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THE VALUE OF DRUGS COMMONLY USED IN
THE TREATMENT OF *T. RHODESIENSE* SLEEPING
SICKNESS

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THE VALUE OF DRUGS COMMONLY USED IN
THE TREATMENT OF *T. RHODESIENSE* SLEEPING
SICKNESS (*) ⁽¹⁾

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It was a resolution of the 5th meeting of the I.S.C.T.R., held in Pretoria in September 1954, that an appraisal of the trypanocidal drugs should be prepared by each of the countries presented, and handed in at the next meeting.

This paper records our observations in Mozambique and deals with the *T. rhodesiense* sleeping sickness from 1942 up to the end of 1955.

From 1942 to 1947, Bayer 205 (or antrypol) and tryparsamide were the only drugs in use.

In 1942 we started with pentamidine (isethionate) and in 1951 we treated a few cases with Mel B Friedheim (arsobal) for the first time.

Our observations refer to 1,346 cases in the various clinical stages.

The diagnosis was based, invariably, on the existence of trypan-

(*) Paper presented at the 6th meeting of the International Scientific Committee for Trypanosomiasis Research (I.S.C.T.R.) held in Salisbury in September 1956.

(¹) Entregue para publicação em 2-4-957.

nosomes either in the blood (the majority) or in the spinal fluid (in rare suspected cases where the blood was negative).

All cases were carefully classified by C.S.F. examination before the commencement of treatment.

The tables included are similar to those in Neujean's paper discussed in the last meeting. They give the time factor, presence or absence of trypanosomes, changes in spinal fluid composition and data on mortality.

After treatment the general procedure was to examine the patients again the 2nd and the 6th month and from then onwards every three months.

Cases treated with Bayer 205 or pentamidine, showing trypanosomes or C.S.F. pathological changes after two months, were subjected to another drug.

Cases still showing spinal fluid changes, six months after treatment with tryparsamide, were either given the same drug or arsobal.

As a rise in the leukocytosis and albumin contents is often observed after arsobal, we had to change the general procedure, as described above, in cases treated with this drug: the first examination taking place the 6th month after treatment.

Now we are going to analyse the results obtained with each drug.

BAYER 205 (OR ANTRYPOL)

Treatment of early cases (36)

The majority of these cases was treated with antrypol (31 cases). Bayer 205 was given to only 5.

The spinal fluid was normal in 22 cases. The other 14 cases showed normal protein contents and a slight increase of cells but in spite of this they were considered early cases. (See Table I).

The dosage of antrypol or Bayer was 15 to 20 mgrs. per Kgr. of body weight, per injection. Usually weekly injections.

In order to check the tolerance of the patients to the drug, the first injection was half the dosage later given, but as a rule it was

well tolerated. However, in some cases treatment had to be discontinued owing to the appearance of albuminuria.

There were regular complaints of palmar and plantar pruritus or even pain on the days of injection.

Favourable results — Of these cases, 9 can be considered to be cured, all having normal spinal fluid before treatment. 8 cases are under observation for too short a time.

Relapses — In one case with a cell count of $5/\text{mm}^3$ before treatment, a parasitological relapse (in blood) was observed nine months after treatment. The spinal fluid at the time was normal in view of which a reinfection is presumed.

One patient with normal C.S.F. before treatment showed pathological changes, including increased protein, 9 months after treatment.

The same happened in 2 cases with cell counts of 5 and 8 before the treatment.

Deaths — In one case, with normal spinal fluid, the disease took an acute course and death occurred during treatment.

One case died of amoebiasis in the hospital.

Another case having a cell count of 5 per mm^3 , died three months after treatment.

It was not possible to ascertain the exact cause of death in 4 cases as they died in their villages.

Use of antrypol in nervous cases (737)

In these cases antrypol was used only together with tryparsamide. As a rule the dosage was the same as in the early cases.

We would begin treatment with a course of antrypol, or Bayer 205, followed by the administration of tryparsamide (see Table III).

In a few cases we injected both drugs at the same time, mixing them in the syringe at the proportion of 0,5 grs. of antrypol to 1 or 1,5 gr. of tryparsamide.

DIAMIDINES

Treatment of early cases (46)

Pentamidine (isethionate) was used in 46 early cases. Some showed cell counts varying from 4 to 9 per mm^3 , but normal protein in the spinal fluid (see Table II).

The general condition of these cases was good and by questioning we gained the impression that the infection was recent.

The dose per daily intramuscular injection was 3 to 4 mgr. per Kgr. of body weight.

Pentamidine is well tolerated provided the patient is lying down when the injection is given and remain in same position for 15 minutes.

