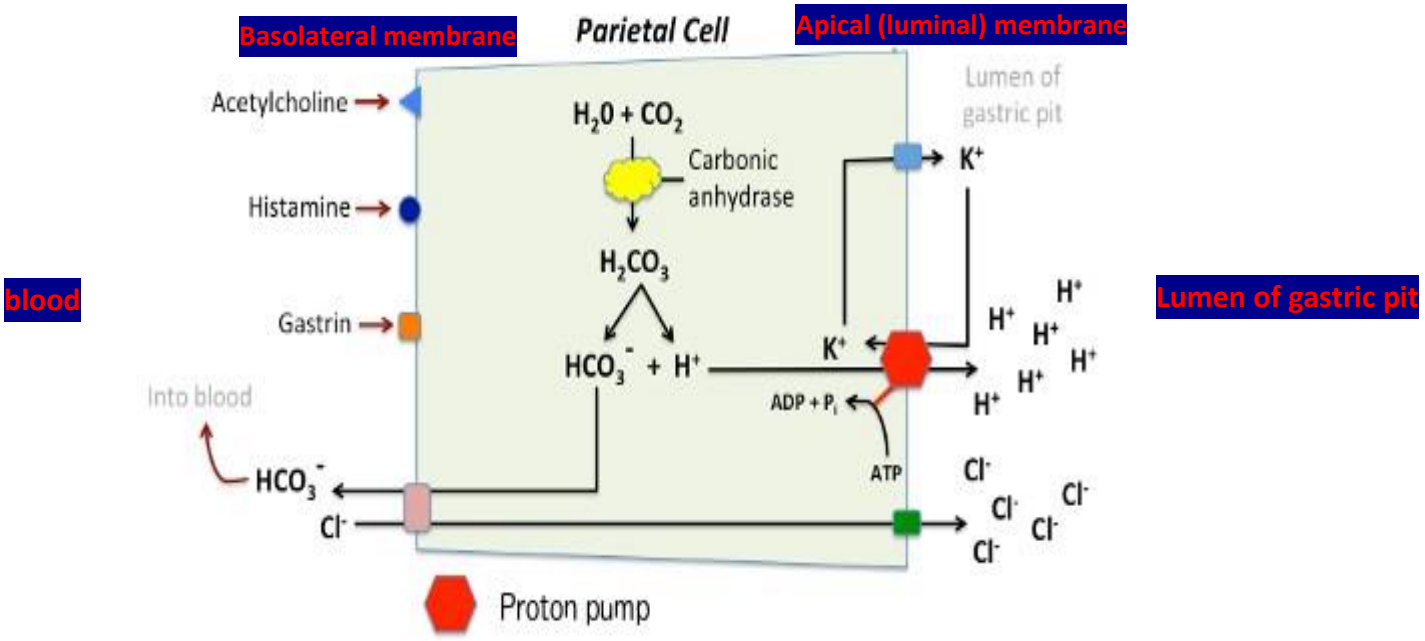
Cont. # Gastric secretion

-Gastric acid secretion:



CO2 has two sources: metabolism reactions in the parietal cell, and from the blood. CO2 reacts with water (H2O) to form carbonic acid (H2CO3), this reaction is stimulated by carbonic anhydrase enzyme. Carbonic acid (H2CO3) is dissociated to a proton (H+) and bicarbonate (HCO3-). Bicarbonate (HCO3-) is transported (outflow) at the basolateral membrane in exchange for chloride (Cl-). Outflow (efflux) of bicarbonate (HCO3-) into blood makes it slightly alkaline.

