Islets of Langerhans

TDC Part III
Paper –V, Group D

Learning Objectives

- Definition of Islets of Langerhans.
- Description of the morphology and function of the pancreatic islets
- Compare and contrast the functions of insulin and glucagon

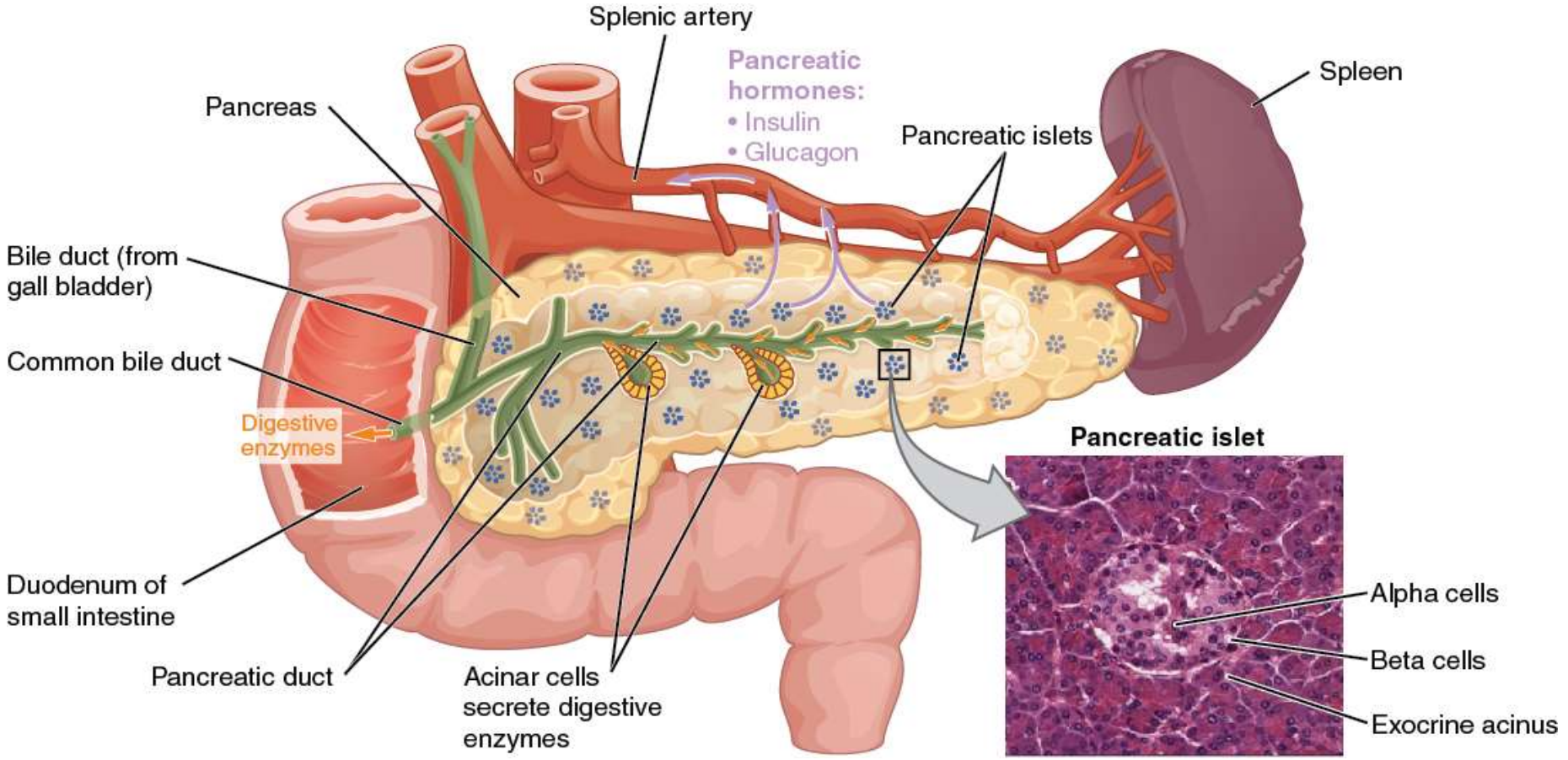
Definition

- “The islets of Langerhans are a cluster of cells within the pancreas that are responsible for the production and release of hormones that regulate glucose levels.”
- Also called as Pancreatic Islets.

