Endocrine and Exocrine Functions of the Pancreas

The pancreas is a 2-in-1 organ: an exocrine and endocrine gland. It is essential for digestion and the carbohydrate metabolism. Thus, a loss in pancreatic function leads to severe clinical symptoms. In this article, you will get a compact overview of the structure, functions, and diseases of the pancreas.

Macroscopic Anatomy of the Pancreas
Location of the pancreas

The pancreas is an elongated, tapered organ that is located across the back of the abdomen, right behind the stomach. It has a sigmoid shape and is organized in lobules, which are separated from each other by projections of the thin, fibrous capsule that surrounds the organ and by fine connective tissue septa.

Apart from the tail, the pancreas is a retroperitoneal organ that lies behind the peritoneal cavity and is located deeply within the upper abdomen in the epigastrical and left hypochondriac regions. Some of its relations include the stomach superiorly and anteriorly and the colon and spleen laterally on the right and left, respectively. The head of the pancreas is located on the right side of the abdomen and is connected to the duodenum through a small tube called the `pancreatic duct`.

The different parts can be distinguished as follows.

- **The caput pancreatis** (head of the pancreas) lies in the concave aspect of the duodenum (duodenal C) and has a hook-shaped process (uncinate process) that surrounds the superior mesenteric artery and vein.
- **The corpus pancreatis** (body of the pancreas) represents the main part of the pancreas and is contained within the posterior, retroperitoneal abdominal wall. The anterior part is covered with peritoneum and forms the posterior wall of the omental bursa.
- **The cauda pancreatis** (tail of the pancreas) stretches to the spleen and cannot be differentiated from the body of the pancreas.
The microscopic anatomy of the pancreas involves 99% exocrine and 1% endocrine tissue by weight that is organized into acini that surround multiple ducts. The ducts eventually drain into the excretory duct, which is the main pancreatic duct (or Wirsung’s duct). It runs across the whole gland and leads to the major duodenal papilla along with the common bile duct.

Because the pancreas develops out of two separate anlages (ventral and dorsal), another accessory pancreatic duct (or Santorini’s duct) commonly exists, which leads to the minor duodenal papilla. The pancreatic duct runs along the length of the pancreas, uniting with the common bile duct and forming what is called the hepatopancreatic ampulla of Vater. This structure opens into the duodenum.

Vascular supply of the pancreas

The celiac trunk and the superior mesenteric artery ensure arterial blood supply to the pancreas. The arteries reach the organ from both the cranial and the caudal sides of the pancreas and form anastomoses in the area of the pancreatic head. This construction is referred to as the pancreatic arcade. It includes the following:

- The posterior and anterior superior pancreaticoduodenal artery (from the gastroduodenal artery, which originates from the celiac trunk)
- The inferior pancreaticoduodenal artery (out of the superior mesenteric artery)

In addition, the splenic artery in the area of the body and the tail of the pancreas gives rise to pancreatic rami, the dorsal pancreatic artery, and the greater pancreatic artery, which form an anastomosis with the inferior pancreatic artery at the lower margin of the pancreas.

The pancreas drains into the splenic vein and the superior mesenteric vein, which eventually form the portal vein. Because of the close relationship between the pancreatic head and these vessels, cancer of the pancreatic head may cause constriction of the portal vein, resulting in portal hypertension and stasis with ascites.
Relationships of the pancreas with surrounding organs

The pancreas is located in the posterior abdominal wall in a retroperitoneal manner. Thus, it has close topographic relations with many structures.

- **Stomach**: The omental bursa separates the two organs. It lies anteriorly and superiorly.

- **Small intestine and duodenum**: While the small intestine can reach the lower margin of the pancreas anteriorly and medially, the pancreatic head clings closely to the duodenum.

- **Left kidney**: The pancreatic tail runs over the kidney.

- **Spleen**: The tail of the pancreas ends at the hilum of the spleen. The spleen is located posteriorly and laterally to the pancreas and is connected by ligaments to its tail.

- **Common bile duct**: This can be embedded in the pancreas. Cancer of the pancreatic head can block the common bile duct, which results in obstructive jaundice.

- **Superior mesenteric artery and vein**: The vessels run dorsally to the head of the pancreas and emerge on the front side at the pancreatic notch. This is where they are entwined by the uncinate process. Cancer of the pancreatic head can spread to these two vessels, which can lead to circulatory disorders in several organs.

