STUDIES ON THE PATHOLOGY OF MURINE LEPROSY

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This paper presents a summary of the results of studies of the pathology of murine leprosy carried out in our laboratory since 1941. In naturally infected rats very few metastases are seen in their viscera. In experimentally infected animals, on the contrary, remarkably severe lesions appear in the internal organs. We therefore investigated the disease in histological preparations of various organs, and at the same time studied the genesis of the murine lepra cells by vital staining of the animals.

I. FINDINGS IN INFECTED RATS

This study was made with 109 white rats which had been inoculated subcutaneously with specimens of lepromas as large as the end of the little finger, the animals being examined after from 100 to 648 days of inoculation. In this work there were used 26 strains of murine bacilli acquired by Nishimura (5) in the Osaka-Kobe district. The visceral organs and nerves were examined by Nishimura (6, 7, 8, 9, 10), the organs of vision by Ikeda (2), the bones and bone marrow by Sarashi (12), and the nasal cavity and teeth by Hirai (1).

Frequencies of lesions in the various organs.—After subcutaneous inoculation of the bacilli, they not only produce lepromas in the inoculated sites but intrude extensively into the viscera, sense organs, teeth, bones and other parts of the body and give rise to lesions. The frequencies of lesions in the various organs and tissues are shown in Table 1, where the percentages are given. In descending order of frequency, ranging from 92.6 per cent to 3.1 per cent, the organs involved were as follows: bone marrow (femur), visceral lymph glands, spleen, liver, lung, thymus, stomach, nasal cavity, uterus, intestines, heart, blood vessels (aorta and large veins in the thorax), salivary gland, kidney, tongue, trachea, ovary, thyroid, adrenal, esophagus, seminal vesicles, spermatic duct, epididymis, testis, oviduct, bladder, pancreas, and parathyroid. Moreover, in the severest cases we found lesions in the dura mater, peripheral

nerves, eye ball, periorbital tissue, optic nerve, and teeth (these not arranged in order of frequency, see Table 1).

TABLE 1.—*Sites and frequencies of lesions in experimentally infected rats.*

Organ	Number of examinations	Number of infections	Percentage	Localization
Respiratory organs				
Lung	109	61	56.0	Adventitia of vessels and lymph spaces
Trachea	109	27	28.4	Connective tissue of outer membrane
Nasal cavity	74	33	44.6	Submucous connective tissue
Circulatory organs				
Heart	109	42	38.5	Interstitial tissue, myo- and pericardium
Vessels	109	40	36.7	Adventitia
Digestive organs				
Tongue	98	31	31.6	Interstitial tissue of muscle
Salivary glands	83	32	38.6	Interstitial tissue
Esophagus	109	20	18.5	Outer membrane, muscle, interstitial tissue
Stomach	97	48	49.5	Submucous tissue, mucous membrane of glands
Pancreas	62	4	6.4	Interstitial tissue
Intestines	83	32	38.6	Submucous tissue
Liver	109	76	69.7	Wall of vessels (veins)
Urinary organs				
Kidney	106	36	34.0	Outer fatty membrane
Bladder	14	1	7.1	Muscle layer
Genital organs				
Testis	54	7	13.0	Interstitial tissue, tunica albuginea
Epididymis	54	9	17.0	Interstitial tissue
Spermatic duct	46	8	17.4	Outer membrane
Seminal vesicles	26	5	19.4	Outer membrane
Ovary	42	11	26.2	Connective tissue of medullary substance
Oviduct	42	4	9.5	Outer membrane
Uterus	46	18	39.1	Interstitial tissue of muscle
Blood producing organs				
Bone marrow	27	25	92.6	
Spleen	101	75	74.2	Follicles, sinuses
Lymph gland	106	84	79.2	Outer membrane, cortical and medullary substance
Endocrine glands				
Thymus	108	55	50.8	Capsule, interstitial tissue
Thyroid	108	29	26.9	Outer membrane, interstitial tissue
Parathyroid	96	3	3.1	Outer membrane
Adrenal	75	18	24.0	Fatty tissue of outer membrane
Nervous system				
Central	41	17	41.0	Meninges
Peripheral	41	22	53.6	Epineurium
Sight organ				
Eye ball	47	15	31.9	Sclera
Periorbital tissue	47	34	72.3	Subconjunctiva
Optic nerve	47	5	10.6	Capillary wall of neurilemma bundles
Teeth	60	19	31.7	Periodontium

These results demonstrate that the lesions of murine leprosy appear most frequently in the blood-producing and other organs rich in reticuloendothelial tissue. There can be seen no differences of lesion frequencies due to the different physical functions of the respective organs, and they have no tendency to appear oftenest in the nasal cavity, testis and other organs as is the case in human leprosy.

Period between subcutaneous inoculation and appearance of visceral lesions.—The period from the time of inoculation to the occurrence of lesions in the visceral organs was, at the shortest, 110 days for the visceral lymph glands and 128 days for the spleen. On the whole, in 52 per cent of 27 animals, a full one-half, which were sacrificed after from 100 to 200 days there were lesions in some of the organs, in 87 per cent of 23 animals after from 201 to 300 days, in 97 per cent of 31 after 301 to 400 days, and in 100 per cent of 28 after more than 400 days. These percentages enable us to conclude that the majority of lesions occur in viscera after 100 days in the earlier cases, after six months in most animals, and after a year in all of them.

