

BACTERIOLOGICAL CHANGES UNDER DDS  
TREATMENT OF LEPROSY

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*(Reprinted from Leprosy in India, April, 1951 by kind permission)*

Much has been written in recent months about 4 : 4' diamino-diphenylsulphone (DDS) in the treatment of leprosy. Some have condemned it as too toxic for safe use, while others have found it at least as effective as its derivatives—promin, diasone and sulphetrone. Indeed there is evidence that the first two of these largely owe their effectiveness to the DDS which they liberate inside the body.

This paper is in continuation of one recently published (Muir, 1950). It is based chiefly on a study of a hundred cases under oral treatment with DDS. Details of 58 of these, selected as being of the lepromatous type and as having undergone treatment for periods of one year or more, are given in table I. (See page 68.)

A number of tuberculoid and indeterminate cases have also been treated with DDS with good results, but these are not dealt with in this paper which is limited to a study of bacteriological changes.

Each of the 100 patients was seen daily by the writer and given orally what was considered the maximum dose of DDS which could be safely and comfortably tolerated. After a series of trials, 24 mg. of DDS per kilogram of body weight came to be considered the normal weekly amount tolerated by patients in good general health. This was divided into six daily doses, one being given every day except Sunday. As the average weight of the adult patient was about 50 kg., the average normal amount was 200 mg. a day or 1.2 gm. per week. As may be seen on studying table I, column 7, only in 4 cases (nos. 17, 29, 54, 55) was 24 mg./kg. body weight maintained during the whole period of this study. In 21 cases (36 per cent) it was half or less than half that amount, and in 3 it was less than a quarter.

## BACTERIOLOGICAL IMPROVEMENT

An examination of each patient was made every three months. An attempt is made in columns 8, 9 and 10 of table I to assess and compare the bacteriological findings at the beginning of treatment with those after the number of weeks of treatment shown in column 3. At each examination five smears were made from the skin at places where experience indicated the most bacilli were likely to be

