Liver and Pancreas

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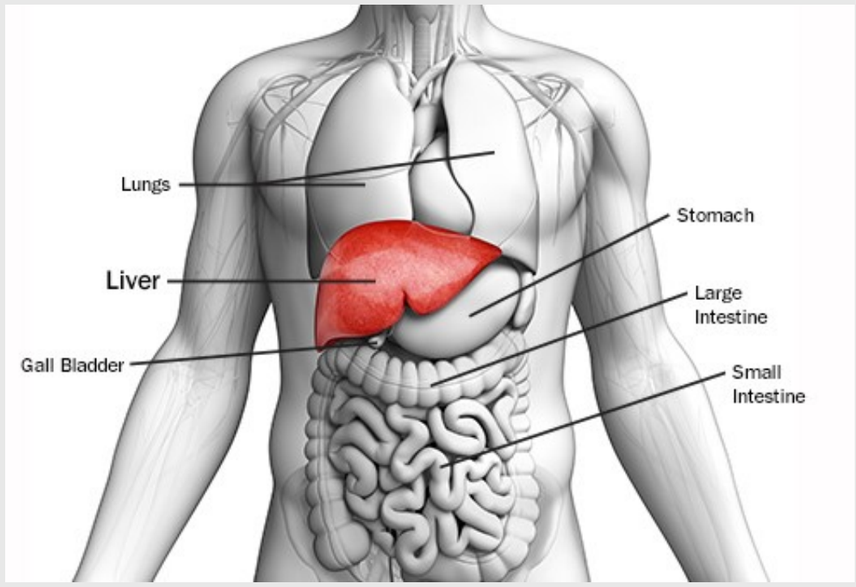
Liver

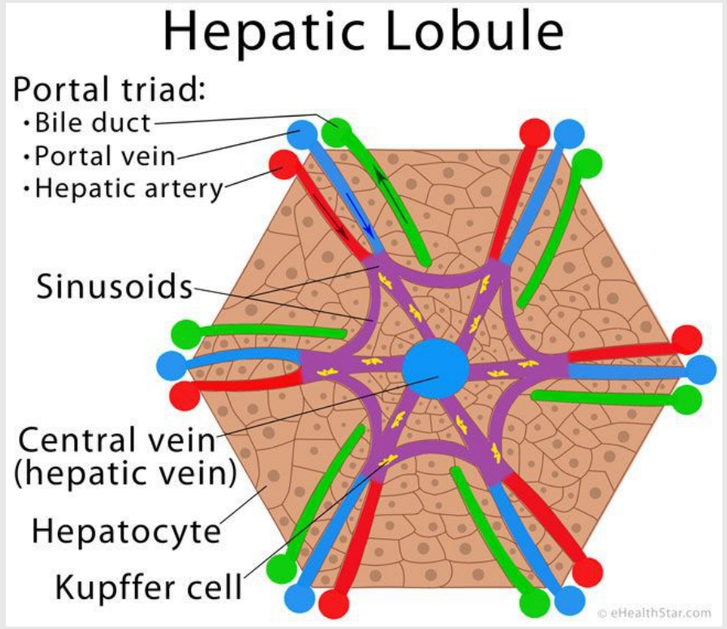
- The liver is an organ that detoxifies various metabolites, synthesizes proteins and produces biochemicals necessary for digestion
- Located in the right upper quadrant of the abdomen, below the diaphragm
- Its other roles in metabolism include the regulation of glycogen storage, decomposition of red blood cells and the production of hormones



webmd

Liver

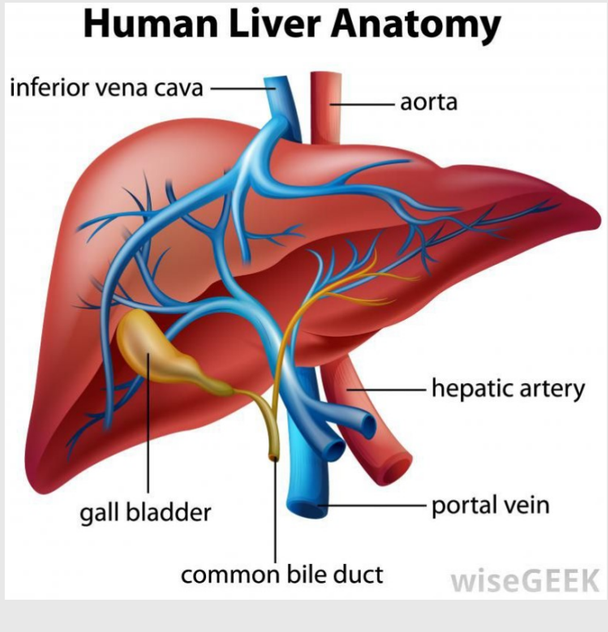
- Is a reddish-brown, wedge-shaped organ with four lobes of unequal size and shape
- Located in the right upper quadrant of the abdominal cavity, it rests just below the diaphragm, to the right of the stomach and overlies the gallbladder
- Connected to two large blood vessels: the hepatic artery and the portal vein and common hepatic duct
- Lobules are the functional units of the liver
- The liver is grossly divided into two parts when viewed from above – a right and a left lobe - and four parts when viewed from below (left, right, caudate, and quadrate lobes)



Liver

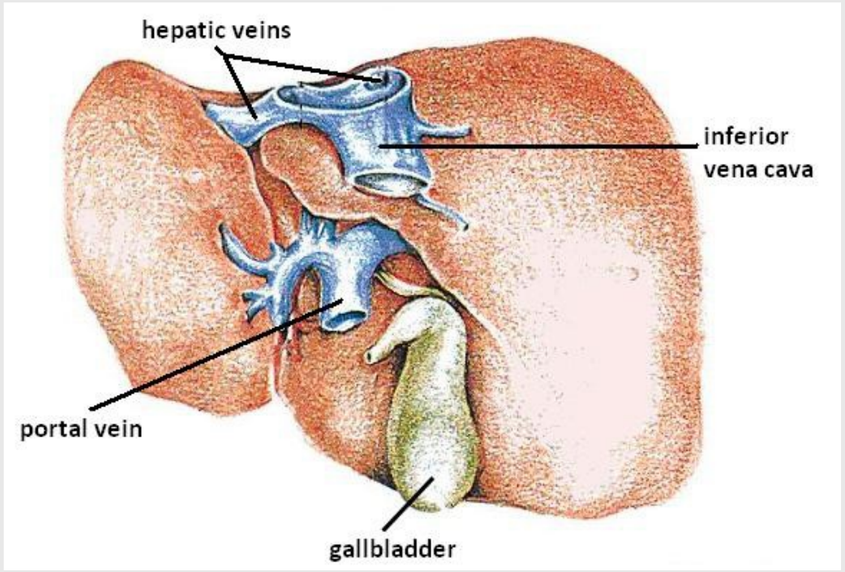
Blood supply

- Receives a dual blood supply from the hepatic portal vein and hepatic arteries
- The hepatic portal vein delivers around 75% of the liver's blood supply, and carries venous blood drained from the spleen, gastrointestinal tract, and its associated organs
- The hepatic arteries supply arterial blood to the liver, accounting for the remaining quarter of its blood flow



Liver

- The hepatic artery also has both alpha- and beta-adrenergic receptors; therefore, flow through the artery is controlled, in part, by the splanchnic nerves of the autonomic nervous system.
- The central veins coalesce into hepatic veins, which leave the liver and drain into the inferior vena cava

