blood sugar and of sugar in the urine to about the same level as had been reached without insulin on a diet of 1,400 calories. There was also an increase, though a smaller one, in the total acid bodies. The nitrogen balance continued positive up to as much as +5 grams a day. After the above-mentioned excess of food was given, in a further fortnight of observation, not shown on the chart, the insulin was increased and the total food was reduced to about 2,500 calories.

8. The patient's weight increased steadily; 8 lb. were put on in six weeks of treatment.

9. The blood sugar was never brought below 0.11 per cent., and no symptoms of hypoglycaemia were observed.

10. The respiratory quotient was determined several times, but in this case similar figures were obtained with and without insulin. The reflection occurs that the case might not be severe enough or the dosage of insulin large enough to produce considerable changes in the quotient; especially as no attempt was made to enable the patient to assimilate much exogenous carbohydrate.

11. The investigation showed that a suitable régime for this patient is a diet of about 2,500 calories with low carbohydrate, and 30 units of insulin daily.

12. The change in appearance and attitude to life after insulin was given was unmistakable, and was remarked by the members of the staff, who, of course, know the patient well. He grumbled sometimes, as anyone might, at having to have injections and still having to look after his diet, but was interested in his various pursuits and had a look of health and keenness.

It was advised that 20 units of insulin be given just before breakfast and 10 before the evening meal, the smaller dose being given in the evening to avoid reducing the blood sugar too much in the night. This patient when at home sometimes prefers to omit lunch and make two main meals a day, with a little tea in the afternoon. In that case it was advised that the insulin should be given in two equal doses just before the two meals.

The fasting days formerly practised were omitted, but he was advised as a safeguard to take half quantities of food on one day a week. Progress will be watched, and an occasional fast day prescribed if needed.

The following is an example of a day's diet of about 2,500 calories as taken by this patient.

Diet taken on May 26th, 1923.

	Grams.					Cal.	Grams.		
	B.	L.	T.	D.	Total.		Carb.	Prot.	Fat.
*Duff House casein bread	30	15	30	15	90	196		47	
Milk	105		105		210	156	11	7	9
Butter	20	10	20	10	60	476		1	51
Cheese		30		30	60	270		17	22
Eggs	2	1		2	5	400		34	29
Fish—lemon sole ...				120	120	107		25	1
Bacon	60				60	320		10	30
Meat—lean beef—stewed		50			50	293		36	16
Filletted steak ...				60	60				
Vegetables—									
Cabbage	280				280	58	8	5	1
Tomato (raw) ...	150				150	101	16	5	2
Lettuce (raw) ...			300		300				
Kale		400			400	76	4	14	
Asparagus				400	400	92	10	12	
K. iller's sugarless marmalade or jam	30		30		60	9	2	1	
Tea	340		340						
Clear meat soup ...				200					
						2,554	51	214	161

* *Lancet*, 1921, ii, 960; *BRITISH MEDICAL JOURNAL*, 1921, ii, 707; also *Duff House Papers*, vol. i, Oxford Medical Press, 1923.

It will be noticed that in most cases the weights are given in multiples of 30 grams or cubic centimetres, so that the corresponding number of ounces can be approximately calculated by dividing by 30.

Summary.

In a detailed study of a moderately severe case of diabetes in which tolerance had been diminishing for the last three years, it was found that with the help of two daily hypodermic injections of insulin, on a measured diet, the excess of sugar in the blood, the sugar in the urine, and the acidosis could be controlled; also that the patient could take more than double the amount of food he had previously been able to take without the appearance of sugar in the urine. Regulation of diet is still needed, for if an excess of food was taken above the new and higher level of tolerance, the hyperglycaemia, glycosuria, and acidosis reappeared.

The treatment led to improvement in the nutrition, physical capacity, mental outlook, and appearance of the patient.

THE BEHAVIOUR OF THE BLOOD SUGAR UNDER THE ACTION OF INSULIN AND OTHER AGENTS.

BY

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IN view of the failure to demonstrate any action of insulin on the oxidation of glucose *in vitro* either in presence of defibrinated blood, muscle juice, a combination of these, or pus,¹ it seems likely that its action is indirect. Winter and Smith² have recently published some experiments which led them to the conclusion that there is present in normal blood a kind of sugar differing from an equilibrated mixture of the α , β varieties in having a lower specific rotation. They fail to find any evidence of this in the blood of diabetic patients, and consider that the diminished carbohydrate metabolism of the diabetic is due to the lack of this more reactive form. It became of interest, therefore, to see if their results could be repeated and to study the effects of epinephrine and insulin. The following is a preliminary account of some of these experiments. No interpretation will be attempted.

Method.

