

## Visceral Lesions in Lepromatous Leprosy Study of Sixty Necropsies<sup>1</sup>

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Autopsy studies of leprosy are scarce, and some of those reported present scanty details. The earliest series is that of Hansen and Looft in 1895 reporting on 125 necropsies (<sup>11</sup>). Subsequent reports by Mitsuda and Ogawa (<sup>15</sup>), Black (<sup>5</sup>), Kean and Childress (<sup>13</sup>), Powell and Swann (<sup>16</sup>) and Desikan and Job (<sup>8</sup>), provide comparative data from several geographic areas.

The present report extends the range of findings from Argentina, first published in 1966, covering 40 necropsies (3).

### MATERIALS AND METHODS

Sixty complete autopsies on lepromatous leprosy subjects in the Baldomero Sommer Leprosarium in Argentina were performed in the period of 1965-1971, and are the subject of this report. The subjects ranged in age from 25 to 97, with the majority being between 50 and 70 years. The autopsies reflected the fact that the sanitarium's population is predominantly male.

After gross examination of all the viscera, specimens were taken from representative areas fixed in 10% neutral formalin and processed by the standard paraffin technic. Sections cut at 7 microns thickness were stained by hematoxylin and eosin. The Ziehl-Neelson stain with Kinyoun modification was used. Congo red and methyl violet stains were employed for amyloid. The Van Gieson, Gomori and Rio Hortega technics were utilized also.

### OBSERVATIONS

Two categories of lepromatous patients were observed: 26 instances of active,

bacilliferous leprosy with visceral dissemination, and 34 instances of residual or quiescent leprosy characterized by absence of bacilli and scarring with fibrosis.

**Skin lesions.** There were 29 instances of active lepromatous lesions, 14 being bacilliferous, and 26 cases where the skin was atrophic and fibrotic at autopsy. The latter were in the inactive and residual cases.

Associated lesions seen were: ulcers, 13; *erythema nodosum*, 6; edema, 4; and calcified nodules, 2. Additional lesions unrelated specifically to leprosy were: icterus, 5; basal cell carcinoma, 1; epidermoid carcinoma, 3.

**Cardiovascular system.** Specific leprosy involvement of blood vessels was most significant in small blood vessels and no lesions were found in the heart (<sup>10</sup>).

Leprous arteriolitis was found in 23 cases (in liver, spleen, skin, lymph nodes). Amyloid vasculitis was frequently seen in liver, spleen, kidneys, adrenals and pituitary glands. All cases had aortic atherosclerosis with ulcerated and calcified plaques. These findings differ from those of Desikan and Job (<sup>8</sup>) who observed a low incidence of aortic atheromatous lesions.

There were two instances of myocardial infarction in aged patients having coronary atherosclerosis. Five other cases showed myocardial fibrosis. Additionally, there were two cases with rheumatic mitral stenosis associated with myocardial hypertrophy and dilatation.

**Respiratory system.** Lepromas were present in the epiglottis in two cases. Acid-fast bacilli, not associated with tuberculosis, were found in alveolar macrophages in one instance. There were 15 cases of bronchopneumonia, lobar pneumonia and hemorrhagic pneumonia. There were five cases of pleural adhesions, four of fibrosis and pachypleuritis and two of pleural abscesses.

The incidence, of pulmonary tuberculosis

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was found to be very low. This was the opposite of the findings of Desikan and Job<sup>(8)</sup>, and Mitsuda and Ogawa<sup>(15)</sup> in Japan, who considered that it is the most frequent associated disease and cause of death in leprosy patients.

There were only eight cases, two being miliary, with dissemination to liver, spleen, lymph nodes and kidneys. Four cases were chronic fibrocaceous and two were of acute nodular caseous tuberculosis.

Other lesions found were: eleven cases of pulmonary edema, eight cases of fibrosis and pulmonary emphysema, four cases of atelectasis, four of pulmonary carcinoma (three epidermoid, one "oat cell" type).

**Digestive system.** There were rare bacilliferous infiltrates between bowel muscle bundles. There were eight instances of esophagitis, five gastroduodenal ulcers, one esophageal and one gastric carcinoma, three instances of nonspecific colitis and one case of acute perforation of colonic diverticuli.

The liver showed three kinds of leprosy lesions: a) miliary lepromas in the portal spaces (Figs. 1 & 2) composed of foam cells and containing acid-fast bacilli; b)

Kuffer cells infiltration, the cells containing acid-fast bacilli; and c) reticular hyperplasia in the portal spaces. Such lesions were found in six cases of the active lepromatous type.

