SOME OBSERVATIONS ON

ABNORMAL CARBOHYDRATE METABOLISM

IN CERTAIN CONDITIONS OTHER THAN UN
COMPLICATED DIABETES BASED CHIEFLY UPON

BLOOD-SUGAR ESTIMATIONS AND GLUCOSE

TOLERANCE TESTS.

THESIS

PRESENTED FOR THE DEGREE OF DOCTOR OF MEDICINE OF THE UNIVERSITY OF GLASGOW

· BY

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INTRODUCTION.

Before proceeding to the subject proper of this paper, it is interesting to note some points regarding the means by which the investigations were carried out - namely, the estimation of the blood sugar percentage and the glucose tolerance test.

A. The Blood Sugar.

Though it was recognised as far back as the days of Willis, 1674, that the urine in diabetes contained a sweet substance, later identified as sugar, it was not until 1775 that Dobson discovered that the blood serum in diabetic persons had a sweet taste. In 1892 Freund found that normal blood contained small quantities of a reducing substance, and later Lepine and Boulud found that there was an increase of the reducing power of the blood in depancreatized animals. It was not, however, until comparatively recently that methods of estimating the actual percentage of sugar in the blood were worked out.

Many of the earlier methods of blood sugar estimation were of little value, inasmuch as they did not aim at removing all traces of protein which vitiate the result. Of the various methods of estimation elaborated, the one employed in this case was McLean's, as being a

thoroughly practicable one for use in the wards of a hospital, and dependable in its results - provided the solutions employed be reasonably fresh. The main advantage of the method is that only a small quantity of blood, 0.2 cc., is required, obviously a point of great importance where repeated estimations have to be made within a short period of time.

Method of Blood Sugar Estimation.

A brief outline of the process may be given as follows:-

The required amount of blood, 0.2 c.c., is taken by means of a special graduated pipette from a prick in the ear or finger (in most cases the ear will be found more satisfactory), and run into a small flask containing a measured amount of a 15% solution of sodium sulphate which has been slightly acidified just before use. The contents of the flask are brought to the boil, dialysed iron is added to precipitate the proteins, and the mixture is cooled then filtered. The filtrate is boiled with an alkaline copper iodide solution, a precipitate of cuprous oxide being thrown down; after boiling six minutes the flask is cooled and an excess of sulphuric acid added, with a resulting effervescence and the liberation of free iodine. The amount of free iodine is now estimated by titration with a 1/400 sodium thiosulphate solution, starch being used as indicator.

By comparing the results of titration with a control containing no blood and that obtained with the blood filtrate, the percentage amount of sugar can be made out on reference to special tables drawn up by McLean.

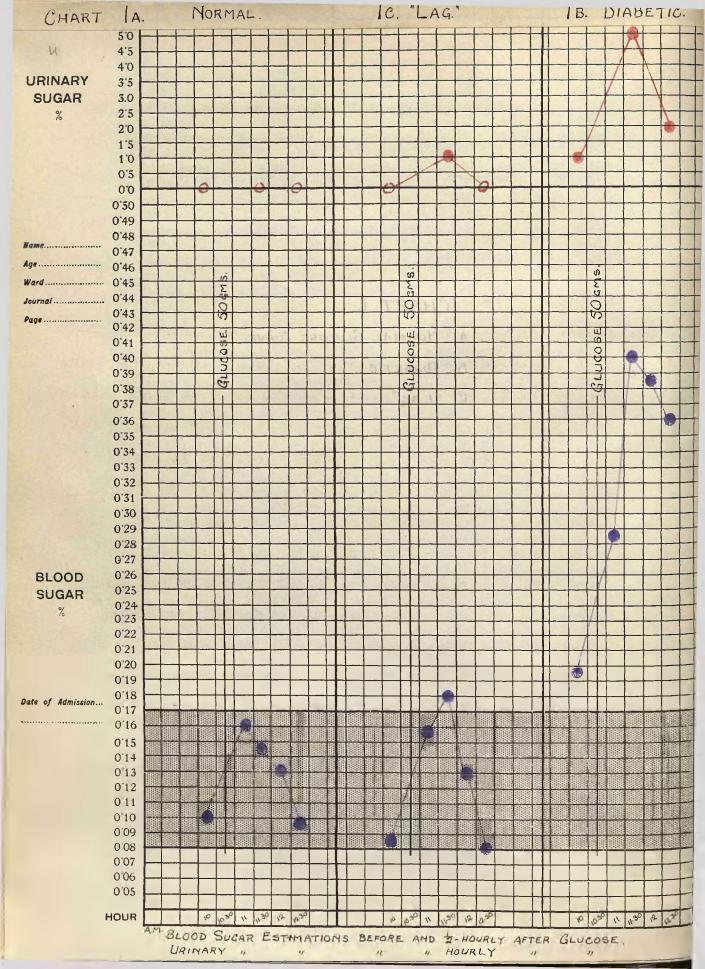
The Glucose Tolerance Test.

A single estimation of the blood sugar is obviously of little value in investigating a case, since various governing factors, such as diet, may be at work at the time of investigation. A method had therefore to be devised whereby the varying sugar-content of the blood could be followed by investigation under certain fixed conditions. The one adopted was one in which tolerance of carbohydrate food was tested by giving the patient a fairly large quantity of pure glucose by mouth, and then testing the blood at intervals. Throughout this investigation the method of carrying out a glucose test was as follows:-

If possible, the patient received no food for at least three hours prior to the commencement of the test. The requisite amount of blood was taken off for a sugar estimation, and a sample of urine was obtained and tested for sugar. The patient was then required to drink 50 grammes of pure glucose dissolved in about 100 c.cs. of water, with the juice of a lemon added to make the draught less nauseating. Half an hour later a second sample of

CHART 1.

- A. NORMAL GLUCOSE CURVE
- B. DIABETIC
- C. "LAG"



blood was taken; and further samples of blood were taken off at half hourly intervals up till two hours after the glucose. One hour and two hours after the glucose a sample of urine was obtained and tested for sugar.

The results obtained by this method are best illustrated by means of a charted curve. Chart I2 shows the type of curve obtained in a normal person. In such a person the blood sugar rises for $\frac{1}{6}$ - 1 hour after glucose from its pre-glucose level of about 0.1%; the maximum level reached seldom exceeds 0.16%, and from this it falls rapidly back to normal or slightly below the starting-level, reaching this point within $1\frac{1}{2}$ - 2 hours after the taking of glucose. No sugar appears in the urine since the "renal threshold" of approximately 0.17% is not exceeded.

In an abnormal case the blood sugar at some one or at several points exceeds the "renal threshold" and sugar appears in the urine; the rate at which the blood sugar returns to the starting-level depends upon the degree of carbohydrate intolerance. In a well-established case of diabetes, for example, the blood sugar is still high at the end of two hours - in the most severe cases it may be still mounting. This type of curve is illustrated in Chart IC.

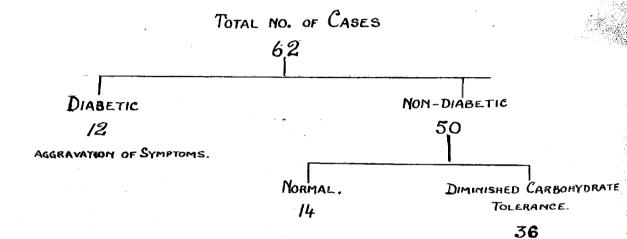
Other cases show a curve which rises sharply above the "threshold" of 0.17% with the consequent appearance, as a rule, of sugar in the urine, but which describes an equally abrupt fall to the original level within $1\frac{1}{2}$ - 2

To this type the name "lag" curve has been given, and an example of it is shown in Chart IDI. explanation of this form of curve appears to be that the sudden ingestion of a large quantity of sugar causes a delay in the action of the inhibiting mechanism which ordinarily prevents sugar passing into the circulation, with the result that a temporary rise of the blood sugar, accompanied by glycosuria, takes place. Presently, however, the normal mechanism comes into play and the remainder of the curve follows the ordinary course. A curve of this type may be considered as indicative of some degree of abnormal carbohydrate metabolism. It is interesting to note in this connection that one or two cases of early diabetes personally investigated yielded a "lag" curve, but later on, when the disease had progressed considerably, a typically diabetic curve such as that seen in Chart IC. was obtained.

EFFECT OF SEPSIS

NO

CARBOHYDRATE METABOLISM.



ABNORMAL CARBOHYDRATE METABOLISM IN CASES OF SEPSIS AND IN INFECTIONS.

It is well-known to those who have had to deal frequently with cases of diabetes that the incidence of sepsis in the course of the disease almost invariably leads to aggravation of the symptoms already present. It has also long been observed that glycosuria is a common occurrence in cases of sepsis. Obviously, then, sepsis produces a similar effect on diabetics and on apparently normal people. Comparatively little, however, appears to have been written concerning the immediate effect of sepsis on the sugar-content of the blood and on carbohydrate metabolism. It was with a view to ascertaining something of this effect and in the hope that it might throw some light on the cause of diabetes that the investigation of the following cases of sepsis, &c. was undertaken.

In all a series of 62 cases with active sepsis was investigated.

Of this number 11 cases or 17.5% were known to have suffered from diabetes before the incidence of the sepsis which was presently active; one case was probably a diabetic before admission but the evidence was not conclusive. The remaining 50 cases gave no history of diabetic symptoms, nor was there any reason to suspect hyperglycaemia or glycosuria prior to the onset of sepsis. Investigation during active sepsis, however, yielded evidence of abnormal

carbohydrate metabolism in 36 cases, or 72%, leaving only
14, or 28%, which showed no abnormality. Wherever possible,
observations made at a time when the patient had no sepsis
were used as controls, and the results of such controls were,
as will be seen, very striking. Except where otherwise stated,
however, the tests were carried out during active sepsis.

(a) The Influence of Sepsis in Diabetic Subjects.

In several of these cases the presence of diabetes had not even been suspected until with the incidence of sepsis the symptoms became obvious, and in others the symptoms had been so slight as to call for little or no attention or treatment. In the latter cases (cases 1, 2, 3, & 11.) a subsequent investigation of tolerance was carried out and yielded a typical diabetic curve. The question of whether this diabetic condition was likely to have been present before the onset of sepsis, or whether it had developed as a direct result of the latter remains to be discussed later. (See page 88) In the meantime they are considered as coming under the heading of diabetics with superadded infection.

CASE 1. D. MeI.

DIABETES + CARBUNCLES.

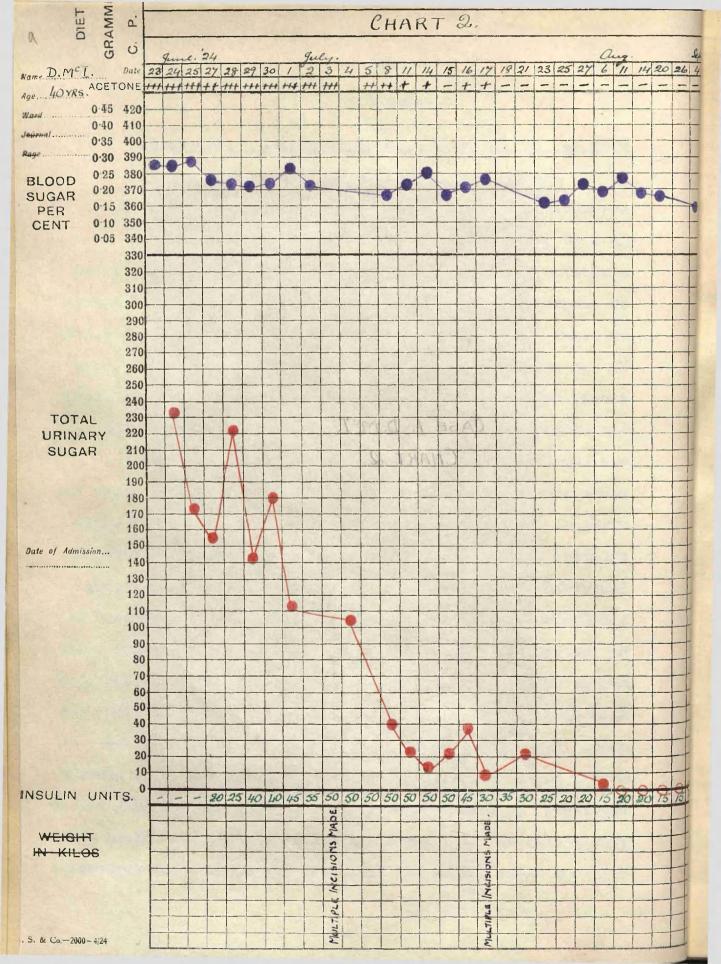




CASES.

Case I. D. Mc. I. Aged 40 years. Storeman.

Admitted in June, 1924, suffering from a large carbuncle involving the right suprascapular region. He gave no previous history of diabetic symptoms, but on admission was found to be smelling strongly of acetone, and on examination the urine was found to contain a large amount of sugar and acetone bodies, while the blood sugar was 0.275%. He was put at once on a suitable diet with insulin in large The carbuncle was freely opened by a crucial incision, doses. but infection spread until the whole surface area of the back was involved in small carbuncles and pustules. (See accompanying photograph.) On 3/7/24, about 10 days after the original incision, multiple incisions were made under ethyl chloride anaesthesia. The urinary sugar excretion gradually diminished but the blood sugar remained high - about 0.2%; the acetone gradually lessened until on 18/7/24 it ceased to be present. The infection next spread to the right arm which became greatly swollen, and on 17/7/24 further incisions were made under ethyl chloride. In all, thirtyfive incisions were made. From that time on infection ceased to spread, the wounds began to heal, and the man's general condition greatly improved. He became sugar-free on 22/7/24 and remained so, or practically so. till his dismissal on 4/9/24. The blood sugar remained rather high, his threshold for sugar being apparently

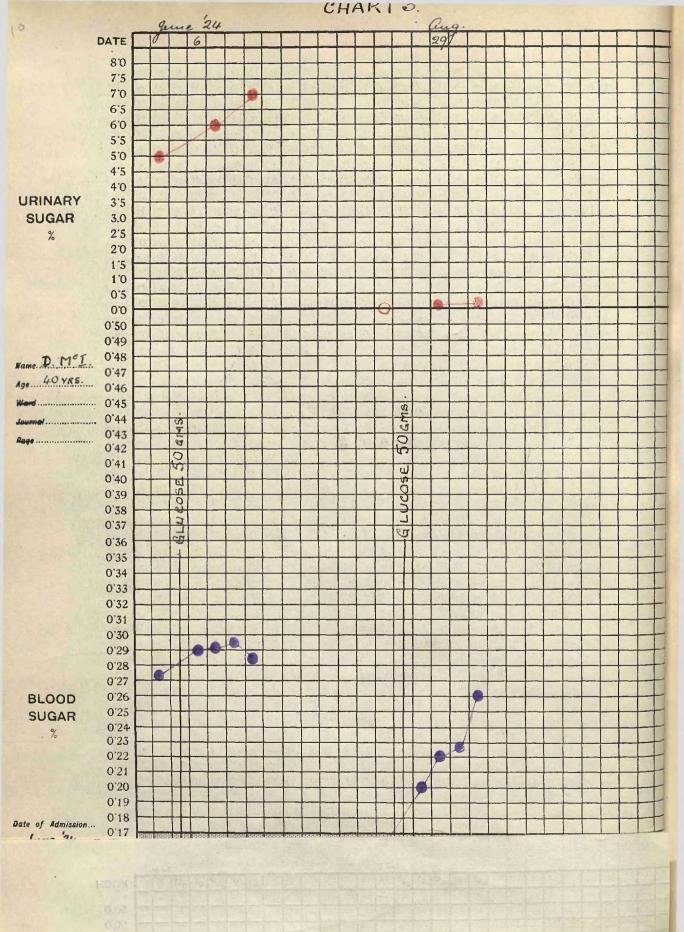


raised. The dose of insulin was gradually reduced from the original one of 50 units per day down to 10 units at the date of dismissal.

The course of this man's illness, the variations in the blood sugar, &c. are well illustrated in Chart 2. His condition on admission has been already described; for the following ten days blood sugar, urinary sugar and acetone remained abundant in spite of suitable dieting and large doses of insulin. Immediately after surgical treatment on 5/7/24, however, a striking fall of the urinary sugar output and of acetone was evident, and by 22/7/24, when the sepsis was still further under control, the urinary sugar was reduced to a mere trace and acetone was absent, in spite of the fact that the dose of insulin was now reduced to half the original amount. Good progress continued, the sepsis gradually cleared up entirely, and the man remained sugar-free on an ample diet with only 10 units of insulin.

The blood sugar curve showed no such striking fall to normal; so long as the sepsis was active it remained at a comparatively high level with few variations, in spite of the large doses of insulin. Doubtless the level of the curve would have been very much higher had it been uncontrolled by insulin. It was only after three months' treatment when sepsis was reduced to a minimum that the blood sugar reached a normal level. Three weeks after dismissal it had risen again to 0.23%, possibly owing to neglect of diet, more

Case I. D.MºI. CHART. 3

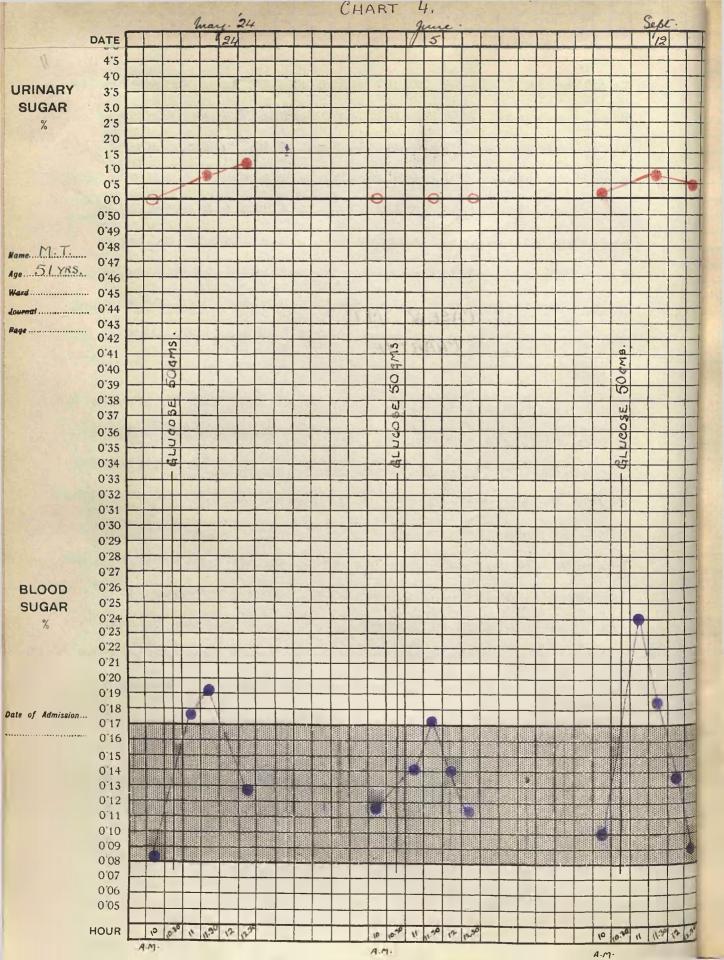


probably as the result of another factor which had now come into play. For some time he had complained of cough and spit, and on examination of the sputum on 26/9/24 it was found to contain fairly abundant tubercle bacilli. The chest yielded dullness and tubular breathing at the right apex, but very little rale was audible. The X-Ray revealed extensive consolidation at the right apex. He was admitted to a sanatorium where he improved considerably, but refused to stay more than two months and died at home a month or two later.

Chart 3 shows the results of two glucose tests, the first of which was carried out a day or two after admission when sepsis was at its height; the second after an interval of two months when sepsis was minimal, the temperature normal and glycosuria absent. Both curves are obviously diabetic in type. In the earlier one, however, the blood sugar level throughout is much higher and glycosuria is considerable, while only a trace of sugar appears in the later curve. Tolerance had evidently been regained to a certain degree.

The striking points, obviously, in this case are the entire absence of diabetic symptoms prior to the onset of sepsis, and the rapid development of extremely urgent symptoms as the latter advanced; and the gradual subsidence of the diabetic condition along with the clearing-up of the septic foci.

CASE 2. M.T. CHART 4.



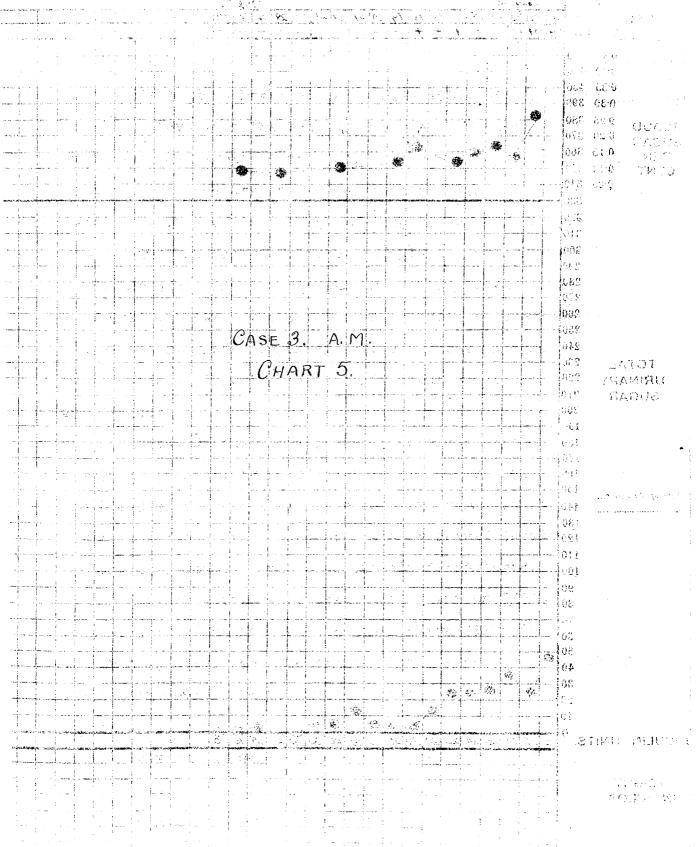
Case No. 2. M.T. Male. Aged 51 years. Carbuncle.

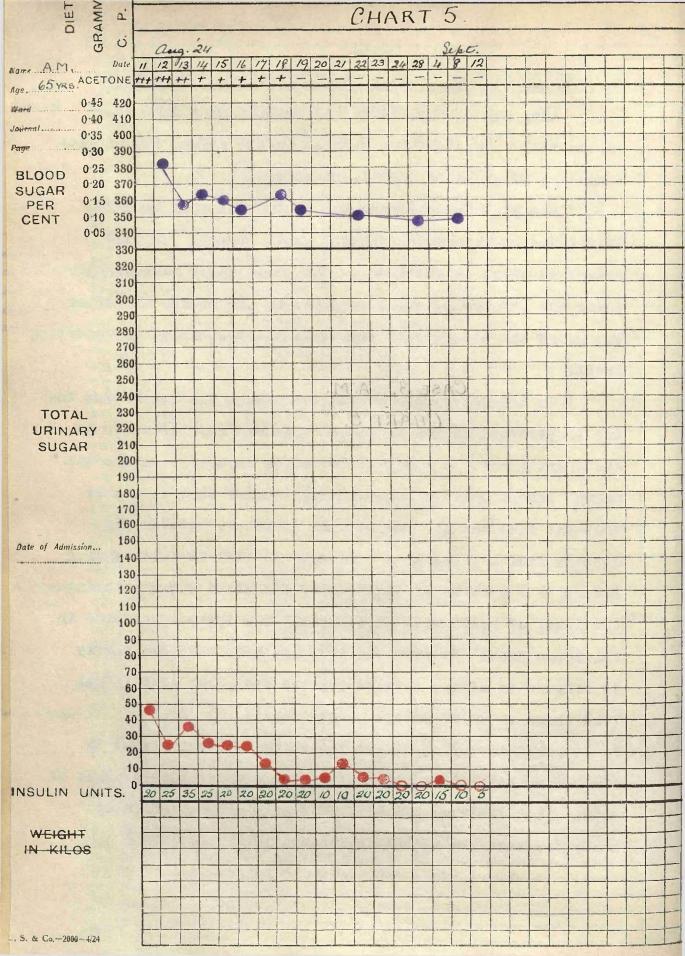
Admitted in May, 1924, suffering from a carbuncle on the neck. No sugar was present in the urine, but he gave a history of moderate thirst and polyuria.

His glucose tolerance was investigated on 24/5/24, when the temperature was running about 100-101° and the result is shown in Chart 4. The blood sugar rose sharply above the threshold, sugar appeared in the urine, and after two hours the blood sugar was still somewhat above the starting level.

On 5/6/24, by which time the slough was separating and the temperature normal, a second test was carried out. As the Chart (Chart 4) shows, the curve on this occasion was normal except that it rose slightly higher than is usual. That the case was now one of mild diabetes, however, is certain from a third test performed on 12/9/24 which showed (Chart 4) a curve of "lag" type, the blood sugar reaching the level of 0.24% with glycosuria. The obvious decrease in tolerance since the previous test may have been due partly to failure to adhere to a restricted diet, but also in all likelihood to added damage by the sepsis.

The history of slight thirst and polyuria point to his having been the subject of diabetes prior to the onset of sepsis, but the symptoms were evidently not sufficiently marked to make him consult his doctor.





Case No. 3. A.M. Male. Aged 65 years. Carbuncle.

Admitted to hospital in August, 1924, with a large carbuncle involving the back of the neck. On admission he was drowsy and smelt of acetone. The blood sugar was 0.26%, urinary sugar and acetone bodies were abundant. The carbuncle was freely opened and insulin was begun. By 20/8/24 the blood sugar had fallen to 0.10% and glycosuria was minimal, while the general condition was greatly improved. Good progress continued, the insulin was reduced to 5 units daily, and he was dismissed sugar and acetone free, on a fair diet and 5 units of insulin and with his wound practically healed on 18/9/24.

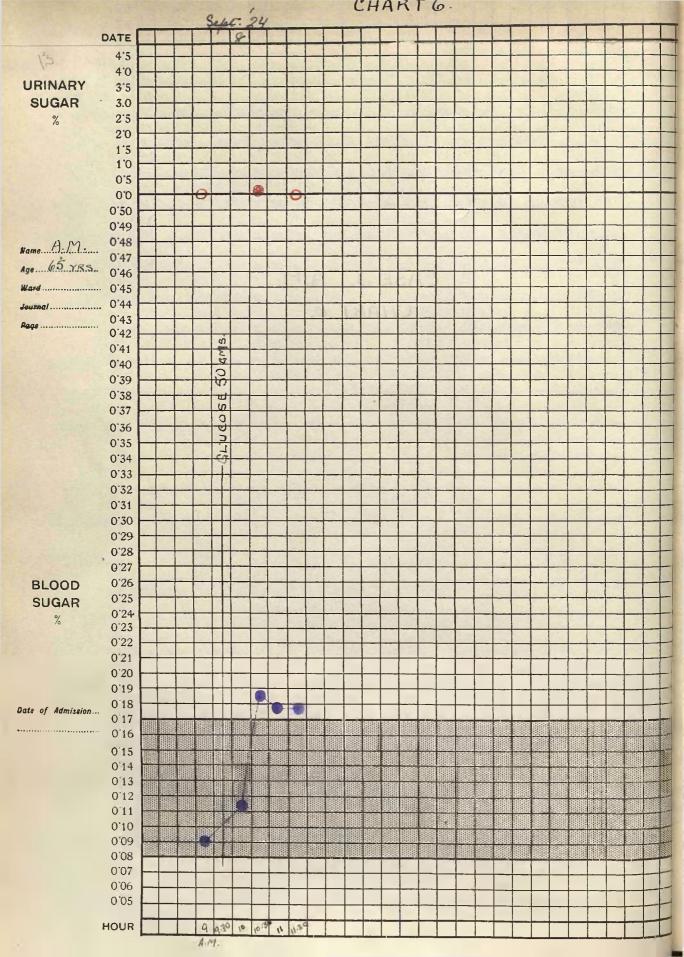
Chart 5 shows the patient's progress while in hospital. It will be noted that as sepsis gradually subsided the blood sugar percentage came down and remained at a normal level in spite of increased diet and decreased insulin.

Acetone and urinary sugar also rapidly disappeared.

