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THE HISTOID VARIETY OF LEPROMATOUS LEPROSY¹

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In the past decade and more, many of the specimens of lepromatous leprosy added—more or less sporadically—to my biopsy collection have proved to be of an atypical kind which I have come to call “histoid.”

That name, which signifies “composed of, or developed from, a single tissue and not a complex structure” (Stedman), is regarded as appropriate because of its usage in connection with tumors⁽³⁾. In contrast with the complex “organoid” tumors, as for example adenomas, the simple “histoid” ones are composed primarily of a single tissue element, as fibromas and the like.

The histoid leproma, in its typical form best seen in young and active subcutaneous nodules—nodules which are neither modified by “local reactionary” conditions nor by the secondary fibrosis that occurs with chronicity—has the nature of a simple, organized, spindle-cell (histiocytic) tissue, rather than the “inflammatory” granulomatous structure of the ordinary leproma.

These lesions are not at all ascribable to “fibrosis” of ordinary lepromas, as they have usually been thought to be. The collagen element which is present in the mature lesions, increasing with their age, is a secondary feature.

CASES INVOLVED

Typically, the cases which have been particularly studied once had, whatever their earlier history, ordinary lepromatous leprosy for a period of years. Under treatment in that phase they underwent improvement in various degrees, even in some instances to the point of bacteriologic negativity, but, later on, reactivation or relapse occurred.

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The new lesions, in general conspicuously nodular and for the most part primarily subcutaneous in origin, are relatively or absolutely resistant to treatment. A point of more than passing interest, observed by Dr. C. B. Lara, is that such cases do not undergo the erythema nodosum leprosum type of reaction.

By no means are all of the cases of generalized or systemic involvement. Some with only limited histoid manifestations from whom biopsy specimens were obtained several years ago have cleared up under treatment. Nevertheless, the ultimate prognosis of the more seriously affected cases is decidedly unfavorable,—which is something of an understatement.

CLINICAL FEATURES OF THE LESIONS

Subcutaneous nodules.—The clinical description of the histoid lesions properly begins with the independent subcutaneous nodules, to which ordinarily so little attention is paid. In the first place, they are the source, as the result of a sort of outward migration, of most of the lesions that affect the dermis. Secondly, such nodules of normal activity present the best histologic pictures of their nongranulomatous, nonfibromatous, tissue-like but still histiocytic character, and also many variations of “local reactional” nature. Lastly, such subcutaneous lesions are something that do not—to my knowledge—occur in the ordinary form of lepromatous leprosy.



FIG. 1. Demonstrating a large nodule in the subcutis of the posterior surface of the right upper arm. This lesion was chronic, and sections were of fibrous-tissue appearance. (Cf Fig. 13.)

These nodules vary in size from the smallest that can be palpated in the subcutaneous tissue to about 5 cm. in diameter. The smaller nodules are soft, and on scraping a cut surface it yields abundant pulp-material for smears; the larger nodules are old and relatively—but secondarily—fibrotic, and so the cut surface is likely to be pale and tough. Our nodule material consists mostly of specimens large enough to be removed for the making of lepromin. Although a few very small and

early ones have been encountered, nothing that could be considered the actual initial stage of the lesion has been observed.

The nodule is an *expansile* lesion, enlarging primarily by a process of expansion and not by the infiltration that is characteristic of ordinary lepromas. As the nodule enlarges it pushes aside the connective-tissue element of the subcutis (if located there), thus forming a sort of pseudocapsule.

