Endocrine Functions of Pancreas

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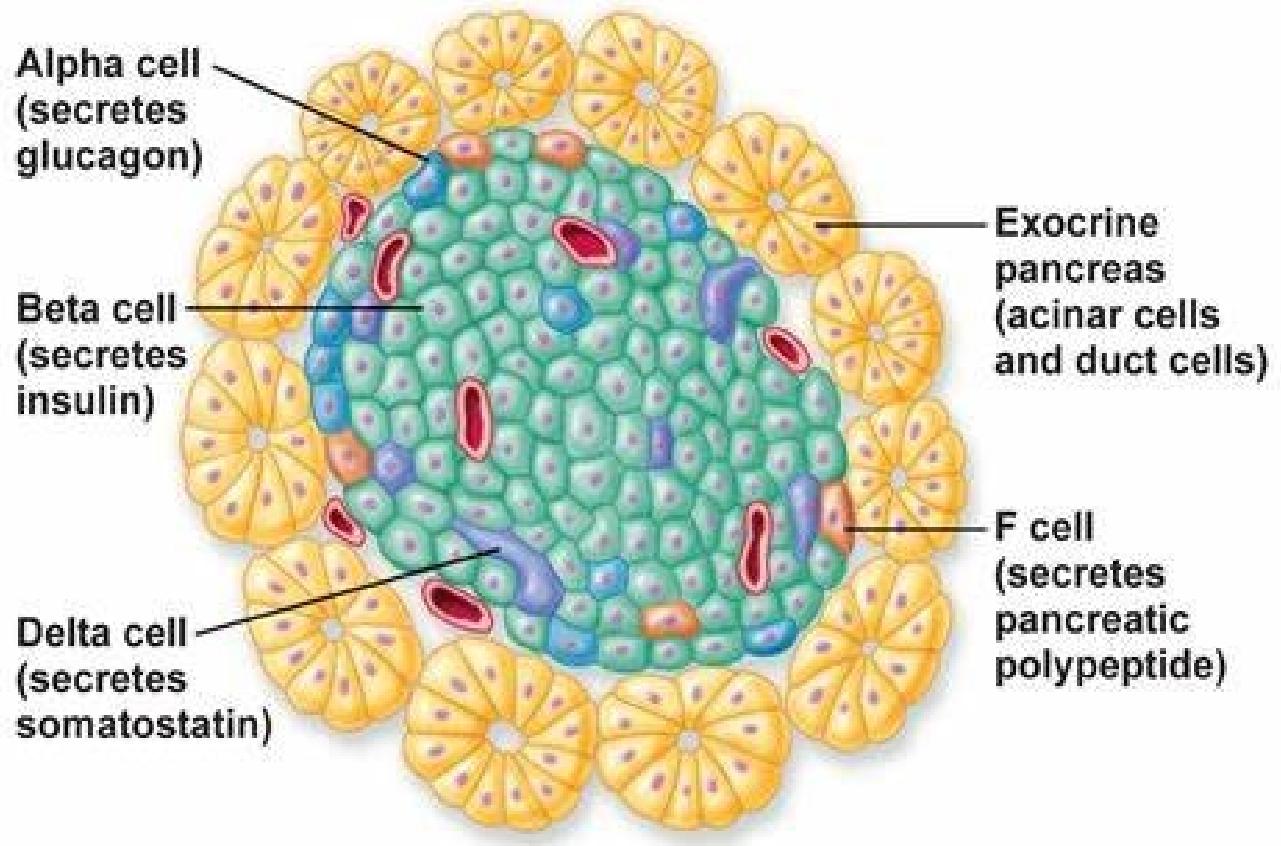
ISLETS OF LANGERHANS

- Endocrine function of pancreas is performed by the islets of Langerhans.
- Human pancreas contains about 1 to 2 million islets.
- Islets of Langerhans consist of four types of cells:

1. A cells or **α-cells :** which secrete **glucagon**
2. B cells or **β-cells :** which secrete **insulin**
3. D cells or **δ-cells :** which secrete **somatostatin**
4. F cells or **PP cells :** which secrete **pancreatic polypeptide**



INSULIN

SOURCE OF SECRETION

- Insulin is secreted by B cells or the β-cells in the islets of Langerhans of pancreas.

CHEMISTRY, HALF-LIFE AND PLASMA LEVEL

- Insulin is a polypeptide with 51 amino acids and a molecular weight of 5,808.
- It has two amino acid chains called α and β chains, which are linked by disulfide bridges.
- The α-chain of insulin contains 21 amino acids and β-chain contains 30 amino acids.
- The biological half-life of insulin is 5 minutes.
- Basal level of insulin in plasma is 10 μU/mL.