- **Splenic artery and vein**: The splenic artery is located on the upper margin of the pancreas, while the splenic vein runs deeper and behind the gland.
Malformations of the pancreas

The pancreas develops as two outpouchings from the embryonic foregut: the dorsal and ventral pancreatic buds. Both remain attached to the gut, and as the duodenum rotates during development, it takes with it the dorsal anlage, leading to fusion of the dorsal and ventral anlages to form the adult pancreas.

The dorsal anlage forms the head, neck, body, and tail of the pancreas, whereas the ventral anlage forms the uncinate process of the pancreas.

Pancreas divisum

If the ventral and dorsal pancreatic anlages do not merge during development of the pancreas, a pancreas divisum occurs, which is characterized by two separate glands. The merging of the two pancreatic ducts stops here so that they can flow separately into the duodenum: the major pancreatic duct at the major duodenal papilla and the minor pancreatic duct at the more cranially positioned minor duodenal papilla. This is a frequently occurring abnormality, which mostly does not cause any symptoms. In some cases, this anomaly is associated with recurrent episodes of pancreatitis. However, its role as a predisposition for pancreatitis is controversial.

Annular pancreas

During the development of the pancreas, a part of the ventral anlage (the right bud) moves around the duodenum from a dorsal location, whereas the other part (the left bud) regresses. If this regression does not occur, the left bud rotates around the duodenum ventrally and fuses with the right bud, which results in an annular pancreas. The descending part of the duodenum is encircled by pancreatic tissue. This rare anomaly can cause duodenal atresia.

Accessory pancreatic lobe

Accessory pancreatic lobe is a rare condition that presents with an additional lobe arising from the main pancreatic gland with its aberrant duct. The anomaly may present with recurrent pancreatitis.
Agenesis/hypoplasia of the pancreas

Total agenesis is incompatible with life and rarely occurs. However, hypoplasia/lack of development of one anlage may be seen. It may predispose the individual to diabetes mellitus, especially if the dorsal anlage, where islet cells are located, is involved.

Microscopic Anatomy of the Pancreas

In contrast to the macroscopic anatomy, the pancreas’s organization in the exocrine and endocrine pancreas becomes apparent in histologic sections.

Exocrine part of the pancreas

Histologically, the exocrine part of the pancreas shows the typical structure of the serous gland and represents roughly 98% of the organ’s tissue. The acini consist of strong basophilic cells, which contain numerous secretory granules. Acini are made of zymogenic cells that surround a central lumen and are arranged in lobules.

Each lobule contains a ductule, and many ductules join together to make intralobular ducts, which then form interlobular ducts that drain into branches of the main pancreatic duct. They contain inactive precursors of digestive enzymes, which are activated outside the pancreas (see below) to prevent the organ from digesting itself. The acini are followed by intercalated ducts, which connect the acini to the ductal system.

A special feature concerning the histology of the pancreas are the centroacinar cells, which represent invaginations of the intercalated ducts into the acinar lumen. With their bright coloration, they form a contrast to the acini and are easily identified in a histologic image. The pancreas lacks striated ducts, which can be found, for example, in the parotid gland. The ductal system consists of intralobular ducts with cuboidal epithelium, which fuse to form interlobular ducts with columnar epithelium. Eventually, these ducts lead to the major or minor pancreatic duct.

Endocrine part of the pancreas

About 2% of the pancreatic tissue has an endocrine function. It is represented by accumulations of cells (islets of Langerhans) within the exocrine tissue. With their weak eosinophilic coloration, they differ from the dark acini of the exocrine part. The islets can be found mainly in the tail of the pancreas.

With the use of specialized immunohistochemical stains, four different cell populations, each producing different hormones, can be distinguished within the islets of Langerhans: alpha cells (20%; appear particularly in the periphery and function in glucagon production), beta cells (70%; evenly spread and function in insulin production), delta cells (5%; function in somatostatin production), and PP cells (5%; function in pancreatic polypeptide production).

Function of the Pancreas

An essential pancreatic function is the conversion of food into fuel for the body’s cells. The exocrine part produces mainly digestive enzymes and helps in digestion, whereas the endocrine part is responsible for the regulation of carbohydrate metabolism (i.e. blood
sugar), with its insulin and glucagon production.

**Exocrine function of the pancreas**

The pancreas produces roughly 1.5–2 L of digestive secretions, which travel to the duodenum via the pancreatic duct. These secretions consist of bicarbonate, which makes the fluid alkaline (pH 8), and several enzymes that are essential for digestion.

