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On a global scale, there has been a startling rise of diabetes in developing countries in recent years, especially type 2. One theory is that this may be linked to the switch to a diet more typical of developed countries – that is, one rich in high glycaemic index foods (World Health Organization, 2016; Carrera-Bastos et al, 2011).

It is the most common endocrine disease; since 1980, prevalence has risen from 4.7% to 8.5% of the adult population (WHO, 2016).

For the UK show that there were around 3.2 million people with a diagnosis of diabetes in 2013. About 90% have the more common type 2 and 10% the rarer type 1 diabetes (National Institute for Health and Care Excellence, 2015).

Diabetes management 1: disease types, symptoms and diagnosis

Key points

1. The defining feature of diabetes is increased blood glucose (hyperglycaemia).

2. Type 1 diabetes is characterised by a lack of insulin production, type 2 by insulin resistance.

3. Gestational diabetes increases the risk of higher birth weight in the child and subsequent type 2 diabetes in the mother.

4. Warning signs of diabetes include polyuria, glycosuria, polydipsia, polyphagia, ketoacidosis, weight loss, lethargy and visual disturbances.

5. Diagnostic tests comprise the oral glucose tolerance test, measuring fasting or random blood glucose levels, and measuring glycated haemoglobin.

Authors John Knight is senior lecturer in biomedical science; Yamni Nigam is associate professor in biomedical science; Maria Andrade is senior lecturer in interprofessional studies; all at the College of Human Health and Science, Swansea University.

Abstract Insulin is the only major hormone that reduces blood glucose levels, so people with insulin resistance or impaired insulin production display hyperglycaemia, which is the defining feature of diabetes. The two most common forms are type 1 diabetes (an autoimmune disease where the immune system destroys the insulin-producing cells of the pancreas) and type 2 (characterised by gradual resistance to the effects of insulin). This article, the first of a three-part series on diabetes management, gives an overview of the different types of diabetes (including rarer forms), causes and triggers, symptoms and warning signs, and diagnostic tests.

blood glucose to supply extra energy to the muscles when the body prepares for immediate action;
- Cortisol: produced by the adrenal gland (cortex); released following prolonged stress or starvation. It increases the conversion of fat and protein into glucose and ketones such as acetone, which can be used in metabolism;
- Glucagon: produced by the alpha cells of the pancreas when blood glucose levels drop; it increases and maintains blood glucose between major meals and during sleep.

**The insulin response**

While several hormones increase blood glucose, only one major hormone has the opposite effect, that of reducing the amount of glucose in the blood: insulin. This is a small polypeptide hormone that is released directly into the blood and rapidly circulated to all areas of the body (Van-Putte et al, 2013). The insulin response (Fig 1) works as follows: after a meal rich in carbohydrates:
- Blood glucose levels rise quickly;
- Insulin-producing beta cells in the pancreas respond rapidly by releasing insulin;
- Insulin is released into the blood and circulated to all areas of the body;
- Insulin binds to receptors present on the surface of all human cells;
- Small-channel proteins called glucose transporters (Gluts) move onto the cell membrane, allowing glucose to move rapidly from the blood into the cells, where it can be used for energy;
- Most of the glucose enters the liver and muscle cells, where it can be stored in the form of starch (glycogen) for later use (Marieb and Hoehn, 2015).

**Role of insulin in fat deposition**

If excess carbohydrate is consumed, insulin promotes the uptake of glucose into the adipocytes – which form adipose tissues under the skin and around many of the internal organs, where it is rapidly converted into fat and stored (Guyton and Hall, 2015). Insulin is the key hormone in fat deposition, and low-carbohydrate diets are effective because they result in decreased insulin production and therefore reduced fat deposition.

**Types of diabetes**

**Type 1**

The rare form of diabetes is type 1 (Table 1); it has a prevalence of about 10% in those diagnosed with the condition, equating to over 40 million people worldwide (WHO, 2016). It usually occurs in childhood: it is most frequently diagnosed between the ages of four and five years or in adolescence; diagnoses then become progressively rarer with age (Ozougwu et al, 2013).