Pancres and Islets of Langerhans

- The pancreas is a long, slender organ, most of which is located posterior to the bottom half of the stomach . Although it is primarily an exocrine gland secreting a variety of digestive enzymes, but it also possesses hormones secreting cells in cluster, thus have endocrine functions too.
- Islets of Langerhans are microscopic structures 50–250 µm in diameter scattered throughout the pancreas, with a maximum density in the tail. Microscopically, the islets are composed of small uniform cells with round nuclei and scant cytoplasm. Routine microscopy does not permit differentiation of the various types of cells contained within the islets; this requires immunohistochemistry
- .

The pancreas



. **Pancreas. The pancreatic exocrine function involves the acinar cells secreting digestive enzymes that are transported into the small intestine by the pancreatic duct. Its endocrine function involves the secretion of insulin (produced by beta cells) and glucagon (produced by alpha cells) within the pancreatic islets. These two hormones regulate the rate of glucose metabolism in the body. The micrograph reveals pancreatic islets. LM × 760. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)**

- Islets of Langerhans in the human can be identified with electron microscopy based upon ultrastructural differences in their secretory granules:

1) beta granules, which are round or rectangular with a crystalline structure
2) alpha granules which are round with a central dense core; and
3) delta granules, which are round, less dense than alpha granules and have an amorphous appearance.

CELLS AND SECRETIONS OF THE PANCREATIC ISLETS

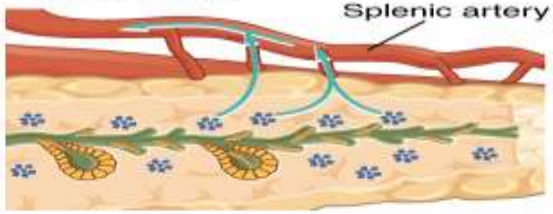
The pancreatic islets each contain four varieties of cells:

1. The **alpha cell** produces the hormone glucagon and makes up approximately 20 percent of each islet. Glucagon plays an important role in blood glucose regulation; low blood glucose levels stimulate its release.
2. The **beta cell** produces the hormone insulin and makes up approximately 75 percent of each islet. Elevated blood glucose levels stimulate the release of insulin.
3. The **delta cell** accounts for four percent of the islet cells and secretes the peptide hormone somatostatin. Recall that somatostatin is also released by the hypothalamus (as GHIH), and the stomach and intestines also secrete it. An inhibiting hormone, pancreatic somatostatin inhibits the release of both glucagon and insulin.
4. The **PP cell** accounts for about one percent of islet cells and secretes the pancreatic polypeptide hormone. It is thought to play a role in appetite, as well as in the regulation of pancreatic exocrine and endocrine secretions. Pancreatic polypeptide released following a meal may reduce further food consumption; however, it is also released in response to fasting.

REGULATION OF BLOOD GLUCOSE LEVELS BY INSULIN AND GLUCAGON

- Glucose is required for cellular respiration and is the preferred fuel for all body cells. The body derives glucose from the breakdown of the carbohydrate-containing foods and drinks we consume. Glucose not immediately taken up by cells for fuel can be stored by the liver and muscles as glycogen, or converted to triglycerides and stored in the adipose tissue. Hormones regulate both the storage and the utilization of glucose as required. Receptors located in the pancreas sense blood glucose levels, and subsequently the pancreatic cells secrete glucagon or insulin to maintain normal levels.

Insulin release:
- Beta cells of pancreas release insulin



Insulin effects:
- Triggers body cells to take up glucose from the blood and utilize it in cellular respiration
- Inhibits glycogenolysis
  – glucose is removed from the blood and stored as glycogen in the liver
- Inhibits gluconeogenesis
  – amino acids and free glycerol are NOT converted to glucose in the ER



Hyperglycemia
(elevated blood glucose)

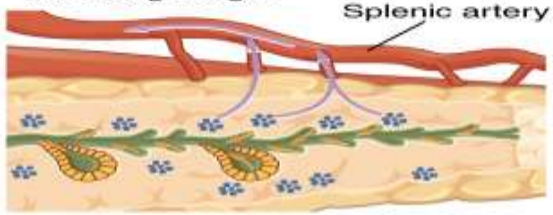
START: Homeostasis
(70–110 mg/dL)

