3 c.cm. for the tenth and 2 c.cm. for the eleventh injection. She had no asthma all this time, though previously she was confined to bed every two or three weeks. She has remained well, except for two slight attacks in about three months.

In view of the fact that she had tried everything previously with no benefit, this case was very striking, and showed the rapidity with which the peptoned serum agar acted.

A man, aged 27, was sent to me by Dr. Randall of Wimbledon on November 24th, 1926. He had had asthma since he was 17. It is in his family. He went to Shanklin one year and was so bad that he had to leave. Then he went another year and was never better. This is a curious fact. I asked Dr. Randall to give him peptone, which he did intramuscularly, with but little effect. I then gave him nine injections of peptoned serum agar, from 1½ c.cm. to 4 c.cm. During the first three or four injections his asthma was but little better. It then entirely disappeared. Dr. Randall gave him the last three injections—2 c.cm., 1½ c.cm., and 1 c.cm. He remained quite well for about six weeks. Then he took a change, which made the asthma come back a little. He is now free from attacks, but is a little wheezy at night some-times. He writes that he is highly satisfied with his condition.

These are cases of great interest, and show the treatment to be very valuable. But I have had a few cases which did not respond to it; these form a very small percentage.

Women are much more subject to endocrine disturbance than men. The thyroid and the ovaries are the principal offenders.

A girl, aged 12, was brought to me from Lichfield by her mother. She looked healthy and was well grown. Her sister had horse asthma. I ordered peptone for her, which was given by her school doctor intramuscularly. She was no better. Dr. Rowlands of Lichfield then injected it into the vein, when she greatly improved, but the asthma returned. She was brought back to me in September, 1926. Her mother told me she had menstruated, but it was very scanty. I ordered her 1 grain of thyroid extract a day, and 5 grains of ovarian extract twice a day. I also prepared peptoned serum agar for her, and Dr. Rowlands gave her the injections. She has been quite well since. Her menses became much more profuse after the tablets of ovarian substance.

It will be noted that though intramuscular injections of peptone did her little good, yet she was much better after those given intravenously. I do not consider a patient should be left without trying the intravenous method. I give the intramuscular (in the back of the upper arm) only in young children and weak elderly persons. But, although quite safe, the majority of doctors do not like giving it intravenously.

The ovaries contain a hormone which has been much inquired into lately. Pratt⁸ declares that it exists in the Graafian follicles, corpus luteum, and placenta. S. Asdell and F. Marshall, F.R.S.,⁹ state that the hormone injected subcutaneously produces typical pro-oestrous change in the uterus of the bitch and changes in the vaginal epithelium.

Some (Coca, etc.) consider that asthma and hay fever are allergies, but they are not anaphylactic. I believe that, though they are allergies, they are of the family of "toxic idiopathies," and are to be considered anaphylactic. An allergy differs from an artificial anaphylaxis, as an allergic patient will react the first time he comes in contact with a protein to which he is naturally sensitive. Allergy has the same fundamental nature as anaphylaxis; I have discussed this elsewhere.¹⁰ Huber and Koessler¹¹ place the pollen extracts as antigens, producing characteristic anaphylactic reactions in guinea-pigs, and antibodies are found in the blood of properly sensitized animals, also positive broncho-constriction is produced. The view of Coca has been adversely criticized by van Leeuwen in his recent work on allergic diseases.

Peptoned serum agar must be prepared very carefully. The greatest care must also be made in injecting it into the vein, which must be done slowly. I always use a No. 12 needle. The piston of the syringe must always be withdrawn a little when the needle is supposed to be in the vein, and if some blood comes into it, it is all right. Otherwise trouble may ensue. Those who make and give it properly will be well rewarded.

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THE TREATMENT OF DIABETICS AS HOSPITAL OUT-PATIENTS.*

BY

C. J. C. EARL, M.R.C.P. (IREL.),

MEDICAL REGISTRAR, SALFORD ROYAL HOSPITAL.

THE difficulties in the way of the successful investigation and treatment of diabetes mellitus in the ordinary out-patient department of a general hospital are familiar to every physician. At the Salford Royal Hospital an attempt has been made to meet them in a special out-patients' clinic for all diabetic cases. The clinic has been in my charge under the direction of the honorary medical staff.

