

A Narrative Review about the Pancreas

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ABSTRACT

The pancreas is an organ in the back of the abdomen (belly). It is part of the digestive system. It is an organ and a gland. Glands are organs that produce and release substances in the body. It performs a vital essential role in converting the food we eat into fuel for the body's cells. The pancreas has two main functions: an exocrine function that helps in digestion and an endocrine function that regulates blood sugar. The head of the pancreas is the enlarged part of the gland that is surrounded by the C-shaped curve of the duodenum. In the normal, healthy human adult, the pancreas weighs approximately 100 g, has a length of 14 to 25 cm [7], a volume of approximately $72.4 \pm 25.8 \text{ cm}^3$ and is both lobular and elongated in shape. Lying obliquely behind the posterior and upper abdominal wall, this highly parenchymatous organ is divided into five anatomical parts: the head, uncinate process (located in the ventral lobe of the head), neck, body and tail. A healthy pancreas produces the correct chemicals in the proper quantities, at the right times, to digest the foods we eat. In this article, we will explore the anatomy of the pancreas, including its location, blood supply, innervation, lymphatics, function, and some relevant clinical aspects.

KEYWORDS: INSULIN, GLUCAGON, BETA CELLS

I. INTRODUCTION

The pancreas is an organ in the back of your stomach (belly). It is part of the digestive system. It is an organ and a gland. Glands are organs that produce and release substances in the body. It performs a vital essential role in converting the food we eat into fuel for the body's cells. The pancreas has two main functions: an exocrine function that helps in digestion and an endocrine function that regulates blood sugar. [1]

The pancreas is special and unique in that it's both an endocrine and exocrine gland. In other words, the pancreas has the dual function of secreting hormones into blood (endocrine) and secreting enzymes through ducts (exocrine). The pancreas belongs to the endocrine and digestive systems with most of its cells (more than 90%) working on the digestive side. However, the pancreas plays the vital duty of producing hormones most notably insulin to maintain the balance of blood glucose (sugar) and salt in the body. Without this balance, the body is susceptible to serious complications, such as diabetes. [2] The pancreas is a composite organ derived from two buds, dorsal and ventral, that occur from either side of the distal foregut endoderm. It contains a distinctive combination of cell lineages. The exocrine tissue includes acinar cells that secrete digestive fluid and a duct system by which the fluid drains into the intestine. The endocrine component is organized as discrete islets of Langerhans, which comprise multiple distinct cell types secreting (at least) five different hormones into the circulation (α -cells, glucagon; β -cells, insulin; δ -cells, somatostatin; ϵ -cells, ghrelin; and γ [or PP]-cells, pancreatic polypeptide). [3] The pancreas is an accessory organ and exocrine gland of the digestive system, as well as a hormone producing endocrine gland. It is a retroperitoneal organ consisting of five parts and an internal system of ducts. The pancreas is furnished with the aid of pancreatic arteries stemming from surrounding vessels and is innervated by means of the vagus nerve (CN X), celiac plexus, and superior mesenteric plexus. This organ is incredibly potent; unregulated, excessive functioning can result in auto-digestion, while insufficiency can lead to coma. Spotting the latter scenario commonly involves an unconscious (diabetic) person who may additionally have fruity breath. [4] In this article, we'll explore the anatomy of the pancreas, along with its location, blood supply, innervation, lymphatics, function, and some relevant clinical aspects.

STRUCTURE OF PANCREAS

Divisions

The pancreas is divided into 4 parts: head, neck, body, and tail.

The head of the pancreas is the enlarged section of the gland that is surrounded by using the C-shaped curve of the duodenum. On its way to into the descending section of the duodenum, the bile duct lies in a groove on the posterosuperior surface of the head or is embedded in its substance.

The body of the pancreas continues from the neck passes over the aorta and L2 vertebra. The anterior surface of the body of the pancreas is covered with peritoneum. The posterior surface of the body is devoid of peritoneum and is in contact with the aorta, the superior mesenteric artery (SMA), the left suprarenal gland, left kidney, and renal vessels.

The neck of the pancreas is short. The tail of the pancreas lies anterior to the left kidney, where it is closely related to the splenic hilum and the left colic flexure. The main pancreatic duct carrying the pancreatic secretions joins with bile

duct to form hepatopancreatic ampulla, which opens into the descending section of the duodenum. The hepatopancreatic sphincter of Oddi around the hepatopancreatic ampulla is a smooth muscle sphincter that controls the flow of bile and pancreatic juice into the ampulla and inhibits reflux of duodenal substances into the ampulla. [5]

