MUSCULAR EXERCISE IN DIABETES MELLITUS.

BY

K. S. HETZEL, M.B., B.S.ADELAIDE,

M.R.C.P.LOND.,

ASSISTANT IN THE MEDICAL UNIT, UNIVERSITY COLLEGE HOSPITAL.

IN conjunction with Mr. C. N. H. Long, M.Sc., experiments are in progress on the effect of muscular exercise in patients suffering from diabetes mellitus. We hope shortly to publish the results in full dealing with lactic acid, acidosis, and the respiratory metabolism. This preliminary communication on the blood sugar and urinary changes brought about by exercise is written more from the clinical standpoint.

Allen and his followers have insisted that in the treatment of patients suffering from diabetes mellitus it is beneficial for them during the time of their dietetic adjustment and subsequently to take moderate exercise and not to remain in bed for prolonged periods. The present experiments show that in a diabetic whose diet contains a moderate proportion of carbohydrate and who receives an adequate supply of insulin the effect of exercise is beneficial, rapidly lowering the blood glucose to a normal level and diminishing the production and therefore the excretion of ketones and so rendering tissue metabolism more complete. But in a patient even with adequate carbohydrate foodstuff or carbohydrate stores whose diabetes is moderately severe and who is without sufficient insulin, endogenous or exogenous, exercise produces little or no effect on blood glucose and ketosis is increased.

The patients who are the subjects of these experiments had been treated for some time previous to the experiments by dietetic restriction and adjustment with insulin, and they are now continuing their ordinary routine life.

The exercise which has been done is that of "standing running" in which the subject doubles rapidly on his toes with the elbows flexed and the arms drawn to the side of the chest, but he does not move forward and he maintains his position on about one to two square feet of floor space in the laboratory, drawing the knees well up. The number of steps a minute is noted, the patient keeping time with a metronome which is set to a certain rate; in this way the subject keeps up the rate of exercise for the stipulated time. The exercise done—for instance, 156 steps per minute—is only moderate, and a normal subject can readily do it for the time over which these patients were exercised, and with no great fatigue. By "all out" exercise is meant that the subject doubles as rapidly as he can so as just to last out the time, at the end of which he is "done." Samples of blood and urine are taken at intervals before and after the exercise. A rough estimate of the amount of urinary ketones has been made by the depth of the colour which is attained in one minute by the Rothera or sodium nitro-prusside test. These are designated $\pm$ for a faint trace, + trace, ++ and +++ for deeper colorations. All the samples of urine are examined at the same time and set side by side so as to get the comparative variation in colour produced.

CASE I.

Male, aged 36; decorator. Weight 10 st. 10 lb. Diet 2,090 calories: Carbohydrate 69 grams, protein 77 grams, fat 167 grams. Insulin 30 units a day, given in two doses, of 20 and 10 units each. This patient had received insulin for seven weeks and he had been discharged from hospital on the above diet for three weeks when the first experiments—for example, experiments B and E—were done. The experiments were made at intervals over a period of five and a half months. This man leads an active life and he feels and looks a fit man.

EXPERIMENT A.—Control for ordinary fall of blood sugar without exercise. Without insulin for thirteen hours—last meal two hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10 a.m.	Resting	0.210	0.06%	$\pm$
10.30 a.m.	Resting	0.190		
11.10 a.m.	Resting	0.180	Nil	$\pm$
11.35 a.m.	Resting	0.155		
12.10 p.m.	Resting	0.135	Nil	$\pm$
12.55 p.m.	Resting	0.115	Nil	$\pm$

EXPERIMENT B.—Insulin two and a half hours and food two hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.30 a.m.	Resting	0.110	Nil	Nil
10.50 a.m.	Exercise $3\frac{1}{2}$ mins. "standing running" at 210 steps per minute			
11 a.m.	Recovery	0.115		
11.15 a.m.	Recovery	0.105		
11.30 a.m.	Recovery	0.105		
11.45 a.m.	Recovery	0.095	Nil	Nil