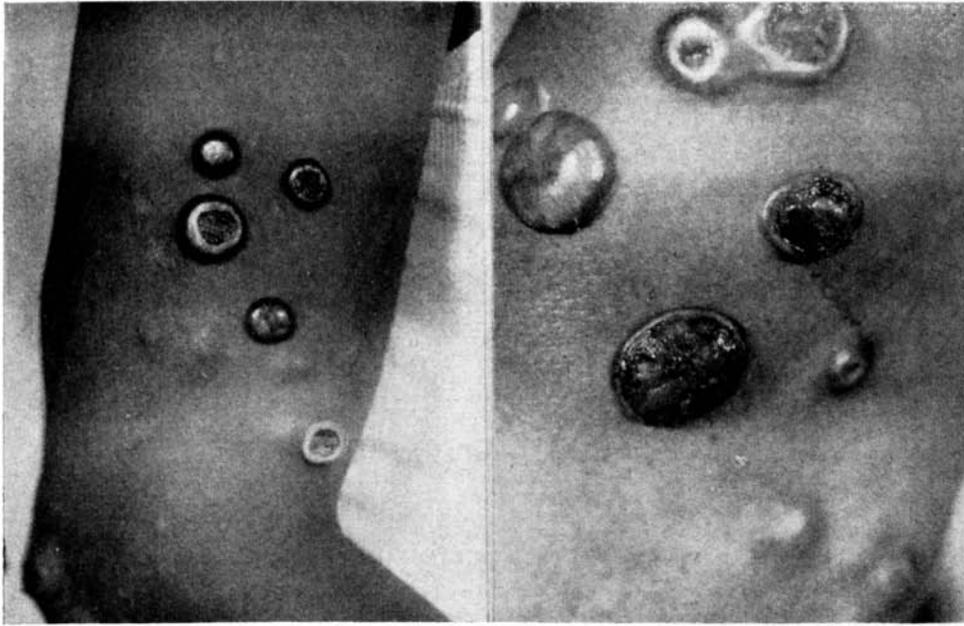


FIG. 2. A succession of lesions of different stages, on the external surface of the right arm (a) Seen by their shadows is a transverse row of four nodules still in the subcutis, and another deep one associated with the lowermost of the ruptured lesions. (b) Upper most is an intact nodule recently emerged from the depth, and (c) elsewhere are four larger lesions three of which have broken down.

FIG. 3. Stages of evolution of broken-down nodules, two of them showing different degrees of the characteristic "pulled-back" condition of the surface layer around the raw—but not ulcerative—surface.

Such nodules may remain subcutaneous indefinitely, and become of considerable size (Fig. 1). In many instances, however, they tend somehow to migrate toward the surface and to fuse with the dermis, and later they may become elevated or protuberant (Fig. 2). If the protuberant nodule has broken down by the central softening process that is common in such lesions, it may rupture and discharge, and later heal slowly with distinctive scar formation. The raw-surfaced lesions thus produced, the epidermis of which may be peculiarly pulled back (Fig. 3) are to be distinguished from actually ulcerated lesions, a matter for future demonstration.

Cutaneous nodules.—An occasional case may present histoid nodules definitely of cutaneous origin, arising from the upper reticular layer. Such lesions promptly become elevated (Fig. 4), and they may

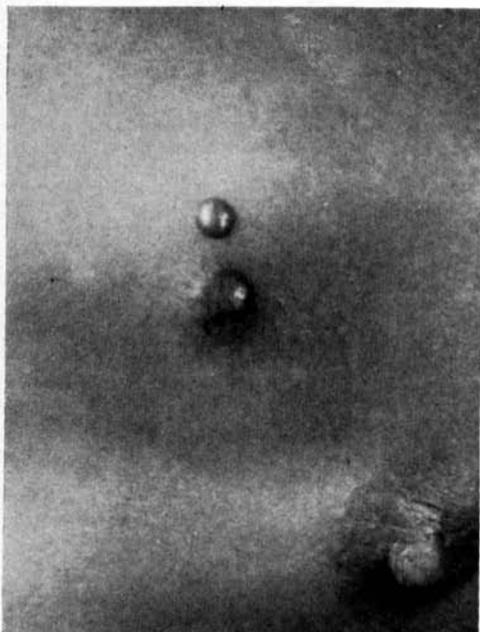


FIG. 4. A very small, very recent, protuberant nodule, of superficial cutaneous origin, on left chest above nipple. Below it is a larger, less simple, less protuberant, nodule of deeper—but still cutaneous—origin.

become protuberant and even pedunculated (Fig. 5). They are as strictly limited as those of the subcutis; the skin immediately around them seems quite normal (Fig. 6), and smears from that skin are negative.

Cases with lesions of precisely the kind shown in the last two figures are apparently rare. In my collection there is only one case. One such case, quite unmistakable, is pictured in Fig. 117 of Dharmendra's Notes⁽¹⁾, and two in Figs. 25 and 29 of the Atlas of Orestes Diniz *et al.*⁽²⁾; in that book several other definite or probable histoid cases are also to be found.

Cutaneous plaques.—This refers to a very different kind of histoid lesion, not of nodular character. It is of different growth habit from the nodules, but of the same nature cytologically and bacteriologically. These are exemplified by the thick, scaling pads which in some cases develop on points of pressure, especially the elbows, but there are also independent plaques. They are as sharply delimited as are the nodules—or as a tuberculoid plaque would be (Fig. 7).

HISTOPATHOLOGY OF THE LESIONS

The histoid lesions have certain characteristic features of structure, cytology, and bacteriology which serve to distinguish them from the ordinary lepromas wherever they are met. Most of these are ordinarily best seen in young, active subcutaneous nodules, although nodules in general are liable to show changes of aging on the one hand, and on the other hand changes of local reactional nature—too numerous and complex to be discussed here.

Technique.—The tissues studied were processed by our routine method for research specimens, as recently described (6). All specimens were Zenker-fixed, of recent years for only 5-6 hours. In all instances sections were stained by (a) hematoxylin and eosin and, after 1957, by (b) Wade's modification (5) of Fite's first (1938) method (WF-I; also by (c) Mallory's aniline-blue stain which differentiates the collagenous elements, and (d) his phosphotungstic hematoxylin stain for other special features.

The most striking feature of the typical, active histoid lesion is the intertwining of cellular strands which in the sections are cut longitudinally, obliquely, and transversely, and—although the cells are primarily spindle-shaped histiocytes more or less loaded with bacilli and not fibrocytes—the lesions resemble more or less closely certain fibromas and fibrosarcomas (Figs. 8 and 9) as shown in Mallory (4).