TABLE I

1	2	3	4	5	6	7	8	9	10	11	12
Case number	Name	Length of treatment in weeks	Total DDS in gm.	Average DDS per week in mg.	Average weight of patient in kg.	Average weekly DDS in mg/kg.	B.I. before treatment	B.I. at end of period	Percentage B.I. increase	Percentage B.I. decrease	Number of days reaction
1	B. J.	83	58.1	700	43	16	13	14	7	—	21
4	M. D.	73	45.1	620	44	14	20	19	—	5	51
5	S. L.	81	61.1	750	49	15	14	9	—	35	9
6	S. V.	81	33.1	400	35	11	20	19	—	5	105
7	G. B.	56	38.2	680	50	13	20	20	—	—	20
8	B. L.	80	61.3	760	49	16	14	14	—	—	52
10	D. K.	80	57.7	720	45	16	18	14	—	22	66
11	H. G.	80	55.9	690	46	15	20	8	—	60	17
12	H. P.	82	35.9	440	33	14	15	11	—	26	129
13	S. D.	81	32.6	400	34	12	15	17	13	—	85
14	S. T.	83	34.3	410	29	14	15	4	—	77	187
15	R. J.	53	20.1	370	53	7	20	20	—	—	9
16	B. L.	81	29.0	360	24	15	10	0	—	100	0
17	D. U.	81	70.3	860	31	28	8	2	—	75	2
18	G. T.	74	27.3	360	28	13	20	11	—	45	55
19	B. R.	75	35.2	450	33	14	13	8	—	38	43
20	R. P.	72	13.1	180	22	8	18	15	—	16	137
21	L. U.	74	16.1	210	29	7	19	9	—	52	191
22	J. F.	77	35.0	450	33	14	18	15	—	16	58
23	C. T.	81	61.4	750	47	16	18	18	—	—	68
25	L. C.	81	59.1	720	52	14	20	20	—	—	42
26	D. T.	81	50.0	610	45	14	20	17	—	15	87
27	R. H.	56	50.5	900	43	21	20	20	—	—	0
28	B. L.	81	70.1	850	48	18	18	18	—	—	27
29	C. L.	81	79.3	980	42	23	13	2	—	84	14
31	J. M.	79	82.0	1,030	58	18	20	20	—	—	8
32	A. T.	64	51.0	780	52	15	6	0	—	100	0
35	N. D.	82	67.5	810	57	14	19	18	—	5	31
39	G. N.	52	24.6	470	41	11	20	20	—	—	60
41	S. M.	78	4.2	50	41	1	20	20	—	—	302
42	R. L.	56	25.0	450	51	9	7	1	—	85	45
43	T. L.	79	46.6	590	51	12	20	19	—	5	21
44	J. R.	74	35.2	470	51	9	10	7	—	30	54
46	B. N.	56	50.7	900	44	20	20	19	—	5	6
47	J. H.	70	52.1	730	52	14	20	18	—	10	12
48	A. M.	70	15.4	220	40	5	20	20	—	—	125
49	J. R.	52	33.8	650	59	11	18	13	—	27	15
50	D. J.	70	23.2	330	38	9	19	9	—	52	75
51	M. G.	69	23.2	340	59	5	20	20	—	—	81
52	M. I.	68	30.7	450	43	10	10	13	30	—	37
54	S. F.	67	63.5	950	35	27	7	5	—	28	3
55	L. S.	67	68.3	1,020	40	25	10	6	—	40	7
56	J. E.	68	30.6	450	47	9	20	17	—	15	44
57	R. D.	68	52.9	770	55	14	19	19	—	—	9
58	R. A.	68	30.7	450	60	7	18	13	—	27	21
59	S. K.	71	25.7	420	46	9	20	20	—	—	36
60	M. H.	60	37.8	630	50	13	6	2	—	66	0
61	V. E.	57	35.4	450	55	8	10	7	—	30	61
62	A. T.	57	38.6	670	43	16	20	18	—	10	10
63	B. D.	57	33.2	580	37	16	18	15	—	16	3
64	G. R.	57	31.1	540	47	12	20	20	—	—	22
65	G. S.	57	29.4	510	39	13	12	4	—	66	36
66	B. H.	57	29.2	510	52	10	10	2	—	80	0
68	B. D.	57	49.0	850	46	18	17	19	11	—	2
69	P. T.	57	40.8	710	37	19	20	14	—	30	3
70	S. R.	57	49.8	870	48	18	16	5	—	68	30
71	M. K.	57	38.4	670	51	13	15	14	—	6	2
74	P. M.	55	51.7	940	48	20	7	6	—	14	0

found, cutaneous or subcutaneous nodules being chosen when present. Each smear when found positive was counted in one of four grades with one, two, three or four points respectively: one point indicating a few bacilli, four points a massive infection, and two and three points intermediate grades. The total of points at an examination is known as the 'Bacteriological Index' or B.I., the maximum being 20 for the five smears. In columns 8 and 9 there is shown the B.I. of each patient at the first and at the last examination, and in columns 10 and 11 the amount of increase or diminution in percentages of points. It will be noticed that in only four cases (nos. 1, 13, 52, 68) is there an increase in the number of bacilli and only to a total of 8 points, whereas there is a diminution in 39 cases to a total of 197 points, and 15 cases appear to remain stationary. Moreover, these figures are loaded against more favourable results in two ways: (a) the 4-point grade represents a massive infection over a wide range, and the smears of many patients who had made considerable bacteriological improvement were still in this grade at the final examination, and accordingly showed either no improvement or less improvement than had actually taken place; (b) the constant examination of patients made one more skilled in choosing the places where most bacilli could be found, and also improved the technique for taking and staining smears; thus there was a tendency to find higher grades at the final examination. Indeed in the four cases which showed increased points, and in the 15 which showed no change, there had been definite clinical and bacteriological improvement, but at the final examinations more strongly positive sites happened to be discovered. The total of the points gained by all the 58 cases at the first examination was 936 and at the last 747, showing an overall diminution of 20 per cent.

No mention is made in table I of clinical improvement, but in fact every case made definite clinical progress, and the majority improved very considerably.