EXPERIMENT C.—Insulin three and a half hours and food three hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.25 a.m.	Resting	0.150	Nil	Nil
10.33 a.m.	Exercise 1 min. at 156 steps per minute			
11.5 a.m.	Recovery	0.140		
11.21 a.m.	Exercise 8 mins. at 155 steps per minute			
11.31 a.m.	Recovery	0.115		
12.1 p.m.	Recovery	0.105		
12.35 p.m.	Recovery	0.105	Nil	Nil

EXPERIMENT D.—Insulin and food (with extra carbohydrate) three and a half and three hours before respectively.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.30 a.m.	Resting	0.195	Trace	+
10.45 a.m.	Exercise 3 mins. at 156 steps per minute			
10.51 a.m.	Recovery	0.150		
11.21 a.m.	Recovery	0.115		
11.35 a.m.	Exercise 5 mins. at 156 steps per minute			
11.43 a.m.	Recovery	0.110		
12.35 p.m.	Recovery	0.115	Nil	$\pm$

EXPERIMENT E.—Last insulin fourteen hours and last meal two and a half hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.40 a.m.	Resting	0.240	0.44%	++
10.46 a.m.	Exercise $3\frac{1}{2}$ mins. at 210 steps per minute			
10.54 a.m.	Recovery	0.140		
11.5 a.m.	Recovery	0.120		
11.30 a.m.	Recovery	0.120		
12 noon	Recovery	0.120		
12.50 p.m.	Recovery	0.110	Faint trace	Nil

EXPERIMENT F.—Insulin omitted with evening meal eleven hours previously, but taken with breakfast two hours before experiment.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.10 a.m.	Resting	0.290	0.09%*	Nil
10.15 a.m.	Exercise $\frac{1}{2}$ min. at 156 steps per minute			
10.47 a.m.	Recovery	0.255		
11 a.m.	Exercise $4\frac{1}{2}$ mins. at 156 steps per minute			
11.10 a.m.	Recovery	0.195		
11.40 a.m.	Recovery	0.145		
12.10 p.m.	Recovery	0.110	0.16%†	Nil

* Total 0.05 gram. † Total 0.41 gram.

EXPERIMENT G.—Without insulin for twenty-seven hours; last meal two and a half hours before.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.20 a.m.	Resting	0.195	Trace	Nil
10.38 a.m.	Exercise 8 mins. at 156 steps per minute			
10.48 a.m.	Recovery	0.140		
11.8 a.m.	Recovery	0.100		
11.32 a.m.	Recovery	0.100		
12.2 p.m.	Recovery	0.095		
12.18 p.m.	Recovery	0.100	Nil	Nil

EXPERIMENT H.—Without insulin for fifteen hours; last meal two and a half hours before.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.55 a.m.	Resting	0.140	Nil	Nil
11.10 a.m.	Exercise 104 secs. "all out"			
11.17 a.m.	Recovery	0.125		
11.53 a.m.	Recovery	0.125	Nil	Nil
11.57 a.m.	30 grams of glucose by mouth			
12.27 p.m.	Resting	0.180		
12.31 p.m.	Exercise 101 secs. "all out"			
12.35 p.m.	Recovery	0.190		
1.13 p.m.	Recovery	0.135	Nil	Nil

EXPERIMENT I.—Without insulin for twenty-seven hours; last meal three hours before.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.35 a.m.	Resting	0.190	Trace	Nil
10.48 a.m.	Exercise 30 secs. at 156 steps per minute			
11.15 a.m.	Recovery	0.140		
11.30 a.m.			Nil	Nil
11.33 a.m.	Exercise 5 mins. at 156 steps per minute			
11.45 a.m.	Recovery	0.105		
12.5 p.m.	Recovery	0.090		
12.25 p.m.	Recovery	0.085		
12.45 p.m.	Recovery	0.090	Nil	Nil

Experiment A is shown graphically by curve A in Fig. 1. Fig. 1 also demonstrates the results of Experiments B and E.

CASE II.