SYNTHESIS AND METABOLISM

- Synthesis of insulin occurs in the rough endoplasmic reticulum of β-cells in islets of Langerhans.
- It is synthesized as **preproinsulin,** that gives rise to **proinsulin.**
- Proinsulin is converted into insulin.
- Insulin is degraded in liver and kidney by a cellular enzyme called **insulin protease** or **insulin-degrading enzyme.**

ACTIONS OF INSULIN

- Insulin is the important hormone that is concerned with the regulation of carbohydrate metabolism and blood glucose level.
- It is also concerned with the metabolism of proteins and fats.

1. ON CARBOHYDRATE METABOLISM

- Insulin is the only antidiabetic hormone secreted in the body, i.e. it is the only hormone in the body that reduces blood glucose level.
- Insulin reduces the blood glucose level by its following actions on carbohydrate metabolism:

A. Increases transport and uptake of glucose by the cells

- Insulin facilitates the transport of glucose from blood into the cells by increasing the permeability of cell membrane to glucose.

B. Promotes peripheral utilization of glucose

- Insulin promotes the peripheral utilization of glucose.
- In presence of insulin, glucose which enters the cell is oxidized immediately.
- The rate of utilization depends upon the intake of glucose.

C. Promotes storage of glucose – glycogenesis

- Insulin promotes the rapid conversion of glucose into glycogen (glycogenesis), which is stored in the muscle and liver.
- In liver, when glycogen content increases beyond its storing capacity, insulin causes conversion of glucose into fatty acids.

D. Inhibits glycogenolysis

- Insulin prevents glycogenolysis, i.e. the breakdown of glycogen into glucose in muscle and liver.

E. Inhibits gluconeogenesis

- Insulin prevents gluconeogenesis, i.e. the formation of glucose from proteins by inhibiting the release of amino acids from muscle and by inhibiting the activities of enzymes involved in gluconeogenesis.

2. ON PROTEIN METABOLISM

- Insulin facilitates the synthesis and storage of proteins and inhibits the cellular utilization of proteins by the following actions:

A. Facilitating the transport of amino acids into the cell from blood, by increasing the permeability of cell membrane for amino acids.

B. Accelerating protein synthesis by influencing the transcription of DNA and by increasing the translation of mRNA

C. Preventing protein catabolism by decreasing the activity of cellular enzymes which act on proteins

D. Preventing conversion of proteins into glucose. Thus, insulin is responsible for the conservation and storage of proteins in the body.

3. ON FAT METABOLISM

- Insulin stimulates the synthesis of fat and increases the storage of fat in the adipose tissue.
- Actions of insulin on fat metabolism are:

A. Synthesis of fatty acids and triglycerides

- Insulin promotes the transport of excess glucose into liver cells. This glucose is utilized for the synthesis of fatty acids and triglycerides.
- Insulin promotes the synthesis of lipids by activating the enzymes which convert:

i. Glucose into fatty acids

ii. Fatty acids into triglycerides.

B. Transport of fatty acids into adipose tissue

- Insulin facilitates the transport of fatty acids into the adipose tissue.

C. STORAGE OF FAT

- Insulin promotes the storage of fat in adipose tissue by inhibiting the enzymes which degrade the triglycerides.

4. ON GROWTH

- Along with growth hormone, insulin promotes growth of body by its anabolic action on proteins.
- It enhances the transport of amino acids into the cell and synthesis of proteins in the cells.

REGULATION OF INSULIN SECRETION

- Insulin secretion is mainly regulated by blood glucose level.
- In addition, other factors like amino acids, lipid derivatives, gastrointestinal and endocrine hormones and autonomic nerve fibers also stimulate insulin secretion.

1. ROLE OF BLOOD GLUCOSE LEVEL

- When blood glucose level is normal (80 to 100 mg/dL), the rate of insulin secretion is low (up to 10 µU/minute).
- When blood glucose level increases between 100 and 120 mg/dL, the rate of insulin secretion rises rapidly to 100 µU/minute.
- When blood glucose level rises above 200 mg/dL, the rate of insulin secretion also rises very rapidly up to 400 µU/minute.

2. ROLE OF PROTEINS

- Excess amino acids in blood also stimulate insulin secretion so it alone can cause a slight increase in secretion of insulin.
- However, amino acids potentiate the action of glucose on insulin secretion so that, in the presence of amino acids, elevated blood glucose level increases insulin secretion to a great extent.

