BONE LESIONS IN LEPROSY[1]

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A valid estimate of the incidence of bone changes in leprosy which is broadly applicable is not possible at present. X-ray studies are essential for the detection of minimal damage, and they have been limited in number and in scope. Even clinical surveys, without x-rays, have dealt for the most part with institutional and other selected groups, rather than with representative samples of all leprosy cases in an area. Institutional patients always include an excessively large proportion of those with advanced disease and disablement.

That bone lesions may be present in a considerable proportion of all who are affected with leprosy is, however, well established. From their sampling survey in the Ryukyus, Doull and Kluth ([16]) estimated that of the lepromatous patients 15 per cent had lost part or all of one or both hands, and 13 per cent part or all of one or both feet. Among the nonlepromatous patients, the comparable figures were 22 per cent for the hands and 25 per cent for the feet. The very high proportions that have been found in x-ray studies in some institutions likewise indicate the importance of the problem. Murdock and Hutter ([37]) found some type of pathology of the hands and feet demonstrable by x-ray in 50 per cent of 140 patients at the Kalihi Hospital, Honolulu; Faget and Mayoral ([20]), in 29 per cent of 505 patients at the Public Health Service Hospital, Carville, La.; Esguerra-Gomez and Acosta ([19]), in 68 per cent of 483 patients in the Agua de Dios leprosarium in Colombia; Paterson ([39, 40]), in 34 per cent of 116 selected patients at the Christian Medical College, Vellore, India; Karaseff ([26]), in 95 per cent of 77 patients in an institution near Irkutsk; and Chardome and Lechat ([10]), in all but 10 of 128 patients in an initial study at the Yonda leprosarium in the Congo. Many other authors might be cited, but it is amply evident that bone involvement is a serious and probably universal feature of leprosy.

Our knowledge of the pathogenesis of the bone lesions of leprosy is very unsatisfactory, because there have been few studies in which clinical, x-ray and pathologic data have been correlated. Two varieties may be distinguished: (*a*) specific leprous osteitis, caused by invasion of the bones by *Mycobacterium leprae;* and (*b*) nonspecific leprous osteitis, in which the fundamental cause is damage to or destruction of the nerves supplying the affected parts.

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A. SPECIFIC LEPROUS OSTEITIS

Satisfactory evidence of a specific process is the presence in the bone of a leprosy patient of granulomatous tissue containing acid-fast bacilli that cannot be cultivated. Few reports meet these criteria. Murdock and Hutter mentioned infection carried to the bones by the vascular supply and stated that marked destruction and cystic degeneration may follow. "Curretings from such a lesion have been found teeming with acid-fast bacilli." They termed the condition "osteitis leprosa multiplex cystica." Faget and Mayoral found, in 160 lepromatous cases, 9 instances of bone involvement. In 4 there was enlargement of the nutritive canals of the phalanges; in 3 there was cyst formation. Aspiration of these cysts revealed acid-fast bacilli. Such cysts are usually multiple (Fig. 1) and are more frequent in lepromatous than in nonlepromatous patients. They were observed by Erickson and Johansen ([18]) and by Lechat and Chardome ([30]) to heal sometimes under sulfone therapy.