#### DOSAGE

A remarkable feature shown in table I is the smallness of the amount of DDS required to bring about very marked improvement in certain cases. In strong healthy well-nourished patients 4 mg. per kg. body weight daily for six days a week is well tolerated over an indefinite period and many out-patients have been taking this quantity for many months without any adverse signs. But the cases in table I were of in-patients many of whom were weak and in an advanced stage of the disease; also for lack of funds

nutrition was inadequate in many cases. Thus of the 58 cases only four (nos. 17, 29, 54, 55) were able to tolerate the average dose of 24 mg./kg. per week during the period of treatment. This gave an opportunity of studying the effect of much smaller doses.

Table II gives the weekly mg./kg. dose of 12 cases who showed a B.I. improvement of over 50 per cent.

TABLE II

Case number ...	11	14	16	17	21	29	32	42	50	65	66	70
Period of treatment in weeks	80	83	81	81	74	81	64	56	70	57	57	57
Percentage B.I. improvement ...	60	77	100	75	52	84	100	85	52	66	80	68
Average weekly mg./kg. dose ...	15	14	15	28	7	23	15	9	9	13	10	18

The mean of the average weekly DDS of these 12 cases was 14.6 mg./kg., just over 2 mg./kg. per day, or about half what experience shows that strong healthy patients tolerate. Higher doses were not given because they caused either a fall in the hæmoglobin or else excessive reaction (note days of reaction in column 12 of table I).

One of the patients who made most clinical as well as bacteriological improvement, although his latest smears still showed the 4-point grade, was case 41. At the beginning of treatment this patient was in a very low condition, covered with lepromatous ulcers and with a bad prognosis for the eyes. Under DDS the ulcers healed quickly and the disease of the eyes was arrested. The patient was however unable to tolerate more than 50 mg. doses every second day, and sometimes this had to be suspended for several weeks at a time as even these small quantities induced considerable reaction and lowered the hæmoglobin. His condition very gradually improved and reactions were reduced to the appearance of only small evanescent nodules. The hæmoglobin remained low, seldom more than 8.6 gm. and was not improved by iron or liver therapy. Note that 362 out of 546 days, almost two-thirds of the period, were spent in reaction. Immediate improvement was brought about by weekly injections of Normocytin (Vitamin B<sub>12</sub> Concentrate) 30 micrograms, and within a few weeks the patient was able to tolerate daily doses of 50 and then 100 mg. of DDS without reaction, while his hæmoglobin slowly rose to 11.7 gm. Spread over the period of treatment under review, this patient had a total of only 4.2 gm. of DDS in minute doses. Although bacteriological examination still revealed massive infection, the bacilli were much fragmented and undergoing disintegration. This

patient is now in good health, and though crippled is able to take an active and useful part in the life of the institution.

#### DDS AND ANÆMIA

Some workers have reported that serious anæmia is produced by DDS and have recommended the administration of iron in full amounts, though the actual type of anæmia and its pathology have not yet been completely elucidated.

In this series of cases it has been found necessary in some of the weaker and more advanced cases to maintain a low dosage of DDS for a considerable time to begin with, partly because of anæmia and partly because larger doses produced severe reactions.

At first all but stronger patients were kept on ferrous sulphate tablets, but later experience showed that most patients improve almost, if not entirely, as well without iron, and it is now seldom used except in an occasional short course for one or two weeks. In fact, though in some patients before beginning DDS treatment the hæmoglobin was low, it has generally gradually risen without iron as the health improved under DDS.

