CCX. CARBOHYDRATE METABOLISM IN HUMAN TRYPANOSOMIASIS.

By ARTHUR WORMALL¹.

From the Human Trypanosomiasis Institute, Entebbe, Uganda.

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DURING recent years much attention has been directed to the study of blood-sugar changes during trypanosomiasis in animals such as the guinea-pig, rat and rabbit, and it has been considered by many that the changes noted play a significant rôle in the pathogenesis of this disease. The observations of Schern [1925] showed that the life of trypanosomes *in vitro* could be prolonged appreciably by the addition of dextrose or laevulose, and that the serum and the liver of normal animals could reactivate trypanosomes which had almost become motionless, whereas the serum and liver of animals which were in the last stages of trypanosomiasis had much less reactivating power. This author concluded that in trypanosomiasis the blood-sugar and the liver-sugar are gradually used up by the trypanosomes and that a very important pathogenic action of the trypanosomes is a disturbance of the power of the liver to store glycogen, accompanied by a significant hypoglycaemia [*cf.* also review by Schern, 1927]. The same author [1928] found that rabbits and a horse infected with *T. equinum* sometimes showed a marked hypoglycaemia and at other times a hyperglycaemia. Scheff [1928; 1929], as a result of experiments with rats, brought forward similar evidence and concluded that the consumption of sugar and oxygen by the trypanosomes plays a very important rôle in the metabolic disturbance of the host; this disturbance of normal metabolic processes and a state of partial asphyxia are followed, according to Scheff, by an acidosis which contributes to a diminution in the reaction capacity of the host.

Other authors have recorded a hypoglycaemia in rats, mice, guinea-pigs and similar animals infected with trypanosomes, but they are not in complete agreement as to the significance of the phenomenon. Regendanz and Tropp [1927] found that a marked hypoglycaemia exists in rats infected with trypanosomes only in the premortal stages, and conclude that death in these infected rats is not due to a lack of sugar. Regendanz [1929] similarly found that the decreases in the blood-sugar of monkeys infected with *T. rhodesiense* did not run parallel with the number of parasites in the blood. Fenyvessy [1926], Cordier [1927], Knowles and Das Gupta [1928], and Fenyvessy and Scheff [1930], amongst other authors also record a hypoglycaemia in trypanosomiasis of guinea-pigs, rats, *etc.* Dubois and Bouckaert [1927] and Bruynoghe,

¹ Seconded from the Department of Physiology, the University of Leeds.

Dubois and Bouckaert [1927] reach the conclusion that the hypoglycaemia is of little or no clinical significance, but Dubois [1928] considers that in certain acute cases of trypanosomiasis in guinea-pigs and mice, death is due to this lowering of the blood-sugar. Zotta and Radacovici [1929], using guinea-pigs infected with *T. brucei*, obtained marked variations in blood-sugar with a constant premortal hypoglycaemia; these authors, however, state that the latter phenomenon is not specific for trypanosomiasis but occurs in a large number of diseases. Linton [1930], working with rats infected with *T. equiperdum*, observed a normal blood-sugar value until a very late period of the disease; the liver-glycogen was found to be markedly decreased. The same author [1929] had previously recorded a normal blood-sugar in rats infected with *T. lewisi*. The relatively enormous sugar consumption by trypanosomes *in vitro* has been well demonstrated by Yorke, Adams and Murgatroyd [1929], who showed that 0.25 cc. of heavily-infected mouse-blood (*T. rhodesiense* infection) when added to 5 cc. of sheep-serum to which glucose had been added caused the disappearance of between 2 and 2.5 mg. of glucose in one hour.

Other authors have investigated the question of excess lactic acid production in trypanosomiasis. Kligler and Geiger [1928] found that in this disease the blood-lactic acid level in the rat shows a progressive rise and that this increase runs parallel with the increase in the number of trypanosomes (*T. evansi*) in the blood. Kligler, Geiger and Comaroff [1929], in a continuation of these investigations, concluded that the increased lactic acid production, as a result of the activities of the trypanosomes, results in an exhaustion of the alkali reserve [cf. also Geiger, Kligler and Comaroff, 1930].

