

EFFECTS OF SULPHETRONE TREATMENT IN FIJI¹

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Sulphetrone treatment, which was introduced into this hospital on a small scale at the end of October, 1948,² was received during 1949 by no less than 444 patients, they being all in the institution with positive bacteriological smears except for a few who were unable to take the treatment. Their distribution as regards race and type of disease is shown in Table 1. Not shown there is the sex distribution, which varies considerably in the different groups, in part because of factors not connected with liability to infection; in total there were 317 males and 127 females.

RESULTS

There is some interest in the differences to be seen in Table 1 between the different racial groups with regard to improvement. The percentages work out as follows:

Group	Cases	Total improved	Much improved
Indian	198	75.3%	32.9%
Fijian	59	59.3%	10.2%
Other islanders	162	60.5%	11.1%
Others	25	88.0%	16.0%

Apart from the small fourth group, consisting of 20 Euroneseans, 2 Europeans and 3 Chinese, the Indians showed most improvement, both total and "marked"—which latter comprises the first two columns of Table 1. Considering various differences between them which might be expected to affect the findings, it is noteworthy that the percentages for the Fijians and for the other islanders are practically identical.

The most striking fact about the results of the year's treatment is that the wards of the hospital proper have been emptied of all of the familiar chronic ulcerated lepromatous patients, whose arms and legs were swathed in bandages and for whom

¹ This article is based on a part of the author's annual report of the Fiji Leprosy Hospital for 1949, used in this way by permission of the Director of Medical Services, Fiji.

² See abstract of 1948 report, *THE JOURNAL*, page 428.

TABLE 1.—Results of treatment with sulphetrone at Makogai, by race and type of disease.

Group	No. of cases	Results					
		Quiescent	Much improved	Improved	Stationary	Worse	Died
<i>By racial groups</i>							
Fijian	59	----	6	29	12	10	2
Indian	198	45	20	84	31	15	3
Solomon I.	10	----	1	6	----	2	1
Rotuman	9	1	3	2	1	2	----
Chinese	3	----	----	3	----	----	----
Samoan	43	1	5	26	5	6	----
Cook I.	25	----	1	14	6	4	----
Niue I.	4	----	1	2	1	----	----
Tongan	11	1	2	5	2	1	----
Gilbert I.	60	1	1	26	19	9	4
Euronesian	20	1	3	13	3	----	----
European	2	----	----	2	----	----	----
Totals	444	50	43	212	80	49	10
<i>By type of the disease</i>							
Lepromatous-1	87	30	1	31	17	6	2
Lepromatous-2	237	5	16	133	50	31	2
Lepromatous-3	89	----	24	42	7	10	6
Tuberculoid-1	13	9	----	1	3	----	----
Tuberculoid-2	18	6	2	5	3	2	----

daily dressings were quite insufficient to render their close neighborhood tolerable. The only lepromatous ulcerations now seen are the occasional acute ones associated with severe reactions. The general exodus of the formerly ulcerated patients from the hospital has produced quite a housing problem in the villages, and illustrates the difficulty in drawing up "five-year plans." No less than 41 of the sulphetrone-treated patients who were surveyed for the purposes of this report called forth the observation "no ulceration," a notation which was made only

when the previous records indicated that ulcerations had been severe and prolonged and therefore resistant to all previously known forms of treatment, including latterly the sulfonamides and penicillin.

Other criteria of improvement, until the hoped-for stage of bacteriological negativity is reached, are less objective in nature and therefore perhaps more open to criticism, but the fact that I was absent for most of the year before undertaking this survey probably enabled me to assess progress more accurately than I could have done had I been seeing the patients daily. No case was classified as "improved" without some very definite evidence of a change for the better, and the 43 patients somewhat tamely recorded as "much improved" would, if I had expressed my feelings more freely, have been described as "astoundingly improved."

The proportions of improved lepromatous cases ("total improved") with respect to degree of advancement are 71.3, 65.0 and 74.2 per cent, respectively, for the L1, L2 and L3 groups, which figures may be compared with 57.4, 44.7 and 20.2 per cent at the end of 1948—at which time only 62 cases had been treated for only 2 months, and some of them had had to be discontinued.

Whereas our previous reports have always stressed the better prognosis in tuberculoid cases our 1949 figures, as the result of the treatment of the lepromatous cases with sulphetrone, have changed this tendency. Of the lepromatous cases 65.1 per cent are regarded as improved, against 62.2 per cent of the tuberculoid cases. This fact raises the question of the use of the sulfones in the tuberculoid form of the disease, and because there appear to be marked differences of opinion in published reports on the subject it is proposed to extend the treatment to a selection of active cases of this kind in 1950.

