ABC of Diabetes

PETER J WATKINS

WHAT IS DIABETES?

Ebers papyrus: early clinical description of diabetes.

Diabetes occurs either because of a lack of insulin or because of the presence of factors that oppose the action of insulin. The result of insufficient action of insulin is an increase in blood glucose concentration (hyperglycaemia). Many other metabolic abnormalities occur, notably an increase in ketone bodies in the blood when there is a severe lack of insulin.

Diagnosis

Blood glucose levels diagnostic of diabetes

Fasting ≥ 8 mmol/l

Random > 11 mmol/l

The diagnosis of diabetes must always be established by measuring blood glucose, although glycosuria nearly always indicates diabetes. Fasting blood glucose concentrations greater than 8 mmol/l and random blood glucose concentrations greater than 11 mmol/l are clearly diagnostic of diabetes; and fasting values less than 6 mmol/l or random levels less than 8 mmol/l exclude diabetes.

Glycosuria usually occurs when blood glucose values are greater than 10 mmol/l but this threshold varies considerably between individuals and increases with age. Only if blood glucose concentrations are borderline and there is cause for doubt about the presence of diabetes should a glucose tolerance test be performed.

Glucose tolerance test

	Glucose concentration (mmol/l)		
	Venous whole blood	Capillary whole blood	Venous plasma
<i>Diabetes mellitus*</i>			
Fasting	≥ 7	≥ 7	≥ 8
2 hours after glucose load	≥ 10	≥ 11	≥ 11
<i>Impaired glucose tolerance†</i>			
Fasting	< 7	< 7	< 8
2 hours after glucose load	$7 - < 10$	$8 - 1 < 11$	$8 - < 11$

*In the absence of symptoms at least one additional abnormal blood glucose is needed to confirm clinical diagnosis—for example, 1-hour value of 11 mmol/l.

†Patients with impaired glucose tolerance are managed at the discretion of the physician. In general, no treatment is given to elderly people but diet and weight reduction are advisable in younger subjects. Pregnant women with "impaired glucose tolerance" must be treated as if they were diabetic.

For reliable results a glucose tolerance test should be performed in the morning after an overnight fast with the patient sitting quietly and not smoking; it is also important that he should have had normal meals for the last three days and should not have been dieting. False results may also occur if the patient has been ill recently or has had prolonged bed rest. Blood glucose concentrations are measured fasting and then every half an hour (for two hours) after a drink of 75 g of glucose in 250-350 ml water (in children 1.75 g/kg to a maximum of 75 g), preferably flavoured—for example, with pure lemon juice. Urine tests should be performed before the glucose drink and at one and two hours. Interpretation of blood glucose values according to WHO criteria is shown.

2-hour blood glucose during
75-g glucose tolerance test

Glucose tolerance tests may also show:

Renal glycosuria, when there is glycosuria but normal blood glucose values; this is a benign condition, only rarely indicating unusual forms of renal disease. It is worth issuing these patients a "certificate" to prevent them from being subjected to repeated glucose tolerance at every medical examination.

A steeple or lag curve, when fasting and 2-hour concentrations are normal but those between are high, causing glycosuria; this is also a benign condition which most commonly occurs after gastrectomy but may occur in healthy people.

Types of diabetes

Diabetes associated with other conditions, and rare syndromes.

All the following may be insulin or non-insulin-dependent:

Pancreatic disease—pancreatectomy, pancreatitis, haemochromatosis, carcinoma of pancreas.

Hormone-induced diabetes—acromegaly, Cushing's syndrome, pheochromocytoma, glucagonoma.

After burns or other severe illness (usually temporary, see latent diabetes).

Drug-induced diabetes—corticosteroid drugs and ACTH, especially in large doses; diazoxide. Thiazide diuretics and the oral contraceptive pill have a weak effect on carbohydrate tolerance.

Lipoatrophic diabetes—associated with complete absence of fat from all tissues, subcutaneous and elsewhere.

Insulin receptor abnormalities, including conditions due to insulin-receptor antibodies.

Incorrectly synthesised proinsulin and insulin

Genetic syndromes—(a) recessive inheritance. Rare families developing insulin-dependent diabetes according to a recessive pattern. Other features are associated, namely diabetes insipidus, optic atrophy causing blindness, and high-tone deafness—the DI DM OA D syndrome; (b) other hereditary syndromes.

