

## Correlation of Histopathologic Changes in the Liver and Bone Marrow of Leprosy Patients<sup>1</sup>

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Lepromatous leprosy is a systemic disorder. In many cases there is extensive involvement not only of the reticuloendothelial system, but also of other organs. Intimal cells of blood vessels may be almost bursting with leprosy bacilli. Liver changes in lepromatous leprosy are well known. They consist chiefly of foam-cell granulomas, with or without acid-fast bacilli, in the portal tissues and elsewhere in the liver lobule and in accumulations of acid-fast bacilli in the Kupffer cells and sinusoidal lining cells.

Comparatively little information, however, exists about histopathologic changes of internal organs in indeterminate, dimorphous (borderline), and tuberculoid leprosy particularly during the life time of the patient. Recently it has been shown that acid-fast bacilli may be present in the liver, and that tuberculoid granulomas can exist in this organ in the case of tuberculoid and indeterminate leprosy (<sup>11, 16, 19</sup>). Shivde and Junnarkar (<sup>18</sup>), however, did not find granulomas in nine liver biopsies from cases of tuberculoid leprosy. Acid-fast bacilli were found by Bru and Rollier (<sup>2</sup>), while Camain *et al.* (<sup>3</sup>) did not find acid-fast bacilli in 13 of 41 liver biopsies with epithelioid granulomas. Job *et al.* (<sup>11</sup>) detected no acid-fast bacilli in liver biopsies of tuberculoid cases, but in granulomas of borderline cases they saw numerous bacilli with the Gomory methenamine silver stain, but not with the Fite stain. Little and sometimes contradictory information exists about liver lesions in indeterminate leprosy.

Bone marrow studies have been made on autopsy material or surgical specimens (<sup>5</sup>) or on sternal marrow aspirates. In lepromatous leprosy, acid-fast bacilli were found frequently in the bone marrow. In other types of leprosy, however, they were rarely reported (<sup>12, 14</sup>). Almost no information is available about histopathologic changes in the bone marrow of leprosy patients during their life time.

In the study here reported we tried to get a clearer conception of these changes in the liver and bone marrow and their relation to the type of leprosy, its clinical course, and the duration of treatment.

### MATERIALS AND METHODS

Forty-one leprosy patients, all male but two, from among patients attending the leprosy clinic of the Christian Medical College at Ludhiana, Punjab, were admitted to the hospital during the period from 1 January 1967 to 15 May 1968. Criteria of selection were their willingness to be investigated as inpatients and to undergo a thorough examination including the following procedures:

1. Clinical examination, routine laboratory investigations, and lepromin test.
2. Skin clippings for acid-fast bacilli.
3. Skin biopsy.

Following this the patients were grouped as lepromatous, dimorphous (borderline), tuberculoid, and primary neuritic leprosy. The criteria for classification were those set forth by Cochrane and Smyly (<sup>4</sup>). Additional studies were carried out only in those patients who could definitely be classified in one of the above named types of leprosy. All cases of doubtful classification were excluded from this study.

4. Liver biopsy.

5. Bone marrow aspirate. In some cases no bone marrow biopsies could be made.

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These are indicated in Table 1.

**Liver biopsies.** The following investigations were made with the biopsy material: One half of each liver biopsy specimen was inoculated on Loewenstein-Jensen medium and cultured for *Mycobacterium tuberculosis* for eight weeks. This was done to exclude, as far as possible, the presence of tuberculous granulomas. The other half of the liver biopsy specimen was placed in 10 per cent formalin, embedded in paraffin, and sectioned at 5 microns. Routinely slides were stained with hematoxylin and eosin and the Ziehl-Neelsen stain for acid-fast bacilli. When no acid-fast bacilli were found, the Fite-Faraco stain was applied. In some cases the silver-reticulum stain of Gordon and Sweets (<sup>6</sup>), Congo red for amyloid, and, in many cases, Hall's bilirubin stain (<sup>7</sup>) were applied.

Twenty to 30 serial sections were studied, if the size of the biopsy specimen permitted. In order to assure an unbiased record, the pathologist did not know the clinical classification of the case under study at the time of the microscopic examination.

**Bone marrow aspirates.** For cytology, smears were stained with the May-Grün-

wald-Giemsa stain (<sup>15</sup>), and for leprosy bacilli with the Ziehl-Neelsen stain. For histopathologic examination, the bone marrow particles were treated in the same manner as the liver biopsy specimens. No material was used for culture.

**Skin biopsies.** These were processed histopathologically in the same way as the liver biopsy specimens, but only about four to six step sections were examined. Skin biopsy specimens were obtained in all cases with the exception of five primary neuritic cases and one case each of lepromatous and of dimorphous (borderline) leprosy.

