GASTRIC ANALYSES IN CASES OF DIABETES AND GLYCOSURIA.

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GASTRIC ANALYSES IN CASES OF DIABETES AND GLYCOSURIA.

Since the discovery by Thomas Willis in 1679 of the presence of sugar in the urine in certain cases of bodily wasting, many attempts at classification of the various forms of a long recognised dystrophy have been made. Amongst the earlier writers, the classification of Von Noorden[1] is perhaps the most interesting in the light of our more recent knowledge.

Sugar is used in the body for two main purposes:-

(1) Energy production.

(2) Fat Synthesis.

For the maintenance of health not only must the sugar ingested be utilised, but a proper balance must be maintained between these two functions.

Von Noorden describes three groups of cases of altered sugar metabolism.

(1) Consumption of sugar for energy and its transformation into fat are both impaired.

(2) Consumption of sugar for energy is impaired but not its synthesis into fat. Instead of being excreted in the urine the Carbohydrates are transformed into fat. Here we have obesity but no glycosuria.

(3) Consumption of sugar for energy is impaired and the fat synthesis/

synthesis is insufficient to take up all the Carbohydrates ingested.

These cases exhibit obesity plus glycosuria.

The first group includes the cases of what most writers classify as true Diabetes Mellitus. Here we have not only a failure to utilise ingested Carbohydrates, but also a breaking-down of the body proteids to form sugar which is excreted in the urine. Thus there is often extreme wasting, and this type constitutes what was, until the introduction of Insulin, a very dangerous and frequently fatal disease, all the more to be dreaded in that it occurs most commonly in persons under forty years.

Recent work on the Blood Sugar Content has shown that cases belonging to the second group are exceedingly common. These patients frequently have a gouty tendency, are of stout plethoric build, have a high Blood Sugar Content, and are liable to many of the complications of Diabetes. Of these complications, perhaps the most common are eye conditions such as soft cataract. Obstinate localised pruritus and other skin conditions often occur and patients are frequently treated for the complications without the underlying hyperglycaemia being suspected.

The third group includes those cases which are usually designated simple glycosuria, and with which every practioner is familiar.

These patients come under observation usually on account of/

of some complication. Attention is drawn to the condition of the blood by the presence of sugar in the urine, and under suitable dietetic treatment the symptoms commonly disappear.

Classifications based on the supposed etiology of the condition have proved unsatisfactory, chiefly on account of the overlapping of the various groups. Thus we have had described Nervous, Hepatogenous, Pancreatic, Alimentary and Renal Glycosurias Of these, the only distinct group is the Renal Glycosuria and this properly does not belong to the dystrophy under consideration at all. Here the fault lies in the kidney, not in the sugar metabolism. The Blood Sugar does not rise above normal and in fact, is usually considerably below that level. The importance of these cases lies in the danger of their being treated as true Diabetes whereby the already low Blood Sugar may be reduced to a dangerous degree. What has been described as Nervous Glycosuria cannot be considered a distinct group. The mental state has a marked effect on the Endocrine Glands and the Sympathetic Nervous System. These in turn control in great measure the functions of the Liver and Alimentary Canal, and many cases of so-called nervous glycosuria, if thoroughly investigated, might equally well be placed in any of the other three categories. The tendency in the past has been to lay greatest stress on abnormalities of liver function in Glycosuria; but in so far as the material reaching the liver by the Portal Vein must first be selected and rendered suitable by the physiological action of stomach and intestine, the functions of these organs are surely also of great importance.

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In the course of investigations into the sugar tolerance of a large number of cases of glycosuria, it was found that certain pronounced types frequently exhibited anomalies of gastric secretion which might well have some significance from the point of view of diagnosis and prognosis. In the present thesis it is proposed to show that cases belonging especially to Group 1, that is, cases of severe Diabetes, have been found to have a deficiency in the Gastric Secretion of Hydrochloric Acid, to formulate a theory as to how this is brought about, and to indicate the significance of the gastric findings in prognosis.

Long and careful investigations by many workers into the pathological condition of various organs in cases of Diabetes Mellitus have given us a certain amount of knowledge on the subject but much remains to be done.

At the end of the eighteenth century, Dr. Dobson of Liverpool affirmed that sugar existed in the blood as well as in the urine of Diabetes. About fifty years later Claude Bernard showed the presence and amount of sugar in normal blood and propounded the theory, with which we are now familiar, of its control by the glycogenic function of the liver. He showed that sugar could be obtained from the liver of animals even when for some time before death they had received no Carbohydrate in the diet. When all the sugar was washed out of the liver immediately after death, he found that in a few hours sugar could/

could again be obtained from the same liver. From these facts he formulated the theory that the liver contains a store of material which is gradually converted into sugar during life and that this function goes on for a short time even in the extirpated liver.

The view that the stored glycogen of the liver is converted into sugar during life was contested by Pavy.(2) He stated that the conversion which took place in the extirpated liver was due to a ferment derived from the tissues after death. He considers that the chief destiny of liver glycogen during life is the formation of fat and that its conversion into sugar is a pathological process brought about by over-oxygenation of the liver through inhibition of the Vaso-constrictors. In the light of this theory it would be expected that section of the Splanchnics (which carry vaso-constrictor impulses to the liver) would produce diabetes. Such is not the case, and most physiologists, while accepting the view that part of the liver glycogen is converted into fat, believe that the greater portion is normally given up as dextrose according to the needs of the body.

That the glycogenic function of the liver is controlled, in part at least, by some secretion of the Pancreas, was shown by Minkowski. He first demonstrated that diabetes was produced in dogs by extirpation of the pancreas, and then, by grafting a piece of pancreas under the skin of the abdomen in depancreatised dogs/

dogs, prevented the occurrence of that diabetes. In cases of diabetes the pancreas is frequently found diseased. In 1900 Opie (3) localised the morbid processes in the Islands of Langerhans.

In most cases the disease can be diagnosed by decrease in the number of the Islands or by hydropic degeneration of the cells.

The older methods of treatment of Diabetes were based on the assumption that the sugar in the blood and in the urine came only from the Carbohydrates of the diet, but at the end of last century Kossel and Pavy produced evidence that Carbohydrates could be split off from the majority of albuminates by treatment with acids and alkalis. It is from the amino acids of the proteins that Carbohydrates are evolved, and a diabetic may not only utilise 58% of the protein of his diet in the formation of sugar, but in a severe case the proteins of the body are broken down in order to provide sugar, which, after all, cannot be utilised by the diabetic organism, and so large quantities are excreted in the urine.

This failure to utilise Carbohydrates prevents the proper metabolism of fats and so the poisonous ketone bodies are produced and Coma may be the result.

That carbohydrates, other than monosaccharides, in order to cause true hyperglycaemia, must first pass to the liver via the alimentary canal and portal vein, is shown by the fact that cane sugar injected subcutaneously can be recovered entirely

from/

from the urine unchanged, whereas, if taken by the mouth, it is assimilated and either stored in liver and muscles as glycogen, or, in a case of diabetes, circulated in the blood and excreted in the urine as dextrose.(4)

Rollo at the beginning of the nineteenth century suggested a disturbance of the digestive functions as having an etiological bearing on Diabetes Mellitus. More recent research appears to show that hyperglycaemia produces certain marked changes in the digestive function which probably intensify the fault in the metabolism of Carbohydrates, Proteins and Fats which we know to be present in Diabetes.

Starch, digested by saliva, yields achroodextrin and only small quantities of glucose. In the stomach, where the reaction is acid, the diastatic ferment loses most of its activity. In the duodenum the amylase of the pancreatic juice acts in the same way as the diastase of the saliva but goes a step further. From starch it produces achroodextrin and this it converts into maltose. The intestinal ferment maltase now comes into action and the maltose is converted into glucose in which form the Carbohydrates are carried by the blood stream via the portal vein to the liver. In the stomach, while starch digestion is more or less in abeyance, the digestion of proteids normally proceeds as far as the production of peptones. For this, the pepsin requires the presence of Hydrochloric Acid. When Hydrochloric Acid is absent or deficient, the Pyloric Sphincter, instead/

instead of merely allowing the normal regurgitation of duodenal contents and the gradual emptying of the stomach, relaxes early in digestion, and the stomach contents are hurried on into the duodenum. Here the trypsin of the pancreatic juice acts on the peptones and on undigested protein to produce amino acids. If digestion in the stomach is defective by reason of the absence of Hydrochloric Acid, there is a greater demand on the pancreatic digestion. The trypsin is increased, but so also is the amylase. There is increased production of maltose and therefore also of glucose. When this occurs in a diabetic patient, who cannot utilise the glucose produced by normal digestion, it is obvious that the disease will be aggravated.

