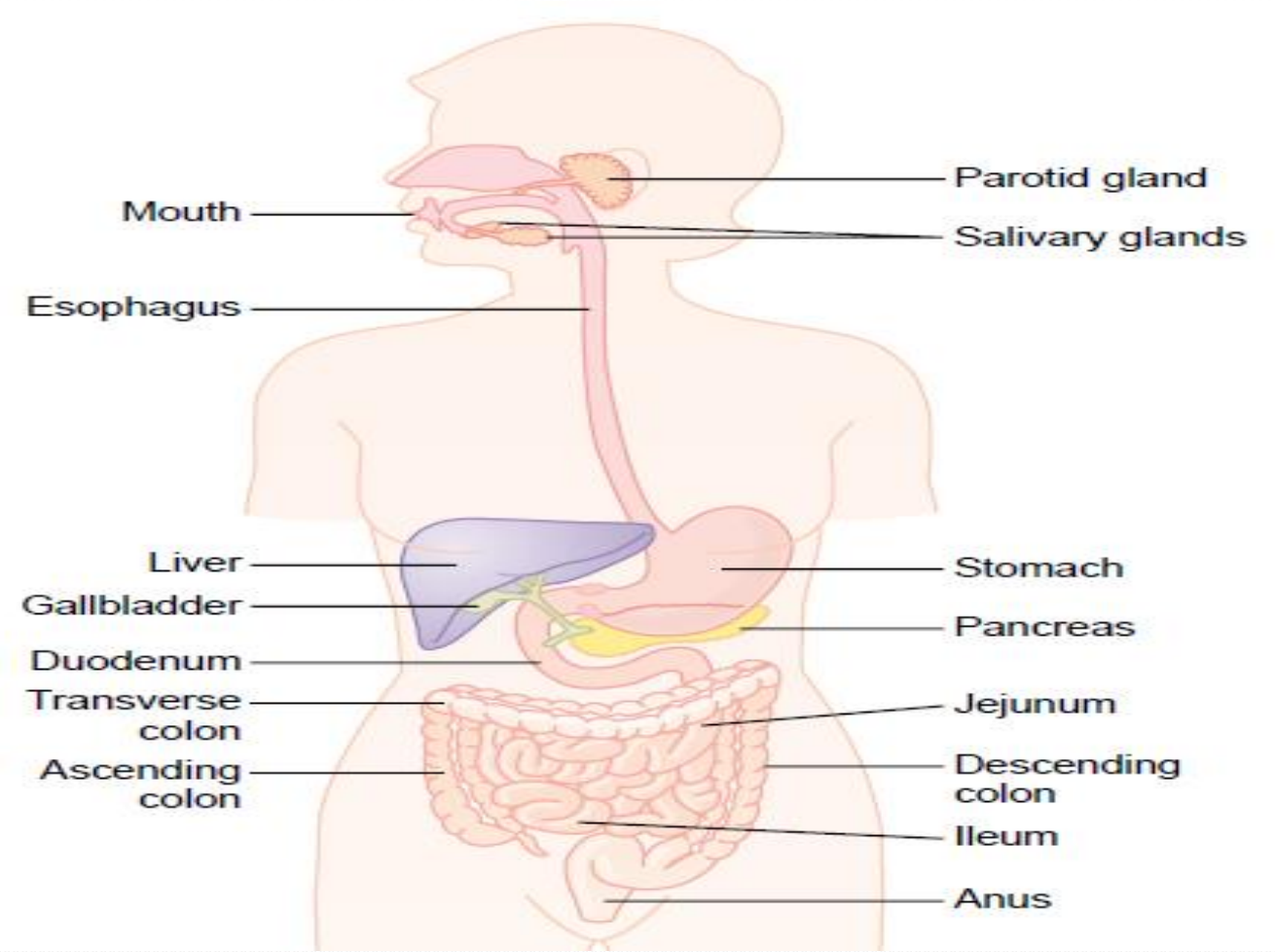
Digestive fluids

Reference Books:

- **Text Book of Medical physiology** (Guyton and Hall) Eleventh edition

- **Fundamentals of Clinical Chemistry** (Tietz) Sixth

Alimentary tract



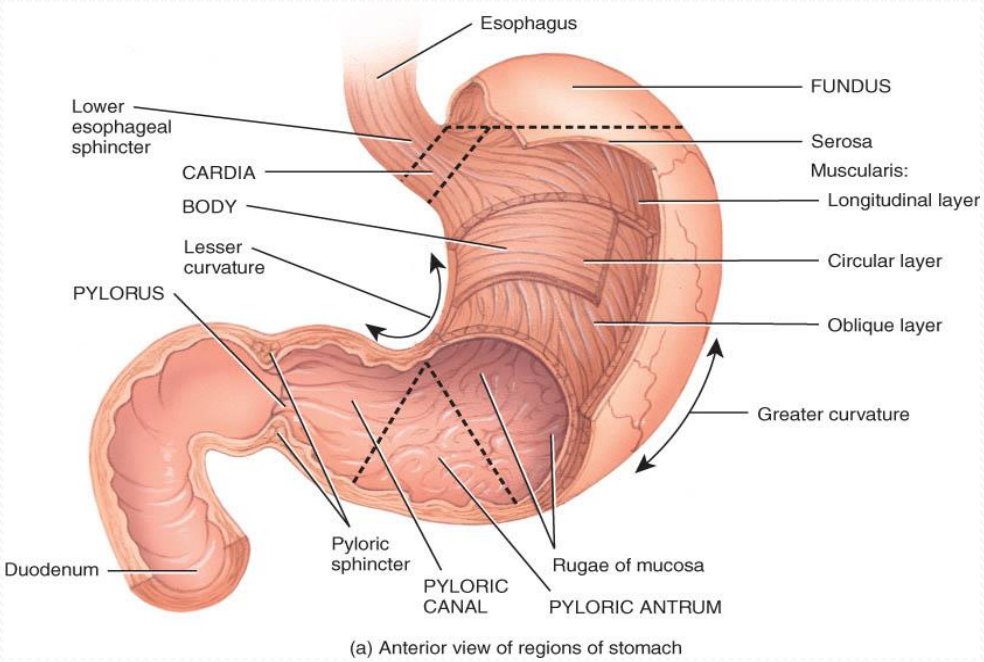
- **Gastric Secretion**
- **Characteristics of the Gastric Secretions**

Mucus-secreting cells that line the entire surface of the stomach.

The stomach mucosa has two important types of tubular glands:

Oxyntic glands. *(also* called *gastric glands)* (acid-forming) glands secrete *hydrochloric acid, pepsinogen, intrinsic factor, and mucus*. The glands are located on the inside surfaces of the body and fundus of the stomach, constituting the proximal 80 per cent of the stomach.