These studies of the blood-sugar changes in trypanosomiasis indicate that some disturbance of the normal metabolism of sugar occurs in this disease. Most of the observations have been made, however, on small animals and in many instances with trypanosomes which differ markedly from those pathogenic to man, and it would be unwise to assume, without further evidence, that the results would be applicable to trypanosomiasis in man. Any disturbance of this type in the case of man would, however, be of clinical significance, although it would not necessarily contribute, directly or indirectly, to the decline of the host. No observations appear to have been made so far on the blood-sugar changes in human trypanosomiasis¹, although Sicé [1930] recorded a diminution in the c.s.f.-sugar in nervous trypanosomiasis, with a return, in the majority of cases, to more normal values when treatment was given.

In the present investigation, determinations of the resting blood-sugar values and the sugar tolerance for natives with trypanosomiasis and the values

¹ Since this work was completed and a preliminary report made (Annual Report for 1931 of the Institute for Human Trypanosomiasis Research, Entebbe, Uganda), a review has appeared in the April number for 1932 of the Tropical Diseases Bulletin [29, 285] of a paper by Walravens [Ann. Soc. Belge de Med. Trop. 1931, 11, 213]. This author has studied the blood-sugar of 12 sleeping sickness patients before, during and after treatment and has observed no definite variations in the blood-sugar titre during these periods. In two of the patients, the titre was very low before treatment.

for normal natives have been made. The first study and the main part of this investigation was made on sleeping sickness patients kept in the hospital attached to the laboratory, and the controls were natives employed in the laboratory. The latter were selected in such manner that they might be regarded as normal in the sense that they were free from trypanosomiasis; probably every one had had malaria at some time and the majority had been infected with syphilis. The patients were given a liberal diet, the food being selected so that qualitatively and, as far as possible, quantitatively it resembled that of the controls. With the patients, and with practically all the controls, it was possible to be confident that no food had been taken in the morning before samples of blood were taken for fasting blood-sugar determinations. Repeated examinations were made on each patient and the effect of treatment was noted. Twelve patients were thus examined over varying lengths of time, the number available being limited partly by the accommodation but mainly by the disinclination on the part of the native to stay in hospital. With one notable exception, it was extremely difficult to persuade the patients to stay for longer than one month under observation, and as soon as an improvement in their general condition occurred as a result of treatment, they expressed a very strong desire to return to their homes. The results of these laboratory investigations, in spite of the rather small number of patients examined, are considered of value as a more or less systematic study of these selected cases of human trypanosomiasis. The original programme included determinations of the resting blood-sugar of sleeping sickness patients and normals in the West Nile area of the Uganda Protectorate, where it was hoped that a large number of treated and untreated cases might be studied. Owing to circumstances over which the author had no control, however, it was not possible to carry out the second half of this programme.

All the blood-sugar determinations were made by the Hagedorn and Jensen method [1923] [*cf.* Beaumont and Dodds, 1930], this method being selected as the most suitable method for work in the field. A few drops of capillary blood were collected, early in the morning, from a finger of the fasting patient (or control), no food having been taken by the subject since the previous evening. This blood was used immediately for sugar determinations. Duplicate determinations were made with each sample, and the figures given here represent the mean of the two values obtained.

EXPERIMENTAL.

Sleeping sickness patients were selected by the Medical Officers in various parts of Uganda and were sent to Entebbe¹. These patients were kept in the small hospital attached to the Human Trypanosomiasis Institute at Entebbe,

¹ The author would like to take this opportunity of thanking Major G. J. Keane, Director of Medical and Sanitary Services, the Uganda Protectorate, and Dr S. W. T. Lee for their generous help in this and other matters. In particular, he is indebted to them for the details of the previous history of these patients and for the very satisfactory arrangements made for him by the Medical Department when the author went on safari to the West Nile district in 1931.