Usually the patients complained of pain where they were injected. Some cases had profuse perspiration, vomiting and felt indisposed soon after the injection.

Favourable results — Of 46 cases, 14 can be considered to be cured, including 4 in which the spinal fluid was not completely normal before treatment. 13 cases were under observation for too short a time.

Two european cases are included in Table II; one had been treated more than four years ago and the other more than two years ago.

Relapses — A parasitological relapse was observed in one case, nine months after treatment. Trypanosomes were found in the blood and also in C.S.F., the composition of which had greatly changed; this case had 5 cells per mm^3 before treatment.

Three C.S.F. relapses occurred: 2 cases had a normal spinal fluid and 1 case had 9 cells per mm^3 before pentamidine was given.

Deaths — One patient suffering also from TB died during the treatment. Other case in bad condition died in hospital soon after treatment. Both had normal spinal fluid.

We could not establish the exact cause of death in 5 cases as

they died in their villages. They had been examined the 2nd and 6th month and had no signs of disease.

Use of pentamidine in nervous cases (222)

As in the case of antrypol, pentamidine was only given as mere trypanocidal together with tryparsamide, the pentamidine preceding the other drug.

Dose given was the same as in early cases.

TRYPARSAMIDE

Treatment of nervous cases

In Mozambique, tryparsamide was the drug most widely used in the treatment of sleeping sickness but its use was limited to nervous cases and then in combination with Bayer 205 (or antrypol) or pentamidine (see Table III and IV).

The usual dose of tryparsamide was 0,04 grs. per kilo of body weight but we also used bigger doses up to 0,06 grs.

The number of injections varied from a minimum of ten to a maximum of twenty five. Weekly injections as a rule.

Where necessary, the tryparsamide was repeated: three injections of antrypol or pentamidine would be given.

The intervals between courses of injections varied from case to case but in general they were longer than three months.

In some cases the drug was given continuously, under the control of lumbar puncture, until the spinal fluid would become normal.

Tryparsamide is well tolerated.

We had optical complications and in some cases blindness followed. At one time the incidence of optical neuritis was high owing to the inferior quality of tryparsamide used. Naturally when this was discovered we destroyed the stock and that particular make was not used again.

In 7 cases already considered hopeless toxic accidents of the drug were perhaps responsible for earlier death.

Treatment of nervous cases with Bayer 205 or antrypol + Tryparsamide (737 cases)

Favourable results — Of all these cases, 33 were alive and well after more than 4 years. It was not possible to follow up these 33 cases for the next two years after treatment. They were considered to be cured as well as 127 others. (See Table III).

Relapses — We have observed numerous parasitological relapses besides the 33 registered in Table III, in cases which eventually died in the hospitals.

The relapsed cases continued treatment either with tryparsamide or arsobal.

It is difficult to say if a highly modified fluid during tryparsamide administration or at intervals between courses of injections, corresponds to a relapse. This, in patients whose C.S.F. does not show tendency to become normal.

In many cases we have observed considerable fluctuation of leukocytosis during and after treatment.

This is the reason why fluid relapses are not mentioned in Tables III and IV.

Deaths — 219 deaths occurred in the hospitals. Cause of death was either trypanosomiasis or trypanosomiasis in association with other diseases or toxic accidents caused by tryparsamide (rare).

94 patients died in their villages and the cause of death could not be ascertained, but we presume that a fair number of cases were victims of sleeping sickness, as they still showed signs of the disease when they were discharged.

Treatment of nervous cases with pentamidine + tryparsamide (222 cases)

In this series of cases we used, as a rule, the dose of tryparsamide of 0.04 grs. per kilo of body weight. We had a lesser percentage of optic neuritis than amongst the cases treated with antrypol + tryparsamide, because of the better quality of the drug.

Favourable results — Of 222 cases, 11 were alive after more than 4 years. They were considered to be cured as well as 23 others (see Table IV).

Relapses — 10 parasitological relapses were observed with the trypanosomes usually in the spinal fluid. Besides these relapses, mentioned in the table, 27 others occurred in cases which later died in the hospitals.

Deaths — 28 deaths occurred in the hospitals and 44 in the villages. Although we ignore the cause of death, we surmise that some cases died of trypanosomiasis, because they still showed pathological modification of the fluid when they were discharged.

MEL B (ARSOBAL)

New nervous cases treated with arsobal (272 cases)

We used arsobal in the treatment of 272 nervous cases where no other drugs had been administered (see Table V).

The table is sufficiently clear as to the doses given. In general, the injections of one course were given either daily (in the majority of cases) or every second or every third day.

