LEPROSY: PATHOLOGIC CHANGES OBSERVED IN FIFTY CONSECUTIVE NECROPSIES *

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The purpose of this presentation is to record the gross and microscopic changes observed in necropsy material from leprosy patients. It consists of a review of 50 consecutive necropsies performed at the National Leprosarium (U.S. Public Health Service Hospital) at Carville, Louisiana.

Relatively few detailed studies have been reported in the English literature of the necropsy findings in leprosy. One of the earliest, that of Hansen and Looft translated into English by Walker[1] in 1895, remains among the best. Their study represents a compilation of 20 years' work following the discovery of the bacillus *Mycobacterium leprae* by Hansen in 1874, and includes a discussion of necropsy findings in 125 cases. Although some of their conclusions are no longer tenable, remarkably little improvement can be made on their original descriptions after 60 years.

An early article by Mitsuda (1902) discussing lepra cells and their distribution in certain organs was translated into English in 1936.[2] In 1937, Mitsuda and Ogawa[3] briefly discussed the gross findings in 150 necropsies from the Aiseien Leprosarium in Japan.

Black,[4] in 1938, reported a number of observations from 75 necropsies performed by him at the National Leprosarium. Kean and Childress,[5] in 1942, summarized the findings in 103 necropsies performed by several pathologists in Panama. The detailed reviews by Fite,[6,7] in 1941 and 1943, are based in part on necropsy material, and include an extensive review of the literature on tissue changes in leprosy in general. Numerous excellent illustrations of necropsy lesions are included in the *Atlas of Leprosy* by Mitsuda[8] published in 1952.

MATERIALS AND METHODS

All of the 50 cases presented in this study concerned patients at the National Leprosarium where 46 of the gross necropsies were performed. The remaining 4 gross necropsies were performed at the New

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Orleans U.S. Public Health Service Hospital, where the tissues from all 50 cases were studied microscopically and the clinical data analyzed.

Routine sections were made of heart, lung, spleen, liver, adrenal gland, kidney, testis, epididymis, skin, peripheral nerves (usually ulnar), gastrointestinal tract, lymph node, thyroid gland, pituitary body, bone, bone marrow, eye, brain, and spinal cord. Tissues were removed from additional sites when indicated. All of the tissues were fixed in 10 per cent formalin. Routine hematoxylin and eosin stains, as well as acid-fast stains, were made of all tissues. The acid-fast quality of *Myco. leprae* is more difficult to demonstrate than that of *Mycobacterium tuberculosis,* and in our experience the Fite-Cambre-Turner[9] technique is superior to other modifications of the Ziehl-Neelsen stain. Bennhold's congo red and the crystal violet stains gave the most satisfactory results for demonstration of amyloid. Mallory's trichrome stain was useful in evaluating late testicular changes.

Analysis of Cases

During the 5½ years covered by this study (September, 1948, through April, 1954), the average census at the National Leprosarium was 385 patients. Seven per cent of these were considered to have leprosy of the tuberculoid type and the majority of the remaining were considered to be of lepromatous type. Of the 50 cases in this series, 48 were of lepromatous type and 2 were of tuberculoid type. Therefore, this review is essentially one of lepromatous leprosy. In addition to being the predominant type at the National Leprosarium, it is also the type most frequently seen in the United States.[10] The 50 cases represent 92.6 per cent of all the deaths that occurred at the National Leprosarium during the 5½-year period of this study.

Thirty-four of the patients in this series were men and 16 were women, giving a 2:1 ratio which is approximately the figure given for the sex distribution of leprosy throughout the world.[11] The race was listed as white in 29 cases, Mexican in 10, colored in 8, and Chinese, Japanese, and Filipino, respectively, in the 3 remaining cases.

The average age at the time of death was 58.8 years, the youngest patient being 31 and the oldest 79 years. The average length of life from the onset of obvious signs and symptoms of leprosy was 20 years. Five of the patients gave a family history of leprosy in one or more relatives.

Sister Hilary Ross who performed the serologic tests for syphilis on these patients has previously reported[12] the high incidence of false positives on patients with leprosy. At least one, and in most cases many different, standard tests for syphilis were performed on all but

one patient in this series. Thirty-four of these patients had at least one positive serologic test, giving an incidence of 68 per cent. In 3 patients a doubtful reaction and in 12 a negative reaction was obtained. Despite this, in no case at necropsy could unequivocal evidence of syphilitic changes be found either grossly or microscopically.

Mycobacterium leprae was found in at least one tissue in 34 of the cases. The tissues in which it was possible to demonstrate these organisms were peripheral nerves (usually ulnar), skin, testis, epididymis, liver, eye, spleen, lymph node, bone, bone marrow, adrenal gland, nasal mucosa, kidney, pharynx, and larynx. In 12 of the cases, *Myco. leprae* was seen within visceral organs such as the spleen, liver, and adrenal gland. In an additional 3 cases old miliary lepromas were seen in the viscera, although no bacilli could be demonstrated. If lepra bacilli were found in the parenchymatous organs, they usually were present also in the skin and peripheral nerves.

Myco. leprae was still clinically demonstrable in skin scrapings up to the time of death in 34 of the patients. Ten of the patients had 12 consecutive negative skin scrapings (clinically arrested), and 6 had several consecutive negative skin scrapings immediately prior to death. In 26 of the cases with positive skin scrapings prior to death, organisms were demonstrated in necropsy tissues available. Of the 10 patients who were considered to be clinically arrested (12 consecutive negative skin scrapings), *Myco. leprae* was demonstrated in the tissues of 6. In the 6 additional cases with several consecutive negative skin scrapings prior to death, organisms were present in the tissues of 2 patients.

Thirty of the 50 patients had received sulfone drug therapy for 2 years or more. In 22 of these cases lepra bacilli were demonstrable in necropsy tissues.

Changes of secondary amyloidosis were seen in 23 of the cases in one or more tissues, the organ most frequently involved being the kidney. Other sites included the spleen, liver, adrenal glands, lymph nodes, stomach and rectal mucosa, and arteriolar walls of the thyroid gland, pituitary body, and pancreas. The sites of amyloid change in the parenchymatous organs such as spleen, liver, adrenal glands, and kidney were unrelated to the presence or absence of bacilli in these organs. No amyloid was found in the bone marrow in the 32 cases in which sections were taken.

