DIAMINODIPHENYLSULPHONE IN LEPROSY

ITS ORAL AND PARENTERAL USE

(A Comparison)

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The compound diaminodiphenylsulphone was first synthesised in 1908 by Fromm and Wittmann. It was first used in 1937 in experimental streptococcal infection. In 1940 Feldman *et al* first used its proprietary preparation " Promin " in experimental tuberculosis with success. Other proprietary preparations such as diasone, sulphetrone, etc. by Abbott Laboratories and Burroughs Wellcome & Co., were promptly made to overcome the reported toxicity of the parent compound. Later in 1949 in spite of these preparations having been found effective in leprosy, their method of administra-

tion and high cost stood in the way to their use in a large number of persons suffering from leprosy in India, China and Africa. The parent compound diaminodiphenylsulphone, or DDS as it is generally termed, in spite of its greater toxicity was suggested for an extensive trial to find out its effect and minimum subtoxic effective dose.

ITS ORAL USE

With the idea stated above, Dr. Muir in Purulia selected 119 lepromatous cases of leprosy at different periods. At this stage, April 1949, the tablets were not manufactured; the DDS powder was given in the form of a 2.5% suspension (0.1 grm. in 4 c.c. or 10 mgs. in 4 c.c.) in sweetened acacia mucilage, and was squirted into the patients mouth from a syringe, but after a year, when the tablets were made by I.C.I., this method of administration was replaced by tablets. The dose was administered according to the tolerance of each individual. Little importance was attached to age and sex. Particular importance was attached to the estimation of hæmoglobin. While assessing the result after 2 years, it was found that the period of treatment in the 98 cases treated orally varied as follows.

Period of treatment	*No. of cases*
24 months	25
22 ,, ...	14
20 ,, ...	20
18 ,, ...	2
16 ,, ...	19
14 ,, ...	7
12 ,, ...	4
10 ,, ...	1
8 ,, ...	4
6 ,, ...	2

Dosage.—The usual dose of the suspension by oral route was 2 c.c. to 8 c.c. (50 mgs. to 200 mgs.) daily, 6 days in a week, and of the tablets ½ to 3 tablets (50 to 300 mgs.) daily, 6 days in a week. The dose was regulated by the reaction and percentage of hæmoglobin. Sulphone was discontinued when the Hb. was below 50%. Tests were done by Sahli's hæmoglobinometer.

The assessment of the results of treatment was made by examining 5 skin smears from the most infected part of the body and finding out the average points for 5 smears; giving 4 points to the smears of highest bacillary concentration, 1 to the lowest concen-

tration and 3 or 2 to the findings between these extremes. Almost negative has been used for those smears which had only a few bacilli in all the 5 smears.

TABLE NO. 1 ORAL TREATMENT

The following result was observed in 98 cases after expiry of 2 years.

Result	*No. of cases*	*%*	*Total DDS given in grms. Average*	*Period of treatment in months Average*
Negative	2	2	45.8	21.5
Almost negative ...	5	5.1	63.5	18.5
75% less bacilli ...	10	10.2	79.6	17.8
50% less bacilli ...	14	14.2	66.1	10.0
Slightly improved (less bacilli, below 50%)	43	43.8	45.9	17.8
Stationary ...	14	14.2	39.5	15.9
Worse	10	10.2	58.9	18.6

ITS PARENTERAL USE

Cochrane[1] in 1947 started injecting 15% suspension of DDS in arachis oil intradermally. Later finding the drug concentrated in the skin, he preferred the subcutaneous injections. He reported very favourable results from the subcutaneous injections of 25% suspension of DDS in groundnut oil, and used 2.5 grm. per week per patient. This experiment was taken up by Molesworth and Narayanswami in Malaya[2]. They used 20% DDS suspension in purified deodorised neutral cocoanut oil. Injecting the suspension subcutaneously 1 grm. per week per patient, their findings on 100 cases after 1 year's treatment were as follows:—Clinically, improved 96 and Stationary 4. Bacteriologically, improved 27, Stationary 64 and Worse 9.

On injecting 2 c.c. of 20% suspension of DDS (400 mgm.) first in hydnocarpus oil and then in cocoanut oil, the following results were found by us, in 140 lepromatous cases, after 1 year's treatment.

TABLE NO. 2 PARENTERAL TREATMENT

Showing the status after 1 years' treatment with DDS of 140 lepromatous cases.

Result	*No. of cases*	*%*	*Total DDS given (in grms)*	*Period of treatment in months*
Negative	Nil	—	—	—
Almost negative ...	12	8.5	18.42	12
75% less bacilli ...	27	13.2	19.90	12

50% less bacilli ...	18	12.8	19.40	12
Slightly improved (less bacilli below 50%)	47	33.5	18.50	12
Stationary	20	14.3	19.40	12
Worse	16	11.4	20.75	12

TABLE NO. 3

TABLE NO. 1 AND TABLE NO. 2 COMPARED

	Oral DDS.	*Parenteral DDS.*
	98 cases	140 cases
Improved average ...	74 or 75%	104 or 74.2%
Average time per case	17.1 months	12 months
Average grm. per case	57 grms.	19.38 grms.
Stationary	14.2%	14.3%
Worse	10.2%	11.4%

Comparing results in Table No. 1 and Table No. 2, it will be found that the negative cases mentioned in Table 1 were very early cases of low bacteriological index, so much stress cannot be put on this finding. The main difference is in the period of treatment and in the quantity of DDS used. With the suspension, the same result has been achieved as that with the sulphone tablets but in half the time. Very little difference can be noticed in the numbers classed " stationary " and " worse ".

Conclusion.—If the trouble of injecting the suspension is not taken into consideration, there is a real advantage in using the suspension of DDS parenterally. Here both the amount of the drug and the period of treatment are lessened. Expense too is thus reduced.

REFERENCES

1. COCHRANE, R. G. et al (1949) . . . *Leprosy Review* 20 (Jan-Apr.)
2. MOLESWORTH, D. and NARAYANSWAMI, P. S. (1949) *Int. Journal of Leprosy*, 17, 197.
3. ROY, A. T. (1951) *I.M.G.* Vol. LXXXVI, 373.