

SPECIFIC AFFECTIONS OF THE FOLLICULAR APPARATUS OF THE SKIN IN LEPROSY¹

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In the examination of leprosy patients my attention has been arrested by a peculiar affection of the follicular structure of the skin that, so far as known to me, has not been described heretofore. In Klingmüller's exhaustive review of leprosy (4), which comprises the world's literature up to 1930, there are no indications that this condition has been recorded. Among the reports on leprosy that have appeared since 1930 I have not found one that refers to it.

In examinations of patients with skin lesions of leprosy the presence of the generally known specific manifestations is noted, manifestations which are responsible for the extreme heterogeneity and diversity of the clinical picture. Among them are different kinds of macules—erythematous, pigmented, depigmented. On the background of these macules striking follicular changes are frequently observed. Thus Henderson described five kinds of such lesions. Besides them there are observed different kinds of infiltrations—marginated and diffuse—as well as leprous nodules, often found together; these can be differentiated from one another by their appearance, which is related to their duration.

More detailed examination of the skin of some patients has disclosed, besides the presence of other elements, small follicular spots, varying in size from that of the head of a pin up to that of a millet seed, that are usually of yellow or yellowish-brownish color though sometimes they are more reddish. Only a smaller part of them, those that are located at the periphery of the affected areas, retain hairs in the centers; as a rule they do not have hairs and, indeed, even the follicular opening may be absent (Plate 16, fig. 1). A characteristic of these follicular spots is superficial atrophy. The epithelium is thin and forms fine wrinkles on lateral pressure, and because of atrophy the spots appear sunken in comparison with the surrounding surface. They are not perceptible on palpation.

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They do not show any character of inflammation; they are hardly noticeable and are only discovered on detailed examination (Plate 16, figs. 2 and 3).

Having become interested in these small lesions, I have made histological examinations of pieces of skin removed from four patients, in order to ascertain their nature. These specimens were taken from the region of the shin-bone and the hip. The microscopic examinations showed the following changes:

The epithelium is somewhat thinner than normal and of atrophic appearance, and the papillary outgrowths of the epithelium are poorly defined. The horny layer is composed of a small number of loosely-laid plates, the stratum granulosum of a series of cells with dark-colored nuclei, the stratum spinosum of several series of cells of usual appearance; the cells of the stratum germinativum are in palisade arrangement, perpendicular to the corium. Here and there are remnants of hair follicles, in the form of epithelial protuberances. The region of the atrophic follicular remnant is lower than the common level of the epidermis.

Immediately under the epithelium is a zone of connective tissue which is free from specific changes. This layer is bordered by a large number of cell accumulations which are of different forms and in general of insignificant size. These infiltrations are at times rounded, at times elongated in form. They are separated from each other by quite wide zones of connective tissue, which is unchanged in appearance. In several places the infiltrates merge into each other to form larger accumulations.

These cellular infiltrations are composed of various cells. The principal ones are large, rounded, and with pale-staining vesicular nuclei. On staining with Sudan III one finds in their cytoplasm lipoid inclosures of different sizes that are characteristic of the Virchow cells. Occasionally these lipoid bodies contain vacuoles of different sizes, which frequently lie close to one another and are notable for their brown borders. On staining for lepra bacilli numbers of them appear in these cells. The bacilli are conglomerated together like packages of cigars, or lie in small groups or individually. Finally, one also finds broken rods and bacillary granules.

Besides the histiocytes and lepra cells, there are present large numbers of small round cells with dark nuclei and very little cytoplasm (lymphocytes). Fibroblasts are also present.

In the deeper layers of the cutis remnants of sweat glands are found. Around them are large specific infiltrations of characteristic structure. In some places one finds, in the depth of the corium bordering the subcutaneous tissue, leprous infiltrations of considerable size. No sebaceous glands or remnants of them and no hair follicles were found in any of the preparations. Only in the peripheral layers of the corium are there bundles of smooth muscle fibers.

The absence of hairs in the affected places and the existence of skin atrophy is confirmed by the microscopic findings. The outgrowths mentioned in the description of epithelial changes represent rare remnants of the markedly atrophied follicular struc-

tures. The histologic findings, which were quite similar in all four cases, prove that the manifestations mentioned are really of leprous nature, caused by the local development of the leprous infiltration, and permit the conclusion that the clinically similar condition seen in other patients is of the same nature.

