7.3 Physiological Activities in Stomach

FUNCTIONAL ANATOMY

GROSS ANATOMY

General features

- Stomach is a J-shaped hollow muscular bag connected to the oesophagus at its upper end and to the duodenum at the lower end.
- Gastric contents are isolated from the rest of gastro-intestinal tract proximally by the lower oesophageal sphincter (LES) and distally by the pyloric sphincter.
- The *volume* of stomach is 1200-1500 ml, but its *capacity* is greater than 3000 ml.
- The stomach has two curvatures. The concavity of the right inner curve is called *lesser curvature*, and the convexity of the left outer curve is the *greater curvature*. An angle along the lesser curvature, the *incisura angularis*, marks the approximate point at which the stomach narrows before its junction with duodenum.

Parts of stomach

The stomach can be divided into five anatomic regions (Fig. 7.3-1):

- *Cardia* is the narrow conical portion of the stomach immediately distal to the gastroesophageal junction.
- *Fundus* is the dome-shaped proximal portion of the stomach.
- *Body or corpus*, is the main part of the stomach that extends upto the incisura angularis.
- *Pyloric antrum* extends from the incisura angularis to the pyloric canal.
- *Pyloric canal or pylorus* is the distal most one inch long tubular part of stomach.

Note. Anatomically the antrum and pylorus are continuous and respond to nervous control as a unit. Functionally,

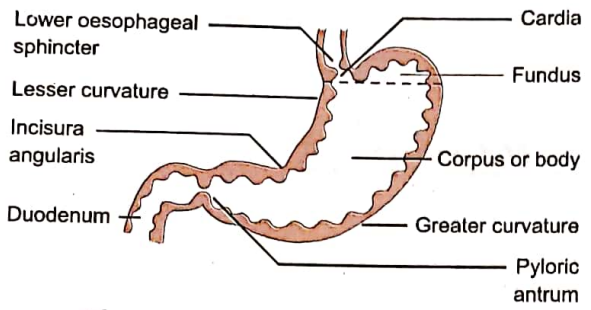


Fig. 7.3-1. Gross anatomy of stomach.

first part of duodenum is associated with the pyloric part of stomach.

STRUCTURAL CHARACTERISTICS

As elsewhere in the gut (page 583), the gastric wall consists of mucosa, submucosa, muscular coat, and serosa (serous layer). The mucosa and muscular coat of stomach need to be described in detail to understand physiology of stomach.

Gastric mucosa

Gross features

- The inner surface of stomach exhibits coarse *rugae*. These infoldings of mucosa and submucosa extend longitudinally and are most prominent in the proximal stomach.
- A finger mosaic-like pattern is delineated by small furrows in the mucosa.
- The delicate texture of the mucosa is punctured by millions of gastric foveolae or pits, leading to the mucosal glands.

Histological features

Gastric mucosa comprises (Fig. 7.3-2):

Surface foveolar cells are tall columnar mucin secreting cells which line the entire gastric mucosa as well as the gastric pits. These cells have basal nuclei and mucin-containing granules in the supranuclear region.

Mucous neck cells are present deeper in the gastric pits. These cells have a lower content of mucin granules and are thought to be the progenitors of both, the surface epithelium and the cells of gastric glands.

Glandular cells form the gastric glands. There are three types of gastric glands, main gastric glands, cardiac tubular glands, and pyloric (antral) glands.

1. *Main gastric glands,* found in the body and fundus of stomach, are much more in number than the other gastric glands. These are simple tubular glands (Fig. 7.3-2). The

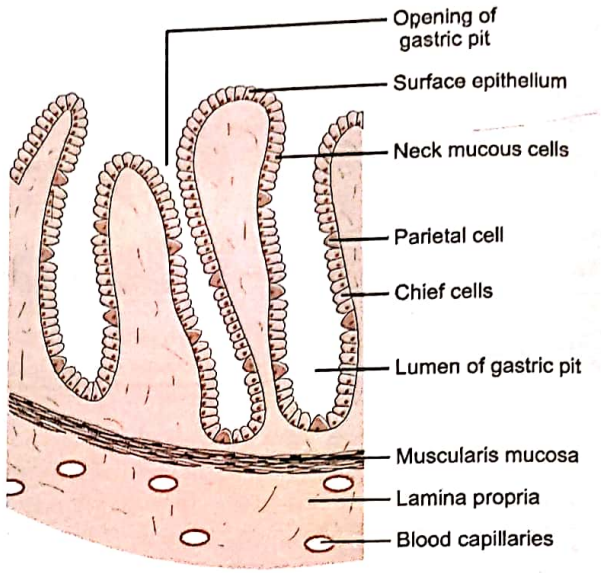


Fig. 7.3-2. Histological features of gastric mucosa.

alveoli of main gastric glands contain two types of cells:

- *Chief cells*, also known as peptic or zymogen cells are basophilic. These cells are concentrated at the base of main gastric glands. These cells secrete proteolytic proenzymes, pepsinogen I and II.
- *Parietal cells*, also known as oxyntic cells are acidophilic. These cells line predominantly the upper half of glands and have an extensive intracellular canalicular system. These secrete *hydrochloric acid* (HCl) and the *intrinsic factor*.

2. *Cardiac tubular glands* are found in the mucosa of cardia (a small conical part of the stomach) just around the distal end of oesophagus. These secrete *soluble mucus*.

3. *Pyloric (antral) glands* are found in the antrum and pylorus region of the stomach. These glands contain two types of cells:

- *Mucus cells*, which secrete *soluble mucus*, and
- *G-Cells*, are responsible for release of the hormone gastrin.

Musculature of stomach

Characteristic features of gastric musculature are:

- The muscle coat of stomach has three layers, an outer longitudinal, middle circular, and an inner oblique (Fig. 7.3-3).
- As elsewhere in the gut, each muscle layer in the stomach forms a *functional syncytium* and, therefore, acts as a unit. In the fundus, where the layers are relatively thin, the strength of contraction is weak; in

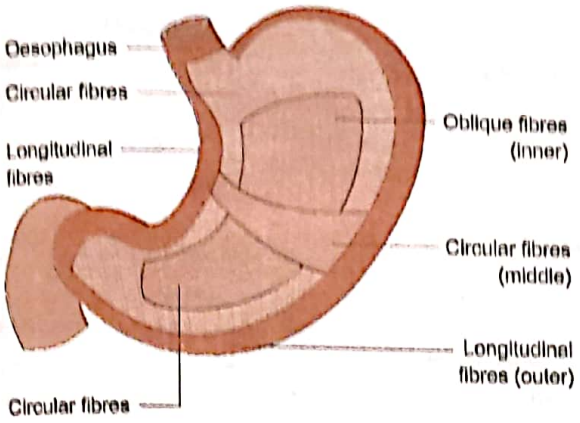


Fig. 7.3-3. Three layers of gastric mucosa.

the antrum, where the muscle layers are thick, the strength of contraction is greater.

- The stomach and duodenum are divided by a thickened circular smooth muscle layer called *pyloric sphincter*.

INNERVATION OF STOMACH

Innervation of stomach, as elsewhere in the gut (page 583), includes an intrinsic and an extrinsic system.

1. ***Intrinsic innervation*** comprises two interconnected plexuses:

- *Myenteric (Auerbach's) plexus*, located between the layers of circular and longitudinal muscles of the stomach, and
- *Submucosal (Meissner's) plexus*, located in the submucosal layer.

The intrinsic innervation is directly responsible for peristalsis and other contractions. Because this system is continuous between the stomach and duodenum, peristalsis in the antrum influences the duodenal bulb.

2. ***Extrinsic innervation*** modifies the co-ordinated motor activity that arises independently in the intrinsic nervous system. It consists of the two components of autonomic nervous system:

- *Sympathetic innervation* comes via coeliac plexus and *inhibits motility*, and
- *Parasympathetic innervation* comes via the vagus nerve and *stimulates motility*.

PHYSIOLOGY OF GASTRIC SECRETION

The gastric secretions include:

- *Exocrine secretions*, i.e. gastric juice, and
- *Endocrine secretions*, i.e. gastrin hormone (see regulation of gastric secretion, page 604).

GASTRIC JUICE

COMPOSITION

Gastric glands secrete about 2-2.5L of gastric juice in the lumen of stomach per day. It is acidic with a pH varying from 1 to 2. Important constituents of gastric juice are:

Water – 99.45%

Solids – 0.55%, which include:

Electrolytes such as Na^+, K^+, Mg^{2+}, Cl^-, HCO^-_3, HPO^{-2}_4 and SO^{-2}_4. The electrolyte content of gastric juice varies with the rate of secretions. At low secretory rates, Na^+ concentration is high and H^+ concentration is low, but as acid secretion increases Na^+ concentration falls.

Enzymes present in the gastric juice are:

- *Pepsin* is a proteolytic enzyme which is secreted by chief cells of gastric glands in an inactive form pepsinogen. Pepsinogen is activated to pepsin in the presence of HCl at an optimal pH of about 2.
- *Gastric lipase* is a weak fat splitting enzyme. It is of little importance in fat digestion except in pancreatic insufficiency.
- *Gastric gelatinase* liquefies gelatin, a protein contained in connective tissue.
- *Gastric amylase* is present in small amounts.
- *Lysozyme* is bactericidal.
- *Carbonic anhydrase* is present in small amounts.

Mucin or mucus is of two types:

- *Soluble mucus* secreted by mucus cells of pyloric and cardiac glands, and
- *Insoluble mucus* secreted by surface foveolar cells (tall columnar mucin secreting cells) lining the entire gastric mucosa.

Intrinsic factor is secreted by parietal cells of gastric glands.

SECRETION OF GASTRIC JUICE

Secretion of HCl

General consideration

- Hydrochloric acid (HCl) is secreted by the *parietal cells* (also called oxyntic cells). These cells show, under electron microscope, a complex network of *intracellular canaliculi* (Fig.7.3-4) into which HCl is secreted
- Gastric glands secrete about 2.5L of HCl in a day. The HCl secreted by gastric glands is concentrated having a pH of approximately 1.0.

into enough small pieces (typically less than 1 mm^3) to fit through the pyloric sphincter.

- Each time the chyme is pushed against the pyloric sphincter, contraction ahead of advancing gastric contents prevent bigger food particles from entering the duodenum. Therefore, chyme is pumped in a bit (2-7 ml) at a time into the small intestine.
- The peristaltic waves which provide this pumping action are known as *pyloric pump*.
- Regurgitation from duodenum, normally does not occur, because the contraction of pyloric segment tends to persist slightly longer than that of duodenum. The prevention of regurgitation may also be due to the stimulating action of CCK and secretin on the pyloric sphincter.

Factors regulating the gastric emptying

After a normal meal, the emptying time is 2-3 hours. The gastric emptying is regulated by various factors:

1. ***Fluidity of the chyme***. The rate of gastric emptying of solids depends on the rate at which the chyme is broken down into smaller particles. Liquids empty much faster than solids. The rate at which liquids empty is proportional to the pressure within the oral stomach, which increases slowly during the digestive period.