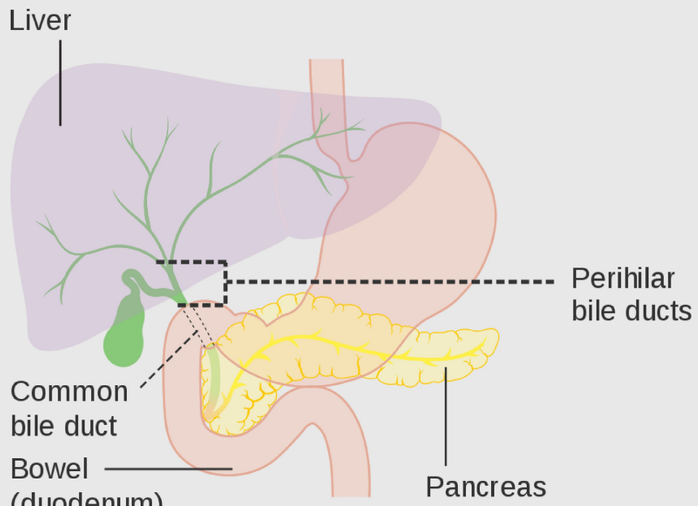


wikipedia

Liver

Biliary flow

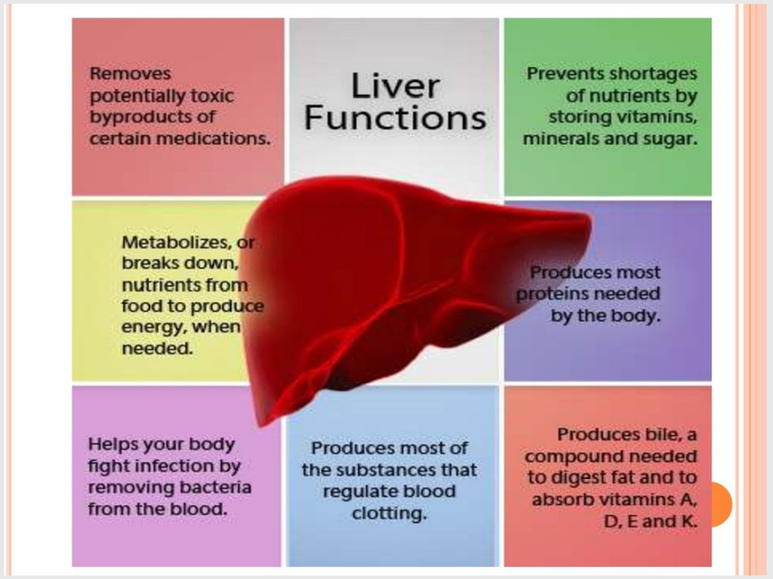
- The biliary tract is derived from the branches of the bile ducts
- Is the path by which bile is secreted by the liver then transported to the first part of the small intestine, the duodenum
- The cystic duct from the gallbladder joins with the common hepatic duct to form the common bile duct
- The biliary system and connective tissue is supplied by the hepatic artery alone
- Bile either drains directly into the duodenum via the common bile duct, or is temporarily stored in the gallbladder via the cystic duct
- The common bile duct and the pancreatic duct enter the second part of the duodenum together at the hepatopancreatic ampulla, also known as the ampulla of Vater



Liver

Synthesis

- Major role in carbohydrate, protein, amino acid, and lipid metabolism
- carbohydrate metabolism:
  - The liver synthesizes and stores glycogen via glycogenesis, the formation of glycogen from glucose.
  - When needed, the liver releases glucose into the blood by performing glycogenolysis, the breakdown of glycogen into glucose
  - The liver is also responsible for gluconeogenesis, which is the synthesis of glucose from certain amino acids, lactate, or glycerol.
- Adipose and liver cells produce glycerol by breakdown of fat, which the liver uses for gluconeogenesis



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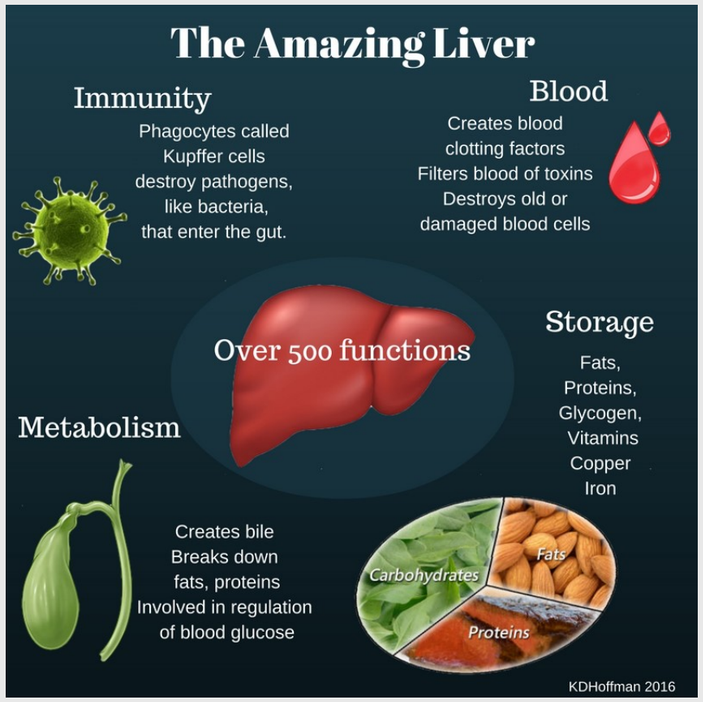
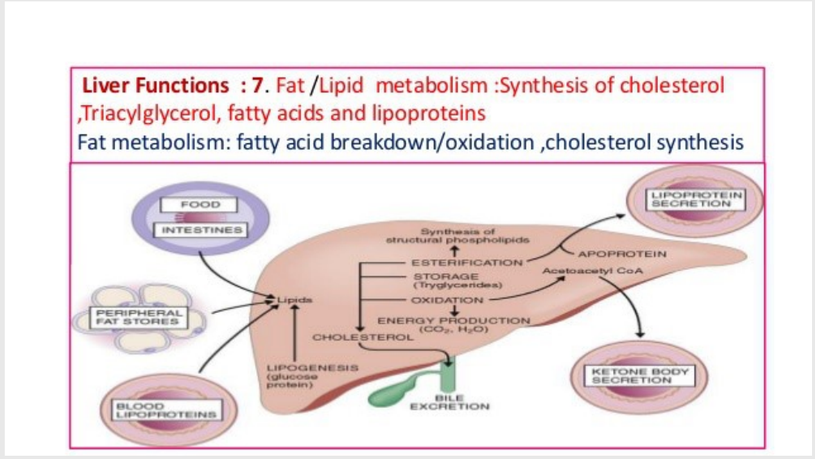
Liver

- Responsible for the mainstay of protein metabolism, synthesis as well as degradation.
- It is also responsible for a large part of amino acid synthesis.
- The liver plays a role in the production of clotting factors, as well as red blood cell production.
- Some of the proteins synthesized by the liver include coagulation factors I (fibrinogen), II (prothrombin), V, VII, VIII, IX, X, XI, XII, XIII, as well as protein C, protein S and antithrombin.
- In the first trimester fetus, the liver is the main site of red blood cell production.
- By the 32nd week of gestation, the bone marrow has almost completely taken over that task.
- The liver is a major site of production for thrombopoietin, hormone that regulates the production of platelets by the bone marrow



Liver

- The liver plays several roles in lipid metabolism:
  - it performs cholesterol synthesis, lipogenesis, and the production of triglycerides, and a bulk of the body's lipoproteins are synthesized in the liver.
  - The liver plays a key role in digestion, as it produces and excretes bile (a yellowish liquid) required for emulsifying fats and help the absorption of vitamin K from the diet. Some of the bile drains directly into the duodenum, and some is stored in the gallbladder.
  - The liver also produces insulin-like growth factor 1, a hormone that plays an important role in childhood growth and continues to have anabolic effects in adults.



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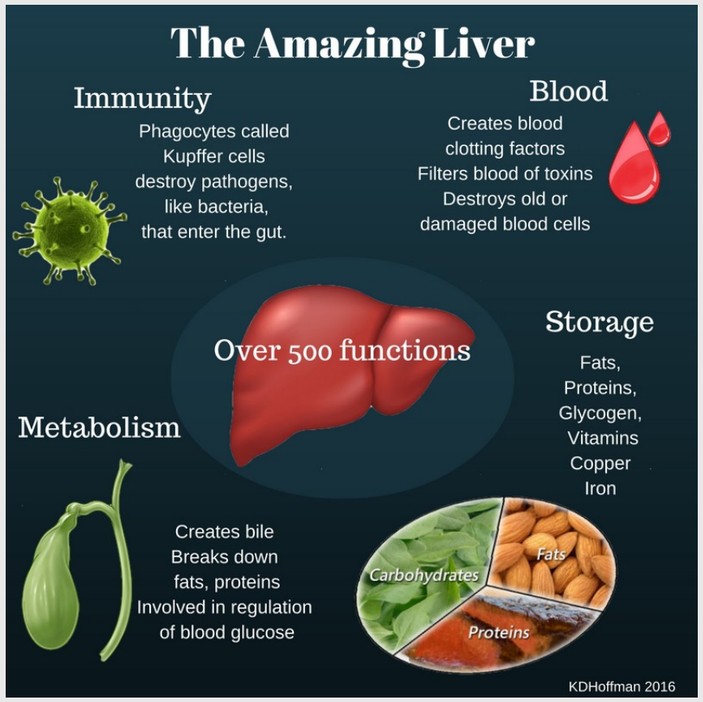
Liver