3. ROLE OF ENDOCRINE HORMONES

- Diabetogenic hormones like glucagon, growth hormone and cortisol also stimulate insulin secretion, indirectly.
- All these hormones increase the blood glucose level, which stimulates β-cells for insulin secretion.
- **Prolonged hypersecretion** of these hormones causes exhaustion of β-cells, resulting in diabetes mellitus.

GLUCAGON

SOURCE OF SECRETION

- Glucagon is secreted from **A cells** or **α-cells** in the islets of Langerhans of pancreas.
- It is also secreted from **A cells** of stomach and **L cells** of intestine.

CHEMISTRY AND HALF-LIFE

- Glucagon is a polypeptide with a molecular weight of 3,485. It contains 29 amino acids.
- Half-life of glucagon is 3 to 6 minutes.

SYNTHESIS AND METABOLISM

- Glucagon is synthesized from **preproglucagon** precursor in the α-cells of islets.
- Preproglucagon is converted into **proglucagon,** which gives rise to glucagon.
- About 30% of glucagon is degraded in liver and 20% in kidney.
- 50% of the circulating glucagon is degraded in blood itself by enzymes such as **serine** and **cysteine proteases.**

ACTIONS OF GLUCAGON

- Actions of glucagon are antagonistic to those of insulin.
- It increases the blood glucose level, peripheral utilization of lipids and the conversion of proteins into glucose.

1. ON CARBOHYDRATE METABOLISM

- Glucagon increases the blood glucose level by :

i. Increasing glycogenolysis in liver and releasing glucose from the liver cells into the blood.

ii. Increasing gluconeogenesis in liver by increasing the transport of amino acids into the liver cells. The amino acids are utilized for glucose formation.

2. ON PROTEIN METABOLISM

- Glucagon increases the transport of amino acids into liver cells. The amino acids are utilized for gluconeogenesis.

3. ON FAT METABOLISM

- Glucagon shows lipolytic and ketogenic actions.
- It increases lipolysis by increasing the release of free fatty acids from adipose tissue.
- The lipolytic activity of glucagon, in turn promotes ketogenesis (formation of ketone bodies) in liver.

4. OTHER ACTIONS GLUCAGON

- Inhibits the secretion of gastric juice
- Increases the secretion of bile from liver.

REGULATION OF GLUCAGON SECRETION

- Secretion of glucagon is controlled mainly by glucose and amino acid levels in the blood.

1. ROLE OF BLOOD GLUCOSE LEVEL

- When blood glucose level decreases below 80 mg/dL of blood, α-cells are stimulated and more glucagon is released.
- Glucagon, in turn increases the blood glucose level.
- On the other hand, when blood glucose level increases, secretion of glucagon decreases.

2. ROLE OF AMINO ACID LEVEL IN BLOOD

- Increase in amino acid level in blood stimulates the secretion of glucagon.
- Glucagon, in turn converts the amino acids into glucose.

3. ROLE OF OTHER FACTORS

- Factors which increase glucagon secretion are Exercise, Stress, Gastrin and Cortisol.
- Factors which inhibit glucagon secretion are Somatostatin, Insulin, Free fatty acids and Ketones.

SOMATOSTATIN

SOURCE OF SECRETION, CHEMISTRY AND HALF-LIFE

- Somatostatin is secreted from:
  i. Hypothalamus
  ii. D cells (δ-cells) in islets of Langerhans of pancreas
  iii. D cells in stomach and upper part of small intestine.
- Somatostatin is a polypeptide. It is synthesized in two forms, namely somatostatin-14 and somatostatin-28.
- Half-life of somatostatin is 2 to 4 minutes.

SYNTHESIS AND METABOLISM

- Somatostatin is synthesized from the precursor prosomatostatin.
- Prosomatostatin is converted mostly into both somatostatin-14 and somatostatin- 28.
- Somatostatin is degraded in liver and kidney.

ACTIONS OF SOMATOSTATIN

- Somatostatin acts within islets of Langerhans and it inhibits the secretion of both glucagon and insulin
- It decreases the motility of stomach, duodenum and gallbladder.
- Hypothalamic somatostatin inhibits the secretion of GH and TSH from anterior pituitary.
- That is why, it is also called **growth hormone-inhibitory hormone** (GHIH).

REGULATION OF SECRETION OF SOMATOSTATIN

- Secretion of pancreatic somatostatin is stimulated by glucose and amino acids.
- Hypersecretion of somatostatin, leads to hyperglycemia and other symptoms of diabetes mellitus.