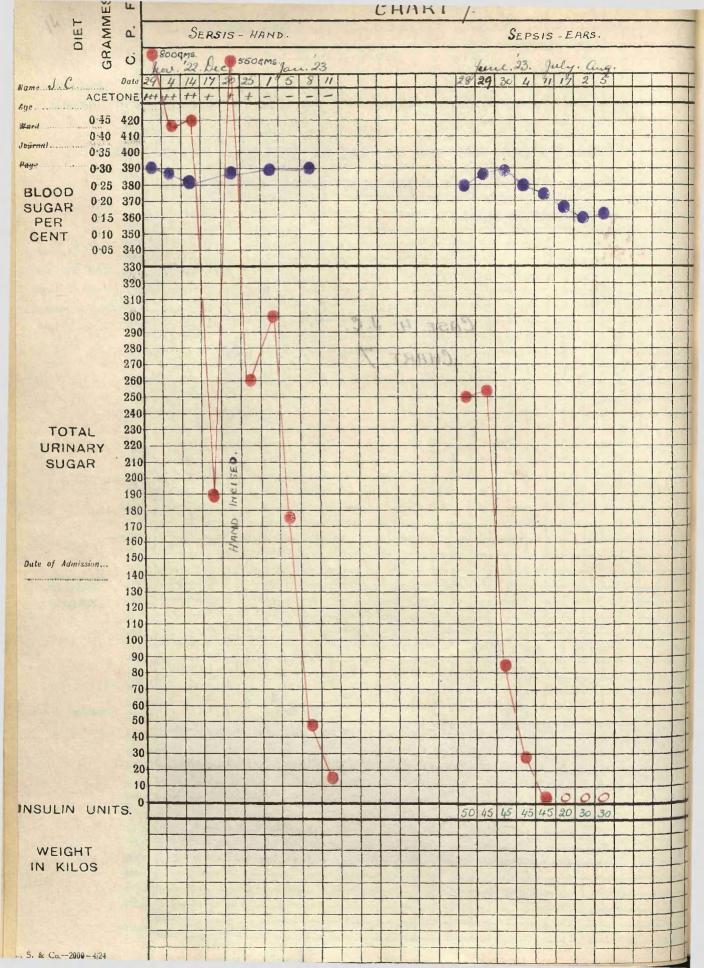
A glucose tolerance test carried out on 8/9/24, after four weeks' treatment, resulted in a curve diabetic in type though only mildly so, the highest level reached by the blood sugar being only 0.186%. Sugar appeared in the urine to the extent of a trace only. Chart 6.

Previous to admission this man had complained of frequency of micturition only, but had no serious symptoms until the onset of the sepsis immediately produced urgent symptoms. The man was undoubtedly a diabetic in September

CASE 3. A.M.



1924; he probably was in July of that year before the onset of sepsis, but the symptomatic evidence is certainly meagre.



Case No. 4. J.C. Male. Aged 42 years.

Previous This man was treated for diabetes in hospital History.

in 1920 and 1921, and on each occasion was dismissed very well.

On 6/11/22, however, he struck his left thumb Sepsis. with a hammer, and the whole hand became in a few days greatly swollen. On admission the hand was swollen with three sinuses discharging pus. the veins of the forearm were red and inflamed, and several enlarged, tender glands were palpable in the axilla. The urine now contained 15% of sugar, and abundant acetone and diacetic acid: the breath smelt strongly of acetone. The blood sugars, as seen from Chart 7 ran high, varying between 0.2% and 0.3%. On one occasion he passed 800 gms. of sugar in the course of 24 hours. On account of the degree of acidosis present strict dieting could not be safely carried out, but as soon as it was deemed advisable this was begun. It was found impossible, however, to get him sugar free.

In April 1923 he was re-admitted for insulin treatment to which he re-acted extremely well, and was dismissed sugar free on a good dietary. Two months later, however, he was re-admitted, this time with a perforation of the right tympanic membrane and discharge from the left ear. An acute

exacerbation of a chronic otitis media was diagnosed. There was no record previously of any deafness or otorrhœa. He was now passing 250 grammes of sugar in the 24 hours, acetone was present, and the blood sugar was 0.25% (See Chart γ) The latter remained high in spite of the fact that large doses of insulin were given, and even when the amount of carbohydrate was reduced to a minimum. As time went on and the sepsis cleared up, however, there was obviously recovery of tolerance to a certain degree - the blood sugar being more constantly about the normal level despite considerable reduction of the dose of insulin. Nevertheless, he was now in a much less satisfactory condition than on his previous dismissal in April, 1923, when he was sugar free on a good dietary. Here again the damaging effect of sepsis is seen.

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Case No. 5. V.G. Male. Aged 32 years. Newspaper Reporter. Carbuncle.

Previous History.

This man was first treated in hospital for diabetes from 17/3/22 till 16/4/22. He was easily rendered sugar and acid free by dieting and was dismissed very well. The blood sugars ran about 0.2%.

A year later, on 21/4/23, he was re-admitted with abundant sugar and acetone, and insulin in fairly large doses was required; he gradually regained a considerable degree of tolerance, however, and the insulin was eventually cut down to 5 units daily. The blood sugar on admission was 0.363%, but it gradually sank below this level, as seen in Chart 8 until it reached normal or practically normal.

Sepsis.

On 3/10/25 patient was again admitted, this time in a serious condition. He had kept well since last dismissal until a week before when a carbuncle developed above the left clavicle. He then began to feel out-of-sorts, weak and giddy, and on several occasions he vomited. On admission he had 3% of sugar and abundant acetone and diacetic acid in the urine, while the alveolar carbon dioxide and blood bicarbonate estimations indicated a severe degree of acidosis. The blood sugar was 0.286%. Under appropriate dieting and large doses of insulin the acidosis gradually disappeared and the urinary sugar lessened. The blood sugar curve, however, (Chart 8), as compared with the

previous ones, indicated a marked deterioration of tolerance, running at a higher level throughout and showing a decided aversity to coming down to anything like normal, in spite of the large doses of insulin given.

Comparing the results obtained during this patient's three admissions to hospital, it is obvious that the cause of his marked loss of tolerance on the last occasion was the incidence of sepsis.

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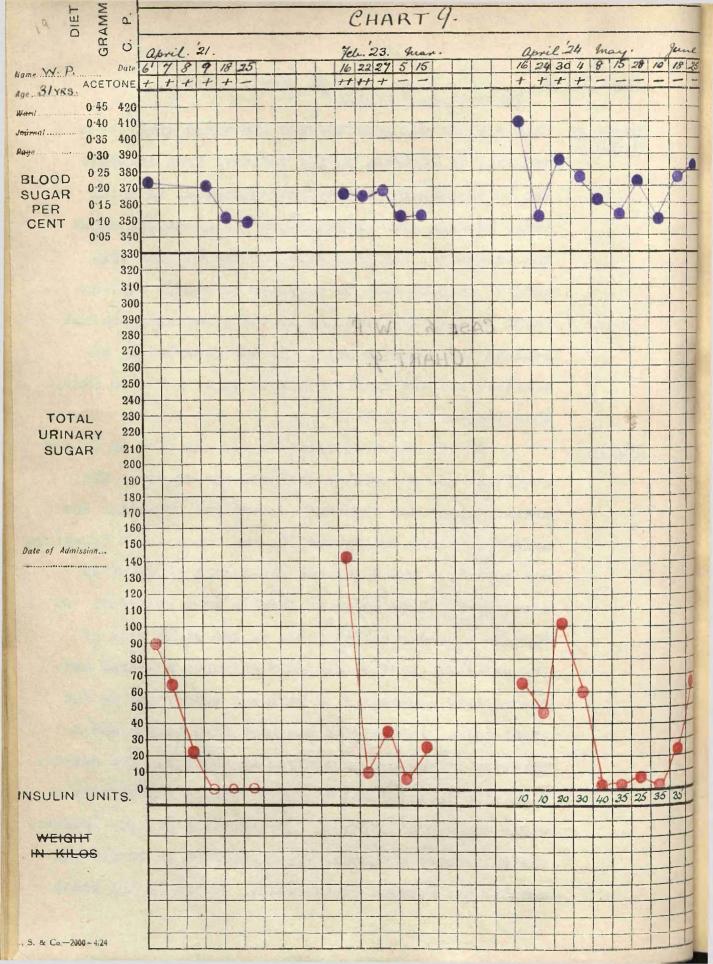
Case No. 6. W.P. Male. Aged 31 years. Clerk.

Perinephric Abscess.

Previous History. This patient was admitted for the third time to hospital on 16/4/24, having suffered from diabetes for three years. On the first occasion, in April 1921, he made good progress and was dismissed sugar and acid free. He kept well and was at work till 15/2/23 when he came to hospital to report and was found to have 15% of sugar in the urine and abundant acetone and diacetic acid. He was accordingly readmitted and was easily rendered sugar and acid free, this time with insulin.

Sepsis.

On the third occasion he was admitted in a weak condition and was rather confused and drowsy. The urinary sugar was 4.5% and acctone was present. The urine was found to contain pus and blood and a balanitis was present. The sugar was persistent in spite of dieting and large doses of insulin were required. On 26/4/24 a tumour was palpable in the right side of the abdomen. Ascites and some anasarca appeared and the patient complained of pain and tenderness in the right loin. An incision was made from behind and a quantity of pus evacuated from an abscess. The general condition improved and the urine became sugar-free, while the pus diminished. As the wound healed, however, the pus became abundant, sugar returned in increasing amount, and acctone re-appeared. Obviously the renal



sepsis was still active. The man's general condition was against further surgical interference and he went home.

of the blood sugar during his three periods of residence in hospital. It is obvious that on the third occasion, when active sepsis was present, the blood sugar reached much higher levels and varied to a much greater extent than on either of the two previous admissions, in spite of heavy insulin desage.

CASE 7. E.C.

CHART 10.

Case No. 7. E.C. Female. Aged 27 years. Nill-worker.
Tonsillitis. "Chill".

Previous History.

This girl was first admitted to hospital on 13/12/23 with symptoms of diabetes of nine months' duration. To keep her sugar free it was found necessary to give her a very low allowance of carbohydrate along with insulin. By this means the blood sugar was kept within the limits of 0.12%

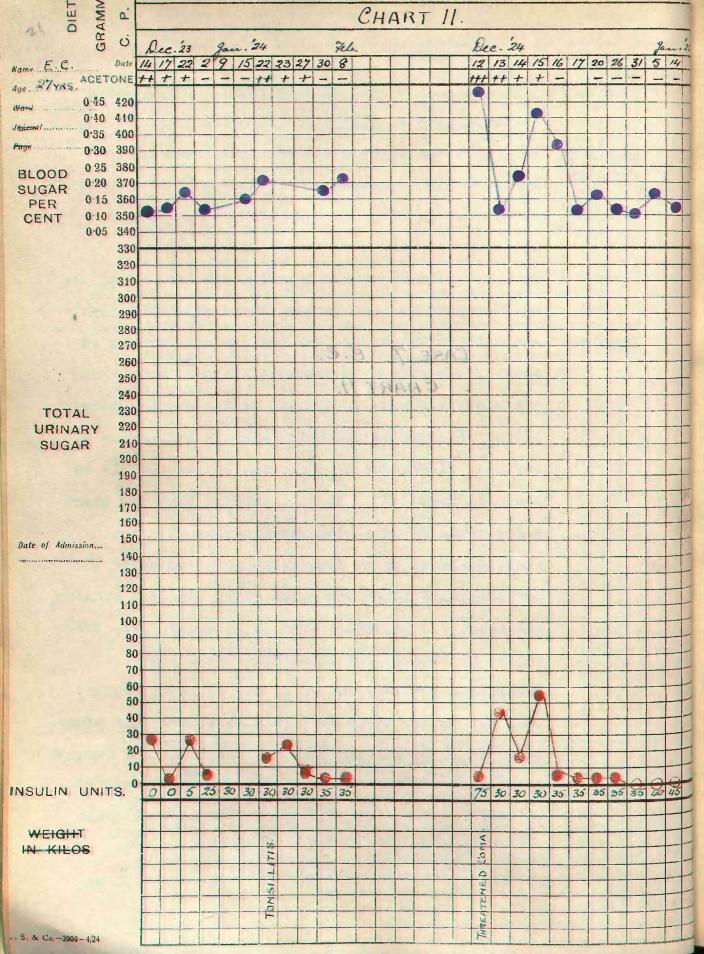
and 0.17%. On 20/1/24 she had a sudden attack of

Sepsis.

tonsillitis with a temperature of 103° which sent the blood sugar up to 0.212%, with a corresponding output of sugar in the urine and the appearance of acetone. A glucose test carried out on 22/1/24 is shown in Chart 10. It will be seen that the blood sugar curve is at a high level throughout, the starting-level being considerably raised above the percentage at which the blood sugar had been running previously. The urine, from being sugar-free, now showed glycosuria throughout the test. Her subsequent progress was good, but it is noteworthy that she now required more insulin to keep the sugar under control, showing that her tolerance had further deteriorated. She was dismissed on 8/2/24, and for the following six months was in good health, with slight lapses which were corrected by further alterations in diet and insulin. She was seen on

CASE 7 E.C. CHART 11.

医乳毒素



22/9/24 when the blood sugar was 0.207% and the urine contained a trace of sugar.

Sepsis. Threatened Coma.

She remained well until 5/12/24 when she caught a chill while standing in a theatre queue. She went to bed, and next day began to suffer from headache, vomiting and drowsiness; on 12/12/24 she was sent in to hospital on the verge of coma. When seen she was collapsed with feeble rapid pulse and marked dyspncea, and could only be roused with difficulty. sugar was now 0.484%, while the urine was loaded with acetone and diacetic acid but contained only 1% of sugar. With stimulation and large doses of insulin she rapidly improved and was out of danger in 48 hours. On the day after admission the blood sugar had fallen to 0.112% but it rose again for two or three days when the initial very large doses of insulin were cut down. Within a week it was again under control and remained about 0.1% to 0.15%. She was dismissed very well on 15/1/25.

Chart // shows clearly the variations in the blood sugar, urinary sugar, &c. during the period from December 1923 till December 1924 when she was under observation. The immediate reaction to infection on two occasions is very striking, showing the marked contrast with her satisfactory condition first during one month's treatment in hospital and later during six

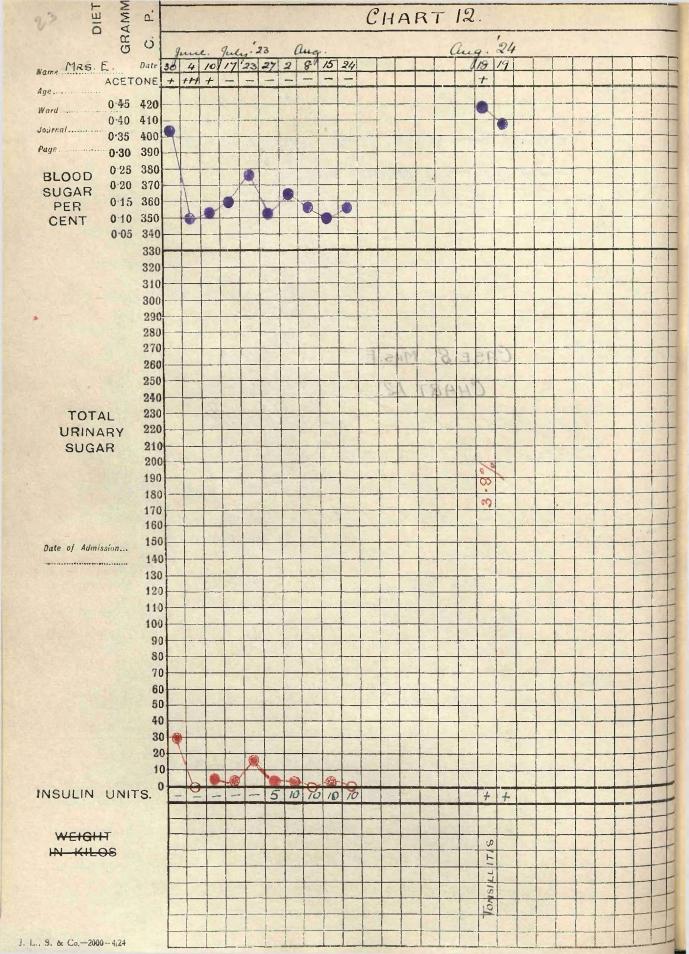
months' observation of her general health, blood sugar and urinary sugar.

CASE 8 MRS E CHART 12.

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Case Mo. 2. Mrs. E. Aged 46 years. Housewife. Tonsillitis.

Previous History.

Patient was admitted to hospital for the first time on 30/6/25, with a history of diabetes of one year's duration. The blood sugar on admission was 0.37% and the urine contained 2% of sugar and some acetone. It was found impossible to control the sugar without insulin and she was accordingly put on a small daily dose. She was for nine weeks in hospital, and during this time the blood sugars ran between 0.08% and 0.18%. After dismissal from hospital she proved unable to keep to a rigid dietary, and a larger dose of insulin was prescribed. The blood sugars now ran higher, 0.23% or 0.24% being the usual level found on estimation.

Sepsis. Death.

The patient remained in fairly good health, however, until 18/8/24 when an attack of tonsillitis developed and four days later she was brought to hospital in a comatose condition. The blood sugar was now 0.44% and the urine contained 3.8% of sugar and a trace of acetone. The following day the blood sugar was 0.386%. In spite of stimulation and large doses of insulin she failed to rally and died that day. Chart /2 shows the blood sugars and urinary sugar at various times during her illness.

In this case the patient's condition had been for a considerable time unsatisfactory, but she had

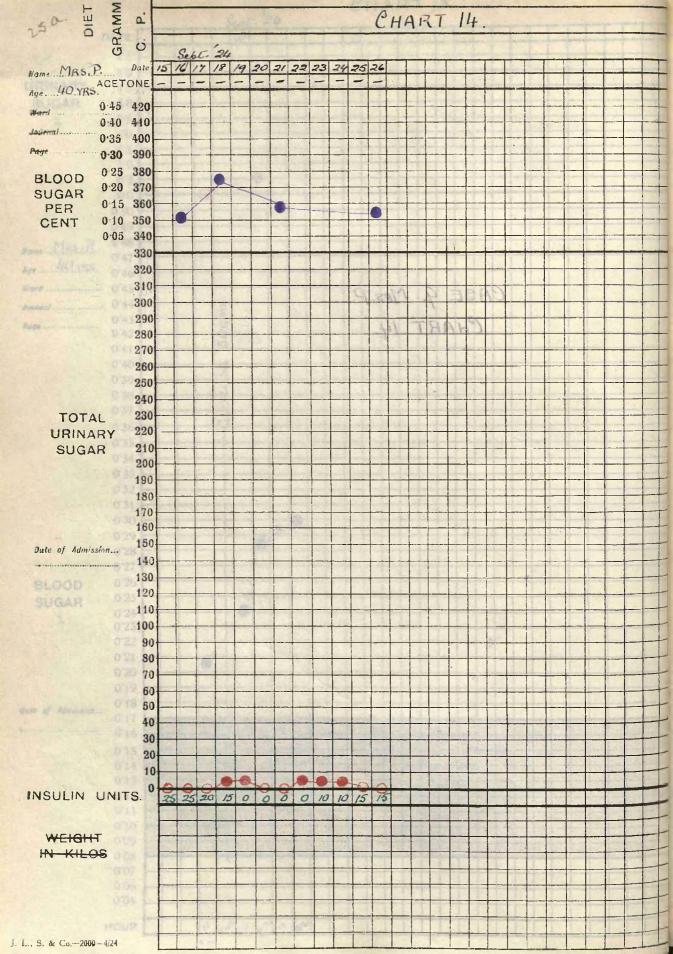
managed to struggle on until, finally, sepsis proved the last straw.

CASE 9. MRS.P.

CHART 13. DATE 4'5 40 URINARY 3.5 SUGAR 3.0 % 2.5 20 1'5 10 0'5 0.0 0.20 0'49 0'48 Name MRS P. 0'47 Age 40 YRS. 0'46 Ward 0'45 0'44 Journal 3 0'43 5 Page 500 0'42 0'41 SE 0'40 0'39 3 0.38 STC. 0'37 0.36 0.32 0'34 0'33 0'32 0'31 0.30 0'29 0'28 0.27 0'26 BLOOD 0.22 SUGAR 0.24 % 0.53 0.55 0'21 0'20 0'19 0'18 Date of Admission... 0'17 0.16 0'15 0'14 0'13 0.13 0'11 Ė 0'10 0'09 0.08 0'07 0.06 0.02 HOUR 10 1030 11 1190 17 1230 A.M.

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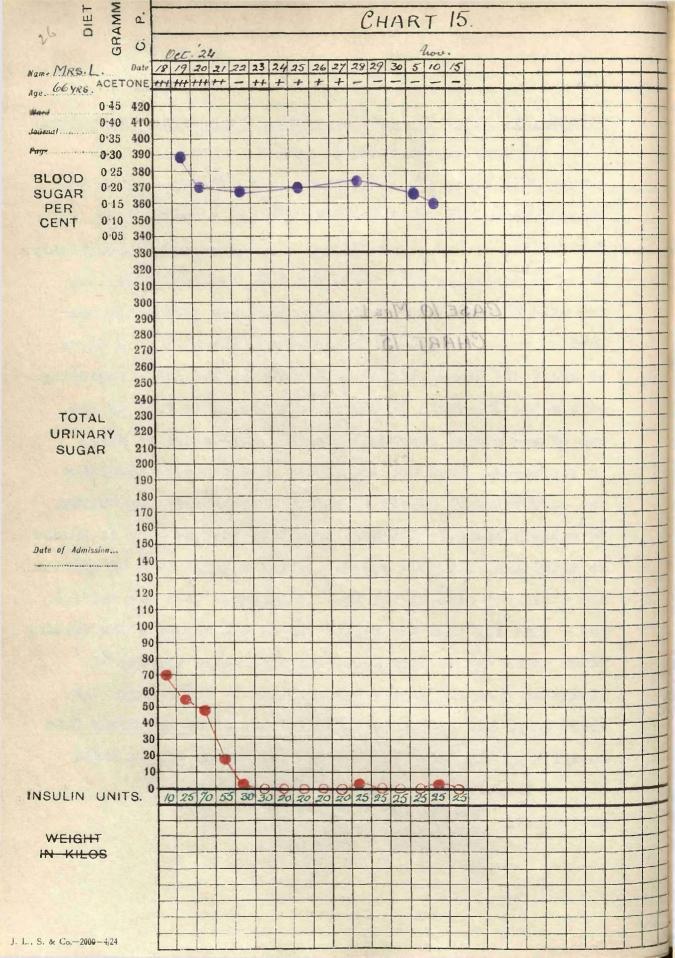
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Case No. 9. Mrs. P. Aged 40 years. Housewife. Cellulitis.

Patient was admitted to hospital suffering from severe Cellulitis involving the left hand. Amputation was considered but it was decided to try and save the hand, fortunately so, as the condition cleared up most successfully. Prior to admission this woman had been treated by dieting for mild diabetes, and a glucose tolerance test which was carried out a few days after admission resulted in a curve of decidedly diabetic type (Chart /3), the curve beginning well above the renal threshold, and rising to 0.3% at the end of two hours; accompanied by the appearance of sugar in the urine. That her ordinarily mild diabetic condition was aggravated by sepsis is hardly obvious from the Charts. To satisfy oneself, however, that this was the case it should be noted that, although she was having a large dose of insulin and a reduced diet at the time the glucose test was carried out - that is, when the sepsis was at its height - the fasting blood sugar was as high as 0.207%; whereas on the day of dismissal when the sepsis had practically cleared up, the blood sugar had fallen to 0.10% and the urine was sugar free in spite of the fact that she was now having only a small dose of insulin and a much more ample diet than previously.

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Case No. 10. Mrs. L. Aged 66 years. Housewife. Gangrene.

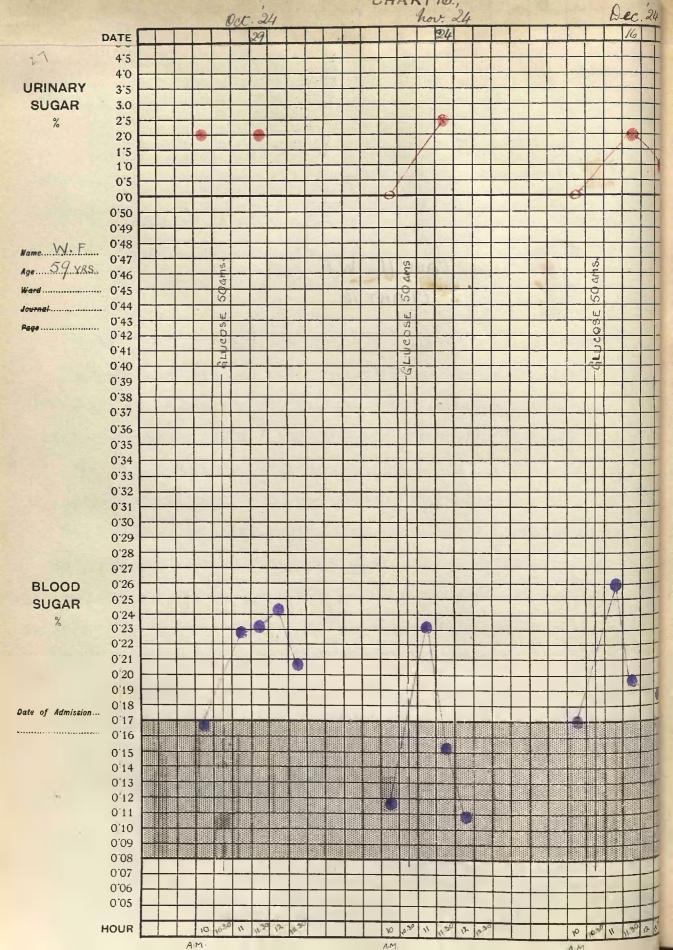
Previous History.

This woman was first admitted in May 1924 with commencing gangrene of two of her toes. At that time there was abundant sugar in the urine which, however, was controlled by dieting. One toe was amputated and she was sent home sugar free and in quite good condition.

Sepsis.

In October 1924 she was re-admitted, again suffering from gangrene, and on admission was very drowsy and on the verge of coma. The urine contained abundant sugar and acetone, and the blood sugar was 0.3%. She rallied and improved considerably with dieting and insulin. The blood sugars, however, continued to run above the normal, and whereas she previously had been sugar free without insulin, she now required a fairly large dose together with a restricted diet to keep her free. Her progress in hospital is shown in chart /5. The marked acidosis and high blood sugar on re-admission should be noted and compared with the satisfactory condition on her first dismissal from hospital. The effect of sepsis in this case was permanent as shown by the continued deterioration of carbohydrate tolerance.

CASE II. W.F.
CHART 16.



Case No. 11. W.F. Male. Aged 59 years. Carbuncle.

This man was admitted with a large carbuncle on the back of the neck. He gave no history whatever of diabetic symptoms prior to admission, and it was only on routine examination of the urine that glycosuria of considerable severity was discovered. The blood sugar was then found to be high. A glucose test carried out on 29/10/24 showed a diabetic curve (see Chart /6) the blood sugar rising to 0.243%, and the urinary sugar reaching 2%. A second curve obtained about a month later on 24/11/24, when the carbuncle was healing well and the sugar was under control, showed a typical "lag" condition with the blood sugar rapidly shooting up to 0.25% and as rapidly returning to the original level. Three weeks later another test was performed; this resulted in a curve which was neither typically diabetic nor typically "lag" in character. It differed from the first in the fact that the return of the blood sugar towards the fastinglevel was more rapid, and also that the urine was free of sugar before glucose was taken; and from the second in running throughout at a much higher level, in fact above the renal threshold. It must be taken into account in contrasting the last test with the previous more favourable one, that towards the end of the man's stay in hospital his diet was much less restricted and at the same time his insulin was reduced.

The striking feature of the case is the entire absence of symptoms of diabetes prior to the onset of sepsis in the

form of carbuncle. This raises the question of whether the man had actually suffered previously from diabetes, or whether he had become diabetic as a result of the sepsis. The presence of hyperglycaemia and glycosuria on admission would seem to indicate that diabetes was already present.

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Cass No. 12. T.D. Male. Aged 16 years. Septic Tound.

This boy had been a patient in the wards on several occasions. Since his last dismissal on 3/8/23 he had kept free of sugar on insulin until scen on 8/5/24, when the blood sugar was found to be 0.212%, the urinary sugar 3% and acetone and diacetic acid abundant. He then gave a history of having fallen heavily on the elbow one week before, sustaining a wound which became septic. On 14/5/24, the wound being still troublesome, the blood sugar was 0.182%, the urinary sugar 1.7%, acetone and diacetic acid less abundant. Three weeks later on 4/6/24, there was no improvement in the sugar tolerance, the blood sugar being 0.25% and the urinary sugar 2.5%, but acetone and diacetic acid were slight in amount. By this time the wound was healing well, and on 25/6/24 the diabetic symptoms were much improved, the blood sugar being now 0.147%, the urine sugar-free and acetone entirely absent. This satisfactory condition has been maintained since. His progress is shown in Chart /7.

This case is interesting from the fact that insulin treatment was being carried out before the incidence of sepsis, and it is noteworthy that what had previously been a sufficiently large dose to maintain the balance of tolerance was now totally inadequate.

SUMMARY.

for themselves. In all of them, obviously, the onset of sepsis brought with it an increase in the severity of symptoms, sometimes to a marked degree, evidenced by high blood sugar percentage, the appearance or increase of glycosuria and acidosis, and aggravation of the general symptoms. In some, the improvement of the diabetic symptoms along with the subsidence of sepsis was striking; in others, there was certainly some recovery from the first acute symptoms, but carbohydrate metabolism was clearly in a much more defective condition than before sepsis arose. (See cases 2, 4, 5, 10 & 12.)

(b) The Influence of Sepsis in Non-diabetic Subjects.

As regards the influence of sepsis upon carbohydrate metabolism in non-diabetic persons, it was long ago pointed out that glycosuria was a very common accompaniment of certain forms of sepsis. The condition was first referred to in 1878 by Prévost who described it as one of "Sapraemic Glycosuria"; it was more fully described in 1886 by Redard. Mr. W.G. Spencer described cases in which he found glycosuria which was reduced to a minimum by the removal of the septic focus, e.g. on amputation of a diseased limb or part of a limb. Cuthbert Wallace 2 described "A Case of Gangrene of the Foot with Sugar in the Urine, successfully treated by Amputation." described a series of cases of gangrene with glycosuria disappearing on amputation, one case of glycosuria which recurred with repeated attacks of gangrene, and cases of carbuncle, ulcer of the rectum, cellulitie, &c. with temporary glycosuria. Cuthbert Wallace used the urinary glucose test first in these cases. In some of his cases there was elevation of temperature, in others there was not from which he concluded that fever was not a necessary factor in the production of glycosuria.

