Anatomy, Functions, and Diseases of the Pancreas

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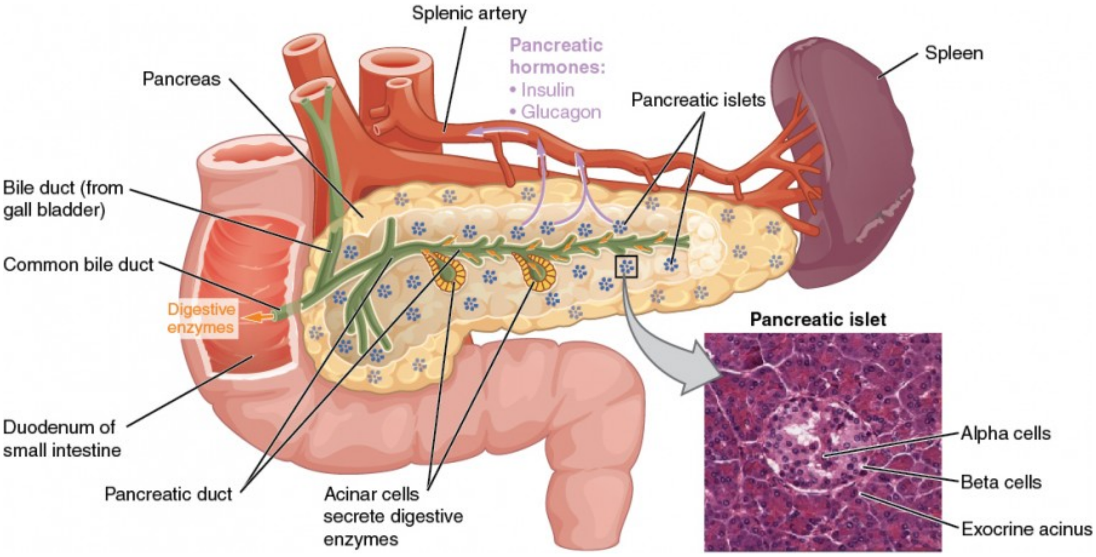
A gland consists of one or more cells that produce and secrete an aqueous (water-based) fluid that generally contains proteins. The pancreas is an organ that actually consists of two glands: one exocrine gland and one endocrine gland. The exocrine gland secretes its fluids through ducts into the intestinal lumen. Endocrine glands also release chemical substances directly into the bloodstream or body tissues. The chemical substances released by the endocrine glands are called hormones. The endocrine gland secretes its substances through the extracellular space into the vascular and lymphatic system. Exocrine glands release chemical substances through ducts to the outside of the body or onto another surface within the body. These two parts of the pancreas differ both in structure and function. The following article offers an overview of the histological features of the two glandular parts of the pancreas.



A Macroscopic View of the Pancreas

Pink or beige in color, the pancreas is an organ that measures about 6 inches in length and is positioned across the back of the abdomen and behind the stomach. The head of the pancreas is connected to the duodenum which is also the first section of the small intestine. The pancreas is covered with a very thin connective tissue capsule which extends inward as septa, partitioning the gland into lobules.

The Exocrine Pancreas

The exocrine pancreas produces 1.5 – 2 liters of fluid which contains enzymes that help to break down carbohydrates and fats, proteolytic proenzymes (preliminary stages of enzymes), and bicarbonate.

Enzymes produced by the exocrine pancreas:

- Trypsinogen and chymotrypsinogen;
- Procarboxypeptidase;
- Proelastase;
- Lipase;
- Cholesterinesterase enzyme;
- α-amylase; and
- Ribonuclease and deoxyribonuclease.

The exocrine pancreas aids in meal digestion through secretions it produces. Malnutrition and malabsorption result without the exocrine pancreas.