- ***Pyloric glands.*** secrete mainly *mucus* for protection of the pyloric mucosa from the stomach acid. They also secrete the hormone *gastrin*. The glands are located in the antral portion of the stomach, the distal 20 per cent of the stomach.



(a) Anterior view of regions of stomach

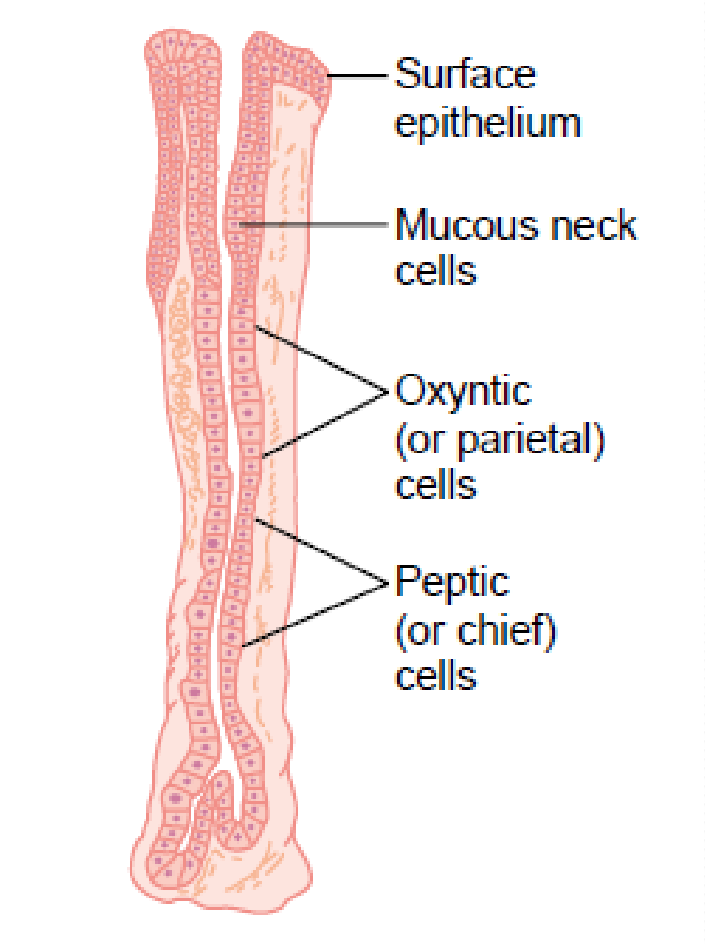
Secretions from the Oxyntic (Gastric) Glands

- A typical stomach oxyntic gland is composed of three types of cells:

(1) mucous neck cells, which secrete mainly mucus.

(2) peptic (or chief) cells, which secrete large quantities of pepsinogen.

(3) parietal (or oxyntic) cells, which secrete hydrochloric acid and intrinsic factor.



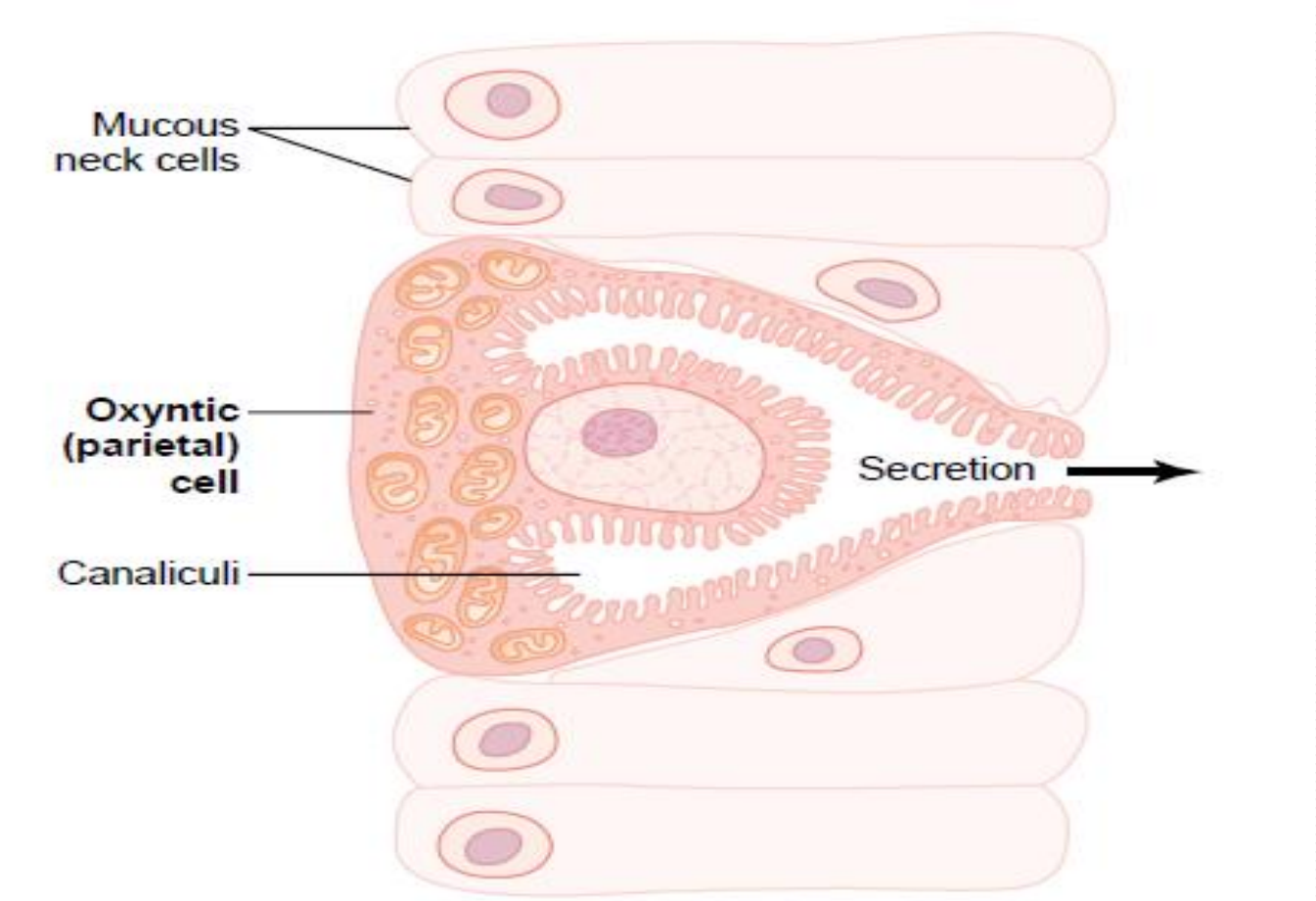
Oxyntic gland from the body of the stomach.