and samples of blood were taken from each patient every day (except Sundays) and examined for trypanosomes, malarial parasites, *etc.* Repeated examinations were also made by the red cell adhesion test [Duke and Wallace, 1930; Wallace and Wormal, 1931] and, on occasions, the C.S.F. was collected and examined. In other cases, the blood of the patient was injected into monkeys, guinea-pigs or mice and further examination of the trypanosomes made. The assumption was made that in all these cases the infection was due to *T. gambiense*, since *T. rhodesiense* infections in man appear to be of very infrequent occurrence in Uganda (*cf.*, however, the report of a case of *T. rhodesiense* infection in man in Uganda by Duke [1930]). The results of the red cell adhesion test, the behaviour of the trypanosome in monkeys and other animals (*i.e.* duration of infection and the result of drug treatment) and the symptoms of the patient were, with one possible exception, in entire agreement with the views that the trypanosome concerned was *T. gambiense*. The possible exception was the infection in the patient Kibuka; this matter will be discussed more fully in a subsequent paper [Wormal, 1932].

The patients had a mixed diet which was particularly rich in carbohydrate, the main bulk of the food being taken in the form of sweet potatoes, muhogo flour and sugar cane. Fish was given on most days and meat twice a week. The daily ration included also small quantities of milk, tea and salt. With most of these patients, drug treatment was started after the patient had been at Entebbe for about three or four weeks, the dates of the injections being given in Tables I and II. Treatment during the blood-sugar investigations consisted of the intravenous injection of a solution containing 1 g. of Bayer 205, except in one case where tryparsamide was used. Regular injections of tryparsamide and Bayer 205 were subsequently given to all the patients. At one period during this study, one of the patients developed malaria and was treated with quinine. No blood-sugar determinations were made on this patient during this period or on the seven days following quinine administration.

The patients can be divided into three groups, although it is not suggested that there should be any sharp differentiation between these groups:

(a) *Those with little or no previous drug treatment:*

Sumba—no treatment.

Lisuwa, Manika, Oditi and Otenyi (with one injection of tryparsamide each).

Kibuka (with one injection of tryparsamide 2 years previously).

(b) *Those with a moderate amount of drug treatment:*

Orachi, Osanda and Atoyo.

(c) *Old-standing cases (with previous drug treatment):*

Wanjira, Zenesio and Achan.

Age, sex and previous history of these patients.

Sumba. Male, age 25–30 years. Trypanosomes first detected (in the blood) 24. xi. 30. No treatment given prior to arrival at Entebbe, 8. xii. 30.

Lisuwa. Male, age 40. Trypanosomes first detected in Feb. 1931 (gland juice). Received 2.5 g. tryparsamide on 18. ii. 31. Arrived at Entebbe, 28. ii. 31.

Manika. Male, age 20. Trypanosomes first detected in gland juice in Sept. 1930. Received 2.5 g. tryparsamide on 15. ix. 30. Arrived at Entebbe, 27. ix. 30.

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Odiiti. Male, age 19. Trypanosomes first detected in the gland juice in Feb. 1931. Received 2.5 g. tryparsamide on 18. ii. 31. Arrived at Entebbe, 28. ii. 31.

Otenyi. Male, age 26. Trypanosomes first detected in the gland juice early in Dec. 1930. Received 2.5 g. tryparsamide on 5. xii. 30. Arrived at Entebbe on 21. xii. 30.

Kibuka. Male, age 25-30. Trypanosomiasis diagnosed in 1928, but no further official details were available. (Patient stated that he received one injection only in 1928; none in 1929 or 1930.) Trypanosomes detected in the blood and gland juice on 4. iii. 31. Arrived at Entebbe, 8. iii. 31.

Orachi. Male, age 29. Trypanosomes first detected in the gland juice. Received injections of tryparsamide (2.5 g. each time) on 7. xi. 30, 14. xi. 30, 2. xii. 30 and 9. xii. 30. Arrived at Entebbe, 21. xii. 30.

Osanda. Male, age 10. Trypanosomes first detected in the gland juice 1930. Received 20 injections of tryparsamide (total of 55 g.) from 18. ii. 30 to 15. ix. 30; over practically the whole of this period gland punctures revealed the presence of trypanosomes. This infection appeared, therefore, to be resistant to treatment with tryparsamide, and experiments carried out by Dr J. M. Wallace showed that guinea-pigs infected with this trypanosome were not completely cured by the normal sterilising doses of atoxyl. A large number of adhesion tests were carried out with the serum of this patient and others with the trypanosomes of animals inoculated with his blood, and in all these tests the infection appeared to be a typical *gambiense* infection.