The route of metastasis of inoculated bacilli.—From the fact that, without exception, the lesions were centered by veins and capillaries and developed primarily around them, it follows that the blood circulation plays a great part in the metastasis of the bacilli. Furthermore, the facts that histiocytes which contained organisms appeared in lymph spaces, and that in every organ leprous lesions occurred in lymph nodules earlier than in the organ tissue, lead us to conclude that the lymphatic circulation also has a close relationship with the metastasis of bacilli.

The sites of predilection.—The bacilli, disseminated through the blood or lymph circulation, proliferated electively in the reticuloendothelial cells, static wandering cells, sparse connective-tissue cells, adventitial cells and cover cells (*Deckzellen* of German terminology) ; they could not be found in the parenchymal cells of the respective organs. Therefore, lesions occurred most frequently in the reticuloendothelial tissue of the bone marrow, spleen and lymph glands. In the liver they appeared around the central veins and the capillaries. In the tubular organs they were observed around the vessels of the submucous connective tissue, and in parenchymatous organs in the fatty membrane, the outer membrane and the interstitial tissue. They presented a specific root-shaped form along the interstitial tissue among muscle fibers. In the teeth, the lesions occurred more frequently in the periosteum than in the

pulp. In this respect they differ from those of human leprosy. These results reveal that the site of predilection of the murine lesions is the interstitial tissue.

Genesis of the murine lepra cells.—The fact that the lesions occur in the mesodermal tissue suggests that they have a close relation with the cells of this tissue. We could follow the transformation of cells derived from the mesodermal tissue into the murine lepra cells by vital staining with trypan blue. In our laboratory, Kajiyama (4) made exact observations of the capillary endothelium of the liver, Sano (11) of the reticular cells and sinus endothelium of the spleen, Sarashi (13) of the reticuloendothelial cells and sinus endothelium of the bone marrow, Takedazu (15) of the fibroblasts and adventitial cells of the subcutaneous connective tissue, and Hirai (1) of the sinus endothelium, reticuloendothelial cells and static wandering cells of the lymph glands.

These observations showed that the phagocytic histiocytes and histiocyte-like cells take in bacilli but do not digest them; instead, they allow their proliferation. In consequence the cytoplasm increases in volume and is filled with innumerable bacilli. The nuclei divide and multiply, and with increase of the cytoplasma there results a form of giant cell in most cases. The so-called murine lepra cells fuse and congregate into nodules, mixed with the above-mentioned giant cells, until they form a very nodal lesion. At this stage of development the centers of the lesions undergo necrosis, while at their peripheries the lesions are spreading.

By this study of the process of transformation it was found that the murine lepra cells are derived from the histiocytes and histiocyte-like cells.

Morphology of murine lepra cells.—The histiocytes and histiocyte-like cells in which only a small number of bacilli and some stained granules are included cannot yet be called "murine lepra cells." The typical cells of that kind are loaded with innumerable bacilli and lack the power of phagocytosing pigment granules and in general they have the following characteristics after hematoxylin-eosin staining: The cytoplasm appears expanded and of light tone. The form is round, oval, spindle-shaped or of polygonal epithelioid appearance, but the contour is not sharp because of the plasmodium-like aggregation of cells. The nuclei are somewhat large, stained light, and eccentrically situated; in shape they are not identical, being round, oval, hemispheric, spindle-shaped, or of other forms.

With sudan III these cells stain slightly, their fatty corpuscles being very fine, and almost no vacuoles can be seen. Although these are the characteristics of these cells, it is quite difficult to distinguish them from the ordinary histiocytes. They can be defined precisely, however, by the existence of numerous bacilli and their presence in leprous nodes or infiltrations.

Morphology of the lesions in the various organs.—The morphology of the lesions differs according to the organ in which they appear. They can be classified in three types: (1) the round node type (Fig. 9), (2) the spindle-shaped stratiform node type (Fig. 1), and (3) the root-shaped infiltration type (Fig. 16).

The tissue surrounding the round node lesion is not reactional, and the border between them is sharp. Lesions of this form occur frequently in the liver, spleen, lymph glands and other organs in which the reticuloendothelial tissue is abundant. Especially in the liver they show the true round form, and there can be seen no inflammatory reaction such as cell infiltration in the normal liver tissue around them (Figs. 9, 10). In the spleen the round nodes appear around the central arteries of the follicles, and have the characteristic form of amyloid degeneration (Figs. 7, 8). In the lymph glands there is a greater tendency for giant cells to appear than elsewhere. Central necrosis frequently occurs (Figs. 4, 9).

The spindle-like nodes are found in the subcutaneous and submucous connective tissues. In this case the lepra cells are spindle-shaped or of epithelioid appearance, and almost no giant cells are observed. These cells congregate into a large spindle-like group, and these groups accumulate to form larger nodal lesions. The centers of these lesions are often necrotic.

