THE USE OF INSULIN IN PRIVATE AND PANEL PRACTICE.

ABSTRACT OF THREE LECTURES DELIVERED AT GUY'S HOSPITAL TO PANEL PRACTITIONERS,

BY

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INSULIN is not a cure for diabetes in the usual sense of the word, but it is a specific treatment, and the results are wonderful. The correct dose of insulin for each individual patient must be established and an appropriate diet prescribed, and the patient must continue the treatment himself under the general supervision of his doctor. It is, of course, possible to send the patient to a specialist, to have the correct dose of insulin, etc., determined, a procedure which requires three or four weeks' special study with estimations of the blood sugar, etc. But it is my purpose to show the possibility of this being done, at any rate in the majority of cases, by the patient's own doctor in his own home, provided the doctor can give the necessary time and take the necessary trouble; and, further, to state the rules that should guide the doctor in his treatment. When once the dose and correct diet have been determined, general supervision by the medical man is not difficult, since the patient should have been taught what diet to take and what symptoms to look out for, in case he becomes unduly sensitive to insulin. Further, he should be able to test his urine periodically for sugar, to make certain that the dose is not much too small. The urine must always be free from sugar.

At the beginning of treatment examination must be made for possible foci of infection—such as septic teeth with apical infection, septic tonsils, gall bladder, or appendix, and suitable measures taken to eradicate them.

TECHNIQUE OF INJECTIONS.

The doctor must teach the patient how the injections are given. If the patient injects himself, his legs and the front and sides of his body are available. Even if he usually has the services of a friend or relative, he should learn how to give the injections himself.

METHODS OF GIVING INSULIN INJECTIONS AT HOME.

Most hypodermic needles and syringes lead to some waste of insulin at each injection owing to the dead space in the nozzle. A special needle (see Fig. 1) which fits into the head of the syringe*

FIG. 1.

has the advantage of minimizing the waste. Money can be saved by teaching the patient how to sharpen his own needles on a stone, using liquid paraffin as a lubricant. Undoubtedly the best plan is to see whether the point is sharp by looking at it under the microscope. In default of this a sufficiently powerful lens can be bought for a few shillings.

Method A.

Absolute alcohol, rectified spirit, ether, and clean lint cut into small squares are required.

The syringe (1 or 2 c.cm.), with needles, is kept on a stand in a bottle with ground-glass stopper, containing absolute alcohol. [If the patient has much travelling to do a metal case in the form of a tube, with screw-on cap, is an advantage. This requires much less of the expensive absolute alcohol.] After washing and drying the hands, the stand with needle case and syringe is removed from the bottle by means of forceps, and the needle is attached to the syringe. By running the plunger up and down several times the alcohol is removed as far as possible from inside the syringe. The outside of the syringe may be wiped with a clean cloth, but the needle must not be touched.

* The syringe and other apparatus mentioned are supplied by Messrs. Down Brothers, St. Thomas's Street, S.E.1.

Suppose that 1/2 c.cm. of insulin is to be injected. The plunger is placed at the 1/2 c.cm. mark so that the syringe contains 1/2 c.cm. air. After cleaning the rubber cap of the insulin tube with ether, the needle is passed through it into the insulin tube, which is held upside down. The plunger is pushed home, so that 1/2 c.cm. air enters the tube. With the point of the needle lying beneath the level of the insulin, the plunger is moved up and down several times to expel the last traces of air into the tube, and on withdrawing the plunger to the 1/2 c.cm. mark the syringe will be filled with 1/2 c.cm. of insulin. The insulin tube is then removed. The injection is made after cleaning the skin with ether.

The syringe and needle are then rinsed out several times with tap water to remove all trace of insulin. After rinsing out two or three times with rectified spirit they are disconnected and returned to the bottle of absolute alcohol. The latter requires to be changed periodically—that is, every week or fortnight.

Method B.

This is less simple, but cheaper. For it are required lysol in methylated spirit (1 in 20), methylated spirit, ether, enamelled bowl, clean houseflannel to cover the bowl, clean lint cut into small squares.

At tea time the bowl is rinsed several times with boiling water from the kettle and then filled with boiling water; the bowl is covered with the houseflannel and allowed to cool.

Just before the injection the syringe and needle are removed with forceps from the lysol and methylated spirit in which they are kept. The needle is attached to the syringe, and rinsed out five or six times with the cold boiled water in the bowl, so as to get rid of the spirit completely. It is important not to let the rinsings run back into the bowl. The water is removed as far as possible from the syringe by moving the plunger up and down. The syringe is filled, and the injection is made exactly as described under Method A. After the injection the syringe and needle are washed out with water and rinsed out with methylated spirit, and returned to the methylated spirit mixture. The latter should be changed every week or fortnight.

THE THEORY OF TREATMENT WITH INSULIN.