Both dogs and rabbits were used. The rabbits were killed by knocking on the head and bled from the carotid artery; two were used in each experiment. In the case of dogs, blood was removed, either from the heart or femoral artery. The blood so obtained (usually 100 c.cm.) was treated as described by Winter and Smith—namely, diluted with seven volumes of water and precipitated with one volume each of 10 per cent. sodium tungstate and 2/3 N. sulphuric acid. It was filtered first through coarse filter paper, then through a Whatman No. 40 or 42. It was then evaporated to dryness under reduced pressure (water pump), using a capillary to prevent bumping, the temperature of the water-bath surrounding the boiling fluid being kept between 30° and 40° C.; 100 c.cm. of 85 per cent. alcohol was then added (proportionately less when less blood was taken) and the mixture let stand for twenty minutes. It was then filtered into a smaller distillation flask, and the extraction repeated with half the volume of alcohol. This was filtered in the same way, and both filtrates were united and evaporated to dryness as before. The residue was then taken up in distilled water, filtered through a No. 50 Whatman paper, and placed in a polarimeter tube. Readings were made on successive days.

The polarimeter used was a half-shade instrument made by Schmidt and Haensch. Successive readings did not vary more than 0.04°. The average of ten readings was taken. Sodium light was used. The tubes were 1.894, 2, and 2.2 cm. in length.

The copper-reducing value was obtained by the method of Shaffer and Hartmann, using the fluid in the polarimeter tube after the completion of the experiment. Blood sugar estimations were made by the same method. The epinephrine and insulin were administered subcutaneously.

Results.

A general table of the results is given. No experiments are omitted except those in which the polarimeter reading was impossible on account of the opacity of the solution.

(a) *Normal*.—With the rabbit three experiments were done. In one of these the rotation gradually rose to a value corresponding to the reducing power. In the others there was little or no change, but the rotation found was markedly lower than that calculated from the reduction. With the

No.	Animal.	Remarks.	Blood Sugar, mg. per 100 c.cm. when sample taken.	Readings on successive days. Degrees.	Reading calculated for reduction. Degrees.	[α] D of lowest reading. Degrees.	Volume of Blood taken. c.cm.	Time required by process. hrs.
1	Rabbit	Normal	—	0.07, 0.07, 0.17, 0.17	0.17	21	100	6
2	"	"	—	0.03, 0.10, 0.07, 0.10	0.17	25	85	6½
3	"	"	—	0.03, 0.10, 0.10	0.20	27	100	7½
4	Dog	"	—	? 0.07, 0.18, 0.20, 0.18	0.21	13	100	9
5	"	"	—	0.07, 0.15, 0.20	0.21	18	100	9
6	"	"	—	0.23, 0.25, 0.30, 0.31, 0.31	0.30	39	95	—
7	Rabbit	Epinephrine	300 & 400	0.58, 0.55, 0.53, 0.53	0.50	56	75	6½
8	Dog	Struggling	222	0.28, 0.28, 0.28	0.34	43	100	7½
9	"	Epinephrine	147	0.20, 0.20, 0.20	0.21	47	100	10½
10	"	"	230	0.63, 0.61, 0.70, 0.70, 0.68	0.70	48	100	—
11	"	Epinephrine + insulin	300	0.08, 0.15, 0.28, 0.31, 0.28	0.20	22	100	10½
12	"	"	240	0.38, 0.50, 0.47	0.50	39	100	—
13	"	"	145	0.17, 0.25, 0.23, 0.23	0.13	66	100	5½
14	"	"	176	0.22, 0.16, 0.18, 0.16, 0.16	0.20	42	100	6½

For the calculation of rotating power from reducing, [α] D = 52.5 was used.

dog also three experiments were done. In each of these there was a gradual rise in the rotating power until it coincided with that calculated from the reducing power.

(b) *In Hyperglycaemia.*—One experiment was done on a rabbit. Here there was a fall in the rotating power until it reached a value equal (within the limits of error) to that calculated from the reduction. In the three experiments on dogs two showed no change in rotation, although one of them was a little below the value calculated from reduction. In the third there was a slight rise to this value.

(c) *Following Insulin and Epinephrine.*—In these experiments 5 c.cm. of 1 in 1,000 adrenaline was given in diluted divided doses, followed by insulin, the blood being taken about half an hour later. In all but one of these there was a rise in the rotating power, which in two cases was considerably greater than the rotation calculated from reduction. The specific rotations for the lower readings recorded have been calculated. For normal blood they are very low (with one exception) and do not approach that of α , β glucose. For blood with epinephrine hyperglycaemia they are in the neighbourhood of that for an equilibrated mixture of α , β glucose, but show a tendency to be low. After epinephrine and insulin, in spite of the hyperglycaemia two of them are about the same as for normal blood.