PANCREATIC POLYPEPTIDE

SOURCE OF SECRETION, CHEMISTRY AND HALF-LIFE

- Pancreatic polypeptide is secreted by F cells or PP cells in the islets of Langerhans. It is also found in small intestine.
- Pancreatic polypeptide is a polypeptide with 36 amino acids.
- Its half-life is 5 minutes.

SYNTHESIS AND METABOLISM

- Pancreatic polypeptide is synthesized from preprohormone precursor called **prepropancreatic polypeptide** in the PP cells of islets.
- Pancreatic polypeptide is degraded and removed from circulation mainly in kidney.

ACTIONS OF PANCREATIC POLYPEPTIDE

- Exact physiological action of pancreatic polypeptide is not known.
- It is believed to increase the secretion of glucagon from α-cells in islets of Langerhans.

REGULATION OF SECRETION

- Secretion of pancreatic polypeptide is stimulated by the presence of chyme containing more proteins in the small intestine.

REGULATION OF BLOOD GLUCOSE LEVEL

NORMAL BLOOD GLUCOSE LEVEL

- In normal persons, blood glucose level is controlled within a narrow range.
- In the early morning after overnight **fasting,** the blood glucose level is low ranging between 70 and 110 mg/dL.
- Between first and second hour after meals **(postprandial),** the blood glucose level rises to 100 to 140 mg/dL.
- Glucose level in blood is brought back to normal at the end of second hour after the meals.

- Blood glucose regulating mechanism is operated through liver and muscle by the influence of the pancreatic hormones – insulin and glucagon.
- Many other hormones are also involved in the regulation of blood glucose level. Among them, insulin is the only hormone that reduces the blood glucose level and it is called the **antidiabetogenic hormone.**

NECESSITY OF REGULATION OF BLOOD GLUCOSE LEVEL

- Regulation of blood glucose (sugar) level is very essential because, glucose is the only nutrient that is utilized for energy by many tissues such as brain tissues, retina and germinal epithelium of the gonads.

ROLE OF LIVER IN THE MAINTENANCE OF BLOOD GLUCOSE LEVEL

- Liver serves as an important **glucose buffer system.**
- When blood glucose level increases after a meal, the excess glucose is converted into glycogen and stored in liver.
- Afterwards, when blood glucose level falls, the glycogen in liver is converted into glucose and released into the blood.
- The storage of glycogen and release of glucose from liver are mainly regulated by insulin and glucagon.

ROLE OF INSULIN IN THE MAINTENANCE OF BLOOD GLUCOSE LEVEL

- Insulin decreases the blood glucose level and it is the only antidiabetic hormone available in the body.

ROLE OF GLUCAGON IN THE MAINTENANCE OF BLOOD GLUCOSE LEVEL

- Glucagon increases the blood glucose level.

ROLE OF OTHER HORMONES IN THE MAINTENANCE OF BLOOD GLUCOSE LEVEL

- Other hormones which increase the blood glucose level are:
  1. Growth hormone
  2. Cortisol
  3. Adrenaline
- Thus, liver helps to maintain the blood glucose level by storing glycogen when blood glucose level is high after meals and by releasing glucose, when blood glucose level is low after 2 to 3 hours of food intake.
- Insulin helps to control the blood glucose level, especially after meals, when it increases.
- Glucagon and other hormones help to maintain the blood glucose level by raising it in between the meals.

APPLIED PHYSIOLOGY

HYPOACTIVITY – DIABETES MELLITUS

- Diabetes mellitus is a metabolic disorder characterized by high blood glucose level, associated with other manifestations.
- **'Diabetes'** means **'polyuria'** and **'mellitus'** means **'honey'.**
- The name 'diabetes mellitus' was coined by Thomas Willis, who discovered sweetness of urine from diabetics in 1675.
- In most of the cases, diabetes mellitus develops due to deficiency of insulin.

CLASSIFICATION OF DIABETES MELLITUS

- Diabetes may be primary or secondary.
- Primary diabetes is unrelated to another disease. Secondary diabetes occurs due to damage or disease of pancreas by another disease or factor.
- Recent classification divides primary diabetes mellitus into two types, Type I and Type II.

TYPE I DIABETES MELLITUS

- Type I diabetes mellitus is due to deficiency of insulin because of destruction of β-cells in islets of Langerhans.
- This type of diabetes mellitus may occur at any age of Life But, it usually occurs before 40 years of age.
- The persons affected by this require insulin injection. So it is also called **insulin-dependent diabetes mellitus (IDDM).**
- Type I diabetes mellitus develops rapidly and progresses at a rapid phase. It is not associated with **obesity**.

