TUBERCULOSIS AT THE UNITED STATES PUBLIC HEALTH SERVICE HOSPITAL, CARVILLE, LOUISIANA, 1922-1950 ¹

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Tuberculosis is universally a common and serious complication in leprosy patients. This is as true at the U. S. Public Health Service Hospital, Carville, Louisiana, as in leprosaria in other countries (1, 2). Of 607 patients dying in the hospital among 1,512 admitted prior to July 1, 1950, 141 have had moderately or far-advanced active tuberculosis at the time of death. Thus tuberculosis was a primary or contributory cause in 23 per cent of all deaths. At the time of death another 16 patients had minimal active tuberculosis and 13 had arrested tuberculosis.

The part which tuberculosis has played in many of the deaths is difficult to assess, for the majority of patients having it in active advanced form also have renal disease, and in the pre-sulfone days at this hospital most of the patients were also suffering from progressively active far-advanced leprosy at time of death. The most common pathological process responsible for death at this hospital is amyloid degeneration of the kidney, probably due to the leprosy itself. Leprosy also at times causes death by suffocation as a result of leprous laryngitis with its laryngeal stenosis and edema. Or, a patient may die during lepra reaction. Therefore, the most that can be said is that tuberculosis is a significant contributory factor and in many cases the chief cause of death.

Admissions to the hospital and deaths occurring there between February 1, 1921² and June 30, 1950 are shown in Table 1. The ratio of males to females among patients ad-

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 $^{^2}$ This was the date when the hospital first became a federal institution. Prior to that time it had been the leprosarium of the State of Louisiana.

mitted has been 2.3 to 1; among deaths from all causes it was 3.1 to 1, and among deaths with tuberculosis it was 6.4 to 1. This shows the relatively greater importance of tuberculosis among males. Mexican and Filipino nationalities are shown separately in this tabulation in order to study the importance of tuberculosis in these groups. The percentages of all patients who at time of death had moderately or far-advanced active tuberculosis among the various nationality groups were as follows: among whites, 17.6; Mexicans, 29.6; Negroes, 32.9; Chinese and Japanese, 35.7, and Filipinos, 66.7. It should be recognized, however, that the excess proportions of tuberculosis deaths among Chinese, Japanese and Filipinos may be explained in part by the fact that over 90 per cent of admissions of these ethnic groups are males.

		Sex		Race						
	Total	Male	Female	White	Mexican	Negro	Chinese and Japanese	Filipino	Other	
Patients admitted	1512	1060	452	877	303	169	79	79	9	
Deaths from all causes	607	458	149	408	71	79	28	15	6	
Deaths with pulmonary tuberculosis:									-	
Far or moder- ately advanced active	141	122	19	72	21	26	10	10	2	
Minimal active	16	11	5	10	3	1	1	0	1	
Arrested	13	10	3	12	0	0	1	0	0	

TABLE 1.—Admissions and deaths by sex and race groups.

Data for the years 1922 to 1950 have been divided into periods, three of seven years each and one of eight years: 1922-1928, 1929-1935, 1936-1942, and 1943-1950. The data are on the basis of fiscal years since the records here, as in other government hospitals, are kept in this manner. Thus the year 1950 includes the interval from July 1, 1949 to June 30, 1950. The last period covers the time since the introduction of sulfone drugs in the treatment of leprosy. This was done in order to compare the occurrence of tuberculosis in the pre-sulfone and sulfone periods, both in patients who have died with it and in those who are known to be still living with either active or arrested tuberculosis.

In any study of tuberculosis among patients at this hospital several factors should be considered: (1) Marked im-

provement in the records kept on patients during the past ten years. This tends to bring to light more cases of tuberculosis in recent years. (2) Change in the tuberculosis case-finding procedure. This would not only uncover more cases of tuberculosis, but would bring them under treatment earlier. (3) Change in isolation procedure of tuberculosis patients. With routine isolation of active cases since 1941, spread of the disease may be assumed to have decreased. (4) Change in the therapy of leprosy. The sulfone drugs have replaced chaulmoogra oil in routine therapy of leprosy at Carville.³ Streptomycin alone and in conjunction with the sulfones has been used since 1946, penicillin since 1945. These changes in therapy have resulted in a remarkable improvement in both clinical status and in bacteriological findings among the patients. Most patients under sulfone therapy have shown marked improvement in their leprosy, with healing of upper respiratory tract lesions, shrinking of lepromatous skin lesions, and marked reduction in the frequency of lepra reactions and of attacks of iridocyclitis, erysipelatoid eruptions, etc. Eventually bacteriological examinations of the skin and nasal mucosa in many patients have shown reductions in numbers of bacilli, finally to the point of becoming negative, with resultant increase in the discharge of arrested cases (3).

