Diabetes mellitus

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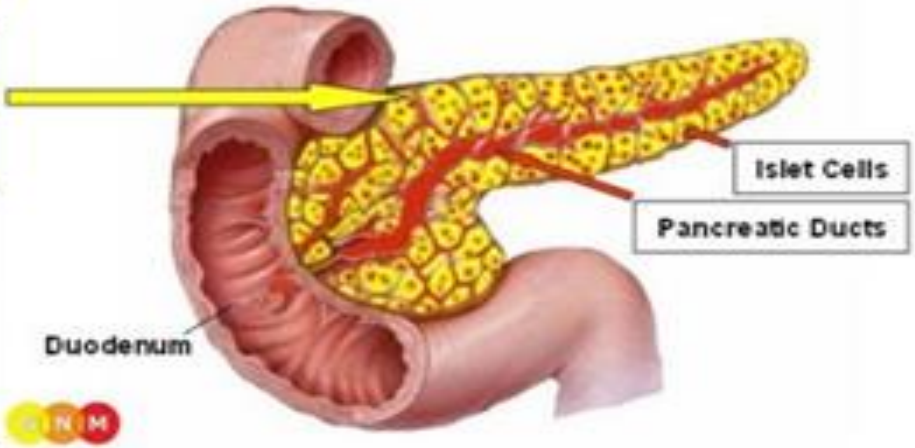
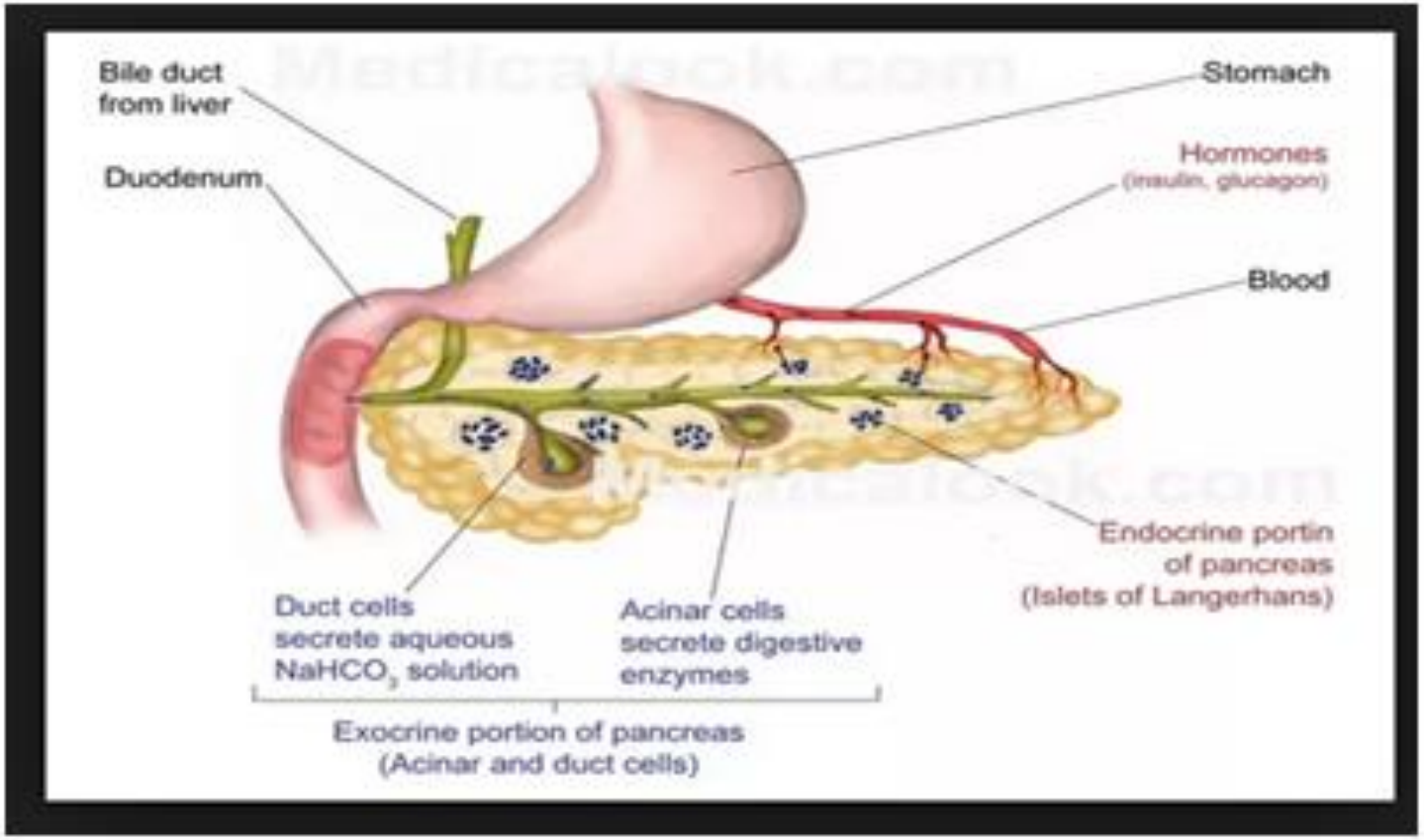
- Diabetes Mellitus is a group of metabolic disorders characterized by chronic **hyperglycaemia** (elevated blood glucose concentration), due to insulin deficiency insulin resistance, or both.

