34. Glass rod 4 inches long. Recto-vesical pouch. Colostomy, four and a half months before. Symptoms were referred to a large wound in the buttock. Removal during an operation for excision of rectum. Dense adhesions but no serious erosion of viscera. Recovery.

35. Flanged glass tube 2 inches long. Under right rectus muscle. Operation for relief of ascites fifteen years before. No symptoms except ventral hernia. The tube is still there and the patient in good health. The ascites is cured. No external sinus present.

36. Hairpin (straightened). Passing from rectum and transfixing the Fallopian tube. Possibly passed into rectum, about two months before. Symptoms: Dysmenorrhoea, rectal pain. Removal by laparotomy. Peritonitis round tube. Ulcer in rectum. No abdominal sinus. Recovery.

37. Bone knitting-needle 5 inches long. Left iliac fossa. Pushed through uterus, fifteen months before. Symptoms: Abdominal pain, increased by movement. Removal by laparotomy. Knitting-needle surrounded by omentum. No damage to viscera. Radiogram taken. No sinus. Recovery.

38. Uterine dilator 8 inches long. Below liver. Pushed through uterus four days before. No symptoms. Removal by laparotomy. No damage to viscera. Radiogram taken. No sinus. Recovery.

39. Bone knitting-needle 10 inches long. Pouch of Douglas. Possibly pushed through vagina. Symptoms: Intestinal obstruction. Removal by laparotomy. No damage to viscera. No sinus. Recovery.

40. Piece of steel needle, 1 cm. long. Appendicectomy two years before. Symptoms: Persistent abdominal sinus. Sinus opened up and needle removed. Recovery.

41. Pin. Back of broad ligament. No previous operation. Possibly swallowed. No symptoms. Removed during ovariectomy for ovarian cyst. Slight adhesions, but no damage to viscera. No sinus. Recovery.

42. Stone. Lower abdomen. Stone was accidentally forced through the rectum three days before. Symptoms: Pain. Removal by laparotomy. Recovery. Royal College of Surgeons Museum 2310 I.

43. Artery forceps (4½-inch). Left iliac fossa, perforating uterus. Two laparotomies, one eighteen months, the other nineteen years previously. Symptoms: Pain, diarrhoea, leucorrhoea. Removal by abdominal hysterectomy and suture of colon. Severe ulceration of colon present. No abdominal sinus. Radiogram taken. Sudden death six weeks later, as recorded in detail above. Royal College of Surgeons Museum.

44. Bone pinholder 5 inches long. Above umbilicus, wrapped in omentum. Pushed through vagina three days before. Symptoms: Pain. Removal by laparotomy. No damage to viscera. Uneventful recovery. University College Hospital Museum.

REFERENCE.

¹ Crossen: *Amer. Journ. Obstet.*, 1909, vol. i; and also *Operative Gynaecology*, 1915, p. 589.

THE TREATMENT OF TRYPANOSOMIASIS.*

(A FURTHER REPORT.)

BY

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CONFRONTED by the problem of the treatment of trypanosomiasis in the field, and at the same time precluded from access to any reference library, the present writers endeavoured to evolve a working hypothesis which would explain the relapses so characteristic of the disease, and on that hypothesis planned a method of treatment which at the time they thought novel, and details of which have already been published in two previous articles.¹ Briefly the procedure comprised an attempt to sterilize the blood stream by the intravenous injection of arsenical compounds and an immediately subsequent attempt to sterilize the central nervous system by the intrathecal injection of salvarsanized serum. When holiday leave, however, afforded opportunity of consulting the literature on the subject it became evident that similar hypotheses must have been adopted by several previous workers, notably Balfour, Van Someren, Thiroux, D'Aufreville, and Reichnow, even as far back as 1906, and the evolution of the idea can be followed by the following references.

Thiroux² suggested that the absence of trypanosomes from the blood of certain patients was due to the presence of specific antibodies; and conversely, the presence of trypanosomes in the cerebro-spinal fluid was due to the absence of such bodies.

Thiroux and D'Aufreville³ conjectured that serotherapy would not give good results in meningeal trypanosomiasis

unless the antitoxin was injected into the spinal canal and cerebral substance, as had been done in tetanus.