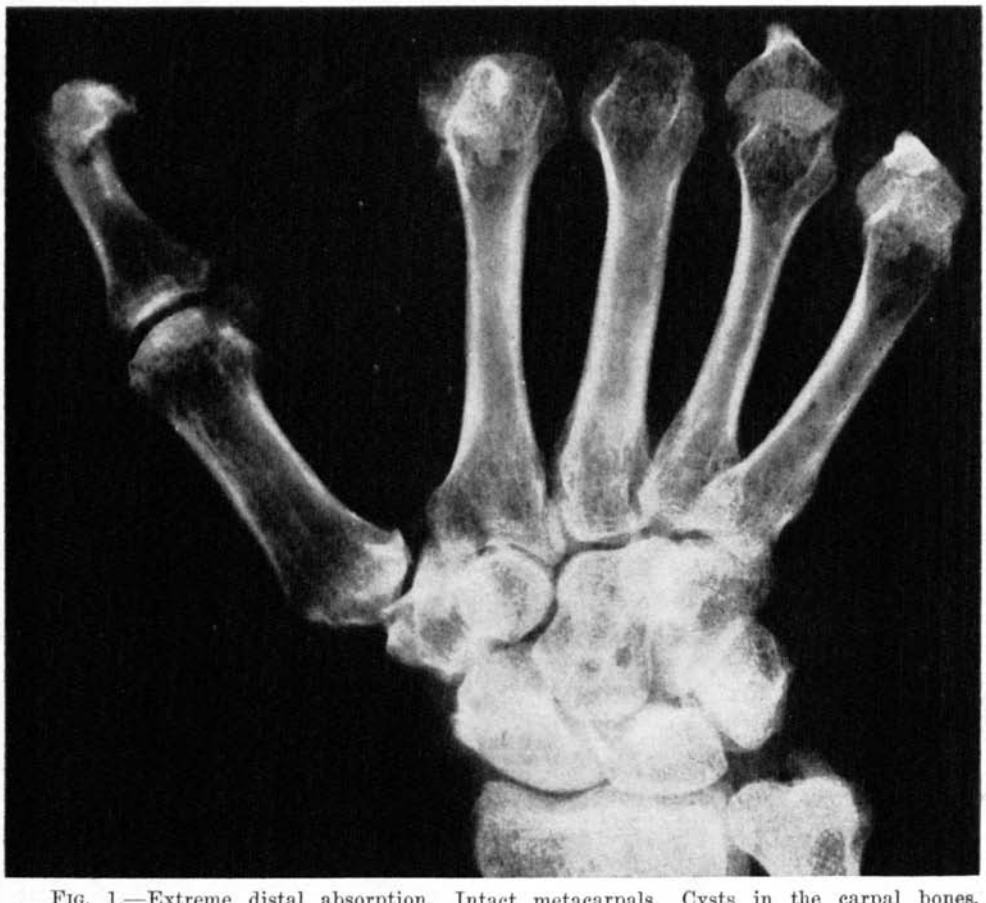

FIG. 1.—Extreme distal absorption. Intact metacarpals. Cysts in the carpal bones. (Lepromatous patient who had the disease for 14 years; arrested for 4 years.)

Acid-fast bacilli have been found by others in the bone marrow ([5,24]). Gass and Rishi ([23]) studied bones removed at operation or obtained at autopsy in 69 cases. The bones included metatarsals, radius, ulna and tibia. Of 21 "cutaneous" (i.e., lepromatous) cases, 17 were positive for bacilli; of 48 "neural" cases, none was positive. Acidfasts have also been found in marrow from the sternum ([6]).

Certain radiologic lesions have been assumed to be specific because they were observed chiefly in the lepromatous type. Periostitis, for example, has been reported in the absence of ulceration, and it may be such a manifestation ([24,38,45]).

Absorption of the anterior nasal spine deserves special attention. Absorption of nasal bones was noted by x-rays in one case by Colombier back in 1914 ([13]). More recently Møller-Christensen ([34-36]) has found absorption of the nasal spine in many skulls, associated with typical changes in the hands and feet, in skeletons excavated in a Danish cemetery near the site of an ancient lazaret. X-ray studies by Melsom ([32]) and by Michman and Sagher ([33]) and a few autopsy findings by Waaler ([47]) are in agreement regarding the leprotic origin of this lesion. A radiologic study by Lechat and Chardome ([29]) of 96 patients in the Congo also gives support to the theory that this lesion is of lepromatous origin. It was found in 78 per cent of 64 lepromatous cases, but it was also found in 22 per cent of burnt-out cases that could not be classified definitely in retrospect but which had no record of positive bacteriology. It was related in most instances to severe lesions of the nasal mucosa.