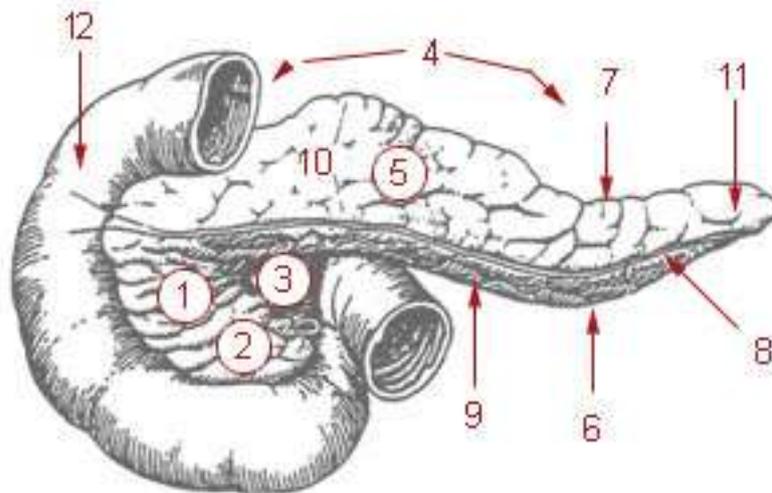
The pancreas has three main sections:

Head: area of pancreas to right of left border of superior mesenteric vein.

Body: area of pancreas between left border of superior mesenteric vein and left border of aorta.

Tail: area of pancreas between left border of aorta and hilum of spleen.

The most common site of primaries is the head of the pancreas. The pancreas has two functional components: endocrine, to produce insulin and other hormones, and exocrine, to produce pancreatic juices for digestion. The pancreas is in direct contact with the stomach, duodenum, spleen, and major vessels of the abdomen.



1. Head of pancreas
2. Uncinate process
3. Pancreatic notch
4. Body of pancreas
5. Anterior surface
6. Inferior surface
7. Superior margin
8. Anterior margin
9. Inferior margin

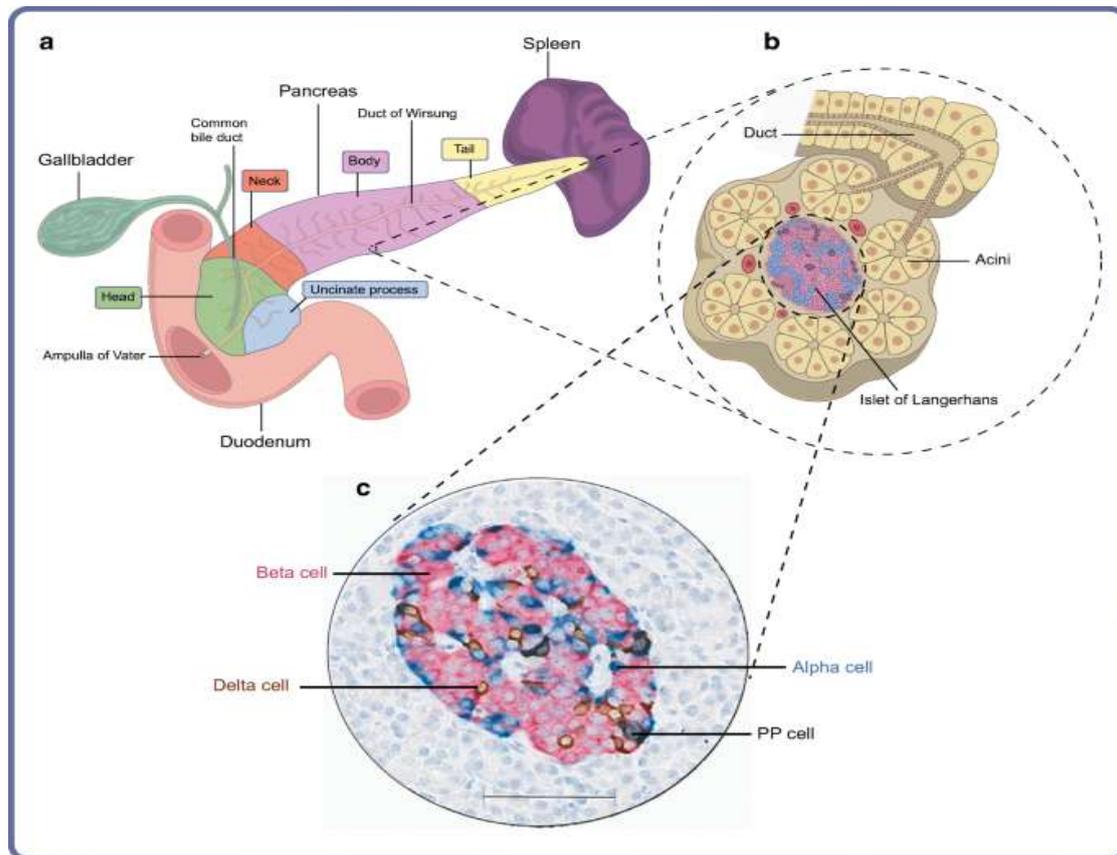
- 10. Omental tuber
- 11. Tail of pancreas
- 12. Duodenum [6]

