UPDATE
Module 1676

This module covers:

- Acute and chronic complications of diabetes
- Hyper- and hypoglycaemia, neuropathy, retinopathy, nephropathy, cardiovascular disease and stroke
- Management of complications of diabetes
- Advice community pharmacists can give to help manage complications that may arise and reduce the risk of them occurring

OCTOBER
Endocrine system

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Diabetic complications

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Diabetes mellitus (DM) is a disorder characterised by varying degrees of insulin hyposecretion or insensitivity, resulting in raised blood glucose (BG) levels, routinely measured using Boehringer Mannheim (BM) sticks.

There are four known types of DM with differing pathophysiology: type 1 (T1DM), type 2 (T2DM), secondary diabetes and gestational diabetes. This article focuses on complications of T1DM and T2DM.

Since 1996, the number of cases of diabetes diagnosed in the UK has increased from 1.4 to 2.9 million and is estimated to increase to more than 4 million by 2025.[1] Diabetes is a major cause of mortality; morbidity from diabetic complications is up to three and a half times higher in socio-economically deprived groups.[2]

Complications vary in their severity and include damage to various organs and blood vessels, blindness, end stage renal failure (ESRF) and lower-limb amputations. Within Europe, Britain has a poor record of blood glucose and blood pressure (BP) control and higher rates of heart attacks, stroke, foot ulcers, renal failure and nerve damage.[2]

Effective management of diabetes aims to both prevent the occurrence of complications and slow their progression. It requires a life-long commitment from patients, family members and a dedicated multidisciplinary team aiming to achieve high-quality care and patient education.

Complications often develop as a result of poor glycaemic control (blood glucose levels consistently below 4mmol/l or above 9mmol/l and a glycosylated haemoglobin concentration (HbA1c) of >7.5 per cent (59mmol/mol).[3] The appearance of symptoms and signs of complications are due either to acute metabolic disturbances or chronic tissue damage.

Acute complications

Acute complications resulting from disturbed glycaemic control include hyperglycaemia, hypoglycaemia, diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS). While DKA and HHS are clinical emergencies requiring urgent referral for emergency treatment, people who have not been diagnosed with diabetes who have hyperglycaemia or individuals on hypoglycaemic treatment who develop hypoglycaemia may initially present for advice in the pharmacy.

Hyperglycaemia, where blood glucose levels are above 11mmol/l, occurs slowly with symptoms developing over a few hours. It often follows omitted antidiabetic medication or inadequate insulin doses. Other causes include drugs affecting diabetic control (such as sugar-containing formulations), foods with high sugar content and stress.

The clinical features of hyperglycaemia include glycosuria, ketonuria (only T1DM and ketosis-prone T2DM), polyuria, nocturia, thirst, polydypsia (excessive thirst) and rapid respiration rate (in DKA as a consequence of ketoacidosis). Hypotension and tachycardia occur at a later stage due to profound dehydration and acidosis.

Hypoglycaemia (blood glucose levels below 4mmol/l in adults; in younger children, these vary according to age and clinical status[3]) develops rapidly, sometimes within minutes, and often results from excessive doses of insulin or antidiabetic medication. Other contributing factors are shown in box 1, below left.

The symptoms of hypoglycaemia are:

- tremor, pallor, sweating, shivering, palpitations, anxiety – caused by enhanced sympathetic activity
- drowsiness, confusion, disorientation, inappropriate behaviour, aggression, delirium and coma due to reduced CNS glucose delivery
- hunger, salivation, weakness, blurred vision.

Box 1. Risk factors contributing to the development of hypoglycaemia

Medically or patient induced

- Long duration of diabetes, loss of hypo awareness
- Impaired renal function
- Renal dialysis
- Excessively tight glycaemic control
- Malabsorption
- Fasting
- Deficiency of counter-regulatory hormone function (Addison's disease and hypopituitarism)

Drug induced

- Injection into lipo-hypertrophied sites
- Drug interactions with hypoglycaemic agents such as quinine or selective serotonin reuptake inhibitors (SSRIs)
- Insulin prescription error (notable in hospitalised patients)
- Alcohol

Chronic complications[4-6]

Chronic complications develop as a direct consequence of poor glycaemic control due to poor adherence to treatment or inadequate lifestyle changes. At-risk patients have blood glucose levels that are often persistently greater than 9mmol/l and HbA1c levels above 7.5 per cent.[6]

Chronic complications involve long-term permanent macro- and microvascular damage affecting various organs and systems, and are shown in box 2, above right.

