TABLE 14.

Infection.	Treatment.	Animal.	Apparent Permanent Recovery.	Per cent.	Temporary Recovery.	Per cent.	Died.	Per cent.	Total No. of Animals Treated.	Remarks.
T. congolense....	(I) Tartar emetic alone....	Ox.....	23 (21, 1, 1, —)	37·1	29 (11, 7[1], 9, 2)	46·8	10 (5, —, 3, 2)	16·1	62 (37, 8, 13[2], 4[3])	[1] Later placed in (II) (*a*) treatment. [2] All in (II) (*b*) treatment. [3] All cases of mixed infection, but suitable for testing efficacy of drugs. [4] A horse in (II) (*b*) treatment [5] A donkey of this lot was later placed in (II) (*a*) treatment. [6] Dog in (II) (*b*) treatment.
		Ox.....								
		Ox.....								
		Ox.....								
		Equine....	—	—	5 (1[4], 4[5])	62·5	3 (—, 3)	37·5	8 (1, 7)	
		Equine....								
		Dog.....	1[6]	—	—	—	—	—	1	
	(II) Tartar emetic in combination with other drugs.									
	(*a*) Tartar emetic preceding other drugs	Ox.....	2	15·4	9	69·2	2[7]	15·4	13	[7] One of these cattle fell into a gulley, which no doubt hastened death
		Equine....	1	—	1	—	—	—	2	
	(*b*) Tartar emetic following other drugs	Ox.....	1	7·1	9	64·3	4	28·6	14	
		Equine....	—	—	—	—	1	—	1	
		Dog.....	1	—	—	—	—	—	1	
	(III) Drugs other than tartar emetic	Ox.....	—	—	1	—	1	—	2	
		Pig.....	1	—	—	—	—	—	1	
Probably *T. congolense*	(I) Tartar emetic alone..	Ox.....	32	84·2	4	10·5	2	5·3	38	
		Equine....	—	—	5	—	—	—	5	
	(II) (*a*) Tartar emetic preceding other drugs	Ox.....	—	—	3	—	1	—	4	
		Equine....	—	—	1	—	1	—	2	
	(III) Drugs other than tartar emetic	Equine....	3	—	—	—	—	—	3	
T. vivax.....	(I) Tartar emetic alone....	Ox.....	4	66·6	1	16·7	1	16·7	6	
T. brucei.....	(II) (*a*) Tartar emetic preceding other drugs	Ox.....	1[8]	—	—	—	—	—	1	[8] Ox being refractory would have recovered in any case.
		Equine	—	—	—	—	1	—	1	
	(III) Drugs other than tartar emetic.....	Equine....	—	—	1	—	3	—	4	
		Dog.....	—	—	—	—	4	—	4	
Mixed Infection.	(I) Tartar emetic alone...	Ox.....	—	—	—	—	2	—	2	
	(II) (*a*) Tartar emetic preceding other drugs	Ox.....	—	—	1	—	—	—	1	
	(*b*) Tartar emetic following other drugs	Ox.....	—	—	1	—	—	—	1	
	(III) Drugs other than tartar emetic	Ox.....	—	—	1	—	1	—	2	

As will be seen from the above statement, the mortality from *T. congolense* disease in bovines was 16 per cent, and in equines was 33 per cent. This applies to the cases treated with tartar emetic alone. The results following other methods of administration are shown quite clearly in the table above.

It is convenient at this stage to emphasize that as a result of the active campaign carried out by the Division of Veterinary Research, the confidence of farmers regarding the future was restored. As an example may be quoted the following extract from the Report * of the Directors of the Zululand Farmers' Co-operative Industries, Ltd.:—"The favourable position as regards the control of nagana in the Ntambanana area, as the result of veterinary research work carried out, is a factor of the greatest importance to your company, and encourages the Board to hope for progressively better results in the early future."

Conclusions in Connexion with Tartar Emetic Treatment.—Although tartar emetic is admittedly far from being an ideal drug, chiefly on account of its temporary beneficial action, and the disadvantages resulting from faulty administration, yet there is at the present time no other drug to compare with it for the following reasons:—

(1) It is easily prepared and administered.
(2) In reliable hands it is safe.
(3) It is easily procured.
(4) It is cheap, costing only 5s. to 6s. per lb.
(5) It does not bring about any severe changes likely to prejudice the health of the patient.
(6) Trypanosomes do not appear readily to acquire resistance to its action.
(7) It has been reported by farmers to be effective for other maladies, e.g. redwater and gall-sickness.

2. Use of Drugs other than Tartar Emetic.

Arsenic and its Derivatives.

In addition to arsenic, the following arsenic-containing compounds have been used in nagana in most cases along with tartar emetic:—

Arsenite of soda.
Cooper's Sheep Dipping Powder† (Badenhorst's Cure).
Atoxyl.
Neosalvarsan.
Preparation 189 (Fourneau).