Trypsinogen and chymotrypsinogen are inactive protease precursors (zymogens); they are activated by enterokinase in the intestinal lumen. These enzymes are secreted by zymogenic cells. The active enzymes trypsin and chymotrypsin are endopeptidases (fission of the peptide bond within a protein). This prevents the pancreatic tissue from digesting itself. Trypsin can activate other inactive enzymes.

Carboxypeptidases are also zymogens, which are exopeptidases (formed by fission of the peptide bond at the end of a protein) in their active form. Active enzymes in the pancreatic digestive secretion are pancreas lipase and phospholipase A2, which hydrolyze triglycerides and phospholipids; pancreas amylase, which breaks bonds in polysaccharides; and deoxyribonucleases, which act in the degradation of nucleic acids.

The release of these enzymes is regulated by hormones of the intestinal wall. Secretin encourages the release of the alkaline secretion in order to neutralize the acidic stomach content. Cholecystokinin stimulates the production and secretion of the enzymes. Gallstones in the common bile duct can cause secretion backflow. This can lead to premature activation of the enzymes and pancreatic self-digestion, which is referred to as acute pancreatitis (see below).

**Endocrine function of the pancreas**

The pancreas is not only a digestive gland but also an endocrine gland. As such, it produces two important hormones of the carbohydrate metabolism: insulin and glucagon, among others. The anabolic hormone insulin is produced in the beta cells and is released basally in an oscillating manner. Its half-life in the blood is only 6–8 minutes. A high blood glucose value acts as the main stimulus for induced release. Insulin then promotes the translocation of the insulin-dependent glucose transporter type 4 (GLUT4) to the plasma membrane so that the target cells can now quickly ingest glucose, which results in a decrease in the blood glucose value.

Insulin also promotes glycolysis and glycogen synthesis. Thus, the absorbed glucose is either transformed into energy or is stored. The direct antagonist of insulin is glucagon, which is produced in the alpha cells of the pancreas. At low blood glucose levels, glucagon promotes glycoenolysis and gluconeogenesis. It inhibits glycolysis and glycogen synthesis so that the blood glucose level rises.

Therefore, it is a catabolic hormone that has an antagonist effect on insulin. Somatostatin, which is produced by the delta cells, inhibits the secretion of insulin, glucagon, pancreatic enzymes, and gastric acid. Pancreatic polypeptide (PP) is produced by PP cells and also has an inhibitory effect. PP inhibits the release of pancreatic enzymes and the gallbladder’s release of bile.
Diseases of the Pancreas

Acute pancreatitis

Acute pancreatitis is characterized by autodigestion of pancreatic tissue due to the premature activation of zymogens. The most frequent causes of this clinical picture are choledocholithiasis and alcohol abuse. Affected patients experience severe pain in the upper abdomen, which can spread to the back in a belt-like manner. Nausea and vomiting can occur, sometimes accompanied by fever. Ileus and jaundice are also possible symptoms. A circulatory shock, acute kidney failure, sepsis, respiratory arrest, heart failure, bleeding in the gastrointestinal tract, and coma are other possible severe complications.

Up to 30% of patients with acute pancreatitis develop a pseudocyst that can regress spontaneously (see below). In the physical examination of a patient with acute pancreatitis, abdominal tenderness (elastic abdominal wall tension), reddening of the face, and sometimes bruising around the umbilicus (Cullen's sign) and in the flank area (Grey Turner's sign) stand out. An increase in serum amylase and lipase (> three times the normal value) can be found on laboratory testing, whereas lipase is specific to the pancreas.
An increase in gamma-glutamyl transferase (GGT), alkaline phosphatase (AP), serum glutamic oxaloacetic transaminase (SGOT), and bilirubin points to obstruction of the common bile duct as a cause for pancreatitis.

**Treatment**

- Keep the patient on a nothing-by-mouth (NPO) regimen to rest the gland and avoid secretions and reactivation of the digestive function.
- Supportive therapy with fluids and electrolytes avoids dehydration and electrolyte imbalances in a patient who is on a NPO regimen and has diarrhea and vomiting.
- Gallstones must be removed. If conservative therapy fails, surgery should be the next step.
The most common cause (80%) of chronic pancreatitis is alcohol abuse. In 10% of the cases, no cause for the disease can be identified (i.e. it is idiopathic). In contrast to their role in acute pancreatitis, gallstones are not considered to be a cause of chronic pancreatitis. The main symptom is recurrent pain in the upper abdomen, which often lasts hours to days and is present in 90% of the patients. In many cases, this leads to further abuse of alcohol and analgesics.

