

SUSPENSION OF DIAMINODIPHENYLSULPHONE IN LEPROSY

A. T. Roy.

When the proprietary sulphones proved successful in the treatment of leprosy, attention naturally turned to the use of the parent sulphone, 4:4' diaminodiphenylsulphone (DDS or DADPS) as a possibly more economic method of therapy.

Cochrane (1) started injecting a suspension of DDS intradermally into the macules. Later on, on skin estimation, he found that DDS could be recovered from the skin tissues in which the sulphone was deposited. This finding made him abandon intradermal injections and adopt the subcutaneous injection. He found very favourable results from subcutaneous injections of 25% suspension of DDS in groundnut oil. This report helped all leprologists to get rid of the alarmingly heavy cost of the proprietary preparations. Molesworth and Narayanswami (2), advised by Cochrane, took up the experiment. They used a 20% suspension in place of 25% in purified and deodorized neutral cocoanut oil and reported favourable results in 100 lepromatous cases, after a year's trial.

In August, 1950, Muir selected 170 cases for DDS injection. Out of these, 140 cases, 75 males, 39 females and 26 children, have been included in this report. All of them were lepromatous cases. The plea for writing this is to show the progress of these cases after the completion of 1 year's treatment.

Preparation of the Suspension.

A 20% suspension was made first in hydnocarpus oil and sterilized in an autoclave at 15 lb. pressure for half an hour. A cork with two glass tubes, one straight and long reaching the bottom, and the other short and bent, were fitted to the container of the sterilized suspension. This bottle was often shaken and emptied in a small sterilized glass bowl, in small quantities at a time. From this bowl the syringes were filled by a laboratory assistant who, after drawing in and out the suspension several times, to make the injectable quantities of the same uniformity, handed them over to the injector. Next the hydnocarpus oil was changed to refined cocoanut oil with the same percentage of DDS.

DOSAGE AND METHOD OF INJECTION.

All injections were given bi-weekly and subcutaneously in the

extensor surfaces of arms and thighs in rotation. All the patients, male, female and children, got the same dose of 1 cc (.2 grm.) of the suspension. Observation of reaction, dosage, examination for depot formations and detailed bacteriological examinations were done only by the doctor in charge of the experiment, to ensure accuracy and uniformity of the result.

METHOD OF BACTERIOLOGICAL EXAMINATION AND ASSESSMENT OF PROGRESS.

This was done before the experiment was started, and repeated after 12 months. Five smears were examined from the most infected positive sites of each case on both occasions, and the average result of the five smears from +4 to +1 was taken as the bacteriological index, e.g. the most positive smear was counted as +4 and the least positive was counted as +1, +2 and +3 for less or more midstages. By adding the counts of the 5 smears, and dividing these 5, the bacteriological index was assessed.

“Partly negative” = Those cases who have improved much, but revealed only a few bacilli in all the 5 smears, e.g. (4 in 30 fields).

“Much improved” = This was reckoned when the present bacteriological index was less by 1 or more, e.g. if the initial B.I. was +4 and became less than +3.

“Moderately improved” was given to those just less by +1 from the initial bacteriological index, e.g. +4 to +3, or +3 to +2.

“Slightly improved” = Those whose bacteriological index had improved by less than 1.

“Stationary” and “Worse” are self explanatory.

RESULTS.

(1) Cases males 10, 30, 54, 72 and 103, females 22, 25, 30, 36 and 55 (total 7.1%), have become partly negative after an average of 18.64 and 18.2 gm. of DDS respectively. The maximum improvement is in case F.36. The Bacteriological Index came down from +4 to +4/5ths, and in case Male 103, B.I. from 1+ to 2 bacilli in all the 5 smears.

(2) 37 cases (26.7%) improved a great deal. The Bacteriological Index became less by more than 1. Cases Male 8, 18, 49, 74, 78, 97, and female 4, 9 have improved more than the other cases of this group. The Bacteriological Index became less than 1 only.

(3) 18 cases (12.8%) became moderately improved. The B.I. lessened after 1 year's treatment just by one.

(4) 47 cases (33.5%) improved slightly.

(5) 20 (14.3%) and 16, or 11.4%, remained stationary or became worse respectively.

TABLE 1.

Results and average total dose of DDS in males and females separately.

Advancement.	No.		Total %	Dosage Avg. in Grm.		Period
	Male	Female		Male	Female	
Partly negative ...	7	5	8.5	18.64	18.2	12 months
Much improved ...	17	10	19.3	18.6	19.2	" "
Mod. improved ...	10	8	12.8	19.1	19.7	" "
Slightly Improved	30	17	33.5	18.9	18.1	" "
Stationary ...	16	4	14.3	19.1	19.7	" "
Worse ...	9	7	11.4	19.8	19.7	" "
	89	51				

TABLE 2--see pages 76, 77 and 78.