Higginson cited cases, including some of his own, of carbuncle and of gangrens complicated by glycosuria which was cleared up by the removal of the sepsis. Fordyce described the case of a girl of 6 years who was being treated for progeria, and in whom a large abscess of the face

developed, with accompanying glycosuria. Both cleared up under treatment. The presence of sugar in the urine was verified by means of the fermentation test.

In all these observations the abnormality noted was the appearance of sugar in the urine, no investigation of the condition of the blood being made; and it was only comparatively recently that the perfecting of methodsof blood sugar estimation made it possible to observe more accurately what actually occurs in cases such as the above.

Grigawt, Brodin and Rouzaud in 1920 found that hyperglycaemia, or excess of sugar in the blood, was the rule in infectious diseases, while Poll and Campagnolle showed that there was a distinct lowering of tolerance for glucose in such cases. Cammidge finds that even in an ordinary febrile cold the fasting level of the blood sugar is raised, and glucose tolerance lowered. Willcox and others have drawn attention to the influence of septic foci in causing hyperglycaemia. The former directs special attention also to the frequency with which glycosuria is associated with dental sepsis, quoting its occurrence as 12% in 100 consecutive cases of the latter. Pringle and Millar find that there is a distinctly lowered glucose tolerance in cases of arthritis. particularly in the severe infective types, and also in periarticular cases and in muscular fibrositie. They point out the complete return to normal on recovery.

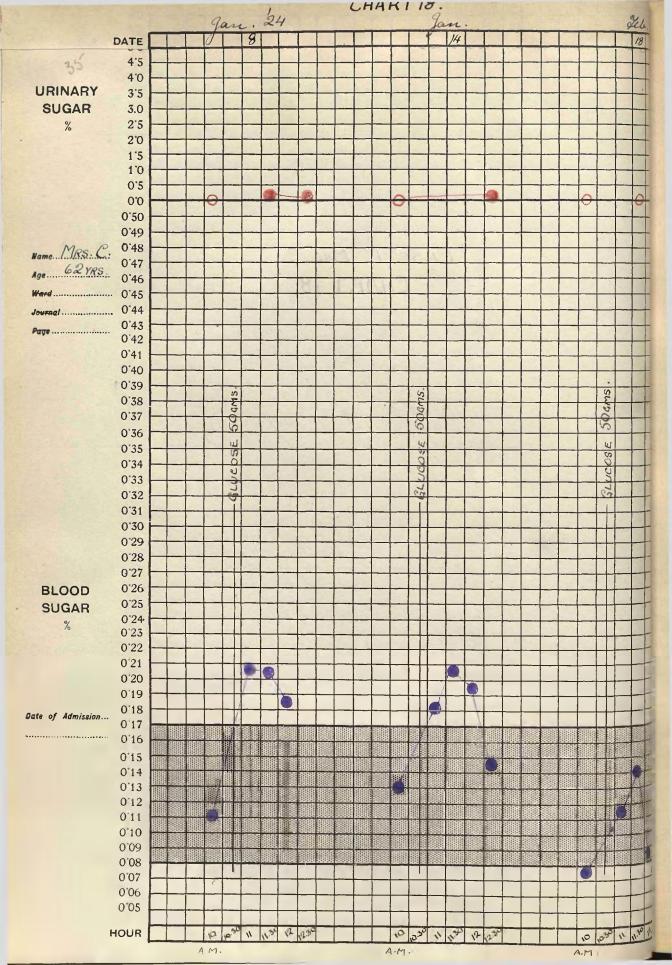
I.M. Rabinowitch, W.D. described some cases of diabetes with infection, showing that while at first they

required large doses of insulin to keep them sugar-free, later, when the sepsis had cleared up, some were able to do entirely without insulin. These were mild diabetics originally whose pancreatic function had been further deranged by infection. The same writer in another article pointed out the frequent association of hyperglycaemia with diseases of the gall-bladder and bile passages, stating that over 80% of cases of cholelithiasis investigated showed some degree of hyperglycaemia. He asserted that the incidence of pancreatitis with cholecystitis and cholelithiasis was much more common than supposed.

R. Owen-Janes described a case of gangrene of the right leg arising at the site of variouse veins, associated with sugar in the urine. After treatment by dieting and insulin the leg was amputated. A week later sugar and acetone returned and the atump flaps began to show signs of secondary infection, sloughs and purulent discharge making their appearance. Treatment with eusol led to separation of the sloughs and the wound became cleaner - with consequent fall of the urinary and blood sugar almost to normal.

To illustrate the association of infectious diseases and diabetes one may quote Dr. Adam Patrick who described three cases (including one of his own) in which acute diabetes developed after an attack of numps. He also referred to a case of Routh's (1912) where sugar

and diacetic acid were found fourteen days after the development of a right-sided parotid swelling, but disappeared in four days. This, he says, was probably a temporary glycosuria associated with septic parotitis, not mumps. CASE 1. MRS. C.
CHART 18.



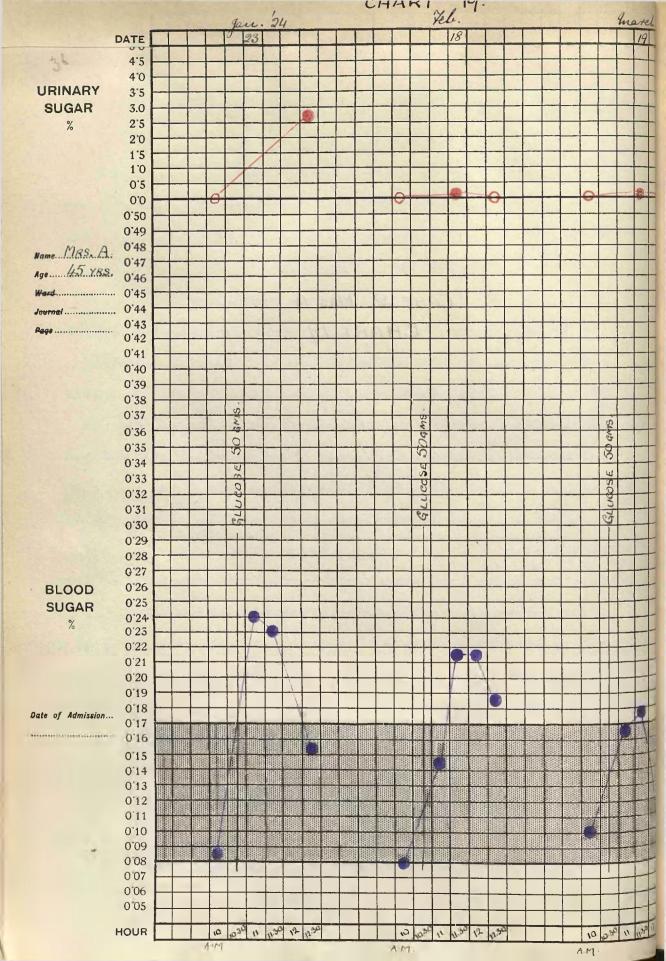
Case 1. Mrs. C. Aged 62 years. Housewife. Carbuncle.

This woman was admitted to hospital on 4/1/24 suffering from a large carbuncle which extended over the back of the neck. Sepsis had then been active for several weeks. The temperature was running at 99 - 100° .

At this stage, on 8/1/24, a glucose tolerance test was carried out. The result, as shown in Chart 18, indicated a marked loss of tolerance, the blood sugar considerably exceeding the threshold and showing delay in the return to pre-glucose level while sugar appeared in the urine. On the following day the carbuncle was thoroughly scraped and sloughs removed under an anaesthetic. Five days later, on 14/1/24, a second glucose test gave a result almost similar to the first.

A month later, on 18/2/24, a third test was performed three weeks after the patient's dismissal from hospital. The result of this presented a striking contrast with that of the previous two. The blood-sugar curve was now absolutely normal, at no point exceeding the threshold and returning within two hours to the starting level. The urine showed no sugar. This result is shown in Chart 18 case / The case is a typical one of temporary lowering of tolerance due to sepsis, and shows in a remarkable way the return to normal when the focus of infection had cleared up.

CASE 2. MRS. A.



Case 2. Mrs. A. Aged 45 years. Housewife.

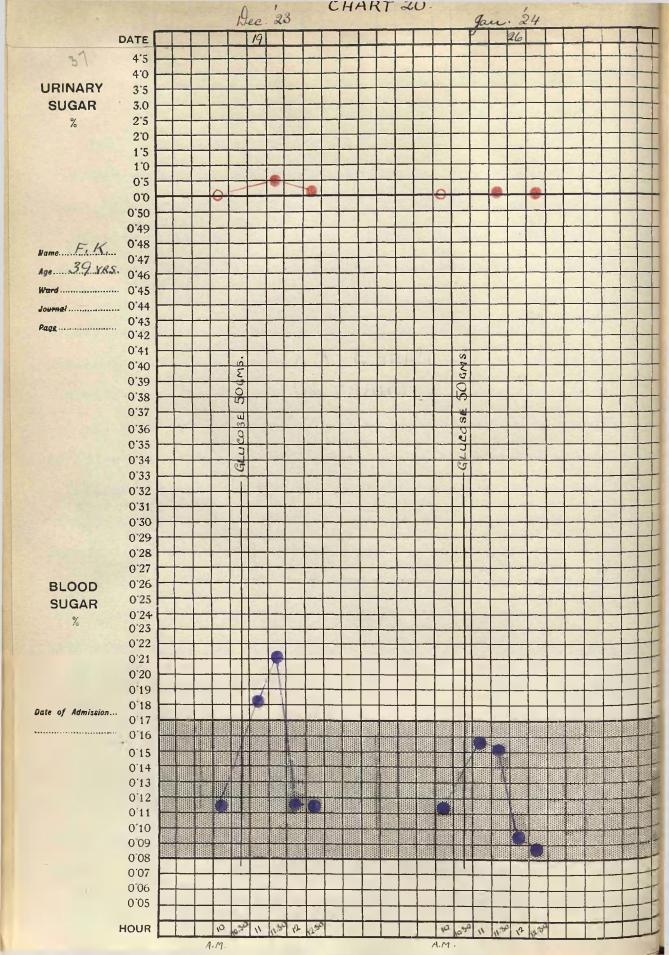
Necrosis of Jaw.

This was a case of necrosis of the jaw attributed by the patient herself to the removal of carious teeth some weeks before. The mouth was in an extremely septic condition, the tissues inside being greatly swollen and necrotic, and the breath was overpoweringly foul. She could swallow only with difficulty and was exhausted and anaemic-looking.

A glucose test on 23/1/24(carried out when sepsis was at its height) as seen in Chart 19, showed a very high blood-sugar curve, and a sample of urine at the end of two hours showed almost 3% of sugar. The patient's condition was slow to improve and a month later, on 18/2/24, the curve was still high although not quite so markedly so as on the first occasion. The patient now began to improve slightly, and a blood-sugar curve obtained a month later, 19/3/24, was practically normal, as will be seen from Chart 19.

In this case as in the last the blood-sugar before the commencement of each test was normal and the urine sugar-free; but the extra strain put upon the organism by giving the 50 gms. of glucose was sufficient to upset the balance and to show to what a precarious condition carbohydrate tolerance had been brought. It should be noticed that even the third test, carried out nearly three months after the commencement of sepsis did not yield a completely normal result, and it is probable that this patient was left with some permanent damage, ready to become aggravated with any fresh infection.

CASE 3. F.K. CHART 20.



Case 3. F.K. Male, Aged 39 years. Septicaemia.

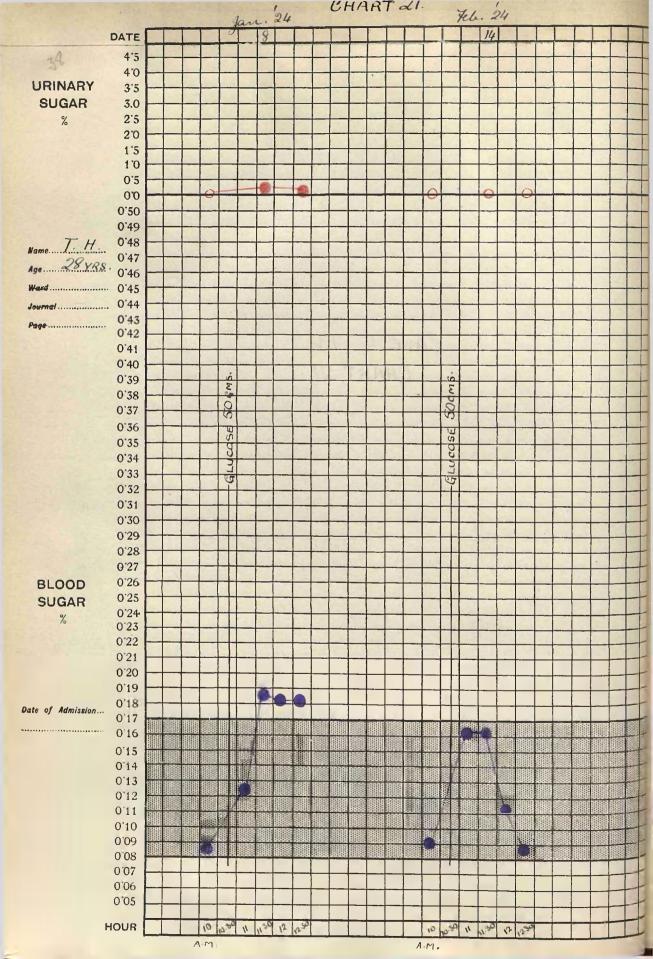
This patient was suffering from a low form of septicaemia. He complained of pain in the right hip and shoulder but no pus was found on incision. A blood culture showed staphylococcus albus. Some endocarditis was present. The temperature ran about 99°. He also showed symptoms of neurasthenia.

A glucose test carried out on 19/12/23 when he had been ill for some weeks gave the abnormally high blood-sugar curve seen in Chart 20, with the appearance also of sugar in the urine.

A month later, on 26/1/24, the curve obtained was normal. The temperature at this time was still slightly elevated but the patient's general condition had greatly improved.

In this case also there was a distinct loss of sugar tolerance although of a very transitory nature.

CASE 4. T.H.
CHART 21.



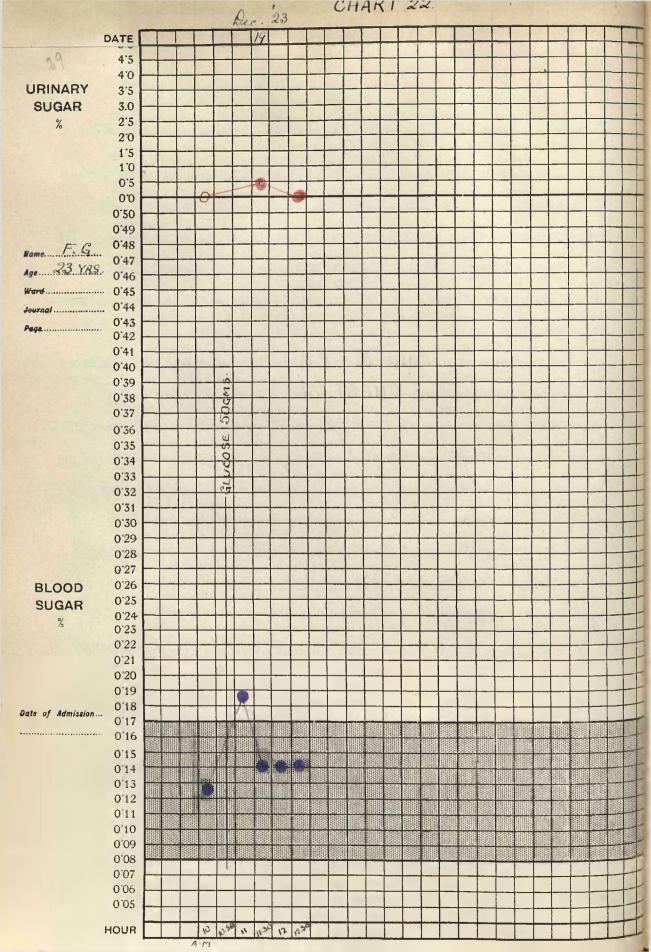
Case 4. T.H. Male, Aged 28 years. Pyaemic Abscesses.

This man was admitted suffering from an acute osteomyelitis of the right femur, and from a pyaemic abscess over the left humerus. He complained also of pain in the ankle. He had previously suffered from similar affections and his body was covered with scars. The temperature varied between 98° and 100°.

A glucose test on 8/1/24 revealed a distinct defect in carbohydrate tolerance, the result being as seen in Chart 21; the blood-sugar exceeded the normal renal threshold, sugar appeared in the urine, and at the end of two hours the blood sugar was still above the threshold. Five weeks later, on 14/2/24, when his condition had very greatly improved a curve was obtained which presented a striking contrast to the first, being in every respect normal, as seen in the chart.

In this case also, the transitory loss of tolerance due to sepsis is well illustrated.

CASE 5, F.G. CHART 22.



Case 5. F.G. Female. Aged 23 years. Dyeworker. Acute Septic Arthritis.

This girl came into hospital with an arthritis affecting the right knee. The joint was swollen and extremely tender to the touch. The temperature was swinging in character.

In this case the resting blood-sugar was rather higher than normal and on the administration of glucose it rose above the threshold and failed to return to its pre-glucose level within the normal two hours. Sugar appeared in both samples of urine (see Chart 22). Her further progress was not observed as she developed erysipelas a few days after admission and was transferred to a fever hospital. The defective tolerance, however, was obvious from the results of the test. The blood-sugar curve in this case is interesting in that its form is suggestive of that of a true diabetic one, except in being at a lower level throughout than the latter.

CASE 6. C.T.

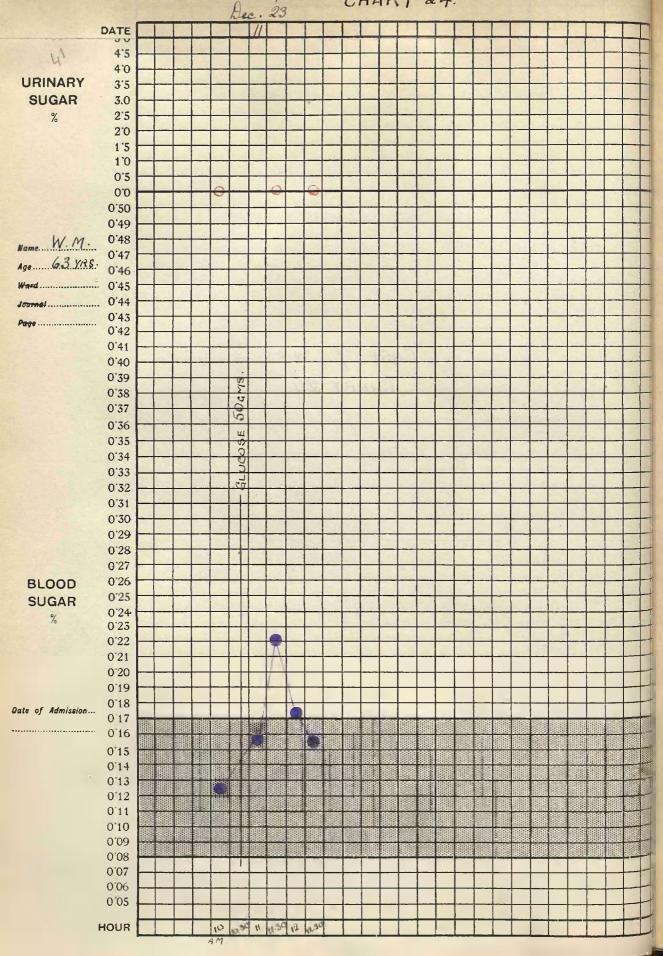
CHART 23. DATE 1.0 4'5 4'0 URINARY 3.5 SUGAR 3.0 2.5 % 20 1'5 10 0.2 0.0 0.20 0'49 0'48 Name C.T. 0'47 Age 30 YRS. 0'46 Ward: 0'45 Journal 0'44 0'43 Page 0'42 0'41 0'40 S CM 0'39 0'38 30 0'37 0.36 Ш 0'35 \$00073 0'34 0.33 0.35 0'31 0.30 0'29 0'28 0.27 0.26 BLOOD 0.22 SUGAR 0.24 % 0.53 0'22 0'21 0'20 0'19 0'18 Date of Admission... 017 0.16 0'15 0.14 0'13 0.12 0.11 0'10 0'09 0.08 0'07 0'06 0 05 HOUR 10 10 30 11 11 30 12 12.30 A.M.

Case 6. C.T. Male. Aged 30 years. Cellulitis.

Patient was admitted with a severe cellulitis of the left hand arising from a crush sustained while at work. Two fingers had to be amputated.

In this case the resting blood-sugar was slightly above normal, and 50 grammes of glucose caused a rapid rise above the threshold and a slow return towards the original level, which was not reached at the end of two hours. A trace of sugar was detected in the urine. This is shown in Chart 23.

CASE 7 WM.



Case 7. W.M. Male. Aged 63 years. Abscess in Groin.

Admitted suffering from an abscess in the groin, the original site of infection being the foot. The lesion healed well.

A glucose test carried out during active sepsis showed the following :-

The pre-glucose blood-sugar level was slightly raised and one hour after glucose it had risen to a very high level from which it fell slowly, reaching only 0.155% at the end of two hours. (see Chart 24). The course of the curve in this case is distinctly diabetic in character.

CASE 8. A.G. CHART 25.

LHANI XU. DATE 4'5 4'0 URINARY 3'5 SUGAR 3.0 2'5 % 20 1'5 10 0.5 0.0 0.20 0'49 0.48 Name A.G. 0'47 Age 35 YRS. 0.46 Ward..... 0'45 Journal 0'44 0'43 Page 0'42 0'41 0'40 BMS. 0.39 0'38 0'37 0'36 Ш 0'35 Lucos 0'34 0'33 0.35 0'31 0.30 0'29 0'28 0.27 0'26 BLOOD 0.22 SUGAR 0'24 % 0.23 0.22 0'21 0'20 0'19 0'18 Date of Admission... 0 17 ************ 0.16 015 0'14 0'13 0.12 0.11 0.10 0'09 0.08 0'07 0'06 0'05 HOUR 10 1030 11 1130 12 12 A.M

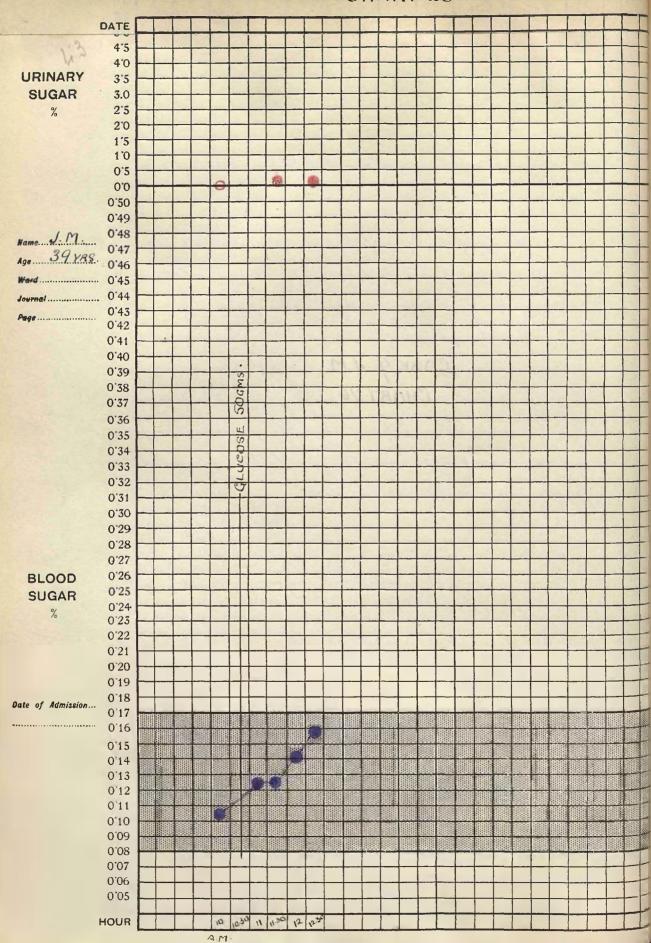
Case 8. A.G. Male. Aged 35 years. Miner. Bronchiectasis.

The nature of this man's condition at the time of investigation was doubtful, but was later diagnosed as bronchiectasis.

The blood-sugar throughout the test was at a higher level than normal, the initial reading was slightly raised, the renal threshold was exceeded with the consequent appearance of sugar in the urine and there was considerable delay in the return to pre-glucose level. (Chart 25)

CASE 9. J.M.
CHART 26.

CHART 26.

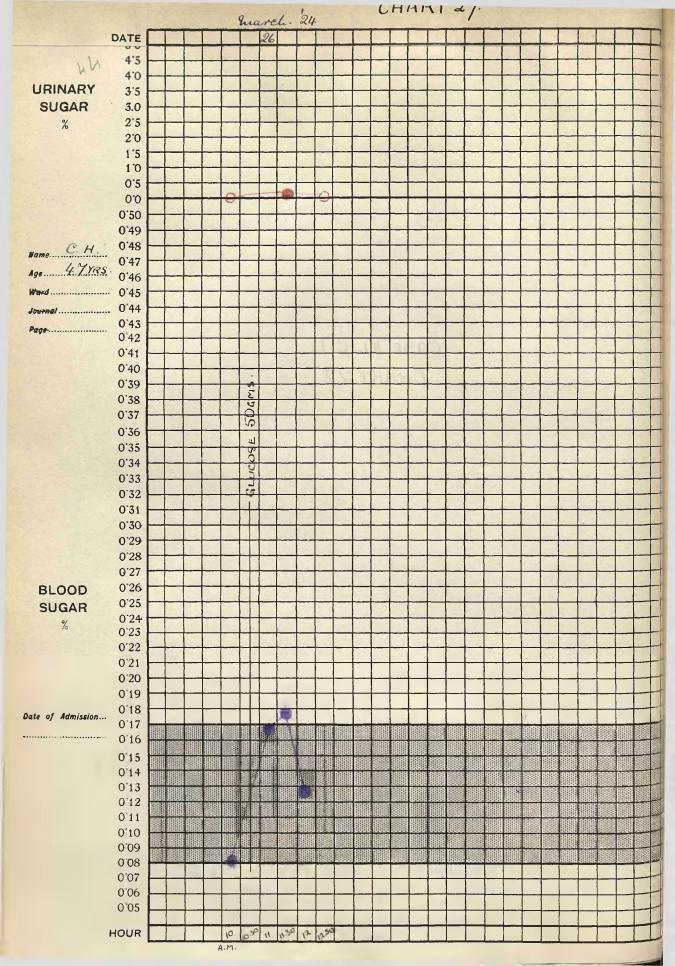


Case 9. J.M. Male. Aged 39 years. Septic Haematoma.

The condition in this case was one of septic haematoma resulting from an accident.

The curve obtained in this case (Chart 26) differs considerably from that given by the cases already described. It shows a delayed absorption of glucose, the blood-sugar rising very gradually and only reaching its height after two hours, by which time it should, of course, have reached its preglucose level. The renal threshold, however, was not exceeded and no glycosuria occurred.

CASE 10. C.H. CHART 27.

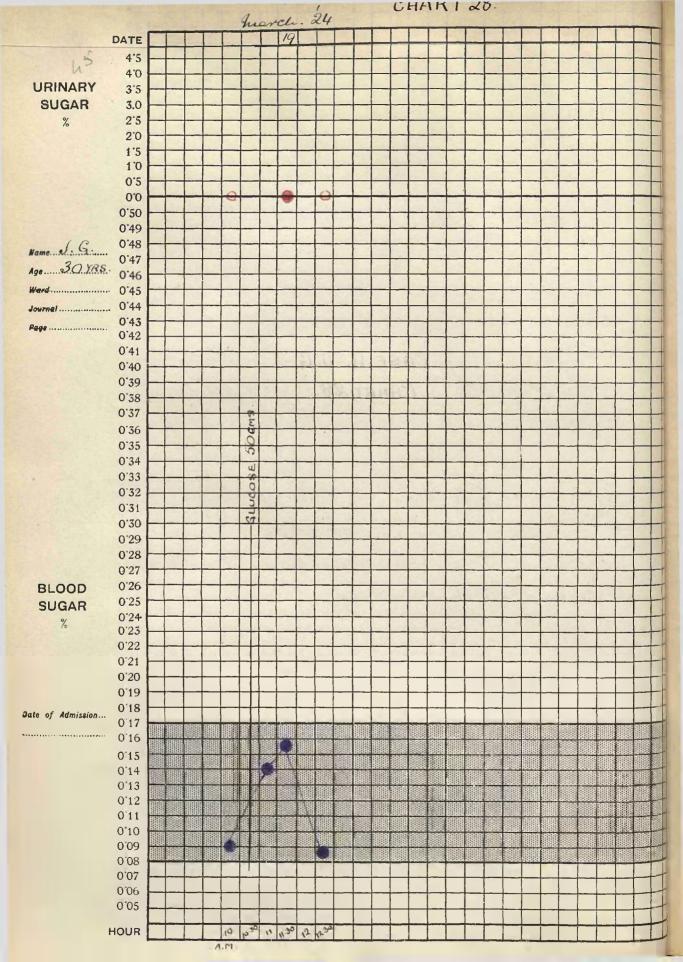


Case 10. C.H. Female. Aged 47 years. Midwife. Cellulitis.