Breakdown

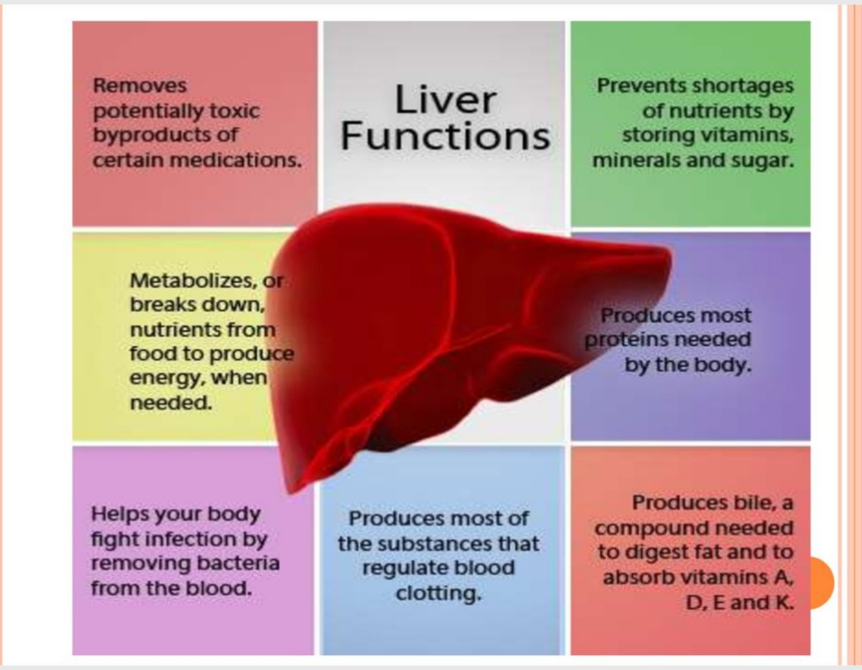
- Responsible for the breakdown of insulin and other hormones.
- The liver breaks down bilirubin via glucuronidation, facilitating its excretion into bile.
- The liver is responsible for the breakdown and excretion of many waste products.
- It plays a key role in breaking down or modifying toxic substances (e.g., methylation) and most medicinal products in a process called drug metabolism. This sometimes results in toxication, when the metabolite is more toxic than its precursor. Preferably, the toxins are conjugated to avail excretion in bile or urine.
- The liver converts ammonia into urea as part of the urea cycle, and the urea is excreted in the urine



Liver

Other

- The liver stores a multitude of substances, including glucose (in the form of glycogen), vitamin A (1–2 years' supply), vitamin D (1–4 months' supply), vitamin B12 (3–5 years' supply), vitamin K, iron, and copper.
- The liver is responsible for immunological effects – the mononuclear phagocyte system of the liver contains many immunologically active cells, acting as a 'sieve' for antigens carried to it via the portal system.
- The liver produces albumin, the most abundant protein in blood serum. It is essential in the maintenance of oncotic pressure, and acts as a transport for fatty acids and steroid hormones.
- The liver synthesizes angiotensinogen, a hormone that is responsible for raising the blood pressure when activated by renin, an enzyme that is released when the kidney senses low blood pressure.
- The liver produces the enzyme catalase in order to break down hydrogen peroxide, a very toxic substance due to it being a powerful oxidising agent, into water and oxygen.



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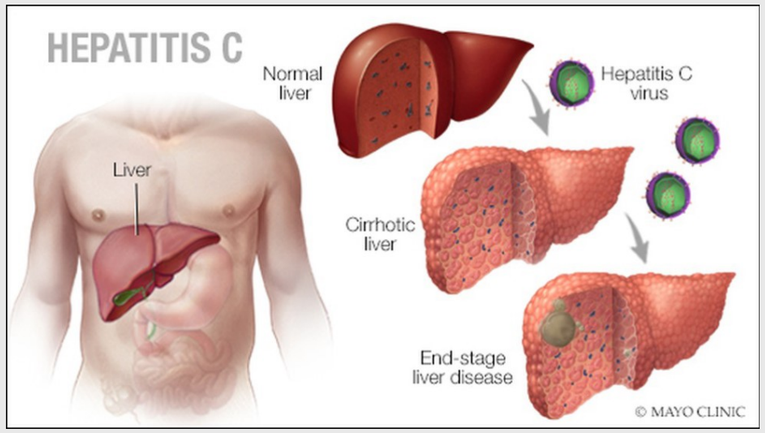
Liver

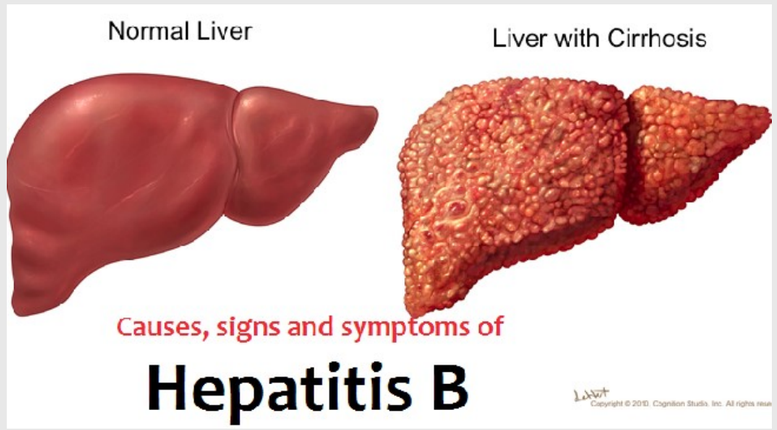
<u>Clinical significance</u>

- A vital organ and supports almost every other organ in the body.
- Because of its strategic location and multidimensional functions, the liver is also prone to many diseases
- The bare area of the liver is a site that is vulnerable to the passing of infection from the abdominal cavity to the thoracic cavity
- <u>Hepatitis</u> is a common condition of inflammation of the liver
  - Most usual cause of this is viral, and the most common of these infections are hepatitis A, B, C, D, and E.
  - Some of these infections are sexually transmitted
  - Other viruses in the family Herpesviridae such as the herpes simplex virus.



Liver

- Chronic infection with hepatitis B virus or hepatitis C virus is the main cause of liver cancer
- Globally, about 248 million individuals are chronically infected with HBV
- 142 million are chronically infected with HCV
- Globally there are about 114 million and 20 million cases of hepatitis A and hepatitis E respectively, but these generally resolve, and do not become chronic
- Hepatitis D virus is a "satellite" of hepatitis B virus (can only infect in the presence of hepatitis B), and co-infects nearly 20 million people with hepatitis B, globally

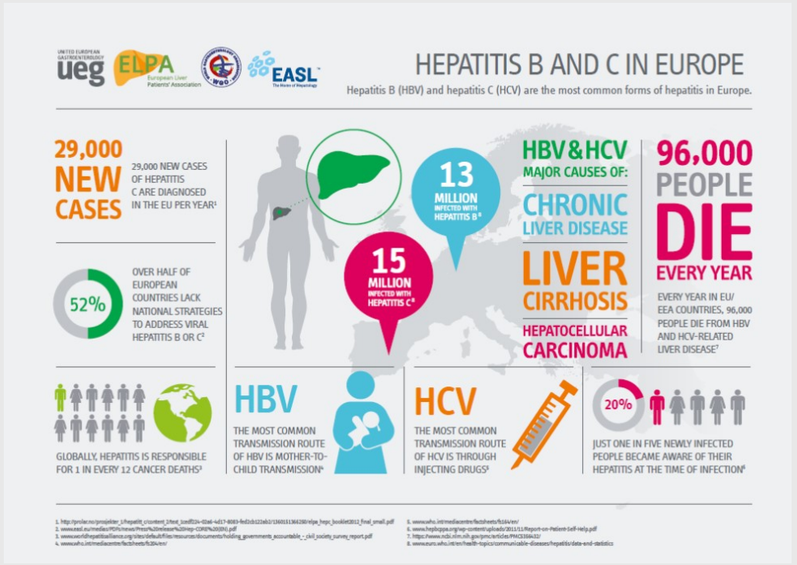


Liver

- Hepatic encephalopathy is caused by an accumulation of toxins in the bloodstream that are normally removed by the liver. This condition can result in coma and can prove fatal
- Alcoholic liver diseases and these include alcoholic hepatitis, fatty liver, and cirrhosis
  - Factors contributing to the development of alcoholic liver diseases are not only the quantity and frequency of alcohol consumption, but can also include gender, genetics, and liver insult
- Liver damage can also be caused by drugs, particularly paracetamol and chemotherapy
- A rupture of the liver can be caused by a liver shot used in combat sports