Two views have been held as regards the objects to be aimed at in treatment with insulin. According to one view it is sufficient to make the urine sugar-free or to allow at most a small trace of sugar to be passed continuously. In the majority of cases treated in this way there will still be considerable hyperglycaemia, as sugar is often only passed when the blood sugar rises considerably higher than normal. According to the other view, which is now generally accepted in this country, the aim should be to keep the blood sugar within the normal limits, and in some cases even below normal, the theory being that a high blood sugar is deleterious because it means a greater strain on a weakened pancreas, while with a low blood sugar the pancreas is rested, and so tolerance may be regained to some extent. It is at present too early to be certain whether the second method really gives better results than the first, though some of our results at Guy's Hospital have been suggestive. However, until we have more definite knowledge on this subject the second view is the safer one to adopt for physiological reasons, and particularly in the case of young patients.

The blood sugar curves of two patients with diabetes in the private ward for insulin treatment at Guy's Hospital, as determined throughout the twenty-four hours by Mr. W. W. Payne, Parsons Research Fellow, are reproduced in Fig. 2.† Doses of insulin were given at 6.30 a.m. and 6 p.m., half an hour before breakfast and supper. The diet consisted of 5 per cent. vegetables, protein, and fat. It will be seen that the curve falls as the result of giving insulin and then rises again, but the important thing is that the rise is just as high during the night and early morning hours as it is in the early afternoon, in spite of the fact that no food was given later than 7 p.m. The explanation is that the maximum metabolism of protein occurs in the later part of the day. Graham and I¹ showed this, since we found in our own case, when we were on a very similar diet, that about 50 per cent. more nitrogen was excreted in the urine from 3 p.m. to 11 p.m. than from 11 p.m. to 7 a.m. or from 7 a.m. to 3 p.m. The output was fairly constant during the two latter periods. Further, Williams, Riche, and Lusk² have shown that the metabolism of protein in the body takes place mostly during the period of high nitrogen excretion in the urine. These considerations are important, as they indicate that when insulin is given twice a day it should be given in approximately equal doses at twelve-hour intervals—

† A full account of our observations will appear in a forthcoming number of the *Guy's Hospital Reports*.

before breakfast and before supper. For the sake of comparison I have shown in Fig. 2 the blood sugar curves of Mr. W. W. Payne and myself on a similar diet. They lie between 0.08 and 0.12 per cent., and on the present theory they serve to show the kind of values that we should strive to reach when treating our diabetics with insulin.

In Fig. 3, A is the diurnal blood sugar curve of a diabetic on a diet of vegetables, protein, and fat of sufficient calorie value, seven days after a single starvation day; B is the curve during treatment with insulin three times a day. At each injection there is a fall in blood sugar, so that there are three waves in the twenty-four hours. Here again the blood sugar rises as high during the night as during the day. This shows that the three doses should be spaced out as evenly as possible during the twenty-four hours. The actual times of the doses were 6 a.m., 12 noon, and 9 p.m., so that the maximum period between the doses is nine hours, and the last dose is given *after* the evening meal, the other two being given before breakfast and lunch.

Physiologically speaking, it is best to give insulin in small doses frequently. But practically the third dose at mid-day

FIG. 2.—Percentage of sugar in blood during twenty-four hours. Two upper curves obtained from two patients in the insulin ward. Two lower curves obtained from E. P. P. and W. W. P.

is usually inconvenient for a man at work; but I have prescribed it in the case of a young man living at home who, I thought, had the chance of regaining a fair measure of tolerance.

TREATMENT WITHOUT BLOOD SUGAR DETERMINATIONS.

According to the theory, the blood sugar is to be kept within normal limits by means of insulin. How can this be brought about without blood sugar determinations? The answer is that advantage is to be taken of our knowledge of the early symptoms of hypoglycaemia. The dose is to be gradually increased until mild symptoms appear, and it is then to be kept just short of this amount. At first sight this sounds a rather alarming method of treatment. But Sir Thomas Lewis³ has advised a similar method in the rational use of digitalis in refractory cases of heart disease; the drug is increased up to the point when symptoms of poisoning are first noticed. However, the last thing I want to do is to discourage any of you from undertaking blood sugar estimations, if such is your intention. Some cases of diabetes cannot very well be treated without them, and in any case they make the treatment easier. They are sometimes necessary to help in the choice of cases suitable for treatment.

Analysis of 31 cases in the insulin ward at Guy's Hospital shows the variety of early symptoms of hypoglycaemia. The numbers in brackets indicate the number of patients

who noticed the particular symptoms: shakiness (21), sweating (19), hunger or emptiness or nausea (10), giddiness or dizziness (9), mental disturbances (7)—that is, anxiety (3), excitement (1), depression (1), confusion (1), simulating drunkenness (1)—headache (6), palpitations and irregularity of heart (4), exhaustion and weakness (4), faintness (3), eye symptoms (3)—heaviness, blurring, and "seeing stars"—numbness (2), feeling of cold (2), diarrhoea (1), "pins-and-needles" (1).

This list was obtained by asking the patients what they noticed. Leading questions about particular symptoms were not asked, though they knew, broadly speaking, what to look out for. Sweating was accompanied by a feeling of heat. One patient recently examined had feelings of hot and cold alternately about four times in two hours, and noticed sweating on the face during the last hot period.

