

THE DIAGNOSIS AND TREATMENT OF GLYCOSURIA

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Part I. The Diagnosis of Glycosuria

Introduction

Since glycosuria is often found only on routine examination of the urine, the importance of this simple procedure in every case is obvious. Unless this symptom is severe or long-standing, many of these patients make no suggestive complaint when first seen.

When a reducing substance is found in the urine, it is necessary to prove that it is glucose. Fehling's solution should not be used, since this reagent is reduced not only by sugar, but also by uric acid, glycuronic acid and creatinine; the degree of reduction is slight, usually only a change in colour to green or yellowish-green. The more delicate Benedict's test may detect such sugars as lactose, laevulose or pentose, which need more elaborate tests for their identification.

Lactosuria is suggested by the presence of sugar in the urine during pregnancy or lactation, or when breast-feeding is suddenly stopped. Lactose is identified by the yeast-fermentation test (glucose being the only sugar which ferments yeast), and by the characteristic 'hedgehog' crystals of lactosazone. Laevulosuria may occur during the course of liver disease. Pentosuria is extremely rare.

The usual type of glycosuria is due to the presence of glucose in the urine. Four varieties will be considered.

- I. Diabetic Glycosuria.
- II. Renal Glycosuria.
- III. Glycosuria of Cerebral Origin.
- IV. Glycosuria of Endocrine (non-pancreatic) origin.

I. Diabetic Glycosuria

When a young adult complains of thirst, excessive hunger, polyuria, exhaustion and loss of weight, the discovery of glycosuria usually confirms an obvious diagnosis of Diabetes Mellitus. Milder cases, especially in patients over middle age, may have less marked symptoms. Minor degrees of wasting and lassitude should not be dismissed without examination of the urine, together with a glucose tolerance test, or at least a fasting blood-sugar estimation, if glycosuria is found.

Sometimes one of the complications of diabetes may first suggest the need to test the urine. Thus the patient may present with recurrent boils, carbuncles or other septic infection. It is important in such cases not to miss a diabetic origin, so that the patient may be properly prepared for any operative treatment needed.

Pulmonary tuberculosis is common in diabetics, and its symptoms may be few and undetected unless the chest be X-rayed in every case. Less often, the pulmonary lesion may cause symptoms before diabetes is suspected; in these cases a urine test is most important.

Nervous symptoms may have a diabetic basis. In addition to peripheral neuritis, pains in the legs resembling sciatica may be associated with diabetes, without other suggestive symptoms.

In severe diabetes the tendon reflexes may be absent, and paraesthesia and signs of posterior column involvement may lead to a suspicion of tabes unless their origin is appreciated. In cases of failing vision, the urine should always be tested; diabetic

cataract and retinitis can be improved, or at least arrested in their progress, by early treatment.

Coma

In every unconscious patient, whatever the history, the urine must be examined for sugar, acetone bodies and albumen. The finding of glycosuria and ketosis strongly suggests diabetic coma, but some cerebral lesions may produce these signs (q.v.). If there is a history of previous diabetes the diagnosis is simple. Useful confirmatory signs are the low ocular tension (rarely found except in conditions of dehydration leading to coma), dry skin, lips and tongue, a smell of acetone in the breath and, if available, laboratory findings showing hyperglycaemia and a lowered alkali reserve.

If blood sugar estimations are not available, the distinction of hypoglycaemia from diabetic coma may be difficult. In the former, the onset is more sudden, the skin moist and sweating and the ocular tension normal. Sugar and acetone are usually absent from the urine, at least, in the second specimen obtained. The immediate response to the giving of sugar in hypoglycaemia is also diagnostic.

Glycosuria may be an incident in coma due to poisoning, uraemia or a cerebral vascular lesion; in such cases there will be characteristic physical signs. Even when glycosuria is found, every comatose patient should be thoroughly examined to make sure that no lesion other than diabetes is present. In particular, one should note the state of the reflexes, cranial nerves and pupil reactions, also, the presence of any needle marks or signs of poisoning. The breath may smell of acetone and so lead to the detection of glycosuria.

When the cause of coma is in doubt, lumbar puncture should be done to exclude the presence of a subarachnoid haemorrhage. In some cases of severe diabetic coma, the presence of albumen and casts in the urine may suggest uraemia and may cause neglect of the essential treatment with insulin and glucose. In every case of coma the urine should be examined for albumen and sugar and, if possible, the blood urea should be estimated.

Alimentary Glycosuria

In this condition, after a large meal of carbohydrate, the patient passes sugar in the urine. There may be no diabetic symptoms, and renal glycosuria may be suspected, but a glucose tolerance test will show that the blood sugar rises abnormally high and takes unduly long to return to its fasting value, which may be above the normal. These cases are essentially mild diabetics, with lowered carbohydrate tolerance, in which the insulin produced is enough to deal with average, but not heavy, carbohydrate meals. The transient glycosuria sometimes found in fat, hypertensive women after middle age, is probably of this nature.