2. ***Gastric factors*** which affect emptying are:

- *Volume of food in the stomach.* Greater the volume of food in the stomach, greater is the stretching of stomach wall. Distension of the stomach triggers long (vagally mediated) and short (intrinsic neural plexus mediated) reflexes leading to strong peristalsis waves and increased rate of gastric emptying.
- *Gastrin hormone.* Presence of certain types of food (e.g. meat) causes release of gastrin from antral mucosa. Gastrin enhances the activity of pyloric pump and therefore promotes gastric emptying.
- *Type of food ingested* (present in the stomach) affects the gastric emptying as:
  - Carbohydrate rich food causes rapid gastric emptying,
  - Protein rich food causes slow gastric emptying, and
  - Fat rich food causes slowest gastric emptying. Because of this reason some people consume fats before a cocktail party. The fat keeps the alcohol in the stomach longer, slowing the absorption and reducing the chances of intoxication.

3. ***Duodenal factors***, which inhibit gastric emptying are:

- *Enterogastric reflex. It* is a neural mediated reflex. It is initiated by stimulation of receptors in the duodenal mucosa. The important stimuli are: distension of duodenum, acidity of the contents (pH <4), high or low osmolarity of chyme, presence of fat and protein digestion products in the chyme.

  The enterogastric reflex is initiated in the duodenum and passes to stomach through the myenteric plexus and also extrinisic nerves to inhibit or even stop emptying by inhibiting antral propulsive contractions and increasing slightly the tone of pyloric sphincter.
- *Enterogastric hormones.* A variety of intestinal hormones, collectively called enterogastrones inhibit gastric contractions. Some of the hormones which have been identified are:
- *Cholecystokinin (CCK).* It is released from the duodenum in response to fat or protein digestion product. CCK probably acts by blocking the excitatory effects of gastrin on gastric smooth muscles.
- *Secretin.* It is released from the duodenum in response to presence of acid. Secretin most likely has a direct inhibitory effect on smooth muscle.
- *Gastric inhibitory peptide (GIP).* It is released from upper small intestine in response to fat in chyme and reduces gastric motility under some conditions.

Purpose of duodenal inhibitory effect on gastric emptying. The duodenal inhibitory effects (exerted through enterogastric reflex and enterogastrones) prevent the flow of chyme from exceeding the ability of intestine to handle it (especially longer time is required for fat digestion). It does not allow disturbance in electrolyte balance even if hypo or hypertonic solutions are drunk.

4. ***Other factors affecting gastric emptying***:

- *Emotions* have a strong effect on gastric motility. Anger and aggression increase gastric motility whereas depression and fear decrease it.
- *Vagotomy* decreases the magnitude and co-ordination of stomach contractions and thus slows emptying.

FUNCTIONS OF STOMACH

After studying the physiological activities of stomach, its functions can be summarized as:

1. ***Mechanical or motor functions*** include:

- *Storage of food.* Stomach serves as a reservoir for the food ingested. Stomach can store about 1 to 2 L of food. Food remains in the stomach for several hours.
- *Mixing of food* with gastric juice is performed by gastric motility until it forms a semisolid paste known as chyme.
- *Slow emptying of food* into duodenum occurs to provide proper time for digestion and absorption by small intestine.

2. Digestive functions. Only small amounts of foods are digested in stomach as:

- *Carbohydrate digestion* in the stomach depends on the action of salivary amylase, which remains active until halted by the low pH of stomach.
- *Protein digestion.* About 10% of ingested protein is broken down completely in the stomach. *Gastric pepsin* facilitates later digestion of protein by breaking protein into peptone.
- *Fat digestion* in stomach is minimal due to the restriction of gastric lipase activity to triglycerides containing short chain (< 10 carbon) fatty acids. Acid and pepsin break emulsions so that fats coalesce into droplets, which float and empty last.

3. Absorptive function. Stomach contributes little in absorption function.

- *Absorption of nutrients.* Very little absorption of nutrients takes place in the stomach. The only substances absorbed to any appreciable extent are highly lipid-soluble substances (e.g. the non-ionized triglycerides of acetic, propionic and butyric acids). *Aspirin* at gastric pH is non-ionized and fat soluble, after absorption it ionizes intracellularly, damaging mucosal cells and ultimately producing bleeding.
- *Ethanol* is absorbed rapidly in proportion to its concentration.
- *Water absorption.* Water moves in both direction across the gastric mucosa. It does not, however, follow osmotic gradients. Water soluble substances, including Na^+, K^+, glucose, and amino acids, are absorbed in insignificant amounts.
- *Intrinsic factor* released from gastric glands helps in absorption of vitamin B_{12} from the small intestine.

4. Excretory function. Stomach excretes following substances:

- Certain toxins, as in case of uraemia, and
- Certain alkaloids, such as morphine.

5. Stimulating functions. Stomach performs stimulatory function for release of:

- Gastrin,
- Enterogastrin, and
- Intrinsic factor of Castle.

6. Reflex functions. Various reflexes initiated from the stomach are:

- Gastro-salivary reflex,
- Gastro-ileal reflex,
- Gastro-colic reflex, and
- Presence of food in the stomach reflexly stimulates secretion of pancreatic juice and expulsion of bile.

7. Antiseptic action. HCl present in the gastric juice kills the bacteria and other harmful substances.

APPLIED ASPECTS

Important applied aspects of stomach which need special attention are:

- Gastric mucosal barrier and pathophysiology of peptic ulcer,
- Physiology of vomiting,
- Gastrectomy, and
- Gastric function tests.

GASTRIC MUCOSAL BARRIER AND PATHOPHYSIOLOGY OF PEPTIC ULCER

GASTRIC MUCOSAL BARRIER

The gastric mucosal barrier protects the gastric mucosa from damage by intraluminal HCl, i.e. autodigestion. Indeed, it is a physiologic marvel, or gastric walls would suffer the same fate as a piece of swallowed meat. It is created by the following:

- *Mucin secretion.* The thin layer of surface mucus in the stomach and duodenum exhibits a diffusion coefficient for H^+ that is one-fourth that of water. Acid-containing and pepsin-containing fluid exits the gastric glands as jets passing through the surface mucus layer, entering the lumen directly without contacting surface epithelial cells.
- *Bicarbonate secretion.* Surface epithelial cells in both the stomach and the duodenum secrete bicarbonate into the boundary zone of adherent mucus, creating an essentially pH neutral microenvironment immediately adjacent to the cell surface.
- *Epithelial barrier.* Intercellular tight junctions provide a barrier to the back-diffusion of H^+. Any damaged cells are quickly replaced, as the turnover rate of gastric mucosa is very high. Approximately $5x10^5$ mucosal cells are shed each minute, replacing the entire mucosa in 1-3 days.
- *High mucosal blood flow.* It rapidly carries away any acid that penetrates the cellular lining. The rich mucosal blood supply also provides oxygen, bicarbonate, and nutrients to epithelial cells.
- *Prostaglandins*, are responsible for maintaining the gastric mucosal barrier.

PATHOPHYSIOLOGY OF PEPTIC ULCER

Peptic ulcer refers to excavation of mucosa of duodenum or pyloric part of stomach caused by the digestive action

7.4 Pancreas, Liver and Gall Bladder

PANCREAS
Functional anatomy
- General considerations
- Structural characteristics of exocrine part
- Vessels and nerves

Pancreatic secretion
- Properties and composition
- Functions
- Mechanism of secretion
- Regulation

Applied aspects
- Disorders of pancreas
- Pancreatic function tests

LIVER AND GALL BLADDER
Physiological anatomy
- General considerations
- Structural characteristics
- Hepatic circulation
- Hepatic biliary system
  - Intrahepatic biliary system
  - Extrahepatic biliary apparatus

Functions of liver

Bile and gall bladder
- General considerations
- Formation and composition of bile
- Functions of gall bladder
- Functions of bile
- Regulation of bile

Applied aspects
- Disorders of liver and gall bladder
- Liver function tests

Pancreas, liver and gall bladder are accessory organs of digestive system. After studying the physiological events occurring in stomach and before considering the physiological activities of small intestine, it will be worthwhile to know about the physiological role of pancreas, liver and gall bladder in digestive system, because secretions of these organs affect the activities of small intestine.

PANCREAS

FUNCTIONAL ANATOMY

General considerations

- The pancreas—an elongated, accessory digestive gland—lies retroperitoneally and transversely across the posterior abdominal wall, posterior to the stomach between the duodenum on the right and spleen on the left (Fig.7.4-1)
- *Anatomically*, for the purpose of description, pancreas is divided into four parts: head, neck, body, and tail.
- *Physiologically*, on the basis of functions performed, the pancreas consists of two parts:
  - *Exocrine part*, which produces a secretion called pancreatic juice that contains enzymes capable of hydrolyzing proteins, fats and carbohydrates.
  - *Endocrine part* of the pancreas, the islets of Langerhans, produce the hormones insulin and glucagon, which play a key role in the carbohydrate metabolism. The endocrine part is discussed elsewhere (page 783).

Structural characteristics of exocrine part of pancreas

The exocrine part of the pancreas is in the form of a serous, compound tubuloalveolar gland, very similar to parotid gland in general structure (Fig. 7.4-2).

Acinar cells lining the alveoli appear triangular in section. Numerous secretory (or zymogen) granules can be demonstrated in the cytoplasm, especially in the apical part of cells. These granules are eosinophilic and decrease considerably after the cells have poured out their secretions.

The acinar cells produce thick secretion containing numerous enzymes (listed in composition of pancreatic juice).

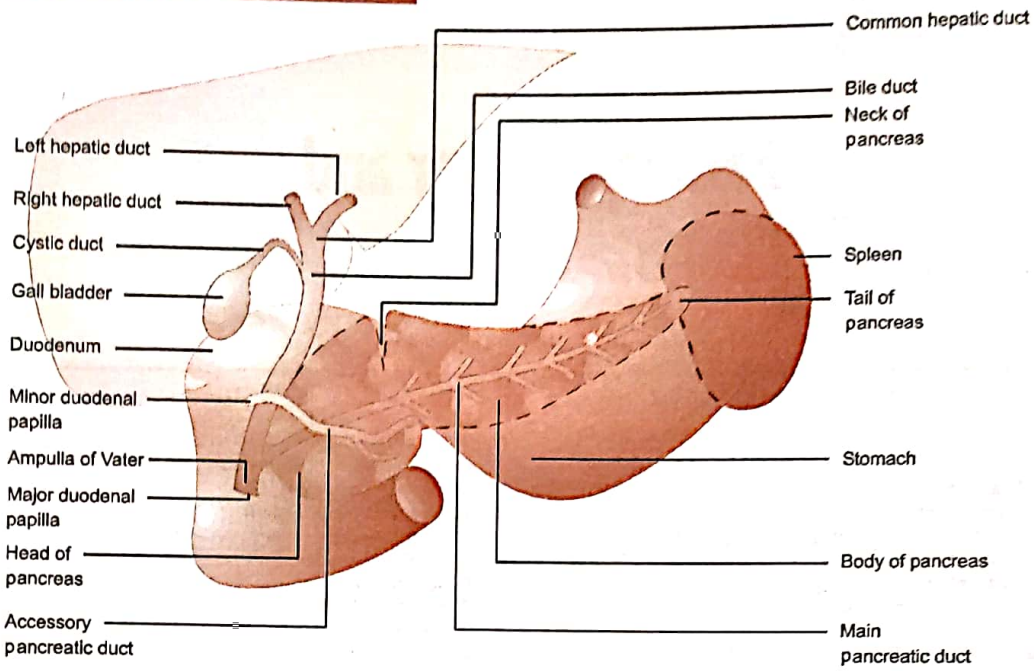


Fig. 7.4-1. Anatomical relations of pancreas, pancreatic duct and extrahepatic biliary system.

