UPDATE
Module 1675

This module covers:

- The causes, diagnosis and management of type 1 diabetes
- Treatment aims for people with type 1 diabetes
- Insulin types used in the management of type 1 diabetes
- How pharmacists can help people manage their diabetes effectively

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Endocrine system

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Managing type 1 diabetes

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Type 1 diabetes mellitus (T1DM) is a disorder characterised by an absence of insulin synthesis. Onset can occur in childhood, around puberty, or in the twenties; it is more prevalent in Caucasians than other ethnicities.

Since 1996, the number of people diagnosed with diabetes in the UK has increased from 1.4 million to 2.9 million. The UK has the fifth highest European incidence of childhood diabetes and by 2025 it is estimated that 5 million people will have diabetes.[1] In England, about 15 per cent of diabetics have T1DM.[2]

There is no cure for T1DM. Pancreatic transplantations have been performed in some T1DM diabetics, but these are complex operations and there is a shortage of suitable donors.

The cost of both disease management and complications places an enormous strain on NHS resources. As such, diabetes in general and T1DM in particular is a key priority for the Department of Health (DH).

What causes type 1 diabetes?

Type 1 diabetics have a poorly functioning pancreas that can no longer produce insulin. This is due to the selective destruction of insulin-producing beta-cells in the islets of Langerhans by the immune system. There is a known genetic correlation, and the risk of developing diabetes is three times greater when the father has diabetes compared with the mother.[3]

Circulating islet cell auto-antibodies (ICAs) are already present in 70 per cent of cases at the time of diagnosis. Their appearance often precedes clinical T1DM onset by up to three years, suggesting slow progressive immunological damage. The final precipitating event leading to clinical presentation may relate to a sudden stress, such as infection, when beta-cell numbers fall below 5 to 10 per cent.[3]

Insulin is synthesised as pre-proinsulin (a polypeptide precursor) in the beta-cells of the islets of Langerhans. Pre-proinsulin is then rapidly converted to pro-insulin that, through the removal of four amino acid residues, forms equal amounts of insulin and C-peptide.

Glucose is the major stimulant for insulin release. The interaction of insulin with its cell surface receptor initiates a signalling cascade within the cell that facilitates the transport of glucose, amino acids and electrolytes.

An intravenous glucose injection causes a biphasic insulin response; an initial rapid response (within two minutes) and a second response (five to 10 minutes later), which is smaller in magnitude and sustained over one hour. The initial response corresponds to the release of stored insulin; the second reflects the discharge of newly synthesised insulin.

An acute insulin deficiency causes simultaneously:

1. Hyperglycaemia due to unrestrained hepatic glycogenolysis and gluconeogenesis resulting in:
- increased hepatic glucose output
- reduced glucose uptake in insulin-sensitive tissues
- increased secretion of counter-regulatory hormones (glucagon, cortisol, catecholamines and growth hormone)
- further increased hepatic glucose production.

2. Removal of insulin's restraining effect on lipolysis:
- non-esterified fatty acids are released into the circulation and taken up by the liver, producing acetyl coenzyme A (acetyl CoA)
- the tricarboxylic acid cycle capacity to metabolise acetyl CoA is rapidly exceeded
- ketone bodies, acetoacetate and hydroxyl-butyrate are formed in large amounts and released into the circulation.

The combination of these effects results in the clinical picture known as diabetic ketoacidosis.

Table 1. Types of insulin[10-11]

Type of action	Onset of action	Peak action	Duration	Chemical name	Brand name
Rapid	5-10 minutes	30-90 minutes	2-4 hours	Insulin lispro	Humalog
				Insulin aspart	NovoRapid
				Insulin glulisine	Apidra
Short	30 minutes	1-2 hours	4-6 hours	Soluble insulin	Actrapid
					Humulin S
					Insuman Rapid
Intermediate	2 hours	3-6 hours	18-24 hours	Isophane insulin suspension/NPH	Humulin I / Insulatard
				Insulin zinc suspension	Hypurin bovine lente
Long	1-3 hours	Flat without a peak	12-24 hours	Insulin glargine	Lantus
				Insulin detemir	Levemir

Diagnosis

Most new cases present with an acute episode but the clinical picture can develop over several weeks to months with sub-acute symptoms.

Acute symptoms:

- sudden and severe onset of polyuria, thirst, tiredness and lethargy
- rapid and unexplained weight loss
- spontaneous ketosis; ketones on breath, dehydration, hyperventilation and coma
- absence of C peptide
- presence of immune markers, such as ICAs.

Sub-acute symptoms:

- thirst
- polyuria, nocturia and urinary incontinence
- tiredness and lethargy
- weight loss
- recurrent skin and genital infections such as thrush
- blurred vision.