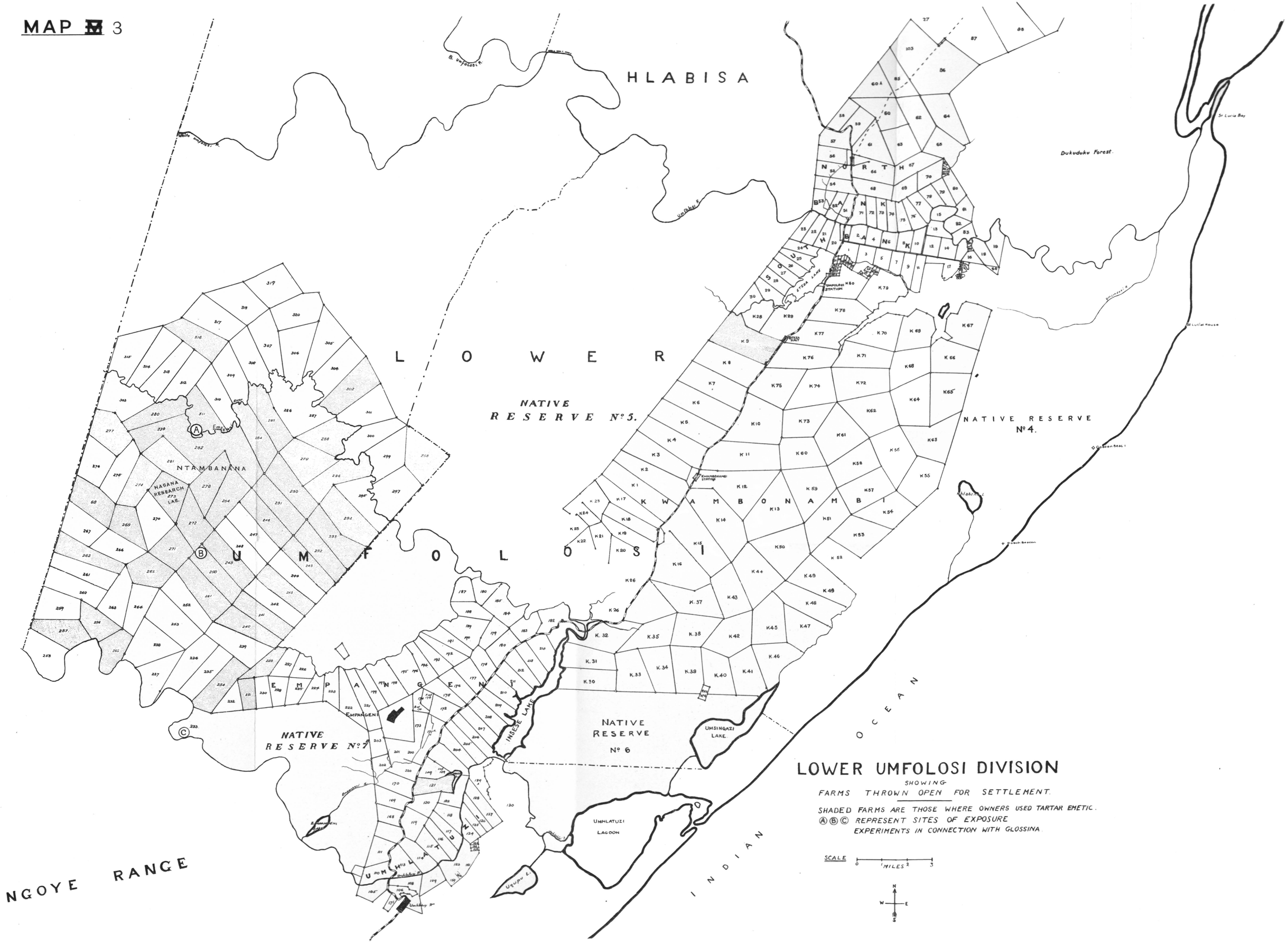
White Arsenic (Arsenious Acid).

This was first employed as a remedy for nagana by Livingstone in 1847 (Boyce and Breinl, 1908). He gave 0.12 gm. of the drug (Knuth and du Toit, 1921) to a horse on seven successive days, but it is doubtful whether the drug was responsible for any beneficial effects. Since the animal lived for six months afterwards, it is more likely

* *Natal Mercury*, Durban, 7th September, 1922.

† A farmer named Badenhorst, residing in the Nkwaleni Settlement, claimed to have used with great success a drug which was indistinguishable in appearance from Cooper's Dip, and which, on analysis, yielded almost identical results.

MAP 3



LOWER UMFOLOSI DIVISION

SHOWING

FARMS THROWN OPEN FOR SETTLEMENT.

SHADED FARMS ARE THOSE WHERE OWNERS USED TARTAR EMETIC.

Ⓐ Ⓑ Ⓒ REPRESENT SITES OF EXPOSURE EXPERIMENTS IN CONNECTION WITH GLOSSINA.

SCALE 0 1 MILES 2 3

N W E S

MAP 3.—Lower Umfolosi Division, showing (1) farms in division: (2) farms where tartar emetic used: (3) sites of "Exposure Experiments."

that infection was due to the less pathogenic *T. congolense*. After the discovery of the trypanosome of surra in 1880, the drug was used, among others, by Lingard. Bruce (1896), who refers to Lingard's preliminary investigations, mentions nine agents employed by the latter, but of these only arsenic seemed at all promising. The case, however, apparently cured by Lingard was treated with liquor arsenicalis (solution of potassium arsenite), and the double iodide of arsenic and mercury (*liquor arsenii et hydrargyri iodidi* or Donovan's Solution). Nevertheless, according to Dale (1923), Lingard successfully treated surra in horses with arsenious acid. Since those days arsenious acid has been employed for most forms of trypanosomiasis, but of far greater importance has been the use of the derivatives of arsenic, notably atoxyl, arsenophenylglycine, salvarsan, and most recently tryparsamide.

Arsenic formed the latter part of Jones' (1915) treatment for *T. congolense*, but probably it was given as much for its alterative properties as for its trypanocidal action. In Zululand it was hoped that, in addition to its tonic effects, it would continue the beneficial trypanocidal effects of tartar emetic. After a few tests, however, it was obvious that such was not the case, and as it was also a dangerous drug to recommend to farmers, it was decided to discontinue its use.