The procedure was indicated especially by the general condition of the patients.

When the course of injections had to be repeated, the interval was one or two weeks.

Sometimes we repeated the treatment after some months.

In previous communications handed in to meetings of the Committee (I.S.C.T.R. (52) 13 and I.S.C.T.R. (54) 4) we referred to the different ways of administration of the drug.

Table V includes cases already mentioned and others treated from then on.

As to accidents caused by arsobal they have been described; they are either benign or extremely grave, such as the toxic encephalopathy.

It is impossible to foresee the appearance of convulsions quickly followed by coma and death.

In our series the major incidence of encephalopathy occurred in 1951 and 1952 in hopeless cases, in very bad condition, where tryparsamide was of no avail.

From then on we have noticed that this serious complication is more frequent in cases showing greatly modified spinal fluid.

Favourable results — Of 272 cases, 65 are considered to be cured. 79 cases were under observation for too short a time to enable us to say whether they will eventually be cured.

Relapses — One parasitological relapse (in the fluid) was observed one year after treatment.

As for the fluid relapses we had observed often a considerable rise of cells and albumin following the administration of arsobal. This reaction lasts sometimes several months and for this reason we have avoided the lumbar puncture before the 6th month.

The definite C.S.F. relapses were based upon examinations taken 6 months after treatment.

Deaths — 44 deaths occurred: in 24 the cause was encephalopathy; 7 patients died of trypanosomiasis; the exact cause in 13 is unknown.

*New nervous cases treated with trypa samide + arsobal
(21 cases)*

We have treated 21 cases which were in a bad condition and with one exception all had increased albumin in the C.S.F.; we used a small dose of tryparsamide and after an interval of 2 to 4 weeks we gave arsobal (see Table VI).

Tryparsamide, acting as a tonic, improved the condition of the patients.

Results obtained were extremely favourable even more so in view of the poor condition of the cases.

No relapses were observed in this series.

No cases of encephalopathy in these patients. Only one death occurred out of the hospital whose cause is not known.

The use of arsobal in nervous cases previously treated with tryparsamide (34 cases)

None of these 34 cases have shown favourable evolution towards cure after they have been treated with tryparsamide.

Favourable results — Of 34 cases, 3 are considered to be cured. Other 11 cases were not long enough under observation to be able to say if they will recover (see Table VII).

Relapses — 2 parasitological relapses were observed (spinal fluid) one year after treatment plus 2 definite fluid relapses.

Deaths — Toxic encephalopathy caused three deaths.

Treatment of early cases with arsobal (12 cases)

We have given arsobal to 8 cases with normal spinal fluid and to further 4 cases which showed a slight leukocytosis.

The same criterion was applied to cases treated with antrypol or pentamidine. The 4 mentioned patients were in good condition and presumably had been recently infected.

Results — They couldn't be more favourable. 4 cases got cured.

Only one death from causes foreign to trypanosomiasis. No relapses.

DISCUSSION AND CONCLUSIONS

1. Our series of cases includes less early than nervous cases. As african patients are not anxious to find medical help, on their own account, this makes it necessary for us to look for them. Consequently, when diagnosed the majority are already nervous cases.

There were 94 early cases (Tables I, II and VIII), which undoubtedly included some borderline cases, and 1.252 nervous cases.

2. As for the early are concerned, Mel B Friedheim (arsobal) gave 100 % favourable results in which 8 cures are included (66,6 %) (¹).

No deaths due to trypanosomiasis. No relapses were observed (see Table VIII).

Obviously the number treated with arsobal was too small to draw any definite conclusions. All the same, results were much better than those obtained with Bayer 205 (or antrypol) or pentamidine.

3. With antrypol, in cases of category I, we had 63,6 % favourable results among which we can count 9 cures (40,9 %). In same category we had 4,5 % spinal fluid relapses but no parasitological relapses. One death due to trypanosomiasis among 22 cases (4,5 %).

In cases of category IB (borderline cases?) we had one parasitological relapse (7,1 %) and two fluid relapses (14,2 %). One death occurred (7,1 %) due to trypanosomiasis (see Table I).

4. With pentamidine, in category I, favourable results were 55,1 %, among which 10 cures (34,1 %). Two definite fluid relapses (6,8 %) and two deaths due to trypanosomiasis.

In category IB favourable results 29,4 %, among which 4 cures (23,5 %). One parasitological relapse (5,8 %) and one fluid relapse were observed.

5. Looking at the results of tryparsamide our attention is drawn to the high rate of mortality.

In cases treated with antrypol + tryparsamide 29,7 % of deaths were due to trypanosomiasis and also to toxic accidents (rare).