Experiments were made to see if alcohol in acid solution had any effect on pure glucose. These were uniformly negative, although the acid alcohol was warmed with glucose in the presence and absence of phosphate for periods of the same length and much longer than those in the experiments with blood filtrates.

My thanks are due to Professor A. Hunter and Professor J. J. R. Macleod, under whose direction the experiments were done.

[It would be rash at the present juncture to conclude that the highly reactive forms of glucose, called gamma glucose, are necessarily responsible for these results. The long and complicated chemical procedure used to prepare the solutions for the polariscope may be responsible for the production of substances with a lower rotating power. The slowness of the change in rotating power (intervals of days), also, does not suggest the presence of a highly reactive substance. Further investigation will therefore be necessary before the important hypothesis suggested by Winter and Smith can be considered as established.—J. J. R. M.]

REFERENCES.

- ¹ Eadie, Macleod, and Noble: *Amer. Journ. Physiol.* (in press).
² Winter and Smith: *Journ. Physiol.*, 1923, lvi, 100; *BRITISH MEDICAL JOURNAL*, January 6th, 1923; *Ibid.*, April 28th, 1923; *Ibid.*, May 26th, 1923.

A CASE OF ACTINOMYCOSIS WITH RECOVERY.

BY

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THE following case is worthy of record on account of certain interesting clinical features which it presented, but especially for the extraordinary recovery which occurred.

A man, aged 22, was admitted to the David Lewis Northern Hospital, Liverpool, on October 8th, 1922, with a history of lobar pneumonia on board ship while crossing from Canada to England; crisis was said to have taken place. The temperature chart which accompanied the patient showed that the maximum temperature had been 103.8°, and that on the fourth day it had fallen to 100°, rising to 101° on the sixth day, and falling to normal on the seventh day (the day before his admission to hospital).

On admission the temperature was 100°, the pulse was 120, and respirations 56. He was cyanosed, exhausted, and had marked dyspnoea. Signs of fluid were detected in the right pleural cavity, and percussion over the right lung caused pain, a common sign of empyema. Exploration of the right chest yielded fluid, and an hour later a rib was resected and the pleura drained. The fluid withdrawn was serous with a flaky deposit, but was not definitely purulent. Pathological examination of the fluid revealed nothing.

The patient's general condition did not improve, though the wound drained freely and only fluid of a serous nature exuded. The pulse rate varied from 100 to 120, the temperature was normal, but the dyspnoea became more and more urgent. The pleural cavity was probed with the hope of finding a loculation of fluid, but without result. The respirations reached 60, and death appeared imminent. With great difficulty Dr. Oram made an x-ray examination, and reported: "The whole of the lower part of the chest on the left side is opaque, the upper border of the opacity following the line of the sixth rib. I fear that it is not possible to say whether this is fluid in the pleura, heart shadow, or pericardium."

On October 14th the patient still appeared to be on the point of death, and it became increasingly evident that the dyspnoea was due to mechanical obstruction and not to a general toxæmia. The cardiac dullness was greatly increased, but breath sounds could be heard clearly all over the dull area, while the heart sounds too were distinctly audible in the region of the nipple. No pericardial friction sound could be heard. Dr. John Owen of the Royal Infirmary saw the patient in consultation, and it was decided that there must be some mediastinal swelling, possibly a pericardial effusion covered by a thin shell of lung. Such a diagnosis was the only possible explanation of the anomalous physical signs, and yet there was the fear that the dullness might be due to a dilated and displaced heart. Exploring needles were inserted, but with such caution that nothing was found.

During the evening, on hearing that the patient was, if possible, worse and unlikely to live till the morning, the pericardium was explored under local anaesthesia, and about 25 ounces of sero-purulent fluid were allowed to escape. Through the incision in the pericardium a typical "bread-and-butter" appearance of the heart could be seen. The fluid was examined bacteriologically, but all cultures were sterile. The patient was very collapsed, but next day his condition improved, though he was still very dyspnoeic.

On October 19th, signs of a pleural effusion on the left side having developed, the cavity was tapped, and 21 ounces of clear fluid were withdrawn; the pathological report on this fluid was: "No tubercle bacilli or other micro-organisms found. Numbers of lymphocytes and lymphoid cells present." Abdominal distension now occurred, but yielded to eserine and pituitrin.

About October 18th it was noticed that the character of the discharge coming from the right pleura and the pericardium had changed, and that it was now thick and yellow. The discharge was examined by Professor Glynn at Liverpool University, and in the material from the right pleural cavity numerous actinomycosis organisms were found. Attempts were made by Professor Glynn to cultivate the organism anaerobically in order to determine its type, but unfortunately the streptothrix would not grow. The sputum was repeatedly examined for the ray fungus, but always with negative results. The pericardial fluid yielded a pure culture of *Staphylococcus aureus*.