The dietary and general living conditions have been good throughout the existence of this hospital, so that no change in effect on tuberculosis could be attributed to them. All patients live in private rooms, in both the men's and women's dormitories, while in the infirmary building also they have singlebed rooms. Hence the possibility of tuberculosis spreading within the hospital is probably not much different from that which would occur among middle-class apartment-house dwellers in a city, many of whom also, similarly to the patients here, eat cafeteria-style in large groups of people. The main difference is that patients tend to congregate in groups during the day for recreation, hence there is fairly constant exposure to the same individuals.

Data relative to tuberculosis were obtained by a search of the clinical record of each patient, note being taken of clinical and X-ray findings, sputum cultures, autopsy reports and

³ Promin was used first in 1942, diasone first in 1944, promizole first in 1946, sulphetrone and promacetin first in 1948, and all were in use at the time of this analysis.

death certificates. To cross-check the information so obtained, microscopic slides of lung sections from all autopsies from 1933, previous to when no slides were available, through 1950 were examined for evidence of tuberculosis. Autopsy charts of patients dying prior to 1933, about one-half of which had microscopic as well as gross descriptions of the organs and tissues, were also read. To be classed as a case of tuberculosis in this study, a patient must have had positive X-ray findings, and, in the case of patients who died and were autopsied, gross pathologic findings characteristic of tuberculosis plus microscopic slide confirmation of the diagnosis if—as was the fact with almost all autopsied cases—slides had been made. The records of sputum cultures and guinea-pig inoculations were of little value, for prior to 1940 cultures had been made for only about one-half of the patients with tuberculosis.

The proportion of deaths in which autopsies have been done has been at a high level at Carville since it became a federal hospital, varying from 66 to 77 per cent during the four periods, as is seen in Table 2. Autopsy records were available for 86 per cent of patients dying with far-advanced active tuberculosis, and for 95 per cent of those with moderately-advanced active disease. All diagnoses of minimal active tuberculosis were made at autopsy, and, since this amount of tuberculous involvement probably played a very minor role—if any—in the deaths of these patients, these cases are not included in the study of patients dying with tuberculosis.

				Tuberculosis									
Time	all	Deaths, all causes			Far- advanced			Moderately- Advanced			Minimal		
period	riod Number, total	With autopsy		No. of deaths	With autopsy		No. of deaths	With autopsy		No. of deaths	With autopsy		
	No.	P.c.	No.		P.c.		No.	P.c.		No.	P.e.		
1922-28	112	81	72	22	19	86	4	3	75	5	5	100	
1929-35	147	97	66	28	25	89	8	7	88	3	3	100	
1936-42	212	164	77	37	29	78	19	19	100	- 6	6	100	
1943-50	136	103	76	14	14	100	9	9	100	2	2	100	
Totals	607	445	73	101	87	86	40	38	95	16	16	100	

 TABLE 2.—Deaths from all causes and from tuberculosis classified as to history of autopsy.

During the period under study there was an increase in the average annual census, especially between 1921 and 1928.

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The bed capacity was expanded in 1921 to take care of the patients admitted from the entire United States. Since 1933 the average annual census has ranged from 350 to 400. The number of deaths from all causes and from tuberculosis for the four time periods are given in Table 3. Deaths for single years are not shown, since the numbers are so small that comparisons would be difficult.

		Deaths, a	all causes	Deaths, tu	berculosis	Ratio:		
Time period	Average annual census	Number of deaths	Average annual rate per 1000	Number of deaths	Average annual rate per 1000	deaths from tuberculosis to deaths from all causes (per cent)		
1922-28	217	112	73.7	26	17.1	23.2		
1929-35	341	147	61.6	36	15.1	24.5		
1936-42	368	212	82.3	56	21.7	26.4		
1943-50	383	136	44.4	23	7.5	16.9		

TABLE 3.—Death rates from all causes and from moderately and far-advanced tuberculosis.