Centroacinar cells. In addition to the secretory acinar cells, the alveoli of exocrine pancreas contain centroacinar cells that are so called because they appear to be located near the centre of the acinus (alveolus). These cells really belong to the intercalated ducts which are invaginated into the acinus (Fig. 7.4-2).

Ductal cells lining the ductal system of pancreas produce watery secretion rich in bicarbonate ions (HCO^-_3), which mix with the thick secretion produced by acinar cells to constitute the pancreatic juice.

Pancreatic ducts

The ***intercalated ducts***, which receive secretions produced by acini, pass it on to interlobular ducts. Ultimately the pancreatic secretion passes into duodenum through the main pancreatic duct and accessory pancreatic duct.

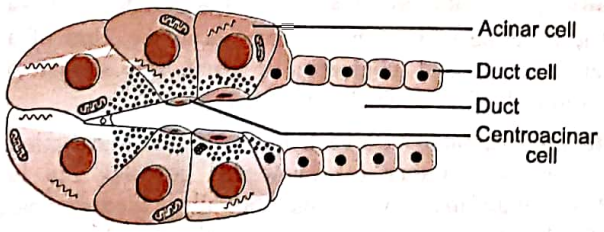


Fig. 7.4-2. Histology of functional unit of pancreas.

Main pancreatic duct, also known as duct of Wirsung, begins in the tail and runs the length of the gland, receiving numerous tributaries on the way. It joins the common bile duct to form the ampulla of Vater, which opens into the second part of the duodenum at about its middle on the major duodenal papilla (Fig. 7.4-1). Ampulla of Vater is guarded by the sphincter of Oddi.

Accessory pancreatic duct, also called a duct of Santorini, when present, drains the upper part of the head and then opens into the duodenum about 2 mm above the main duct on the minor duodenal papilla. The accessory duct frequently communicates with the main duct.

Vessels and nerves of pancreas

Arterial supply to the pancreas comes from splenic and superior as well as inferior pancreaticoduodenal arteries.

Veins, corresponding to arteries, drain into the portal system.

Lymphatics drain into the lymph nodes situated along the arteries that supply the gland. The efferent vessels ultimately drain into the coeliac and superior mesenteric lymph nodes.

Nerve supply comes from both sympathetic and parasympathetic (vagi) nerves. Preganglionic vagal fibres synapse with ganglionic cells embedded in the pancreatic

tissue; the postganglionic fibres innervate both the acinar cells and smooth muscles of the ducts. Vagal stimulation increases pancreatic juice secretion.

PANCREATIC JUICE

PROPERTIES

- Pancreatic juice is a transparent colourless fluid isotonic with plasma.
- About 1200-1500 ml of pancreatic juice is secreted per day.
- Its specific gravity varies from 1.010-1.018.
- Pancreatic juice is markedly alkaline (pH 7.8 to 8.4), due to very high concentration of HCO^-_3 (about 4-5 times that of plasma).

COMPOSITION

Pancreatic juice is composed of 99.5% water and 0.5% solids which include organic and inorganic substances.

Organic constituents of pancreatic juice are certain enzymes and other substances.

Enzymes. The pancreas secretes four major types of enzymes: amylase, lipase, protease and trypsin inhibitor.

Other organic substances present in traces are albumin and globulin.

Inorganic substances present in the pancreatic juice are cations like Na^+, K^+, Ca^{2+}, Mg^{2+}, and Zn^{2+}; and anions such as HCO^-_3, Cl^- and traces of SO_4^{2-} and HPO_4^{2-}. Electrolyte composition varies with rate of secretion (see page 623.

Pancreatic enzymes

Pancreatic acini secrete four major types of enzymes: amylase, lipase, protease and trypsin inhibitor.

1. ***Pancreatic α amylase.*** It is secreted in its active form. It is the only amylytic enzyme present with pancreatic juice. Its action on the carbohydrates is like that of salivary amylase. It hydrolyzes glycogen, starch, and most other complex carbohydrates except cellulose, to form disaccharides.

2. ***Pancreatic lipases*** or lipolytic enzymes include pancreatic lipase, cholesterol ester hydrolase and phospholipase A_1.

- *Pancreatic lipase.* It is a powerful lipolytic enzyme. It hydrolyses neutral fats to glycerol esters and fatty acids. It activity is accelerated in the presence of bile salts.
- *Cholesterol ester hydrolase* converts cholesterol esters to cholesterol.
- *Phospholipase A_1.* It is secreted in an inactive form, the pro-phospholipase A_2 and gets converted to active form the phospholipase A_2 by the action of trypsin. It acts on lysophospholipids, i.e. lysolecithin and lysocephalin and converts them into phosphoryl choline.

It is *important to note* that in acute pancreatitis, phospholipase A_2 gets activated in the pancreatic ducts causing disruption of pancreatic tissue and necrosis of surrounding fat which may be fatal. Acute pancreatitis is invariably associated with high serum amylase level.

3. ***Pancreatic proteases*** or proteolytic enzymes include three endopeptidases (trypsin, chymotrypsin and elastase) and two exopeptidases (carboxypeptidase A and B). Endopeptidases break the peptides somewhere in the middle. Exopeptidases break the peptide chain near its end, releasing single amino acid.

- *Trypsin.* It is the most powerful proteolytic enzyme of the pancreatic juice. It is secreted in an inactive form of trypsinogen which is activated by the enzyme enterokinase (enteropeptidase) secreted by duodenal mucosa. Once formed, trypsin also activates trypsinogen—an autocatalytic reaction.

  $$\text{Trypsinogen} \xrightarrow{\text{Enterokinase}} \text{Trypsin}$$

  $$\text{Trypsinogen} \xrightarrow{\text{Trypsin}} \text{Trypsin}$$

  – Trypsin hydrolyses proteins into proteoses and to polypeptides
  – It activates trypsinogen and other pancreatic enzymes.
- *Chymotrypsin.* It is also secreted in an inactive form chymotrypsinogen and is activated by trypsin. It hydrolyses the proteins into small polypeptides.
- *Elastase.* It is secreted as proelastase which is activated by trypsin. It digests elastin.
- *Carboxypeptidase A and B.* These are secreted as procarboxypeptidase A and B and are activated by enterokinase and trypsin.
  – Carboxypeptidase A cleaves the carboxyl-terminal amino acid that have aromatic or branched aliphatic side chains.
  – Carboxypeptidase B cleaves the carboxy-terminal amino acids that have basic side chains.
- *Nucleases* (ribonuclease and deoxyribonuclease). They split nucleic acids of ribose and deoxyribose type into nucleotides.
- *Collagenase.* It is also activated by trypsin and digests collagen.

4. ***Trypsin inhibitor.*** If even a small amount of trypsin is released into the pancreas, the resulting chain reaction would produce active enzymes that could digest the pancreas. It is therefore, not surprising that the pancreas normally contains a trypsin inhibitor which is secreted by the same cells and at the same time as the pancreatic

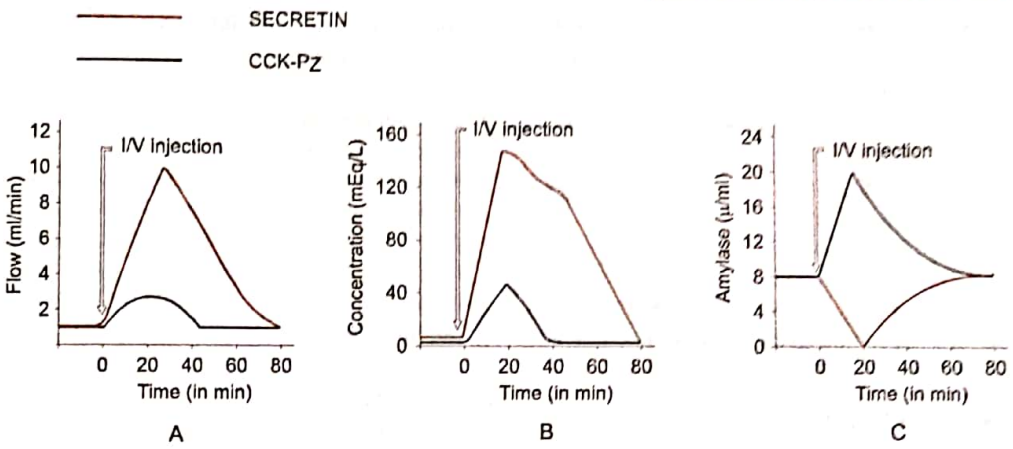


Fig. 7.4-6. Normal curves for combined secretin-cholecystokinin test: A, volume of pancreatic juice; B, HCO_3^- concentration of pancreatic juice; and C, enzyme (amylase) level of pancreatic juice.

Van de Kramer method and results are interpreted as:

- Normally fats are digested by lipase (mainly from pancreas) and about 5-6 gm/day are excreted in stools.
- In patients with exocrine pancreatic insufficiency it may increase to 40-50 gm/day.

2. *Faecal nitrogen excretion test.* Normally, about 7 gm of nitrogen is excreted in the stools per day. In patients with exocrine pancreatic insufficiency due to deficiency of proteolytic enzymes, the nitrogen excretion in stools is increased.

3. *Tripeptide hydrolysis test.* In this test patient is given a synthetic peptide—B_2–T_4-PABA. Normally, B_2–T_4-PABA is cleaved by the chymotrypsin into B_2–T_4 and PABA. PABA is rapidly absorbed and excreted in urine. In exocrine pancreatic insufficiency cleavage of B_2-T_4-PABA is decreased leading to decreased excretion of PABA in the urine. Thus, from the values of PABA in urine, activity of pancreatic chymotrypsin can be studied.

4. *Dual label Schilling test.* In this test ability of the gut to absorb vitamin B_{12} is studied. It is based on the fact that pancreatic proteases (trypsin) play an important role in the absorption mechanism of vitamin B_{12} and that in pancreatic insufficiency the absorption of vitamin B_{12} is abnormal.