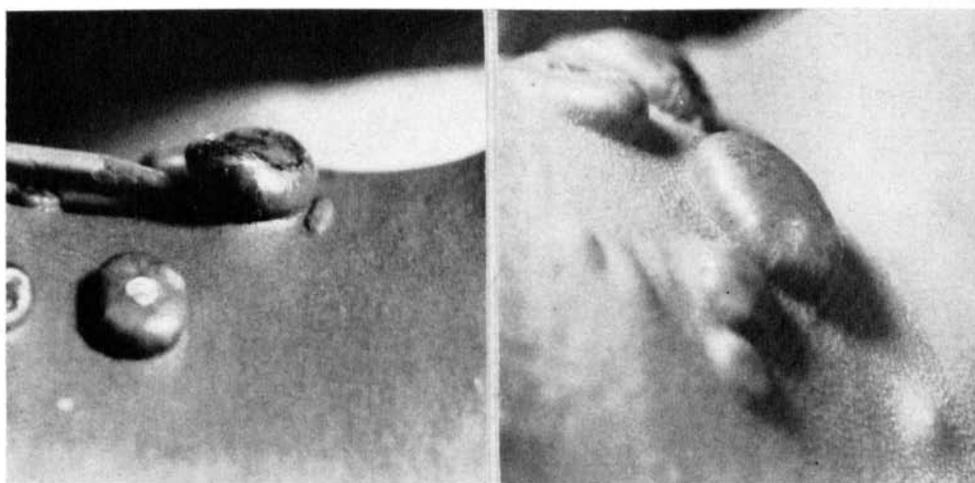


FIG. 5. A nodule, raw-surfaced, lifted (by pencil point) to demonstrate the pedunculation sometimes seen in cases of this particular rare variety.

FIG. 6. Close-up of a nodule in the left lumbar region, to illustrate the normal graining of the skin (bacteriologically negative) up to the very edge of the nodule. This is a characteristic of these self-contained, noninfiltrative lesions.

The structural features of an active histoid nodule are shown in Figs. 10 to 12. Fig. 10, poorly-focused, is nevertheless illustrative of certain features, including the pseudocapsule. In Figs. 11 and 12, of the "parenchyma" of the same nodule, the resemblance to a fibroma-tissue growth is particularly marked; a certain description of a fibrosarcoma, as composed of "strands and whorls," would be perfectly applicable. It is a fact, however—demonstrable only by the special stain and color pictures—that this area contains very few aniline-blue-stained collagenous elements; almost all of the cells are bacillus-laden spindle-shaped histiocytes.

As the subcutaneous nodules mature and age, blue-staining fibrous elements appear and increase in the spindle-cell base, but they never become diffusely dispersed throughout the lesion. A chronic lesion of fibromatous appearance shown in Fig. 13 contains in the aniline-blue-

stained duplicate only a moderate amount of actual fibrous-tissue elements. The oldest, toughest nodule studied, the cut surface of which seemed very fibrous when scraped for bacilli, proved in sections to be composed of fibrous strands in hardly one-half of the total area, the rest being interspersed areas of bacillus-containing spindle cells. In histoid lesions of cutaneous origin, whether nodules or plaques, the fibrotic changes described are seldom marked, when present at all.

This description of the structure applies, on the whole, only to the subcutaneous nodules, and in this simple form it applies only to those that have not undergone any of the various "local reactional" changes.