In the investigation of cases of Diabetes, one is struck by the frequent history of former gastric symptoms. A very common story is that, a few years before coming under observation with the glycosuria, the patient suffered from indigestion with pain after food and other symptoms pointing to hyperchlorhydria. In the majority of cases, he will state that these symtoms have entirely left him and the only way in which his digestion now troubles him is that he is constantly hungry. He can eat anything without fear of indigestion, but complains that his food does not seem to do him any good. A number of cases of this type were investigated in the present series and those who presented a clinical picture of severe diabetes with the diabetic type of sugar tolerance curve, and a history similar to the above, were found to have a definite hypochlorhydria at the time of investigation/

investigation.

Some light appears to be thrown on the manner in which the onset of Diabetes may change hyperchlorhydria into achlorhydria by the work of Lee Foshay,(5) who has made interesting investigations into the Chlorine Content of the blood in cases of Diabetes. He found that the administration of glucose to unanaesthetised dogs, either by stomach-tube or intravenously, causes a transference of Chlorine from serum to corpuscles. On investigating cases of Hyperglycaemia in man he differentiated two groups.

In group 1 he found concentration of circulating blood with diminished relative volume of serum and increased viscosity. These cases showed also increased Chlorine concentration within the Erythrocytes relative to that in the serum.

In group 2 there was a condition of blood dilution with subnormal erythrocyte counts and an extremely variable Chlorine concentration. Group 1, he found to include all his cases of juvenile diabetes and diabetes in young adults, also some elderly diabetics who suffered from severe exacerbations or who were examined in the terminal phase of the disease.

Group 2 consisted chiefly of diabetic patients with recognisable arterio-sclerosis.

Clinical experience shows that Diabetes in the young tends to take the most severe form. Hence Lee Foshay's Group 1 appears to correspond with Von Noorden's Group 1. where consumption

of/

of Carbohydrates for energy and their transformation into fat are both impaired. In such cases the Blood Sugar is usually persistently raised. When the Blood Sugar is decreased by treatment, Lee Foshay finds an increase in serum volume with a decrease in Corpuscular Chlorine. This decrease is greater than could be explained simply by the dilution of the previously concentrated blood. The curves for corpuscular chlorine and relative serum volume he finds, in general, parallel to the Blood Sugar curve in these cases.

The glands of the gastric mucosa, like the other glands of the body, elaborate their secretion from the material brought to them by the circulating blood. From the above investigation, however, it appears that the Chlorine necessary for the elaboration of Hydrochloric Acid, though still present in the blood of diabetics, is in a less available form, being bound up in the corpuscles. Thus the secretion of Hydrochloric Acid becomes less and in a severe case, where the Blood Sugar is constantly high, we may find no free HCl and a very low total acidity.

In addition to the effect which this absence of Hydrochloric Acid secretion has on the digestion, it plays no small part in the production of acidosis. The tension of Carbondioxide in the alveolar air is known to be abnormally low in cases of severe diabetes. So constant is this phenomenon that many writers consider it of great importance in prognosis. The average amount of CO_2 in the alveolar air of the normal adult is/

Gastric and Respiratory Response to Meals

Bennett and Dodds

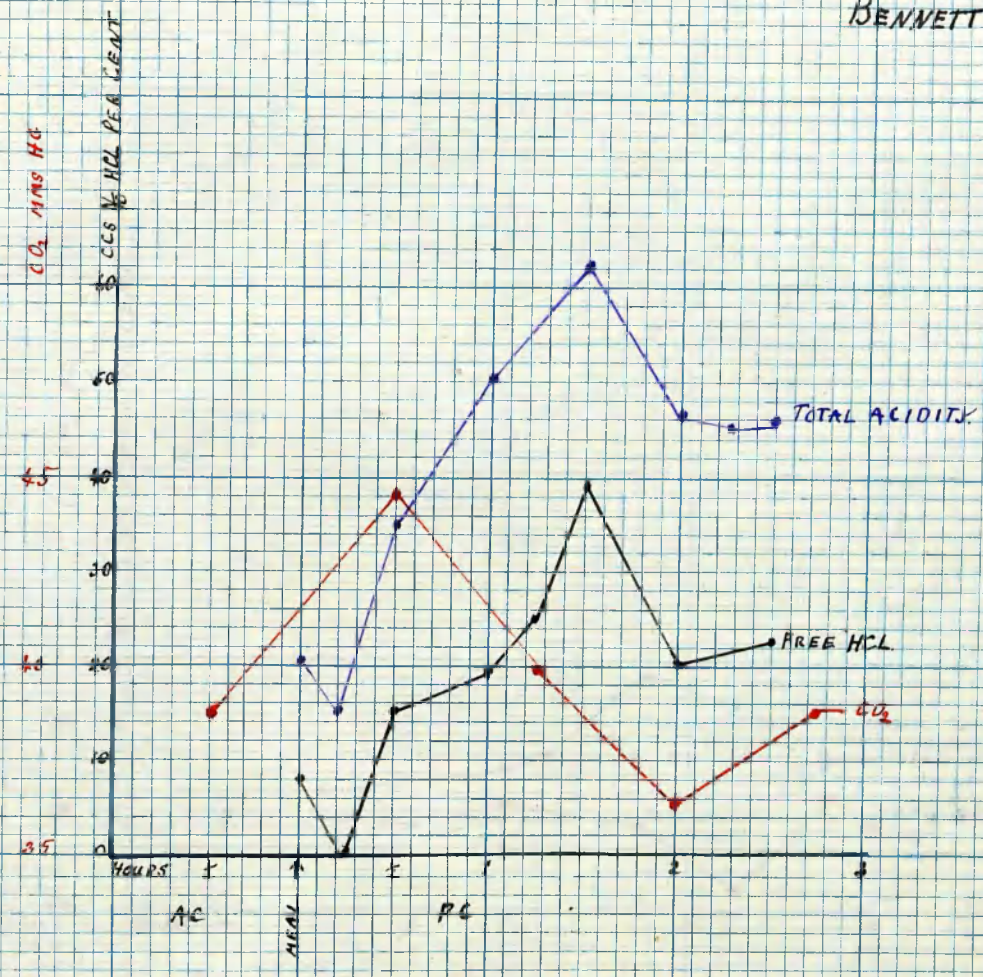


CHART I. NORMAL CASE

GASTRIC AND RESPIRATORY RESPONSE TO MEALS.

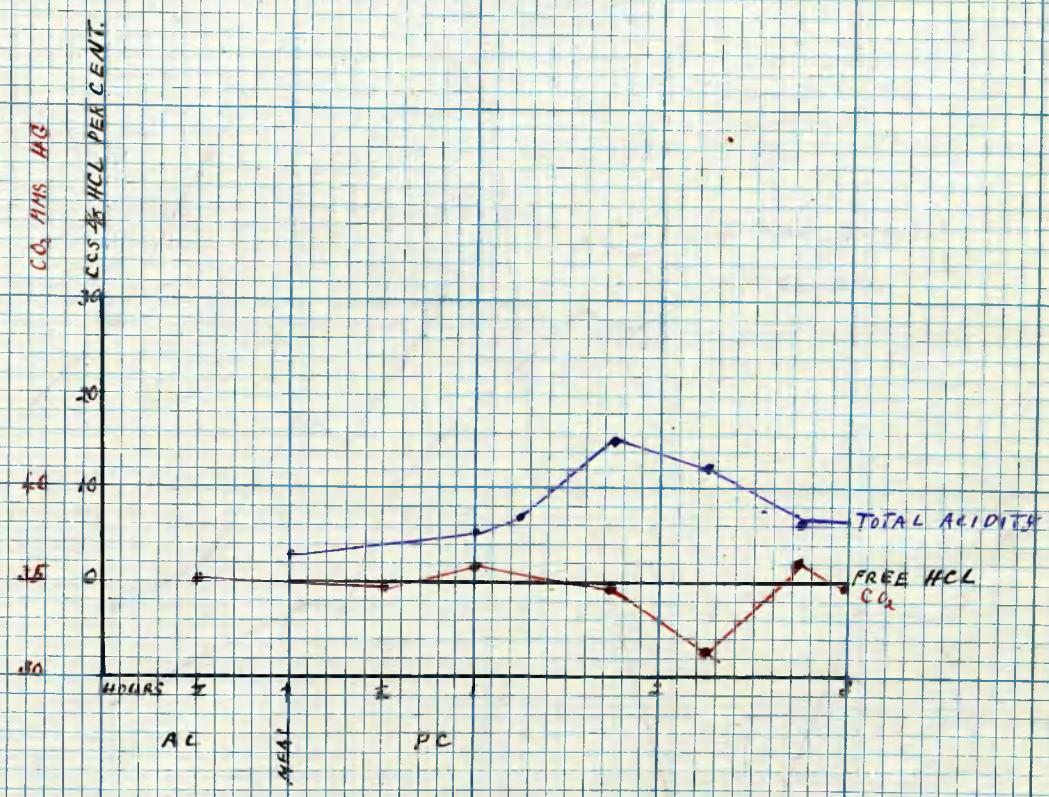


CHART II. ACHLORHYDRIA.