III. Estimation of serum amylase levels

This test is particularly useful to rule out acute pancreatitis in patients presenting with acute pain in upper abdomen. Normal values of serum amylase are 50 to 120 units/L. The levels of serum amylase are markedly raised in patients with acute pancreatitis.

LIVER AND GALL BLADDER

LIVER: PHYSIOLOGICAL ANATOMY

GENERAL CONSIDERATIONS

- Liver, the largest gland in the body, weighs approximately 1500 gm and accounts for approximately 1/40th of adult body weight.
- Traditionally, the liver has been divided into *right and left lobes*. Right lobe is much larger and includes caudate lobe and quadrate lobe. Left lobe is much smaller and consists of 1/6th of total weight of liver.
- In current terminology, the liver consists of right and left functionally independent parts called the *portal lobes*, that are approximately equal in size. Thus, functionally the left part of liver includes the caudate lobe and most of the quadrate lobe (Fig. 7.4-7).

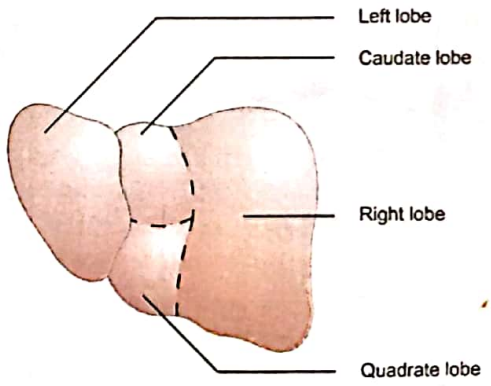


Fig. 7.4-7. Gross anatomy of the liver.

- The right and left functional parts of the liver have their own blood supply from the hepatic artery and portal vein and their own venous and biliary drainage.
- Liver has got considerable physiological reserve. Even after removal of 80% of liver tissues, all *physiological* functions of liver can be accomplished normally. Further, even if 90% of bile ducts are ligated, the volume of bile secreted remains normal.
- The liver possesses considerable *regeneration power*. Original liver mass is restored within 6-8 weeks of removal of upto 3/4th of liver. This occurs due to active mitotic division of the cells.

STRUCTURAL CHARACTERISTICS

- The liver tissue comprises about one lac hexagonal areas that constitute the *hepatic lobules* (Fig. 7.4-8A).
- Each hepatic lobule is made of ramifying columns of hepatic cells (*hepatocytes*) that are arranged in the form of one cell thick plates. In between the cells are present bile canaliculi. These hepatic cell plates are tunelled by a communicating system of lacunae called *blood sinusoids*. The sinusoids open into a central vein present in the centre of each lobule (Fig. 7.4-8B).

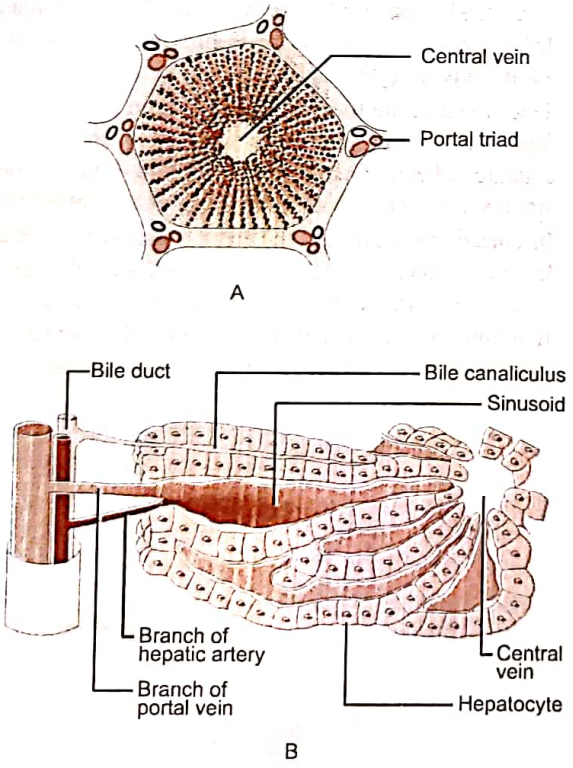


Fig. 7.4-8. Histological characteristics of the liver: A, hexagonal lobule with portal triad; and B, hepatocyte, sinusoid and biliary canaliculi seen under high magnification.

- Blood sinusoids are lined by endothelial cells. Few tissue macrophages called *Kupffer* cells are found at regular intervals in between the endothelial cells. The endothelial cells have large fenestrations thereby forming an intimate contact between the blood and hepatic cells. This helps the liver to transform or modify many of the constituents of blood.
- Along the periphery of each lobule are present *portal triads* consisting of a branch of portal vein, branch of hepatic artery and an interlobular bile duct. Blood from the branch of portal vein and hepatic artery enters the sinusoids which drain into central vein.
- *Concept of portal lobule*, instead of hepatic lobule has been suggested by some workers. It has been described to consist of adjoining part of three hepatic lobules centred on a portal triad.
- Presently acinus is considered the functional unit of liver. Each acinus has been considered to have three zones: 1, 2 and 3.

  Zone 1 refers to central portion of the acinus immediately surrounding the terminal hepatic arteriole and terminal portal venule. This zone is well oxygenated. Enzymes involved in oxidative metabolism and glucogenesis predominate here.

  Zone 3 refers to peripheral most part of the acinus. It is least oxygenated and most susceptible to anoxic injury. It is rich in enzymes involved in glycolysis, lipid and drug metabolism.

  Zone 2, i.e. the intermediate zone, which is present in between zone 1 and 3 is moderately well oxygenated. It contains a mixed complement of enzymes.

HEPATIC CIRCULATION

Liver receives about 1500 ml blood/min from two sources:

Hepatic artery, which is a branch of coeliac trunk supplies about 20 to 25% (300 to 400 ml/min) of total blood which caters to metabolic requirement of the liver tissue.

Portal vein, which collects blood from the mesenteric and splenic vascular bed, supplies about 75 to 80% (1100-1200 ml/min) of the total blood.

Hepatic vein. The hepatic and portal streams of blood meet in the sinusoids. The various substances produced by liver cells, the waste products and CO_2 are discharged into the sinusoids. The sinusoids drain into the central vein of the lobule. The central veins from different lobules unite to form bigger veins. These veins ultimately form the right and left hepatic veins which open into the inferior vena cava.

For details about the hepatic circulation and oxgen consumption see page 382.

is essential for energy production, and their conversion into carbohydrates or fats.
- Liver is the main site of *urea formation.*
- Liver is the main site for formation of all non-essential amino acids by transamination of ketoacids.
- Albumin is solely resynthesized in liver and also to some extent α- and ß-globulins.

III. Detoxicating and protective functions
- Kupffer cells efficiently remove bacteria and other foreign bodies from portal circulation. This is the blood cleansing action of liver.
- Liver detoxifies certain drugs by either oxidation, or hydrolysis, or reduction or conjugation, and excretes out through bile.

IV. Storage functions
Liver stores glucose (in the form of glycogen), vitamin B_{12}, and vitamin A.
- Liver acts as a blood iron buffer and iron storage medium. It stores 60% of excess of iron mainly in the form of ferritin and partly as haemosiderin.

V. Excretory functions
Certain exogenous dyes like bromsulphthalein (BSP) and rose bengal dye are exclusively excreted through liver cells.

VI. Synthesis function
Liver is the site for synthesis of:
- *Plasma proteins*, especially albumin and to some extent α- and β- globulins.
- *Some blood coagulation factors*. Liver cells are responsible for conversion of pre-prothrombin (inactive) to active prothrombin in the presence of vitamin K. It also produces other clotting factors such as fibrinogen (I), factors V, VII, IX and X.
- *Enzymes*, such as alkaline phosphatase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum isocitrate dehydrogenase (SICD).
- *Urea.* Liver removes ammonia from the body to synthesize urea.
- *Cholesterol.* It is synthesized from the active acetate.

VII. Miscellaneous functions
- *Reservoir of blood.* Liver acts as reservoir of blood and it stores about 650 ml of blood. Also helps in regulation of blood volume.
- *Erythropoiesis.* Liver is an important site of erythropoiesis in fetal life.
- *Hormone metabolism.* Liver causes:
  - *Inactivation* of some hormones such as insulin, glucagon and vasopressin.
  - *Reduction and conjugation* of adrenal and gonadal steroid hormones such as cortisol, aldosterone, oestrogen and testosterone.
  - *Conversion of thyroid hormone,* i.e. tetra-iodothyronine (T_4) into tri-iodothyronine (T_3)
- *Destruction of RBCs*, also occurs in liver.
- *Thermal regulation.* Liver also helps in thermo-regulation, as it produces large amount of heat.

BILE AND GALL BLADDER

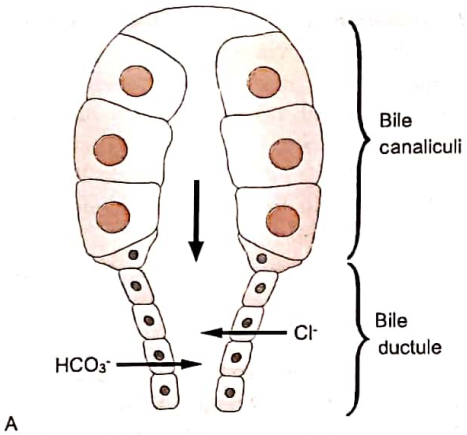
GENERAL CONSIDERATIONS
- Bile is a digestive juice, formed continuously in the liver by the hepatic cells (hepatocytes), and by epithelial cells lining the bile ducts (ductal cells).
- It is poured into the bile canaliculi from where it ultimately goes to common hepatic duct which join with cystic duct to form common bile duct. During interdigestive period when the sphincter of Oddi is closed, the bile is directed via cystic duct to the gall bladder, where it is stored and concentrated.
- During meals, the sphincter of Oddi is relaxed, and when food reaches the duodenum, there occurs release of CCK which causes contraction of gall bladder. Then the bile is released into the duodenum along with the pancreatic juice through the common opening ampulla of Vater.

FORMATION AND COMPOSITION OF BILE
The bile is formed by the hepatocytes and ductal cells lining the hepatic ducts. The hepatocytes, one surface of which is adjacent to the blood sinusoids and other to the biliary canaliculi, pick up some constituents of bile from the blood (e.g. *bile pigments*), synthesize some constituents (e.g. *bile salts*), and secrete a mixture into the biliary canaliculi. Ductular cells contribute HCO^-_3 and Cl^- to the mixture giving rise to *hepatic bile* (Fig. 7.4-9).

The bile so formed is an alkaline juice comprised of:
- Water and solids,
- Solids include organic and inorganic substances,
- Organic substances are bile salts, bile pigments, cholesterol, lecithin, fatty acids and enzyme alkaline phosphatase,
- Inorganic substances are Na^+, K^+, Ca^{2+}, HCO^-_3 and Cl^-.