This woman was suffering from a severe cellulitis of the left arm of ten days' duration when the investigation was made. She developed erysipelas shortly after and was removed to a fever hospital. The arm healed satisfactorily.

A glucose test carried out at the height of sepsis showed a distinct loss of tolerance to glucose in the curve obtained, the blood-sugar rising above the renal threshold with the consequent appearance of sugar in the urine (Chart 27).

CASE II. J.G.

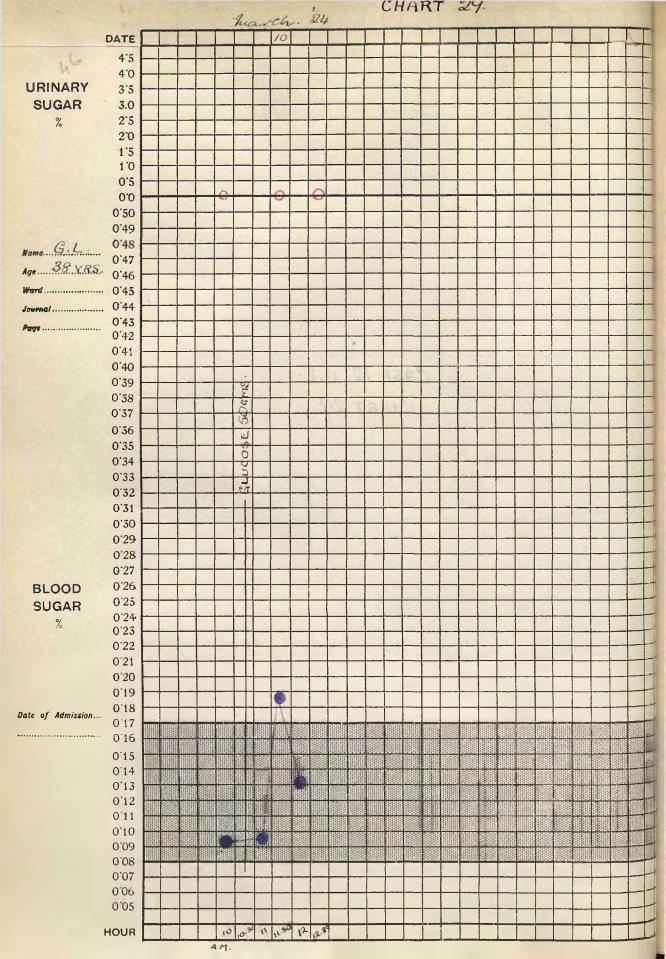


Case 11. J.G. Male. Aged 30 years. Carbuncle.

Patient had a carbuncle on the neck from which he had been suffering for two weeks. The temperature at the time of investigation was slightly elevated.

The glucose test, as is seen in Chart 28, gave a curve which was perfectly normal in character. There was in this case apparently no disturbance of metabolism.

CASE 12, G.L.
CHART 29



Case 12. G.L. Male. Aged 38 years. Cellulitis.

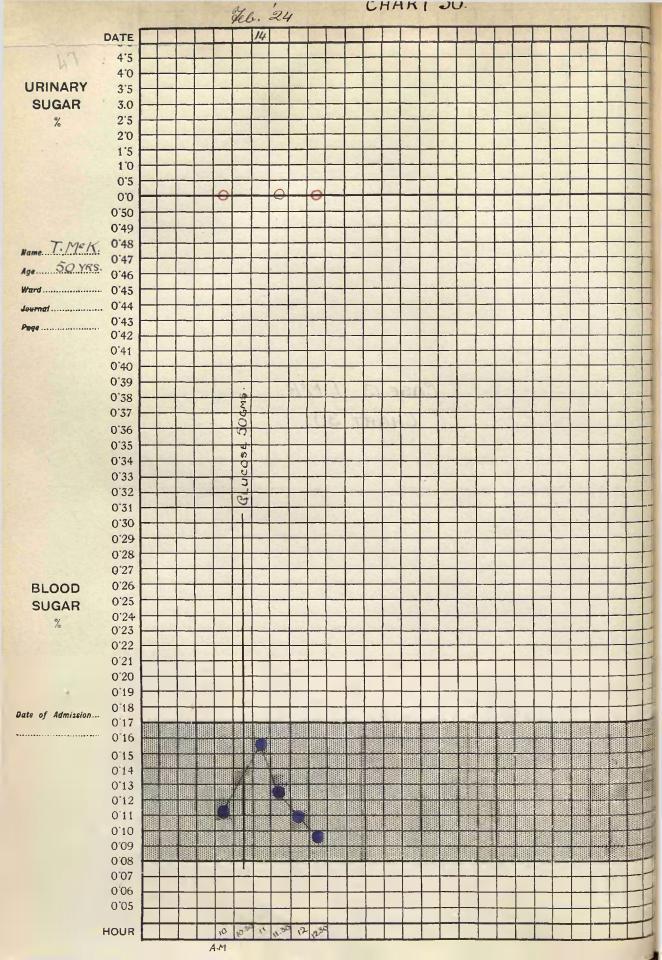
This patient was suffering from cellulitis of the right leg of possible specific origin.

A glucose test during sepsis showed the blood-sugar rising considerably above the threshold, and delay in the return to normal.

No sugar appeared in the urine. The course of the blood-sugar curve indicates disturbed tolerance.

(Chart 29).

Case /3. Т. М°К. Снакт 30.



Case 13. T. McK. Male. Aged 50 years.

Carbuncle.

This man also had a carbuncle present for some weeks. The temperature was normal at the time of examination.

The curve obtained on testing was a normal one, the blood-sugar running within normal limits and no sugar appearing in the urine.

(Chart 30.)

CASE 14. MRS.Q. CHART 31.

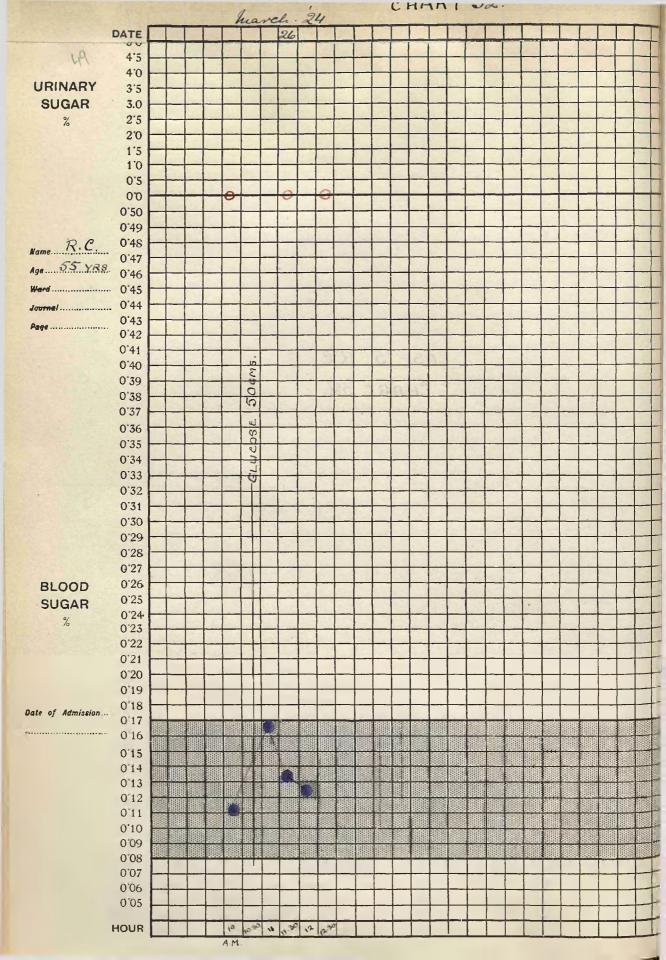
CHART OI. merch. 24 DATE 4.5 40 URINARY 3.2 SUGAR 3.0 2.5 % 20 1'5 10 0.2 0.0 0.20 0'49 0'48 Name MRS. Q. 0'47 Age 45 YRS. 0'46 0.45 0'44 Journal 0'43 Page 0'42 0'41 0'40 0.39 0'38 50gms. 0'37 0.36 0'35 0'34 S 0'33 60 0.35 0.31 0.30 0.29 0'28 0.27 0'26 BLOOD 0.22 SUGAR 0'24 % 0.23 0.55 0.21 0.20 0.19 0'18 Date of Admission... 017 0'16 015 0.14 0.13 012 0'11 0.10 0'09 0.08 0'07 0.06 0 05 10 1030 11 1130 12 12 1230 HOUR

Case 14. Mrs. Q. Aged 45 years. Cellulitis.

This woman had a severe cellulitis of the left leg following the removal of a bursa from the popliteal space. The temperature, which remained up for some weeks, was 1000 at the time of investigation, two days after admission.

In her case the blood-sugar not only rose to a higher level than is normal but remained about the same level for an hour and a half after glucose was given. (see Chart 31) This result indicated a considerable degree of disturbance of carbohydrate metabolism.

CASE 15, R.C. CHART 32.



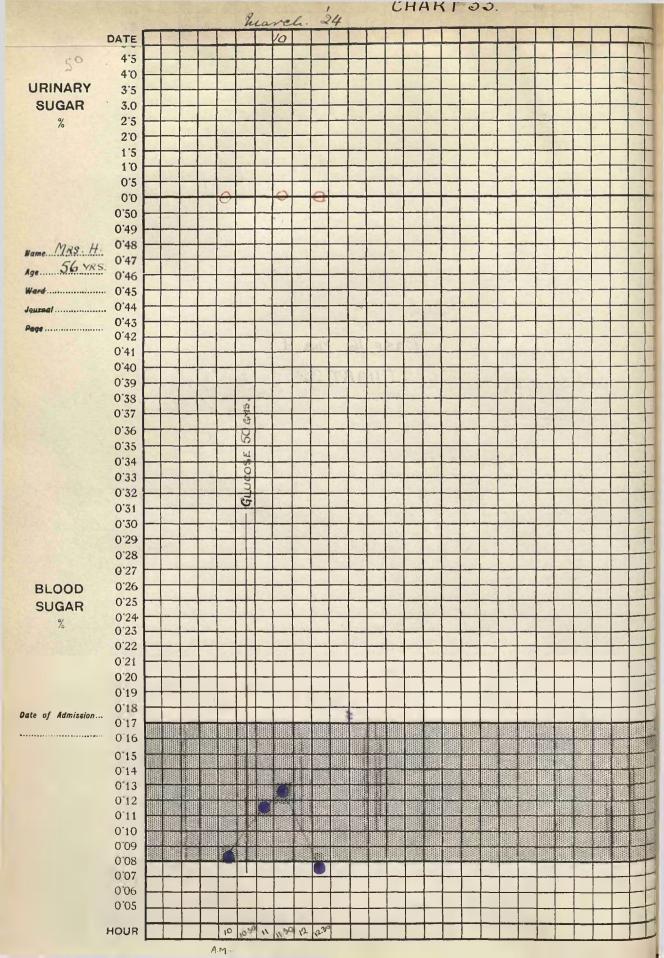
Case 15. R.C. Male. Aged 55 years. Septic Wound.

The patient was admitted to hospital with a discharging wound in the leg, the result of an accident ten days before.

The blood-sugar after glucose rose to a slightly higher level than is usually found, but the curve was otherwise normal. (Chart 32)

There was apparently no interference with normal metabolism.

CASE 16. Mrs. H. CHART 33.

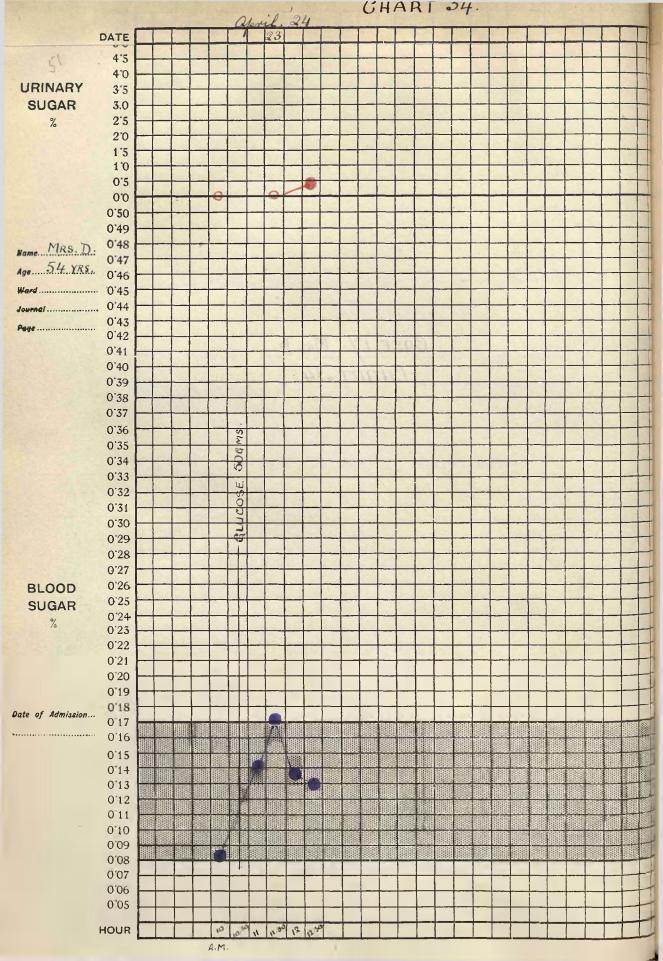


Case 16. Mrs. H. Aged 56 years. Housewife. Sepsis of Hand.

This woman had a septic hand, and at the time her case was investigated had a temperature of 99°.

The result of the test was in every way normal. (Chart 33)

CASE 17. MRS.D.



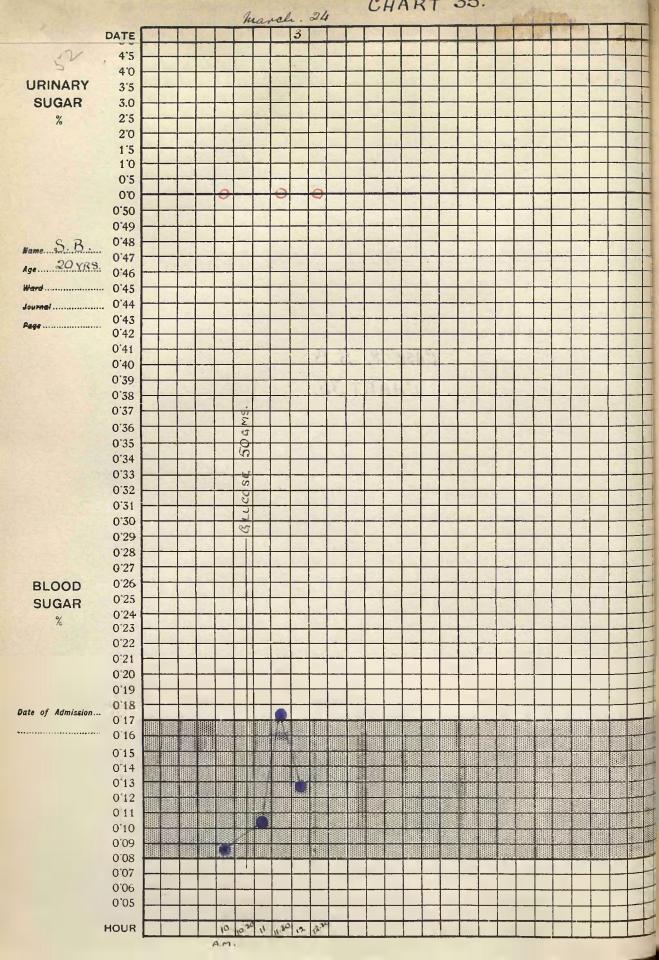
Case 17. Mrs. D. Aged 54 years. Housewife. Cellulitis.

On 4/4/24 this patient pricked her left thumb with a fish bone; two days later the wound suppurated and inflammation spread up the arm, causing a severe cellulitis.

A glucose curve obtained during active sepsis showed a "lag" character, the blood-sugar rising slightly above the threshold, and sugar appearing in the urine in estimable amount.

(Chart 34)

CASE 18. S.B.
CHART 35.

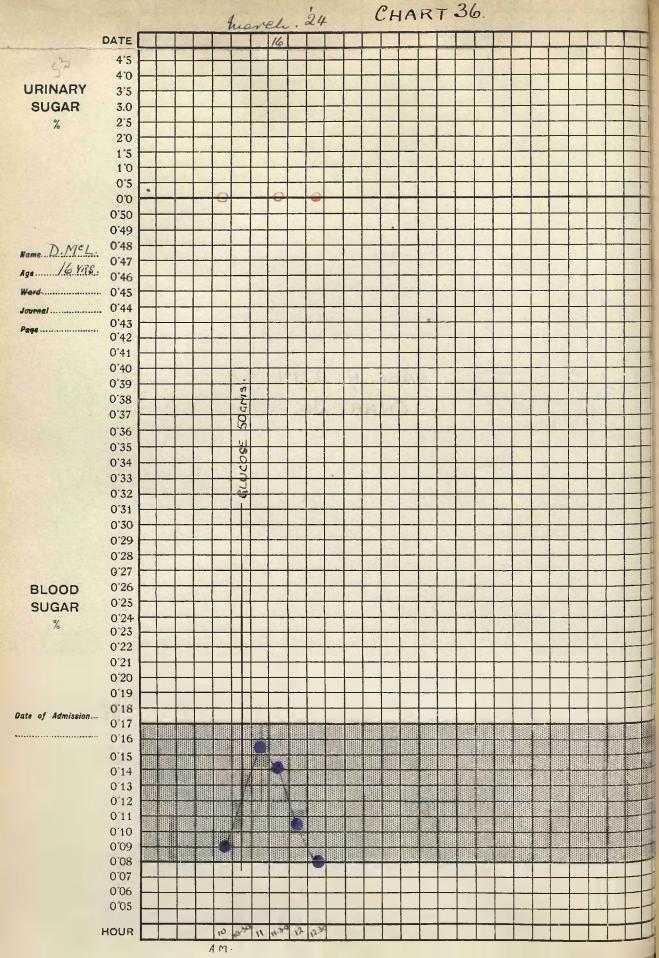


Case 18. S.B. Female. Aged 20 years. Abdominal Abscess.

This girl was suffering on admission from an abdominal abscess which had been incised a few days before her case was investigated.

The glucose curve rose to a rather higher level than usual but was otherwise normal. (Chart 35)

CASE 19. D.MºL. CHART 36.



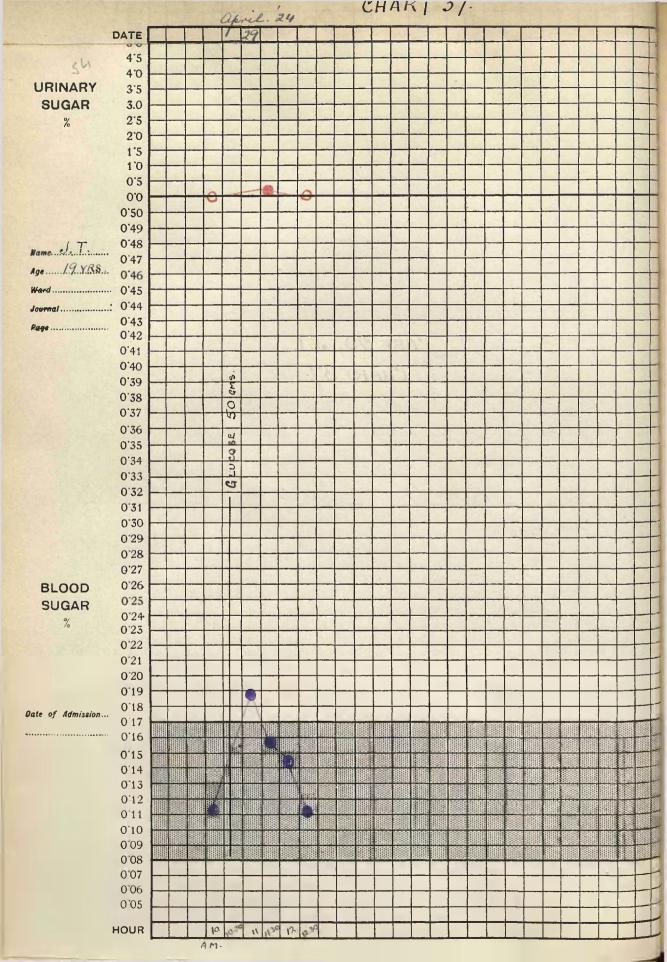
Case 19. D. McL. Male. Aged 16 years.

Tubercular Knee.

This patient had tubercular disease affecting the right knee. His temperature on the day of the test was 99°.

The glucose curve obtained was normal. (Chart 36)

CASE 20. J.T.

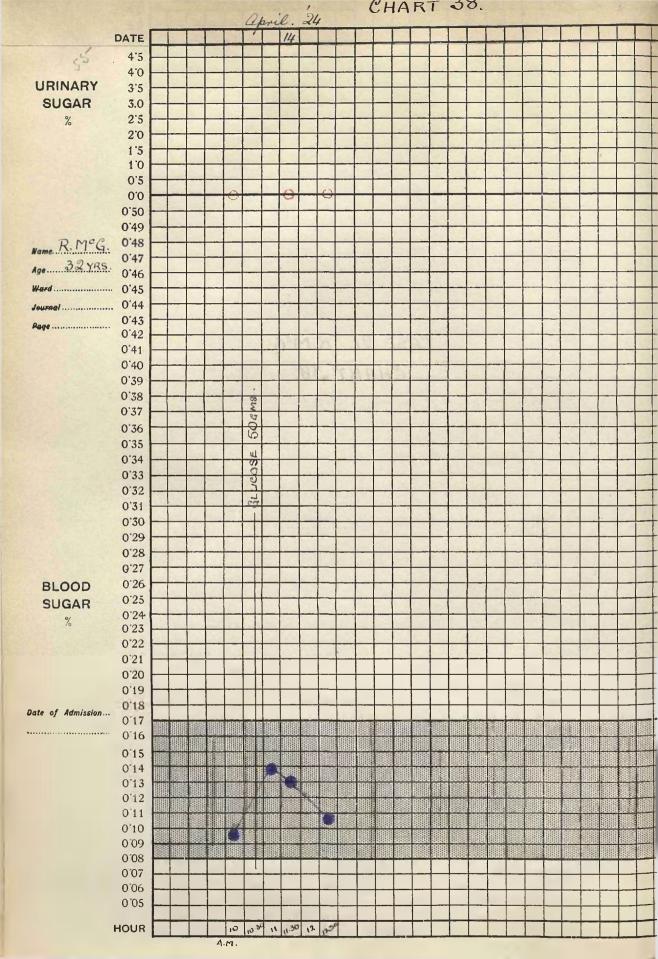


Case 20. J.Y. Male. Aged 19 years. Septic Wound.

This lad was admitted to hospital with a septic wound of the hand arising from an injury received while at work.

A fortnight after his admission, when the hand was still freely discharging pus, the carbohydrate tolerance was investigated. The blood-sugar rose to 0.188% in the first half hour and the urine showed a trace of sugar. There was, however, no delay in the return to normal. (see Chart 37) A. typical "lag" curve.

CASE 21. R.M°G.



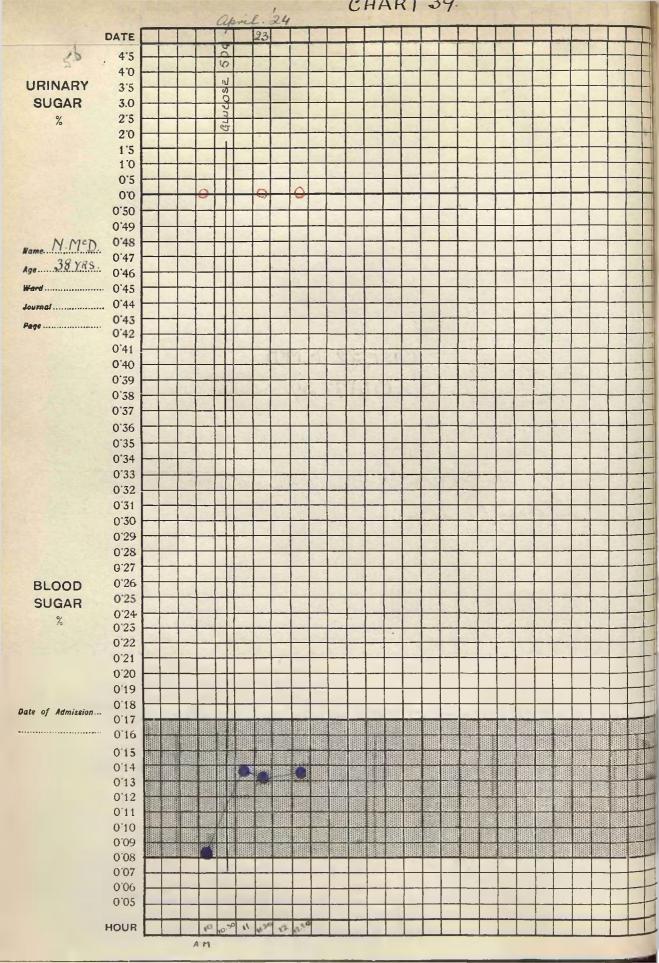
Case 21. R. McG. Male. Aged 32 years. Tubercular Hip.

This man was suffering from tubercular disease of the left hip. Sinuses discharging pus were present in the region of the hip joint, and there was an abscess on the left buttock.

The result of the glucose test was normal. (Chart 38)

CASE 22. N.M°D.

CHART 39.



Case 22. N. McD. Male. Aged 38 years.

Chronic Ulcer.

Patient had suffered from a chronic ulcer (probably perforating) of the foot for some years. In his case there was no abrupt rise in the blood-sugar after glucose but there was obvious delay in the return to normal, as seen in Chart 39.

CASE 23. A.G. CHART 40.

CHART 40 14 DATE 4.5 40 URINARY 3.2 SUGAR 3.0 % 2.5 20 1'5 10 0.2 00 0'50 0'49 Name A.G. 0'48 0'47 Age 9 YRS 0'46 Ward 0'45 0'44 Journal 0'43 Page 0'42 0'41 0.40 0'39 MIS 0'38 500 0.37 0'36 M 0.32 Sabu18 0'34 0'33 0.35 0'31 0.30 0.53 0.58 0'27 0.26 BLOOD 0'25 SUGAR 0'24 0.53 0.55 0.21 0.50 0'19 0'18 Date of Admission ... 0.17 ************************* 0.16 0.15 0'14 0'13 0.12 0.11 0.10 0.09 0.08 0 07 0.06 0.02 10 1039 11 1130 12 1230 HOUR A.M.

Case 23. A.G. Female. Aged 9 years. Septic Wound.

This child was suffering from a wound which had become septic. The temperature was slightly elevated at the time her case was investigated.

The glucose curve was normal in all respects. (Chart 40)

CASE 24 MRS.E.

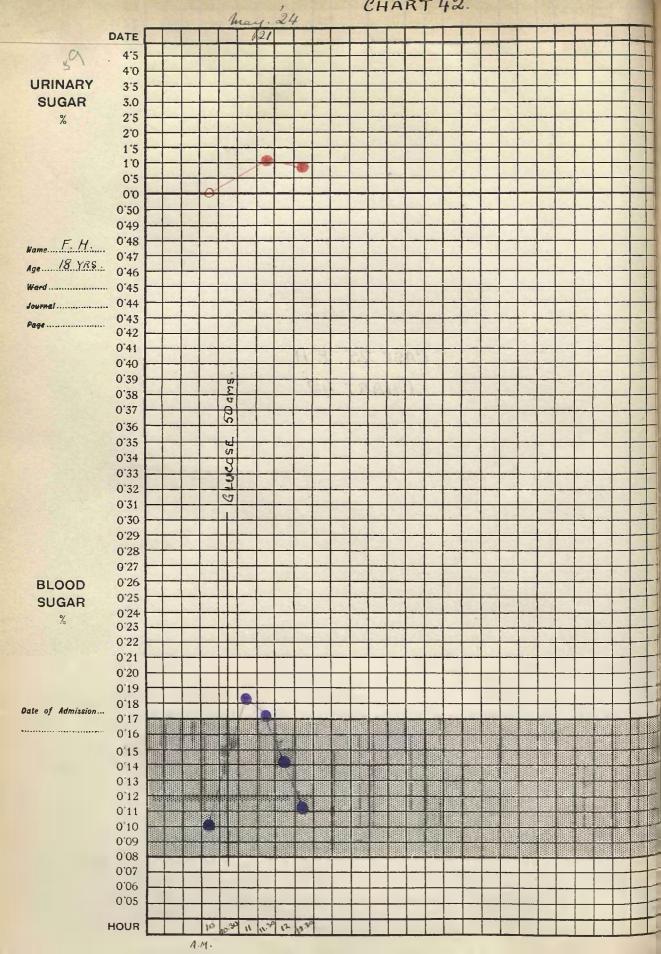
CHAK 1 41-DATE 4.5 40 URINARY 3.2 SUGAR 3.0 2.2 % 20 1'5 10 0.2 0.0 0.20 0'49 0'48 Name MRS.E. 0'47 Age 30 YRS. 0'46 Ward 0'45 0'44 Journal 0'43 0'42 0'41 0'40 0'39 0'38 0.37 0'36 0'35 \$.M 0'34 50 0.33 0'32 SE 0'31 0 0.30 Š 0.29 92 0'28 0.27 0'26 BLOOD 0.25 SUGAR 0.24 % 0.23 0'22 0'21 0.50 0'19 0.18 Date of Admission... 0.17 ********** 0.16 015 0'14 0.13 0'12 0.11 010 0.09 0.08 0.02 0.09 0.02 HOUR 4.M-

Case 24. Mrs. E. Aged 30 years. Housewife. Ischio-rectal Abscess.