Atoyo. Male, age 8. Trypanosomes first detected in the gland juice in June, 1929. Received 8.5 g. tryparsamide and 1 g. Bayer 205 from 21. i. 31 to 9. iv. 31. Arrived at Entebbe, 22. iv. 31.

Wanjira. Male, age 35. Trypanosomiasis diagnosed in 1926. Received 14 g. tryparsamide and 4 g. Bayer 205 in 1927, 42 g. tryparsamide in 1928, and 6 g. tryparsamide in 1929. In 1930, he received 12 g. tryparsamide during Sept., Oct. and Nov. Sent to Entebbe as a possible case of relapse, 8. xii. 30.

Zenesio. Male. Early history not available. 14 g. tryparsamide and 4 g. Bayer 205 given from May to Sept. 1930. Trypanosomes present in the blood on 12. v. 30 and on several subsequent occasions. Arrived at Entebbe in May, 1930.

Achan. Female, age 40. Trypanosomes detected in gland juice in Aug. 1929. From Aug. to Nov. 1929, she received 35 g. tryparsamide, and from 26. viii. 30 to 9. iv. 31 she received 32 g. tryparsamide and 1.5 g. Bayer 205. Arrived at Entebbe, 22. iv. 31.

Wanjira and Sumba were sent from Tororo (East Province, Uganda); Atoyo and Achan came from Gulu, North Province; all the other patients came from the West Nile district of the Uganda Protectorate.

The results of the fasting blood-sugar determinations with the sleeping sickness patients are given in Tables I and II. The date of each examination and the results of the examination of blood films for trypanosomes are also recorded. Whenever drug treatment (the intravenous injection of a solution of Bayer 205 or tryparsamide) was given, reference is made to it in the Tables in order that a direct study might be made of the influence of this treatment on the fasting blood-sugar level. For convenience the results with patients of group (a) are given in Table I and those for groups (b) and (c) in Table II, but it is not suggested that this division into groups is very clear cut, or that it has any special significance. Table III gives average fasting blood-sugar values for these patients.

In these blood-sugar investigations it was necessary to have, for purposes of comparison, satisfactory values for the fasting blood-sugar of natives of Uganda, and in Table IV the results of such determinations with 12 "normal" natives (four determinations with each native, made at approximately weekly intervals) are given. These control natives were normal in the sense that they did not suffer from trypanosomiasis; all of them were apparently healthy, and

Table I. *Fasting blood-sugar values with trypanosomiasis patients in group (a).*

Sugar values as mg. per 100 cc.								
Date	Blood-sugar	Blood examination*	Date	Blood-sugar	Blood examination	Date	Blood-sugar	Blood examination
Sumba			Lisuwa			Manika		
16. xii. 30	82	+	5. iii. 31	106	+	29. ix. 30	95	-
17. xii. 30	97	+	10. iii. 31	98	+	3. x. 30	98	-
19. xii. 30	82	+	13. iii. 31	102	+	10. x. 30	97	-
22. xii. 30	82	+	18. iii. 31	91	+	13. x. 30	88	-
24. xii. 30	94	+	24. iii. 31	91	+	16. x. 30	99	-
29. xii. 30	89	+	26. iii. 31	98	+	20. x. 30	99	-
3. i. 31	72	+	31. iii. 31	99	+	23. x. 30	1 g. Bayer 205	-
9. i. 31	83	+	8. iv. 31	94	-	24. x. 30	100	-
16. i. 31	1 g. Bayer 205	-	9. iv. 31	1 g. Bayer 205	-	30. x. 30	88	-
20. i. 31	90	-	15. iv. 31	99	-	31. x. 30	1 g. Bayer 205	-
24. i. 31	100	-				1. xi. 30	95	-
29. i. 31	93	-				6. xi. 30	97	-
6. ii. 31	95	-						
Odit			Otenyi			Kibuka		
5. iii. 31	105	+	22. xii. 30	69	-	10. iii. 31	93	-
10. iii. 31	96	+	24. xii. 30	86	-	13. iii. 31	100	-
13. iii. 31	100	+	29. xii. 30	93	+	18. iii. 31	90	-
18. iii. 31	87	+	3. i. 31	96	+	20. iii. 31	1 g. Bayer 205	-
24. iii. 31	77	-	7. i. 31	1 g. Bayer 205	-	24. iii. 31	60	-
24. iii. 31	1 g. Bayer 205	-	9. i. 31	96	-	26. iii. 31	81	-
31. iii. 31	91	-				31. iii. 31	87	-
8. iv. 31	84	-				8. iv. 31	77	-
9. iv. 31	1 g. Bayer 205	-				9. iv. 31	1 g. Bayer 205	-
15. iv. 31	72	-				15. iv. 31	94	-