GASTRIC AND RESPIRATORY RESPONSE TO MEALS

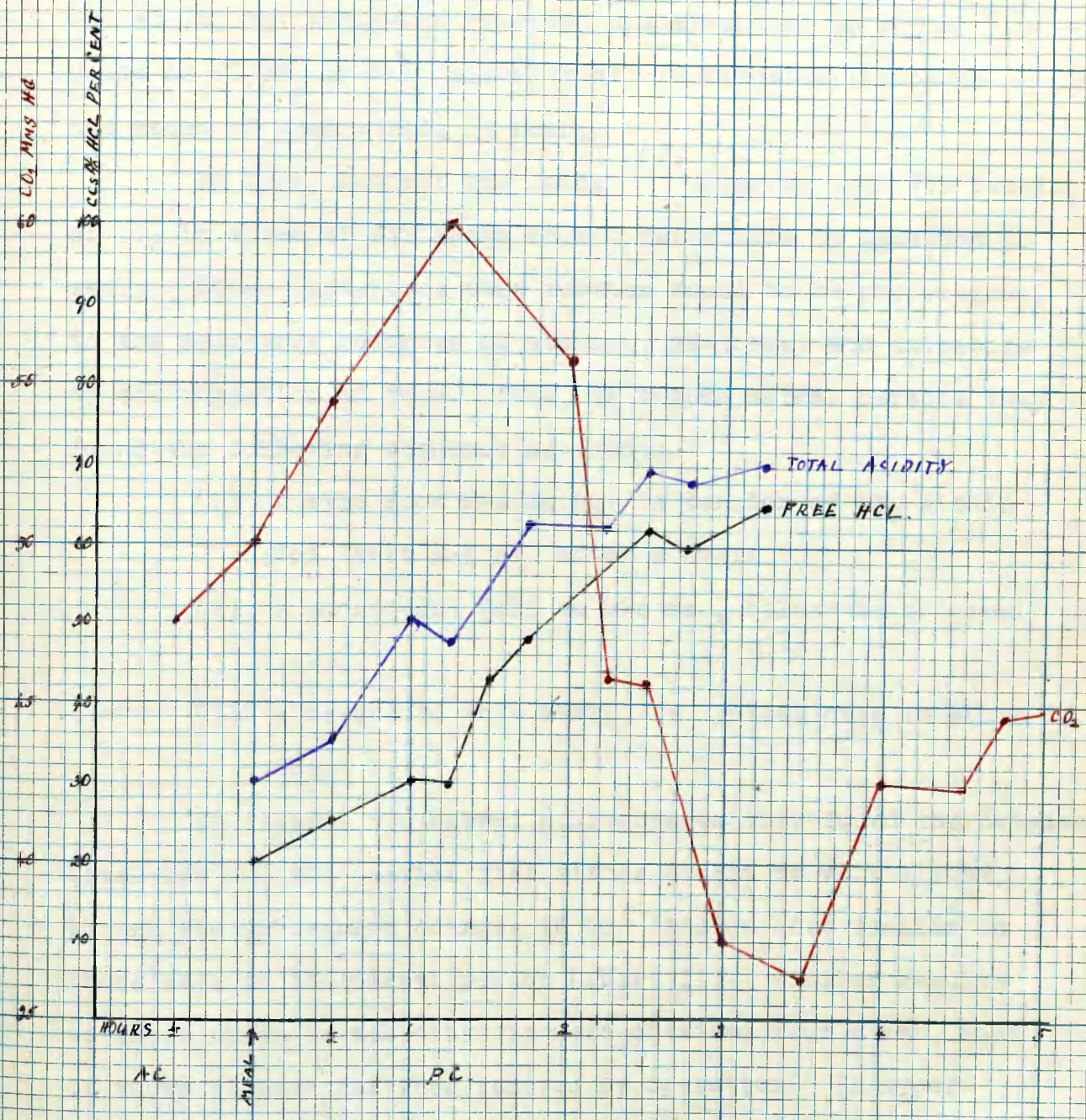


CHART III. HYPERCHLORHYDRIA

is 5% to 5.3%, i.e., the tension is equal to 36-41.8 mm. Hg. at 760 mm. pressure. Poulton[6] states that so low a value as 2% CO_2 in the alveolar air in diabetes indicates the onset of coma within 24 hours.

In 1921, Bennett and Dodds[7] observed that the tension of CO_2 in alveolar air shows marked variations in relation to meals. These variations they further found to be proportional to the secretory response of stomach, pancreas, and intestine to the ingestion of food. Thus, in twelve normal persons they found the following sequence of events.

(1) A rise from 2-6 mm.Hg. in tension of CO_2 within the first $\frac{1}{2}$-$\frac{3}{4}$ hr. after a meal.

(2) A subsequent fall to 2-6 mm., below the original level.

(3) A return to this level; a typical case is shown in Chart I.

In persons who showed achlorhydria they found the original level low and the initial rise either absent or very slight, though the subsequent changes in CO_2 tension were similar to those seen in the normal person (Chart II). Similar results to those shown in achlorhydria were obtained from a man, most of whose stomach had been removed by operation. In hyperchlorhydria, on the other hand, the original tension of CO_2 was high, and the initial rise was very great (Chart III).

Bennett/

Bennett and Dodds deduce from these results that the initial rise is associated with the secretion of gastric juice and the subsequent fall with the later processes of digestion. They consider that the formation of free HCl from the neutral body fluids tends to render the blood alkaline. In order to restore the balance, more CO_2 is retained within the body. This is brought about by lessened ventilation of the lungs and so the tension of alveolar CO_2 rises, the rise being proportional to the free HCl formed.

Conversely, one may infer, when no free HCl is being formed, the normal setting free of bases in the blood during digestion will not take place. In order to counteract the tendency to acidosis as much CO_2 is got rid of by the lungs as will serve to keep the P_H of the blood normal. When this occurs in a diabetic, in whom acidosis is being produced also by the faulty metabolism of fats, the CO_2 tension in the alveolar air may fall very low and the lung ventilation, great as it may be, will still be insufficient to combat the acidosis. Thus it will be seen that a diabetic who has achlorhydria runs graver risk of coma than one in whom the gastric secretion is normal.

For many years it has been recognised that the important factor in a case of glycosuria is not so much the quantity of sugar passed with the urine as the concentration of sugar in the circulating blood. Until recently, however, the methods of/

of estimating blood-sugar concentration were too elaborate for ordinary clinical use and the quantity of blood required was such as to preclude the possibility of performing repeated tests on the same patient. Since, for the thorough investigation of a case of glycosuria, it is necessary to observe the blood-sugar variations over a period of hours, the most useful method of estimation is one which, though accurate, causes least disturbance to the patient and may be carried out with a moderate expenditure of time and care by a worker of average skill. Such a method is that devised by Hugh Maclean (8) in 1915. The quantity of blood required is only 0.2 c.c. This is drawn off by means of a special pipette into a solution of Acid Sodium Sulphate. The protein is removed from the blood by heating this mixture and then adding dialysed iron. A clear filtrate is now obtained by passing the liquid through starch-free filter paper. The sugar in an aliquot part of the filtrate is estimated by boiling under standard conditions with an alkaline solution of copper sulphate containing Potassium Iodide and Potassium Iodate. The liquid now contains Cuprous Oxide in suspension. After cooling it is treated with slight excess of Sulphuric Acid. This interacts with the Potassium Iodide and Potassium Iodate liberating free Iodine. At the same time the Cuprous Oxide goes into solution and is at once oxidised to the Cupric condition by some of the Free Iodine. The remaining Iodine which has not been used in the above reaction or to oxidise the Aldose in

the/

the Gluconic Acid, (which is the form in which the dextrose exists in the solution) is determined by titration with N/400 Sodium Thiosulphate. The amount of Iodine in a solution containing equal amounts of all the reagents to those used in the estimation, but without the addition of blood filtrate, is measured, and the difference between the two results gives the quantity of sugar present in the blood. On estimating the blood-sugar at regular intervals after a meal a definite curve can be plotted out. By the character of this curve, the tolerance of the patient for carbohydrate, i.e. his power to metabolise it without raising his blood-sugar to an abnormal level, is determined.