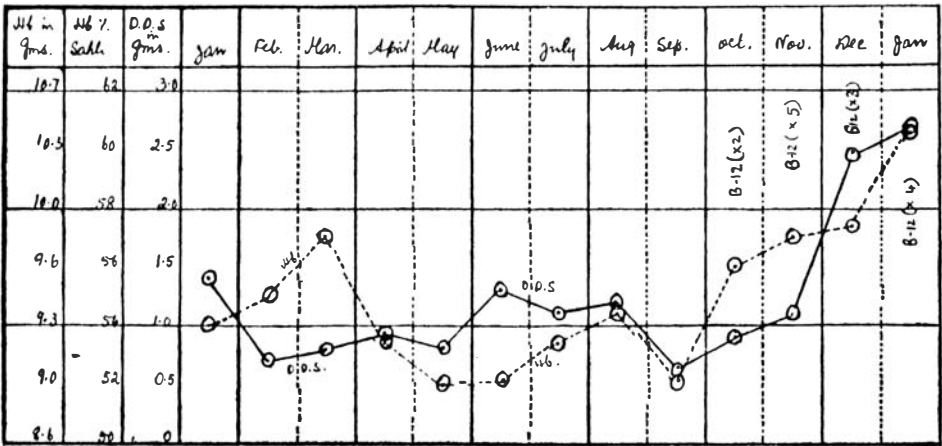
Among the out-patients, who on the whole are stronger and less advanced than the in-patients, we have so far had little or no difficulty with anæmia, either in the 60 oral cases most of whom are getting full weekly doses of 24 mg./kg. in tablet form, or among the 117 parenteral cases who get weekly only 6 to 12 mg./kg. of body weight. Only in occasional cases has iron administration been found necessary.

When the hæmoglobin is lowered by DDS, it is generally sufficient to suspend treatment for a few days, when the hæmoglobin will rise again rapidly.

#### AUXILIARY TREATMENT WITH VITAMIN B<sub>12</sub>

Vitamin B<sub>12</sub> has been found useful in those advanced lepromatous cases which appear to be intolerant of DDS, and in whom even the smallest doses cause frequent reactions and the hæmoglobin remains persistently low in spite of all other forms of treatment.

Below is shown in graphic form the mean of the maximum amount of DDS tolerated each month from January 1950 till February 1951 by 9 such patients, together with the mean of their monthly hæmoglobin. From October onwards weekly injections of B<sub>12</sub> were given in the form of 30 µg. of Normocytin, and the effect was shown in the immediate raising of the hæmoglobin and increase in the amount of DDS tolerated.



$B_{12}$  appears to act primarily in diminishing reaction so that more DDS is tolerated, and then secondarily in raising the hæmoglobin, perhaps partly by relieving the hæmatopoietic system of the repressive effects of reaction.

Further trial is necessary as to the length of  $B_{12}$  treatment required and the most effective dosage. But the results so far obtained give some hope that a class of patients formerly excluded as intolerant can now be brought within the scope of sulphone treatment.

#### IMPORTANCE OF EARLY TREATMENT

The study of these 58 cases shows the importance of early treatment, the word 'early' including all leptomatous cases in which the bacilli have not yet multiplied to a massive degree.

Table III gives particulars of 12 of the 58 cases in which the B.I. points before treatment were not more than 10, that is to say half the maximum number of points. It shows the number of weeks of treatment, and the B.I. at the beginning and end of the period of treatment.

TABLE III

	16	17	32	42	44	52	54	55	60	61	66	74	Total	Mean
Case number ...													—	—
Weeks of treatment ...	81	81	64	56	74	68	67	67	60	57	57	55	787	65.5
B.I. before treatment ...	10	8	6	7	10	10	7	10	6	10	10	7	101	8.4
B.I. after treatment ...	0	2	0	1	7	13	5	6	2	7	2	6	51	4.2

In these comparatively early cases the average period of treatment is 65.5 weeks, and the average reduction in points is 48.5 per cent, a remarkable reduction in so short a time.

## DESTRUCTION AND ABSORPTION OF BACILLI

The effect of DDS on *M. lepræ* is a subject of great importance which is still not well understood. From the speed with which lepromatous ulcers of the skin and nasal mucosa heal up and eye lesions are brought under control, it may be inferred that some immediate profound change takes place in the bacilli or their surroundings. This is also suggested by the 'granulation' of bacilli which is seen in smears after a few weeks' treatment, and which goes on more slowly to fragmentation and absorption. It is difficult to explain these changes except on the supposition that bacilli have been killed in large numbers, although they remain in the tissues and retain their acid-fastness, at least in part, for months or even years. The alternative suggestion that the existing bacilli still remain alive, although their power of reproduction is destroyed scarcely fits in with the immediate changes mentioned above. If the former suggestion is correct then further improvement in treatment should aim not so much at a more rapidly acting bactericide as at some agent which will cause more rapid absorption and disappearance of bacilli.