* Examination of wet and stained blood films for trypanosomes.

Table II. *Fasting blood-sugar values with trypanosomiasis patients of groups (b) and (c).*

Sugar values as mg. per 100 cc.								
Date	Blood-sugar	Blood examination	Date	Blood-sugar	Blood examination	Date	Blood-sugar	Blood examination
Osanda			Wanjira			Zenesio		
6. x. 30	77	+	16. xii. 30	99	-	29. ix. 30	57	-
8. x. 30	91	+	17. xii. 30	105	-	6. x. 30	69	-
10. x. 30	93	+	19. xii. 30	98	-	10. x. 30	70	-
13. x. 30	99	+	22. xii. 30	91	-	11. x. 30	1 g. Bayer 205	-
16. x. 30	90	-	24. xii. 30	97	-	13. x. 30	107	-
20. x. 30	93	+	29. xii. 30	100	-	16. x. 30	86	-
24. x. 30	82	-	3. i. 31	96	-	20. x. 30	77	-
25. x. 30	1 g. tryparsamide	-	9. i. 31	98	-	24. x. 30	79	-
30. x. 30	79	+	20. i. 31	101	-	30. x. 30	73	-
30. x. 30	1 g. Bayer 205	-	24. i. 31	101	-	1. xi. 30	85	-
1. xi. 30	99	-	29. i. 31	104	-	6. xi. 30	83	-
6. xi. 30	94	-	6. ii. 31	107	-	14. xi. 30	72	-
8. xi. 30	1 g. Bayer 205	-				25. xi. 30	74	-
14. xi. 30	91	-				27. xi. 30	86	-
21. xi. 30	1 g. Bayer 205	-						
25. xi. 30	87	-						
Orachi			Atoyo			Achan		
22. xii. 30	85	+	29. iv. 31	91	-	6. v. 31	79	-
24. xii. 30	90	+	6. v. 31	86	-	12. v. 31	77	-
29. xii. 30	86	+	12. v. 31	82	-			
3. i. 31	87	-						
7. i. 31	1 g. Bayer 205	-						
9. i. 31	78	-						

Table III. *Average values for fasting blood-sugar of trypanosomiasis patients.*

Patient	Blood-sugar as mg. per 100 cc.			
	Before treatment at Entebbe		Before and after treatment (all values)	
	No. of determinations	Average	No. of determinations	Average
Sumba	8	85	12	88
Lisuwa	8	97	9	98
Manika	6	96	10	96
Oditi	5	93	8	89
Oteryi	4	86	5	88
Kibuka	3	94	8	85
Osanda	7	89	12	90
Wanjira	12	100	12	100
Zenesio	3	65	13	78
Orachi	4	87	5	85
Atoyo	3	86	3	86
Achan	2	78	2	78

Table IV. *Fasting blood-sugar (mg. per 100 cc.) normals.*

	Determinations				Average
	1	2	3	4	
Lolenti	86	89	81	84	85
Joseph	107	93	95	98	98
Mikaili Mayanja	83	82	88	90	86
Butulumayo	88	94	85	85	88
Matayo Kiwanuka	92	85	102	99	94
Yusufu Kolokojo	99	94	96	100	97
Abinayo Kitakule	104	100	99	109	103
Yokana	97	101	98	92	97
Alajabu	89	92	93	88	90
Asiri Mutasa	77	95	75	82	82
Erika Kasozi	98	81	85	88	88
Isaka Serwangu	94	104	82	96	94

Table V. *Carbohydrate tolerance tests.*

Blood-sugar values (mg. per 100 cc.) after taking 50 g. glucose.