The significance of sugar tolerance curves of various types has been worked out by Hugh Maclean and others. After ingestion of 50 grams of glucose it is found that the blood-sugar in the normal adult rises within the first hour from the fasting level (.08% -.11%) to about .15% or .17%. Before the blood-sugar reaches the level (usually about .18%) at which the normal kidney will begin to excrete sugar, the storage mechanism of liver and muscles comes into action, and the blood-sugar rapidly falls to fasting level or even lower. Usually this occurs within 1½ hours after administration of the glucose. In Diabetes, however, not only is the rise higher, but the high level is longer sustained, and the drop, instead of being rapid, is gradual. Chart IV illustrates the curves/

SUGAR TOLERANCE CURVES

(AFTER HUGH MACLEAN)

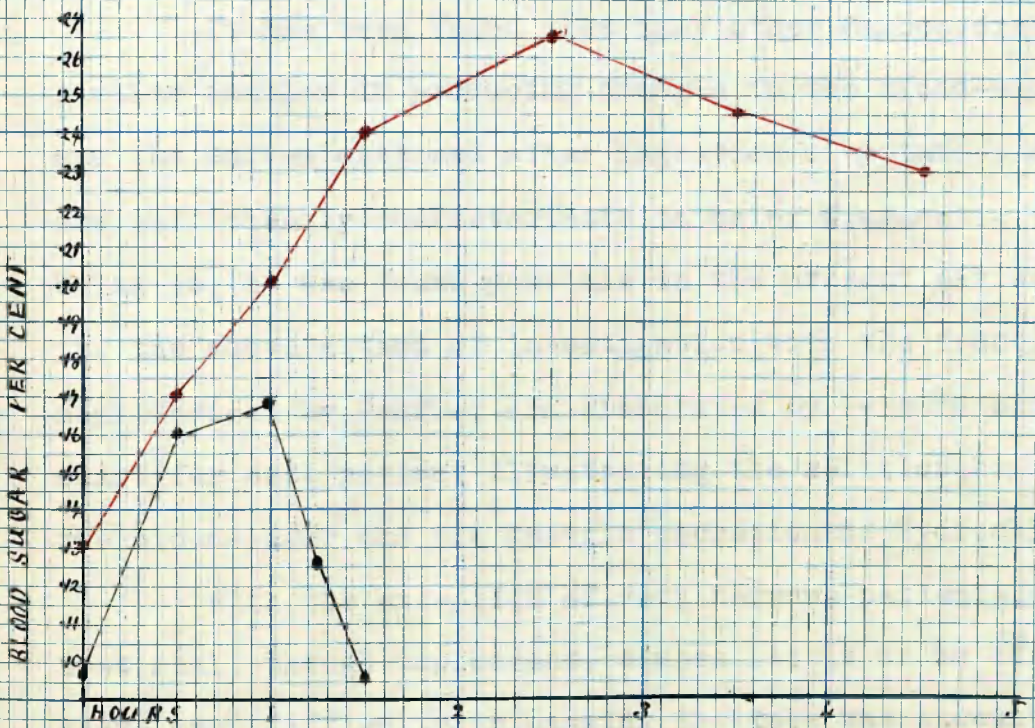


CHART IV.

50 GRAMS OF GLUCOSE INGESTED

— NORMAL

— SEVERE DIABETES

curves obtained by Maclean from:-

(1) the normal adult after ingestion of 50 grams of glucose;

(2) a case of severe Diabetes after ingestion of 40 grams of glucose.

It has been found that many other Carbohydrates act in similar fashion in producing changes in the blood-sugar content, and the curves obtained after ingestion of potatoes or oatmeal are sufficiently characteristic to be of diagnostic value. This being so, it was found possible in the present series, by combining the above method of investigation with the fractional test meal devised by Rehfuss and elaborated by Ryle to obtain a chart for each patient illustrating the relationship between the blood-sugar and the gastric secretion of Hydrochloric acid.

With the exception of very nervous patients, the fractional test meal, though unpleasant, causes little or no disturbance. Where much difficulty in passing the tube was encountered the investigation was usually not persisted in at that time as the excitement was found to cause wide variations in the blood-sugar which rendered the results valueless. In some cases it was found possible, after a longer residence in the hospital wards of nervous patients, to carry out the gastric analyses with the usual ease; but wherever possible the investigation was made before the commencement of treatment.

This method of gastric analysis is performed in the morning, the patient having received no food since the night before. He

is/

is seated upright in bed or on a chair, and told to breathe naturally through his nose. A stomach tube of small bore is now passed. To facilitate swallowing, the tube has a metal bulb let into the blind end. Above this are several small perforations. When the tube has been passed the required distance, any material present in the stomach is withdrawn by means of a syringe, and a specimen kept for investigation of the fasting gastric juice. The tube being kept in situ, the patient now swallows, in the natural fashion, a meal of the composition and consistency which has been found by trial to give the best and most uniform results. The test meal in most common use is a thin oatmeal gruel. By using in every case 4 oz. of oatmeal to make 1 pint of gruel, the conditions in the present series of cases were kept constant. Samples of the gastric contents are drawn off every half hour and analysed for Free Hydrochloric Acid and Total Acidity in the following manner. If free HCl be present the addition of Dimethyl-amino-azo-benzol to the gastric contents will produce a pink colour. To a measured quantity of filtered stomach contents a few drops of this reagent are added. The mixture is then titrated with decinormal Sodium Hydroxide solution till the pink colour is discharged. The number of c.cs. of N/10 NaOH used gives the free HCl. To the same sample a few drops of an alcoholic solution of Phenol-phthalein are now added and the titration is continued till a faint but persistent pink colour appears.

The/

Normal Gastric Function.

After Bennet and Ryle.

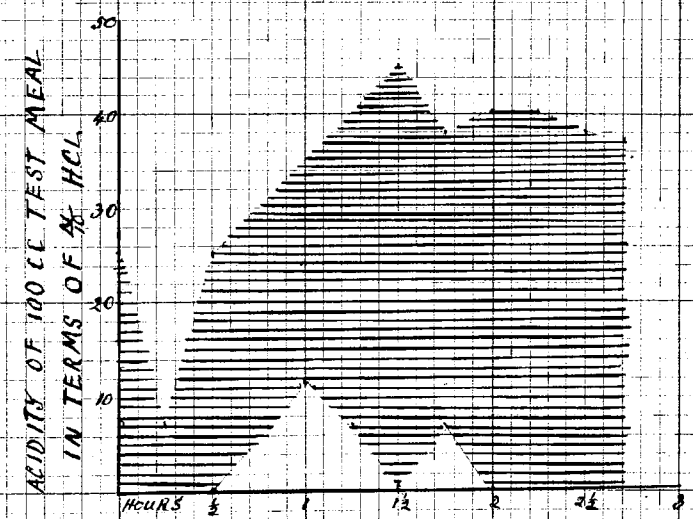


Chart V.

The shaded area represents the limits of free HCl in 80 % of healthy males.

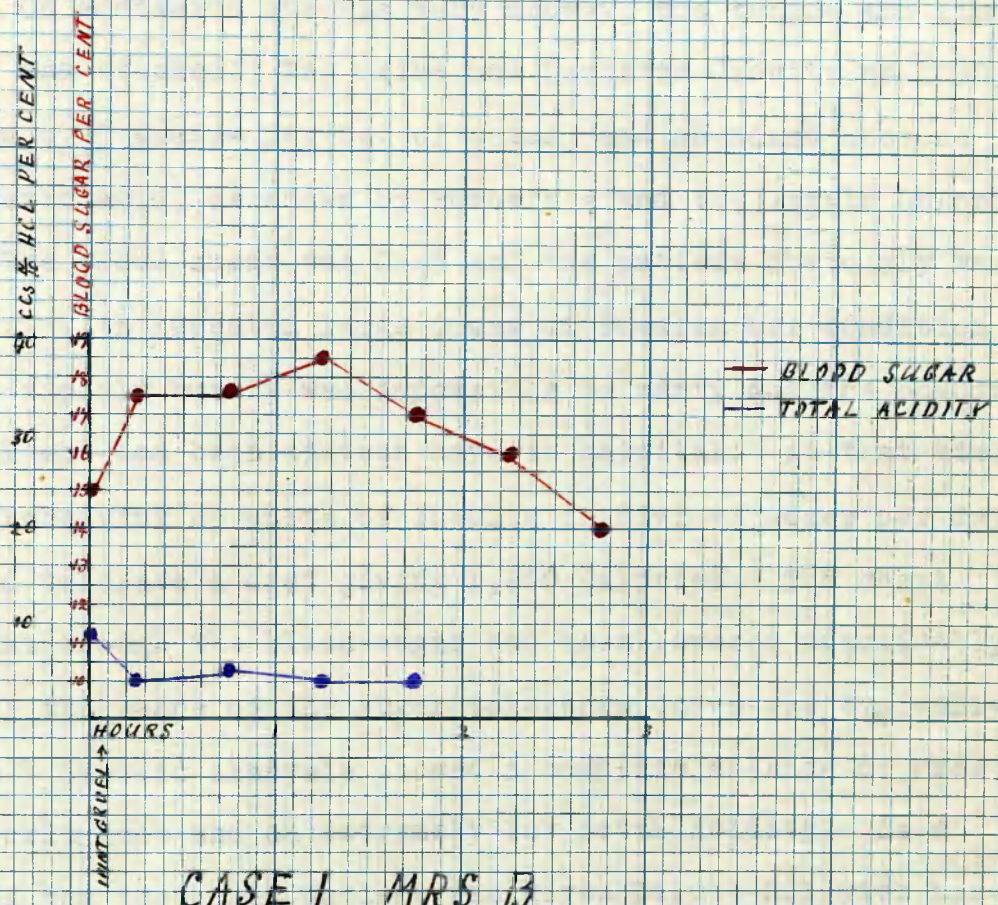
The reading now gives the measurement of total acidity. By calculating the amount of N/10 NaOH required for 100 c.c. of gastric contents one may express the results as percentage of Decinormal Hydrochloric Acid. In this form Chart V gives the upper and lower limits of free HCl as found in 80% of healthy males by Bennet and Ryle.(9) Ryle finds that there is generally a difference between the curves of free and total acidity of 10 to 15 per cent N/10 NaOH, and they run closely parallel. The rate of emptying of the stomach is determined by testing the successive samples for the presence of starch with Iodine.