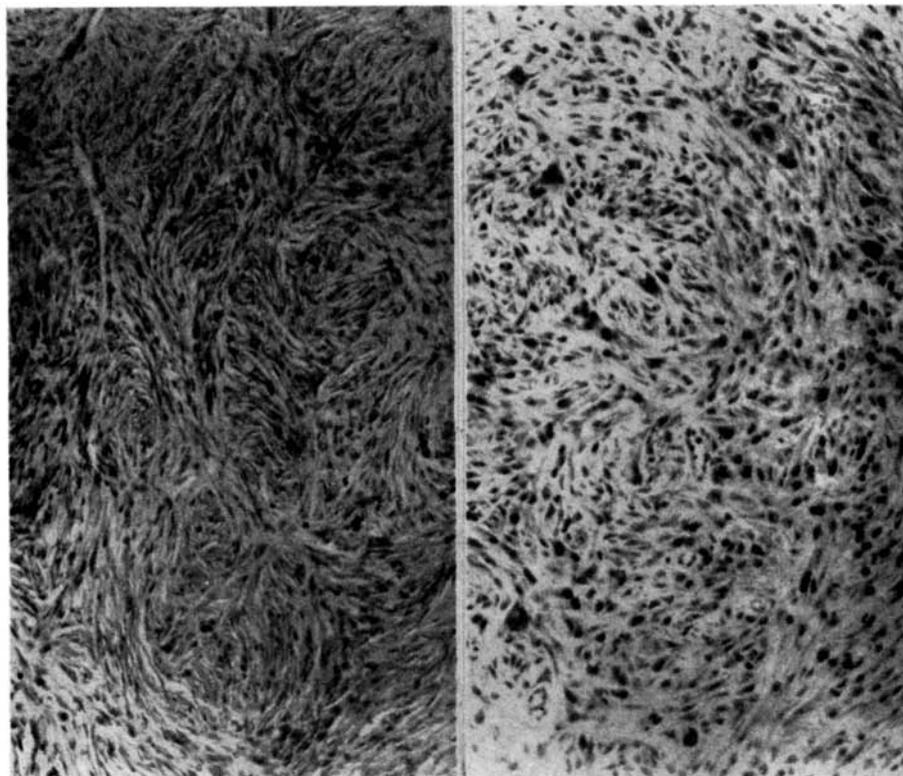


FIG. 7. Elevated histoid plaques of subcutaneous origin, as sharply demarked as are emergent nodules (and tuberculoid lesions). These are by no means the largest plaque-like lesions of this patient, but the picture is of the most illustrative one.

It is to be emphasized, and is therefore repeated, that the next characteristic feature of the nodular histoid lesions is that their growth is expansile, not infiltrative as is the ordinary leproma. The cells of the lesions proliferate *in situ*, evidently by amitosis, and are not brought in by the nutrient blood vessels. Thus, by pushing ahead of it the connective tissue elements of the tissue in which it lies—with coincident pressure atrophy of the fat cells, is formed a sort of pseudo-capsule (Fig. 10), which often appears to be an essential part of the lesion proper but is readily seen to be otherwise.

Also pushed aside by the expanding nodule are any large blood vessels of the vicinity, which are often conspicuous outside the pseudo-capsule, and also any nerves—which are much less frequently seen. The lesion is well supplied with small blood vessels, but no nerve branch has been seen in any specimen.

The expansile condition and pseudoencapsulation are also to be seen in the lesions within the cutis, both those that have invaded from the subcutis and those that originate in the dermis proper. They are



FIGS. 8 and 9. FIG 8, fibroma, and FIG. 9, fibrosarcoma. (From Mallory's Pathologic Histology, by permission of the publisher.) The legends of the two are virtually identical: "Cells and fibrils in small bundles which run in various directions" [alternatively, "in every direction"].

absent only in the cutaneous plaques, but in them the structure is nevertheless an orderly arrangement of the lesion cells which run vertically from the epidermis downward. Clinically those elevated lesions are sharply demarked as if they were of major tuberculoid nature.

Also to be mentioned is the occurrence, although rarely, of *mixed lepromatous* lesions of the skin. Lesions that originate there may be in association with lesions of the ordinary form of leprosy that are by no means residual of a previous process. Of the two specimens of this kind in my collection, one is a typical histoid nodule of the dermis surrounded on three sides by a contrasting mosaic of well-separated small areas of ordinary lepromatous infiltrates. In the other specimen, of a plaque-type lesion, the orderly histoid process changes abruptly in the depth of the dermis, to the ordinary type of leproma. Since the sections of these mixed lesions show the two processes after identical treatment, they are particularly demonstrative of their contrasting individuality.

The bacilli of the histoid lesions constitute one of the most striking and distinctive features of those lesions, first in the *absence of*

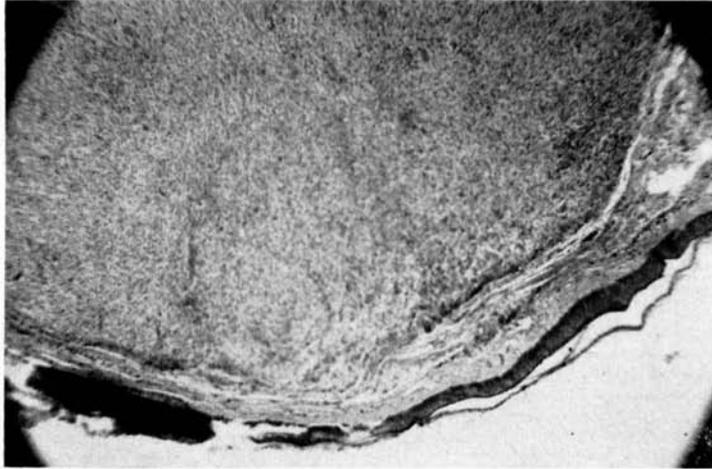
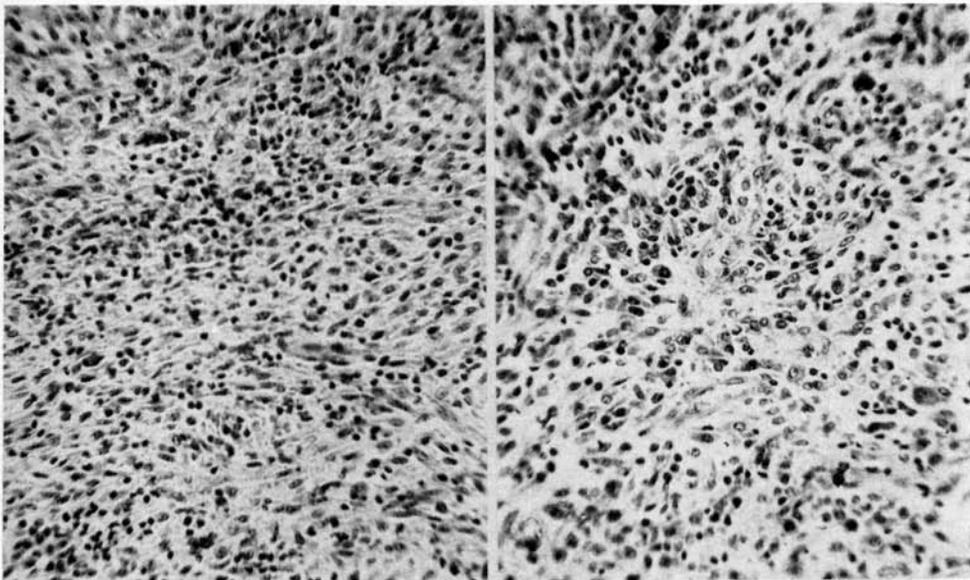