Patient was admitted suffering from an ischiorectal abscess. The abscess at the time of investigation had not been opened, and the temperature was running about 100 - 101°.

The curve following the administration of glucose indicated a distinct interference with normal carbohydrate metabolism, the blood-sugar rising above the threshold within half an hour and failing to return to normal within two hours. The urine remained sugar-free. (Chart 41)

CASE 25 F.H. CHART 42.

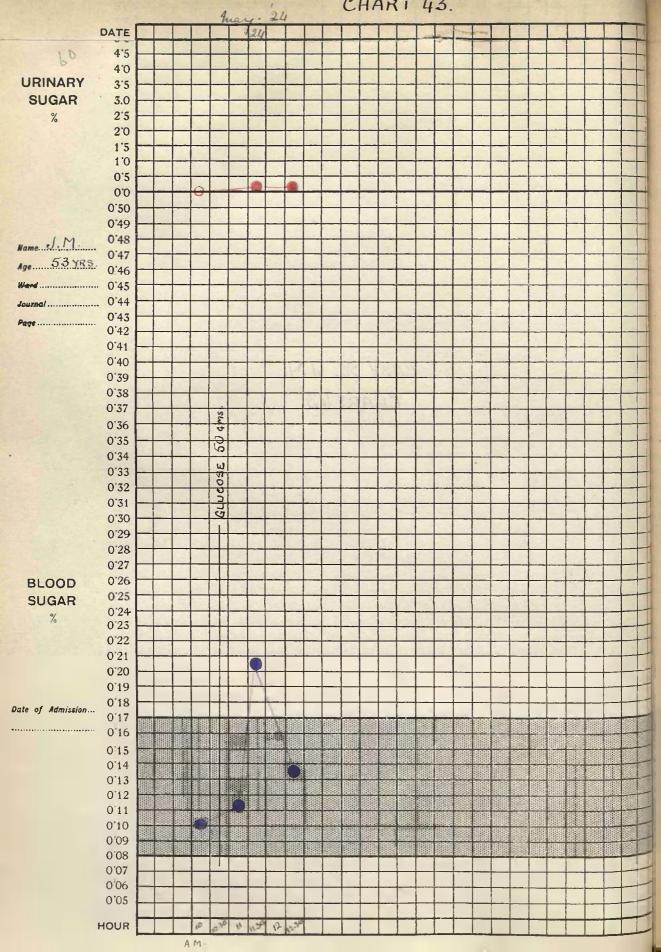


Case 25. F.H. Male. Aged 18 years. Osteomyelitis.

This boy was in hospital suffering from an osteomyelitis affecting the lower end of the right tibia. He had fallen and injured the leg a week before admission.

The glucose test, performed while the disease was active, indicated a marked loss of tolerance, as seen in Chart 42. The blood-sugar reached 0.18% and considerable glycosuria occurred.

CASE 26. J.M.
CHART 43.

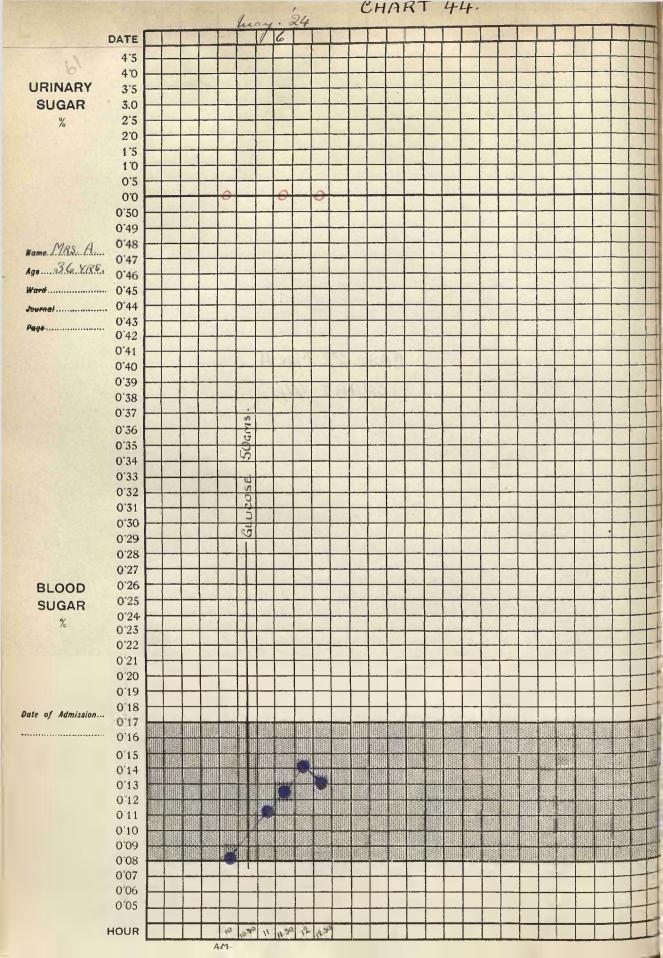


Case 26. J.M. Male. Aged 53 years. Miner. Cellulitis.

A case of very severe septic infection of the right hand and arm resulting from an accident at work. The temperature was running at 100-101°.

The result of a glucose test showed a blood-sugar rising to 0.205% at the end of an hour, and falling only to 0.134% after two hours. Sugar appeared in the urine. (Chart 43) This result indicated a fairly marked disturbance of metabolism.

CASE 27. MRS. A. CHART 44.

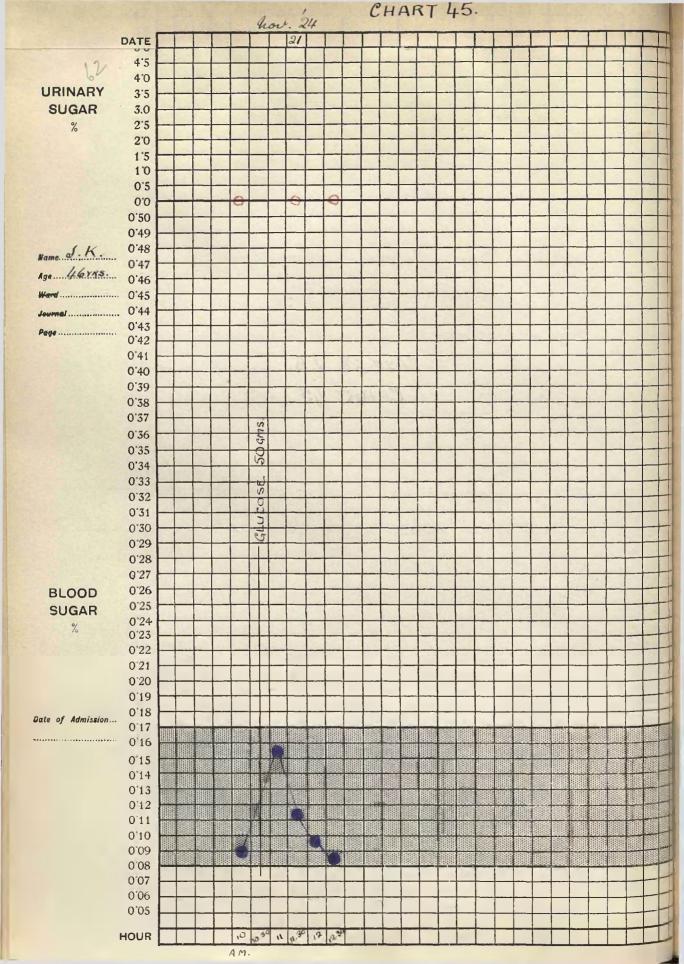


Case 27. Mrs. A. Aged 36 years. Pyorrhoea. Septicaemia.

This patient was, at the time of investigation, supposed to be suffering from an acute form of pyorrhoea alveolaris. She became acutely ill, however, and died a week after the carrying out of the test. The temperature on the day of investigation was 99°.

The blood-sugar after glucose rose slowly for $l\frac{1}{2}$ hours and at the end of two hours was somewhat above the starting level, but at no point did it touch the threshold. It may be considered a normal curve. (See Chart 44)

Case 28. J.K.
Chart 45.

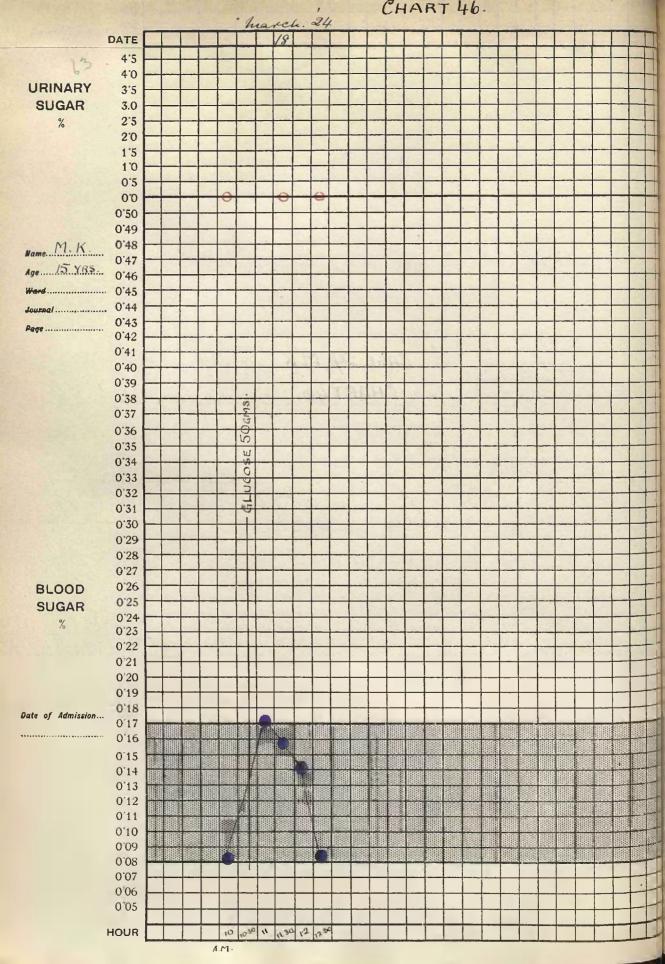


Case 28. J.K. Male. Aged 46 years. Stonehewer. Pleurisy. Tuberculosis.

Patient was admitted with a history of having caught cold two weeks before, and recently had developed pain in the chest and breathlessness. A right-sided pleurisy was diagnosed and the right apex yielded evidence of tubercle. The temperature was 99°.

The glucose curve obtained during the active stage of his illness was normal. (Chart 45.)

CASE 29. M.K. CHART 46.

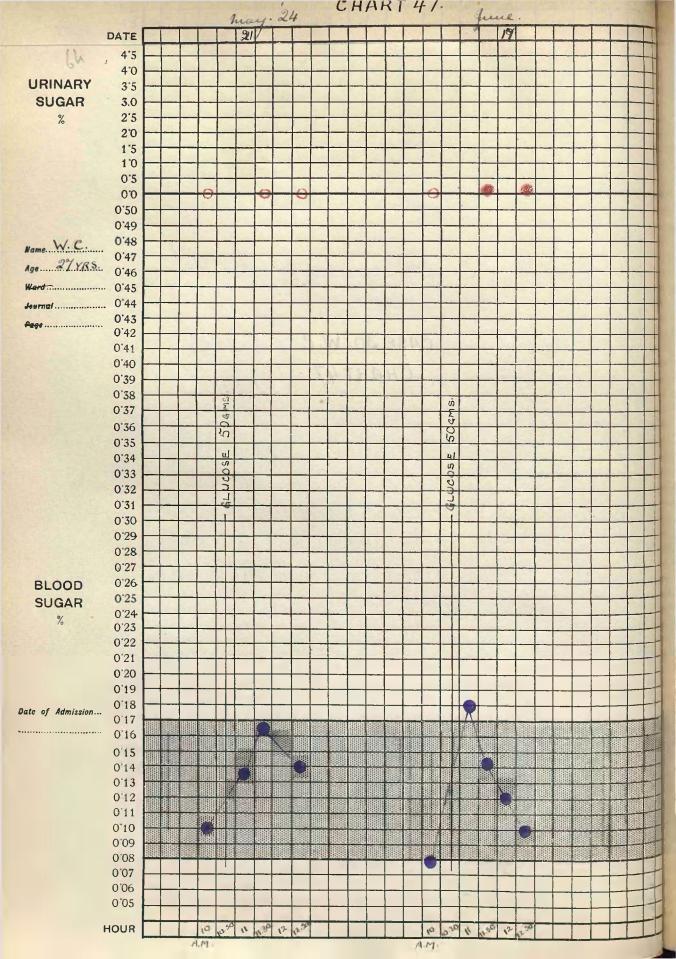


Case 29. M.K. Female. Aged 15 years. Lupus Vulgaris.

This girl had been suffering for some time from lupus vulgaris, complicated by an electrical burn which she had sustained in the course of treatment. The temperature was normal.

A glucose curve obtained on 18/3/24 was probably normal although the blood sugar rose slightly above the threshold in the first half hour. (Chart 46)

CASE 30 W.C.



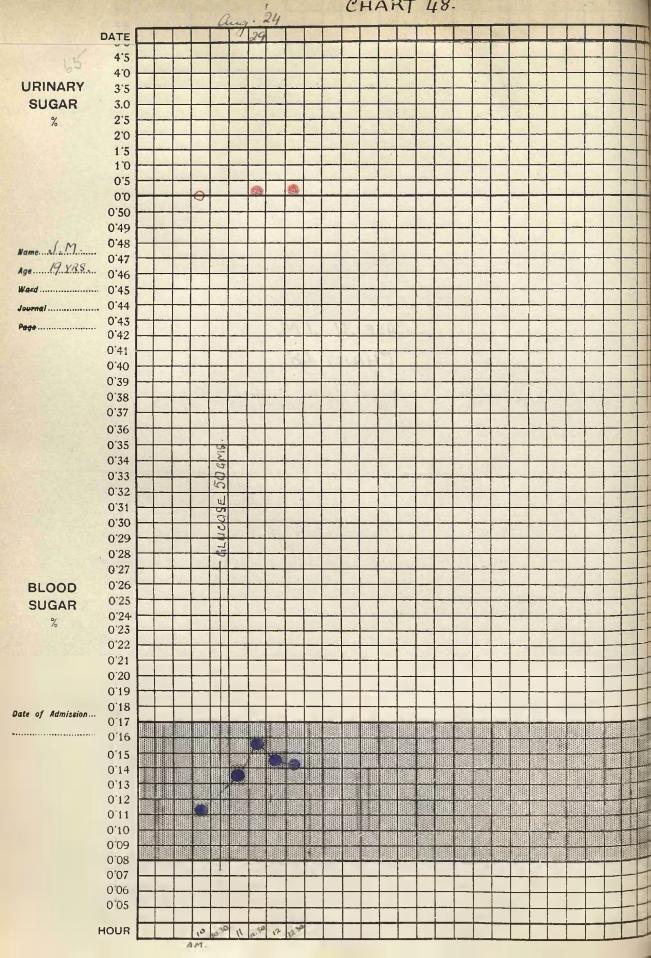
Case 30. W.C. Male. Aged 27 years. Pyaemic Abscesses.

This man was admitted with a severe suppurative condition of the glands in the neck, of two or three weeks' duration. The temperature at the time of investigation was 101°.

The curve rose above the threshold in half an hour and a trace of sugar appeared in the urine.

There was no delay in the return. (Chart 47). A "lag" curve indicating diminished glucose tolerance.

CASE 31. J.M.
CHART 48.



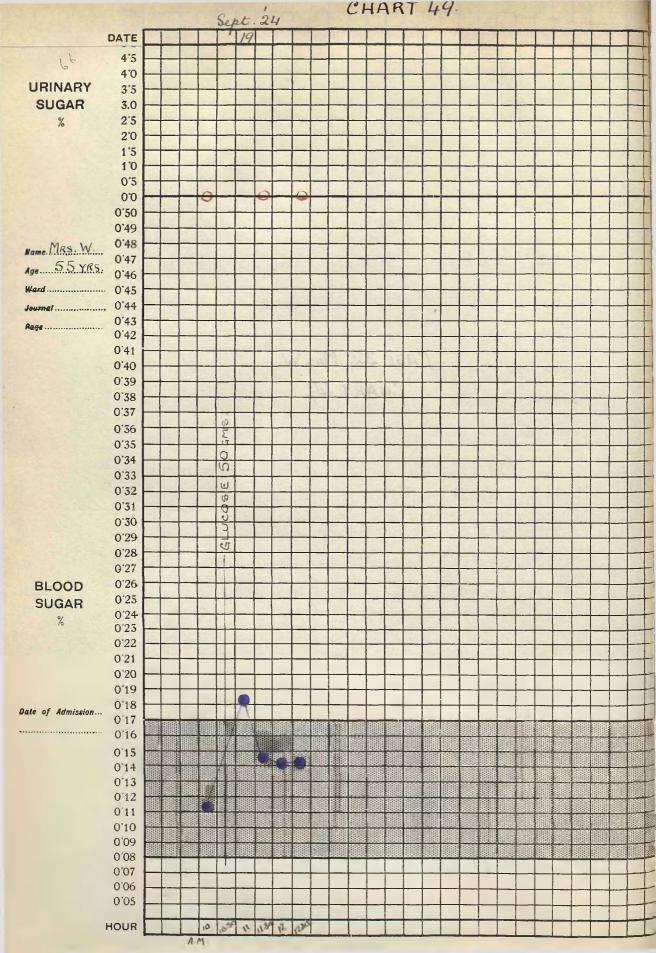
Case 31. J.M. Male. Aged 19 years. Osteomyelitis.

Patient was suffering from osteomyelitis which involved the right humerus and right tibia.

The temperature was swinging. The left leg had been amputated below the knee ten years before.

In this case, as in cases 9 and 22, the blood-sugar did not exceed the threshold, but the disturbance of metabolism was clearly evidenced by the continued high percentage of blood-sugar at the end of two hours. (See Chart 48)

CASE 32. MRS.W.



Case 32. Mrs. W. Aged 55 years. Housewife. Cellulitis.

This was a case of septic bursitis of the right knee followed by cellulitis. The temperature at the time of investigation was 100° .

50 grammes of glucose caused a rise of the blood-sugar to 0.182% within half an hour, followed by a very slow return towards the original level - a curve showing the characters more of a diabetic than of a "lag" type. (Chart 49)

CASE 33. Mrs. M.L. CHART 50.

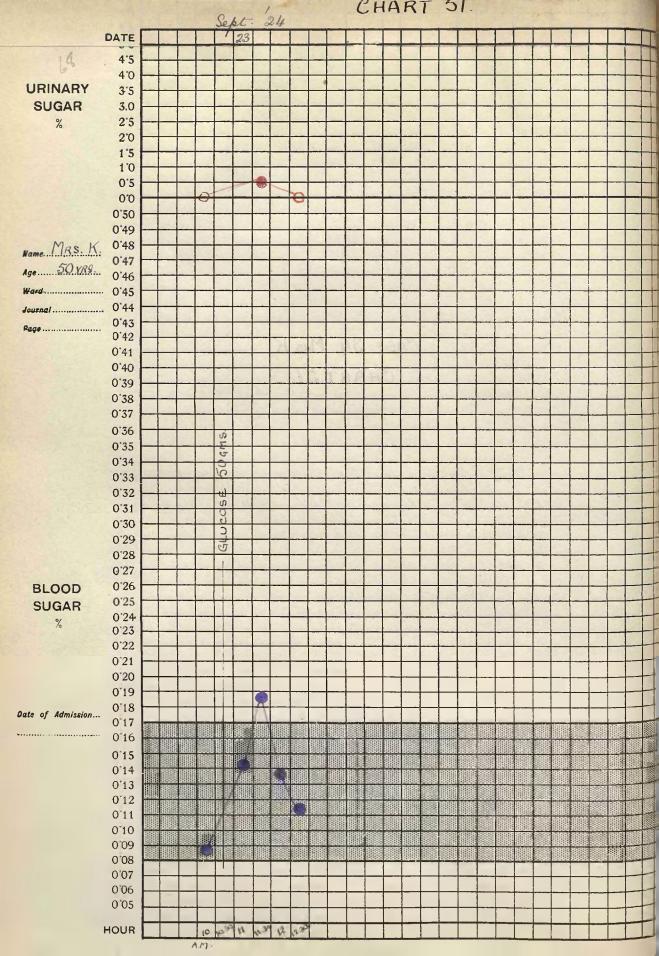
CHART 50. DATE 4'5 40 URINARY 3.5 SUGAR 3.0 % 2.5 20 1'5 10 0.2 0.0 0.20 0.49 0'48 Name MRS. MeL. 0'47 Age 44 YRS 0'46 Ward 0'45 0'44 Journal 0'43 Page 0'42 0'41 0.40 0'39 0'38 0'37 0'36 Mª 0'35 छ 0 0'34 S 0'33 0.35 S 0'31 Lucas 0.30 0.58 S 0.28 0.27 BLOOD 0.26 0.22 SUGAR 0'24 % 0.23 0.25 0'21 0'20 0.19 0'18 Date of Admission... 0'17 ****************************** 0.16 015 0'14 0'13 0.12 0'11 0.10 0.03 0.08 0.07 0.06 0.05 HOUR 10 11 000 A.M.

Case 33. Mrs. McL. Aged 44 years. Housewife. Chronic Osteomyelitis.

Patient had an old-standing osteomyelitis of twenty years' duration affecting the lower end of the right femur. A discharging sinus was present. The temperature was normal during the test.

The result of a test showed a considerable lowering of tolerance, as seen in Chart 50. The blood-sugar level was high throughout and sugar appeared in the urine to the amount of 1%. Another curve inclining to diabetic type.

CASE 34. MRS.K.

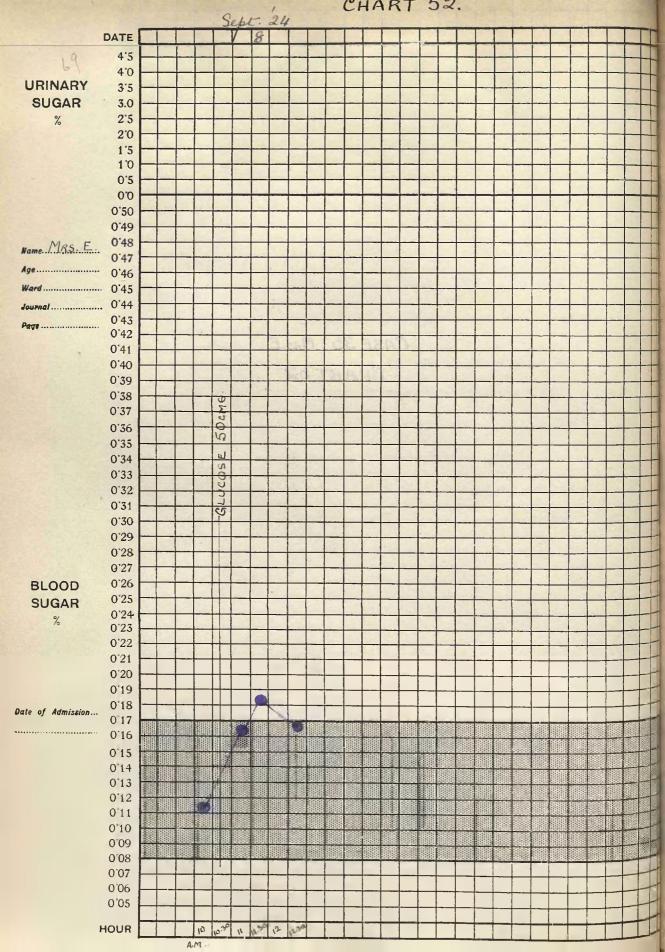


Case 34. Mrs. K. Aged 50 years. Housewife. Varicose Ulcer.

This case was one of long-standing varicose ulcer of nine years' duration, the left leg being affected. The temperature was normal.

The administration of glucose raised the blood-sugar to 0.186% and sugar appeared in the urine; there was, however, no delay in the return to normal. (Chart 51) A "lag" curve.

CASE 35. MRS.E.
CHART 52.



Case 35. Mrs. E. Housewife. Pelvic Cellulitis.

This woman suffered from a rather obscure condition which was diagnosed as pelvic cellulitis. She had also a bed-sore over the sacrum. The temperature was slightly raised

After 50 grammes of glucose the blood-sugar rose sharply, reaching 0.181% at the end of the first hour, and showed considerable delay in returning, being still 0.168% at the end of two hours. (Chart 52) This was obviously a case of considerable disturbance of carbohydrate metabolism.

CASE 36. C.M.B.

CHART 53.

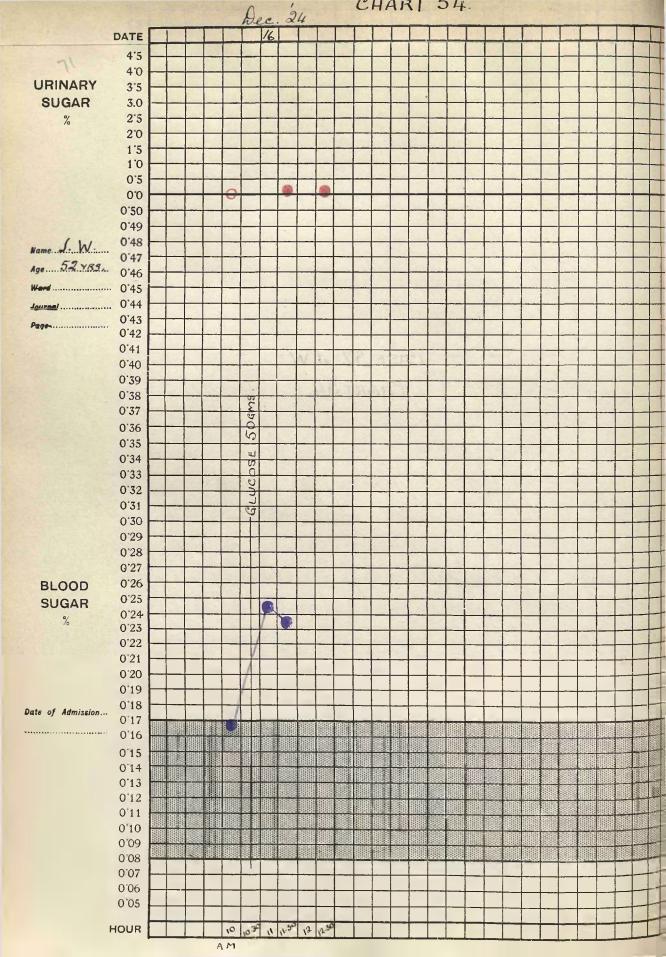
CHART 53. DATE 4.5 40 URINARY 3'5 SUGAR 3.0 2.5 % 20 1'5 10 0.2 0.0 0.20 0'49 Name C. MCB. 0'48 0'47 Age 60 YRS 046 Ward..... 0'45 Journal 0'44 0'43 Page 0'42 0'41 0'40 0'39 0'38 50cm 0'37 0'36 0'35 1.5 0'34 80 0.33 Š 0'32 0'31 0.30 0.59 0'28 0'27 0'26 BLOOD 0.22 SUGAR 0'24 % 0.53 0.23 0.21 0.20 0'19 0'18 Date of Admission... 0 17 ************************* 0'16 015 0'14 013 0.12 0.11 0'10 0.09 0.08 0.07 0'06 0 05 HOUR 1030 11 11:00 12 123 d.M.

Case 36. C. McB. Male. Aged 60 years. Osteomyelitis.

Patient was admitted suffering from an osteomyelitis of the lower jaw. Four weeks previously several teeth had been extracted and the cavities had become infected. A sinus discharging pus was present.

The blood-sugar rose in this case well over the renal threshold within half an hour and continued to rise till the end of an hour. After two hours it was still well above the starting level. (Chart 53) This case also showed marked loss of tolerance.

CASE 37. J.W. CHART 54.



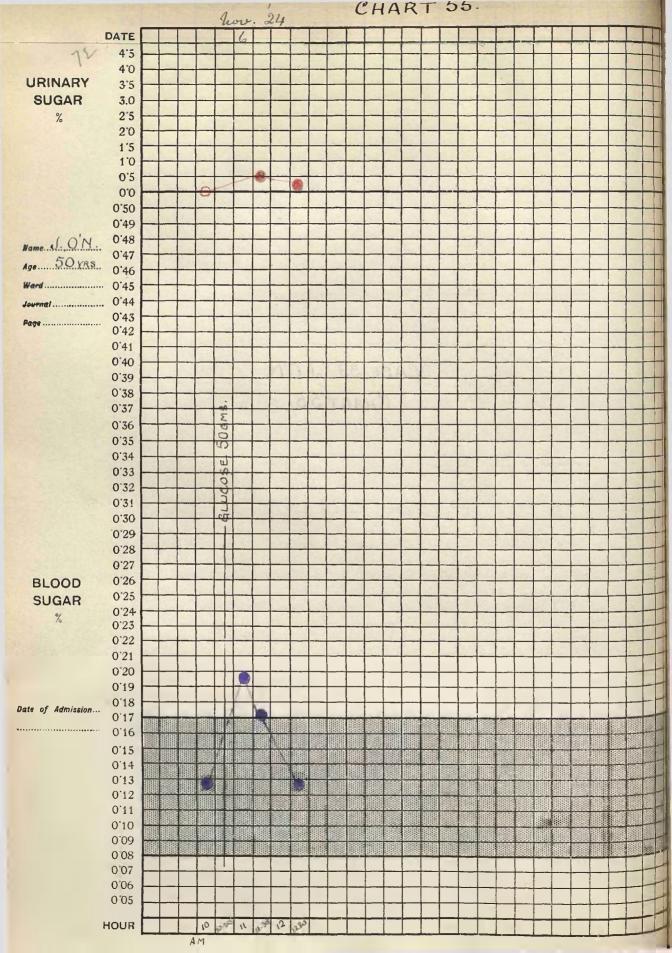
Case 37. J.W. Male. Aged 52 years. Pyaemia.