Nature of Drug.—White arsenic (trioxide of the element arsenic) is a dull, white, heavy crystalline powder, practically insoluble in cold water, but dissolving on warming with alkalies.

Notes on some cases treated:—

(*a*) Bull Cm. 1. A course of eight doses per os, totalling 8 gm., and given during the period 9.12.21-14.1.22, did not prevent return of *T. congolense*, smear being positive 14.2.22.

(*b*) Heifer Cm. 3. Although this animal received 10 gm. between 24.12.21 and 28.1.22, *T. congolense* reappeared on 7.2.22, when 189 was administered with equally unsatisfactory results.

(*c*) Horse 14326. A dose 1 gm. administered 15.2.22 failed to clear the blood of *T. congolense* by 18.2.22, after which Frosch and Knuth's method was given a trial.

As the results with tartar emetic alone were equally good, it was considered a waste of time to dose animals with white arsenic as well.

Sodium Arsenite.

Bruce was the first (with the exception of Lingard) to use sodium arsenite in the treatment of trypanosomiasis, since in 1895 he employed this agent for what was apparently *T. brucei* infection in a horse. The arsenic was dissolved in water with an equal quantity of carbonate of soda, and the solution was "scattered night and morning over his feed of crushed mealies." From experiments carried out later, Bruce "concluded that arsenic is quite useless as a prophylactic agent, but that it is useful in prolonging life and usefulness in the fly-country after the disease has begun." Laveran and Mesnil * (1902) employed the drug and had good results when it was administered subcutaneously. The good effects, however, were only temporary, for trypanosomes (*T. brucei*) soon reappeared in the blood stream. Other

* Quoted by Boyce and Breinl in "Atoxyl and Trypanosomiasis," Ann. Trop. Med. and Para., Vol II, page 6 (1908–1909).

observers also found that sodium arsenite was a convenient form of administering arsenic, but since Thomas' (1905) researches with atoxyl, which he showed was more efficacious, sodium arsenite has been comparatively little used.

Nature of Drug.—A greyish white powder fairly soluble in cold water, but more soluble on warming. It is the most easily procurable poison in South Africa, being extensively used as the metarsenite (approximately 80 per cent. As_2O_3) for dipping. Van Zyl (1924) has drawn attention to the variation in composition of the common brands met with on the market.

Method of Administration.—For adult horses and bovines 0.750 gm. of the powder was dissolved in 40 c.c. normal saline, which had just been boiled. Donkeys received 0.250 gm. in 30 c.c. of fluid. In all cases it was administered intrajugularly, except once, when 0.1 gm. was given subcutaneously to Donkey B.3. In this latter case an abscess formed, but the local reaction was not so serious as that induced by tartar emetic. The same donkey, B.3, at the time of the previous injection, also received 0.100 gm. intrajugularly, and there followed immediately afterwards distress and staggering, the only alarming symptom seen in connexion with arsenite of soda.

Effects of Drug.—The immediate and local effects have been referred to in the previous paragraph, and there now remains to be described the effect of the agent on trypanosomes. The speed at which trypanosomes disappear and the length of time they are kept from blood stream are best shown in the subjoined table:—

TABLE 15.

Type of Trypanosome.	Animal and Number.	Drug Administered. 4 p.m.	5.50 p.m.	6.5 p.m.	9 p.m.	6 a.m.	12 noon.	5 p.m.	February, 1923. 17–25.	26.	27.
		15/2/23.				16/2/23.					
T. congolense.....	Ox 4617	+	+	+	+	+	−	−	−	−	+
T. congolense.....	Ox 1....	+	+	+	+	+	+	−	−	+	

+ and − indicate positive or negative blood-smears stained by Giemsa.

It will be noted that the parasites do not disappear so readily as is the case with tartar emetic, the actual period being at least twelve hours in the first case and eighteen hours in the second. A relapse may be expected according to the above in about ten days. In one observation made on *T. brucei*, Donkey B.3, the trypanosomes were dispelled in nine hours, and the blood was still free four days later, when another drug, iodarshytone, was administered.

In one case where nagana was successfully prevented (Horse 14104), one of the nine injections given after exposure to "fly" was arsenite of soda.

Cooper's Sheep Dipping Powder (Badenhorst's Cure).

This preparation, after sodium arsenite, which is used for dipping cattle, is the next most easily procured trypanocidal agent in South Africa. Being less toxic than arsenite of soda, it is extensively used

for various ailments of stock, particularly for the treatment of worms. It is sold in packets containing approximately 900 gm., which is sufficient to make 25 gallons for the first dipping (and 50 gallons for second dipping).

Nature of Drug.—It is a yellow powder containing about 22 per cent. of arsenic expressed as As_2O_3, of which the bulk is present as water-soluble arsenite and a small proportion as sulphur arsenite and arsenate. The powder also contains over 60 per cent. of sulphur, nearly all of which is in the free state.

Cooper's Dip was largely used in the Lower Umfolosi Division, especially along the Umhlatuzi Valley, during the nagana outbreaks of 1920 and 1921, but with very little success, although an occasional farmer, such as Mr. Badenhorst, stated it had almost proved a specific. The agent was generally given mixed with coarse salt (after finely pulverizing) in proportions varying according to the user, but the general quantities were Cooper's Dip one part and salt ten parts. Mr. Badenhorst claimed that a *teaspoonful** of his "remedy" given as such per os would cure any case of nagana, and as the Magistrate at Mahlabatini had ascertained that of eleven bovines (suffering from nagana) treated, only one had died,† it was decided to give the treatment a trial. Material was accordingly sent to the Laboratory at Maritzburg, and the analysis already referred to, and certain details regarding treatment to be mentioned later, were kindly supplied by Dr. Robinson, Officer in Charge, during 1922.