### HISTOPATHOLOGIC FINDINGS

In Table 1 we show a summary of histopathologic changes in the bone marrow and liver in relation to the type of leprosy, the duration of the disease, and the time of treatment. Details found in the various groups of leprosy patients were as follows:

#### Liver

**Liver changes in lepromatous leprosy.** Liver biopsies were made in all 13 patients of this group. All 13 patients showed granulomatous lesions in the liver. We have studied 416 portal tracts. In 62 per cent of

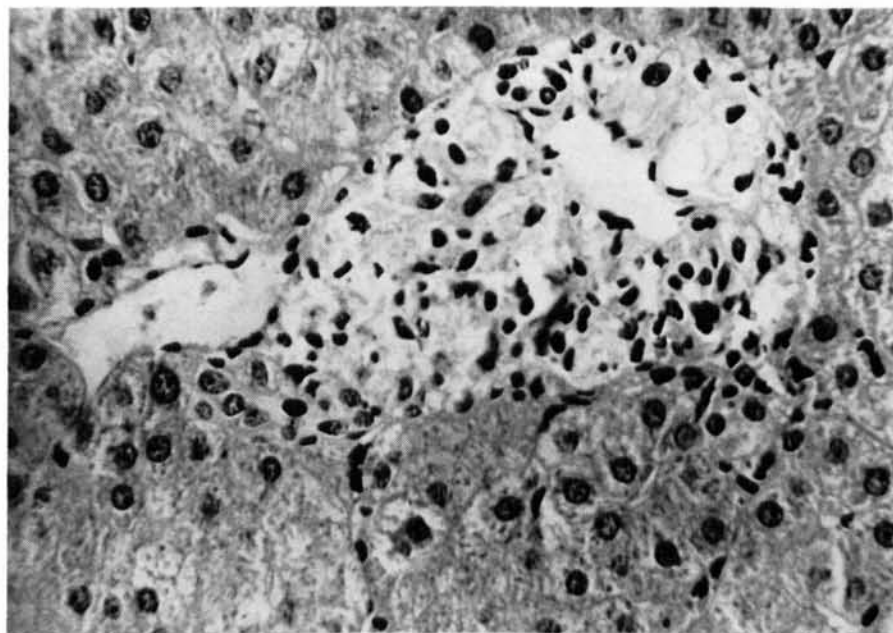


FIG. 1. Foam-cell granuloma in a portal tract of liver (lepromatous leprosy). Hematoxylin and eosin, X520.

TABLE 1. Summary of patients investigated.

Patient No.	Age	Granulomas in liver			AFB in liver	Duration of (yrs.)		Remarks
		Foam cell	Epithelioid	Retothel		Illness	Treatment	
<i>Lepromatous leprosy</i>								
1	22	++	-	-	+	5	2	NB
2	35	+++	-	-	+	5	2 6/12	AFB + in bone marrow smear
3	35	+++	-	-	-	2	6/12	Prolif. reticulum cells in bone marrow
4	41	+++	+	-	-	10	0	NB
5	32	++	-	-	-	2	2 S	Prolif. reticulum cells in bone marrow
6	25	++	-	-	++	1	0	
7	37	++	-	-	++	1	0	
8	32	-	++	-	-	8	1 6/12 S	
9	50	++	-	-	+	5	3/12	
10	27	++	-	-	++	1 6/12	0	NB, NS
11	40	++	++	-	++	?	0	NB
12	20	++	++	-	++	5	0	NB
13	19	+	-	-	-	9-10	Irregular	
Total: 13		12 92.3%	4 30.8%		8 61.5%			
<i>Tuberculoid leprosy</i>								
1	30	-	++	-	-	5	2	Shown necrosis in one liver granuloma
2	36	-	-	-	-	2	0	
3	37	-	++	+	-	3	0	
4	40	-	++	+	-	13	0	
5	30*	-	-	-	-	3	?	NB
6	27	-	-	-	-	1 6/12	0	
7	35	-	-	-	-	2	0	
8	27	-	-	-	-	6/12	0	
9	42	-	-	-	-	8	1	
10	42	-	++	+	-	4	0	NB
Total: 10			4 40%	3 30%				