We must stress the point that it is highly probable that sleeping sickness was responsible for further deaths amongst those cases which died out of the hospitals (94). Parasitological relapses were frequent.

(¹) The percentage for cure, in early cases, was calculated on the number of cases which did not show signs of disease for 1 to 2 years and over. The same percentage, in nervous cases, was calculated on the number of cases not showing signs of disease for 2 years and over.

The percentage for favourable results, in early cases, was calculated on number of cases showing good evolution from the 6th month onwards and the same percentage, in nervous cases, on the number of cases showing good evolution from 1 year onwards.

Favourable results obtained with antrypol + tryparsamide were 27,8 %, among which are 160 cases considered to be cured (21,7 %).

As shown in table III results were considerably better in cases of category II.

Favourable results obtained with pentamidine + tryparsamide in nervous cases, were 26,1 % among which 34 considered cured (15,3 %). Frequent parasitological relapses were observed. The rate of death due to trypanosomiasis was 12,6 % but as in the preceding cases sleeping sickness was probably the cause of further deaths still.

Parasitological relapses were frequent (see Table IV).

For many years tryparsamide was the one and only drug at our disposal to treat the nervous cases. Its trypanocidal action is poor as compared to arsobal, antrypol and pentamidine. Its use in the treatment of *T. rhodesiense* sleeping sickness is considerably less favourable than in gambian trypanosomiasis.

Tryparsamide quickly improves the general condition of cases and in a short time the clinical symptoms disappear, but all this is only deceptive. Yet tryparsamide has been extremely useful as it alters favourably the pathological spinal fluid, especially when the protein content is normal, and it even effects cure in some patients.

5. In nervous cases where only arsobal was used, favourable results were 46,3 %, including 65 cures (27,5 %). Parasitological relapses were negligible. Deaths due to arsenical encephalopathy 8,8 % and to trypanosomiasis 2,5 % (see Table V).

6. We used tryparsamide + arsobal in 21 cases (Table VI). Favourable results 42,8 %. No relapses, no deaths of trypanosomiasis. No encephalopathy.

7. Arsobal was used in 34 cases previously treated with tryparsamide. Favourable results (38,2 %) are very impressive as patients had not improved at all with tryparsamide. These results include 3 cures (8,8 %).

Two parasitological relapses and two definite fluid relapses (5,8 %). The only deaths were caused by encephalopathy (8,8 %).

RESUMO

Dos 1.346 doentes, 293 são considerados curados. O arsobal, tanto no princípio como nos casos nervosos, deu-nos melhores e mais consistentes resultados do que qualquer outra droga.

O número de recaídas foi diminuto e tivemos uma média muito baixa de mortalidade devido ao tripanossoma, entre os 339 casos tratados com a droga.

O único inconveniente do arsobal é a sua alta toxicidade causando às vezes encefalopatias. Em 339 casos, esta grave complicação foi causadora de 27 mortes, cuja percentagem (6,9 %) foi mais alta que a média de mortalidade devido ao tripanossoma.

Quando se usa arsobal temos que nos lembrar sempre disto e observar os doentes cuidadosamente para actuarmos imediatamente quando necessário.

RÉSUMÉ

Des 1.346 malades, 293 se sont guéris. L'arsobal, tantôt au commencement que dans des cas nouveaux, nous a donné des meilleurs et plus consistants résultats, que autre drogue quelconque.

Le nombre de recidives a été exigü et nous avons en une moyenne basse de mortalité dû au trypanosome, chez les 339 cas traités avec la drogue.

Le seul inconvénient de l'arsobal est sa haute toxicité qui quelquefois cause les encéphalopathies. Chez 339 cas, cette grave complication a été la cause de 27 décès, dont le pourcentage (6,9 %), a été plus élevé que la moyenne mortalité dû au trypanosome.

Quand on emploie l'arsobal, nous avons besoin de nous rappeler toujours de sa haute toxicité et, dû à cela, observer les malades soigneusement, pour actuer immédiatement lorsqu'il soit nécessaire.

SUMMARY

Of 1.346 patients, 293 are considered to be cured. Arsobal, both in early and nervous cases, gave us better and more consistent results than any other drug.

The number of relapses was negligible and we had a very low rate of mortality due to trypanosomiasis, among the 339 cases treated with the drug.

The only handicap of arsobal is its high toxicity causing sometimes encephalopathy. In 339 cases this grave complication was responsible for 27 deaths which percentage (6,9 %) was higher than the rate of mortality due to trypanosomiasis.