Male, aged 21; clerk. Weight 9 st. 6 lb. Diet 1,840 calories: Carbohydrate 52 grams, protein 92 grams, fat 140 grams. Insulin 50 units a day, in three doses of 20, 10, and 20 units each. Insulin had been given for twelve months before the experiments began. Three months before these experiments the diet and the insulin were increased to the above values. This subject is a severe case, and, although not as fit as Case I, he is active and he is able to do the exercise briskly.

EXPERIMENT P.—Insulin six hours and food five and a half hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
6.45 p.m.	Resting	0.075	Nil	±
6.55 p.m.	Exercise ½ min. at 156 steps per minute			
7.25 p.m.	Recovery	0.080		
7.35 p.m.	Exercise 1 min. at 156 steps per minute			
7.55 p.m.	Recovery	0.080		
8.5 p.m.	Exercise 3 mins. at 156 steps per minute			
8.38 p.m.	Recovery	0.085	Nil	Nil

C

EXPERIMENT Q.—Insulin five and a half hours and last meal five hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
6.5 p.m.	Resting	0.095	Nil	+
6.23 p.m.	Exercise 5 mins. at 155 steps per minute			
6.33 p.m.	Recovery	0.085		
7.23 p.m.	Recovery	0.075	Nil	±

EXPERIMENT R.—Without insulin for eleven hours; last meal five hours before.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
6.25 p.m.	Resting	0.145	Nil	+++
6.40 p.m.	Exercise 8 mins. at 156 steps per minute			
6.51 p.m.	Recovery	0.135		
7.21 p.m.	Recovery	0.110		
8.1 p.m.	Recovery	0.090	Nil	+

EXPERIMENT S.—Last insulin eleven hours and last meal five hours before.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
6.45 p.m.	Resting	0.160	Nil	+++
7.5 p.m.	Exercise 101 secs. "all out"			
7.6 p.m.	Recovery	0.155		
7.35 p.m.	Recovery	0.155		
8.6 p.m.	Recovery	0.150		
8.36 p.m.	Recovery	0.150	Nil	±

EXPERIMENT T.—Without insulin twenty-four hours; last meal five hours previous'y.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
6.10 p.m.	Resting	0.270	1.9%*	+++
6.35 p.m.	Exercise 3 mins. at 155 steps per minute			
6.43 p.m.	Recovery	0.250		
7.13 p.m.	Recovery	0.280		
7.30 p.m.	Recovery	0.280	1.85%†	+++

* Total 1.06 grams. † Total 5.25 grams.

EXPERIMENT U.—Without insulin for twenty-four hours; last meal five hours before.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
6.20 p.m.	Resting	0.220	0.28%*	++
6.27 p.m.	Exercise 5 mins. at 155 steps per minute			
6.34 p.m.	Recovery	0.225		
6.49 p.m.	Recovery	0.220		
7.19 p.m.	Recovery	0.215	0.78%†	+++

* Total 0.57 gram. † Total 0.40 gram.

EXPERIMENT V.—Without insulin for twenty-two hours; last meal three hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
10.50 a.m.	Resting	0.225	0.48%*	±
11 a.m.	Exercise 30 secs. at 156 steps per minute			
11.23 a.m.	Recovery	0.205	0.83%†	+
11.34 a.m.	Exercise 60 secs. at 156 steps per minute			
11.38 a.m.	Recovery	0.205		
11.58 a.m.	Recovery	0.210		
12.18 p.m.	Recovery	0.225	1.2%‡	+++

* Total 1.2 grams. † Total 0.68 gram. ‡ Total 1.62 grams.

The results of Experiments P, R, and V are represented graphically in Fig. 3.

CASE III.

Male, aged 56; tailor. Weight 9 st. 2 lb. Diet 1,940 calories: Carbohydrate 50 grams, protein 98 grams, fat 150 grams. Insulin 20 units a day in two equal doses. This subject had been stabilized on this diet with insulin for nearly twelve months when these results were obtained. He does the exercise fairly well, but he is not as active as the two younger subjects.

EXPERIMENT X.—Without insulin for eleven hours; last meal six hours before.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
7 p.m.	Resting	0.160	Nil	+
7.18 p.m.	Exercise 80 secs. "all out"			
7.22 p.m.	Recovery	0.155		
7.55 p.m.	Recovery	0.135		
8.25 p.m.	Recovery	0.135		
8.45 p.m.	Recovery	0.130	Nil	±

EXPERIMENT Y.—With insulin five hours and last meal four and a half hours previously (with extra carbohydrate).

