

THE LEPRONIN TEST IN LEpra REACTION

II. HISTOLOGY OF THE REACTION LESIONS AND PERSISTENCE OF THE INJECTED BACILLI¹

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In a previous paper on the lepromin test in 48 lepromatous-type cases in a state of lepra reaction (7) it was concluded that no evidence had been elicited to support the hypothesis that lepra reaction is a manifestation of allergy. The present report is of a study of biopsy material obtained from the tested sites of thirty-five of the patients under observation. This material was taken, first, for the purpose of correlating the histological changes with the different grades of positive and negative reactions as observed clinically, and, second, to investigate the question of persistence of the injected bacilli in the tissues. Six patients not in lepra reaction, all residents of the Female Invalids' Dormitory—four of them secondary neural cases (all N3), bacteriologically negative for periods varying from 3 to 14 years, and two of them lepromatous cases (all L3)—were used as a control group, and the test sites of all of them were also biopsied.

Mariani (6), and more recently Manalang (5), Schujman (12) and Rodriguez (10), have shown that the positive lepromin nodule consists of a dense grouping of epithelioid cells with giant cells and lymphocytic infiltrations or collections—a typical tuberculoid picture. Rabello, Jr. and Rotberg (9) have also shown that the histologic tuberculoid picture resulting from lepromin injection is found not only in tuberculoid cases of leprosy but also in some of the less frequent positive reactions in cases of the lepromatous type.

Schujman was unable to demonstrate the injected bacilli in four out of five tuberculoid cases two days after the injection, or in any of eight other tuberculoid cases examined after from 8 to 30 days. In all of ten lepromatous cases the bacilli were demonstrated two days after injection.

PROCEDURE

Details regarding the classification of the patients used in this study and the technique of making and reading the tests were given

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in the preceding paper (7) and need not be repeated here. The times at which the biopsies were done in the thirty-five cases so examined were as follows: in six cases on the 21st day, in four on the 25th day, in twelve on the 27th day, in ten on the 32nd day, and in three on the 34th day. In the cases biopsied earlier than the fourth week, the final readings were made on the day of the operation, while in all of the other cases the readings of the fourth week were the ones recorded as final. Of the six control cases the biopsies were made on the 42nd day in one case and on the 49th day in the other five. The specimens were fixed in Zenker's fluid and paraffin sections were stained with eosin and hematoxylin and for acid-fast organisms by Wade's modified method (13). Sections were examined serially whenever indicated, at intervals of about 50 micra, to locate the sites of the injections; this was necessary particularly in the negative tests, in which the sites appeared only as brown spots at the time of the biopsies. After the tests were finished an additional specimen was taken from a representative skin lesion on the right chest of the only 3+ reaction case in the experimental group, to determine the possibility of the presence of tuberculoid leprosy in the patient.

Results of the tests in the biopsied cases.—Of the thirty-five cases in the group so studied, one gave a 3+ lepromin reaction, with suppuration of the papule, two were 2+, sixteen were recorded as 1+ and sixteen were negative. Of the six control cases, one of the four of neural type gave a 3+ reaction, also with suppuration, and the other three were 2+; the two lepromatous cases were both negative.

REPORT OF FINDINGS

I. EXPERIMENTAL GROUP

The thirty-five lepra reaction cases here dealt with are conveniently separated into four groups according to the intensity of the lepromin reaction, as follows: (a) three-plus reactions (one case), (b) two-plus reactions (two cases), (c) one-plus reactions (sixteen cases), and (d) negative reactions (sixteen cases). The third group is further divided into two on the basis of the histological findings, depending upon whether the specimens did or did not show changes of tuberculoid or related nature. The descriptions of the reaction lesions are of their appearance on the day of biopsy.

A. Case with a three-plus reaction.—CASE V.T., biopsied on the 27th day. The reaction lesion was a raised nodule measuring 8.5×7.9 mm., the surface eroded due to suppuration.

Histology: There is a large central area of necrosis (Plate 13, fig. 1), bordered at its deepest portion by several tuberculoid foci showing some lymphocytic infiltration (Plate 13, fig. 2). Other sections, cut serially, also show tuberculoid foci with compactly arranged epithelioid cells and lymphocytic infiltration. Degenerating leucocytes, mostly polynuclears, infiltrate the area of necrosis. Numerous acid-fast bacilli, which had been injected were found in this area, and a few below and about it in the thin tuberculoid-reacting zone. No leprotic foci seen. The reacting area under the microscope measures 2.5 mm. long and 2.4 mm. thick.