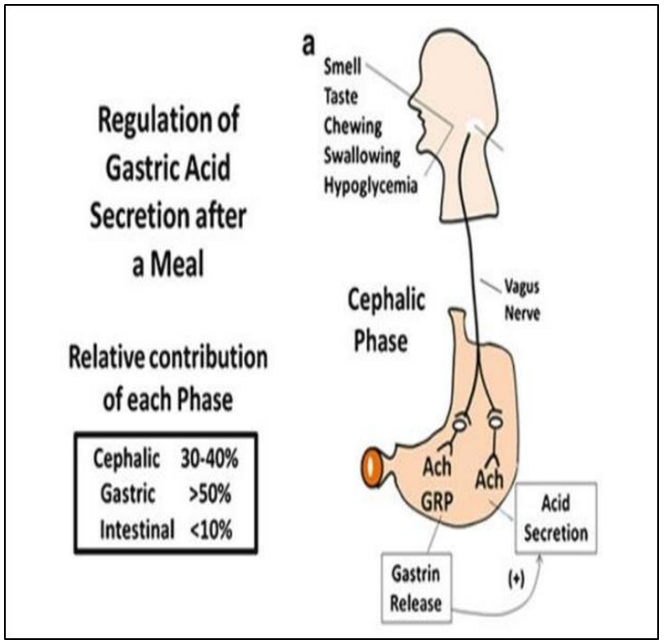
Chloride and potassium ions (Cl-,K+) are transported at the apical membrane into lumen of gastric pit, cuniculus (canicular membrane) specifically. Protons (H+) are transported (outflow) at the apical membrane in exchange for (K+) ions, through proton pump (H-K pump), this is an active transportation with energy consumption. K+ ions that enter the cell through the pump are recycled back into the lumen; this is very important for hydrogen efflux, because the pump cannot work unless there are K+ ions outside of the cell (in lumen).

Accumulation of chloride, hydrogen and potassium ions in the lumen creates an osmotic environment, this contributes to water and Na diffusion from the cell to the lumen. These ions in the lumen react to form gastric juices (acids), such as: HCl, KCl and little amount of NaCl.

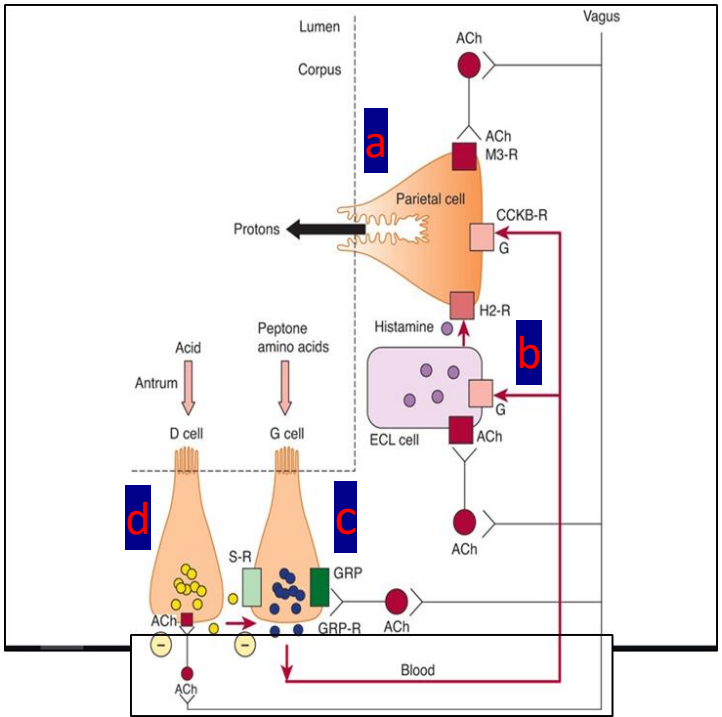
-Regulation of gastric acid secretion (mechanism):

Gastric acid secretion mostly occurs during feeding (eating). Between meals, gastric secretion is usually fluid and mucous, but gastric acid secretin is very low.

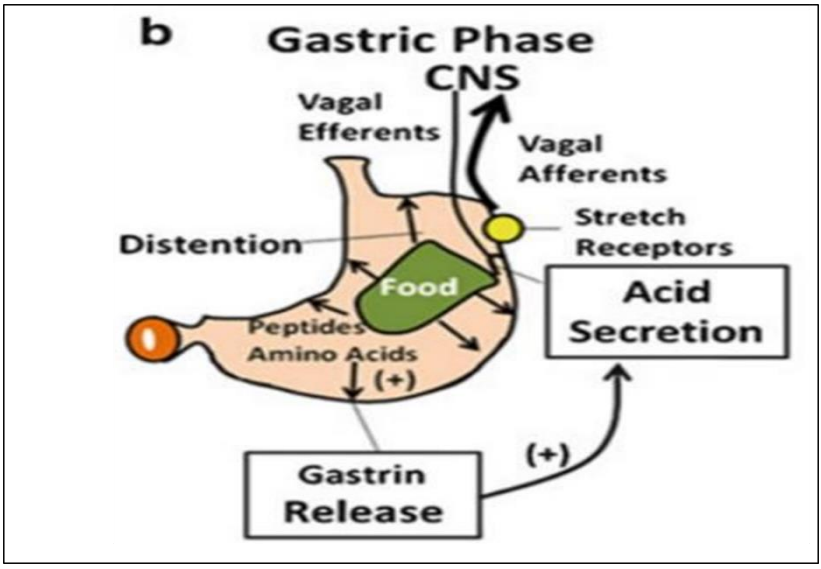
Gastric acid secretion occurs in three phases:



