

## A STUDY OF ONE HUNDRED AND FIFTY AUTOPSIES ON CASES OF LEPROSY

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In a recent issue of *THE JOURNAL* there was published a letter from Arning (1) in which he brought up the question of the visceral changes in leprosy, with particular reference to the occurrence of tuberculoid and necrotic changes of the kind that he had observed in Honolulu and which he considered to be a miliary tuberculoid condition of leprotic nature. He proposed that inquiry be made concerning the prevalence of this condition:

... in different centers, races and climates, and its occurrence in either of the two types of leprosy, calling special attention to its liability to be confounded with tuberculosis and therefore ignored.

The Editor of *THE JOURNAL* submitted this question to one of us (K. M.) with the suggestion that, because many autopsies on cases of leprosy have been done in Japan, it should be particularly interesting to have a statement on the subject from here. The present article was prepared in response to this suggestion.

During his forty years of service in leprosy work, the senior author has personally done more than one thousand autopsies. It was our plan to analyze the records of several hundreds of these cases, but it was not found feasible to do that because of differences in the records made at different periods. During the five years that have elapsed since the opening of the Aiseien leprosarium in 1931, about 150 autopsies have been done here. A summary of the records of these cases suffices to give a general idea of the macroscopic pathology of leprosy in Japan.

### CAUSES OF DEATH

The principal cause of death in Aiseien, as in most other leper colonies, is tuberculosis, with a rate of 54.7 percent. This and other data on causes of death are shown in Table 1. It is especially when patients of the cutaneous type are weakened by lepra reaction (or erythema nodosum leprosum, as it is called in Japan) that they are

liable to be affected by this complication. Tuberculous infection is on the whole much more serious in lepers than in other people, and sometimes it is acute. The rates for Aiseien and the Culion colony in the Philippines are almost identical. According to statistics of the latter place for the nine years from 1924 to 1932, shown for comparison in Table 2,<sup>1</sup> the tuberculosis death rate there has varied from 52 to 55 percent during that period. Tuberculosis as a complication of leprosy constitutes a grave problem in all leprosaria. It has also been, undoubtedly, the cause of misunderstandings concerning visceral leprosy, a matter which will be discussed shortly.

TABLE 1.—*Causes of death in 150 autopsied cases at Aiseien, by types of leprosy.*

Cause of death	Neural cases		Cutaneous cases		Total	
	No.	Percent	No.	Percent	No.	Percent
Tuberculosis .....	6	31.6	76	58.0	82	54.7
Kidney disease.....						
Chronic .....	3	15.8	6	4.6	9	6.0
Acute .....	0	0.0	4	3.0	4	2.7
Uremia.....	1	5.2	6	4.6	7	4.7
(Total) .....	(4)	(21.1)	(16)	(12.2)	(20)	(13.3)
Septicemia.....	4	21.1	10	7.6	14	9.3
Leptous cachexia .....	0	0.0	6	4.6	6	4.0
Laryngeal stenosis.....	0	0.0	2	1.5	2	1.3
Other conditions .....	5	26.3	21	16.0	26	17.3
Totals .....	19	100.0	131	99.9	150	100.0

The second most common cause of death at Aiseien is nephritis; the rate is 13 percent, the same as that for Culion. The third highest figure with us is for septicemia, 9.3 percent. This is very different from the Culion figure of 1.6 percent (or even the 3.0 percent attained by including the cases diagnosed as gangrene), but it is not due to neglect or lack of cleanliness. It is a fact that the Japanese are fond of taking hot baths, and our patients bathe every other day; furthermore, the bandages of their ulcers are changed almost every day. The frequency of septicemia among our patients, in spite of these measures, is due to the fact that leprosy ulceration is much more common here than in warm countries. In the cold winter season the ulcers become more numerous and more serious, with correspondingly greater danger of septic infection.