A classic autoimmune disease, type 1 diabetes is characterised by the progressive destruction of insulin-producing beta cells of the pancreas. Genetics influences individual susceptibility to type 1 diabetes, and around 10% of people with type 1 diabetes have a parent, sibling or child with the condition (Ferrannini et al, 2010). A variety of genes that predispose individuals to autoimmune disease have been associated with type 1 diabetes (Pociot and Lernmark, 2016).

It has been speculated that type 1 diabetes may also be triggered by a viral infection in early childhood, and many viruses have been suggested as potential triggers, including rubella, mumps, cytomegalovirus and a variety of enteroviruses including poliovirus (Filippi and Von Herrath, 2008). Certain foods such as root vegetables, eggs and cow’s milk have also recently been proposed as triggers, particularly when eaten in infancy (Rewers and Ludvigsson, 2016).

Due to the destruction of the insulin-producing beta cells, people with type 1 diabetes either no longer produce any insulin, or produce it in such small amounts that it cannot have any useful physiological effect. Without insulin to bind to receptors on the surface of the cells, Gluts remain in the cells and glucose cannot move from the blood into the cells, resulting in hyperglycaemia. Unlike type 2 diabetes, the onset of type 1 is usually rapid and the disease can be treated only with insulin, usually via regular injection, to normalise the blood glucose concentration. Without insulin therapy, patients would not survive. Before insulin became available, people with diabetes would rapidly enter states of ketoadosis and/or hyperglycaemic coma, or gradually become emaciated, before starving to death (Rajashree et al, 2012).

Technological advances – particularly the introduction of continuous blood glucose monitoring and automated insulin pumps – are revolutionising treatment of type 1 diabetes (Tumminia et al, 2015). Current stem-cell research is examining the feasibility of pancreatic beta cell transplants to restore insulin production, thereby potentially curing the disease (Kim et al, 2016).

**Type 2 diabetes**

Type 2 diabetes (Table 1) is characterised by insulin resistance: affected individuals gradually become less responsive to the hormone. It is recognised as a separate condition to type 1, as most people retain a population of insulin-producing beta cells.

Until recently, the disease was commonly referred to as maturity-onset diabetes, since it usually occurred in overweight people of middle age; this term is no longer used, as type 2 also occurs in younger age groups. It is more frequent in people of African, South Asian and Afro-Caribbean descent, but it can affect people from all ethnic backgrounds (NICE, 2015).

Despite decades of intensive research, the exact cause of type 2 diabetes is still to
Table 1: Features of type 1 and type 2 diabetes

<table>
<thead>
<tr>
<th>Nature of the disease</th>
<th>Type 1 diabetes</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin-producing beta cells in the pancreas are depleted</td>
<td>Insulin resistance; the exact cause has yet to be established, but it is thought to involve problems in insulin's interactions with its receptors</td>
<td></td>
</tr>
<tr>
<td>Onset</td>
<td>Typically rapid</td>
<td>Generally slow and often insidious</td>
</tr>
<tr>
<td>Age of onset</td>
<td>Usually early childhood, but can be any age</td>
<td>Used to be middle age, but now also increasingly younger age</td>
</tr>
<tr>
<td>Prevalence</td>
<td>Around 10%</td>
<td>Around 90%</td>
</tr>
<tr>
<td>Risk factors</td>
<td>Genetic predisposition, particularly certain viral infections, possibly foods such as certain root vegetables, eggs and cow's milk, particularly when eaten in infancy</td>
<td>High body mass index (particularly obese and morbidly obese categories), large waist (&gt;80cm/31.5in in women and &gt;94cm/37in in men), genetic predisposition, African-Caribbean, black African, South Asian and Chinese descent, pre-existing cardiovascular disease, mental health problems or learning difficulties (NICE, 2012)</td>
</tr>
<tr>
<td>Warning signs</td>
<td>Increased thirst and urination, glycosuria, tiredness, weight loss (often rapid), blurred vision, constant hunger</td>
<td>Feeling 'washed out', frequent urination that can disturb sleep, thirst that is difficult to quench, blurred vision, frequent infections (particularly fungal and bacterial), poor/delayed wound healing</td>
</tr>
<tr>
<td>Treatment</td>
<td>Insulin</td>
<td>Diet, exercise, weight loss, oral hypoglycaemics (e.g. metformin); insulin often used as well</td>
</tr>
</tbody>
</table>