Patients may also have diarrhea and weight loss due to poor feeding and increased water losses via diarrheal stools. Only in later stages of the disease can the pain disappear completely. A decline in pancreatic tissue occurs because of the constant inflammation, and this results in an exocrine and endocrine insufficiency.

Exocrine and endocrine insufficiency lead to maldigestion and intolerance of certain kinds of food (mainly fats) with nausea, vomiting, meteorism, weight loss, and diabetes mellitus. In earlier stages, these consequences can be reversible. In later stages with a ‘burnt-out’ gland, however, the pancreatic insufficiency is irreversible.

The detection of elastase-1 in the stool (< 100 μg/dL—insufficiency) can be an indirect measurement of exocrine pancreatic insufficiency. Calcifications in the pancreas can be seen on sonography and are highly suggestive of chronic pancreatitis.

An abdominal computed tomography (CT) scan is the gold standard method for the detection of chronic pancreatitis, because calcifications are easily visualized as hyperdense lesions.

Causal therapy includes strict alcohol abstinence or elimination of the underlying disease. With regard to symptoms, the acute episode should be treated as acute pancreatitis. Treatment of exocrine insufficiency consists of a diet rich in carbohydrates, with many small meals and substitution of pancreatic enzymes.

Endocrine insufficiency leads to patients becoming insulin-dependent (CAVE: risk of hypoglycemia). Because there is a risk of addiction to analgesics, patients with endocrine insufficiency should be enrolled in a pain management program. In most cases, the pain can be reduced by eliminating obstacles to drainage. This can be accomplished by endoscopic retrograde cholangiopancreatography (ERCP) with stent implantation; this procedure decreases the pressure in front of the stenosis. Pain that is resistant to therapy presents an indication for surgery. The prognosis of chronic pancreatitis is poor; mortality rates within 10 years are 30–40%.
Pancreatic pseudocysts can present in the course of pancreatitis and disappear spontaneously in 50% of the cases. They consist of an accumulation of fluids, necrotic tissue, pancreatic enzymes, and old blood. The main symptoms are pain in the upper abdomen, nausea, vomiting, and weight loss. Additional symptoms can occur because of compression of surrounding organs (e.g., intestinal tract, spleen, and kidney).

However, pancreatic pseudocysts are often asymptomatic. Complications are a spontaneous rupture in the abdominal cavity and bleeding into the cyst. Sonography is suitable for diagnosis. On sonographic images, the cysts present as anechoic structures with a hyperechoic rim. If there are cysts with a diameter of more than 5 cm, spontaneous resolution over the ensuing months is less likely, and cyst infection, a local complication, may occur. In these cases, surgery with cystojejunostomy or partial pancreatic resection may be necessary.

Diabetes mellitus

Physicians very often encounter patients with diabetes. Because insulin is the only hormone in the body that can decrease the blood sugar level, insulin deficiency results in an increase in glucose in the blood (hyperglycemia) and increased glucose excretion in the urine (glycosuria). There may be a relative or an absolute insulin deficiency.

With type 1 diabetes, there is an absolute insulin deficiency due to the destruction of the beta cells by autoantibodies. Patients with type 1 diabetes are mostly young (between the ages 15 and 25) and must administer exogenous insulin all their lives. Typical symptoms are increased thirst (polydipsia), increased urination (polyuria), weight loss, and reduced performance.

Type 2 diabetes is more frequent by far and is characterized by resistance to insulin by peripheral cells so that a relative insulin deficiency occurs. It is also referred to as ‘adult-onset diabetes’ because it mainly affects adults. In most patients, adiposis, hypertonia, and hypertriglyceridemia can be diagnosed. These disorders along with diabetes mellitus are referred to as metabolic syndrome. Treatment consists of a balanced diet, normalization of weight, and movement. Oral diabetes drugs are the medications of choice.
Mucoviscidosis

Mucoviscidosis, or cystic fibrosis, is a frequent metabolic disease that is inherited as an autosomal recessive trait. It is a multiorgan disease of exocrine gland function that mainly affects the lungs and the pancreas, leading to chronic respiratory tract infections and pancreatic enzyme insufficiency.

Cystic fibrosis mainly affects the lungs and the pancreas. A mutation in the cystic fibrosis transmembrane regulator (CFTR) gene leads to defective chloride channels in the ducts of exocrine glands which causes them to produce a very viscous secretion that can obstruct the duct system of the gland. Thus, a cystic or fibrous conversion of the affected organ takes place, which gradually leads to loss of function.

