

Sejal is losing weight

You are a GP. Sejal is a 23 year old journalist who comes to see you concerned about her recent weight loss. She grew up in the area, but you have not seen her since she was a child.

She tells you that at first she thought the weight loss was just because she was so busy at work over the last two months. She's been running around a lot, and had been feeling tired and rundown. However, over the last two weeks she's been stuck behind a desk, doing nothing but working on a computer – so much so that she worries she may have damaged her eyes, because her vision has been blurry and she thinks she will have to change the prescription for her contact lenses – and still she seems to be losing weight.

Sejal is terrified that she might have cancer, which she knows can cause weight loss. She also wonders if the weight loss might be connected to her not sleeping; she wakes up at least three times every night. After you question her regarding why she wakes up, she tells you she usually has to pass urine. Upon further questioning, she tells you she has always made sure to drink at least two litres of water a day, because she knows you need to do that to keep your skin healthy. However, she has noticed that she's actually been drinking a lot more than that of late, because she is often thirsty.

You ask Sejal to provide a urine sample, which she does. You test it and find that it is positive for glucose and ketones. You need to explain to Sejal what your preliminary diagnosis is and what needs to happen next.

Mentor notes

Aim

To examine the presentation, differential diagnosis and treatment for type 1 diabetes mellitus.

Learning Objectives

1. Explain how glucose homeostasis is regulated, and how it is altered in diabetes mellitus.
2. Describe how type 1 diabetes mellitus is caused and how it presents.
3. Describe how disrupted glucose homeostasis can lead to micro and macrovascular problems, including retinopathy.
4. Compare and contrast type 1 and type 2 diabetes mellitus.
5. Describe the differential diagnosis of type 1 diabetes mellitus
6. Describe current and future potential treatments for type 1 diabetes mellitus
7. Understand how general some symptoms (e.g. weight loss, insomnia) can be.
8. Appreciate that water intake is related to fluid homeostasis.

Prompt questions

General

Are there any terms, expressions, actions etc. that the students do not understand and need to discuss?

Specifically for:

Learning Objective 1

What is the organ important in regulating blood glucose? What are the hormones involved? What happens to this regulation in diabetes?

Learning Objective 2

Is type 1 diabetes genetic? Is it due to lifestyle? What do you understand by the term 'autoimmune disease'? What tells you someone might have type 1 diabetes?

Learning Objective 3

Why does diabetes influence the cardiovascular system? Why particularly the eyes?

Learning Objective 4

Who develops type 1 and type 2 diabetes? What are the differences between the diseases? Do we treat them the same way?

Learning Objective 5

How can we be sure Sejal has type 1 diabetes? Why is diabetes associated with weight loss? Why is cancer associated with weight loss?

Learning Objective 6

Why does giving insulin not completely normalise health? (type 1 diabetics have lower life expectancy). How else might we treat type 1 diabetes? What might be the problem with transplanting beta cells?

Learning Objective 7

How often do you feel tired? Or have a headache? Are these symptoms useful for diagnosis? What might tell you Sejal's problem is serious?

Learning Objective 8

How much water do you drink a day? How do you know? What makes you drink?

Background

(Please note this section is a précis – more detailed information can be obtained from the lecture slides for the Endocrinology courses for Year 1 and Year 2 if required).

Insulin is a hormone produced by the beta cells of the Islets of Langerhans of the pancreas. Insulin is released from the pancreas when blood glucose levels rise, e.g. after a meal or an oral glucose tolerance test. Insulin causes glucose to be removed from the blood and metabolised to provide energy or stored as glycogen or fat.

Diabetes mellitus is caused by insulin deficiency, and resistance to insulin action can also contribute. Diabetes mellitus causes heart disease, blindness and kidney failure, and is treated by restoring insulin action.

Type 1 diabetes is an organ-specific autoimmune disease that leaves patients with an absolute insulin deficiency.

Presentation of type 1 diabetes:

Symptoms: polyuria, nocturia, polydipsia, blurring of vision, 'thrush', weight loss, fatigue.

Signs: dehydration, cachexia, hyperventilation, smell of ketones, glycosuria, ketonuria.

Causes of type 1 diabetes: Hypothesised environmental trigger leads to autoimmune destruction of the beta cells, leading to hyperglycaemia due to insulin deficiency.

Treatment of type 1 diabetes mellitus aims to prevent short term metabolic complications and long term vascular complications. Most type 1 diabetes patients are now treated with human insulin or forms of human insulin modified for more desirable properties e.g. rapid onset, long acting.