When using arsobal we always have to keep this in mind and watch the patients under treatment, carefully, in order to act immediately when necessary.

TABLE I
Treatment of early cases with antrypol
Results obtained — (Figures show number of cases)

Classification of cases (1)	Dose given (2)	Favourable evolution with no signs of disease after treatment for :			No signs for less than 6 months	Relapses (3)			Deaths (4)	Total	
		2 years and over	1 to 2 years	6 to 12 months		Parasitological	C. S. F.			Per series	General
							Definite	Doubtful			
I	3 grs.	—	1	—	—	—	—	—	—	1	—
	4 grs.	—	—	1	—	—	—	—	1	2	—
	6 grs.	3	2	1	2	—	1	—	2	10	—
	6.5 grs.	—	—	1	—	—	—	—	—	2	—
	7.5 grs.	1	—	2	—	—	—	—	—	3	—
	8.5 grs.	1	—	—	1	—	—	—	—	2	—
	9.5 grs.	—	—	—	1	—	—	—	—	1	—
	10 grs.	1	—	—	—	—	—	—	—	1	22
	3 grs.	—	—	—	—	—	1	—	—	1	—
	4 grs.	—	—	—	—	—	—	—	1	1	—
IB	4.5 grs.	—	—	—	—	—	—	—	1	1	—
	5 grs.	—	—	—	1	—	—	—	1	1	—
	7.5 grs.	—	—	—	2	—	—	—	2	6	—
	8 grs.	—	—	—	1	1	—	—	—	2	—
	10 grs.	—	—	—	—	—	2	—	—	2	—
	Total of results . . .	6	3	5	8	1	3	3	7	—	36

(1) The cases were classified according to the picture given by an examination of the spinal fluid, before treatment:

I — Cases with less than 3 cells per mm³ and a maximum of 0.25 grs. %/00 of protein.

IB — Included: 9 cases with 3 cells per mm³; 1 case with 6 cells per mm³; 4 cases with 8 cells per mm³. In all these cases the maximum protein contents was 0.25 grs. %/00.

(2) Usual dose per injection 1 to 1.5 grs., in adults.

(3) Treatment continued with tryparsamide in 6 cases and with arsobal in 1 case.

(4) Trypanosomiasis was the cause of death in 2 cases; 1 patient died of amoebiasis; 4 patients died out of the hospitals in their villages.

TABLE II

Treatment of early cases with diamidine (pentamidine isethionate)

Results obtained — (Figures refer number of cases)

Classification of cases (1)	Dose given (2)	Favourable evolution with no signs of disease after treatment for :			No signs for less than 6 months	Relapses (3)			Deaths (4)	Total	
		2 years and over	1 to 2 years	6 to 12 months		Parasitological	C. S. F.			Per series	General
							Definite	Doubtful			
I	1x 26 + 7x 52 mgrs.	—	—	—	1	—	—	—	—	1	—
	6x 100 »	—	—	—	—	—	—	—	1	1	—
	6x 140 »	—	—	1	—	—	—	—	—	1	—
	5x 200 »	—	—	—	1	—	—	—	—	1	—
	7x 150 »	1	1	—	1	—	—	—	—	3	—
	10x 120 »	1	—	—	—	—	—	—	—	1	—
	1x 100 + 6x 200 »	1	2	1	2	—	—	1	1	8	—
	7x 200 »	—	1	—	—	—	1	—	—	4	—
	1x 100 + 7x 200 »	1	—	1	—	—	—	—	1	3	—
	10x 175 »	—	—	—	—	—	1	—	—	1	—
	10x 190 »	—	—	2	—	—	—	—	—	2	—
	1x 100 + 9x 200 »	1	1	1	—	—	—	—	—	2	—
	10x 200 »	—	—	—	—	—	—	—	—	1	29
IB	1x 60 + 7x 120 mgrs.	1	—	—	—	—	—	—	—	1	—
	6x 150 »	—	—	—	—	1	—	—	—	1	—
	6x 160 »	—	—	—	—	—	1	—	—	1	—
	10x 170 »	—	—	—	1	—	—	—	—	1	—
	10x 187 »	—	—	—	1	—	—	—	—	1	—
	2x 200 »	—	—	—	—	—	—	—	1	1	—
	6x 200 »	—	—	—	2	—	—	—	1	3	—
	1x 100 + 7x 200 »	—	1	1	2	—	—	—	—	4	—
	2x 100 + 7x 200 »	—	—	—	—	—	—	—	1	1	—
	9x 200 »	—	1	—	—	—	—	—	—	1	—
	10x 200 »	—	1	—	—	—	—	—	—	1	—
	1x 100 + 10x 200 »	—	—	—	—	—	—	—	1	1	—
	Total of results.		6	8	7	13	1	3	1	7	—

(1) Category I — Cases with less than 3 celles per mm³ and a maximum of 0.25 grs. 0/100 of protein.Category IB — Includes: 1 case with 4 celles; 7 cases with 5 celles; 1 case with 6 celles; 6 cases with 8 celles; 2 cases with 9 celles per mm³ Maximum protein contents 0.25 0/100.

