Diabetes Mellitus

Diabetes mellitus is a disease caused by deficiency or diminished effectiveness of endogenous insulin. It is characterised by hyperglycaemia, deranged metabolism and sequelae predominantly affecting the vasculature. The main types of diabetes mellitus are:

- **Type 1 diabetes mellitus**: results from the body's failure to produce sufficient insulin.
- **Type 2 diabetes mellitus**: results from resistance to the insulin, often initially with normal or increased levels of circulating insulin.
- **Gestational diabetes**: pregnant women who have never had diabetes before but who have high blood glucose levels during pregnancy are said to have gestational diabetes. Gestational diabetes affects about 4% of all pregnant women. It may precede development of type 2 (or rarely type 1) diabetes.
- **Maturity-onset diabetes of the young (MODY)** includes several forms of diabetes with monogenetic defects of beta-cell function (impaired insulin secretion), usually manifesting as mild hyperglycaemia at a young age and usually inherited in an autosomal-dominant manner.\(^1\)
- **Secondary diabetes**: accounts for only 1-2% of patients with diabetes mellitus. Causes include:
  - Pancreatic disease: cystic fibrosis, chronic pancreatitis, pancreatectomy, carcinoma of the pancreas.
  - Endocrine: Cushing's syndrome, acromegaly, thyrotoxicosis, phaeochromocytoma, glucagonoma.
  - Drug-induced: thiazide diuretics, corticosteroids, atypical antipsychotics, antiretroviral protease inhibitors.
  - Congenital lipodystrophy.
  - Acanthosis nigricans.
  - Genetic:
    - Wolfram's syndrome (which is also referred to as DIDMOAD: diabetes insipidus, diabetes mellitus, optic atrophy and deafness).\(^2\)
    - Friedreich's ataxia.
    - Dystrophia myotonica.
    - Haemochromatosis.
    - Glycogen storage diseases.

Some patients with type 2 diabetes require insulin, so the old terms of insulin-dependent diabetes mellitus (IDDM) for type 1 diabetes and non-insulin-dependent diabetes mellitus (NIDDM) for type 2 diabetes are inappropriate. Type 2 diabetes is increasingly diagnosed in children and adolescents and so the old term maturity-onset diabetes for type 2 diabetes is also inappropriate.

### Type 1 diabetes mellitus

The development of type 1 diabetes mellitus is based on a combination of a genetic predisposition and an autoimmune process that results in gradual destruction of the beta cells of the pancreas, leading to absolute insulin deficiency. There is usually a pre-diabetic phase where autoimmunity has already developed but with no clinically apparent insulin dependency. Insulin autoantibodies can be detected in genetically predisposed individuals as early as 6-12 months of age.\(^3\)

Possible triggers for the process may include viruses, dietary factors, environmental toxins, and emotional or physical stress. Early cessation of breast-feeding has also been linked to increased risk of developing type 1 diabetes, but the association is unproven and controversial.\(^4\)

- Approximately 15% of those with diabetes have type 1 diabetes - usually juvenile-onset, but it may occur at any age. It may be associated with other autoimmune diseases. It is characterised by insulin deficiency.
There is 30-50% concordance in identical twins and a positive family history in 10% of people with type 1 diabetes. Screening for the diagnosis of diabetes in first-degree relatives of patients with type 1 is therefore reasonable, keeping in mind that the absolute risk is quite low. Associated with HLA DR3 and DR4 and islet cell antibodies around the time of diagnosis. Patients always need insulin treatment and are prone to ketoacidosis. The most at-risk population for type 1 diabetes is Caucasian of northern European ancestry. Incidence is high in Scandinavian people.

**Type 2 diabetes mellitus**

- Approximately 85% of those with diabetes; they are usually older at presentation (usually >30 years of age) but it is increasingly diagnosed in children and adolescents.
- Type 2 diabetes is associated with excess body weight and physical inactivity.
- All racial groups are affected but there is increased prevalence in people of South Asian, African, African-Caribbean, Polynesian, Middle-Eastern and American-Indian ancestry.
- It is caused by impaired insulin secretion and insulin resistance and has a gradual onset.
- Those with type 2 diabetes may eventually need insulin treatment.

**Epidemiology**

The increasing prevalence of diabetes worldwide has led to a situation where approximately 360 million people had diabetes in 2011, of whom more than 95% would have had type 2 diabetes. This number is estimated to increase to 552 million by 2030 and it is thought that about half of those will be unaware of their diagnosis.\(^5\)

**Risk factors for type 2 diabetes\(^6\)**

- Obesity, especially central (truncal) obesity.
- Lack of physical activity.
- Ethnicity: people of South Asian, African, African-Caribbean, Polynesian, Middle-Eastern and American-Indian descent are at greater risk of type 2 diabetes, compared with the white population.
- History of gestational diabetes.
- Impaired glucose tolerance.
- Impaired fasting glucose.
- Drug therapy - eg, combined use of a thiazide diuretic with a beta-blocker.
- Low-fibre, high-glycaemic index diet.
- Metabolic syndrome.
- Polycystic ovary syndrome.
- Family history (2.4-fold increased risk for type 2 diabetes).
- Adults who had low birth weight for gestational age.
- Statins have been associated with a small, but statistically significant risk of new-onset diabetes.

