



Activity 2 – Understanding the symptoms and complications of Type 2 diabetes mellitus

What initial symptoms do diabetic patients report, and why?

Doctors will enquire about certain symptoms when taking a patient's medical history, to establish a firm diagnosis. Together with the background of a patient (see *Epidemiology* in Activity 1) and a blood test (for glucose), the presence of certain symptoms can assist a doctor in diagnosing T2DM. Such symptoms include:

<http://www.diabetes.co.uk/diabetes-symptoms.html> .

Why do these various symptoms of T2DM arise?

1. Effects of having to get rid of a lot of glucose:
 - *Urination, dehydration and thirst*: The word 'diabetes' means 'siphon', which alludes to the excessive urination that accompanies diabetes mellitus. When a large amount of glucose is removed through the kidneys as urine, this glucose draws water out of the body together with it. Poorly controlled diabetes can therefore lead to dehydration and persistent thirst.
 - The high levels of glucose in the urine may encourage infections (e.g. yeast, bacteria) of the skin around the genitals.
2. Effects of glucose not being used for the right purposes:
 - *Fatigue, weight loss and hunger*: Insulin is an 'anabolic' hormone, i.e. it promotes energy storage in the body in the form of larger molecules, promoting fat deposition, muscle growth etc. When insulin is no longer able to tell target organs to store and use energy in the right ways, this leads to lethargy, weight loss and increased appetite.
 - *Nausea and dizziness*: When glucose cannot be metabolized by the normal routes, the proportion of glucose being shunted down unusual pathways increases, leading to the appearance of certain metabolic intermediates in the blood. By affecting osmotic balances or acting as toxins, these intermediates may cause nausea and dizziness in Type 2 diabetics.
3. Effects of glucose not being in the right places:
 - *Blurred vision*: High levels of glucose in the aqueous humour of the eye lead to glucose accumulation within the lens of the eye. Enzymes within the lens convert the glucose to sorbitol, which draws water into the lens, swelling it, and blurring vision.

What health problems do diabetics go on to develop, and why?

As T2DM becomes more severe over months or years, some late-stage complications may surface. These arise because T2DM can cause damage to tiny blood vessels (capillaries) and large blood vessels, affecting many organs in the body.

1. Problems with smaller blood vessels, namely capillaries: When glucose cannot be metabolized by the normal routes, the proportion of glucose being sent down unusual metabolic pathways increases, leading to an accumulation of certain



chemical intermediates (e.g. 'polyols'). Some of these can combine with and alter the properties of cell signalling molecules, or contribute free radicals that physically damage cells ('oxidative stress'). High glucose levels are particularly damaging to the small blood vessels that supply all tissues.

- When starved of a blood supply ('ischaemia'), metabolically-active tissues such as the kidney, nerves and the retina are very susceptible to damage. This leads to the common complications of T2DM – diabetic nephropathy (kidney damage), neuropathy (nerve damage) and retinopathy (retinal damage).
 - A poor blood supply, together with other factors can lead to poor wound healing in diabetics, which is one of the factors contributing to the development of diabetic foot ulcers.
2. Problems with larger blood vessels: In T2DM, the way the body handles lipids (fat) is also abnormal. In particular, the high levels of triglycerides and fatty acids in the bloodstream and poorly-regulated immune function lead to the build-up of plaques that block large blood vessels ('atherosclerosis'). This can elevate blood pressure. Furthermore, when atherosclerotic plaques build up in important blood vessels supplying the heart or brain, heart attacks and strokes can also result.
- For an animation illustrating atherosclerosis, see <http://vimeo.com/41301385>