Among our 1,200 patients at Aiseien there are 20 (nearly 2 percent) who carry tracheotomy cannulas, but in spite of the frequency

<sup>1</sup>Data obtained from Dr. C. B. Lara, chief physician at Culion, by Dr. F. Hayashi, during his recent visit there.

of this operation 1.3 percent of our deaths have been due to laryngeal stenosis. That condition is seldom seen at Culion. This fact, as well as the severity of ulcerations and certain other conditions (e. g., eye and scalp affections) among our patients supports the view expressed by Hayashi (4) that our cold climate aggravates seriously the effects of leprosy.

That leprosy itself is comparatively seldom the cause of death is common knowledge among leprologists. Our figure is 4 percent, which is in agreement with that at Culion (5 percent) in recent years. Before 1922, when there was an insufficient number of doctors at Culion and no autopsies were done, "leprous cachexia" was recorded as the cause of death in 3,001 out of 9,369 cases, nearly one-third, which was obviously incorrect.

TABLE 2.—*Causes of death at the Culion Leper Colony, 1924 to 1932.*

Diagnosis	Number of cases	Percent of deaths
Tuberculosis .....	1,533	48.6 <sup>a</sup>
Nephritis, all kinds .....	411	13.0
Heart disease, organic .....	234	7.4
Leprosy .....	174	5.5
Pneumonia, broncho- .....	83	2.6
Pneumonia, lobar .....	82	2.6
Ileocolitis, nonspecific .....	76	2.4
Beriberi .....	63	2.0
Septicemia .....	50	1.6
Gangrene .....	44	1.4
Malaria .....	37	1.2
Dysentery .....	24	0.7
Other causes .....	344	10.9
Total .....	3,155	99.9

<sup>a</sup>Since 1929 tuberculosis has been the cause of death in from 51.6 to 54.6 percent of deaths.

In general, it may be said that the causes of death at Aiseien are similar to those in leprosy hospitals in other parts of the world.

#### LEPROUS CHANGES

Many studies of the leprous changes of the viscera and other structures examined at autopsy have been made. Mitsuda has carefully gone into this matter, especially in a study published in the Japanese language in 1918 and recently republished in an English translation (5). The findings in the 150 cases that have been examined at Aiseien are shown in Table 3 and discussed briefly here.

With regard to changes in the viscera, it need only be recalled that macroscopic changes of the viscera are found in the liver, spleen, suprarenal and testis. Microscopically, leprosy changes are also found in the heart, stomach, intestine, kidney, urinary bladder, ovary, etc. It is to be understood that such changes are to be found only in cutaneous-type cases, and not in those of the neural type. Reports of such changes in the latter type, except for those of the testis, are due to erroneous classification. It is true that such lesions (consisting of lepra cells with scanty bacilli) are to be found in the so-called "secondary neural" cases, but these are only cutaneous cases in which the lepromatous infiltrations have been absorbed, and are to be classified as primarily of that type.

TABLE 3.—Manifestations of leprosy in the internal organs in 150 autopsies at Aiseien.

Organs affected	Neural type				Cutaneous type				
	Macular <sup>a</sup> (5 cases)	Ordinary (14 cases)	Total (19 cases)	Percent affected	C1 (11 cases)	C2 (83 cases)	C3 (37 cases)	Total (131 cases)	Percent affected
Lymph glands ..	0	0	0	0.0	11	83	37	131	100.0
Viscera .....	0	0	0	0.0	10	80	37	127	96.9
Cranium .....	0	0	0	0.0	1	2	7	10	7.6
Spinal cord.....	3	10	13	68.4	5	37	24	66	50.4
Peripheral nerves	5	14	19	100.0	9	74	33	116	88.5
Vagus, right....	1	3	4	—	5	38	20	63	—
Vagus, left .....	1	0	1	—	0	2	4	6	—
Vagus, both.....	0	3	3	—	2	4	6	12	—
(Vagus, total)	(2)	(6)	(8)	42.1	(7)	(44)	(30)	(81)	61.8

<sup>a</sup>Cases designated as "macula tuberculoid" in Japan.