Mention should be made also of osteochondritis deformans of the fingers described in the lepromatous type during acute reaction ([8,9,26]). This lesion, which is accompanied by painful swelling of the fingers. has been well studied by Paterson in India ([39]) and has been observed by me in a few cases in the Congo. It is characterized by pseudocyst formation in the phalanges, collapse of the articular surfaces, and joint-cupping deformities resulting in the radiologic picture known as "twisted fingers." Acidfasts have been observed in biopsies of bone ([39,41]).

B. NONSPECIFIC LEPROSY OSTEITIS

Nonspecific osteitis is very much more common than the specific kind, occurring in both types of the disease. Evidence of nerve damage can always be detected, such as anesthesia, muscular weakness and vasomotor disturbances.

To help in the clarification of nonspecific osteitis, I would tentatively propose a mechanistic classification which is in harmony with the established facts and with radiologic observations.

1. Bone lesions of hands and feet associated with anesthesia and

with evidence of interference with the dynamics of the blood vessels: Distal absorption.

2. Bone lesions of the walking foot associated with anesthesia and with displacement of the supporting parts of the plantar arch: Metatarsophalangeal osteoarthritis.

3. Bone lesions of the hands and feet associated with anesthesia and secondary infection: Secondary osteomyelitis.

4. Bone lesions associated with anesthesia and disuse: Osteoporosis, These several types of damage may be present in the same patient and even in the same limb.

1. *Distal absorption.*—Distal absorption, or acroosteolysis, begins by notching of the tufts in the terminal phalanges. It is often bilateral, but rarely symmetric as regards location or stage of development. It occurs in both lepromatous and tuberculoid types. Barnetson ([4]), who studied the histologic pictures in 5 cases, noted that fraying of the tuft was associated with breaks in continuity of the cortical bone, the gaps being filled by connective tissue which extended from periosteum to marrow. The shaft undergoes gradual absorption, and when the bone disappears the process is continued in the proximal bone. The metacarpals are seldom involved, even when the process becomes advanced (Fig. 1). A curious feature was noted by Barnetson, namely, that osteoclastic activity, the generally accepted mechanism for bone absorption, was rarely seen in the histologic sections. The evolution of the absorptive process in the terminal phalanges of the hands is illustrated in (Fig. 2).

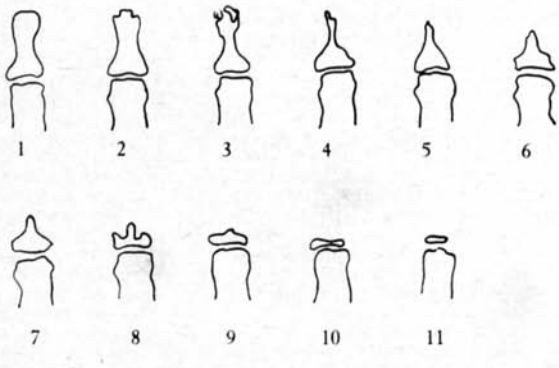

FIG. 2.—Diagrammatic representaiton of successive stages of absorption of distal phalanx of the fingers.

Several theories have been proposed to explain distal absorption ([25,38]). Practically all leprologists emphasize "neurotrophic atrophy." The meaning of this term is not altogether clear. The possible role of vascular changes is discussed later.

Paterson has suggested the interesting hypothesis that bone absorption in leprosy is caused by infection of anesthetic digits. "It is the soft tissue infection that gives rise to the absorptive type of leprosy."

Infection releases and activates the absorptive process. This assumption is important, because it determines the measures to be undertaken for the prevention of disabilities.

It has been generally accepted by leprologists that there is a close relationship between anesthesia and distal absorption. In a study of 284 hands in the Congo, I found ([28]) that the two phenomena were positively associated. Nevertheless, there were some cases of dissociation, suggesting a common factor in their background rather than a causal relationship between anesthesia and absorption or vice-versa.

