Digestive System:

Esophagus, Stomach and Intestines

The gastrointestinal tract (GIT) or alimentary canal is a long muscular tube that begins at the oral cavity and ends in the anus. Different parts of the tract are specialised to perform different functions, and hence structural modifications are seen in various parts of the GIT.

The esophagus and anal canal are merely transport passages. The part of the alimentary canal from the stomach to the rectum is the proper digestive tract, responsible for digestion and absorption of food. Reabsorption of secreted fluids is an important function of the large intestine.

General Structure of GIT

The structure of the alimentary canal, from the esophagus up to the anal canal, shows several features that are common to all these parts. We shall consider these common features before examining the structure of individual parts of the canal.

The walls of the oral cavity and pharynx are partly bony, and partly muscular. From the upper end of the esophagus up to the lower end of the anal canal the alimentary canal has the form of a fibro muscular tube. The wall of the tube is made up of the following layers (from inner to outer side) (Fig. 16.1).

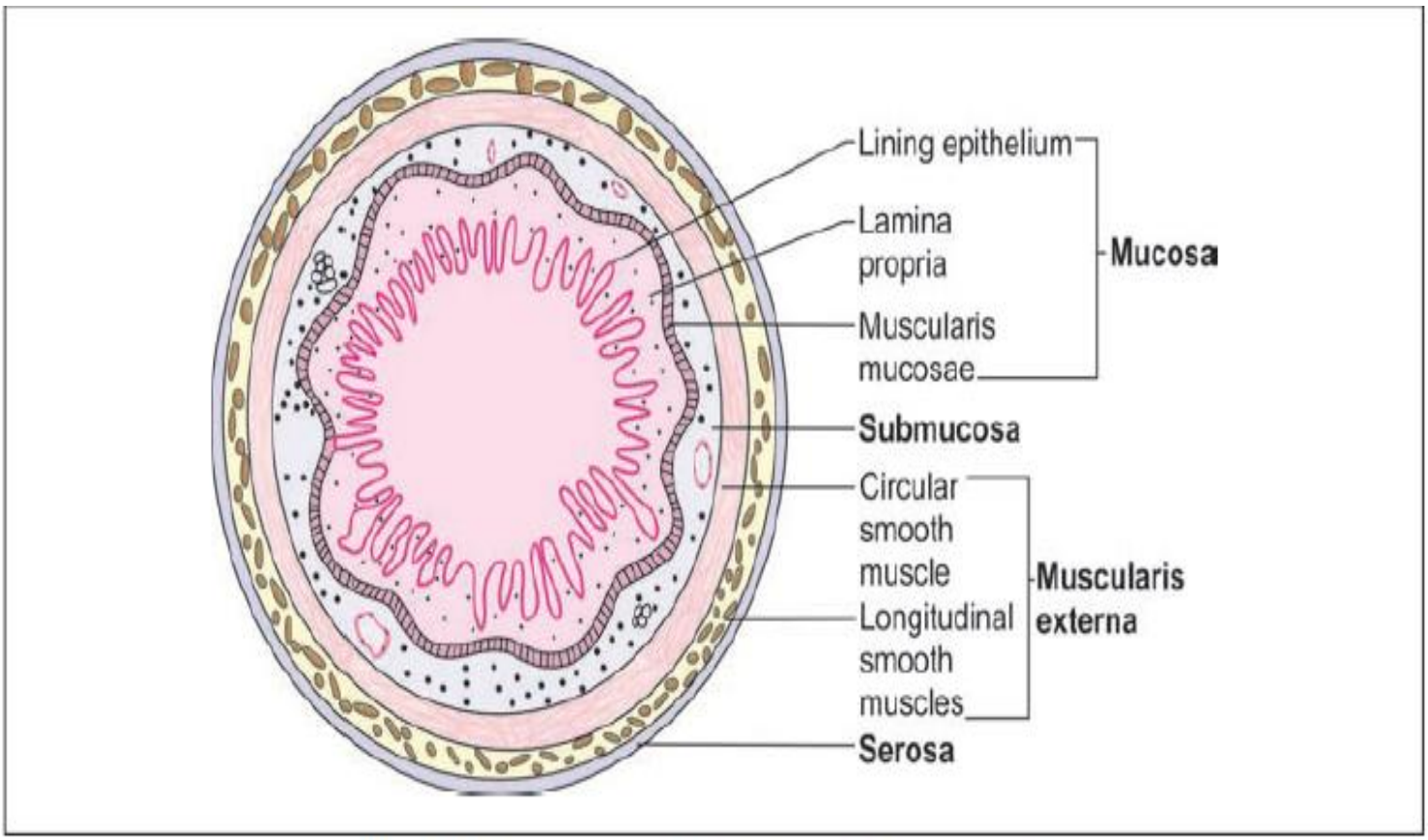


Fig. 16.1: Layers of the gut (Schematic representation)

1. The innermost layer is the ***mucous membrane*** that is made up of:
a. A lining epithelium
b. A layer of connective tissue, the ***lamina propria***, that supports the epithelium
c. A thin layer of smooth muscle called the ***muscularis mucosae***.
2. The mucous membrane rests on a layer of loose areolar tissue called the ***submucosa***.
3. The gut wall derives its main strength and form because of a thick layer of muscle (***muscularis externa***) that surrounds the submucosa.
4. Covering the muscularis externa there is a ***serous layer*** or (alternatively) an ***adventitial layer***.

Primarily, it is the mucosa in which changes are seen in the alimentary tract; the other layers remain almost the same.

The Mucosa

The Lining Epithelium

The lining epithelium is columnar all over the gut; except in the esophagus, and in the lower part of the anal canal, where it is stratified squamous. This stratified squamous epithelium has a protective function in these situations. The cells of the more typical columnar epithelium are either absorptive or secretory.

The epithelium of the gut presents an extensive absorptive surface. The factors contributing to the extent of the surface are as follows:

1. The ***considerable length*** of the alimentary canal, and specially that of the small intestine.
2. The presence of ***numerous folds*** involving the entire thickness of the mucous membrane. These folds can be seen by naked eye. The submucosa extends into the folds.
3. At numerous places the epithelium dips into the lamina propria forming ***crypts***.
4. In the ***small intestine*** the mucosa bears numerous finger-like processes that project into the lumen. These processes are called ***villi***. Each villus has a surface lining of epithelium and a core formed by an extension of the connective tissue of the lamina propria. The luminal surfaces of the epithelial cells bear numerous microvilli.

The epithelium of the gut also performs a very important secretory function. The secretory cells are arranged in the form of numerous glands as follows:

a. Some glands are unicellular, the secretory cells being scattered among the cells of the lining epithelium.
b. In many situations, the epithelium dips into the lamina propria forming simple tubular glands (These are the crypts referred to above).
c. In other situations (e.g., in the esophagus, duodenum) there are compound tubuloalveolar glands lying in the submucosa. They open into the lumen of the gut through ducts traversing the mucosa.

d. Finally, there are the pancreas and the liver that form distinct organs lying outside the gut wall. They pour their secretions into the lumen of the gut through large ducts (In this respect, these glands are similar to the salivary glands).

The Lamina Propria

The lamina propria is made up of collagen and reticular fibers embedded in a glycosaminoglycan matrix. Some fibroblasts, blood capillaries, lymph vessels, and nerves are seen in this layer. In the small intestine the lamina propria forms the core of each villus. It surrounds and supports glandular elements and the overlying epithelium.

Prominent aggregations of lymphoid tissue (as well as scattered lymphocytes) are present in the lamina propria. Some of this lymphoid tissue extends into the submucosa and is called as gut associated lymphoid tissue (GALT).

The Muscularis Mucosae

This is a thin layer of smooth muscle that separates the connective tissue of the lamina propria from the submucosa. It consists of an ***inner layer*** in which the muscle fibers are arranged ***circularly*** (around the lumen) and an ***outer layer*** in which the muscle fibers run ***longitudinally***. The muscularis mucosae extends into mucosal folds, but not into villi. Contractions of the muscularis mucosae are important for the local mixing of intestinal contents.

The Submucosa

This layer of loose areolar tissue connects the mucosa to the muscularis externa. Its looseness permits some mobility of the mucosa over the muscle. Numerous blood vessels, lymphatics and nerve fibres traverse the submucosa.

The Muscularis Externa

Over the greater part of the gut the muscularis externa consists of smooth muscle. ***The only exception is the upper part of the esophagus where this layer contains striated muscle fibers.*** Some striated muscle fibers are also closely associated with the wall of the anal canal.

The muscle layer consists (typically) of an ***inner layer of circularly arranged muscle fibers, and an outer longitudinal layer.*** Both layers really consist of spirally arranged fasciculi, the turns of the spiral being compact in the circular layer, and elongated in the longitudinal layer.

The arrangement of muscle fibers shows some variation from region to region. In the stomach an additional oblique layer is present. In the colon the longitudinal fibers are gathered to form prominent bundles called the ***taenia coli***.

Localized thickenings of circular muscle fibers form ***sphincters*** that can occlude the lumen of the gut. For example, the ***pyloric sphincter*** is present around the pyloric end of the stomach, and the ***internal anal sphincter*** surrounds the anal canal. A functional sphincter is seen at the junction of the esophagus with the stomach. A valvular arrangement at the ileocaecal junction (ileocaecal valve) prevents regurgitation of caecal contents into the ileum.

The Serous and Adventitial Layers

Covering the muscle coat, there is the serous layer which is the outermost layer of the alimentary canal. This layer is merely the visceral peritoneum that covers most parts of the gastrointestinal tract. In some places where a peritoneal covering is absent (e.g., over part of the oesophagus) the muscle coat is covered by an adventitia made up of connective tissue.

Nerve Plexuses

The gut is richly supplied with nerves. A number of nerve plexuses are present as follows:

1. The ***myenteric plexus*** (***of Auerbach***) lies between the circular and longitudinal coats of muscularis externa.
2. The ***submucosal plexus*** (***of Meissner***) lies in the submucosa (near its junction with the circular muscle layer).
3. A third plexus is present near the muscularis mucosae. The nerve fibers in these plexuses are both afferent and efferent. The efferent fibers supply smooth muscle and glands.

The Esophagus

The esophagus is a long muscular tube beginning at the end of cricoid cartilage and opens into the cardiac end of stomach. It conducts chewed food (bolus) and liquids to stomach.

Microscopic Features

The wall of esophagus has the usual four layers viz., mucosa, submucosa, muscularis externa and an external adventitia (Fig. 16.2 and Plate 16.1). The esophagus does not have a serous covering except over a short length near its lower end.

The Mucosa

a. The mucous membrane of the esophagus shows several longitudinal folds that disappear when the tube is distended.
b. The mucosa is lined by stratified squamous epithelium, which is normally not keratinized.
c. Occasional melanocytes and endocrine cells are present. A columnar epithelium, similar to that lining the cardiac end of the stomach, may extend for some distance into the abdominal part of the esophagus.
d. Finger-like processes (or papillae) of the connective tissue of the lamina propria project into the epithelial layer (just like dermal papillae). This helps to prevent separation of epithelium from underlying connective tissue.
e. At the upper and lower ends of the esophagus some tubuloalveolar mucous glands are present in the lamina propria.
f. The muscularis mucosae is absent or poorly developed in the upper part of the esophagus. It is distinct in the lower part of the esophagus, and is thickest near the esophagogastric

junction. It consists chiefly of longitudinal muscular fibers, but a few circular fibers are also present.

The Submucosa

The only special feature of the submucosa is the presence of compound tubuloalveolar mucous glands. Small aggregations of lymphoid tissue may be present in the submucosa, specially near the lower end. Some plasma cells and macrophages are also present.