Symptoms may come on when the blood sugar is not abnormally low. This is probably due to the body in diabetes becoming adapted to hyperglycaemia, with the result that symptoms are produced when the blood sugar falls below its accustomed level. Lieutenant Commander M., aged 33, was a good example of this. He had a bad headache felt at the vertex after 10 units, when the blood sugar was 0.11 per cent. Sometimes the blood sugar may be much higher still.

Mr. Payne and I have been able to demonstrate the possibility of treating patients efficiently with insulin without doing blood sugar determinations, in the following way.

FIG. 3.—Diurnal blood sugar curve from a single patient.

In Figs. 2 and 3 the determinations were begun about 10 a.m. and carried through to the next morning. To make the character of the curves clearer the morning values have in most cases been placed both at the beginning and end of the chart. The arrows mark the administration and the numbers refer to the units of insulin.

We have chosen certain typical cases of diabetes and determined the blood sugar on two occasions only—one at the beginning of treatment, to prove that there was true hyperglycaemia, and again at the end of treatment, when the dose of insulin and the diet had been finally prescribed, to show that the blood sugar had been brought down to a satisfactorily low level.

D. B., a woman aged 23, in domestic service, admitted to Mary Ward, had had diabetes with typical symptoms for nearly one and a half years. On a diet of vegetable, protein, and fat the blood sugar was 0.26 per cent. at 10 a.m. Insulin was given in doses of 5 units, then 10, then 15, then 20, then 25, and then 30 units twice a day at 6 a.m. and 6 p.m., the dose being increased every three or four days. The urine had by this time become free from sugar, but as there was no reaction, a mid-day dose was added and the evening dose was shifted to 9 p.m. The doses were 30, 15, and 20; after three days 30, 15, and 25; after four days 30, 20, and 25. Two days later there was a reaction—namely, slight shakiness, giddiness, faintness, and palpitations. A reaction was noticed again three days later. The blood sugar at 11 a.m. was found to be 0.104 per cent., which proves that treatment had been successful. This patient was an unusually refractory case. This may have been due to some infection with slight rise of temperature during part of the time (a well known cause), as it has been since found possible to omit the mid-day dose altogether and reduce the morning and evening dose to 20 units, and yet some very mild symptoms have been experienced occasionally.

If the dose of insulin is gradually increased in this way there is, in my opinion, no danger of serious hypoglycaemic symptoms. In domiciliary treatment it would be undoubtedly safer to proceed more slowly still—increasing by 2 units at a time, and beginning with 4 units twice a day. The morning and evening dose of insulin need not necessarily be the same. With equal doses some patients may experience symptoms in the evening, and others in the morning. The dose that causes symptoms must be diminished. They act as a valuable guide to the dose, but there is another reason for arranging that the patient should experience them early in the treatment: they will be his guide during the rest of his life, as to whether the dose is becoming too large.

It sometimes happens that hypoglycaemic symptoms are noticed quite early in the treatment, vanish, and only appear again when the dose has been increased considerably. This increased sensitiveness to insulin at the beginning of treatment has been commented on elsewhere.*

B. M., a man aged 24, was a case of mild diabetes with a history of nine months. He had hypoglycaemic symptoms one day after the beginning of treatment, when he was having 10 units of insulin a day. The symptoms disappeared, and this coincided with a gain in weight of 4 lb. Slight symptoms were noticed again, when he was having 40 units a day, about three weeks later, and there was a marked reaction with 60 units another week later. He had put on another 2 lb. in weight. The diet consisted of vegetables, protein, and fat. When the patient gets a mild reaction there is no reason to give him sugar or bread or biscuits—treatment which may unduly raise the blood sugar. A cup of tea with some kind of diabetic biscuit and perhaps a little butter will be quite effective in getting rid of the symptoms.

DIET.

I must insist again on the utmost importance of prescribing for patients a diet suitable as regards protein and carbohydrate content and of the correct calorie value. A list of various foodstuffs, with their analyses, etc., is quite essential. It need not be long. In fact, for the patients in the medical wards at Guy's a list is printed on the back of the bed-letter, and they are given this on leaving. A very short list is given below.

	1 oz. contains approximately:			
	Carbo- hydrate.	Protein	Fat.	Calories.
	gm.	gm.	gm.	
Vegetables (see list below) ...	1	—	—	6
Grape fruit or small orange ...	10	—	—	40
Brazil nuts ...	2	5	20	210
Potatoes (boiled) ...	16	1	0	30
Oatmeal ...	20	5	2	120
Bread ...	15	3	—	75
Meat (cooked, lean) ...	0	8	5	75
Poultry, game (cooked) ...	0	8	3	65
Fish (cooked) ...	0	6	0	25
Bacon (medium fat) ...	0	5	15	150
One egg ...	0	6	6	75
Butter ...	0	0	25	225
Cheese ...	0	8	10	130
Milk ...	1.5	1	1	20
Cream (40 per cent.) ...	1	1	12	120
Midolia biscuits, three ...	4	5	9	120

*Vegetables arranged approximately according to percentage of carbohydrates: lettuce, cucumber, spinach, rhubarb, marrow, celery, tomatoes, greens, sprouts, watercress, cauliflower, cabbage, radishes, leeks, runner beans, turnips, swedes.