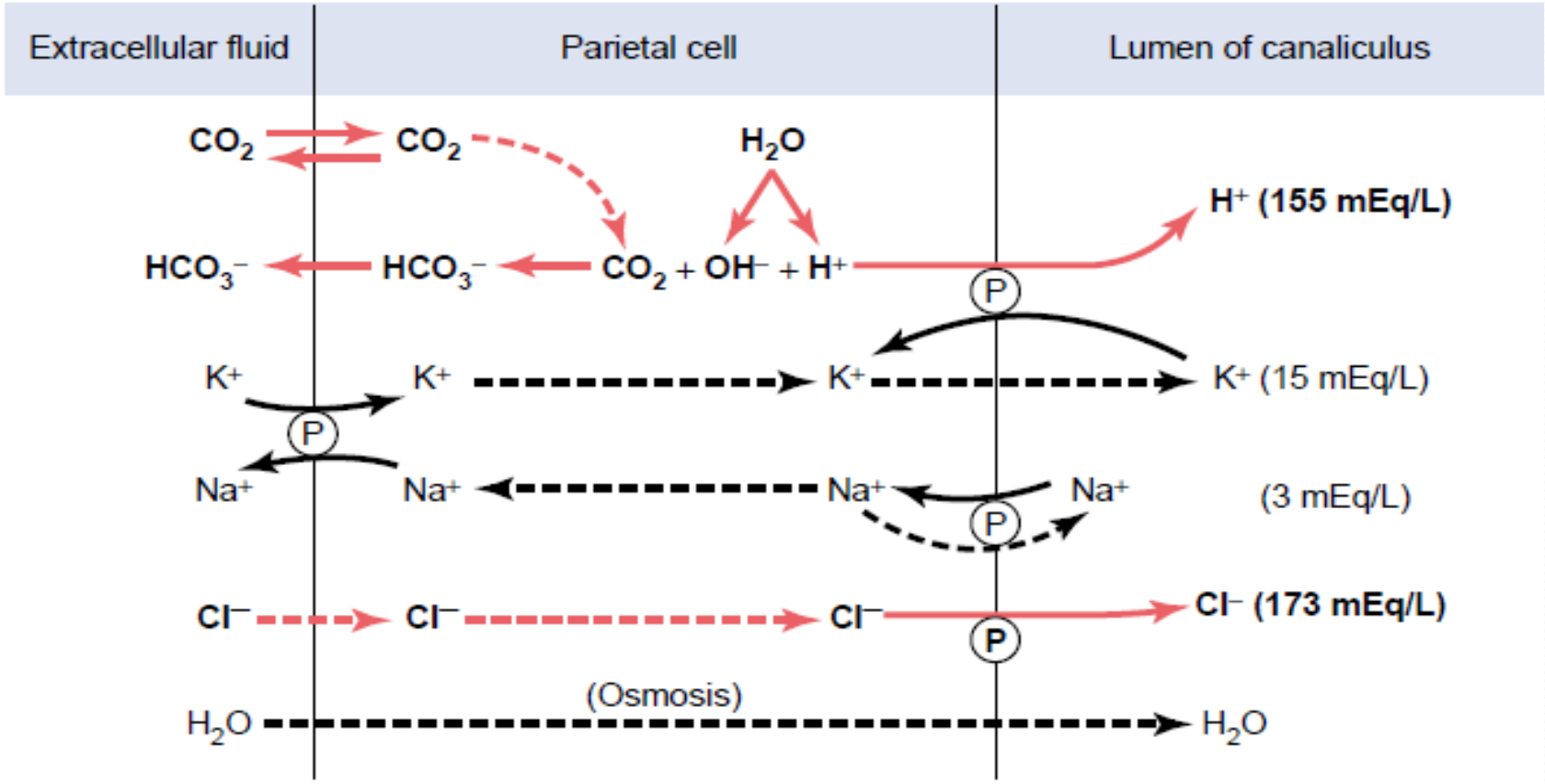
Basic Mechanism of Hydrochloric Acid Secretion.

- When stimulated, the parietal cells secrete an acid solution that contains about 160 millimoles of hydrochloric acid per liter.

- The pH of this acid is about 0.8. At this pH, the hydrogen ion concentration is about 3 million times that of the arterial blood.

Schematic anatomy of the canaliculi in a parietal (oxyntic) cell.





Postulated mechanism for secretion of hydrochloric acid. (The points labeled "P" indicate active pumps, and the dashed lines represent free diffusion and osmosis.)

1. Chloride ion is actively transported from the cytoplasm of the parietal cell into the lumen of the canaliculus, and sodium ions are actively transported out of the canaliculus into the cytoplasm of the parietal cell. These two effects together create a negative potential of -40 to -70 millivolts in the canaliculus, which in turn causes diffusion of positively charged potassium ions and a small number of sodium ions from the cell cytoplasm into the canaliculus. Thus, in effect, mainly potassium chloride and much smaller amounts of sodium chloride enter the canaliculus.

2. Water becomes dissociated into *hydrogen ions* and *hydroxyl ions* in the cell cytoplasm. The hydrogen ions are then actively secreted into the canaliculus in exchange for potassium ions: catalyzed by H^+,K^+- ATPase. The sodium ions are actively reabsorbed by a separate sodium pump. Thus, most of the potassium and sodium ions that had diffused into the canaliculus are reabsorbed into the cell cytoplasm, and hydrogen ions take their place in the canaliculus, giving a strong solution of hydrochloric acid in the canaliculus. The hydrochloric acid is then secreted outward through the open end of the canaliculus into the lumen of the gland.

3. Water passes into the canaliculus by osmosis because of extra ions secreted into the canaliculus. Thus, **the final secretion from the canaliculus contains water, hydrochloric acid at a concentration of about 150 to 160 mEq/L, potassium chloride at a concentration of 15 mEq/L, and a small amount of sodium chloride.**

4. Finally, carbon dioxide, either formed during metabolism in the cell or entering the cell from the blood, combines under the influence of carbonic anhydrase with the hydroxyl ions (from step 2) to form bicarbonate ions. These then diffuse out of the cell cytoplasm into the extracellular fluid in exchange for chloride ions that enter the cell from the extracellular fluid and are later secreted into the canaliculus.

Secretion and Activation of Pepsinogen.

- Different types of pepsinogen are secreted by the peptic and mucous cells of the gastric glands.
- Pepsinogen has no digestive activity. However, as soon as it comes in contact with hydrochloric acid, it is activated to form active pepsin. (pepsinogen molecular weight of about 42,500 split to form a pepsin molecular weight of about 35,000). Pepsin act as active proteolytic enzyme in a highly acid medium (pH 1.8 to 3.5), but above a pH of about 5 it has almost no proteolytic activity and becomes completely inactivated in a short time.

Secretion of Intrinsic Factor.