The Muscularis Externa

The muscle layer consists of the usual circular and longitudinal layers. However, it is unusual in that the muscle fibers are partly striated and partly smooth. In the upper one-third of the esophagus the muscle fibers are entirely of the striated variety, while in the lower one third all the fibers are of the smooth variety. Both types of fibers are present in the middle one third of the esophagus.

Note: The circular muscle fibers present at the lower end of the esophagus could possibly act as a sphincter guarding the cardio-esophageal junction. However, the circular muscle is not thicker here than elsewhere in the esophagus, and its role as a sphincter is not generally accepted.

However, a ***physiological sphincter*** does appear to exist. The anatomical factors that could account for this sphincteric action are not agreed upon.

The Adventitia

The muscle layer of the esophagus is surrounded by dense fibrous tissue that forms an adventitial coat for the esophagus. The lowest part of the esophagus is intra-abdominal and has a covering of peritoneum.

Pathological Correlation

Achalasia (Cardio spasm): Achalasia of the esophagus is a neuromuscular dysfunction due to which the cardiac sphincter fails to relax during swallowing and results in progressive dysphagia and dilatation of the esophagus (mega-esophagus).

Barrett's Esophagus: This is a condition in which, following reflux esophagitis, stratified squamous epithelium of the lower esophagus is replaced by columnar epithelium (columnar metaplasia). The condition is seen more commonly in later age and is caused by factors producing gastro-esophageal reflux disease.

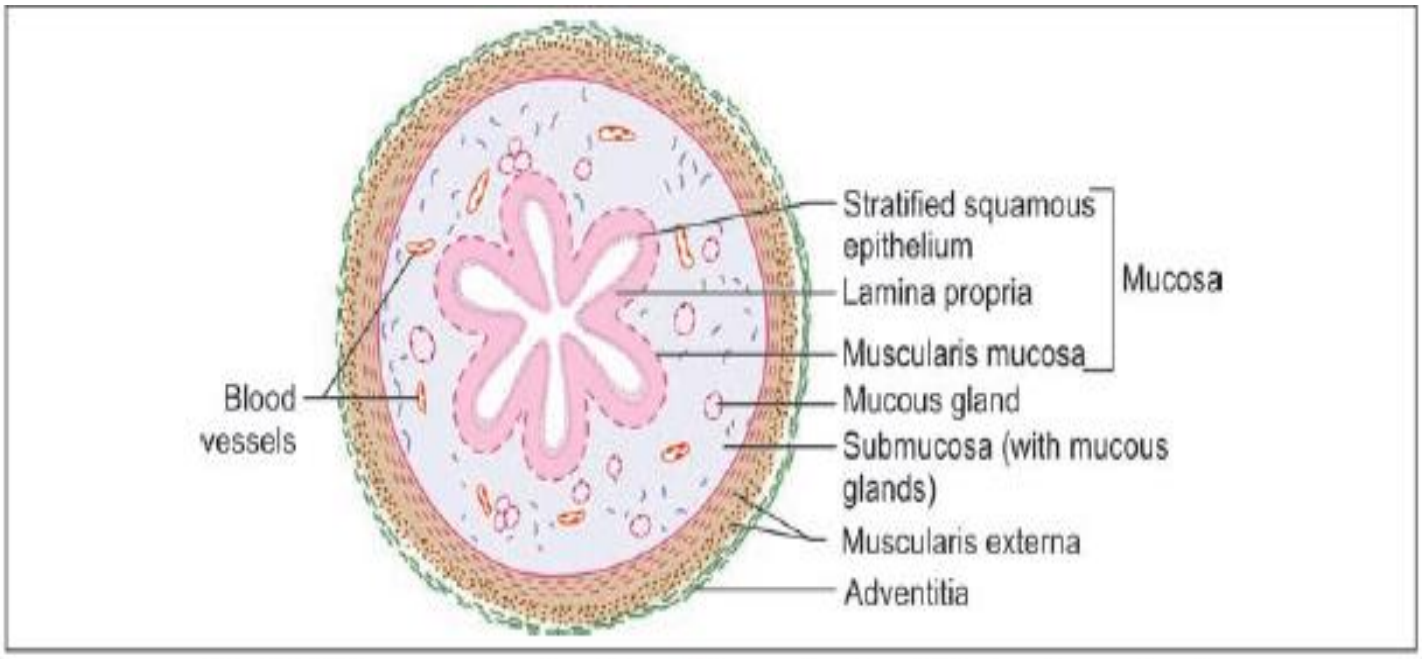
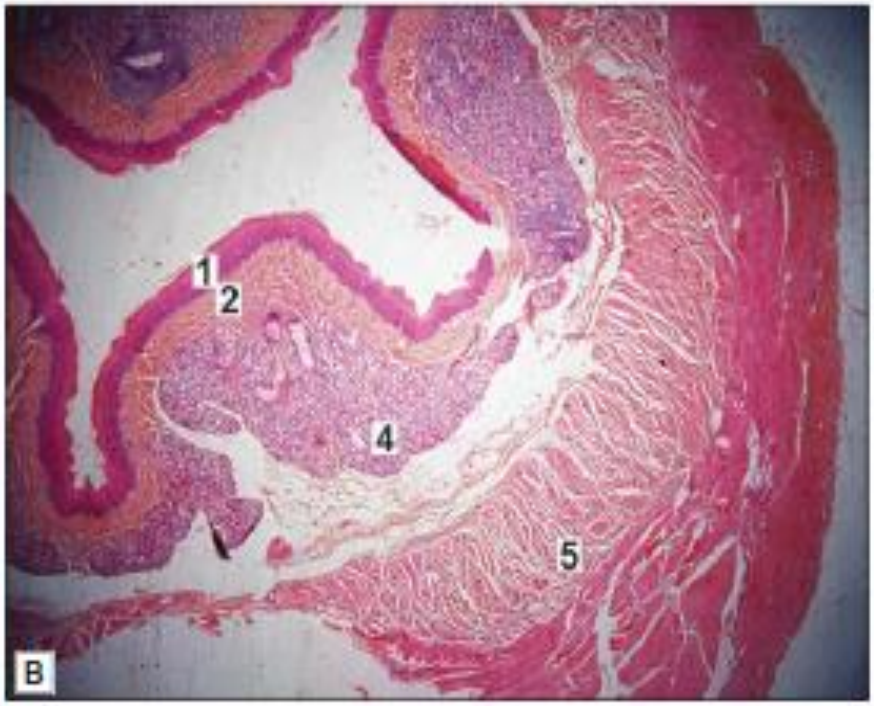


Fig. 16.2: Transverse section of oesophagus showing all the four layers of wall. The lumen of oesophagus is star shaped (Schematic representation)

Plate 16.1: Oesophagus



Oesophagus. A. As seen in drawing [to be provided by author]; B. Photomicrograph

In transverse section the oesophagus shows the following layers:

- Lining of non-keratinised stratified squamous epithelium
- The underlying connective tissue of the lamina propria
- The muscularis mucosae in which the muscle fibres are cut transversely
- The lining epithelium, lamina propria and muscularis mucosa collectively constitute the mucosa
- The submucosa having esophageal glands (mucous acini)
- The layer of circular muscle, and the layer of longitudinal muscle constituting the muscularis externa. In muscularis externa the muscle is of the striated variety in the upper one-third of the oesophagus, mixed in the middle one-third, and smooth in the lower one third.

Note: In the photomicrograph muscularis mucosa cannot be differentiated.

Key

1. Muscosa lined by stratified squamous epithelium
2. Lamina propria
3. Muscularis mucosa
4. Submucosa displaying mucous acini.
5. Muscularis externa
   a. Inner circular layer
   b. Outer circular layer
6. Adventitia

Ma. Mucous acini.

The Stomach

Stomach is a muscular bag that receives food bolus from esophagus. The food passes through the esophagus and enters the stomach where it is converted into a thick paste known as ***Chyme***. Anatomically, stomach is divided into four regions: ***Cardia, fundus, body and pylorus*** (Fig. 16.3).

Histologically fundus and body of stomach have a similar structure.

Microscopic Features

The wall of the stomach has the four basic layers a mucous membrane, a submucosa, a muscularis externa, and a serous layer. The mucous membrane and the muscularis externa have some special features that are described below.

The Mucous Membrane

As seen with the naked eye the mucous membrane shows numerous folds (or ***rugae***) that disappear when the stomach is distended.

Lining Epithelium

The lining epithelium is columnar and mucous secreting. The apical parts of the lining cells are filled by mucin that is usually removed during processing of tissues so that the cells look empty (or vacuolated). Mucous secreted by cells of the lining epithelium protects the gastric mucosa against acid and enzymes produced by the mucosa itself. (The mucous cells lining the surface are also believed to produce blood group factors).

At numerous places the lining epithelium dips into the lamina propria to form the walls of depressions called ***Gastric pits*** (Fig. 16.4). These pits extend for a variable distance into the thickness of the mucosa. Deep to the gastric pits the mucous membrane is packed with numerous ***gastric glands***. These glands are of three types: main gastric, cardiac and pyloric (depending on their presence in different regions of stomach).

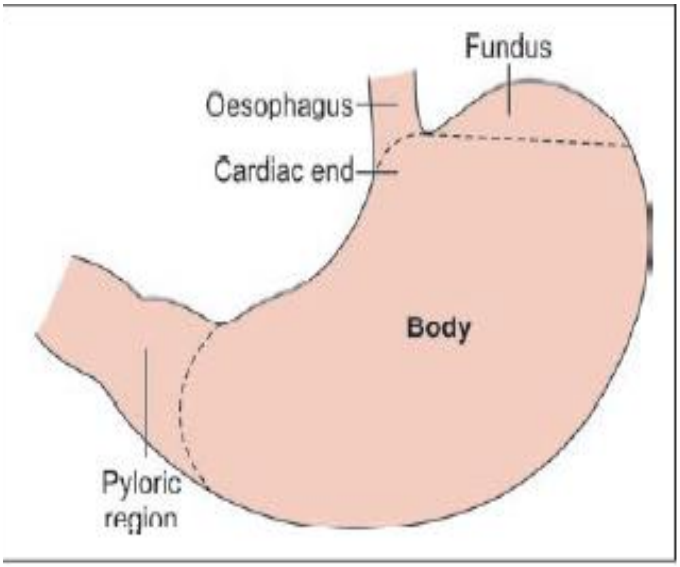


Fig. 16.3: Anatomical regions of stomach (Schematic representation)

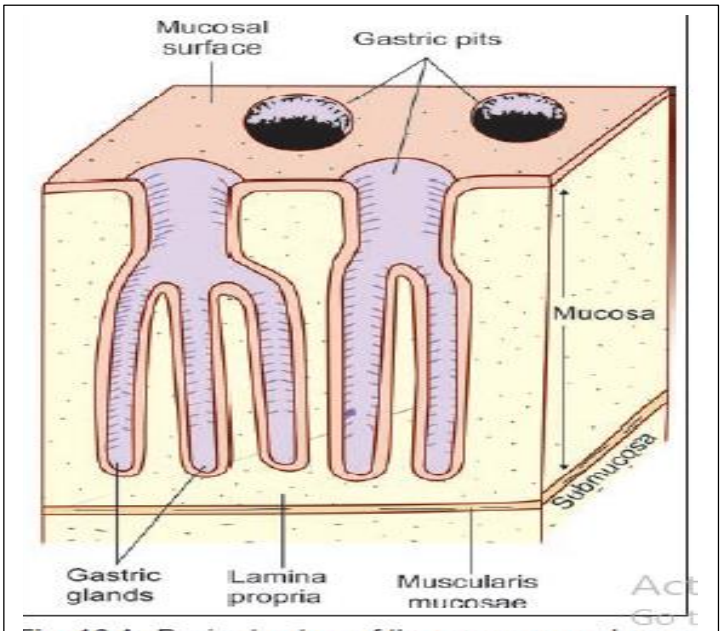


Fig. 16.4: Basic structure of the mucous membrane of the stomach (Schematic representation)

The Lamina Propria

As the mucous membrane of the stomach is packed with glands, the connective tissue of the lamina propria is, therefore, scanty. It contains the usual connective tissue cells. Occasional aggregations of lymphoid tissue are present in it.