If soft-tissue infection due to wounds is responsible for bone absorption, the right hand, which is more exposed to injury, would be expected to show earlier and more extensive absorption than the left. Also, certain fingers should exhibit more absorption than others. A study of 169 patients in the Congo revealed that the absorption in the right and the left hands were of equal importance. In 285 hands, the observed frequency of involvement of the various fingers did not differ significantly from the expected frequency as calculated from the entire experience.

The etiology of distal absorption seems to be more complex than is provided for by the infection theory. The occurrence of soft tissue infection in a high proportion of cases does not necessarily establish a causal relationship. Before far-reaching conclusions can be drawn the frequency of absorption in otherwise comparable patients without infection must likewise be studied. No report of such a comparison has as yet appeared.

Similarities between Raynaud's disease and leprosy with respect to the radiologic aspects of bone absorption suggest that some peripheral vascular disturbances may play a part in bone damage of leprosy.

It has been observed that the skin temperature in the fingers of leprosy patients shows large irregularities ([31]). In a preliminary study of the differences in temperature between pairs of fingertips in 110 patients in the Congo, I found that the variations between healthy pairs of adjacent or corresponding fingers was somewhat less than that between pairs of mutilated fingers. Further study of this point should be of interest, as for example that of S. N. Chatterjee ([12]).

Reflex vasodilatation, after immersion of the other limb in hot water, has been found to be slow or absent in leprosy patients ([3]). Morphologically, Fite ([21]) has reported lesions of the blood vessels, but only in the lepromatous type. Capillaroscopy has shown ([2,7,43]) a diminution in the number of capillaries; those persisting are of irregular size, shape and course, especially in patients affected with anesthesia and mutilations.

Arteriography of the extremities, performed on leprosy patients *in vivo* or postmortem, has shown a narrowing of the arteries in the lepromatous type of the disease ([20]) and in the presence of perforating ulcers ([42,46]). Paterson, studying 12 patients, has observed that the

terminal vascular nets are not filled in the areas of bone resorption.

Serial arteriography performed on 50 patients by Chardome and Lechat ([11,28]), 12 on the hand and 38 on the foot, demonstrated two types of lesions: (*a*) Communications between arteries and veins revealed by the existence of many tiny anastomoses, acceleration of the circulation, and early venous filling; and (*b*) obstruction of the small arteries with consequent loss of opacity in peripheral areas, slow circulation, and prolonged venous return.

Vascular alterations, however, may extend farther than the mutilations and reach either the undamaged neighboring fingers or the roots of partially absorbed fingers. Although the observations that have been cited deal only with peripheral vessels, it is logical to assume that if the nutrient vessels of the bone could be examined similar changes would be found.

The hypothesis has been advanced that absorption of bone occurs when the nervous mechanism controlling vasoregulation in the skin is interfered with. The terminal vascular system is no longer able to adapt the flow of the peripheral blood, especially following repeated but perhaps minor traumatism. Such a relationship does not constitute an explanation, unless we can describe (1) the mechanism by which a disturbed peripheral circulation might affect absorption, and (2) the basic mechanism of interference with the circulation. .

We know that the functioning of the terminal sympathetic system is definitely abnormal in leprosy patients. Arnold ([1]) has described the lack of pilomotor response after intradermic injection of nicotine picrate. The Pavlov test ([41])—intravenous injection of nicotinic acid—may reveal latent macules in the skin. A lack of the triple response of Lewis after histamine is to be seen in anesthetic areas ([44]). The existence of a dissociation between the histamin reaction and anesthesia