Blood glucose concentration decreases

Hypoglycemia
(low blood glucose)

Blood glucose concentration increases

Glucagon release:
- Alpha cells of pancreas release glucagon



Glucagon effects:
- Inhibits body cells from taking up glucose from the blood and utilizing it in cellular respiration
- Stimulates glycogenolysis
  – glycogen in the liver is broken down into glucose and released into the blood
- Stimulates gluconeogenesis
  – amino acids and free glycerol are converted to glucose in the ER and released into the blood



GLUCAGON

- Receptors in the pancreas can sense the decline in blood glucose levels, such as during periods of fasting or during prolonged labor or exercise . In response, the alpha cells of the pancreas secrete the hormone **glucagon**, which has several effects:
- It stimulates the liver to convert its stores of glycogen back into glucose. This response is known as glycogenolysis. The glucose is then released into the circulation for use by body cells.

- It stimulates the liver to take up amino acids from the blood and convert them into glucose. This response is known as gluconeogenesis.
- It stimulates lipolysis, the breakdown of stored triglycerides into free fatty acids and glycerol. Some of the free glycerol released into the bloodstream travels to the liver, which converts it into glucose. This is also a form of gluconeogenesis.
- Taken together, these actions increase blood glucose levels. The activity of glucagon is regulated through a negative feedback mechanism; rising blood glucose levels inhibit further glucagon production and secretion.

INSULIN

- The primary function of **insulin** is to facilitate the uptake of glucose into body cells. Red blood cells, as well as cells of the brain, liver, kidneys, and the lining of the small intestine, do not have insulin receptors on their cell membranes and do not require insulin for glucose uptake. Although all other body cells do require insulin if they are to take glucose from the bloodstream, skeletal muscle cells and adipose cells are the primary targets of insulin.
- The presence of food in the intestine triggers the release of gastrointestinal tract hormones such as glucose-dependent insulinotropic peptide (previously known as gastric inhibitory peptide). This is in turn the initial trigger for insulin production and secretion by the beta cells of the pancreas. Once nutrient absorption occurs, the resulting surge in blood glucose levels further stimulates insulin secretion.

- Precisely how insulin facilitates glucose uptake is not entirely clear. However, insulin appears to activate a tyrosine kinase receptor, triggering the phosphorylation of many substrates within the cell. These multiple biochemical reactions converge to support the movement of intracellular vesicles containing facilitative glucose transporters to the cell membrane. In the absence of insulin, these transport proteins are normally recycled slowly between the cell membrane and cell interior. Insulin triggers the rapid movement of a pool of glucose transporter vesicles to the cell membrane, where they fuse and expose the glucose transporters to the extracellular fluid. The transporters then move glucose by facilitated diffusion into the cell interior.

- Insulin also reduces blood glucose levels by stimulating glycolysis, the metabolism of glucose for generation of ATP. Moreover, it stimulates the liver to convert excess glucose into glycogen for storage, and it inhibits enzymes involved in glycogenolysis and gluconeogenesis. Finally, insulin promotes triglyceride and protein synthesis. The secretion of insulin is regulated through a negative feedback mechanism.

Hormones of the Pancreatic Islets

Associated hormones	Chemical class	Effect
Insulin (beta cells)	Protein	Reduces blood glucose levels
Glucagon (alpha cells)	Protein	Increases blood glucose levels
Somatostatin (delta cells)	Protein	Inhibits insulin and glucagon release
Pancreatic polypeptide (PP cells)	Protein	Role in appetite

Summary

- The endocrine pancreas has a central role in maintaining energy homeostasis by regulating nutrient uptake and release by the hormone-sensitive storage tissues, liver, fat, and muscle. When the circulating levels of nutrient fuels, such as glucose and FFA, are high, energy metabolism within islet β-cells is increased, and intracellular signals that increase insulin secretion are generated. At the same time, glucagon secretion from islet α-cells is inhibited. Thus, high insulin to glucagon ratio signals nutrient storage, and a low ratio signals nutrient release. The islet response is further regulated by autonomic and sensory nerves and by blood-borne hormones produced at distant sites of the gastrointestinal tract