Contrary to Klingmüller's assumption that degeneration of the hair follicles appears only in advanced stages of the formation of the leprous granuloma, my investigation shows that that change occurs relatively early, while as yet no typical granulomata are evident to the naked eye. The infiltrations begin to develop around the follicular vessels, as has been observed by Lie, and rapidly lead to falling out of the hairs and destruction of the follicles, which is observable clinically as well as histologically.

After the leprous character of the follicular spots was established, an effort was made to ascertain how often this manifestation of leprosy occurs and in what forms, what changes they undergo and how soon they disappear under the action of treatment with derivatives of chaulmoogra oil. Of the available 249 patients under treatment such lesions were found in 85, or 33.3 percent. The figures are given in Table 1, from which it appears that they are somewhat more common in women than in men.

TABLE 1.—*Frequency of follicular spots.*

Sex	Cases	Spots present	Spots absent
Male.....	149	47 (31%)	102 (69%)
Female.....	100	38 (38%)	62 (62%)
TOTAL.....	249	85 (33%)	164 (67%)

Duration of the disease seems not to have any special importance in connection with this manifestation of leprosy (Table 2). Up to 20 years approximately the same proportions of patients show it, namely, about one-third.

Data regarding the relation of this condition to the type and degree of advancement of the disease are given in Table 3. It is to be seen that such changes are observed most frequently in the moderately severe lepromatous and mixed forms. In the least marked cases (L1) they were found in only one-third (10 out of 30)—also, it is to be noted, in nearly the same proportion in the L3 group (11 out of 29)—but in the medium group (L2) it was more frequent (in 64 out of 151 cases, or 42 percent). In this intermediate period of leprosy of the skin, that of generalization, the

TABLE 2.—Relation of duration of the disease and occurrence of follicular spots.

Duration	Cases	Spots present	Spots absent
0-5 years.....	33	13 (39%)	20 (61%)
6-10 years.....	68	26 (40%)	42 (60%)
11-15 years.....	80	30 (37%)	50 (63%)
16-20 years.....	37	12 (32%)	25 (68%)
21-25 years.....	17	3 (18%)	14 (82%)
Over 25 years.....	14	1 (7%)	13 (93%)
TOTAL.....	249	85 (33%)	164 (67%)

strongly-defined progressive infection constantly attacks new regions, whereas in the more advanced stage there occur deeper changes—destruction and ulceration—in the already present lesions. It is in the medium stage of the lepromatous condition that the follicular apparatus, which is the starting point of the leprous granuloma in the skin, shows most frequently the clinically evident change here described. It is noteworthy that it was not found in any of the 39 neural cases examined.

These follicular lesions do not occur with equal frequency on all parts of the body. The distribution in the 85 cases that had them was: shin only, 5 cases; hip only, 21 cases; shin and hip, 35 cases; upper and lower extremities, 14 cases, upper and lower

TABLE 3.—Relation of type and degree of advancement of the disease to the occurrence of follicular spots.

Type	Cases	Spots present	Spots absent
L1.....	6	4	2
L1-N1.....	7	2	5
L1-N2.....	10	3	7
L1-N3.....	7	1	6
L2.....	12	6	6
L2-N1.....	13	5	8
L2-N2.....	70	32	38
L2-N3.....	56	21	35
L3-N1.....	3	1	2
L3-N2.....	15	7	8
L3-N3.....	11	3	8
N1.....	1	0	1
N2.....	9	0	9
N3.....	29	0	29
TOTAL.....	249	85	164

extremities and body, 10 cases. The part most commonly involved is, therefore, the lower extremity; the condition was present there in all of the affected cases, and found only there in 61 of them, about two-thirds of the whole. The upper extremities were involved in 24 cases, the trunk in only 10.

This distribution of the lesions, the presence of which indicates the existence of the specific leprous process in the regions affected, changes our ideas of the distribution of that process. It is also important in the type diagnosis of cases under the international classification. A considerable number of the cases investigated, which had been called L1, L1-N1, L1-N2 or L1-N3, had to be considered moderately advanced lepromatous leprosy and mixed leprosy.