Since the bile is concentrated in the gall bladder, so the concentration of its ingredients in the liver bile and gall bladder bile is bound to differ as shown in Table 7.4-2.

Salient features of the some of the ingredients of bile are described here:



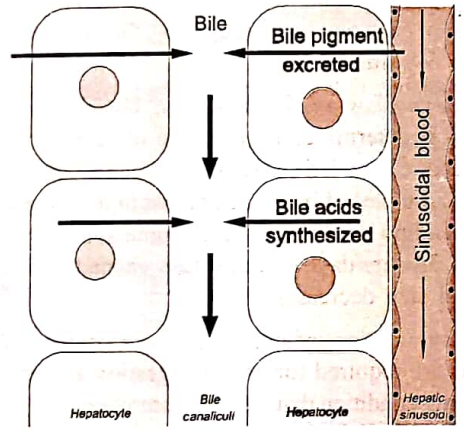


Fig. 7.4-9. Mechanism of bile formation: A, secretion by hepatocytes and ductal cells; and B, bile pigments picked up from blood sinusoids are excreted while bile salts are synthesized and secreted by hepatocytes.

Table 7.4-2 : Liver bile versus gall bladder bile

Properties and composition	Liver bile	Gall bladder bile
• pH	8 to 8.6	7 to 7.6
• Specific gravity	1010-1011	1026-1032
• Water	97.5%	87.5%
• Solids	2.5%	12.5%
Organic substances		
• Bile salts	1.10 gm%	8.0 gm%
• Bile pigments	0.20 gm%	1.0 gm%
• Cholesterol	0.10 gm%	0.5 gm%
• Fatty acid	0.15 gm%	0.5 gm%
• Fat	0.10 gm%	0 gm%
• Lecithin	0.1 gm%	0.8 gm%
• Mucin	Absent	Present
Inorganic substances	0.75 gm%	8.7 gm%

1. Bile salts

Formation of bile salts

Bile salts are sodium and potassium salts of bile acids conjugated with either taurine or glycine. Bile acids are of two types: primary and secondary. Steps in the formation of bile salts (Fig. 7.4-10) are:

- *Primary bile acids* are cholic acid and chenodeoxycholic acid. These are synthesized by hepatocytes from cholesterol.
- *Secondary bile acids*, are deoxycholic acid and lithocholic acid. These are formed from the primary bile acids in the colon by the action of intestinal bacteria.
- *The conjugation of bile acids*. In the liver the bile acids are conjugated with either glycine (an amino acid) or taurine (an amino acid derivative) forming the conjugated bile acids.
- The conjugated bile acids namely glycocholic acid and taurocholic acid form bile salts in combination with sodium or potassium.

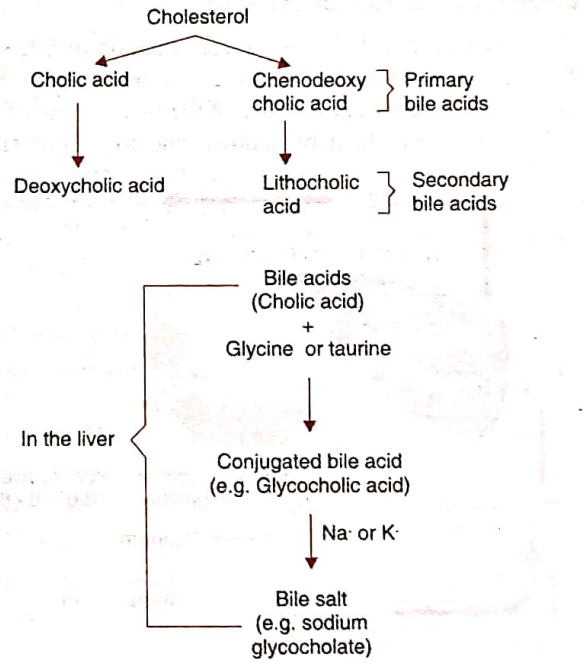


Fig.7.4-10. Formation of bile salts from the bile acids.

Functions of bile salts

Bile salts help in digestion as well as absorption of fat by their following actions:

- *Emulsification of fat*, i.e. breaking of large fat drops into smaller droplets and their stabilization is caused by the bile salts because of their power of lowering surface tension. The emulsification is a prerequisite for action of pancreatic lipase, which is water soluble and

acts only on the surface of a lipid droplet.

- *Acceleration of action of pancreatic lipase* occurs in the presence of bile salts due to binding of colipase for the lipase.
- *Micelle formation.* The bile salts combine with the products of hydrolysis of triglycerides to form *small water soluble cylindrical disc-shaped particles called* micelle, which are transported to the brush border of the epithelial cells for absorption.
- *Absorption of fat soluble vitamins* (A, D, E and K) is aided by the bile salts by forming complexes more soluble in water (hydrotrophic action).
- *Choleretic action*, i.e. they stimulate liver to secrete bile (as long as bile salts are absorbed) and then make more bile salts available for fat digestion.
- *Cholesterol is kept in soluble form* in the gall bladder bile by the bile salts. This property of bile salts prevents formation of gall stone.
- *Intestinal motility* is stimulated by bile salts. This action of bile salts help in defaecation (laxative action).

Enterohepatic circulation of bile salts

Enterohepatic circulation is the recirculation of bile salts from the liver to small intestine and back again. This circulation is necessary because of the *limited pool of bile salts available* to help breakdown and to absorb fat.

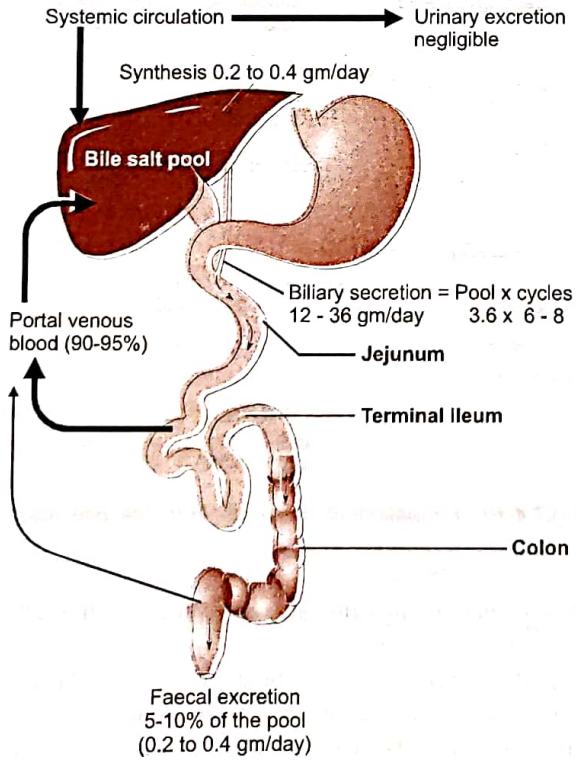


Fig. 7.4-11. Enterohepatic circulation of bile salts.

Path of circulation (Fig. 7.4-11). Bile salts travel from the liver to duodenum via the common bile duct.

- When the bile salts reach *terminal ileum*, 90 to 95% of bile salts are reabsorbed into the portal circulation. It is important to note that no absorption of bile salts occurs in the duodenum and jejunum. The liver then extracts the bile salts from the portal blood and secretes them once again into the bile.
- The remaining 5-10% of bile salts are excreted into the faeces.

Circulating pool. The total circulating pool of bile salts (consisting of salts of primary and secondary bile acids) is approximately 3.6 gm. About 4-8 gm of bile salts are required (more if the meal is high in fat) for digestion of fats during each meal; thus the total content of bile salts in the body (3.6 gm), most circulate twice during the digestion of each meal. Consequently, the bile salts usually circulate 6-8 times daily.

Bile salt synthesis and replacement. The rate of bile salt synthesis is determined by the rate of return to liver by enterohepatic circulation. Usually only 0.2 to 0.4 gm (5 to 10% of 3.6 gm) of bile salts are lost in the faeces, which are replaced by synthesis. The maximal synthesis rate can go up to 3-6 gm/day. If faecal loss exceed this rate, the total pool size decreases.

Clinical implications of enterohepatic circulation. Because bile salts are required for proper digestion and absorption of fats, only condition that disrupts enterohepatic circulation (e.g. ileal resection or small intestinal diseases such as sprue or Crohn's disease) leads to decreased bile salt pool and malabsorption of fat and fat soluble vitamins. The clinical manifestations of such conditions are:

- Steatorrhoea, i.e. increased fat content in the stools,
- Nutritional deficiency due to malabsorption,
- Watery diarrhoea because the bile salts which inhibit water and sodium absorption from the colon are decreased due to excessive loss in stools.

2. Bile pigments

- The two principal bile pigments, *bilirubin* and *biliverdin* are the other major constituents of bile which have no digestive function.
- Bile pigments are metabolites of haemoglobin formed in the liver.
- The hepatic cells extract bilirubin and biliverdin from the blood, conjugate them with glucuronic acid and transfer them into the bile canaliculi by an active transport mechanism (Fig. 7.4-12). They are responsible for golden yellow colour of bile.
- Intestinal bacteria metabolize bilirubin further to urobilinogen, which is responsible for the brown colour

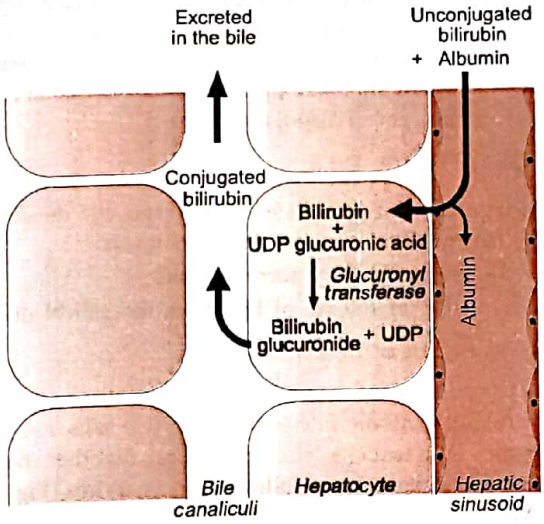


Fig. 7.4-12. Bile pigment metabolism in the hepatocyte.

of stools.

- Hepatocellular dysfunction leading to failure of bilirubin passages causes accumulation of bile pigments in the blood producing hepatic or post-hepatic jaundice, respectively.

Formation and circulation of bile pigments and jaundice are described on page 160.

3. Phospholipids

- The phospholipids (primarily lecithins) are, after bile salts, the most abundant organic compound in bile.
- Phospholipids, which are normally insoluble in water, are solubilized by the bile salt micelles.
- Micelles are able to solubilize other lipids more effectively when they are composed of bile salts and phospholipids than when they are composed of bile salts alone.

