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PRELIMINARY REPORT ON DIASONE* IN THE TREATMENT OF LEPROSY

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The favorable results reported from the use of diasone in the treatment of tuberculosis suggested the possibility that it might be beneficial also in leprosy, a disease which presents many resemblances to tuberculosis. Plans were made therefore for its use in patients at the Chacachacara Leprosarium, Trinidad. Sufficient time has not elapsed to assay fully the results of the trial, but as the writer is leaving the institution a preliminary report may be of interest.

A progress report on promin therapy was published by Faget and his colleagues (1) before the supply of diasone became available. The result of the use of promin, a drug similar to diasone, over a period of two years at the National Leprosarium at Carville, Louisiana, showed that promin was less toxic by intravenous than by oral administration. These authors stated that "—promin can be safely administered intravenously for prolonged periods, provided the blood and urine are examined frequently. When these precautions are taken, toxic manifestations are relatively rare and mild. The most important of them, hemolysis, if recognized early, is usually controllable and not a cause of discontinuance of treatment." Dosage of promin varied from 1 to 5 Gm. daily for six days a week, the majority of the patients receiving 5 Gm. daily. Treatment was continuous for months, except for rest periods of one to two weeks three times a year.

Methods of administration. In the light of experience with promin, it was decided to give diasone intravenously. The material was prepared by

* Diasone is di-sodium formaldehyde sulfoxylate, a derivative of diaminodiphenyl sulfone. It is prepared by Abbott Laboratories, which furnished the supply used in the test. This compound was independently synthesized by Raiziss and his associates of the Dermatological Research Laboratories, Division of Abbott Laboratories, and by Bauer and Rosenthal of the United States Public Health Service, at approximately the same time.

Editorial note: Early in 1945 Dr. Muir resumed his position as Medical Secretary of the British Empire Leprosy Relief Association (B.E.L.R.A.).

dissolving or suspending 0.3 Gm. of the powder in 1 cc. of sterile normal saline. This was then filtered through three layers of sterile gauze, and injected slowly. At first, injections were given six days a week, the dose being raised gradually from 2 cc. to 8 cc.

Twelve patients, all of the lepromatous type, were first selected for treatment. Due to inadequacy of staff it was found impossible to do frequent blood counts, but the hemoglobin index was made the criterion of any serious anemia-producing effects of the drug. The early results in several patients were remarkable in clearing up the lepromatous ulcers and in producing a general feeling of well being. The immediate effect was that other patients clamored for treatment. In some patients, however, the hemoglobin percentage began to decrease and there were signs of weakness, loss of appetite, and fever. In these cases the treatment was either suspended or the dosage was diminished. Later the injections were restricted to three a week, with dosage varying from 2 cc. to 8 cc.

The restriction in number of doses made it possible to place more patients under treatment. The number was raised to about one hundred when a larger supply of diasone was available. Approximately half the patients were given intravenous injections, the others received the drug orally in capsules. Ferrous sulphate was given also to all patients with a hemoglobin percentage below 78. The dosage of diasone was restricted to 1.3 Gm. or less, three times a week, to all those with hemoglobin below 71. It is possible that the effects were less rapid with the lower scale of administration, but all toxic results were eliminated both with intravenous and oral treatment. In no case was the continuous use of diasone found to affect the kidneys, and when administered to those with albuminuria there was no increase in the amount of albumin or other renal signs.

Results obtained. The beneficial results noted were: (1) a feeling of well-being with increased appetite and improvement in general health; (2) flattening out of nodules and drying up of lepromatous ulcers of the skin; (3) clearing of nasal lesions; (4) improvement of inflammatory condition of the eye, and (5) disappearance of chronic fever and lepra reaction.

In assessing the results patients were divided into two groups, those treated for more than three months and those treated for two but not three months. Those treated for less than two months are not considered at this time.