Liver

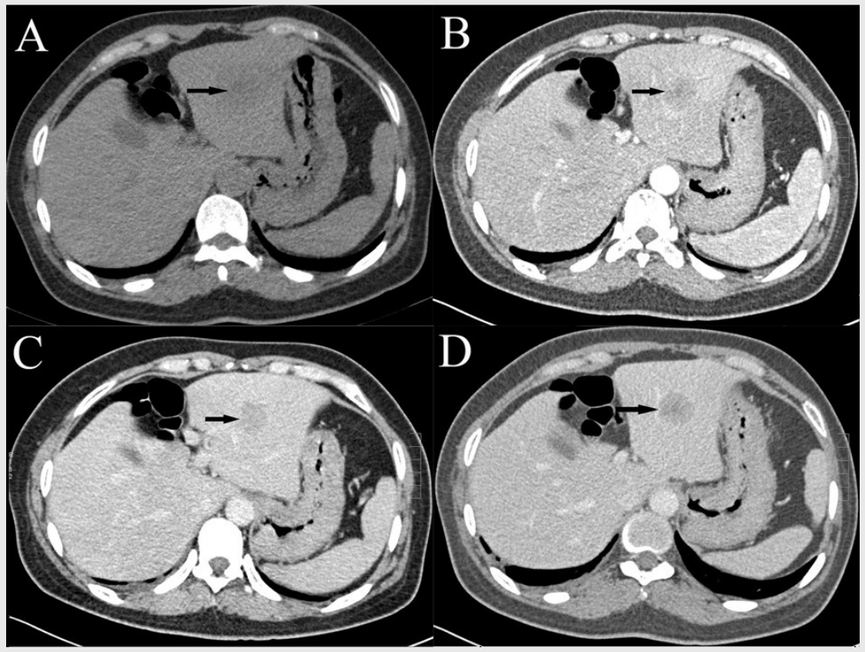
- Budd–Chiari syndrome is a condition caused by blockage of the hepatic veins (including thrombosis) that drain the liver. It presents with the classical triad of abdominal pain, ascites and liver enlargement
- Primary biliary cholangitis is an autoimmune disease of the liver.
- It is marked by slow progressive destruction of the small bile ducts of the liver, with the intralobular ducts (Canals of Hering) affected early in the disease. When these ducts are damaged, bile and other toxins build up in the liver (cholestasis) and over time damages the liver tissue in combination with ongoing immune related damage. This can lead to scarring (fibrosis) and cirrhosis



Liver

Hepatocellular carcinoma

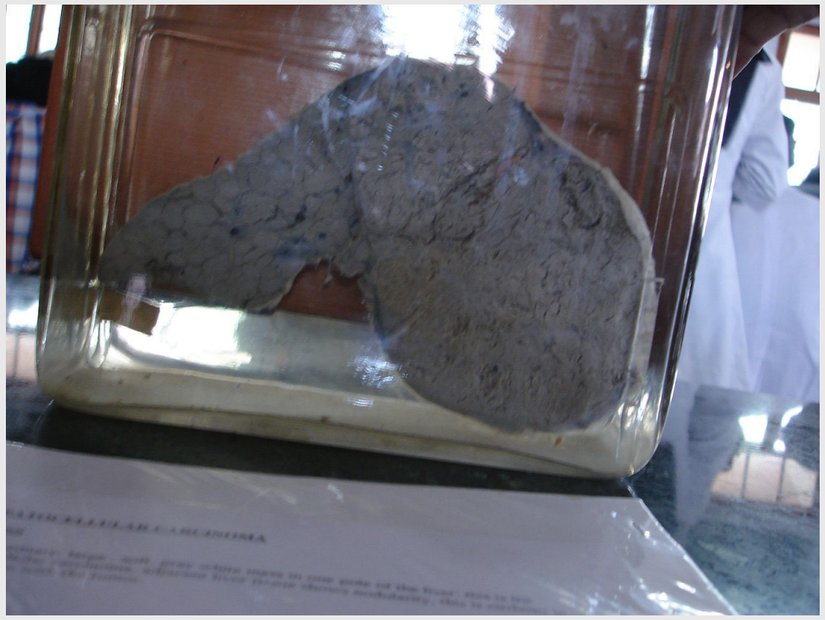
- The most common type of primary liver cancer in adults, and is the most common cause of death in people with cirrhosis
- It occurs in the setting of chronic liver inflammation(hepatitis B or C) or exposure to toxins such as alcohol or aflatoxin
- hemochromatosis and alpha 1-antitrypsin deficiency, markedly increase the risk of developing HCC. Metabolic syndrome and non alcoholic fatty liver disease are also increasingly recognized as risk factors for HCC.



By Zhenyu Pan, Guozi Yang, Tingting Yuan, Lihua Dong, Lihua Dong - (2014). "Leptomeningeal metastasis from hepatocellular carcinoma with other unusual metastases: a case report". BMC Cancer 14 (1). DOI:10.1186/1471-2407-14-399. ISSN 1471-2407.CC-BY 2.0, CC BY 4.0, https://commons.wikimedia.org/w/index.php?curid=76774959

Liver

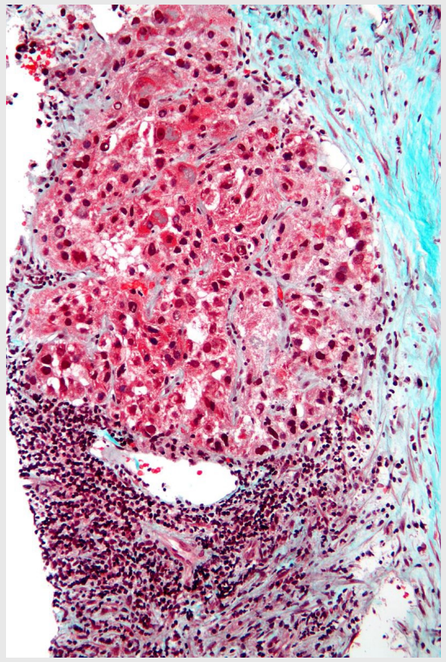
- As with any cancer, the <u>treatment and prognosis</u> of HCC vary depending on the specifics of tumor histology, size, spread, and overall health
- The vast majority of HCC occurs in Asia and sub-Saharan Africa, in countries where hepatitis B infection is endemic and many are infected from birth
- The incidence of HCC in the United States and other developing countries is increasing due to an increase in hepatitis C virus infections
- It is more common in males than females for unknown reasons



Liver

Risk factors

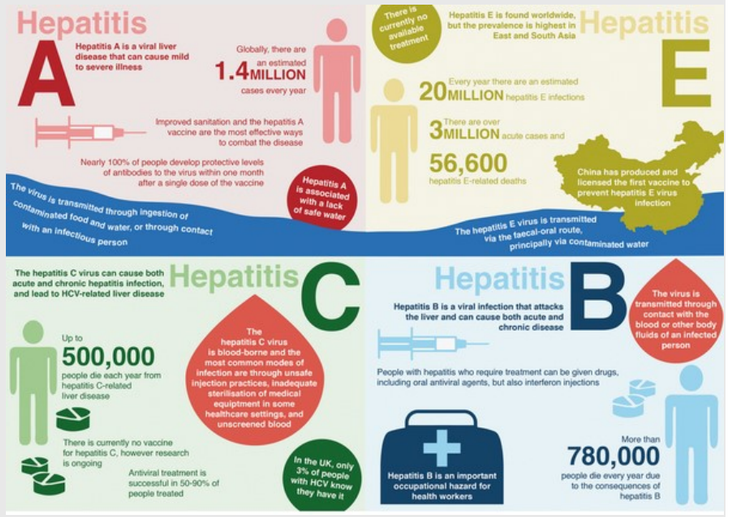
- Chronic viral hepatitis (80% cases globally)
  - Chronic hepatitis B (about 50% cases)
  - Chronic hepatitis C (about 25% cases)
- Toxins:
  - Alcohol abuse: the most common cause of cirrhosis
  - Aflatoxin
  - Iron overload state (hemochromatosis)
- Metabolic:
  - Nonalcoholic steatohepatitis: up to 20% progress to cirrhosis
  - Type 2 diabetes (probably aided by obesity)
- Congenital disorders:
  - Alpha 1-antitrypsin deficiency
  - Wilson's disease(controversial)
  - Hemophilia, although statistically associated with higher risk of HCC, this is due to coincident chronic viral hepatitis infection related to repeated blood transfusions over lifetime



