TREATMENT OF BILHARZIASIS WITH ANTIMONY DIMERCAPTOSUCCINATE

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TWSb (antimony-a, a'-dimercaptosuccinate) was synthesized by E. A. H. Friedheim, New York. It is put up in powder form in multiple dose vials for intravenous (diluent 20-50% sterile hypertonic glucose solution) or intramuscular (diluent sterile normal saline) use. In these trials all patients were given the drug by the intramuscular route.

Material

The patients were all apparently healthy Bantu male recruits between 20 and 40 years old, from the Transvaal or Mozambique to Havelock Asbestos Mine in Swaziland. The mine is in a bilharzia-free area and the chances of reinfection were therefore minimal. Patients selected for treatment all had double infections with *Schistosoma haematobium* and *S. mansoni*.

Diagnosis was made by simple gravity sedimentation and examination of urine, and concentration of *S. mansoni* ova by sieving and sedimenting the faeces with water and pouring off the supernatant fluid until clear. One examination of urine and faeces was done. The cases were admitted to

TABLE I. TESTS OF CURE

Case	Dosage	Urine examinations		Faeces examinations		Rectal snip result	Side-reactions
		Number	Result	Number	Result weeks after treatment		
1	0·2 g.	10	Neg.	10	Neg.	Dead h. and m.	Nil
2	daily × 10	9	Neg.	2	Pos. (7)	Dead h. and m.	Nil
3		Not done		Not done		Not done	Nil
4		8	Neg.	9	Neg.	Not done	Nil
5	0·4 g.	Not done		Not done		Not done	Nil
6	daily × 5	9	Neg.	3	Pos. (8)	Dead h. and m.	Nil
7		10	Neg.	10	Pos. (10)	Dead h. and m.	Nil
8		Not done		Not done		Not done	Nil
9		4	Neg.	1	Neg.	Not done	Nil
10		3	Neg.	1	Pos. (10)	Dead h. Vi. m.	Nil
11		4	Neg.	1	Pos. (7)	Dead h. Vi. m.	Nil
12		2	Neg.	2	Neg.	Not done	Nil
13	0·34 g.	3	Neg.	2	Pos. (9)	Dead h. and m.	Nil
14		1	Neg.	1	Neg.	Not done	Nil
15	*t.d.s.*	4	Neg.	2	Pos. (6)	Neg	Nil
16		Not done		Not done		Not done	Nil
17	for 2 days	5	Neg.	4	Pos. (11)	Dead h. and m.	Coughing after 1st three injections
18		Not done		Not done		Not done	Vomiting after 4th injection, Temp. 100°F.
19		Not done		Not done		Not done	Vomiting after 4th injection
20		4	Neg.	1	Pos. (8)	Neg.	Vomiting after 4th injection, Temp. 99°F.
21		5	Neg.	5	Pos. (11)	Dead h. Vi. m.	Vomiting after 4th injection
22		5	Neg.	5	Neg.	Not done	Vomiting after treatment completed, Temp. 99°F.
23		8	Neg.	6	Pos. (11)	Dead h. and m.	Vomiting after treatment completed, Temp. 100°F.
24	0·4 g. 8-hourly × 3	Not done		Not done		Not done	Severe vomiting after third injection
25	0·4 g. 8-hourly × 5	3	Neg.	3	Neg.	Not done	Severe vomiting, abdominal pain, liver tenderness, bile in urine after 5th injection
26		3	Neg.	3	Pos. (10)	Not done	Nil
27		3	Neg.	1	Pos. (5)	Not done	Nil
28	0·4 g.	6	Neg.	5	Neg.	Not done	Same as No. 25 after 6th injection
29	8-hourly × 6	2	Neg.	2	Pos. (9)	Not done	Bile in urine after 6th injection
30		3	Neg.	2	Pos. (10)	Not done	Severe vomiting, bile in urine after 6th injection
31		1	Neg.	1	Pos.	Not done	Severe vomiting, bile in urine after 6th injection
32		3	Neg.	3	Neg.	Not done	Rise of temperature after treatment completed
33		3	Neg.	3	Neg.	Not done	Nil
34	0·4 g.	3	Neg.	3	Neg.	Not done	Nil
35	8-hourly × 7	2	Neg.	2	Neg.	Not done	Nil
36		5	Neg.	2	Pos. (4)	Not done	Nil

h.=haematobium m.=mansoni Vi.=viable

hospital for the duration of, and 1 day following, treatment.

Dosage Schedules

A. *Total dose* 2·0 *g.* (1) 0·2 g. daily for 10 days, 4 patients; (2) 0·4 g. daily for 5 days, 3 patients; and (3) 0·34 g. thrice daily for 2 days, 16 patients.

