ARSOBAL IN THE TREATMENT OF RHODESIAN SLEEPING-SICKNESS

M. A. DE ANDRADE SILVA, A. CASEIRO,
R. P. CARMO and A. X. DE BASTO

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In our comunication to I.S.C.T.R. in September 1952 we announced the treatment of the first cases of *T. rhodesiense* sleeping--sickness, in Mozambique, with arsobal (S. 854 R. P. Specia). Those cases all showed serious involvement of the nervous system.

As the results were encouraging we decided to treat a larger number of patients with the same drug. Our paper today is a general view on the subject.

We used three batches of arsobal (N.º 102, 103, 104).

Most of the cases mentioned here were diagnosed during 1951, 1952 and 1953.

In order to put things clearly we divide the cases in three major groups:

Group I — New nervous cases.

Group II — Old cases, also in the nervous stage, previously treated with antrypol + tryparsamide or pentamidine + tryparsamide.

Group III — Early cases (haemolynphatic stage).

All patients were hospitalised during treatment and were submited to: a general examination, blood tests for trypanosomes and other

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parasites, urine test for albumin and microscopic examination of the sediment, microscopic examination of the feces and lumbar punctures before and after treatment. Weight was ascertained before and after treatment.

The patients had, as a rule, two days rest before starting arsobal treatment on account of the usual headaches following lumbar puncture.

The injections of arsobal were given always very slowly, in the morning, with the patients in jejune and in bed.

B.A.L. was at hand injections were given when necessary at the dosage indicated in the circular accompanying the ampoules.

As a rule the patients were discharged one week after treatment and followed up during several months.

I Group — *New nervous cases treated with arsobal.*

To these patients a dose equivalent to 3,6 mgr. per kgr. of body weight was given.

Various ways were used for the sequence of the injections, as follows:

Some cases were treated with two courses of four daily injections separated by an interval of 7 to 14 days (I A.).

Other cases were treated with a single course consisting of one injection on each of 4 consecutive days (I B.).

Others again were treated with four injections, one in every third day (I C.).

We treated other cases with one or two courses of injections but differently from the cases mentioned under I A. or I B. (I D.).

In some cases we proceeded in the following manner: first antrypol or pentamidine + tryparsamide; after a period of 15 to 30 days a course of four daily injections of arsobal was given (I E.).

Lastly, in some patients we repeated the arsobal treatment once more. (I F.).

I A. *Cases treated with two courses of four daily injections separated by an interval of one or two weeks* — A total of 23 cases all showing trypanosomes in the C.S.F. with protein contents between

28 and 80 mgrs. and cell counts always higher than 20/mm^3 were treated.

The cerebrospinal fluid examinations supply us with the following data:

The cell count came down to less than 5/mm^3: in 1 case after 5 months, in 1 case after 9 months and in 9 cases between 9 and 20 months after treatment.

The cell count remained above 5 per c.mm. in 12 cases.

As for the protein content it was normal in 5 cases between 4 and 5 months and in 6 cases between 8 and 12 months after treatment. The protein remained above normal in 1 case after 8 months, in 1 case after 12 months, in 1 case after 13 months and in 2 cases after 15 months after treatment. The protein content increased in 2 patients. One of these patients had a much higher protein content 2 months after the treatment and died two months later.

The C.S.F. was not examined in 3 cases after treatment because one of them escaped and the other two were females in advanced stage of pregnancy.

The cerebrospinal fluid composition became normal (protein 25 mgs. or less, cell count 1-2/mm^3) in 7 cases: 1 case in 8 months, 1 case in 9 months, 1 case in 11 months, 2 cases in 12 months, 1 case in 13 months and 1 case in 14 months after treatment.

These results lead us to the conclusion that we have obtained the cure in 7 cases (30 %) and very marked improvement in 11 cases (47 %) with arsobal treatment using two courses of four injections.

Accidents — With the exception of hyperthermia observed in all cases after the first injection and vomiting in some, no serious accidents are recorded with this manner of treatment.