Although the number of deaths increased in each of the first three periods, they decreased markedly in the last period, 1943-1950. This decrease, coupled with an increase in the average annual census, resulted in a lowering of the average annual death rate from all causes from 82.3 per 1000 in 1936-1942 to 44.4 in 1943-1950. This decrease, of about 46 per cent, would appear to be related to the introduction of the sulfone drugs. Among those dying with tuberculosis, there was little change in the rates between 1922 and 1942. Since the advent of the sulfone era, however, there has been a marked decrease, the rate for 1943-1950 being only about 35 per cent of that for the preceding period. These decreases are much more marked than in the general population of the country. The death rate from all causes in the United States in 1939 was 10.6 per 1000, and in 1949 it had dropped to 9.7, a decrease of approximately 8 per cent. This is about one-sixth of the proportional decrease at Carville. The death rate from pulmonary tuberculosis in the United States in 1929 was 43.2 per 100,000, and this had dropped by 1949 to 26.3, a decrease of 39 per cent. This is slightly more than one-half of the proportional decrease at Carville. It can be stated, then, that the death rates from all causes and among those with pulmonary tuberculosis have decreased much more at Carville than in the general population.

The effect of the change in the therapy of leprosy on the death rate from tuberculosis appears to be more striking when the deaths are studied closely. Of the 23 patients dying with this disease in 1943-1950, 13 had never received sulfone treatment (11 of these were patients who died in 1943-1945, before sulfone treatment had become routine), and 1 of the 10 who did have sulfone treatment received it (promin) for only 2 weeks. Among the other 9 tuberculosis patients dying after receiving some sulfone treatment, there were 6 who had had promin for periods varying from 4 to 29 months, and 3 who had received diasone for 1 month, 33 months and 45 months, respectively.

To study this matter further, another approach was tried. All patients who were at Carville for any or all of the time between July 1, 1942 and June 30, 1950 were divided into two groups, according to whether or not they had had sulfone therapy. In the former group were included only patients who had had six months or more of such treatment. For each group the number of person-years of life at each year of age was then determined for this period. For example, a person who was in Carville during the entire period and who was 29 years of age on July 1, 1942 would have lived one year at 29 years of age, one year at 30 years, and one year at each year of age up to and including age 37. The person-years were then totaled for the white and non-white races separately for the two groups. Next, the age-specific mortality rates for the white and non-white population of Louisiana from all causes and from tuberculosis were calculated for data recorded in 1940. On the basis of these rates the number of deaths expected at each age for the person-years lived by the white and non-white groups of the Carville population were calculated. The total deaths expected in each group are shown in Table 4.

Examination of this table reveals, first, that the observed deaths are from 1.1 to 19.7 times as many as those expected on the basis of the age-specific rates of the Louisiana population. There is, however, a striking difference between the non-sulfone and sulfone groups. The number of deaths from all causes in the non-sulfone group is nearly 5 times the ex-

		Person-years of observation	Dea	ths, all cau	ises	Deaths, tuberculosis			
Treatment status	Race		Observed	Expected	Ratio O/E	Observed	Expected	Ratio O/E	
Not sulfone treated	White	701	84	15.7	5.4	8	0.5	14.6	
	Non-White	207	17	5.3	3.2	5	0.3	19.7	
	Total	908	101	21.0	4.8	13	0.8	16.2	
Sulfone	White	2014	27	24.0	1.1	7	1.2	5.6	
treated	Non-white	477	8	7.3	1.1	3	0.6	4.9	
	Total	2491	35	31.1	1.1	10	0.9	5.4	

TABLE 4.—Comparison of observed deaths from all causes and from tuberculosis with those expected on the basis of the age specific death rates in Louisiana, 1940, for patients treated and not treated with sulfones. (Time period 1942-1950)

pected, while in the sulfone-treated group it is only about 10 per cent higher. In comparison, the deaths from tuberculosis show a much greater excess of actual deaths over those expected, being 16 times as high in the non-sulfone group and 5 times as high in the sulfone group. While the proportional decrease in the ratio of the observed to the expected deaths is not as great for tuberculosis (3:1) as for all causes (4.4:1), it is nevertheless striking. This is especially so when one considers that in many of these patients the tuberculosis was already far-advanced before sulfone therapy was started.

There has been a marked increase in the average age at death of patients dying with tuberculosis, as shown in Table 5. There was a gradual increase from 33.9 years in the first period to 42.6 years in the third period, but a sharp increase to 51.9 years in the sulfone period. This is striking when the average ages at death from those without tuberculosis are compared, which have remained fairly constant during the entire span of 28 years. The fact that the average age on admission has increased only about 4 years during the period, with approximately the same increase in the average age of patients in the hospital, makes this increase in the average age at death of patients with tuberculosis of even greater significance.

An attempt was also made to determine as nearly as possible the average duration of the tuberculosis. In the early periods adequate histories were available for only about one-half of the patients dying with it. The average duration at that

Average age in years									
		At time of death							
At admission	Of patients in hospital	From causes other than tuberculosis	With tuberculosis						
36.1	39.3	50.7	33.9						
37.6	39.2	45.4	40.5						
39.6	42.1	50.6	42.6						
40.1	43.2	54.6	51.2						
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 TABLE 5.—Average age at admission of patients in the hospital, and at death with and without tuberculosis.

time was approximately one year. This increased in the third period to one and one-half years, estimated from the histories of about 70 per cent of the patients. In the last period the histories of 84 per cent of the patients gave an average duration of nearly four years.