Effects of Cooper's Dip given at Nagana Research Laboratory.—These may be conveniently described under the following:—

(*a*) Effect on animal.
(*b*) Effect on trypanosomes.

(*a*) The dose generally given was 8 gm., which was thrown at the back of the tongue with a spoon and washed down the gullet with a little water. In seven cases out of eight, marked purgation followed from 24-48 hours after administration, in spite of the fact that drinking water and grazing on dew-sodden grass were not allowed on the day of administration. The purging lasted from one to three days, and had the effect of reducing the weight of the patient, an unsatisfactory result in weak and emaciated animals.

(*b*) The following table shows at a glance the intervals between administration and disappearance of parasites, and between the latter phenomenon and their return in the peripheral circulation:—

---

* Most farmers use a "heaped" spoonful. In any case teaspoons not only differ in size, but vary considerably in capacity according to whether the contents are "levelled" or "heaped." Tests show that the weight of Cooper's Dip in "levelled" spoons may vary from 2·2 gm. to 3·5 gm., whereas when "heaped" these figures become 11 gm. and 17 gm. respectively.

† Other details, such as time disease noted, when animals dosed, and eventual fate, are lacking.

TABLE 16.

SHOWING ACTION OF COOPER'S DIP POWDER ON *T. CONGOLENSE* (STAINED SMEARS).

Drug Administered.

No.	Animal.	6 a.m.	10 a.m.	11 a.m.	4 p.m.	6 a.m.	11 a.m.	4 p.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.	6 a.m.
		2/2/23				3/2/23			4/2/22	5/2/23	6/2/23	7/2/23	8/2/23	9/2/23	10/2/23	11/2/23	12/2/23	13/2/23	14/2/23	15/2/23	16/2/23	17/2/23
1	Ox 13	+	+	+	+	+	+	+		+	1	+	‖									
2	Ox 7	+	+	+	+	+	+	−	−	−	−	−	−	−	+				‖			
3	Ox 1	+	+	+	+	+	+	+	+	−	−	−	−	−	−	−	−	+		‖		
4	Ox 96	+	+	+	+	+	+	−	−	−	−	−	−	−	−	−	−	+		‖		
5	Ox 4617	+	+	+	+	+	+	+	+	−	−	−	−	−	−	−	−	−	+	‖		
6	Ox 3628	+	+	+	+	+	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	+, ‖

+ Indicates positive smear. − Indicates negative smear. ‖ Indicates other treatment adopted.

1. On 5th and 6th February, 1923, ox was on transport work to White Umfolosi River.

Ox 1, which also received Cooper's powder at 10 a.m., 2.12.22, showed negative blood-slides at 6 a.m., 3.12.22, trypanosomes thus disappearing within twenty-four hours. They, however, reappeared nine days later (12.12.22). Ox 4, after being treated on 8.12.22, showed negative blood-smears twenty-four hours later. It may be concluded then that, as a rule, the parasites disappear within 24-48 hours of administration, and that a reappearance may be expected in a week or thereabouts.

Maritzburg Experiments.—These carried out on *T. congolense* by Dr. Robinson gave the following results, Badenhorst's remedy being employed:—

TABLE 17.

Animal.	Dose Administered.	Date.	Trypanosomes Disappeared.	Trypanosomes Reappeared.	Remarks.
Cow 224....	12 grams....	27/10/22	29/10/22	Not seen again	Died 8/11/22 from overdose.
Ox 101.....	8 grams....	15/11/22	16/11/22	29/11/22	No improvement.
Cow 221....	8 grams....	5/12/22	7/12/22	18/12/22	No improvement.

In addition, two bovines, Heifer 130 (*T. congolense*) and Ox 325 (mixed infection), received tartar emetic along with Badenhorst's remedy, but, as will be seen from Dr. Robinson's notes, with no better results.

"Heifer 130. . . . Treatment with 1.5 gm. tartar emetic in 30 c.c. normal saline on 5.1.23, and subsequently with 1 gm. on each of five successive days (8th-12th January), making 6.5 gm. in all. In addition, on 13th January, 8 gm. Badenhorst's powder was given. This was repeated on 25th idem. No trypanosomes were seen from 6th-17th January, but they reappeared with a rise of temperature to 104°, and have been fairly frequent every day since.

"Ox 325. Commenced to show *T. brucei* in blood on 23.12.22 and *T. congolense* as well on 24th idem. Later only *T. congolense* was present. On 5.1.23, 1.5 gm. tartar emetic was given intravenously in 30 c.c. normal saline. This animal immediately afterwards showed great distress, laboured breathing, staring eyes for a few minutes, and falling to the ground, but recovered within half an hour. On 8.1.23, and daily until 12.1.23, 1 gm. of tartar emetic was given intravenously in 20 c.c. saline, and on 13.1.23 8 gm. Badenhorst's powder was administered. From 5.1.23 the blood remained negative, but parasites reappeared in small numbers and have been present ever since. It would therefore seem that tartar emetic alone may be as effective in sufficient doses as its combination with other drugs."

Advantages Claimed by those using Cooper's Dip.