I B. *Cases treated with a single course of four injections of arsobal. An injection on each of four consecutive days* — 83 cases were treated in the above mentioned way. The C.S.F. examinations showed before treatment protein contents between 30 and 90 mgrs. cell counts between 4 and over 1.000; trypanosomes from a few to many were found in 57 patients.

After treatment the cell count came down considerably in 51 cases, 39 of which returned to normal.

This took:

3	months	in	1	case
4	»	»	2	cases
5	»	»	3	»
6	»	»	1	case
7	»	»	7	cases
8	»	»	8	»
9	»	»	7	»
10	»	»	5	»
12	»	»	12	»
14	»	»	4	»
16	»	»	1	case

The cell count remained high in 15 cases:

In	5	cases	after	4 months
»	2	»	»	5 »
»	3	»	»	7 »
»	2	»	»	8 »
»	1	case	»	9 »
»	1	»	»	11 »
»	1	»	»	12 »

Protein contents returned to normal in 43 cases:

In	1	case	after	3 months
»	4	cases	»	4 »
»	6	»	»	5 »
»	3	»	»	6 »
»	8	»	»	7 »
»	7	»	»	8 »
»	5	»	»	9 »
»	4	»	»	10 »
»	4	»	»	14 »
»	1	case	»	16 »

In 23 cases the protein continued increased:

In	14	cases	after	4 months
»	2	»	»	7 »
»	2	»	»	9 »
»	1	case	»	11 »
»	2	cases	»	12 »
»	1	case	»	14 »
»	1	»	»	15 »

In none of the 83 patients trypanosomes were found in the C.S.F. after treatment.

39 patients had a normal C.S.F. (protein 25 mgs. or less, cell count under 4):

4	cases	after	4	months
6	»	»	5	»
2	»	»	6	»
5	»	»	7	»
10	»	»	8	»
5	»	»	9	»
2	»	»	10	»
2	»	»	12	»
2	»	»	14	»
1	case	»	16	»

Consequently, 39 cases are considered to be cured (percentage 46,9 %).

The C.S.F. was not examined in 4 cases. We lost sight of one case and the other three are still under observation and apparently well.

In 12 patients the C.S.F. is to be considered almost normal after treatment. 15 cases continued to show seriaus disturbance of the C.S.F. composition.

Of the total 83 death occurred in 13 cases. We attribute the cause of death in 7 cases to toxic accidents caused by arsobal which gives a percentage of mortality of 8,4 % in this series of cases.

Accidents — A feverish condition was observed in all patients after the first injection.

As slight incidents we mention vomiting, tremors and diarrhoea, in some cases, during the course of injections.

We have to report 8 very serious toxic accidents resulting death in 7. A description of these eight cases follows.

Case n.º 4/53 — African male, age about 48.

Before treatment:

Blood:	Tryps +
C.S.F.:	Tryps —
	Protein 39 mgrs.
	Cell count 38/mm³
Urine:	Ova of Sch. haematobium

Two days after treatment the patients complained of headache. Prostration. B.A.L. Temp. 37º,5. Kernig and Romberg signs positive. Next day prostation continues and patient becomes unconscious. Next day generalised tremor and coma in the afternoon. Death occurred the 5th day after treatment.

Total dosage of B.A.L.: 14 ampoules.

Case n.º 24/53 — African female, aged about 25.

Before treatment:

Blood:	Tryps +
C.S.F.:	Tryps ++
	Protein 56 mgrs.
	Cell count 153/mm³
Urine:	Without albumin

After the 4th injection of arsobal the patient started having tremors. B.A.L. Next day trismus appeared and in the afternoon coma. Death occurred the 5th day after treatment.

Case n.º 36/53 — African male, aged abouth 60. He was admited to hospital in very bad condition, unconscious. Somnolence.

Before treatment:

Blood: Tryps ++
C.S.F.: Tryps —
Protein 138 mgrs.
Cell count 71/mm³
Urine: Without albumin

3 days after treatment the somnolence of the patient increased profuse diarrhoea.

B.A.L. (2 cc. every four hours during two days; the third day 2 cc. every 6 hours). The patient recovered and was discharged eight days later.

4 months later:

Blood: Tryps —
C.S.F.: Tryps —
Protein 30 mgrs.
Cell count 4/mm³

Case n.º 55/53 — An african female, aged about 45.