Control specimen: A second specimen from this patient, taken from a lesion on the right chest to determine the nature of the disease process, showed a rather unusual histologic picture. Although the predominating changes were lepromatous (Plate 13, fig. 3), it also showed in some places a decided tendency to epithelioid change, with more or less admixture of foamy cells, and also occasional collections of lymphoid cells, as is seen in tuberculoid rather than lepromatous lesions. For the most part the epithelioid condition is diffuse and irregular (Plate 14, fig. 4); but at one point, deep in the section, there is definite focal tuberculoid grouping, with an attempt to produce the usual kind of giant cells (Plate 14, fig. 5). Here, then, is a mixed condition, an evident attempt to change from the lepromatous to the tuberculoid type of tissue reaction, which is undoubtedly related to the seemingly anomalous reaction to the lepromin injection.

B. Cases (two) with two-plus reactions.—(1) CASE S.C., biopsied on the 27th day. The reaction lesion was a raised brownish nodule, 5.1×5.5 mm.

Histology: There are some giant cells in a thin area diffusely and loosely infiltrated with large monocytes, which shows one or two foreign-body tubercles. Connective-tissue cells increased. No tuberculoid lesion, and no small-round cell or lymphocytic collections. Other serial sections show isolated foreign-body tubercles with loosely arranged cells. Injected bacilli were found in large numbers in this area. In the corium are small intrinsic leprotic foci of foamy cells, these also containing bacilli. The reacting area under the microscope measures 3.6 mm. long by 0.7 mm.

(2) CASE P.F., biopsied on the 21st day. The reaction lesion was a brownish nodule, 6.5×6.4 mm., the surface eroded because of scratching.

Histology: There are some giant cells in a fairly diffuse, thick zone of cellular reaction with slight edema, the other cells consisting mainly of large monocytes with some epithelioid cells, degenerating polynuclears and proliferating connective-tissue cells. This area is limited by a zone of tuberculoid foci, composed of rather compactly arranged epithelioid cells with slight lymphocytic infiltration, seen throughout the serial sections. The edema and degenerating polynuclears present are possibly due to the traumatic effect of scratching. Numerous injected bacilli were found within isolated large monocytes in the superficial portion of the corium. Two small leprotic foci, also positive for acid-fast bacilli, are present around sweat glands far from the site of injection. The reacting area under the microscope measures 2.7 mm. long and 1.5 mm. thick.

C. Cases with one-plus reactions, (a) Reaction lesions showing foreign-body tubercles, tuberculoid, or subtuberculoid foci (six cases).—

(1) CASE F.U., biopsied on the 27th day. The reaction lesion, a barely palpable brownish spot, measured 3.2×4.4 mm.

Histology: In the serial sections there is found a single foreign-body tubercle at one point in the deeper corium, with slight fibrosis without lymphocytic infiltration (Plate 14, fig. 6). No other lesion referable to the injection is seen except slight fibrosis. Minute leprotic foci present in the corium, and larger ones in the subcutis. Many bacilli were found in the foreign-body tubercle, and numerous ones in the leprotic foci. The reacting area under the microscope measures only 1.1 mm. long by 0.7 mm.

(2) CASE E.F., biopsied on the 25th day. Reaction lesion a pale nodule, 3.7×3.3 mm.

Histology: There is moderate fibrosis at the site of injection, with a diffuse proliferation of connective-tissue cells and infiltration of large monocytes mixed with some vacuolated foreign-body giant cells. Some foreign-body tubercles in the mass of cellular reaction. In one spot along the border is a small subtuberculoid focus, its cells somewhat loosely arranged, and very slight, almost imperceptible, lymphocytic infiltration. Minute foci of foamy cells found in the corium far from the site of injection. Acid-fast bacilli were abundant in the injection site, and a few were found in the foci of foamy cells. The reacting area under the microscope measures 2.0 mm. long and 1.6 mm. thick.

(3) CASE R.U., biopsied on the 32nd day. Reaction lesion a barely palpable thickening, 4.1×5.9 mm.