In presenting this account of the first year's working of the clinic it must be pointed out that the work has not been undertaken from the "research" point of view, but as a matter of necessity, and that nearly all our patients are of the labouring class, uneducated and financially badly off—not at all promising material for elaborate dietetic treatment. A few were of the artisan class, one a clerk, and one—an incorrigible carbohydrate "smuggler"—was a schoolmistress.

The functions of the clinic are investigation and control of patients who are sent to the clinic from the wards, from the general out-patient department, and occasionally direct from the practitioner.

All cases were divided, before investigation, into the two groups of severe diabetes mellitus, and of glycosuria of other origin. In the first group were included all cases with ketosis or a short acute history, and all cases in young adults and children. Such patients were immediately admitted to the wards for full investigation and control before re-discharge to the clinic. The second group consisted of patients whom it was thought safe to investigate as out-patients. Investigation consisted of blood and urinary analysis and of sugar tolerance curves; the latter, unfortunately, were not always possible to perform owing to pressure of work, but they were performed in at least all doubtful cases. In a few instances patients were admitted to the wards for a day or two for tolerance estimation.

Classification of Cases.

After investigation all cases were classified into four groups. Group I consisted of all cases considered on clinical grounds to be definite diabetes mellitus. Group II consisted of diabetics of the milder elderly type, whose blood sugar—taken four hours after breakfast—was constantly at or about 0.180 per cent. or more; whose urine contained sugar, often in large amount, but no acetone; and whose weight remained constant or even increased. This group corresponds roughly to the hepatic group of Maclean,¹ and it is supposed that these are primarily cases of defective storage by the liver. The patients in this group were nearly all of obese type, and, with one exception, were over 45 years of age. It is certain that such persons tend to develop a condition of true diabetes mellitus, though of a mild type. Group III consisted of patients—clinically midway between the other two groups—supposedly in this category. Group IV contained three cases.

One woman of 70 had a glucose tolerance normal for her age and some glycosuria. She was considered to be a case of the "normal glycosuria of the elderly" described by Langley.² The other two cases in the group were glycosuria of renal origin. Their progress was interesting. The first cleared up entirely in a few weeks. The second, after remaining at a normal blood sugar level for three months, presented herself at the clinic one day with acetoneuria and a blood sugar of 0.285 per cent. This patient has not attended the clinic since, but it is known that she is being treated with insulin by her own doctor.

TABLE I.—Classification of Cases.

Group.	No. of Cases.
I. Diabetes mellitus	20
II. Elderly hepatic type	14
III. Elderly mellitus type	10
IV. Non-diabetic glycosuria	3
Total	47

There were five additional cases, but they are not included in the table as their investigation was not completed.

* A paper read before the Salford Division of the British Medical Association.

Not all the elderly cases fall into Groups II and III. Group I contained four patients over 50 years of age, one of whom was a severe case difficult to control. All four patients were of spare habit, in contrast to the obesity which was the rule in the other groups.

Conduct of the Clinic.

The clinic was held on one day a week (Friday) from 11.45 a.m. to 12.45 p.m. Each patient brought with him a sample of urine, which he handed to the nurse to be tested. He then went into the examining room and was weighed, after which he interviewed the medical officer, gave particulars of progress, home tests of urine, etc., and received any advice or help which he might require. He then went to the laboratory, where blood samples were taken by the house-physician, or by the laboratory assistant. The whole procedure took less than half an hour as a rule.

An informal atmosphere was cultivated; patients were encouraged to compare notes of their progress, blood sugar content, and so forth. Nearly all of them inquired anxiously about the "blood tests," and many of them learned to read their charts at a glance. Patients were encouraged also to watch their urine being tested, and some of the more responsible type were allowed to take charge of the weighing at times. Considerable importance was attached to this matter of "atmosphere." It kept the patients cheerful and good-tempered, enabled one to obtain their confidence, and kept them interested in their progress with the least possible tendency to depression. Those who were convicted of dietary indiscretions were good-humouredly but roundly rated in front of their fellow patients, and whilst these scoldings were always taken in good part, they seemed to have an excellent effect, and the offence was rarely repeated.