## EFFECT OF LEPRO REACTION

In table I, column 12, is given the number of days which each patient spent in lepra reaction. In order to study the effect of this condition on the progress of the disease and the elimination of bacilli, the 58 cases have been divided into four groups according to the number of days that reaction was present, and these are compared in table IV. The four groups consist respectively of those with reaction from 0 to 10 days, 11 to 50 days, 51 to 100 days and over 100 days. There is given under each group the mean of: the days of reaction, the average weekly amount of DDS in mg./kg., the first and last B.I. and the percentage decrease of the B.I.

TABLE IV

Group	Days in 'lepra reaction	Number of cases	Days reacting	DDS in weekly mg./kg.	First B.I.	Last B.I.	Decrease per cent
I	0-10 ...	19	3.8	17.3	14.0	11.0	21.4
II	11-50 ...	19	28.1	13.2	16.7	13.2	20.9
III	51-100...	13	66.4	12.0	17.0	14.4	15.3
IV	Over 100	7	176.5	8.5	18.5	14.0	24.3

It will be noticed that while there was a B.I. decrease in all groups it was most in group IV (24.3 per cent) although the amount of DDS tolerated and taken was just under half the amount in group I. The decrease would indeed have been much greater

(35.5 per cent) but for two cases in the group, 41 and 48, in whom although there was very considerable clinical improvement and diminution of bacilli the original infection was so gross that all their smears still remained in the 4-point grade.

Disappearance of bacilli therefore appears to be accelerated in patients who, while taking DDS, have severe and prolonged lepra reactions.

In non-reacting cases elimination is a slow process, the bacilli first becoming granular then fragmented and broken down into debris, leaving at last only the slightly acid-fast lipid globules into which they appear to have melted. But in reacting cases the bacilli are phagocytosed by monocytes, and in the more severe reactions by polymorphs, while sometimes small abscesses full of lepra bacilli and pus cells are discharged, thus bringing about much more rapid elimination.

The reaction caused by DDS, or due to some other cause (such as malaria) while the patient is under DDS treatment, should be distinguished from the ordinary classical form of lepra reaction. The symptoms of both are very similar, but while the latter results in deterioration of the patient's condition, the former usually leaves him better after each successive attack.

So noticeable is this, that patients who have observed these results in themselves and others willingly undergo the accompanying pain and discomfort in the hope of improvement.

The course of lepra reaction is made clearer by a short description of three of the cases in group IV, table IV (nos. 14, 20 and 21).

Case 14 shows rapid improvement in a boy of 29 kg. average weight. During the 83 weeks of treatment his bacillary index fell from 18 to 4 points, an improvement of 77 per cent. His average weekly dose during the period was 14 mg./kg. It will be noticed that he spent 187 out of 581 days, almost one-third of the period, in lepra reaction. This was induced to a certain extent and accompanied by attacks of malaria.

Case 20, a small boy of 22 kilos average weight, had suffered from reaction with ulcerating nodules for months. One eye was entirely, and the other almost entirely destroyed. After a few 50 mg. doses of DDS given every second day the temperature became normal and the disease in the remaining eye was arrested. He still had bouts of febrile reaction, but these gradually diminished in degree and duration, and after each the clinical condition showed progressive improvement. Latterly, the reaction was confined to short attacks of leprous orchitis which cleared up



each time after suspending DDS for a few days. He suffered from reaction for 137 out of the 504 days under consideration, more than a quarter of the period. The bacteriological index shows a fall of only 16 per cent from 18 to 15 points, but this apparent slightness of improvement was due almost entirely to thick lepromatous infiltration of the skin and subcutaneous tissue covering the triceps muscles, which still showed 4-plus grade though the bacilli appeared to be rapidly disintegrating. In the previous examination before these foci were noticed the points of smears taken from the rest of the body totalled only 7.

Case 21 is similar, a boy of 29 kg. average weight. During the 74 weeks of treatment his bacillary index diminished from 19 to 9 points, a percentage of 52. He spent 191 out of the 518 days, more than a third of the period, in lepra reaction. His average weekly dose was only 7 mg./kg.