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
1.45 p.m.	Resting	0.205	0.92%	+++
2.9 p.m.	Exercise 3½ mins. at 204 steps per minute			
2.15 p.m.	Recovery	0.200		
2.45 p.m.	Recovery	0.185		
3.15 p.m.	Recovery	0.170		
3.45 p.m.	Recovery	0.160	Trace	Nil

EXPERIMENT Z.—Without insulin for twenty-four hours; last meal five hours previously.

Time.		Blood Sugar per Cent.	Urine.	
			Glucose.	Ketones.
7 p.m.	Resting	0.175	Trace	±
7.20 p.m.	Exercise 80 secs. "all out"			
7.24 p.m.	Recovery	0.160		
7.55 p.m.	Recovery	0.135		
8.25 p.m.	Recovery	0.120		
8.55 p.m.	Recovery	0.115	Nil	Nil

In the diabetic patient at rest the hyperglycaemia due to ingestion of food tends to decrease slowly. This fall in blood sugar is slower the more diabetic the patient is—that is, the less endogenous insulin there is present capable of metabolizing the glucose. This gradually decreasing hyperglycaemia is demonstrated in the ordinary glucose tolerance curves.

Fig. 1 represents the results of Experiment A, in which the blood sugar falls slowly and continuously to the normal and the ketosis, which is slight, is not affected. The effect of exercise is to lower this hyperglycaemia very rapidly to a normal blood sugar level ranging between 0.07 and 0.10 per cent. When the blood sugar is low to begin with, and within

FIG. 1.—The gradual and continuous fall in the blood sugar to nearly normal during three hours in the resting diabetic patient, without insulin for thirteen hours, and having had food two hours previously. A trace of ketosis is maintained throughout. Curves marked A are the results of Experiment A, Case I. The effect of the same exercise (three and a half minutes "standing running" at 210 steps per minute) on the blood sugar and ketosis in the same subject (Case I) when insulin had been given two and a half hours before — (1 in square) and seventeen hours previously — (2 in circle). The curves marked with the same numerals correspond. The curves with definite points are the blood sugar curves, and the others represent the urinary ketones. Exercise was started at zero time.

the normal range of 0.07 to 0.10 per cent., exercise has little or no effect on it. If ketones are present in the urine before the muscular exercise they are always absent or diminished in amount after the exercise, even when the blood sugar is low at the start, provided insulin has been administered not many hours previously.

The less severe cases of diabetes show these results—that is, a rapid fall in the blood sugar and a decrease in ketosis up to twenty-four hours since the last administration of insulin; but in the severe diabetic this result is only shown when insulin has been administered within the last fourteen to twenty hours. After the lapse of twenty-four hours in the severe diabetic, the production of endogenous insulin being smaller, very little or no effect is noticed on the concentration of glucose in the blood, as is shown in Experiments T, U, and V. In

these circumstances too the ketosis is increased, showing that tissue metabolism is less perfect, and especially that of carbohydrate, for only in the perfect and complete metabolism of carbohydrate is the katabolism of fats perfect. The excretion of glucose in the urine is increased also, presumably owing to increased blood flow and increased excretion by the kidney after the exercise.

Curve A, Fig. 2, represents the patient's glucose tolerance eight weeks before Experiment H. The quantity of insulin he is now taking is the same as when he was discharged from hospital, so he has not gained tolerance to any marked degree.

Curve B, Fig. 2, represents this patient's glucose toler-

FIG. 2.—The glucose tolerance of Case I, with 40 grams of glucose before treatment with insulin was begun (Curve A), and seven months later after continuous insulin treatment (Curve B). See text. Curve A, after forty hours' starvation. Curve B, no insulin for sixteen hours; last meal five hours before the glucose was given.

ance with the same quantity of glucose seven months later. The configuration of the curves approximate closely, the difference in absolute blood sugar percentages being due to the fact that when Curve A was taken the patient's urine was not sugar-free and so the whole curve was displaced to a higher level. In the case of Curve B the patient's initial blood sugar was at a lower level and he was not passing sugar in his urine when the 40 grams of glucose were administered. So from the glucose tolerance tests and from the fact that his daily quantity of insulin has not been altered one would conclude that there had been little or no gain in carbohydrate tolerance.