Balfour (1908) in a memorandum, "The treatment of sleeping sickness," presented to the Sudan Sleeping Sickness Commission, drew attention to the treatment of cerebro-spinal meningitis by intrathecal injection of immune serum, and suggested a combined therapy for sleeping sickness, the trypanosomes being attacked in the blood by some of the more promising of the chemical trypanocides, and in the cerebro-spinal fluid by the injection of the patient's own serum or the serum from a case under treatment, obtained by defibrinating or centrifuging the blood.

Van Someren,⁴ putting Balfour's suggestion into practice, treated six cases, but concluded that the results were not encouraging. He added, however, that the method was tried only in cerebral cases, usually too far gone for other treatment.

Reichnow (1914), in the Kameruns, treated his cases on similar lines, but added 0.04 gram neo-salvarsan to his salvarsanized blood serum, a procedure which he himself admitted was far from devoid of danger and the risk attendant upon which caused him to abandon the method, as other observers had already done in the treatment of syphilis of the central nervous system.

From the above extracts it is quite clear that those whose duties included the treatment of sleeping sickness in endemic areas were even then—as they are now—dissatisfied with the adequacy of the methods at their command; so that it is almost incomprehensible to the present writers that the fact that they were following (even if unwittingly) the suggestion of such a keen observer and logical thinker as Balfour should have aroused so much and so uncompromising a hostility.

Moreover, the method we now advocate is administratively and economically sound. The patient's treatment is completed in two or three days, when he is free to return to his village and friends. Large hospitals and camps are no longer required, nor is the patient's life made irksome by continuous drugging for long periods of time. The natives themselves appreciate these advantages and now come in of their own volition asking for treatment.

Recently Warrington Yorke, in a critical review of recent work on the treatment of sleeping sickness in the *Tropical Diseases Bulletin*,⁵ has done us the compliment of massing much of the evidence he has collected from the literature around the debatable points in our work in such a manner as to make it evident that he, like ourselves, is primarily interested in the elucidation of the disease. As we have now completed a further survey of the cases we have had under treatment by various methods, we wish to present the results to the impartial reader so as to make it clear where we are in agreement with Yorke's arguments and where we consider our observations justify a totally different interpretation. But first we would deal with some general observations in connexion with sleeping sickness.

Naturally the first point that arises in connexion with the work has reference to the virulence of the particular strain or strains of trypanosomes that are met with in the Uganda Protectorate. With a nomadic population it is sometimes difficult to collect the necessary figures in support of any particular view, but we now have notes relating to the Northern Province of nearly 100 cases which have been diagnosed clinically and by laboratory methods and have been under observation for a year and a half, and another 200 cases which have been under observation for a shorter period (six or seven months). For facilities in following up these cases we are indebted to the Hon. E. C. Eliot, Acting Chief Secretary of the Protectorate.

The following table shows the course of the disease in the district under natural conditions and without treatment, and may be of value in another direction also—namely, that of extending Yorke's Table II. We have here adopted Yorke's plan of setting out the percentage mortality under two headings—in the first place assuming that all the cases missing at the time of the second census were alive, and under the second heading assuming that those missing had died of the disease. From our table it will be seen that the mortality varied from a minimum of 14.7 per cent. in one series of cases of six months' duration to a maximum of 70 per cent. in the small series under observation from twenty months. The true mortality percentage obviously lies somewhere between these extremes, but in any case the inference is justified that the disease, as it occurs in Uganda, is a serious one, and that the strain of trypanosome which is encountered there is fairly virulent.

* This report was received on September 11th, 1922.

TABLE I.

District.	No. of Untreated Cases.	Months since first seen.	No. Alive.	No. Missing.	No. Dead.
Gulu	25	20	10	0	16
Arua	40	18	12	8	20
Toro and Katwe ...	28	18	11	8	9
East Madi	123	6	90	15	18
West Madi	118	7	73	20	25

The percentage mortality of these cases would therefore be as follows:

District.	Percentage "A."	Percentage "B."
Gulu	61	61
Arua	50	70
Toro and Katwe ...	31	60
East Madi	14.7	18.6
West Madi	21	38

Note.—The cases here shown are the cases still alive and not those "alive and well"; if only the latter were included, the percentage would be very different indeed—for example, of the 12 cases alive in Arua, 6 are in an advanced state of sleeping sickness.

The East Madi figures are by Dr. G. D. H. Carpenter, who was in that area in September, 1921; of the cases he examined then, he only noted one as being in an advanced state, yet by February, 1922, eighteen had died. Further, in the same area, another sixty cases were discovered in March, 1922, but it is difficult to say if these were recent infections or were cases that had eluded observation during Carpenter's previous tour.