(2) Dosage per injection, 3 to 4 mgrs. per Kg. of body weight.

(3) Treatment continued with arsobal in 3 cases and with trypanamide in 2 cases.

(4) Trypanosomiasis was the cause of death in 2 cases, of which one was also a TB case. 5 patients died out of the hospitals.

TABLE III

Nervous cases treated with antrypol + trypanamide (2)
Results obtained — (Figures refer number of cases)

Classification of cases (1)	Trypanamide given (3)	Favourable evolution with no signs of disease after treatment for:			No signs for less than 6 months	Cases not followed up properly but still alive after 4 years	Parasitological relapses	Deaths (4)	Per series
		2 years and over	1 to 2 years	6 to 12 months					
II	1 course of less than 20 grs. . . .	—	—	1	—	—	—	5	6
	1 » » 20 to 40 grs. . . .	—	15	5	5	3	3	19	50
	2 courses of 24 to 40 grs. . . .	1	3	13	1	1	2	5	26
	3 » » 24 » 40 grs. . . .	—	2	5	—	—	—	1	8
	2 » » 40 » 60 grs. . . .	—	1	4	1	—	—	1	7
	3 » » 40 » 60 grs. . . .	—	1	—	1	—	—	2	7
	1 course of 100 grs. . . .	80	6	2	—	2	3	53	143
	2 courses of 100 grs. . . .	—	—	—	4	—	3	10	17
	3 » » 100 grs. . . .	—	—	—	—	—	2	3	5
	4 » » 100 grs. . . .	—	—	—	—	—	—	1	1
	1 course of less than 20 grs. . . .	—	—	—	—	—	—	5	5
III	2 courses of less than 20 grs. . . .	—	1	2	—	—	—	2	5
	1 course of 24 to 40 grs. . . .	—	—	8	27	3	1	30	69
	2 courses of 24 to 40 grs. . . .	—	—	22	37	2	5	18	84
	3 » » 24 » 40 grs. . . .	—	4	—	10	6	1	9	30
	4 » » 24 » 40 grs. . . .	—	6	—	10	1	—	6	23
	1 course of 100 grs. . . .	31	1	—	—	4	4	70	110
	2 courses of 100 grs. . . .	3	—	—	—	2	8	14	27
	3 » » 100 grs. . . .	1	—	—	—	2	—	6	9
	4 » » 100 grs. . . .	—	—	—	—	—	1	—	1
	1 course of less than 20 grs. . . .	—	—	—	—	—	—	6	6
	1 » » 24 to 40 grs. . . .	—	1	—	9	—	1	6	27
IV	2 courses of 24 to 40 grs. . . .	—	3	2	5	1	1	16	27
	3 » » 24 » 40 grs. . . .	—	—	1	3	2	—	6	18
	4 » » 24 » 40 grs. . . .	—	1	3	—	—	—	1	7
	1 course of 40 to 60 grs. . . .	1	—	—	—	—	—	—	4
	2 courses of 40 to 60 grs. . . .	—	—	—	—	—	2	—	1
	1 course of 100 grs. . . .	6	—	—	—	3	1	20	30
	2 courses of 100 grs. . . .	4	—	—	—	1	—	2	7
	3 » » 100 grs. . . .	—	—	—	—	—	—	1	1
	Total of results	127	45	68	113	33	38	313	—

(1) Cases were classified according to the picture given by the examination of the spinal fluid before treatment:

II — Cases with more than 3 cells per mm³ and a maximum of 0.25 grs % of protein.

III — Cases with less than 100 cells per mm³ and more than 0.25 grs of protein.

IV — Cases with more than 100 cells per mm³ and more than 0.25 grs of protein.