- **Cardiovascular disease (CVD) and stroke** DM is a major risk factor for

Box 2. Microvascular and macrovascular complications of diabetes

Microvascular complications
- Retinopathy
- Glaucoma
- Cataract
- Sensory polyneuropathy (may be painful)
- Autonomic neuropathy
- Proximal neuropathy and amyotrophy
- Mononeuropathies and mononeuritis multiplex
- Nephropathy
- Focal segmental glomerulosclerosis, chronic kidney disease and end stage renal failure

Macrovascular complications
- Ischaemic heart disease
- Peripheral vascular disease and ulcers
- Stroke

ischaemic heart disease (IHD) and stroke. The risk is twice that for non-diabetics. Both conditions tend to occur at an earlier age. There is also a greater fatal outcome post heart attacks. The main cause of CVD and stroke is development of atherosclerosis in coronary arteries and cerebral vasculature; over time, this leads to increased atheromatous deposits in vessels and results in various degrees of occlusion. BP control is more important than BG control in the prevention of macrovascular complications.

- **Peripheral vascular disease (PVD)** manifests as insufficient tissue perfusion caused by existing atherosclerosis in the peripheral vasculature that may be acutely compounded by either emboli or thrombi. The disease tends to affect lower rather than upper limbs, is typically segmental and causes claudication. Limb ischaemia is rare but life-threatening and requires emergency intervention. Risk factors include smoking, hyperlipidemia and hyperviscosity. PVD often coexists with CVD, indicating an increased burden of atheroma.
- **Nephropathy** occurs in T1DM and T2DM as a consequence of chronic hyperglycaemia. Diabetic kidney disease is a glomerulopathy defined by characteristic structural and functional changes. The main clinical manifestations are: albuminuria, occasionally microhaematuria and, in many patients, progressive chronic kidney disease, which can be slowed or prevented with optimisation of therapy.
- **Retinopathy (DR)** presents as non-proliferative and proliferative, named for the absence or presence of abnormal new blood vessels emanating from the retina. DR can be further classified by severity. However, each patient has a unique combination of findings, symptoms and progression rate, which require an individualised approach to treatment.
- **Neuropathy** develops in the presence of hyperglycaemia and progression of symptoms depends upon the duration of hyperglycaemic episode. The presenting symptoms vary from leg discomfort or pain to complete loss of function.

Management of complications

Optimal management endeavours to achieve a delicate balance of preventing excessive glucose levels without causing hypoglycaemia. The approach aims to reduce the frequency of acute complications and slow the occurrence of chronic complications, thereby improving the patient's quality of life, prognosis and outcome, achieved by combining non-pharmacological and pharmacological methods.

- **Patient education**[7]

Educational interventions should aim to promote: a better understanding of DM and its management; support implementation of lifestyle changes such as weight control, smoking cessation, physical exercise, nutrition and diet; and understanding of pharmacological treatment and adherence to avoid hyperglycaemic/hypoglycaemic events. Sessions should be accessible, taking into account the individual's culture, ethnicity, disability and geographical issues. Educational techniques should vary to promote active learning.

- **Hypoglyacemic agents**

Treatment should reflect the most up-to-date guidelines and recommendations according to the type of diabetes. Hyperglycaemia can be avoided by increasing insulin or antidiabetic agent dose or improving adherence. Hypoglycaemia can be avoided by avoiding tight blood glucose control and/or reducing insulin dose.

- **Primary and secondary prevention of CVD and stroke**[8]

If BP is consistently above 140/80mmHg (or above 130/80mmHg in patients with kidney, eye or cerebrovascular damage), lifestyle changes should be started, supplemented by medication. A renin-angiotensin enzyme inhibitor (ACEi) should be commenced as first-line treatment in all patients particularly if there is evidence of renal impairment or proteinuria (unless contraindicated, for example in bilateral renal artery stenosis). If an ACEi is not tolerated, an angiotensin II receptor antagonist (A2RB) should be initiated.

A combination of ACEi with a calcium-channel blocker (CCBs) or a diuretic is recommended as first-line treatment in those of Afro-Caribbean origin.

- **Lipid modification**

Statin therapy should usually be added to lifestyle therapy regardless of baseline lipid levels for diabetic patients with CVD, and those without CVD who are more than 40 years old, or have more than one other CVD risk factors. For lower risk patients without overt CVD and under 40 years old, statins should be considered if LDL remains >2.6mmol/l despite lifestyle therapy (weight loss, dietary modification), or if there are multiple CVD risk factors.

- **Renal disease** Patients should have urine checks annually or more frequently (if suspected diabetic nephropathy) to measure serum creatinine and estimate the glomerular filtration rate. Treatment with an ACEi should be commenced to achieve BP <130/80mmHg. An A2RB can be prescribed if the albumin/creatinine ratio is abnormal or the ACEi is poorly tolerated.
- **Footcare** Patients should receive annual foot examinations to identify changes in sensation, shape, new ulcerations, swellings or skin discoloration.
- **Eyecare** Patients should have annual eye checks and maintain good blood glucose control. Checks aim to identify changes in the visual field, the apparition of black spots, the occurrence of glaucoma and loss of vision.
- **Anxiety and depression** Diabetes care teams should be aware that patients may develop anxiety and/or depression. Patients with persistently poor blood glucose monitoring should be offered screening for anxiety and depression. Those suspected of anxiety and/or depression should be referred promptly to mental health professionals.

Role of the pharmacist

By proactively providing health and wellbeing advice and engaging appropriate public health services, community pharmacists can help support effective diabetes management to achieve better outcomes.