It is interesting to compare the figures relating to Gulu in this table with some details of a small series of treated cases discovered about June, 1920, in the same area; apart from the 26 untreated cases recorded in Table I, 11 others were conveyed a distance of some three hundred miles to one of us (S. M. V.) and were then treated in the latter part of the year as indicated in Table II. They returned home, two advanced cases dying on the road. Owing to difficulties of transport, etc., no further observations were possible till March, 1922—that is, about fifteen months after treatment—when it was found that a third case had died, giving a mortality of 28 per cent. The remaining eight cases absolutely refused blood, gland, or any other form of examination, so that, though alive and to all appearances well, we have no definite evidence to offer as to their condition, and have therefore omitted them entirely from our calculations.

TABLE II.—Treatment and Results of the Gulu Cases.

Case No.	Date of Treatment.	Treatment.	Result.	Period under Observation.	Remarks.
40	4.10.20	Intrathecal salvarsanized serum	Died	Months.	Advanced cases; died on road.
41	4.10.20	Ditto	Died	—	
44	4.10.20	Ditto	Well	15	
47	15.11.20	Ditto	Well	14	C.S.F. positive (neo-kharsivan).
48	15.11.20	Ditto	Well	14	C.S.F. negative (atoxyl).
49	2.12.20	Ditto	Died	—	C.S.F. negative (atoxyl).
50	2.12.20	Intramuscular salvarsanized serum	Well	14	Atoxyl.
51	6.12.20	Intrathecal heterogeneous serum	Well	14	C.S.F. negative (atoxyl).
52	6.12.20	Intrathecal salvarsanized serum	Well	14	C.S.F. negative (atoxyl).
53	6.12.20	Intramuscular salvarsanized serum (heterogeneous)	Well	14	Atoxyl.
54	6.12.20	Intrathecal heterogeneous serum	Well	14	C.S.F. negative (atoxyl).

If it had been possible to carry this experiment to a definite conclusion the results would have been of considerable value, since both the treated cases and the controls lived under identical conditions in an infected district, and in close contact with other cases of disease, for there is even now in Gulu and the surrounding districts a serious epidemic of sleeping sickness.

The next criticism—and a very reasonable one—that the cases we have recorded as still alive and well are not necessarily cured, cannot easily be controverted at this stage, owing to the widely varying interpretations placed upon the word "cure" by different authorities. In a discussion which followed the paper by the present writers at the Royal Society of Medicine in 1921 a five years' limit was suggested as desirable. Whilst regarding this as a counsel of perfection, we are not in the least inclined to take exception to it, and judged by this criterion we are ready to agree that all our cases are still "under observation"—although it may be noted that from time to time cases are reported in the medical press as "cured" well within this period. Hitherto, however, if clinical symptoms are totally absent and examination of the blood, glands, and, whenever possible, the cerebrospinal fluid, is repeatedly negative within a period of two to three years, we have assumed that such an uninterrupted convalescence normally proceeds to a permanent cure. Such cases are referred to in all our subsequent tables as "alive and well."

Turning now to Yorke's criticisms, he is correct in emphasizing the fundamental character of our statement that "most authorities are agreed that although the (intravenous) administration of one dose of salvarsan, neo-salvarsan, or atoxyl may be sufficient to sterilize the blood stream, yet within a variable period, averaging about four months, the symptoms reappear and the disease progresses to a fatal termination." Table III, although it only comprises six cases that we have treated in the first instance with only a single dose of neo-kharsivan or novarsenobillon, does include some of the coincidences characteristic of the disease in Uganda which originally stimulated our interest in the treatment of trypanosomiasis.

TABLE III.—Showing Results of Intravenous Treatment Only.

Case No.	Date of Diagnosis.	Intravenous Dosage.	Result.	Period under Observation.	Remarks.
7	10.7.19	0.6 gm. neo-kharsivan.	Relapsed. C.S.F. + 27.10.19	Months. —	Re-treated completely 28.10.19. See Table I.
14	22.11.19	0.6 gm. ditto	Well	26	
28	21.4.20	0.4 gm. ditto	Well	21	
56	13.1.21	0.4 gm. ditto	Died	—	Sleeping sickness 20.9.21.
68	2.8.21	0.3 gm. novarsenobillon	Recurred	—	Trypanosomes in blood 20.1.22.
69	15.12.21	0.6 gm. neo-kharsivan	Died	—	Sleeping sickness 17.4.22.