The patients, in all of whom the disease was of the lepromatous type, have also been classified for the purpose of assessment as being in one of four stages at the beginning of treatment: (1) diffusion, when the disease is spreading through the skin and before the appearance of marked thickening or nodules; (2) thickening and nodulation of the skin; (3) elimination, when frequent lepra reactions occur and nodules and thickened lepromatous areas break down and ulcerate, and (4) anorexia, in which prolonged feverish re-

actions have resulted in a condition of weakness and anemia, accompanied not infrequently by renal disease.

TABLE 1. *Results of treatment of leprosy patients with diasone, classified as to stage of disease at beginning of treatment, method and duration of treatment, and results of treatment.*

Stage of Disease	Treated more than 3 months									Treated between 2 and 3 months								
	Injection			Mouth			Total			Injection			Mouth			Total		
	M.I.	S.I.	S.	M.I.	S.I.	S.	M.I.	S.I.	S.	M.I.	S.I.	S.	M.I.	S.I.	S.	M.I.	S.I.	S.
1	0	2	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0
2	3	8	0	0	2	0	3	10	0	0	5	3	0	7	0	0	12	3
3	10	0	1	5	0	0	15	0	1	0	1	0	0	9	0	0	10	0
1 & 2	4	1	0	1	0	0	5	1	0	0	4	1	0	3	1	0	7	2
2 & 3	0	4	0	0	0	1	0	4	1	0	5	0	0	1	0	0	6	0
3 & 4	0	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0
Total	17	15	1	7	2	1	24	17	2	0	15	4	0	21	1	0	36	5

M.I. = Marked improvement
S.I. = Slight improvement
S. = Stationary

The results of treatment of 43 patients treated for more than three months and of 41 patients treated for two but not for three months are given in table 1, classified as to method of treatment and stage of disease at beginning of treatment. Of those treated for more than three months 24 out of 43 showed marked improvement and 17 additional showed slight improvement. Only two are classed as stationary. Of those treated less than three months none showed marked improvement but 36 of 41 showed slight improvement, five remaining stationary. It is interesting that in neither group did the condition of a single patient become worse. On the basis of these figures it is evident that those treated for the longer period show the greater improvement.

Of 83 patients for whom complete data are available, 24 had at the beginning of treatment a hemoglobin percentage of less than 65; 52 of between 65 and 80 per cent, and 7 of over 80 per cent. Of those with a hemoglobin of less than 65 per cent, 14 had during the course of treatment an increase in hemoglobin of more than 5 per cent; in none of these patients was there a decrease of more than 5 per cent. In only 12 of the 83 patients was there a decrease in hemoglobin of more than 5 percent; in all of these 12 patients the original hemoglobin was 71 per cent or over. Two of the 12 showed a decrease of 6 per cent, 9 a decrease of 7 per cent, and one a decrease of 14 per cent.

In table 2 the patients are classified as to duration of treatment, stage of disease, change in hemoglobin, and results of treatment. There is no evidence that the decrease in hemoglobin influenced the outcome of treatment, but no conclusion can be based on such small numbers.

TABLE 2. *Relationship between change in hemoglobin, stage of disease, and results of treatment in those treated for 3 months or more compared with those treated less than 3 months.*

Duration of treatment	Stage of disease*	Decrease in hemoglobin of more than 5 per cent			Decrease in hemoglobin of less than 5 per cent, no change or increase			Total**
		M. I.	S. I.	S.	M. I.	S. I.	S.	
More	1	0	2	0	0	0	0	2
than	2	1	2	0	7	8	0	18
three	3	3	1	1	12	3	1	21
months	4	0	0	0	1	0	0	1
Between	1	0	0	0	0	0	0	0
two and	2	0	0	0	0	19	5	24
three	3	0	2	0	0	14	0	16
months	4	0	0	0	0	1	0	1
Total		4	7	1	20	45	6	83

* Patients classified in Table 1 as in two stages of the disease are here classified according to the more advanced stage.