Enzymes for:

Carbohydrates	Fats	Proteins	Nucleotides	Ions and water
Amylase	• Lipase • Pro-phospholipase A2 • Cholesterol esterase	• Trypsinogen • Chymotrypsinogen • Pro-elastase • Pro-carboxy-peptidase	• Ribonuclease • Deoxyribonuclease	HCO_{3-}

Bicarbonate is responsible for the alkaline pH level of the pancreatic fluid and raises the pH of the contents in the duodenum. The pancreas produces alkaline pancreatic fluid naturally, and a pH level for the pancreas that ranges between 7.8 – 8.0 is considered healthy. This range also helps to neutralize the acid content of the stomach in the duodenum. The pancreatic fluid is secreted through the ductus pancreaticus into the lumen of the duodenum. The duodenal cuticular layer and the Brunner´s glands secrete the enzyme enterokinase that transforms trypsinogen into trypsin. Trypsin transforms all of the other pancreatic proenzymes into their active forms.

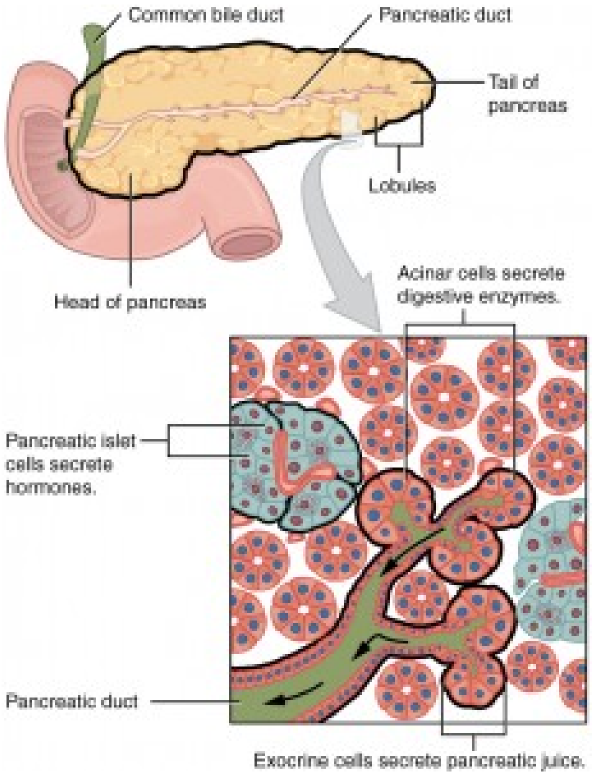


Image: "Exocrine and Endocrine Pancreas" by OpenStax College.
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- The exocrine pancreas secretes a serous fluid. These fluids contain proteins and bear thin viscosity levels.
- The method of secretion is merocrine which involves producing a secretion that does not contain cellular components and that is discharged without major damage to the secreting cell. The secretion happens by way of exocytosis that keeps the cell intact.
- It is a composed gland where the excretory ducts branch out.
- It is an acinar gland, and the acini—where secretion happens—are small spherical clusters with a small lumen.

The lobe-like structure of the pancreas can be seen macroscopically. These lobes consist of hundreds of serous acini. Every acinus contains approximately 70 pyramid-shaped gland cells located on a basal lamina with large, round and basal-lying nuclei. The basal lamina can be described as a layer of extracellular matrix secreted by the epithelial cells on which the epithelium sits; the epithelium is the cellular covering of internal and external surfaces of the body.

The basal portion of the exocrine cells shows a strong basophilic part which is the rough endoplasmic reticulum. The apical portion of these cells shows a strong acidophilic part and contains the proenzymes that are wrapped in zymogenic granules. These are emitted by way of the apical cell-pole which is mounted with microvilli.

Intercalated ducts—cells of cubic to flat epithelium—connect several acini with the excretory ducts by sliding into the acini and creating the microscopic image of centroacinar cells. There are no striated ducts as they can be found in the excretory ducts of the parotid gland.