1)Cephalic phase: responsible for 30-40% of gastric acid secretion. Cephalic phase is stimulated by higher brain centers even before food entrance to the stomach. Stimuli of this phase include: appetite, smell and taste of food, etc. When higher brain centers are stimulated, they send signal through the vagus nerve to the stomach → Ach release →
a)directly increase acid secretion,
b)stimulates ECL cells to secrete histamine,
c)stimulate G cells to secrete gastrin,
d)inhibit D cells secretion of somatostatin.



2)Gastric phase: responsible for >50% of gastric acid secretion. This phase is stimulated by:



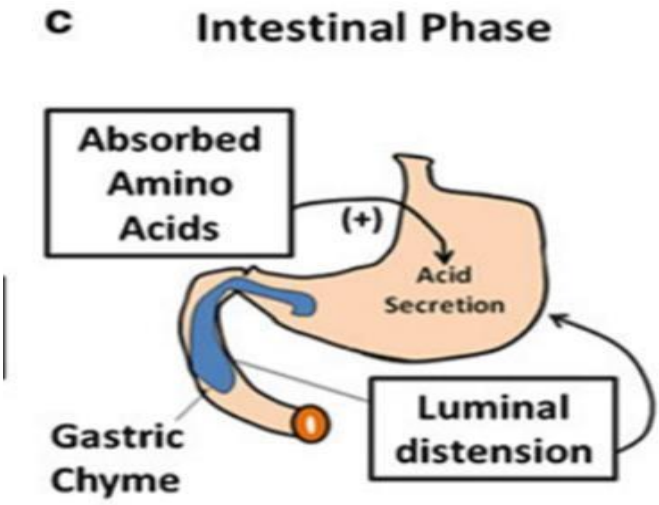
a) distention of gastric wall (by food), which leads to:

i) A vagovagal reflex (vagal afferent and efferent neurons): distention activates stretch receptors, which send a signal to CNS through afferent vagal neurons, and then CNS carry out a response and sends a signal to stomach through efferent vagal neurons → release of Ach → stimulates parietal cells to secrete gastric acid. This neural mechanism is predominant, especially in minimal distention.

ii) stimulation of G cells → gastrin release. (this is a local intrinsic mechanism).

b) peptides and amino acids in stomach: they stimulate G cells to secrete gastrin, directly or through stimulation of the enteric nervous system (submucosal plexus).

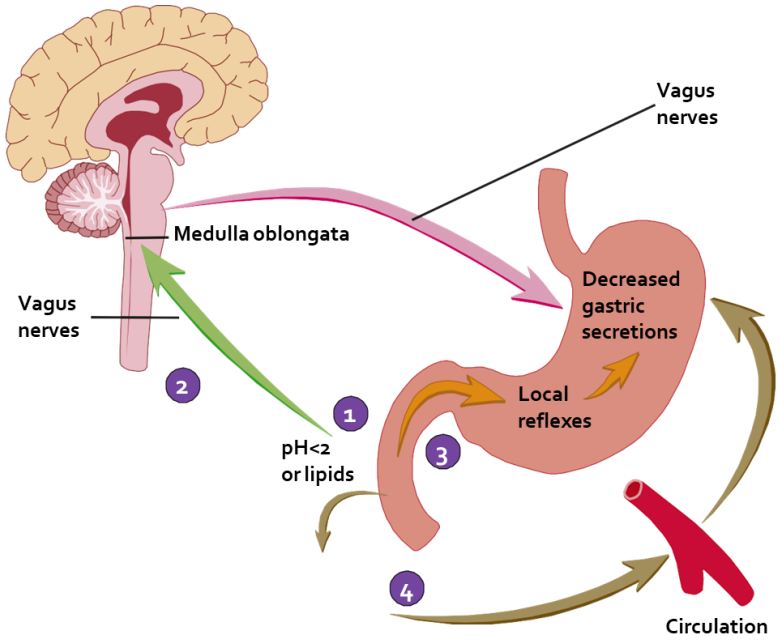
3)Intestinal phase: responsible for <10% of gastric acid secretion. This phase is stimulated by the presence of food (chyme) in the duodenum → stimulation of intestinal G cells to secrete gastrin. This phase is not significant to gastric acid secretion, in fact it is a regulatory phase, because chyme (in intestine) initiates a reverse entero-gastric reflex which inhibits gastric motility and secretion, to give intestinal content adequate time for efficient digestion and absorption.