(The small amount of protein contained in the vegetables need not be counted in the daily protein ration.)

It is first of all necessary to find out the basal requirement of the individual—that is, the number of calories he uses in the twenty-four hours if he is at rest. These are given in the following table calculated from Dreyer's formula. The values depend on the age and weight of the person. But a warning is necessary here. It is necessary to find out

Basal Metabolism. (Dreyer.)

Weight.	Calories—Males.									
	Age— 5	10	15	20	30	40	50	60	70	80
1b.										
10	535									
20	758	390	657							
30	928	846	804	773	733	704	683	657	653	642
45	1133	1037	986	946	838	863	838	818	801	788
60	1315	1158	1140	1094	1038	998	963	945	926	910
80	1517	1382	1315	1262	1197	1151	1117	1090	1068	1050
100	1593	1543	1457	1408	1336	1285	1247	1217	1192	1172
120		1689	1605	1542	1463	1407	1367	1332	1305	1283
140		1827	1738	1637	1582	1521	1476	1440	1411	1383
160			1858	1785	1592	1626	1573	1540	1509	1483
180				1883	1792	1723	1672	1632	1599	1571
200				2020	1917	1843	1783	1746	1710	1681

Basal metabolism is expressed as calories per twenty-four hours. In the case of females the values are 10 per cent. lower.

Relation between Body Length and Body Weight. (Ainley Walker and Dreyer.)

Body Length (inches).	Body Weight.	
	Males.	Females.
20	...	24
22	...	32
24	...	42
26	...	54
28	...	68
30	...	84
32	...	103
34	...	125
36	...	150
38	...	177
40	...	208

the weight he should be, according to his dimensions—that is, his "predicted weight"—and for this purpose the most valuable measurement is the length of the body. The subject sits down on the floor with his back pressed firmly against the wall and his knees bent. The body length is measured from the floor to the top of the head in inches, and the body weight corresponding to this length is obtained from Dr. E. W. Ainley Walker's measurements, as recalculated by Professor Dreyer.* They are also included in a small pamphlet* that I have arranged for my patients. The predicted weight should be noted in calculating the basal requirement, because otherwise a patient who is too fat would get too much food, and one who is too thin too little. The relationship between body length and body weight varies to some extent. The predicted weight need not be used in the calculation unless there is a big discrepancy—that is, unless the body length corresponding to the actual weight is more than 5 per cent. greater or less than the actual body length. A discrepancy of 7 per cent. is the outside limit of the normal variation.

Example.—The weight of a fat female patient was 224 lb. The mean body length corresponding to this is just over 40 inches. The actual body length was 34 inches. The difference is 6 inches, which is much more than 5 per cent. of the actual body length, consequently the predicted weight—namely, 131 lb.—should be used in calculating the calorie value of the diet.

This method of calculating the normal requirement is specially valuable in the case of children. It will be noticed that it is not simply proportioned to the body weight. Dreyer* has suggested that the circumference of the chest at the end of expiration should also be used to obtain the predicted weight, and has published corresponding tables. This is, in my opinion, a much less valuable measurement than Ainley Walker's "length of body," because, owing to the loss of subcutaneous fat from the chest wall in wasted patients and its excessive amount in obese patients, the measurements give unreliable results—that is, the predicted weight is much too low in a wasted individual and much too high in an obese one.

The protein content of the daily diet should be 1/2 gram per lb. of the predicted body weight—that is, 75 grams in a

patient weighing 150 lb. The protein part of the diet should be arranged first. The patient might have:

	Protein.	Calories.
Breakfast:		
2 oz. bacon	10 gm.	310
2 eggs	12 "	150
Lunch:		
2 oz. meat	16 gm.	150
1 egg for cream custard ...	6 "	75
Tea:		
3 midolia biscuits (1 oz.) ..	5 gm.	120
Supper:		
3 oz. fish	18 gm.	75
1 oz. cheese	8 "	130
	75 gm.	1,010

We will imagine that the patient is a man aged 30. The basal requirement is about 1,475. We have then 465 additional calories to provide. It is best not to allow him any carbohydrate other than that contained in 5 per cent. vegetables during the period of testing the insulin dosage, but I allow an unlimited quantity of these, as it is a great advantage for the patient to feel that there is some kind of food he can take without stinting himself. If he takes 24 oz. in the day he will get 144 calories. The vegetables might be taken as follows: 4 oz. tomatoes fried with the bacon at breakfast, 12 oz. greens and cooked celery at lunch, 8 oz. in the form of (1) salad—that is, lettuce, cucumber, etc.—(2) rhubarb, for supper.