#### INDUCTION OF REACTION

As it appears that reaction is beneficial in causing elimination of bacilli, the question arises of the desirability of promoting their absorption by deliberately inducing reaction.

In most of the cases in table IV reaction was brought about by DDS; thus there is an indication that it may be well to give over a period of days sufficient DDS to cause reaction, and then follow with a rest till the reaction passes off. It may be better to do this than to give smaller non-reaction-producing amounts which would not have to be intermitted.

Case 14 described above is typical of cases in which malaria, a cause other than DDS was responsible for inducing reaction, which had beneficial results since there was a concentration of DDS in the body.

If reaction fails to be caused by DDS given in safe quantities, that is to say in quantities which do not produce anæmia or other toxic symptoms, then the question of inducing it by means of iodides may be considered at least in strong healthy patients. We have been trying this out in a small number of such patients. It is first necessary to find out the minimum dose of (potassium or sodium) iodide which will induce reaction, by administering rising doses: 5, 10, 20, etc., grains every second day till a definite reaction is produced. The reaction-producing dose is then repeated once a week, always provided the previous reaction has fully passed off. According as the reaction is too great or too small the next dose is diminished or increased. Care must be taken that this combined iodide and DDS treatment is not pushed beyond the strength or tolerance of the patient. There has not yet been time to determine

the results of this form of combined treatment, but a few notes on three cases, all with a B.I. of 20, illustrate what results may be expected.

K. T. (weight 64 kg.) was given iodide in rising doses up to 4 gm. which last amount produced a slight reaction lasting 3 days. On two subsequent occasions at weekly intervals this same dose caused an even slighter reaction. The amount was then gradually increased. Even 8 gm. only produced a slight rise of temperature and glandular pain for 2 days. There was no fall in the hæmoglobin which remained at 13.8 gm.

J. M. (weight 56 kg.) was given daily doses of 0.16 gm. of iodide for a month except for 3 occasions when it was interrupted for 1 to 3 days for slight reaction. Iodide had then to be stopped as the hæmoglobin had fallen from 12.1 to 8.6 gm. On its rising again after 7 weeks to 14.5 gm. he was given 1.3 gm. of iodide on two occasions with an interval of one day, which resulted in the hæmoglobin falling to 12.1 gm. Thereafter 30 grains was given once a week with only slight signs of reaction till, after the third dose, there was a sharp reaction lasting 3 days and a fall of hæmoglobin from 12.8 gm. to 11. After 3 weeks, the hæmoglobin having risen to 13.8 gm., 2 gm. of iodide were given, and after one week 2.6 gm. This resulted in a fall of hæmoglobin to 10.7 gm. with only slight signs of reaction.

D. G. was given weekly doses of 1.3 gm. of iodide on three occasions. After the third dose there was a violent reaction with high fever, intense pain in the bones of the limbs and the appearance of multiple nodules. This reaction lasted 10 days. Two weeks after it had passed off the same dose was repeated, but this time the reaction, though severe, only lasted 4 days. Two days after recovery the dose was repeated with again four days of reaction, but still less severe. There was practically no change in the hæmoglobin, and the patient's general health was apparently not affected by these reactions. The clinical improvement in this patient was very striking, though his original B.I. was too gross to record any bacteriological improvement.

These three cases, though all 4-grade bacteriologically, were affected by iodide in markedly different ways. The benefit appeared to be in direct proportion not to the amount of iodide given but to the severity of the reaction. They received the usual full daily dose of DDS during the iodide treatment except on days of severe reaction.

#### LOCAL TREATMENT

Another method of speeding up the absorption of bacilli is by

means of local treatment applied to the skin. Perhaps the most effective method of local treatment is intradermal injections of hydnocarpus oil, or where there are nodules injection into them of a few drops of an irritant substance such as 1 in 5 or 6 solution of turpentine in arachis oil. The use of caustics such as painting with trichloroacetic acid 1 in 3 watery solution, or the application of CO<sub>2</sub> snow, has a similar effect in speeding up the absorption of bacilli.