Definitive diagnosis of T1DM is based on criteria specified by the 1999 World Health Organization report[4] as a fasting venous plasma glucose (FPG) greater than 7mmol/l or a venous plasma glucose greater than 11.1mml/l two hours after a 75g oral glucose load. This should be confirmed by a single diagnostic laboratory glucose measurement in the presence of classical symptoms, or by a further laboratory glucose measurement. The diagnosis may be supported by a raised glycosylated haemoglobin level (HbA1c).[5]

The diagnosis should also exclude underlying causes suggestive of type 2 diabetes mellitus (T2DM) such as obesity or family history of T2DM, particularly in non-Caucasians.

Tests to detect specific auto-antibodies or C-peptide deficiency should not be used routinely, but are available to specialists to predict the rate of decline of islet beta-cell function and to discriminate between cases of T1DM from T2DM where there is uncertainty.

Management

All patients with T1DM require lifelong insulin therapy. The aim of the treatment is to mimic the body's natural insulin response to glucose stimulation.

In the national service framework (NSF) for diabetes, the DH specifically outlines the need for both a specialist and multidisciplinary approach to successful disease management. The NSF also stresses the importance of involving and educating patients (and/or their family in the case of a child) with the aim of empowering them to self-manage their diabetes. Long-term prognosis strongly correlates with patients' understanding of their condition and adherence to treatment. The aim of management is to achieve a tight control of blood glucose, blood pressure and lipids (see box 1, p17).

The initiation of insulin treatment often occurs within hospital settings and is usually started at 0.25 to 0.5 units/kg/day, then titrated according to blood glucose levels. The choice of insulin regimen should be determined by a number of factors including the patient's compliance or reluctance to inject, hypoglycaemic risk, lifestyle, religious beliefs, age and risk of complications.

Multiple injection regimens combine the use of short-acting insulin or rapid-acting insulin analogues (before meals) and intermediate-acting or long-acting insulins once or twice daily.[6]

Continuous subcutaneous insulin infusion (CSII) is recommended as an option in adults and children over 12 years old who suffer repeated or unpredictable hypoglycaemia, while attempting to achieve optimal glycaemic control with multiple-injection regimens. It is also used for those whose glycaemic control remains inadequate despite optimised multiple-injection regimens.

CSII is also recommended for children under 12 years old with T1DM when multiple-injection regimens are considered impractical or inappropriate. Children on insulin pumps should undergo a trial of multiple-injection therapy between the ages of 12 and 18 years.

Insulin can be animal-derived (usually porcine or bovine), semi-synthetic, eg enzymatically-

modified porcine insulin (emp), or bio-synthesised by recombinant DNA technology using bacteria (crb, prb) or yeast (pyr). Insulins can be further classified according to their onset and duration of action, as shown in table 1 on page 14.

The second aspect of the management of T1DM involves non-pharmacological measures to affect modifiable factors aiming to reduce the risk of early mortality from vascular disease, morbidity (blindness, renal disease leading to dialysis), neuropathies and to improve quality of life. These include changes in lifestyle, physical exercise and dietary modifications.

The role of the pharmacist

Community pharmacists are an accessible point of contact for further information for patients with T1DM. Pharmacists can provide education about indications for treatment, administration timings, side effects, interactions, appropriate storage and needle supply. They should familiarise themselves with the different types of insulin and insulin devices, blood glucose monitors and needle types.

Dispensing errors can be minimised by using patients' insulin passports to ensure the correct insulin type and device are issued every time.[7] Pharmacists should ensure prescriptions for blood glucose monitoring test strips provide adequate supply to meet clinical needs.[8]

It is essential that the correct needle size is provided; if it is too long it may penetrate through the subcutaneous tissue layer into the muscle. It is also important patients receive sufficient quantity to ensure they can change needles with every administration. This reduces the risks of infection from dirty needles and receiving partial doses from blocked needles.[9]

Many cough and cold syrups contain both simple sugars and alcohol, which metabolise into carbohydrate in the body. This provides a sugar load into the bloodstream that can cause sudden increases in blood glucose. Sugar-free formulations should be recommended instead, such as those containing fructose. Herbal remedies can also affect diabetes, for example, diet pills frequently contain chromium, which increases metabolism thus impacting upon glucose and insulin processing.

Pharmacists can also use MURs to review and optimise concomitant medications such as statins and antihypertensives that reduce cardiovascular risk.

Storage of insulin is important and patients or parents should be advised to:

- keep unused insulin vials or pens in their boxes in the fridge, but avoid freezing
- keep the vial or pen in use at room temperature and use within one month
- check expiry dates and not use if out of date
- not expose insulin to sunlight or high temperatures (eg leaving in the car on a hot day or next to the cooker)
- check what to do with insulin when planning a holiday.

Patients should also be reminded of the sick day rules – what to do if they become unwell:

- never stop taking insulin, even when not eating, there may be a need to increase the dose
- test blood glucose more often (at least four times a day)
- drink lots of fluids to prevent dehydration
- replace normal drink with carbohydrate drinks if necessary
- test urine for ketones
- seek medical advice if vomiting develops.