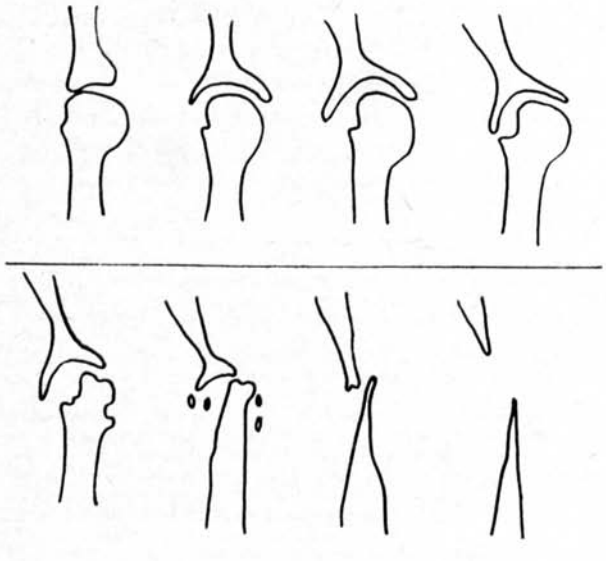

FIG. 3.—Destruction of the adjacent bones in particular during evolution of metatarsophalangeal osteoarthritis; absorption in the proximal end of the phalangeal bones as opposed to the distal end.

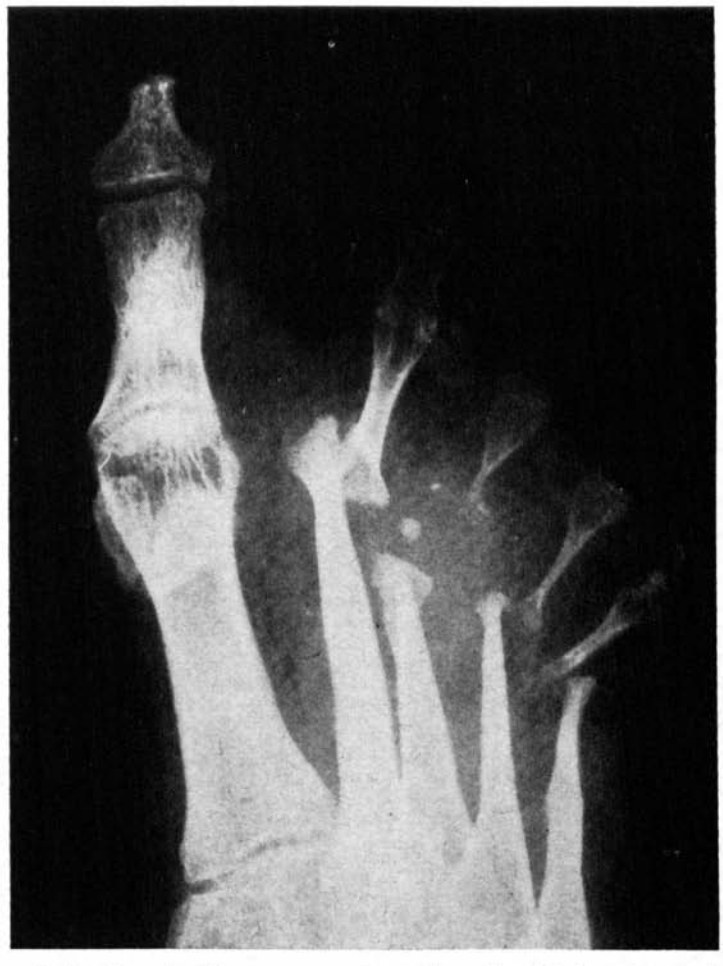

FIG. 4. Metatarsophalangeal osteo arthritis.

has been emphasized in borderline cases by Convit, Sisiruca and Lapenta ([14]). These facts suggest that disturbance of the tonus exercised by the sympathetic fibers on the peripheral vessels should be taken into account in studying abnormalities of the terminal circulation in leprosy patients. It would be helpful to obtain more data concerning the histopathologic changes in the sympathetic nerves innervating the peripheral vessels of the extremities.

It is not established that sulfone treatment can slow down the process of distal absorption. Erickson and Johansen ([18]), in a group of 82 patients followed for 1½ to 5 years, noted that a further progression of atrophic bone absorption probably occurs.