In addition to the lungs and the pancreas, the intestine, liver, bile ducts, and gonads can be affected, and the symptoms depend heavily on the affected organ. For the pancreas, exocrine insufficiency is the most important symptom; its consequences are indigestion with diarrhea and weight loss up to the point of cachexia. Diabetes mellitus can result from the destruction of the islet tissue and, therefore, deficient insulin production. Respiratory symptoms include a persistent cough, wheezing, and restlessness.

The pilocarpine iontophoresis sweat test (which measures the chloride content in sweat; values are pathologic at > 60 mmol/L) can be performed to ensure the correct diagnosis. Because mucoviscidosis is not curable, only symptomatic therapy can be provided. Life expectancy is mainly limited by respiratory insufficiency and is roughly 40 years.

Note: An early diagnosis (if possible in the first half of the first year of life) is important in order to increase life expectancy.

Pancreatic carcinoma

Pancreatic carcinoma is the third most frequent tumor of the digestive tract. It affects men more frequently than women. The peak disease onset is between the ages of 60 and 80. The causes are unknown, but smoking, adiposis, and heavy alcohol consumption are suspected to be risk factors. This adenocarcinoma originates from the epithelium of the duct and, in roughly 70% of the cases, it is located in the head of the pancreas.

The absence of early symptoms makes pancreatic cancer hard to diagnose; its recognition very late in the course of the disease results in a dire prognosis. Symptoms such as upper abdominal pain, nausea, and weight loss make the differential diagnosis of chronic pancreatitis possible. Many patients report pain spreading to the back and jaundice, which points to a progressed stage of the disease.

Another rather rare symptom is a recurrent risk for thrombosis. If the body or the tail of the pancreas is affected, symptoms generally occur even later than with cancer in the head of the pancreas so that the prognosis is worse.
Normally, the tumor is not palpable. However, the gallbladder is palpable if the tumor obstructs the common bile duct. Jaundice also results in this situation (Courvoisier's sign). Tumor markers CA 19-9 and carcinoembryonic (CEA) should not serve for early diagnosis but are helpful in the postsurgery follow-up.

Only a few patients can be cured with resection of the tumor because in most cases, metastasis has already occurred by the time the diagnosis is made.

The results of chemotherapy and radiation therapy are also not satisfactory. The latter is helpful, however, in treatment of pancreatic pain. In most patients, palliative interventions (biliodigestive anastomosis, percutaneous stenting, and biliary drainage) are indicated. These can prolong life for 6–9 months.

**Note:** Pancreatic carcinoma is a difficult diagnosis to make, its treatment is also difficult, and it has a poor prognosis.

### Examination of the Pancreas

Because of its location in the retroperitoneal space, the pancreas can neither be palpated nor auscultated or imaged using conventional X-ray imaging. Pain expresses itself in the upper abdomen in a belt-like manner.

**Note:** The pancreas is not accessible for a simple physical examination. Often, a pancreatic disease is not noticed until symptoms occur. With a carcinoma of the pancreatic head, jaundice can result from obstruction of the common bile duct (see above).

| **Sonography** | The main structure for the localization of the pancreas is the splenic vein, which lies dorsally to the pancreas. Its echogenicity is similar to that of the liver's; echogenicity increases with adiposis and increasing age (leading to pancreatic lipomatosis). Pancreatic tumors are normally hypoechoic. Calcifications are evidence of chronic pancreatitis. For better imaging of the tail of the pancreas, the head of the ultrasound should be rotated slightly clockwise. |
| **CT/MRT (magnetic resonance tomography)** | In the sectional views, the pancreas lies in front of the vertebrae in a hoof shape. |
| **ERCP** | Imaging of the bile ducts and pancreatic ducts is performed with an application of contrast agents via the major duodenal papilla and screening afterward. If needed, a direct therapeutic intervention (papillotomy, stone extraction, or drain placement) is possible. |
| **MRCP (magnetic resonance cholangiopancreatography)** | This is noninvasive and does not involve radiation exposure. Fluids in the pancreatic ducts and the bile ducts are detectable on imaging as areas with high signal intensity, but no direct therapeutic intervention is possible. |
Patients frequently ask

Can you live without a pancreas?

Medically, it is possible to survive after the complete removal of the pancreas. However, in the absence of the pancreas, the body is incapable of producing digestive enzymes, insulin, and other hormones to digest food and control blood sugar levels. Thus, the patient develops diabetes and must rely completely on an exogenous insulin supply and other medications to maintain blood sugar levels.

References


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