The intrinsic factor, essential for absorption of vitamin B12 in the ileum, is secreted by the parietal cells along with the secretion of hydrochloric acid. When the acid-producing parietal cells of the stomach are destroyed, which frequently occurs in chronic gastritis, the person develops not only a chlorhydria (lack of stomach acid secretion) but often also pernicious anemia because of failure of maturation of the red blood cells in the absence of vitamin B12 stimulation of the bone marrow.

Pyloric Glands: Secretion of Mucus and Gastrin

The pyloric glands are structurally similar to the oxyntic glands but contain few peptic cells and almost no parietal cells. Instead, they contain mostly mucous cells that are identical with the mucous neck cells of the oxyntic glands. These cells secrete a small amount of pepsinogen, and an especially large amount of thin mucus that helps to lubricate food movement, as well as to protect the stomach wall from digestion by the gastric enzymes. The pyloric glands also secrete the hormone **gastrin**, which plays a key role in controlling gastric secretion.

Surface Mucous Cells

- The entire surface of the stomach mucosa between glands has a continuous layer of a special type of mucous cells called simply "**surface mucous cells**." They secrete large quantities of a very viscid mucus that coats the stomach mucosa with a gel layer of mucus often more than 1 millimeter thick, thus providing a major shell of protection for the stomach wall as well as contributing to lubrication of food transport.
- Another characteristic of this mucus is that it is alkaline. Therefore, the normal underlying stomach wall is not directly exposed to the highly acidic, proteolytic stomach secretion. Even the slightest contact with food or any irritation of the mucosa directly stimulates the surface mucous cells to secrete additional quantities of this thick, alkaline, viscid mucus.

Stimulation of Gastric Acid Secretion

- The parietal cells secrete hydrochloric acid. the parietal cells operate in close association with another type of cell called **enterochromaffin- like cells** (ECL cells), the primary function of which is to secrete **histamine.**
- Gastrin is itself a hormone secreted by gastrin cells, also called G cells. These cells are located in the pyloric glands in the distal end of the stomach. Gastrin is a large polypeptide secreted in two forms: a large form called G-34, which contains 34 amino acids, and a smaller form, G-17, which contains 17 amino acids. Although both of these are important, the smaller is more abundant.

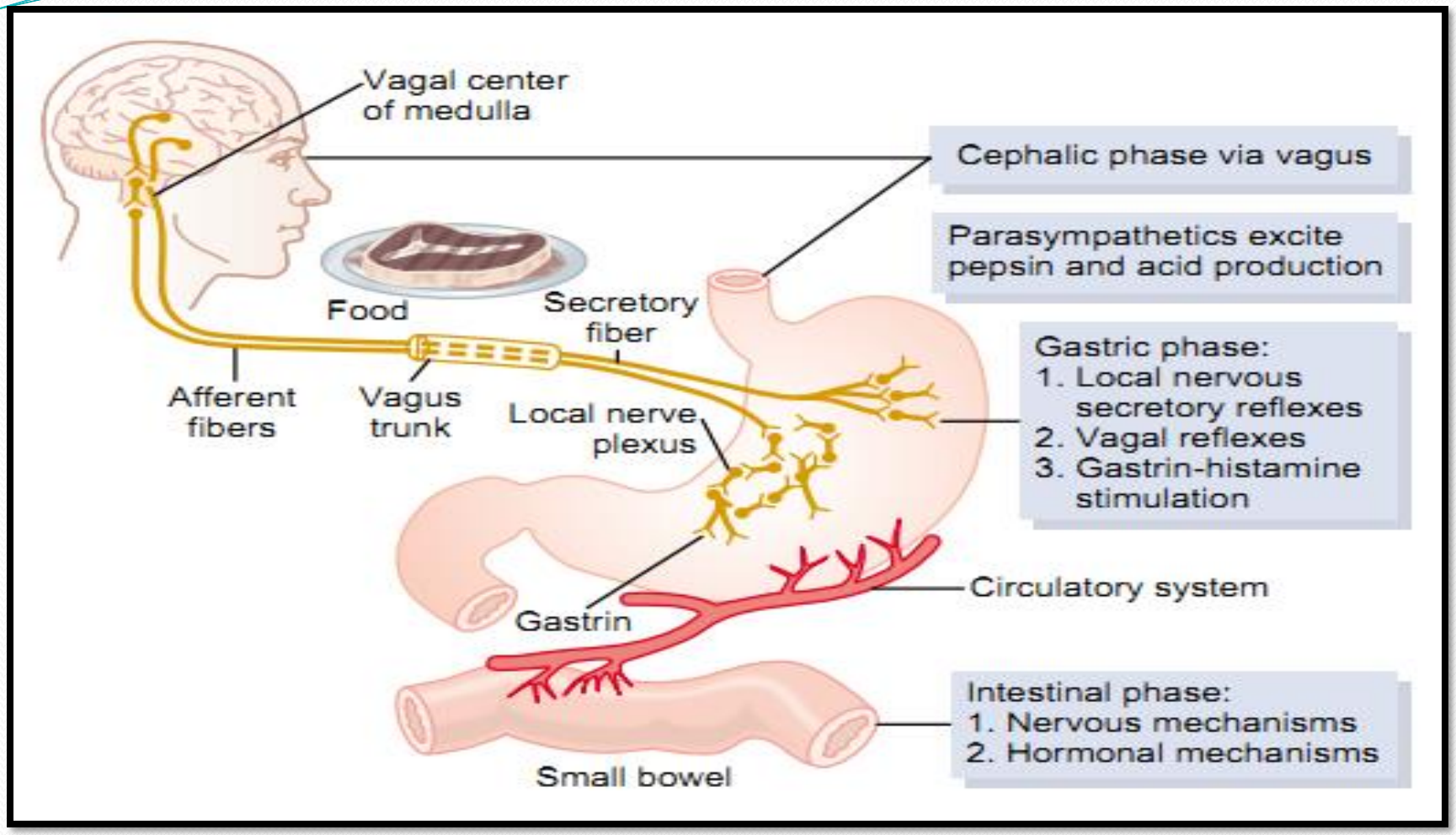
When meats or other protein-containing foods reach the antral end of the stomach, some of the proteins from these foods have a special stimulatory effect on the gastrin cells in the pyloric glands to cause release of gastrin into the digestive juices of the stomach. The vigorous mixing of the gastric juices transports the gastrin rapidly to the ECL cells in the body of the stomach, causing release of **histamine** directly into the **deep oxyntic glands.** The histamine then acts quickly to stimulate gastric hydrochloric acid secretion.