Histology: Numerous vacuolated foreign-body giant cells and large monocytes, fairly densely arranged, infiltrate the injection site. In serial sections are found one or two tuberculoid and some subtuberculoid areas deep in the corium, along the border of the reaction lesion; the cells are compactly arranged, with slight lymphocytic infiltration. The picture as a whole, however, is predominantly that of a foreign body reaction. No lepromatous lesions found. Injected bacilli were present in large numbers. The reacting area under the microscope measures 3.0 by 1.1 mm.

(4) CASE F.G., biopsied on the 32nd day. Reaction lesion a brownish nodule, 4.7×4.2 mm.

Histology: There is slight fibrosis, with many vacuolated foreign-body giant cells and several foreign-body tubercles in the injection site. No tuberculoid or subtuberculoid lesions found in serial sections. Minute lepromatous foci present in the superficial corium and medium-sized ones surrounding sweat-gland coils close to the subcutis. Numerous acid-fast bacilli were demonstrated in the site of injection and in the lepromatous foci. The reacting area under the microscope measures 2.3 by 1.2 mm.

(5) CASE V.C., biopsied on the 32nd day. Reaction lesion a palpable brownish nodule, 4.6×4.7 mm.

Histology: There is moderate fibrosis, and several vacuolated foreign-body giant cells with some foreign-body tubercles in the injected area.

Other sections in the series show in the deeper corium two small areas of subtubercloid lesions containing vacuolated giant cells and loosely arranged large monocytes with vacuolated pinkish cytoplasm, the whole showing an apparent tendency to produce the definite tubercloid picture. Lymphocytic infiltration scanty or very slight. Several minute, isolated foamy-cell collections present in the corium. Abundant acid-fast bacilli were found in the injection site, and a few in the isolated foamy cell collections. The reacting area under the microscope measures 2.5 by 0.8 mm.

(6) CASE F.A., biopsied on the 32nd day. Reaction lesion a palpable brownish nodule, 3.7×3.8 mm.

Histology: There is some proliferation of connective tissue, with many vacuolated foreign-body giant cells, large vacuolated monocytes and some foreign-body tubercles in the injected area (Plate 14, fig. 7). No tubercloid or subtubercloid foci found in serial sections. Several small lepromatous foci present in the superficial and deep corium. Numerous acid-fast bacilli were found in the site of injection and in the lepromatous foci. The reacting area under the microscope measures 1.6 by 0.8 mm.

C. Cases with one-plus reactions, (b) Reaction lesions without foreign-body tubercles (ten cases).—In these ten cases, biopsied between the 20th and the 34th days after injection, the reaction lesions varied in size from 3.2×3 mm. to 5×5 mm. As described at the time of the last observations, their appearances were as follows: raised nodule, raised pale brownish nodule, palpable brownish nodule, raised spot, barely palpable thickening, brownish raised nodule, raised or slightly raised palpable nodule, or barely palpable brown spot.

Histology: The specimens from these ten cases show no tubercles. Instead, two show a markedly cellular compact mass superimposed on lepromatous lesions, five show proliferation of connective tissue and large monocytic infiltration mixed with foreign-body giant cells, two show slight fibrosis and cellular infiltration with large monocytes, and one, excised on the 34th day, shows marked nodular thickening of connective tissue, almost free from cellular infiltration, in one small round spot which measures under the microscope 1.1 mm. long×1.2 mm. thick (Case J. D., Plate 15, figs. 8 and 9). This last lesion was a raised palpable nodule measuring 3.2×2.9 mm. Eight of these ten cases showed leprotic lesions in the corium, while two had none.

With regard to the presence of the injected bacilli, these were found in large numbers in the sites of the injection in all instances. All of the leprotic foci in the eight specimens that contained them were found also positive.

D. Cases (sixteen) with negative reactions (sixteen cases).—In these cases the test sites were described as follows: no trace of the injection (eight), brownish spot (three), barely palpable brownish spot (two), barely palpable trace (two), and very slight pigmented trace (one).

Histology: In five cases no trace of the injection could be demonstrated in serial sections, none of them showing any apparent changes except for the presence of from very slight to moderate lepromatous lesions in the corium or subcutis. The remaining eleven showed no histological tubercle formation, only from slight to moderate or marked connective tissue proliferation with a few foreign-body giant cells (seven cases), dense connective tissue, almost free from cellular infiltration, in a very small spot around some small lepromatous lesions (one case), slight hypertrophy of the epidermal pegs (two cases), and vacuoles of the injected lepromin suspension in the connective-tissue interstices, without apparent cellular reaction (one case). In all of these last eleven cases leprotic lesions, from slight to moderate in degree, were also found in the sections.