Location	Retroperitoneal Spans the epigastric, left hypochondriac, and a portion of the umbilical abdominal regions
Parts	External: head, uncinete process, neck, body, tail Internal: main pancreatic duct (of Wirsung), accessory pancreatic duct
Function	Digestion by releasing peptidases, lipases, nucleases, amylases Hormonal regulation by releasing insulin (beta cells), glucagon (alpha cells), and somatostatin (delta cells)
Blood vessels	Pancreaticoduodenal, splenic, gastroduodenal, and superior mesenteric arteries
Innervation	Parasympathetic: vagus nerve (CN X) Sympathetic: greater and lesser splanchnic nerves
Lymphatics	Pancreaticosplenic and pyloric lymph nodes
Clinical point	Pancreatitis

PANCREAS ANATOMY

In the normal, healthful human adult, the pancreas weights approximately 100 g, has a length of 14 to 25 cm [7], a volume of approximately 72.4±25.8 cm³ [8] and is both lobular and elongated in shape (reviewed previously [9]).

Lying obliquely in the back of posterior and upper abdominal wall, this highly parenchymatous organ is divided into five anatomical parts: the head, uncinete process [10] (located in the ventral lobe of the head), neck, body and tail (Fig. 2).



Key anatomical features of the human pancreas. (a) Diagram of the pancreas, and surrounding organs. (b) Schematic representation of organisation of the endocrine and exocrine pancreas at the cellular level. (c) Human pancreatic islet showing the four endocrine cell types. Scale bar, 100 μ m

Located in the upper abdomen, with its head residing immediately adjacent to the duodenum, the body and tail areas of the pancreas lengthen throughout the body's midline to a factor close the spleen. More specifically, the head lies directly against the descending and horizontal components of the C-shaped duodenum. The uncinate process projects inferiorly from the head and extends posteriorly towards the superior mesenteric artery.

The neck portion extends laterally from the head where it connects to the pancreatic body. Posterior to the neck is the superior mesenteric artery and vein, as well as the origin of the hepatic portal vein. The aorta, superior mesenteric artery, left renal vessels and left kidney are each situated posterior to the pancreatic body. Finally, the tail is in near proximity to the hilum of the spleen. These

anatomical parameters are key to the function of the organ.

The vast majority of pancreatic tissue is devoted to its exocrine function, in which digestive enzymes are produced and secreted by a complicated ductal tree into the duodenum. The cells in the pancreas that produce these digestive enzymes are acinar cells, derived from the Latin phrase 'acinus', meaning grape, as they are cellular aggregates that form bundles akin to clusters of grapes (Fig. 2) [11]. Acinar cells make up almost 85% of the pancreas, are organized in acini, and synthesize and secrete enzymes active in protein, fat and carbohydrate digestion, together with trypsin, lipase and amylase [12]. Each acinar bundle connects to the pancreatic duct system. Centroacinar cells signify the most peripheral duct system and partially cover the apical surface of the acinar cells. Centroacinar cells connect to the intercalated ducts that converge and form the intralobular and interlobular ducts, which, in turn, subsequently drain into the main pancreatic duct. The main duct, the duct of Wirsung, empties into the duodenum. The residual portion of the main pancreatic duct located in the dorsal lobe, the so-called duct of Santorini, empties into the duodenum

as the accessory pancreatic duct. The main duct additionally connects with the bile duct in the head of the pancreas to form the hepatopancreatic duct (i.e. the ampulla of Vater). Flow via the ampulla of Vater is managed by using muscular sphincter of Oddi, to open during digestion and to close for prevention of reflux of duodenal content into the pancreatic ductal tree postprandially.

Acinar enzymes are secreted into a bicarbonate-rich fluid produced with the aid of the ductal epithelium. Pancreatic secretions appear at a low rate between meals (0.2–0.3 ml/min) and markedly enlarge throughout ingredients during meals (4.0 ml/min) for a total daily volume of ~2.5 l [13]. Pancreatic fluid output is regulated with the aid of several hormones, as well as by the autonomic nervous system. As food enters the duodenum, enteroendocrine cells found in the mucosal lining release hormones (e.g., secretin, cholecystokinin) into the bloodstream that, in turn, stimulate the pancreas to produce and release large amounts of water, bicarbonate and digestive enzymes (e.g., amylase and lipase) and zymogens (e.g., trypsinogen, chymotrypsinogen, proelastase and procarboxypeptidase), which are inactive enzyme precursors that are activated via proteolytic enzymes as soon as they are secreted. These enzymes are critical in the digestion of food that enters the small intestine from the stomach.

