

## HISTOPATHOLOGICAL CHANGES DUE TO SULFONE THERAPY

### OBSERVATIONS OF 449 LEPROMATOUS LEPROSY CASES<sup>1</sup>

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The histopathological changes of lepromatous leprosy cases submitted to treatment by sulfone drugs have not been studied extensively as yet.

In 1947, Fite and Gemar (1) reported a study of this subject. Of 32 patients submitted to sulfone treatment for periods of 18 months to 4 years none showed modification as to the structural type. In 1948, Lauro de Souza Lima (4), who had dealt with 1,287 lepromatous cases treated by sulfone drugs for 4 to 5 months, claimed to have found not only retrogressive changes like those reported by Rath de Souza and Alayon (2) in cases improving under other treatment, but also transformation from lepromatous infiltration to both the indeterminate condition and reactional tuberculoid infiltrations. Later, in 1950, Rath de Souza and Moacir de Souza Lima (3) called attention to the greater frequency of "regressional lepromatous lesions" since the introduction of sulfone therapy than previously.

As a contribution to the study of this subject, which we consider of importance, we present this paper whose purpose is to record our findings concerning the basic structural changes in lepromatous leprosy patients under treatment by the sulfone drugs. Minor changes, such as the persistence or not of the appendages or the atrophy of the hair muscles, are not dealt with, for we believe them to be unimportant. Our interest is to discover how the lepromatous structure behaves under the sulfone treatment. In Brazil this question of structural change is of practical importance because of Law No. 1,045, which deals with the discharge of lepromatous cases.

<sup>1</sup> Work from the Laboratory of the Epidemiological Section (Dr. João Baptista Risi) of the National Leprosy Service (Dr. Ernani Agricola), Rio de Janeiro, Brazil. Read at the III Pan-American Conference on Leprosy, held in Buenos Aires, December 1951.

## MATERIAL

This study is based on biopsy specimens from 449 cases of lepromatous leprosy submitted to sulfone treatment for periods of from 1 to 3 years. Before treatment these cases were classified as lepromatous on clinical and histological grounds in 116 instances, on clinical and bacteriological grounds in 124 instances, and on clinical grounds alone in 209 instances.

The specimens were fixed in formol-saline solution. Paraffin sections were stained with hematoxylin and eosin and by the Gram-Weigert and Ziehl-Klingmüller techniques. Frozen sections were stained with Sudan III or Scharlach R for the demonstration of lipids. The examination for *M. leprae* was not confined to paraffin sections, for smears were also made from the biopsy material and stained by the Ziehl-Gabbett technique.

## FINDINGS

The histopathological study of the 449 specimens has revealed different types of pictures, which may be classified as below. The data are summarized in Table 1.

TABLE 1.—*Findings in biopsy specimens from 449 clinically lepromatous cases after sulfone treatment.*

Bases of diagnosis, before treatment	Histological diagnosis										Total
	Lepromatous infiltration (with bacilli)		Regressive lepromatous infiltration/a		Indeterminate infiltration with bacilli		Indeterminate infiltration without bacilli		Normal		
	Cases	P. c.	Cases	P. c.	Cases	P. c.	Cases	P. c.	Cases	P. c.	
Clinical and histological	69	59.5	27	23.3	.....	....	20	17.2	...	...	116
Clinical and bacteriological	78	62.9	26	21.0	2	1.6	18	14.5	...	...	124
Clinical	86	41.1	52	24.9	.....	....	68	32.5	3	1.4	209
Total	233	51.9	105	23.4	2	0.4	106	23.6	3	0.7	449

a As defined, bacilli not demonstrable.

(1) *Lepromatous infiltration*.—In spite of the treatment, 233 cases (51.9%) showed lepromatous infiltration, i.e., the presence of small or large foci, or even bands of infiltration, composed of histiocytes many of which presented lipoid degeneration of the cytoplasm (Virchow's cells). Some plasmocytes and lymphocytes were also found, and some sections showed some degree of fibrosis. In general, the bacilli presented alterations of morphology. As a rule they were granular but still rod-shaped; in some cases only alcohol-acid-fast and Gram-positive granules were found; in some other cases there were both forms, granular rods and granules.