-Mechanisms of inhibition of gastric secretion:

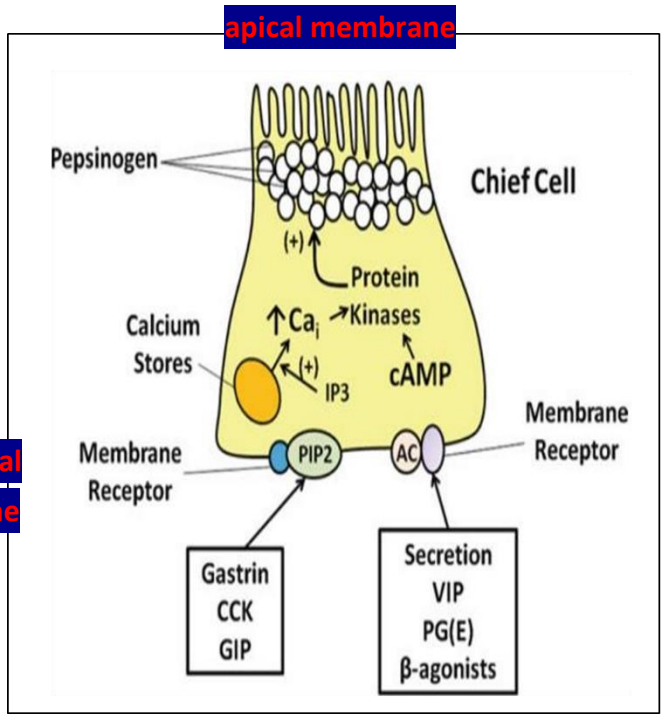
1)neural mechanism:

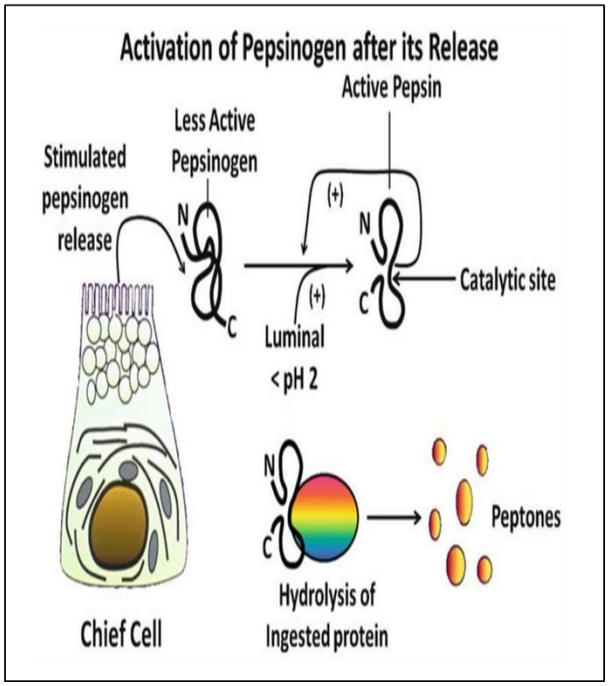
Chyme in intestine initiates a reverse entero-gastric reflex which inhibits gastric motility through myenteric plexus, and gastric secretion through submucosal plexus. Reverse entero-gastric reflex can be intrinsic (local) → independent of external stimulation, or extrinsic (sympathetic or parasympathetic stimulation). Stimuli of this reflex include: distention (by chyme), acids, food like lipid, etc.