Observation and Discussion.

SUSPENSION OF DDS POWDER.

Cochrane used groundnut oil, though he has not given any details regarding its purification, acidity etc. It may well be surmised that he used purified and injectable oil. Molesworth et al changed the groundnut oil to the acid free purified cocoanut oil, which was thinner than groundnut oil and could be injected easily, using a medium sized (Gauze 23) hypodermic needle. The author used filtered groundnut oil, hydnocarpus oil and acid free, purified and deodorised cocoanut oil, all sterilised. Groundnut oil was found to be the thickest, and difficulties were encountered specially for mass treatment. Hydnocarpus and cocoanut oil could be used easily.

DEPOTS.

The formation of depots was found in all. Groundnut oil took a longer time to be absorbed, but if massaged well, as has been done here, the number of depots become minimised. It is interesting to note that cases M. 44, 45, 85 and 114 always formed depots after DDS injection, be the suspension in cocoanut, hydnocarpus or groundnut oil.

Doses:—As has been mentioned, 1 cc of 20% (0.2 gm) was all along given twice a week (per week .4 gm), irrespective of age

TABLE 2.

Showing the results of the examinations in details, sex by sex.

PARTLY NEGATIVE Males							PARTLY NEGATIVE Females						
Case No.	Name	Length of treatment in weeks.	Total DDS in grms.	Bacteriological index before treatment.	B.I. at end of period.	No. of days reaction.	Case No.	Name	Length of treatment in weeks.	Total DDS in grms.	Bacteriological index before treatment.	B.I. at end of period.	No. of days reaction.
10	Ronu	39	15.6	+2	$\frac{4}{5}$	—	22	Mano	51	20.4	+2 $\frac{1}{5}$	$\frac{4}{5}$	—
30	Nobin	47 $\frac{1}{2}$	19.4	3 $\frac{3}{5}$	$\frac{4}{5}$	—	25	Sushila	43	17.2	+3 $\frac{1}{5}$	$\frac{4}{5}$	52
54	Opindra	45 $\frac{1}{2}$	18.2	2 $\frac{4}{5}$	$\frac{1}{5}$	15	30	Nishu	50	20.4	+2	3 $\frac{3}{5}$	—
72	Nobin	51	20.4	+1	+ $\frac{1}{5}$	—	36	Kehsori	32 $\frac{1}{2}$	13.4	+4	$\frac{4}{5}$	61
76	Amrit	47	18.8	+2 $\frac{3}{5}$	+ $\frac{4}{5}$	3	55	Jotsna	51	20.4	+2 $\frac{2}{5}$	$\frac{4}{5}$	—
79	Joseph	50 $\frac{1}{2}$	20.2	+1 $\frac{3}{5}$	+ $\frac{1}{5}$	—							
103	Jogu	50	20.4	+1 $\frac{1}{5}$	2 bacilli	9							
MUCH IMPROVED													
8	Khudu	32	12.8	+3 $\frac{1}{5}$	+1	24	4	Subni	46	18.4	+2 $\frac{4}{5}$	+1	31
18	Bokul	20	8.0	+3 $\frac{4}{5}$	+1	31	9	Singho	48	19.2	+2 $\frac{2}{5}$	+1	7
21	Mongol	51 $\frac{1}{2}$	20.6	+4	+2 $\frac{4}{5}$	—	10	Ambika	47	18.8	+3 $\frac{3}{5}$	+1 $\frac{3}{5}$	10
22	Bhim	50 $\frac{1}{2}$	20.2	+3	+1	—	17	Jhabri	49 $\frac{1}{2}$	19.8	+3 $\frac{1}{5}$	+1 $\frac{3}{5}$	—
43	Durjon	45 $\frac{1}{2}$	18.2	+3 $\frac{2}{5}$	+1 $\frac{1}{5}$	18	24	Thelia	45 $\frac{1}{2}$	18.1	+3 $\frac{3}{5}$	+2	21
46	Chuttu	38	19.2	+3 $\frac{4}{5}$	+2 $\frac{1}{5}$	15	31	Kemola	49	19.6	+4	+2 $\frac{4}{5}$	17
49	Sorbo	49	19.6	+4	+1 $\frac{1}{5}$	7	34	Ruou	50	20.4	+4	+2 $\frac{3}{5}$	10
53	Pundee	48	19.2	+3 $\frac{1}{5}$	+1 $\frac{4}{5}$	21	38	Hira	47	18.8	+4	+2 $\frac{4}{5}$	21
62	Horinath	50	20.4	+4	+2 $\frac{1}{5}$	—	42	Sauri	46	18.4	+3 $\frac{1}{5}$	1 $\frac{4}{5}$	49
64	Akhoy	47 $\frac{1}{2}$	19.4	+2 $\frac{2}{5}$	+1 $\frac{1}{5}$	21	50	Jamila	51 $\frac{1}{2}$	20.6	2 $\frac{3}{5}$	1 $\frac{1}{5}$	—
70	Monu	49	19.6	+2	+1	9							
74	Nokul	47 $\frac{1}{2}$	19.4	+3 $\frac{1}{5}$	+1	—							
78	Menon	48 $\frac{1}{2}$	19.4	+2 $\frac{1}{5}$	+1	—							
81	Nimai	49	19.6	+4	+2 $\frac{3}{5}$	—							
86	Gobardhan	50 $\frac{1}{2}$	20.2	+4	+1 $\frac{4}{5}$	—							
97	Bihai	51 $\frac{1}{2}$	20.6	+2 $\frac{1}{5}$	+1	—							
99	Motilal	50	20.4	+4	+1 $\frac{1}{5}$	—							
MODERATELY IMPROVED													
14	Gopal	48	19.2	+3 $\frac{1}{5}$	2 $\frac{1}{5}$	14	26	Indi	50	20.4	+1 $\frac{2}{5}$	+ $\frac{2}{5}$	7
33	Akhey	50 $\frac{1}{2}$	20.2	+3 $\frac{2}{5}$	2 $\frac{2}{5}$	3	28	Rupi	49 $\frac{1}{2}$	19.8	+3 $\frac{3}{5}$	+2 $\frac{2}{5}$	10
35	Konthiram	50 $\frac{1}{2}$	20.2	+3 $\frac{3}{5}$	2 $\frac{3}{5}$	3	35	Mongli	50	20.4	+3 $\frac{4}{5}$	+2 $\frac{4}{5}$	3