In a series of cases it was possible to observe the further progress of these spots. Frequently their color acquires a more intense yellowish-brownish tone, often quite copperish, and they become elevated above the surface of the surrounding skin. In these cases the condition reminds one very strongly of the so-called goose-flesh. On palpation, tiny elevations of thick consistency are felt (Plate 17, fig. 4). When the patient disrobes in a cool room the lesions acquire a livid color, increasing the similarity to *cutis anserina*. Contrary to that condition, however, these lesions are permanent; because of the absence of hair they are not dependent upon the pilomotor reflex; their color is variable because of admixture with clearly defined yellow; finally, the affected areas are sharply defined, in contrast to *cutis anserina*. Histologic examination of lesions in this stage reveals the following:

The epithelium is markedly atrophied and considerably thinner than in the preparations of the previous cases described. The horny layer is composed of several layers; the stratum granulosum consists of a row of cells with deeply staining nuclei; the stratum spinosum is composed of two or three rows of cells; the basal layer is flattened; and the papillary outgrowths of the epithelium are absent. The relief of the surface of the epidermis is changed—a quite steep elevation (miliary papulation) is present, due to the infiltration in the corium. In the outermost layer of the cutis, immediately below the subepidermal zone that is free from involvement, is a quite large infiltration of specific structure with Virchow cells that contain lipoids and lepra bacilli.

In several patients there were found areas of skin that showed miliary lepromas and leprous granulomata of considerable size, in addition to the follicular spots. Here there were transitional forms of the spots, varying from the size of a millet seed up to the usual lepromatous nodules.

It is of interest to mention that in treating cases with methylene blue by Montel's method, in which treatment only the infiltrated leprous granulomata become colored, it was observed that the dye was taken up by these transitional lesions and also by some of the follicular spots themselves.

On the basis of the results of the histologic examinations we may speak of the presence of miliary lepromatous granulomata in such cases. Some lesions of that nature were found to enlarge, acquiring a hemispherical form and undergoing conversion to small leprous papules of the size of millet seeds and of typical appearance. Thus it is seen that the follicular spots form the starting points of leproma formation, such lesions later attaining considerable size and acquiring a characteristic clinical appearance.

One of the development forms of the leprous follicular spots is apparently the seldom-recorded lichenoid form of the leprosy that has been described by Archibald (1), Tschernogubow and Pawlow (5), Chavarria and Barrera (2) and Gonzalez Urueña (3).

Though, as described, some of the follicular spots may become infiltrated, others remain for an indefinite time without undergoing notable changes. It is interesting to note that these lesions yield to treatment. It has been observed that, after the disappearance of the leprous granuloma, the follicular spots persist for a long time, but ultimately they disappear.

CONCLUSIONS

The observations here recorded permit of the following conclusions:

1. The follicular structures of the skin are quite frequently involved in leprosy (33 percent of cases) by specific processes in the form of follicular spots.
2. This leprous manifestation appears clinically as yellowish-brown, somewhat sunken follicular spots with atrophic epithelium. Histologically there is found a specific granuloma with lepra cells and bacilli, which lesion rapidly destroys the hair follicles and the hairs.
3. The skin of the lower extremities is principally attacked.
4. The follicular lesions described form starting points for the formation of leprous granulomata.

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DESCRIPTION OF PLATES

PLATE 16

FIGS. 1-3. Yellowish-brownish follicular spots of pin-head size in different regions of the body.