When the kidney was involved by amyloid change it was usually quite markedly altered. As a result, in 19 of the cases (38 per cent), the mechanism of death was one of renal insufficiency with terminal uremia, bronchopneumonia, and/or pulmonary edema. In 9 of the

cases a malignant neoplasm was the cause of death. In 7 cases active pulmonary tuberculosis was the primary cause of death. In the remaining 15 cases various diseases such as hemorrhagic pancreatitis, myocardial infarction, and cerebral hemorrhage were responsible for the patient's demise. In only one case in the entire series (A-1950), a patient with active tuberculosis, was active widespread lepromatous leprosy believed to be a major contributing factor in the mechanism of death.

GROSS PATHOLOGIC FINDINGS

In the following sections describing the gross and microscopic findings, many of the observations are of necessity composite. Upon inspection of the body, the disfigurement of the nose, eyes, extremities, and skin was quite obvious. Corneal opacities were frequent and in some cases the eyes had been enucleated. "Saddle" nose deformity of varying degrees usually was present. The ear lobes were often enlarged and redundant. The eyebrows and eyelashes were sparse, especially laterally, and some patients had none at all. Considerable induration of the facial skin and underlying tissues resulted in the typical leonine facies of leprosy.

The skin lesions varied considerably, depending upon the activity of the disease at the time of death. Areas of irregular pigmentation, old scars from burns or lepromatous nodules, and a diffuse atrophy of skin over wide areas of the body, with thin "onion skin" wrinkling, were seen. Hypopigmented areas were frequent in the skin of deeply pigmented persons. A few patients presented raised, sometimes erythematous areas of apparently active lesions.

Obvious deformities of the hands (*"main-en-griffe"*) and feet often were present with resorption of bone and shortening of fingers, toes, and sometimes other bones. Usually the shortened finger or toe had a small, distorted nail remaining at its tip, for the digits in fact seldom "fall off" as in the cicatrizing disease ainhum, but rather undergo a progressive resorption from the tip. Many patients had trophic ulcers of the extremities and some had had previous amputations. Muscle atrophy, especially of the interossei of the hands, was prominent in many cases with marked nerve involvement. Usually the ulnar nerves were palpably enlarged. Testicular atrophy was usually quite marked. Several cases presented gynecomastia.

Review of Organ Systems

Respiratory System. The lesions of leprosy seen in the respiratory system of these 50 patients were confined entirely to the upper portion

of the tract. In the 3 cases in which the nasal mucous membrane was examined the characteristic picture was a diffuse infiltration by chronic inflammatory cells, chiefly lymphocytes and many vacuolated histiocytes ("lepra" or Virchow cells) with occasional globi. Globi are rounded, compact masses of lepra bacilli in the center of vacuoles or spaces that measure up to 100 μ in diameter. Globi are situated within giant cells or sometimes within macrophages having only a single nucleus.[13,14] Sometimes, the vacuole becomes so large the nucleus of the cell is hard to see or is not present at all.

In the more advanced cases, numerous acid-fast bacilli were seen within the lepra cells and globi, as well as diffusely throughout the intercellular spaces and overlying epithelium. Ulceration and perforation of the nasal septum were common, with destruction of nasal cartilage and bone resulting in varying degrees of "saddle" deformity. In a few of the more severe cases the nasopharynx, oropharynx, peritonsillar tissues, and larynx were involved by diffuse lepromatous infiltrate similar to that described in the nasal septum.

The respiratory tract below the larynx was not involved in any of the 50 cases. Three of our cases presented lipid granulomas of the lung parenchyma which were attributed to the use of chaulmoogra oil nasal spray or nose drops over a period of many years. In another case (A-2005) lesions of classical Boeck's sarcoid were seen in the lungs as well as in intrathoracic and retroperitoneal lymph nodes. No relationship could be ascertained between the sarcoid lesions and the patient's leprosy, which did not involve the lymph nodes examined.

Cardiovascular System. Direct involvement of the heart, aorta, or other great vessels was not seen. In one case (A-1723) a few *Myco. leprae* were seen within the media of the aorta adjacent to a large lymphosarcomatous mass in which there were large numbers of organisms. Involvement of blood vessel walls of the skin, nerves, and testes was very frequent and was uniformly present in the more active lesions.

Spleen. The weight of the spleen varied from 40 to 520 gm., and averaged 240 gm. Externally, the spleen was not remarkable except for its size and for a rare plaque of white, glistening, fibrous tissue or adhesions. Only rarely were miliary lepromas or amyloid deposits large enough to be visible grossly and therefore distinguishable from malpighian corpuscles.

Microscopically, 8 of the 49 spleens sectioned contained miliary lepromas. These were composed of vacuolated histiocytes, lymphocytes, and occasional globi and were located in every part of the

parenchyma in both the red and white pulp, often around blood vessels (Fig. 1). In 6 of the 8 cases with lepromas, acid-fast organisms were demonstrable.

Amyloid was seen in 17 of the spleens sectioned. It was located chiefly within the thickened walls of arteries of medium and small size as well as in distinct masses in the centers of malpighian corpuscles and elsewhere in the pulp (Fig. 1).

Liver. The weight of the liver varied from 890 to 2,550 gm., and averaged 1,604 gm. As in the spleen, the lepromas usually were too small to be seen grossly. In those cases with marked amyloid change the liver was usually enlarged, and the cut surface presented irregular tan areas throughout (Fig. 3).

Miliary lepromas were seen microscopically in 12 of the 50 livers sectioned and in 10 of the lepromas organisms were demonstrable. The lepromas often were located around portal triads and central veins, but were seen also along the sinusoids, apparently arising in Kupffer cells as well (Fig. 2). The gallbladder and bile ducts were never seen to be involved, although lymph nodes around the duodenum and major biliary ducts sometimes contained lepromas with organisms. Replacement of liver cord cells by amyloid was seen in 17 of the cases (Fig. 2).