The root-shaped infiltrations are seen in muscle and gland tissue, its special form being due to the infiltration of the lepra cells along the interstitial connective tissue or the sparse tissue of the organs. After hematoxylin-eosin staining this form can hardly be recognized, but the pretty root-shaped infiltration is easily seen after the Ziehl-Neelsen stain (Figs. 15, 16, 17).

Besides these three morphological types, we can mention as characteristics of the murine leprosy lesions the weak proliferation of connective tissues in the nodes or infiltrations, and the marked tendency to softening and necrosis, as compared with human leprosy lesions. Furthermore, the murine disease produces no proliferative inflammation of the interstitial tissue of the testis and liver, and no reaction in the

endothelium of the vessels. The disproportionately innumerable bacilli with which the cells are stuffed is in striking contrast to the slight grade of the lesions (Fig. 22). These observations lead us to conclude that the virulence of the murine leprosy bacillus is very weak against the vital force of the body cells of rats.

Murine leprosy lesions in the nervous system.—In rat leprosy we can see no type of the disease corresponding to the human nerve type. This coincides with the histopathological observations. In the central nervous system no change is produced in the parenchyma; on the other hand, marked affection of the meninges may be seen. The adventitial cells near the confluens sinuum of the veins of the encephalon take in a few bacilli in slight cases. In severe cases, however, the lymph spaces are filled with lepra cells loaded with numerous bacilli, and the meninges are thickened by infiltration of these cells (Fig. 31). In the pia mater a small number of bacilli may be observed in the connective tissue cells around vessels, but only when the meninges are heavily infected. In the spinal cord, the invasion of bacilli into the meninges has been seen, but only in a few cases.

In the peripheral nerves (plexus brachialis, nervus ischiadicus, n. hypoglossus and n. opticus) the leprous infiltration has been found only in the epineurium, the lepra cells appearing around the vessels there, and not in the perineurium, the endoneurium, or the neurilemma. In severely infected cases the whole tissue is transformed into a granulomatous mass, invading as far as the epineurium where it is intercepted sharply. The endoneurium, neurilemma and nerve fibers are indifferent to infection, and no inflammatory reaction is seen in the interstitial tissue (Fig. 30). In a few cases a solitary lepra cell or a small group of them had come out around the central capillaries of the neurilemma bundles, although the tissue surrounding them expressed no reaction (Fig. 32).

These results reveal that murine leprous lesions occur not in the parenchyma of the nervous system, but chiefly around the vessels of the meninges and in the epineurium of the peripheral nerves. Sometimes the walls of the capillaries in the neurilemma bundles are affected, without any inflammatory change of the interstitial tissue.

Relation of the severity of lesions and the strains of bacilli.—From the fact that different strains of murine leprosy bacilli show slight morphological differences, it can be imagined with-

out difficulty that there may also be differences of pathogenicity. In this study it has been found that strains Nos. 38, 39 and 5081 produced the most marked changes, and No. 6569 comparatively slight lesions; the rest fall between these extremes. Variations in the susceptibility of the animals caused more marked differences in the seriousness of the disease than did differences in the strains of the bacilli.

Sex and the lesions produced.—The frequencies of lesions in the two sexes were 81.7 per cent in males and 87.9 per cent in females. This difference was due only to the findings in the genital organs, which were affected in 24.0 per cent of the males and 41.7 per cent of the females, the female genital organs showing the higher ratio of infection. This is the reverse of what is seen in the human disease.

II. FINDINGS IN INFECTED MICE

The material for this experiment was 55 mice with lepromata, sacrificed after from 100 to 400 days after inoculation (by Tani) with murine bacilli, Kumamoto strain, which had been passed repeatedly through rats. Tani (17) examined the lung, liver, heart, mediastinal organs, spleen and kidney, Shimizu (14) the brain, stomach, intestines, penis, testis, uterus, ovary and skeletal muscle, Sarashi (12) the bones (marrow), and Ikeda (3) the organs of sight.

Frequencies of lesions in the various organs.—The frequencies of lesions in the various organs, shown in detail in Table 2, were in the following order, from 61.7 per cent to 5.4 per cent: liver, testis, penis, spleen, ovary, intestines, bone marrow (femur), kidney, lung, uterus, heart and vessels, esophagus and stomach, adrenal, trachea, and brain. By further examinations, the leprous change was found in the periocular tissue in 83.3 per cent of the animals, in the eyeballs themselves in 30.0 per cent, and in the optic nerve in 6.7 per cent.