Patient No.	Age	Granulomas in liver				AFB in liver	Duration of (yrs.)		Re marks
		Foam cell	Epithe- lioid	Retothel	Illness		Treatment		
<i>Dimorphous (borderline) leprosy</i>									
1	35	-	++	+	-	2	8/12	4 liver and 3 bone marrow biopsies.	
2	35	-	-	-	-	1	0	Epithelioid granulomas in bone marrow smear	
3	33	-	-	-	-	4	0	NB	
4	26	-	+	-	-	8/12	8/12		
5	45	-	+	-	-	2	1 6/12		
6	35	-	+	-	-	8	1		
7	41	-	+	+	-	3	0		
8	41	-	+	+	-	7	0		
9	39	-	-	-	-	7	0		
10	25	-	-	-	-	1 6/12	4/12		
11	47	-	-	-	-	11/12	0		
12	31	-	-	-	-	18	5	AFB + in bone marrow smears	
13	28*	-	-	-	-	3	0		
Total: 13			5 38.4%	3 23%					
<i>Primary neuritic leprosy</i>									
1	27	-	-	-	-	12	8	NS	
2	64	-	-	-	-	3/12	1/12	NS	
3	22	-	-	-	-	3	1/12	NS	
4	21	-	-	-	-	8-10	0	NS	
5	21	-	-	-	-	6/12	0	NS	
Total: 5									
Grand total: 41		12 29.3%	13 31.7%	6 14.6%	8 19.5%				

*Liver granulomas:*  
+ = 1-2 granulomas in biopsy.  
++ = Approx. 1/3 of all portal tracts in biopsy involved.  
+++ = 1/2-3/4 of all portal tracts in biopsy involved.  
++++ = Extensive involvement.  
\* = Female patient, all others male.

- = Negative findings.  
S = Treatment received only at start of illness.  
Bone marrow, liver and skin biopsies performed except:  
NB = No bone marrow biopsy.  
NS = No skin biopsy.

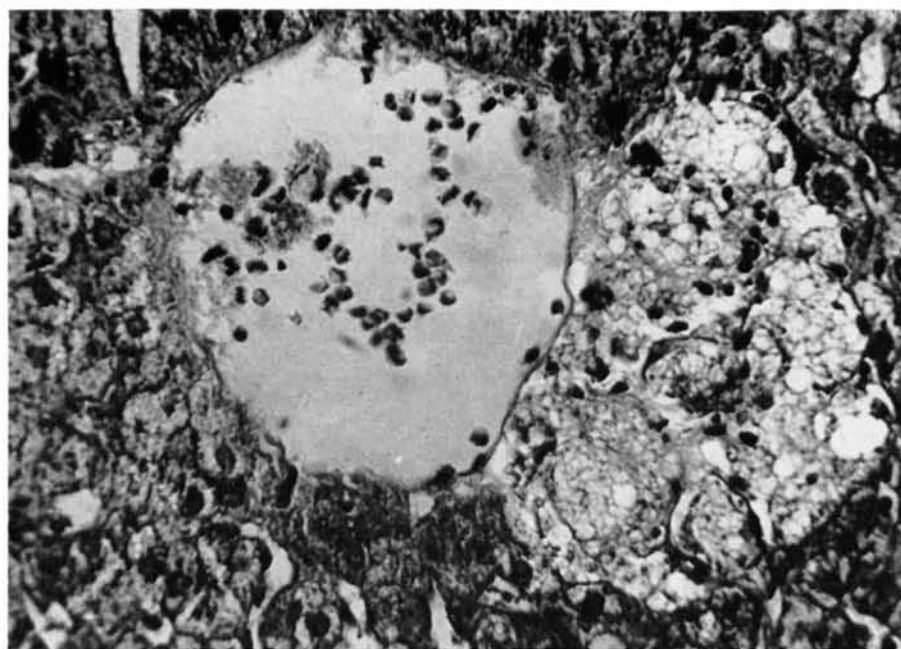


FIG. 2. Lepromatous leprosy: foam-cell granuloma immediately adjacent to the intima of a central vein of a liver lobule. This showed 2+, a moderate number of acid-fast, presumably leprosy, bacilli. Weigert's iron hematoxylin and eosin, X520.