Located between the clusters of acinar cells are scattered patches of endocrine secretory tissue, known as the islets of Langerhans. Approximately one million of these micro-organs [14] exist in the pancreas, altogether weighing about 1 g and forming 1–2% of the total pancreas mass [15]. In human pancreas development, islets occur from the endodermal tissue compartment and are determined in the ventral and dorsal lobes. In humans, approximately about 40–60% of the endocrine cells are insulin-producing beta cells, with the remainder being alpha, delta, pancreatic polypeptide (PP; also additionally known as F) and epsilon cells which secrete glucagon, somatostatin, pancreatic polypeptide and ghrelin, respectively. However, the proportion of these various endocrine cell types within an islet varies as a characteristics of islet size, age and location within the organ (reviewed previously [16]). Smaller islets are comprised chiefly of beta cells, while larger islets may additionally have almost equal numbers of beta and alpha cells [17]. Islets derived from the ventral lobe contain PP cell-rich areas, with few beta and alpha cells, that are determined exclusively in the posterior head and uncinate regions of the pancreas [18].

Each islet is furnished through one or more small arteries (arterioles) that branch into numerous capillaries. These capillaries emerge and coalesce into small veins outside the islet. Regarding pancreatic innervation, motor nerve fibres carry impulses to both acinar cells and pancreatic islets [19]. Parasympathetic fibres induce secretion from acinar cells, ultimately resulting in the release of pancreatic juice, as well as stimulating islets to secrete insulin, glucagon and other polypeptide hormones required for normal blood glucose regulation. In contrast, sympathetic fibres cause inhibition of exocrine and endocrine secretions (previously reviewed)[20]. Thus, islet features are regulated by means of signals initiated by autonomic nerves, circulating metabolites (e.g., glucose, amino acids and ketone bodies), circulating hormones and local (paracrine) hormones.

Pancreas function and its contribution to diabetes

The particular contributions of both the endocrine and exocrine pancreas to diabetes in its many varieties are described throughout this special edition in *Diabetologia*. However, as a collective, diabetes is a disorder of carbohydrate metabolism, characterised with the aid of the inability of the body to produce sufficient amounts of, or respond appropriately to, insulin. In addition, dysregulated glucagon secretion via alpha cells is a key characteristics functions of both type 1 and type 2 diabetes. Therefore, the significant importance of the endocrine pancreas lies in the fact that it secretes the two major hormones, glucagon and insulin, that play a central function role in the regulation of energy metabolism.

The pancreas in type 1 diabetes

Beta cell loss

Type 1 diabetes consequences from autoimmune-mediated destruction of islet beta cells due to complicated interactions between genetic and environmental factors [21]. The pathology of what we now reflect consideration on type 1 diabetes was reported over 100 years ago, primarily based on autopsy findings from individuals at the onset of the disease (reviewed previously). These studies established the defining feature of the disease as a significant loss of islet beta cells, with 50–90% of islets having no beta cells (depending on disease duration) despite having other islet endocrine cells present at expected numbers. Loss of islet beta cells has additionally been discovered in islet-autoantibody-positive non-diabetic organ

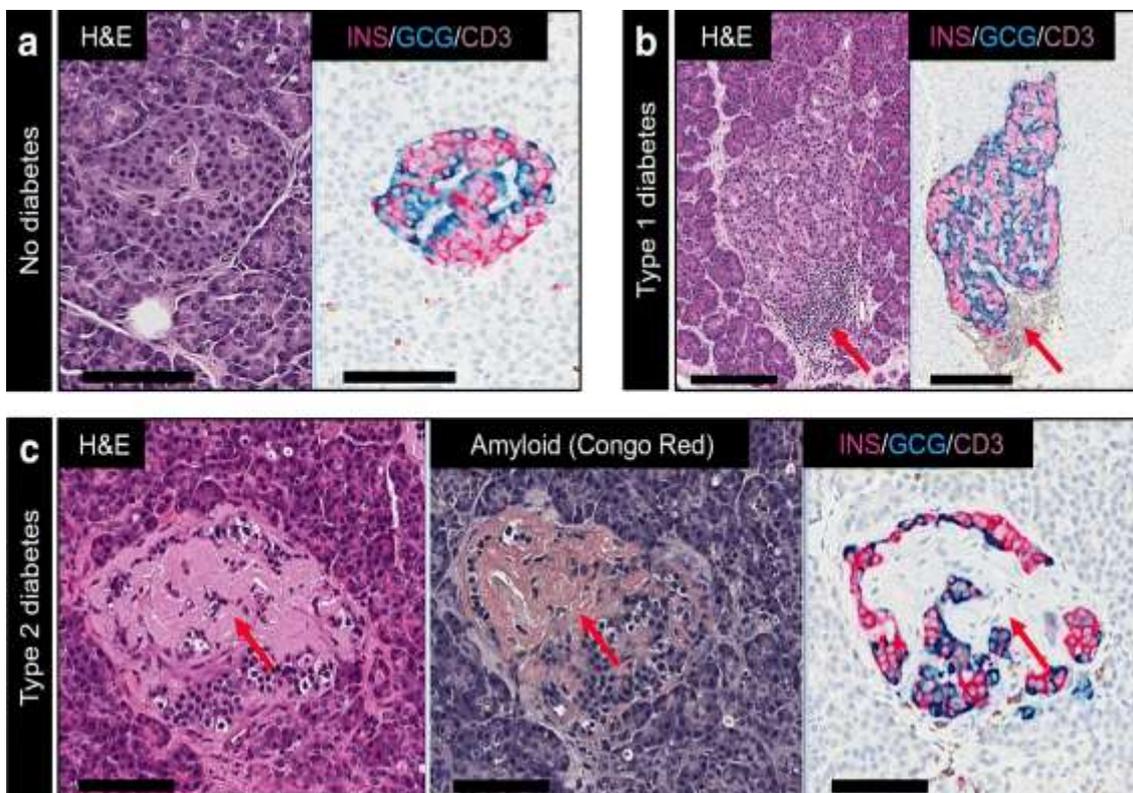
donors [22]. Significant heterogeneity exists in the numbers of islets with residual beta cells (insulin⁺) vs those with partial or complete loss of beta cells (insulin⁻). The insulin⁺ islets additionally exhibit a excessive degree of heterogeneity, ranging from normal to greatly reduced beta cell numbers.