Gastrointestinal Tract. The esophagus, stomach, and small and large intestines were free of involvement by lesions due to leprosy per se. In 3 cases, however, amyloid change was prominent in the mucosa and submucosa of the stomach and in one case the rectal mucosa showed similar amyloid change. The pancreas was not involved in any of the cases examined. Occasionally, in a case with widespread amyloid disease, the pancreatic vessel walls shared in the change.

Urinary Tract. The weight of the kidneys varied from 75 to 300 gm., and averaged 148 gm. The predominant lesion seen in 19 of the 50 cases was a varying degree of usually quite severe amyloidosis. The corticomedullary junctions often were indistinct and the kidneys pale, especially the cortical portions (Fig. 4). In a number of cases nephrosclerotic changes were associated with those due to amyloid, but the latter were usually predominant. Microscopically, the amyloid was seen beneath the basement membranes of the glomerular tufts and convoluted tubules and also within the walls of many smaller arteries and arterioles. Many glomeruli were completely replaced by amyloid (Fig. 5). Protein casts were seen in some kidneys.

In 2 cases a few small collections of vacuolated histiocytes containing *Myco. leprae* were seen within glomerular tufts. The ureters, bladder, prostate, and urethra were not involved by lepromatous changes in any case.

Reproductive Organs. Lesions of the female genital tract were not seen in any of the 16 women. In the male, however, the testes were seldom free of lesions and usually were quite small.[15] In 24 of the 33 cases in which sections of a testis were available, there was marked atrophy, with moderate to minimal atrophy in all but one of the remaining cases. The picture varied from a very active lepromatous infiltrate of lymphocytes, vacuolated histiocytes, and globi within and primarily between seminiferous tubules, to one of increasing degrees of hyalinization and thickening of the basement membranes and eventual complete fibrous replacement of all tubules (Fig. 6). Blood vessel involvement by an active lepromatous lesion frequently was seen as an early lesion, especially near the tunicae of the testes (Fig. 7). *Myco. leprae* was found in 16 of the 33 testes examined. Islands of interstitial cells were prominent in many of the advanced cases and in a few there actually appeared to be hyperplasia of these cells. In many cases the epididymides were involved by a lepromatous infiltrate similar to that seen in the adjacent testicular body.

Endocrine Glands. As in the liver and spleen, adrenal lesions consisted of miliary lepromas seen most frequently near the junction of the cortex with the medulla and within the medulla. Acid-fast organisms within lepromas were found in 5 of the 46 cases in which adrenal sections were available. In 16 of the adrenal glands sectioned, amyloid change was noted, principally between and replacing cords of cells in all three layers of the cortex (Fig. 8).

Few changes were observed in the thyroid or pituitary glands except for occasional deposition of amyloid within the walls of small arterioles. In a few cases with marked testicular atrophy, eosinophilic cells in the anterior lobe of the pituitary body were quite prominent. Clear cell hyperplasia of the parathyroid glands was seen in some cases with marked renal amyloidosis.

Hematopoietic System. The bone marrow shared in the widespread miliary lesions in some of the advanced cases. In 6 of the 32 bone marrows sectioned, *Myco. leprae* was demonstrable within lepromas (Fig. 9). No specific clinical hematologic pattern was seen; however, a severe hypochromic microcytic anemia was present in several cases. Several of the more active cases with widespread miliary lesions had very hyperplastic bone marrow. Amyloid was not seen in the marrow.

Lymphatic System. The lymph nodes draining skin areas involved by lepromatous infiltrate and often those in the thoracic and abdominal cavities were enlarged and contained collections of vacuolated histiocytes (Fig. 10). *Myco. leprae* was found in the lymph nodes in 7 of the 25 cases in which sections were made. One lymph node contained

large deposits of amyloid as well. The peritonsillar tissues were involved by lepromatous infiltrate in one patient who had many active lesions from the nose to the larynx.

Skin. The gross changes of the skin have been discussed. In 21 of the 44 cases with skin sections available, *Myco. leprae* was demonstrated in characteristic lepromatous infiltrates of the dermis. Usually a "free zone" of varying width was seen between the epidermis and the infiltrate (Fig. 11). The infiltrate consisted of coalescing aggregates of vacuolated histiocytes, lymphocytes, and occasional globi characteristically situated around blood vessels and nerves, and occasionally around adnexal structures (Fig. 12). Sweat glands and other adnexal structures in old lesions often were atrophic or replaced completely by the inflammatory reaction. Organisms were found within the vacuoles of histiocytes, within globi, and within adnexal structures, as well as lying free in the dermis and occasionally in the epidermis. They were seen frequently within the walls of small blood vessels and in several cases within the walls of larger vessels in the dermis.

Many cases exhibited only varying degrees of thinning of the epidermis and atrophy of dermal structures with a scattering of residual chronic inflammatory cells. The skin sections from the 2 cases listed as of tuberculoid type fell into this category with only residual atrophic changes.

Central Nervous System. The brain was examined in 37 and the spinal cord in 13 cases. Unequivocal involvement of the central nervous system by *Myco. leprae* was not found.

Peripheral Nerves. The ulnar and superficial peroneal nerves were enlarged in most cases as were other nerves in some. Many nerves contained small lepromatous lesions while in others the infiltration was quite extensive and largely obliterated the normal architecture (Fig. 13). *Myco. leprae* was demonstrable in 25 of the 47 cases in which peripheral nerve sections were made. Organisms were found within vacuolated histiocytes and globi, within axis cylinders, and within blood vessel walls both within and around the nerve trunks (Fig. 13). In almost every case, including the 2 tuberculoid cases, there was varying but usually quite extensive, fibrous thickening of the endoneurium, perineurium, and epineurium. In the nerves with the more extensive fibrous tissue replacement, few or no organisms were seen. Calcification of the ulnar nerve with extensive fibrosis was found in one patient (A-2113) who had had lepromatous leprosy for over 60 years (Fig. 14).