Regulation of Pepsinogen Secretion

pepsinogen secreted by the peptic cells in the oxyntic glands occurs in response to two types of signals:

(1) stimulation of the peptic cells by acetylcholine released from the vagus nerves or from the gastric enteric nervous plexus, and (2) stimulation of peptic cell secretion in response to acid in the stomach. The acid probably does not stimulate the peptic cells directly but instead elicits additional enteric nervous reflexes that support the original nervous signals to the peptic cells. Therefore, the rate of secretion of pepsinogen.

the precursor of the enzyme pepsin that causes protein digestion, is strongly influenced by the amount of acid in the stomach. In people who have lost the ability to secrete normal amounts of acid, secretion of pepsinogen is also decreased, even though the peptic cells may otherwise appear to be normal



Phases of gastric secretion and their regulation

Phases of Gastric Secretion

- Gastric secretion occur in three phases: cephalic phase, gastric phase, and an intestinal phase.

Cephalic Phase.

The cephalic phase of gastric secretion occurs even before food enters the stomach, especially while it is being eaten. It results from the sight, smell, thought, or taste of food, and the greater the appetite, the more intense is the stimulation. Neurogenic signals that cause the cephalic phase of gastric secretion originate in the cerebral cortex and in the appetite centers of the amygdala and hypothalamus.

They are transmitted through the dorsal motor nuclei of the vagi and hence through the vagus nerves to the stomach. This phase of secretion normally accounts for about 20 per cent of the gastric secretion associated with eating a meal.

Gastric Phase.

Once food enters the stomach, it excites (1) long vagovagal reflexes from the stomach to the brain and back to the stomach, (2) local enteric reflexes, and (3) the gastrin mechanism, all of which in turn cause secretion of gastric juice during several hours while food remains in the stomach.

The gastric phase of secretion accounts for about 70 per cent of the total gastric secretion associated with eating a meal and therefore accounts for most of the total daily gastric secretion of about 1500 milliliters.

Intestinal Phase.

The presence of food in the upper portion of the small intestine, particularly in the duodenum, will continue to cause stomach secretion of small amounts of gastric juice, probably partly because of small amounts of gastrin released by the duodenal mucosa.

Inhibition of Gastric Secretion by Other Post Stomach Intestinal Factors

Intestinal chyme inhibits gastric secretion This inhibition results from at least two influences.

1. The presence of food in the small intestine initiates a reverse enterogastric reflex, transmitted through the myenteric nervous system as well as through extrinsic sympathetic and vagus nerves, that inhibits stomach secretion. This reflex can be initiated by distending the small bowel, by the presence of acid in the upper intestine, by the presence of protein breakdown products, or by irritation of the mucosa.

2. The presence of acid, fat, protein breakdown products, hyperosmotic or hypo-osmotic fluids, or any irritating factor in the upper small intestine causes release of several intestinal hormones. One of these is **secretin**, which is especially important for control of pancreatic secretion. However, secretin opposes stomach secretion. Three other hormones—gastric inhibitory peptide, vasoactive intestinal polypeptide, and somatostatin—also have slight to moderate effects in inhibiting gastric secretion.

Disorders of the Stomach

- **Gastritis—Inflammation of the Gastric Mucosa.**
- **Gastric Atrophy.**
- **Achlorhydria (and Hypochlorhydria).**
- **Pernicious Anemia in Gastric Atrophy.**
- **Peptic Ulcer**

Peptic Ulcer.

Basic Cause of Peptic Ulceration.

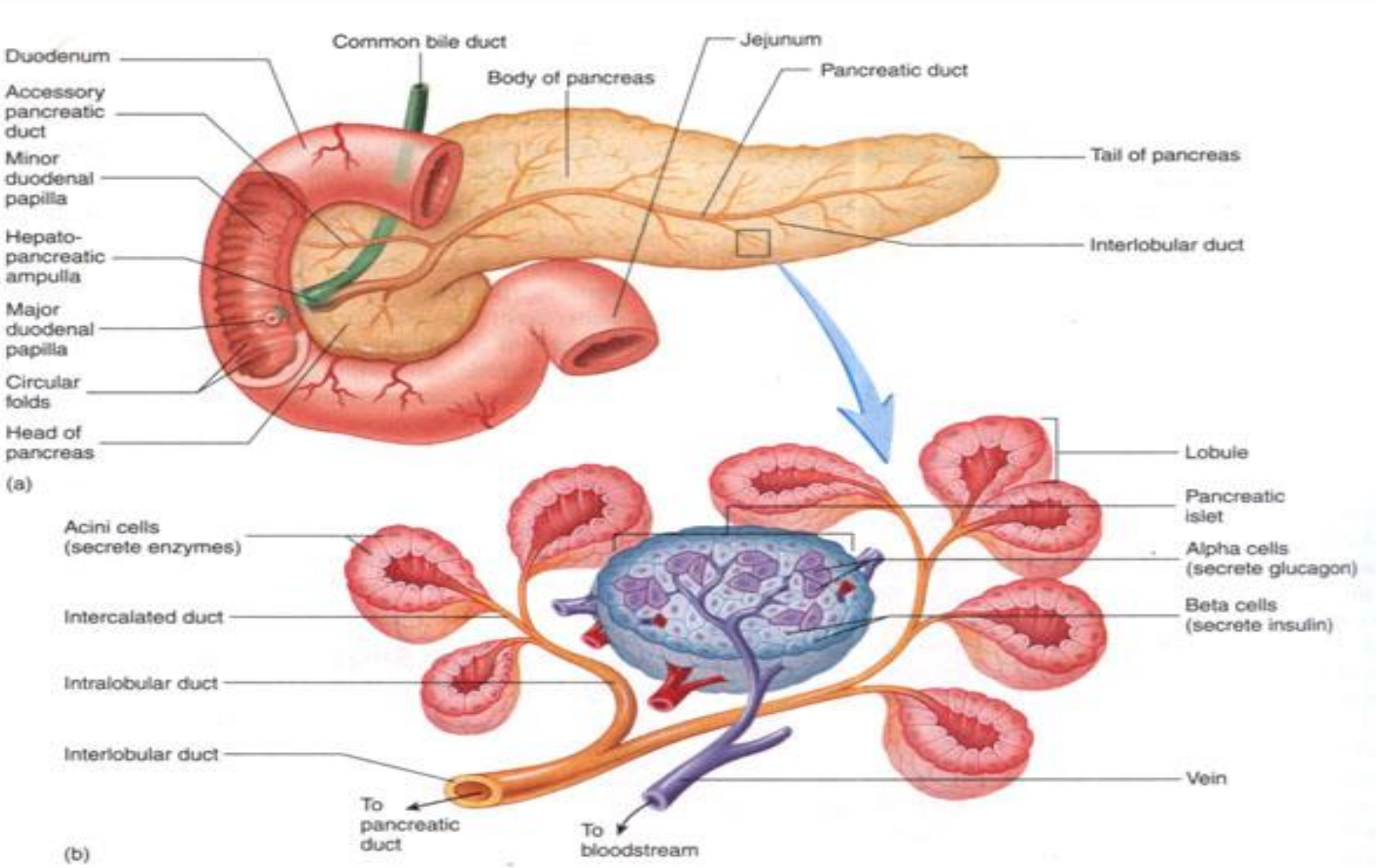
1. High acid and peptic content
2. Irritation
3. Poor blood supply
4. Poor secretion of mucus
5. Infection, H. pylori

Other factors that predispose to ulcers include (1) smoking, presumably because of increased nervous stimulation of the stomach secretory glands; (2) alcohol, because it tends to break down the mucosal barrier; and (3) aspirin and other non-steroidal anti-inflammatory drugs that also have a strong propensity for breaking down this barrier.