The Muscularis Mucosae

The muscularis mucosae of the stomach is well developed. Apart from the usual circular (inner) and longitudinal (outer) layers an additional circular layer may be present outside the longitudinal layer.

The Muscularis Externa

The muscularis externa of the stomach is well developed. Three layers, oblique, circular and longitudinal (from inside out). The appearance of the layers in sections is, however, highly variable depending upon the part of the stomach sectioned. The circular fibers are greatly thickened at the pylorus where they form the pyloric sphincter. There is no corresponding thickening at the cardiac end. Salient features of cardiac, fundus and pyloric part of stomach have been summarised in Table 16.1 and discussed in detail in Plates 16.2, 16.3 and 16.4.

Table 16.1: Salient features of each region of stomach

Cardia	Fundus and body	Pylorus
Presence of cardiac glands (mucous secreting glands) in lamina propria of mucosa. Cardiac glands are either simple tubular, or compound tubulo alveolar	Presence of gastric glands in the lamina propria of mucosa. Gastric glands are simple or branched tubular glands. They secrete enzymes and hydrochloric acid	Presence of pyloric glands in the lamina propria of mucosa. Pyloric glands (mucous glands) are simple or branched tubular glands that are coiled.
Shallow gastric pits	Shallow gastric pits occupying superficial 1/4th or less of the mucosa	Deep gastric pits occupying 2/3rd of the depth of the mucosa
Change of epithelium from stratified squamous of the oesophagus to simple columnar epithelium in stomach	Epithelium is simple columnar.	Epithelium is simple columnar. Circular muscle layer is thick and is called as pyloric sphincter.

Gastric glands

The cardiac glands

These are confined to a small area (cardia) near the opening of the esophagus. In this region the mucosa is relatively thin (Plate 16.2). Gastric pits are shallow (as in the body of the stomach). The cardiac glands are either simple tubular, or compound tubulo-alveolar. They are mucous secreting. An occasional oxyntic or peptic cell may be present.

The Main gastric glands

The main gastric glands are present over most of the stomach, but not in the pyloric region and in a small area near the cardiac end. In other words they are present in the body of the stomach, and in the fundus (Plate 16.3 and Fig. 16.6).

Note: These glands are often inappropriately called fundic glands in many books of histology: they are not confined to the fundus.

The main gastric glands are simple or branched tubular glands that lie at right angles to the mucosal surface. The glands open into gastric pits, each pit receiving the openings of several glands. Here the gastric pits occupy the superficial one-fourth or less of the mucosa, the remaining thickness being closely packed with gastric glands. The following varieties of cells are present in the epithelium lining the glands.

Chief cells: The most numerous cells are called ***chief cells***, ***peptic cells***, or ***zymogen cells***. They are particularly numerous in the basal parts of the glands. The cells are cuboidal or low columnar. Their cytoplasm is basophilic. With special methods the chief cells are seen to contain prominent secretory granules in the apical parts of their cytoplasm.

The granules contain pepsinogen that is a precursor of pepsin. With the EM the cytoplasm is seen to contain abundant rough endoplasmic reticulum and a prominent Golgi complex. The luminal surfaces of the cells bear small irregular microvilli.

Note: Chief cells secrete the digestive enzymes of the stomach including pepsin. Pepsin is produced by action of gastric acid on pepsinogen. Pepsin breaks down proteins into small peptides. It is mainly through the action of pepsin that solid food is liquefied.

Oxyntic cells: The ***oxyntic*** or ***parietal cells*** are large, ovoid or polyhedral, with a large central nucleus (Fig. 16.5). They are present singly, amongst the peptic cells. They are more numerous in the upper half of the gland than in its lower half. They are called oxyntic cells because they stain strongly with eosin. They are called parietal cells as they lie against the basement membrane, and often bulge outwards (into the lamina propria) creating a beaded appearance. With the light microscope they appear to be buried amongst the chief cells.

The EM shows, however, that each parietal cell has a narrow apical part that reaches the lumen of the gland. The cell membrane of this apical region shows several invaginations

into the cytoplasm, producing tortuous intracellular canaliculi that communicate with the glandular lumen.

The walls of the canaliculi bear microvilli that project into the canaliculi. The cytoplasm (in the intervals between the canaliculi) is packed with mitochondria. The mitochondria are responsible for the granular appearance and eosinophilia of the cytoplasm (seen with the light microscope). Secretory granules are not present.

Note: Oxyntic cells are responsible for the secretion of hydrochloric acid. They also produce an ***intrinsic factor*** (a glucoprotein) that combines with vitamin B12 (present in ingested food and constituting an ***extrinsic factor***) to form a complex necessary for normal formation of erythrocytes.

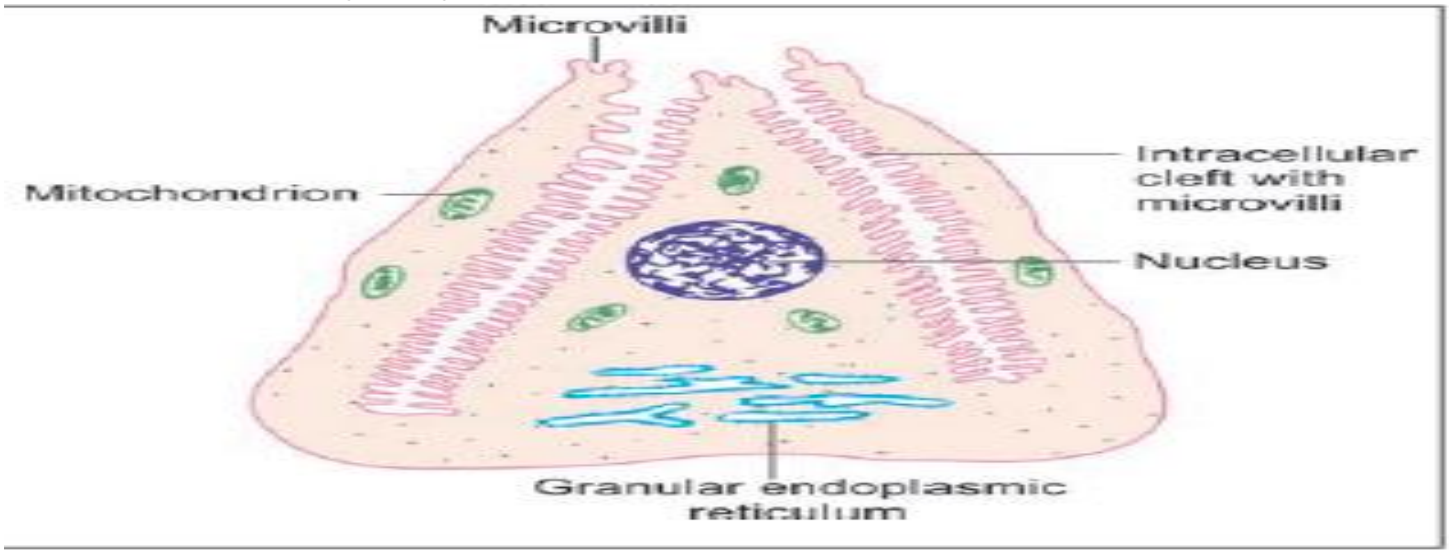


Fig. 16.5: Some features of the electrone microscope structure of an oxyntic cell (schematic representation)

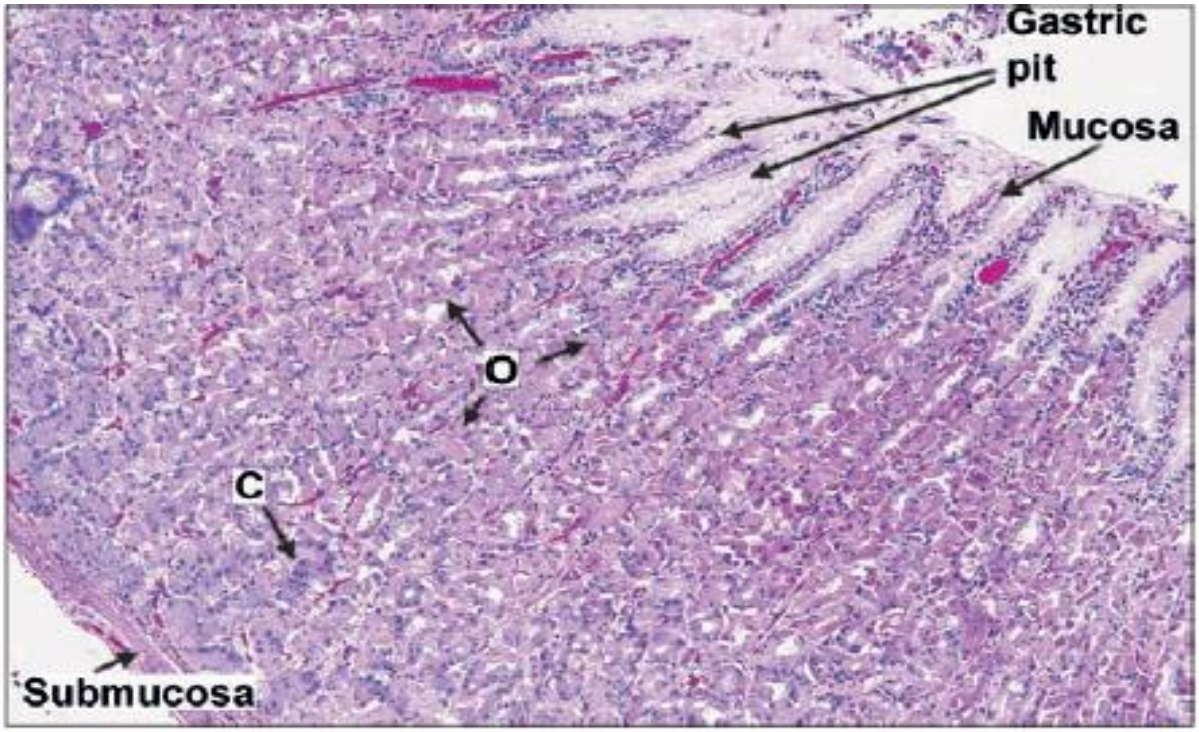


Fig. 16.6: Photomicrograph of body of stomach to show the different types of cells in gastric glands
O–oxyntic cells; C–chief cells

Mucous neck cells: Near the upper end (or 'neck') of the glands there are mucous secreting cells that are called ***mucous neck cells***. These are large cells with a clear

cytoplasm. The nucleus is flattened and is pushed to the base of the cell by accumulated mucous. The supranuclear part of the cell contains prominent granules. The chemical structure of the mucous secreted by these cells is different from that secreted by mucous cells lining the surface of the gastric mucosa.

Endocrine cells: Near the basal parts of the gastric glands there are ***endocrine cells*** that contain membrane bound neurosecretory granules. As the granules stain with silver salts these have, in the past, been called ***argentaffin cells.*** These cells are flattened. They do not reach the lumen, but lie between the chief cells and the basement membrane. These cells probably secrete the hormone ***gastrin***. Some of the cells can be shown to contain serotonin.

Stem cells: Some undifferentiated cells (stem cells) that multiply to replace other cells are also present. They increase in number when the gastric epithelium is damaged (for example when there is a gastric ulcer), and play an important role in healing.