In Experiment H the subject had had no insulin for sixteen hours when the 30 grams of glucose were given, so there can be little doubt that the exercise prevented glycosuria, and more than this, the exercise caused a rapid fall in the blood sugar. Most of the glucose must have been metabolized or rendered non-reducing as the result of insulin produced by the patient's pancreas consequent on exercise and increased blood flow, and probably to some extent by insulin previously stored in the tissues.

Hence for practical purposes we may state that in the mild and less severe diabetic with insulin moderate exercise has a beneficial effect by increasing tissue metabolism, burning glycogen, depleting the blood sugar, and more completely

FIG. 3.—The effect of muscular exercise on the blood sugar and ketosis in the same patient (Case II) when insulin had been administered six hours before (1 in square); not for eleven hours (2 in circle); and when he was without insulin for twenty-two hours (3 in triangle). All curves are read from left to right.

burning fats. In the severer case with insulin the same beneficial effect is noticed with exercise, but without adequate insulin exercise has no depleting effect on the blood sugar, and it increases the production of ketones. It amounts to the fact that with insulin most cases of diabetes can be rendered nearly normal as regards the tissue metabolism, but the severer cases depend much more on adequate quantities of insulin.

It was definitely recognized before the introduction of insulin that excessive exercise was a potent factor in causing diabetic coma in patients suffering from diabetes mellitus, and the explanation is readily understood when it is realized that the energy is produced at the expense of the incomplete tissue metabolism in the absence of a sufficient insulin supply, thus increasing the production of ketone bodies and resulting in acidosis and coma. Experiment V demonstrates this. The likelihood of acidosis and coma supervening as the result of exercise in the diabetic is small provided there are adequate supplies of carbohydrate or material capable of being readily converted to such and a sufficient supply of insulin.

These patients have been able to do the exercise without undue fatigue, and no difference has been noticed by them either in the nature of muscular stiffness or fatigue with and without insulin. No hypoglycaemic reactions have occurred even in such experiments as P and Q, where the blood sugar was low before the exercise, so even though the blood sugar is depleted there is apparently no check in

transformation of the glycogen stores to glucose as the result of muscular exercise. A fall in the blood sugar concentration on exercise doubtless occurs in the normal healthy man, but the changes are not readily demonstrable, because of the small range over which the normal glycaemia fluctuates, any change being relatively small. However, when the range of glycaemia is increased, as in the diabetic, this fall in blood glucose on muscular exercise is more readily demonstrated.

CONCLUSIONS.

From these observations we might advance certain theoretical considerations. As the result of the muscular exercise a certain amount of glycogen must be katabolized in the muscles and a vacuum created which would necessitate a more rapid inpouring from the blood of glucose to make this good. Already there is pouring into the blood glucose derived from other glycogen stores—for example, the liver—but this influx of glucose is not accelerated unless the blood sugar falls to below 0.070 per cent., and so the blood sugar would fall from exercise to this level. When the blood sugar at the beginning of exercise is low, as the same exercise is done the transformation of glycogen in the muscles must be at least equal to the transformation in circumstances when the blood sugar is relatively higher, and so the vacuum in the muscles must be made good at the expense of the blood sugar; but the blood sugar itself is replenished concurrently from the glycogen stores, but the glucose does not flow in in excess and the blood sugar remains at its initial low level. This would postulate a delicate balance between blood sugar and glycogen stores, the transformation of the latter to glucose not being in excess of its normal rate unless the blood sugar falls below 0.07 per cent.

Our conception of hypoglycaemia occurring from an excessive amount of insulin is that the blood is being depleted of its glucose more rapidly than the glycogen stores can be transformed into glucose, and so this latter process cannot keep pace with the former, and the blood sugar falls to the hypoglycaemic level and below it.