Bennet and Ryle, examining 100 students by means of the Fractional Test Meal, found Achlorhydria present in only 4%. Campbell had a similar result. It is therefore usually considered that congenital Achlorhydria occurs in 4% of normal people.(10) This percentage, however, cannot be taken as an explanation of the very constant Hypochlorhydria found in the present series of cases.

The patients investigated were all sent into Glasgow Royal Infirmary on account of sugar having been found in the urine. On admission, unless the patient was dangerously ill, each was given for 24 hours a test diet providing 2,500 Calories per day, in order that the blood and urinary sugar under known conditions might be investigated. Thereafter the diet was gradually reduced and if necessary a starvation day was given. Thus usually rendered the urine sugar free and can be done in hospital without/

without risk of dangerous acidosis in the majority of cases. When the blood-sugar had been lowered as far as was thought advisable the diet was gradually increased till the patient was taking a diet calculated to suffice for his needs. If this could not be accomplished by very gradual increase of diet, Insulin Treatment was instituted in order to permit of sufficient nourishment being given without the blood-sugar being raised above normal. This line of treatment was not of course applicable to cases received in Coma or with very severe acidosis. In such cases Insulin was given at once and the sugar tolerance curve may have been altered by the Insulin administration. Even so, it was very constantly found that in such cases the gastric secretion was devoid of free HCl, or, if it did appear, it was very small in quantity and the total acidity was low.

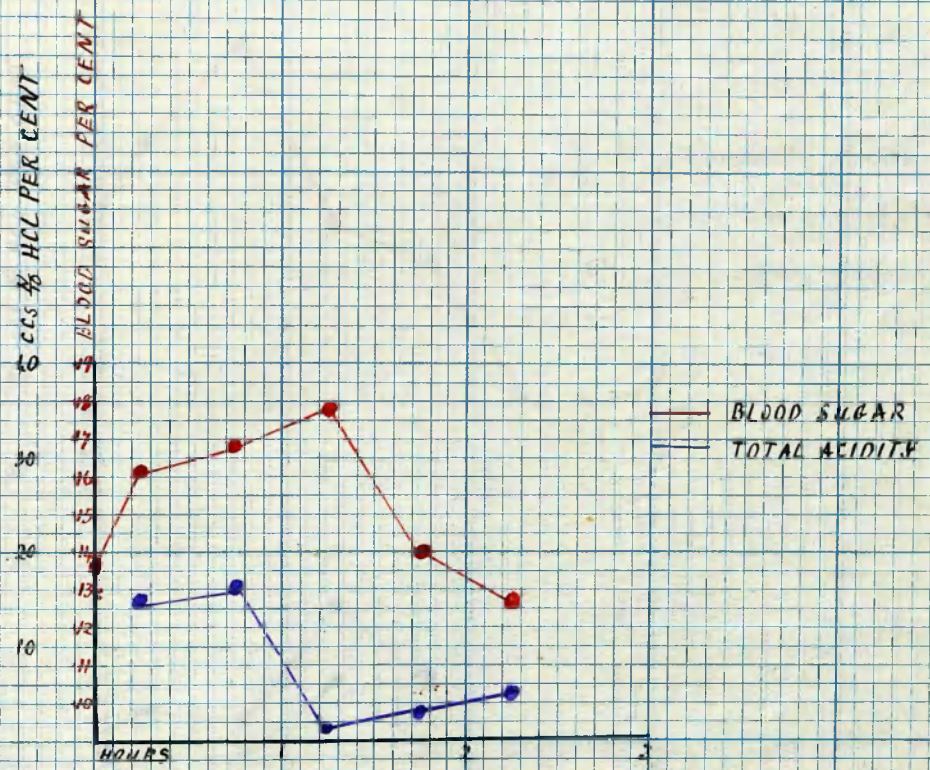
The cases illustrated by charts have been chosen as showing the findings in different types of glycosuria. With the exception of Case 7, all were confined to bed at the time of the analysis. The tests were performed in the morning, the patients having had no food or drink for the previous 12 hours. As each sample of gastric contents was obtained a specimen of blood also was taken for blood-sugar estimation. Thus, while the effect of the gruel on the gastric secretion was investigated, a sugar tolerance curve was simultaneously worked out, using the Carbohydrate of the oatmeal as glucose was used in the original sugar tolerance investigations.


CCS. N/10 HCL PER CENT
BLOOD SUGAR PER CENT
HOURS
MEAT GRUEL
BLOOD SUGAR
TOTAL ACIDITY

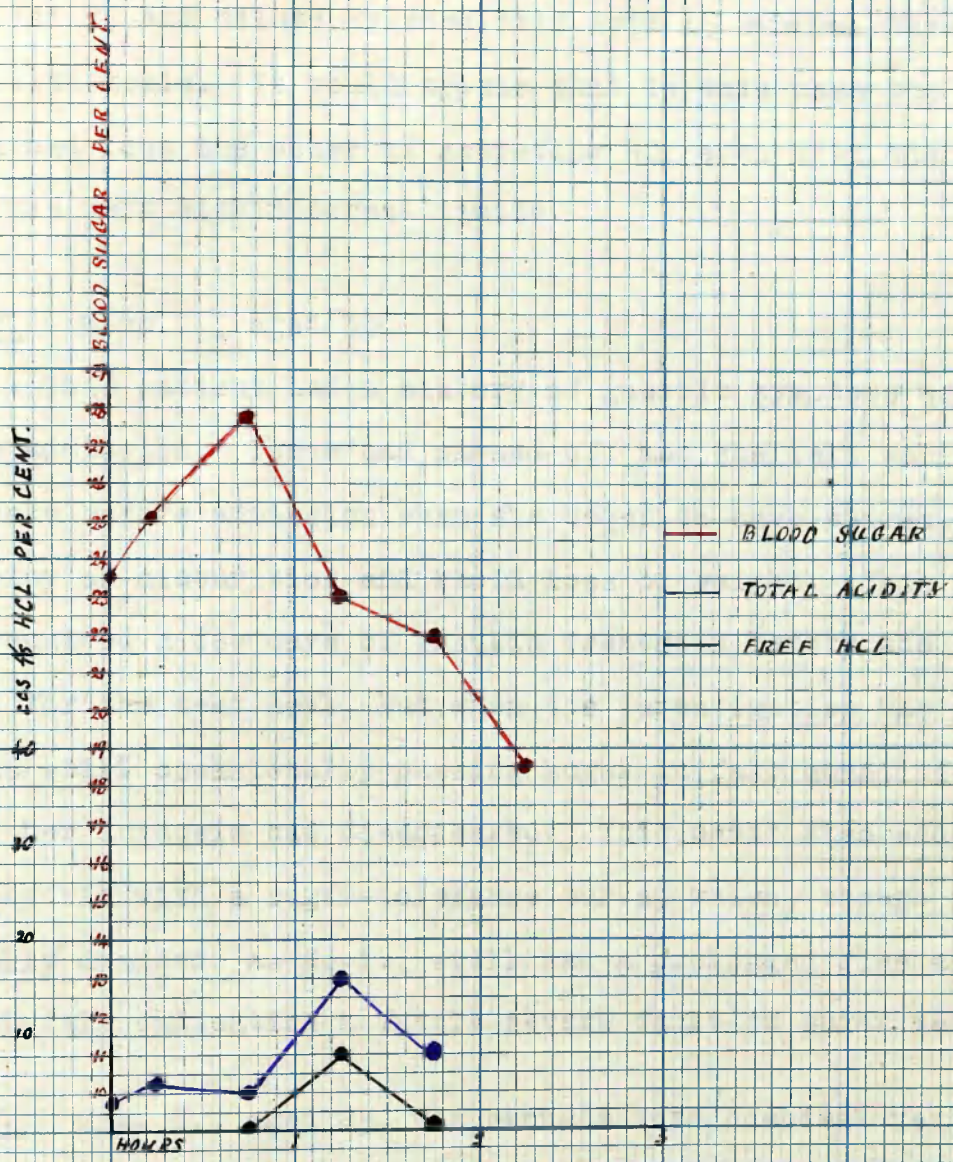
CASE I MRS B

Case 1. Mrs. B., aged 40, had a history of polyuria and loss in weight for six months. Two years before admission she was curetted for Pruritus Vulvae with little result. Since then she had suffered from headaches, insomnia, weakness and constipation. On admission she was very drowsy, the tongue and lips were dry and cracked. The urine had Specific Gravity of 1030, contained 8.75 grains per oz. of sugar, and abundant acetone and diacetic acid, as shown by Rothera's and the Ferric Chloride tests. The blood-sugar was 0.4% and the patient obviously was very ill. With repeated large doses of Insulin her condition improved rapidly but it was impossible to carry out the combined test till she had been sixteen days in hospital. At that time she was receiving 25 units of Insulin in divided doses per day and could tolerate a diet giving 1,200 Calories. The chart shows that though the blood-sugar had been lowered practically to normal the shape of the sugar tolerance curve was typically diabetic. Gastric analysis showed a complete absence of Free Hydrochloric Acid and an extremely low Total Acidity. As a result of the test this patient was given Dilute HCl with her meals. It was then found possible to reduce the Insulin dosage to 20 units. She was dismissed on a diet giving 1,500 Calories and attended as an out-patient. Five months later it was found that, while she was taking HCl, 15 units of Insulin sufficed to enable her to utilise an adequate diet, but if the HCl was stopped the Insulin had to be increased. A year after admission this patient was looking and feeling well. Her diet had been