Eyes. The principal lesions in the eyes of the lepromatous cases were

iridocyclitis and keratitis, both superficial and deep. Diffuse lepromatous infiltration of the ciliary body, iris, and choroid was seen and *Myco. leprae* was demonstrated in many of these cases (Fig. 15). The cornea and periorbital tissues also shared in the lepromatous infiltrate in some cases. Occasionally the ocular lesions appeared quite active when the rest of the tissues of the body contained only residual changes which were apparently inactive or healed. In no case were there demonstrable lesions in the posterior half of the eye or in the optic nerve.

Musculoskeletal System. In several cases in which the calf muscles were examined there was extensive yellowish fatty replacement of large bundles of muscle fibers. The circumference of the calf and the bulk of the muscles remained normal in these cases. Microscopically, the sarcolemma remained intact, but the sarcoplasm had lost its striations and was partially or entirely replaced by fat (Fig. 16).

Characteristically, there was resorption of the bones of the phalanges and in some cases resorption of more proximal bones. Grossly, these bones were cut easily without decalcification. Microscopically, varying areas of bone resorption and new bone or osteoid formation were seen occurring simultaneously. These were associated with chronic inflammatory cellular infiltration and extensive fibrous tissue reaction. Lepromatous infiltrates within the fatty marrow spaces and within the fibrous tissue in and around the periosteum contained acid-fast organisms.

Discussion

It must be remembered that the foregoing presents the pattern of lepromatous leprosy as seen in necropsies at the National Leprosarium in the United States and that the pattern of leprosy in many other parts of the world is quite different. It should be recalled, also, that in the natural history of the disease the tendency is toward spontaneous remission after many years. The so-called "burned out" cases may reveal few or no organisms and are left only with the residual neural and other tissue damage as described in many of the present cases. One of the oldest patients in this series became blind from leprous changes in 1898, 8 years after the clinical onset of his leprosy. He refused virtually all specific therapy except for sporadic doses of chaulmoogra oil totalling approximately 1,000 cc. Several years prior to death, over 60 years after the onset of his leprosy, skin scrapings were positive only occasionally. No organisms were demonstrable at necropsy.

It should be pointed out that 30 of these patients (60 per cent) re-

ceived sulfone therapy for at least 2 years, and 10 patients received sulfone therapy for a shorter period. It is believed that this treatment has influenced to some extent the pattern of the disease in some of these patients. Undeniably beneficial effects are produced clinically by the sulfones, as reported recently by Chang, Wolcott, and Doull[16]; however, they pointed out that bacteriologic improvement may lag behind clinical improvement for years. Skin scrapings were positive clinically just prior to death in 23 of the 30 patients who received sulfone therapy for at least 2 years. As mentioned before, *Myco. leprae* was demonstrable also in necropsy tissues in 22 of these cases. Moreover, it is believed that if additional multiple sections of skin and nerve had been taken, organisms would have been found in a higher percentage of cases.

As seen by the average duration of life of 20 years after the recorded onset of obvious signs and symptoms, leprosy per se is not a rapidly fatal disease. Also, the average age at the time of death of just under 59 years is less than 10 years below that of the population as a whole. As mentioned, in only one patient in this series was widespread leprosy itself considered to be a major factor in the immediate cause of death. However, the disabling features of leprosy often were seen, as in the contractures, resorbed digits, neurotrophic ulcers, renal insufficiency, and blindness.

While leprosy was not an immediate cause of death, it very frequently produced secondary changes which in turn were responsible eventually for the patient's demise. Thus in 38 per cent of the cases, amyloidosis of the kidney, secondary to the leprous infection, produced renal insufficiency with uremia, often coma, bronchopneumonia and/or pulmonary edema, and death. The cause of death in another 14 per cent was active pulmonary tuberculosis to which the patient might have been predisposed by the debilitating effects of the leprous infection. One might assume, then, that in approximately 50 per cent of the cases, leprosy was indirectly responsible for death. In the other 50 per cent, diseases to which any person might succumb, such as neoplasms and myocardial infarction, were the causes of death.

From the foregoing descriptions, it can be seen that few tissues in the body were free from demonstrable involvement by lepromatous leprosy at necropsy. The principal ones not involved included the lower respiratory tract, the heart and great vessels, the gastrointestinal tract, the central nervous system, and the female reproductive organs. Isolated instances of involvement of most of these sites have been reported in the literature,[2,7] but their occurrence must be exceedingly uncom-

mon. Viscera such as spleen, liver, and adrenal gland contained lepromatous lesions in one third of the cases in this series. In 6 of the 10 patients believed to be clinically arrested (12 consecutive negative skin scrapings), organisms were demonstrated at necropsy.

A striking feature secondary to leprosy in these patients was the frequency with which amyloid was seen (almost one half of the cases). When the kidney was involved by amyloidosis, it usually was very markedly altered and resulted, as mentioned, in marked renal insufficiency which was incompatible with life. The pathogenesis of the deposition of amyloid, while obviously related to the leprous infection of the body in general, still remains theoretical.[17]

Summary

The pathologic changes of leprosy as seen in the United States are presented by reviewing in detail 50 consecutive necropsies from the National Leprosarium (U.S. Public Health Service Hospital) at Carville, Louisiana.

Two of the cases were considered to be of the tuberculoid type and 48 of the lepromatous type of leprosy, the predominant type at the National Leprosarium as well as in the United States in general.

Mycobacterium leprae was demonstrable in at least one tissue in 34 of the cases (68 per cent). These tissues included peripheral nerves (usually ulnar), skin, testis and epididymis, liver, eye, spleen, lymph node, bone, bone marrow, adrenal gland, nasal mucosa, kidney, pharynx, and larynx. Organs such as spleen, liver, and adrenal gland contained lepromatous lesions in one third of the cases.

The average duration of life after the onset of obvious signs and symptoms was 20 years and the average age at the time of death was just under 59 years. While leprosy is seldom a rapidly fatal disease, over a period of many years it often results in the marked debilitating effects of contractures, neurotrophic ulcers, renal insufficiency, and blindness.

Secondary amyloid changes were seen in 23 cases in one or more tissues, the organ most frequently involved being the kidney. Renal insufficiency secondary to the amyloid change was the most frequent cause of death in the series (38 per cent).