As for the injected bacilli, these were found in large numbers in the injection sites in the eleven cases in which those sites could be identified. The lepromatous foci were also loaded with bacilli. In the five cases where no trace of the injection could be detected histologically, acid-fast bacilli were found only in the lepromatous foci.

II. CONTROL GROUP

This group comprised six cases, four of neural type (all N3) and two lepromatous (L3-N1 and L3-N2), biopsied on the 42nd or 49th day after the injection.

A. Case with three-plus reactions.—CASE E.S., biopsied on the 42nd day. The test site suppurated and ulcerated, and on the 28th day there was a pinkish raised nodule measuring 19.6×15.2 mm.

Histology: There is a large tuberculoid lesion with lymphocytic collections and infiltrations (Plate 15, fig. 10), involving the entire thickness of the corium and even the superficial layers of the subcutis, and centrally in it is a subsiding suppurative process. This lesion measures under the microscope 9.45 mm. long and 3.2 mm. thick. No lepromatous lesion found. Acid-fast bacilli were very rare, and none were found in the first four sections stained. In the fifth preparation twelve bacilli were counted, eleven in the papillary layer of the corium and one in the deepest portion of the reacting lesion at the border of a tuberculoid focus. None could be demonstrated in the mass of the tuberculoid reaction.

B. Cases (three) with two-plus reactions.—These cases were all biopsied on the 49th day. The test sites were: a pinkish indurated nodule measuring 5.5×5.7 mm., a bluish nodule 5.6×6.5 mm., and a bluish, indurated, somewhat soft nodule 8.5×7 mm.

Histology: The specimens all show a tuberculoid picture, with quite conspicuous lymphocytic collections. One is a thick tuberculoid nodule or diffused epithelioid reaction measuring under the microscope 2.5 mm. long and 3 mm. thick; the second is a thin tuberculoid lesion 4.3 mm. long and 1.3 mm. thick (with eroded surface due to scratching), containing a small purulent exudate; and the third is also a thin tuberculoid lesion, 3.4 mm. long and 1.1 mm. thick. No lepromatous infiltration found.

Concerning the presence of injected bacilli, in the first case several of them were found easily, in the second a few occurring singly were found with difficulty, and in the third there were many, easily found in the superficial and deep portions of the tuberculoid lesion.

C. Cases (two) with negative reactions.—Both of these cases were biopsied on the 49th day. The test sites showed on palpation only very slight traces of infiltration, the areas of which could not be measured.

Histology: Both sections contain lepromatous lesions. One shows in the site of injection dense connective tissue in a small spot superimposed on a group of small lepromatous lesions. In the other no evidence of the injection was found in serial sections of the entire specimen. In both instances the lepromatous lesions contained numerous bacilli.

DISCUSSION

From what has been found in the histological sections of the biopsy specimens in the experimental group, it would appear that the one-plus reactions cannot all be taken as definitely lepromin-positive, if for a definitely positive reaction we accept the criterion of tuberculoid changes in the reaction lesions, as found by previous workers (5, 6, 9, 10, 12). The presence of proliferating connective tissue, or slight or dense fibrosis (Plate 15, figs. 8 and 9), or of infiltrations with large monocytes, foreign-body giant cells and tubercles without any tuberculoid structure (Plate 14, figs. 6 and 7), as noted histologically in thirteen—over 80 percent of these sixteen one-plus reaction lesions—may be regarded as simple foreign-body reactions to the injected lepromin emulsion. It follows that one-plus reactions should be taken with reserve; the small nodules formed (3 to 5 mm. in diameter) may represent only false or non-specific reactions due to the injected lepromin suspension. Only in three of the sixteen cases (Cases E.F., R.U. and V.C.) did the biopsy specimens present histologic evidences of tuberculoid or subtuberculoid changes, found in places within or along the border of the cellular reaction, concomitantly with foreign-body tubercles. The histological findings in the other thirteen cases lend support to Rotberg's suggestion that it would be:

... preferable to put such borderline reactions in a "doubtful" class, considering it better to let them go unclassified than to adopt an imperfect qualification.

The proposal would certainly remove the false positive tests that are due to the foreign-body response of the tissues to the lepromin suspension.