** 1 with hemoglobin unknown is omitted.

It will be noted that the patients who were in the third stage at the beginning of treatment showed the most marked improvement. These were patients with reactive symptoms, ulcers caused by breaking down of nodules and thickened lepromatous skin, ulcers of the nasal lining, and inflammatory lepromatous iridocyclitis. At this stage of the test it is undoubtedly those with these conditions who have shown the most striking improvement.

In one patient (I.D.) who had suffered for years from ulceration of the face, hands, and other parts of the body, which had not improved under any of the former remedies tried, the ulcers all healed up rapidly. Diasone had to be discontinued, however, because fever and anemia developed (Hb. 44 per cent). Under liver injections and iron these gradually disappeared, but there was no relapse of the ulcerative condition even during the febrile and anemic period. Previously a chronic invalid, he is now able to do active work.

In two other patients (R.S. and B.A.) there was a febrile reaction with acute iridocyclitis and rapid invasion of the cornea with vascularization. Previous experience presaged complete blindness, but under diasone the condition cleared up rapidly, leaving damaged but useful eyes.

One of the most serious complications of leprosy is tuberculosis. A patient (J.I.) suffering from severe tuberculosis of the left elbow joint with septic complications had had the arm amputated. The tarsal bones of the right foot were involved and there were large tuberculous glands on both sides of the neck. Under diasone the foot condition cleared up rapidly, the swinging temperature became normal and the glands shrunk in size. This patient has

gained in general health and strength and the lepromatous condition has improved considerably.

Another patient (R.N.), once crippled with ulcers of the limbs and a chronic febrile condition, is now well and able to do hard manual work as a carpenter. Similar improvement has been produced in others (O.D., R.B., C.H., R.W., H.K., and A.R.). Still another patient (E.L.), in the early stage of leprosy but a chronic invalid for a year with continuous low fever, has become strong and well after a few weeks of diasone.

In the third stage of the lepromatous type anemia is a common complication as it is in malaria, kala-azar, and other conditions where there is gross reticulocytosis. Since diasone also has a tendency to produce anemia particular care must be taken at the beginning of treatment. Liver extract and iron will in most cases improve the anemia, but the initial doses of diasone must be small and only increased as the hemoglobin index improves. Care must also be exercised in administering iron in large doses, as iron like other metals tends to produce lepra reactions when given in excess.

While the majority of the patients which are reported on received diasone intravenously, there was similar improvement in those treated orally. A sufficient number of patients has not been treated to assay the relative merits of the two methods of administration.

The question arises as to whether diasone has a direct effect in destroying or preventing growth of the leprosy bacillus, or whether improvement is attributable only to the destruction of complicating pyogenic microorganisms. To determine this a few patients in the first stage of the lepromatous type have been treated. These have shown improvement, but it is still too soon to determine whether the treatment will lead to complete elimination of the bacilli. Even if it does, there will be no proof that there is direct action on the bacilli. Leprosy has under favorable circumstances a tendency towards self-healing and it may be that diasone by improving the general condition, as it appears to be doing in these cases, would indirectly promote self-healing.

There seems no doubt that diasone is of definite value in the treatment of leprosy, especially in clearing up febrile and inflammatory conditions associated with lepra reaction. The heavy metals, especially antimony, and certain aniline dyes when given intravenously in small doses have a similar effect in some cases. Their value, however, is limited by the fact that when given over a long period they tend to produce the opposite effect and increase the inflammatory signs. It seems probable that diasone on the other hand can be given continuously over long periods, during which it will continue to give beneficial effects.

The results obtained so far correspond closely with those reported on the use of promin at Carville. The general effects are also similar to those obtained with diasone in the treatment of tuberculosis by Petter and Prenz-

lau (2). The latter report that 87 per cent of patients receiving diasone over periods ranging from 60 to 275 days were considered definitely improved. The most decided changes for the better occurred in the moderately advanced cases treated for 90 or more days.

The results obtained with diasone so far are encouraging, and though it is still too soon to make any definite statement as to the extent to which this drug will be of use, there is reason to believe that a distinct step forward has been made in the treatment of leprosy.

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