4. Cholesterol

- Cholesterol is an other important constituent of bile that does not have digestive function. Its presence in the bile seems to be a byproduct of bile salt synthesis in the hepatic cells. Normal biliary content of cholesterol is about 100 mg% (60 to 170 mg%) as compared to 150-240 mg% in blood.
- Cholesterol is essentially insoluble in water and thus must be solubilized by bile salt micelles before it can be secreted in the bile.
- Biliary secretion of cholesterol is important because it is one of the few ways in which cholesterol stores can be regulated.
- Biliary cholesterol forms an important component of gall stones (large sand) like particles found in the gall bladder of some patients.

5. Electrolytes

- Biliary content of inorganic substances is about 0.75 gm%.
- The cations Na^+, K^+, and Ca^{2+} are all present in concentration about 20% greater than in the plasma.
- Two major anions are Cl^- and HCO^-_3, Cl^- is present in concentrations lesser than in plasma while HCO^-_3 is far greater than in plasma, which makes the bile juice considerably alkaline. Further, HCO^-_3 concentration increases with an increased rate of bile secretion. Intravenous administration of acetazolamide (in high doses), decreases HCO^-_3 concentration of bile, thereby decreases pH from 8.6 to 7.4.

FUNCTIONS OF GALL BLADDER

Gall bladder is a thin walled sac-like structure with a storage capacity of about 50 ml. It is not essential for life. Removal of gall bladder (cholecystectomy) in patients suffering from dysfunction of gall bladder not result in any major disadvantages. Functions of gall bladder are :

1. Storage of bile. The bile secreted during interdigestive period is stored in the gall bladder. The gall bladder, typically stores 30-50 ml of bile. During meals, the gall bladder contracts and releases its contents into the duodenum.

2. Concentration of bile. The mucosa of gall bladder is extensively folded and can actively absorb fluid and electrolytes. In this way, the gall bladder bile, in comparison to liver bile (also see page 631).

- Becomes thicker, viscous and darker in colour.
- Water content is decreased (from 97 to 87.5%).
- All organic constituents which are not absorbed become 5-6 times concentrated.
- Cl^- and HCO^-_3 ions decrease by 5-6 times (due to active absorption).
- Ca^{2+} and K^+ which are not absorbed increased by 2 times.

3. Effect on the pH of bile. In the gall bladder, alkalinity of the stored bile is reduced due to rapid absorption of HCO^-_3 (mainly), Na^+ and Cl^-. The pH of bile is decreased from 8-8.6 to 7-7.6.

4. Secretion of mucus. Gall bladder secretes mucin which is added to the bile stored in it. The mucin acts as a lubricant in the intestine for the chyme.

5. Regulates equalization of pressure in biliary system. Due to continuous absorption of water from the stored bile the gall bladder regulates equalization of pressure in the biliary system. This fact can be understood by following observations:

- When both the bile duct and cystic duct are clamped, the pressure in the biliary system rises to above 30 cm

of bile in 30 minutes, and bile secretion is stopped.

- When the bile duct is clamped alone, water is continuously reabosrbed in the gall bladder, and the pressure in the biliary system rises to only 10 cm of bile in several hours. Thus, gall bladder prevents the rise of pressure in biliary system.

Control of gall bladder functioning See page 635.

Effects of cholecystectomy

As mentioned earlier, bile, not the gall bladder is essential for digestion and absorption of fats. After removal of gall bladder (cholecystectomy), bile empties slowly but continuously into the intestine, allowing digestion of fats sufficient to maintain good health and nutrition. Only high-fat meals need to be avoided.

- Bile ducts become dilated to accommodate some of the bile which is continuously secreted by liver.

FUNCTIONS OF BILE

Functions subserved by the bile poured into the duodenum are because of its constituents (mainly bile salts) which have already been discussed. However, they are compiled and summarized once again:

1. *Digestive function.* Bile salts help in digestion of fats by *emulsifying fat drops* (see page 663).
2. *Absorptive functions.* Bile salts help in absorption of fats (by micelle formation) and fat soluble vitamins (see page 664).
3. *Excretory function.* Bile pigments are the major excretory products of the bile. The other substances excreted in bile are, heavy metals (e.g. copper and iron), some toxins, some bacteria (e.g. typhoid bacteria), cholesterol, lecithin and alkaline phosphatase.
4. *Laxative action.* Bile salts increase the gastrointestinal motility and act as laxative.
5. *Protective action.* Bile is a natural detergent. So, it inhibits the growth of certain bacteria in the lumen of intestine.
6. *Choleretic action,* i.e. bile salts stimulate the liver to secrete bile.
7. *Maintenance of pH of GIT.* Being highly alkaline the bile juice neutralizes the gastric HCI present in the chyme entering the small intestine. Thus, an optimum pH is maintained for the action of digestive enzymes.
8. *Prevention of gall stone formation.* Bile salts keep the cholesterol and lecithin in solution and thus prevents the formation of gall stones. In the absence of bile salts the cholesterol precipitates along with lecithin and may form gall stones.
9. *Lubricating function.* The mucin secreted by gall bladder mucosa into the bile lubricates the chyme in the intestine.
10. *Cholagogue function.* Cholagogue is an agent, which increases the release of bile from gall bladder into the intestine. The bile salts perform this function indirectly. The bile salts stimulate the secretion of hormone CCK, which has got cholagogue action.

REGULATION OF BILE

The regulation of bile juice released into the duodenum after the meals is performed at two levels:

- Regulation of biliary secretion, and
- Regulation of release of bile from the gall bladder.

A. Regulation of biliary secretion

The secretion of aqueous component (water and electrolytes) and the bile (containing bile salts and other organic substances), though occur together but is controlled separately by following mechanisms (Fig. 7.4-13A):

- Regulation of bile-independent fraction of biliary secretion, and
- Regulation of bile-dependent fraction of biliary secretion.

I. *Regulation of bile-independent fraction of biliary secretion.* The bile-independent fraction of biliary secretion refers to the amount of *fluid containing water and electrolytes*. Secretion of this fraction of the bile juice is (similar to the fluid secreted by ductal cells of pancreas) controlled by secretin and vagal stimulation.

- *Secretin* is a hormone secreted by S-cells of duodenum and jejunum in response to stimulation of acidic chyme (for details see page 624). It acts on the ductal cells of hepatic ducts (Fig. 7.4-13.A) via cyclic AMP, second messenger and produces large amount of watery fluid with high concentration of HCO^-_3.
- *Vagovagal reflex* initiated during intestinal phase of digestion also affects the ductal secretion by potentiating the effects of secretion through the acetylcholine.

Note. The agents (e.g. secretin and acetylcholine) which cause secretion of bile from liver with more amount of water and less amount of solids are called hydrocholeretics.

II. *Regulation of bile-dependent fraction of biliary secretion.* The bile-dependent fraction of biliary secretion refers to the quantity of bile salts secreted by the liver. It depends upon following factors (Fig. 7.4-13):

- The amount of bile salts secreted by the hepatocytes is directly proportional to the *amount of bile salts reabsorbed* by them from portal circulation. As the bile salts are recycled in the enterohepatic circulation, they maintain high level of bile secretion during digestive period. The secretion of bile increases about 1 hour after a meal (when the gastric emptying starts). The maximum rate of bile secretion is achieved 3-5 hours

7.5 Physiological Activities in Small Intestine

FUNCTIONAL ANATOMY

GROSS ANATOMICAL CONSIDERATIONS

The small intestine is convoluted tube which extends from the pylorus to the ileocaecal valve, where it joins with caecum, the first part of large intestine. It is about 6-7 metre in length and its diameter gradually diminishes from its commencement to its termination. It is divided into three parts: the duodenum, the jejunum and the ileum (see Fig. 7.1-1.).

Duodenum. The first and *shortest* part (25 cm long) of the small intestine is also the *widest* and most fixed part. It is C-shaped and for descriptive purposes is divided into four parts: superior (Ist) part, descending (2nd) part, horizontal (3rd) part, and ascending (4th part). Superior part of duodenum is also called *duodenal cap* or bulb. It is the region which is struck by acidic gastric contents when they pass through pylorus and is a *common site for peptic ulcer*. The bile and pancreatic ducts open by a common hepatopancreatic ampulla of Vater on the posteromedial wall of descending (2nd) part of duodenum. Ligament of Treitz demarcates the continuation of duodenum with jejunum.

Jejunum and ileum. Jejunum and ileum form respectively, the proximal 2/5th and distal 3/5th of the remaining part of small intestine. There is no sharp demarcation between jejunum and ileum. The inner mucosal surfaces of jejunum and ileum, however, can be differentiated from each other.

STRUCTURAL CHARACTERISTICS OF SMALL INTESTINE

Histologically the wall of small intestine is made up of 4 layers, which from within to outwards consist of: mucosa, submucosa, muscle coat, and serosa (for details see page 583).

Characteristic features of mucous membrane of small intestine

Characteristic features of mucous membrane of small intestine need special emphasis.

Although the small intestine is about 6 metre long, it has an absorptive area of over 250 square metres. This larger surface is created by:

- Numerous folds of the intestinal mucosa *plicae circulares* (Fig. 7.5-1),
- Densely packed villi, which line the entire mucosal surface,
- *Microvilli*, which protrude from the surface of intestinal cells, and the presence of numerous depression (crypts of Lieberkuhn) that invade the lamina propria.

Plica circulares

The mucosal surface shows numerous circular folds (*plicae circulares* or valvulae conniventes) which are

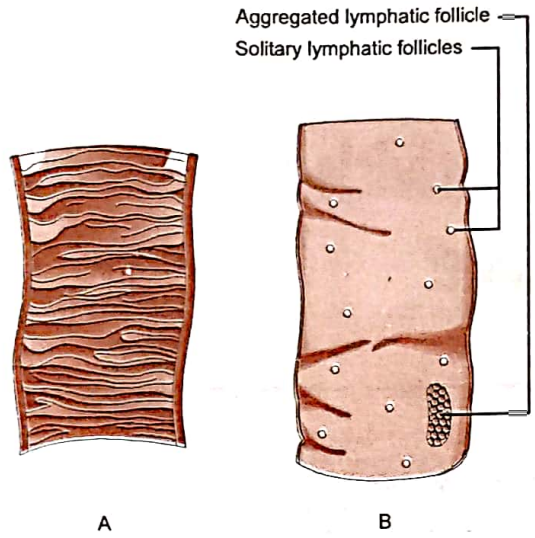


Fig. 7.5-1. The mucosal surface of jejunum (A) and ileum (B).

absent in first 2 inches of duodenum but are larger, more numerous, and closely set in rest of the duodenum and jejunum, whereas in the upper part of ileum they are smaller and more widely separated and in the lower part they are absent (Fig. 7.5-1). Unlike the folds in stomach, the plicae circulares are permanent and do not obliterate when intestine is distended. Each fold is made up of all layers of the mucosa (lining epithelium, lamina propria, and muscularis mucosa). The submucosa also extends into the fold. The circular folds serve following functions:

- Increase surface area for absorption, and also slow down the passage of contents through small intestine which facilitate absorption.