Thus (1) in two very early cases the single dose (intravenous) apparently acted as the desired *therapia sterilisans magna* and resulted in the individual remaining "alive and well" after twenty one (Case 28) and twenty-six (Case 14) months respectively; (2) in four cases the single dose was insufficient to sterilize the blood stream and/or the central nervous system; and (3) in three of these relapse occurred in three and three-quarter months (Case 7), four and three-quarter months (Case 68), and four and a half months, when death occurred (Case 69); Yorke, too, quotes Lurz as recording nine relapses out of eleven after salvarsan within one and a half months, and four out of six treated with atoxyl within one month.

Further, in many instances sleeping sickness is a disease of slow progress, and, although symptoms may reappear within a short time of one therapeutic dose, the subsequent progress may be very tardy; such, however, is not usually the case—for example, Case 56, Table III. With regard to the fatal character of the disease Yorke quotes one batch of cases undergoing various prolonged treatments (Table IV, *Bull. Trop. Med.*, 18, 1921, p. 172), which in this connexion is very significant—namely:

"Hodges, Uganda, states that of 1,185 cases admitted between December, 1906, and November, 1907, 734 were dead at the end of two years and only 49 could be found four years later, whilst 912 were known to be dead; of the 49 still alive, 27 were clinically advanced cases, 19 showed definite signs of disease, and only 3 were cases we should count as 'alive and well.'"

Other similar instances become at once apparent from an examination of Table IV, where we have completed Yorke's Table IV in this sense.

TABLE IV.

Author.	No. of Cases.	Condition before Treatment.	Treatment.	Length of Observation Period.	No. Disappeared.	No. Dead.	No. Alive.	Percentage of original total alive assuming all who had disappeared are		Remarks.	On our Basis "Alive and Well."	
								"A" Dead.	"B" Alive.		"A" percentage.	"B" percentage.
Hodges. Uganda: all sleeping sickness camps, 1910	1185	Unselected cases	Various prolonged treatments, chiefly arsenical	2 years 4 years	182 224	734 912	269 49	22.7 4.1	38.2 23.0	Of 49 alive: 3 good health; 19 definite signs of disease; 27 advanced	— 0.2	— 10.5
Hodges. Uganda: Busino Camp, 1906-7	399	Unselected cases	Various prolonged treatments	3½-4 years	65	313	21	5.2	21.5	All showed signs of disease	0	0
Bagshawe, 1910	50	Europeans	Ditto	3-7 years	7	30	13	26.0	40.0	No details	—	—
Simson. Yei Camp, Sudan, 1920	35	15 early, 20 advanced cases	Metallic antimony, 8 injections	7 years	7	20	8	22.8	42.8	6 good condition	15.0	37.0
	29	Selected cases	15 injections antimony, 2 injections salvarsan	6 years	0	11	18	62.0	62.0	All good condition (2 died of small-pox and cerebro-spinal meningitis)	62.0	62.0
	23	Selected cases	15 injections antimony	6 years	0	4	19	82.6	82.6	17 good condition	74.0	74.0
	96	Unselected cases	36 injections atoxyl 2 years' continuous treatment	6-7 years	2	43	51	53.1	55.2	33 good condition 13 fair 5 poor	34.0	36.0
	63	Unselected cases	Atoxyl, prolonged treatment	7-8 years	0	23	40	63.5	63.5	26 good condition 6 fair 3 poor (* 2 died small-pox)	41.0	41.0
	11	Unselected cases	Ditto	7 years	0	5	6	54.5	54.5	No details	54.5	51.5
	7	Unselected cases	Ditto	6 years	0	3	4	57.1	57.1	2 good condition 1 fair 1 bad	28.0	28.0
	19	—	Ditto	5 years	0	6	13	68.4	68.4	6 good condition 3 fair 4 poor	47.0	47.0
	5	—	Salvarsan and atoxyl, 1 year	3 years	0	1	4	80.0	80.0	2 good condition 2 fair	40.0	40.0
Marshall and Vassallo, 1918-1922	12	Unselected cases	1 dose neo-kharsivan 1 injection intrathecal serum	2-3½ years	2	2	8	66.6	83.0	All "alive and well"	66.6	83.0
	17	(2 advanced) Unselected cases	Ditto	18-21 mos.	1	0	16	94.0	100.0	All "alive and well"	94.0	100.0