Before treatment (25.5.953).

Blood: Tryps +
C.S.F.: Tryps +
Protein 30 mgrs.
Cell count 55/mm³
Urine: No albumin

A rise of temperature (39º,8) was noticed after the first injection of arsobal.

Five days after the treatment the patient complained of headache and became somnolent. Epileptiform convulsions started on the morning of the following day. B.A.L. injections (2 cc. every 4 hours) were given to the patient. Entered in coma in the afternoon and death occurred the 7th day.

Case n.º 69/53 — An african female, aged about 35.

Before treatment:

Blood: Tryps —
C.S.F.: Tryps +
Protein 40 mgrs.
Cell count 375/mm³
Urine: No albumin

Temperature 38º,2 after the first injection. On the 4th day after treatment started with tremors firstly of the limbs and soon generalised. B.A.L. (2 cc. every 4 hours). Temperature 40º. Quickly the patient entered in deep coma and died the following day.

Case n.º 83/53 — An african male, aged about 24.

Before treatment:

Blood: Tryps ++
C.S.F.: Tryps ++
Protein 50 mgrs.
Cell count 51/mm³
Urine: Albumin

Temperature 39º,6 after the first injection. After treatment the urine was albumin free. On the 3rd day after the last injection of arsobal patient complained of headache. Temperature 37º,6. A few hours afterwards restlessness and trismus developed. We started to give B.A.L. injections. Death occurred in the afternoon of the following day.

Case n.º 7/54 — African male, aged about 60.

Before treatment:

Blood: Tryps +
C.S.F.: Tryps ++
Protein 56 mgrs.
Cell count 23/mm³
Urine No albumin

Two days after treatment a slight but generalised fibrillation of the muscles. B.A.L. (2 cc. every four hours). In the morning of the 4th day condition worsens. Albuminuria. Temperature 40°. Tremor increases. Patient entered coma and died four days after treatment.

Case n.° 9/54 — African male, aged about 32. Weight 62 kgs.

Before treatment:

Blood:	Tryps +	
C.S.F.:	Tryps —	
	Protein	31 mgrs.
	Cell count	33/mm³
Urine	Albumine free	

In the afternoon of the last day of treatment the patient suddenly became unconscious and quickly entered coma. B. A. L. Cheynes Stokes breathing, fever. He remained in coma until he died the 5th day after treatment.

I C. *Cases treated with one course of 4 injections of arsobal. One injection every third day* — We treated 2 patients in this way. One had nephritis and 9 months after treatment his general condition was excellent, the C.S.F. cell count was normal but protein was still increased.

The second case was in poor condition before treatment and died of toxic encephalopathy.

The description of this case follows.

Case n.° 78/53 — An african male, aged about 55.

Before treatment:

Blood:	Tryps +	
C.S.F.:	Tryps ++	
	Protein	35 mgrs.
	Cell count	27/mm³
Urine:	Albumin	

A slight rise of temperature after the first injection. One day after treatment the patient had hiccups, he became confused. B.A.L. (2 cc. every 4 hours). Next day the patient complained of intense cephaloea. Tremors started and later on violent epileptiform convulsions. Temperature 38°,6. Cheynes Stokes breathing the following day and deep. coma. Death occurred the 4th day after treatment.

I D. *Cases treated with one or two courses of arsobal, the sequence of the injections beeing irregular* — We have used several ways of treatment owing to the condition of the patients.

a) One patient received two courses of 3 daily injections with one week's interval.

Case n.° 84/53 — Before treatment (12.8.953).

Blood:	Tryps +
C.S.F.:	Tryps +
	Protein 40 mgrs.
	Cell count 87/mm³
Urine	No albumin.

Weight 45 kgr.

7 months after treatment:

Blood:	Tryps —
C.S.F.:	Tryps —
	Protein 25 mgrs.
	Cell count 9,3/mm³

Weight 51 kgr.

b) One case received two courses of 4 injections with the interval of one week. The injections of this first course were given on four consecutive days and those of the second course were given every second day.

Case n.° 71/53 — African male, aged about 42.

