Lecture #: 2

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Histology of Esophagus, Stomach & Small Intestines

- **Histology of Esophagus:**

Esophagus is a muscular tube that starts at the lower border of the pharynx (at the level of C6 cervical vertebra) and ends at the level of cardia of stomach (cardiac orifice). Esophagus differs from pharynx that it’s all muscular, the muscles in esophagus are divided into 3 parts; upper third, middle third and lower third. Upper third contains skeletal (voluntary) muscles, while the middle third contains skeletal and smooth muscles (mixed), and the lower third contains only smooth muscles (involuntary).

The function of esophagus is to propel (push) the bolus to the stomach. The lower end which is called cardia is a physiological sphincter, it works as a sphincter to prevent regurgitation of contents of stomach upward to the esophagus. It’s physiological (not anatomical) because there’s no thickening in the smooth muscles.

Histology of esophagus has the normal 4 layers of GI tract; the first layer is mucosa, then submucosa, then muscularis externa and the last layer is adventitia as large portion of esophagus is located in the thorax (only 1.3 cm under the diaphragm). Adventitia is a connective tissue layer rich in blood vessels and lymphatics.

The first layer is called lining epithelium, it’s **stratified squamous non-keratinized**, after this layer there’s lamina propria, it’s loose connective tissue and in esophagus it
has a gland found specially in the lower end of esophagus; it’s called cardiac gland that is similar to the cardia of the stomach.

Then comes muscularis mucosa, it’s composed of 2 or 3 ribbons of smooth muscles. After this there’s submucosa, in esophagus the submucosa contains glands; they are called esophageal gland proper (note: along the GI tract, there are only 2 organs that have glands in their submucosa; the esophagus (esophageal glands) and the duodenum). The function of these glands is secretion and lubrication, they’re mucus-secreting glands and this facilitates the transport of food and protect the mucosa. A plexus of nerves is found in submucosa, Meissner’s plexus, it’s mainly parasympathetic.

Then we have muscularis externa, it has 2 layers of muscles; inner circular and outer longitudinal layers (remember how the esophagus is divided into 3 parts according to the types of muscles in the muscularis externa; upper third has only skeletal muscles, middle third has skeletal and smooth muscles, whereas the lower third has smooth muscles only). Between the circular and the longitudinal layers there’s a plexus of nerves; the myenteric plexus.

Notice this section in the esophagus, you can see smooth muscles, lamina propria, and notice the esophageal gland in the submucosa.
- **Histology of Stomach:**

In histology, stomach is divided into 3 parts, the first one is the cardia, it’s the end of esophagus and beginning of stomach (cardiac orifice; فتحة الفؤاد), it’s different histologically from the fundus and body of stomach (which have the same histological features) and from Pylorus, the last part of stomach; which is divided into pyloric antrum, pyloric canal & pyloric sphincter. This sphincter is different from cardiac sphincter which is physiological and prevent regurgitation of stomach contents upward to the esophagus, but pyloric sphincter is anatomical sphincter which means it has thickening in smooth muscles and this controls the passage of digested material (acidic chyme) in stomach to duodenum, chyme passes from pylorus to duodenum (duodenum usually receives acidic chime, this causes irritation of mucosa of duodenum, but in duodenum there is a huge amount of alkaline secretions to neutralize the acidic chyme.

Function of stomach is digestion and formation of acidic chyme (bolus starts from oral cavity till esophagus, in stomach it becomes chyme as in stomach a lot of secretions convert this bolus into acidic chyme such as HCl, pepsinogen and gastrin, these are secretion from cells of mucosa in stomach).

Many types of cells are found in mucosa of the stomach; paraïtal cells which secret HCl, chief cells that secret pepsinogen and mucus cells which secret mucus to protect the mucosa of the stomach from its own digestion, also we have gastrin cells that secret gastrin hormone and they’re considered endocrine cells.

In anatomy the mucosa of the stomach has folds (Histologically, they are invaginations of submucosa through the mucosa to increase the surface area for absorption), these folds are called Rugae.
A section in the stomach shows the same 4 layers; 1) mucosa which has lamina propria (it contains glands and it’s loose connective tissue layer) and muscularis mucosa. 2) submucosa. 3) muscularis externa. 4) serosa (serosa not adventitia as the stomach is located inside the abdomen covered by peritoneum).

Gastric mucosa has gastric glands that open on the surface as gastric pits (pits are the opening of the gastric glands into the mucosa).