Other lesions seen were: amyloidosis, fatty degeneration and fibrosis. Amyloidosis was the most frequent lesion in the liver (14 cases). There was among these an instance of insufficiency due to amyloidosis with compression and atrophy of hepatic cells but without amyloidosis in other organs. This case has been previously published<sup>(2, 4, 14)</sup>. Fatty degeneration was found in ten cases, three being massive, one perilobular and the rest being centrilobular. Fibrosis was noted in seven cases.

Additional lesions seen were: congestion, ten; cirrhosis, two; miliary tuberculosis, two; metastatic carcinoma, two; pigmentary lesions, three; lipofuscin, two; and one of hematoidin. There were three cases of acute pancreatitis and two of pancreatic fibrosis. The gall bladder and bile ducts showed no abnormalities and no gall stones were found.

**Urinary system.** There were no specific leprosy lesions. Amyloidosis and nephro-

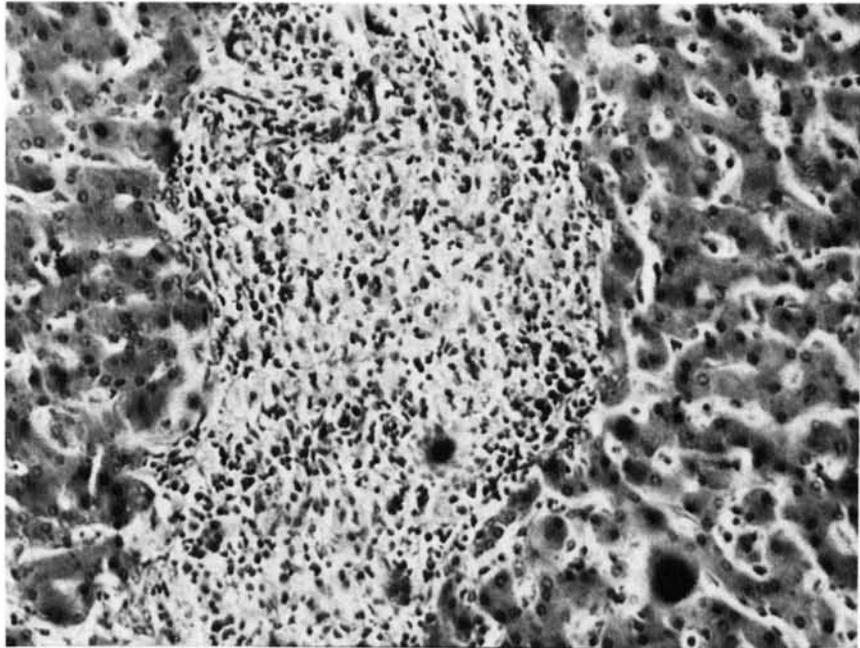


FIG. 1. Interstitial leproma in Kiernan's space in the liver of a lepromatous patient. (Ziel-Neelsen stain with the Kinyoun modification)

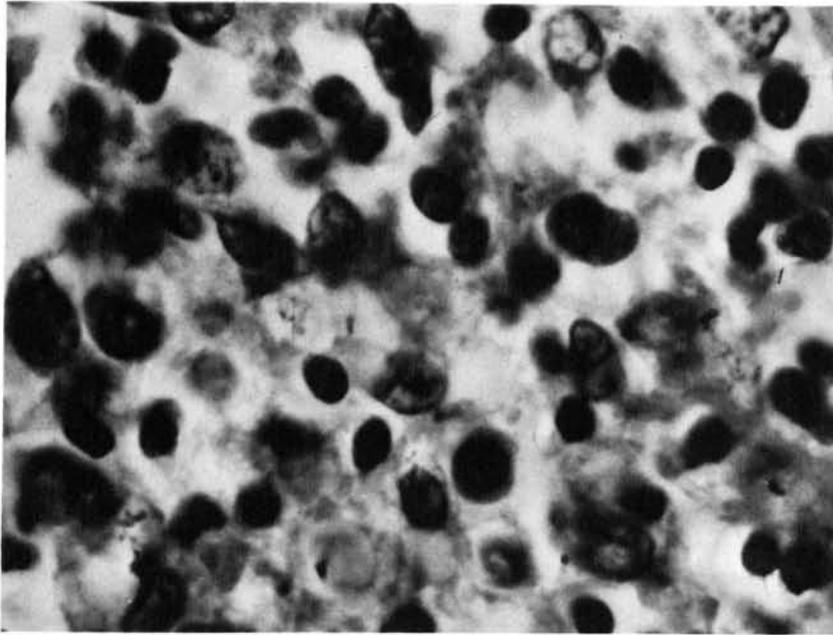


FIG. 2. Leproma in the liver (in Kiernan's space). Vacuolated Virchow cells contain bacilli. (Ziehl-Neelsen with the Kinyoun modification)