Before treatment:

Blood: Tryps +
C.S.F.: Tryps +
Protein 55 mgrs.
Cell count 270/mm³

Weight 51 kgrs.

10 months after treatment:

Blood: Tryps —
C.S.F.: Tryps —
Protein 18 mgrs.
Cell count 4,1/mm³

Weight 65 kgrs.

c) One case received two courses of injections with the interval of one week. The first course consisted of 4 injections and the second of three. All the injections were given every other day.

Case n.° 77/53 — Before treatment:

Blood: Tryps +
C.S.F.: Tryps +
Protein 30 mgrs.
Cell count 82/mm³

Weight 49,5 kgrs.

8 months after treatment:

Blood: Tryps —
C.S.F.: Tryps —
Protein 20 mgrs.
Cell count 5 /mm³

Weight 55 kgrs.

d) 2 patients received two courses of 2 injections, at one week's interval, given every third day.

Case n.º 52/53 — Before treatment:

Blood: Tryps ++
C.S.F.: Tryps ++
Protein 60 mgrs.
Cell count 138/mm³

Weight 42 kgrs.

9 months after treatment:

Blood: Tryps —
C.S.F.: Tryps —
Protein 35 mgrs.
Cell count 13/mm³

Weight 63 kgrs.

Case n.º 54/53 — Case in very bad condition.

Before treatment:

Blood: Tryps —
C.S.F.: Tryps +
Protein 62 mgrs.
Cell count 186/mm³

Weight 30 kgrs.

The patient died four days after the last injection of arsobal of hearth failure.

In this series of 5 patients treated with arsobal we have obtained the cure in 2 cases; in 2 cases the cell count and protein content decreased to near normal.

I E. *Cases treated first with antrypol or pentamidine + tryparsamide in small doses. After an interval of 15 to 30 days they received one course of 4 injections of arsobal on consecutive days* — Three cases showing very bad condition were treated in this way as we feared ill effects of the arsobal upon them. We tried to improve their general condition with the tryparsamide in small dosage.

Case n.° 73/53 — An african female, aged 20.

Before treatment:

Blood: Tryps ++
C.S.F.: Tryps +
Protein 30 mgrs.
Cell count 36/mm³
Urine: Ova of Sch. haematobium

Weight 43 kgrs.

She was treated first with antrypol (5,5 grs.) + tryparsamide (4,3 grs.). After a rest of 15 days we gave a course of 4 injections in consecutive days.

No feverish condition after the first injection. After beeing treated of her bilharzial infection was discharged.

9 months after treatment:

Blood: Tryps —
C.S.F.: Tryps —
Protein 25 mgrs.
Cell count 1,6/mm³

Weight 52 kgrs.

Case n.º 75/53 — An african female, aged 40.

Before treatment:

Blood: Tryps ++
C.S.F.: Tryps +++
Protein 40 mgrs.
Cell count 30/mm³
Urine: Albumin.

Weight 47 kgrs.

The patient received seven injections of pentamidine + Tryparsamide (6 grs.). After an interval of two weeks without treatment a course of 4 injections of arsobal was given. One injection on each consecutive day. No fever after the first injection of arsobal.

9 months after treatment:

Blood: Tryps —
C.S.F.: Tryps —
Protein 18 mgrs.
Cell count 2,3/mm³

Weight 53 kgrs.

Case n.º 88/53 — African male, aged about 25.

Before treatment:

Blood: Tryps ++
C.S.F.: Tryps +
Protein 35 mgrs.
Cell count 80/mm³
Urine: Ova of Sch. haematobium

Weight 59 kgrs.

Treated first with antrypol (5,5 grs.) + tryparsamide (7,80 grs). The patient had voluminous ascites and oedemas of the feet and legs.

After an interval of 30 days we started with a course of 4 injections of arsobal each given on every three days. No fever after the first injection.

The ascites disappeared and the patient was discharged 20 days after treatment.

*

According to C.S.F. examinations we can say that two out of these 3 patients got cured.

I F. *Cases treated twice with arsobal at intervals of several months* — 11 cases selected from those showing good general condition months after the arsobal treatment received a second one.