II. Renal Glycosuria

The normal renal threshold for sugar is about 180 mgm. per cent. and above this level the storage mechanisms prevent a further rise of blood sugar. In cases of renal glycosuria, the renal threshold is lower than normal, and these patients pass sugar in the urine when the blood sugar is only 140-150 mgm. per cent., or less. The patient is usually a healthy young adult without diabetic symptoms. He may complain of recurrent boils, or of local pruritus, but the glycosuria is often found only on routine examination. A glucose tolerance test shows that the fasting blood sugar is rather low and that the blood sugar never rises above 180 mgm. per cent.—usually not above 150 mgm. per cent.—but that sugar appears in the urine each time its blood level exceeds 140-150 mgm. per cent. This test is the only certain method of diagnosing renal glycosuria.

III. Glycosuria of Cerebral Origin

Since Claude Bernard first described glycosuria following puncture of the floor of the fourth ventricle, the condition has been noted in many basal cerebral lesions. When neurological signs predominate the case, and glycosuria is incidentally found, there is no difficulty in diagnosis. Some difficulty may arise from lesions near the fourth ventricle in which glycosuria precedes other signs.

In some cases of cerebral haemorrhage, glycosuria and even acetonuria may occur—the latter following starvation and vomiting.

Subarachnoid haemorrhage is suggested by the sudden onset of intense headache, coma and signs of meningeal irritation, often with glycosuria. The cerebrospinal fluid, first bloodstained and later stained yellow, is under greatly increased pressure, and is diagnostic.

Internal capsular haemorrhage may track into the ventricle; but in this coma the onset is more rapid than in diabetic coma, and there are some localizing signs, *e.g.*, hemiplegia and conjugate deviation of the eyes.

Tuberculous meningitis occurs especially in childhood, in which diabetes is uncommon. Even through glycosuria may coexist, the presence of meningeal irritation, ocular pareses and raised intracranial pressure should establish the diagnosis.

IV. Endocrine Glycosuria

Sometimes diabetes is part of a generalized pancreatic insufficiency; these cases show other signs such as chronic dyspepsia, steatorrhoea, raised blood and urinary diastase, and a positive Loewi's adrenalin test. The signs may be due to pancreatitis, neoplasm or syphilitic infection.

Glycosuria is not uncommon in thyroid and pituitary diseases; the thyroid, pituitary and suprarenal hormones antagonize insulin, so that their hypersecretion may cause a state of lowered carbohydrate tolerance. In hyperthyroidism, glycosuria and some degree of hyperglycaemia are common. If clinical signs are not obvious, a glucose tolerance test will usually show a normal fasting level but high blood sugar readings after food.

A more difficult problem is the early diagnosis of acromegaly, in which glycosuria may also occur. The blood sugar findings are the same as in hyperthyroidism. Enlargement of the nose, tongue, supraorbital ridges, hands and feet; pressure signs such as headaches and hemianopia, may show that the glycosuria is due to pituitary disease. A rarer lesion is the basophil adenoma (Cushing syndrome), which causes obesity, hypertrichosis, genital atrophy, glycosuria, albuminuria and hypertension.

With the exception of the rare chromaffin tumour (hypersecretory adenoma) of the medulla, suprarenal disease is rarely associated with glycosuria, in spite of the effect of

adrenalin upon the blood sugar. Great emotional disturbances may possibly produce glycosuria by means of an outpouring of adrenalin. Such an effect would be transient, but it is possible that prolonged mental strain might, by the same mechanism, cause diabetes. This would explain the common development of diabetes in times of stress. Any disturbance of function of the ductless glands which antagonize the pancreas may, if sustained, cause true diabetes. Glycosuria occurring, for example, in hyperthyroidism, cannot therefore be dismissed as unimportant.

Summary of Differential Diagnosis of Glycosuria

1. The importance of routine examination of the urine is stressed.
2. If sugar is found, it must first be identified as glucose.
3. If glycosuria is accompanied by hunger, thirst, polyuria, loss of weight and lassitude, the diagnosis is diabetes mellitus.
4. Recurrent septic infections, cataract or retinitis, pulmonary tuberculosis or other well-known complications of diabetes, should always call for an examination of the urine.
5. Inconstant glycosuria in a healthy young adult is probably due to a low renal threshold for sugar. This should be confirmed by a glucose tolerance test.
6. If glycosuria only follows a heavy carbohydrate meal, and there are no diabetic symptoms, the possibility of a low carbohydrate tolerance must be confirmed, and distinguished from renal glycosuria, by a glucose tolerance test.
7. Signs of raised intracranial pressure, or localizing cerebral signs, or evidence of meningitis or subarachnoid haemorrhage in a case of glycosuria, should suggest that the latter is only incidental.
8. In every case of glycosuria it is important to exclude hyperthyroidism, acromegaly or other endocrine disorder which might explain this symptom without the presence of true diabetes.

