CHAPTER 1

Diagnosing Diabetes

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OVERVIEW

- Diabetes produces a variety of clinical presentations, from acute to gradual onset
- Currently, the diagnosis should be based on two separate tests unless the patient is clearly symptomatic in which case only one positive test is required
- New World Health Organization diagnostic criteria based on glycosylated haemoglobin are expected in the near future
- A combination of genetic and environmental factors contribute to the risk of diabetes
- Impaired glucose regulation is an important risk factor both for future diabetes and cardiovascular disease
- Distinction between random and fasting samples is essential in interpreting the significance of borderline blood glucose levels
- Impaired glucose tolerance can only be diagnosed by oral glucose tolerance test

Introduction

Diabetes mellitus is a common metabolic disorder that is defined by chronic hyperglycaemia. Besides symptoms related to hyperglycaemia itself such as thirst, polyuria and weight loss, it may also cause potentially life-threatening acute hyperglycaemic emergencies. It is a major cause of morbidity and premature mortality from long-term complications such as cardiovascular disease, blindness, renal failure, amputations and stroke. With good control of hyperglycaemia established early on and continued life-long, an individual with diabetes can enjoy a good quality of life and reduce the risk of these long-term complications that are so detrimental to their life and wellbeing.

Prevalence of diabetes

In the United Kingdom we have an estimated 1.8 million people with diabetes. However, based on screening studies it is believed that up to a million more may be undiagnosed (see pages 15 and 17).

ABC of Diabetes, 6th edition. By T. Holt and S. Kumar.
Published 2010 by Blackwell Publishing.

The prevalences of both type 1 and type 2 diabetes are increasing. Type 2 diabetes is increasing far more rapidly, driven by increasing life expectancy and the epidemic of obesity. It is believed that there will be as many as 300 million people with diabetes worldwide by the year 2025. Most of this increase will occur in developing countries. The majority of children have insulin-requiring type 1 diabetes, whilst the vast majority of those aged >25 years will have type 2 diabetes (Figure 1.1).

Types of diabetes

The types of diabetes have been classified by the WHO. Type 1 diabetes (previously referred to as insulin-dependent diabetes mellitus or IDDM) is due to absolute insulin deficiency and is usually an autoimmune disease leading to the destruction of the insulin-secreting beta cells in the pancreas. In some cases the cause of destruction of the beta cells is not known.

Type 2 (previously known as non-insulin dependent diabetes mellitus or NIDDM) results from relative insulin deficiency that may be associated with varying degrees of insulin action defects known collectively as insulin resistance.

For a practising clinician the implication of this diagnosis is that patients with type 1 diabetes require insulin straight away and insulin should not be stopped as it is life-preserving. Type 2 patients can progress through several stages and may require insulin later on in their disease.

Risk factors for diabetes

Genetics. Genetic susceptibility is important for both types of diabetes. Family history of type 1 diabetes or other autoimmune diseases such as autoimmune thyroid disease is associated with a higher risk of developing type 1 diabetes in the family. Inheritance in type 2 diabetes is far more complex as there are many underlying causes. Furthermore, the risk varies according to the particular sub-type of type 2 diabetes. A family history of type 2 diabetes in a first degree relative is a strong risk factor for diabetes in that individual.

Obesity. Apart from family history, obesity is a very important risk factor for diabetes. For a given degree of obesity, central or 'apple-shaped' obesity is associated with a much higher risk of