CAUSES OF TYPE I DIABETES MELLITUS

i. Degeneration of β-cells in the islets of Langerhans of pancreas
ii. Destruction of β-cells by viral infection
iii. Congenital disorder of β-cells
iv. Destruction of β-cells during autoimmune diseases.

TYPE II DIABETES MELLITUS

- Type II diabetes mellitus is due to insulin resistance (failure of insulin receptors to give response to insulin). So, the body is unable to use insulin.
- About 90% of diabetic patients have type II diabetes mellitus. It usually occurs after 40 years.
- Only some forms of Type II diabetes require insulin.
- In most cases, it can be controlled by oral hypoglycemic drugs. So it is also called **noninsulindependent diabetes mellitus (NIDDM).**
- Type II diabetes mellitus is associated with obesity.

COMMON CAUSES OF TYPE II DIABETES MELLITUS (INSULIN RESISTANCE) ARE:

- Genetic disorders (significant factors causing type II diabetes mellitus)
- Lifestyle changes such as bad eating habits and physical inactivity, leading to obesity
- Stress.

SIGNS AND SYMPTOMS OF DIABETES MELLITUS

- Various manifestations of diabetes mellitus develop because of insulin deficiency.
- Increased blood glucose level (300 to 400 mg/dL) due to reduced utilization.
- Mobilization of fats for energy purpose, leading to elevated fatty acid content in blood. This causes deposition of fat on the wall of arteries and development of atherosclerosis.
- Depletion of proteins from the tissues.

- Following are the signs and symptoms of diabetes mellitus:

A. GLUCOSURIA

- Glucosuria is the loss of glucose in urine.
- Normally, glucose does not appear in urine.
- When glucose level rises above 180 mg/dL in blood, glucose appears in urine. It is the renal threshold level for glucose.

B. POLYURIA

- Excess urine formation with increase in the frequency of voiding urine is called polyuria.

C. POLYDIPSIA

- Increase in water intake is called polydipsia.
- Excess loss of water decreases the water content and increases the salt content in the body. This stimulates the thirst center in hypothalamus.

D. POLYPHAGIA

- Polyphagia means the intake of excess food. It is very common in diabetes mellitus.

E. ASTHENIA

- Loss of strength is called asthenia.
- Body becomes very weak because of this. Asthenia occurs due to protein Depletion.

F. ACIDOSIS

- During insulin deficiency, a large amount of fat is broken down to release energy.
- It causes the formation of excess **ketoacids,** leading to acidosis.

G. COMA

- Due to Kussmaul breathing, (increase in rate and depth of respiration caused by severe acidosis) large amount of carbon dioxide is lost during expiration.
- It leads to drastic reduction in the concentration of bicarbonate ions causing severe acidosis and coma.
- It occurs in severe cases of diabetes mellitus.
- Increase in the blood glucose level develops hyperosmolarity of plasma which also leads to coma. It is called **hyperosmolar coma.**

COMPLICATIONS OF DIABETES MELLITUS

- Prolonged hyperglycemia in diabetes mellitus causes some complications.
- However, the patients with well controlled diabetes can postpone the onset or reduce the rate of progression of these complications.
- Initially, the untreated chronic hyperglycemia affects the blood vessels, resulting in vascular complications like atherosclerosis.
- Vascular complications are responsible for the development of most of the complications of diabetes such as:

A. Cardiovascular complications like:
   I. Hypertension
   II. Myocardial infarction
B. Degenerative changes in retina called diabetic retinopathy.
C. Degenerative changes in kidney known as diabetic nephropathy.
D. Degeneration of autonomic and peripheral nerves called diabetic neuropathy.

HYPERACTIVITY – HYPERINSULINISM

- Hyperinsulinism is the hypersecretion of insulin.

SIGNS AND SYMPTOMS OF HYPERINSULINISM

1. HYPOGLYCEMIA

- Blood glucose level falls below 50 mg/dL.

2. MANIFESTATIONS OF CENTRAL NERVOUS SYSTEM

- Manifestations of central nervous system occur when the blood glucose level decreases.
- All the manifestations are together called **neuroglycopenic symptoms.**
- Initially, the activity of neurons increases, resulting in nervousness, tremor all over the body and sweating.
- If not treated immediately, it leads to **clonic convulsions** and **unconsciousness.**
- Slowly, the convulsions cease and **coma** occurs due to the damage of neurons.

THANK YOU