The Pyloric glands

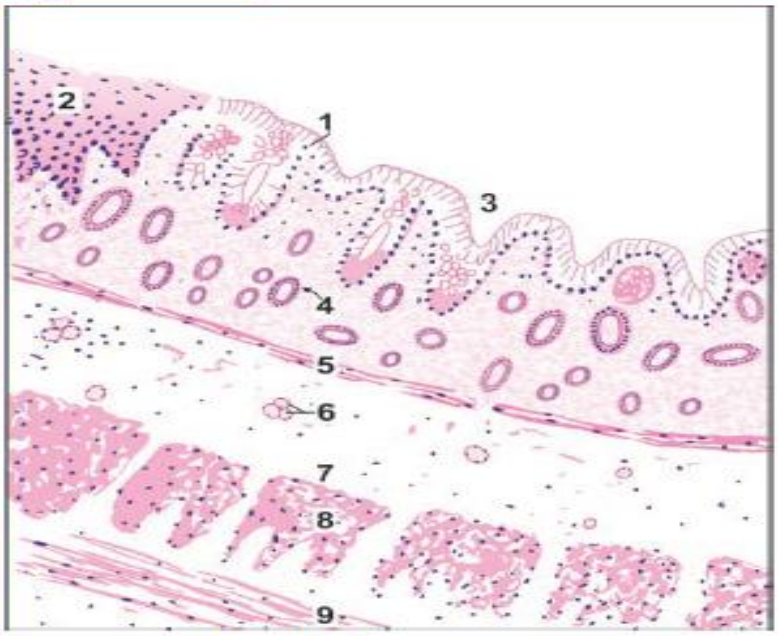
In the pyloric region of the stomach the gastric pits are deep and occupy two-third of the depth of the mucosa. The pyloric glands that open into these pits are short and occupy the deeper one-third of the mucosa. They are simple or branched tubular glands that are coiled. The glands are lined by mucous secreting cells (Plate 16.4). Occasional oxyntic and argentaffin cells may be present. In addition to other substances, pyloric glands secrete the hormone gastrin.

Clinical Correlation

Gastritis: The term ‘gastritis’ is commonly employed for any clinical condition with upper abdominal discomfort like indigestion or dyspepsia in which the specific clinical signs and radiological abnormalities are absent. The condition is of great importance due to its relationship with peptic ulcer and gastric cancer.

Gastric ulcer: Gastric ulcer may occur due to damage to the gastric mucosa barrier. It is most common along the lesser curvature and pyloric antrum. Food-pain pattern, vomiting, significant weight loss and deep tenderness in the midline in epigastrium are the main presentations.

PLATE 16.2: Stomach (Cardia)



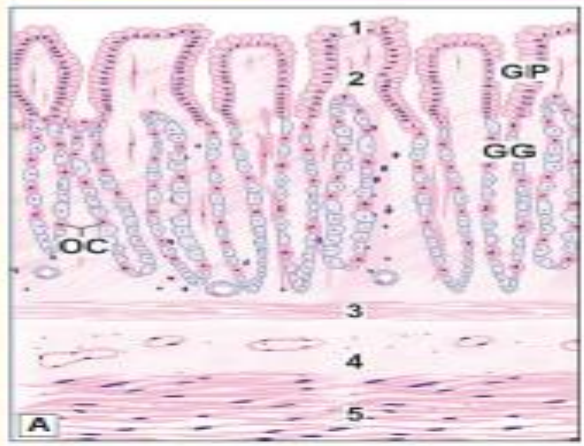
Stomach (cardia). As seen in drawing

- At low magnification, the cardiac end of stomach shows all the four layers seen in stomach:
  - Mucosa
  - Submucosa
  - Muscularis externa
  - Serosa
- At its cardiac end the stomach is lined by simple columnar cells. The epithelium is sharply demarcated from the stratified squamous epithelium lining the lower end of the oesophagus
- Important distinguishing points of cardiac end of stomach are the columnar epithelium lining, the absence of goblet cells, and the simple tubular nature of cardiac glands. If the lower end of the oesophagus is included in the section, the diagnosis becomes obvious (as seen in the drawing).

Key

1. Columnar epithelium
2. Stratified squamous lining of lower end of oesophagus
3. Gastric pit
4. Cardiac gland in mucosa
5. Muscularis mucosae
6. Oesophageal gland in submucosa
7. Submucosa
8. Circular muscle
9. Longitudinal muscle

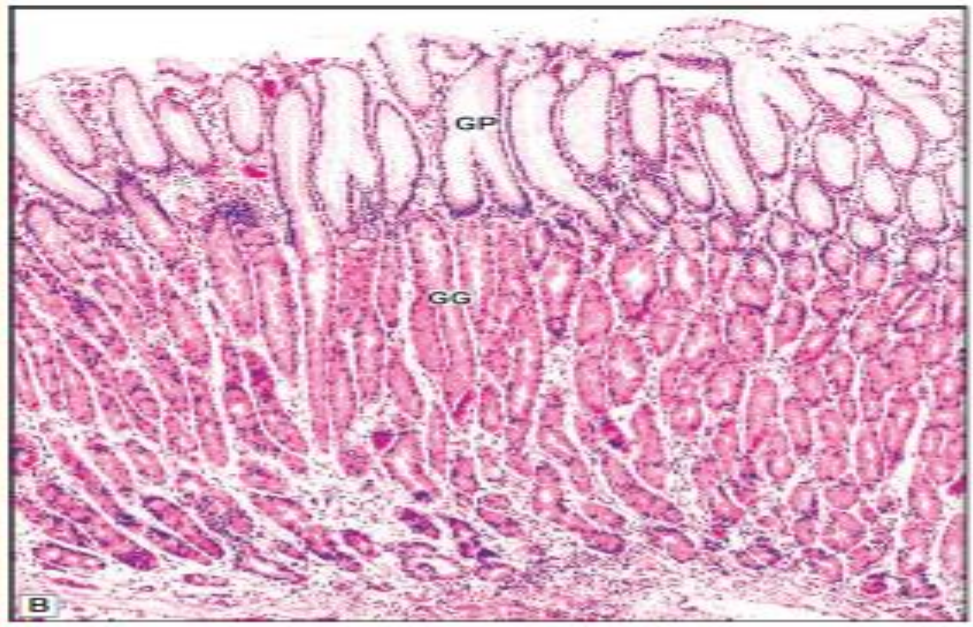
PLATE 16.3: Stomach (Body/Fundus)



The basic structure of stomach is similar to oesophagus i.e. it is composed of:

- Mucosa
- Submucosa
- Muscularis externa
- Serosa

- Mucosa is lined by simple tall columnar epithelium. It shows invaginations called gastric pits that occupy the superficial one fourth of the mucosa
- The area between the pits and the muscularis mucosae is packed with tubular gastric glands. The glands are lined mainly by blue staining chief cells or peptic cells. Amongst these there are pink staining oxyntic cells. These are large cells that are placed peripherally in the wall of the gland. They are more numerous in the upper parts of the gastric glands. The main point to note is that in the region of the glands we see different types of cells that appear to be closely packed together



- Muscularis externa is composed of three layers of smooth muscle–inner oblique, middle circular and outer longitudinal.

A photomicrograph of the body of the stomach is shown in Plate 16.3B. The gastric pits and gastric glands can be distinguished. Observe that the gastric pits occupy the upper one fourth of the lamina propria of mucosa.

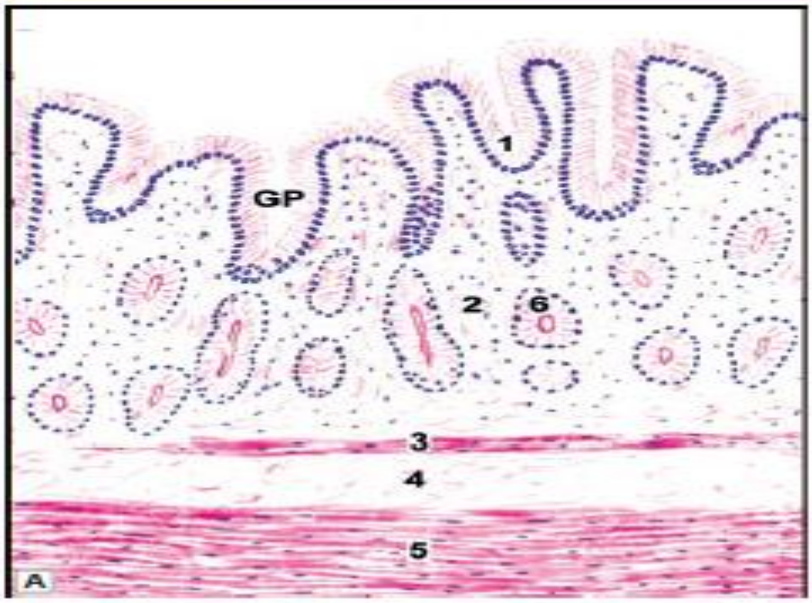
Key

1. Columnar epithelium lining
2. Lamina propria
3. Muscularis mucosa
4. Submucosa
5. Muscularis externa

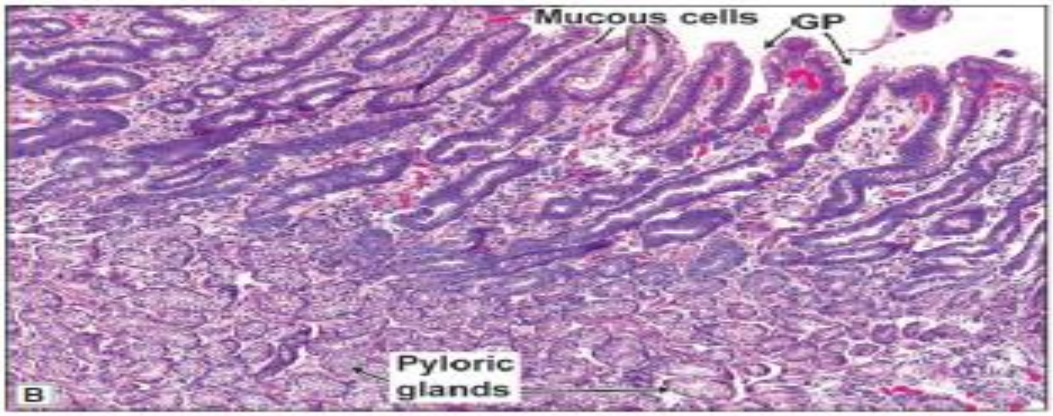
GP. Gastric pit
GG. Gastric gland
OC. Oxyntic cells

Stomach (body/fundus). A. As seen in drawing; B. Photomicrograph

PLATE 16.4: Stomach (Pylorus)



- In the pyloric part of the stomach the gastric pits are much deeper than in the body of the stomach (occupying up to two-third of the depth of the mucosa)
- Deep to the pits there are pyloric glands that are lined by mucous secreting cells. These are pale staining
- The muscularis mucosae, submucosa, and part of the muscle coat are also seen
- It is important to note that the stomach does not have villi. In the photomicrograph folds of epithelial lining may be confused with villi. Observe that each fold merges with underlying connective tissue completely. When true villi are present (as in the small intestine), small parts of them appear as circular or oval masses not attached to a villus or to the submucosa. These are villi that have been cut transversely or obliquely
- Another important feature to note is that the lining epithelium does not have typical goblet cells, but some epithelial cells are mucous secreting.



Key
1. Columnar epithelium lining
2. Lamina propria
3. Muscularis mucosa
4. Submucosa
5. Muscularis externa
6. Pyloric gland

GP. Gastric pit

Stomach (body/fundus). A. As seen in drawing; B. Photomicrograph
Courtesy: Atlas of Histopathology. Ist Edition. Ivan Damjanov. Jaypee Brothers. 2012. p 104

THE SMALL INTESTINE

The small intestine is a tube about five meters long. It is divided into three parts. These are (in craniocaudal sequence) the ***Duodenum*** (about 25 cm long); the ***Jejunum*** (about 2 meters long); and the ***Ileum*** (about 3 meters long). (Gut length is shorter in the living person than in a cadaver, because of muscle tone). It is the principal site for absorption of products of digestion.