increased/


CCS ½ HCL PER CENT
BLOOD SUGAR PER CENT
10
20
HOURS
1
2
3
BLOOD SUGAR
TOTAL ACIDITY

CASE 2. MISS M


BLOOD SUGAR PER CENT.
FREE HCL PER CENT.
40
30
20
10
HOURS
1
2
3
BLOOD SUGAR
TOTAL ACIDITY
FREE HCL

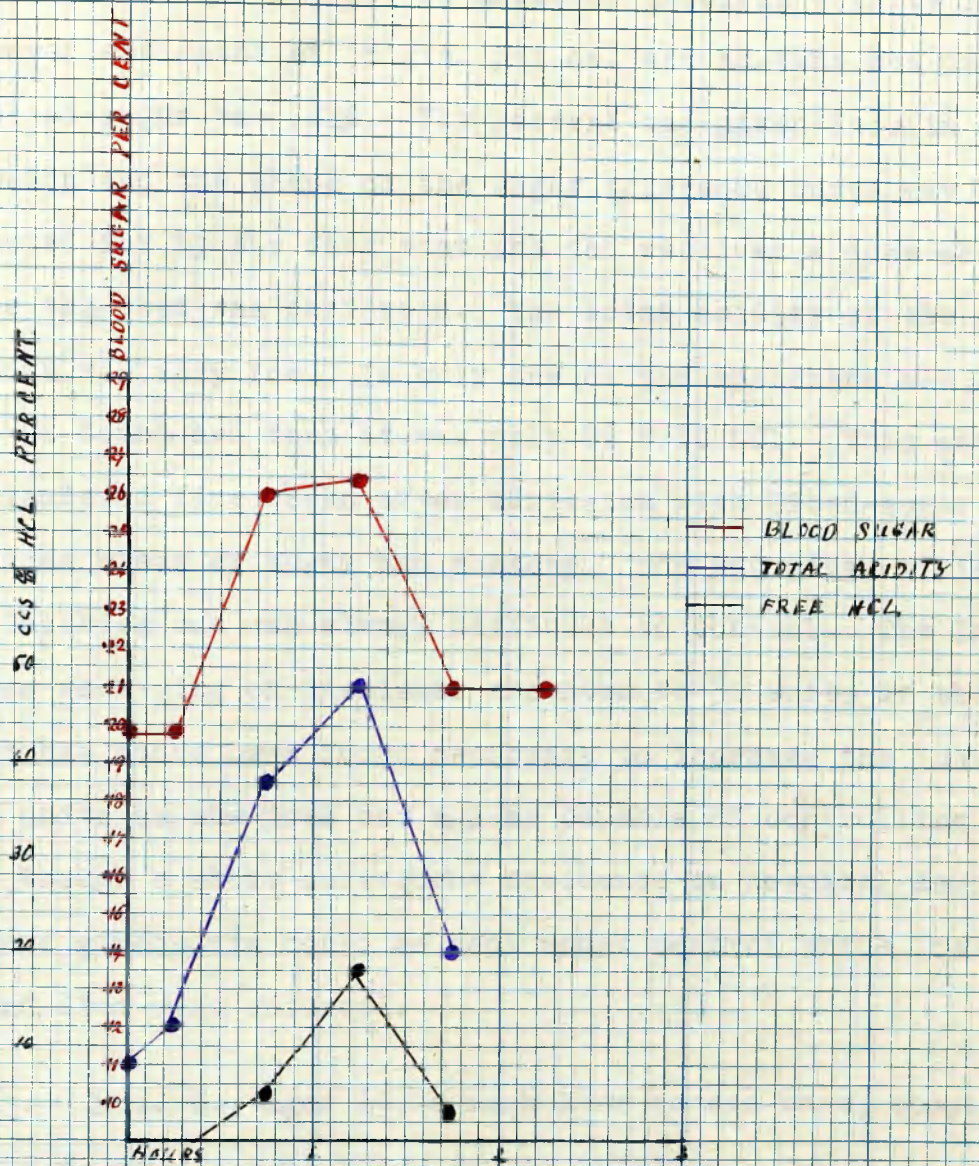
CASE 3 MRS G.

increased to 1,800 Calories, she was taking Insulin, 10 units, twice daily, and dilute Hydrochloric Acid 15 minims three times a day with meals. It would appear that in this case the gastric mucosa had lost the power of secreting HCl even when the blood-sugar was kept within normal limits.

Case 2. Miss M., aged 38.

This patient had a history of gastric symptoms some years before admission. These had passed off and she felt well till six weeks before admission when she began to have thirst, frequency of micturition and rapid loss of weight. This patient also required a few days of Insulin Treatment before she was well enough for the test meal, but when the investigation was made she was still occasionally passing sugar in fair quantities, though her acidosis had disappeared. This chart also shows Achlorhydria with a sugar-tolerance curve, which, though not so typically diabetic as No.1., still had a prolonged rise and gradual fall indicating a fairly severe fault in sugar metabolism.

Case 3. Mrs. G., aged 25, was brought into hospital verging on coma. Her mother died from Diabetes, aged 36. The patient had suffered from thirst, polyuria, and pruritus vulvae for ten months. In the last six months she had lost 2 st. weight and had suffered from boils. She had amenorrhoea (pregnancy was excluded) and loss of the knee-jerks. On admission she was passing/


BLOOD SUGAR PER CENT
CCS OF HCL PER CENT
BLOOD SUGAR
TOTAL ACIDITY
FREE HCL
HOURS

CASE 4. MRS C.

passing in the day 105 oz. of urine of Specific Gravity 1045. The sugar estimated at 36 grs. per oz. and acetone was present. The blood-sugar was .24%. The patient was given Insulin on admission and the shape of the sugar tolerance curve may be accounted for by the fact that she had received a dose shortly before the test was performed. The total acidity of the gastric contents was very low. In only one of the specimens was any Free HCl found and then it was only 8% N/10 HCl. This patient was dismissed five weeks after admission with Blood-sugar .153% and urine clear of sugar and acetone. She was given a diet of 1400 Calories but was always difficult to control. The Insulin she was receiving on dismissal amounted to 30 units in the day, but it has since been found necessary to increase the Insulin to 45 units as she does not appear capable of controlling her diet, though a short subsequent residence in hospital demonstrated that her glycosuria could be kept under control while Insulin, HCl and diet were enforced.

Case 4. Mrs. C., aged 65, a much less severe case, complained chiefly of pruritus of three years' duration.