sclerosis were the most significant lesions found. The kidneys were the organs most frequently involved in amyloidosis and were usually severely damaged by it. As a result, in 19 cases (31.2%) the cause of death was renal insufficiency with terminal uremia, bronchopneumonia and pulmonary edema (<sup>2</sup>).

Amyloidosis of the kidneys presented as two varieties. In one the organs were large with smooth surfaces and having associated vascular nephrosis. Stains showed amyloid glomeruli. The second form presented as small kidneys with granular surfaces, arteriosclerosis and interstitial infiltrations by mononuclear cells (<sup>3</sup>). The former variety was found in the active lepromatous cases and the latter was most frequently seen in the quiescent cases.

Other lesions were: pyelonephritis, five; acute glomerulonephritis, two; renal miliary tuberculosis, two; hydronephrosis, two; and nine cases of cystitis.

**Male genital system.** Active leprosy orchitis was present in two cases, with Virchow cells and bacilli in them. However, the most frequent lesions in the testes were atrophy and hyalinization found in 26

cases. The latter probably represented the end phase of leprosy orchitis or other disease (<sup>9, 11, 12</sup>). There was prostatic adenomatous hyperplasia in 18 cases, gynecomatous changes in 6 cases and acute prostatitis in 2 cases.

**Female genital system.** There were no specific leprosy lesions found. There was uterine and ovarian atrophy in six cases, chronic cystitis in four; uterine myomatosis in five; and glandulocystic hyperplasia of the endometrium in two cases.

**Hemolymphatic system.** Spleen and lymph nodes were the structures most frequently affected. The spleen showed diffuse infiltration of sinusoids with foamy macrophages which were filled with acid-fast bacilli in four cases. There was amyloid deposition in 16 instances, (Fig. 3) congestion in 10 and hemosiderin pigment in one instance.

The lymph nodes showed reticular hyperplasia of sinuses in 18 cases and miliary lepromas with acid-fast bacilli in five. There were two instances of miliary tuberculosis.

**Endocrine system.** The adrenal glands were the most involved with specific

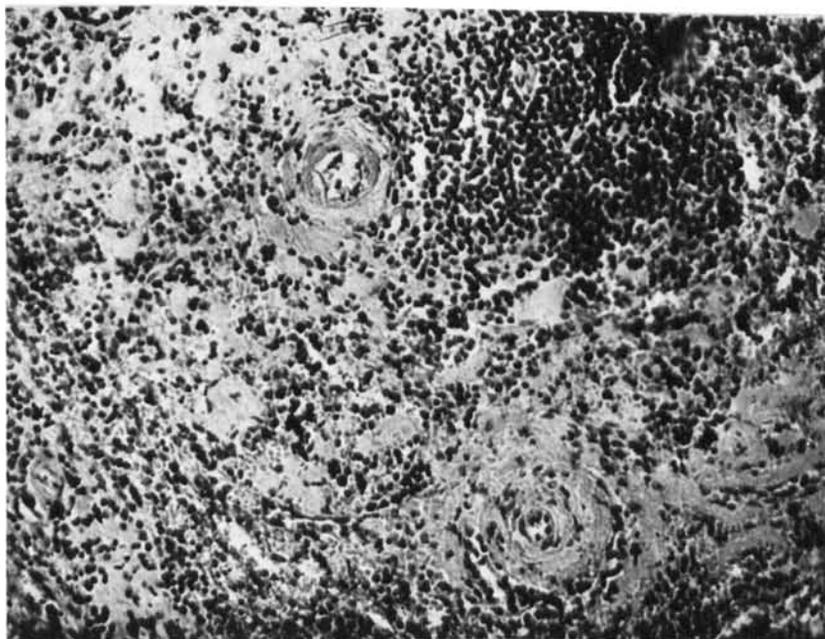


FIG. 3. Splenic amyloid with the typical Malpighian bodies and lymphocytes between the amyloid arteriolitis. (Hematoxylin and eosin)

lesions. Miliary lepromas, with Virchow cells containing acid-fast bacilli were found in the cortex in two cases. Amyloidosis (Fig. 4) was the most important lesion in

quiescent patients (14 cases). Amyloid was found in the pituitary gland in three cases and fibrosis in one. In 47 cases, there was decrease in adrenal cortical lipids, colloid