Pancreatic Secretion

Pancreatic juice is secreted most abundantly in response to the presence of chyme in the upper portions of the small intestine, and the characteristics of the pancreatic juice are determined to some extent by the types of food in the chyme. (The pancreas also secretes insulin directly into the blood not into the intestine by the islets of Langerhans that occur in islet patches throughout the pancreas.

Pancreas:


Duodenum
Common bile duct
Jejunum
Body of pancreas
Pancreatic duct
Accessory pancreatic duct
Minor duodenal papilla
Tail of pancreas
Hepato-pancreatic ampulla
Interlobular duct
Major duodenal papilla
Circular folds
Head of pancreas
(a)
Lobule
Pancreatic islet
Acini cells (secrete enzymes)
Alpha cells (secrete glucagon)
Intercalated duct
Beta cells (secrete insulin)
Intralobular duct
Interlobular duct
Vein
To pancreatic duct
To bloodstream
(b)

Pancreatic Digestive Enzymes

- Pancreatic secretion contains multiple enzymes for digesting all of the three major types of food: proteins, carbohydrates, and fats. It also contains large quantities of bicarbonate ions, which play an important role in neutralizing the acidity of the chyme emptied from the stomach into the duodenum.
- The most important of the pancreatic enzymes for digesting proteins are **trypsin**, **chymotrypsin**, and **carboxypolypeptidase**.
- **Trypsin** and **chymotrypsin** split whole and partially digested proteins into peptides of various sizes but do not cause release of individual amino acids. However,

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carboxypolypeptidase does split some peptides into individual amino acids, thus completing digestion of some proteins all the way to the amino acid state.

- The pancreatic enzyme for digesting carbohydrates is **pancreatic amylase**, which hydrolyzes starches, glycogen, and most other carbohydrates (except cellulose) to form mostly disaccharides and a few tri-saccharides.
- The main enzymes for fat digestion are (1) **pancreatic lipase**, which is capable of hydrolyzing neutral fat into fatty acids and mono-glycerides; (2) **cholesterol esterase**, which causes hydrolysis of cholesterol esters; and (3) **phospholipase**, which splits fatty acids from phospholipids.

Activation of Pancreatic Enzymes

When first synthesized in the pancreatic cells, the proteolytic digestive enzymes are in the inactive forms trypsinogen, chymo-trypsinogen, and procarboxy-polypeptidase, which are all inactive enzymatically. They become activated only after they are secreted into the intestinal tract. Trypsinogen activated by an enzyme called enterokinase, which is secreted by the intestinal mucosa when chyme comes in contact with the mucosa. Also, trypsinogen can be autocatalytically activated by trypsin that has already been formed from previously secreted trypsinogen. Chymotrypsinogen is activated by trypsin to form chymotrypsin, and procarboxypolypeptidase is activated in a similar manner.

Secretion of Bicarbonate Ions

The enzymes of the pancreatic juice are secreted entirely by the acini of the pancreatic glands, the other two important components of pancreatic juice, bicarbonate ions and water, are secreted mainly by the epithelial cells of the ductules and ducts that lead from the acini. When the pancreas is stimulated to secrete copious quantities of pancreatic juice, the bicarbonate ion concentration can rise to as high as 145 mEq/L, a value about five times that of bicarbonate ions in the plasma. This provides a large quantity of alkali in the pancreatic juice that serves to neutralize the hydrochloric acid emptied into the duodenum from the stomach.

Regulation of Pancreatic Secretion

Basic Stimuli That Cause Pancreatic Secretion

1. **Acetylcholine,** which is released from the parasympathetic vagus nerve endings and from other cholinergic nerves in the enteric nervous system
2. **Cholecystokinin,** which is secreted by the duodenal and upper jejunal mucosa when food enters the small intestine
3. **Secretin,** which is also secreted by the duodenal and jejunal mucosa when highly acid food enters the small intestine

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- The first two of these stimuli, **acetylcholine** and **cholecystokinin**, stimulate the acinar cells of the pancreas, causing production of large quantities of pancreatic digestive enzymes but relatively small quantities of water and electrolytes to go with the enzymes.
- **Secretin**, stimulates secretion of large quantities of water solution of sodium bicarbonate by the pancreatic ductal epithelium.

Phases of Pancreatic Secretion

- Pancreatic secretion occurs in three phases: the cephalic phase, the gastric phase, and the intestinal phase.

Cephalic and Gastric Phases.

During the cephalic phase of pancreatic secretion, the same nervous signals from the brain that cause secretion in the stomach also cause acetylcholine release by the vagal nerve endings in the pancreas. This causes moderate amounts of enzymes to be secreted into the pancreatic acini, accounting for about 20 per cent of the total secretion of pancreatic enzymes after a meal.

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During the gastric phase, the nervous stimulation of enzyme secretion continues, accounting for another 5 to 10 per cent of pancreatic enzymes secreted after a meal. But, again, only small amounts reach the duodenum because of continued lack of significant fluid secretion

Intestinal Phase.

After chyme leaves the stomach and enters the small intestine, pancreatic secretion becomes copious, mainly in response to the hormone **secretin**.

Secretion of Bile by the Liver.

- The liver secrete bile, normally between 600 and 1000 ml/day.
- Bile serves two important functions: **First**, bile plays an important role in fat digestion and absorption of fats , because bile acids in the bile do two things: (1) they help to emulsify the large fat particles of the food into many minute particles, the surface of which can then be attacked by lipase enzymes secreted in pancreatic juice, and (2) they aid in absorption of the digested fat end products through the intestinal mucosal membrane.

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Second, bile serves as a means for excretion of several important waste products from the blood. These include especially bilirubin, an end product of hemoglobin destruction, and excesses of cholesterol.

Biliary Secretion

Bile is secreted in two stages by the liver: (1) The initial portion is secreted by the principal functional cells of the liver, the hepatocytes; this initial secretion contains large amounts of bile acids, cholesterol, and other organic constituents.

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(2) Next, the bile flows in the canaliculi toward the interlobular septa, where the canaliculi empty into terminal bile ducts and then into progressively larger ducts, finally reaching the hepatic duct and common bile duct.

Storing and Concentrating Bile in the Gallbladder.