On admission the urine contained 8.45 grs. of sugar per oz. There was no acetone or diacetic acid. The blood sugar was .20% The test was performed while the patient was on the usual admission diet. The chart shows a fairly high blood-sugar content, with a deficiency in gastric secretion as shown by the fact that in only three of the specimens was a small amount/

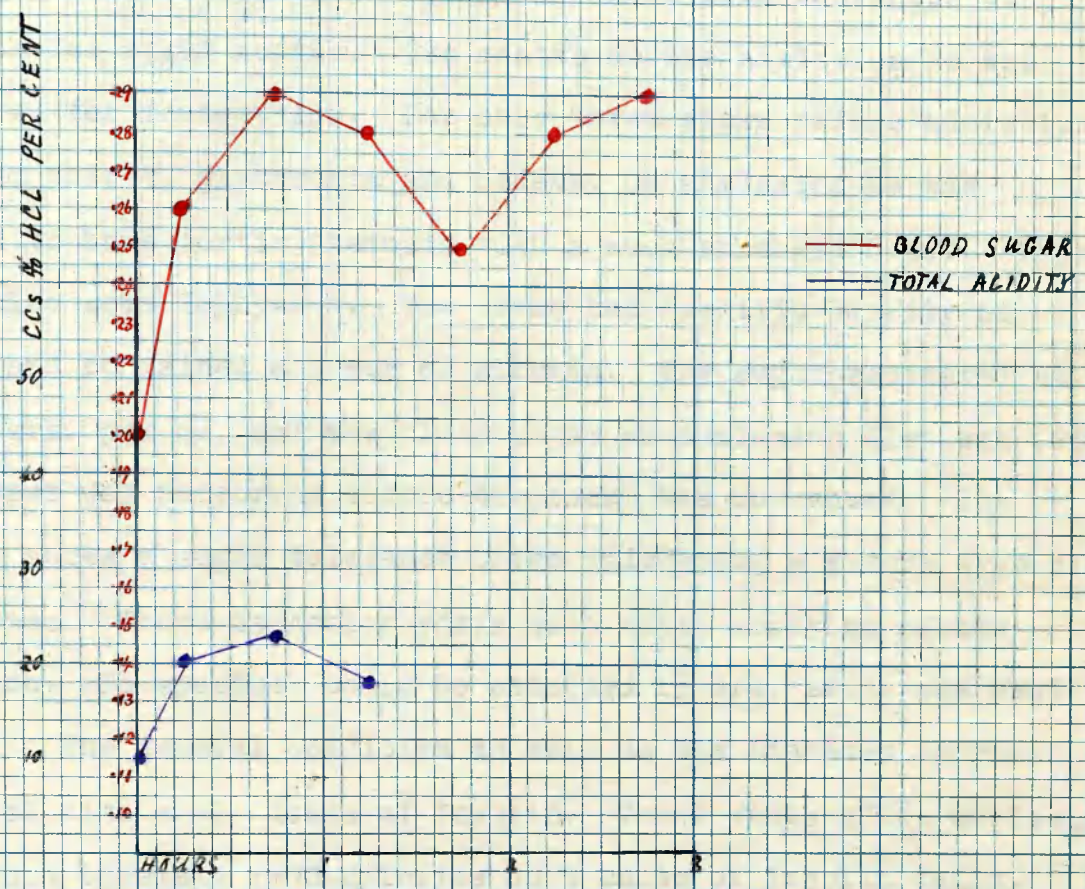
amount of Free HCl found. A notable feature is the rapid emptying of the stomach. This case was found to do well on dietetic treatment alone.

Case 5. David B., aged 61, had suffered from shortness of breath for eight months. Ten months before admission he was treated for Indigestion. For only three weeks before admission he had thirst, glycosuria and oedema. On admission he was found to have Aortic Stenosis with a much enlarged heart. There was also some Emphysema. The urine had Specific Gravity of 1034 and contained a trace of albumin. The sugar estimated at 19.6 grs. per oz. and the blood-sugar on admission diet was .26% The test was performed before treatment was commenced. The chart shows a sugar tolerance curve indicating a severe type of Diabetes. There is Achlorhydria with rapid emptying of the stomach. No specimen could be obtained 1¾ hrs. after the meal.

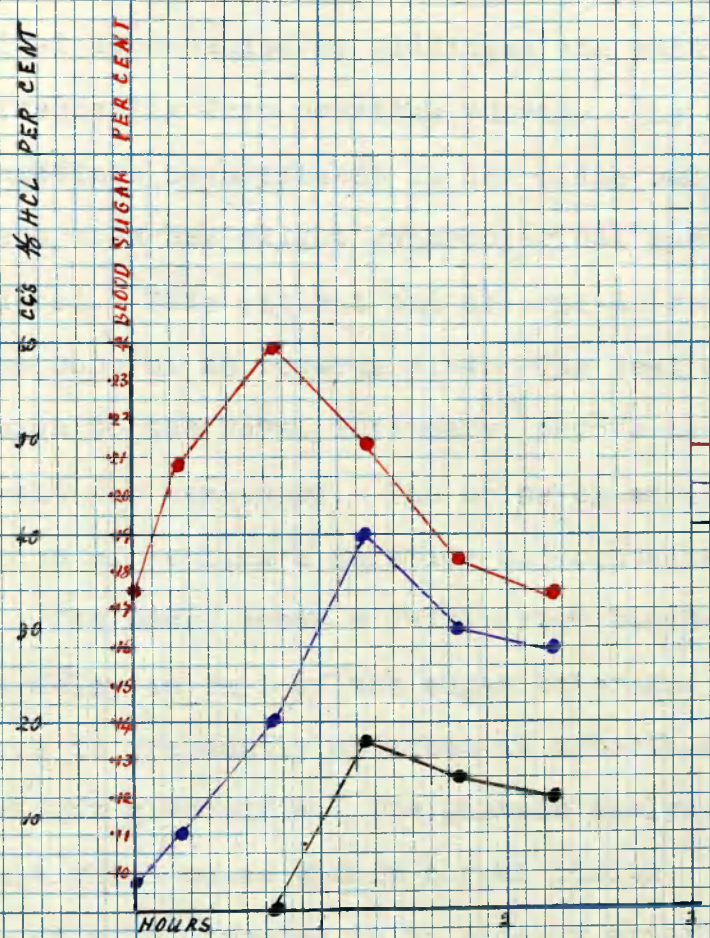
The general condition as well as the Diabetes improved on diet with small doses of Insulin. Three weeks after admission he could tolerate 1200 Calories on 5 units of Insulin daily.

Shortly after dismissal the heart condition became worse and the patient died. No record was obtained of the urinary condition after he left hospital.

Case 6. Mrs K., aged 62, was sent for investigation because two days after an operation (performed outside the Royal Infirmary) she had become comatose, and sugar was found in the/


CCs ½ HCL PER CENT
50
40
30
20
10
HOURS
1
2
3
BLOOD SUGAR
TOTAL ACIDITY

CASE 5 D B


BLOOD SUGAR PER CENT
CCS N/5 HCL PER CENT
HOURS
BLOOD SUGAR
TOTAL ACIDITY
FREE HCL

CASE 6 MRS K

the urine. She recovered on administration of Insulin for four days and had remained well until admission three weeks after the operation. On inquiry into her previous history it was found that she had suffered for ten years from attacks of thirst accompanied by giddiness and pain in her legs, and also frequently from pruritus vulvae. She knew that sugar had sometimes been present in her urine but did not mention the fact when her slight gynaecological operation was being considered. This patient had arterio-sclerosis and was difficult to control as regards diet. The test was performed on admission to the Royal Infirmary, before dietetics or Insulin treatment was commenced. The urine on admission gave a slight reduction of Fehling's Solution but contained no Acetone.

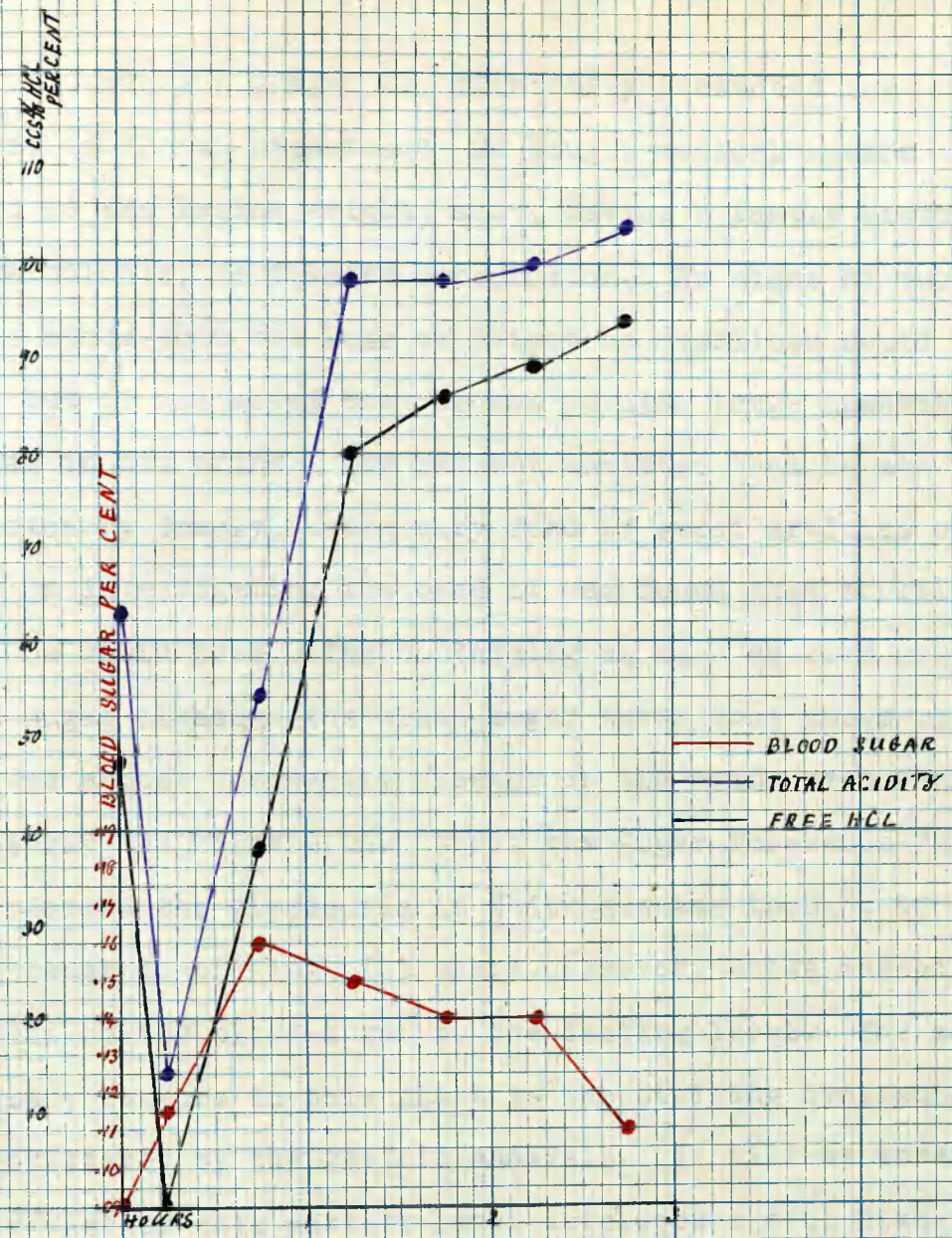
The chart shows a fairly high blood-sugar content and slight delay in fall of the sugar tolerance curve. This type of curve is frequently obtained in arterio-sclerotic patients with slight glycosuria. The gastric analysis in this case gives a result which comes within normal limits. This is evidently a case of mild diabetes in an elderly arterio-sclerotic which was converted into a temporarily acute type by the circumstance of the patient receiving an anaesthetic. The rapid recovery under Insulin with reversion to the mild type not requiring Insulin Treatment is interesting when taken in conjunction with the Sugar Tolerance Curve and Gastric Analysis.