TOXICITY

Turning to the other side of the picture, the experience in this institution leaves no doubt that sulphetrone is markedly toxic. Without careful and regular blood examinations it would be much too dangerous a drug for routine use in our patients. In spite of one week's rest in four, a number of patients have had to be taken off the drug from time to time, although in the great majority of cases a simple iron preparation or combined iron and liver treatment has restored the blood picture to normal and permitted resumption of the drug. A few patients, however, have failed to react to this treatment and have consequently had to forego the use of sulphetrone.

In May, Dr. P. E. C. Manson-Bahr, as physician specialist, came to investigate the anemias produced by sulphetrone, and he summarized his results as follows:

Examination of the figures for haemoglobin, mean corpuscular volume, mean haemoglobin concentration, and red cell count revealed that the anaemia was mild and was microcytic and normochromic. Examination of the marrow smears showed no megaloblasts and no evidence of any maturation defect such as would be produced by a lack of the haemopoietic liver factor. Only one case showed any evidence for haemolysis with an Icteric Index of 20 and a serum bilirubin of 1.25 mgms; in this case there was no reticulocytosis. Only one case showed hookworm infestation.

Later in the year something of the nature of a cumulative effect began to be shown, and although in most cases the anemia remained mild, patients seemed to take longer to recover and a number of them required more prolonged iron treatment and longer periods of rest before it was felt safe to resume the drug, and even then only with concurrent iron therapy.

No less than 45 patients have been unable to stand full dosage of the drug because of continual or frequently repeated and severe reactions. Some of these patients were already subject to frequent reactions before starting treatment, but in other cases the reactions appear to have been provoked by the sulphetrone. On the other hand, a few patients who previously had been suffering from frequent reactions appear to have lost that tendency under the drug. A curious finding is that many of the patients stood the first six months of treatment without untoward incident, but then began to suffer from reactions from which they found it difficult to recover. These reactions are themselves productive of anemia, and for this reason it has frequently proved impossible to follow the advice given, particularly by Cochrane, to continue treatment throughout the reaction.

A form of itchy desquamative dermatitis, sufficiently severe in more than 20 cases to justify injections of sodium thiosulphate, and in one case going on to a severe generalized exfoliative dermatitis, has been a further cause of interruption and very careful and tentative resumption of treatment after varying periods of rest. The exfoliative dermatitis patient, a Fijian, after several attempts were made in vain to resume treatment, was given eight weeks freedom from the drug before it was felt safe to make another attempt. Within two hours after taking one 0.5 gm. tablet he was covered with the usual irritating rash. It is proposed to make a later trial with this patient under cover of benadryl.

A large proportion of the patients, particularly among the

women, had to be given more or less prolonged rests from treatment at the end of the year because of marked loss of weight. When the drug was resumed with these patients a lower maximum dose was aimed at—2.0 gm. in the case of the less sturdy among the women, instead of the usual 3.0-6.0 gm.—to give the weight, which in most cases had still not reached its former height, a further chance to recover.

The Indians not only show a higher improvement rate under treatment than the other races, as has been pointed out, but apparently they also find the drug less toxic. Although 10 of them are recorded as having suffered from dermatitis during treatment, it has apparently been of a comparatively mild character and has caused less interruption to treatment than in the case of the Islanders. It is only in the long-standing advanced Indian cases, moreover, that very marked anemia has developed, in two cases with jaundice.

Of the 10 deaths in the sulphetrone-treated group, 6 occurred in L3 cases, 2 in the L2 group, and 2 among those classified as L1. One of the last two was due to coronary thrombosis, and the other to a nephritis apparently not connected with the leprosy. In one of the L2 cases death was due to tuberculosis; and the second one, dead of nephritis, had a clear history of severe nephritis in childhood, prior to the development of leprosy. One L3 patient, who died of pulmonary tuberculosis as a terminal cause, had been an advanced ulcerated case for many years, and his ulceration had completely cleared up under sulphetrone. As another lepromatous patient remarked in this connection, "When I have got to die, I would rather die clean!" These lepromatous cases had naturally been able to stand only minimal doses of the drug owing to general debility and anemia.

CONCLUSIONS

Considering all factors, there is no question but that the introduction of the sulfones represents a very real advance in the treatment of lepromatous cases of leprosy. The results of the year's treatment with sulphetrone here recorded have been highly gratifying, in spite of all the drawbacks mentioned. Since all workers with long experience with the sulfones emphasize the fact that continued treatment produces steadily increasing improvement together with less evidence of toxicity, we are justified in hoping that our results in 1950 will be even more encouraging.