INTERNATIONAL JOURNAL OF LEPROSY

VOLUME 15, NUMBER 3 JULY-SEPTEMBER, 1947

PRELIMINARY REPORT ON A NEW SULPHONE DRUG "SULPHETRONE"

L. H. WHARTON

Mahaica Leprosarium, British Guiana

Sulphetrone is tetrasodiumphenylpropylamino — diphenyl sulphone tetrasulphonate. The use of three "sulphone" compounds has already been reported in the literature in leprosy therapy. These sulphones are all derivatives of diaminodiphenylsulphone, the parent compound.

DIAMINODIPHENYLSULPHONE

PROMIN DIASONE PROMIZOLE SULPHETRONE

The use of sulphetrone in the treatment of tuberculosis is based on its anti-tuberculous activity in the guinea pig. It inhibits the development of experimental tuberculosis in this animal and prolongs the life of infected animals as compared with controls.

So promising have been the results in human tuberculosis with experiments by Anderson at Glasgow, that it was decided that clinical trials in leprosy should be made. Through the courtesy of Dr. Ernest Muir, C.I.E. Medical Secretary of the British Empire Leprosy Relief Association, a sample of the drug was sent to this leprosarium, and we were asked to work out a suitable dosage, and to report on its clinical effect.

The present report gives the preliminary results of a therapeutic trial with sulphetrone in six cases of leprosy for a period of six months.

Six young adults were selected varying in age from 16 to 35 years, five males and one female, all suffering from lepromatous leprosy (type L_1) and all lepromin-negative. These patients had all received prolonged treatment with chaulmoogra oil, and had not benefitted. Treatment consisted of sulphetrone tablets 0.5 Gm. for fifteen weeks continuously with four weeks rest at the end of each course of treatment. As sulphetrone produces hypochromic anemia,

we gave each patient one month's treatment with ferrous sulphate, 3 grs. three times a day, and yeast, prior to the administration of sulphetrone.

Starting with a dose of 0.5 Gm. daily we gradually increased the dose until we reached the maximum which could be tolerated by the patients. This was 3.0 Gm. daily. Estimations of concentration of the drug in body fluids were done weekly for the first four weeks and fortnightly thereafter; these included blood counts, hemoglobin estimation, and urinalysis. Throughout the course of treatment no abnormalities were noted by urinalysis. The drug was well tolerated and we have been greatly impressed by its action.

The following tables give details of our findings:

Average daily dose of drug 3.0 grams.

Table 1. Concentration of drug in blood in mg. %

Case 1	7 to 12	Average	9
" 2	6 to 12	"	10
" 3	7 to 12	"	9
" 4	6 to 12	"	9
" 5	6 to 10	"	8
" 6	6 to 12	"	9

Concentration of drug in cerebrospinal fluid in mg. %. All cases 2 mg. %.

Table 2. Concentration of drug in urine in mg %

Case 1	4 to 12	Average	6
" 2	6 to 12	"	8
" 3	6 to 12	"	9
" 4	6 to 12	"	9
" 5	6 to 12	"	10
" 6	6 to 12	"	8

Table 3. Hemoglobin % (Haldane)

	At commencement	After 6 months
Case 1	70	90
" 2	60	78
" 3	80	80
" 4	80	85
" 5	60	65
" 6	75	78

Table 4. Red cell count (Erythrocytes)

	At commencement	After 6 months
Case 1	5,410,000	4,600,000
" 2	4,100,000	3,140,000
" 3	5,200,000	3,920,000
" 4	4,260,000	4,300.000
" 5	4,330,000	3,000,000
" 6	4,260,000	3,300,000

This shows mild anemia in all cases except Number 4. Every case showing a red cell count below 3½ million was given ferrous sulphate orally 5 grains 3 times a day.

Table 5. White blood cell count

	At commencement	After 6 months
Case 1	10,900	8,800
" 2	6,900	6,300
" 3	4,700	5,400
" 4	5,400	5,300
" 5	4,500	4,700
" 6	8,000	5,200

There was no marked leukopenia. The differential white count showed very slight variation in the percentage counts of polymorphonuclears, leukocytes, and eosinophiles.

Table 6. Sedimentation rate (mm/hr.)

	At commencement	After 6 months
Case 1	4.5	9.0
" 2	49.2	30.0
" 3	10.0	9.0
" 4	10.0	16.0
" 5	12.5	6.0
" 6	15.5	19.0

Table 7. Increase of weight in almost all cases

	At commencement	After 6 months
Case 1	140 lbs.	162 lbs.
" 2	118 "	123 "
" 3	186 "	190 "
" 4	147 "	144 "
" 5	109 "	109 "
" 6	131 "	133 "

Table 8. Mild toxic effects

	Nausea	Cyanosis	Disturbance of vision
Case 1	Present 1st week	Nil	Nil
" 2	Nil	Nil	Nil
" 3	Nil	Nil	Nil
" 4	Nil	Nil	Nil
" 5	Present 2 weeks	Nil	Nil
" 6	Nil	Nil	Nil

Table 9. Monthly nasal and skin bacilli counts*

Cases	Months											
	1st		2nd		3rd		4th		5th		6th	
	N.	S.	N.	S.	N.	S.	N.	S.	N.	S.	N.	S.
1	9/10	12/10	3/10	5/10	Neg.	5/10	Neg.	3/10	Neg.	Neg.	Neg.	Neg.
2	22/10	30/10	18/10	22/10	Not exam.		13/10	20/10	10/10	16/10	8/10	13/10
3	38/10	§§	30/10	37/10	20/10	25/10	15/10	22/10	9/10	18/10	5/10	13/10
4	20/10	32/10	16/10	22/10	10/10	18/10	8/10	16/10	6/10	13/10	4/10	9/10
5	18/10	20/10	15/10	22/10	9/10	15/10	6/10	12/10	4/10	9/10	Neg.	6/10
6	Neg.	15/10	Neg.	10/10	Not exam.		Neg.	6/10	Neg.	4/10	Neg.	6/10

* The numerator denotes the number of bacilli and the denominator the number of fields examined.

Neg.:—Negative; §§:—More than 10 in each field; Not exam.:—Not examined.

In all cases a marked reduction in bacilli is seen.

SUMMARY

Sulphetrone in 3.0 Gm. daily dose, giving 1 tablet (0.5 Gm.) every four hours, has proved to be safe. We have seen only very mild toxic effects from the drug, nausea, which was quickly relieved by administering sodium bicarbonate, 30 gr. three times a day orally. There has been marked improvement in clinical symp-

toms, with flattening out of nodules. Bacteriological smears from nose and skin have shown marked improvement from month to month and one patient with positive nose and skin smears became bacteriologically negative in the fifth month.

It should be noted that this trial was made on early L_1 cases that were free from any complications of the disease. Clinical trials continue and will be extended to include patients with more advanced lesions, and with complications.

CONCLUSIONS

We consider the results obtained by the use of sulphetrone after six months clinical trial sufficiently promising to warrant further investigation. We have found the drug less toxic than other sulphones we have used.

We look forward to literature from other workers on this new sulphone.

(We wish to express thanks to Dr. Ernest Muir, and Dr. F. Prescott of the Wellcome Research Institute, London, for supplying us this drug gratis. This drug is still in the experimental stage.)