The sites of predilection and histopathology of the lesions.—In every organ, without exception, the leprous change appeared first in mesodermal tissue in contact with vessels or along the endothelium of venous sinuses, and in the reticuloendothelial tissue of the spleen, lymph nodes and bone marrow. In the liver it was observed in the walls of veins, particularly the central veins. In many cases the transformation of Kupffer's cells containing bacilli into lepra cells was observed (Fig. 10). In the kidney the capsule was most often infected, and in rare cases bacilli and leprous lesions were found in the glomeruli,

TABLE 2.—*Sites and frequencies of lesions in experimentally infected mice.*

Organ	Number of examinations	Number of infections	Percentage	Localization
Respiratory organs				
Lung	54	19	35.0	Pleura, adventitia of vessels
Trachea	53	10	19.0	Outer membrane
Circulatory organs				
Heart	50	14	28.0	Pericardium, interstitial tissue of muscle
Vessels	53	15	28.0	Adventitia
Digestive organs				
Esophagus	55	12	21.5	Outer membrane, interstitial tissue of muscle
Stomach	59	12	21.5	Submucous tissue
Intestines	59	23	39.0	Submucous tissue
Liver	54	33	61.0	Wall of vessels (veins)
Urinary organ				
Kidney	51	19	37.0	Outer fatty membrane
Genital organs				
Testis	31	18	58.1	Interstitial tissue, tunica albugnea
Penis	29	13	44.0	Subcutaneous connectiye tissue
Ovary	24	10	41.7	Cortical substance, connective tissue of medullary substance
Uterus	28	8	28.6	Connective tissue of muscle layer
Blood-producing organs				
Bone marrow	42	16	38.0	
Spleen	54	23	43.0	Follicles, red pulp
Nervous system				
Brain	56	3	5.4	Meninges
Endocrine glands				
Adrenal	41	8	20.0	Connective tissue of cortical substance
Sight organs				
Eye ball	30	9	30.0	Sclera
Periocular tissue	30	25	83.3	Palpebra, fatty tissue around eye ball
Optic nerve	30	25	6.7	Capillary wall of neurilemma bundles

Bowmann's capsules and ducti controiti of the renal parenchyma (Fig. 21). Lepra cells also appeared along the capillaries of the submucous tissue of the stomach and intestines, the subcutaneous connective tissue of the penis, the tunica albuginea, the interstitial tissue of the testis, the muscular layer of the uterus, the cortical and medullary connective tissues of the ovary, the meninges of the brain, and the interstitial tissue among muscle fibers.

The histopathology of the lesions in the respective organs was the same as that of rats. We could see the round nodes in the liver, spleen and bone marrow, the spindle-like nodes in the adventitia or subcutaneous tissue, and the root-shaped infiltrations in the glandular tissues or among muscle fibers. In general, however, the tendency is to produce smaller nodes and diffuse infiltrations of the lepra cells. In every lesion the proliferation of the connective tissue was slight, and the centers of the larger nodes degenerated and softened. As in the case of the rats, no inflammatory reaction could be seen in the tissue around them.

SUMMARY AND CONCLUSIONS

When murine leprosy is studied as an experimental procedure for the research of human leprosy, the following points should be borne in mind from the histopathological point of view:

1. Similarities: (*a*) Murine leprosy produces node lesions of epithelioid-like cells and giant cells loaded with innumerable bacilli. (*b*) The lesions occur in the skin and every other organ of the animal. (*c*) The site of predilection is the mesodermal tissue. (*d*) The lesions appear along blood or lymph vessels. (*e*) Both murine and human lepra cells are derived from the histiocytes or histiocyte-like cells. (*f*) Both cells contain more or less of a fatty substance.

2. Differences: (*a*) The murine leprosy bacillus has no affinity for the nervous system, and produces no interstitial inflammation of the nerves. (*b*) In the murine disease there are seen nodules and infiltrations, but no lesions of macular form. (*c*) Murine bacilli are found only in the cells of the mesodermal system, and not in mucous epithelial cells, the endothelium of the larger vessels, the gland epithelium, or other parenchymatous cells. (*d*) The bacilli contained in the lepra cells are in larger numbers than in the human leproma, and they are irregularly arranged. (*e*) In the murine lepra cells the fatty granules are quite fine, and no vacuoles can be found. (*f*) The tissues around the lesions are not infiltrated with cells and are not reactional, although sometimes they are slightly infected. (*g*) Murine nodes are poor in connective tissue and soft, and they readily undergo necrosis. (*h*) The murine disease causes no proliferative interstitial inflammation of the testis, liver or meninges, as is seen in the human disease. (*i*) The murine disease has no tendency to produce lesions in particular

organs, as has the human disease in the nasal mucosa, the testis, and the adrenal, but occurs most frequently in those tissues which are rich in reticuloendothelial cells.

In short, these results reveal that murine leprosy consists of nodules and infiltrations of leprous cells in the subcutaneous tissue, lymph glands and other organs, by symbiosis of the bacilli in cells of the mesodermal tissues. The virulence of the Stefansky bacillus for the rat family is much less than that of Hansen's bacillus for the human being. Their attitude toward the body cells is quite different from that of the human bacilli, being a mere symbiosis. The difference between the bacilli of murine and human leprosy is much greater than that between bovine and human tubercle bacilli. It remains as an interesting problem if this difference should be attributed to the factor of virulence of the bacilli, or to the specific resistance of the rats.

RESÚMEN

Este trabajo sintetiza los estudios hechos en el laboratorio del autor desde el 1941, per various investigadares, sobre la diseminación sistémica de la lepra murina experimental en la rata y el ratoncillo, con observaciones acerca de la predilección tisular, la morfología de las lesiones, y la génesis de la célula de la lepra murine según revela la tinción vital. Al comparar las lesiones de ésta infección con las de la lepra humana, los seguientes puntos deben tenerse en mente:

1. Semejanzas: (a) La lepra murina produce nodulillos de células epitelioides y células gigantes repletas de innumerables bacilos. (b) Las lesiones ocurren en la piel y en todos otros órganos del animal. (c) El titio predilecto es el tejido mesodérmico. (d) Las lesiones ocurren cerca de vasos linfáticos o sanguíneos. (e) Tanto la célula de lepra murina como la humana se deriva de histiocitos o células parecidas a histiocitos. (f) Ambas células contienen algun material graso.