Liver

Symptoms

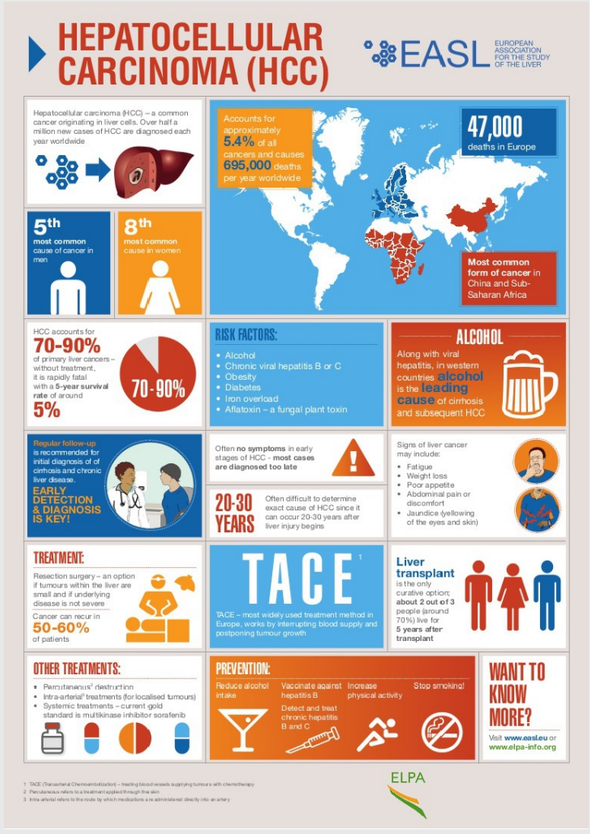
- The classic symptoms of liver damage include the following:
- Pale stools occur when stercobilin, a brown pigment, is absent from the stool. Stercobilin is derived from bilirubin metabolites produced in the liver.
- Dark urine occurs when bilirubin mixes with urine
- Jaundice.This is where bilirubin deposits in skin, causing an intense itch. Itching is the most common complaint by people who have liver failure. Often this itch cannot be relieved by drugs.
- Swelling of the abdomen, and swelling of the ankles and feet occurs because the liver fails to make albumin.
- Excessive fatigue occurs from a <u>generalized loss of nutrients, minerals and vitamins</u>
- Bruising and easy bleeding are other features of liver disease. The liver makes clotting factors.When liver damage occurs, these factors are no longer present and severe bleeding can occur
- Pain in the upper right quadrant can result from the stretching of Glisson's capsule in conditions of hepatitis and pre-eclampsia.



Liver

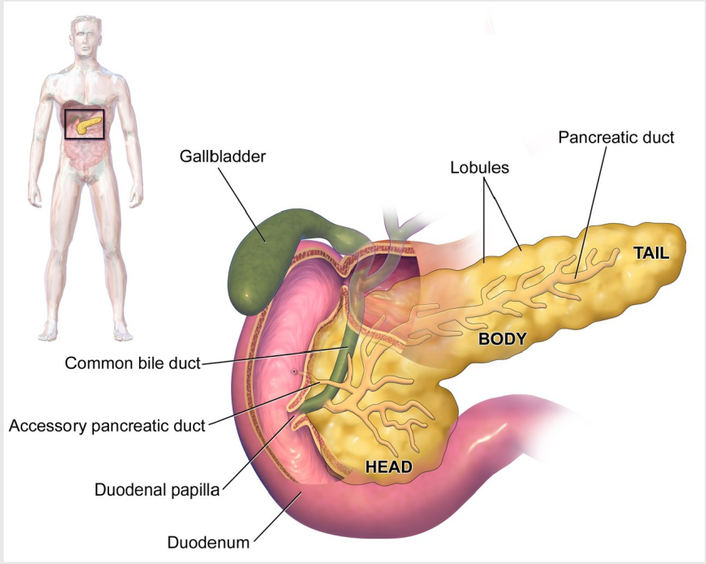
Diagnosis

- The diagnosis of liver disease is made by liver function tests, groups of blood tests, that can readily show the extent of liver damage.
- If infection is suspected, then other serological tests will be carried out.
- A physical examination of the liver can only reveal its size and any tenderness, and some form of imaging such as an ultrasound or CT scan may also be needed.
- Sometimes a liver biopsy will be necessary, and a tissue sample is taken through a needle inserted into the skin just below the rib cage. This procedure may be helped by a sonographer providing ultrasound guidance to an interventional radiologist



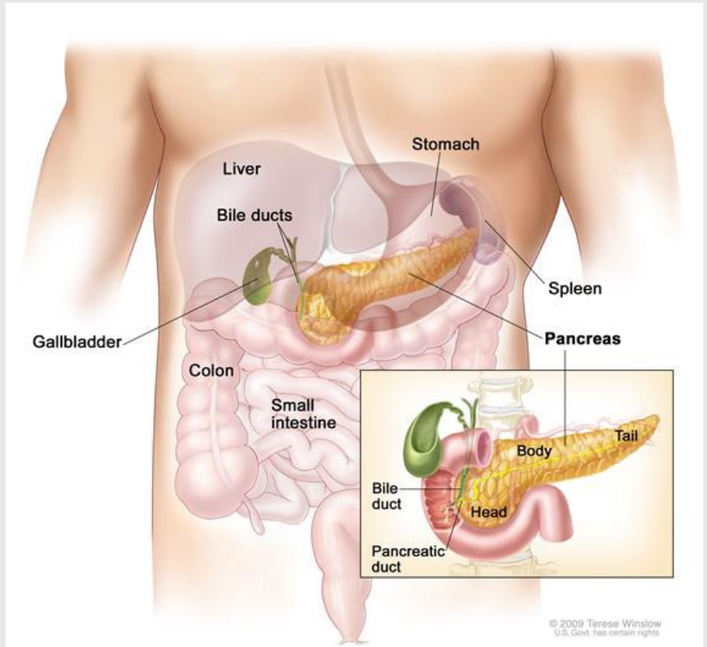
Pancreas

- Is an organ of the digestive system and endocrine system
- Located in the abdomen behind the stomach and functions as a gland
- It has both an endocrine and a digestive exocrine function
- As an endocrine gland, it functions mostly to regulate blood sugar levels, secreting the hormones insulin, glucagon, somatostatin, and pancreatic polypeptide
- As a part of the digestive system, it functions as an exocrine gland secreting pancreatic juice into the duodenum through the pancreatic duct. This juice contains bicarbonate, which neutralizes acid entering the duodenum from the stomach; and digestive enzymes, which break down carbohydrates, proteins, and fats in food entering the duodenum from the stomach



Pancreas

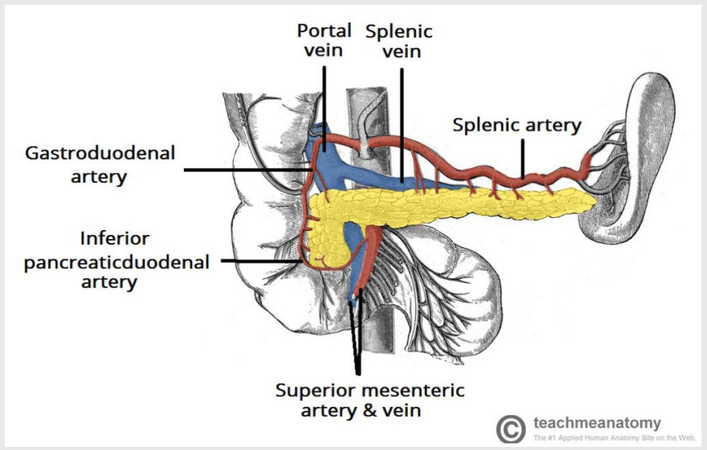
- The pancreas is an organ that lies in the upper left part of the abdomen. In adults, it is about 12–15 centimetres long, lobulated, and salmon-coloured in appearance
- Anatomically, the pancreas is divided into a <u>head, neck, body, and tail.</u>
- The pancreas stretches from the inner curvature of the duodenum, where the head surrounds two blood vessels, the superior mesenteric artery, and vein.
- The longest part of the pancreas, the body, stretches across behind the stomach, and the tail of the pancreas ends adjacent to the spleen
- Two ducts, the main <u>pancreatic duct</u> and a smaller <u>accessory pancreatic duct</u>, run through the body of the pancreas, joining with the common bile duct near a small ballooning called the ampulla of Vater. Surrounded by a muscle, the sphincter of Oddi, this opens into the descending part of the duodenum