PANCREAS GLAND




Bile duct
from liver
Duodenum
Stomach
Hormones
(insulin, glucagon)
Blood
Endocrine portin
of pancreas
(Islets of Langerhans)
Duct cells
secrete aqueous
NaHCO3 solution
Acinar cells
secrete digestive
enzymes
Exocrine portion of pancreas
(Acinar and duct cells)

- Type 1 diabetes
- Type 2 diabetes

- **Type 1 diabetes:**

- commonest type in the young.
- characterised by the progressive loss of all or most of the pancreatic -cells.
- is rapidly fatal if not treated.
- must be treated with insulin

- **Type 2 diabetes**:

• affects a large number of usually older individuals.

• characterised by the slow progressive loss of -cells but with disorders of insulin secretion and tissue resistance to insulin.

• may be present for a long time before diagnosis.

• may not initially need treatment with insulin but all do eventually

Staging of diabetes

In type 1

people can be found with the relevant HLA markers and autoantibodies

but without glucose or insulin abnormalities

In type 2

people can be found with insulin resistance then as insulin production fails they develop impaired glucose tolerance

Size of the problem

- Approximately 2.6 million people in the UK have diabetes (2009 figure), the majority (~90%) with type 2 disease

Type 1

- genetic predisposition to the disease interacts with an
- environmental trigger to produce immune activation. This leads to the production of killer lymphocytes and macrophages and antibodies that attack and progressively destroy -cells (an auto-immune process) The genetic predisposition is associated with the genetic markers HLA DR3 and HLA DR4. There is a strong seasonal variation,
- suggesting a link with a viral infection acting as a trigger to a rapid deterioration

triad of symptoms

- **Polyuria –** excess urine
- **Thirst** (polydipsia drinking a lot)
- **Weight loss** as fat and protein are metabolised by tissues because insulin is absent

diabetic ketoacidosis

- The high rates of -oxidation of fats in the liver coupled to the low insulin/antiinsulin ratio leads to the production of huge amounts of ketone bodies, such as acetoacetate, acetone and -hydroxybutyrate.

Clinical feature

- The features of keto-acidosis are
- prostration
- hyperventilation
- nausea vomiting
- dehydration and abdominal pain.
- Keto-acidosis is a very dangerous condition.

Type 2 diabetes

- The estimated prevalence in the UK is about 2%.
- Typically, the patients are older and often overweight.
- The disease has often been present for some time, maybe years, before diagnosis.

- At diagnosis patients retain about 50% of their -cells, however as the number of these cells falls patients develop disorders of insulin secretion or insulin resistance, so blood glucose is raised.

Clinical feature

- Patients may present with the classical triad of symptoms
- lack of energy
- persistent infections,
- thrush infections of the genitalia, or infections of the feet, slow healing minor skin damage
- visual problems

Diagnosis of diabetes

- a random venous plasma glucose concentration 11.1 mmol.l^{-1} **or**
- a fasting plasma glucose concentration 7.0 mmol.l^{-1} (whole blood 6.1 mmol.l^{-1}) **or**
- plasma glucose concentration 11.1 mmol.l^{-1} 2 hours after 75g anhydrous glucose in an oral glucose tolerance test (OGTT).