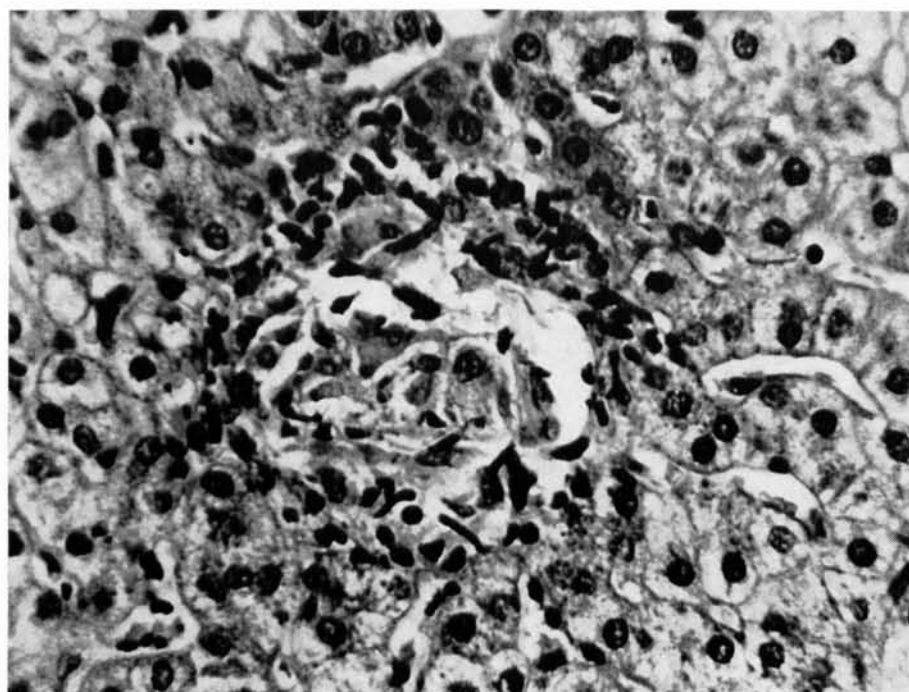


FIG. 3. Dimorphous (borderline) leprosy: Reticulated nodule in midzone of a liver lobule. Degenerating liver cells are present in the center, and Kupffer cell proliferation in the periphery. For detailed description see text. Hematoxylin and eosin, X520.



these (255), typical lepromatous granulomas composed of foam-cells, often with a small proportion of histiocytes and epithelioid cells with few peripheral lymphocytes and occasionally polymorphonuclear leucocytes, were present (Fig. 1). Other cell types were rarely seen. The diameter of lepromatous granulomas in portal fields varied from 45 to 180 microns. They were placed eccentrically in the portal tracts or involved the whole portal tissue. A slight star-shaped fibrous portal extension was seen only in two cases. In five of the 13 cases, additional granulomas of vacuolated cells were found, scattered throughout the liver lobules, and even directly adjacent to the intimal lining of central veins (Fig. 2). In one case no foam-cells were found, but only parportal granulomas composed of nonvacuolated histiocytes and epithelioid cells. In the periphery of these lesions there was usually a scattering of lymphocytes and, rarely, of polymorphonuclear leucocytes. No acid-fast bacilli were seen in this case. Eight of the 13 cases, however, had acid-fast bacilli in the portal granulomas, and, in six of these eight, acid-fast bacilli were seen, also in Kupffer cells or in granulomas in other locations. Liver cells showed little evidence of degeneration except for a moderate variation in nuclear size and staining. No unusual degree of pigmentation was seen. Kupffer cells were definitely prominent in nine cases.

**Liver changes in tuberculoid leprosy.** Liver biopsies of all 10 patients of this group were studied. Four showed parportal granulomas (40%), but only approximately 30 per cent of all the portal tracts were involved. The granulomas consisted of epithelioid cells and, in smaller number, histiocytes. Particularly in the periphery of the lesions, although not in all granulomas, there was a scattering of lymphocytes and a few polymorphonuclear leucocytes. In one portal tract an epithelioid lesion was found, with large central necrosis resembling a caseous tubercle. No acid-fast bacilli were seen in any of these liver biopsy specimens in cases of tuberculoid leprosy.

Occasionally an epithelioid cell granuloma was seen in any location of the liver lobule, not related to the portal tract. In

three liver biopsy specimens, however, we observed small infiltrates that appeared to be different in nature from the typical epithelioid granuloma. These infiltrates were not related to the portal tract. Their diameters ranged from 40 to 140 microns, usually between 40 and 80 microns. A few of these cell nodules showed disintegrating, degenerate or necrotic liver cells in their centers (Fig. 3). The infiltrates consisted of cells with elongated or plump-, kidney-, or spindle-shaped, or irregularly configured nuclei. There was a conspicuous chromatin content of the nuclei. The cells appeared to be located in the sinusoids, and the cell character suggested derivation from proliferating Kupffer cells (Fig. 4). Occasionally these cell groups were encircled by endothelial cells and the nodules showed well defined margins. Others were radiated irregularly into the surrounding liver tissue. By serial sections and reticulum stain we excluded the possibility that these nodules were marginal sections of portal tracts. Usually, also, some infiltration with lymphocytes, a few polymorphonuclear leucocytes, and frequently, but not always, eosinophils, were seen. Plasma cells were rarely found. Leprosy bacilli were never found in those nodules. Following the suggestion of Hamperl<sup>(8)</sup> and Ringleb<sup>(17)</sup> henceforth we shall call these nodules "retothel nodules" (abbreviation of *reticulo-endothelial cell nodules*).

Kupffer cells were prominent in three cases of tuberculoid leprosy, and two of these three showed retothel nodules. Nuclei of liver cells were moderately irregular in most of the biopsies. Lipofuscin pigment appeared to be more prominent, on the whole, than in lepromatous leprosy. Acid-fast bacilli were not seen in any of these biopsies.

**Liver changes in dimorphous (borderline) leprosy.** In 12 patients liver biopsies were made once. In an additional case four liver biopsies were made at intervals of six, eight and 16 weeks.