45	Thakurlal	...	47	18.7	+2	+1	24	39	Nilmoni	...	42	16.8	+24 $\frac{1}{5}$	+14 $\frac{4}{5}$	9
63	Noru	...	46 $\frac{1}{2}$	18.6	+2	+1	18	43	Babi	...	51	20.4	+13 $\frac{3}{5}$	+3 $\frac{1}{5}$	—
89	Chamru	...	39 $\frac{1}{2}$	15.5	+4	+3	51	49	Taramoni	...	50 $\frac{1}{2}$	20.2	+23 $\frac{3}{5}$	+12 $\frac{3}{5}$	7
95	Biswaneth	...	51 $\frac{1}{2}$	20.6	+13 $\frac{3}{5}$	+3 $\frac{1}{5}$	—	51	Habi	...	49 $\frac{3}{5}$	19.8	+12 $\frac{3}{5}$	+4 $\frac{1}{5}$	7
98	Purna	...	45 $\frac{1}{2}$	18.2	+32 $\frac{3}{5}$	+12 $\frac{3}{5}$	38	52	Khetu	...	51 $\frac{1}{2}$	20.6	+33 $\frac{3}{5}$	+23 $\frac{3}{5}$	—
100	Jogeswar	...	50 $\frac{1}{2}$	20.2	+12 $\frac{3}{5}$	+3 $\frac{1}{5}$	—								
101	Banka	...	49	19.6	+33 $\frac{3}{5}$	+23 $\frac{3}{5}$	—								