Even of the two cases considered to have given two-plus reactions, one measuring 5.5×5.1 mm. on the 27th day and

the other 6.5×6.4 mm. on the 21st day, only the specimen from the latter showed the tuberculoid histology. The first showed only foreign-body tubercles.

Of the negative reactions, no trace of the injection could be identified in serial sections of the specimens from five of the sixteen cases in this group. Schujman, in his eight lepromin-negative cases (also of lepromatous type) that were biopsied one, two and four weeks after the injections, found almost normal skin sections; in these cases the body tissues had apparently lost all ability to react to the injected lepromin emulsion. In the present experiment the specimens from eleven of the sixteen negative cases showed no histological tubercle formation but only from slight to marked connective-tissue proliferation, with a few foreign-body giant cells in seven instances, dense connective tissue in a very small spot in one, slight hypertrophy of the epidermal pegs in two, and vacuoles of the injected lepromin in the interstices of the connective tissue, without apparent cellular reaction, in one.

The only three-plus reaction in the experimental group should also be referred to. The biopsied lepromin lesion showed the tuberculoid histology, besides suppuration and necrosis. In the specimen biopsied from the right chest of this patient, the presence of epithelioid or tuberculoid elements mixed with a predominantly lepromatous picture (Plate 13, fig. 3 and Plate 14, figs. 4 and 5) may explain the anomalously positive lepromin test. It is possible that the observations of Rabello Jr. and Rotberg (9), which led them to say that the histologic tuberculoid picture is also found in some of the infrequent positive reactions in cases of the lepromatous type, may be due to the existence of mixed lesions. The patient referred to in the present report, when examined two and a half years later, appeared so clean of skin lesions that no site could be selected for biopsy. This isolated observation lends support to Hayashi's claim (1) that a positive lepromin reaction in nodular leprosy may be looked upon as a sign of favorable prognosis.

Concerning the persistence of the injected bacilli in the tissue, special care was taken in the search for them, and when none were found in the first examination other preparations were studied. Of the thirty-two cases in the experimental group that gave one-plus and negative reactions, biopsied from the 20th to the 34th days, injected bacilli were demonstrated in large numbers in all of the twenty-seven specimens in which the sites of the injections were identified histologically. In the sections from the other five cases,

in which the injection sites could not be so identified, injected bacilli were not searched for because in all of them lepromatous lesions, very slight to moderate in degree, that contained bacilli were also present. In the specimens from the two cases of the experimental group that gave two-plus reactions, biopsied on the 21st and 27th days respectively, bacilli in large numbers were also found at the sites of the injections. These sections also contained small lepromatous foci which were positive. In the one three-plus reaction lesion of that group, biopsied on the 27th day (see above), there were numerous bacilli in the suppurative necrotic spot but only a few in the tuberculoid reacting areas.

The four neural controls (all N3), one giving a three-plus lepromin reaction, biopsied on the 42nd day, and three giving two-plus reactions, all biopsied on the 49th day, supplied interesting material as regards the presence of the injected bacilli. All of these specimens showed the histological picture of tuberculoid reaction, and no leptotic foci were present. In the three two-plus reaction lesions the injected bacilli were not found in large numbers, as in the experimental cases, but were recorded as "several bacilli easily found," "a few bacilli occurring singly and found with difficulty," and "many bacilli in the superficial and deep portions of the reaction lesion." The difficulty of demonstrating bacilli in the specimen from the other (three-plus) control case, of which four sections examined at length were negative and only twelve could be demonstrated in the fifth (located only in the papillary layer of the corium and at the border of a deep tuberculoid focus, none in the mass of tuberculoid reaction), suggests that a large proportion of the injected bacillary suspension must have suffered destruction and absorption.

Concerning the manner of disposal, by the tissues in the tuberculoid areas in these four neural controls, of the large number of injected bacilli, the experiments of Lurie (3) on tuberculosis in rabbits have to be mentioned. By correlating the cultural and histological findings in rabbits injected with human and bovine bacilli, he concluded that the bacilli are usually destroyed effectively within epithelioid cells of all organs in the case of the human type of tubercle bacilli; that in the lung and kidney, the bovine bacilli persist within epithelioid cells, but that in other organs they are usually destroyed; and that where the mononuclears are transformed into mature epithelioid cells and tubercles have reached their maximum development, the bacilli have already undergone extensive destruction and are disappearing. Opie (8), in a general

review on the cellular reactions of tuberculosis, in which another experiment by Lurie (2) on tuberculous reinfection in rabbits is mentioned, states that the most important factor in the destruction of the tubercle bacillus is the young epithelioid cell, and that in reinfected animals the formation of epithelioid and giant cells proceeds more promptly and with greater intensity than in previously uninfected animals.