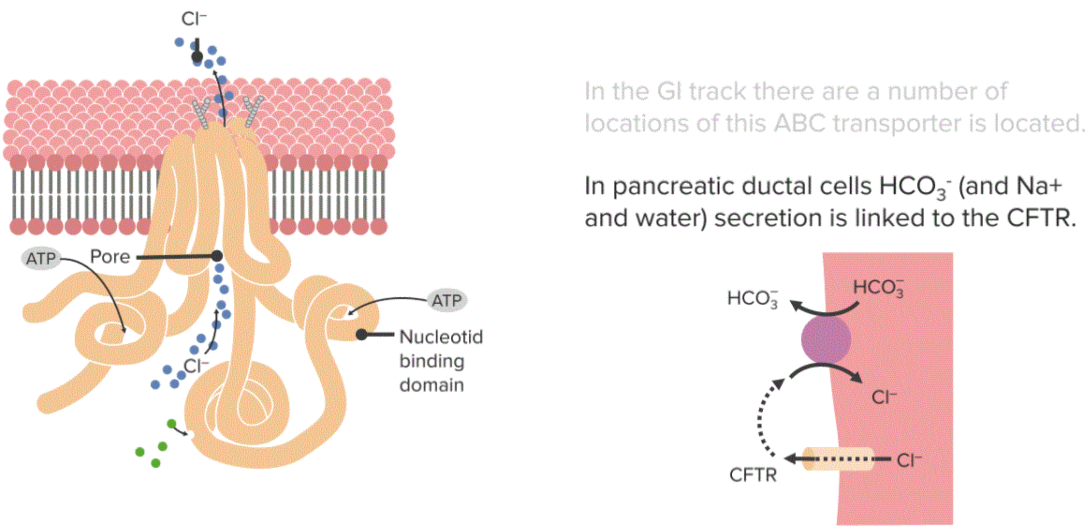
Excretory ducts are intralobular and can be found inside every lobule; these ducts can also be recognized by their simple cylindrical epithelium.

Excretory ducts connect inside the septa—partitions separating two chambers—to extra tubular excretory ducts with a stratified epithelium containing both goblet cells and enterochromaffin cells.

The ducts inside the septa connect again to larger ducts before leading to the one large excretory duct of the pancreas–the pancreatic duct. Together with the common bile duct, the pancreatic duct leads to the major duodenal papilla, a small mucosal elevation in the duodenum. It is in the duodenal lumen where the pancreatic fluid and its enzymes are activated.

The cystic fibrosis transmembrane conductance regulator CFTR

The cystic fibrosis transmembrane conductance regulator (CFTR) is a membrane protein that functions as a channel across the membrane of cells that produce mucus, sweat, saliva, tears, and digestive enzymes. The CFTR protein is encoded by the CFTR gene which provides instructions for making the CFTR protein.



"Cystic fibrosis transmembrane regulator" Image by Lecturio

On the basolateral side of the acinar cells, potassium, sodium, and chloride are transported into the cells using adenosine triphosphate (ATP), a complex organic chemical that provides energy to drive processes in living cells. A transporter for chloride on the apical side—or cystic fibrosis transmembrane conductance regulator (CFTR)—pumps chloride from the stroma inside the cellular lumen which causes sodium and water to follow. The intercalated ducts take the chloride in exchange for bicarbonate.

Patients with cystic fibrosis (mucoviscidosis) have a mutated gene that codes CFTR. In such cases, less chloride and water are transported into the glandular lumen. The secretion becomes viscous and backed up which leads to inflammation. In the intercalated ducts, the lack of chloride leads to a lower exchange with the bicarbonate that is essential to neutralize the thymus in the duodenal lumen and activate the pancreatic enzymes. The consequences result in digestive disorders that are typical for cystic fibrosis.

The Endocrine Pancreas

The endocrine pancreas is the portion of the pancreas that reacts to signals from the vascular system by secreting hormones which include but are not limited to insulin–B cells, glucagon–A cells, somatostatin–D cells, pancreatic polypeptide–PP cells, and gastrin. There are several types of endocrine cells, and each cell type produces a special hormone that regulates the carbohydrate metabolism.

The endocrine pancreas — histochemical differentiation of cells

Insular clusters of endocrine cells are found inside the pancreatic lobules between the acini. These endocrine cells are irregularly shaped patches of endocrine tissue and are also known as islets of Langerhans or islands of Langerhans. They are named for the German physician, Paul Langerhans, who first described them in 1869. The normal adult pancreas contains about 1 million of these islets. The islets consist of four distinct cell types where three types (alpha, beta, and delta cells) produce important hormones, and the fourth type (the C cell) has no explicit function.