This hypothesis would hold good when there was an adequate quantity of insulin in the tissues. But when there is inadequate insulin present in the tissues there is no increased depletion in the glucose concentration of the blood, and the production of ketones is increased on exercise. Since the exercise is done just as efficiently the muscle metabolism must be as good, and just as much energy is needed for an exercise of equal length and rapidity to that in circumstances where insulin has been given shortly before. However, in the absence of adequate insulin the loss of glycogen or like products in the muscle tissue is not made good by the blood in excess of the amount which would be pouring into them when these structures were at rest, and so the blood sugar percentage does not fall more rapidly than it would have done had the subject remained at rest. Again, in the absence of sufficient insulin carbohydrate metabolism is less perfect, and so there is an increase of ketone bodies in the urine from the incomplete combustion of fats.

Hence insulin is essentially associated with the metabolic processes in the muscles, but apparently it is not necessary for the transformation of glycogen to lactic acid in the contraction of muscle, but the transformation of glucose into glycogen precursors and the intrinsic metabolic processes of muscle depend on its presence.

SUMMARY.

1. Muscular exercise in patients suffering from diabetes mellitus depletes the blood glucose provided there is an adequate supply of insulin in the tissues.
2. The more perfect and complete tissue metabolism is demonstrated by the disappearance of ketones from the urine under these conditions.
3. As the result of exercise the blood sugar tends to fall rapidly to between 0.07 and 0.10 per cent., but it does not become lowered further.
4. No hypoglycaemic reactions have occurred on exercise even if the initial blood sugar was as low as 0.07 per cent.
5. Muscular exercise does not tend to cause acidosis provided there are adequate carbohydrate and insulin for its transformation.

6. Exercise in patients without sufficient insulin, endogenous or exogenous, causes no change in the concentration of glucose in the blood, but markedly increases the production of ketone bodies, with resultant acidosis and the likelihood of the supervention of a diabetic coma.

7. An hypothesis for the action of insulin is suggested from these experiments.

SOME OBSERVATIONS ON BLACKWATER FEVER.

BY

ERNEST P. CARMODY, M.B.E., M.R.C.S., L.R.C.P.,
DISTRICT SURGEON, BINDURA, SOUTHERN RHODESIA.

"I am of opinion that our first duty is to inquire whether a thing be or be not, before asking wherefore it is."—HARVEY.

ENCOURAGED by my success in the treatment of blackwater fever, I feel justified in publishing my observations on 36 consecutive cases, and an account of the method of treatment I have followed.

The district of Bindura, situated about the middle of the Mazoe Valley, which runs from west to east for some sixty miles, has a somewhat scattered European population of 350. The district is traversed by the Salisbury-Shamva branch railway. Bindura station, 70 miles north-east of Salisbury, and 1,730 miles distant from Capetown, lies at an elevation of 3,737 feet above sea-level, and is the most northerly point on the railway system of Southern Rhodesia.

Bindura has the reputation of being the worst blackwater district in the country. The average mortality from blackwater fever in Southern Rhodesia, taken over a period of twenty years, is, according to the medical director's report for the year 1921, 20 per cent.

Since my arrival here in February, 1921, I have studied the local history of the disease and its treatment, both by the Roman Catholic sisters—who were the earliest nurses in the country—and the early settlers. It appears that they considered it imperative that blackwater cases should not be moved, but nursed on the spot where the disease was developed.

Blackwater fever may be defined as an acute non-infective disease associated with characteristic dark urine and grave constitutional disturbances. It is a condition affecting Europeans, very rarely natives, occurring at all ages, and most prevalent in males; it is consequent on chronic subtertian malaria, even though there be no definite paroxysms of fever.

I consider that blackwater fever should be regarded as para-malaria, and that its possible cause is a chronic anaemia, fulminated by a sudden lowering of the vitality from any cause; this leads to a temporary rapid hypotonic osmotic condition of the blood plasma, and consequent bursting of the red blood corpuscles.