These are:—

(*a*) The preparation is cheap and easily procured.
(*b*) It is easily administered per os, a native being able to carry out the dosing.
(*c*) One dose, i.e. a teaspoonful, is sufficient to bring about recovery.

Disadvantages of Cooper's Dip.

These are as follows:—

(*a*) Since it contains a large proportion of arsenic, the agent is far too dangerous to place in the hands of a native, and for that matter to entrust to an inexperienced European for administration.

(*b*) An 8-gm. dose, which is approximately the minimum dose given by farmers, failed to effect a cure. In fact this amount was sufficient to produce violent purgation, which is a serious complication in an animal already enfeebled by nagana.

(*c*) Animals are to be kept in a paddock away from water for 18-24 hours after administration, which is a severe handicap to animals losing condition daily.

(*d*) Any improvement which follows is seen about a week after administration, whereas the beneficial effects of tartar emetic are almost immediate.

Atoxyl.

This drug was first used in the treatment of trypanosomiasis by Thomas (1905). It still forms, or at any rate did so until comparatively recently, part of the routine treatment for sleeping sickness in the Belgian Congo (Pearce, 1921). It was employed by Thomas in at least half a dozen forms of trypanosomiasis, and he found it more effective than arsenite of soda, in that it was less toxic, it produced less sloughing, and, more important still, it possessed a longer trypanocidal action. The few tests carried out in Zululand were with material prepared by the Vereinigte Chemische Werke Aktiengesellschaft, of Charlottenburg. The white crystalline powder was easily soluble in normal saline brought to boiling point. The solution was administered either subcutaneously or intravenously, and was particularly useful where the jugular veins had been excised.

Notes on Some Cases Treated.—The following table shows the effects of the drug on *T. congolense*:—

TABLE 18.

Animal.	Dose.	Time and Date of Administration.	Route of Administration.	Trypanosomes Disappeared after.	Trypanosomes Reappeared after.
Ox 134.....	4 grams.....	12.30 p.m. 6/2/23	Intravenous....	18½-hours.....	11 days.
Ox 40.....	6 grams.....	6 p.m. 15/2/23	Intravenous....	23 hours.....	10 days.

The most striking case of the efficacy of atoxyl was that reported by Mr. Coffey, of Farm No. 302. The available details are that of three pedigree pigs introduced from Natal, one died from an acute attack of *T. congolense* six weeks after arrival on the farm. The second pig, which was also ill (blood-smear positive 4.9.22), was treated subcutaneously with several 1-gm. doses, and as a result an apparently permanent recovery followed. Nothing is related concerning the third pig. The few animals treated at the Laboratory appeared to benefit as a result of the treatment, but tartar emetic was preferred, in that it was far cheaper.

Neosalvarsan.

This agent, manufactured by Meister, Lucius & Bruning, Hoechst a/M., is a fine yellow powder, which is so prepared that 1 gm., when added to 22 c.c. of water, distilled for preference, gives an isotonic solution suitable for intravenous administration. The drug was one of three agents employed by Frosch and Knuth (1914) in their successful treatment of *T. brucei* disease of the horse.

Notes on Some Cases Treated.—A horse, 14326, suffering from *T. congolense* infection received intrajugularly at 8 a.m., 18.2.22, 18 gm. of the powder dissolved in 400 c.c. of distilled water. Along with this was given 40 gm. of optochin in a drench of 500 c.c., and a second drench containing 200 gm. of salicylate of soda dissolved in 1 litre of water. Trypanosomes had not disappeared by the 20th February at 6.15 a.m., but were absent the following day. They, however, reappeared on 17.3.22. A slight local reaction occurred at the site of inoculation, and the treatment was no doubt responsible for two or three weeks of improvement in condition which followed.

Dr. Robinson has kindly supplied the following details of cases treated by him in Maritzburg:—

TABLE 19.

Animal.	Type of Infection.	Dose.	Route.	Date of Infection.	Trypanosomes Disappear.	Trypanosomes Reappear.
Bovine 278.	*T. congolense.*	2 grams...	Intravenous	4/1/23	5/1/23	6/1/23
Ox 334.....	*T. congolense.*	2 grams...	Intravenous	24/1/23	"No marked effect was noticed on the trypanosomes, but on 27th January, a number of degenerate forms was seen."	
		2 grams...	Intravenous	26/1/23		
Horse 262..	*T. brucei*....	3 grams...	Intravenous	24/1/23	25/1/23	27/1/23
		3 grams...	Intravenous	26/1/23		

From the above record it would appear that when given alone neosalvarsan is less effective than when given according to Frosch and Knuth's method.

Dr. Robinson also treated Ox 276, *T. congolense* infection, with neosalvarsan combined with tartar emetic, the result appearing more satisfactory than when neosalvarsan was used alone. In this particular case the parasites were driven from the peripheral circulation for over a month, but it is probable that tartar emetic alone was responsible for this disappearance.

Preparation 189 (*Fourneau*).

After the glowing account of the trypanocidal effects of the above drug by Martin (1922), it was hoped that an efficacious agent was at last available for combating nagana. The drug is prepared by Messrs. Poulenc Fréres, of Paris, and small quantities were obtained from the Director of Veterinary Education and Research and Dr. W. A. Murray, of Durban. The drug is a finely pulverized yellow-brown powder, dissolving easily in water with the production of a dark brown solution. Chemically it represents the hydroxy-amino-phenylarsenate of soda, and closely resembles atoxyl in its composition. According to the author quoted above, its therapeutic coefficient

is superior (at least for *T. rhodesiense* and *T. brucei*) to any of the other arsenicals, being at least 1 : 5. It is recommended that the solution be freshly prepared before injection. At Onderstepoort a horse weighing approximately 340 kgm. was given 4 gm. without untoward result, and a second horse weighing about 300 kgm. stood 10 gm., the only change being an acceleration of pulse rate and respiration. The drug after preparation may be given intravenously (when the strength of the solution must not exceed 10 per cent.), and subcutaneously or intramuscularly, when a 20 per cent. dilution may be employed.