The first treatment consisted of: in 8 cases, one course of 4 injections on each of four consecutive days; in 3 cases, two courses of 4 daily injections at the interval of two weeks.

The second treatment for all the 11 cases consisted of a course of 4 injections given on consecutive days.

Hereunder follows a table registering the results.

New cases treated twice with arsobal

Case n.o	Before Arsobal				After Arsobal						
	Blood Tryps	C. S. F.			C. S. F. after Ist. treatment			Interval in months between Ist. and 2nd. treatment	C. S. F. after 2nd. treatment		
		Tryps	Protein	Cells	Protein	Cells	Period in months		Protein	Cells	Period in months
10-52	+	—	40	120	31-35	3-3	4-8	10	31	1	4
15-52	+	—	31	2	29-29	12-4	5-9	9	35	3	5
16-52	+	—	20	9	28-31	2-2	4-8	10	29	2	4
9-53	+	—	71	429	48-31	38-9	4-10	10	?	?	—
12-53	+	++	42	38	31-31	8-3	5-8	0	31	3	4
15-53	+	—	92	102	40-42	22-8	5-9	9	40	9	5
20-53	+	++	26	7	25-40	15-3	4-8	15	31	7	5
21-53	+	++	71	368	40-35	20-11	5-9	9	?	?	—
22-53	+	++	36	20	31-28	12-5	5-9	9	31	3	4
25-53	—	+	71	156	40-31	17-3	5-9	9	?	?	—
27-53	+	—	26	9	31-40	1-1	4-9	11	?	?	—

No serious accidents took place in these cases.

Comparing the results on the table we note a slight or no improvement at all of the C.S.F. composition after the second arsobal treatment.

*

We include in this major group of new nervous cases (Group I) three patients who died during treatment and after the second injection of arsobal.

Case n.º 63/53 — African female, aged about 37.

Before treatment:

Blood: Tryps ++
C.S.F.: Tryps ++
Protein 25 mgrs.
Cell count 22/mm³
Urine: Without albumin

Feverish reaction of 40º after the first injection. Next day the temperature was normal and the second injection given. Next day temperature 37º,5, inflammation of the buccal mucous membrane, restlessness. In the afternoon prostration, tremors. Death occurred at night.

Case n.º 65/53 — African male, aged about 17.

Before treatment:

Blood: Tryps ++
C.S.F.: Tryps +
Protein 25 mgrs.
Cell count 7/mm³

After the second injection of arsobal the patient had fever (40º,3), cephaloea and tremors. B.A.L. During night restlessness, aphasia. Next day in the morning the patient died.

Case n.° 79/53 — African male, aged about 50.

Before treatment:

Blood:	Tryps ++	
C.S.F.:	Tryps ++	
	Protein	50 mgrs.
	Cell count	195/mm³
Urine:	Albumin	

Some hours after the injection the patient had tremors, apathy and entered coma. He received 6 cc. of B.A.L. and died the following day.

*

This group of nervous cases newly diagnosed (Group I) numbers a total of 130. 50 of these patients, 38,4 % can be considered cured: both blood and C.S.F. were free from trypanosomes and repeated examination of same fluid revealed its normal composition several months after arsobal treatment.

In 31 cases the protein content and cell count of the cerebrospinal fluid came down considerably. In some of these patients the C.S.F. composition became nearly normal.

In 21 cases there are still serious disturbances of the C.S.F. several months after treatment.

19 patients died. We relate the cause of death in 11 of the fatal cases to toxic encephalopathy caused by arsobal. Of the 130 patients this means a percentage of 8,4 % of deaths due to the drug.

II Group — *Old nervous cases previously treated with Antrypol or Pentamidine + Tryparsamide.*

34 nervous cases, previously treated with one or more courses of antrypol or pentamidine + tryparsamide received arsobal at the dosage of 3,6 mgrs. per kgr. of body weight.

