ELRAZI UNIVERSITY

Faculty of medicine

ENDOCRINE PATHOLOGY
ENDOCRINE PANCREAS
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- The pancreas consists of two functionally distinct components:
  - The exocrine pancreas, which secretes digestive enzymes into the duodenum
  - The islets of Langerhans, scattered within the tissues of the exocrine pancreas act together as an endocrine gland.

CELL TYPES IN THE ISLETS OF LANGERHANS

Cell Type	Average Prevalence (%) in islets	Hormone produced	
		Identity	Action
Beta	70	Insulin	Promotes glucose entry, Glucagon synthesis (and inhibits breakdown). Lipogenesis(and inhibit lipolysis)and protein synthesis(together with growth hormone
Alpha	20	Glucagon	Promotes breakdown of glycogen(only in liver) and gluconeogenesis (from proteins)
Delta	8	Somatostatin	Inhibits insulin and glucagon secretion
PP	2	Pancreatic polypeptides	Function in humans unknown

DIABETES MELLITUS

- Abnormal metabolic state characterised by glucose intolerance due to inadequate insulin action
- Type 1 (juvenile onset) due to destruction of Bela cells (probably a result of virus infection and genetic factors); Insulin dependent
- Type 2 (maturity onset) due to defective insulin action; treatment by weight reduction and oral hypoglycaemlc agents
- Complications include
  - ❑ Accelerated atherosclerosis,
  - ❑ Susceptibility to infections, and
  - ❑ Microangiopathy affecting many organs

- Diagnosis is based on the clinical demonstration of glucose intolerance
- Insulin is unique, in that it is the only hormone with a hypoglycaemlc effect.
- There are live hormones that tend to exert a hyperglycaemic effect
  - **Glucagon,**
  - **Glucocorticoids,**
  - **Growth hormone,**
  - **Adrenaline (epinephrine)**
  - **And non-adrenaline (norepinephrine),**
- The hyperglycaemic effects of these hormones cannot be counterbalanced if there is inadequate insulin action.

PATHOGENESIS

- The actions of insulin are all anabolic, that is, they promote the laying down of tissue stores from circulating nutrients.
- The consequences of insulin deficiency are therefore catabolic, that is, there is breakdown of tissue energy stores.
- The major features of diabetes mellitus are:
  - **Inability to utilise, and overproduction of, glucose(hyperglycaemia)**
  - **Diminished protein synthesis**
  - **Lipolysis resulting in hyperlipidaemia, hence there is rapid wasting and weight loss.**

- In hyperglycaemia the renal threshold for glucose conservation is exceeded, so that there is osmotic diuresis resulting in polyuria, dehydration and thirst.
- Lipolysis may also have serious consequences.
- Free fatty acids are converted in the liver to ketone bodies, such as acetoacetate, acetone and beta-hydroxybutyrate.
- These dissociate to release hydrogen ions, and a profound metabolic acidosis may ensue.

- The combined result of severe ketosis, acidosis, hyperglycaemia, hyperosmolarity and electrolyte disturbance is to impair cerebral function, producing diabetic ketoacidotic coma.
- This is quite distinct from the hypoglycaemic coma that may also be found in diabetic patients; this is due to insulin overdosage, and has entirely different clinical features.

CLASSIFICATION

- **Type 1 (juvenile-onset, insulin-dependent diabetes)**
- Typically presents in childhood.
- The patient usually shows the catabolic effects and is prone to develop ketoacidosis.
- The central defect is inadequate insulin secretion by the beta cells of the pancreas, and this can be corrected only by the life-long administration of exogenous insulin.

- Postmortem examination of the pancreas in patients who had recently developed type 1 diabetes but died from other causes (e.g. road traffic accident) shows lymphocytic Infiltration of the islets with specific destruction of the beta-cells.
- There are three major theories concerning the aetiology of these changes:
  - **Autoimmune destruction,**
  - **Genetic factors and**
  - **Viral infection.**

- ***Autoimmune destruction***. The majority of patients have circulatory antibodies to several different types of islet cell.
- ***Genetic factors***. As with other ‘organ-specific' autoimmune diseases, there is an association with certain HLA types. It seems that environmental factors also play a role.
- ***Viral infection***. Titers of antibodies to viruses such as Coxsackie B types and mumps are elevated in some patients developing this type of diabetes

- **Type 2 (maturity-onset, non-insulin-dependent diabetes)**
  - is more common than type 1 and usually presents in middle age, being commonest in the obese.
  - Patients are not prone to ketoacidosis, but occasionally develop a non-ketotic coma in which there is extreme hyperosmolarity of the plasma.
  - Insulin secretion is normal or increased and the central defect may therefore be a reduction in the number of cell surface receptors for insulin.

- Type 2 (maturity-onset, non-insulin-dependent diabetes)
- Genetic factors clearly play an important part in the aetiology of type 2 diabetes.
- Treatment is usually by weight reduction coupled with orally administered drugs that potentiate the action of insulin.

- **Secondary diabetes**
- Hypersecretion of any of the hormones that tend to exert a hyperglycaemic effect may cause glucose intolerance.
- Thus Cushing's syndrome, phaeochromocytoma, acromegaly and glucagonomas may cause secondary diabetes.
- Generalized destruction of the pancreas by acute and chronic pancreatitis, haemochromatosis and occasionally, carcinoma may cause insulin deficiency.

COMPLICATIONS

- The commonest complications are seen in blood vessels.
- Atheroma, often ultimately severe and extensive, develops at an earlier age than in the non-diabetic population. Small blood vessels show basal lamina thickening and endothelial cell proliferation (diabetic microangiopathy), frequently causing retinal and renal damage.
- About 80% of adult diabetics die from cardiovascular disease, while patients with longstanding diabetes, especially type 1, frequently develop serious renal and retinal disease.

TUMOURS

- Less common than pancreatic adenocarcinoma
- Present with endocrine effects and may be malignant
- Insulinoma: causes hypoglycaemia
- Glucagonoma: causes secondary diabetes and skin rash
- Adenomas and carcinomas derived from the islet cells are quite rare.

TUMOURS

- **Insulinoma**

  - Insulinoma is the commonest islet cell tumour and produces hypoglycaemia through hypersecretion of insulin.

  - During hypoglycaemic attacks, the patient develops confusion, psychiatric disturbances and possibly coma. Diagnosis is urgent because hypoglycaemia may produce permanent cerebral damage.

- **Other islet cell tumours** are very rare, but include somatostatinomas and tumours secreting vasoactive intestinal peptide (VIP), which leads to watery diarrhoea.

- **Gastrinomas :** Although gastrin is usually produced in the G-cells of the stomach, tumours of the G-cells, called gastrinomas, most commonly originate in the pancreas.

- Islet cell tumours and gastrinomas may occur as part of one of the MEN syndromes , most commonly MEN type 1.

THANK YOU