Data Concerning Cases Treated in Zululand.

The position regarding the use of the drug for *T. congolense* and *T. brucei* can be best studied from the following tables:—

T. congolense *Disease.*

TABLE 20.

Giving General Information Regarding Cases Treated.

(For results of blood examinations, see Table 21.)

No.	Animal.	Approximate Weight in kilograms.	Date, Trypanosome seen for First Time.	Infection, Artifical or Natural.	Condition of Animal.	Dose (first) in grams.	Date.	Dose (second) in grams.	Date.	Dose (third) in grams.	Date.	Dose (fourth) in grams.	Date.	Clinical Result.
1	Ox 863..	250	28/12/21	A.	Poor....	2·5	1/2/22	5	4/2/22	5	7/2/22	6	11/2/22	Condition worse
2	Ox J4...	250	26/1/22	N.	Fair.....	2·5	1/2/22	5	4/2/22	5	7/2/22	6	11/2/22	Condition worse.
3	Ox 867..	175	8/12/21	A.	Poor....	5	4/2/22	5	7/2/22	6	11/2/22			Condition worse.
4	Horse 14326	350	11/2/22	N.	Good, only first symptoms	7	7/2/22	7	11/2/22					Condition worse.
5	Ox 17...	350	4/3/22	N.	e.g. photophobia,	7	7/3/22	10	15/3/22					Condition same.
6	Ox 18...	400	4/3/22	N.	eating of earth and scouring noticeable	6·5	7/3/22	10	15/3/22					Condition same.
7	Bull S1..	200	10/3/22	N.	Very poor	10	21/3/22							Condition worse.

TABLE 21.

Showing Action of 189 *on* T. congolense (*Stained Blood-smears*).

No.	Animal.	Injection. 7 a.m. 31/1/22	Injection. 8·30 a.m.	9·45 a.m.	11 a.m.	12 noon. 1/2/22	6 a.m. 2/2/22	6 p.m. 3/2/22	Injection. 8 a.m.	9·30 a.m.	2 30 p.m. 4/2/22	6 a.m. 5/2/22	6 a.m. 6/2/22	Injection. 8 a.m.	12 noon. 7/2/22	6 a.m. 8/2/22	6 a.m. 9/2/22	Injection. 8 a.m.	9 a.m.	1 p.m. 11/2/22	8 a.m. 13/2/22	8 a.m.	2 p.m. 14/2/22	7 a.m. 17/2/22	8 a.m.	12 noon 18/2/22
1	Ox 863...	+	+	−			+	−	−	+	+	−	−	−	−	−			+	+	−	−	−		−	−
2	Ox J4...		+	+	+	+	+		+	+	+	−	−						+	+	−	+	−		−	−
3	Ox 867..		+				+		−	+	+	−	−	+	+	−	−		+	+	-	+	−		+	
4	Horse 14326	−					−	−	−				−	−	−	−			−	+	−	+		+	+	+

No.	Animal.	9 a.m. 4/3/22	Injection. 7 a.m.	6 p.m. 7/3/22	7 a.m. 8/3/22	7 a.m. 9/3/22	6 a.m. 10/3/22	7 a.m. 11/3/22	6 a.m. 13/3/22	7 a.m. 14/3/22	Injection. 7 a.m.	6 p.m. 15/3/22	8 a.m. 16/3/22	4 p.m. 10/3/22	Injection. 7 p.m.	6 a.m. 21/3/22	23/3/22
5	Ox J7...	+	−	+	+	+	+	−	−	+	+	+	−				
6	Ox J8...	+	−	−	+	+	−	−	−	−	−	+	−				
7	Bull S1..													+	+	+	

The injections were either subcutaneous or intravenous.
= Other treatment adopted.
<— Occasions 189 administered.
+ Presence of trypanosome.
− Absence of trypanosomes.
Blank, no smears taken.

Conclusions.—Not only did the drug fail to clear the peripheral blood stream of parasites, but, more important still, the loss of condition associated with nagana was not checked in the least. For the latter reason the drug was far less promising than tartar emetic. Martin's work, it must be remembered, was performed under laboratory conditions on white mice suffering from *T. brucei* and *T. rhodesiense.*

T. brucei *Disease.*

As no suitable natural cases were available, the drug was given to artificially infected animals as shown below:—

TABLE 22.

Giving General Information Regarding Cases Treated.

(For results of blood examination, see Table 23.)