With regard to leprotic changes not dealt with in the article by Mitsuda referred to, the gross manifestations may be described briefly.

*Lymph glands.*—In cutaneous leprosy the lymph glands are affected in various degrees. In the femoral, inguinal and portal glands especially, the involvement is so marked that changes are to be seen even in cases of slight degree, and in cases in which the skin lesions have become completely absorbed. The finding of the characteristic grayish or yellowish (lipoid) degeneration in the glands of a case is conclusive proof that it was of the cutaneous type. While the bacilli are fresh and abundant, and the lipoid substance is scarce, the lesion-foci are whitish and somewhat translucent, but as the bacilli undergo degeneration and the lipoid material increases they become proportionately more distinct and yellowish in color.



*Testis.*—It has been our practice to examine the testis at autopsy only with regard to consistence and the appearance of the surface. Because cutting the organ open before fixation disturbs the topography, we examine it on section only after it has been fixed in formalin. Hence the findings in this organ are omitted from this article.

*Bone involvement.*—Leprotic periostitis and involvement of the osseous structure are found in various bones, such as the tibia and the phalanges. At Aiseien we are accustomed to examine only the cranium, after the brain is removed. In a considerable number (7 percent) of the cutaneous cases we find leprotic bone changes there. This involvement is manifested by yellowish, flat raised areas with rough surfaces; these are seen only in cutaneous cases, and as a rule only in advanced ones. Microscopically the leprotic lesions are usually seen to develop from the periosteum or the diploe, but sometimes lepromatous infiltrations or nodules of the scalp give rise to this cranial change.

*Degeneration of the posterior spinal column.*—The only macroscopic change seen in the central nervous system is that of the spinal cord, described by Lie in 1904 (5) and Mitsuda (6) in 1906. This is a grayish coloration of the tracts of Goll and Burdach, caused by an ascending degeneration due to leprotic peripheral neuritis and dependent in its degree upon the degree of the nerve change. This degeneration is especially marked in the cervical portion of the cord, from where the nerves of the upper extremities arise. We have found it in 68 percent of neural cases and 50 percent of the cutaneous type.

*Enlargement of peripheral nerves.*—In the clinical examination of lepers one can detect enlargement of the median and radial nerves in their upper and lower portions, and of the ulnar in its middle portion, at the elbow. At autopsy we usually examine these nerves and, when there is indication for it, the peroneal and posterior tibial nerves as well.

There are two kinds of nerve enlargement, one characteristic of cutaneous leprosy and the other of neural. In the former type the swollen portions show lepromatous changes histologically, and in general contain more bacilli than do the lesions in neural cases. In the latter type tuberculoid changes are often found in the enlarged nerves, sometimes with caseation or calcification. These changes are often associated with tuberculoid macules of the skin. In these nerve lesions bacilli are very scanty, as reported by Chatterji (2) and others. Contrary to the usual rule, smear examination is better than histological search for bacilli in the caseous lesions of the nerve.

As a result of atrophy the affected nerves sometimes become thinner than normal, but in that case their consistence is firmer. As is shown in Table 3, enlargement of nerves was found in **all** of the neural cases and 88 percent of the cutaneous ones. In the other cases the nerves were atrophic or of normal size, but in either case bacilli were to be found, together with histological changes characteristic of one or the other type of the disease.

*Affection of the vagus nerves.*—It is our practice to examine the vagus nerve at autopsy, and we often find enlargement, usually between the subclavian artery and the bronchial bifurcation. The left vagus is less frequently enlarged than the right. The latter contains more sympathetic fibers and these usually contain many bacilli, which explains the greater enlargement of this nerve. The frequencies with which swelling is found on the right side, the left side, and both sides, are approximately 4:1:3 in neural cases and 5:1:2 in cutaneous cases. In total, enlargement of this nerve was found in 42 percent of neural cases and 62 percent of cutaneous cases.