The lining epithelium of stomach is simple columnar epithelium without goblet cells (important). In stomach there’s no goblet cells, they start to appear in small intestines, and as we move distally the number of goblet cells increases; in large intestines they are very numerous.

Submucosa is a layer of connective tissue, rich in lymphatics and blood vessels, it has no glands, the glands are found in the lamina propria of mucosa. As it's said before submucosa has a plexus of nerves, it’s Meissner's plexus. It’s an autonomic system; it sends sympathetic and parasympathetic signals to the mucosa.

Muscularis externa usually has inner circular and outer longitudinal layers, between these 2 layers of muscles we have myenteric plexus, this one is also autonomic, it’s responsible for the peristaltic movement of smooth muscles especially in small intestines and it’s secretomotor for glands.

Muscularis externa in stomach has 3 layers (muscularis externa here is different from the entire GI tract); inner circular, outer longitudinal and most inner oblique layer (smooth muscles) so these layers are ordered like this: oblique, inner, outer, but myenteric plexus is found between the inner circular and the outer longitudinal.

Note: stomach has 3 layers of muscles because its function is digestion so it needs more strength.

Serosa is simple squamous epithelium (peritoneum).
Notice the gastric pits in mucosa, which are the opening of the glands in mucosa, notice the duct of the gland, and when we say “gastric pit” this includes the duct and the opening of the gland on the surface. The type of the gastric glands is tubular; simple or branched (simple tubular or branched tubular, notice figure 3 (cardia), the gland that is in the center is simple tubular, while the glands which are on both sides are branched tubular).

It’s important to know the ration between the length of the gastric pits and the length of the gastric glands. For example, in cardia the duct is longer than the gland whereas in body most of it is gland so pits are shorter. In pylorus the duct is longer and gland is smaller. These changes are important (the ration of pits to glands), notice them in the figures below.

Remember that these glands are found in lamina propria of mucosa, submucosa here has no glands.

Notice figure 4 (body & fundus), pits are short and wide (for secretions to reach the mucosa) while the glands have more thickening (they are longer); glands here are large and compose 4/5 of the mucosa.
Remember that the lining epithelium is simple columnar, and its main secretion is mucus. (important)

Notice figure 4, the gland is divided into 3 parts; isthmus, neck and base. This is important.

Parietal (oxyntic) cells (figure 6), (it is acidophilic and pale or orange in color) are located and concentrated in isthmus and neck, and less as we move to the base. Parietal cells are few in cardia, but very numerous in fundus and body, and absent or very few in pylorus, they secret 1) HCl and 2) intrinsic factor that helps in absorption of vitamin B12 in ileum.

Chief (zymogenic) cells (figure 7) are located in the base (the lower region of tubular glands), they secret pepsinogen and sometimes amylase and rennin, in human these cells secret gastric lipase but most importantly pepsinogen that is converted into pepsin that is important in stomach. The base is basophilic due to the abundant rough endoplasmic reticulum and ribosomes (RNA), the apex is acidophilic as a result from the presence of enzyme. Chief cells are located only in fundus and body, no chief cells in pylorus or cardia.

Mucous neck cells (figure 5) are located in isthmus and neck. These cells (glands) are simple columnar epithelial cells, mucus is important on surface as we said, but it’s also important here in the gland because it’s responsible in stomach for neutralization of acids and protection of lining mucosa from its own digestion.

Stem cells (regenerative cells; figure 8) are located at the neck or under isthmus (so the newly formed cells could move toward the surface or downward to the base), its’ called regenerative because it can be converted into other types of cells, its turnover is 3-7 days.

Gastrin cells (enteroendocrine cells; G-cells) are found at the base, they secret gastrin and serotonin.
Figure 5: Mucous neck cells

Figure 6: Parietal cells (the cells in the box); they tend to appear pale (acidophilic) at the neck and isthmus, but at the base chief cells (basophilic) appear dark.

Figure 7: Chief cells

Figure 8: Stem cells. Notice the lining epithelium which is simple columnar, and note the white color which is mucus because it dissolves during preparation.
The most cells we can see are Mucus, parietal and chief cells, stem cells and enteroendocrine cells cannot be seen by light microscope, they need electron microscope, but mucus cells can be seen light microscope.

Note: mucous neck cells are found in the neck, they secret mucous, you can find them in the cardia, fundus and body but they are more numerous in the pylorus because it receives the acidic chyme so mucus neutralizes it to decrease the acidity.