This man was suffering from Pyaemia.

Both legs had been amputated as the result of an accident and sepsis had supervened. The temperature was swinging.

The blood sugar curve could, unfortunately, not be completed, but its course so far as it went, and the **pe**currence of glycosuria, were sufficient to show defective metabolism.

CASE.38. J.O'N. CHART 55.

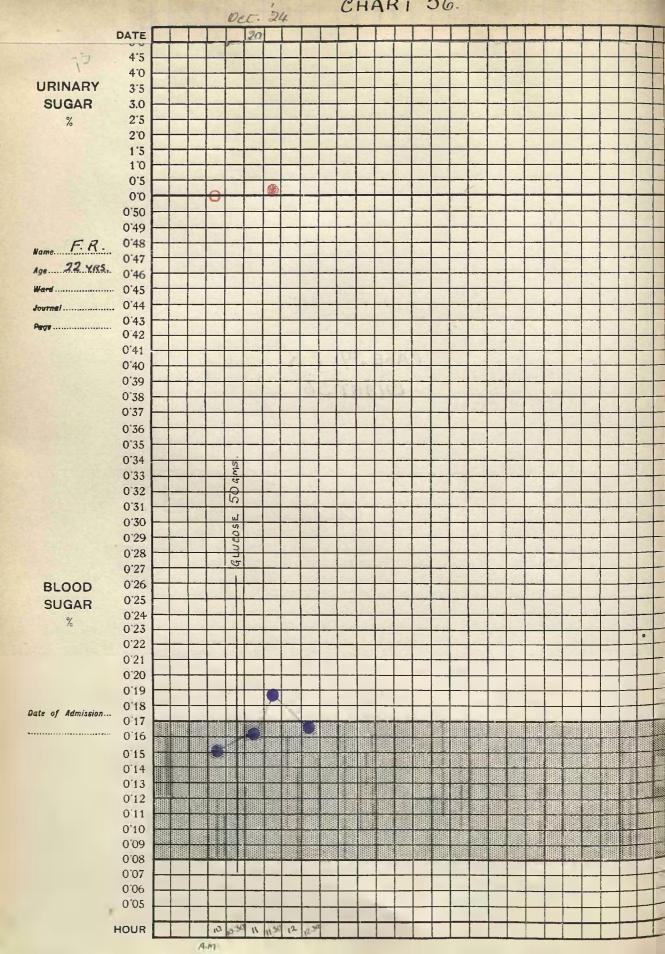


Case 38. J. O'N. Male. Aged 50 years. Cellulitis - Pyaemia.

This man had a severe cellulitis of the left hand of four weeks' duration at the time of investigation. He developed a pyaemic condition and died. The temperature at the time of investigation was 99°.

The fasting level of the blood-sugar in this case was rather above the normal, as seen in Chart 55, and after glucose it rose sharply within the first half hour to 0.196%. Within two hours it had fallen to the pre-glucose level.

CASE 39. F.R. CHART 56.



Case 39. F.R. Male. Aged 22 years. ? Abscess in Lung.

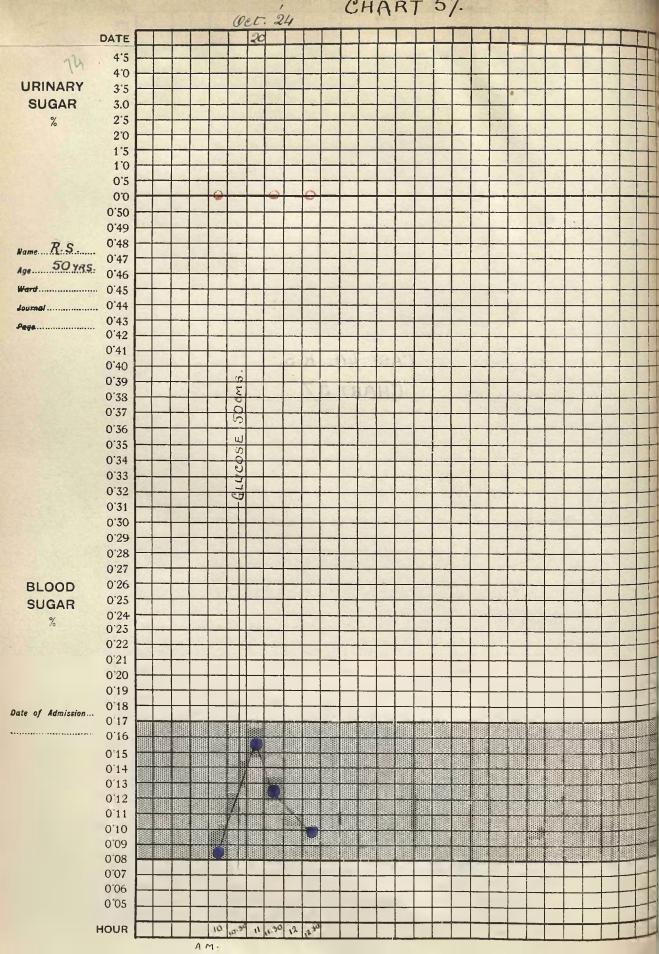
Patient had sustained a compound fracture of the right arm seven weeks before. He had recently developed a cough with abundant foulsmelling sputum. The temperature was elevated.

In this case also the resting blood-sugar was above normal and after glucose its course indicated a considerably diminished tolerance.

The curve, in fact, is of mild diabetic character.

(Chart 56)

CASE 40 R.S. CHART 57.

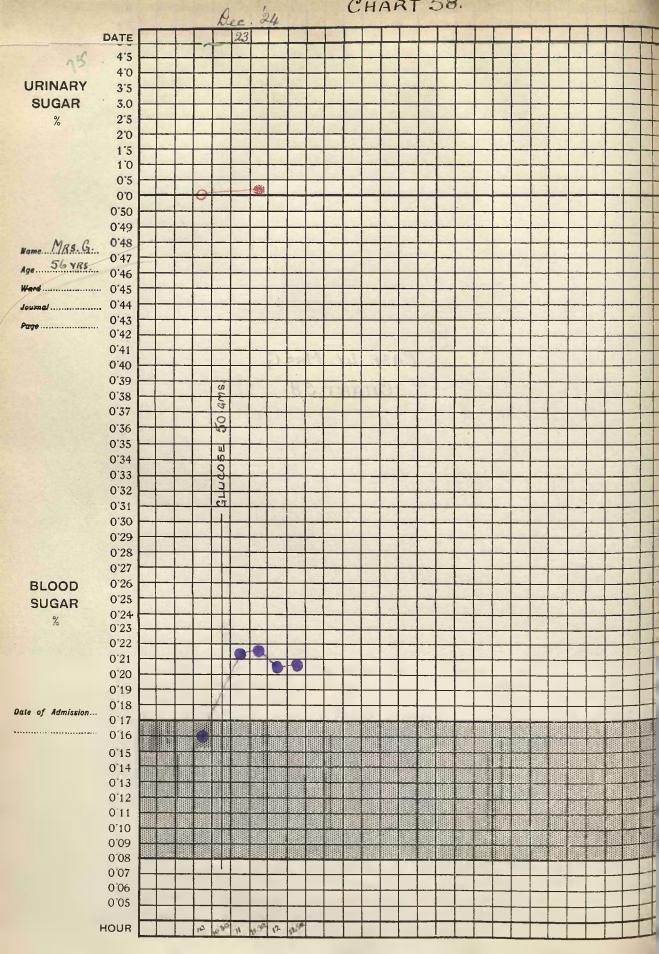


Case 40. R.S. Male. Aged 50 years. Carbuncle.

This man was suffering from a carbuncle on the back of the neck. The carbuncle was of five weeks' duration. At the time of investigation the temperature was normal.

A glucose test yielded a normal curve. (Chart 57)

CASE 4/. MRS.G. CHART 58.



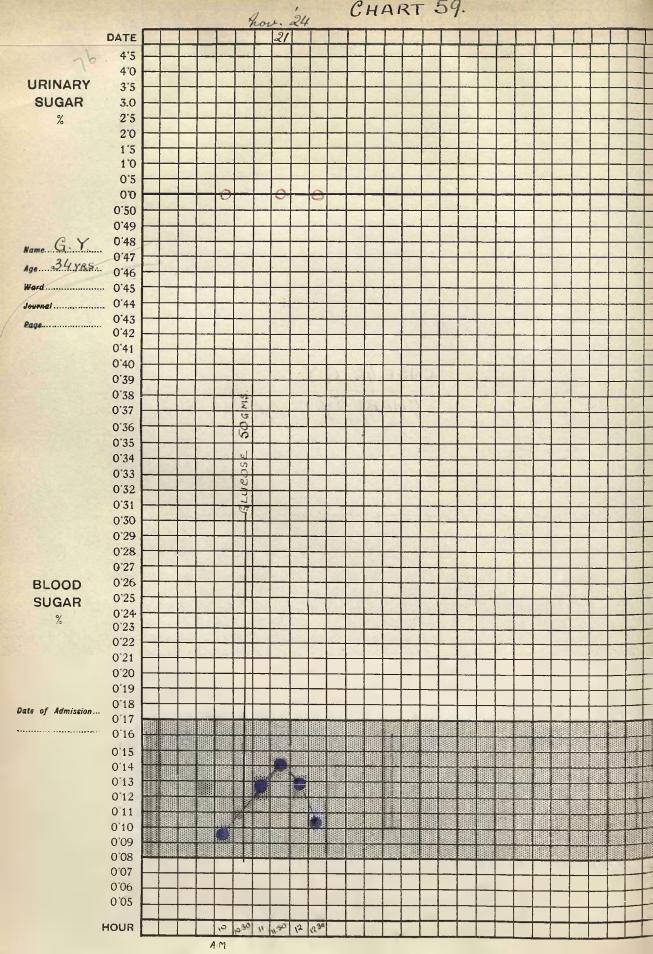
Case 41. Mrs. G. Aged 56 years. Osteomyelitis.

This woman was suffering from osteomyelitis of the right leg arising from an old focus of infection which dated from many years before. This had recently been lit up by a blow on the leg. The temperature at the time of investigation was 100°.

The blood-sugar curve indicated a marked loss of tolerance, beginning at the high level of 0.16%, rising to 0.216% and remaining at practically that height till the end. (Chart 58)

This curve is distinctly diabetic in type in spite of the absence of glycosuria. The resting blood-sugar was high - 0.16%. This might be due to the effect of the long-standing infection which was present, and the non-appearance of sugar in the urine to raising of the renal threshold, which so often occurs in diabetes of long duration.

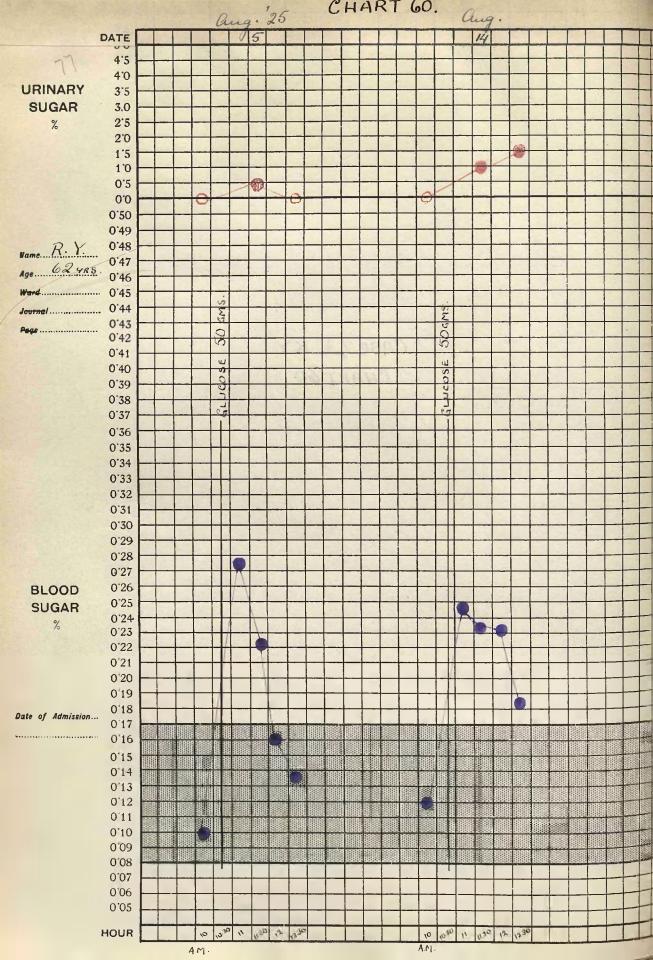
CASE 42. G.Y. CHART 59.



Case 42. G.Y. Male. Aged 34 years. Engineer. Pneumonia.

This man had an attack of pneumonia which began with a rigor on 23/10/24. The left base was consolidated. The crisis was reached on 31/10/24 but his general condition did not improve greatly and on 13/11/24 he began to bring up large quantities of purulent sputum. This continued for some days, then retention occurred, as shown by a rise in temperature. On 21/11/24 when the temperature was back to normal a glucose test was carried out, resulting in a normal curve. (See Chart 59)

CASE 43. R.Y.



Case 43. R.Y. Male. Aged 62 years. Labourer. Septic Dermatitis.

Patient was admitted with a severe eczematous condition of the legs, and a similar but practically healed condition of the arms. Six days after admission he developed a temperature of 103° and two days later when a glucose test was carried out the temperature was 100.4°. The legs showed signs of increased inflammatory reaction, and the man was very unwell.

Ten days later a second test was carried out. The temperature at this time was 101° and the man's general condition was worse than before.

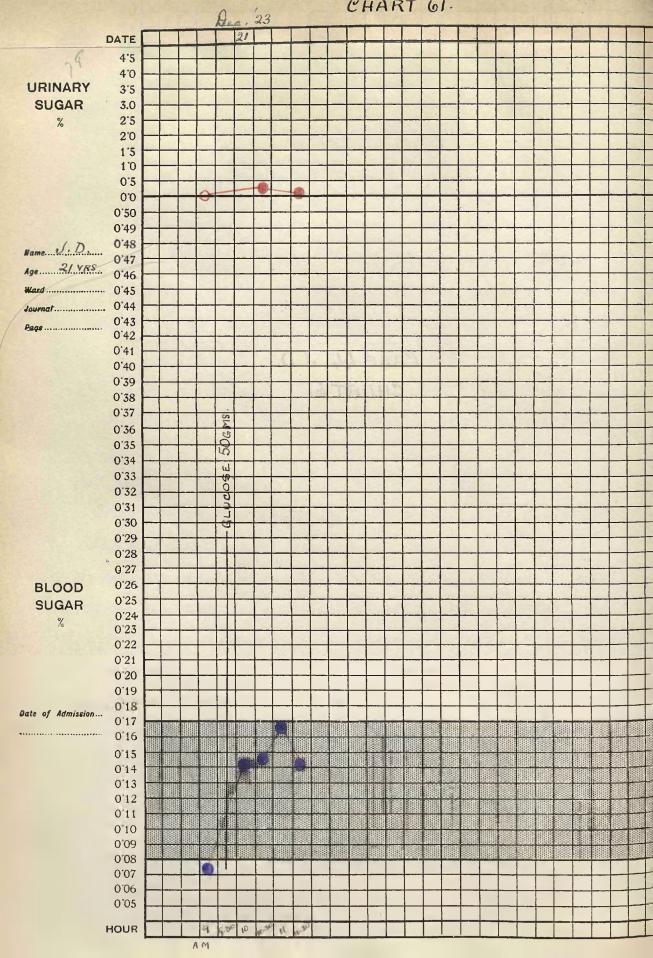
Chart 60 shows the result of these two tests. They indicate a very considerable degree of loss of tolerance.

In the first the blood-sugar shoots up to the high level of 0.276%, coming down fairly rapidly but not reaching the original level in two hours. Sugar appears in the urine. This curve shows the characters of a "lag".

The second curve is a striking one for an apparently non-diabetic subject. The rise in blood-sugar is not quite so high as in the previous test, but it shows a prolonged elevation, with accompanying glycosuria, which gives the curve an appearance very nearly approaching that of a true diabetic one.

The case demonstrates in a very striking manner the progressive loss of telerance with increase of sepsis.

CASE 44. J.D.

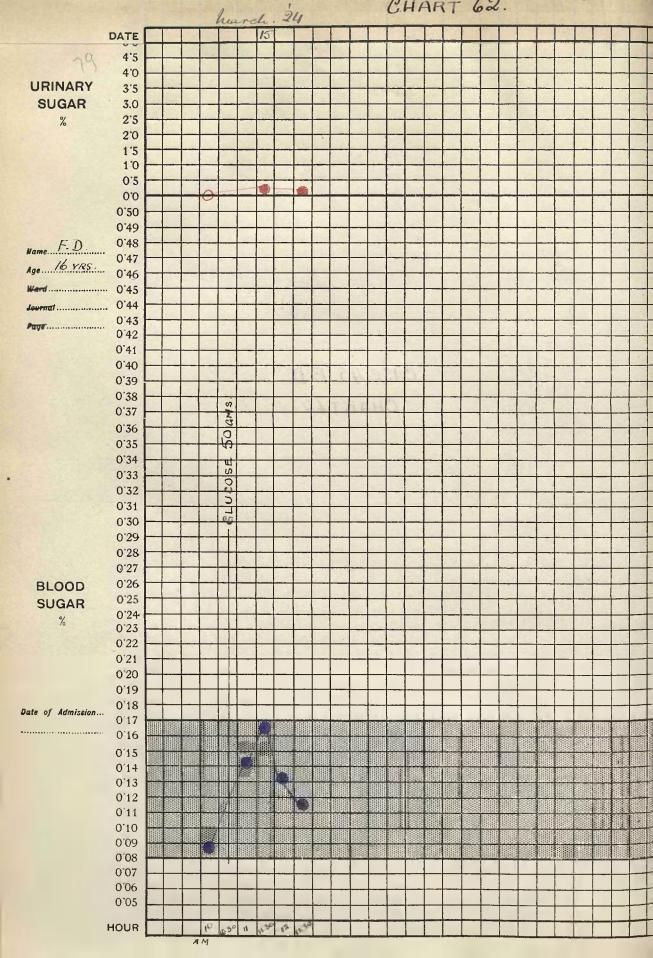


Case 44. J.D. Male. Aged 21 years. Pit pony driver. Acute Rheumatism.

This patient was admitted suffering from an attack of acute rheumatism which had begun six days before. Both knees and the right shoulder were affected at the time of investigation on 21/12/23 (four days after admission) being swollen and tender. The temperature had fallen to normal.

The glucose curve (Chart 61) shows that the renal threshold is not exceeded, but there is delay in regaining the pre-glucose level.

CASE.45. F. D. CHART 62

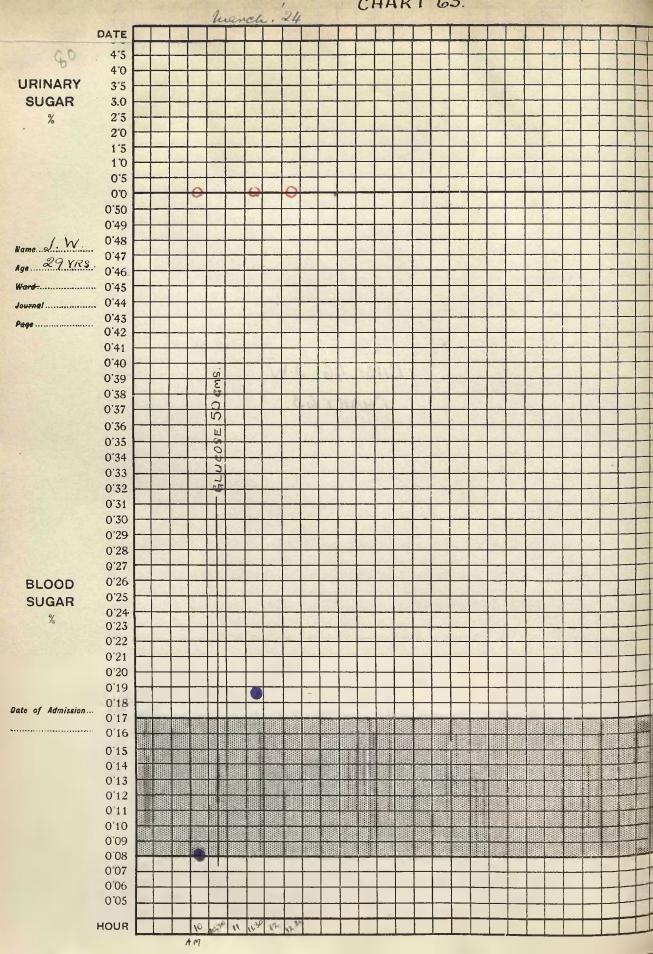


Case 45. F.D. Male. Aged 16 years. Pneumonia. Sore Throat.

This boy developed pneumonia on 15/1/24 and made good progress up till 14-3-24 when he complained of sore throat. The tonsils were found to be inflamed and showing greyish spots. The temperature rose to 103° but fell on 15/3/24 to 99°.

A glucose curve on 15/3/24 showed a fairly sharp rise in blood-sugar with the appearance of sugar in the urine (Chart 62) Here also there was defective metabolism, as shown by the "lag" form of the curve.

CASE 46. J.W. CHART 63.



Case 46. J.W. Male. Aged 29 years. Miner. Bronchopneumonia.

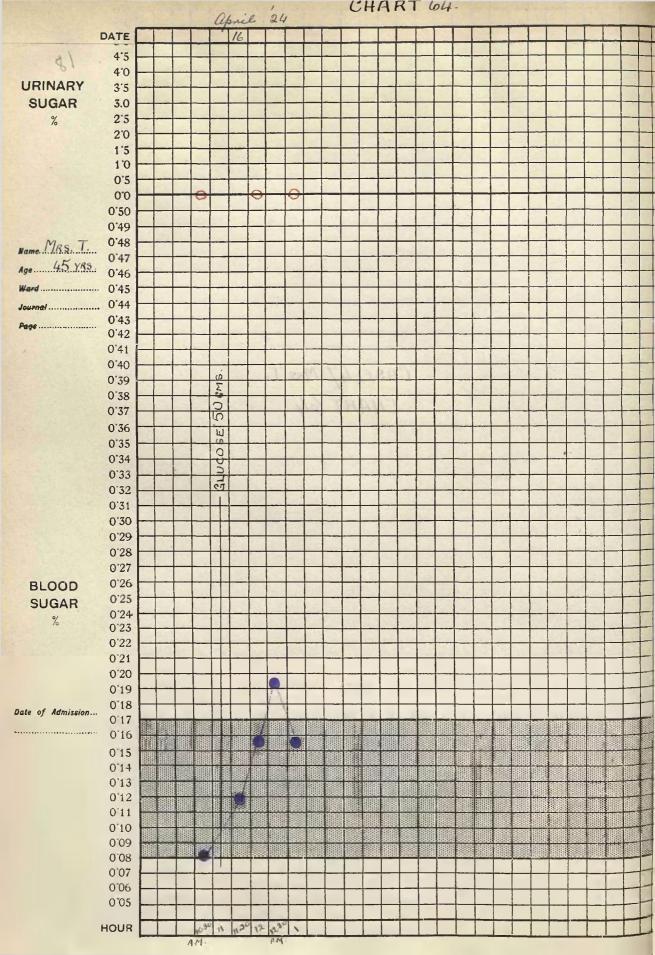
This man's illness began about 10/3/24 and was diagnosed as bronchopneumonia. There was consolidation at both apices and pleurisy was present at the right base. The temperature on the day of investigation was 100° .

A diagnosis of phthisis was made later on.

Chart 63 shows the result of the glucose test on

/8-3-24. The blood-sugar rose within an hour of
the giving of glucose to 0.187% and sugar appeared
in the urine. Unfortunately the blood tests were
not carried further, but there was already sufficient
evidence of intolerance. Two hours later the urine
still showed a trace of sugar, and from this it may
be concluded that there was some delay in the return
of the blood-sugar to normal.

CASE 47 MRS. T.

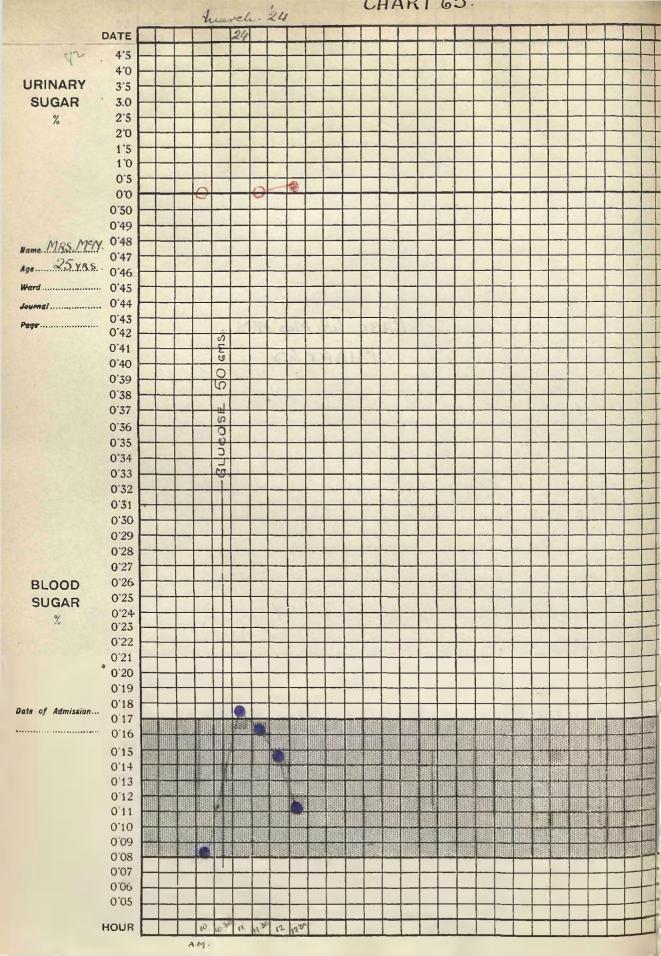


Case 47. Mrs. T. Aged 45 years. Housewife. Acute Rheumatism.

Patient was admitted to hospital on 10/4/24 suffering from acute rheumatism. Before its onset she had had an attack of influenza. The knees were swollen and the joints of the left arm painful at the time of investigation. The temperature was normal

A glucose test carried out on 16/4/24 shows a curve (Chart 64) rising gradually for an hour and a half, reaching 0.193% and coming down slowly. There was no glycosuria. The gradual rise gives the curve the characters of the diabetic rather than of the "lag" type.

CASE 48 MRS. MªN. CHART 65

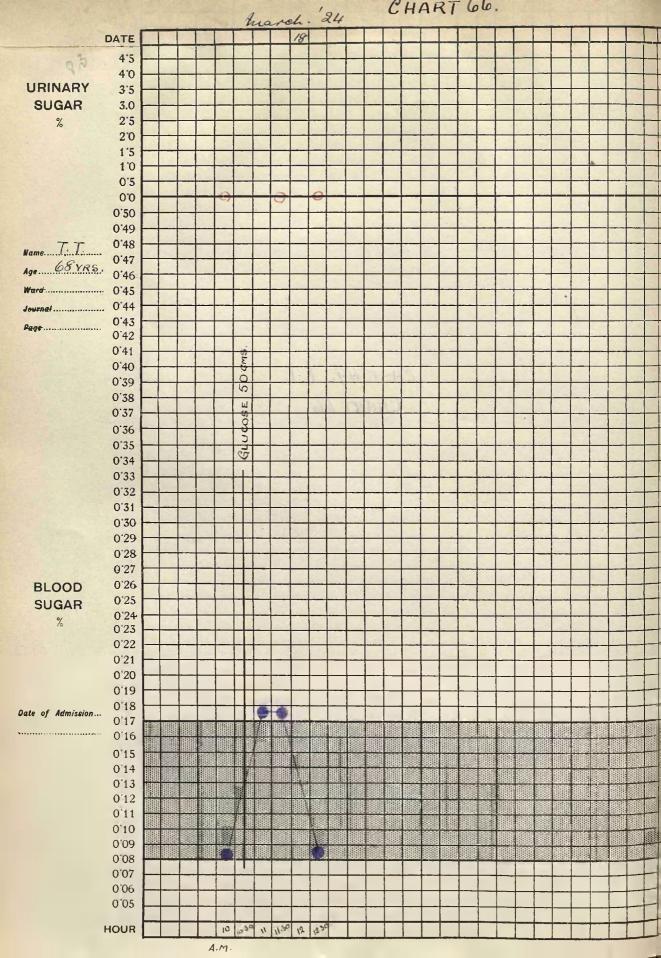


Case 48. Nrs. McN. Aged 25 years. Housewife. Superficial Burn.

Patient was admitted to hospital suffering from superficial burning involving the thighs and lower abdomen.