Type 2 diabetes is also frequently accompanied by some or all of the features of the so-called metabolic syndrome (NICE, 2015), which include:

- A body mass index in the 'overweight', 'obese' or 'morbidly obese' categories;
- Hypertension (high blood pressure);
- Raised cholesterol levels;
- Increased risk of blood vessel damage and thrombosis (clot formation).

**Gestational diabetes**

Gestational diabetes is a temporary form of the disease seen in about one in nine pregnant women. It results in more sugar crossing the placenta, which often increases fat deposition in the foetus and makes it grow larger. These macrosomic (large-bodied) babies typically have a much higher birth weight than average (commonly over 4.5kg), which means that an assisted delivery is often needed.

In most affected women, blood sugar levels return to normal after delivery; however, research indicates that they are at increased risk of developing type 2 diabetes later in life (Baz et al, 2016).

**Impaired glucose tolerance**

In impaired glucose tolerance (IGT), blood glucose levels are above normal but below those seen in diabetes, so IGT is often referred to as 'pre-diabetes'. It is most easily diagnosed with a standard oral glucose tolerance test (OGTT) where the results fall between the normal and diabetes curves. Individuals with IGT are regarded as pre-diabetic and at great risk of developing type 2 diabetes unless they make significant lifestyle changes.

Having IGT also appears to increase the risk of coronary artery disease and myocardial infarction (George et al, 2015; Xu et al, 2015). Research indicates that IGT can be improved or even reversed by exercise and diet (Hordern et al, 2012).

**Rare forms of diabetes**

There are rarer forms of diabetes, which account for 2% or less of the total number of cases.

**Maturity-onset diabetes of the young**

Maturity-onset diabetes of the young is a dominant genetic disorder with signs and symptoms similar to type 2 diabetes but with a much earlier onset, usually in childhood. Since it is caused by a single gene mutation, it is a mononuclear genetic disorder and can usually be traced through a family’s generations in a predictable manner (Diabetes UK, 2017a).

**Secondary diabetes**

Secondary diabetes, as its name implies, arises as an effect of either another disease or a medication. Pancreatitis, pancreatic cancer and cystic fibrosis often cause extensive damage to the pancreas. If enough insulin-producing beta cells are destroyed in the process, patients with these conditions will develop a poor response to insulin, which in turn will produce the signs and symptoms of diabetes.

Many steroidal drugs, particularly those given at high doses to treat long-term inflammatory conditions, can lead to elevated blood glucose levels. Steroid-induced diabetes is not a ‘true’ form of diabetes, because it may subside when steroids are discontinued. As a result, it is often
referred to as pseudo diabetes; however, it often produces many of the classic signs and symptoms of diabetes.

When investigating patients with suspected diabetes, it is important to consider the possibility of secondary diabetes, as many people have been wrongly diagnosed with type 2 diabetes when they actually had pancreatic disease or adverse drug reactions (Diabetes UK, 2015; Chun, 2015).

**Clinical features**

The defining feature of diabetes is hyperglycaemia. In a type 1 diabetes patient, it can occur rapidly with pronounced symptoms, as pancreatic insulin-producing beta cells are rapidly destroyed. In a patient with type 2 diabetes, hyperglycaemia usually develops gradually over a longer period of time, leading to less pronounced symptoms that many learn to live with.

Some people with type 2 diabetes may be asymptomatic at the time of diagnosis. As a result, in type 2 diabetes, diagnosis is often delayed, sometimes by many years, and when the disease is finally confirmed, irreversible damage to many organs and tissues may have already occurred.

The gradual and often insidious onset of type 2 diabetes also helps explain why there are an estimated 1.1 million undiagnosed people in the UK today (Diabetes UK, 2016). Box 1 lists the key symptoms that should raise suspicion of diabetes in undiagnosed patients. Patients describing any or a combination of the symptoms listed in Box 1 should ideally be tested to establish whether or not they have diabetes, as well as to rule out other medical conditions.