The time fixed had several advantages. It enabled women to attend and to get home in time to prepare dinner; it enabled working men to attend in their dinner hour; and, most important of all, blood specimens were taken at a uniform time. Patients were told to have breakfast at 8 a.m. so that blood specimens were taken four hours after the meal—a standard which is, for practical purposes, as good as the ideal, but obviously impossible "true starvation" level.

Control of Cases.

The tests used as a routine in controlling the cases were (1) blood sugar estimations, (2) urinary analysis, and (3) weight.

Blood Sugar Estimations.—These were performed at each visit in nearly all cases. Maclean's method for capillary blood was used. An attempt was made to keep the blood sugar of all Group I cases down to a figure below 0.135 per cent. in specimens taken four hours after breakfast. This was generally easy, the more so as cases in this group nearly all came to the clinic from the wards of the hospital, where they had been fully controlled and trained before discharge. Some of our best cases in this group had for months at a time readings varying from 0.085 to 0.130 per cent. Any sudden alteration was at once inquired into. Caution in increasing insulin dosage prevented any alarming drop. The commonest cause of a rise was found to be a "cold" or similar minor ailment. Overstrain and worry of any kind also showed their traces immediately in the blood sugar percentage. It may not be out of place to mention here that all our working-men patients reported glycosuria on the first morning of the general strike of last May. Illicit food was surprisingly rare as a cause of sporadic rises in blood sugar content. In the elderly type of case regulation was not so strict. Figures of 0.105 to 0.250 per cent. were commonest, and were found harmless; I have had more than one patient whose blood sugar, taken four hours after breakfast, was constantly 0.300 per cent. or more, who remained perfectly fit, the urine loaded with sugar but acetone-free, the weight maintained or even definitely increased, and no general symptoms of any kind occurring.

Urinary Analysis.—Patients were instructed to pass water into a clean receptacle immediately before going to bed, and upon rising next morning to urinate again into

the same receptacle. In this way a composite sample was obtained of "starving" and "feeding" urine, which was regular and fairly average in composition. The urine was tested by Fehling's method. Quantitative tests were not performed, the sugar content being entered as +, ++, or +++, according to the reduction obtained. Acetone bodies were tested for by a modification of Rothera's method, which was most satisfactory. The presence of acetone was quite rare and was regarded as indicative of a serious breakdown in control, usually sufficient to warrant admission to the wards. Home examination of urine for sugar was encouraged, and in most cases insisted upon. It was found quite easy to teach patients to perform the tests. The result of the daily testing was reported at each visit and was duly charted. We attach great importance to this home testing of urine. It gives early and fairly accurate information, it keeps the patient interested in his progress, and provides a constant reminder of the need for care.

Weight.—Patients were weighed at each attendance. The week-to-week variations were not found to be of any value, but, watched over longer periods, the weight proved an index to progress, more especially in cases from Groups II and III. The behaviour of the weight was frequently the only means of distinguishing between these groups. In the true diabetic group a drop at the commencement of treatment was not uncommon, but after a certain stage had been reached the level became constant, or rose a little. In Groups II and III this preliminary loss practically never occurred. We have had patients weighing 12 st. who have been changed suddenly from an unrestricted diet to one of 1,800 calories or less who have never lost a pound in weight.

Diet.

The diet used had to be cheap and simple, but sufficient to maintain the patient at his or her usual occupation. The food ratios taken were based on those recommended by Langley,³ and in use in the wards of the hospital for some time past. The actual carbohydrate:fat ratio in the diet most used was 1.37:1 in grams (molecular ratio—fatty acid to total available glucose=0.48:1). In some cases Langley's original ratio of 1.6:1 was used (molecular ratio—fatty acid:total glucose=0.38:1). In both cases the protein content was about 0.75 to 1 gram per kilo body weight, or rather less in elderly patients. In no case was the gram ratio C:F lower than 1:1. These ratios are much higher than are commonly used, though Sansum⁴ uses not only higher C:F ratios, but much higher calorie values with good results.