Only about 18.4 per cent of all the portal tracts studied, but approximately 40 per cent of all patients<sup>(5)</sup>, showed any infiltrating or granulomatous lesions. These consisted chiefly of epithelioid-histocytic

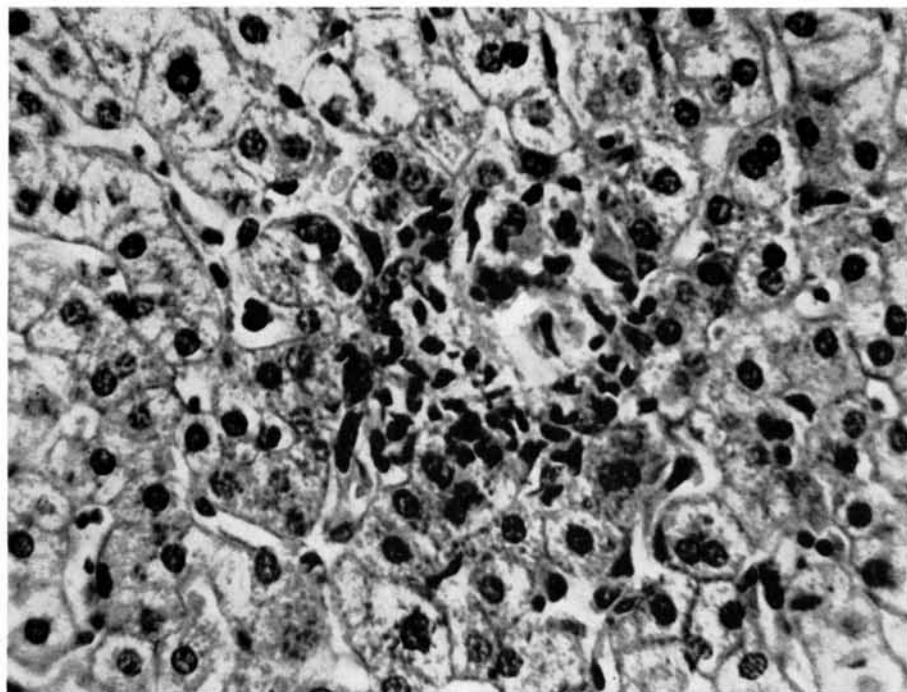


FIG. 4. Dimorphous (borderline) leprosy: Small reticulated nodule with a few central necrotic liver cells and proliferation of Kupffer cells also in sinusoids peripheral to nodule. This nodule has no relationship to a portal tract. Hematoxylin and eosin, X520.

cells, and in one case only also of vacuolated Virchow cells. Occasionally a few lymphocytes and plasma cells also were present. In four patients a slight star-shaped fibrous extension of portal tracts was seen. One of these livers showed already some fibrous joining of portal tracts. No granulomas were found in the portal tracts of this patient.

Reticulated nodules, ranging from 40 to 110 microns in diameter, were found in the biopsies of three patients. In one additional case small accumulations of lymphocytes were noticed in some sinusoids. The appearance and location of reticulated nodules was the same as seen in tuberculoid leprosy. Liver cell degeneration in dimorphous (borderline) leprosy reached grade 2 in six cases. The Kupffer cells were prominent in two biopsies only. Acid-fast bacilli were not found in any of the sections.

**Liver changes in primary neuritic leprosy.** In all five cases one liver biopsy specimen each was obtained. Only a single tract showed a small infiltrate, composed of histiocytes and epithelioid cells with very

few lymphocytes and polymorphonuclear leucocytes. No reticulated nodules were found, and no acid-fast bacilli. Liver cells were unremarkable and Kupffer cells were prominent only in one case in which the granuloma was present in a portal tract.

*Mycobacterium tuberculosis* was not grown by culture from any of the 41 liver biopsy specimens.

#### Bone Marrow Changes

In *lepromatous leprosy*, acid-fast bacilli were found in one of eight cases in the bone marrow smears, but not in the histologic sections. In two biopsy specimens large scattered reticulum cells, some showing epithelioid appearances, were seen. No granulomas were present in any of these sections. The cytology of the bone marrow smears was essentially normal.