SLIGHTLY IMPROVED

1	Radha	...	49	19.6	+4	+34 $\frac{1}{5}$	14	1	Golapi	...	50 $\frac{1}{2}$	20.6	+2 $\frac{3}{5}$	2 granules	3
6	Charu	...	48	19.2	+24 $\frac{3}{5}$	+22 $\frac{3}{5}$	7	6	Alomoni	...	48 $\frac{1}{2}$	19.3	+14 $\frac{4}{5}$	+1	10
9	Rakhal	...	50	20.4	+33 $\frac{3}{5}$	+3	3	7	Sundora	...	46	18.4	+14 $\frac{4}{5}$	+12 $\frac{3}{5}$	17
16	Gulba	...	47 $\frac{1}{2}$	19.0	+12 $\frac{3}{5}$	+1	14	8	Opi	...	48	19.2	+14 $\frac{4}{5}$	+12 $\frac{3}{5}$	17
17	Baneswar	...	49	19.6	+4	+31 $\frac{3}{5}$	—	12	Phudi	...	42	16.8	+2 $\frac{3}{5}$	+11 $\frac{1}{5}$	21
20	Damri	...	47 $\frac{1}{2}$	19.4	+4	+31 $\frac{3}{5}$	14	14	Buchi	...	51 $\frac{1}{2}$	20.6	+1	+11 $\frac{1}{5}$	—
27	Bhuru	...	50	20.4	+33 $\frac{3}{5}$	+33 $\frac{3}{5}$	7	15	Rojoni	...	46	18.4	+4	+33 $\frac{3}{5}$	52
28	Bijoy	...	47 $\frac{1}{2}$	18.9	+31 $\frac{3}{5}$	+24 $\frac{4}{5}$	21	18	Rudun	...	47	18.8	+34 $\frac{4}{5}$	+33 $\frac{3}{5}$	14
32	Sarjoram	...	42	16.7	+4	+34 $\frac{4}{5}$	24	19	Rongi	...	51	20.4	+1	+11 $\frac{1}{5}$	—
37	Haradhan	...	48 $\frac{1}{2}$	19.3	+4	+32 $\frac{3}{5}$	14	23	Phulu	...	51	20.4	+34 $\frac{4}{5}$	+32 $\frac{3}{5}$	—
47	Bhaskar	...	36 $\frac{1}{2}$	14.6	+34 $\frac{4}{5}$	+32 $\frac{3}{5}$	45	27	Binoti	...	49	19.6	+4	31 $\frac{1}{5}$	14
48	Kashinath	...	33	13.2	+4	+31 $\frac{3}{5}$	31	29	Champa	...	47 $\frac{1}{2}$	19.4	+21 $\frac{1}{5}$	13 $\frac{3}{5}$	38
50	Nilamber	...	45	17.9	+11 $\frac{1}{5}$	+4 $\frac{1}{5}$	35	37	Khandhi	...	50	20.4	+11 $\frac{1}{5}$	4 $\frac{1}{5}$	—
51	Balak	...	48 $\frac{1}{2}$	19.4	+11 $\frac{1}{5}$	3 $\frac{1}{5}$	21	46	Dugi	...	46	18.4	+31 $\frac{1}{5}$	24 $\frac{4}{5}$	35
52	Lalmohan	...	35	14.0	+11 $\frac{1}{5}$	4 $\frac{1}{5}$	—	47	Gendu	...	51	20.4	+24 $\frac{4}{5}$	23 $\frac{3}{5}$	—
55	Ghasiram	...	47 $\frac{1}{2}$	19.4	+4	+4 $\frac{1}{5}$	21	48	Adu	...	49 $\frac{1}{2}$	19.8	+22 $\frac{3}{5}$	14 $\frac{4}{5}$	10
60	Menon	...	50 $\frac{1}{2}$	20.6	+3	+22 $\frac{3}{5}$	—	53	Balika	...	37 $\frac{1}{2}$	15.4	+4	—	—

SLIGHTLY IMPROVED

		Males					
67	Horish	...	51	20.4	+13 $\frac{3}{5}$	+1	—
68	Dhonu	...	50	20.4	+12 $\frac{3}{5}$	+1	—
77	Kitu	...	50 $\frac{1}{2}$	20.2	+4	+34 $\frac{4}{5}$	7
80	Purna	...	51	20.4	+14 $\frac{4}{5}$	+1	7
82	Rothu	...	49 $\frac{1}{2}$	19.8	+4	+32 $\frac{3}{5}$	10
86	Ebadot	...	48	19.2	+33 $\frac{3}{5}$	+31 $\frac{3}{5}$	14
90	Dibaker	...	46	18.4	+4	+31 $\frac{3}{5}$	56
93	Suru	...	48 $\frac{1}{2}$	19.4	+2	+14 $\frac{4}{5}$	14
96	Ronjit	...	51	20.4	+12 $\frac{3}{5}$	+4 $\frac{1}{5}$	3
102	Kartik	...	51 $\frac{1}{2}$	20.6	+24 $\frac{4}{5}$	+23 $\frac{3}{5}$	—
107	Sibsankar	...	48 $\frac{1}{2}$	19.3	+32 $\frac{3}{5}$	+24 $\frac{4}{5}$	7
108	Kopildee	...	49 $\frac{1}{2}$	19.8	+4	+34 $\frac{4}{5}$	16
114	Lachmi	...	51	20.4	+2	+14 $\frac{4}{5}$	—