The remaining 321 calories are given in the form of fat at the various meals—namely, 1 oz. butter (225 calories) and 1 oz. cream (120 calories)—making in all a little more than the theoretical amount.

Since the protein ration is strictly limited many so-called diabetic foods are highly unsatisfactory equivalents for bread owing to the high proportion of protein contained in them. Bran and agar cakes according to F. M. Allen's receipt⁵ can be taken in any quantity, but they may cause indigestion. Patients often get to like them quite well if taken with plenty of butter. They should be made thin and crisp. Almond bread (Callard's) or midolia biscuits (Van Abbot's) contain less protein than many other diabetic foods. I now never make the patient fast, but it might be useful to reduce the weight rapidly if the patient was very fat.

The diet just described is adequate for the patient as long as he is having an easy time at home, but when he begins to take exercise the calorie value may be increased by 10 or 20 per cent. The protein should not be altered, but fat in the form of butter and cream may be given. Most people become in time accustomed to a diet of this kind and are happy on it. But all rules are apt to need modifications. Some people seem definitely to require more food. Each case must be decided on its merits.

The problem remains as to whether carbohydrate should be added after the maximum dose of insulin has been determined while the patient has been taking the above diet. When the discovery of insulin was first reported it was naturally thought by many that a patient while under treatment with the drug might be allowed an unlimited amount of carbohydrate. The obvious objection to this "luxury" use of insulin is its cost and the increasing demand for its use; but there are two other grave objections. In the normal body insulin is being delivered into the blood stream in the amount required at any period of the day, so that the blood sugar is kept within normal limits. Artificially, it can only be given two or three times a day. If large doses of insulin are used to counteract much extra carbohydrate, the timing may not be quite right on some occasions—possibly absorption of carbohydrate is delayed owing to indigestion—and the patient will suddenly get severe hypoglycaemic symptoms. Again, it is desirable to keep the blood sugar within normal limits or even on the low side of normal. Precision in this respect will be possible if insulin is required to counteract relatively small amounts of carbohydrate, but much more difficult if both are increased. Still the restricted use of carbohydrate may be allowed in certain circumstances. In elderly patients there is no object in trying to obtain any increase in carbohydrate tolerance. Such people may be given 1 oz. of bread* containing 15 grams of carbohydrate

*A standard bread containing 20 per cent. starch, made by adding bran and middlings to whole-meal, would be a great boon to diabetics

for breakfast, and 1 oz. for supper—that is, shortly after their injection. Perhaps 2 or 3 oz. of potatoes may be added at supper. The dose of insulin must be increased to some extent (perhaps at the rate of 1 unit for 4 grams of the extra carbohydrate). Instead of the bread the patient may take an orange, or apple, or half a grape fruit, or 3/4 oz. of oatmeal, etc., as the fancy takes him; but he must remember to take a strictly measured amount of carbohydrate in this way. In mild cases requiring less insulin proportionately more carbohydrate may be allowed.

In younger subjects up to the age of 30 or 40 the case is rather different. A large part of their life is in front of them, and it would be a pity to throw away any chance they may have of ameliorating their condition for the sake of a little extra freedom in their diet during the next two or three years. I do not advise these patients to take extra carbohydrate unless the urine consistently shows ketosis by the presence of a well marked "positive" Rothera reaction—that is, a dark purple colour, gradually developing when excess of ammonium sulphate crystals and ammonia and a tiny crystal of sodium nitroprusside are added to the urine. In this case I prescribe a small orange or half a grape fruit at breakfast or supper, and perhaps slightly increase the insulin. This seems to me a better plan than giving a definite amount of carbohydrate based on a rather problematical antiketogenous ratio between carbohydrate and fat as Woodyatt,⁷ Wilder,⁸ and Campbell⁹ have suggested.

Allen¹⁰ has recently pointed out the fallacy of a very high fat diet in treatment with insulin, since excess of fat is also a cause of hyperglycaemia. One of my patients in the insulin ward, an ex-officer aged 28, illustrates this point very well. He was one of my early cases and his diurnal blood sugar curves with and without insulin have been given (Fig. 3, curves A and B). When I began using insulin, I must confess that I inclined to the view that patients might be allowed as much food as they liked, apart from carbohydrates. During the greater part of a month's treatment this patient was having a diet (vegetables, protein, fat) of 3,310 calories, containing 110 grams of protein, and at the end 65 units of insulin a day. His age was 28; his actual weight was 162 lb., and his predicted weight 169 lb. The basal requirement was 1,570 calories. At the end of the month he had put on 10 lb. in weight. After omitting insulin for thirty-six hours the diurnal blood sugar (Fig. 3, curve C) was found to be very much higher than before treatment was begun. In view of this unsatisfactory result the diet was immediately cut down to 2,050 calories and 59 grams of protein, and he took 20 units of insulin a day. About six weeks later some determinations of the blood sugar during treatment, and thirty-six hours after stopping insulin, were again carried out. The results (Fig. 3, D and E) show a great improvement. This case is a good illustration of the fact that moderation in diet is absolutely essential during treatment with insulin.