The advantages claimed are several. First, from the point of view of practicability, it is simple and cheap—its average cost is about 10s. a week—and easy to manage for even the most stupid patient. Furthermore, its generosity in carbohydrate makes it far more tolerable to the patient than the more conventional diet, with a corresponding increase in the probability of its being adhered to.

From the metabolic point of view the advantages are also important. The high carbohydrate:fat ratio gives a much lower ketogenic:antiketogenic ratio than the more usual diets based on the figures of Wilder⁵ or Woodyatt.⁶ It follows that in any sudden decrease of carbohydrate tolerance—from such a cause as an acute infection, etc.—there will be a larger margin of safety before the onset of acidosis in our diets than in diets based on their figures. Further, should such acidosis occur, the blood sugar content will—on our diets—rise more quickly and to a greater height, warning symptoms will be earlier and more marked, and an increased insulin dose will be safer than when diets of low carbohydrate:fat ratios are used.

It is quite certain that, apart from gross ketonuria, patients taking diets on the older basis are constantly on the verge of a milder acidotic state, with consequent detriment to their general health and diminution in what may be called the "pre-comatose margin of safety," in the event of a further breakdown. It is worthy of note that Campbell,⁷ using a molecular ratio fatty acid:glucose :: 1.3:1, finds that it is common in patients whose blood sugar is fully controlled to find acetone in the early morning urine specimen.

A further point is that patients appear to be satisfied

and maintain weight on a surprisingly low calorie intake. This seemed to apply specially to the elderly "hepatic" type, several of whom were able to do their housework on a diet barely sufficient—on the Aub Dubois standard—for their basal metabolic requirements. Not all the elderly cases were subjected to the full dietary régime. In some cases "restriction of bread and potato" was considered sufficient, and in one or two no dietary regulation was imposed.

Insulin.

The use of insulin in the clinic had to be modified by the two considerations of safety and expense. With regard to the first, it is obvious that some few of the patients attending such a clinic as this are quite unfitted to be allowed to administer insulin to themselves, except in cases of absolute necessity. This difficulty was in one or two cases obviated by having the injections given by the patient's own doctor, but this plan is obviously unsatisfactory, and, in general, patients of this type were treated on dietetic lines alone. The expense of insulin therapy was a bar to its use in many cases. Patients who were insured persons were, of course, able to obtain supplies free, but in other cases the supply had often to be limited, or its use entirely discontinued on the grounds of expense. Only in exceptional cases did the hospital supply insulin free of charge.

Subject to these limitations insulin was used freely. Its use was never commenced in the clinic itself, patients being always admitted to the ward if it was considered necessary. Before discharge to the clinic again, patients were made to give their own injections, and thoroughly educated in the use of the syringe, and it was surprising what unpromising patients could be educated to the routine by tactful ward sisters. No trouble was experienced with the injections. The hospital supplied syringes and needles at cost price, and issued spirit for sterilizing as required.

Dosage varied from 6 to 80 units daily, given in two doses before the two principal meals. There were no serious cases of hypoglycaemia. Patients were fully warned of the danger of the condition, and told to carry lumps of sugar in case of accident. Mild hypoglycaemic reactions, lasting a few minutes only, occurred in several patients from time to time, and were considered to be of good prognostic significance. The patients knew what was happening to them, and allowed the reaction to go on to the stage of acute discomfort, if necessary, before taking sugar. It was found that in these cases the insulin dose could be gradually reduced, being kept at each lower level in turn, till the patient complained again of hypoglycaemic reaction, before again reducing the dose (one case reduced from 40 to 8 units daily).

In Table II are given the results of insulin therapy, the standard of increased pancreatic function being reduction of insulin dosage without detriment to the blood sugar. The lack of improvement in cases in Groups II and III is probably due to the fact that no serious attempt was made to bring their blood sugar to normal, consequently "pancreatic rest" was never obtained. Of the two patients in Group I whose pancreatic function decreased, one has a surgical affection—probably tubercle—of the kidney, for which he is being admitted for surgical investigation, etc.; the other is a woman who has several times been convicted of dietary "sprees."