No.	Animal.	Approx. Weight in kgm.	Date of Infection	Trypanosomes seen for First Time.	Condition.	Dose (first).	Date.	Dose (second).	Date.
1	Dog 15	20	2/1/22	10/1/22	Emaciated.	0·25 gm. subcutaneous	1/2/22	·75 gm. subcutaneous	4/2/22
2	Dog 16	20	2/1/22	10/1/22	Emaciated.	0·25 gm. subcutaneous	1/2/22	·75 gm. subcutaneous	4/2/22
3	Horse 14301	325	6/1/22	14/1/22	Poor.....	3·5 gm. subcutaneous	1/2/22	6 gm. intravenous	4/2/22
4	Dog 14	20	*	1/2/22	Emaciated.	0·5 gm. subcutaneous	7/2/22	·5 gm. subcutaneous	11/2/22

The solutions were 10 per cent., and all injections were made subcutaneously, except the second injection given to the horse which at the time was *in extremis.* The only other points calling for attention are those associated with temperature and pulse in the case of Dog 16. The particulars are as follows:—

Temperature at 8.30 a.m., 1.2.22, was 103.8°, and at 9.45 a.m. 101.2 On the other hand, it rose from 100° at 9.30 a.m., 4.2.22. to 104° by 2.30 p.m., 4.2.22. This remission and exacerbation are probably quite independent of action of drug. Pulse rate after second injection was increased, but respiration unaffected. Animal seemed brighter six hours after second dose, but this was only temporary and most likely the transient improvement often seen in cases of nagana. Next day, 5.2.22, dog was again dull and listless.

The second injection in Dogs 15 and 16 was undoubtedly irritating, for both animals scratched violently at site of inoculation (behind shoulder) for a few minutes.

* Infection was probably accidental as a result of taking blood-smears with contaminated needle. Infection probably took place between the 18th and 24th January.

TABLE 23.

Showing Action of 189 *on* T. brucei (*Stained Smears*).

	6.30 a.m.	6.30 a.m.	8.30 a.m.	9.45 a.m.	11 a.m.	12 noon.	6 a.m.	6.30 a.m.	8 a.m.	9.30 a.m.	2.30 p.m.	6 a.m.	12 noon.	8 a.m.	12 noon.	6 a.m.	6 a.m.	6 a.m.	8 a.m.	9 a.m.	1 p.m.	8 a.m.	8 a.m.	
		Injection. ↑						Injection. ↑						Injection. ↑						Injection. ↑					
	31/1/22	1/2/22					2/2/22	4/2/22				5/2/22	6/2/22	7/2/22		8/2/22	9/2/22	10/2/22	11/2/22			13/2/22	14/2/22	15/2/22
Dog 15 ..		+	+	+	+	+	+	+	+	+	+	+	dead											
Dog 16..		+	+	+	+	+	+	+	+	+	+	+dead												
Horse14301	+		+	+	+	−	+	−		−	dead													
Dog 14..														+	−	+	+	+		+	+	+	+	dead

↑ Occasions 189 administered. + Presence of trypanosomes. − Absence of trypanosomes. Blank, no smears taken.

Conclusion.—As in the *T. congolense* experiment, the drug had little or no effect on the trypanosomes in the peripheral blood stream.

Enésol.

The above is the trade name for salicyl arsenate of mercury prepared by the Clin Laboratories, Paris. The compound contains 38.46 per cent. mercury and 14 per cent. arsenic, and is administered (1 c.c. of solution contains 0.03 gm. of the drug) either intramuscularly or intravenously. There was unfortunately not sufficient material for a fair trial.

Thiarsol.

Thiarsol represents a colloidal solution of trisulphide of arsenic. It is a yellow fluorescent solution dispensed in ampoules, of which 1 c.c. contains 0.002 gm. of the drug. According to a booklet on the therapeutic colloids issued by the Clin Laboratories, this agent "has been shown to be remarkably active in trypanosomiasis." The drug was administered subcutaneously to Donkey B.3 (*T. brucei*) on 23.12.21, but it failed to disperse the trypanosomes.

Iodarshytone.

This compound of arsenic, the triple peptonate of iodine, arsenic, and mercury, was not given a fair trial, so nothing more need be said regarding its action and uses. To the Messrs. Union Commerciale Francaise, of Durban, are extended thanks for kindly supplying samples of the above three drugs.

Electrargol.

Messrs. Union Commerciale Francaise, Durban, kindly supplied gratis several ampoules of this preparation, which in France is recommended for several contagious diseases. It is an isotonic solution containing extremely minute particles of colloidal silver which have been submitted to an electric charge.

Notes on Two Cases Treated.—Donkey B.3 received two subcutaneous injections on the 19th and 20th December, 1921, respectively, but trypanosomes were not dispelled from blood circulation. Donkey B.6, which was positive on 19.12.21 and treated intravenously the same day, was free of parasites the following day. This does not necessarily mean that electrargol possesses trypanocidal action, for, as is well known, the organisms of nagana appear and disappear at irregular intervals. Both donkeys were infected with *T. brucei.*

Quinine Sulphate.

Quinine was used by Lingard for surra in the early nineties, it being one of the drugs mentioned by Bruce (1896) that proved ineffective. According to Boyce and Breinl (1908), Surgeon-Major Ranking, previous to this, stated that "by the employment of full doses of quinine and arsenic he has been able to cure the disease." Bruce employed the drug in cases of nagana in dogs, but it proved useless (1903). Helm (1911) reported two cases of recovery from *T. brucei* infection in West Africa. He treated a dog and a horse

with quinine per os and atoxyl subcutaneously or intravenously, and both animals apparently recovered. It is as well to mention that Ranking's and Helm's results might be attributed to the arsenical preparations alone. Andrews (1913) was unsuccessful in his endeavours to cure *T. congolense* disease of sheep by combined quinine and atoxyl treatment.