#### METHODS OF ADMINISTERING DDS

DDS is supplied by the makers either as a white powder or in tablets of 100 mg. It is a stable substance, not easily disintegrated on sterilization by heat and of very low solubility in water. Smith (1949) has shown that when it is given orally less than 10 per cent is recovered in the fæces. Absorption is therefore almost complete. He has also shown that excretion is slow and that traces can be found in the blood 14 days after cessation of a six weeks' period of administration. Oral administration is therefore an economical and efficient method.

Given parenterally as a 20 per cent suspension in pure coconut oil\* as recommended by Molesworth and Narayanaswami (1949) equally good results are obtained. Smith has shown that a single subcutaneous injection of 1.5 ml. of this suspension gives a blood level of 0.1 to 0.15 mg. per cent for a period of six days, and subsequent injections given at weekly intervals would necessarily raise the level higher. This prolonged blood level is due to the slow solubility of DDS, which gives it an advantage over its more soluble derivatives.

When the relative merits of oral and parenteral administration of DDS are considered no great superiority can be claimed for either as regards blood levels. For strong healthy patients who are not likely to have severe reactions and who can be trusted to follow instructions regularly tablets given orally are more convenient.

We have found it now possible to discharge patients who have become bacteriologically negative, whereas in the past it was necessary to retain them as in-patients for a further few years to prevent

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\* Some have recommended the addition of beeswax to the suspension to prevent sedimentation, but this makes injection much more difficult and, without beeswax, occasional shaking of the emulsion keeps the powder in suspension. Arachis oil also has been recommended, but in our experience this tends to form painful subcutaneous 'depots' of unabsorbed DDS. Coconut oil seems to be most suitable, but it must be pure and of low acid value. The suspension can be sterilized by placing the container in an oil-bath or pressure sterilizer at a temperature of 120°C. for 30 minutes. Subcutaneous injection is preferable to intramuscular, and 'depots' are seldom formed if thorough massage is applied at once to flatten out the lump raised by the suspension.

relapse. On leaving, they are given a supply of 75 tablets sufficient for 3 months taking one daily six days a week. They pay the small amount of one rupee eight annas, which helps to ensure that the tablets are actually taken. They are instructed to return for inspection and a fresh supply of tablets after that period. This practice is still under trial, but there is reason to believe it will be successful provided patients are willing to persist with maintenance doses over a period of 2 or 3 years.

But in a country like India where a large proportion of leprosy patients are ignorant and prejudiced and also have to attend from a considerable distance for treatment at weekly intervals, subcutaneous injection seems to be the method of choice. In the Purulia institution where this investigation has been made both methods are used according to the nature of the patients. For the ordinary out-patient a weekly injection of 1.5 ml. of the oily emulsion is found safe and effective. It has not yet been found to produce any serious anæmia or lepra reaction. The suspension is easy to prepare and can be conveniently and safely sterilized in a pressure sterilizer or on an oil-bath at a temperature of 120° for ten minutes. The suspension has generally to be heated at the time of injection to make it thin enough to pass easily through the needle, and the bottle should be shaken from time to time.

Another of the advantages of DDS is that on account of the small effective dose the cost is small (the weekly dose of suspension costs less than an anna) and therefore the treatment is within the reach of the poorest.

#### SUMMARY

(1) 4 : 4' diaminodiphenylsulphone (DDS) has been found effective in leprosy in very small amounts.

(2) In such amounts it is not more toxic than its derivatives.

(3) The effect is shown of vitamin B<sub>12</sub> in controlling reaction and anæmia in cases intolerant to DDS.

(4) In 58 cases there was an average improvement of over 20 per cent in the bacillary index, while in 12 cases in which the original bacillary index was 10 or less there was an average improvement of almost 50 per cent.

(5) There is evidence that lepra reaction induced by DDS, or by another cause during treatment with DDS, favours the more rapid absorption of lepra bacilli.

(6) On this account the advisability is discussed of inducing lepra reaction in cases in which it does not otherwise occur.

(7) The question of combining local treatment with DDS therapy is discussed.

(8) The oral and parenteral methods of giving DDS are compared.

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