2)Hormonal mechanism: chyme in intestine stimulates the release of enterogastrone hormones (we talked about them before in gastric emptying), such as: Secretin, GIP, VIP and CCK. Enterogastrones inhibit gastric motility and secretion.

-Pepsinogen secretion:





Multiple agents (shown in figure above) are responsible for activating signaling pathways (cAMP or IP3 and Ca) in chief cells → fusion and exocytosis of pepsinogen → secretion of pepsinogen (inactive form).

Pepsinogen is then activated by two mechanisms:

1)by acids (HCl) in the lumen to form pepsin (active form).

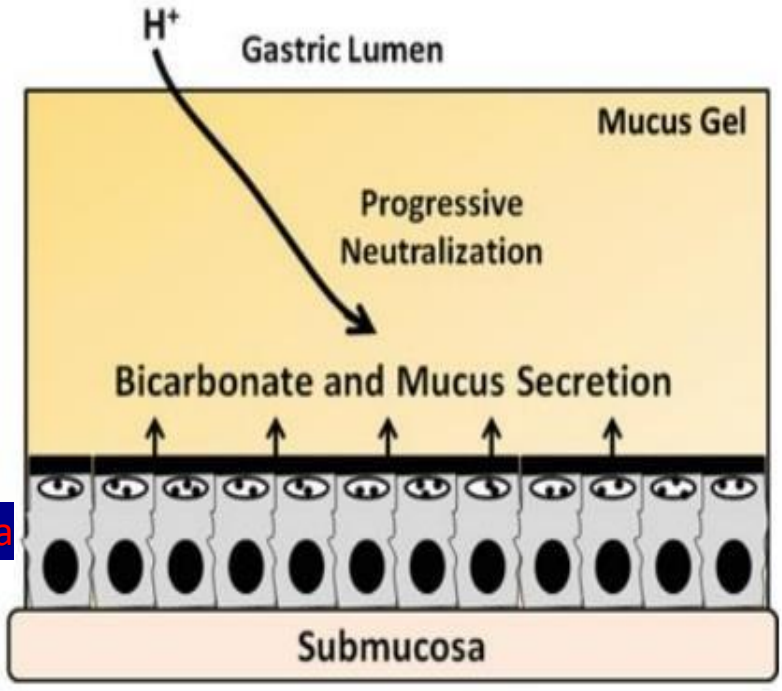
2)Pepsin has a positive feedback; pepsin stimulates pepsinogen activation to make more pepsin.

-pepsinogen is not exclusively secreted by chief cells; mucous cells secret it too.

-HCl is not the only agent that causes gastric and duodenal ulceration, pepsin is an important agent too.

-pepsin has an important role in digesting proteins, especially collagen; which is present in animal proteins. Proteins are partially digested by pepsin; pepsin converts proteins to smaller polypeptides called "peptones" (not amino acids).

-Mucous secretion:



Mucous surface cells secrete insoluble mucous → forming a layer between lumen and gastric mucosa called 'mucous gel', this layer is alkaline due to secretion of bicarbonate (HCO_3^-) by mucous cells. So, gastric mucosa is not directly exposed to the acidic environment of the lumen.

Neck mucous cells secrete soluble mucous.

Insoluble mucous→ protection

Soluble mucous→ lubrication

Other protective mechanisms of gastric mucosa include: tight junctions between the cells.

- Factors that affect mucus secretion:

Cholinergic stimulation (neural).

Serotonin.

Prostaglandins A & F.

-Factors that affect Bicarbonate Secretion:

Cl^-/HCO_3^- channel (exchange of chloride and bicarbonate ions).