In human tuberculosis it is sometimes almost impossible to demonstrate the tubercle bacillus in the lesions, except by inoculation into a susceptible animal (4). In the tuberculoid type of leprosy the same difficulty in demonstrating the leprosy bacillus in the sections is not infrequently encountered. *M. leprae*, being an acid-fast microorganism and morphologically very much like *M. tuberculosis*, may possibly undergo in the tuberculoid lesions a destructive process by the epithelioid cells similar to that which occurs in tuberculosis. In the study here reported the paucity of the injected microorganisms that were demonstrable in some of the specimens of the four neural, lepromin-positive controls, compared with the findings in the experimental lepromatous group, suggests that the epithelioid cell may have an important rôle in the destruction of the leprosy bacillus.

SUMMARY AND CONCLUSIONS

1. Biopsy specimens of the sites of lepromin tests in two groups of leprosy patients, thirty-five lepromatous cases in lepra reaction and six nonreaction control cases (four N3 and two L3), were removed from 21 to 49 days after the test injections were made and examined histologically and for the presence of the injected bacilli in the tissues.

2. In the first, or experimental, group the reactions were: three-plus, one case; two-plus, two cases; one-plus, sixteen cases; and negative, sixteen cases. In the second, or control, group the four neural cases gave: three-plus reaction, one case; and two-plus, three cases; the two lepromatous cases were both negative.

3. The specimens from both cases giving the three-plus reactions (one experimental and one control) showed histological tuberculoid pictures. Of the total of five cases in both groups giving two-plus reactions, four showed histological tuberculoid pictures—an 80 percent agreement if the tuberculoid picture in the reaction lesion is to be considered the criterion for a definitely positive test.

4. Of the sixteen cases recorded as giving one-plus reactions, only three, or 19 percent, showed tuberculoid or subtuberculoid pictures, concomitantly with foreign-body tubercles. In the other thirteen, or 81 percent, the histological changes consisted only of more or less marked cellular compact masses, proliferation of connective tissue with slight or dense fibrosis and infiltrations with vacuolated large monocytes, foreign-body giant cells, or foreign-body tubercles. These changes are interpreted to be false positive or nonspecific reactions to the injected lepromin emulsion.

5. Of the total of eighteen negative reactions, in none could either the tuberculoid picture or the foreign-body tubercle be demonstrated. Instead, there was only connective-tissue proliferation or from slight to dense fibrosis, with slight infiltration of large monocytes and foreign-body giant cells (nine cases), slight hypertrophy of the epidermal pegs (two cases), and vacuoles of the injected lepromin in the interstices of connective tissue without cellular reaction (one case). In six instances no trace of the injection could be demonstrated.

6. The only three-plus reaction in the experimental group showed, in a biopsy specimen of a representative lesion from the right chest, the presence of epithelioid or tuberculoid picture mixed with a predominantly lepromatous condition. To this unusual feature is attributed the unusual, strongly positive lepromin reaction.

7. In the one-plus and negative reactions of the two groups (thirty-four cases), the injected bacilli were demonstrated in large numbers in the sites of the injections in the twenty-eight specimens in which the sites of injections were identified histologically. In the six specimens in which no trace of the injection could be made out, injected bacilli were not looked for because all of the sections showed lepromatous lesions containing bacilli.

8. In the two-plus reaction lesions of the experimental group (two cases) injected bacilli were demonstrated in large or fairly large numbers, whereas in the reaction lesions of the same degree in the neural cases of the control group (three cases) they were numerous in only one specimen, few or very few in the others.

9. In the two three-plus reactions both test sites suppurred. In the specimen from the experimental case numerous bacilli were found in the suppurative necrotic focus but only a few in the tuberculoid zone around it. In that from the control case (neural), bacilli were very rare and demonstrated only in the fifth section examined.

10. Although the lepromin tests were made only in apparently normal skin areas, leptotic foci were demonstrated histologically in thirty-three of the thirty-seven lepromatous cases studied.