The pancreas in type 2 diabetes

Increased amyloid deposition

Insulin-secreting beta cells are remarkable for their ability to adapt to metabolic demand. In fact, trained athletes secrete up to three times less insulin to achieve euglycaemia than untrained individuals; conversely, non-diabetic obese people can secrete five times more insulin than control participants in response to a glucose challenge [23]. However, the adaptive response of beta cells is not limitless and when it fails, type 2 diabetes ensues.

In contrast to the dramatic changes in islet morphology and immune infiltration described for type 1 diabetes above, there is no stereotyped histology of the pancreas in type 2 diabetes (Table 1). One histological feature that has historically garnered interest is the deposition of amyloid, an extracellular protein aggregate derived from IAPP (Fig. 3). While islet amyloid is existing present in some islets of the majority of individuals with type 2 diabetes, its causal function role in diabetes pathogenesis has not been established. In addition, it is no longer a definitive histological marker since a significant fraction of individuals with type 2 diabetes do not have amyloid in their islets, while these deposits can be existing present in the islets of euglycaemic individuals and, as mentioned earlier, of those with type 1 diabetes [24,25,26].



Functions of the Pancreas

A wholesome healthy pancreas produces the correct chemicals substances in the proper quantities, at the right times, to digest the foods we eat.

Exocrine Function:

The pancreas contains exocrine glands that produce enzymes essential important to

digestion. These enzymes encompass trypsin and chymotrypsin to digest proteins; amylase for the digestion of carbohydrates; and lipase to destroy or break down fats. When food enters the stomach, these pancreatic juices are released into a system of ducts that culminate in the main pancreatic duct. The pancreatic duct joins the common bile duct to form the ampulla of Vater which is present at the first portion of the small intestine, called

the duodenum. The common bile duct originates in the liver and the gallbladder and produces any other necessary important digestive juice referred to as called bile. The pancreatic juices and bile that are launched into the duodenum, help the body to digest fats, carbohydrates, and proteins.

Endocrine Function:

The endocrine factor of the pancreas consists of islet cells (islets of Langerhans) that create and launch necessary hormones directly into the bloodstream. Two of the foremost main pancreatic hormones are insulin, which acts to decrease blood sugar, and glucagon, which acts to elevate blood sugar. Maintaining proper suitable blood sugar levels is crucial to the functioning of key organs such as the brain, liver, and kidneys.

Pancreatic enzymes

Your pancreas creates herbal natural juices called pancreatic enzymes to destroy or break down foods. These juices travel through your pancreas by the ducts. They empty into the upper part of your small intestine referred to as the duodenum. Each day, your pancreas makes about 8 ounces of digestive juice filled with enzymes. These are the different enzymes:

Lipase. This enzyme works together with bile, which your liver produces, to break down fat in your diet. If you don't have adequate lipase, your body will have trouble absorbing fat and the important fat-soluble vitamins (A, D, E, K). Symptoms of poor fat absorption encompass diarrhea and fatty bowel movements.

Protease. This enzyme breaks down proteins in your diet. It additionally helps protect you from germs that might also stay live in your intestines, like certain bacteria and yeast. Undigested proteins can reason allergic reactions in some people.

Amylase. This enzyme helps break down starches into sugar, which your body can use for energy. If you don't have sufficient amylase, you might also get diarrhea from undigested carbohydrates.