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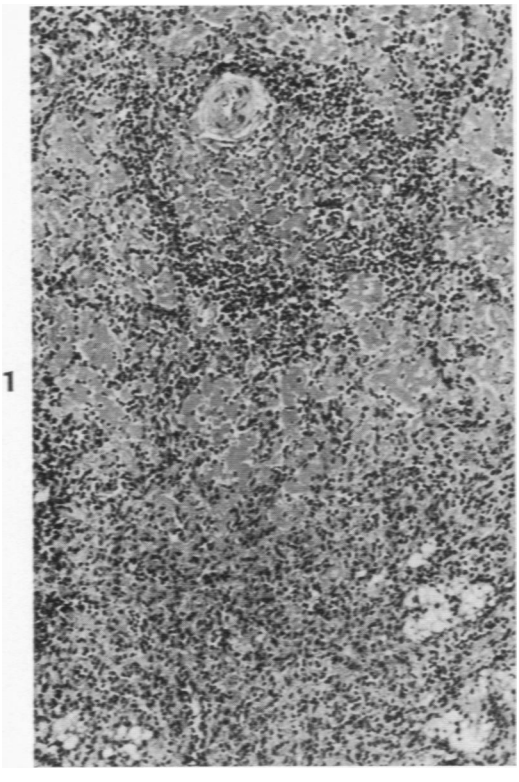
LEGENDS FOR FIGURES

FIG. 1. Spleen showing deposition of amyloid material within and around a malpighian corpuscle as well as clusters of vacuolated histiocytes (miliary lepromas) below. Hematoxylin and eosin stain. × 228.

FIG. 2. Liver. Centrally, there is a miliary leproma surrounded by large areas of replacement of liver cords by pale-staining amyloid material. Small, darker cells are remaining liver cord cells. Hematoxylin and eosin stain. × 300.

FIG. 3. Cut section of liver showing widespread, diffuse, pale tan areas of amyloid.

FIG. 4. Cut section of kidney showing loss of normal markings with large, pale areas of amyloid in both cortex and medulla.



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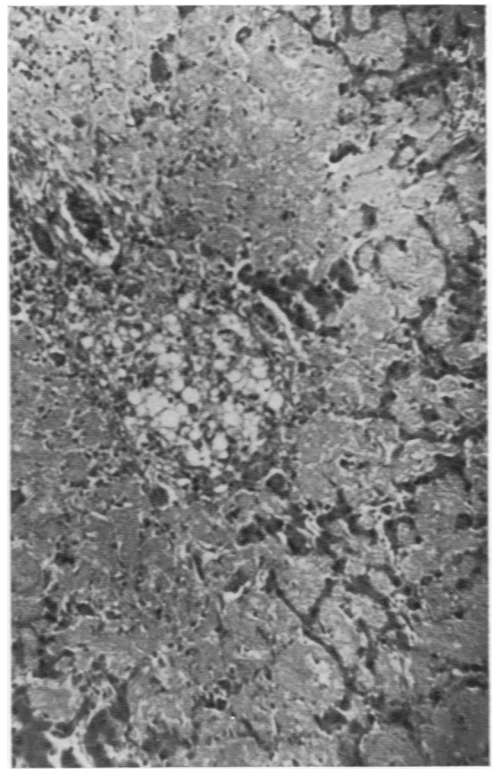

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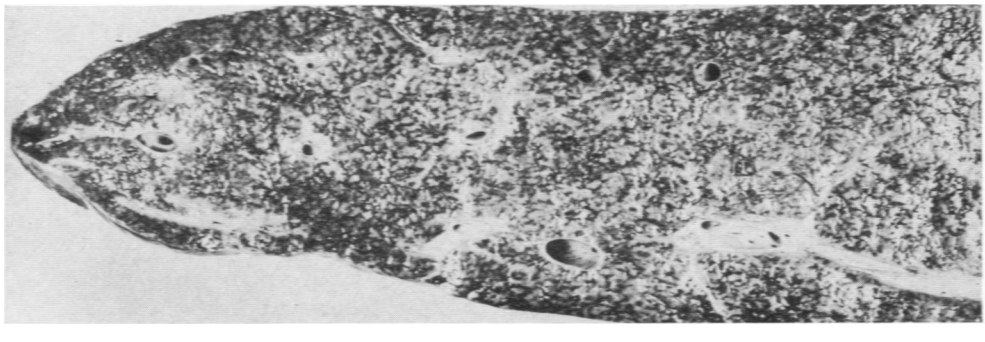

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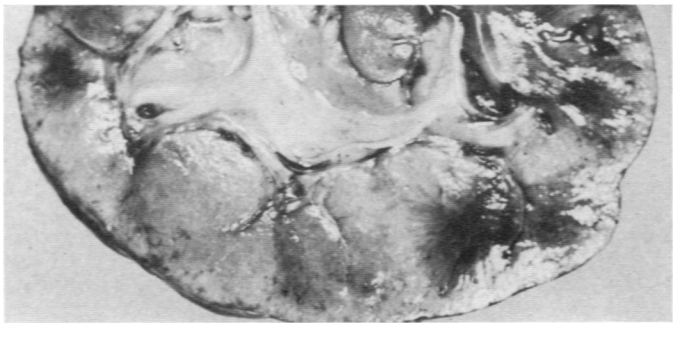