They were diagnosed from 1950 to 1952. Before the arsobal treatment all cases showed increased protein contents and cell counts of the C.S.F. Trypanosomes were found in 9 cases. One patient was treated with two courses of 4 dally injections at one week's interval. This case had trypanosomes, 151 cells per mm³ and 45 mgrs. of

Old cases treated with a single series of 4 injections of arsobal, one on each of four consecutive days

Case N.°	Before arsobal						After arsobal					
	Previous treatment	Weight (Kgrs)	Blood tryps	C. S. F.			Weight (Kgrs)	Blood tryps	C. S. F.			Period in months
				Tryps	Protein	Cells			Tryps	Protein	Cells	
2–50	Antryp.	45	+	+	30	56	49		–	25	3,4	11
	+ trypar-sam.						45	–	–	30	2,7	13
3–50	Pent. + trypars.	80	–	+ +	70	192	85	–	–	35	9	3
							80	–	–	28	7,5	8
10–50	Pent. + trypars.	54	–	–	35	54	64	–	–	25	2	11
							64	–	–	25	2	15
7–51	Pent. + trypars.	45	+	+ +	45	85	55	–	–	56	80	9
3–52	Antryp.	43	–	–	20	42	?	–	–	31	3	5
	+ trypar-sam.						56	–	–	25	1	9
							55	–	–	22	2	16
4–52	Pent. + trypars.	58	–	+	25	51	57	–	–	22	6,5	7
							57	–	–	25	1,6	20
5–52	Pent. + trypars.	64	–	+	40	55	56	–	–	18	1,6	8
9–52	Pent. + trypars.	49	–	+ +	40	38	50	–	–	30	6,8	5
							50	–	–	20	4,4	10
15–52	Pent. + trypars. (2 courses)	63	–	+	35	146	62	–	–	25	3,7	5
							60	–	–	25	1,5	14
20–52	Antryp. + trypars. (2 courses)	44	–	–	28	109	49	–	–	18	2,4	8
34–52	Antryp. + trypars.	32	–	–	30	59	37	–	–	22	2	13
44–52	Pent. + trypars.	44	–	–	40	119	45	–	–	20	3,8	4
							43	–	–	18	1,9	12
58–25	Antryp. + trypars.	53	–	–	72	421	58	–	–	32	4,2	3
							55	–	–	28	4,3	8
										25	1,7	17
5–53	Antryp. + trypars. (2 courses)	56	–	–	31	11	61	–	–	31	16	5

protein in the C.S.F. before treatment. 9 months later the cell count was 1,2/mm³ and had 20 mgrs. of protein. This patients is considered to be cured.

26 cases were treated with one course of 4 injections of arsobal.

The C.S.F. of 11 cases has not yet been examined but we know that they are alive and well.

One patient in poor condition before treatment died of toxic encephalopathy after the second injection of arsobal.

Of the remaining 14 cases, shown on the table, 9 (40,9 %) are considered to be cured; another case had a near normal C.S.F. several months after treatment.

The other 4 cases are more or less in the same condition as for C.S.F. composition.

Tests were negative for trypanosomes in all cases after treatment.

For a better understanding of trypansamide and later arsobal treatment we give the history of one case included on the table.

Case n.º 7/51 — African male, aged about 36. On admission to the hospital he complained of headache, pain in the legs. Fever, difficult walking, dysarthria. No oedemas. Pulse 76/m. Blood test negative for trypanosomes.

C.S.F. examination (17.4.951):

Tryps: ++
Protein: 60 mgrs.
Cells: 442

Treatment: antrypol (5 grs.) + tryparsamide (45 grs.).

After treatment the patient was called for periodical observation. The results of the C.S.F. examination and his weight were:

	Tryps	Protein	Cells	Weight
8- 8-951	—	48	53	69
13-12-951	—	40	50	72
17- 9-952	—	64	152	82
17- 2-953	—	48	40	79
12- 8-953	++	71	192	80

Tryparsamide (123 grs.) was given during this period of time.

In 12-8-53 the patient had a serious relapse. Tryps in the blood and C.S.F. oedema of the legs and feet, dysarthria, somnolence. Walking impossible.

The patient received 2 grs. of antrypol and we decided to give arsobal: an injection on each of four consecutive days.

The patient was discharged a month later without oedemas; normal walking and much improved general conditions.