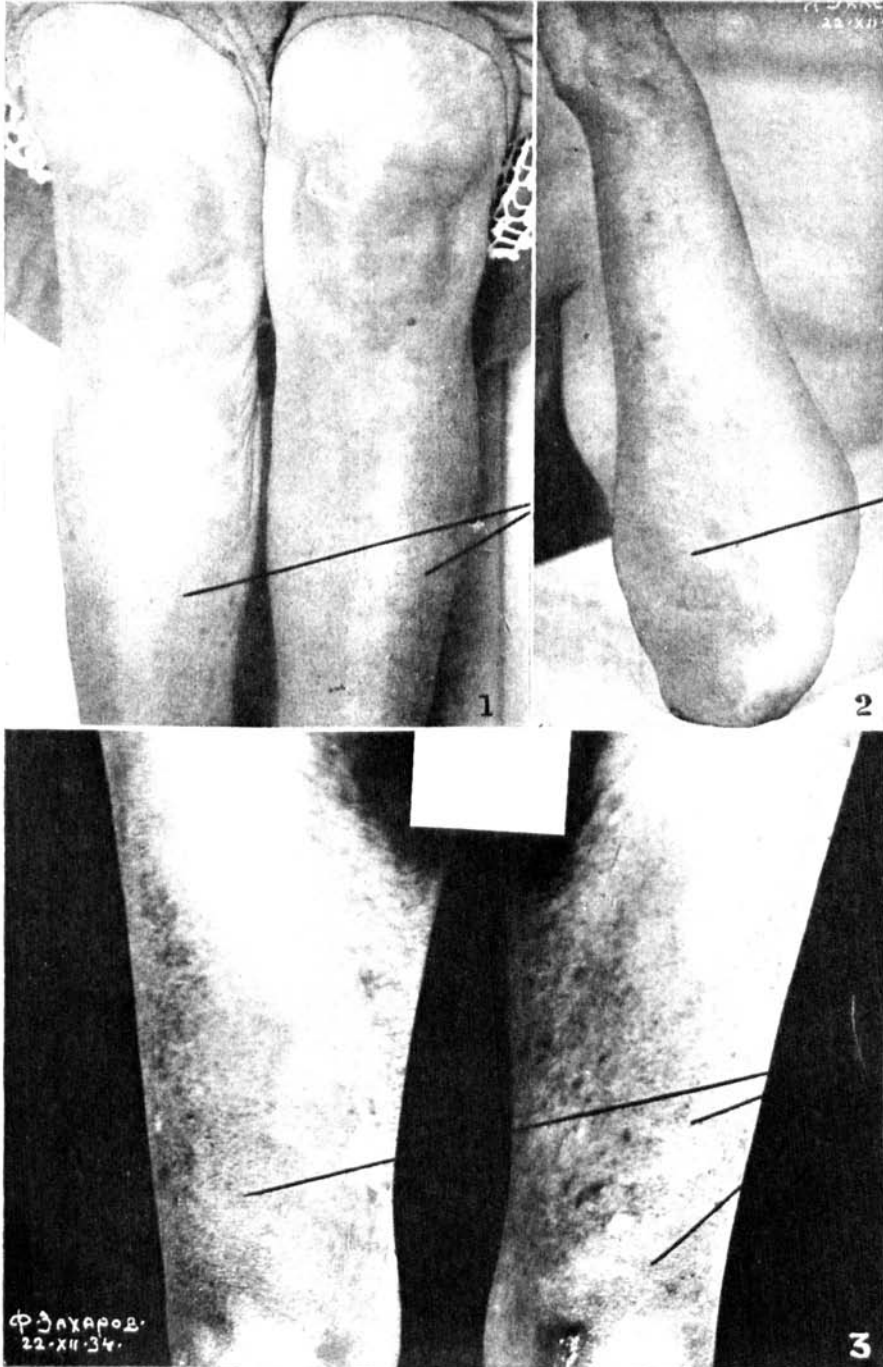


PLATE 16

PLATE 17

FIG. 4. Leprosy with small nodulations, resembling strongly cutis anserina ("goose-flesh").

FIG. 5. Photomicrograph of a small nodule from the patient shown in Fig. 4. Typical leprous granuloma.

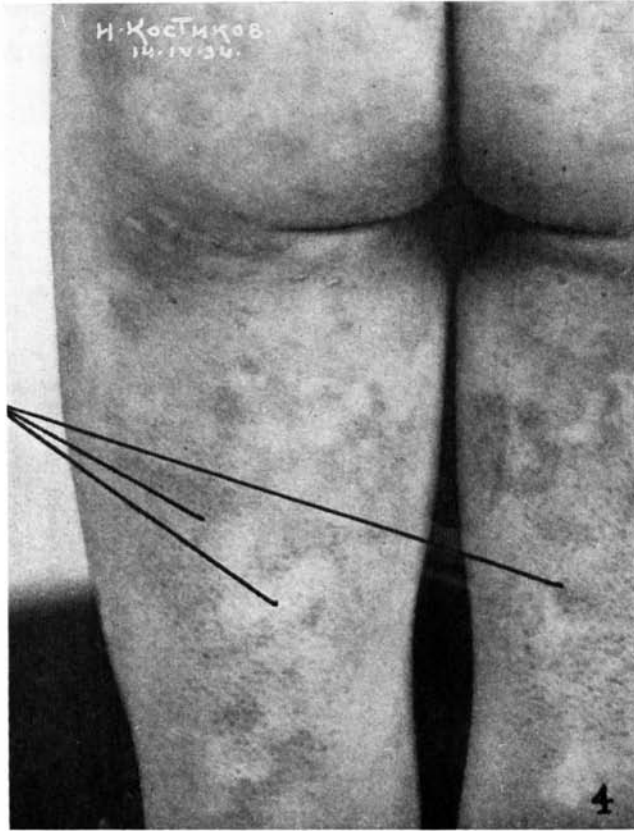


PLATE 17