The short duration of tuberculosis in patients with advanced lepromatous leprosy in the pre-sulfone days is illustrated by the following case report:

CASE No. 1017 .- White female, admitted in 1934, aged 27. The first symptoms of leprosy appeared in 1923, with anesthetic macules. In 1929, nodules developed. On admission she had widespread lepromatous infiltrations of the skin and upper respiratory tract. She faithfully took benzocaine-chaulmoogra oil, 2 cc. weekly, from 1934 until 1939, but the progression of leprosy was relentless. She gained some weight in her first year, and this was sustained until 1938, when frequent lepra reactions began. The massive nodular involvement around her mouth, with repeated ulcerations of these peroral lepromata, led to cicatricial healing and a button-hole mouth which caused great difficulty in eating solid foods. Also, it prevented dental care, so that her teeth became carious and the gums infected. A plastic operation to enlarge the mouth opening and facilitate dental care was done in 1938; the dental work was done, and eating became easier. Soon, however, the mouth scarring recurred. From January 1939 until her death in September 1940 she was in the infirmary at bed rest with repeated lepra reactions and loss of weight and strength. She became emaciated in 1940, and trophic ulcers on her legs as well as ulceration of the skin lepromata became more severe. She developed gastric distress, anorexia and insomnia in June 1940. Chest X-rays in 1937, 1939 and April 1940 showed normal lungs. In June 1940, however, there was found an exudative lesion in the right upper lobe, with a circular area of decreased density. A sputum specimen inoculated into a guinea-pig in July 1940 was positive for tuberculosis. The patient died two months later. Autopsy revealed that both lungs were honeycombed with tubercles and small cavities, with several larger cavities up to 4 cm. in diameter.

There were also some tubercles in the ileum. In addition to advanced leprosy and tuberculosis, the patient had amyloid degeneration of the kidneys, adrenals, spleen and liver. In conclusion, then, this patient died of far-advanced tuberculosis, with a duration of only 4 months.

Other cases could be cited showing similarly rapid progression of tuberculosis in patients with advanced lepromatous leprosy. Of the 10 persons who died of tuberculosis after having received sulfone therapy, the disease was present and already far-advanced in 6 before that treatment was started. Compared with similar cases seen in the pre-sulfone period, these patients lived somewhat longer, perhaps because their leprosy was improving and thus their general health was better. On the other hand, there may also have been a more direct effect of the drugs on the tuberculosis itself.

To complete the picture regarding the patients who at death had tuberculosis, there were 13 individuals not included in the above analysis in whom there was *arrested* tuberculosis of moderately or far-advanced grades. Of these, 4 died before sulfone drugs were available; in 4, arrest of the tuberculosis had occurred before that time and the patients were not later given sulfone treatment; in 1 patient given that treatment the condition was diagnosed at autopsy; in the other 4, sulfone treatment was given—as far as can be determined—after arrest of the tuberculosis had occurred.

Of the 15 patients in whom minimal active tuberculosis was found at autopsy, also not included in the previous figures, 14 occurred before the sulfone era. The additional patient had had promin, 2.5 gm. daily, for ten months, but had discontinued treatment about five months before death because of anemia. Whether tuberculosis developed prior to, during, or subsequent to the treatment could not be determined. No additional evidence as to the relationship of the sulfones to tuberculosis can be derived from these data.

More light may be thrown on the direct effect of sulfones on tuberculosis by an examination of living patients in whom that complication is found. There have been 61 such patients in whom the disease was either active or arrested. Of them, 25 (41%) were diagnosed as having arrested tuberculosis at time of admission, 20 (33%) had active tuberculosis, and 16 (26%) were negative on admission but developed tuberculosis afterward. Of the 25 cases diagnosed at admission as arrested cases, all have been admitted since 1938, 20 of them since 1941. This no doubt reflects the effect of the routine X-ray examination on admission, begun in 1941.

There has been reactivation of arrested tuberculosis in only four instances. Three of these patients are included in the mortality data.

One of these patients was a woman who died of far-advanced tuberculosis three months after reactivation. She had menopausal melancholia and refused to eat or take sulfones. The second was an old man with advanced arteriosclerosis, under sulfone treatment for two years with considerable improvement of his severe lepromatous leprosy. He died with far-advanced tuberculosis four months after the first active tuberculous lesions, superimposed on an old pulmonary fibrosis probably of tuberculous origin, were seen in his lungs. The third reactivated under sulfone therapy and died with far-advanced pulmonary tuberculosis.