2. Diferencias: (a) El bacilo de la lepra murina no tiene afinidad por el tejido nervioso, y no produce inflamación interesticial de los nervios. (b) En la enfermedad murina, se observan nodulillos e infiltrados, pero no hay lesiones maculares. (c) Bacilos murinos se hallan solamente en células de origen mesodérmico, y no en células epiteliales mucosas, en el endotelio de los grandes vasos, ni en epitelio grandular o parenquimatoso. (d) Los bacilos dentro de las células de lepra son más abundantes que en el leproma humano, están dispuestos en forma irregular. (e) En la célula de lepra murina las partículas grasas son muy finas y no hay grandes vacuolas. (f) Los tejidos alrededor de las lesiones no están infiltrados y no muestran reacción tisular, aunque aveces estén ligeramente infectados. (g) Los nodulillos murinos son blandos y tienden a la necrosis rápidamente. (h) La enfermedad murina no produce inflamación proliferativa interesticial testicular, hepática o meníngea, como en la enfermedad humana. (i) La enfermedad murina no tiende a afectar ningún órgano en particular, como la enfermedad humana afecta la mucosa nasal, el testículo y la suprarenal,

pero afecta más frecuentemente aquellos tejidos ricos en células reticuloendoteliales.

En breve, la lepra murina consiste de nodulillos e infiltraciones de células leprosas en tejido subcutáneo, los ganglios linfáticos y otros órganos, por simbiosis de los bacilos y las células mesodermales. La virulencia del bacilo de Stefansky en ratas y ratones, es menos que la virulencia del bacilo de Hansen en el ser humano. La relación hacia células del huesped es distinta, siendo una mera simbiosis. La diferencia entre el bacilo de lepra murina y el humano es más que en el caso de tuberculosis bovina y humana. Queda como un problema interesante decidir si ésta diferencia entre el bacilo de lepra murina y el de lepra humana es debido a diferencia en virulencia o a resistencia específica de la rata.

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DESCRIPTION OF PLATES

PLATE (4)

FIG. 1. Rat, skin. Spindle-shaped stratiform lesion in the subcutaneous muscle layer. (Hematoxylin-eosin.)

FIG. 2. Rat, skin. Lepra cells developing from the adventitia of a small blood vessel in the subcutaneous connective tissue. (Ziehl-Neelsen.)

FIG. 3. Rat, skin. Lepra cells developing from the supporting tissue of the subcutaneous fatty tissue, and bacilli included in them. (Ziehl-Neelsen.)

FIG. 4. Rat, lymph gland. Large nodal lesion with central necrosis. (Hematoxylin-eosin.)

FIG. 5. Rat, lymph gland. Node lesion stained for reticulum. (Bielschowsky.)

FIG. 6. Rat, lymph gland. The connective tissue surrounding a necrotic lesion, stained for reticulum. (Bielschowsky.)

FIG. 7. Rat, spleen. Lepromata around the arteries, showing the appearance of amyloid degeneration. (Ziehl-Neelsen.)

FIG. 8. Rat, spleen. Leproma in a spleen follicle, stained for reticulum. (Bielschowsky.)