FIG. 10. Low-power view (poorly focused) of a very active, recent, emerging nodule. Conspicuous features are: (a) the flattening and breakdown of the epidermis, (b) the distinct pseudocapsular layer above (but not integral with) the nodular lesion on the left, and (c) the merging, on the right, of that capsular layer with the subepidermal connective-tissue layer.

globus formation, and also in their arrangement, abundance and size, and the consequent ease of observation (at least in sections stained by the WF-I method).

The arrangement of the bacilli, the "histoid habitus," corresponds to the form of the cells involved, and is very different from that in the ordinary leproma. In the spindle-cell lesions the groups or clumps of bacilli are correspondingly elongate. Their numbers vary widely according to the ages of the lesions. In the immature younger ones they are not as numerous as in the typical mature ones; in the latter they



FIGS. 11 and 12. Structure of a typical, normally active histoid nodule; low and high-dry magnifications.

are very abundant, more so than in the ordinary kind of leproma; later on, as the lesion ages, they become less abundant, so much so that such lesions may be unsuitable for use in making lepromin.

In certain "local reactional" areas of the subcutaneous nodules the spindle cells are changed to large rounded phagocytes (i.e., of the usual histiocyte type, but large), and in these particularly "active" cells the bacillus load is simply incredible. It seems impossible for a cell to carry so many bacilli without disturbance of its morphology, yet usually the most that can be seen in the hematoxylin-eosin section is a fine irregularity of the cytoplasm that suggests the minute "vacuolation" of xanthomatous lesions. Occasionally coarser vacuolation is seen, always within the cytoplasm but not large enough to penetrate the thickness of a 6-micron section; hence it has no resemblance to globus formation.

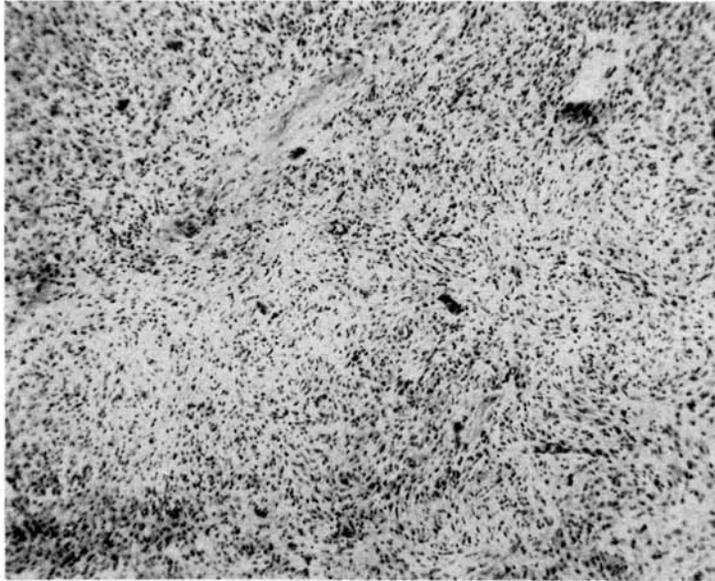


FIG. 13. Structure of an inactive, rather chronic histoid nodule. The aniline-blue section of this specimen shows much less collagen than would be expected from the appearance of the hematoxylin-eosin section.

In size, the bacilli (as stained) are notably larger than those in the ordinary leproma, even in the same section. In consequence, a low-power objective (the 20X especially) is sufficient for their general observation. This is in sharp contrast with the ordinary lepromatous lesions, to study which the oil immersion lens is needed.