Weight and C.S.F. examination after arsobal:

	Tryps	Protein	Cells	Weight
11-11-953	—	35	9	85
22- 4-953	—	26	7,5	80

Arsobal was given twice, at an average interval of nine months, to 7 cases. We selected these 7 cases from amongst those with ocular complications caused by tryparsamide. In nearly all these cases improvement of the general condition was noticed. As for their cerebrospinal fluid the protein and cells generally decreased after the first treatment; in the hope of even better results we administered the second course but it was disappointing as the C.S.F. remained more or less the same (see table).

Old cases treated twice with arsobal

Case N.°	Previous treatment	Before arsobal			After arsobal						
		C. S. F.			C. S. F. after Ist. treatment			Interval in months betœeen Ist. & 2nd treatments	C. S. F. after 2nd treatment		
		Tryps	Pro-tein	Cells	Pro-tein	Cells	Period months		Pro-tein	Cells	Period months
3–47	Antryp. + trypars. (4 courses)	—	64	113	31 31	2 3	4 8	9,5	30	3	4
4–50	Antryp. + trypars. (2 courses)	+	56	207	40 35	9 8	4 9	9	28	5	4
2–51	Antryp. + trypars. (2 courses)	–	90	429	64 64	7 6	4 9	9	56 14	4 4	5 9
10–51	Antryp. + trypars.	—	35	9	56 56	36 36	5 8	9	?	?	
15–51	Antryp + trypars.	—	31	13	40 31	23 5	4 8	9	31 35	11 11	4 8
6–52	Pent + trypars.	—	70	over 1.000	31 31	3 2	4 10	10	31	2	4
8–53	Antryp + trypars.	—	59	159	35 31	2 4	5 9	9	?	?	

III Group — *Early cases treated with arsobal.*

Only one early case was treated with arsobal.

Case n.° 53/53 — African male, aged about 35. At the date of diagnose:

Blood: Tryps +
C.S.F.: Tryps —
Protein 20 mgrs.
Cell count 3,1/mm^3

Treatment: Arsobal at the dosage of 3,6 mgrs. per kgr. of body weight. Two injections. The first injection gave rise to a feverish reaction. Next day the patient received the second injection.

Case discharged five days after treatment.

11 months later:

Blood: Tryps —
C.S.F.: Tryps —
Protein 25 mgrs.
Cell count 1,2/mm^3

The patient is excellent condition.

DISCUSSION

We have treated all in all 165 cases of *T. rhodesiense* sleeping sickness: 130 were nervous cases newly diagnosed and arsobal was given from the start; 34 were nervouscases as well but diagnosed one to three years before and already treated with antrypol or pentamidine + tryparsamide before receiving arsobal; lastly 1 early case treated with arsobal.

The arsobal was administered in different ways at the dosage of 3,6 mgrs. per kg. of body weight. In some cases we have repeated the treatment after several months.

As the great majority of the nervous cases are considered incurable when being treated with tryparsamid, the results obtained in our series of 165 cases speak for themselves.

We feel that the use of arsobal or Mel B is of great interest and importance in the treatment of rhodesian sleeping-sickness.

The least we can say is that arsobal is a great advance over tryparsamide.

As a rule the patients are natives and come too late under medical care, being already in the nervous stage of the disease. At this stage the classical treatment — antrypol or pentamidine + tryparsamide — is more or less useless: rare cures result.

It is true that tryparsamide in many cases greatly tones up the general condition but improvement is apparent and the disease runs its fatal course as an average in two years.

Results varied. When arsobal was given in one or in two courses of injections, following each other at an interval of 7 to 15 days, the results were good in both nervous newly diagnosed and previously treated cases.

We feel that it is of no use to repeat the arsobal within a year of the first treatment. Moreover we think that the patients once they did not respond to he first treatment, will not do so either with a second treatment within a year.

We have found helpful in patients in bad condition to administer a small dosage of tryparsamide before giving the arsobal. Although we only treated 3 cases in this manner, all three of them responded well to arsobal, probably because of the improvement in the general condition owing to tryparsamide. Further experiments are being carried out.

Various slight accidents occurred during the course of injections. The first injection always caused fever in all cases except in those who received tryparsamide immediately before arsobal.