Management of Diabetes

Type 1 diabetes

- Insulin
- treat Infection
- social and psychological
- dietary management
- regular exercise
- Treat hypoglycaemia

Management of Diabetes

Type 2 diabetes

- Diet
- oral hypoglycaemic
  - sulphonylureas that increase insulin release from the remaining –cells and reduce insulin resistance and particularly
  - metformin that reduces gluconeogenesis.
- exercise

Prevention of type 2 diabetes

- Diet
- exercise

Metabolic consequences of persistent hyperglycaemia

- Persistent hyperglycaemia is associated, in some tissues, with the abnormal metabolism of glucose to products that may be harmful to cells

- This is because the uptake of glucose into cells of tissues such as peripheral nerves, the eye and the kidney does not require insulin and is determined by the extracellular glucose concentration.

Glucose + NADPH + H^+ ⟶ Sorbitol + NADP

- glycosylation of plasma proteins

+

Glycosylated haemoglobin (HbA1c)

- Glucose in the blood will react with the terminal valine of the haemoglobin molecule to produce glycosylated haemoglobin (HbA1c).

Clinical complications of Diabetes

Macrovascular

- Increased risk of stroke.
- Increased risk of myocardial infarction.
- Poor circulation to the periphery - particularly the feet.

Microvascular

- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy
- Diabetic feet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100
140
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260

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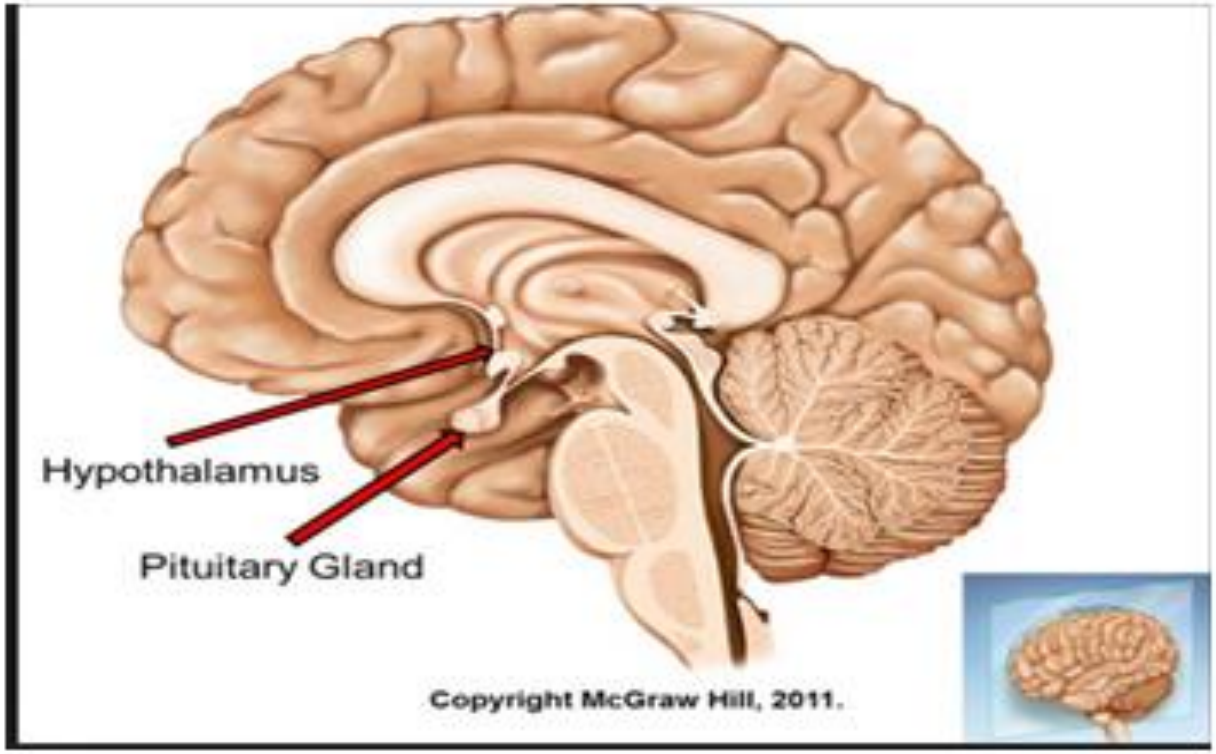
Control of Appetite