My conclusions are based on my successful application, in the early stages of the disease, of normal saline injected subcutaneously, and sodium bicarbonate administered by the mouth. My belief is confirmed by the views expressed by various medical writers, including Manson (*Tropical Diseases*, seventh edition), of the value of subcutaneous and intravenous hypertonic and isotonic salt solutions. Further corroborative evidence lies in the fact that chronic malaria is associated with profuse sweating and consequent loss of salt.

SYMPTOMS.

Premonitory.—A relatively large number of patients complain of severe abdominal pain with constipation, about twenty-four to forty-eight hours before the onset of blackwater fever.

The *onset* is usually characterized by the passing of six to ten ounces of very dark urine, in colour and frothiness like porter, but when viewed in a thin layer of a dark red colour; this is the first warning to the patient that he has blackwater fever, although he may not have been feeling very well, and has assumed the onset of malaria. The patient looks ill and the pulse is rapid, but pyrexia is by no means a feature of the disease in all cases. Headache,

loin-ache, and nausea are usually present, and a rigor may occur. Jaundice in a slight degree may be present before the onset of blackwater, but usually it comes on some hours after, and grows very profound if the patient is moved or shaken. The liver and spleen are nearly always palpably enlarged and the latter tender.

Danger of Moving.

Mortality in cases who have been moved, even for a short distance, is very much higher than in those who have not been moved. Before I realized this two patients I moved with the utmost care, and only for a short distance, became suddenly intensely yellow and very collapsed within a few minutes of being lifted, and subsequently had two or three severe relapses in the following five or six days. One case, a slight one, moved ten days after the onset and seven days after the water was quite clear, was run slowly by car for a distance of five miles over a rather rough road, and immediately developed one of the severest attacks of blackwater I have seen. Another recent case went by train to Capetown twenty-seven days after the onset, and had a relapse.

Complications.—Acute nephritis, scanty urine, and complete suppression are perhaps the most trying and dangerous complications one has to be on the look-out for. Abdominal complications seem to figure largely; the pain is of a gripping character, and seems to be referred to the colon, and in most cases I have seen there has been obstinate constipation. In one case this appeared to lead to lighting up an old appendix, and in another to intussusception; in each of these cases the patient was too collapsed for operation to be urged. Two of my cases developed bronchopneumonia, and this, I think, was due to getting uncovered whilst hot and sweating profusely.

The diagnosis as a rule should present no difficulty in a patient who has lived in a country where malignant tertian malaria is prevalent, and whose first symptom of real illness is the characteristic urine.

TREATMENT.

Prophylactic treatment consists in protection from mosquitos (and therefore malarial infection), early diagnosis, especially in incipient cases of malaria, and efficient quinine treatment over a sufficiently long period, and maintenance of good general health by means of good food and housing, the removal of all scrub near dwellings, and the draining or protection of all pools of water wherein mosquitos might breed. The successful treatment of blackwater fever depends on taking care not to move or shake the patient in any way. Therefore, if the patient is not near any dwelling, every effort should be made to bring a bed to him and erect a shelter over him.

Having got the patient to bed and well covered, I now, as a routine, immediately inject subcutaneously 5 to 10 ounces of normal saline, and repeat it if necessary. With this I find the urine, even in severe cases, clears up more quickly, sometimes in a few hours, whilst the jaundice and the constitutional symptoms are less marked. I also give from 1/2 to 1 ounce of magnesium sulphate at the beginning. This is probably beneficial from its depletive effects.

As 20 grains of sodium bicarbonate hourly is found to be beneficial in these cases, and as nausea and restlessness are nearly always troublesome features, I generally give a mixture such as the following:

R Sodii bicarb.	gr. xx
Bismuth carb.	gr. x
Tr. chlorof. et morph. co.	℥ v

S. To be taken every hour in 5 oz. of water.

I have found vomiting less severe since giving up "Sternberg's mixture"; this, I think, is due to the fact that the mixture contains mercury perchloride. Abdominal or loin pains are best treated with hot-water bottles or antiphlogistine.

As a rule I do not prescribe quinine, but see no reason why it should not be given, and when symptoms of acute malaria have been present I have given it with good results; but it is best administered by intramuscular injection.