The absence of globus formation is obviously due to the lack of production by the bacilli of the essential matrix substance, or gloea—the "electron transparent substance" of the electron microscopist. This is evidently a failure, or deviation, of the metabolism of the bacilli, about the cause of which one can only speculate.

It is to be said, however, that the failure to produce globi is absolutely characteristic but not absolutely invariable. A few histoid specimens have been encountered in which areas of the lesions have undergone the reverse change and produced globi. Areas showing this condition have never been very extensive, and they have not perceptibly affected the character of the rest of the lesion in which they occurred.

TUBERCULOID "CONTAMINATION" OF HISTOID LESIONS

A feature of some of the specimens of histoid nodules which caused amazement when first observed and still remains inexplicable, is the occurrence of definite tuberculoid foci within the lesion substance or in the encircling fibrous-tissue encapsulation. This "contamination," seen only in nodules of subcutaneous location or origin, is not rare, for it has been found in a fairly large percentage of the specimens. Nothing like it has ever been seen in ordinary lepromatous lesions.

These foci are usually small, less than the diameter of the 20X objective; in the largest, encountered in two specimens, the area of the 20X objective hardly encompasses that of the epithelioid center of the lesion.

The smaller foci—but not the larger ones—may be easily overlooked in the hematoxylin-eosin sections, but they are fairly conspicuous in those stained for bacilli. The epithelioid centers are almost free from bacilli, in sharp contrast with the normal abundance in the surrounding, unaffected histoid tissue.

In numbers per specimen block they are often single, not infrequently two to several, only very rarely numerous. None has ever shown any suggestion of a tendency to multiply, i.e., to form satellite foci in its immediate neighborhood.

No explanation of the occurrence of these tuberculoid foci in these lesions has been offered by persons consulted, and none can be offered by me; speculation will not be indulged in. It may be remarked, however, that lesions so contaminated cannot be called "borderline," or even "dimorphous."

DISCUSSION

To appreciate the basically histiocytic nature of the spindle-cell structure of the histoid lesions, and the secondary role of the fibrous tissue element—i.e., to realize that the lesions are not fibrous or fibromatous, as they are likely to be thought to be from the appearance of ordinary hematoxylin-eosin sections—a good differential stain for collagen must be applied routinely to all specimens. That requires Zenker fixation of the specimens, at least if the Mallory aniline-blue stain is to be used—and also if the structural alterations due to the shrinkage inherent in formalin-fixed tissue is to be avoided, which is greatly to be desired.

Only in the earliest nodular lesions is the spindle-shaped histiocytic element to be seen in pure culture, without any collagenous fibers except in the pseudocapsules. Infiltration by strands of fibrocytes and, later, advancing fibrosis, are features of maturing and aging of the nodules.

The demonstration of the bacilli in the histoid lesions by the method employed in this laboratory exclusively since 1957 (⁴) is extraordinarily good. The "histoid habitus" of their arrangement in the ordinary spindle-cell lesion is very distinctive. In the histiocytic areas of some of the more active lesions there is a simply incredible massing of the bacilli. The contrast between the bacilli seen in these lesions and those in the ordinary lepromatous lesions is well shown in certain infrequent "mixed" lesions, of which there are only two in my collection.

That the bacillus groups and masses of the histoid lesions do not produce globi—recognition of which fact requires recognition of what globi are—is obviously a matter of metabolism. The bacilli do not produce the matrix substance, or gloea, that characterizes the globus. Beyond that, the explanation is a matter of speculation.

An unexplained clinical feature of evident significance is that reactions of the erythema nodosum leprosum kind seem not to occur in histoid cases.

Until detailed case reports can be presented, little can be said about clinical variations of the cases presenting histoid lesions. Several that can properly be called *histoid leprosy* (lepromatous) because the condition was systemic, have died of it in the course of time. Unfortunately, none has been autopsied. In other cases the histoid lesions seem to have been local, with no systemic manifestations, and without particularly unfavorable prognosis.

The not infrequent finding of tuberculoid foci in the nodules of subcutaneous origin, either in the substance ("parenchyma") or the capsular layer, constitutes a particularly intriguing problem. These foci are evidently of metastatic nature, but from what or where do they originate? Here, again, speculation is avoided.

SUMMARY

1. The "histoid" variety of lepromatous leprosy here discussed is so named because histologically the typical lesions resemble, rather than the inflammatory granuloma that the ordinary leproma is, a tumor developed from a single, spindle-shaped tissue element. The condition is commonly mistaken for fibrosis of ordinary lepromatous lesions.

2. Lesions of this sort are most likely to be found in old cases which for years had progressed as ordinary lepromatous leprosy, responding to treatment, but had later retrogressed, or relapsed, developing lesions resistant to treatment. They are therefore of a kind seldom seen

except in leprosaria, and patients of such kinds in such environment are not likely to arouse sufficient interest to lead to the making of biopsies.

3. The essential clinical feature is nodule formation, notably subcutaneous but also cutaneous. In their manner of growth the nodules are primarily expansile, and consequently are usually surrounded by a pseudocapsule derived from the tissue in which they are located. They are well vascularized, but they contain no nerve branches.