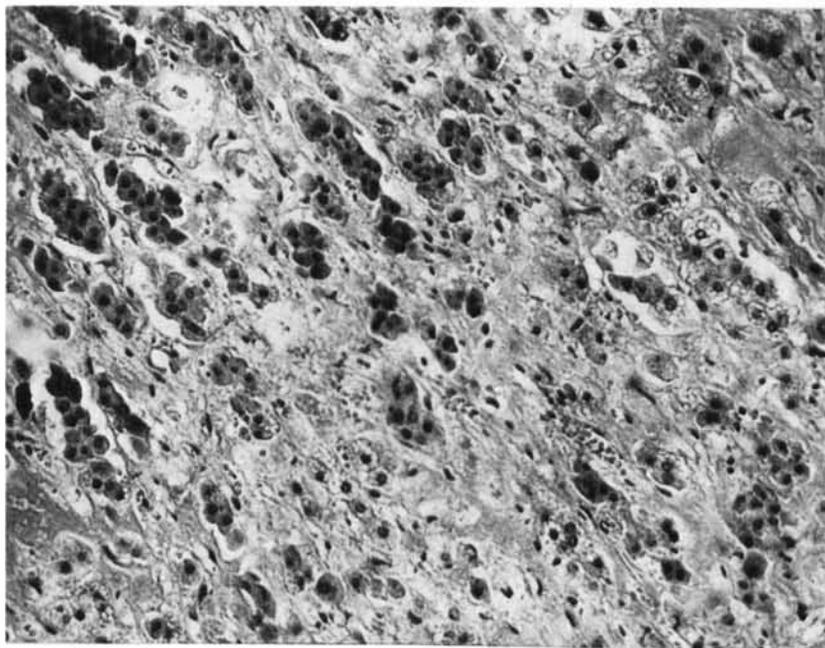


FIG. 4. Adrenal gland showing depletion of cortical lipids and amyloid infiltration. (Hematoxylin and eosin)

adenoma of the thyroid in two instances and cortical adenomas of the adrenal cortex in two cases. One eosinophile adenoma of the pituitary gland, one benign pheochromocytoma, three cases of carcinomatous metastasis to the adrenals, and one case of medullary adrenal hemorrhage completed the findings.

**Nervous system.** Specific leprosy lesions found consisted of peripheral neuritis with bacillary infiltration. Infiltration of many acid-fast bacilli in the macrophages in leptomeninges appeared in two cases. Multiple coronal sections, though, the cerebellum and cerebral hemispheres, showed no gross lesions. Sections of specimens taken from several representative areas of the brain showed no significant lesions.

Nonleprosy lesions found were: four brain hemorrhages, four instances of meningeal edema and one glioblastoma multiforme. Ocular lesions were: iridocyclitis with associated diffuse leptomeningeal infiltration of the ciliary body. There was ocular calcification in six cases. In no cases were there demonstrable lesions in the posterior half of the eye or in the optic nerve.

### DISCUSSION

Table 1 summarizes the findings with respect to visceral lesions as found in the

autopsy reports from 1895 to 1971, as culled from the literature.

The earliest reported autopsy series in leprosy is that of 1894 by Hansen and Looft which was translated into English by Walker in 1895. In 1937, Mitsuda and Ogawa<sup>(15)</sup> published a study of 150 autopsies at the Aiseien Leprosarium. They found that tuberculosis was the most important complicating disease (54.7%) while others of a lesser incidence were renal insufficiency (13.3%), septicemias (9.3%) and cardiac insufficiency (7.4%). These findings could be expected before the age of chemotherapy.

However, in 1968 Desikan and Job<sup>(8)</sup>, in a review of post-mortem findings in 37 cases of leprosy found tuberculosis to be the cause of death in 29%; tetanus was second (13.2%) in their series; and renal insufficiency third (11.3%).

In 1942, Kean and Childress<sup>(13)</sup> with 103 necropsies in Panama, also found tuberculosis to be the most important disease associated with leprosy (24%). This series was derived from the period when the construction of the Panama Canal was taking place and the local laboring populace was reinforced by immigration of Negroes (of 103 autopsies, 59 were Negro). Renal insufficiency (22%) was the second most frequent cause of death, while cachexia

TABLE 1. Comparative table of causes of death in leprosy in various countries.