Bile is secreted continually by the liver cells, but most of it is normally stored in the gallbladder until needed in the duodenum. The maximum volume that the gallbladder can hold is only 30 to 60 milliliters.

Nevertheless, as much as 12 hours of bile secretion (usually about 450 milliliters) can be stored in the gallbladder because water, sodium, chloride, and most other small electrolytes are continually absorbed through the gallbladder mucosa, concentrating the remaining bile constituents that contain the bile salts, cholesterol, lecithin, and bilirubin.

Composition of Bile.

The following table gives the composition of bile when it is first secreted by the liver and then after it has been concentrated in the gallbladder.

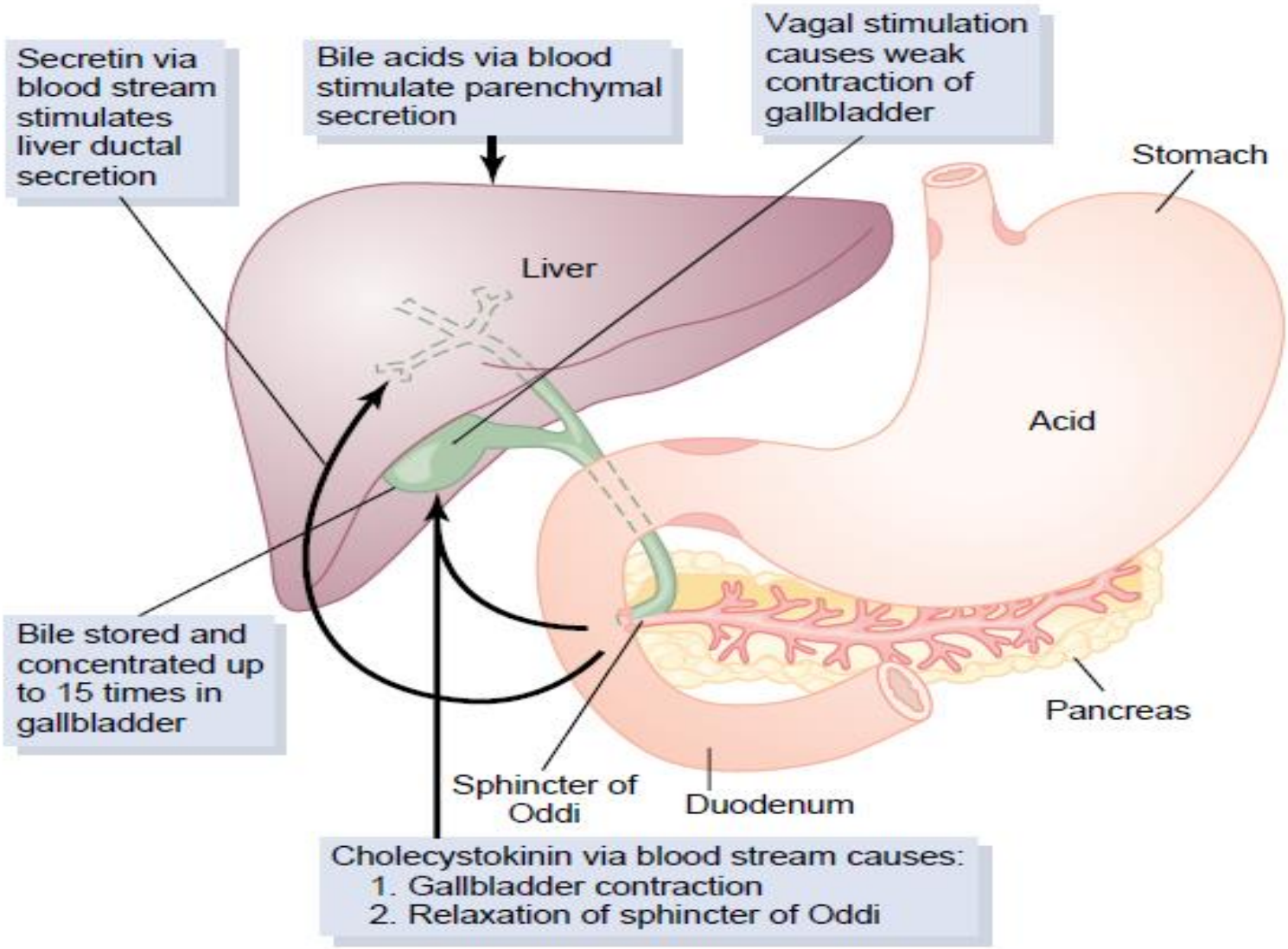
Composition of Bile

	Liver Bile	Gallbladder Bile
Water	97.5 g/dl	92 g/dl
Bile salts	1.1 g/dl	6 g/dl
Bilirubin	0.04 g/dl	0.3 g/dl
Cholesterol	0.1 g/dl	0.3 to 0.9 g/dl
Fatty acids	0.12 g/dl	0.3 to 1.2 g/dl
Lecithin	0.04 g/dl	0.3 g/dl
Na^+	145.04 mEq/L	130 mEq/L
K^+	5 mEq/L	12 mEq/L
Ca^{++}	5 mEq/L	23 mEq/L
Cl^-	100 mEq/L	25 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L

Emptying of the Gallbladder Stimulatory Role of Cholecystokinin.

- The gallbladder empties its store of concentrated bile into the duodenum mainly in response to the cholecystokinin stimulus that itself is initiated mainly by fatty foods. When fat is not in the food, the gallbladder empties poorly, but when significant quantities of fat are present, the gallbladder normally empties completely in about 1 hour.

Liver secretion and gallbladder emptying.