General advice

Highlight the importance of medication adherence, attending regular check-ups including eye exams and dental checks, ongoing optimal care and yearly vaccinations such as influenza A and pneumonia. For special populations, including ethnic groups (black/south Asian), increase outreach by making information available in different languages (see Diabetes UK) and advise those who are fasting or unwell that dose adjustment may be required.

Over the counter advice

- Support patients to achieve better control of BP, BG and blood cholesterol – some pharmacies offer free testing services[9]
- Promote awareness and recognition of signs and symptoms of hyperglycaemia and hypoglycaemia
- Warn about the loss of hypo awareness occurring in the long term
- Warn about the possibility of blurred symptoms of hypoglycaemia in those on beta-blocking treatment
- Promote smoking cessation by offering a range of products and referring to relevant services for follow-up
- Advise patients to wash their feet daily and to dry them well, especially between the toes. Remind them not to ignore cuts or broken skin and to see their GP if these worsen or do not improve
- Caution against overuse of sugar-free medicines containing fructose, which can have a laxative effect, increasing dehydration risk
- Refer patients presenting with resistant/recurrent vaginal thrush to their GP
- Offer diet and lifestyle advice (including to clients with pre-diabetes) plus waist/BG measurement.

Medicines use reviews

- Provide information about dosing, administration times and side effects
- Recommend the GP optimises doses if there are no contraindications and it is tolerable
- Identify and optimise overall treatment, eg statins
- Identify and address barriers to adherence. Missed doses may be due to lack of understanding: education can alleviate concerns. In cases of intolerance or allergies, refer to the GP for alternatives
- Identify potential insulin misuse by young female patients, who may be using this method to control their weight
- Poor eyesight and inability to read labels may be barriers to adherence. This can be identified during the consultation by observation and questioning. Large print labels may help.

Hospital admissions and clinic appointments

- Medicines reconciliation should identify recent medication changes, especially following specialist review, and prevent medicines wastage
- Medicines withheld temporarily – due to impaired renal function or blood pressure, such as metformin or ACEi - may need GP review before restarting.

Useful websites for patients

- Diabetes UK has a calculator for checking the risk of type 2 diabetes: riskscore.diabetes.org.uk/type2risk
- The diabetes.co.uk website has information about complications: diabetes.co.uk/diabetes-complications/diabetes-complications.html

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5 minute test

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Take the 5 Minute Test

1. The development of complications in diabetes is often a result of poor glycaemic control.
True or false?
2. Hyperglycaemia is defined as blood glucose levels above 6mmol/l.
True or false?
3. The symptoms of hyperglycaemia include tremor, pallor, sweating, shivering and anxiety.
True or false?
4. Hypoglycaemia usually occurs slowly with symptoms developing over a number of hours.
True or false?
5. Risk factors for hypoglycaemia include long duration of diabetes, reduced renal function and malabsorption.
True or false?
6. Microvascular complications of diabetes include ischaemic heart disease, peripheral vascular disease and cardiomyopathy.
True or false?
7. Studies have shown hyperglycaemia to be a direct cause of cardiovascular disease.
True or false?
8. Statin therapy is recommended for the primary prevention of CVD for adults who have a 10 per cent risk of developing the condition.
True or false?
9. Renal disease in diabetes should be treated with an ACE inhibitor.
True or false?
10. Diabetics should be reminded that overuse of sugar-free medicines containing fructose can have a laxative effect.
True or false?

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Tips for your CPD entry on diabetic complications

Reflect **What risk factors contribute to the development of hypoglycaemia? What are the two types of diabetic retinopathy? How can cardiovascular disease risk be reduced in diabetic patients?**

Plan **This article describes complications associated with diabetes and includes information about hyper- and hypoglycaemia, neuropathy, retinopathy, nephropathy and cardiovascular disease and stroke. The role of the pharmacist in diabetes management and advice that can be given to patients is also discussed.**

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

Read more about the symptoms of hyper- and hypoglycaemia from diabetes.co.uk
http://tinyurl.com/diabetescomplication1
http://tinyurl.com/diabetescomplication2

More information about diabetes complications, which may be useful for patients, is on diabetes.co.uk
http://tinyurl.com/diabetescomplication3

Find out more about peripheral neuropathy on the NHS Choices website
http://tinyurl.com/diabetescomplication4

Revise your knowledge of diabetic retinopathy on the Royal National Institute of Blind People's website
http://tinyurl.com/diabetescomplications5

Read more about nephropathy and cardiovascular disease in diabetes on the Diabetes UK website
http://tinyurl.com/diabetescomplication6
http://tinyurl.com/diabetescomplication7

Evaluate **Are you confident in your knowledge of the complications that may affect patients with diabetes? Could you give advice to patients about reducing the risks of these complications?**

ASK THE EXPERT

October is endocrine system month and our expert is on hand to answer your queries. From diabetes to thyroid disease submit your questions by email: **steve.titmarsh@ubm.com**