Year	1895	1902	1942	1955	1967	1968	1971
Country	Germany	Japan	Panama	U.S.A.	Argentina	India	Argentina
Authors	Hansen and Looft	Mitsuda and Ogawa	Kean and Childress	Powell and Swann	Bernard	Desikan and Job	Bernard and Vazquez
No. of cases	125	150	103	50	40	37	60
Renal failure		13.3%	22.0%	38.0%	42.5%	11.2%	31.6%
Acute pulmonary infections		5.0%	3.0%	15.0%	7.5%	7.9%	15.0%
Tuberculosis		54.7%	24.0%	14.0%	17.5%	29.2%	11.7%
Cardiac failure		7.4%	10.0%	9.0%	5.0%	7.9%	10.0%
Septicemia		9.3%	2.0%		7.5%	7.8%	8.3%
Internal hemorrhage			3.0%		5.0%	5.8%	6.6%
Brain hemorrhage			2.0%		2.5%	2.7%	5.0%
Liver failure			1.0%				1.6%
Tetanus						13.2%	
Malaria		1.2%	3.0%				
Other causes		5.2%	11.0%		5.0%		9.0%

TABLE 2. Causes of death in lepromatous leprosy in the Sommer Leprosarium (autopsy).

Disease	Total	Quiescent leprosy	Active leprosy
Renal failure	19	7	12
Acute	2	—	2
Chronic	17	7	10
Acute pulmonary infections	9	2	7
Tuberculosis	7	4	3
Hemorrhagic shock	4	3	1
Cachexia	3	3	—
Cardiac failure	6	4	2
Brain hemorrhage	3	3	—
Liver failure	1	1	—

(15%) and cardiac insufficiency (10%) ranked third and fourth. Powell and Swann (16) in 1955, presented 50 necropsies from the National Leprosarium at Carville, Louisiana. They found renal insufficiency to be the cause of death in 38% of their cases while respiratory insufficiency and tuberculosis occurred in only 14%. In our 1966 series of 40 cases (3), renal insufficiency due to amyloidosis was the most important cause of death in leprosy (42.5%), while tuberculosis held second place with 17.7%. In the present series of 60 cases (Table 2) there was a lower incidence (31.65%) of renal insufficiency while 15% of the cases had respiratory insufficiency associated with pulmonary infections, and there were 11.7% with tuberculosis.

Thus, in Oriental countries such as India and Japan, tuberculosis is the most important cause of death in leprosy while renal insufficiency occupies second place, Table

3. In Occidental countries, such as Scandinavia, U.S.A., Panama and Argentina, the most important cause of death has been renal insufficiency generally due to amyloidosis while respiratory diseases and tuberculosis have been of secondary importance. It may be speculated that the incidence of amyloidosis may be related to variations in diets since in Oriental countries there often is a lower protein intake. It might be postulated that amyloidosis is very high in Argentina because of high protein consumption. However, leprosy reactions and chronic osteomyelitis both occur in India and Argentina.

There has been much discussion in recent years of cross-immunity between tuberculosis and leprosy. Chaussinand (7) was among the first to put forward this concept, basing it on his observation that as tuberculosis increased in Western countries, leprosy decreased. We find that both diseases are independent and often association is very common in Argentina, but they seem to have no effect on each others prevalence.

We found lepromatous visceral lesions in 23% of active leprosy (bacteriologically positive) cases and in 10% of all cases.

Desikan and Job discovered leprosy lesions not only in active cases of lepromatous leprosy but also in bacteriologically negative and clinically quiescent cases. They found such lesions in the testes in four cases, in the liver in two cases and in one case each in lymph nodes, adrenal and spleen. They also emphasized the danger of relapse in treated cases and the need to continue treatment for a long time after skin lesions have cleared.

TABLE 3. Comparative causes of death in leprosy.

	COUNTRIES			
	OCCIDENTALS		ORIENTALS	
U.S.A.	PANAMA	ARGENTINA	JAPAN	INDIA
Renal failure	38%	Renal failure 22%	Renal failure 43%	Tuberculosis 55%
Tuberculosis 14%	Tuberculosis 24%	Tuberculosis 12%	Renal failure 13%	Tuberculosis 29%
				Renal failure 11%

TABLE 4. Manifestations of leprosy in the internal organs.