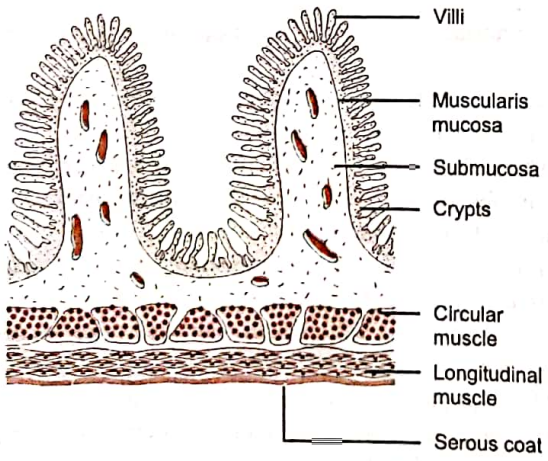


Fig. 7.5-2. Longitudinal section of small intestine showing plica circulares and villi.

Villi

Villi are finger-like projections of mucous membrane seen throughout the length of small intestine (Fig. 7.5-2).

Total number of villi is about 5 million and they are distributed about 20-40 villi per square millimetre. Each villus is about 0.5 to 1 mm long.

Structure. Each villus is covered by a single layer of columnar epithelial cells called enterocytes. The core of each villus contains (Fig. 7.5-3):

- An arteriole and venule with their communicating capillary plexus; the venules of the villi which carry absorbed nutrients ultimately drain into the portal vein. Blind ended lymphatic vessel called lacteal which carry the absorbed fats to the thoracic duct, few smooth muscle fibres extending from the muscularis mucosa, and
- A fine network of nerves which has connections with submucosal and myenteric plexus.

Activity. During digestion and absorption, the villi contract quickly with an irregular rhythm and relax slowly. Their muscular fibres serve to pump the lymph from core of villi towards the submucosal lacteals.

The crypts of Lieberkuhn

The crypts of Lieberkuhn are single tubular intestinal

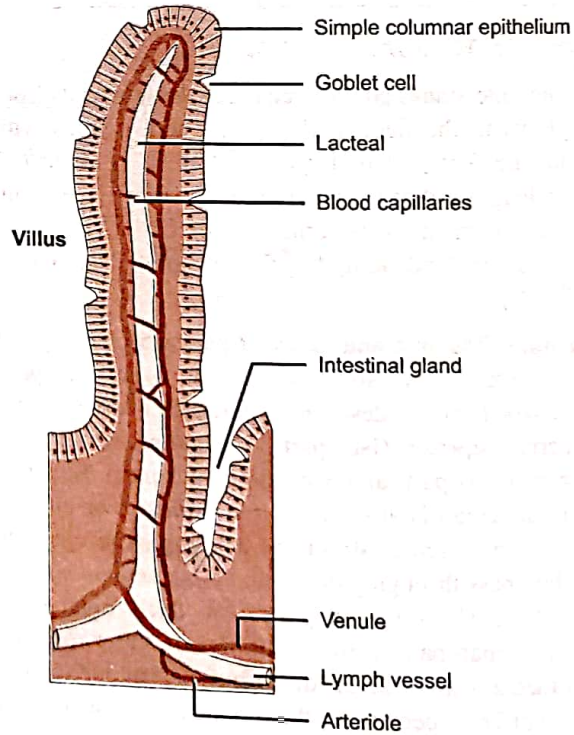


Fig. 7.5-3. Structure of an intestinal villus, crypts of Lieberkuhn and an enterocyte.

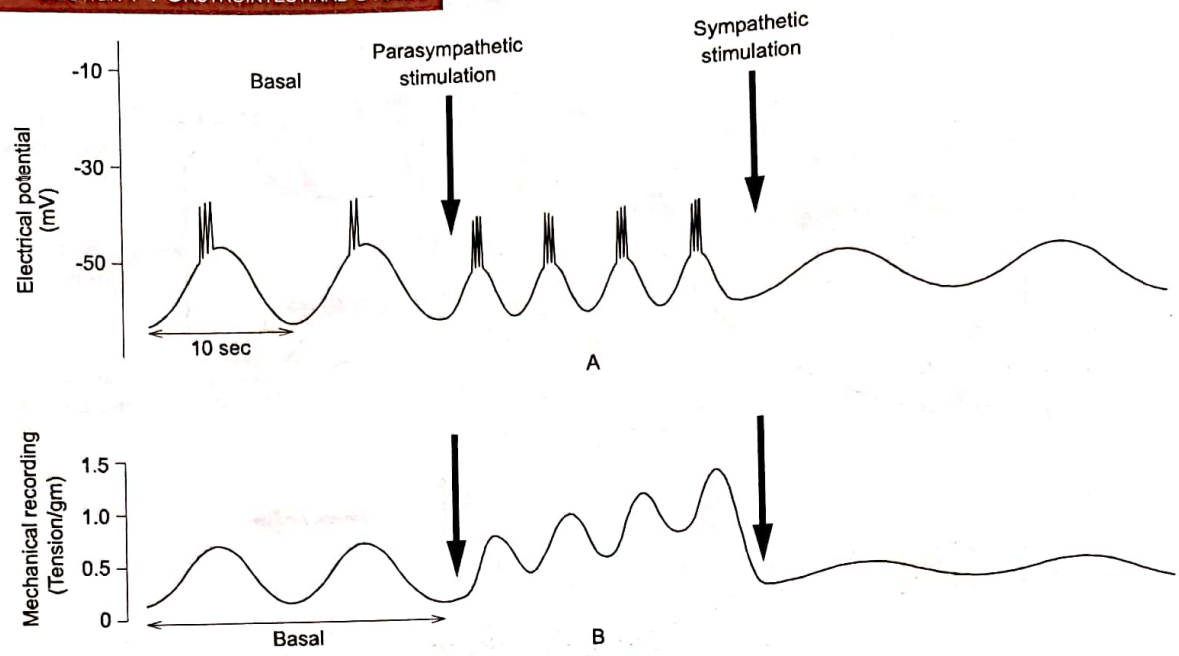


Fig. 7.5-8. Effect of parasympathetic stimulation and sympathetic stimulation on membrane potential (A) and mechanical activity (B) of small intestine.

Features. Movements of villi consist of alternate shortening and elongation of the villi caused by contraction and relaxation of the muscle.

Functions. Movements of villi help in emptying lymph from the central lacteal into the lymphatic system. The surface area of villi is increased during elongation. This helps in absorption of digested foodstuffs from the lumen of intestine.

Initiation. Local nervous reflexes, which occur in response to the presence of chyme in small intestine initiate the movements of villi. *Villikinin*, a hormone secreted from small intestinal mucosa is also believed to play an important role in increasing the movements of villi.

MOTILITY REFLEXES

1. Gastroileal reflex

- Gastroileal reflex refers to marked increase in the peristaltic contractions of ileum associated with relaxation of ileocaecal sphincter which occur immediately after the meals. As a result, the intestinal contents are delivered to the large intestine.
- This reflex is initiated by the distension of stomach by the food.
- The peristaltic contractions are caused by reflex stimulation of vagus and the relaxation of ileocaecal sphincter seems to be produced by the hormone gastrin.

2. Intestinointestinal reflex

Intestinointestinal reflex refers to relaxation of smooth muscles of the rest of the small intestine in response to overdistension of one segment of the intestine.

FUNCTIONS OF SMALL INTESTINE

After going through the physiology of intestinal secretion and intestinal motility, the functions of small intestine can be summarized as:

1. ***Mechanical functions.*** The mixing and propulsive movements of the small intestine help in thorough mixing of chyme with the digestive juices (pancreatic juice, bile juice and succus entericus) and propel it towards the large intestine.

2. ***Digestive functions*** of small intestine are carried out by the digestive enzymes present in the succus entericus (see page 641), pancreatic enzymes (see page 621) and bile (see page 630).

3. ***Absorptive function*** is accomplished by the huge surface area created by the presence of plicae circulares, villi and microvilli. The end products of digestion of carbohydrates, proteins and fats are absorbed through portal system or through the lymph. For details of absorption, see page 657.

4. *Hormonal functions.* The small intestine secretes certain hormones which exert their effect on the secretions and motility of gastrointestinal tract. These hormones include *enterogastrone secretin* (page 624), and *cholecystokinin* (page 625).

5. *Activator function.* The enzyme enterokinase secreted by small intestine activates trypsinogen into trypsin which in turn activates other enzymes.

6. *Protective function.* The mucus secreted into the succus entericus protects the intestinal wall from the gastric acid chyme.

7. *Hydrolytic function.* The aqueous component of the succus entericus provides water and thus helps in all the hydrolytic processes of enzymatic reactions of digestion of various food particles.

APPLIED ASPECTS

Paralytic ileus

Paralytic ileus or the adynamic ileus refers to a condition in which the intestinal motility is markedly decreased leading to retention of its contents (because the contents cannot be propelled into the colon). This produces irregular distension of the small intestine by pockets of gas and fluid.

Causes. Paralytic ileus may occur due to:

1. Direct inhibition of smooth muscles of small intestine due to handling of intestine:

- During intra-abdominal operations, and
- During trauma.

2. Reflex inhibition of smooth muscles of small intestine due to increased discharge of noradrenergic fibres in splanchnic nerves, as seen in irritation of peritoneum (in patients with peritonitis, and injury to peritoneum).

Intestinal obstruction

Causes. Obstruction of the lumen of small intestine may occur due to many causes, such as tumours, strictures and fibrotic bands in the abdomen.

Features. The intestinal obstruction is characterized by:

- *Intestinal colic*, i.e. severe abdominal pain. Pain is caused by peristaltic rush (intense peristaltic wave initiated due to irritation of intestinal mucosa at the site of obstruciton).
- *Distension of small intestine* with pockets of fluid and gas occur proximal to the site of obstruction.
- *Local ischaemia* of intestinal wall may occur due to increased intraluminal pressure.
- *Stimulation of visceral afferent* nerves by the increased intraluminal pressure may cause sweating, hypotension and severe vomiting.
- *When the obstruction is in the upper half of small intestine*, the antiperistaltic reflux causes intestinal juices to flow into the stomach, and these juices are vomitted along with the secretions of stomach. The person becomes severely dehydrated, but the loss of acids and bases may be approximately equal, so that little change occurs in acid-base balance.
- *When the obstruction is near the lower end of the small intestine*, it is possible to vomit more basic than acidic substances; in this case acidosis may result. In addition, after a few days of obstruction the vomitus becomes faecal in character.