It also secretes some hormones through entero-endocrine cells. Digestion is completed in small intestine.

Microscopic features

The wall of the small intestine is made up of the four layers: mucousa, submucousa, muscularis externa and serousa. The serousa and muscular layers correspond exactly to the general structure of alimentary canal. The submucosa is also typical except in the duodenum, where it contains the ***Glands of Brunner***. The mucous membrane exhibits several special features that are described below.

The Mucous Membrane

The surface area of the mucous membrane of the small intestine is extensive (to allow adequate absorption of food). This is achieved by virtue of the following:

a. The considerable length of the intestine.
b. The presence of numerous circular folds in the mucosa.
c. The presence of numerous finger-like processes, or ***villi***, that project from the surface of the mucosa into the lumen.
d. The presence of numerous depressions or ***crypts*** that invade the lamina propria.
e. The presence of microvilli on the luminal surfaces of the cells lining the mucosa (Fig. 16.7).

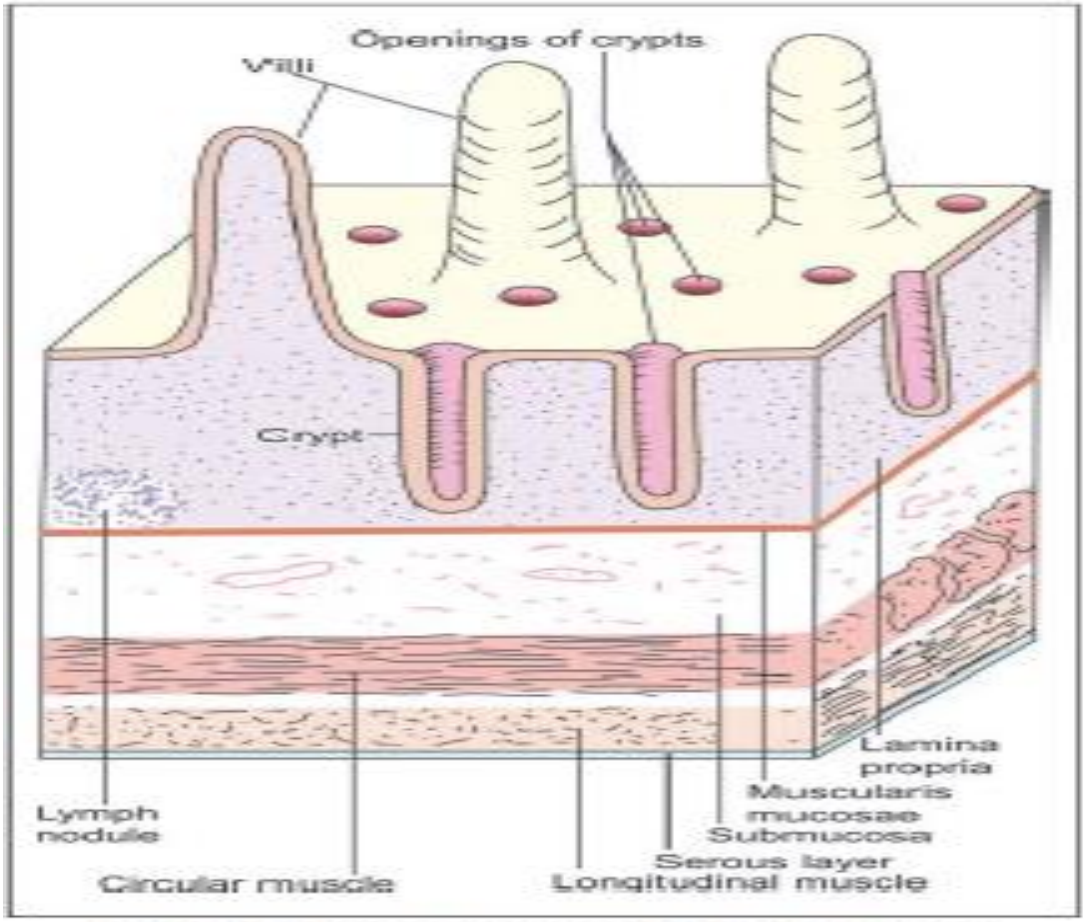


Fig. 16.7: Basic structure of the small intestine

Circular Folds

The circular folds are also called the ***valves of Kerkring***. Each fold is made up of all layers of the mucosa (lining epithelium, lamina propria and muscularis mucosae). The submucosa also extends into the folds. The folds are large and readily seen with the naked eye. They are absent in the first one or two inches of the duodenum. They are prominent in the rest of the duodenum, and in the whole of the jejunum. The folds gradually become fewer and less marked in the ileum. The terminal parts of the ileum have no such folds.

Apart from adding considerably to the surface area of the mucous membrane, the circular folds tend to slow down the passage of contents through the small intestine thus facilitating absorption.

The Villi

The villi are, typically, finger-like projections consisting of a core of reticular tissue covered by a surface epithelium (Fig. 16.8). The connective tissue core contains numerous blood capillaries forming a plexus. The endothelium lining the capillaries is fenestrated thus allowing rapid absorption of nutrients into the blood. Each villus contains a central lymphatic vessel called a lacteal. Distally, the lacteal ends blindly near the tip of the villus; and proximally it ends in a plexus of lymphatic vessels present in the lamina propria. Occasionally, the lacteal may be double. Some muscle fibres derived from the muscularis mucosae extend into the villus core.

NOTE: In some situations the villi, instead of being finger-like, are flattened and leaf-like, while in some other situations they are in the form of ridges. The villi are greatest and most numerous (for a given area) in the duodenum. They progressively decrease in size, and in number, in proceeding caudally along the small intestine. It has been estimated that the presence of villi increases the surface area of the epithelial lining of the small intestine about eight times.

The Crypts

The crypts (of Lieberkuhn) are tubular invaginations of the epithelium into the lamina propria. They are really simple tubular intestinal glands that are lined by epithelium (Plate 16.4). The epithelium is supported on the outside by a basement membrane.

The Epithelium Lining

The epithelium covering the villi, and areas of the mucosal surface intervening between them, consists predominantly of columnar cells that are specialised for absorption. These are called ***enterocytes***. Scattered amongst the columnar cells there are mucous secreting goblet cells.

The cells lining the crypts (intestinal glands) are predominantly undifferentiated. These cells multiply to give rise to absorptive columnar cells and to goblet cells. Near the bases of the crypts there are ***Paneth cells*** that secrete enzymes. Endocrine cells (bearing membrane bound granules filled with various neuroactive peptides) are also present.

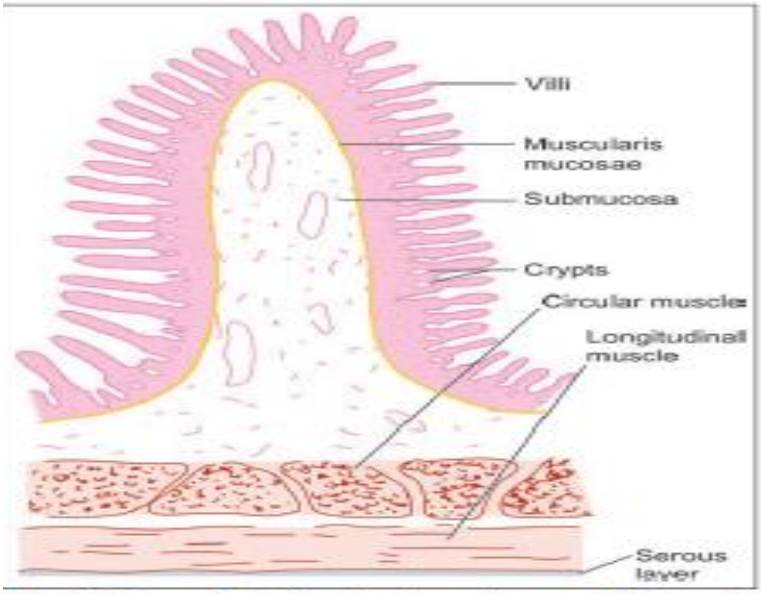


Fig. 16.8: Longitudinal section through a part of the small intestine seen at a very low magnification to show a circular mucosal fold (Schematic representation) Note the submucosa extending into the mucosal fold.

Cells of Small intestine

Absorptive Columnar Cells

Each cell has an oval nucleus located in its lower part. When seen with the light microscope the luminal surface of the cell appears to be thickened and to have striations in it, perpendicular to the surface (Fig. 16.9).

With the EM this ***striated border*** is seen to be made up of microvilli arranged in a very regular manner. The presence of microvilli greatly increases the absorptive surface of the cell. Each microvillus has a wall of plasma membrane within which there are fine filaments. that form the ***terminal web***.

The surface of each microvillus is covered by a layer of fine fibrils and mucous (***glycocalyx***).

The plasma membrane on the lateral sides of absorptive cells shows folds that interdigitate with those of adjoining cells.

Adjacent cells are united by typical junctional complexes and by scattered desmosomes.

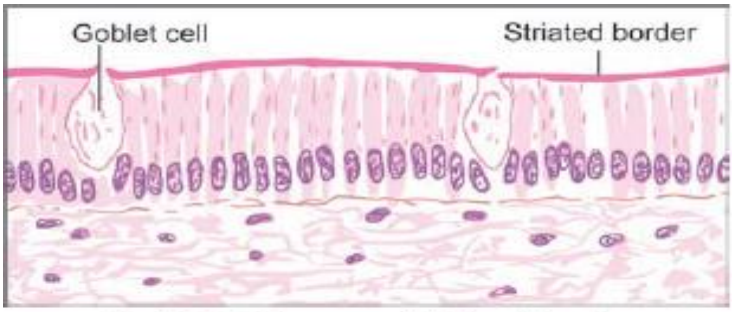


Fig. 16.9: Columnar epithelium lining the small intestine. Note the striated border and some goblet cells (Schematic representation)

Intercellular canals may be present between adjacent cells. The cytoplasm of absorptive cells contains the usual organelles, including lysosomes and smooth ER. These cells are responsible for absorption of amino acids, carbohydrates, and lipids present in digested food.

Goblet Cells

A goblet is literally a drinking glass that is broad above, and has a narrow stem attached to a base. Goblet cells are so named because of a similar shape. Each goblet cell has an expanded upper part that is distended with mucin granules (Figs. 16.9 and 16.10). The nucleus is flattened and is situated near the base of the cell. Goblet cells are mucous secreting cells. In consonance with their secretory function these cells have a prominent Golgi complex and abundant rough endoplasmic reticulum. The luminal surface of the cell bears some irregular microvilli. In haematoxylin and eosin stained preparations, the mucin content of goblet cells appears to be unstained. It stains brightly with the PAS technique. Mucous cells increase in number as we pass down the small intestine, being few in the duodenum and most numerous in the terminal ileum.

Undifferentiated Cells

These are columnar cells present in the walls of intestinal crypts. They are similar to absorptive cells, but their microvilli and terminal webs are not so well developed. The cytoplasm contains secretory granules. Undifferentiated cells proliferate actively by mitosis. The newly formed cells migrate upwards from the crypt to reach the walls of villi. Here they differentiate either into typical absorptive cells, or into goblet cells. These cells migrate towards the tips of the villi where they are shed off. In this way, the

epithelial lining is being constantly replaced, each cell having a life of only a few days. The term ***intermediate cells*** has been applied to differentiating stem cells that show features intermediate between those of stem cells and fully differentiated cells.