	Before glucose	$\frac{1}{2}$ hr. after glucose	1 hr.	1½ hrs.	2 hrs.	3 hrs.
Manika	98	111	166	141	107	100
Osanda 1)	91	137	131	124	108	91
„ (2)	90	104	100	102	88	77
„ (3)	93	125	121	90	70	91
Zenesio (1)	70	107	117	105	105	77
„ (2)	72	97	148	109	105	74
„ (3)	74	124	162	122	115	87
Sumba (1)	97	102	127	119	112	94
„ (2)	94	104	127	135	130	105
Lisuwa (1)	94	123	152	114	89	87
„ (2)	99	153	166	97	92	93
Normal native (1)	84	109	101	100	88	77
„ (2)	86	161	201	181	115	90
„ (3)	81	123	111	106	74	82
„ (4)	91	125	121	110	89	90
„ (5)	92	131	137	129	92	85

were not suffering from malaria during the period when their blood-sugar values were determined.

In view of the suggestion made by several authors that in trypanosomiasis of small animals there is a general disturbance of carbohydrate metabolism involving a derangement of the storage of glycogen by the liver, it was decided to make glucose tolerance tests with certain of the sleeping sickness patients and normal natives. Table V gives the results of the tests with the patients and a few typical results with controls. None of the patients and only one of the controls (normal native No. 2 in the Table) passed sugar in the urine during these tolerance tests.

DISCUSSION.

The results of determinations of the fasting blood-sugar of natives suffering from trypanosomiasis (Tables I and II) indicate that in this condition the fasting blood-sugar is not markedly lower than that for a native who does not suffer from this disease (*cf.* Table IV for the controls). Marked variations from time to time in the fasting blood-sugar of any one patient certainly occur, but such variations also occur with normal natives. The fluctuations are perhaps somewhat greater with the patients, but the difference between the patients and the controls in this respect does not appear to be significant. Nor are the average values for the sleeping sickness patients very definitely lower than the average values for the control normal natives (*cf.* Tables III and IV), and it is only in isolated instances that there is any suggestion of a marked hypoglycaemia.

It is perhaps difficult to decide what might be regarded as the lower limit for normal fasting blood-sugar values. With the controls used in this work (natives of various tribes in Uganda) the lowest value was 75 mg. per 100 cc. In some investigations carried out on two tribes in Kenya (Special Report Series, No. 155, of the Medical Research Council, Edited by J. B. Orr and J. L. Gilks, 1931), figures of 77 to 136 mg. per 100 cc. are given for the fasting blood-sugar values of normal natives, with perhaps slightly lower values in cases of tropical ulcer (one low value of 65 mg.). In the course of another investigation, Dr F. W. Vint and Dr D. Harvey in Nairobi, using a modification of the Hagedorn and Jensen blood-sugar method, obtained, with natives, fasting blood-sugar values which were usually about 100 mg., or slightly more, per 100 cc. The lowest value in 25 determinations was 75 mg. per 100 cc. (private communication from Dr Harvey in 1931). From these figures for normal natives in Uganda and Kenya, it might be considered, therefore, that the following values for the sleeping sickness patients investigated in the work described here were subnormal; 57, 69, 70, 72 and 73 mg. per 100 cc. with Zenesio, 60 mg. with Kibuka and 69 mg. with Otenyi. These low values, although they may offer some support for the view that there is a hypoglycaemia in human trypanosomiasis, do not occur sufficiently often to suggest a very marked disturbance of carbohydrate metabolism in this disease. The results of the glucose tolerance tests with the patients and a few

of the controls (Table V) also indicate that, in the early stages of trypanosomiasis at least, there is no very serious inability of the liver to deal with glucose. Several of the sugar tolerance curves were of the lag type, and this finding is in agreement with the observations of Bhatia and Coelho [1925], who carried out tests on Indians. The latter authors obtained values between 83 and 246 mg. per 100 cc. for the fasting blood-sugar of these people accustomed to a vegetarian diet.