**Diagnostic tests**

**Oral glucose tolerance test**

The OGTT is the gold standard for diagnosing diabetes (Sacks, 2011); it is the only test that gives a ‘real-time’ assessment of the insulin response. It requires:

- Overnight fasting of at least eight hours;
- Admission to a clinic and having a fasting blood glucose measurement;
- Consumption of an oral solution containing a fixed amount of glucose (normally 75g);
- Blood glucose levels being measured every 30 minutes thereafter during a two-hour period.

In a healthy patient the test will show:

- Fasting blood glucose level to be normal (3.9–5.5mmol/L);
- After the glucose solution has been drunk, blood sugar levels will rise rapidly, triggering the release of insulin;
- Insulin will promote the rapid uptake of glucose into cells and the gradual reduction of glucose in the blood;
- At the end of the two-hour period, glucose concentrations will be close to, or just above, the fasting reading.

In a patient with diabetes, the test results will show:

- Fasting blood glucose concentration will be higher than normal (>7mmol/L);
- After the glucose solution has been drunk, blood glucose levels can rise as high as 11mmol/L or beyond;
- Due to the lack of an insulin response, blood glucose levels will remain high for the remainder of the two-hour test.

**Fasting and random blood glucose levels**

Other methods used to diagnose diabetes have gradually become accepted (WHO, 2006); their advantage is that they can be readily carried out by a health professional in a GP surgery or even in the patient’s home:

- A fasting blood glucose level >7mmol/L (NICE, 2016), ideally recorded on two separate occasions (fasting means having no calorific intake from food or beverages for at least eight hours);
- A random blood glucose level >11mmol/L in a patient with classic symptoms of hyperglycaemia (Diabetes UK, 2017b); this reading can be taken at any time of day or night. Results should be treated with caution and it is a good idea to ask about the patient’s food
Glycated haemoglobin

Erythrocytes (red blood cells) are unusual in that they have permanent Gluts in their cell membranes. Glucose is therefore continually entering erythrocytes, where it binds to red-pigment haemoglobin, resulting in glycated (or glycosylated) haemoglobin (HbA1c). The more glucose in the blood, the greater the amount of HbA1c in the erythrocytes. Unlike white blood cells (leukocytes), erythrocytes have a long lifespan, typically circulating for over 100 days (Guyton and Hall, 2015). Assessing HbA1c therefore gives GPs and diabetes clinics a good overall picture of patients’ blood glucose control over the past two to three months.

HbA1c testing is traditionally used as a method of assessing a patient’s adherence to their prescribed treatment. However, in 2011, the WHO recognised it as an additional method of diagnosis. In health, normal values are <59; values consistently >6.5% are taken to be strongly indicative of diabetes (NICE, 2016; WHO, 2011).

There are limitations to the use of HbA1c as a diagnostic tool for diabetes. It is of most value in diagnosing classic type 2 diabetes and is not appropriate for the following patient groups (Diabetes UK, 2017b):

- Children and young people;
- Those of any age suspected of having type 1 diabetes;
- Patients who have had symptoms of diabetes for less than two months;
- Patients at high risk of diabetes who are acutely ill (for example, those who require hospital admission);
- Patients taking medication that may cause rapid blood glucose levels rise, for example, steroids or antipsychotics;
- Patients with acute pancreatic damage, including those who have undergone pancreatic surgery;
- Pregnant women;
- Patients who have genetic, haematological and illness-related factors that may influence HbA1c and its measurement.

- This three-part series discusses current knowledge about diabetes, its effects on the human body and the implications for patients and health professionals. The second article (page 45) explores associated pathologies and examines the cumulative effects of poorly controlled blood glucose on the body; the third, to be published in the May issue of Nursing Times, will cover the diabetic foot and its treatment. NT

References


Diabetes UK (2017a) Maturity-Onset Diabetes of the Young (MODY). Bit.ly/DiabetesUK_MODY.