Case 7. Charles S., aged 26, clinically presented the features of "Renal Diabetes." He sought medical advice because he was losing weight, and , having a family history of Tuberculosis, he dreaded consumption. No signs of tuberculosis other than the loss of weight he described could be found, but it was noted that he was passing large quantities of sugar in his urine. The patient admitted that he ate confectionery freely, being very fond of sweet articles of diet. On investigating the case it was found that shortly after a meal he would pass urine containing as much as 21.8 grs. per oz. of sugar although the blood-sugar never rose above .18%. Sugar was almost constantly present in the urine even when the blood-sugar was below .10%. Until the Sugar Tolerance Test was performed the glycosuria in this case was thought to be purely renal in origin. The chart, however, shows marked delay in return of the blood-sugar to the fasting level. The most noteworthy feature in this chart is the striking hyperchlorhydria as demonstrated by the gastric analysis. It will be interesting to note whether this patient later developes a true Diabetes with acidosis, and, if he does, what changes, if any, occur in his gastric secretion.

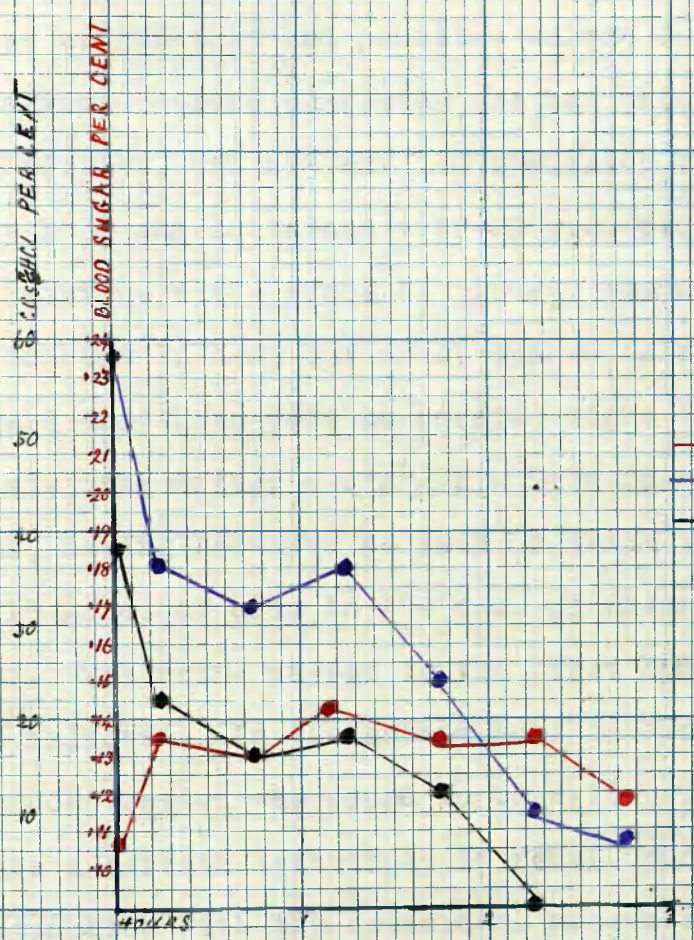
Case 8. Mrs H., aged 65, also presented some of the features of Renal Diabetes as she constantly passed sugar at a blood-sugar concentration of .10% to .15%. Her blood sugar, however, occasionally rose to a high level, being on admission .32%. She presented/

presented also many of the clinical features of true Diabetes. She complained of weakness and loss of weight of six months' duration, and had suffered from thirst, frequency of micturition, numbness of the feet and pruritus vulvae for about three months. About a month before admission she had three troublesome abscesses which, however, had healed. On admission the urine had Specific Gravity 1038 and contained over 20 grs. per oz. of sugar. There was no acetone but a trace of albumin was present. This cleared off with rest in bed, but as it tended to reappear at irregular intervals and there were no cardiac signs beyond slight arteriosclerosis, the writer performed a Urea Concentration Test. The patient, having received no food or drink for twelve hours, was given 15 grams of urea in 100 c.c. of water after emptying her bladder. The urine passed in the first hour was over 120 c.c. so was rejected. In the second hour 84 c.c. was passed and the urea concentration was found to be 2.1%. This was taken to indicate a certain deficiency in renal function, which, taken in conjunction with the occasional presence of albumin and casts, pointed to chronic nephritis of azotaemic type.

The faulty kidneys were apparently allowing sugar to pass at a lower blood-sugar concentration than they would have done if normal, and thus the blood sugar was, perhaps fortunately for the patient, kept at a reasonably low level in spite of the failure in Carbohydrate Metabolism, except when she had an/


CCS N/10 HCL PERCENT
110
100
90
80
70
60
50
40
30
20
10
BLOOD SUGAR PER CENT
.19
.18
.17
.16
.15
.14
.13
.12
.11
.10
.09
HOURS
1
2
3
BLOOD SUGAR
TOTAL ACIDITY
FREE HCL

CASE 7 C.S.


C.C.S. HCL PER LEVT
BLOOD SUGAR PER CENT
60
50
40
30
20
10
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
HOURS
1
2
3
BLOOD SUGAR
TOTAL ACIDITY
FREE HCL

CASE 8 MRS H.

an exacerbation of the Diabetes. On consulting this chart it will be seen that the sugar tolerance curve, though low, is of a typical diabetic shape. It is interesting to note that in this case of definite diabetes in which the blood-sugar was kept low by what one might term the compensating kidney lesion the gastric analysis produced a normal result.

This case, when considered along with cases 6 and 7, would appear to show that it is only when the blood-sugar is persistently high that achlorhydria results from diabetes. It might be contended that Case 2 shows achlorhydria with a low blood-sugar concentration, but Miss M had a severe diabetes and was on Insulin Treatment at the time the test was performed. The Insulin could lower the blood-sugar but could not restore the lost power of gastric secretion of HCl.

Conclusions.

1. Diabetes is due to failure of the glycogenic function of the liver brought about by abnormality of the internal secretion of the pancreas.

2. In persistent hyperglycaemia there is a transference of Chlorine from the blood serum to the corpuscles.

3. Poverty of blood serum in Chlorine causes a diminution of gastric secretion of Hydrochloric Acid amounting in some cases to complete Achlorhydria.

4. The hypochlorhydria produced by hyperglycaemia has itself a deleterious effect on the metabolism of proteins, carbohydrates and fats and also intensifies the acidosis which is a feature of severe diabetes.

5. When achlorhydria has been present for some time, the gastric mucosa loses its power to secrete HCl even when the blood-sugar is normal. Thus HCl administration is frequently found to improve cases of long-standing diabetes.

6. Forms of Glycosuria in which the blood-sugar is not persistently high have no effect on the gastric secretion of HCl.

7. When a case of hyperchlorhydria undergoes apparently spontaneous cure, this may be a sign of failure in the carbohydrate mechanism and the condition of the blood-sugar should be investigated.

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