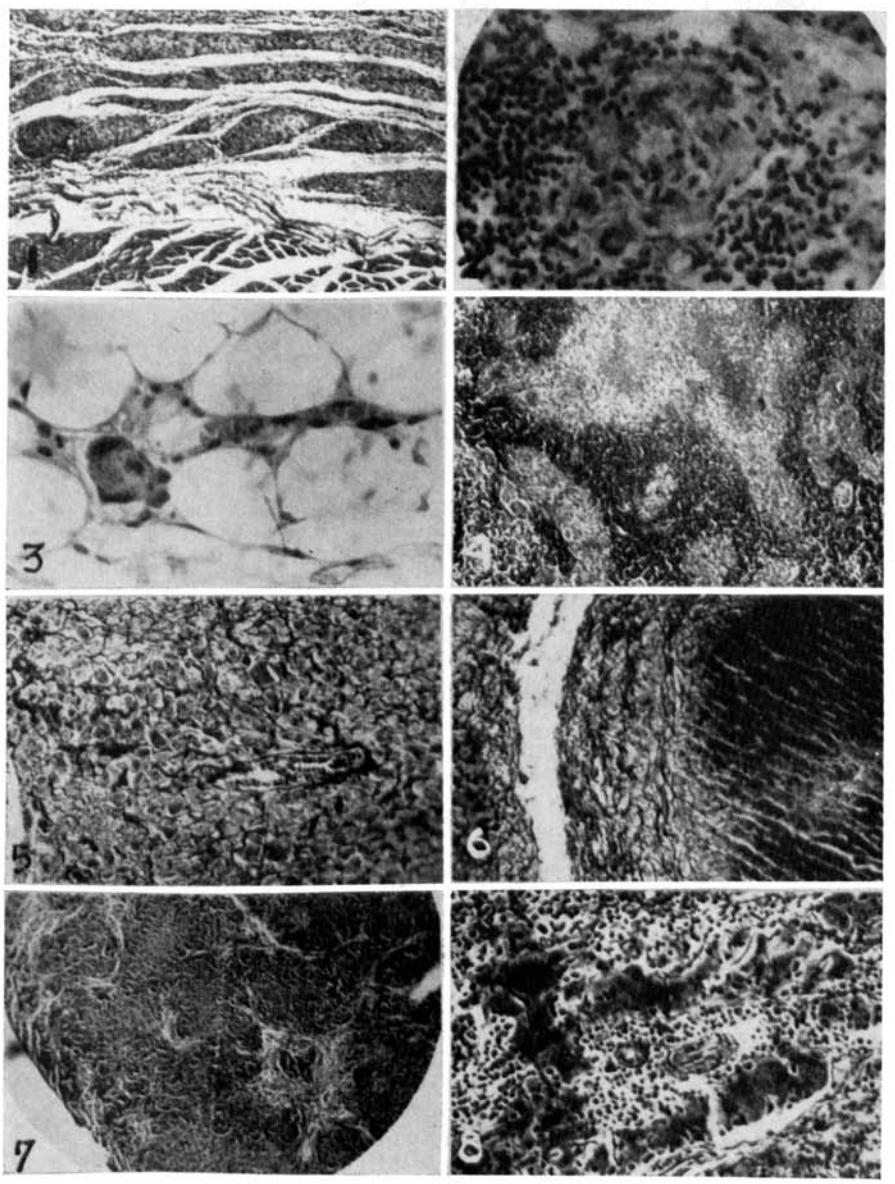

PLATE 4.

PLATE (5)

FIG. 9. Rat, liver. Round nodes, poor in lepra cells and with central necrosis. (Hematoxylin-eosin.)

FIG. 10. Rat, liver. Massed bacilli in greatly enlarged Kupffer's cells. (Ziehl-Neelsen.)

FIG. 11. Rat, lung. Small lepromata in the lymph spaces. (Hematoxylin-eosin.)

FIG. 12. Mouse, lung. Masses of bacilli loaded in cells around a large capillary blood vessel. (Ziehl-Neelsen.)

FIG. 13. Rat, lung. A leproma centered around a capillary of a lung septum. (Hematoxylin-eosin.)

FIG. 14. Rat, trachea. Lepromata in the outer membrane. (Hematoxylin-eosin.)

FIG. 15. Rat, heart. Verrucous lepromata of the endocardium, and root-shaped infiltrations in the muscle. (Ziehl-Neelsen.)

FIG. 16. Rat, heart. Root-shaped infiltrative collections of lepra cells in the muscle. (Hematoxylin-eosin.)

