3%)
Total	79	53 (67.1%)	28 (52.8%)	16 (30.1%)	9 (17.1%)

now gave 3+ reactions. Of the 7 that had been doubtfully positive all but 1 now definitely reacted, most of them weakly. All of the 15 original positives were still positive, and (not shown in the table) there was observed intensification of the reactions.

(c) *Comparison of the Fernandez and Mitsuda reactions, first and second injections.*—We believe that there is great interest in the comparative study of the results of the Fernandez reaction (hypersensitivity) and the Mitsuda reaction (resistance). Here only the positive and negative results are dealt with, eliminating the doubtful ones. The results obtained are given in Table 3. Both the early and the late readings of the first lepromin injection were made in 71 persons, and those of the second injection in only 51.

TABLE 3.—*Comparison of the early and late reactions after the first and second injections, in 71 and 51 individuals, respectively, with summary concerning concordance versus discordance.*

Test	No. of cases	Both reactions negative	Both reactions positive	Early negative Late positive	Early positive Late negative
First	71	4 (5.6%)	15 (21.1%)	52 (73.2%)	0 (0%)
Second	51	2 (3.9%)	41 (80.4%)	8 (15.7%)	0 (0%)

<i>Concordance/Discordance</i>					
Test	No. of cases	Concordance		Discordance	
First	71	19 (26.8%)		52 (73.2%)	
Second	51	43 (84.3%)		8 (15.7%)	

The category with both reactions negative shows no significant difference between the first and the second tests, namely, 5.6 and 3.9 per cent of the cases, respectively.

The category with both reactions positive, however, shows significant differences. In the first test such cases were 21.1 per cent, and in the second one they were 80.4 per cent, the increase in the percentage being 59.3.

In the discordant category with negative Fernandez and positive Mitsuda reactions there is naturally a striking and complementary difference, with a decrease from 73.2 to 15.7 per cent, the percentage difference 57.5.

In neither test was there any case with the reverse discordance, namely, positive Fernandez and negative Mitsuda reactions.

The total figures for concordance and discordance of the two reactions are given in the second part of Table 3. There it is shown that, whereas in the first test there was 73.2 per cent discordance, in the second test the concordance amounted to 84.3 per cent.

SUMMARY AND CONCLUSIONS

1. A study has been made of the results of two successive lepromin tests in residents of San Miguel de Tucumán aged 20 years or more, supposedly healthy (except for various dermatologic conditions) and without

known contacts with leprosy. The second-test injections were made 21 days after the first ones, at the time of reading of the Mitsuda reaction. The reactions of hypersensitivity (Fernandez) and of resistance (Mitsuda) are compared.

2. In the first test the frequency of the reaction of hypersensitivity in the 214 persons in whom it was read was 11.7 per cent, and the frequency of the reaction of resistance in the 92 persons who returned for that reading was 96.7 per cent—results which are not uncommon for noncontact adults.

3. In the second test special attention was paid the Fernandez reaction, because so few had been Mitsuda negative that there could be no significant numerical changes in the retesting. Of the 57 original Fernandez negatives, 56.1 per cent now gave positive reactions, as did 6 of the 7 in whom the first reactions had been of doubtful grade.

4. A comparative study of the reactions of hypersensitivity and of resistance among those in whom both reactions were read shows that:

(a) Those who gave negative results with both reactions were relatively few in both tests, 5.6 per cent in the first one and 3.9 per cent in the second.

(b) Those who in the first test gave negative hypersensitivity but positive resistance reactions were many, 73.2 per cent, but in the second test only 15.7 per cent, a large proportion of the Fernandez negatives having been sensitized by the first injection.

(c) The proportion of cases showing both reactions positive in the first test was not high, only 21.1 per cent, but it increased greatly, to 81.4 per cent, in the second test because of the large number who had acquired hypersensitivity.