In *dimorphous (borderline) leprosy* many acid-fast bacilli were seen in the smears of one case, but not in the histologic sections. In another case, however, distinct epithelioid granulomas, but not acid-fast bacilli, were present in histologic sections

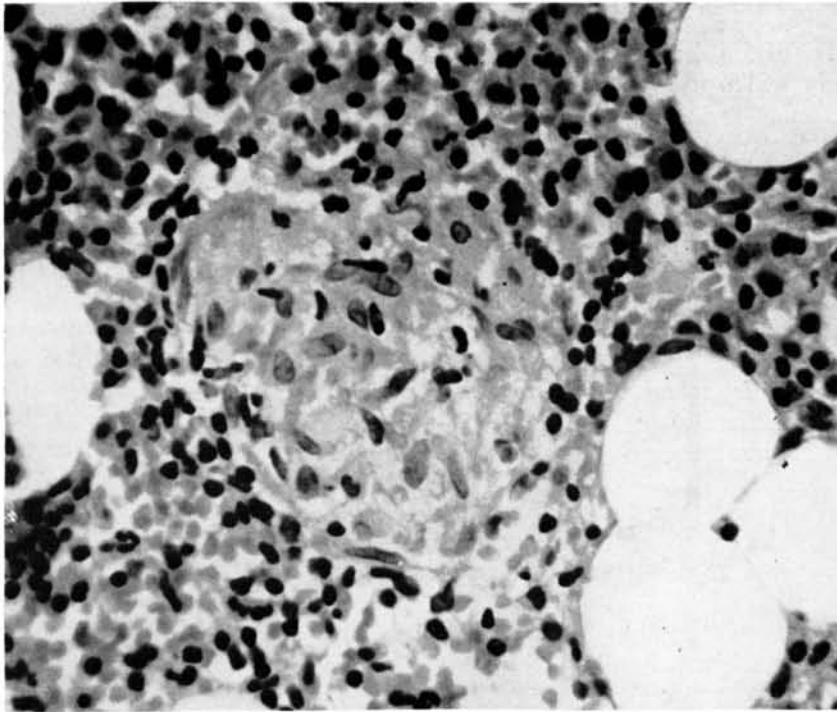


FIG. 5. Dimorphous (borderline) leprosy: Epithelioid cell granuloma in a bone marrow biopsy. Note different cell character of epithelioid cells from cells of reticulated nodule in Figures 3 and 4. Hematoxylin and eosin, X520.

(Fig. 5). No changes were noticed in the bone marrow cytology of all these cases.

**Tuberculoid leprosy and primary neuritic leprosy.** Acid-fast bacilli and pathologic changes were not detected in the smears or the histologic sections.

**Skin biopsies.** The clinical diagnosis was confirmed in all cases studied histologically.

### DISCUSSION

Specific granulomas were found in the liver biopsies of all cases of lepromatous leprosy, and in about 40 per cent each of cases of dimorphous (borderline) and of tuberculoid leprosy. However, the proportionate number of portal tracts involved by granulomatous lesions was greatest in lepromatous leprosy (62%), and declined over 40 per cent in tuberculoid cases to only 18.4 per cent in dimorphous (borderline) leprosy. The more prominent the activity of the skin lesions, as evaluated by clinical appearance and bacteriologic index, the more intense were the granuloma-

tous lesions in the liver. We were not able to find any relation between the duration of the disease and the presence of lepromatous granulomas in the liver. Verghese and Job (<sup>19</sup>) stated that all their lepromatous patients with granulomas in the liver had suffered from the disease for more than four years. Among our 13 lepromatous patients with liver biopsies, however, two had leprosy for only one year and one for one and a half years. All three patients were without treatment prior to liver biopsy. All three showed extensive foam-cell granulomas, not only in the portal tracts but also scattered in other areas of the liver lobules. Other patients with two to 10 years' duration of the disease who were under treatment between three months and two and a half years had, as a rule, no more extensive lesions, and a smaller proportion of portal tracts was involved than in the untreated cases of shorter duration. This suggests that once the skin lesions in lepromatous leprosy become apparent, rapid hematogenous spread of leprosy bacilli takes place. The



liver appears to be involved relatively early in the course of the disease, since after one year already wide-spread and large foam-cell granulomas are encountered in the liver. Treatment appears to reduce the number and the size of the granulomas. It also seems to reduce the number of extra-portal lesions.

In *tuberculoid and dimorphous (borderline) leprosy*, predominantly epithelioid granulomas were seen. They were located in portal tracts, but also scattered in any zone of the lobule. In addition, we found small cell proliferations randomly distributed throughout the liver lobes. They consisted essentially of proliferated Kupffer cells, with an admixture of lymphocytes and a few polymorphonuclear leucocytes and eosinophils. Hamperl<sup>(8)</sup> and Ringleb<sup>(17)</sup> described these nodules in separate papers in 1953. Ringleb<sup>(17)</sup> found them in 26.5 per cent of biopsies of 465 patients suffering from pulmonary tuberculosis. As noted above Hamperl<sup>(8)</sup> suggested the term "retothel nodules" (reticuloendothelial cell nodules). In systematic investigations these authors showed the following characteristics:

1. Typical epithelioid cells are usually not present and the nodules are distinct from small tubercles.
2. The cell nodules originate in the sinusoids, presumably from Kupffer cells.
3. They do not include reticulum fibers.
4. The proliferation may cause degeneration and necrosis of adjacent liver cells. Degenerating liver cells may be engulfed by Kupffer cells.
5. Retothel nodules may vary in size. Finally they may disappear without leaving a scar. They do not develop into tubercles.
6. By serial sections and reticulum stain it was excluded that tangential sections of portal tracts were erroneously interpreted as retothel nodules.
7. In cases of tuberculosis, tubercle bacilli were never found in retothel nodules.

