Lec. 8: Pancreatic hormones

The pancreases' is an intra-abdominal organ, it has endocrine and exocrine parts,

- **The exocrine part** is responsible for the production and releases of digestive enzymes
- **The endocrine part** (the islets of Langerhans) secrets hormones, There are four major cell types in the islets of Langerhans:
  1) α cell, responsible for the production of glucagon.
  2) β-cell for production of insulin,
  3) δ (Delta)-cell for production of somatostatin, and
  4) F (or PP) cell responsible for the production of pancreatic polypeptide.

Insulin

- Is a peptide hormone made up of 51 amino acids, arranged as two polypeptide chains, the A chain has 21 amino acids and is linked to the B chain (30 a.a) by two disulfide bridges.
- **Biosynthesis** of insulin occurs from a precursor called preproinsulin (109 aminoacids), which consists of proinsulin plus an extension of 23 amino acids. It is cleaved by peptidase, and converted to proinsulin (86AA). proinsulin is a single polypeptide, It has A and B chains, the A chain is linked to the B chain by a connecting peptide (C-peptide), then Proinsulin is converted to insulin by proteolysis and is secreted into the circulation upon stimulation,the process liberates inactive C-peptide.
- The **main effect** of insulin is to lower blood glucose level as described below
- **What stimulate insulin secretion?**
  Carbohydrates as Glucose, Fructose
  Hormones as Glucagon and Growth hormone
  Some amino Acids, Fatty acids

Glucagon

- Produced by the α cells of the islets of Langerhans, it is polypeptide hormone. It is synthesized from a larger precursor (proglucagon).
- It acts through cell membrane receptor.
- Its **main effect** is to elevate blood glucose level.
- **Stimulators of glucagon secretion**
  Hypoglycemia, Amino Acids (i.e., Arginine), adrenaline, noradrenaline.

Pancreatic Polypeptide (PP)

PP is peptide hormones. It is synthesized and secreted by F cells (or PP cells). The level of PP is increased with ingestion of a mixed meal.

Somatostatin

- It is secreted by δ-cells of the pancreas, is a 14 amino acid peptide, identical to somatostatin secreted by the hypothalamus.
- In neural tissue somatostatin inhibits GH secretion and thus has systemic effects.

In the pancreas, somatostatin acts as a paracrine inhibitor of other pancreatic hormones. Increasing as blood glucose levels rise and thus leading to down-regulation of glucagon secretion.

Role of pancreatic hormones

Insulin and glucagon have very important role in the maintenance of blood glucose within normal range; Glucagon and insulin have antagonistic effects, with glucagon promoting glucose production and release into the bloodstream, and insulin promoting the transport of glucose into cells from the bloodstream and inhibiting glucose production.

i. in the feeding state

Insulin is the major hormone of the fed state, the ingestion of a meal increases insulin secretion immediately. The rise in serum insulin is proportional to the rise in serum glucose, it lower blood glucose by the the following ways:

a) Insulin **increases the rate of uptake of glucose into cells** by stimulating glucose transport across the plasma membrane.

b) Insulin **reduces the rate of release of glucose from the liver.** It does this by:

1) inhibiting glycogenolysis (which is the breakdown of glycogen to glucose)
2) stimulate glycolysis(which is the oxidation of glucose to obtain energy)
3) Enhance glycogen synthesis which is the synthesis of glycogen from glucose.
4) Insulin inhibit gluconeogenesis (gluconeogenesis is the convertion of certain molecules as amino acid, fatty acid to glucose) by inhibition of fatty acid mobilization from adipose tissue.

c) Other Insulin effects

In addition to its role in regulating glucose metabolism, insulin is anabolic hormone ,it stimulates lipogenesis, diminishes lipolysis, and increases amino acid transport into cells. Insulin also modulates transcription, altering the cell content of mRNAs. It stimulates growth, DNA synthesis, and cell replication.

ii. In the Fasting State:

Glucagon, catecholamines and cortisol are the major hormones during fasting state they are called counterregulatory hormones.
Glucagon from the pancrease raises blood glucose levels by:

a) Stimulating the breakdown of glycogen into glucose (glycogenolysis)
b) Stimulating glucose production from amino acids and fatty acids (gluconeogenesis)
c) Glucagon also stimulates **ketogenesis,** providing an alternative fuel for those tissues that can use it and sparing glucose for those that cannot act without.
d) Also causes **lipolysis** in adipose tissue (which provides FFAs and glycerol for gluconeogenesis).