With reference to our own cases which we have incorporated in this table we would point out: (1) Of the three cases we record as missing, two, we believe, died during the famine, while the third, we are informed, is working on an estate in a distant part of the country and is perfectly well; but as we have put the worst possible construction on our returns these "missing" do not really affect our percentage any more than those of Simson's cases who died of small-pox or cerebro-spinal meningitis. We have, however, excluded the two cases of reinfection, and the one case who died, possibly from delayed chloroform poisoning. (2) All our cases are unselected, as compared to some of Simson's returns, and the deaths occurred in very advanced cases, which would not have been included if we had exercised any selection. (3) The cases here included have only received one complete treatment—that is, one intravenous injection of arsenic and one intrathecal injection of serum the following day, as against the prolonged treatments of others—a point completely ignored by Yorke.

We would therefore suggest that this table in its present form not only affords considerable support to our first assumption, but also goes far to confirm our statement that our routine method of treatment has furnished better results than any one hitherto published treatment of a series of cases.

Again, in Yorke's Table I there are given details of 46 cases where it is claimed that (a) trypanosomes disappeared from the cerebro-spinal fluid after treatment, and (b) treated cases survived for long periods after their cerebro-spinal fluid was found to be infected. There are no details with regard to 4 cases, which leaves us 42 to deal with. Martin, Leboenf, and Ringenbach record a series of 31 cases, and of these 11 disappeared and 10 died. Of the remaining 10, which were followed up, only 3 were found negative after twelve, nine, and seven and a half months respectively—that is, out of 31 cases under 10 per cent. were found to be negative.

Incidentally the period of observation of all these cases is much less than ours.

The other 11 may be regarded as isolated cases. Eight are examples of negative cerebro-spinal fluid after treatment when examined at intervals of one and a half to nine months, but the cell count in most instances suggests that infection is merely latent. Of the remaining 3 cases (Gray and Tulloch) one gave post-treatment positive results until his death at the end of twenty-three months, and the other two were positive up to the end of 230 and 195 days respectively. These cases are of academic interest undoubtedly, but for all practical purposes merely indicate the slow progress of the disease in some individuals.

Yorke's Table II⁶ is interesting, as in the first two instances it suggests that the chances of infected individuals remaining alive are equal whether they are treated or not; for example, 100 per cent. (calculated on 3 cases) and 80 per cent. (calculated on 5 cases) were still alive without any form of treatment. In a third instance the information that 5 were known to be well and working after four years out of a total of 102 cases is held to justify a percentage of 33 living (Dutton and Todd). The absence of any details with regard to the number dead, number alive, and number missing would, on the basis of our calculations, give less than 6 per cent. "alive and well."

The second assumption, a threefold one, is as to its first sentence—"Quite early in the disease the trypanosomes appear to gain an impregnable position in the central nervous system"—avowedly an alternative to the "drug-fast" theory. As to its second part—"in this position they are protected from the action of drugs"—it may be remarked that syphilologists as a body fail to find arsenic in this situation after using salvarsan and its derivatives in the medicinal doses at present employed. It further derives a certain amount of support even from the personal communication from Voegtlin to Yorke (which is all that is offered in contradiction of our

statement) that arsenic reaches the cerebro-spinal fluid in low concentration only after massive and toxic doses have been administered intravenously. The further observation of Voegtlin (unpublished), "that parasites in the cerebro-spinal fluid of experimental animals diminish within twenty-four hours of large doses of these drugs administered intravenously," might, it is true, be explained by the action of that trace of arsenic in the cerebro-spinal fluid; but we would hazard another explanation more in consonance with our own conceptions—namely, that trypanolysin is formed as a result of the action of the intravenous arsenic upon the trypanosomes in the circulating blood, and this trypanolysin is then secreted into the cerebro-spinal fluid by the choroidal cells.

The third part of this assumption, supported though it is by cases in which the cerebro-spinal fluid was originally apparently sterile, but was found to be infected at the time of the post-treatment relapse (for example, Case 7, Table II), is, we are willing to admit, still lacking in experimental proof, since on this point we can only offer the experimental work of Reichnow (one observer again) that infection does take place from the cerebro-spinal fluid to the blood stream. As to the exact route, until experimental proof is forthcoming we are willing to accept either of the suggestions put forward—namely, that infections in the basal systems travel via the nerve sheaths (Keith) or via the arachnoid villi (Halliburton), since either structure, in our opinion, might be permeated by the living trypanosome just as readily as it is by the amoebic activity of the leucocyte.