11. The possible rôle played by the epithelioid cell in the disposal of the injected bacilli is discussed.

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DESCRIPTION OF PLATES

PLATE 13

FIG. 1. Low magnification of a three-plus reaction lesion which suppurated, biopsied on the 27th day after the injection (Case V.T.). Showing the area of necrosis (A) and the tuberculoid zone (B).

FIG. 2. Detail of the tuberculoid area in Fig. 1. Note the lymphocytic infiltration.

FIG. 3. Section of a representative lesion from the right chest of the same patient, showing a lepromatous area composed chiefly of large foamy cells massed together.

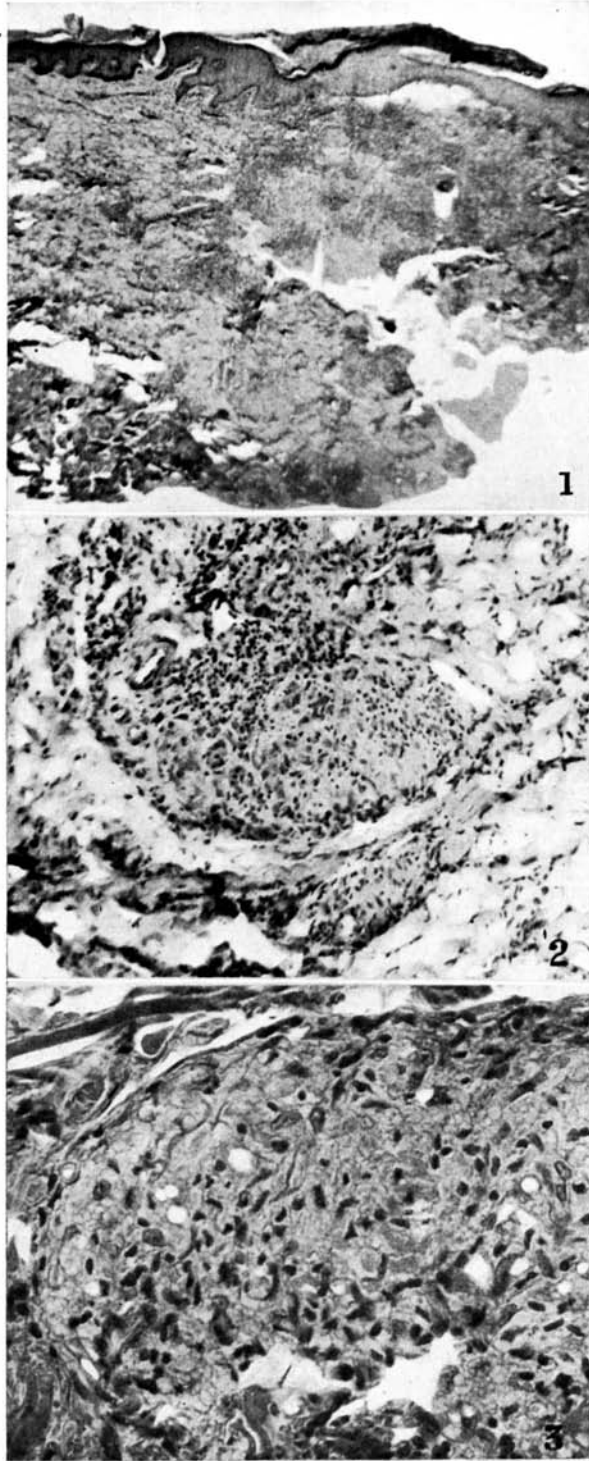


PLATE 13

PLATE 14

FIG. 4. From the same specimen Fig. 3, showing diffuse epithelioid cells, with a lymphocytic accumulation at one side and in places (as at X, X) an admixture of foamy cells.

FIG. 5. From the same specimen as Figs. 3 and 4, showing a focal area of tuberculoid grouping, with a tendency to form giant cells.

FIG. 6. A small foreign-body tubercle, the only lesion found in a one-plus reaction specimen (Case F.U.). Note absence of lymphocytic infiltration, compared with Fig. 2. Clinically, the site of injection was a barely palpable brownish spot, 3.2×4.4 mm., when biopsied on the 27th day.

FIG. 7. Proliferation of connective tissue, some large monocytic infiltration, and giant cells forming foreign-body tubercles, without lymphocytic infiltration. Clinically, it was a brownish palpable nodule 3.7×3.8 mm.; biopsied on the 32nd day after the injection (Case F.A.)