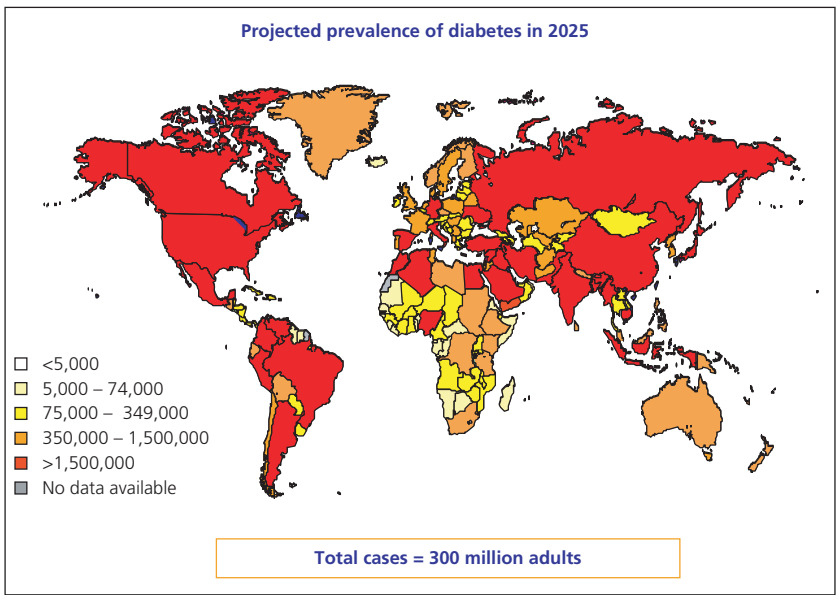

Figure 1.1 Projected prevalence of diabetes in 2025. Reproduced with permission from the World Health Organisation. The World Health Report. Life in the 21st Century: a vision for all. Geneva: WHO, 1998.

progression to type 2 diabetes than those who have lower body obesity or are 'pear-shaped'. Those with a body mass index (BMI) of >25 k/m^2 or high waist circumference (Table 1.1) are at a higher risk of developing diabetes and should be encouraged to take regular exercise and eat healthily (Figure 1.2).

Age. Beta cell function declines with age, indeed if we live long enough all of us have the potential to develop diabetes at some stage. With an aging population an increase in prevalence of diabetes can be expected.

Ethnicity. People of South Asian or Afro-Caribbean origin are at higher risk of developing diabetes. They are also more likely to have type 2 diabetes presenting at a young age and usually have poorer risk factor control. South Asian patients have a high risk of developing diabetic renal disease and also coronary artery disease. Afro-Caribbean patients are more likely to have strokes and have a higher risk of gestational diabetes. South Asian and Hispanic children may develop type 2 diabetes.

Table 1.1 The International Classification of adult underweight, overweight and obesity according to BMI (adapted from WHO guidelines, http://apps.who.int/bmi/index.jsp?introPage=intro_3.html)

	BMI(kg/m^2)	
Classification	**Principal cut-off points**	**Additional cut-off points**
Underweight	<18.50	<18.50
Normal range	18.50–24.99	18.50–22.99
		23.00–24.99
Overweight	≥25.00	≥25.00
Pre-obese	25.00–29.99	25.00–27.49
		27.50–29.99
Obese	≥30.00	≥30.00
Obese class I	30.00–34.99	30.00–32.49
		32.50–34.99
Obese class II	35.00–39.99	35.00–37.49
		37.50–39.99
Obese class III	≥40.00	≥40.00

Source: Adapted from (WHO 1995, 2000, 2004).

Initial presentation and diagnosis

The commonest presentation is tiredness, thirst, polyuria, weight loss, pruritus vulvae or balanitis. It is not uncommon for this

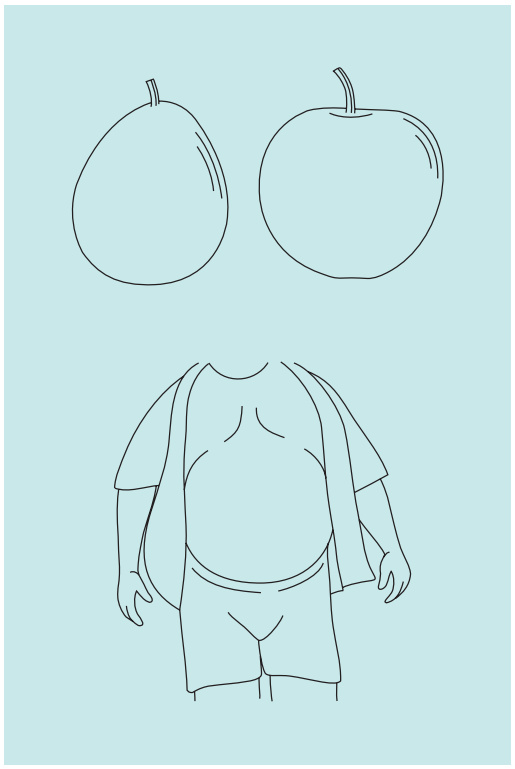

Figure 1.2 'Apple'-shaped fat distribution (central obesity with intra-abdominal adiposity) carries a higher cardiovascular and diabetes risk than 'pear'-shaped fat distribution.

diagnosis to be missed for years, and a significant proportion of those with type 2 diabetes remain undiagnosed. Insidious symptoms mean that the patients generally tend to ignore them. This is one reason why complications are often seen at diagnosis in patients with type 2 diabetes. A number of cases with type 2 diabetes are now diagnosed at insurance examinations or through opportunistic testing when the patient has presented for some other problem to the general practice or hospital.