These cases must be classified as lepromatous and treated as such under the regulations governing the prophylaxis of leprosy in Brazil.

(2) *Regressive lepromatous infiltration*.—In another 105 cases (23.4%) there was the same histopathological picture as just described, but no alcohol-acid-fast or Gram-positive rods or granules were found in repeated examinations. We apply the term "regressive lepromatous infiltration" to the histological condition in which we find foci of infiltration, whether small or large ones, with one or more Virchow's cells, but with negative findings for *M. leprae*.

The clinical conception of regressive lepromatous leprosy we hold to be a lepromatous case which, after treatment, may or may not show clinical residuae of old lesions, has given negative results in twelve successive, monthly bacteriological examinations, and shows the histopathological structure of regressive lepromatous infiltration as here described.

Before making this diagnosis histologically one must always be careful to repeat the examination for bacilli, using both the Ziehl-Klingmüller and Gram-Weigert techniques. The latter is employed because of the possibility that nonacid-fast forms of the bacillus may be present.

(3) *Simple chronic inflammatory picture*.—Of the cases studied, 108 (24.1%) presented, after treatment, only discrete foci of large and small round cells around vessels, nerves and appendages; rarely, fibrosis was seen; the epidermis usually showed some degree of atrophy, but very rarely it was normal. Regarding the bacilli, in only two instances were there found a very few granular rods; in the other 106 no bacilli were found in spite of repeated examinations of several slides.

(4) *Normal skin*.—In 3 instances the specimens examined showed no infiltration at all, and no bacilli were found in the dermis; the epidermis was also normal. Whether this finding resulted from total clearing up of a previous lesion or from error in selection of the biopsy site cannot be said.

It should be said that, although in this report only one specimen from each patient is considered, in a few cases not more than one was actually examined. In several instances the specimens taken from different sites at the same time showed different histopathological pictures. In such instances only the more severe condition was considered as when one specimen showed the indeterminate picture and another one a leproma-

tous infiltration; such cases were necessarily put among the lepromatous ones. The histological examination should be repeated as frequently as required by changes in the clinical condition.

In view of reports by other observers that change of type of structure has been observed after sulfone treatment, that was borne especially in mind in making our examinations. If those cases in which only the simple chronic inflammatory picture was found were classified correctly at the outset as lepromatous, the logical conclusion is that the lepromatous infiltration had receded to leave only a residual round-cell infiltration. This is not regarded as a change of type of the patients' condition, but a residual condition. In no instance was there found the tuberculoid structure, reactional or otherwise.

#### SUMMARY AND CONCLUSIONS

1. The histological findings in biopsy specimens from 449 cases of leprosy diagnosed as lepromatous, which had been treated by sulfone drugs for periods of from 1 to 3 years, are reported.

2. In 223 instances, or 51.9 per cent, the lepromatous structure was still present, with demonstrable bacilli.

3. In 105 instances, or 23.4 per cent, there was found what we call the regressive lepromatous structure, with the cell type, of the lepromatous infiltration but without demonstrable bacilli.

4. In 108 cases, or 24.1 per cent, only simple chronic inflammatory infiltration was found. In only two of these specimens were bacilli found, and they only a very few granular rods. In the others no bacterial elements of any kind could be demonstrated. These lesions are regarded as residual and not as representing a change of type.

5. In 3 instances, or 0.7 per cent, no infiltrative changes of any kind were found.

6. In no instance was there any evidence of transformation towards the tuberculoid structure.

#### RESÚMEN

El autor reporta los hallazgos histopatológicos de biopsias en 449 casos de lepra lepromatosa que fueron tratados con sulfonas por períodos del a 3 años. En 51.9%, correspondiente a 223 exámenes se constató la estructura de la lesión lepromatosa, con bacilos demostrables. En 23.4%, correspondiente a 105 exámenes se encontró lo que puede llamarse la lesión regressiva lepromatosa, sin bacilos demostrables. En 24.1% o sea 108 exámenes, se observó solamente una inflamación crónica simple, con bacilos en 2 casos solamente. En 3 casos, o sea el 0.7% no se encontró

cambio infiltrativo alguno. En ningún caso se observó transformación al tipo de lesión tuberculoide.

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