7.6 Physiological Activities in Large Intestine

FUNCTIONAL ANATOMY
- Gross anatomical considerations
- Structural characteristics

LARGE INTESTINAL SECRETIONS AND BACTERIAL ACTIVITY
- Large intestinal secretions
- Intestinal bacterial activity

MOTILITY OF LARGE INTESTINE
- Haustral shuttling
- Peristalsis
- Mass movements
  - Gastrocolic reflex
  - Transit time in the gut

DEFAECATION
- Functional anatomy
- The act of defaecation
- Applied aspects of defaecation
- Faeces

FUNCTIONS OF LARGE INTESTINE

APPLIED ASPECTS
- Role of dietary fibres
- Disorders of large intestine motility

FUNCTIONAL ANATOMY

GROSS ANATOMICAL CONSIDERATIONS

Functional organization

The large intestine is a tube about 6 cm in diameter and 100 cm in length. It normally arches around and encloses the coils of small intestine and tends to be more fixed than the small intestine. It is divided into following parts (Fig. 7.6-1):

- *Caecum* is a blind ended sac into which opens the lower end of ileum. The ileocaecal junction is guarded by the ileocaecal valve which allows inflow but prevents backflow of intestinal contents.
- *Appendix* is worm-shaped tube that arises from the medial side of caecum which in human being is a vestigial organ.
- *Ascending colon* extends upward from the caecum along the right side of abdomen upto the liver. On reaching the liver it bends to the left, forming the right hepatic flexure.
- *Transverse colon* extends from the right hepatic flexure to the left splenic flexure. It forms a wide U-shaped curve.
- *Descending colon* extends from the left splenic flexure to the pelvic inlet below.
- *Sigmoid colon* begins at the pelvic inlet as continuation of the descending colon and joins the rectum in front of the sacrum.
- *Rectum* descends in front of the sacrum to leave the pelvis by piercing the pelvic floor. Here it becomes continuous with anal canal in the perineum.

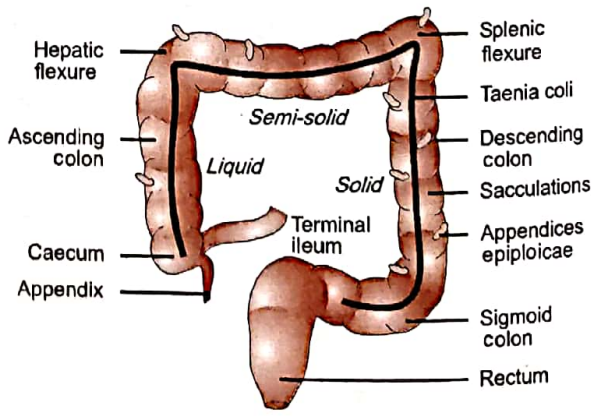


Fig. 7.6-1. *Functional organization of the large intestine and consistency of faecal contents in its different segments.*

- *Anal canal* opens to the exterior through the anus the opening which is guarded by two sphincters.

Ileocaecal valve

Structure. Ileocaecal valve functioning occurs due to invagination of ileum into the caecum at the ileocaecal junction and a very small ileal opening (only 2-3 mm in diameter),

Functions. The principal function of the ileocaecal valve is to prevent back flow of the faecal matter from the caecum into ileum. The valvular mechanism works in such a way that when the caecal pressure is increased the ileocaecal opening is closed.

Role of ileocaecal sphincter. Ileocaecal sphincter refers to thickened band of circular muscle coat of the terminal part of ileum just above the ileocaecal junction. The rhythmic contractions of ileocaecal sphincter leading to rhythmic opening and closing occurs after every 30 seconds after a meal. During every rhythmic opening small jet of ileal fluid (approximately 15 ml) escapes into the caecum. The ileocaecal sphincter slows down the emptying of ileal contents into the caecum and thus, helps in completion of the absorption of nutrients in the ileum.

Control. Gastrin produces relaxation and secretin causes contraction of ileocaecal sphincter. It is important to note that these hormones show opposite effects on cardiac sphincter.

STRUCTURAL CHARACTERISTICS

Histological structure of large intestines is similar to that described in general (see page 583) with following special characteristics. Mucosa of large intestine is characterized by:

- Absence of plica circulares and villi (seen in small intestine).
- It is thrown into folds opposite to the contractions seen in wall of large intestine which produce sacculations.
- A large number of simple tubular glands (crypts of Lieberkuhn) lined by simple columnar epithelial cells with large number of goblet cells which secrete mucus are the histological characteristics of mucosa of large intestine (Fig. 7.6-2). Epithelial cells contain no enzyme.
- The epithelium overlying solitary lymphatic follicles (in ascending colon, caecum and appendix) contains M-cells similar to those seen in small intestine.

Longitudinal layer of muscle coat of colon is unusual

- Most of the fibres in it are collected to form three thick bands, the taenia coli which can be seen through the serous layer (Fig. 7.6-1). A thin layer of longitudinal fibres is present in the intestines between the taenia.
- The taenia coli are shorter in length than other layers of the wall of colon. This results in the production of *sacculations* (also called *haustrations*) on the wall of colon.

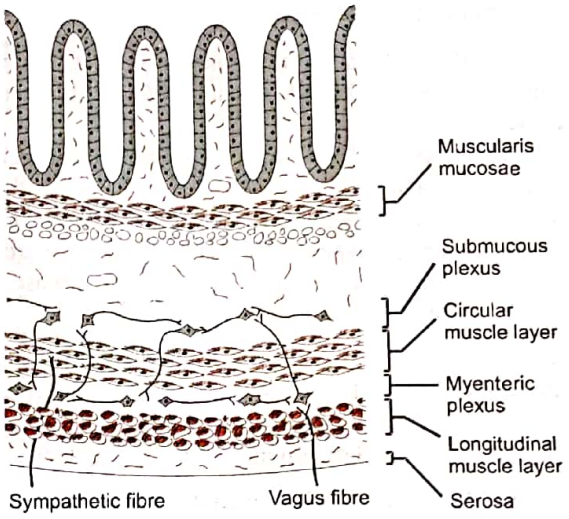


Fig. 7.6-2. Histological structure of the colon.

Serous layer is missing over the posterior aspect of the ascending and descending colon. At places small peritoneal bags of fat, called *appendices epiploicae*, project from the colonic serosa.

LARGE INTESTINAL SECRETIONS AND BACTERIAL ACTIVITY

LARGE INTESTINAL SECRETIONS

- The large intestinal secretions mainly comprise mucus secreted by the goblet cells which are in abundance among the epithelial cells of mucosa; and some water and lot of HCO^-_3 are secreted by glands of Lieberkuhn.
- The mucus lubricates the faecal matter and also protects the mucous membrane of large intestine by preventing the damage caused by mechanical injury or chemical substances.
- The alkaline nature (pH 8.0) of the mucoid secretions of the large intestine is due to the presence of HCO^-_3. It serves to neutralize the acids formed by bacterial action on the faecal matter.
- Large quantities of water and electrolytes are secreted by mucosa of large intestine only when it is intensely irritated.

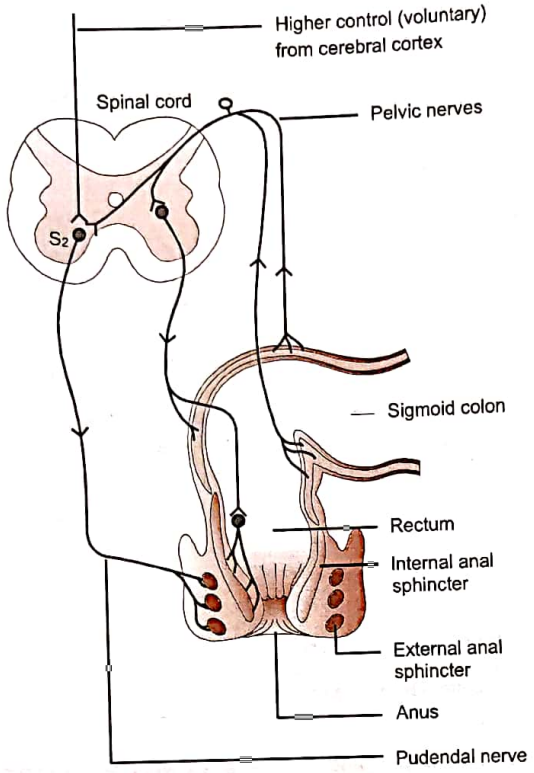


Fig. 7.6-4. Pathway of spinal defaecation reflex and its voluntary control.

contribute 25% to total faecal matter weight. These include: inorganic material, mostly calcium and phosphate, undigested plant fibres, epithelial cells, dead bacteria, constituents of intestinal secretions including bile pigments, fats and proteins. It is important to note that:

- *Proteins* in the stools are not of dietary origin but comes from bacteria and cellular debris.
- *Fats* in the stools come some from the dietary intake but most of it is also derived from desquamated epithelial cells and from bacterial synthesis. On an average fat intake of 100 gm/day 5-6 gm/day is normally lost in faeces. Stool fat content is increased in steatorrhoea.
- Since a large fraction of the faecal matter is of non-dietary origin, faeces during starvation though decreased in bulk but differ little in composition from those of normally fed persons.

pH of stools is slightly acidic (5-7) due to the organic acids formed from carbohydrates by colonic bacteria.

Brown colour of stools is due to the pigment *urobilin* which formed from oxidation of urobilinogen which is colourless. Urobilinogen is formed from bile pigments by the intestinal bacteria. Oxidation of residual urobilinogen in the stools accounts for the darkening of faeces which occurs upon standing in the air. When the bile fails to enter the intestine, stools become white (*acholic stools*), as seen in obstructive jaundice.

Odour of stools is due to the presence of substances like indole, skatole, mercaptans and hydrogen sulphide. These substances are formed by the action of colonic bacteria on the food.

FUNCTIONS OF LARGE INTESTINE

After going through the physiology of large intestine secretion and motility, the functions of large intestine can be summarized as:

1. ***Secretory functions.*** The large intestinal secretion mainly comprise mucin which helps to lubricate the faecal matter. The alkaline nature (pH 8) of the secretion serves to neutralize the acids formed by bacterial action on the faecal matter.

2. ***Synthesis functions.*** The bacterial flora of the large intestine synthesize folic acid, vitamin B_{12} and vitamin K.

3. ***Absorptive functions.*** Absorption of water and electrolytes is the chief function of proximal part of the colon. Organic substances like glucose, alcohol, and some drugs like anaesthetic agents, sedatives and steroids can also be absorbed in large intestine. The vitamin K and a number of B complex vitamins which are synthesized in colon by bacterial flora are also absorbed in the large intestine.

4. ***Excretory functions.*** Heavy metals like mercury, lead, bismuth and arsenic are excreted by large intestine through the faeces.

5. ***Storage function.*** After the absorption of nutrients, water and other substances, the unwanted substances form faeces. The faeces are stored in pelvic colon until they can be expelled by the process of defaecation.

APPLIED ASPECTS

ROLE OF DIETARY FIBRES

Physiological role of dietary fibres on intestinal food transit

Dietary fibres are constituted by the cellulose, hemicellulose and lignin components of the vegetable products in diet.

- In human beings, there is no appreciable digestion of the dietary fibres, at all. The ingested dietary fibres