4. The "parenchyma" of the earliest nodules is composed solely of spindle-shaped, bacillated cells of histiocytic nature, but an irregularly-distributed fibrocytic "stroma" develops later, and the amount of the fibrous-tissue element within the lesion increases with age.

5. Other characteristic and noteworthy histologic features include the frequent reactional, or activation, change of the parenchyma cells in limited areas from the normal spindle shape to typical rounded phagocytes, and the frequent occurrence of areas of local softening ("local reactional" breakdown), even amounting to "abscess" formation but seldom such lesions containing polynuclear leucocytes.

6. Bacteriologically, the most striking and significant feature is the normal absence of globus formation, regardless of the abundance of the bacilli. Their numbers in the active spindle-cell parenchyma are usually large, and in the rounded phagocytes they are usually extremely numerous, at times incredibly so. The arrangement of the bacilli as elongate clumps in the spindle cells, together with the occurrence of dense, rounded masses in the areas of free phagocytes, constitutes the "histoid habitus" of the bacilli, strikingly different from the arrangement in the ordinary leproma.

7. Extraneous to the histoid lesions in sections of the affected skin, never in association with the subcutaneous nodules, there may be found residual foamy-cell areas, usually small, which are merely residuae of the previously-existing ordinary lepromatous process. More rarely, there may be found, in association with active histoid skin lesions, more or less active infiltrates of the ordinary lepromatous process; these infrequent lesions are of double or mixed nature.

8. Finally, but important, is the not infrequent occurrence of definite foci of epithelioid cells located in (i.e., "contaminating") certain of the histoid lesions—an unexplained, and inexplicable condition. This tuberculoid involvement is, in my experience, confined to the nodules of subcutaneous location or origin.

RESUMEN

1. Variedad "histoidea" de la lepra lepromatosa aquí discutida se denomina así porque, histológicamente, las típicas lesiones semejan, más bien que el granuloma inflamatorio como es el leproma ordinario, un tumor formado de un solo elemento histoideo

fusiforme. La dolencia se confunde comúnmente con la fibrosis de las ordinarias lesiones lepromatosas.

2. Las lesiones de este género son más susceptibles de encontrarse en los casos antiguos que por años han avanzado como si fueren de la ordinaria lepra lepromatosa, respondiendo al tratamiento, pero más tarde han involucionado o recidivado, manifestando lesiones resistentes a la terapéutica. Son por lo tanto de una especie rara vez observada excepto en los leprosarios, y los enfermos de esos géneros no son susceptibles de despertar suficiente interés para conducir a la obtención de biopsias.

3. La indispensable característica clínica es la formación de nódulos, notablemente subcutáneos, pero también cutáneos. En su modo de crecimiento, los nódulos son primariamente expansibles y por consiguiente suelen estar rodeados por una pseudocápsula derivada del tejido en que se hallan situados. Están bien vascularizados, mas no contienen ramas nerviosas.

4. El parénquima de los primeros nódulos está compuesto exclusivamente de células baciladas fusiformes de naturaleza histiocítica, pero se forma más tarde un "estroma" repartido irregulamente y la proporción del elemento de tejido fibroso dentro de la lesión aumenta con la edad.

5. Otras características histológicas típicas y dignas de nota comprenden el frecuente cambio reaccional, o estivación, de las células parenquimatosts en zonas limitadas de la forma normal de huso a típicos fagocitos redondeados, y la frecuencia de zonas de ablandamiento local (desintegración "reaccional local"), llegando hasta la formación de abscesos," pero conteniendo rara vez esas lesiones leucocitos polinucleares.

6. Bacteriológicamente, la característica más notable y significativa es la falta normal de la formación de globos, independientemente de la abundancia de los bacilos. Su número en el parénquima fusiforme activo suele ser elevado, y en los fagocitos redondeados suele ser sumamente crecido, y a veces hasta increíble. La disposición de los bacilos en conglutinaciones alargadas en las células fusiformes, junto con la existencia de espesas masas redondeadas en las zonas de fagocitos libres, constituye el "hábito histoiideo" de los bacilos, que es notablemente distinto de su disposición en el leproma ordinario.

7. Aparte de las lesiones histoiideas en los cortes de la piel afectada y jamás asociadas con los nódulos subcutáneos, pueden encontrarse zonas de Mikulicz residuales, por lo general pequeñas, que son meramente residuos del ordinario proceso lepromatoso que existió antes. Más raramente, pueden encontrarse, en asociación con las lesiones cutáneas histoiideas activas, infiltraciones más o menos activas del ordinario proceso lepromatoso; estas lesiones infrecuentes son de naturaleza doble o mixta.

8. Por fin, pero importante, tenemos la existencia, que no es rara, de focos bien definidos de células epitelioides situadas en (o sea "contaminando") ciertas lesiones de las histoiideas—situación esta inexplicada, e inexplicable. Esta invasión tuberculoidea se halla, en lo que haya observado el A., limitada a los nódulos subcutáneos en su localización u origen.