TABLE II.—Results of Insulin Therapy.

Group.	Number Taking Insulin.	Pancreatic Function.			Weight.		
		Increased.	Maintained.	Decreased.	Gained.	Maintained.	Lost.
I.	16	7	7	2	11	3	2
II.	1	0	1	0	1	0	0
III.	3	0	3	0	1	2	0

Conclusions.

The results of the first year's working of the clinic were considered good, and showed a marked improvement over the results obtained for the period during which such cases were treated in the general out-patient department. The

credit for this seems to be due to careful supervision acting partly as a check on the dietary régime, etc., and partly as an early warning of any trouble commencing.

The diet employed seems to have had a good effect, and its simplicity and palatability are probably largely responsible for the small number of failures to adhere to it.

Of the 44 cases in Groups I, II, and III dealt with in Table I, two—both diabetes mellitus—refused treatment after a week or so. The remaining 42 are dealt with in Table III.

TABLE III.

Group.	Improved.	Condition Maintained.	Worse.
I. ...	8 ...	7 ...	3 ...
II. ...	2 ...	11 ...	1 ...
III. ...	1 ...	7 ...	2 ...

The standards by which progress has been judged in this table are: weight and blood sugar level, and in insulin cases decreased dosage required. No case has been considered "improved" or "maintained" unless the blood sugar was lowered or remained at its original level respectively. The larger number of good results in Group I is greatly due to the fact that in Groups II and III we were satisfied with maintenance of weight and blood sugar level, whilst in Group I we were much more strict, and made every effort to keep the blood sugar down and to recover pancreatic function. Of the three cases in this group who had deteriorated at the time of review, two had been convicted of dietary indiscretions on a large scale, whilst the third is the renal subject referred to in a previous paragraph.

The method of handling these cases described needed no extra staff and no elaborate biochemical work, whilst the results obtained seemed more than to compensate for the extra trouble involved. It is hoped next year to improve the department in several respects, notably in the earlier and more complete investigation of cases in Groups II and III.

My thanks are due to the honorary physicians of this hospital for allowing me to treat these cases, and for the courtesy and kindness I have always received from them; also to Dr. W. B. Roantree, late house-physician to this hospital, for his efficient and enthusiastic help.

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A SEVERE CASE OF HYPOGLYCAEMIA.

BY

H. CECIL BARLOW, M.B.LOND., M.R.C.S.,
L.R.C.P.,

HONORARY PHYSICIAN, LINCOLN COUNTY HOSPITAL.

HYPOGLYCAEMIA is almost always preceded for a short period by highly suggestive symptoms of its onset. The following case is an exception.

H. B., aged 16, was sent into hospital on February 1st, 1927. He had been ailing for a month with loss of appetite, thirst, and loss of weight. When seen by Dr. Sydney Scott on January 22nd he complained of a nasty taste, his tongue was dirty, and throat sore, but he looked well. On January 31st he complained greatly of thirst, and the urine was found to be full of sugar. Two days later he had changed greatly for the worse; he was much emaciated, somnolent, and had air-hunger. The house reeked with the smell of acetone.

On admission he was very drowsy, the tongue dry and furred, breath heavy with acetone, body extremely emaciated and shrunken, eyeballs very soft. The urine was loaded with sugar, diacetic acid, and acetone, and the reaction was very acid. Respiration was rapid and deep, the pulse rapid, small, and feeble; the temperature was subnormal. No septic focus could be found. The onset of coma seemed imminent.

He was given 40 units of insulin hypodermically, with 40 grams of glucose and 8 grams of sodium bicarbonate by the mouth. He drank copiously of water and black coffee. The bowels were moved by an enema.

He was given 20 units of insulin with glucose and bicarbonate every two hours for the next twenty hours—in all 240 units; the urine, examined every two hours, contained much sugar; frequent blood sugar estimations could not be made. His general condition was improving, respiration was less rapid, the pulse stronger, and he was less drowsy.

Insulin was increased to 30 units and given with glucose and bicarbonate every two hours for the next twelve hours; the urine