In my own study in the Congo an attempt was made to determine the rate at which the phalangeal bones of the hand became involved before and after sulfone treatment. The data relate to the x-ray findings, in two examinations, on 1,092 phalangeal bones (39 patients with 28 bones each). The average interval between the examinations was 2.7

years. A linear graph was drawn connecting these frequencies. This line was then projected backwards 3.6 years to the date at which, on the average, sulfone treatment had been commenced. The slope of this line was taken to represent the rate of bone involvement during treatment. At the commencement of treatment there were estimated to have been 783 intact bones; at the second x-ray examination there were 694. That is, 89 bones are assumed to have become involved in 6.3 years (3.6 + 2.7), or 14 per year. The estimated average date of onset of leprosy in these cases was 8.8 years before the commencement of sulfone treatment. All bones were assumed to have been intact at the date when the first recognized signs of the disease appeared. From that date until the commencement of sulfone therapy, when 309 bones (1,092 — 793) were estimated to have been affected, it was calculated that involvement had taken place at the rate of 35 bones per year—a much higher rate than that during therapy. These results are only suggestive; prospective studies are required to determine the value of sulfones in arresting the absorptive process.

2. *Metatarsophalangeal osteoarthritis.*—In the feet, absorption of the phalanges and metatarsal bones often begins in the metatarsophalangeal joints. This process therefore differs from a true distal absorption. Repeated radiographs made on patients in the Congo at intervals of from 7 to 48 months, and comparison of the various aspects in more than 200 patients, permit a tentative description of the evolution of this lesion and of its various modifications. A possible sequence in the transition is shown diagramatically in Fig. 3.

Although the peculiar aspects of this kind of bone absorption have been emphasized ([9, 15, 26]), metatarsophalangeal osteoarthritis has nevertheless been confused with distal absorption. Arguments in favor of its individuality are: the peculiar beginning of absorption in the proximal as opposed to the distal end of the bone, the lack of a positive association between distal absorption proper and osteoarthritis in the same foot, and the association with enlargement of the nerve tranks ([28]) which is not observed in distal absorption (Fig. 2). Certain facts suggest that trauma plays a definite role in metatarsophalangeal osteoarthritis, such as the restriction of the lesions to the feet except in those crippled patients who walk on all fours, and the more frequent involvement of joints on the outer side of the foot in patients who walk barefooted, and of joints on the inner side in those who wear sandals ([27, 45]). Displacement of the supporting structures of the plantar arch, following muscular paresis or paralysis, is an invitation to trauma at a site where the loss of sensitivity has impaired the reflex response to injury.

This assumption of a neuromuscular mechanism would be strengthened if we could demonstrate paralysis of the muscles of the legs in patients with osteoarthritis. Chronaximetry, i.e., the measure of the time that a current twice the rheobasic (galvanic threshold) intensity

must flow in order to excite the tissue being tested, seems a good tool for this purpose. In a group of 53 patients without bone damage, or with various types of lesions (28), gross anomalies of chronaxy were found in the legs of 35, confirming the previous observations of Freitas