A glucose test was carried out on the eleventh day, when the temperature was running about 100-101°. The result was a curve rising above the threshold with the appearance of sugar in the urine, but practically no delay. Another example of the "lag" indicating disturbance of metabolism. (Chart 65).

CASE,49. T.T. CHART 66.

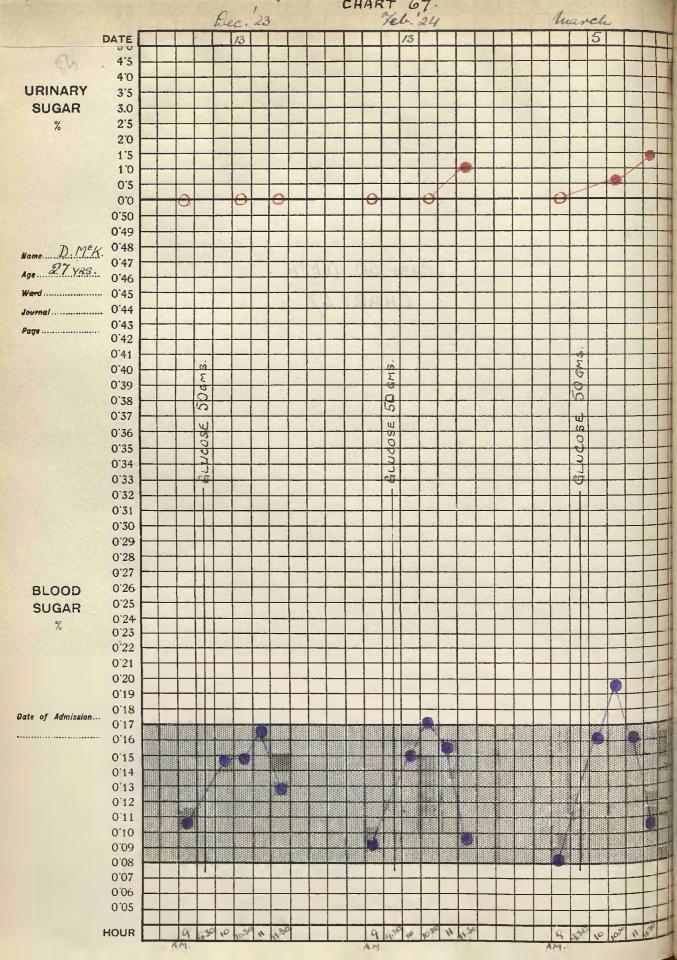


Case 49. T.T. Male. Male. Aged 68 years. Dermatitis emfoliata.

This old man had been suffering from the above skin condition for one month prior to investigation. The temperature was slightly above normal at the time the test was made.

A glucose test resulted in a blood-sugar curve of "lag" type, as seen in Chart 66, but glycosuria did not occur.

CASE 50. D.MºK.



Case 50. D. McK. Female. Aged 27 years. Domestic Servant. "Common Cold" and Tonsillitis.

This girl was undergoing treatment in hospital for emophthalmic goitre. There was no obvious emophthalmos but tachycardia was marked. Her progress was good but was interrupted on two occasions. On the first occasion she caught cold and on the second she developed tonsillitis.

The results of glucose tests done during these febrile attacks and of one carried out previously are shown in Chart 67. The first is normal. The second shows the "lag" type of curve, and the third, obtained during the more severe infection, shows a still more pronounced "lag" character. Comparison of the first curve with the two later ones shows in a striking manner the effect of sepsis.

SUMMARY.

It is evident from the results of investigation of the foregoing fifty cases that in a large majority of people in whom some form of infection arises there is definite disturbance of normal carbohydrate metabolism, evidenced by the production of increased blood-sugar percentage, or glycosuria, or both, when increased strain is put upon the mechanism. The disturbance may be - and in most of these cases was - so slight as to escape detection in the ordinary course of investigation, and only discoverable by a test such as the one employed. Presumably it is due to the absorption of toxins from the focus of infection, although in what way these act remains to be discovered.

Fever apparently does not play a part in the disturbance since in many of cases showing abnormal metabolism the temperature was normal.

Age did not appear to be a factor, although this can hardly be accepted as certain since neither the very young nor the aged happened to come into this series of cases.

It is somewhat difficult to say whether the severity of infection plays an important part, but a careful survey of the cases seems to show that the more general the infection the more likelihood there is of disturbed carbohydrate metabolism occurring. Cases of long-standing sepsis probably show a more prenounced degree of intolerance than those of recent origin.

The cases which gave a normal result remain to be accounted for. As already pointed out, the conditions which obtained in them as regards severity, duration, fever, &c. were the same as in the others. It may be that they had naturally a greater power of dealing with the toxins involved, or, on the other hand, the cases giving abnormal results may have undergone repeated strain from more frequent infection, with the result that they had reached a point where their limit of tolerance was easily over-reached.

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CONCLUSIONS.

In comparing the findings in these two groups of cases one cannot but draw an analogy between them. In both sepsis appears to have the same effect - that of lowering carbohydrate tolerance. In the first group, those cases in which carbohydrate metabolism is known to be already defective, the defect is increased; in the second, the effect is the production of lowered tolerance in persons who have been hitherto apparently normal. In cases belonging to the latter category the disturbance is in most cases slight and only made evident by special investigation; it may be only a temporary defect, but at the same time there is left in all likelihood some permanent damage.

The nature and severity of the infection do not seem to be of importance in determining the effect on metabolism, since cases of similar nature and equal severity led in some cases to considerable disturbance, in some to slight, and in others to no disturbance at all.

It seems reasonable to conclude from this similarity in the effect of sepsis on diabetic and non-diabetic subjects that one form of diabetes at any rate is the result of damage through sepsis; that the damage here has been greater than in those persons belonging to the second group of cases; and that these latter are potential diabetics. Whether or not these people will eventually become true diabetics may depend on the individual resisting-power, on subsequent sepsis or infection,

or upon extra strain from over-indulgence in starchy foods - a factor which, according to American observers especially, is of great importance in the production of diabetes.

In support of this theory of the influence of sepsis in producing defective carbohydrate metabolism one might draw attention to those cases in Group "A" (Sepsis in Diabetic Subjects) in which symptoms or signs of diabetes were entirely absent or only doubtfully present prior to the onset of sepsis. Owing partly to the marked severity of the symptoms which developed and partly to the typically diabetic nature of the curves obtained after subsidence of the sepsis these cases were assumed to be previously undiagnosed diabetics. Might it not be the case, however, that these were individuals who by reason of naturally low resistance, repeated strain from infections, or continued strain from excessive carbohydrate diet, had now reached a point at which this added tax of severe infection had produced in their already enfeebled sugar-dealing mechanism a permanent and obvious defect - in other words, a condition of true diabetes?

ABNORMALITIES OF CARBOHYDRATE METABOLISM IN ENOPHTHALMIC GOITRE.

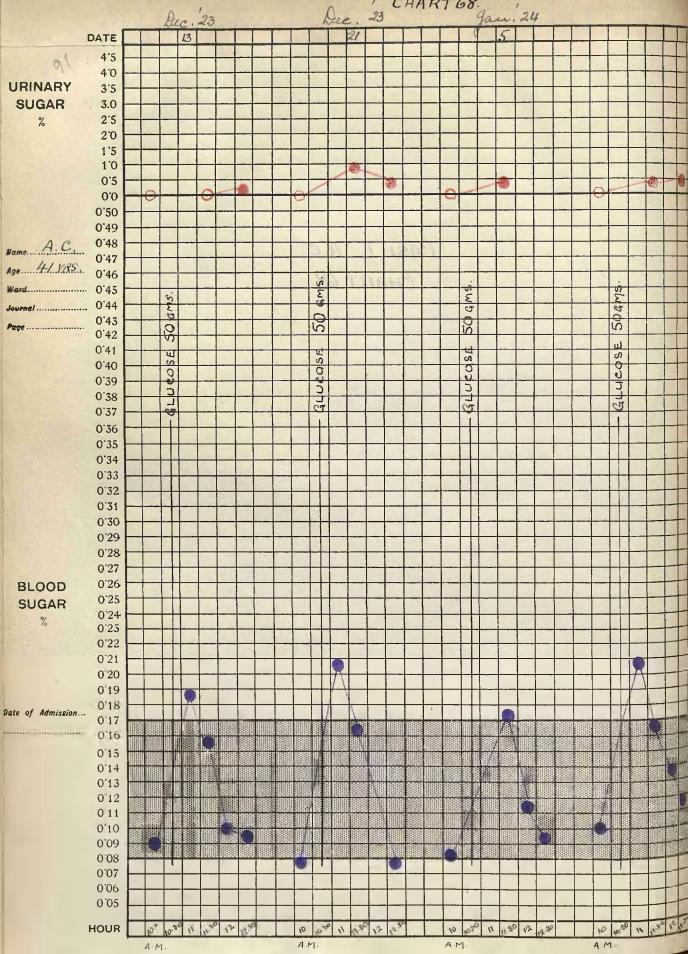
(a) Exophthalmic Goitre.

As regards the influence of the thyroid gland on carbohydrate metabolism, it has been pointed out by Lauder Brunton, Hartmann and others that glycosuria frequently occurs in cases of emophthalmic goitre. Investigating further Langdon Brown stated that he invariably found a marked rise in the blood-sugar after the administration of glucose in emophthalmic goitre. His experience was that even in those cases where glycosuria was absent or was difficult to induce, the blood-sugar rose to a level at which glycosuria would occur in a normal person, and there was delay in return to the fasting level. He described a case of a woman with emophthalmic goitre of fifteen years' standing whose resting blood sugar was normal but who after glucose showed the blood-sugar curve of a severe diabetic.

Of the following thirteen cases investigated by means of glucose tolerance tests, two gave a curve which was in all respects normal. The remaining eleven all showed some abnormality - in the majority the blood-sugar rose above the threshold in $\frac{1}{2}$ - 1 hour and there was delay in the return to normal. In one case the blood-sugar continued to rise for an hour and a half. Nine showed glycosuria. In one of the

most severe cases of goitre the curve showed no abnormality; this patient died immediately following upon an operation for partial thyroidectomy.

CASEI. A.C. CHART 68



Case 1. A.C. Female. Aged 41 years.

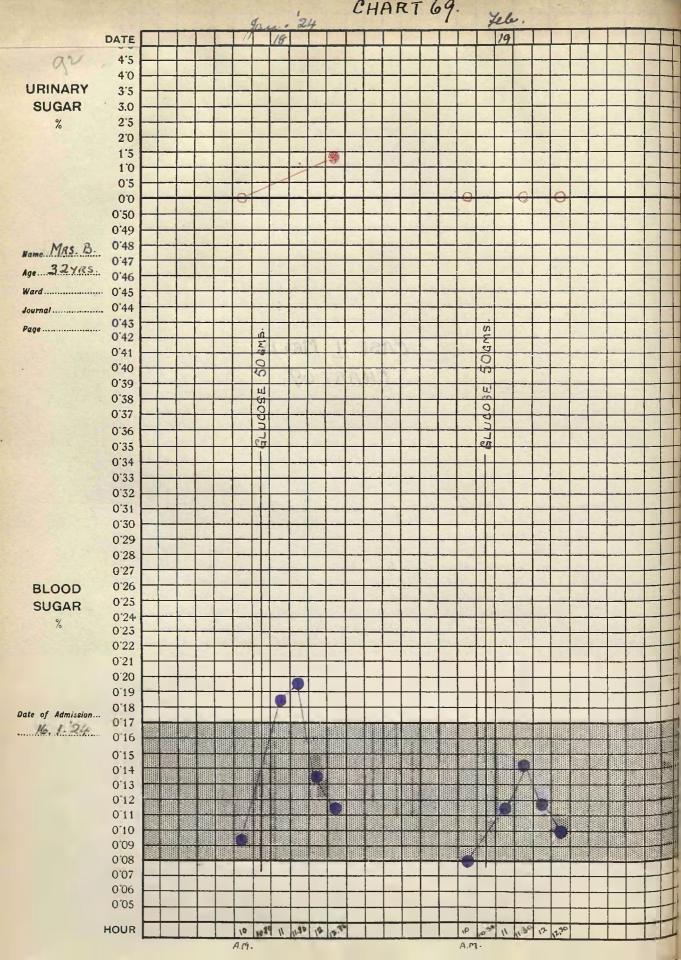
This patient gave on admission a history of palpitation of ten years' duration, enlargement of the thyroid of three months' and emophthalmos of ten months' duration. Within the past seven years she had experienced several severe mental shocks.

On admission to hospital on 7/12/23 the thyroid was soft and pulsatile; there was marked tachycardia and some tremor of the hands and tongue. She made some progress under treatment during the first fortnight then received bad news from home and gradually sank, dying on 7/3/24.

A series of four glucose tests carried out at intervals all showed the same characters, viz:- a blood-sugar curve beginning at the normal level, rising within $\frac{1}{2}$ - 1 hour to exceed the renal threshold and returning to the starting level within two hours. Typical "lag" curves. (Chart 68). In the last one of the series, carried out when the patient was obviously going downhill, the return of the blood-sugar was more prolonged than it had been in the previous tests. In all the tests sugar appeared in the urine.

This case is a striking example of the association of Grave's disease with disturbed carbohydrate metabolism.

CASE II. MRS.B.



Case II. Mrs. B. Aged 32 years.

This patient was admitted on 16/1/24 with a history of breathlessness on exertion, weakness and sleeplessness of three years' duration, worse during the past three months.

On admission the thyroid was enlarged, firm and pulsatile. There was no definite emophthalmos but the right palpebral fissure was larger than the left and the right eye more prominent. Some tremor of the hands was present. The pulse was 120 per minute.

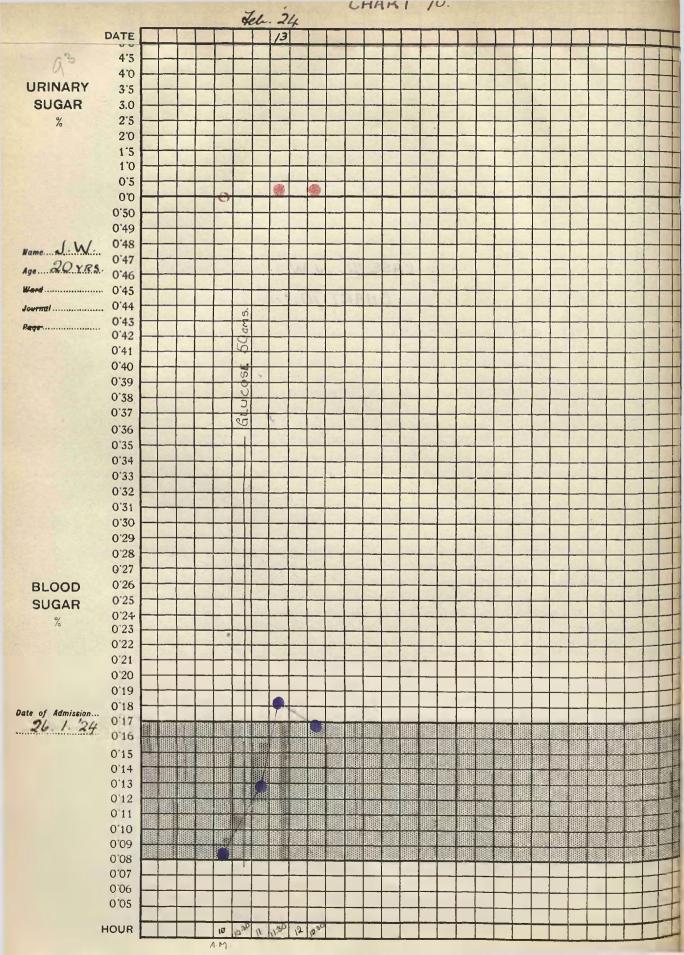
Site did well on treatment and was dismissed much improved on 8/4/24.

A glucose test carried out two days after admission indicated considerably defective tolerance, the blood-sugar rising well over the threshold during the first hour, with a resulting glycosuria amounting to over 1%. (Chart 69)

A month later when the patient's condition had greatly improved under treatment, the thyroid being smaller and firmer and the pulse 90, a second curve obtained was in all respects normal. (Chart 69)

The difference between these two results is striking and should be convincing evidence of the influence of disease of the thyroid gland in leading to disturbance of normal carbohydrate tolerance.

CASE III. J.W.



Case III. J.W. Female. Aged 20 years.

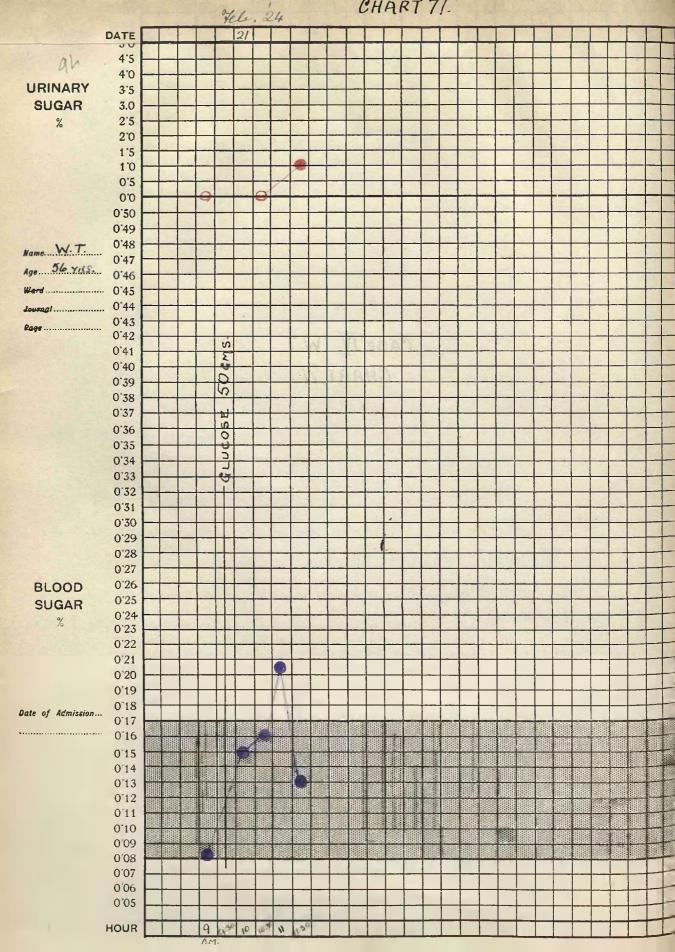
Bookseller's Assistant.

Patient was admitted to hospital on 26/1/24. She gave a history of nervousness, shortness of breath and palpitation of sixteen months' duration, and of enlargement of the thyroid of two months' duration.

On admission the thyroid was enlarged, soft and pulsatile, particularly on the right side. There was no emophthalmos, but Stellwag's sign was positive. The pulse was 130 and a systolic murmur was audible at the apex. A slight degree of tremor was present.

A glucose curve obtained three weeks after admission showed a considerable loss of tolerance. At the end of one hour the blood-sugar was above the threshold and an hour later it had fallen only slightly from that point, the reading being 0.168%. A trace of sugar appeared in the urine. (Chart 70) This curve inclines to the diabetic type.

CASE IV W.T.



Case IV. W.T. Male. Aged 56 years. Auger Temperer.

This was a well-marked case of Emophthalmic Goitre. He gave a history of some heart trouble eight years before admission to hospital. One year ago he began to have palpitation and breathlessness and his legs became weak and shaky. At the same time he grew very nervous and excitable.

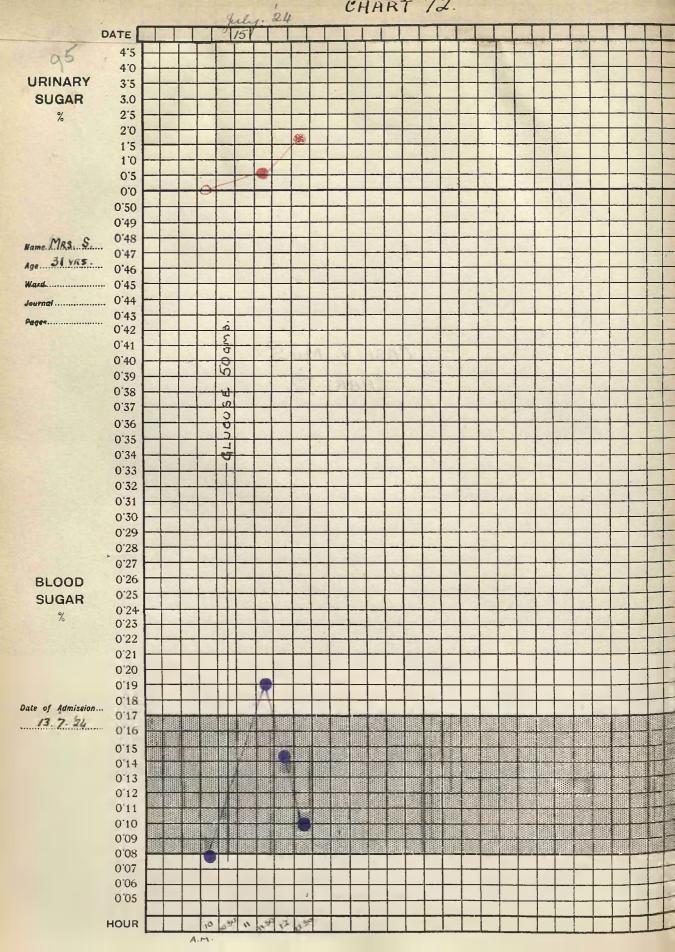
On admission the pulse was 120, emophthalmos was present but there was no obvious thyroid swelling.

Pulsation was marked in the neck and suprasternal notch.

He made considerable progress in hospital.

Carbohydrate tolerance was found on investigation to be greatly diminished; as shown in Chart 71. The blood-sugar level continued to rise for an hour and a half after glucose and at the end of two hours was still well above the starting level. Glycosuria appeared after two hours. A diabetic type of curve.

CASE V. MRS.S.
CHART 72.



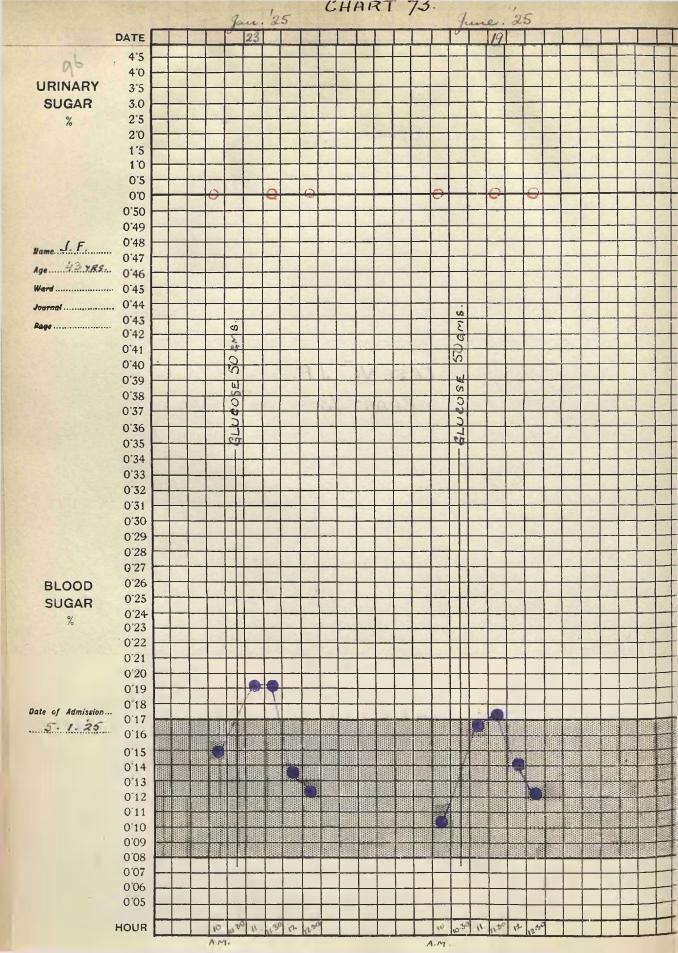
Case V. Mrs. S. Aged 31 years. Housewife.

Patient was admitted on 13/7/24 with complaint of palpitation, sleeplessness and nervous excitability. Her symptoms dated from six or seven years back and she had on two previous occasions been treated in hospital.

There was only slight emophthalmos and the thyroid swelling was barely perceptible partly owing to the amount of subcutaneous fat. There was tachycardia to the extent of 112 beats per minute; tremor was not noticeable.

A glucose test on 15/7/24 showed that in this case also carbohydrate metabolism was defective. The curve was of "lag" type with considerable glycosuria. (Chart 72). The association of such marked disturbance of metabolism with a comparatively mild case of Grave's disease should be noted.

CASE.VI. J.F.



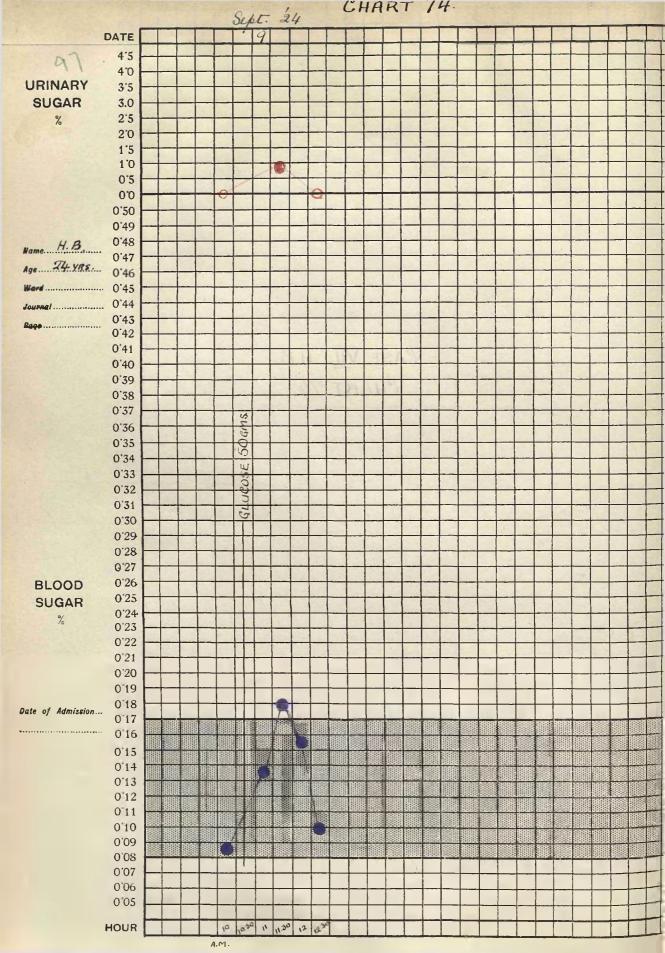
Case VI. J.F. Male. Aged 45 years.

This man was admitted on 5/1/25 complaining of breathlessness, nervousness, shaking of hands and failing eyesight of five months' duration.

On admission there was no obvious enlargement of the thyroid. The eyes were slightly prominent and staring and von Graepe's sign was present. Fine tremor of the hands was also present. The pulse was about 90. A glucose curve obtained on 23/1/25 was of "lag" type. Glycosuria was absent, but the blood-sugar reached a fairly high level. (Chart 73).

Patient was dismissed very well on 21/3/25. On 9/6/25 he reported and was then very well and less nervous. A second test was carried out and again a "lag" curve was obtained, but this differed from the first in remaining throughout at a much lower level. (Chart 73). Presumably this return towards a normal curve was coincident with the improvement in the man's condition.

CASE VII. H.B. CHART 74.



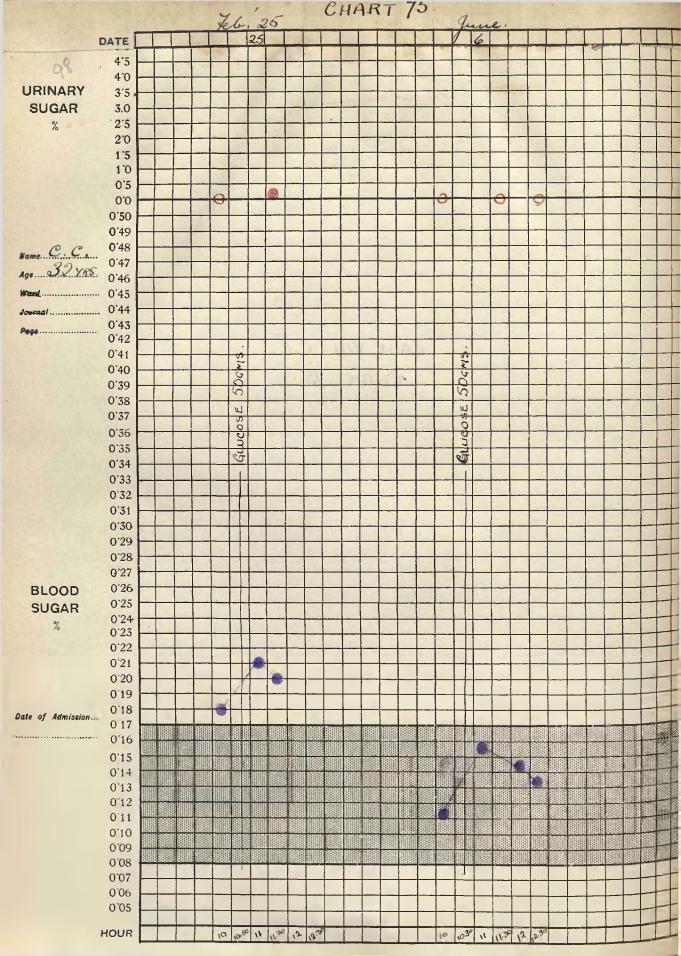
Case VII. H.B. Female. Aged 24 years. Domestic Servant.