Still, with regard to the second assumption, we may perhaps deal further with some of Yorke's criticisms. In the first place he argues that if there are no nervous symptoms and the lumbar puncture is negative, there is no evidence that the central nervous system is involved, and therefore it is not justifiable to tamper with it. To this we would reply that a negative lumbar puncture does not necessarily mean that the cerebro-spinal fluid is sterile; the trypanosomes might be present in so small a number as to be overlooked or even to be actually absent from the quantum of fluid taken for examination—an argument which Yorke himself advances when it serves his purposes (that is, when he suggests that relapses are due to a few trypanosomes in the blood, so few as to escape detection when the blood is examined). That the parasites have other hiding places than in the cerebro-spinal fluid, we are quite willing to admit is more than a probability (we have already referred to van Sacheghem's work on the bone marrow); it is almost a certainty, and could be paralleled by the relapses which occur in malaria after apparent sterilization of the blood stream by drugs, under circumstances where reinfection is impossible and where there is no suspicion either from the symptoms or from the subsequent history that the central nervous system has ever been involved. In face of the well known fact that nervous symptoms are practically always the accompaniment of advanced cases of sleeping sickness, we are of opinion that the central nervous system is the seat of election. Stevenson, too, has recently demonstrated trypanosomes in the central nervous system cells.

There is, of course, the possibility that Yorke, like many others even in the present year of grace, has a personal aversion to the local treatment of infections of the central nervous system, despite the brilliant results achieved in this direction by the scientific use of suitable serums in the treatment of cerebro-spinal meningitis, tetanus, and syphilis of the central nervous system. Others have already advocated local treatment for demonstrable trypanosome infections in this situation, and more recently Mayer urges intrathecal injection of "Bayer 205" and Pearce of tryparsamide. But in view of the opposition of the native to repeated lumbar punctures and the possibility of the existence of central nervous system infection at the moment treatment is undertaken, we consider it more politic to administer the drug through the needle employed to collect the specimen of cerebro-spinal fluid for examination. On the result of the subsequent examination we can decide whether we have employed the salvarsanized serum as a prophylactic or a therapeutic agent. In other words, on the clinical evidence at our disposal, we have gone a step farther than other workers and employed the method as *sur routine* treatment, and we have the temerity to assert that our results have justified our action.

We are now in a position to present our own results to date in concrete form.

TABLE V.—Cases Treated by Intrathecal Salvarsanized Serum and Results to Date.

Case No.	Report up to 31.1.20.		Report up to 31.1.21.		Report up to 31.1.22.	
	Months since Treatment.	Remarks.	Months since Treatment.	Remarks.	Months since Treatment.	Remarks.
2	16	Well	28	Well	40	Well.
3	1	Disappeared				
4	12	Well	21	Well	33	Well.
5	1	Died (cause unknown)				
7	2	Well	14	Well	26	Well.
8	4	Well	16	Well	23	Well.
9	1½	Died				
10	2½	Died				
11	1½	Well	13½	Well	25½	Well.
12	1½	Well	13½	Well	25½	Well.
13	1½	Well	13½	Well	25½	Well.
15	1½	Well	13½	Well	25½	Well.
16	—	—	8	Well	21	Well.
17	—	—	8	Well	21	Well.
18	—	—	8	Well	21	Well.
19	—	—	8	Well	21	Well.
20	—	—	8	Missing	21	Well.
21	—	—	8	Missing	21	Well.
22	—	—	8	Well	21	Well.
23	—	—	8	Well	21	Well.
24	—	—	8	Well	21	Well.
25	—	—	8	Well	21	Well.
26	—	—	7½	Well	20½	Missing.
27	—	—	7½	Well	20½	Well.
28	—	—	7½	Well	20½	Well.
29	—	—	6½	Well	19½	Well.
30	—	—	6½	Well	19½	Well.
31	—	—	1 day	Died*		
32	—	—	—	—	16½	Well.
33	—	—	—	—	13	Well.
34	—	—	—	—	11	Well.
35	—	—	—	—	11	Well.

* ? Chloroform poisoning.