Paneth Cells (Zymogen Cells)

These cells are found only in the deeper parts of intestinal crypts. They contain prominent eosinophilic secretory granules (Figs 16.10 and 16.11). With the EM Paneth cells are seen to contain considerable rough endoplasmic reticulum. Other organelles and some irregular microvilli are present. The cells are rich in zinc. The function of zymogen cells is not well known. They are known to produce lysozyme that destroys bacteria. They may also produce other enzymes.

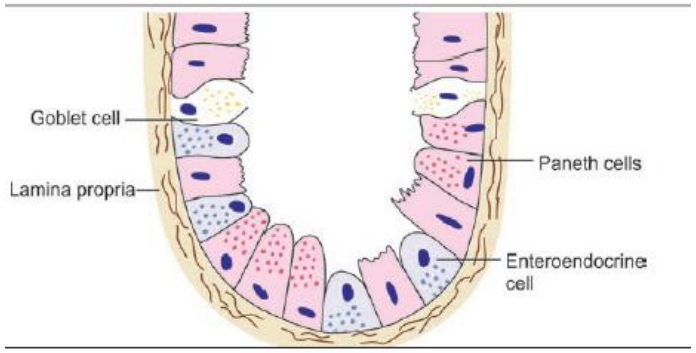


Fig. 16.10: Cells of small intestine (Schematic representation)

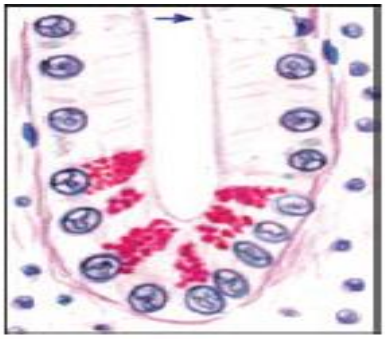


Fig. 16.11: High power view of an intestinal crypt showing Paneth cells with red staining supranuclear granules (Schematic representation)

Endocrine Cells

Cells containing membrane bound vesicles filled with neuroactive substances are present in the epithelial lining of the small intestine. They are most numerous near the lower ends of crypts. As the granules in them stain with silver salts these cells have, in the past, been termed argentaffin cells (Figs 16.11 and 16.12). Some of them also give a positive chromaffin reaction. They are, therefore, also called ***enterochromaffin cells***. With the introduction of immunohistochemical techniques it has now been demonstrated that these cells are of various functional types, and contain many amines having an endocrine function.


Fig. 16.12: High power view of intestinal crypt showing argentaffin cell with black staining granules that are mostly infranuclear (Schematic representation)

Other Cells in the Lamina Propria

Apart from connective tissue associated fibroblasts, and lymphocytes (mentioned above) the lamina propria of the small intestine contains eosinophil leucocytes, macrophages, and mast cells. Plasma cells are present in relation to aggregations of lymphoid tissue.

Lymphoid Tissue of the Small intestine

Solitary and aggregated lymphatic follicles (Peyer's patches) are present in the lamina propria of the small intestine. The solitary follicles become more numerous, and the aggregated follicles larger, in proceeding caudally along the small intestine. They are most prominent in the terminal ileum (Plate 16.5).

Their lymphoid tissue may occasionally extend into the submucosa. Villi are few or missing in the mucosa overlying aggregated follicles.

The epithelium overlying lymphatic follicles contains special ***Follicle-associated epithelial cells*** or ***M-cells*** (M for 'microfold' or 'membrane'). These cells are columnar.

They are believed to take up antigens present in the lumen of the intestine and to transport them to subjacent lymphoid tissue, which can then produce antibodies against the antigens.

Peyer's Patches

Small collections of lymphoid tissue, similar in structure to the follicles of lymph nodes, may be present anywhere along the length of the gut. They are called ***solitary lymphatic follicles***. Larger aggregations of lymphoid tissue, each consisting of 10 to 200 follicles are also present in the small intestine. They are called ***aggregated lymphatic follicles*** or ***Peyer's patches*** (Plate 16.7). These patches can be seen by naked eye, and about 200 of them can be counted in the human gut. The mucosa overlying them may be devoid of villi or may have rudimentary villi. Peyer's patches always lie along the ante-mesenteric border of the intestine and measure 2 cm to 10 cm.

Both solitary and aggregated follicles increase in number and size in proceeding caudally along the small intestine, being most numerous and largest in the terminal ileum. In addition to lymphoid follicles, a large number of lymphocytes and plasma cells are present in the connective tissue of the gut wall.

It has been held that gut associated lymphoid tissue may possibly have a role to play in the processing of B-lymphocytes (similar to that of T-lymphocytes in the thymus), but at present there is not much evidence to support this view.

Distinguishing Features OF Duodenum, Jejunum, and Ilum

Sections through the small intestine are readily distinguished from those of other parts of the gut because of the presence of villi.

Duodenum (Plate 16.6)

The duodenum is easily distinguished from the jejunum or ileum because of the presence of glands in the submucosa. (No glands are present in the submucosa of the jejunum or ileum). These ***duodenal glands*** (of Brunner) are compound tubulo-alveolar glands (Plate 16.6). Their ducts pass through the muscularis mucosae to open into the intestinal crypts (of Lieberkuhn).

The cells lining the alveoli of duodenal glands are predominantly mucous secreting columnar cells having flattened basal nuclei. Some endocrine cells are also present. The duodenal glands are most numerous in the proximal part of the duodenum. They are few (or missing) in the distal part. The secretions of the duodenal glands contain mucous, bicarbonate ions (to neutralise gastric acid entering the duodenum) and an enzyme that activates trypsinogen produced by the pancreas.

Jejunum (Plate 16.5)

The proximal part of the jejunum shows significant differences in structure from the terminal part of the ileum. The changes take place gradually in proceeding caudally along the small intestine, there being no hard and fast line of distinction between the jejunum and the ileum.

As compared to the ileum the jejunum has the following features:

a. A larger diameter
b. A thicker wall
c. Larger and more numerous circular folds
d. Larger villi
e. Fewer solitary lymphatic follicles. Aggregated lymphatic follicles are absent in the proximal jejunum, and small in the distal jejunum
f. Greater vascularity

Ileum

The villi are thin and slender in the region of ileum. The submucosa contains the Peyer's patches. M cells are found overlying the lymphoid follicles.

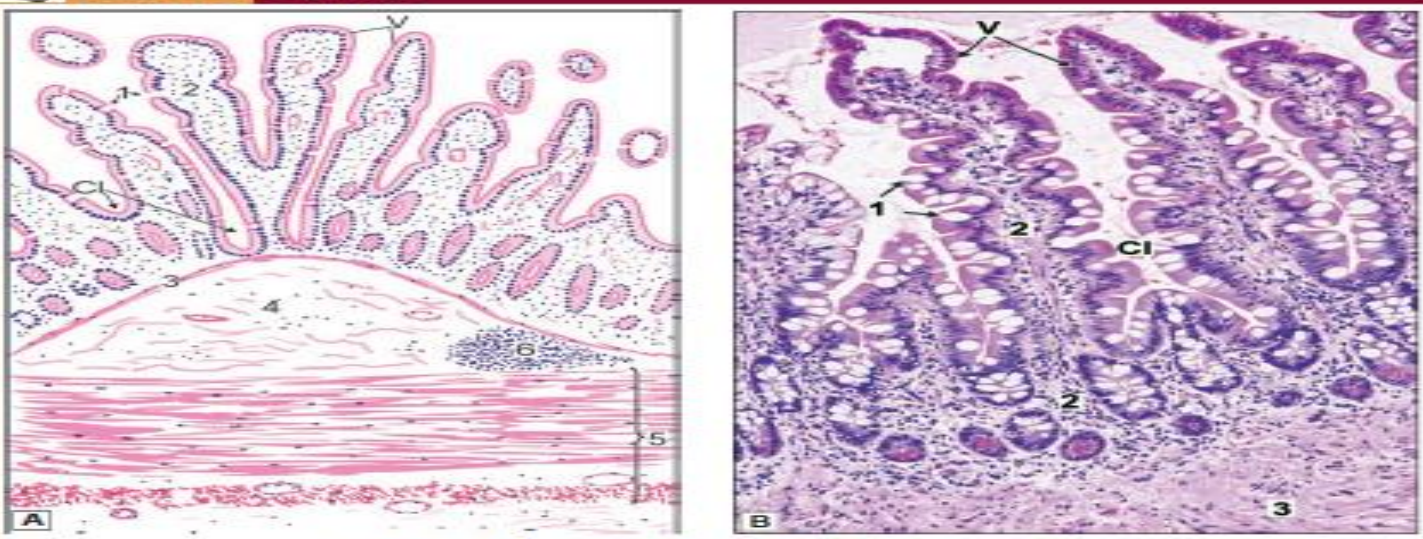
Pathological Correlation

Crohn's Disease or Regional Enteritis is an idiopathic chronic ulcerative inflammatory bowel disease, characterised by transmural, non-caseating granulomatous inflammation, affecting most commonly the segment of terminal ileum and/or colon, though any part of the gastrointestinal tract may be involved.

Coeliac Sprue is the most important cause of primary malabsorption occurring in temperate climates. The condition is characterised by significant loss of villi in the small intestine and thence diminished absorptive surface area. The condition occurs in 2 forms:

A. Childhood form, seen in infants and children and is commonly referred to as coeliac disease.
B. Adult form, seen in adolescents and early adult life and used to be called idiopathic steatorrhoea.

Plate 16.5: Jejunum



Jejunum. A. As seen in drawing; B. Photomicrograph

Courtesy: Atlas of Histopathology. Ist Edition. Ivan Damjanov. Jaypee Brothers. 2012. p 117

In this figure we see features of the typical structure of the small intestine. The mucosa shows numerous finger-like projections or villi. Each villus has a covering of columnar epithelium that covers a core of delicate connective tissue. Some goblet cells are also seen. Numerous tubular depressions, or crypts dip into the lamina propria. These crypts are also lined by columnar cells. The mucosa is separated from the submucosa by the muscularis mucosae. The intestine is surrounded by circular and longitudinal layers of smooth muscle which constitutue muscularis externa.

Note: A solitary lymph nodule is present in the submucosa in the drawing.

The photomicrograph shows the finger-like villi lined by columnar epithelial cells and goblet cells. The villi dip down into the crypts of Lieberkuhn. At the bases of these are Paneth cells with eosinophilic supranuclear granules.