References

1. Diabetes prevalence 2012 (March 2013) www.diabetes.org.uk/About_us/What-we-say/Statistics/Diabetes-in-the-UK-2012/ accessed 31.08.13
2. National Service Framework for Diabetes. www.gov.uk/government/uploads/system/uploads/attachment_data/file/198836/ accessed 15.09.13
3. Walker R, Edwards C. Clinical Pharmacy and Therapeutics: Diabetes mellitus, pages 657-659
4. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. www.who.int/diabetes/publications/diagnosis_diabetes2006/en/index.html
5. Nice (CG 15) publications.nice.org.uk/type-1-diabetes-cg15/guidance#the-diagnosis-of-type-1-diabetes
6. BNF 65, March to September 2013, pages 438-9
7. National Patient Safety Agency npsa.nhs.uk/corporate/news/passport-to-safer-use-of-insulin/
8. Importance of finger prick tests in managing type 1 diabetes highlighted document www.gov.uk/government/publications/importance-of-finger-prick-tests-in-managing-type-1-diabetes-highlighted, published 8 Feb 2013
9. BD How to use an insulin pen www.bd.com/resource.aspx?IDX=10256
10. Nice(CG15) guidance.nice.org.uk/CG15
11. Greene RJ, Harris ND. Pathology and Therapeutics for Pharmacists – A basis for clinical pharmacy practice. 2nd Ed. Pharmaceutical Press, London: 536-7.
12. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1994;329:977-86.
13. Clinical evidence. Glycaemic control in diabetes. In: Clinical Evidence. Issue 9. London: BMJ Publishing Group, 2003;661-7.
14. Diabetes UK. Recommendations for the management of diabetes in primary care. London: Diabetes UK, 2000.
15. Williams B, Poulter NR, Brown MJ, et al. Guidelines for the management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS IV. J Hum Hypertens 2004;18:139-85.

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5 minute test

■ Sign up to take the 5 Minute Test and get your answers marked online: chemistanddruggist.co.uk/update

Take the 5 Minute Test

1. The UK has the highest European incidence of childhood diabetes.
True or false?
2. In England about 15 per cent of diabetics have type 1 diabetes.
True or false?
3. An intravenous glucose injection causes a biphasic insulin response.
True or false?
4. Acute symptoms of type 1 diabetes include polyuria, thirst and rapid weight loss.
True or false?
5. Treatment for type 1 diabetics aims for an HbA1c of less than 53 to 59mmol/mol.
True or false?
6. Continuous subcutaneous insulin infusion is not suitable for children under 12 years old.
True or false?
7. Short-acting insulin has an onset of action of five to 10 minutes.
True or false?
8. Long-acting insulin has a peak action of three to six hours.
True or false?
9. Herbal remedies such as diet pills containing chromium, which increases metabolism, can affect diabetes management.
True or false?
10. Insulin vials or pens currently in use should be kept at room temperature and used within one month.
True or false?

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Tips for your CPD entry on managing type 1 diabetes

Reflect **What are the treatment aims for type 1 diabetes? For which patient groups is continuous subcutaneous insulin infusion recommended? What advice should be given to patients about insulin storage?**

Plan **This article describes the causes, diagnosis and management of type 1 diabetes and includes information about treatment aims, insulin types and advice pharmacists can give patients.**

Act **Read the Update article and the suggested reading (below), then take the 5 Minute Test (left). Update and Update Plus subscribers can access their answers and a pre-filled CPD logsheet at chemistanddruggist.co.uk/mycpd**

Read more about type 1 diabetes from NHS Choices
tinyurl.com/type1diabetes1

Revise your knowledge of different types of insulin and diagnostic and monitoring devices for diabetes from the BNF Section 6.1 Drugs used in diabetes

Find out more about insulin pens, needles and pumps on the diabetes.co.uk website
tinyurl.com/type1diabetes2
tinyurl.com/type1diabetes3

Read about the healthcare essentials that all diabetics should receive on the check list produced by Diabetes UK
tinyurl.com/type1diabetes4

Read the MUR tips for diabetes on the C+D website. Identify any patients who might benefit from an MUR
tinyurl.com/type1diabetes5

Evaluate **Are you now confident in your knowledge of the management of type 1 diabetes? Could you give lifestyle advice to patients with type 1 diabetes?**

Box 1. Treatment aims for type 1 diabetes[12–15]

- HbA1c less than 53 to 59mmol/mol (less than 7.0 to 7.5 per cent)
- Blood pressure less than 140/80mmHg or less than 130/80mmHg for adolescents or those with renal, cerebrovascular, ophthamological and cardiovascular disease with a good life expectancy
- Fasting blood glucose between 4.4 and 6.1mmol/l
- Postprandial blood glucose between 4.4 and 8.0mmol/l
- No glycosuria
- Total cholesterol less than 4.0mmol/l
- Low density lipoprotein cholesterol less than 2.0mmol/l
- Fasting triglycerides less than 1.7mmol/l
- Body mass index of 20 to 25 for men and 19 to 24 for women