Although all types of diabetes have hyperglycaemia in common, the causes vary, as does treatment and long-term outlook. Nearly all diabetics have "primary" diabetes, and most of the other syndromes and associations shown in the table are rare.

Primary diabetes mellitus is of two types: insulin-dependent diabetes non-insulin-dependent diabetes.

This division is important clinically in assessing the need for treatment and in understanding the causes of diabetes, which are different in the two groups. Nevertheless, although most patients can be clearly distinguished as having one type of diabetes or the other, some non-insulin-dependent diabetics come to need insulin for good health, if not survival, and this does to some extent blur the edges of an apparently simple classification.

Other terms

Gestational diabetes—diabetes which is diagnosed during pregnancy but remits afterwards.

Latent diabetes—in patients known to have been previously diabetic but who are now normal.

Potential diabetes—in those at special risk of becoming diabetic for various reasons—strong family history, bad obstetric history (unexplained fetal death), or very large babies at birth.

Insulin-dependent diabetes

An islet with lymphocytic infiltration.

Insulin-dependent diabetes is due to damage to and eventual loss of the B cells of the pancreatic islets of Langerhans with resulting loss of insulin production. The agent that damages the islets is not known; in some cases it may be a virus; in others the damage may be due to autoimmunity. Islet-cell antibodies have been identified, though their precise role is not known.

The incidence of Addison's disease, thyroid disease, and pernicious anaemia are increased in insulin-dependent diabetics, and appear to occur especially in those with persisting islet-cell antibodies.

Insulin-dependent diabetes is not directly inherited, though individuals may inherit a predisposition in that those with certain HLA types show increased susceptibility to this type of diabetes. Only about half the pairs of identical twins with insulin-dependent diabetes are concordant for diabetes; among the rest one of the pair is diabetic and the other is not.

Non-insulin-dependent diabetes

Non-insulin-dependent diabetics secrete insulin, and their serum insulin concentrations may be diminished, normal, or even increased. The cause of the diabetes is unknown; several factors are implicated and there is increasing interest in neural mechanisms of metabolic control, which may be at fault.

The best-known association is with obesity; women who have had large babies or large families are also more prone to develop this type of diabetes later in life. In many of these cases there is a strong genetic component, unrelated to the HLA system, and sometimes a strong family history of diabetes. In some families this follows a dominant pattern of inheritance: the diabetes is always non-insulin-dependent, even among the young, and these patients seem to be less prone to long-term complications (Mason-type diabetes). Most of the diabetics in these families show a chlorpropamide alcohol flush. Identical twins are almost always concordant for non-insulin diabetes—that is, both members of the pair are diabetic.

Insulin dependent	Non-insulin dependent
Inflammatory reaction in islets	No insulinitis
Islet B cells destroyed	B cells function
Islet cell antibodies	No islet cell antibodies
HLA related	Not HLA related
Not directly inherited	Strong genetic basis (some cases)

Risks of inheriting diabetes

A child of an insulin-dependent mother or father has an increased risk of developing the same type of diabetes before he is 20, but the risk is still small—probably about 1%. If both have insulin-dependent diabetes the risk is increased by an uncertain amount; though the risk is probably not too serious, these rare couples would be wise to seek genetic counselling.

Prevalence

In Great Britain 1-2% of the population have diabetes—about half are known to have the condition and the rest can be found by population studies. Among schoolchildren about 2 in 1000 have diabetes.

Diabetes can occur at any age. Non-insulin-dependent diabetes is most common after middle age and occurs most often at 50-70 years of age. The peak incidence of insulin-dependent diabetes is at 10-12 years. Nevertheless, elderly people can also be insulin dependent and a few children are non-insulin dependent.

Overall more women than men have diabetes, but under 30 years of age there is a slight male predominance.

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The illustration of an islet cell was reproduced, by permission of Professor W Gepts, from *Insulin: Islet Pathology, Islet Function, Insulin Treatment*, ed Rolf Luft, published by Nordisk Insulinlaboratorium; that of Mason-type diabetes from Tattersall RB. *Q J Med* 1974;43:339-57; and the prevalence chart from Malins JM. *Clinical Diabetes Mellitus* published by Eyre and Spottiswoode.