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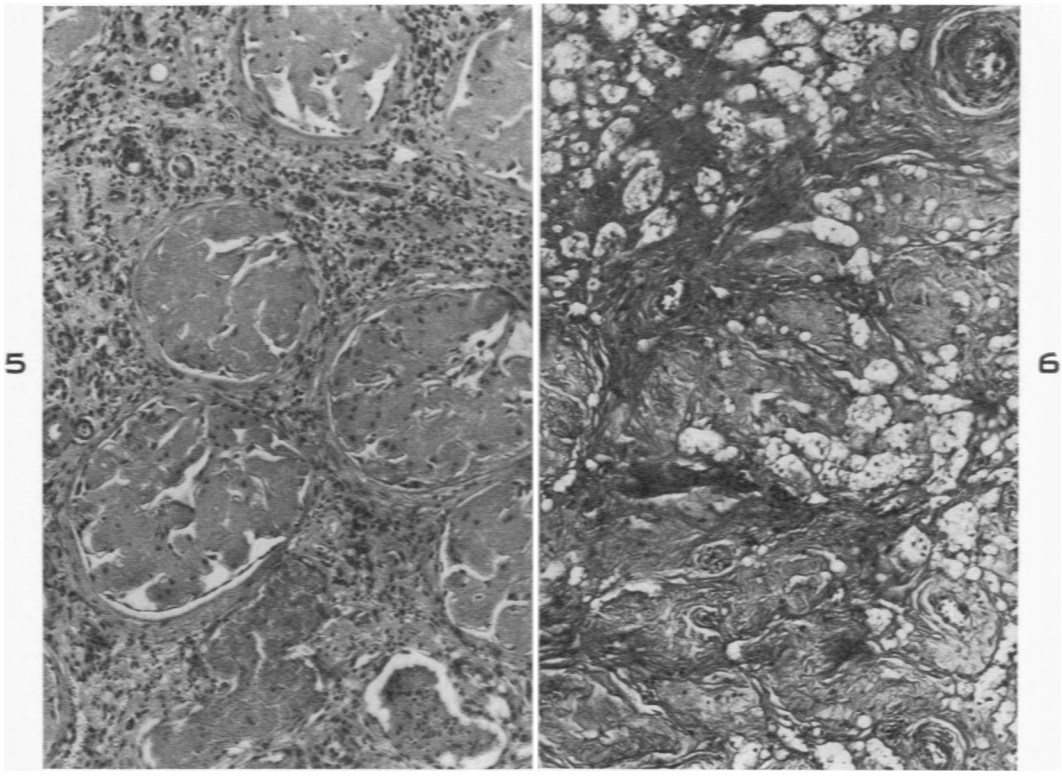


FIG. 5. Kidney with enlarged glomerular tufts showing marked replacement by amyloid. Extensive loss of intervening tubules may be noted also. Hematoxylin and eosin stain. × 228.

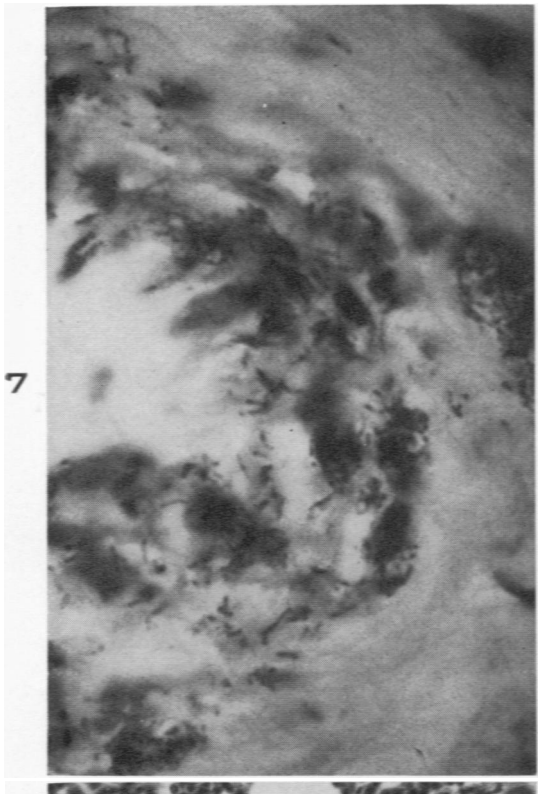
FIG. 6. Testis. No normal seminiferous tubules can be seen. In the central area some can be seen completely replaced by dense, hyalinized, fibrous tissue. Marked thickening of blood vessel walls is seen at the right. The pale, vacuolated areas consist entirely of diffuse lepromatous infiltrate. Hematoxylin and eosin stain. × 228.

FIG. 7. Oil-immersion photomicrograph of a testicular blood vessel showing marked infiltration of *Mycobacterium leprae* bacilli within the enlarged endothelial cells and within cells and globi deeper in the arterial wall. Acid-fast stain. × 900.

FIG. 8. Adrenal gland with extensive replacement of cortical tissue by pale-staining amyloid. Residual dark cortical cells can be seen beneath the capsule. Hematoxylin and eosin stain. × 228.

FIG. 9. Lumbar vertebral bone marrow showing normal hematopoietic tissue above and lepromatous infiltrate below. Of note are the normal appearing, large fat cells above, which are in contrast to the smaller, numerous, vacuolated histiocytes below. Hematoxylin and eosin stain. × 524.

FIG. 10. Lymph node with large area of lepromatous infiltrate (vacuolated histiocytes) below and small deposits of amyloid above (some within the thickened walls of arterioles). The lymph node capsule is seen in the upper right corner. Hematoxylin and eosin stain. × 228.



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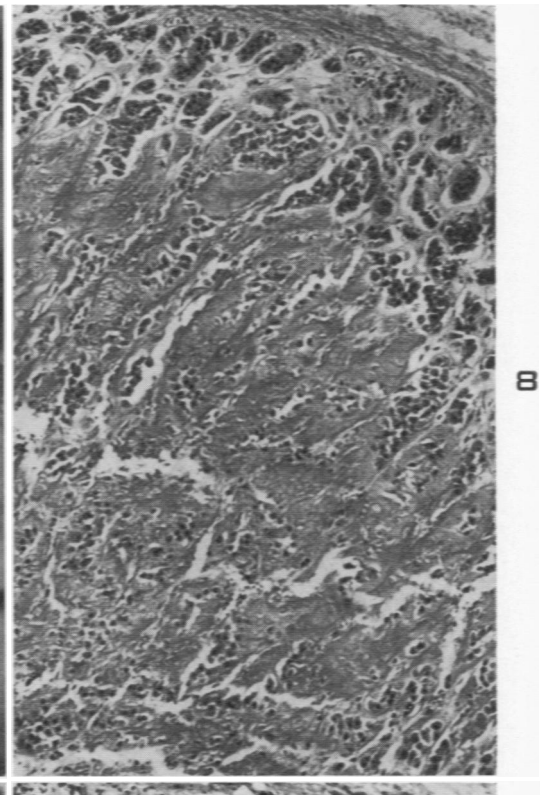