#### RELATION BETWEEN TUBERCULOSIS AND LEPROSY

As stated above, tuberculosis is very common among lepers. It is the cause of at least one-half of the deaths, and is also found at autopsy in many cases that die of other causes. The total frequency in our group under discussion was 85 percent—121 out of 142 cases.

The variety of the neural type of the disease which we call "macula tuberculoid" has been much discussed in recent years, especially since Wade's visit to Japan, South Africa and other countries (8). Arning (1) has recently recalled his experience in Hawaii, where he found tubercle-like lesions in the viscera of several autopsies. He is now uncertain whether these lesions were tuberculous or were of the same nature as the tuberculoid macules so commonly seen in the skin. Many investigators in the past have made the same mistake of assuming tuberculosis of the viscera to be of leprotic nature.

The findings in our autopsies that bear on this question are shown in Table 4. If Arning is correct in his view, it would be expected that lesions of the kind to which he refers would have been frequent in our macular tuberculoid cases, if in no others. The fact is that only one of the five cases in that group showed tuberculosis-like lesions. On the other hand, among our cutaneous-type cases, the group in which tuberculoid changes are never seen in the skin, 107 out of 123 cases (87 percent) showed tuberculous changes.

These findings indicate that the leprotic tuberculoid change is found only in the skin (and, as stated, in the nerves), and that the lesions of the same general appearance that are found in the viscera are actually due to complicating tuberculosis. This fact was noticed in 1894 by Hansen and Looft (3). The following is quoted from their publication:

Arning hat eine Miliarlepra beschrieben und in den Producten dieser Affektion Riesenzellen gefunden und auch leprose Darmulcera. Dr. Arning hat uns freundlichst einige Praeparate dieser Miliarlepra geschickt; in diesen finden wir ueberall, dass es sich um Tuberculose handelt. . . .

TABLE 4.—*Relation between the existence of tuberculous foci in the viscera and the type of leprosy.*

Type	Number of cases	Tuberculosis present		Tuberculosis absent	
		Cases	Percent	Cases	Percent
Neural leprosy					
Tuberculoid . . . . .	5	1	20.0	4	80.0
Ordinary . . . . .	14	13	92.9	1	7.1
Cutaneous leprosy					
(All stages) . . . . .	123	107	87.0	16	13.0
Total . . . . .	142	121	85.2	21	14.8

Most of Arning's autopsies were probably of cutaneous cases, and when such cases are complicated by tuberculosis we often find tubercles and lepromata side by side in the same viscera. The occurrence of tuberculoid macules is an indication of resistance to the leprous infection in neural cases, and is in contrast with the condition in the cutaneous type, in which the resistance is very low. This has been the opinion of Mitsuda for thirty years, and it has recently been recognized by other leprologists. The tuberculoid macular change and the lepromatous lesion are histologically incompatible and never occur together in the same individual.

#### CONCLUSIONS

1. In the past forty years more than one thousand autopsies on cases of leprosy have been performed by one of us (K. M.). The findings in the most recent 150 autopsies, done at the Aiseien leprosarium, are representative and are analyzed here. Certain of the conditions found are discussed.

2. In this group of cases the most common cause of death was tuberculosis, which is in agreement with experiences in the Philippines and other foreign countries.

3. Leprotic lesions of the viscera, aside from those of the testis, are found only in cases of the cutaneous type, and not in neural cases. They are found in "secondary neural" cases, but these cases are to be classified as primarily cutaneous.

4. Lepromatous involvement of the lymph glands is also limited to the cutaneous type, and it is found in such cases even when they are of slight degree of advancement.

5. Tuberculosis-like changes in the viscera have no relation to the tuberculoid changes found in the tuberculoid macules of the skin; such visceral changes are only a manifestation of generalized tuberculosis.

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