Females

STATIONARY

Case No.	Name	Length of treatment in weeks.	Total DDS in grms.	Bacteriological index before treatment.	B.I. at end of period.	No. of days reaction.
4	Budhu	50½	20.2	+3/5	+3/5	7
15	Dhanonjoy	44½	17.8	+4	+4	42
23	Umesh	49	19.6	+1 1/5	+1 1/5	10
25	Premasaran	51½	20.6	+1 1/5	+1 1/5	—
34	Sashee	46	18.4	+4	+4	28
39	Domon	50	20.4	+1	+1	—
41	Chuttu	41	16.4	+3	+3	63
42	Satrugghna	48½	19.4	+2 2/5	+2 2/5	—
56	Sripeti	40	16.0	+4	+4	66
59	Doyasagar	50	20.4	+4	+4	—
69	Budhan	50	20.4	+4	+4	—
83	Robi	47	18.8	+3 3/5	+3 3/5	14
85	Ganesh	50½	20.2	+2 4/5	+2 4/5	3
91	Dinobondhu	49	19.6	+4	+4	—
92	Domon	50	20.4	+4	+4	—
104	Nodu	46	19.2	+4	+4	—

Case No.	Name	Length of treatment in weeks.	Total DDS in grms.	Bacteriological index before treatment.	B.I. at end of period.	No. of days reaction.
3	Rotni	48	19.2	+4	+4	4
5	Sashee	50	20.4	+4	+4	—
41	Dashi	51½	20.6	+4	+4	—
44	Chepi	47½	19.4	+4	+4	14

WORSE

11	Rashu	48	19.2	+1 3/5	+3	21
13	Dulal	50	20.4	+1	+1 1/5	—
26	Usman	48½	19.4	+3 3/5	+3 3/5	14
29	Phakir	48½	19.4	+2	+2 2/5	21
87	Ismael	47½	19.0	+3 3/5	+3 3/5	10
94	Sashee	51½	20.6	+2 1/5	+3 3/5	—
105	Motilal	51	20.4	+3 1/5	3 3/5	—
110	Joseph	51	20.4	+1 4/5	+2 2/5	—
113	Sakir	51	20.4	+2 1/5	+3 3/5	—

11	Kodom	41	16.4	+2 1/5	+3	52
15	Bhadu	51½	20.6	+3 3/5	+3 3/5	—
16	Subodhani	49½	19.8	neg.	2 bac.	—
21	Dongi	48½	19.4	+2 4/5	+3 3/5	14
33	Rosoana	45	18.0	+1 4/5	+3 3/5	45
40	Ulia	49½	19.8	+3 3/5	+4	3
45	Beji	51	20.4	+4/5	+1	—

and sex. Cochrane used .5 gm. to 2.5 gm. per week in most of his cases. Molesworth used .2 gm. to 1 gm. per week.

LEPRA REACTION.

Eighty-nine cases, or 63.5%, suffered from reaction. Cases F. 53, 25, 11, 15, 33 suffered most from 77, 52, 52, 52, 45 days respectively; of these 3 improved slightly and 2 became worse. Cases M. 56, 41, 90, 47, 15 suffered from 66, 63, 56, 45, 42 days respectively. Three improved slightly, 3 remained stationary and none became worse.

In the reactionary stages while being treated with the parent sulphone, the nodules have been observed as diffuse swellings. Discrete nodules were fewer in acute reaction. In 4 cases the swellings softened and, on incision, thick pus came out. On staining, the specimen contained *M. leprae* and pus cells only. In one case, most of the eruptions ulcerated.

SUMMARY.

One hundred and forty cases have been treated with 20% DDS suspension for 1 year. Groundnut oil, hydnocarpus oil and refined deodorised cocoanut oil have been used as suspending agents. Bacteriological improvements are shown in Tables 1 and 2 in short and in detail, sex by sex: Lepra reaction has been discussed. Depot formation has been observed.

CONCLUSIONS.

One hundred and four, or 74.1% of cases, have improved with a dose of .4 gm. per week for one year. There was very little difficulty and treatment could be continued easily without any supplementary treatment, to almost all. Except in 4 cases out of 89, or 63%, reaction cases needed very little special care for the continuation of treatment. DDS can be suspended easily in any vehicle. Refined hydnocarpus oil costs only two-thirds of the purified cocoanut oil, and depots may be seen with any of the vehicles used for the suspension of DDS, but more particularly when arachis oil is used.

REFERENCES.

1. Leprosy Review, Vol. XX, 1949, p. 4.
Cochrane, Ramanujam and Paul.
2. International Journal of Leprosy, Vol. 17, 1949, p. 197.
Molesworth and Narayanswami.