Pancreas

Blood supply

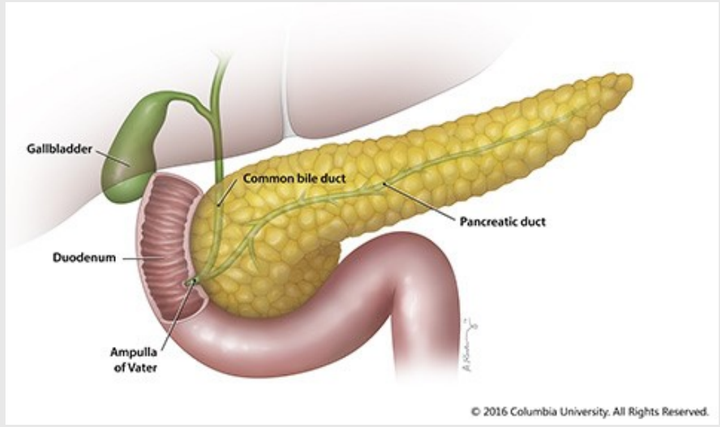
- The pancreas has a rich blood supply, with vessels originating as branches of both the coeliac artery and superior mesenteric artery
- The splenic artery runs along the top margin of the pancreas, and supplies the left part of the body and the tail of the pancreas through its pancreatic branches, the largest of which is called the greater pancreatic artery
- The superior and inferior pancreaticoduodenal arteries run along the anterior and posterior surfaces of the head of the pancreas at its border with the duodenum. These supply the head of the pancreas. These vessels anastamose in the middle
- The body and neck of the pancreas drain into the splenic vein, which sits behind the pancreas. The head drains into, and wraps around, the superior mesenteric and portal veins.
- The pancreas drains into lymphatic vessels that travel alongside its arteries. These lymphatic vessels drain primarily into pancreaticosplenic lymph nodes, and some into the lymph nodes that lie in front of the aorta



Pancreas

Function

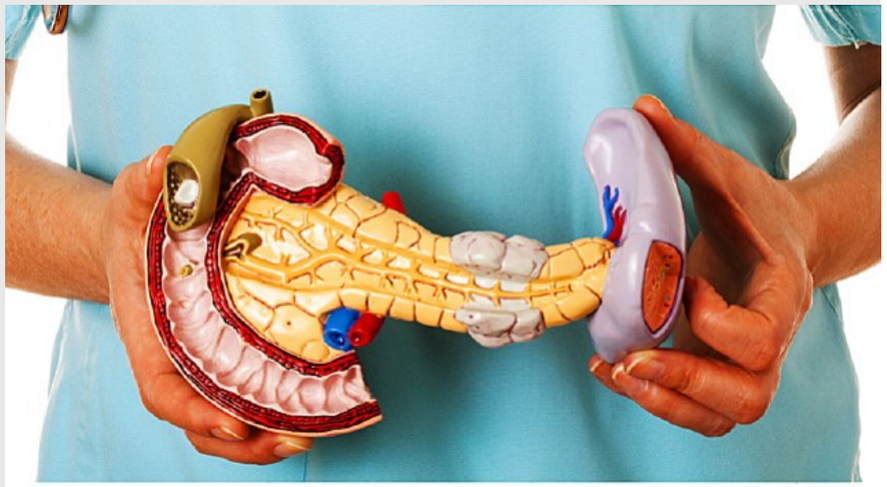
- The pancreas is involved in blood sugar control and metabolism within the body, and also in the secretion of substances (pancreatic juice) which help digestion.
- These are divided into an
  - "endocrine" function , relating to the secretion of insulin and other substances within pancreatic islets and helping control blood sugar levels and metabolism within the body
  - "exocrine" function, relating to the secretion of enzymes involved in digesting substances from outside of the body



Pancreas

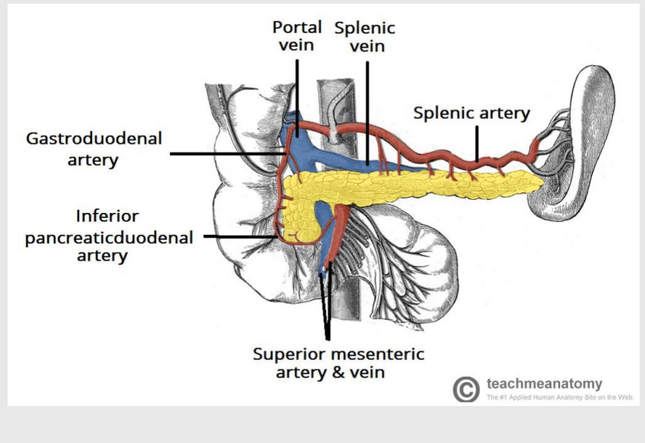
Blood glucose regulation

- Cells within the pancreas help to maintain blood sugar levels (homeostasis).
- The cells that do this are located within the pancreatic islets that are present throughout the pancreas.
- When blood glucose levels are low, alpha cells secrete glucagon, which increases blood glucose levels.
- When blood glucose levels are high beta cells secrete insulin to decrease glucose in blood.
- Delta cells in the islet also secrete somatostatin which decreases the release of insulin and glucose



Pancreas

- Insulin acts to decrease blood glucose levels by facilitating uptake by cells (particularly skeletal muscle), and promoting its use in the creation of proteins, fats and carbohydrates.
- Insulin is initially created as a precursor form called preproinsulin. This is converted to proinsulin and cleaved by C-peptide to insulin which is then stored in granules in beta cells.
- Glucose is taken into the beta cells and degraded. The end effect of this is to cause depolarisation of the cell membrane which stimulates the release of the insulin.

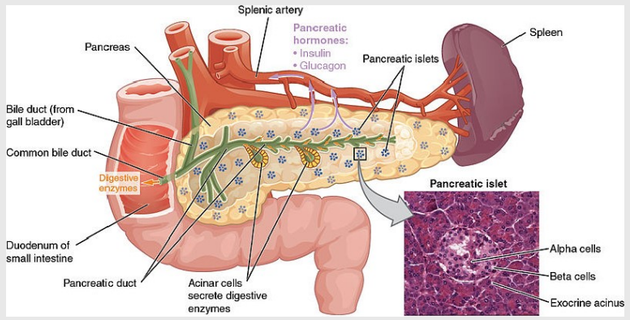


- Activity of the cells in the islets is also affected by the autonomic nervous system.
- <u>Sympathetic (adrenergic)</u>
  - α2: decreases secretion from beta cells, increases secretion from alpha cells, β2: increases secretion from beta cells
- <u>Parasympathetic (muscarinic)</u>
  - M3: increases stimulation of alpha cells and beta cells

Pancreas

Digestion

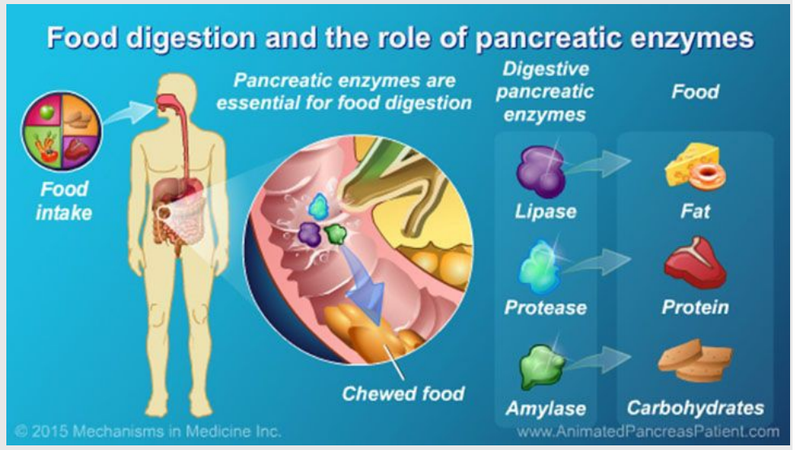
- Plays a vital role in the digestive system
- secreting a fluid that contains digestive enzymes into the duodenum
- These enzymes help to break down carbohydrates, proteins and lipids ("exocrine" pancreas)
- The cells that do this are arranged in clusters called acini.
- Secretions into the middle of the acinus accumulate in intralobular ducts, which drain to the main pancreatic duct, which drains directly into the duodenum.
- About 1.5 - 3L of fluid are secreted in this manner every day
- The cells in each acinus are filled with granules containing the digestive enzymes.
- These are secreted in an inactive form termed <u>zymogens or proenzymes.</u>
- When released into the duodenum, they are activated by the enzyme enterokinase present in the lining of the duodenum. The proenzymes are cleaved, creating a cascade of activating enzymes