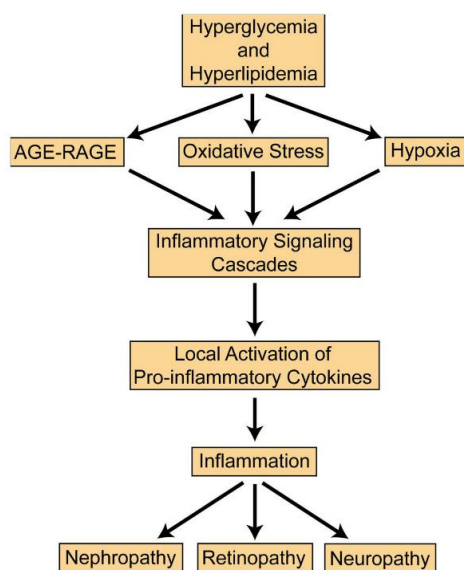
Diabetes damages blood vessels. Damage to the large vessels cause MACROvascular complications (being covered later today). Damage to very small blood vessels causes MICROvascular complications.

There are three important microvascular complications of diabetes.

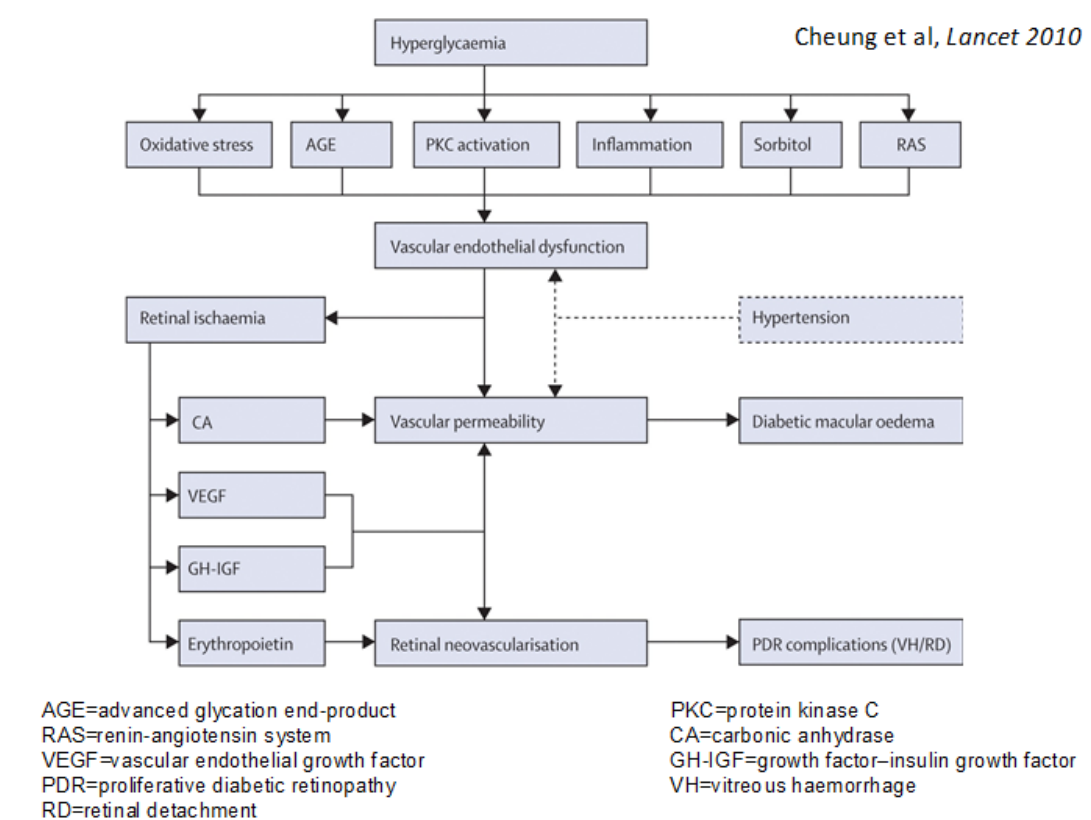
1. Diabetic retinopathy
2. Diabetic nephropathy
3. Diabetic neuropathy

The blood supply of the eye and in particular the retina includes many very small blood vessels, and when these get blocked, retinopathy results. Small blood vessels are also found in the glomeruli, and damage to these causes nephropathy. Damage to the vasa nervorum (the very small blood vessels that keep nerves alive) causes neuropathy.

Mechanisms of glucose damage



- Polyol pathway
- AGEs
- Protein kinase C
- Hexosamine



Possible future treatments for type 1 diabetes include the artificial pancreas (e.g. insulin pump which responds intelligently to real-time glucose sensing) or islet transplantation (from donors, or perhaps implantation of beta cells grown from patient's own stem cells), though a potential problem is that they may suffer from autoimmune attack like the original islets.

In type 1, usually see childhood onset, glycaemia can only be reduced with exogenous insulin, and left untreated, fatal ketoacidosis develops rapidly.

In type 2, usually see adult onset, glycaemia can be reduced without exogenous insulin, and left untreated, microvascular, macrovascular, renal, retinal and neural pathology develops gradually.