Patients with risk factors for developing diabetes mellitus may be at higher risk. This risk is likely outweighed by the benefits of reducing cardiovascular risk.\(^7\)

**Presentation**

- Patients with all types of diabetes may present with polyuria, polydipsia, lethargy, boils, pruritus vulvae or with frequent, recurrent or prolonged infections.
- Patients with type 1 diabetes may also present with weight loss, dehydration, ketonuria and hyperventilation. Presentation of type 1 diabetes tends to be acute with a short duration of symptoms.
- Presentation in patients with type 2 diabetes tends to be subacute with a longer duration of symptoms.
- Patients with diabetes may present with acute or chronic complications, as outlined in the section 'Complications', below.

**Diagnosis**

- Diabetes may be diagnosed on the basis of one abnormal plasma glucose (random ≥11.1 mmol/L or fasting ≥7 mmol/L) in the presence of diabetic symptoms such as thirst, increased urination, recurrent infections, weight loss, drowsiness and coma.
- In asymptomatic people with an abnormal random plasma glucose, two fasting venous plasma glucose samples in the abnormal range (≥7 mmol/L) are recommended for diagnosis.
- Two-hour venous plasma glucose concentration ≥11.1 mmol/L two hours after 75 g anhydrous glucose in an oral glucose tolerance test (OGTT).
- The World Health Organization (WHO) now recommends that glycated haemoglobin (HbA1c) can be used as a diagnostic test for diabetes. An HbA1c of 48 mmol/mol (6.5%) is recommended as the cut-off point for diagnosing diabetes. A value less than 48 mmol/mol does not exclude diabetes diagnosed using glucose tests.[8] See also the separate Glycated Haemoglobin (HbA1c) article.

**Assessment and monitoring**

- Assessment: see the separate Assessment of the Patient with Established Diabetes article.
- Monitoring: see the separate Glycated Haemoglobin (HbA1c) and Self-Monitoring in Diabetes Mellitus articles.

**Management**

The management plan for a person with diabetes includes:[6]

- Diabetes education: structured education and self-management (at diagnosis and regularly reviewed and reinforced) to promote awareness.
- Diet and lifestyle: healthy diet, weight loss if the person is overweight, smoking cessation, regular physical exercise.
- Maximising glucose control while minimising adverse effects of treatment, such as hypoglycaemia.
- Reduction of other risk factors for complications of diabetes, including the early detection and management of hypertension, drug treatment to modify lipid levels and consideration of antiplatelet therapy with aspirin.
- Monitoring and early intervention for complications of diabetes, including cardiovascular disease, feet problems, eye problems, kidney problems and neuropathy.

A global assessment of an individual's cardiovascular risk is essential. See the separate Cardiovascular Risk Assessment article.

See the separate articles:

- Management of Type 1 Diabetes.
- Management of Type 2 Diabetes.
- The Patient with Newly-diagnosed Diabetes.
- Diabetes Diet and Exercise.
- Diabetes Education and Self-management Programmes.
- Antihyperglycaemic Agents used for Type 2 Diabetes.
- Insulin Regimens.
- Precautions with Patients with Diabetes Undergoing Surgery.
- Diabetes and Intercurrent Illness.
- Diabetes in Pregnancy.
- Gestational Diabetes.

**Acute complications**

- See Diabetic Ketoacidosis and Hyperosmolar Hyperglycaemic State.
- See Emergency Management of Hypoglycaemia.

**Chronic complications**

- Cardiovascular disease: see coronary heart disease (Stable Angina, Acute Coronary Syndrome), Cerebrovascular Events and Peripheral Arterial Disease.
- See Diabetic Nephropathy.
- See Diabetic Retinopathy and Diabetic Eye Problems.
- See Diabetic Neuropathy, Autonomic Neuropathy and Neuropathic Pain and its Management.
- See Diabetic Foot, Leg Ulcers and Painful Foot.
- Frequent, recurrent and persistent infections.
Prognosis

Type 1 diabetes\[9\]

- Many people with type 1 diabetes have good health but there is an increased risk of severe sight impairment, end-stage kidney disease, cardiovascular disease and, in some cases, early death.
- Controlling blood glucose, lipids, blood pressure and weight are important prognostic factors.

Type 2 diabetes\[6\]

- 75% of people with type 2 diabetes will die of heart disease and 15% of stroke.
- The mortality rate from cardiovascular disease is up to five times higher in people with diabetes than in people without diabetes.
- For every 1% increase in HbA1c level, the risk of death from a diabetes-related cause increases by 21%.

Prevention

Type 1: despite a great deal of ongoing research, there are currently no interventions before diagnosis that have shown any benefit.\[10, 11\]

There is now an emerging interest as to whether vaccination can be applied in autoimmune and inflammatory conditions. Vaccination may have a future role in the prevention of type 1 diabetes.\[12\]

Type 2: see the separate Prevention of Type 2 Diabetes article.

Further reading & references

- Diabetes; NICE
- Diabetes UK
- Diabetes in adults; NICE Quality Standard (August 2016)

1. Maturity-onset Diabetes of The Young; Online Mendelian Inheritance in Man (OMIM)
2. Wolfram Syndrome 1, WFS1; Online Mendelian Inheritance in Man (OMIM)
5. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD; European Heart Journal (2013)
6. Diabetes - type 2; NICE CKS, October 2015 (UK access only)
8. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus ; World Health Organization, 2011
9. Diabetes - type 1; NICE CKS, December 2014 (UK access only)

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