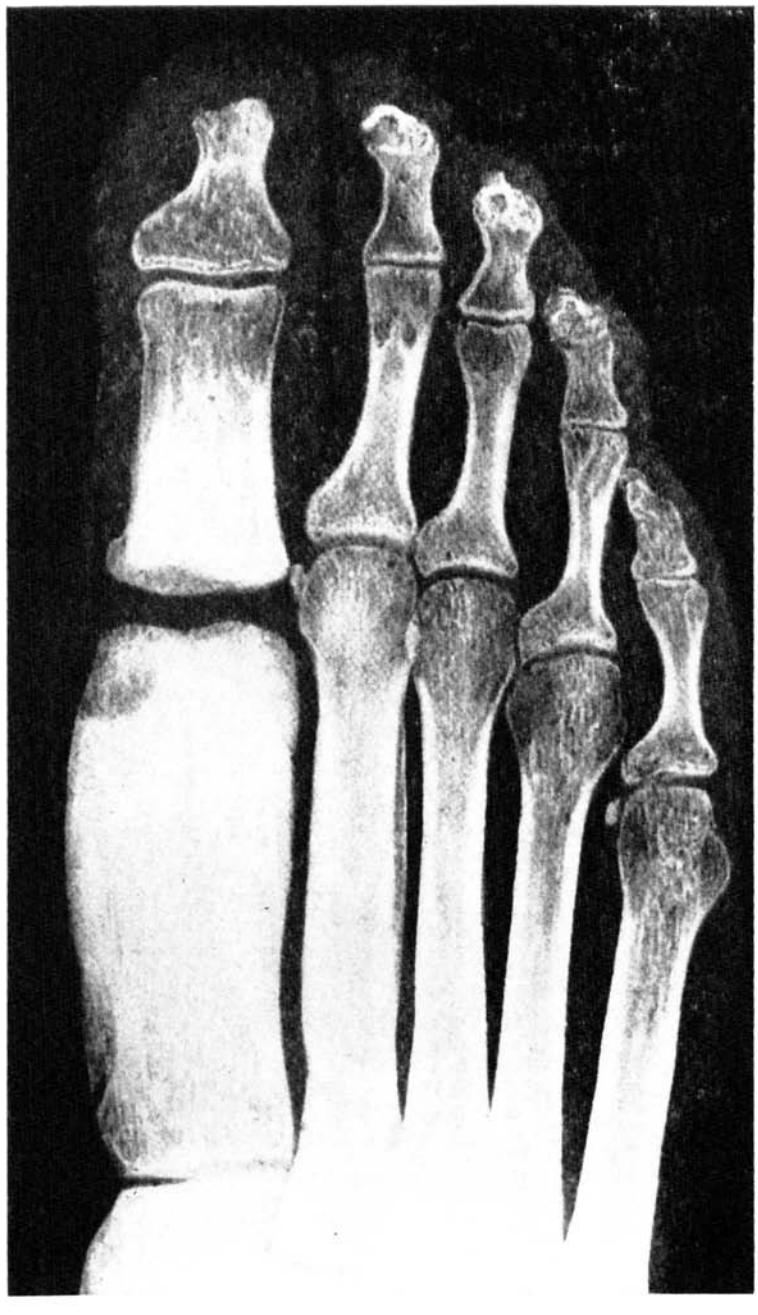

FIG. 5.—Secondary osteitis of the great toe, with history of corresponding ulceration.

Juliao ([22]) and of Dubois and Radermecker ([17]). It has not been possible, however, to relate those abnormal values to the type of bone lesions, or even to the presence of mutilation.

3. *Osteitis and hyperostosis.*—In patients with plantar ulcers, we find rough and nonsystematized lesions of osteitis characterized by decalcification, periostitis, sequestrum formation and hyperostosis. The topographic correspondence between ulcers and osteitis is not very close, except for osteitis adjacent to the first metatarsophalangeal joint which sometimes follows ulceration of the great toe (Fig. 3). Osteitis of the fingers can be found in patients with infection of the soft tissues. Hyperostosis in leprosy is always associated with secondary infection.

4. *Osteoporosis.*—The condition known as osteoporosis is sometimes found in leprosy. Radiographs show in the early stages a reduction in the number of trabeculae, and later a thinning of the inner layers of the cortex. Osteoporotic changes are associated with disuse. There is apparently no peculiarity about the form observed in leprosy but, for the present, because of the association with anesthesia it is included with nonspecific leprous osteitis. Much further study of the condition is needed. A point of special interest is the possible occurrence of osteoporosis in clawhand, in which the bones are often intact.

SUMMARY

Enough is known of the occurrence of bone damage in leprosy to establish it as a serious and probably very frequent complication. For practical purposes although, other bones may be involved, the principal problem relates to the small bones of the hands and feet.