All of these cell clusters together build one functional unit. Every endocrine gland and the islets of Langerhans lose connection to the epithelium during the fetal period and do not emit secretion through excretory ducts. The secretion happens first on the basal side into the stroma and finally by way of the vascular and lymphatic systems to the place where it is needed.

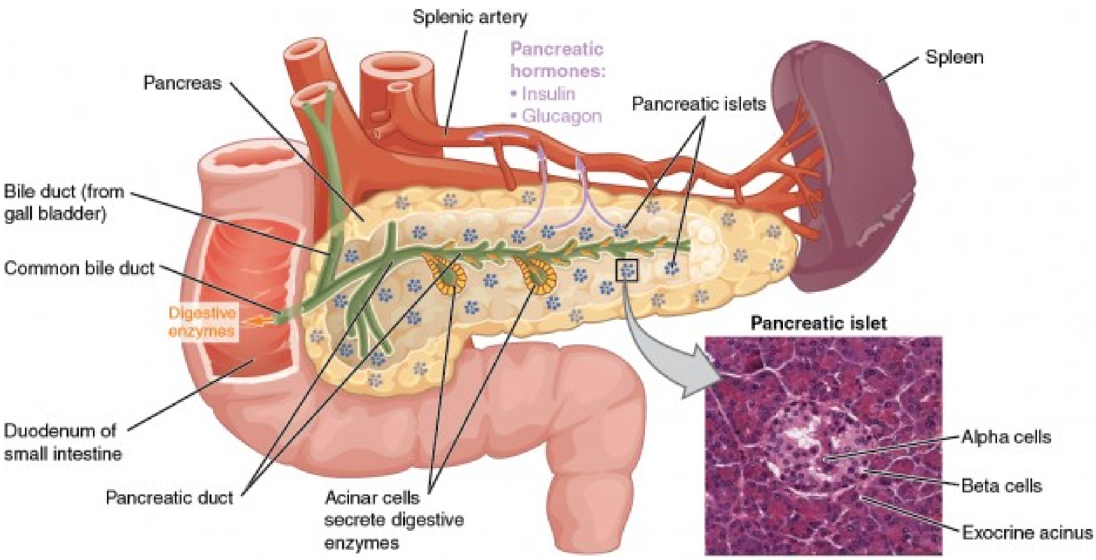


Image: "Pancreas" by philschatz. License: CC BY 4.0

The endocrine pancreas as it is seen under the microscope

The endocrine islets are distributed between the exocrine pancreatic tissue and can have a spherical to ovoid, or strung-out, form. The thread-like arrangement of the epithelial cells and the dense meshwork of capillaries are apparent. The glandular cells are chromophobic, meaning they cannot be dyed very well; for this reason, they can be recognized by their light color when dyed with hematoxylin-eosin. Special dyes help to make the various types of cells visible because the secretory granules appear in different colors.

The endocrine pancreas — neural control

The endocrine pancreas has adrenergic and cholinergic synapses. Neurites of the sympathetic nerve stimulate the release of glucagon. The secretion of insulin is activated by the vagus nerve and inhibited by the sympathetic nervous system.