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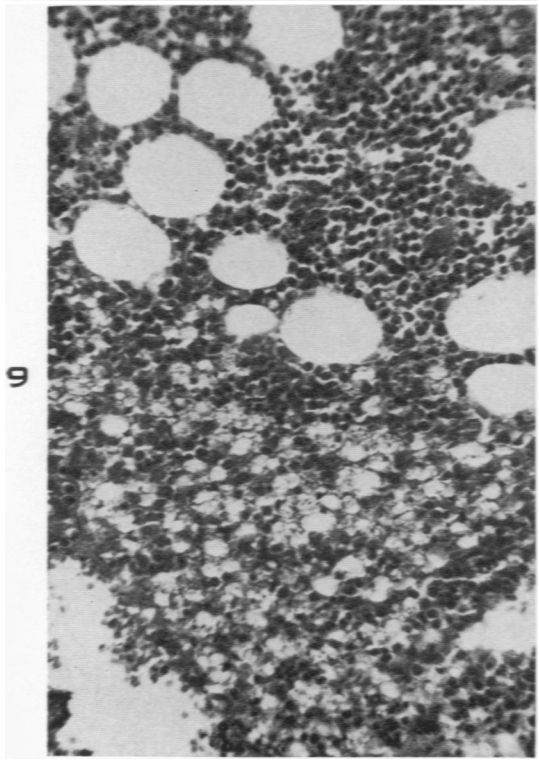

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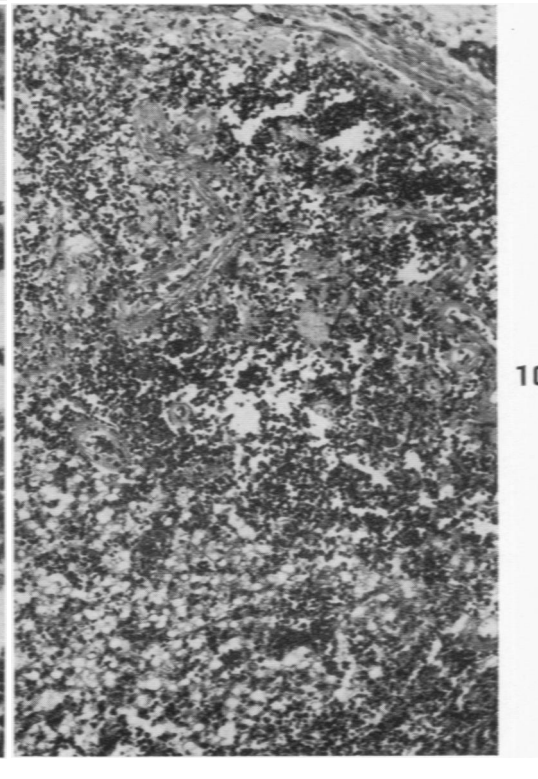

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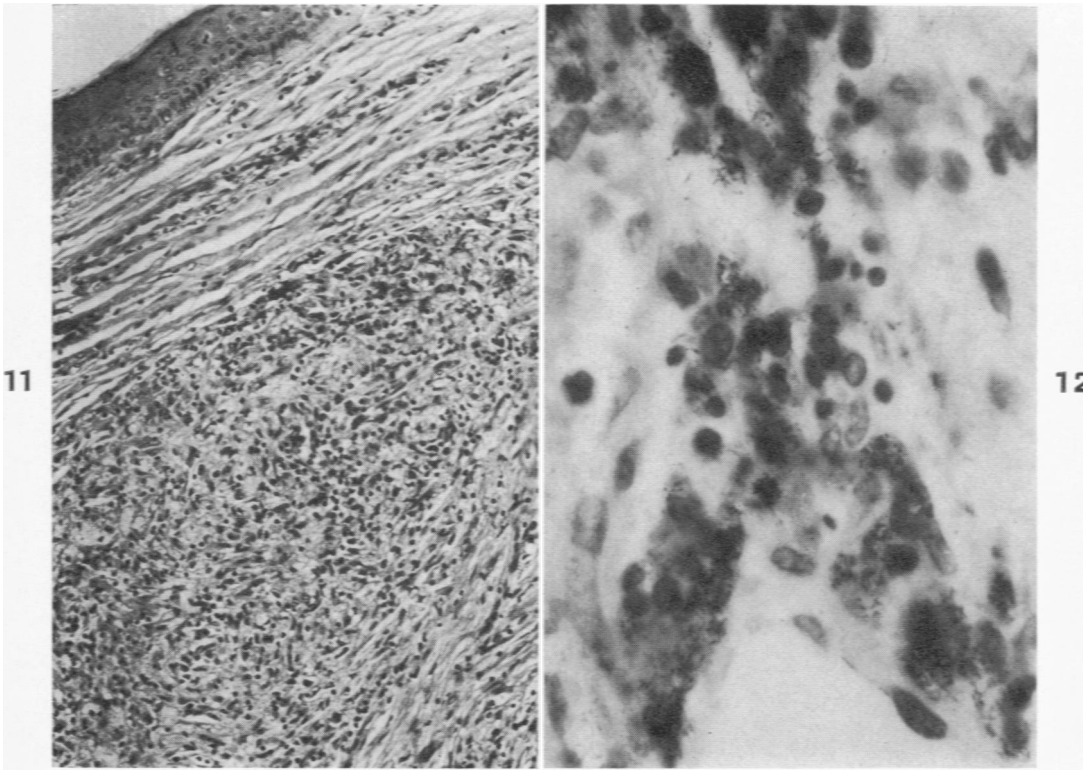

FIG. 11. Skin showing characteristic "free zone" between epithelium and lepromatous infiltrate in the dermis. Coalescing aggregates of lymphocytes and macrophages make up the bulk of the infiltrate. The vacuoles in the macrophages in this case are quite small. There is some blunting and loss of rete pegs of the epithelium but little atrophy. Hematoxylin and eosin stain. × 228.