Both authors realized that retothel nodules are nonspecific lesions. Although frequently present in pulmonary tuberculosis, they were found also in salmonellosis,

brucellosis, various other infections, and Hodgkin's disease. Hamperl<sup>(8)</sup>, and Ringleb<sup>(17)</sup> interpreted these nodules as an expression of a nonspecific particular state of reactivity against tubercle bacilli or their products. Bock *et al.*<sup>(1)</sup> subsequently showed that there were differences in the response to tuberculin in patients with and without retothel nodules. Subsequently the nodules were seen by other authors<sup>(9)</sup> also. The name "retothel nodules" is convenient and descriptive, so that we see no reason for introducing another term. As far as we are aware, retothel nodules have not been recognized previously in liver biopsies of leprosy patients. Their presence is not surprising, since there is considerable cross sensitivity in leprosy patients, resulting from contact with other mycobacteria, especially *M. tuberculosis*<sup>(4)</sup>. This may explain the similar appearance of these nodules in many cases of tuberculosis as well as in leprosy. The fact that we found these nodules only in cases of dimorphous (borderline) and tuberculoid but not lepromatous leprosy, supports the view that their etiology is related to an immunologic response of the tissue. Their presence in liver biopsies may be of limited diagnostic value in the absence of specific granulomas.

Few positive results were obtained in the tissue of the bone marrow. In only one case each of lepromatous and dimorphous (borderline) leprosy were acid-fast bacilli found. One case of dimorphous (borderline) leprosy showed pure epithelioid cell granulomas in the bone marrow, but no acid-fast bacilli. It is interesting that in four successive liver biopsies of this patient typical epithelioid granulomas were present each time. In one of these biopsies a foam-cell lesion was found in addition to the epithelioid lesion. The lepromatous case that was positive for acid-fast bacilli in bone marrow smears had very active skin lesions and had a large number of Virchow cells and acid-fast bacilli in the liver. The same activity of skin lesions was seen in two other lepromatous cases with proliferated reticulum cells of the bone marrow.

We did not find acid-fast bacilli in the bone marrow as frequently as other workers<sup>(5, 10, 12, 14)</sup>, although we used more

elaborate techniques, viz., smears and histopathologic sections for the detection of granulomas and of acid-fast bacilli. The bone marrow seemed to be less commonly affected by granulomatous leprosy lesions than the liver. However, the minute size of the bone marrow fragments may not give a very representative picture if lesions are more scattered than, for instance, in the liver. One of the interesting findings in the liver biopsies was the fact that not only the relative number of cases involved, but also the distribution of lesions appears to have a distinct pattern for each type of leprosy. This may apply to other organs also. We are not aware that attention has been paid to this question previously.

In dimorphous (borderline) and tuberculoid leprosy we confirmed the presence of scattered epithelioid granulomas in the liver as described by previous workers.

Like Karat (<sup>12</sup>), we did not find bone marrow changes in any of our cases of tuberculoid leprosy. The same negative result was obtained in primary neuritic leprosy.

### SUMMARY

Forty-one leprosy patients were investigated by liver, skin, and bone marrow biopsies, by bacteriologic culture of liver biopsy specimens for tubercle bacilli, and by bone marrow smears. The patients had been grouped clinically and histologically as lepromatous (13), tuberculoid (10), dimorphous (borderline) (13), and primary neuritic (5).

All 13 lepromatous patients showed specific granulomas in the liver, and acid-fast bacilli were found in eight of these. A relationship between the intensity of skin lesions and involvement of liver and bone marrow was noted, but there was no correlation between the duration of the disease and the extent of lesions.

Four of the 10 cases of tuberculoid leprosy showed epithelioid cell granulomas in the portal tracts and occasionally elsewhere, but no acid-fast bacilli were found in the liver tissue.

In dimorphous (borderline) leprosy five of 13 cases had specific granulomas in the liver, and two patients had bone marrow

changes. One of these had epithelioid cell granulomas in skin, liver, and bone marrow. No acid-fast bacilli were found in histologic sections, but they were found in one bone marrow smear.

Particular emphasis is placed on the finding of reticuloendothelial ("retothel") nodules in the livers of six patients with dimorphous (3) and with tuberculoid (3) leprosy. These nodules, consisting essentially of proliferated Kupffer cells, are probably nonspecific. They are probably related to a hypersensitivity to mycobacteria or their products. Acid-fast bacilli were not found in them.