This girl gave a history of palpitation, nervousness and insomnia of five months' duration, and of swelling of the neck of three months' duration.

The thyroid was enlarged and slightly pulsatile; there was no emophthalmos or tremor. The pulse was 120 and a systolic murmur was audible at the mitral and pulmonic areas. She improved considerably under treatment, the pulse rate falling to 90 and the thyroid swelling becoming much less. She gained appreciably in weight and was very well on dismissal.

Her glucose tolerance was investigated on 9/9/24, a few days after admission, and was found to be rather lower than normal - the blood sugar reaching the renal threshold, with the appearance of sugar in the urine. Some slight disturbance of metabolism was indicated. (Chart 74)

CASE VIII. C.C. CHART 75.



Case VIII. C.C. Female. Aged 32 years. Waitress.

Admitted on 9/2/25 complaining of nervousness, palpitation and general weakness of about eighteen months' duration; and of swelling of the neck and prominence of the eyes of about six months' duration. She had also been subject to excessive appetite, thirst and polyuria.

On admission the thyroid was enlarged, soft and pulsatile, and systolic and diastolic murmurs were audible over it. The eyes were fairly prominent, and von Graefe's and Stellwag's signs were present. The heart was enlarged and a systolic murmur audible at the apex. The pulse was 130.

A glucose test attempted on 25/2/25 could not be completed on account of the patient's nervousness, but the result so far as it went was distinctly of diabetic type, as will be seen from Chart 75. The starting level of the blood-sugar was very high.

Considerable improvement was made with treatment, emophthalmos becoming less and the goitre smaller, and a glucose curve obtained on 10/6/25 was normal in character, showing a marked contrast to the first.

After showing improvement for some months this patient relapsed; her cardiac condition became progressively more serious, diarrhoea set in, and she eventually died eight months from the date of admission to hospital.

It is interesting to note the presence of excessive thirst and polyuria on admission, associated with a resting

blood-sugar considerably above the normal level.

The absence of glycosuria was probably due to raising of the renal threshold.

CASE IX MAS IN

CASE.<u>IX</u>. Mrs.N. CHART 76 Case IX. Mrs. N. Aged 30 years. Housewife.

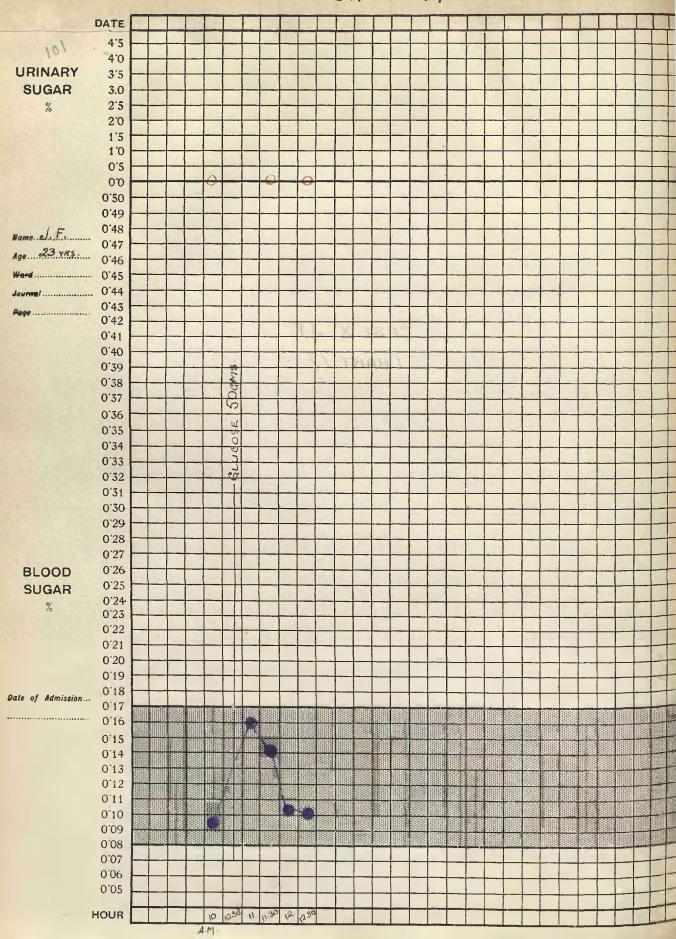
This woman complained of nervousness, pains in the head, dizziness and failing vision in the right eye.

There was no emophthalmos; tachycardia and tremor were, however, present and a provisional diagnosis of emophthalmic goitre was made. Unfortunately the patient left hospital in a few days and the case was not investigated further.

Investigation of her tolerance, however, yielded a striking result. The blood sugar rose during the first hour to the considerable height of 0.237%, and at the end of two hours was still well above the starting level. There was no glycosuria, but the blood-sugar curve indicated severe carbohydrate intolerance. (Chart 76)

CASE X. J.F.

CHART 77



Case X. J.F. Male. Aged 23 years. Motor Mechanic. This man on admission gave the following history; for ten months he had noticed increasing prominence of the eyes and three months before had first observed swelling of the neck in front. During the last three months he had suffered from palpitation, giddy turns, and at times double vision.

On admission the eyes were very prominent and von Graefe's and Stellwag's signs were obtained. Both lobes and the isthmus of the thyroid were much swollen; the swelling was pulsatile and a systolic murmur was audible all over. There was marked precordial heaving, and tachycardia was severe. He failed to make satisfactory progress for the first two months in hospital, then there was a little improvement - he gained slightly in weight and was eating fairly well, but his other symptoms remained unchanged. He was accordingly operated on, the left lobe being easily removed, but the pulse rate rose to 166 and he died twentyfour hours later.

A glucose test carried out about a month after admission to hospital gave a curve which was in every respect normal. It is interesting to compare this result obtained in such a well-marked case of Grave's disease, with the abnormal findings in some of the foregoing cases, such as cases V. and VI. where the symptoms of the disease were comparatively slight. (Chart 77.)

Case XI. J.H. Chart 78.

Case XI. J.H. Female. Aged 41 years.

As a girl this patient had suffered from sick headaches and "bilious" attacks. Eleven years ago, at the age of thirty, she began to have pain in the right eye with failing vision. About this time she suffered a severe mental shock, and following upon this she suffered from nervousness, loss of weight, prominence of the eyes and swelling of the neck. She lost the sight of the right eye through cataract. Her symptoms continued and had recently become more pronounced.

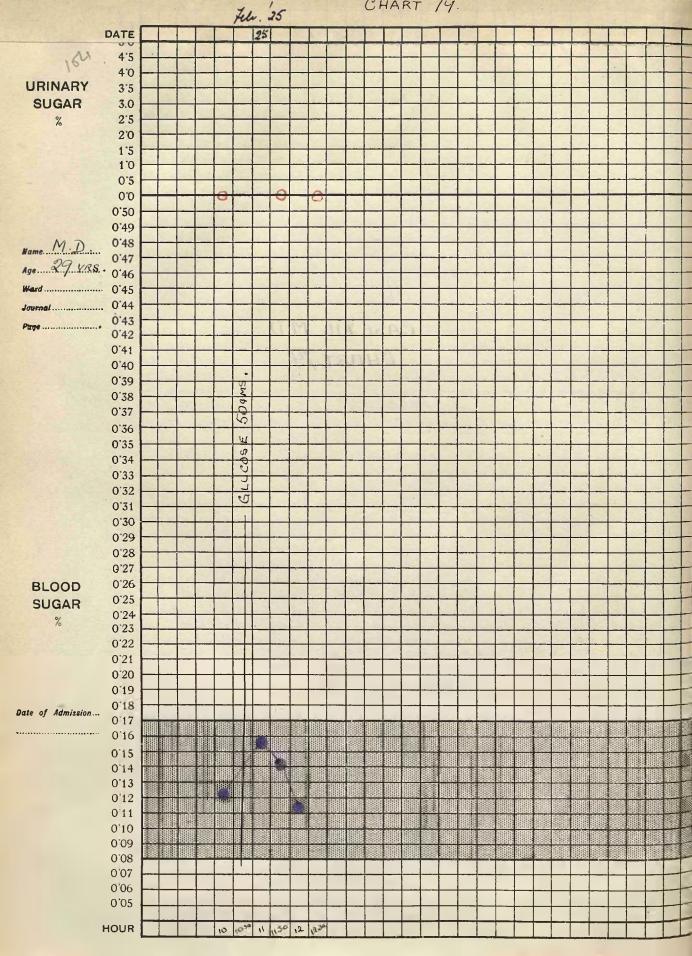
On admission she was greatly emaciated and exhausted. The eyes were rather prominent; the thyroid was enlarged equally on both sides and was soft and pulsatile. Systolic and diastolic murmurs were audible over it. There was tremor of the hands and tongue, and gross restless movements of the limbs. The pulse was 120, irregular and feeble in character. The cardiac dulness was slightly enlarged. She had frequent short attacks of auricular fibrillation during her residence in hospital. Glycosuria was observed at times.

A glucose test carried out on 19/1/25 yielded a curve which was clearly diabetic in type, starting above the renal threshold, rising to the considerable height of 0.282% and showing delay in return. Glycosuria, absent before glucose presumably owing to raising of the renal threshold, occurred in increasing amount. (Chart 78)

The question arises in this case whether the patient was suffering from true pancreatic diabetes coincidently with emophthalmic goitre, or whether her diabetic condition had been brought about by the latter.

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CASE XII M.D.
CHART 79.



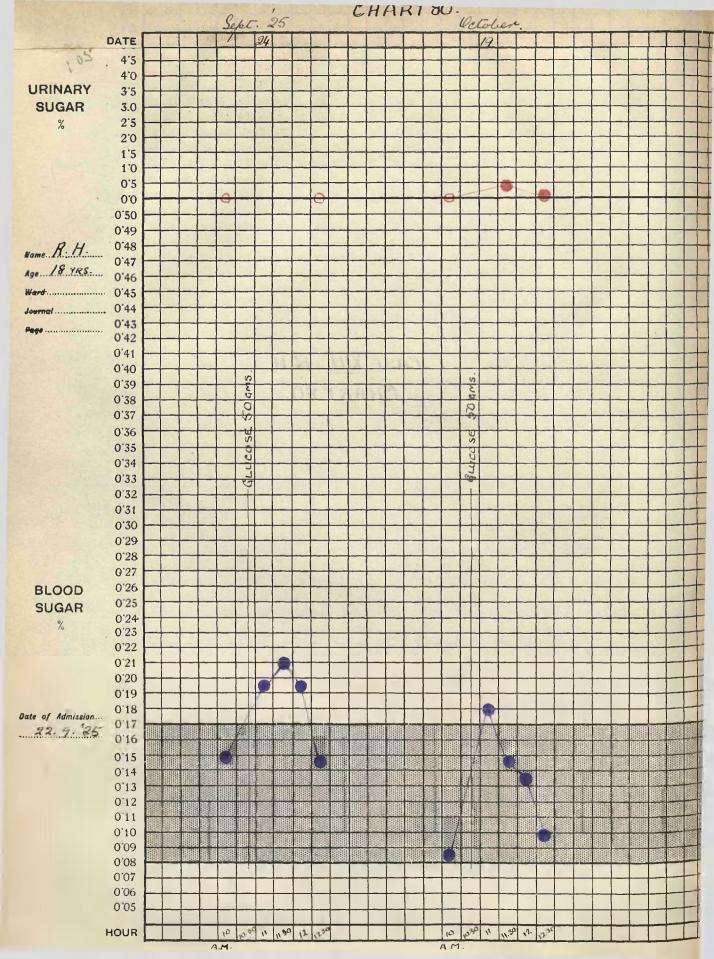
Case XII. M.D. Female. Aged 29 years. Warehouse Assistant. This girl was admitted on 5/2/25 complaining of difficulty in breathing and swelling of the right side of the neck. A year before she had had tonsillitis and had her teeth removed. Shortly afterwards she noticed swelling of the neck. Six months later she complained of headaches and noticed that the swelling was increasing in size. Two months ago she began to suffer from breathlessness and palpitation.

On admission the right eye was slightly more prominent and the right palpebral fissure slightly wider than the left. There was a slight lag of the eyelids on looking down. The right lobe of the thyroid was enlarged, the left slightly. The swelling was fairly firm and non-pulsatile. A systolic murmur was audible over it. Theheart was enlarged a little to the left and a systolic murmur was audible at the pulmonary area. The pulse was 100. The patient was not very ill. The pulse came down and her condition showed general improvement.

It is of interest to note that this patient's mother died of diabetes.

A glucose curve obtained on 25/2/25, three weeks after admission, was normal, indicating undisturbed carbohydrate metabolism. (Chart 79). It should be noted, however, that her case was a mild one to begin with and at the time of the test she had been under treatment for three weeks and had greatly improved in health.

CASE XIII. R.H. CHART 80.



Case XIII. R.H. Male. Aged 18 years. Grocer.

This boy's history was as follows: - in February, 1923, he had an attack of acute rheumatism with cardiac involvement. Four months later he was admitted to hospital recovering from pleurisy. He remained well till May, 1925, when he began to complain of attacks of sickness and vomiting and of palpitation with weakness and a chronic cough. He was readmitted to hospital with these symptoms on 22/9/25. The Thyroid was found to be slightly enlarged and the eyes slightly prominent. The pulse was rapid (120) and irregular; diffuse epigastric pulsation was present and there was a systolic murmur at the apex. Nervousness was fairly marked. No tremor was present. He made excellent progress in hospital and was dismissed very well, with no symptoms.

A glucose test carried out on 24/9/25, two days after admission, resulted in a decidedly abnormal curve. The blood-sugar was considerably above the normal to begin with, and rose in an hour to 0.21%. Within two hours, however, it had fallen to the original level and no sugar appeared in the urine. The curve is of "lag" type but unusual in being at such a high level throughout. A second test was carried out about a month later, on 19/10/25 when his condition had greatly improved, nervousness being less and the pulse 100. In this case the curve obtained was of true "lag" type, and indicated a great improvement in tolerance in the normal level of the blood-sugar at the beginning and end of the test. That there was still some disturbance, however, was shown by the rise to

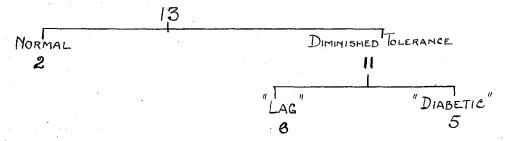
0.18% and by the occurrence of glycosuria. These results are indicated in Chart 80.

CARBOHYDRATE METABOLISM

IN

EXOPHTHALMIC GOITRE.

TOTAL NO. OF CASES.



SUMMARY.

The results obtained from investigation of the carbohydrate tolerance of this series of cases are ample evidence of the disturbance of metabolism which Of the total number of thirteen cases dealt with, no fewer than ten showed a considerable degree of loss of tolerance, one showed a slight defect, and only two gave a normal result. Six of the abnormal cases yielded curves of the "lag" type, while the remaining five curves were distinctly diabetic in character. (Cases III. IV. VIII. IX. XI.) Of the "lag" cases, two were unusual in running at a high level throughout. (Cases VI. and XIII.) Attention has already been drawn to the fact that in one of the cases where anormal curve was obtained (Case X.) the subject was at an advanced stage of the disease, whereas in cases V. and VI. where a considerable defect in tolerance was observed, the symptoms and physical signs of Grave's disease were of comparatively mild type.

The fact that hyperthyroidism frequently leads to hyperglycaemia and glycosuria is borne out by the evidence that treatment of mympedema by thyroid preparations has in not a few instances brought about these conditions.

ABNORMAL CARBOHYDRATE METABOLISM IN

(b) DISEASES OF THE PITUITARY GLAND.

In 1911, Goetsch, Cushing and Jacobson described the results of experiments on animals in whom the hypophysis cerebri had been encised. Cane sugar dissolved in warm water was given, with resulting transient glycosuria. In several cases where total hypophysectomy was performed reduction of tolerance was followed by an increased tolerance. Removal of the anterior lobe alone caused a high post-operative tolerance. Removal of the posterior lobe and a small part of the anterior lobe caused transient glycosuria followed by increased tolerance. Removal of the posterior lobe only (leaving the pars intermedia untouched) caused an immediate rise of tolerance - without previous fall.

These workers also found that in acromegaly and gigantism, at first, when there was stimulation of the posterior lobe, glycosuria was the rule. Later, when glandular insufficiency supervened, there was increased carbohydrate . tolerance.

ACROMEGALY.

Various observers, such as Hansemann, Hinsdale and Borchardt drew attention to cases where glycosuria was associated with acromegaly.

A.W.M. Eilis described a case of hypergrycaemia and

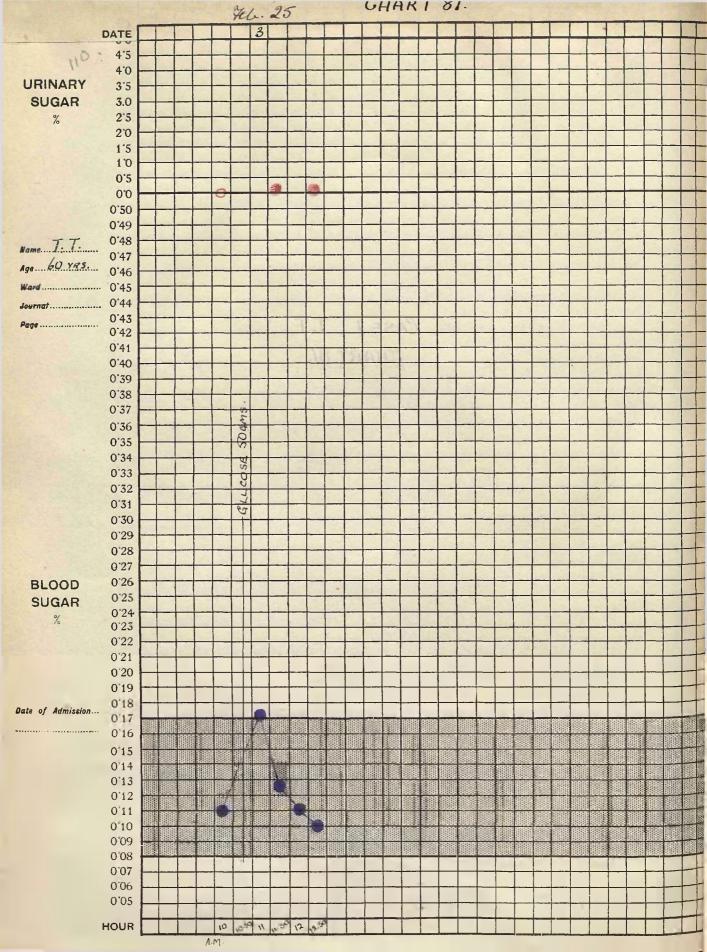
glycosuria in acromegaly, in a woman of fortytwo years. Typical symptoms of acromegaly had been present for seven years; and diabetic symptoms were first noticed eight months before admission to hospital. The urinary sugar was 10%, the blood sugar 0.43%. After dieting an operation was performed - a soft pituitary tumour was removed which was found by Professor Turnbull to have arisen either from the pars intermedia or from the posterior part of the anterior lobe. The urine became at once sugar-free and the blood sugar fell to 0.15%. Three months later the urine was still sugar-free and the blood-sugar 0.12%. Two years later the urine was free of sugar but a sugar tolerance test showed diminished tolerance. Three years after, urine still sugar-free but some hyperglycaemia present and tolerance diminished.

In January, 1924, Langdon Brown spoke of pituitary glycosuria as being due to over-activity of the pars intermedia and referred to its frequent association with signs due to involvement of other parts of the gland, e.g. if the anterior lobe were overacting there would be acromegaly as well, if underacting, diminished sexual development; and if the posterior lobe were underacting there would be obesity and diabetes insipidus.

Opie states that chronic pancreatitis has frequently been observed at autopsy in association with acromegaly.

Case 1. T.T.
CHART 81.

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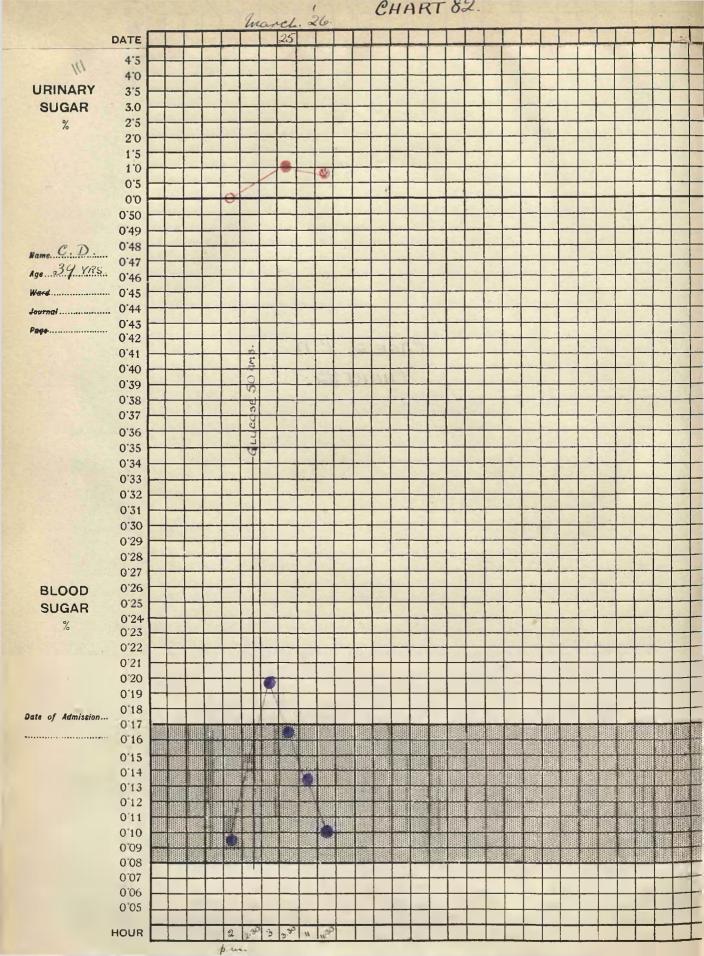
Case I. T.T. Male. Aged 60 years. Acromegaly.

This was a well-marked case of acromegaly. His illness began about 1909 when he suffered from severe frontal headache for which he was treated in hospital. In 1912 he was again in hospital and on this occasion an increase in height and in the size of his head was noted. His face was long with prominent supra-orbital ridges and protruding lower jaw. The hands and feet were enlarged, the former spade-like. Kyphosis was present, and the voice was husky. He suffered from severe frontal headache and impaired eyesight. The thyroid gland was not enlarged.

Seven years later, in 1919, he was re-admitted with increasing weakness, and increase in the size of head, body, hands and feet. He had a fairly large appetite and suffered from excessive thirst. In 1925 he was again in hospital. Headaches were now very severe and he suffered from bronchitis. He was still growing. Ophthalmoscopic examination revealed double partial optic atrophy, and an X-Ray photograph showed a long sella turcica. He died a month or two later at home.

A glucose test carried out on 3/2/25 yielded a "lag" curve with glycosuria (Chart 81) showing that a tendency to carbohydrate intolerance was present.

CASE, 2. C.D. CHART 82.



Case 2. C.D. Male. Aged 39 years. Labourer. Acromegaly.

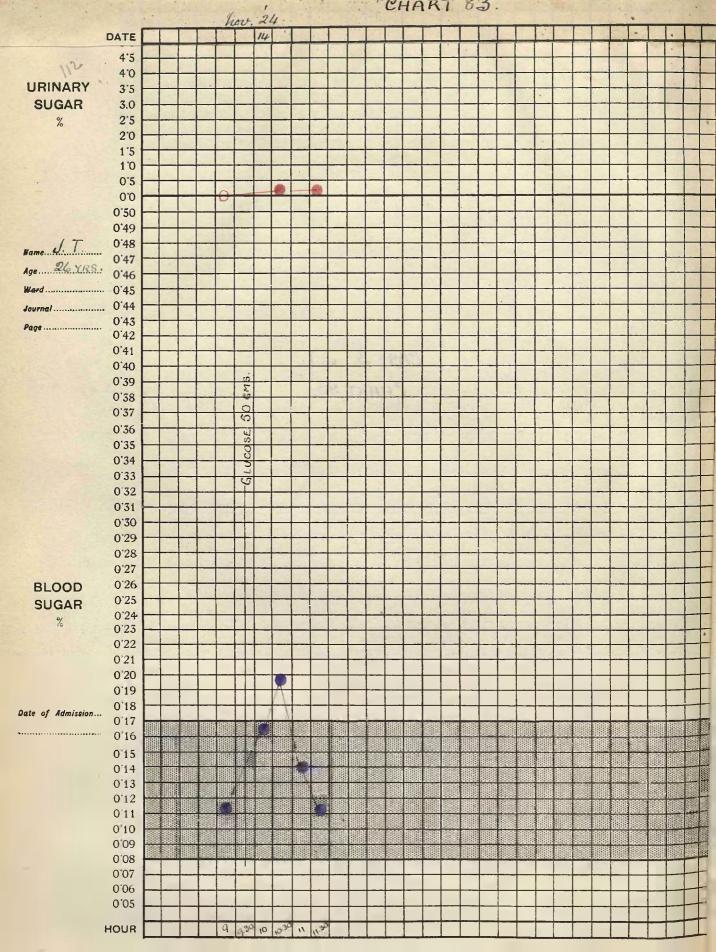
This man was admitted to hospital with a complaint of pains in the back and front of the legs for 12 to 14 years.

On examination he showed prominence of the lower jaw and of the frontal eminences. The lips and tongue were thickened. The shoulder blades were large and thick, the wrists and forearms broad and flat, and the hands spade-like. The chest was long and flat, the ribs thick and prominent at their sternal ends. The bones of the legs and feet were large, but doubtfully out of proportion. There was no kyphosis.

Recently he had been sleepy, and thick speech and salivation had been noted. His mentality was slow, but he was quite sensible. The X-Ray plates showed no definite deformity of hands, wrists, knees, ankles, &c. except that the prominences were rather prominent. The Wassermann was negative.

The result of a glucose test on 25/3/26 was a well-marked "lag" curve with glycosuria, showing a definite defect in carbohydrate tolerance. This is shown in Chart 82.

CASE 3. J.T. CHART 83.



Case 3. J.T. Male. Aged 26 years. Hypopituitarism. Frőhlich's Syndrome.

This patient was first admitted to hospital on 9/12/19, at the age of 21 years. His height was then 4 feet 9 inches, and his appearance suggested that of a boy of 13 years. He was unduly fat, and muscular development was poor. There was no hair on the body. Temporal hemianopia was present in the left eye, and the right eye was blind.

Re-admitted on 22/9/24. His height was now 4 feet 10 inches. He was stouter, and lordosis was marked. Mystagmus was present. Both eyes showed simple optic atrophy. An X-Ray photograph suggested a pituitary growth.

A glucose test was carried out on 14/11/24. The result, shown in Chart 83, was a curve of "lag" type with accompanying glycosuria. Diminished carbohydrate tolerance was indicated.

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The findings in these three cases go
to support the observations by other workers
that disease of the pituitary gland is frequently
accompanied by glycosuria or by a tendency to loss
of carbohydrate tolerance. The theory generally
accepted is that this is due to an excessive
production of pituitary secretion which disorganises
the normal inhibitory action of the internal secretion
of the pancreas on excessive sugar production.

POST MORTEM FINDINGS IN DIABETIC SUBJECTS.

In going over the post mortem records of cases in which diabetes has been the cause of death, one is struck by the very small number in which the pancreas shows signs of any gross lesion such as cancer, tubercle, In the majority, naked-eye examination reveals nothing abnormal. Owing to the liability of the organ to undergo rapid decomposition after death it is apparently impossible in many cases to carry out a microscopic examination, but where this is possible the commonest lesion appears to be increase of fibrous tissue and vacuolation of the cells of the Islands of Langerhans. Some cases show signs of atrophy of a part of the pancreas, others of hypertrophy. It has, however, not yet been proved conclusively that every case of diabetes unaccompanied by gross lesion of the pancreas exhibits the microscopic appearances described. A great deal of work has yet to be done on this subject.

In connection with glycosuria associated with acromegaly, it has already been pointed out that chronic pancreatitis has frequently been found in such cases. As regards the findings in the pancreas in emophthalmic goitre associated with glycosuria, no literature appears to be available.

In conclusion, then, it would appear that there are at least three distinct types of disturbed carbohydrate metabolism. First, that in which there is a definite, gross pancreatic lesion to account for the disturbance of function; secondly, that in which some abnormality of one of the endocrine organs seems to be the cause; and thirdly, that most commonly found of all to which neither of the foregoing causes appear to contribute, and in which there may or may not be microscopic evidence of pancreatic disease. This is the type which is most difficult to explain, and so far little or no light has been thrown on the subject. is reasonable to suppose that some toxin or toxins produced within the body are at the root of the trouble, but how they are produced and in what way they act remain to be explained. There can, however, be no doubt that, judging from the results of the foregoing investigation, sepsis plays an important part in the lowering of carbohydrate tolerance, whether it be in the direction of increasing loss of tolerance in a diabetic subject or of producing such a condition in a person previously normal.

It would be interesting to examine microscopically the pancreas of persons dying from the effects of severe sepsis; so far this has not been done.

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