FIG. 12. Oil-immersion photomicrograph of skin showing large number of *Myco. leprae* within the vacuoles of macrophages in the lepromatous infiltrate in the dermis. A lymphatic space is seen below. Acid-fast stain. × 958.

FIG. 13. Longitudinal section of ulnar nerve showing lepromatous infiltrate with numerous large globi, some of which contain masses of dark-staining acid-fast bacilli. Acid-fast stain. × 524.

FIG. 14. Transverse section of ulnar nerve with extensive fibrosis and a large area of calcification. Most of the calcium has fallen out during processing; however, fragments can be seen within the defect. Hematoxylin and eosin stain. × 55.

FIG. 15. Oil-immersion photomicrograph of ciliary body of eye showing pigmented layer, upper right. Below numerous *Myco. leprae* can be seen within the lepromatous infiltrate and within a large globus in a giant cell. Acid-fast stain. × 700.

FIG. 16. Gastrocnemius muscle showing replacement of sarcoplasm and distortion of sarcolemma by fat. Hematoxylin and eosin stain. × 300.

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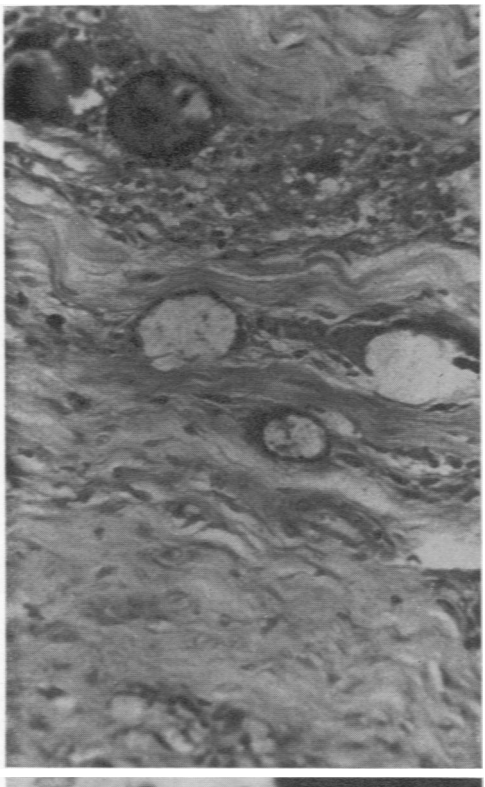

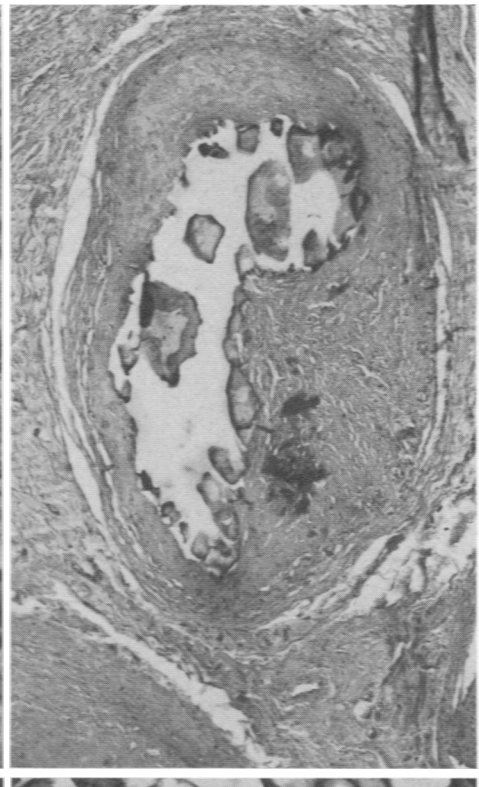

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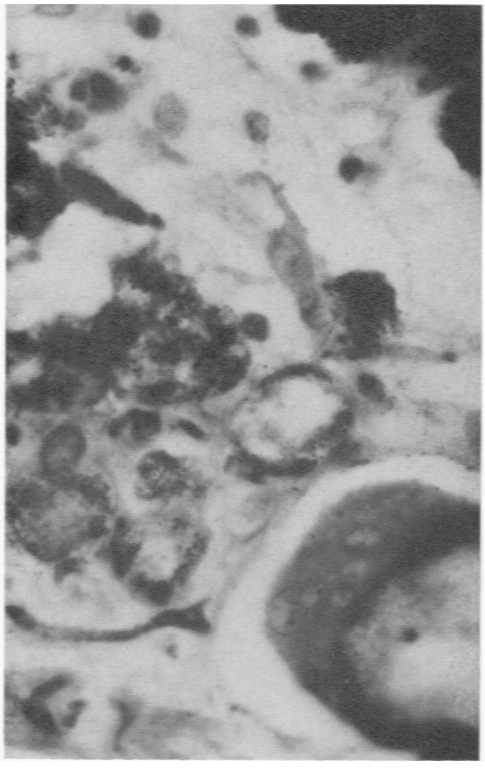

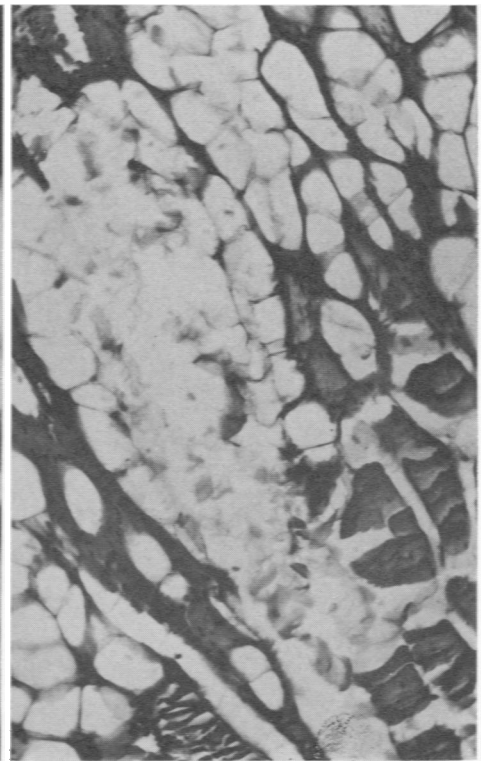

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