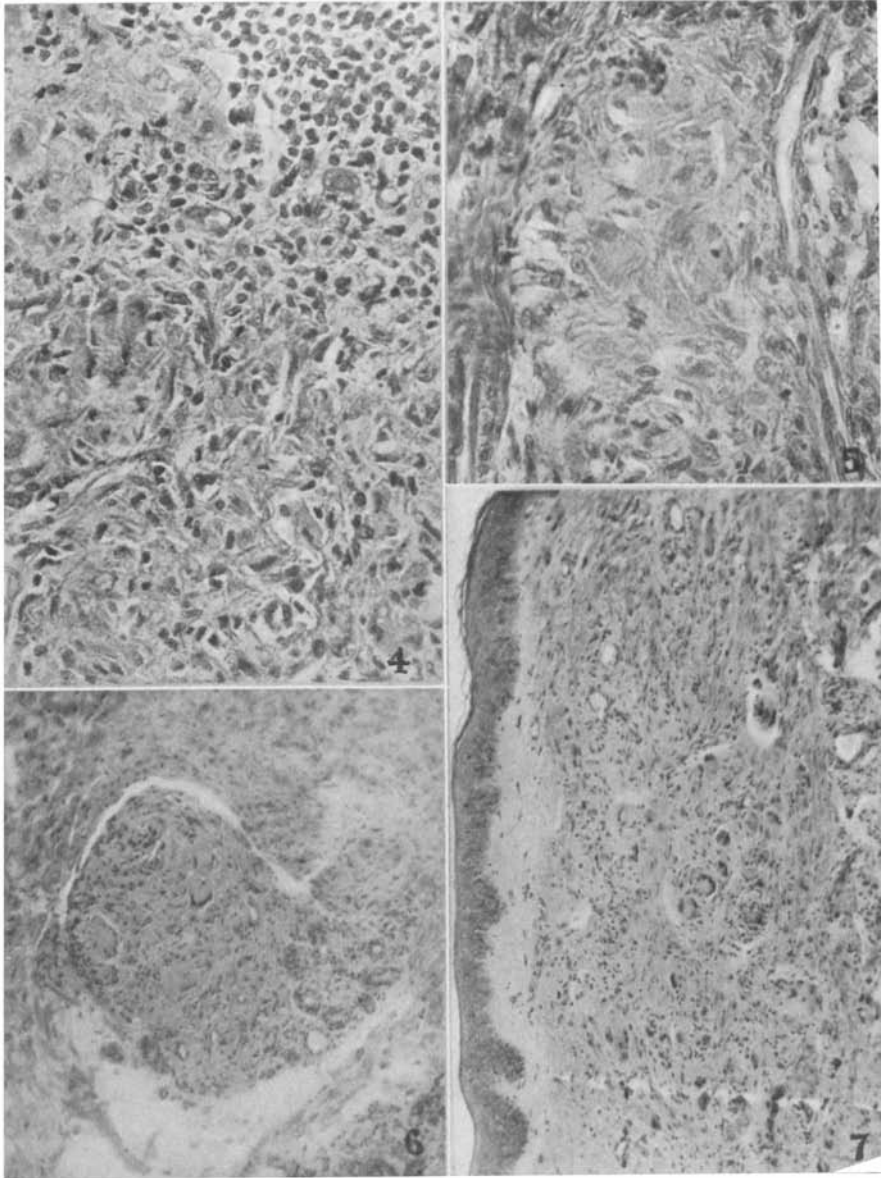


PLATE 14

PLATE 15

FIG. 8. Marked nodular thickening of connective tissue in a small round spot (A) measuring 1.1×1.2 mm. Clinically, it was a raised palpable nodule 3.2×2.9 mm.; biopsied on the 34th day after the injection (Case J.D.).

FIG. 9. Detail of the fibrous area shown in Fig. 6. Note the thick connective tissue, almost free from cellular infiltration. Stained for injected acid-fast bacilli, many were found in this fibrous spot, mostly in the few large monocytes and in connective tissue cells.

FIG. 10. Showing the tuberculoid nature of the reaction lesion below the epidermis in the neural control case that gave a three-plus suppurative reaction which measured 19.6×15.2 mm. on the 28th day after the injection (Case E.S.). Biopsied on the 42nd day. Note the lymphocytic collection.