AFTER-TREATMENT.

In the first place the patient must keep to the diet that has been prescribed for him. So long as the protein and carbohydrate content and the calorie value are not increased, variations in the kind of food taken may, of course, be made. The insulin must be continued in doses that just fail to produce hypoglycaemic symptoms. In the case of young subjects it is a good plan to increase the dose slightly on occasions—that is, by two units at a time, until mild symptoms appear—to be sure that the dose is still proving enough to keep the blood sugar low. The urine should, of course, never contain any sugar when it is tested.

Several of my patients have noticed reactions a few weeks after leaving the ward, while taking the dose of insulin prescribed. It is difficult to say whether this really means a gain in tolerance or whether it is due to the gradual increase in the strength of insulin supplied. If reactions occur, the dose must be gradually diminished until they cease.

Fallacies connected with the after-treatment are well illustrated by two of my cases. One patient thought that the pancreas wanted mildly exercising like a fractured

limb, and gradually increased the intake of carbohydrate till sugar appeared in the urine. The blood sugar at 3.30 p.m. rose from 0.126 to 0.187. Another who had experienced reactions with the dose of insulin prescribed gradually diminished it from 45 units a day to 15 before sugar appeared in the urine. The blood sugar was then found to be 0.23 per cent., which is undesirably high.

CHOICE OF CASE.

In my opinion insulin may be used with benefit in every case of true diabetes, young and old. I have not yet come across a case where it has failed to bring some relief. This is, I admit, surprising, especially as we often hear it suggested that diabetes is a syndrome due to many different causes. There is a striking unanimity among patients as to the effect of insulin. They say that they feel stronger and less tired. Insulin is of particular use in the various complications of diabetes. I have had special experience of its value in gangrene.

At present it is a common practice to try a régime of dieting for some weeks in order to get the urine sugar-free, and to use insulin only in cases where these measures fail. Mr. W. W. Payne and I realized the fallacy of this method when we found in three cases, who had become sugar-free or nearly so, that the diurnal blood sugar was considerably above normal (see Fig. 3, curve A). In spite of the consistently high blood sugar indicated by curve A, this patient only passed a trace of sugar on this day and the urine was sugar-free the day before. For a patient who can afford the continuous use of insulin, the latter should be used from the beginning of treatment. Insulin is supplied free to panel patients.

In early cases the prompt use of insulin is essential. It is dangerous to waste time with dietetic measures alone, because the disease may progress, and more insulin will eventually be required. In two of my cases, aged 33 and 25, treatment with insulin was begun within two months of the diagnosis; 15 and 20 units of insulin a day were sufficient to produce mild hypoglycaemic symptoms. In five other cases, aged 42, 40, 28, 24, and 12, treatment was begun from three months to one year from the diagnosis. The following daily amounts of insulin produced symptoms: 20, 35, 30, >40, 20. These cases, though few in number, point to the importance of early treatment.

The conclusion is that all cases who have, or have had, the ordinary symptoms of diabetes (not merely glycosuria) may be treated with insulin. Where the diagnosis can be made from the symptoms, there is no necessity to estimate the blood sugar first of all.

Insulin is unsuitable for cases of renal glycosuria. In these patients sugar is found in the urine, often during examination for life insurance, but they have never themselves suffered from the symptoms of diabetes mellitus. It is usually very difficult to distinguish clinically between renal glycosuria and very mild diabetes. The only safe way is to determine the blood sugar tolerance curve—that is, the blood sugar before and at stated intervals after taking 50 (or 100) grams of dextrose. This is an elaborate test, but considering that the question of treatment for the rest of the patient's life depends upon it, it should always be carried out.

DIABETIC AND HYPOGLYCAEMIC COMA.

Severe hypoglycaemic symptoms—for example, convulsions and coma—will not occur in the ordinary treatment of diabetes with insulin if the dose of insulin is slowly increased and a careful watch is kept for the earlier symptoms. I do not think that if a patient is treated in this way there will be any danger of his developing hypoglycaemic coma while asleep at night. Those of my patients who have experienced symptoms at night have been awakened by the symptoms at the beginning of the reaction.

But in certain circumstances there is not only a great likelihood of hypoglycaemic coma supervening, but its diagnosis may be extremely difficult. These circumstances arise during the treatment of diabetic coma, because vigorous treatment with insulin is essential, and the patient may pass into hypoglycaemic coma without coming round properly from diabetic coma.

At the beginning of treatment of diabetic coma a large dose of insulin should be given both intravenously and subcutaneously, and the subcutaneous injection should be repeated at four-hourly intervals, until the urine becomes sugar-free; insulin is then stopped until sugar appears again in the urine, and it is then continued in smaller doses at longer intervals. I cannot impress upon you sufficiently the importance of testing every specimen of urine for sugar as it is passed, and of catheterizing the patient in order to get a specimen, if there has been no urine to test for three or four hours.