B. *Total dose* 2·4 *g.* 0·4 g. 8-hourly, 8 patients.

C. *Total dose* 2·8 *g.* 0·4 g. 8-hourly, 5 patients.

Schedule A was used initially until it was found that the curative effect on *S. mansoni* was poor, when schedules B and C were used.

RESULTS

Tests of Cure

Tests of cure were carried out from the 4th week onwards after completion of treatment. The total contents of the bladder was called for after hard exercise; it was sedimented by gravity, and the whole of the sediment examined for ova. Water concentration of the whole stool was used for the detection of *S. mansoni* ova. A rectal snip was done on some cases in addition to the examination of the faeces. Viability of ova was determined by producing motile miracidia from the ova. All positive cases recorded were discharging viable ova.

S. haematobium. None of the cases examined after treatment were found discharging viable ova of *S. haematobium.* This is in accordance with Alves' (1958) findings in Rhodesia.[1] He used a different dosage schedule (0·4 g. daily for 4 days) and a different (intravenous) route of administration.

S. mansoni. Of the 29 cases examined after treatment, 17 (56.6%) were still discharging viable *S. mansoni* ova and probably must be considered failures. *Table I* shows that there was no difference in the number of positives with the different dosages used. The superiority of faeces examination over 1 rectal snip is obvious; only 3 rectal snips contained viable ova in 11 cases with viable ova in their faeces. Several cases in whom *S. mansoni* ova were not found received a limited number of tests of cure. This was mainly due to their leaving the mine before sufficient tests could be done, and accounts for some cases not receiving any tests of cure

Side-reactions

Dosage schedules A (1) *and* (2). No side-reactions were noted in any of the 7 cases.

Schedule A (3). Of the 16 cases 9 had no side-reactions and 1 (No. 17) had coughing only after the first 3 injections. Six cases vomited; in 4 this happened after the 4th injection—2 had a concommitant rise of temperature, and the other 2 had a rise of temperature after the treatment had been completed. In the cases who vomited after the 4th injection, the last 2 injections were postponed for 8 hours. No further vomiting occurred and the temperatures subsided. In none of these 6 cases was the vomiting severe or prolonged.

Schedule B. Eight cases were put on this schedule. Two of them (Nos. 24 and 25) were unable to complete the course owing to severe side-reactions with signs of acute liver damage. One of these (No. 24) received a total of 1·2 g. TWSb in 24 hours and the other 2·0 g. in 40 hours. Of the remaining 6 cases 2 had no side-reactions, but 4 showed signs of liver damage, with bile in the urine, or severe and prolonged vomiting, or liver tenderness. These signs became evident after treatment had been completed and necessitated drastic action.

Schedule C. Strangely enough the only side-reaction in these 5 cases was a rise of temperature in 1 patient after treatment had been completed.

It was obvious that side-reactions in patients receiving a heavy dose of TWSb (0·4 g. 8-hourly) were severe and dangerous. With the less heavy doses (0·34 g. *t.d.s.*) side-reactions were too numerous, though in this series not dangerous, for the drug to be used in ambulant cases. With the light doses of 0·2 and 0·4 g. daily no side-reactions were noted, which supports Alves' findings in Rhodesia[1] on 25 ambulatory patients treated with 0·4 g. of the drug daily for 4 days.

Conclusions

1. TWSb is probably an effective drug in the treatment of *S. haematobium* in doses that do not give rise to severe side-reactions.

2. The drug is not effective in the treatment of *S. mansoni* in any dosage schedule used in the present series in patients from the Transvaal or Mozambique.

3. Side-reactions in patients with double infections of *S. haematobium* and *S. mansoni*, except those receiving light doses of the drug, were numerous, severe and sometimes dangerous.

SUMMARY

Thirty-six patients suffering from *S. haematobium* and *S. mansoni* infection were treated with TWSb.

Of the 29 patients who submitted themselves for re-examination after treatment none were found shedding viable ova of *S. haematobium*; 17 of them were found to be shedding viable *S. mansoni* ova.

Side-reactions were severe in patients receiving the larger doses of the drug.

We wish to thank Mr. L. A. West, Manager, Havelock Mine, for allowing us to do these trials, and other members of the mine staff for their cooperation; Dr. B. de Meillon, Honorary Director of Bilharzia Research, for his criticism, and the South African Council for Scientific and Industrial Research for permission to publish this paper.

1. Alves, W. (1958): Cent. Afr. J. Med., 4, 15.