Primary neuritic leprosy (5 cases) was localized to the peripheral nerves, and no definite spread was found to the liver and bone marrow histologically.

Half of the tissue from each liver biopsy specimen was cultured for tubercle bacilli. No positive results were obtained.

### RESUMEN

Cuarenta y un enfermos de lepra fueron investigados con biopsias de hígado, piel y médula ósea, por medio de cultivos bacteriológicos de muestras de biopsias del hígado para bacilos tuberculosos, y por frotis de médula ósea. Los pacientes habían sido agrupados clínica e histológicamente como lepromatosos (13), tuberculoides (10), dimorfos (borderline) (13), y neuríticos primarios (5).

Los 13 pacientes lepromatosos mostraron granulomas específicos en el hígado, y bacilos ácido-resistentes fueron encontrados en ocho de éstos. Una relación entre la intensidad de las lesiones de la piel y el compromiso del hígado y de la médula ósea fué notado, pero no hubo correlación entre la duración de la enfermedad y la extensión de las lesiones.

Cuatro de los 10 casos de lepra tuberculoides mostraron células epitelioides granulomatosas, en los sistemas portales y ocasionalmente en otras partes, pero no fueron encontrados bacilos ácidos-resistentes en el tejido hepático.

En lepra dimorfa (borderline) 5 de 13 casos tenían granulomas específicos en el hígado y dos pacientes tenían cambios en la médula ósea. Uno de estos tenía células epitelioides en los granulomas de la piel, hígado, y médula ósea. No se encontraron bacilos ácido-resistentes en los cortes histológicos, pero ellos fueron encontrados en un frotis de médula ósea.

Se pone énfasis particular en los hallazgos de nodulos rethothes en el hígado de 6 enfermos con lepra dimorfa y con lepra tuberculoide. Estos nódulos, consistiendo esencialmente de células de Kupffer proliferadas, son no específicos probablemente. Ellos están probablemente relacionados a una hipersensibilidad a las micobacterias o sus productos. Bacilos ácido-resistentes no fueron encontrados en ellos.

Lepra neurítica primaria (5 casos) fué localizada en los nervios periféricos, y no se encontró histológicamente una extensión clara al hígado o la médula ósea. La mitad del tejido de cada muestra de biopsia hepático fué cultivada para bacilos tuberculosos. No se encontraron resultados positivos.

### RÉSUMÉ

On a étudié 41 malades atteints de lèpre, en ayant recours aux biopsies de foie, de peau et de moëlle osseuse, à la culture bactériologique d'échantillons de biopsies hépatiques pour les bacilles tuberculeux, et par des frottis de moëlle osseuse. Les malades avaient été groupés, cliniquement et histologiquement, comme lépromateux (13), tuberculoides (10), dimorphes, c'est-à-dire borderline (13), et névritiques primaires (5).

Tous les malades lépromateux, au nombre de 13, ont révélé des granulomes spécifiques dans le foie; des bacilles acido-résistants ont été observés chez 8 d'entre eux. On a noté une relation entre l'intensité des lésions cutanées et l'atteinte du foie et de la moëlle osseuse; par ailleurs, il n'y avait pas de relation entre la durée de la maladie et l'étendue des lésions.

Quatre des 10 cas de lèpre tuberculoide montraient des granulomes à cellules épithélioïdes dans les espaces portes, ainsi qu'autre part à l'occasion; néanmoins, aucun bacille acido-résistant n'a été trouvé dans le tissu hépatique.

En ce qui concerne la lèpre dimorphe (borderline), 5 des 13 cas présentaient des granulomes spécifiques dans le foie et deux malades montraient des modifications de la moëlle osseuse. Un de ces malades présentait des granulomes à cellules épithélioïdes dans la peau, le foie, et la moëlle osseuse. Aucun bacille acido-résistant n'a été trouvé dans les coupes histologiques, mais bien, dans un cas, dans le frottis de moëlle osseuse.

On souligne de manière toute particulière le fait que des nodules rethothes ont été observés dans le foie de 6 malades, 3 atteints de

lèpre dimorphe, et 3 atteints de lèpre tuberculoide. Ces nodules, qui consistent essentiellement en une prolifération des cellules de Kupffer, sont probablement non spécifiques. Ils sont vraisemblablement reliés à une hypersensibilité aux mycobactéries ou à leurs produits. Aucun bacille acido-résistant n'a été observé dans ces nodules.

La lèpre névritique primaire (5 cas) était située au niveau des nerfs périphériques, et aucune dissémination nette n'a été observée, sur la plan histologique, dans le foie ou dans la moëlle osseuse.

La moitié du tissu provenant de chaque échantillon de biopsie hépatique a été cultivée, afin de mettre en évidence des bacilles tuberculeux. Aucun résultat positif n'a été obtenu.

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