5. The great discordance between the two reactions in the first test (73.2%), changed to marked concordance (84.3%) in the second one. In other words, the persons under study reacted to the second injection of lepromin in much the same way as do leprosy contacts on first test. (3).²

6. From the results observed it is concluded that, in persons without known contact and presumably free from leprosy, a single injection of

² As seen in Table 2, the 79 persons who were retested (including 15 original positives and 7 original doubtfuls) were 67.1 per cent Fernandez positive, against the original 11.6 per cent. In a recent study, as yet unpublished, we reviewed the results of tests with various lepromins made on 756 leprosy contacts of various ages during the period 1942-1956. Among the 324 individuals of the same age group as our present cases (i.e., 20 years or more), 55 per cent were Fernandez positive and 89 per cent gave positive Mitsuda reactions. Incidentally, in the entire group a statistically significantly higher percentage of those whose contact sources were lepromatous cases gave early reactions than did the contacts of tuberculoid cases, whereas there was no significant difference in this respect between the percentages of Mitsuda positives.

integral lepromin can sensitize an appreciable proportion (well over 50%) of Fernandez-reaction negatives so that they become positive reactors.

RESUME Y CONCLUSIONES

1. Se establece la frecuencia de las reacciones de hipersensibilidad (reacción de Fernandez) en personas supuestas sanas, no convivientes de leprosos, de 20 y más años de edad, a una primera y segunda inyección intradérmica de lepromina integral, y se efectúa un estudio comparativo, de la hipersensibilidad (reacción de Fernandez) y resistencia (reacción de Mitsuda). Las personas testificadas residen en San Miguel de Tucumán.

2. La frecuencia de las reacciones de hipersensibilidad fué de 11.6 por ciento para la primera inyección de lepromina y la de resistencia 96.8 por ciento.

3. Los no reactores y reactores dudosos, a la reacción de Fernandez, en la primera inyección de lepromina, vuélvense hipersensibles a la segunda, en porcentajes de 56.1 y 85.7 por ciento, respectivamente.

4. El estudio comparativo de las reacciones de hipersensibilidad y resistencia demuestran que:

(a) Los que no demuestran hipersensibilidad ni resistencia son un porcentaje pequeño (5.6%) para la primera inyección de lepromina, no modificándose apreciablemente a una segunda inyección (3.9%).

(b) Las que a una primera inyección de lepromina no demuestran hipersensibilidad, pero si capacidad de resistencia, se sensibilizan por la primera inyección en un apreciable porcentaje (58.2 a 60.8%).

(c) Los hipersensibles a resistentes a una primera inyección (21.1%), aumentan su porcentaje apreciablemente (81.9%) a la segunda inyección.

5. La gran discordancia entre las reacciones de hipersensibilidad y resistencia (73.2%) a una primera inyección de lepromina, se transforma en una manifiesta concordancia (84.3%) a la segunda inyección; en otros términos las personas en estudio, se comportan a una segunda inyección de lepromina, en forma semejante a los convivientes.

6. De los resultados expuestos, se concluye que, una sola inyección de lepromina integral, en sujetos supuestos sanos de lepra, no convivientes, los sensibiliza en un apreciable porcentaje (56.1 a 60.8%).

REFERENCES

1. FERNANDEZ, J. M. M. and OLMOS CASTRO, N. La reacción precoz provocada por la lepromina; investigaciones efectuadas con diversos antígenos derivados del *Mycobacterium leprae*. Rev. argentina Dermatosisif. **26** (1942) 556-580.
2. FERNANDEZ, J. M. M. Sensitization to lepromin in presumably nonleprous individuals. Internat. J. Leprosy **11** (1943) 15-22.
3. OLMOS CASTRO, N. and ARCURI, P. B. Early and late reactions to lepromin in contacts. Internat. J. Leprosy **15** (1947) 175-177.
4. WADE, H. W. The lepromin reaction in normal dogs; preliminary report. Internat. J. Leprosy **9** (1941) 39-56.
5. WADE, H. W. Induction of lepromin reactivity by repeated lepromin testing. Internat. J. Leprosy **23** (1955) 310-315 (editorial).