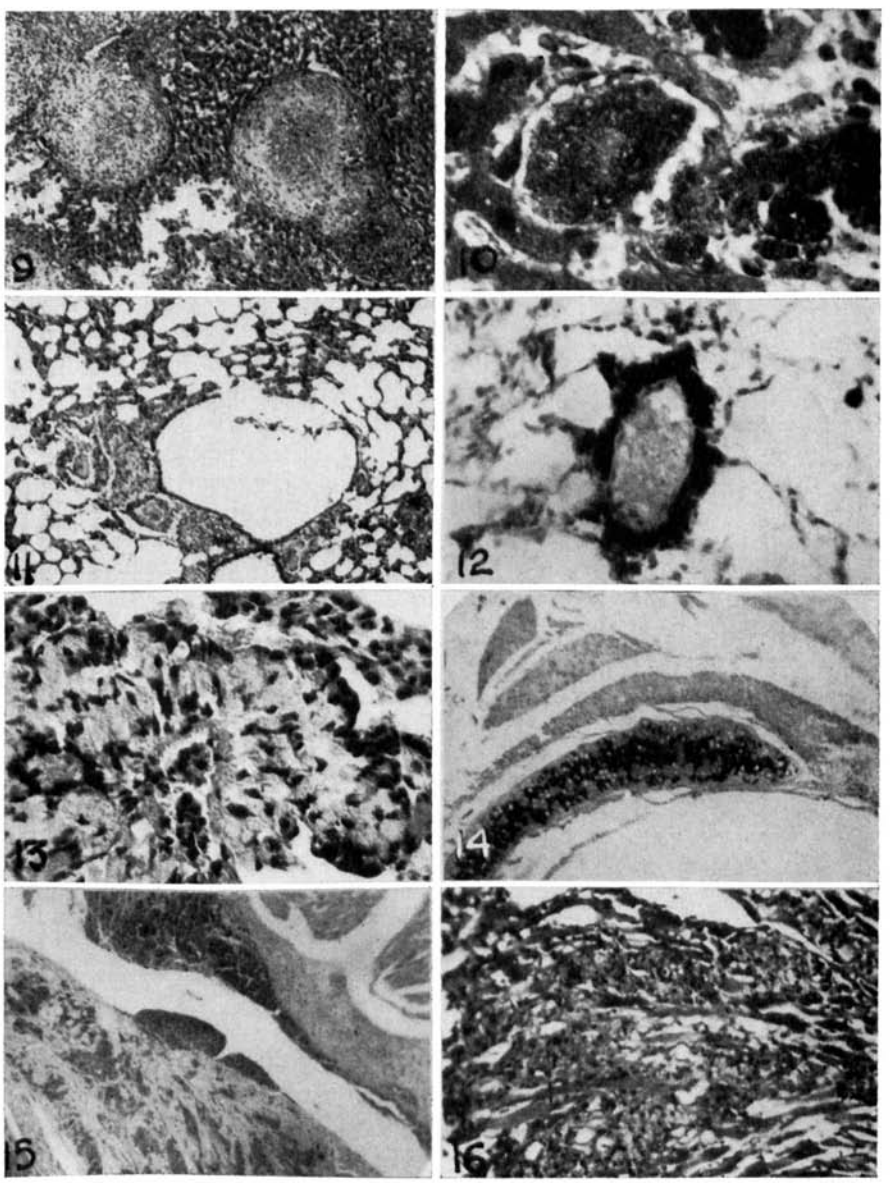

PLATE 5.

PLATE (6)

FIG. 17. Rat, salivary gland. Lepromatous infiltration in the interstitial tissue. (Hematoxylin-eosin.)

FIG. 18. Rat, esophagus. Lepromata under the tunica propria. (Hematoxylin-eosin.)

FIG. 19. Rat, stomach. Leproma in the submucous muscle layer beneath the gastric glands. (Hematoxylin-eosin.)

FIG. 20. Rat, colon. Lepromata under the mucous membrane. (Hematoxylin-eosin.)

FIG. 21. Mouse, kidney. Small nodes in glomeruli; a very rare case. (Ziehl-Neelsen.)

FIG. 22. Rat, testis. Leproma in the interstitial tissue. (Hematoxylin-eosin.)

FIG. 23. Rat, ovary. Lepromatous infiltration. (Hematoxylin-eosin.)

FIG. 24. Rat, uterus. Uterine glands pressed aside by a developing leproma. (Hematoxylin-eosin.)

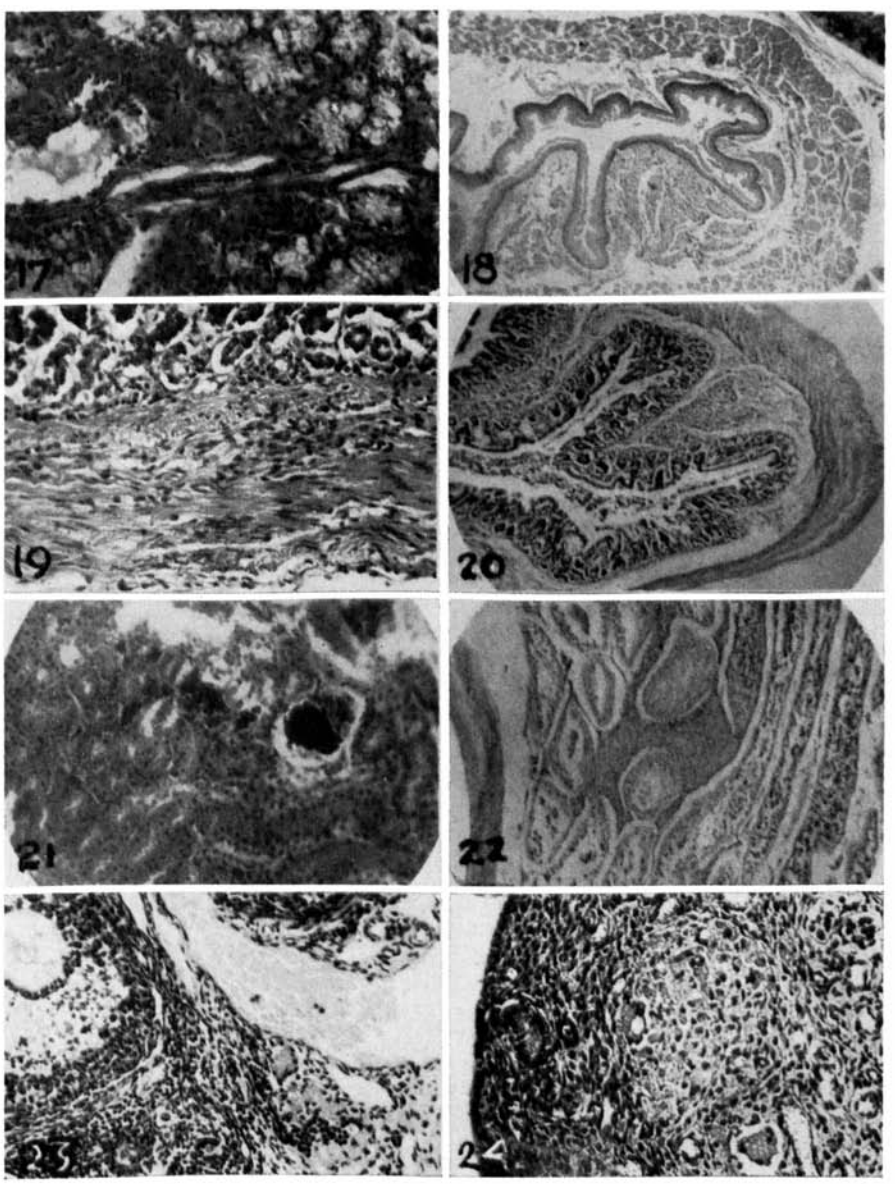

PLATE 6.