Table V gives the cases treated by the method we suggest should become a routine one, with the reports at the various time periods presented on former occasions. Apart from two cases this needs no comment. We must, however, draw attention to Cases 18 and 20. These were found at a subsequent examination several months after treatment to harbour trypanosomes in their glands, but in both cases the cerebro-spinal fluid was negative.

Case 18 was treated on April 18th, 1920; three subsequent examinations were all negative: a fourth one on July 27th, 1921, showed trypanosomes in glands.

Case 20 was treated on April 25th, 1920; subsequent examinations were all negative, but on April 20th, 1921, trypanosomes were recovered from a gland by puncture.

Obviously these two cases would be claimed, by hostile critics, as instances of the failure of our routine treatment; we, however, consider them as reinfections—the only ones we have noted; the circumstantial evidence that influences our opinion is as follows:

1. The glands of both cases had disappeared after the first treatment, and there had been consistent negative results of blood, glands, and cerebro-spinal fluid.

2. There had been no clinical signs or symptoms of any sort during these twelve months, and it would therefore appear probable that the disease had been arrested at the time of the first treatment.

3. Both patients live at Nakibira, a village in the cleared part of the sleeping sickness infected area on the Mpologma River, from which place, however, a succession of fresh infections have been derived (Cases 36, 37, 66, 67, and 68).

4. Investigation showed that the people from this village were crossing to an uncleared and heavily fly-infested promontory, Budobo, for the purpose of devil worship.

5. Acting on the belief that they were not relapses but reinfections, and early cases at that, we treated them by a single intravenous injection of arsenic. Up to the present date they both remain quite well, and blood, glands, and cerebro-spinal fluid are completely negative. (Another case treated with plain serum, who also comes from Nakibira, showed trypanosomes in glands, and he also is possibly a reinfection.)

In view of a suggestion made to us by Dr. Shaw Mackenzie of King's College, that the results obtained from serum treatment might be due to the stimulation of fat splitting by the autogenous serum, we have treated a number of cases by injecting the serum intramuscularly instead of intrathecally. The number so treated, however, is too small for any conclusions to be drawn from them. Dr. Shaw Mackenzie also gave us two preparations to try—"A" and "B"—on which we are experimenting; further, he suggests that autogenous serum is one of the best stimulants of lipase.

In our endeavour to ascertain clinically the most satisfactory procedure we have used other methods; these are set out in Table VI, which is again self-explanatory.

TABLE VI.—Showing all Cases Treated, Method Employed, and Result to Date.

No.	Method.	Total Treated.	Alive and Well.	Dead or Relapsed.	Number Missing.
1	Intrathecal serum	41	31	8	2
2	Plain serum—that is, no preliminary drug injection	4	3	1*	0
3	Non-autogenous serum: injected intrathecally or intramuscularly	7	4	3	0
4	Intramuscular serum—as 1, but intramuscularly†	7	5	1	1
5	Drug only intravenously	5‡	2	3	0
6	Drug direct into spinal canal	2	0	2	0

* Possibly reinfection. See report.

† See Shaw Mackenzie's suggestions.

‡ See Table II.

Towards the end of 1920 Dr. Ashton Bond of the Church Missionary Society, Toro, at our request treated some cases by the salvarsanized serum method. He writes as follows (January 31st, 1922):

"About two months ago I was at Katwe and Kazinga, where the sleeping sickness cases mostly are. I saw a number of those whom we treated with intravenous neo-kharsivan and intrathecal injections of serum (about eighteen months ago) and in most cases there was general improvement of general health and also the glands had mostly become so small as to be hardly palpable, or else were not palpable at all."

Bond has, in addition, treated 12 other cases; after an average period of twelve to eighteen months these were re-examined, and the following report sent to us about them: "Dead, 2; 'alive and well,' 5; and migrated to Belgian Congo, 5." (The latter are therefore probably quite well.)

Apart from the appended figures we have, since the beginning of 1922, treated some 200 cases at the suggestion of the Uganda Government. These we have grouped under various treatments as follows:

1. Intrathecal salvarsanized serum.
2. Intramuscular salvarsanized serum.
3. Intramuscular plain serum.
4. Intrathecal plain serum.
5. Non-autogenous intrathecal serum.
6. "A" (Shaw Mackenzie) intravenously only.
7. "B" (Shaw Mackenzie) intravenously, followed by serum.
8. "B" (Shaw Mackenzie) intravenously only.
9. "B" (Shaw Mackenzie) intramuscularly only.