The most frequent imediate reactions besides fever were pain at the site of the injections, nausea, vomiting and diarrhoea.

Serious toxic accidents were observed in 12 cases. One patient recovered and 11 died. In 7 cases death occurred the 4th or the 5th day after treatment. 4 patients died during treatment and after the second injection.

We have used batches n.° 102, 103 and 104 of the drug; in our opinion batch n.° 102 was less toxic than the others because encephalopathy occurred in 7 cases and slight accidents were more frequent using batches n.° 103 and 104.

In spite of the good results obtained arsobal has one big drawback: its toxicity, which oblige us to use it with great care and which almost prevents its general use in the bush.

We want to point out again that the use of arsobal should be confined only to hospitals.

We treated one early case only with arsobal.

The case got cured.

As we have the antrypol (or Bayer 205, or moranyl and the pentamidine (isethionate) with which the early cases are easily cured, the use of arsobal (or Mel B) seem superfluous in these cases even more so because of its dangerous character.

RESUMO

Descrevemos acima os resultados obtidos com o arsobal. Foram tratados três grupos num total de 165 casos.

Todos os doentes estiveram hospitalizados durante o tratamento que é o procedimento geral em Moçambique.

A dose do arsobal em todos os casos foi de 3,6 mgrs. por kg. do peso do corpo. O número e a sequência das injecções variou algumas vezes com o fim de experimentar a droga, outras vezes conforme as condições dos doentes.

Quase todos os casos foram acompanhados durante um período médio de 6 a 14 meses.

Conforme as nossas pesquisas o arsobal é de real valor no tratamento do *T. rhodesiense* da doença do sono no estado nervoso, mesmo nos casos em que o uso prévio da triparsamide tinha falhado.

Relatámos os casos fatais que se seguiram ao tratamento do arsobal.

Só um único caso foi tratado no princípio da doença. O doente curou-se.

Achamos que o arsobal é demasiado perigoso para ser aplicado no princípio da doença, visto que o antrypol e a pentamidine fàcilmente curam estes casos.

RÉSUMÉ

Nous avons décrite ci-dessus les résultats obtenus avec l'arsobal. Trois groupes dans un total de 165 cas ont été traités.

Tous les malades furent à l'hôpital pendant le traitement selon l'habitude en Mozambique.

La dose de l'arsobal en tous les cas a été de 3,6 mgr., pour 1 kilo du poids. Le nombre et la cure des injections a varié parfois à fin d'essayer la drogue et selon les conditions des malades.

Presque tous les cas ont été accompagnés pendant un période moyen de 6 à 14 mois.

En conformité avec nos observations l'arsobal est d'une valeur efficace dans le traitement du *T. rhodesiense* de la maladie du sommeil au stade nerveux, même dans les cas dont l'usage préalable de la tryparsamid n'avait pas réussie.

Nous avons mentioné les accidents mortels lesquels se sont suivis au traitement de l'arsobal.

Seulement un cas a été traité au commencement de la maladie. Le Malade s'est guéri.

Nous trouvons que l'arsobal est très dangereux pour être appliqué au commencement de la maladie vu que l'antrypol et la pentamidine (isethionate) guérissent facilement ces cas.

SUMMARY

We have described above the results obtained with arsobal. Three groups with a total of 165 cases were treated.

All patients were in hospital during treatment this being the procedure in Mozambique.

The dosage arsobal in all cases was one of 3,6 mgrs. per kgr. of body weight. The number and the sequence of the injections varied sometimes for the sake of experimenting with the drug, other times according to the condition of the patients.

Nearly all cases were followed up for an average period of 6 to 14 months.

According to our findings arsobal is of definite value in the treatment of *T. rhodesiense* sleeping sickness in the nervous stage, even in those cases where previous use of tryparsamide had failed.

We have mentioned the fatal accidents following the arsobal treatment.

Only one early case was treated. The patient got cured.

We think that arsobal is too dangerous to be used in the early stage of the disease since antrypol and pentamidine (isethionate) easily cure these cases.

Imprensa Portuguesa ★ Rua Formosa, 108-116 ★ Porto