In my opinion another very important method of treatment is to give large amounts of fluid, containing dextrose (or cane sugar) and sodium bicarbonate with a little sodium chloride. This will have the effect of keeping up the flow of urine, and so will help to get rid of the poisonous aceto-acetic acid, which is probably the cause of diabetic coma. A stomach tube, Einhorn's tube (or Ryle's modification), or, preferably, a long nasal tube and funnel, are absolutely essential for administering the fluid. The patient is made to lie on the right side so that the fluid will gravitate at once into the duodenum. A pint of warm sterile isotonic solution is given every hour. On no account should this treatment be stopped if the patient vomits, but the actual time of administration should be prolonged so as to prevent distension of the stomach. Care must be taken by frequent examination to see that oedema of the lungs does not develop. It is to be noted, as originally pointed out by Einhorn, that this is by far the most efficient way of introducing large quantities of fluid into the body, owing to the rapid absorption by the intestinal villi. If this method is used there is no necessity to inject fluid intravenously or subcutaneously.* Food other than dextrose should not be given while the patient is unconscious.

The following may be regarded as the characteristic symptoms of diabetic coma. The respiration is greatly increased in depth (air hunger); the rate may be either increased or diminished. The pulse is feeble, the tension of the eyeballs low, the veins collapsed, and the skin dry. The urine contains sugar, and gives a positive ferriochloride and Rothera's reaction. The symptoms of hypoglycaemic coma are to some extent the converse: the pulse is full and bounding, the veins stand out prominently; there is profuse sweating. I have seen some oedema of the lungs with consequent cyanosis, and fluid expectoration. The patient is convulsed as well as comatose. The urine is sugar-free, and ketones are absent. The respiration (as noted in one case) consisted of short shallow gasps, the rate not being much altered.

The treatment of diabetic coma is well illustrated by a case seen in consultation with Dr. Clough, and I am greatly indebted to him for many of the details. A woman about 50 years old became sick and drowsy and developed typical diabetic coma two days later. Diabetes had not been suspected before the attack. At 9 a.m. on October 11th she was difficult to arouse, and at 3 p.m., when treatment was begun, unconsciousness was complete. Forty units of insulin were at once given subcutaneously, and 20 units intravenously. A Ryle's tube was passed by pushing it down with the finger placed at the back of the throat. When once the end of the tube had entered the oesophagus further progress took place by peristaltic action. With the tube well inside the stomach, and the patient lying on her right side, two pints of the following mixture at body temperature were passed down the tube: Cane sugar 1 tablespoonful, sodium bicarbonate 1/2 teaspoonful, sodium chloride 1/4 teaspoonful, boiled tap-water to 1 pint. The tube was kept in position and one pint of the mixture was ordered to be given every hour until consciousness had been completely regained; 36 pints were given in this way over a period of forty-two hours. The urine was copious all the time and there were watery evacuations. The lungs remained clear from oedema.

Forty units of insulin were given subcutaneously at 7 p.m., 11 p.m., and 7 a.m. the next day and at noon. At 5 p.m. the urine was sugar-free and there were no ketones. There was profuse sweating and a bounding pulse (almost certainly indicating some hypoglycaemia). At 9 p.m. she seemed to recognize her husband. She had been in deep coma for thirty-six hours. The urine was still sugar-free. On October 13th the urine at 4 a.m. and 9 a.m. contained sugar, but no ketones. She said "Good morning, doctor." The tube was then removed from the stomach.

* In a case of coma recently treated in this way considerable anasarca developed after the patient had regained consciousness. This may have been due to the excess of sodium in the mixture, as Blum has suggested. A more suitable isotonic solution would contain the following: dextrose 3 per cent., sodium bicarbonate 0.5 per cent., potassium chloride 0.05 per cent., calcium chloride 0.03 per cent.

Treatment with insulin was continued in doses of 20 units every four hours during the day, and at 9 a.m. on October 14th the patient was fully conscious and food was begun. On October 17th she was able to chat, and said that she had been seeing animals, and in particular rats, up to this time. She was finally given 15, 10, and 20 units three times a day.

I have met with at least two cases of diabetic coma who have not become fully conscious, in spite of vigorous treatment with insulin, and have eventually died. The blood sugar was high, the values being 0.45 and 0.46 per cent., so that there was no question of hypoglycaemia. Ketones had disappeared from the urine, but the volume of the latter was suddenly greatly reduced, and there was a corresponding retention of urea in the body. In one case the blood urea was 0.2 per cent., and in the other the urea in the cerebrospinal fluid was 0.15 per cent. Death was probably due to uraemia. It is possible that the administration of fluid in bulk, as already described, may prevent the onset of this unexpected complication.

Treatment of Hypoglycaemic Coma.