- **Fasting** is defined as the condition where the body is deprived of food for at least four hours. Hypoglycemia is a stressful condition for the body; Glucagon favors use of amino acids, especially alanine, to produce glucose (gluconeogenesis), and stimulation of glycogenolysis to increase glucose production. Insulin is decreased in the fasting state, so the anti-lipolytic effect of insulin is reduced. This, along with some increase in catecholamines, stimulates breakdown of tissue triglyceride to glycerol and FFA (lipolysis). Fatty acids are used as energy source.
- Therefore, in the fasting state, in addition to reduction of insulin secretion, three major hormones which have the opposite effect to that of insulin (and hence are called counterregulatory hormones) are increased. These hormones are: glucagon, catecholamines, and cortisol. Growth hormone may also contribute to this mechanism as a fourth counterregulatory hormone. Fasting, results in reduced insulin and increased counterregulatory hormones.

❖ ***hormone resistance syndrome***

A condition caused by a reduced or absent end-organ responsiveness to a biologically active hormone, which may be due to a hormone receptor defect or a post-receptor defect.

❖ ***Diabetes mellitus***

It is a chronic disease of impaired carbohydrate metabolism. β-cells of islets of Langerhans fail to secrete adequate amounts of insulin (type1 DM)or it may be due to the resistance to insulin action (type 2DM) or both, this causes hyperglycemia and glycosuria Secondary changes in the protein, lipid, water & electrolytes metabolism may also occur.

Adipose tissue derived hormones (Adipocytokines)

Adipose tissue is an active metabolic and endocrine organ. it secretes hormones with important endocrine functions. These include for example leptin, adiponectin and resistin. Adipose tissue is also a major site for metabolism of sex steroids and glucocorticoids.example of adipocytes derived hormones**:**

Leptin

Leptin is a hormone produced by adipocytes.

It is involved in the maintenance of a stable body fat mass. Leptin is important in the regulation of appetite, food intake and energy expenditure, sexual maturation and fertility, haematopoiesis and activity of the hypothalamic-pituitary-gonadal axis.

Hormones of the Kidney

The human kidney secretes two hormones:

1) **Erythropoietin (EPO):** is a glycoprotein. It acts on the bone marrow to increase the production of red blood cells. Stimuli such as bleeding or moving to high altitudes (where oxygen is less) trigger the release of EPO.
2) **Calcitriol** acts on the cells of the **intestine** to promote the absorption of calcium from food, **bone** to mobilize calcium from the bone to the blood.

Hormones of the Skin

- When ultraviolet radiation strikes the skin, it triggers the conversion of dehydrocholesterol (a cholesterol derivative) into **calciferol** (vitamin D_3). Calciferol travels in the blood to the liver where it is converted into 25[OH] vitamin D_3.
- This compound travels to the kidneys where it is converted into **calcitriol** (1,25 $[OH]_2$ vitamin D_3). This final step is promoted by the parathyroid hormone (PTH)
- Although called a vitamin, calciferol and its products fully qualify as hormones because they are
    - made in certain cells,
    - carried in the blood,
    - affect gene transcription in target cells.

Hormones of the Heart

- **Natriuretic Peptides** In response to a rise in blood pressure, the heart releases two peptides:
    1) **A-type Natriuretic Peptide** (ANP) released from stretched **atria**
    2) **B-type Natriuretic Peptide** (BNP) released from the **ventricles**.
- Both hormones lower blood pressure.