Energy intake/energy output balance

satiety centre in the hypothalamus which controls the timing and amount of food intake


Hypothalamus
Pituitary Gland
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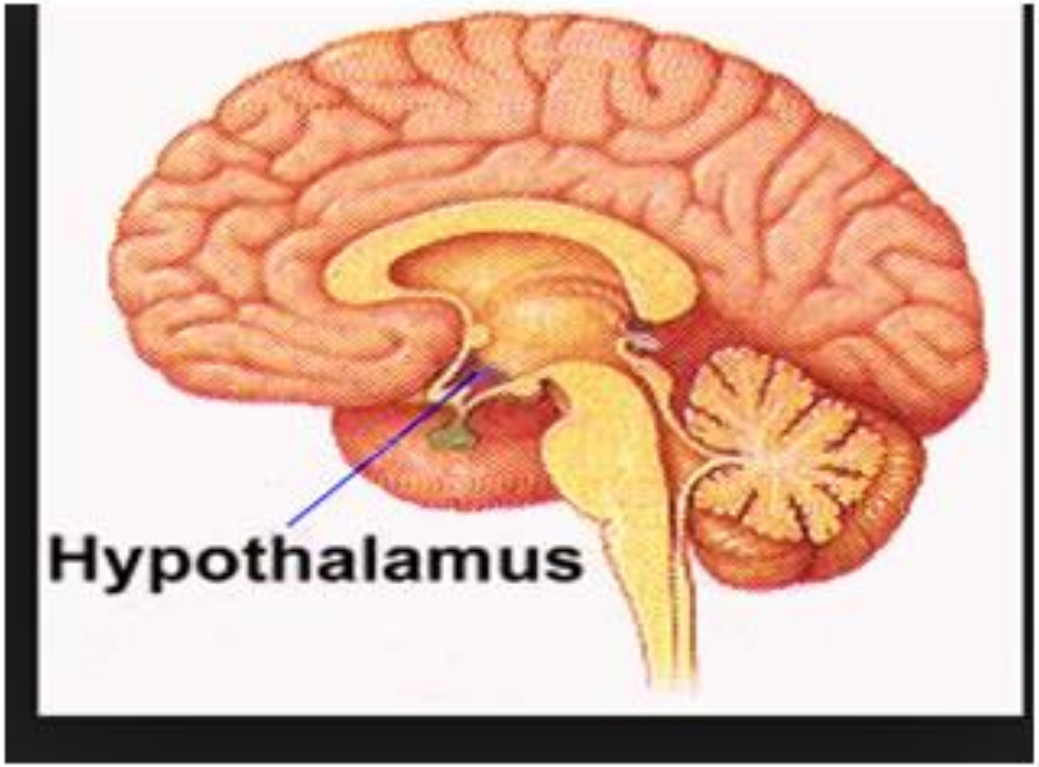
Hypothalamus

Control of appetite

- arcuate nucleus in the hypothalamus
  - primary neurones
    excitatory and inhibitory
  - secondary neurones

- The excitatory neurones stimulate appetite via the release of two peptides:
  - neuropeptide Y (NPY)
  - agouti-related peptide (AgRP).
- inhibitory neurones
  -releasing pro-opiomelanocortin (POMC)

- a reward system in the brain So, in response to the stomach being filled with food, there is a release of POMC in the brain which suppresses appetite, but also the -endorphin derived from this produces feelings of euphoria and tiredness.

feedback from the body to the hypothalamus, and this is provided by several hormones

Ghrelin

- is a peptide hormone released from the wall of the empty stomach, which activates the stimulatory neurones in the arcuate nucleus stimulating appetite
- Stretch of the stomach wall caused by food intake inhibits ghrelin

Hormone leptin

- Leptin is a peptide hormone released into the blood by adipocytes in fat stores in the body.
- Leptin acts by stimulating inhibitory neurones and inhibiting stimulatory neurones in the arcuate nucleus to suppress appetite

- A lack of leptin production or insensitivity to leptin has been associated with obesity.

Insulin

Insulin suppresses appetite via the same mechanism as leptin

Hormone Control of Hunger.mp4

Metabolic Syndrome

- insulin resistance
- dyslipidaemia
- glucose intolerance
- hypertension
- central adiposity

What is Metabolic Syndrome.mp4