TABLE IV
Nervous cases treated with pentamidine + tryparsamide (2)
Results obtained — (Figures refer number of cases)

Classificação of cases (1)	Tryparsamide given (3)	Favourable evolution with no signs of disease after treatment for :			No signs for less than 6 months	Cases not followed up properly but still alive after 4 years	Parasitological relapses	Deaths (4)	Total	
		2 years and over	1 to 2 years	6 to 12 months					Per series	General
II	1 course of less than 20 grs. . .	—	—	1	1	—	—	1	3	—
	1 » » 24 to 40 grs. . .	13	4	51	9	—	4	10	55	—
	2 courses of 24 to 40 grs. . .	2	7	5	4	—	—	3	21	—
	3 » » 24 » 40 grs. . .	—	—	—	—	—	1	1	2	—
III	4 » » 24 » 40 grs. . .	—	—	—	—	—	1	1	2	83
	1 course of less than 10 grs. . .	—	1	1	—	—	—	1	3	—
	1 » » » 20 grs. . .	—	—	2	—	—	—	—	2	—
	1 » » » 24 to 40 grs. . .	1	4	4	6	8	—	14	37	—
IV	2 courses of 24 to 40 grs. . .	1	2	5	1	2	2	4	17	—
	3 » » 24 » 40 grs. . .	—	—	—	2	—	—	2	4	—
	4 » » » 24 » 40 grs. . .	3	1	2	8	—	—	4	18	—
	5 » » » 24 » 40 grs. . .	—	1	—	1	—	—	1	3	84
	1 course of less than 10 grs. . .	—	—	—	—	—	—	1	1	—
	1 » » » 20 grs. . .	2	—	—	3	—	—	8	13	—
	1 » » » 24 to 40 grs. . .	—	2	3	1	—	1	5	12	—
	2 courses of 24 to 40 grs. . .	—	1	—	2	—	1	8	12	—
	3 » » 24 » 40 grs. . .	1	1	—	1	—	—	3	6	—
	4 » » » 24 » 40 grs. . .	—	—	—	2	1	—	4	7	—
	1 course of 40 » 60 grs. . .	—	—	1	2	—	—	1	4	55
	Total of results . . .	23	24	39	43	11	10	72	—	222

- (1) Classification of cases as in Table III.
 (2) Dosage of pentamidine as in Table II.
 (3) Dosage of tryparsamide, per injection, was an average of 0.04 grs./kg. of body weight.
 (4) 44 patients died out of the hospitals in their villages.

TABLE V
New nervous cases treated with arsobal
Results obtained — (Figures refer number of cases)

Classification of cases (1)	Dose given	Favourable evolution with no signs of disease after treatment for :			No signs for less than 6 months	Parasitological	Relapses		Deaths (2)	Per series
		2 years and over	1 to 2 years	6 to 12 months			C. S. F.			
							Definite	Doubtful		
II	3x3,6 mgr./Kgr.	—	2	2	5	—	—	—	4	13
	4x3,6 mgr./Kgr.	25	14	8	1	—	2	—	5	55
	2x3x3,6 mgr./Kgr.	—	1	2	—	—	—	—	—	3
	2x4x3,6 mgr./Kgr.	2	—	—	—	—	1	—	—	3
	3x4x3,6 mgr./Kgr.	—	—	—	—	—	—	1	—	1
III	3x3,6 mgr./Kgr.	—	6	4	3	—	—	—	9	22
	4x3,6 mgr./Kgr.	13	13	4	10	—	—	—	11	51
	5x3,6 mgr./Kgr.	—	—	—	2	—	—	—	—	2
	2x3x3,6 mgr./Kgr.	2	7	8	11	—	—	—	1	29
	2x4x3,6 mgr./Kgr.	11	7	—	—	—	1	4	1	24
IV	2x4x3,6 mgr./Kgr.	—	—	—	—	—	—	1	—	2
	3x3,6 mgr./Kgr.	—	—	—	—	—	—	—	2	2
	4x3,6 mgr./Kgr.	3	3	3	6	—	1	—	9	25
	2x3x3,6 mgr./Kgr.	—	—	—	2	—	—	—	—	2
	2x4x3,6 mgr./Kgr.	9	3	—	—	—	—	4	1	17
Total of results . . .	3x3x3,6 mgr./Kgr.	—	4	5	3	—	—	—	1	13
	3x4x3,6 mgr./Kgr.	—	—	—	—	—	1	3	—	5
	4x4x3,6 mgr./Kgr.	—	1	—	—	—	—	2	—	3
	Total of results . . .	65	61	36	43	1	7	15	44	—

- (1) Classification of cases as in Table III.
 (2) 24 patients died of encephalopathy: 5 cases belonging to category II, 13 cases to category III and 6 cases to category IV. 7 deaths caused by 13 patients died out of the hospitals; cause of death not exactly known.