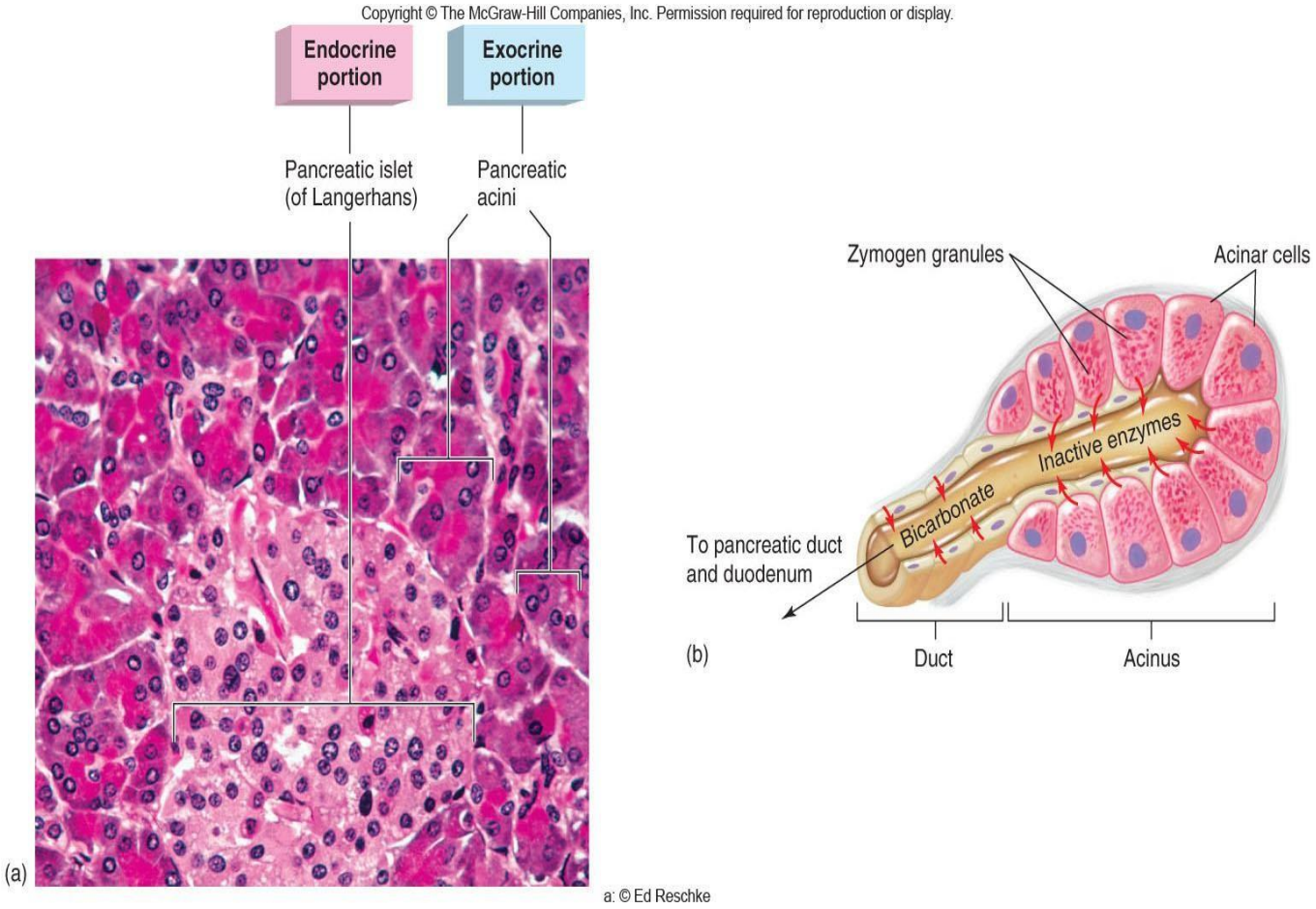
Vagal nerve.

Prostaglandins E.

-note: excessive use of NSAIDs (aspirin, ibuprofen,…) can lead to ulceration, by blocking the Cox-1 enzyme and disrupting the production of prostaglandins in the stomach → disrupted mucous and bicarbonate secretion in the stomach.

-Pancreatic secretion:

Pancreas is an associated (accessory) gland in the digestive system. Pancreas consists of two types of tissues: exocrine portion (90%) and endocrine portion (10%).



Acinar cells secrete digestive enzymes, and the cells of the ducts secrete fluids such as bicarbonate.

The pancreatic exocrine portion is similar to salivary glands; it consists of acini and ducts that transport pancreatic secretion to the duodenum.