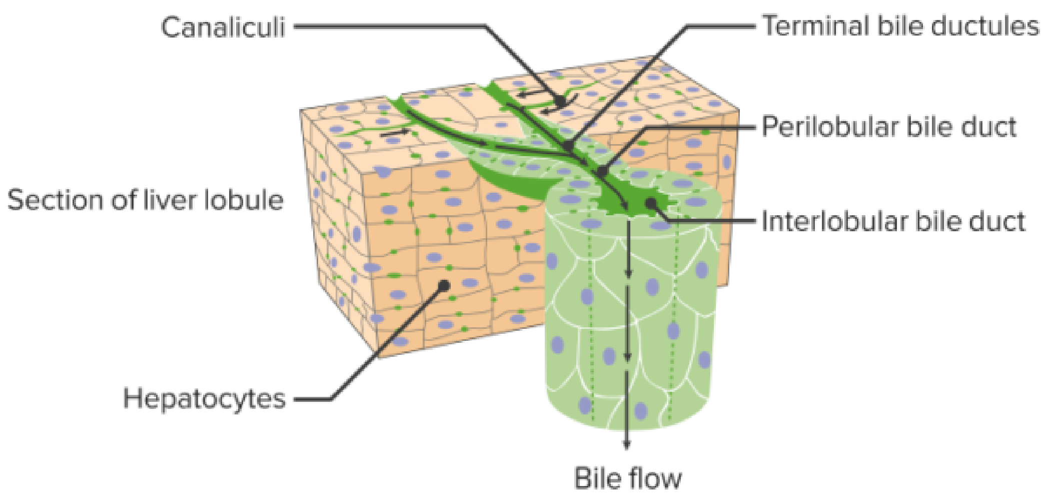
Hepatobiliary — Secretion Constituents

Biliary secretion contains:

- Three bile salts: Cholesterol, Lecithin, and Bilirubin
- Ions

Concentration (5—20%) of these constituents occurs in the gallbladder.

Structure and Functions



Hepatobiliary – Structure and Functions

Diseases of the Pancreas

Mucoviscidosis = cystic fibrosis

Mucoviscidosis, also known as cystic fibrosis, is a hereditary disease that affects the pancreas, lungs, and sweat glands. Mutations of the gene that codes the cystic fibrosis transmembrane conductance regulator (CFTR) protein are the root cause of mucoviscidosis.

Since CFTR is the apical transporter for chloride ions, its absence induces disturbances in the exchange of electrolytes and liquids of the glandular cells. The produced secretion is not serous anymore but mucous which causes the secretion to back up, resulting in chronic inflammation. The parenchyma of the pancreas is then replaced by fibrotic fibers and cannot fulfill its task anymore. This causes conditions such as dyspepsia and failure to thrive. The lungs react with chronic bronchitis, and the sweat glands excrete higher levels of salt. A simple examination of the sweat, or a stool sample, can serve as an effective diagnostic method.

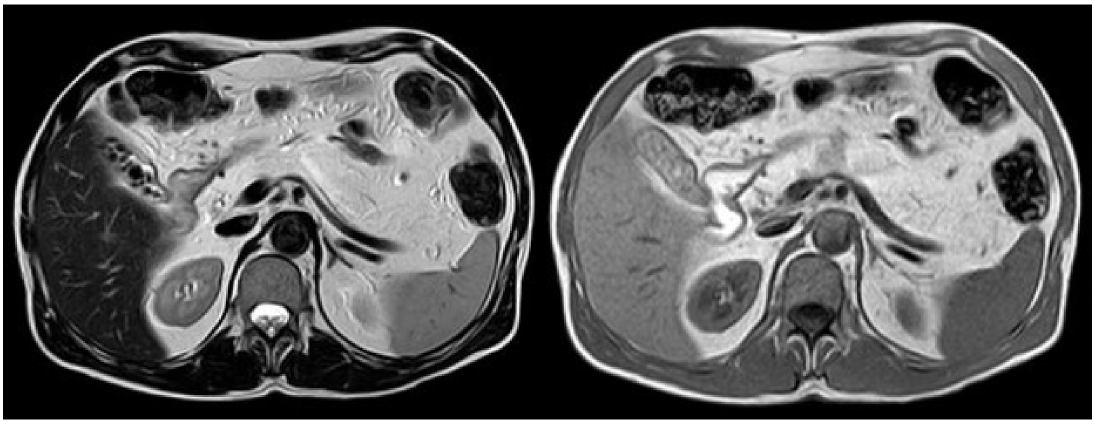


Image: “Complete lipomatous conversation of the pancreas in a 45-year-old cystic fibrosis patient. MRI T2 axial left, right T1 axial, where median anterior to the splenic vein yet divined a fabric with slightly darker signal.” by Hellerhoff. License: CC BY-SA 3.0