The diagnosis of diabetes must not be taken lightly by a clinician as the consequences for the individual are significant and life-long. For those presenting with severe symptoms, evidence of long-term complications or severe hyperglycaemia at presentation, the diagnosis is quite straightforward and can be made using only one diagnostic blood glucose measurement. In asymptomatic individuals presenting with mild hyperglycaemia, the diagnosis should only be established on the basis of at least two abnormal test results. In future, the recently published recommendation is that HbA1c values will be used rather than plasma glucose as it has been in the past (Box 1.1).

Box 1.1 **Recommendation of the International Expert Committee**

For the diagnosis of diabetes:

- The HbA1c assay is an accurate, precise measure of chronic glycaemic levels and correlates well with the risk of diabetes complications.
- The HbA1c assay has several advantages over laboratory measures of glucose.
- Diabetes should be diagnosed when HbA1c is ≥6.5%. Diagnosis should be confirmed with a repeat HbA1c test. Confirmation is not required in symptomatic subjects with plasma glucose levels ≥11.1 mmol/l.
- If HbA1c testing is not possible, previously recommended diagnostic methods (e.g. FPG or 2 hour OGTT, with confirmation) are acceptable.
- HbA1c testing is indicated in children in whom diabetes is suspected but the classic symptoms and a casual plasma glucose ≥11.1 mmol/l are not found.

For the identification of those at high risk for diabetes:

- The risk for diabetes based on levels of glycemia is a continuum; therefore, there is no lower glycemic threshold at which risk clearly begins.
- The categorical clinical states pre-diabetes, IFG, and IGT fail to capture the continuum of risk and will be phased out of use as HbA1c measurements replace glucose measurements.
- Those with HbA1c levels below the threshold for diabetes but ≥6.0% should receive demonstrably effective preventive interventions. Those with HbA1c below this range may still be at risk and, depending on the presence of other diabetes risk factors, may also benefit from prevention efforts.

(Adapted from: The International Expert Committee. International Expert Committee Report on the role of the HbA1c assay in the diagnosis of diabetes. *Diabetes Care* 2009;32:1327–34; 2009)

Glucose tolerance test

A glucose tolerance test should be performed in the morning after an overnight fast. It is important that the patient should have had a normal diet for the preceding 3 days and should not restrict carbohydrate intake drastically. The test should also not be performed during an acute illness or following prolonged bedrest. Plasma glucose concentrations are measured fasting and then 2 hours after a drink of 75 g of glucose in 250–350 ml of water (in children: 1.75 g/kg up to maximum of 75 g). Several proprietary preparations are available and these are often flavoured to make items palatable. Table 1.2 shows normal values and interpretation of abnormal values during an oral glucose tolerance test (OGTT). The role of oral glucose tolerance tests is set to change given the recent recommendations over the use of HbA1c as a preferred means of diagnosing diabetes (Box 1.1).

Interpretation of the oral glucose tolerance test results

Impaired fasting glycaemia (IGF)

Fasting glucose between 6.1 and 6.9 mmol/l in the absence of abnormal values after the glucose load is defined as impaired fasting glycaemia. Conversion to diabetes is not invariable but it is important to reassess once a year, and in future this is likely to be through HbA1c measurement (see Box 1.1). Individuals with IFG should be advised about a healthy life-style and to avoid obesity.

Impaired glucose tolerance (IGT)

Once again conversion to diabetes is not invariable and patients may either persist with impaired glucose tolerance, revert to normal glucose tolerance or progress to type 2 diabetes. Obese individuals should be advised to try and lose weight through diet and exercise. The implications of this diagnosis for pregnancy are different and this is considered further in Chapter 17.