Part II. The Treatment of Glycosuria

Glycosuria being only a symptom, treatment must be directed towards its underlying cause;

the principles of treatment being understood, the detailed management will depend upon the special features of each individual case.

I. Diabetes Mellitus

The diagnosis being certain, the ideal procedure is initially to stabilize each case under hospital conditions. The essential points are:

1. Permanent elimination from the urine of every trace of acetone, with due attention to the detection and treatment of focal infections.

2. Arrest, or reduction to a minimum, of the loss of sugar in the urine.

These aims are fulfilled by giving a diet containing sufficient carbohydrate to prevent the formation of acetone bodies and, if necessary, insulin to enable the patient to utilize this carbohydrate.

Diet

In planning the diet and mode of life of a stabilized patient, it should be remembered that 'a happy diabetic is better than a sugar-free man.' It is best to work with key diets devised by a specialist in dietetics. The following diets would be suitably balanced:

Calories	Carbohydrate (gms.)	Protein (gms.)	Fat (gms.)
1,500	120-150	80	60-70
1,750	170	80	80
2,000	200	80	90
2,250	248	80	100

The patient's calorie requirements can be judged sufficiently from his general appearance. A big, active man will need at least 2,300, a sedentary worker 2,000, most women 1,750 and some small people 1,500. Children, especially adolescents, need proportionately more calories and more protein. The vitamin content of the diet should be adequate, particularly as regards vitamins B₁ and C.

The patient should be taught how to weigh out his diet and, when balanced, he should continue to do this regularly on one day a week.

During stabilization, it is impossible to decide whether a given case will prove to be mild or severe until the reaction to treatment can be seen. It is therefore better to begin with a strict regime and then to slacken, rather than to begin leniently and increase

restrictions later, when the patient will be less amenable.

Balancing

During stabilization, the patient should be allowed as much normal activity as possible, if complications are absent and ketosis slight.

Supposing that the diet needed is one of 2,000 calories, one would start by giving a 1,500 calorie diet; the following day, specimens of urine are obtained half-an-hour before and two hours after each of the three main meals: breakfast, midday meal and supper. Each specimen is tested for sugar and acetone and treatment is determined by these results. If acetone is present in any specimen in more than a trace, insulin should be started.

Details of insulin dosage will be given later.

At the end of a week, the calorie value of the diet is increased and the insulin dosage increased if necessary. Insulin will be needed permanently in every case showing persistent acetonuria and also when glycosuria of more than a moderate degree is continued.

Provided that the patient's renal threshold for glucose be known as a result of an initial glucose tolerance test, it is not necessary to make repeated blood sugar estimations during treatment. When the patient is thought to be balanced, this may be confirmed by four-hourly estimations of the blood sugar during one day, e.g., at 8 a.m., 12 noon, 4 p.m. and 8 p.m.

Insulin

If the urine picture during stabilization shows the need for insulin, it is best to start by giving 5-10 units of soluble insulin at 6 a.m., 12 noon and 6 p.m. (half-an-hour before each meal). After four days the urine picture is reviewed and as long as acetonuria persists, each dose of insulin is increased by five units. When acetone has disappeared and only sugar remains, it is best to allow a week for spontaneous improvement before making any further increase in insulin dosage. Week by week, the diet is increased until the patient is receiving his correct number of calories, the insulin being concurrently increased until the urine picture is satisfactory.

Whenever possible, the total dose of insulin should finally be given as a single injection.

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before breakfast of Protamine Zinc insulin or Globin insulin combined with soluble insulin. Thus if a patient is balanced on soluble insulin, 25, 20 and 25 units, this can be replaced by P.Z. insulin 40 units and soluble insulin 25 units each morning, the results being checked and dosage adjusted by urine and blood sugar tests.

A diabetic is considered to be balanced when he is receiving his full complement of calories and not more than two of the six urine specimens of the day contain sugar.

Before leaving hospital, the patient should be able to give his own insulin, test his own urine and understand the nature of his complaint and its chief risks, including hypoglycaemia.

Diabetes is an outstanding example of the need to study the patient as well as his disease. Most diabetics are fairly intelligent and appreciate the fact that their future health will depend largely upon their own co-operation. It is important to inculcate the idea that, with his diet and insulin maintained in order, a diabetic can live as a normal man and is not in any way to be considered as an invalid.

Routine care and observation should be maintained at fortnightly and, later, monthly intervals. Children may need to be seen more often.