A subcutaneous injection of 15 or 20 minims of adrenaline (1 in 1,000), or, failing this, the same dose of pituitrin, is given. This treatment will be of value if the liver contains a good store of glycogen. Plenty of sugar—that is, 4 to 8 oz. of cane sugar or dextrose—is given by mouth or by stomach tube. If the patient does not recover consciousness rapidly, an intravenous injection of 5 to 6 per cent. solution of dextrose is given. Up to one pint may be given, but 100 c.cm. will usually be ample. Dr. Hinds Howell¹¹ has recently reported the occurrence of hypoglycaemic coma as the result of exercise at golf in a patient who was being treated with 30 units of insulin twice a day. It has been suggested that such patients should carry sugar with them and wear a label round their necks with instructions what to do in case they are found by anyone in an unconscious condition.

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THE EARLY MECHANICAL TREATMENT OF ACUTE ANTERIOR POLIOMYELITIS.*

BY

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It has long been recognized that the serious disablement resulting from acute anterior poliomyelitis is, in many cases, dependent more on the existence of deformities than on the paralysis *per se*. In the treatment of such residual disabilities it is customary to obtain correction of all deformity by appropriate non-operative or operative measures, before carrying out any definitive reconstructive operation designed either to restore muscle balance or to stabilize a flail joint. In children who present multiple contractures of the lower limbs and who have never walked since the onset of the paralysis the preliminary treatment of the deformities may occupy many months. A whole series of manipulative or operative procedures may be required, the deformities being gradually unfolded in successive stages. We have no reason to feel dissatisfied with the functional results obtained under such conditions, because it is rare to meet with a child to-day who cannot be made to walk once deformities have been eliminated, no matter how severe the degree of residual paralysis, provided only that the patient is competent to hold crutches. But every patient so treated brings vividly before the mind a picture of the earliest phases of acute poliomyelitis, a stage when deformities are non-existent. The prevention

of deformity is, of course, by no means a new doctrine. It was expounded many years ago by Hugh Owen Thomas of Liverpool, and has always formed an integral part of the teaching of his distinguished successor, Sir Robert Jones. In this connexion we are also unlikely to forget the work of the late Frederick Batten of London, a physician endowed with surgical instincts. Yet, if we are to judge from the mass of neglected cases, we might be led to the conclusion that such teaching has failed to exert a widespread and lasting influence. On the whole, however, in recent years we are to chronicle a definite advance in the treatment and general handling of poliomyelitis in its earliest stages. To a large extent this has been brought about by the unique experience of a number of American observers, and more particularly perhaps of Lovett of Boston, who has made comprehensive observations on 5,100 cases which have come under his personal supervision since 1916. In the United States acute poliomyelitis is a veritable scourge, and many of the individual States have been compelled to develop special organizations in readiness to handle large epidemics from the outset, and to provide for the subsequent efficient treatment of patients during the recovery period.

In the British Isles the greater proportion of cases continue to arise sporadically, or in small groups, but a number of relatively formidable epidemics have been recorded. Thus, in the late summer of 1911 in the county of Westmorland, some 50 cases were encountered in epidemic form. In 1922 in the same area there was a small epidemic of 15 cases. Many of the children with the late sequelae of the 1911 epidemic have passed through my hands at the Ethel Hedley Hospital for Crippled Children, Windermere, and 9 cases of the 1922 group were admitted to this hospital in the acute stage. Future epidemics in the Lake Country will, I believe, be adequately provided for, the hospital acting in liaison with the health authorities, and thus fulfilling an educational mission to the medical profession and public in the area it serves. In this work we are following the lead given by the Shropshire Orthopaedic Hospital, Oswestry, and the Wingfield Hospital, Oxford. It is a relatively simple matter to cope with an epidemic of poliomyelitis when a well equipped special hospital with a team of expert workers is available, but the mass of sporadic cases seen both in the larger cities and country districts cannot at present be handled under such ideal conditions.

SYMPTOMATOLOGY.

Opportunities for early treatment depend on prompt diagnosis, and the principles on which treatment must be based will be determined by a clear understanding of the character of the primary pathological changes and their mechanical sequelae. It is thus desirable to consider briefly some of the more important clinical features of anterior poliomyelitis, and the nature and extent of the lesions in the central nervous system. It may be suggested that, as a surgeon, I am traversing ground outside my immediate province, but there is an ever-increasing body of surgeons who are best described in the striking phrase of Sir Berkeley Moynihan as "physicians doomed to practise surgery," or who fulfil the spirit of Harvey Cushing's conception that "the physician has become his own surgeon."

Three clinical stages with somewhat arbitrary limits are generally described:

- (1) The *acute stage*, which lasts usually not longer than four to six weeks.
- (2) The *recovery stage*, which extends approximately to the end of the second year.
- (3) The *chronic stage*, from the third year onwards; a period when all the resources of reconstructive surgery are demanded.

It would appear that the initial syndrome is comparatively unfamiliar to practitioners of medicine in general. The variability of the symptoms which usher in an attack of acute poliomyelitis is of course well known, and it is appreciated also that the clinical picture may bear a close resemblance to some of the more commonplace acute illnesses of childhood. Of the signs which may be considered as especially significant three have been found to

* A paper introducing a discussion on this subject before the Manchester Medical Society on January 9th, 1924.