IGF and IGT are collectively known as *impaired glucose regulation* but these terms may become outdated as HbA1c becomes the recommended means of diagnosing diabetes and identifying those at risk (see Box 1.1).

Diabetes mellitus

A fasting glucose of greater than or equal to 7.0 mmol/l or a 2-hour glucose value of greater than or equal to 11.1 mmol/l suggests

Table 1.2 WHO criteria for the diagnosis of diabetes mellitus based on venous plasma samples.

	Fasting (mmol/l)	2-hour sample following oral glucose challenge (mmol/l) in OGTT
Normal	<6.1	<7.8
Impaired fasting glycaemia (IFG)	6.1–6.9	<7.8
Impaired glucose tolerance (IGT)	<7.0	7.8–11.0
Diabetes mellitus	≥7.0	≥11.1

Table 1.3 Conversion of DCCT aligned HbA1c measurements to the new IFCC standard.

HbA1c	
DCCT aligned (%)	**IFCC (mmol/mol)**
4	20
5	31
6	42
6.5	48
7	53
7.5	59
8	64
9	75
10	86
11	97
12	108

diabetes, but in future this will be based on HbA1c (Box 1.1). The glucose tolerance test does not indicate the type of diabetes, this is usually determined on the basis of other presenting features and is discussed further below. Young age at presentation (especially less than 17 years), presence of other autoimmune endocrine diseases (such as hypothyroidism, pernicious anaemia, Addison's disease, vitiligo) in the patient or family members, or significant weight loss are features that suggest type 1 diabetes.

Diabetes in children

Abnormal blood glucose readings in a child or adolescent up to the age of 17 years should be taken seriously as they may have type 1 diabetes and it is important to avoid delay in treatment, especially when they present with very high blood glucose levels. In those with mild hyperglycaemia or where there is doubt, HbA1c should be measured (see Box 1.1).

New units for reporting HbA1c (glycosylated haemoglobin)

Diagnosing diabetes has in the past been based on blood glucose values, but this is likely to change in the near future to a definition based on glycosylated haemoglobin (HbA1c). The measurement of HbA1c has required standardisation of reporting across the world. Table 1.3 gives a chart for converting the older DCCT aligned units (%) to the new International Federation of Clinical Chemistry (IFCC) units (mmol/mol).

Identifying patients in need of insulin or urgent referral to hospital

Insulin is life-saving in those with type 1 diabetes and is also indicated in all patients with marked hyperglycaemia or significant weight loss particularly if ketosis is detected in the urine or blood. Children are much more likely to have type 1 diabetes. Any form of hyperglycaemia in pregnancy is also an indication for insulin. Patients who fail to achieve adequate glycaemic control on oral agents should also be given insulin. A patient who is unable to eat and drink normally and has marked hyperglycaemia due to a concomitant illness will require insulin and may need to be seen in hospital urgently.

Metabolic syndrome

Type 2 diabetes, hypertension, dyslipidaemia and central obesity often present in the same individual. This clustering of chronic risk factors has been called the metabolic syndrome. Therefore, the presence of central obesity, hypertension or dyslipidaemia should prompt the clinician to look for diabetes. It should be noted that the majority of patients with metabolic syndrome do not yet have overt type 2 diabetes but may have either undiagnosed diabetes or impaired glucose tolerance. It is here that the concept of metabolic syndrome is particularly useful. As patients with diabetes should have other cardiovascular risk factors treated intensively anyway, identifying metabolic syndrome in such patients may not alter management.

Delaying the onset of type 2 diabetes

In those identified as being 'at risk', life-style changes to increase physical activity and a diet with modest calorie restriction, less saturated fat and more dietary fibre can significantly reduce the rate at which impaired glucose tolerance progresses to type 2 diabetes. It has been demonstrated that even older people can successfully undertake the life-style programmes required. This is discussed in more detail in Chapter 4.

Further reading

DECODE Study Group. Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and non-cardiovascular diseases? *Diabetes Care* 2003;**26**:688–96.

Freemantle N, Holmes J, Hockey A, Kumar S. How strong is the association between abdominal obesity and the incidence of type 2 diabetes? *Int J Clin Pract* 2008;**62**:1391–6.

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