The acute pancreatitis

Acute pancreatitis is a sudden inflammation of the pancreas that can be a mild or life-threatening condition. With effective treatment, many patients generally recover. Acute pancreatitis occurs when the digestive enzymes are activated before they are released into the small intestine and thus begin attacking the pancreas. If the enzymes enter the blood stream, other organs might become affected which can lead to life-threatening shock symptoms. Gallstones (40%) and alcohol abuse (30%) are the main causes of acute pancreatitis and represent 70% of the cases; however, acute pancreatitis is also hereditary for some individuals. Gene mutations that predispose individuals acute pancreatitis have been identified. Individuals with cystic fibrosis or who carry the cystic fibrosis genes also have an increased risk of developing acute pancreatitis.

Image: “Acute exudative pancreatitis in computed tomography with extensive liquid streets around the pancreas” by Hellerhoff. License: CC BY-SA 3.0

Causes of acute pancreatitis may be:

- Obstruction of the bile ducts or the pancreatic duct by stones or tumorous processes;
- Chronic alcohol abuse
- Viral infections, e.g. epidemic parotitis (mumps)
- Collagenosis (e.g., systemic lupus erythematosus).

Diabetes mellitus

Diabetes mellitus literally translates as “honey flow.” The name refers to symptoms of this disease—the consequence of high blood sugar levels and the increased amount of glucose in the urine which leads to polyuria.

Diabetes mellitus type 1

Note: The pancreas produces no more insulin.

Image: “Overview of the most significant possible symptoms of diabetes.” by Mikael Häggström. License: Public domain

In diabetes mellitus type 1, also known as type 1 diabetes, the beta cells are destroyed because of an immune-mediated reaction that causes a complete insulin deficiency. Because of this, the body is not able to secrete any amount of insulin. Life-long exogenous insulin must be administered subcutaneously or intravenously. Patients are also at increased risk of diabetic complications such as hypoglycemia and ketoacidosis as the exogenous insulin does not accurately mimic the body’s physiological functions.

Diabetes mellitus type 2

Note: the produced insulin has no effect!

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Diabetes mellitus type 2, also known as type 2 diabetes, arises due to an insulin resistance of receptors which results in a relative insulin deficiency. Genetic dispositions as well as changes in the metabolic system (e.g., Syndrome X) may be the trigger for this disease, but scientists continue to search for the actual causes of insulin resistance.

In the past, some assumed that type 2 diabetes primarily affected older patients; however, type 2 diabetes occurs at all ages. Practices such as weight loss, regular physical activity, and dietary changes have had positive results for many patients.

Review Questions

The correct answers are below the references.

1. Which statement about the exocrine pancreas is right?

A. The exocrine pancreas is a serous, tubuloalveolar gland.
B. The cells are secreting the fluids together with a part of the plasmalemma (cell membrane) and the cytoplasm.
C. The glandular cells have only one excretory duct, but several acini are leading to it.
D. The typical microscopic appearance of the exocrine pancreas is a branch-like system of excretory ducts with striated ducts and intercalated ducts.
E. The histological image shows centroacinar cells as parts of the intercalated ducts.

2. Which statement about the islets of Langerhans is wrong?

A. The islets of Langerhans consist of about 1 million cell-clusters that are spread like islands between the exocrine parts of the pancreas.
B. Beta-cells are producing the peptide hormone insulin, which decreases the blood sugar level.
C. Somatostatin can be found in the Delta-cells of the entire gastrointestinal tract and it is inhibiting the secretion of pancreatic fluid.
D. About 70 % of the islets' cells contain the peptide hormone insulin inside their β-granules.
E. Glucagon activates the synthesis of glycogen.

3. Which statement about diabetes mellitus is right?

A. Diabetes type 2 is characterized by absolute insulin deficiency.
B. Diabetes type 2 occurs only in old people.
C. Diabetes type 1 can be cured completely with the right treatment.
D. Diabetes mellitus means "honeyed flow" and refers to this name to polyuria as one symptom of the disease.
E. The insulin receptors are becoming resistant against insulin at diabetes type 1.

References

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Correct answers: 1E, 2E, 3D

Notes