On theoretical grounds alone it is perhaps rather difficult to conceive of a hypoglycaemia in man due entirely to a heavy sugar consumption by the trypanosomes. With a supply to the body of 300 g. at the minimum and usually considerably more than 400 g. of carbohydrate daily in the form of food, it appears unlikely that the amount of sugar used by the trypanosomes would, in itself, result in any marked diminution in the fasting blood-sugar level or in the amount of glycogen stored in the liver and muscles of the patient. It may be, however, as has been suggested by several authors as a result of experiments on smaller animals, that the consumption of glucose by the trypanosomes leads indirectly (perhaps as a result of the production of certain metabolites) to a disturbance of the mechanism concerned with maintaining a minimum blood-sugar level, and it is perhaps only to be expected that these disturbances would not be manifested until the infection had been established for some time. For this reason it would be of interest to know whether there are any marked changes (diminution in glucose content, *etc.*) in the C.S.F. of patients in the advanced stages of sleeping sickness.

Intimately linked up with this problem of carbohydrate metabolism is the oxygen consumption of the trypanosomes, and it is not impossible that a serious disturbance of normal metabolic processes occurs as a result of the trypanosomes depriving certain organs and tissues of part of their supplies of carbohydrate and oxygen. In the course of this investigation in Uganda it was noticed that the blood taken from the finger of the trypanosomiasis patient was in practically every case considerably darker than samples of blood from the control natives. This difference was best observed when the blood was collected, with the minimum of shaking, in a very small conical test-glass containing a trace of potassium oxalate, or preferably when the blood was immediately sucked up under a layer of liquid paraffin into a capillary pipette containing potassium oxalate or sodium citrate, and observed against a white background. The darker, less oxygenated, bloods could then be picked out at once. Similar differences were observed in tests with samples of blood from monkeys infected with trypanosomes and normal monkeys. This darkness did not appear to be evident only when trypanosomes were present in the blood, since it was observed with these sleeping sickness patients when no trypanosomes could be detected in wet and stained blood films. Thus it does not appear to be due entirely to the using up for metabolic purposes of part of the oxygen of the oxyhaemoglobin by trypanosomes present in the sample of blood tested. If these samples were then shaken with air they became as red as the control

samples similarly shaken, but when they had stood again for a short time there was usually but not invariably more reduction in the blood from the sleeping sickness patients. With the blood of infected monkeys, and to a lesser extent with the human bloods which contained trypanosomes, this later reduction can undoubtedly be attributed to a diminution of the oxygen content as a result of the oxidation of glucose by the trypanosomes [*cf.* Yorke, Adams and Murgatroyd, 1929, p. 510]. In the instances where no significant number of trypanosomes are present in the blood, these observations seem to indicate a higher reducing power of the plasma. It was intended to carry out experiments along these lines, including determinations of the oxygen content and capacity of arterial and venous bloods of the sleeping sickness patients and the reducing power of the serum or plasma, but unfortunately it was not possible to complete these investigations.

SUMMARY.

1. In view of the findings of various authors, that in trypanosomiasis of small animals there is a significant hypoglycaemia, which according to some is partially, if not entirely, responsible for the decline of the host, repeated blood-sugar determinations have been carried out on 12 sleeping sickness patients in Uganda (*T. gambiense* infections).

2. Determinations carried out with these patients and with suitable controls (natives not suffering from trypanosomiasis) over varying periods of time indicate that in man there is no general hypoglycaemia during the earlier stages of this disease. In certain instances, however, a definitely low blood-sugar value was obtained, these low values being significantly lower than the lowest value with a normal native.

3. Treatment of these patients with Bayer 205 gives variable results in relation to the blood-sugar; sometimes there is a fall, sometimes a rise, and in other cases no change in the blood-sugar level. With the patient with the lowest blood-sugar values, the injection of 1 g. Bayer 205 resulted in a speedy return to normal (or perhaps slightly high) values.

4. No relationship could be demonstrated between the blood-sugar level and the presence in or absence from the blood of trypanosomes.

5. Glucose tolerance tests carried out on a few of the patients and some of the controls do not suggest that in trypanosomiasis there is a very marked impairment of the capacity of the liver to deal with glucose.

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