Hormones of the Pancreas

The production of pancreatic hormones, including insulin, somatostatin, gastrin, and glucagon, play an vital important role in maintaining sugar and salt balance in our bodies.

Primary hormones secreted by the pancreas include:

Gastrin: This hormone aids digestion through stimulating certain cells in the stomach to produce acid.

Glucagon: Glucagon helps insulin preserve normal blood glucose via working in the opposite way of

insulin. It stimulates cells to release glucose, and this raises the blood glucose levels.

Insulin: This hormone regulates blood glucose through allowing many of your body's cells to absorb and use glucose. In turn, this drops blood glucose levels.

Somatostatin: When levels of other different pancreatic hormones, such as insulin and glucagon, get too high, somatostatin is secreted to keep a balance stability of glucose and/or salt in the blood.

Vasoactive intestinal peptide (VIP): This hormone helps control and manage water secretion and absorption from the intestines by stimulating the intestinal cells to release water and salts into the intestines.

Common pancreatic problems and digestion

Diabetes, pancreatitis, and pancreatic cancer are three common problems that affect the pancreas. Here is how they can have an effect on digestion.

Diabetes: If the pancreatic beta cells do not produce enough insulin or body can't use the insulin your pancreas produces, you can develop diabetes. Diabetes can cause gastroparesis, a reduction in the motor function of the digestive system. Diabetes additionally affects what occur after digestion. If the person don't have enough insulin and eat a meal high in carbohydrates, sugar can go up and cause symptoms like hunger and weight loss. Over the long term, it can lead to heart and kidney disease among other problems.

Pancreatitis: Pancreatitis takes place when the pancreas will becomes inflamed. It is frequently very painful. In pancreatitis, the digestive enzymes your pancreas make attack your pancreas and cause severe abdominal pain. The main cause of acute pancreatitis is gall stones blocking the common bile duct. Too much alcohol can cause pancreatitis that does not clear up. This is recognized as chronic pancreatitis. Pancreatitis influences digestion because due to the fact of enzymes are not available. This leads to diarrhea, weight loss, and malnutrition. About 90% of the pancreas must stop working to cause these symptoms.

Pancreatic cancer: About 95% of pancreatic cancers begin in the cells that make enzymes for digestion. Not having adequate pancreatic enzymes for normal digestion is very common in pancreatic cancer. Symptoms can include weight loss, loss of appetite, indigestion, and fatty stools.

Pancreas is important for digesting food and managing your use of sugar for energy after digestion. If you have any symptoms of pancreatic digestion problems, like loss of appetite, abdominal pain, fatty stools, or weight loss, call your healthcare provider. [13]

Diseases and Disorders of the Pancreas :

Problems in the production or regulation of pancreatic hormones will cause complications related to blood sugar imbalance.

Of all the diseases and disorders of the pancreas, the most well-known is diabetes.

Type 1 diabetes: If you have type 1 diabetes, then your body doesn't produce any insulin to handle the glucose in your body. Insulin deficiency causes a range of complications, so people with type 1 diabetes have to take insulin to help their body use glucose appropriately.

Type 2 diabetes: Type 2 diabetes is much more prevalent than type 1. People with type 2 diabetes may be able to produce insulin, but their bodies don't use it correctly. They might also be unable to produce enough insulin to handle the glucose in their body. Lifestyle choices, such as diet and exercise, play a major role in managing and preventing type 2 diabetes.

Other common diseases and disorders associated with the pancreas are:

Hyperglycemia: This condition is caused by abnormally excessive blood glucose levels. It can be caused by overproduction of the hormone glucagon.

Hypoglycemia: Conversely, hypoglycemia is caused by less level of blood glucose levels. It is caused by a relative overproduction of insulin.

Despite the fact that the great majority of pancreatic cells are devoted to digestive function, the endocrine cells play a major role in your overall health. By regulating blood sugar levels, the pancreatic hormones are directly related to some of the most common diseases of today, including diabetes.

Fast facts on the pancreas

The pancreas is a gland organ with a key important role in digestion and glucose control.

Problems associated to the pancreas include diabetes and cancer.

A healthful diet can contribute to maintaining a healthy pancreas.

Disorders

Problems with the pancreas can affect the whole entire body.

If the pancreas does not produce enough digestive enzymes, for example, food will not be properly absorbed. This can lead to weight loss and diarrhea. The islets of Langerhans are responsible for regulating blood glucose. Too little insulin production will increase the risk of diabetes, and blood glucose levels will rise.

Pancreatitis

Pancreatitis can cause abdominal pain. Pancreatitis refers to an acute or chronic inflammation of the pancreas. It can lead to secondary diabetes.

Inflammation can occur if the main duct from the pancreas is blocked by a gallstone or tumor.