The study of these cases should provide an instructive commentary on the efficacy of the treatment we advocate.

We wish to express our deep obligation and thanks to Dr. C. A. Higgins, P.M.O. Uganda, for permission to publish this report, and also for his great assistance in enabling us to

carry out this method on a large scale; also in Uganda to Drs. Mary Martin, Griffin, Bond, and Rawson; and in England we are deeply indebted to Professors Simpson and Eyre and to Dr. Shaw Mackenzie for their very valued interest and assistance.

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HISTOLOGICAL CONDITIONS IN A CASE OF ADDISON'S DISEASE.

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It is not easy to find any detailed description of the microscopical appearance of the organs in Addison's disease; the following details may therefore be of interest, more especially in view of the prominent part that is being assigned to the endocrine organs at the present time.

History.—The patient was a storeman, aged 42. In September, 1921, he began to suffer from indigestion accompanied by vomiting, and about the same time his wife noticed that his skin began to darken; she stated that the deep bronze colour noted on his admission to hospital was reached within a few weeks. In January, 1922, the patient gave up work, and took to his bed on account of progressive weakness; at this time he also complained of pains in his limbs and chest, and was treated for "influenza." On February 14th, 1922, he was admitted to hospital suffering from extreme weakness. He had had no previous illness except severe influenza thirty years ago. The family history is good and he has five healthy children.

Condition on Admission.—The patient was emaciated, although well built and muscular. He was extremely weak, and sweated freely on the slightest movement. Temperature 94° F., but no shivering. The skin was brown all over, the pigment being most marked over the hands, face, penis, scrotum, nipples, and anterior folds of the axilla; there were also brown spots within the cheeks. There was some deep tenderness over the liver; no superficial abdominal hyperaesthesia. There was slight dullness over the apex of the right lung. Knee and ankle jerks absent; flexor plantar reflex. The urine was alkaline, sp. gr. 1026; otherwise nothing abnormal detected. Respirations 20, shallow. Circulation: Radial pulse not felt; blood pressure (by auscultatory method) 55 mm. Hg; blood film normal. A blood count showed red blood corpuscles 4,800,000; haemoglobin 65 per cent.

The temperature rose to 98° F. on February 15th. On the morning of the 18th, the fourth day after admission, he suddenly became weaker and died.

Post-mortem Report.

Lungs: Old pleural adhesions present over the whole of the right lung; a few scars of old healed tubercle at right apex. Bronchial glands show no evidence of tubercle. Heart: 230 grams, normal. Liver: 1,450 grams, slightly nutmeg. Gall bladder: Distended; contains a single small black stone; no evidence of inflammation. Spleen: 200 grams, moderate perisplenitis. Kidneys: 330 grams, normal.

Suprarenals.—Right, 16 grams; left, 22 grams. The right is small and fibrous, the left shows much fibrosis and some areas of caseating material. No evidence of accessory suprarenal tissue.

Microscopical Appearance of Organs.

The material obtained at autopsy was fixed immediately in formol-acetic-Müller, and embedded in paraffin; the sections were stained with Scott's haematoxylin and Biebrich scarlet, with Mallory's connective tissue stain, with Weigert's resorcin-fuchsin stain, and by the Ziehl-Neelsen method for the tubercle bacillus.

Suprarenal.—Only one small area of cortical tissue found involved in a chronic tuberculous process with round-cell infiltration showing an unusually high percentage of plasma cells. There was much fibrosis, some calcification, and formation of many giant cell systems. The cells of the cortical tissue were of the type belonging to the zona fasciculata, many of them spherical with strongly eosinophil cytoplasm and excentric nuclei; other cells were very irregular, with poorly staining nuclei. The unusual appearance of these cells might have been due to post-mortem changes, but more probably indicates the breakdown of the last remnants of true cortical tissue. No medullary tissue was found. The surrounding fat was unusually rich in small round cells. A small ganglion just outside the organ showed some cellular degeneration and pigment deposition.

Pancreas.—No gross lesion was detected. The islets of Langerhans appeared normal, and contained some lymphocytes. The organ was extremely vascular, and there was some fibrous increase in the blood vessel walls.

Thyroid.—The organ was not so vascular as usual. There was very little intervascular parenchyma, but frequent aggregations