Diabetic Coma

Immediate treatment is needed for:

I. *Ketosis*. Any causative infection must be found and treated. Adequate therapy must be given with glucose and soluble insulin, if necessary, by the intravenous route. The initial dose should be 50 units of soluble insulin and 50 gm. of glucose, repeated 2-4 hourly as indicated by the urine picture. Some cases need as much as 1,000 units of insulin, covered by glucose, in the first 24 hours.

II. *Dehydration*. Fluid and salt loss should be made good by giving normal saline intravenously and by mouth without delay. Six pints may be needed by slow drip over two hours or longer.

III. *Circulatory failure*. Whether it be established or only threatening, this most serious complication needs warmth, absolute rest and circulatory stimulants, e.g.,

Strophanthin gr. 1/100 subcutaneously.	
Coramine 1-2 c.c.,	„
Caffeine, gr., 3,	„
Adrenalin m. 3,	„

IV. *Constipation* is treated by enema or aperient. Drastic purgation may cause collapse.

Subsequent stabilization will be necessary.

Alimentary Glycosuria

These cases can usually be controlled by reducing the total amount of carbohydrate in the day's diet and dividing what is allowed equally between the four meals taken. The patient should be seen at regular intervals in case diabetes supervenes, especially if he or she be over middle age.

II. Renal Glycosuria

These patients should be kept on a suitably planned diet, in which the carbohydrate content must be kept in the neighbourhood of 150-180 gm. per day, equally divided between four meals. The calorie value should be made good by extra protein and fat. If glycosuria be not minimized in these patients, they tend to develop furunculosis and local pruritus.

III. Glycosuria of Cerebral Origin

Treatment in each case is directed to the causative disease.

IV. Endocrine Glycosuria

I. *Generalized lesions of the pancreas*

The possibility of a syphilitic fibrosis may have to be considered. If the Wassermann reaction is found to be positive, the appropriate treatment must be given.

In pancreatitis of the chronic type, the diet

should be planned so that the patient receives no more protein and fat than he can digest. Carbohydrate should be given, as far as possible, as sugar, not as starch. In severe pancreatitis and in haemochromatosis, insulin therapy will be needed.

In pancreatic neoplasm the treatment is surgical.

II. *Hyperthyroidism*. The glycosuria is usually controlled by adequate treatment of the thyroid condition. Since these patients have

a raised metabolism, it is unwise to restrict their intake of carbohydrate.

III. *Acromegaly and pituitary basophilism*

Treatment is by surgical measures when possible or by radiotherapy. The carbohydrate intake should not be unduly restricted pending treatment.

IV. *Suprarenal disease*

The paroxysmal hyperglycaemia associated with the hypersecretory adenoma of the medulla is cured if the tumour can be removed.

NERVE SUTURE

By J. H. KIRKHAM, M.B., CH.B., F.R.C.S.(Ed.)

As there are no means yet available by which we can accelerate the regeneration of nerves after their division, it follows that the best results can be attained only by so repairing the site of division that conditions are optimum for the natural downgrowth of the axons from the proximal end to the periphery.¹

It will be seen by anyone who has attempted nerve suture that the usual method of end-to-end suture, by fine sutures through the sheath only, tends to cause a bunching up of the axons at the site of approximation and, in addition, a varying number of axons from both distal and proximal ends protrude through the line of anastomosis (Fig. 1).

The axons which protrude from the proximal end will naturally become lost in the surrounding tissues, and can never function again. Those which protrude from the distal end will cause loss of the tubes of connective tissue and Schwann cells, by which means alone the downgrowing axons from the proximal end can attain their peripheral destinations, as the entrances to the tubes now lie outside the nerve sheath.

This loss of the possible number of axons which can ever reach the periphery must appreciably affect the perfection of the final result.

In order to obviate this, the following method has been adopted, and although the opportunity for its employment has arisen in only two cases, the final results have been so near perfection that I consider the method worthy of extended trial. It may be applied to both primary and secondary nerve suture, although both the above cases were primary sutures.

The nerve ends having been identified, they are first trimmed square, preferably with very sharp-pointed scissors in a primary suture or a razor blade held in artery forceps in a secondary suture, as this causes minimal trauma. No instrument is used to hold the nerve itself, and the sheath is best held in fine conjunctival fixation forceps, or better still, iris forceps. The delicacy of touch required for the operation is equivalent to that necessary for the majority of ophthalmological operations.

The distal end of the sheath is then incised longitudinally for about $\frac{1}{8}$ in. at points diametrically opposite to each other, the two halves then being very carefully dissected from the underlying nerve fibres and reflected distally as two cuffs of sheath. It will then be possible to cut back the nerve fibres $\frac{1}{8}$ in. further distally than the end of the sheath, thus leaving an empty tube of sheath $\frac{1}{8}$ in.