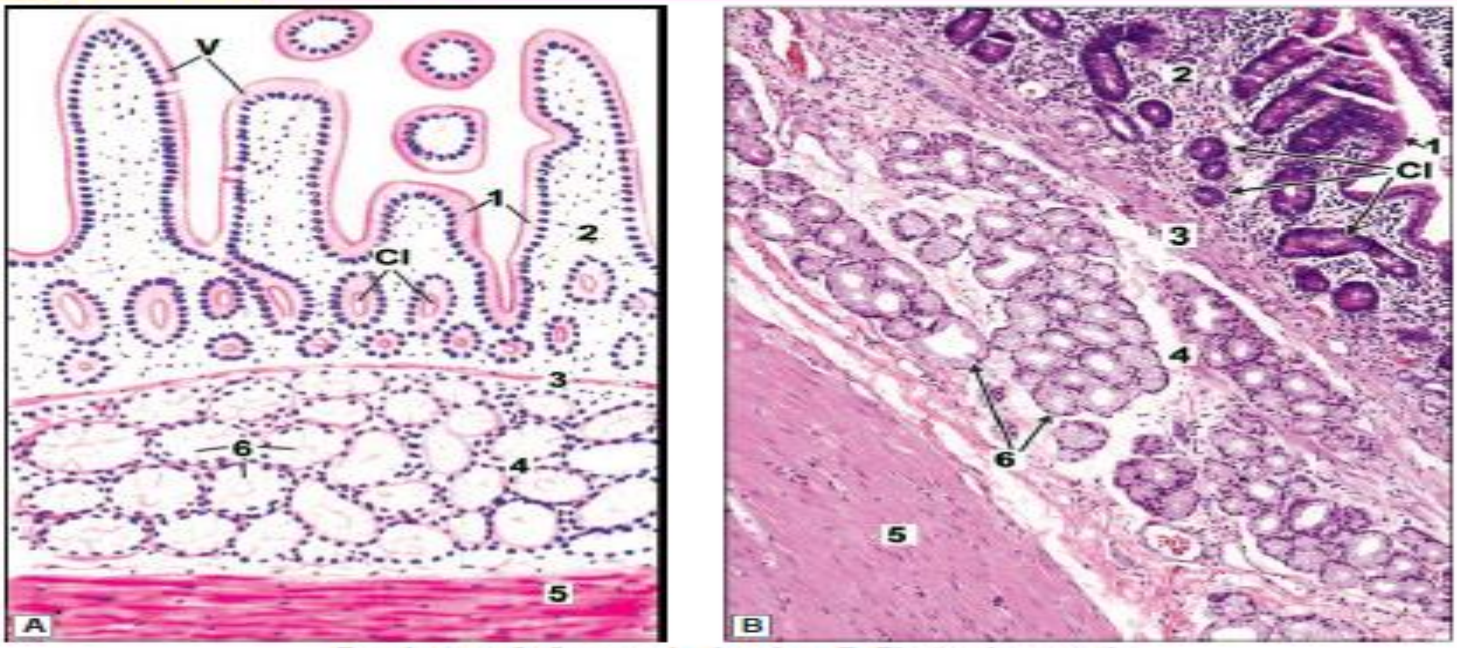
Key

1. Columnar epithelial lining with goblet cells
2. Lamina propria
3. Muscularis mucosa
4. Submucosa
5. Muscularis externa
6. Lymph nodule

V. Villi

Cl. Crypts of Lieberkuhn

Plate 16.6: Duodenum



Duodenum. A. As seen in drawing; B. Photomicrograph

Courtesy: Atlas of Histopathology. Ist Edition. Ivan Damjanov. Jaypee Brothers. 2012. p 117

The general structure of the duodenum is the same as that described for the jejunum, except that the submucosa is packed with mucous secreting glands of Brunner.

Note: The intestinal crypts lie 'above' the muscularis mucosae while the glands of Brunner lie 'below' it. The presence of the glands of Brunner is a distinctive feature of the duodenum.

The photomicrograph shows Brunner's glands which are mucous glands present in the submucosa of the duodenum.

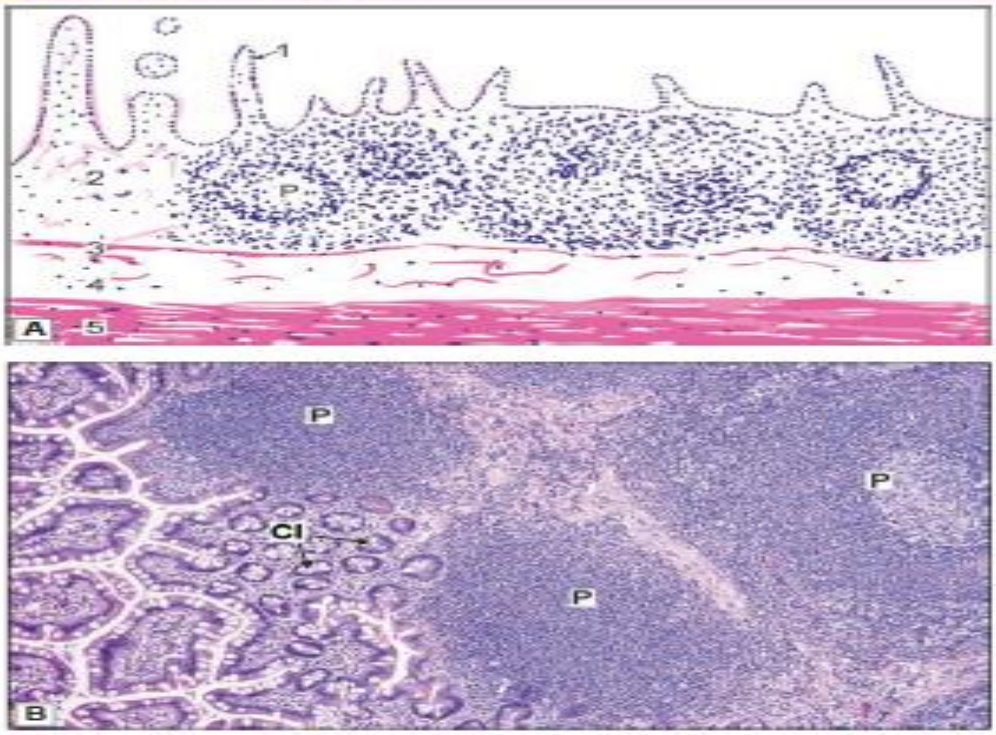
Key

1. Columnar epithelial lining with goblet cells
2. Lamina propria
3. Muscularis mucosa
4. Submucosa with duodenal glands of Brunner
5. Muscularis externa
6. Glands of Brunner

V. Villi

Cl. Crypts of Lieberkuhn

PLATE 16.7: Ileum (Peyers Patch)



Duodenum. A. As seen in drawing; B. Photomicrograph.
Courtesy: Atlas of Histopathology. Ist Edition. Ivan Damjanov. Jaypee Brothers. 2012. p 117

The general structure of the ileum is similar to that of the jejunum except for

- The entire thickness of the lamina propria is infiltrated with lymphocytes amongst which typical lymphatic follicles can be seen which may extend into the submucosa. These lymphatic follicles are called as Peyer's patches
- In the region overlying the 'Peyer's patch' villi may be rudimentary or absent.

Note: Presence of Peyer's patches is the most distinguishing feature of ileum.

Key

1. Columnar epithelial lining with goblet cells
2. Lamina propria
3. Muscularis mucosa
4. Submucosa
5. Muscularis externa

P. Peyer's patches
Cl. Crypts of Lieberkuhn

The Large intestine (colon)

It consists of the caecum, appendix, colon, rectum and anal canal. The main functions of the large intestine are absorption of water and conversion of the liquid, undigested material into solid faeces. It harbor's some nonpathogenic bacteria that produce vitamin B12 and vitamin K. The former is necessary for haemopoiesis and the latter for coagulation of blood.

The Colon

The structure of the colon conforms to the general description of the structure of the gut. The following additional points may be noted (Fig. 16.13 and Plate 16.7).

Mucous Membrane

The mucous membrane of the colon shows numerous crescent-shaped folds. There are no villi. The mucosa shows numerous closely arranged tubular glands or crypts similar to those in the small intestine. The mucosal surface, and the glands, are lined by an epithelium made up predominantly of columnar cells. Their main function is to absorb excess water and electrolytes from intestinal contents.

Many columnar cells secrete mucous and antibodies (IgA). The antibodies provide protection against pathogenic organisms. Numerous goblet cells are present, their number increasing in proceeding caudally. The mucous secreted by them serves as a lubricant that facilitates the passage of semisolid contents through the colon. Paneth cells are not present. Some endocrine cells, and some stem cells, are seen.

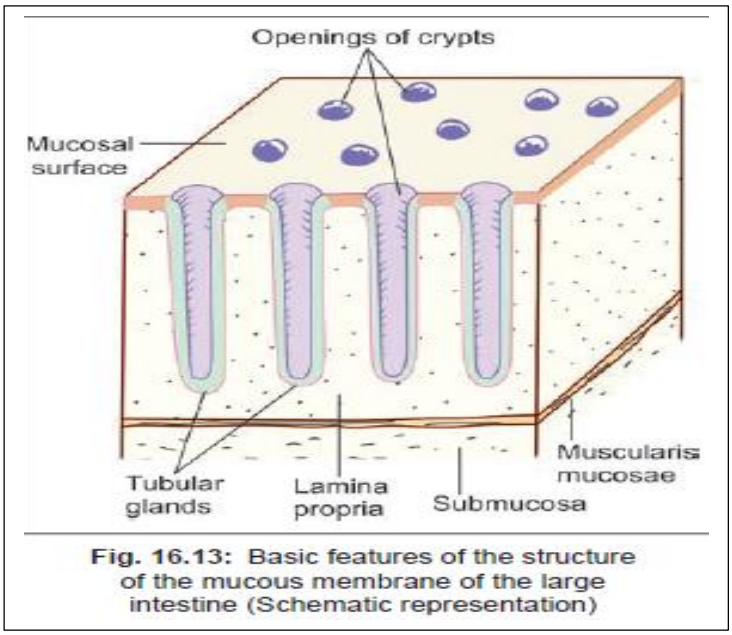


Fig. 16.13: Basic features of the structure of the mucous membrane of the large intestine (Schematic representation)

The epithelium overlying solitary lymphatic follicles (present in the lamina propria) contains M-cells similar to those described in the small intestine. Scattered cells bearing tufts of long microvilli are also seen. They are probably sensory cells.

Sub mucosa

The submucosa often contains fat cells. Some cells that contain PAS-positive granules, termed ***Muciphages***, are also present. These are most numerous in the rectum.

Muscularis Externa

The longitudinal layer of muscle is unusual. Most of the fibers in it are collected to form three thick bands, the ***Taenia Coli*** (Fig. 16.14). A thin layer of longitudinal fibers is present in the intervals between the taenia. The taenia are shorter in length than other layers of the wall of the colon. This results in the production of ***sacculations*** on the wall of the colon.

Serosa

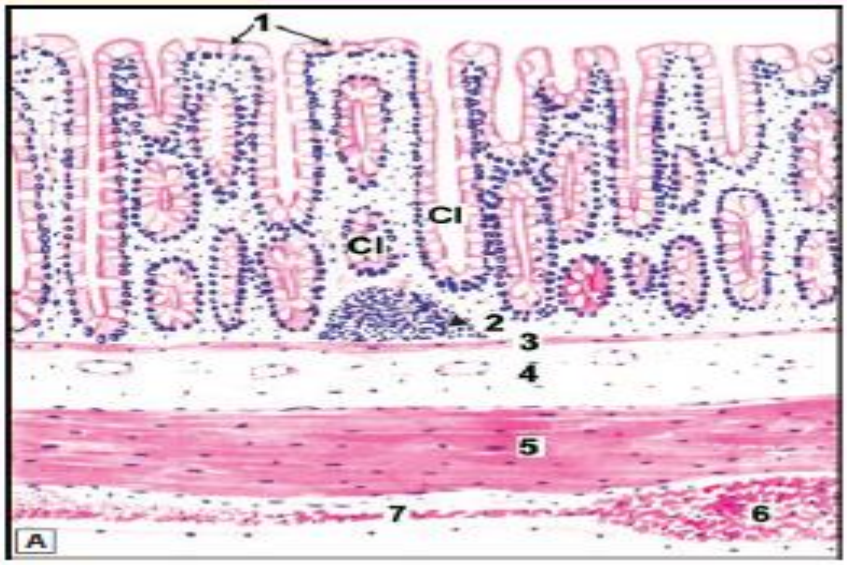
The serous layer is missing over the posterior aspect of the ascending and descending colon. In many situations the peritoneum forms small pouch-like processes that are filled with fat. These yellow masses are called the ***appendices epiploicae***.