Pancreatic juices will accumulate in the pancreas, causing damage to the pancreas. The pancreas may start to digest itself.

Pancreatitis can happen as a result of mumps, gallstones, trauma and the use of alcohol, steroids, and drugs.

Acute pancreatitis is rare, but it needs immediate medical attention.

Symptoms include:

- intense abdominal pain, tenderness, and swelling
- nausea and vomiting
- fever
- muscle aches

Immediate treatment is normally with fluids and painkillers. Patients often do not want to eat at the beginning, but if the pancreatitis is mild, they will start to eat again relatively quickly.

If a secondary infection has occurred, surgery may be necessary.

Chronic pancreatitis can develop if acute pancreatitis happens repeatedly, resulting in permanent damage.

The most common cause is alcohol abuse, and it mostly affects middle-aged men.

Symptoms include:

- persistent pain in the upper abdomen and back
- weight loss
- diarrhea
- diabetes
- mild jaundice

Hereditary pancreatitis can show up if there is an inherited problem in the pancreas or the intestine. A person under 30 years of age may additionally experience repeated acute pancreatitis, leading to a chronic condition.

It is a progressive condition that can lead to permanent damage. The person may experience pain, diarrhea, malnutrition or diabetes. Treatment aims to control pain to replace lost enzymes.

Genetic testing is available for patients who may be at risk.

Pancreatic cancer

Cancer can develop in the pancreas. The exact cause is often unknown, but it is often linked to smoking or heavy drinking.

Other risk factors include:

- diabetes
- chronic pancreatitis
- liver problems
- stomach infections

Symptoms include:

- pain in the upper abdomen as the tumor pushes against the nerves
- jaundice, a yellowing of the skin and eyes and darkening of the urine as the cancer interferes with the bile duct and the liver
- loss of appetite, nausea, and vomiting
- significant weight loss and weakness
- pale or gray stool, and excess fat in the stool

Symptoms may not appear until the cancer is in the advanced stages. By then, it may be too late for successful treatment. The prognosis for pancreatic cancer tends to be poor.

Treatment usually involves surgery, chemotherapy, radiation, or a combination these.

Palliative treatment will focus on reducing the pain. Pancreatic cancer is the fourth most common cause of cancer in men in the United States (U.S.) and the fifth in women. Over 37,000 new cases are diagnosed each year.

Diabetes

Type 1 diabetes is an autoimmune disease. It takes place when the immune system attacks and destroys the beta cells in the pancreas so that they can no longer produce insulin. The exact cause remains unknown, but it may be due to genetic and environmental factors, including viruses.

Type 2 diabetes begins when the body's muscle, fat, and liver cells become unabled trusted source to process glucose. The pancreas reacts by producing extra insulin, but in time, it cannot produce enough insulin. The body can no longer control blood glucose levels.

Other problems that can occur include:

- Exocrine pancreatic insufficiency (EPI): The pancreas does not produce enough enzymes
- Pancreatic cysts: These can be removed by surgery if there is a risk of cancer
- Pancreatic fluid collections: Resulting from a range of conditions, this can lead to pain and fever

- Zollinger-Ellison syndrome: A tumor known as a gastrinoma develops in the pancreas or duodenum

II. CONCLUSION

The pancreas is an internal organ that plays a key role in the transformation of essential nutrients that provide energy for cells. Problems with its functioning may negatively affect the health of the human body. Even healthy and relatively young people should take care of healthy nutrition and an appropriate lifestyle, which will guarantee optimal pancreatic functioning for many years.

Inappropriate work of the pancreas has a negative impact on the proper functioning of the body, contributing to the development of diseases related to the pancreas, as well as obesity. Likewise, leading a wrong lifestyle and poor diet can cause problems in the proper functioning of this organ. The mere presence of chronic diseases such as obesity may also be a contributing factor to the development of pancreatic disorders.

REFERENCE

- [1]. <https://columbiasurgery.org/pancreas/pancreas-and-its-function>
- [2]. <https://www.endocrineweb.com/endocrinology/overview-pancreas>
- [3]. <https://journals.biologists.com/dev/article/142/18/3126/46880/Human-pancreas-development>
- [4]. <https://www.kenhub.com/en/library/anatomy/the-pancreas>
- [5]. <https://training.seer.cancer.gov/biliary/anatomy/>
- [6]. <https://www.kenhub.com/en/library/anatomy/the-pancreas>
- [7]. Longnecker DS, Gorelick F, Thompson ED. Anatomy, histology, and fine structure of the pancreas. The pancreas: an integrated textbook of basic science, medicine, and surgery. 2018 Mar 7:10-23.
- [8]. Saisho Y, Butler AE, Meier JJ, Monchamp T, Allen-Auerbach M, Rizza RA, Butler PC. Pancreas volumes in humans from birth to age one hundred taking into account sex, obesity, and presence of type-2 diabetes. *Clinical anatomy*. 2007 Nov;20(8):933-42.
- [9]. Williams JA. Regulation of acinar cell function in the pancreas. *Current opinion in gastroenterology*. 2010 Sep;26(5):478.