Two general kinds of bone damage are recognized: specific leprous osteitis, caused by invasion of the bone by *M. leprae,* and nonspecific leprous osteitis, in which the basic cause is damage or destruction due to invasion by *M. leprae* of the nerves supplying the extremities. The latter is nonspecific in the sense that the osteitis is not a direct result of invasion of the bone by the leprosy bacillus.

From the mechanistic point of view, nonspecific osteitis may be tentatively classified as:

1. Distal absorption, in which vascular disturbances and/or secondary infection in the anesthetic extremity play a role;
2. Metatarsophalangeal osteoarthritis, which is associated with repeated injury of an anesthetic site following displacement of the supporting structures of the plantar arch;
3. Osteitis, which is a sequel to ulceration and secondary infection; and
4. Osteoporosis, which follows disuse.

There is a need for more extensive sequential studies, correlating clinical, x-ray and histopathologic data. It would be useful and enlightening to have such studies carried out in several widely separated parts of the world.

RESUMEN

Conócese lo suficiente acerca de la aparición de lesiones óseas en la lepra para establecerlas como complicación grave y probablement muy frecuente. Para fines prácticos, aunque pueden afectarse otros huesos, el problema principal se enlaze con los huesecillos de las manos y los pies.

Están reconocidas dos clases generales de lesiones óseas: osteítis leprosa específic ocasionada por la invasión del hueso por el *M. leprae;* y osteítis leprosa anespecífica, en la que la causa fundamental es el daño o destrucción debidos a la invasión por el *M. leprae* de los nervios que sirven los miembros. La última es anespecífica en el sentido de que no es resultado directo de la invasión del hueso por los bacilos leprosos.

Desde el punto de vista mecánico, cabe clasificar tantativamente la osteítis anespecífica como:

1. Absorción distal, en la cual desempeñan un papel los trastornos vasculares y/o la infección secundaria en el miembro anestésico;
2. Osteoartritis metatarsofalangiana, que se vincula con el repetido traumatismo de un sitio anestésico consecutivamente al desplazamiento de los tejidos de sostén del arco plantar;
3. Osteítis, que es una secuela de la ulceración y la infección secundaria; y
4. Osteoporosis, que sigue al desuso.

Se necesitan estudios secuenciales más extensos, que correlacionen los datos clínicos, roentgenológicos e histopatológicos. Resultaría útil e instructivo el llevar a cabo estos estudios en varias regiones muy apartadas del mundo.

RESUMÉ

Ce que l'on said des mutilitations dans la lèpre suffit pour affirmer qu'il s'agit là d'une complication sérieuse, et probablement fort fréquente. Quoique d'autres parties du squelette puissent être atteintes, ce sont, pour des raisons pratiques, les petits os des mains et des pieds qui posent le problème le plus grave.

On admet qu'interviennent deux grands types de lésions osseuses: l'ostéite lépreuse spécifique, due á l'invasion de l'os par *M. leprae* et l'ostéite lépreuse non spécifique, dont la cause lointaine réside dans l'attaque ou dans la destruction par *M. leprae* des nerfs desservant les extrémités. Ce dernier type de lésions est non spécifique en ce sens que l'ostéite n'y apparaît pas comme le résultat direct de l'invasion de l'os par le bacille de la lèpre.

Sommairement, considérant l'aspect des lésions et leur évolution, on peut provisoirement classer l'ostéite nonspécifique en plusieurs groupes distincts:

1. La résorption distale: y jouent un rôle les troubles vasculaires, la surinfection, ou les deux phénomènes associés.
2. L'ostéo-arthrite métatarsophalangienne: ce type de lésion est associé aux traumatismes répétés qui, par suite de l'effrondrement des structures de l'arcade plantaire, se produisent au niveau d'un point de support anesthésique.
3. L'ostéite: c'est une séquelle des manifestations d'ulcération et de la surinfection.
4. L'ostéoporose, par absence d'exercice.

Des recherches plus étendues s'imposent, afin de comparer les données cliniques, radiologiques et histopathologiques. Il serait utile et instructif que ces études soient menées en plusieurs points du globe.

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