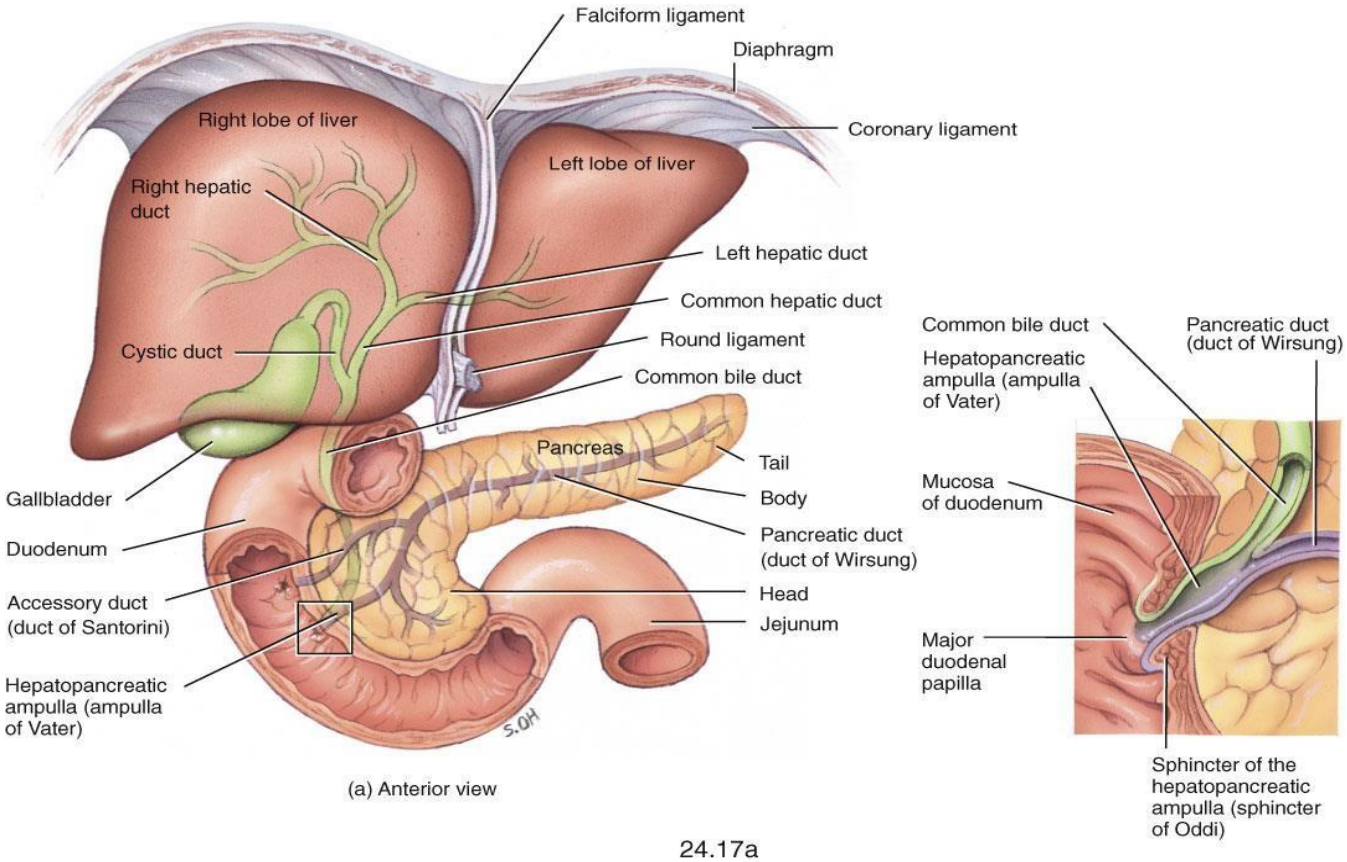
There are two ducts that emerge out of the pancreas:

1)the main duct (wirsung duct). (major duct)

This duct is joined by the common bile duct to form the ampulla of Vater (hepato-pancreatic ampulla) → If there are gallstones in bile duct → the ampulla is blocked → accumulation of pancreatic secretions in the pancreas → pancreatitis, or pancreatic insufficiency.

The ampulla of vater is guarded by the sphincter of Oddi, this sphincter regulates both pancreatic secretions and bile, this sphincter also prevents the reflux of acidic duodenal fluids → prevent damage of pancreas and gallbladder.

2)the accessory duct (Santorini duct).



(a) Anterior view

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