The Vermiform Appendix

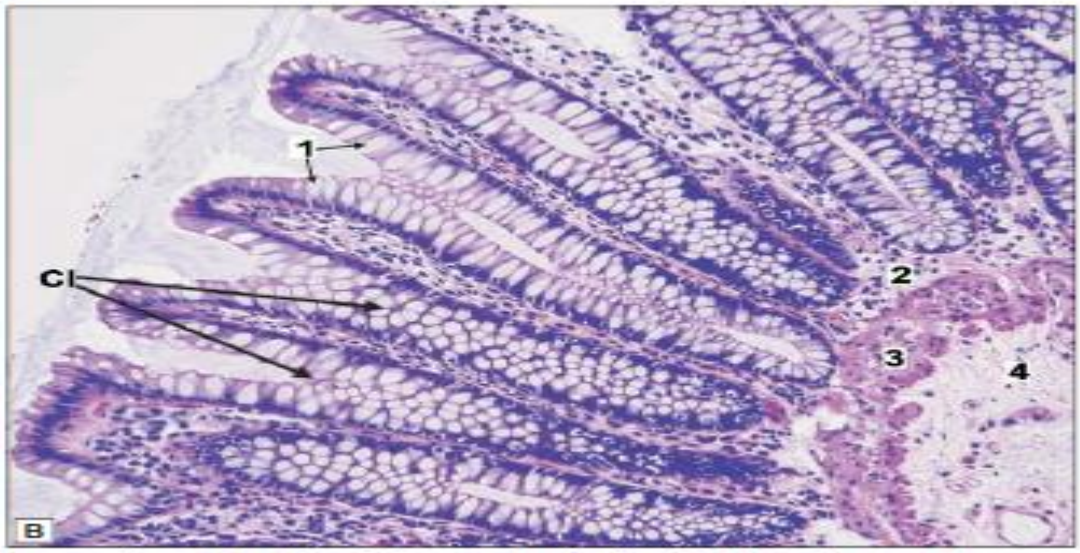
The appendix is the narrowest part of the gut. The structure of the vermiform appendix resembles that of the colon with the following differences (Plate 16.8):

A. The crypts are poorly formed.
B. The longitudinal muscle coat is complete and equally thick all round. Taenia coli are not present.
C. The submucosa contains abundant lymphoid tissue that may completely fill the submucosa. The lymphoid tissue is not present at birth. It gradually increases and is best seen in children about 10 years old. Subsequently, there is progressive reduction in quantity of lymphoid tissue.

PLATE 16.8: Large Intestine



- The most important feature to note is the absence of villi
- The mucosa shows numerous tubular glands or crypts. The surface of the mucosa, and the crypts, are lined by columnar cells amongst which there are numerous goblet cells
- A section of the large intestine is easily distinguished from that of the small intestine because of the absence of villi; and from the stomach because of the presence of goblet cells (which are absent in the stomach)
- The muscularis mucosae, submucosa and circular muscle coat are similar to those in the small intestine
- However, the longitudinal muscle coat is gathered into three thick bands called taenia coli (as shown in drawing). The longitudinal muscle is thin in the intervals between the taenia.



Note: A lymphatic nodule can be seen in the lamina propria (as shown by arrow head) in the drawing.

Key

1. Columnar epithelial lining with goblet cells
2. Lamina propria
3. Muscularis mucosa
4. Submucosa
5. Muscle coat
6. Taenia coli
7. Longitudinal muscle

Cl. Crypts of Lieberkuhn

Large Intestine. A. As seen in drawing; B. Photomicrograph

The Rectum

The structure of the rectum is similar to that of the colon except for the following:

1. A continuous coat of longitudinal muscle is present. There are no taenia.
2. Peritoneum covers the front and sides of the upper one third of the rectum; and only the front of the middle third.
   The rest of the rectum is devoid of a serous covering.
3. There are no appendices epiploicae.

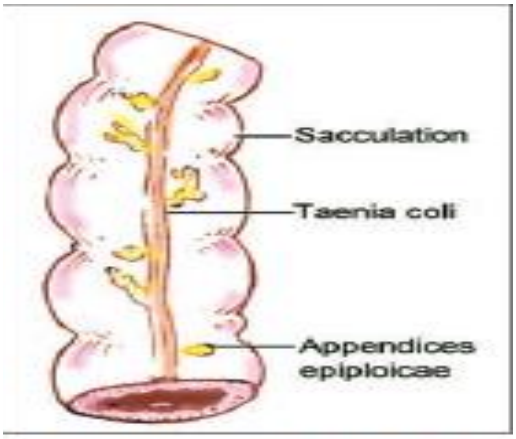


Fig. 16.14: Segment of the colon (Schematic representation)

The Anal canal

The anal canal is about 4 cm long. The upper 3 cm are lined by mucous membrane, and the lower 1 cm by skin.

Mucosa

The mucous membrane of the upper 15 mm of the canal is lined by columnar epithelium. The mucous membrane of this part shows six to twelve longitudinal folds that are called the ***anal columns***. The lower ends of the anal columns are united to each other by short transverse folds called the ***anal valves***. The anal valves together form a transverse line that runs all round the anal canal, this is the ***pectinate line*** (Fig. 16.15). The mucous membrane of the next 15 mm of the rectum is lined by non-keratinised stratified squamous epithelium. This region does not have anal columns. The mucosa has a bluish appearance because of the presence of a dense venous plexus between it and the muscle coat.

This region is called the ***pecten*** or ***transitional zone***. The lower limit of the pecten forms the ***white line*** (***of Hilton***). The lowest 8 to 10 mm of the anal canal are lined by true skin in which hair follicles, sebaceous glands and sweat glands are present.

Above each anal valve there is a depression called the anal sinus. Atypical (apocrine) sweatglands open into each sinus. They are called the anal (or circumanal) glnds.

Submucosa

Prominent venous plexuses are present in the submucosa of the anal canal. The internal haemorrhoidal plexus lies above the level of the pectinate line, while the external haemorrhoidal plexus lies near the lower end of the canal.

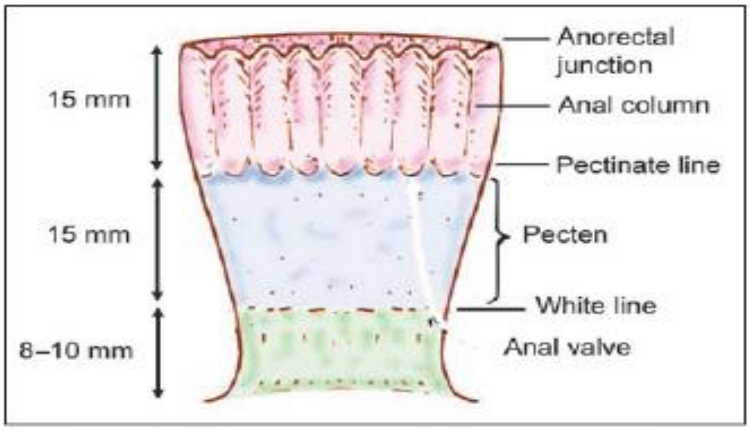


Fig. 16.15: Some features in the interior of the anal canal (Schematic representation)

Muscularis Externa

The anal canal is surrounded by circular and longitudinal layers of muscle continuous with those of the rectum. The circular muscle is thickened to form the ***internal anal sphincter***. Outside the layer of smooth muscle, there is the ***external anal sphincter*** that is made up of striated muscle. For further details of the anal musculature see a book on gross anatomy.

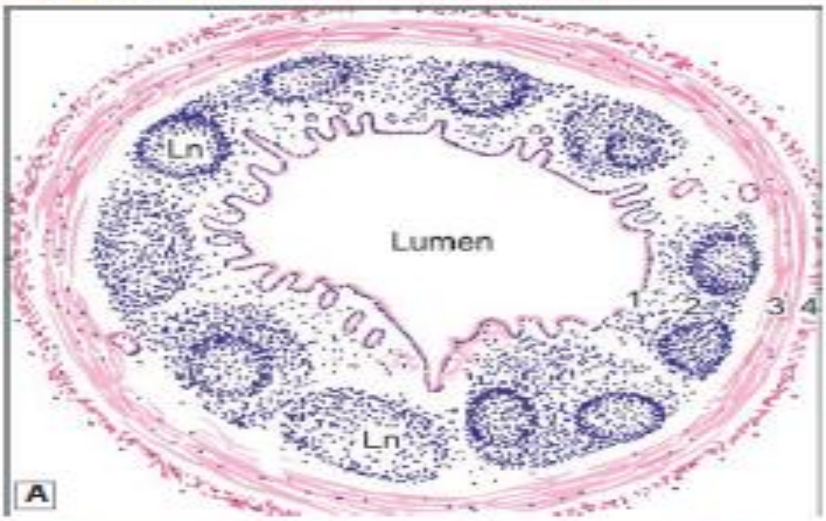
Clinical Correlation

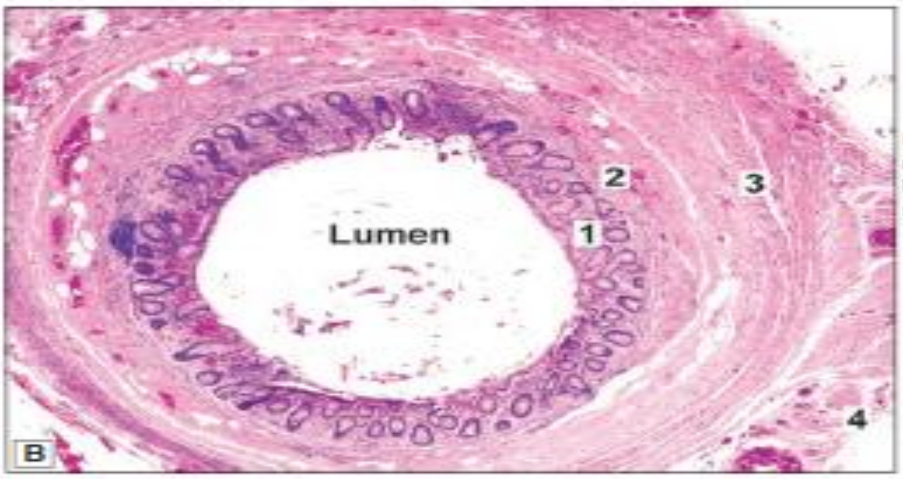
Ulcerative colitis is an idiopathic form of acute and chronic ulcero-inflammatory colitis affecting chiefly the mucosa and submucosa of the rectum and descending colon, though sometimes it may involve the entire length of the large bowel.

Acute inflammation of the appendix, acute appendicitis, is the most common acute abdominal condition confronting the surgeon. The condition is seen more commonly in older children and young adults, and is uncommon at the extremes of age. The disease is seen more frequently in the West and in affluent societies which may be due to variation in diet—a diet with low bulk or cellulose and high protein intake more often causes appendicitis.

Hemorrhoids or piles are the varicosities of the Hemorrhoidal veins. They are called 'internal piles' if dilatation is of superior Hemorrhoidal plexus covered over by mucous membrane, and 'external piles' if they involve inferior haemorrhoidal plexus covered over by the skin. They are common lesions in elderly and pregnant women. They commonly result from increased venous pressure.

Plate 16.9: Vermiform Appendix





Vermiform appendix. A. As seen in drawing; B. Photomicrograph

- The vermiform appendix is the narrowest part of the gastrointestinal canal and is seen as a tubular structure
- The innermost layer of the mucosa, is lined by simple columnar epithelium with goblet cells
- The crypts are poorly formed
- Scattered lymphocytes and aggregated nodules are present in the lamina propria and they may extend into the next layer.
- The next layer, the submucosa may show a variable number of lymphatic nodules
- The submucosa is surrounded by smooth muscle layer (muscularis externa) followed by serosa
- The longitudinal muscle coat is complete and equally thick all round. Taenia coli are not present.

Note: In the photomicrograph the lymphatic nodules are seen mainly in the lamina propria but in the drawing they are shown occupying the submucosa also.

Key

1. Mucosa
2. Submucosa
3. Muscularis externa
4. Serosa

Ln. Lymphatic nodule