PLATE (7)

FIG. 25. Rat, thyroid. Invasion and proliferation of bacilli in the interstitial tissue. (Ziehl-Neelsen.)

FIG. 26. Rat, nasal cavity. Leproma in the perichondrium. (Ziehl-Neelsen.)

FIG. 27. Rat, tooth. Leproma in the periosteum, between the enamel substance and the alveolus. (Hematoxylin-eosin.)

FIG. 28. Rat, bone (femur). Haversian canals and the medulla filled with bacilli. (Ziehl-Neelsen.)

FIG. 29. Rat, bone (femur). Destruction of the marrow space and thinning of the bone substance. (Ziehl-Neelsen.)

FIG. 30. Rat, subcutaneous nerves. Demonstrating their noninvolvement by the infiltration around them. (Hematoxylin-eosin.)

FIG. 31. Rat, venae encephali. Large leproma near the confluens sinuum. (Hematoxylin-eosin.)

FIG. 32. Rat, optic nerve. Small node in the nerve, with no inflammation of the interstitial tissue. (Hematoxylin-eosin.)

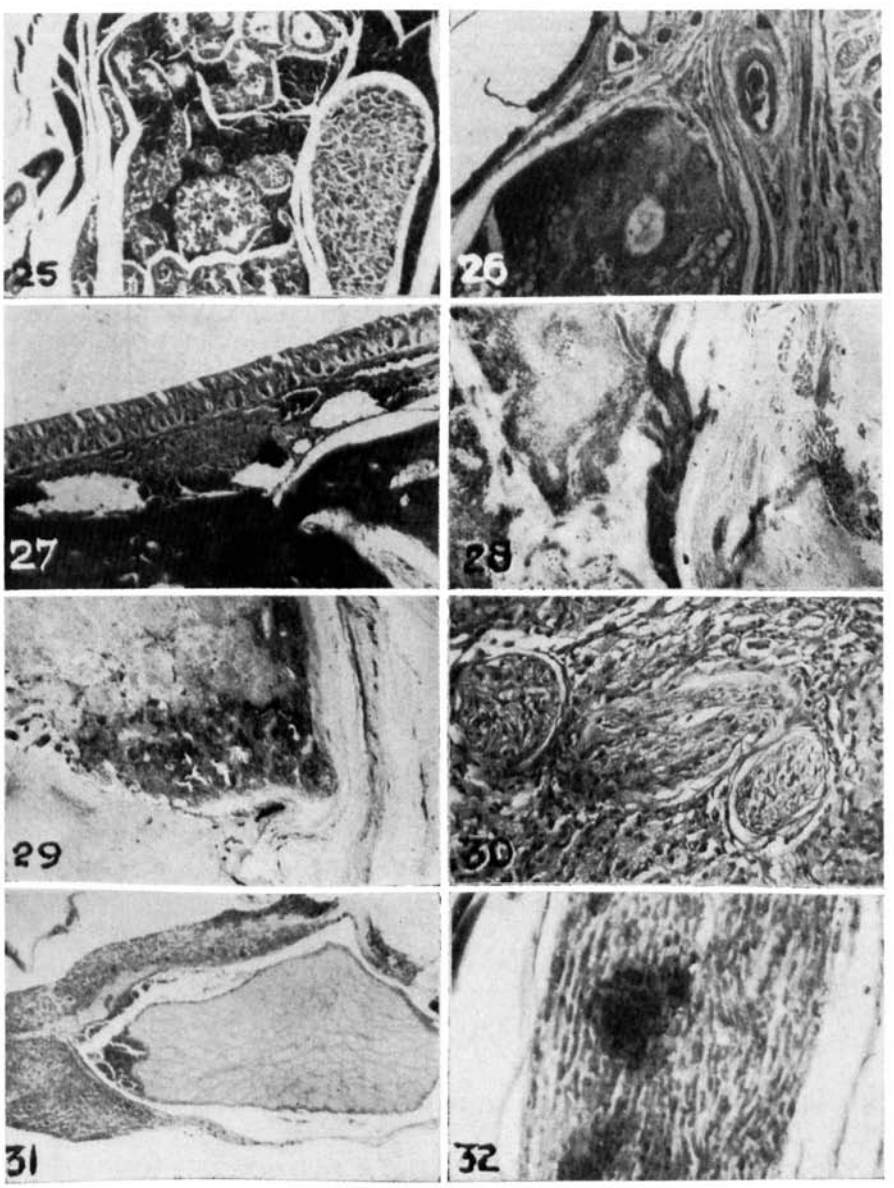

PLATE 7.