Pancreas

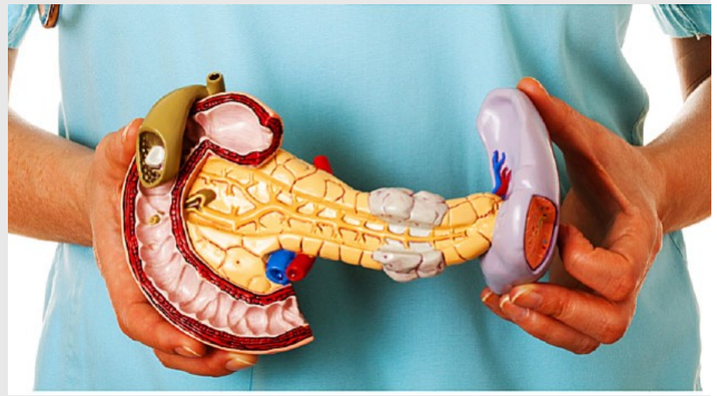
<u>Pancreatic enzymes</u>

- Enzymes that break down proteins begin with activation of trypsinogen to trypsin. The free trypsin then cleaves the rest of the trypsinogen, as well as chymotrypsinogen to its active form <u>chymotrypsin</u>.
- Enzymes secreted involved in the digestion of fats include <u>lipase, phospholipase A2, lysophospholipase, and cholesterol esterase</u>.
- Enzymes that breakdown starch and other carbohydrates include <u>amylase</u>
- These enzymes are secreted in a fluid rich in bicarbonate.
- Bicarbonate helps maintain an alkaline pH for the fluid, a pH in which most of the enzymes act most efficiently, and also helps to neutralise the stomach acids that enter the duodenum



Pancreas

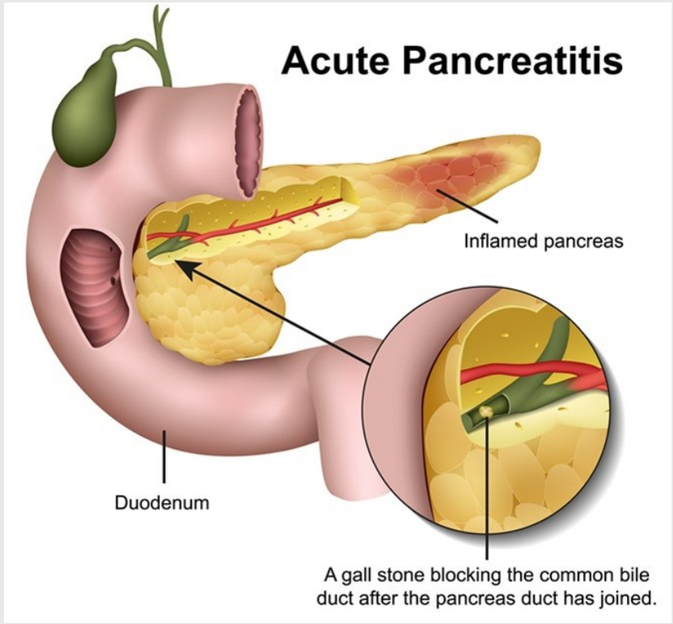
- Secretion is influenced by hormones including <u>secretin, cholecystokinin, and VIP, as well as acetylcholine stimulation</u> from the vagus nerve.
- <u>Secretin</u> is released from the S cells which form part of the lining of the duodenum in response to stimulation by gastric acid. Along with VIP, it increases the secretion of enzymes and bicarbonate.
- <u>Cholecystokinin</u> is released from Ito cells of the lining of the duodenum and jejunum mostly in response to long chain fatty acids, and increases the effects of secretin
- A <u>variety of mechanisms</u> act to ensure that the digestive action of the pancreas does not act to digest pancreatic tissue itself.
- These include the secretion of inactive enzymes (zymogens), the secretion of the protective enzyme trypsin inhibitor, which inactivates trypsin, the changes in pH that occur with bicarbonate secretion that stimulate digestion only when the pancreas is stimulated, and the fact that the low calcium within cells causes inactivation of trypsin
- The pancreas also secretes VIP and pancreatic polypeptide. Enterochromaffin cells secrete the hormones motilin, serotonin and substance P



Pancreas

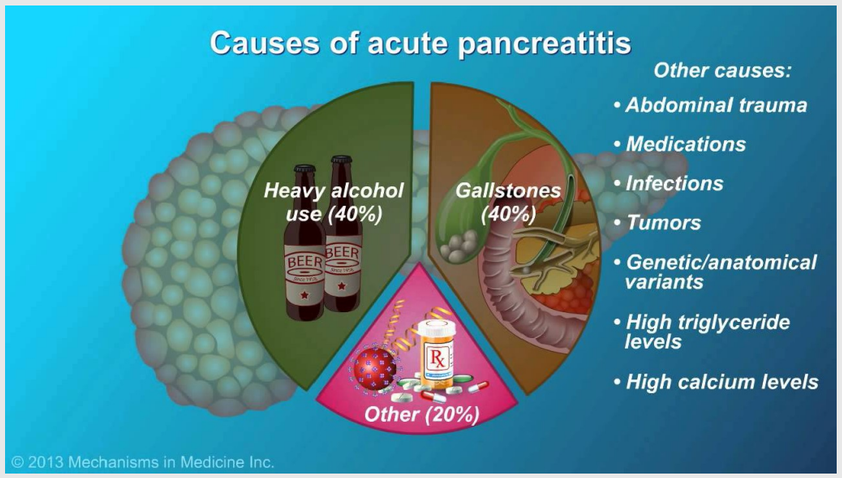
Clinical significance

- **Inflammation**
  - Inflammation of the pancreas is known as pancreatitis. Pancreatitis is most often associated with recurrent gallstones or chronic alcohol use, with other common causes including traumatic damage, damage following an ERCP, some medications, infections such as mumps and very high blood triglyceride levels
  - Acute pancreatitis is likely to cause intense pain in the central abdomen, that often radiates to the back, and may be associated with nausea or vomiting.
  - Severe pancreatitis may lead to bleeding or perforation of the pancreas resulting in shock or a systemic inflammatory response syndrome, bruising of the flanks or the region around the belly button. These severe complications are often managed in an intensive care unit.



Pancreas

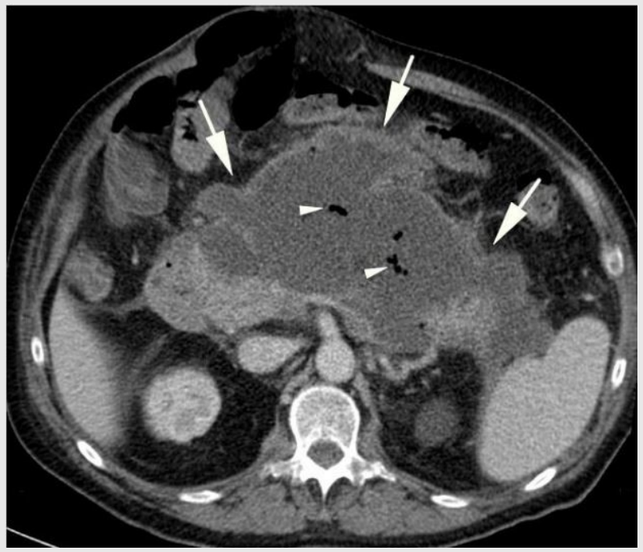
- In pancreatitis, enzymes of the exocrine pancreas damage the structure and tissue of the pancreas.
- Detection of some of these enzymes, such as amylase and lipase in the blood, along with symptoms and findings on medical imaging such as ultrasound or a CT scan, are often used to indicate that a person has pancreatitis.
- Pancreatitis is often managed medically with pain reliefs, and monitoring to prevent or manage shock, and management of any identified underlying causes.
- This may include removal of gallstones, lowering of blood triglyceride or glucose levels, the use of corticosteroids for autoimmune pancreatitis, and the cessation of any medication triggers.