Organ	Miliary lepromata	Lepromatous infiltrations	Fibrosis
Skin	23	14	8
Liver	6	2	6
Spleen	4	3	10
Larynx	2	1	2
Lymph nodes	6	4	10
Nerves	—	6	—
Eyes	—	—	6
Testes	2	5	26
Leptomeninges	—	2	—

In the present study, the liver, lymph nodes, spleen and adrenal glands were found to be the internal organs most commonly having leprosy lesions, Table 4. In the liver the earliest lesions were seen in Kiernan's spaces as miliary lepromas and also as infiltration of the sinusoids by bacillus-laden lepra cells. Desikan and Job<sup>(8)</sup> observed that the respiratory, urinary and digestive tracts did not show lepromatous lesions and they remarked that the lymph nodes draining them, viz, the mesenteric and thoracic, did not show lepromatous lesions. However, in our study we observed pulmonary alveolar macrophages containing bacilli and intestinal lepromas between bowel muscle bundles. We think that the reticuloendothelial system may phagocytose bacilli and these organisms may be found in any place in the body. We observed them in the meninges, for example.

Renal lesions were those most frequently observed in all reported studies (Powell and Swann 38%, Kean and Childress 51%, Guasp 63%<sup>(10)</sup> and presently in 42.5%), and they expired due to renal insufficiency. Interstitial nephritis and pyelonephritis were common findings in the present study. *Erythema nodosum leprosum*, toxic states, and viral infections may be causes of renal diseases. Brusco and Masanti<sup>(6)</sup> in Argentina, observed that 59% of lepromatous cases in reaction developed kidney disease by the time of death as compared to 26% in patients without reaction.

While it is generally held that death in leprosy is due to some other associated disease, Mitsuda and Ogawa<sup>(15)</sup> found

that in 4% of their cases death was due to the virulent form of leprosy. The latter was not a finding in this study.

### SUMMARY

Autopsy findings in 60 cases of leprosy are presented. This is the second such report from Argentina.

Lepromas in visceral dissemination were demonstrated in 10% of cases in liver, spleen, lymph nodes, testes, meninges, bowel, eye (iridocyclitis), adrenal gland and larynx (epiglottis).

Renal insufficiency due to amyloidosis was the most important cause of death (31.2%), with tuberculosis (11.7%) occupying second place.

Previous reports of autopsy findings in leprosy from several parts of the world are compared with the present series.

### RESUMEN

Relatamos 60 casos completos de autopsias del Sanatorio Baldomero Sommer de la República Argentina. Siendo el segundo del país.

En él observamos un 10% de diseminaciones viscerales en forma de lepromas miliares a hígado, bazo, ganglios linfáticos, testículos, meninges, intestino, ojos (iridociclitis) adrenal y larínge (epiglotis).

La causa más importante de muerte en ellos ha sido la insuficiencia renal por amiloidosis (31.2%) siendo la tuberculosis una enfermedad secundaria en estos casos (11.7%).

Se efectuó además una reseña bibliográfica e histórica de los distintos relatos de autopsias en la literatura mundial, observando que en los países orientales (India y Japón) la tuberculosis es la causa más importante de muerte en los lepromatosos, mientras que en los occidentales (E.E.U.U., Panamá y Argentina), la misma resulta secundaria, siendo el problema más importante en ellos la insuficiencia renal por amiloidosis.

### RÉSUMÉ

Nous avons présenté ici 60 cas complètes d'autopsies du Leprosarium Sommer de la R. Argentine. C'est le second étude fait dans ce pays. Nous avons trouvé un 10% de diseminations viscérales de lésions lépromateuses dans la forme de lépromes miliares dans le foie le rat, les ganglions lymphatiques, les testicules, les intestines, les méninges, et les yeux (iridocyclitis), l'adrénale et la larynx (épiglotis).

L'insuffisance rénale par l'amyloidosis

(31.2%) c'est la cause la plus importante de mort, suivit de la tuberculosis (11.7%), maladie qui est secondaire chez eux.

On a fait aussi une révision bibliographique et historique des diverses publications d'autopsies de lèpre dans la littérature mondiale, ayant observé que dans les pays orientales (India y Japon), la tuberculosis est la cause la plus importante de mort chez les lépromateux, pendant que dans les occidentales (E.E.U.U., Panamá et Argentine) la même était secondaire, ayant le problème le plus importante à l'insuffisance rénale par l'amyloidosis.

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