Of the 36 patients in whom active tuberculosis was present at admission or in whom it developed during residence in the hospital, 23 have had their disease arrested. Of these 23, the disease became arrested in 10 while under sulfone therapy, while the other 13 became arrested without sulfone therapy. Of the 13 still remaining active, 7 were discharged with active tuberculosis. Five of the latter were discharged before the sulfone era (one of them was improving at time of discharge), while the other two had been given sulfone therapy and were improving. The present status of these patients is unknown. Six patients, including the fourth reactivated case, are now being treated for tuberculosis, most of them by bed rest and a combination of streptomycin and promin.

That the sulfones alone are not nearly so effective as sulfone plus streptomycin therapy for tuberculosis is shown by the fact that 4 of these 6 patients had received sulfones (2 promin, 2 diasone) for two to four years. All had positive sputum cultures. After two to four months of the combined treatment (promin, 5 gm. daily intravenously; streptomycin, 0.5 gm. intramuscularly every 12 hours), in 3 of the 4 patients (one with far-advanced and 2 with moderately-advanced pulmonary tuberculosis) sputum cultures became negative and are still negative after several months. One of these patients did not tolerate the therapy because of severe amyloid renal disease. In the other two, treatment was started only four months ago and the results are not yet apparent.

DISCUSSION

Sulfone therapy at this hospital has produced a marked improvement in the leprous condition and general health of the

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patients. This has resulted in a striking reduction in the death rate from all causes. The reduction in deaths of patients with tuberculosis has been even greater than in deaths from all causes. One is led to believe, therefore, that there may be some specific effect of the sulfone compounds on tuberculosis. It seems probable that a combination of streptomycin and sulfone is a more powerful method of treating tuberculosis than is sulfone alone. This is evidenced by the three cases who showed negative sputum cultures only after addition of streptomycin to the sulfone therapy which they had been receiving for several years.

Another fact also should be noted, namely, that no new cases of tuberculosis developed among patients treated with sulfones prior to July 1950, although a few have been observed since then.⁴ In two patients, reactivation of old lesions probably occurred while the patients were under sulfone therapy. One of these patients is now dead and the other is improving.

SUMMARY AND CONCLUSIONS

1. Tuberculosis is an important cause of death in leprosy patients.

2. The records of all patients admitted to the U. S. Public Health Service Hospital at Carville, Louisiana, between 1922 and 1950 were examined for evidence of the presence of active or arrested tuberculosis.

3. Sulfone therapy, over a period of several years, has improved the leprosy in these patients, with a marked reduction in deaths from all causes. The reduction in deaths of patients with tuberculosis has been even greater than in deaths of patients without tuberculosis.

4. There has been an increase in the age at time of death of tuberculosis patients since sulfone therapy has been instituted.

5. The duration of the tuberculous infection before death has increased since the use of sulfones.

⁴ In the two years from July 1950 to June 1952, one new case of minimal pulmonary tuberculosis developed after a month of promin treatment, and also two moderately-advanced cases, one of them after nine months of promin and the other after nine years of promin and nine months of diasone. There was also a reactivation of moderately-advanced pulmonary tuberculosis in one patient after two and one-half years of inactivity, with promin treatment during this interval.

6. Patients with tuberculosis and leprosy have had their tuberculosis arrested with sulfone treatment alone. A combination of a sulfone and streptomycin appears to be more effective than sulfone alone.

RESÚMEN

Los records de todos los pacientes hospitalizados en el U.S. Public Health Service Hospital, en Carville, Louisiana, entre los años 1922 y 1950, fueron cuidadosamente examinados para determinar evidencia de tuberculosis, ya activa o ya arrestada, en dichos pacientes. Se constató que la tuberculosis es una importante causa de muerte en los leprosos. Durante los años 1936 a 1942 bubo un promedio de 82.3 muertes por cada 1000 pacientes, y durante el mismo periódo 21.7 de ellas fueron atribuidas a tuberculosis. Sinembargo, durante los años 1943 a 1950 el promedio de muertes por cada 1000 pacientes fué de 44.4, de las cuales solo 7.5 fueron atribuidas a la tuberculosis. Se puede concluir, por tanto, que no sólo el promedio de muertes ha disminuído, durante los años subsiguientes a la introducción de las sulfonas, sinó que el promedio de muertes por tuberculosis ha dismunuído aún más que el promedio general.

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