Pancreas

- Chronic pancreatitis refers to the development of pancreatitis over time.
- It shares many similar causes, with the most common being chronic alcohol use, with other causes including recurrent acute episodes and cystic fibrosis.
- Abdominal pain, characteristically relieved by sitting forward or drinking alcohol, is the most common symptom.
- When the digestive function of the pancreas is severely affected, this may lead to problems with fat digestion and the development of steatorrhoea
- when the endocrine function is affected, this may lead to diabetes.
- Chronic pancreatitis is investigated in a similar way to acute pancreatitis.
- In addition to management of pain and nausea, and management of any identified causes (which may include alcohol cessation), because of the digestive role of the pancreas, enzyme replacement may be needed to prevent malabsorption

Acute pancreatitis



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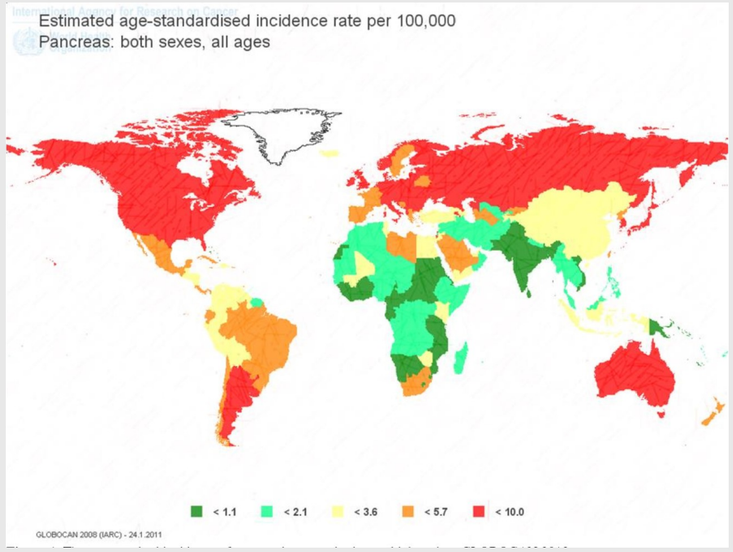
Pancreas

Cancer

- Pancreatic cancers, particularly the most common type, pancreatic adenocarcinoma, remain very difficult to treat, and are mostly diagnosed only at a stage that is too late for surgery, which is the only curative treatment.
- Pancreatic cancer is rare in those younger than 40, and the median age of diagnosis is 71
- Risk factors include chronic pancreatitis, older age, smoking, obesity, diabetes, and certain rare genetic conditions including multiple endocrine neoplasia type 1, hereditary nonpolyposis colon cancer and dysplastic nevus syndrome among others.
- About 25% of cases are attributable to tobacco smoking,while 5–10% of cases are linked to inherited genes



Pancreas

- Pancreatic adenocarcinoma is the most common form of pancreatic cancer, and is cancer arising from the exocrine digestive part of the pancreas. Most occur in the head of the pancreas.
- Symptoms tend to arise late in the course of the cancer, when it causes abdominal pain, weight loss, or jaundice
- Jaundice occurs when the outflow of bile is blocked by the cancer.
- Other less common symptoms include nausea, vomiting, pancreatitis, diabetes or recurrent venous thrombosis.
- Pancreatic cancer is usually diagnosed by medical imaging in the form of an ultrasound or CT scan with contrast enhancement.
- An endoscopic ultrasound may be used if a tumour is being considered for surgical removal, and biopsy guided by ERCP or ultrasound can be used to confirm an uncertain diagnosis.

Pancreas

- Because of the late development of symptoms, most cancer presents at an advanced stage.
- Only 10 - 15% of tumours are suitable for surgical resection.[19] As of 2018, when chemotherapy is given the FOLFIRINOX regimen containing fluorouracil, irinotecan, oxaliplatin and leucovorin has been shown to extend survival beyond traditional gemcitabine regimens.
- For the most part, treatment is palliative, focus on the management of symptoms that develop. This may include management of itch, a choledochojejunostomy or the insertion of stents with ERCP to facilitate the drainage of bile, and medications to help control pain.
- In the United States pancreatic cancer is the fourth most common cause of deaths due to cancer
- The disease occurs more often in the developed world, which had 68% of new cases in 2012.
- Pancreatic adenocarcinoma typically has poor outcomes with the average percentage alive for at least one and five years after diagnosis being 25% and 5% respectively.
- In localized disease where the cancer is small (< 2 cm) the number alive at five years is approximately 20%

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Pancreas

- There are several types of pancreatic cancer, involving both the endocrine and exocrine tissue. The many types of pancreatic endocrine tumors are all uncommon or rare, and have varied outlooks.
- The incidence of these cancers has been rising sharply; it is not clear to what extent this reflects increased detection, especially through medical imaging, of tumors that would be very slow to develop.
- Insulinomas (largely benign) and gastrinomas are the most common types.
- For those with neuroendocrine cancers the number alive after five years is much better at 65%, varying considerably with type
- A solid pseudopapillary tumour is a low-grade malignant tumour of the pancreas of papillary architecture that typically afflicts young women

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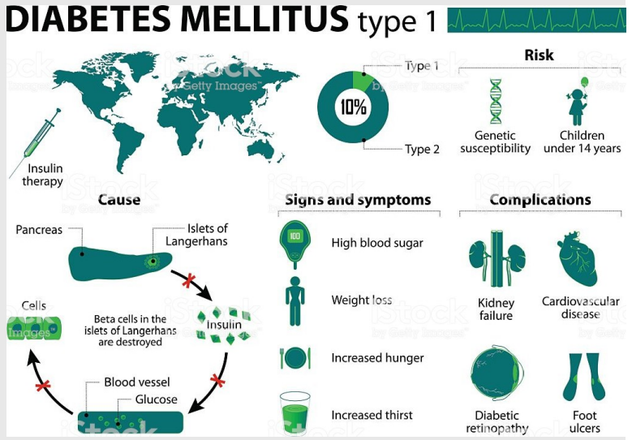
Pancreas

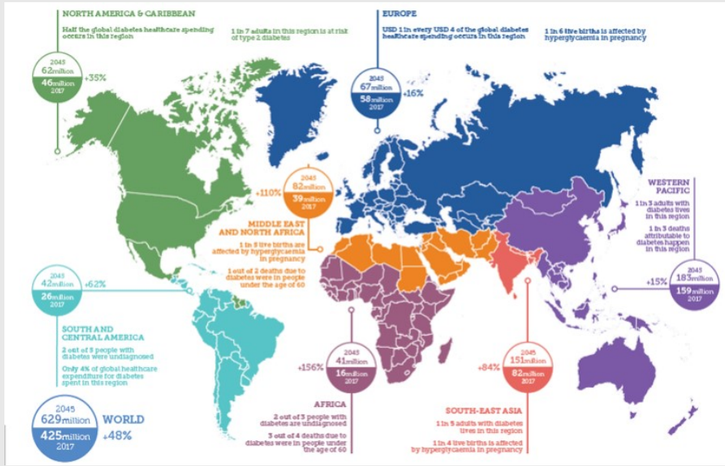
Diabetes mellitus

- Type 1 diabetes
  - a chronic autoimmune disorder in which the immune system attacks the insulin-secreting cells of the pancreas.
  - Insulin is needed to keep blood sugar levels within optimal ranges, and its lack can lead to high blood sugar. As an untreated chronic condition, diabetic neuropathy can result.
  - In addition, if there is not enough insulin for glucose to be used within cells, the medical emergency diabetic ketoacidosis, which is often the first symptom that a person with type 1 diabetes may have, can result.
  - Type 1 diabetes can develop at any age but is most often diagnosed before adulthood For people living with type 1 diabetes, insulin injections are critical for survival.
  - An experimental procedure to treat type 1 diabetes is the transplantation of pancreatic islet cells from a donor into the patient's liver so that the cells can produce the deficient insulin



Pancreas

- **<u>Type 2 diabetes</u>**
  - Diabetes mellitus type 2 is the most common form of diabetes.
  - The causes for high blood sugar in this form of diabetes usually are a combination of insulin resistance and impaired insulin secretion, with both genetic and environmental factors playing an important role in the development of the disease.
  - The management of type 2 diabetes relies on a series of changes in diet and physical activity with the purpose of reducing blood sugar levels to normal ranges and increasing insulin sensitivity.
  - Biguanides such as metformin are also used as part of the treatment along with insulin therapy.

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