- [10]. Matsuda Y. Age-related morphological changes in the pancreas and their association with pancreatic carcinogenesis. *Pathology International*. 2019 Aug;69(8):450-62.
- [11]. Atkinson MA, Campbell-Thompson M, Kusmartseva I, Kaestner KH. Organisation of the human pancreas in health and in diabetes. *Diabetologia*. 2020 Oct;63(10):1966-73.
- [12]. In't Veld P, Marichal M. Microscopic anatomy of the human islet of Langerhans. *The islets of Langerhans*. 2010:1-9.
- [13]. Kilimnik G, Jo J, Periwai V, Zielinski MC, Hara M. Quantification of islet size and architecture. *Islets*. 2012 Mar 1;4(2):167-72.
- [14]. Inada A, Nienaber C, Katsuta H, Fujitani Y, Levine J, Morita R, Sharma A, Bonner-Weir S. Carbonic anhydrase II-positive pancreatic cells are progenitors for both endocrine and exocrine pancreas after birth. *Proceedings of the National Academy of Sciences*. 2008 Dec 16;105(50):19915-9.
- [15]. Savari O, Zielinski MC, Wang X, Misawa R, Millis JM, Witkowski P, Hara M. Distinct function of the head region of human pancreas in the pathogenesis of diabetes. *Islets*. 2013 Sep 13;5(5):226-8.
- [16]. Ahrén B. Islet nerves in focus—defining their neurobiological and clinical role. *Diabetologia*. 2012 Dec;55(12):3152-4.
- [17]. Schwartz MW, Seeley RJ, Tschöp MH, Woods SC, Morton GJ, Myers MG, D'Alessio D. Cooperation between brain and islet in glucose homeostasis and diabetes. *Nature*. 2013 Nov;503(7474):59-66.
- [18]. Rodriguez-Diaz R, Abdulreda MH, Formoso AL, Gans I, Ricordi C, Berggren PO, Caicedo A. Autonomic axons in the human endocrine pancreas show unique innervation patterns. *Cell metabolism*. 2011 Jul 7;14(1):45.
- [19]. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. *The Lancet*. 2014 Jan 4;383(9911):69-82.
- [20]. Campbell-Thompson M, Fu A, Kaddis JS, Wasserfall C, Schatz DA, Pugliese A, Atkinson MA. Insulinitis and β -cell mass in the natural history of type 1 diabetes. *Diabetes*. 2016 Mar 1;65(3):719-31.
- [21]. Campbell-Thompson ML, Atkinson MA, Butler AE, Chapman NM, Frisk G, Gianani R, Giepmans BN, Von Herrath MG, Hyöty H, Kay TW, Korsgren O. The diagnosis of insulinitis in human type 1 diabetes. *Diabetologia*. 2013 Nov;56(11):2541-3.
- [22]. Wang YJ, Traum D, Schug J, Gao L, Liu C, Atkinson MA, Powers AC, Feldman MD, Naji A, Chang KM, Kaestner KH. Multiplexed in situ imaging mass cytometry analysis of the human endocrine pancreas and immune system in type 1 diabetes. *Cell metabolism*. 2019 Mar 5;29(3):769-83.
- [23]. Leete P, Willcox A, Krogvold L, Dahl-Jørgensen K, Foulis AK, Richardson SJ, Morgan NG. Differential insulinitic profiles determine the extent of β -cell destruction and the age at onset of type 1 diabetes. *Diabetes*. 2016 May 1;65(5):1362-9.
- [24]. Yu MG, Keenan HA, Shah HS, Frodsham SG, Pober D, He Z, Wolfson EA, D'Eon S, Tinsley LJ, Bonner-Weir S, Pezolesi MG. Residual β cell function and monogenic variants in long-duration type 1 diabetes patients. *The Journal of clinical investigation*. 2019 Aug 1;129(8):3252-63.
- [25]. Seay HR, Yusko E, Rothweiler SJ, Zhang L, Posgai AL, Campbell-Thompson M, Vignali M, Emerson RO, Kaddis JS, Ko D, Nakayama M. Tissue distribution and clonal diversity of the T and B cell repertoire in type 1 diabetes. *JCI insight*. 2016 Dec 12;1(20).
- [26]. Martino L, Masini M, Bugliani M, Marselli L, Suleiman M, Boggi U, Nogueira TC, Filipponi F, Occhipinti M, Campani D, Dotta F. Mast cells infiltrate pancreatic islets in human type 1 diabetes. *Diabetologia*. 2015 Nov;58(11):2554-62.