RESUMÉ

1. La variété "histoiide" de lèpre lépromateuse discutée dans cet article tire son nom du fait que d'un point de vue histologique la lésion typique ressemble à une tumeur développée à partir d'un élément tissulaire d'une seule espèce, en forme de fuseau, plutôt qu'au granulome inflammatoire qui constitue le léprome courant. Cette condition est généralement prise à tort pour de la fibrose survenant dans des lésions lépromateuses ordinaires.

2. On a le plus de chances de trouver des lésions de cette espèce chez des vieux cas qui, durant des années, ont progressé comme une lèpre lépromateuse ordinaire, répondant à la thérapeutique, mais qui plus tard ont repris, ou récidivé, développant des lésions résistantes au traitement. Dès lors, ce sont des particularités rarement vues sinon en

léproserie, et les malades de cette espèce, dans un tel environnement, ne sont pas susceptibles, semble-t-il, d'éveiller assez l'intérêt que pour mener au prélèvement de biopsies.

3. La particularité clinique essentielle est la formation de nodules, principalement sous-cutanés, mais cutanés également. Leur type de croissance est tel que ces nodules tendent avant tout à se dilater; en conséquence ils sont généralement entourés d'une pseudo-capsule dérivée du tissu où ils sont situés. Ils sont bien vascularisés, mais ne contiennent pas de filets nerveux.

4. Le "parenchyme" des nodules à leur stade le plus précoce est composé uniquement de cellules de nature histiocyttaire, remplies de bacilles, en forme de fuseau, mais à un stade ultérieur se développe un "stroma" fibrocytaire irrégulièrement distribué, et la quantité d'éléments tissulaires fibreux dans la lésion augmente avec le temps.

5. Parmi les autres caractéristiques et particularités notables d'un point de vue histologique, on relève fréquemment, dans des zones limitées, une modification réactionnelle, une activation des cellules parenchymateuses qui de cellules à aspect normal en fuseau se transforment en phagocytes arrondis typiques, ainsi que souvent la formation de régions à structure dissociée localement, (effondrement "réactionnel local"), allant même jusqu'à la formation d'abcès, mais il est rare que de telles lésions contiennent des leucocytes polymorphonucléaires.

6. D'un point de vue bactériologique, la caractéristique la plus frappante et la plus significative est l'absence régulière de formation en globi, sans égard pour la quantité de bacilles. Le nombre de ceux-ci, dans le parenchyme formé de cellules en fuseau en pleine activité, est généralement élevé, et dans les phagocytes ronds les bacilles sont généralement extrêmement nombreux, si nombreux à l'occasion que c'en est incroyable. La disposition des bacilles en amas allongés dans les cellules en fuseau, ainsi que la formation de masses arrondies et denses dans les phagocytes libres, constituent l'"habitus histoiide" des bacilles, qui diffère de manière frappante de leur arrangement dans les lépromes ordinaires.

7. En dehors des lésions histoiides, et jamais en association avec les nodules sous-cutanés, on peut, dans des coupes de peau malade, trouver des zones résiduelles, généralement petites, avec cellules spumeuses, qui représentent simplement les vestiges du processus lépromateux qui a précédé. Plus rarement, en association avec des lésions histoiides actives de la peau, on peut trouver des infiltrats lépromateux ordinaires, plus ou moins actifs; ces lésions peu fréquentes sont de nature mixte, ou double.

8. Enfin, et ceci est important, il n'est pas rare que surviennent des foyers bien définis de cellules épithélioïdes situées dans (on devrait dire "contaminant") certaines des lésions histoiides—ce qui constitue une condition non expliquée et non explicable. Cette participation de nature tuberculoïde est, d'après mon expérience, restreinte aux nodules situés dans le tissu sous-cutané, ou qui y ont leur origine.

(Note: Most of these pictures are from D. Sanchez, one of the first of the histoid cases studied and one with an unusually wide variety of uncomplicated lesions.

REFERENCES

1. DHARMENDRA. Notes on Leprosy. New Delhi: Ministry of Health, Government of India, 1960.
2. DINIZ, O., MARIANO, J. and RABELLO, F. E. Atlas de Leprologia. Rio de Janeiro: National Service of Health Education, 1960.
3. EWING, J. Neoplastic Diseases. A Treatise on Tumors, 4th Ed. Philadelphia and London: W. B. Saunders Company, 1942, p. 33.
4. MALLORY, F. B. The Principles of Pathologic Histology. Philadelphia and London: W. B. Saunders Company, 1914, pp. 283 and 285.
5. WADE, H. W. A modification of the Fite formaldehyde (Fite I) method for staining acid-fast bacilli in paraffin sections. Stain Tech. **32** (1957) 287-292.
6. WADE, H. W. Zenker vs formalin fixation for the histopathology of leprosy tissues, and other desirable features of technique. Internat. J. Leprosy **30** (1962) 477-488.