Notes on Two Cases Treated.—Realizing that quinine administered per os was ineffective, the drug was given intrajugularly to Horse 14326 and Ox 863. The quinine was dissolved in alcohol, and then to this was added normal saline prior to sterilization. The horse showed increased repiratory effort after the first dose of 0.5 gm. given 16.6.22, but showed no untoward effects after the second dose of 5 gm. on the 29.6.22. Trypanosomes were still present half an hour after first injection, but blood was negative thereafter until 12.7.22, when treatment was changed. The quinine seemed to have a marked effect on the ticks, which disappeared after the first injection. The general improvement of condition noticeable after the 16.6.22 was temporary dulness again being manifested during the first week of July. Bovine 863 received four injections, the final one, given 28.6.22, producing stiffness and disinclination to rise. The beast was emaciated, and the large dose, 4 gm., probably proved too much. The treatment did not appear to benefit the animal at all, and death occurred 14.7.22. The blood was cleared of trypanosomes an hour after the first dose was administered on 16.6.22, and remained free until death. In both these cases the infecting organism was *T. congolense*.

Optochin Hydrochloride.

Optochin or ethylhydrocupreine, an artificial member of the cinchona series of alkaloids, was used with success by Morgenroth in 1911 for pneumococcic septicaemia (Dale, 1923). Later it was used by Frosch and Knuth in the treatment of *T. brucei* infection of the horse. It is a white powder possessing the characteristic taste of quinine and administered per os. Its only use in Zululand was along with neosalvarsan and salicylate of soda.

*Trypan Blue.**

This dye was first used in trypanosomiasis by Mesnil and Nicolle (1906), but, apart from Tshuzuki's (1911) favourable report on its efficacy for nagana in mice, it does not appear to have been of much value as a trypanocide. An illustration of its inefficacy for *T. congolense* (and at the same time of its value for *B. bigemina*) is provided by the following:—

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* Unpublished experiments carried out by the author in 1919 and 1920 show that the various brands of trypan blue on the market vary considerably in their therapeutic effects on *B. canis*.

TABLE 24.

(*Cow* 343.)

Showing Action of Trypan Blue on Babesia *and* Trypanosoma.

250 c.c. of 1 per cent. trypan blue administered intrajugularly at 11.30 a.m., 3.8.22 (see dotted line in table).

Per 1,000 erythrocyes.

Date.	Time.	Smear No.	D.	P.	P_2.	A.	Trypano-somes.	Tempera-ture.	Further Remarks.
3/8/22	7 a.m....	5063	—	—	8	1	1	105·5	Redwater and nagana diagnosed in Smear 5063.
„	11.30 a.m.	5069	2	3	4	7	3	105·2	
„	2.30 p.m.	5070	—	—	2	—	2	104·6	D.—Dividing forms.
„	4 p.m....	5071	—	—	1	1	2	104·6	P.—One pear-shaped organism in cell.
4/8/22	7 a.m....	5074	—	—	—	1	1	100·6	P_2.—Two pear-shaped organisms in cell
5/8/22	7 a.m....	5078	—	—	—	—	2	100·8	A.—One amoeboid.

It will be observed from the above that the drug, while dispersing redwater parasites and reducing the temperature, failed to clear the blood stream of *T. congolense*, although given intrajugularly. In two other cases, Dog O.1 and Ox 189, identical results were obtained.

Potassium Citrate.

As it had been observed that the only successful case of transmission * of *T. vivax* artificially had been by the use of fresh blood, and that all citrated blood had given negative results, it naturally appeared that the above agent had been to some extent responsible for some trypanocidal action. *T. congolense*, it must be pointed out, was transmitted whether the blood was fresh or citrated. To ascertain whether any trypanocidal effect existed for *T. brucei*, Dog 56 was injected subcutaneously at 11.30 a.m., 24.7.22, with 28 c.c. of normal saline containing 7 gm. of potassium citrate. The blood was unaffected one hour and three hours after injection, and 20 hours afterwards the trypanosomes were scanty. At 28½ hours the blood was negative. During this period a huge abscess had formed at the site of inoculation, and when it broke on the morning of the 26th July the dog was brighter for a few hours. Death, however, occurred on the 27th idem, but trypanosomes did not reappear.

Preparation 1811 (*Morgenroth*).

A small supply of the above drug was sent by Professor Morgenroth, of Berlin, to the Director of Veterinary Education and Research, with the request that it be used for trypanosomiasis. The material was accordingly dispatched to Zululand, where a single test was made. The drug is a bright yellow powder easily soluble in physiological water. Its chemical composition is not known. It had been established at Onderstepoort that, whereas a horse stood a dose of 1 gm. administered intrajugularly, a dose of 4 gm. proved fatal to a second animal. Donkey 14738, suffering from *T. brucei* disease, and which had relapsed 16.9.22 after a dose of arsenite of soda, received 0.250 gm. intrajugularly as a 1 per cent. solution at 8 a.m., 23.9.22. At noon the blood was free of trypanosomes, but they reappeared on the

* From Cow Cry 1 to Ox 4024.

morning of the 25th September. On the 27th idem a further 1 gm. was administered in the same way as the first dose, but it failed this occasion to disperse the parasites. Death occurred on the 29th September.

Other drugs used on a few occasions include the following:— Santonin and salicylate of soda in Zululand. Brilliant phosphin, oscol arsenicum, oscol sulphur, 685, Bayer 205, and tryparsamide were also employed by Dr. Robinson in Maritzburg.

3. Extracts from Protocols.

An outline showing the system adopted in connexion with drug treatment (as given at the Nagana Research Laboratory) having already appeared under Table 14, it now remains for an extract of the protocols to be appended, since owing to the large number of animals under experiment the complete protocols cannot be included. Typical examples of the various groups have been selected, and from these it should be quite evident how the results of treatment have been arrived at.