Function of Bile Salts in Fat Digestion and Absorption

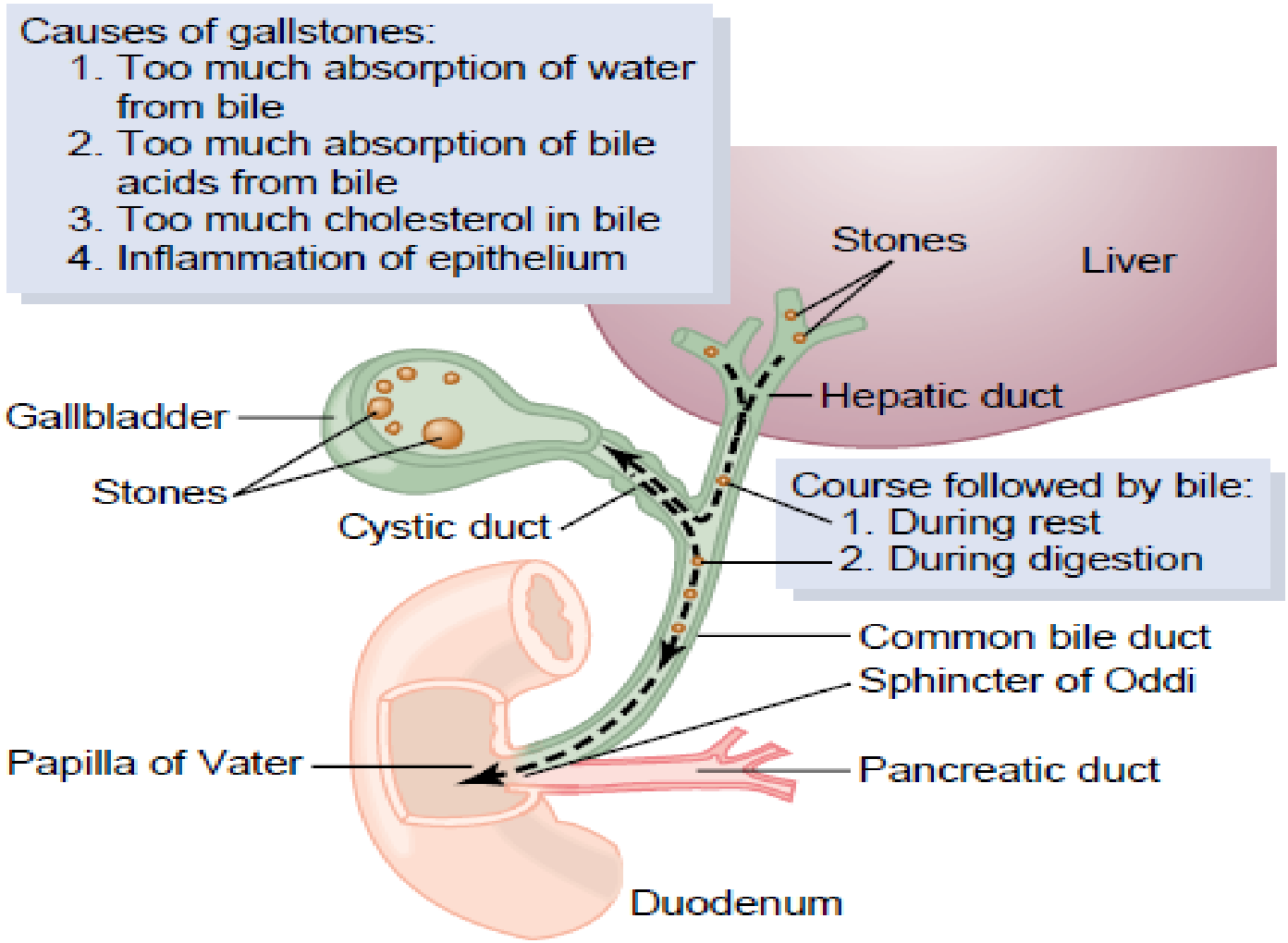
- The liver cells synthesize about 6 grams of bile salts daily.
- The precursor of the bile salts is cholesterol (diet or synthesized in the liver cells during the course of fat metabolism).
- The cholesterol is converted to **cholic acid** or **chenodeoxycholic acid** in equal quantities.
- These acids combine principally with **glycine** and **taurine** to form **glyco-** and **tauroconjugated bile acids**. The salts of these acids, mainly sodium salts, are then secreted in the bile.

The bile salts have two important actions in the intestinal tract: **First**, they have a detergent action on the fat particles in the food. This decreases the surface tension of the particles and allows agitation in the intestinal tract to break the fat globules into minute sizes. This is called the emulsifying or detergent function of bile salts.

Second, and even more important than the emulsifying function, bile salts help in the absorption of (1) fatty acids, (2) monoglycerides, (3) cholesterol, and (4) other lipids from the intestinal tract.

They do this by forming very small physical complexes with these lipids; the complexes are called micelles, and they are semi-soluble in the chyme because of the electrical charges of the bile salts.

Gallstone Formation



Secretions of the Small Intestine

Secretion of Mucus by Brunner's Glands in the Duodenum

- Brunner's glands (mucous gland, is located in the wall of the first few centimeters of the duodenum).
- These glands secrete large amounts of alkaline mucus in response to (1) tactile or irritating stimuli on the duodenal mucosa; (2) vagal stimulation, which causes increased Brunner's glands secretion concurrently with increase in stomach secretion; and (3) gastrointestinal hormones, especially secretin.

The function of the mucus secreted by Brunner's glands is to protect the duodenal wall from digestion by the highly acid gastric juice emptying from the stomach. The mucus contains a large excess of bicarbonate ions, which add to the bicarbonate ions from pancreatic secretion and liver bile in neutralizing the hydrochloric acid entering the duodenum from the stomach.

Secretion of Intestinal Digestive Juices by the Crypts of Lieberkühn

- **Crypts of Lieberkühn** small pits are Located over the entire surface of the small intestine, lie between the intestinal villi.
- The surfaces of both the crypts and the villi are covered by an epithelium composed of two types of cells: (1) a moderate number of goblet cells, which secrete mucus that lubricates and protects the intestinal surfaces, and (2) a large number of enterocytes, which, in the crypts, secrete large quantities of water and electrolytes and, over the surfaces of adjacent villi, reabsorb the water and electrolytes along with end products of digestion.

- Digestive Enzymes in the Small Intestinal Secretion.
- The enterocytes of the mucosa especially those that cover the villi, do contain digestive enzymes that digest specific food substances while they are being absorbed through the epithelium. These enzymes are the following: (1) several peptidases for splitting small peptides into amino acids, (2) four enzymes—sucrase, maltase, isomaltase, and lactase—for splitting disaccharides into monosaccharides, and (3) small amounts of intestinal lipase for splitting neutral fats into glycerol and fatty acids.

Secretions of the Large Intestine

Mucus Secretion. The mucosa of the large intestine, has many crypts of Lieberkühn; however, unlike the small intestine, there are no villi. The epithelial cells contain almost no enzymes. Instead, they consist mainly of mucous cells that secrete only mucus. This mucus contains moderate amounts of bicarbonate ions.

- Mucus in the large intestine protects the intestinal wall against excoriation, but in addition, it provides an adherent medium for holding fecal matter together. Furthermore, it protects the intestinal wall from the inside the feces, and, finally, the mucus plus the alkalinity of the secretion (pH of 8.0 caused by large amounts of sodium bicarbonate) provides a barrier to keep acids formed in the feces from attacking the intestinal wall.

Diarrhea Caused by Excess Secretion of Water and Electrolytes in Response to Irritation

Whenever a segment of the large intestine becomes intensely irritated, as occurs when bacterial infection becomes rampant during enteritis, the mucosa secretes extra large quantities of water and electrolytes in addition to the normal viscid alkaline mucous. This acts to dilute the irritating factors and to cause rapid movement of the feces toward the anus. The result is diarrhea, with loss of large quantities of water and electrolytes. But the diarrhea also washes away irritant factors, which promotes earlier recovery from the disease than might otherwise occur.