TABLE VI
Treatment of new nervous cases with trypanamide + arsobal (1)
Results obtained — (Figures refer number of cases)

Classification of cases (2)	Arsobal given	Favourable evolution with no signs of disease after treatment for :			No signs for less than 6 months	Relapses			Deaths (3)	Total	
		2 years and over	1 to 2 years	6 to 12 months		Parasitological	C. S. F.			Per series	General
							Definite	Doubtful			
II	4x3,6 mgr./Kgr.	—	1	—	—	—	—	—	—	1	1
		—	—	—	—	—	—	—	—	—	—
		—	2	1	—	—	—	—	—	—	—
		—	1	4	—	—	—	—	1	—	—
III	{ 3x3,6 mgr./Kgr. 4x3,6 mgr./Kgr. 2x3x3,6 mgr./Kgr. 2x4x3,6 mgr./Kgr.	—	1	—	—	—	—	—	—	1	12
		—	—	—	—	—	—	—	—	—	—
		—	3	—	—	—	—	—	—	—	—
		—	—	—	—	—	—	—	—	—	—
IV	{ 4x3,6 mgr./Kgr. 2x3x3,6 mgr./Kgr. 3x3x3,6 mgr./Kgr.	—	1	—	—	—	—	—	—	3	—
		—	—	—	—	—	—	—	—	3	—
Total of results . . .		—	9	5	6	—	—	—	1	—	21

- (1) The dose of trypanamide was always small, an average of 4 injections (0,04 grs. per Kgr. of body weight). Interval between trypanamide and arsobal, two to four weeks.
- (2) The same classification as in table III.
- (3) The patient died out of the hospital. Unknown cause.

TABLE VII

The use of arsobal in old nervous cases previously treated with triparasamide (1)

Result obtained — (Figures refer number of cases)

Classification of cases (1)	Arsobal given	Favourable evolution with no signs o disease after treatment for :			No signs for less than 6 months	Relapses		Deaths (3)	To Per series	
		2 years and over	1 to 2 years	6 to 12 months		Parasitological	C. S. F.			
							Definite			Doubtful
II	$\left\{ \begin{array}{l} 1x3,6 \text{ mgr./Kgr.} \\ 4x3,6 \text{ mgr./Kgr.} \end{array} \right.$	—	—	—	—	—	—	1	1	
		—	4	4	2	—	—	—	10	
III	$\left\{ \begin{array}{l} 4x3,6 \text{ mgr./Kgr.} \\ 2x4x3,6 \text{ mgr./Kgr.} \\ 3x4x3,6 \text{ mgr./Kgr.} \end{array} \right.$	1	4	—	5	—	1	—	12	
		—	—	—	—	—	—	1	1	
		—	—	—	—	—	1	—	3	
IV	$\left\{ \begin{array}{l} 4x3,6 \text{ mgr./Kgr.} \\ 2x4x3,6 \text{ mgr./Kgr.} \\ 3x4x3,6 \text{ mgr./Kgr.} \end{array} \right.$	1	—	—	—	1	—	—	2	
		—	2	—	—	—	—	1	3	
		1	—	—	—	1	—	—	2	
Total of results . . .		3	10	4	7	2	2	3	—	

(1) Doses of triparasamide as in table III (1 to 3 courses of injections).

(2) The same classification as in table III.

(3) Deaths caused by arsenical encephalopathy.

TABLE VIII
Treatment of early cases with arsobal
Results obtained — (Figures refer number of cases)

Classification of cases (1)	Arsobal given	Favourable evolution with no signs of disease after treatment for :					No signs for less than 6 months	Relapses			Deaths (2)	Total	
		2 years and over	1 to 2 years	6 to 12 months	Parasitological	C. S. F.		Per series	General				
						Definite				Doubtful			
I	1x3,6 mgr./Kgr. 2x3,6 mgr./Kgr. 3x3,6 mgr./Kgr.	1	2	1	—	—	—	—	—	4	—		
		2	—	—	—	—	—	—	—	2	—		
		1	—	—	—	—	—	—	1	2	8		
IB	2x3,6 mgr./Kgr. 3x3,6 mgr./Kgr.	—	1	—	—	—	—	—	—	1	—		
		—	1	2	—	—	—	—	—	3	4		
		4	4	3	—	—	—	—	—	—	12		
Total of results													

- (1) Classification according to the picture given by an examination of the spinal fluid before treatment:
- 1 — Cases with less than 3 celles per mm³ and a maximum of 0,25 grs. 0/00 of protein.
- IB — Included: 2 cases with 6 celles per mm³ and 2 cases with 8 celles per mm³. In all these 4 cases the maximum of protein was 0,25 grs. 0/00.
- (2) This patient died in his village of snake-bite poisoning eight months after the treatment.

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