The function of parietal cells is to form and secret HCl, so it has 2 stages; active and inactive. Active means that HCl has been formed and it’s very close to the lumen and stored in canaliculi system (intracellular canaliculus), when these canaliculi are found this means that the cell is in the active stage. When these cells are inactive there’ll be tubulovesicular cytoplasm (cytoplasm contains tubules and vesicle) and this means that these cells haven’t synthesized HCl yet.

Pylorus differs from cardia, body and fundus in many things, like: 1) Parietal cells: it has no parietal cells (or it might be very few).

2) Chief cells: it also has no chief cells.

3) Mucous cells are common in pylorus.

4) Gastric pits and glands: pits are very long and narrow, glands are short and might have coils, the pit is three times longer than the gland.
In pylorus there’re lymphatic nodules (aggregation of lymphocytes). Lymphocytes are found along the GI tract but in the pylorus there’re aggregations of these lymphocytes because their function is filtration of foreign bodies, bacteria and viruses resulting in aggregations of lymphocytes that form lymphatic nodules. Also we said that pylorus has pyloric sphincter, it’s a true one (thickening of inner circular smooth muscle).

Do not forget that there’s no goblet cells in the stomach.

![Figure 11: Layers and glands in the stomach](image)

Note: how to differentiate between the parts of stomach according to the pits & glands?

In carida: gastric glands are short. In body (or fundus): gastric glands are long and thick (4/5 of the thickening of the mucosa), and pits are short and wide. In pylorus pits are longer than glands.
- **Histology of Small Intestines:**

Small intestine is composed of 3 parts: duodenum, jejunum and ileum, the length of small intestine is about 6 meters. Duodenum is 10 inch in length, about 25 cm. Duodenum is very important; it’s retroperitoneal (behind the peritoneum) whereas jejunum and ileum are intraoperitoneal and they have mesentery. Duodenum also receives common bile duct and pancreatic duct and their secretions so it has a role in fat digestion. Absorption mainly occurs in jejunum and ileum.

As you know the main function of small intestine is absorption, so the mucosa is different, it has finger-like projections to increase the surface area for absorption. The lining epithelium of small intestine is simple columnar epithelium (like stomach), but it has goblet cells found on the projections. In the base there’re glands, called glands of Lieberkühn (German scientisit), it’s located in the lamina propria of mucosa for secretion.

The function of small intestines after completing digestion is absorption. Layers in small intestines are: mucosa, submucosa, muscularis extera and serosa or adventitia (duodenum is retroperitoneal so it’s covered by adventitia except one surface, whereas jejunum and ileum are completely covered by serosa). Muscularis extera has 2 layers; inner circular and outer longitudinal and between them is myenteric plexus responsible for peristaltic movements.
Submucosa is connective tissue layer rich in blood vessels, it has Meissner’s plexus. Submucosa in duodenum has glands, called Brunner's glands, they secret alkaline secretion to neutralize the acidic chyme of stomach to prevent peptic ulcer, so common peptic ulcer occurs in the first inch of duodenum because more acidic chyme reaches the first inch, then there’ll be neutralization.

Duodenum completes the digestion as it receives the common bile duct and pancreatic duct; its function is to complete digestion.

To increase the surface area of mucosa, there are invaginations of submucosa through the mucosa, in stomach they are called rugae, but here in duodenum they are called plicae cirulares (Kerckring's valves).

Villi in small intestines are 0.5-1.5 mm in length, making a brush border (surface). Glands of Lieberkühn have ducts that open between villi. Mucosa of small intestine is said to be like fingers, each finger has 2 halves, the lower half has glands of Lieberkühn (crypts) and the upper one is villi.

Upper half or villi are unique structures; 1) they have microvilli that make brush border to increase surface area. 2) The lining epithelium is simple columnar epithelial cells in addition it has goblet cells. 3) Smooth muscles are found in lamina propria; the extension of lamina propria reaches to the tip of the villus. Lamina propria is loose connective layer, it has plasma cells lymphocytes, fibrocytes, and the rest of cells we find in connective tissue, but the important thing is that it has lymphatic capillary (lacteal); it’s a blind end of lymph vessels and it helps in absorption of lipid and fat. (You might have a
question about the contents of lamina propria in the exam). Main function of villi is absorption by villi, microvilli and Lacteal lymphatics.

Base (lower half) has glands of Lieberkühn, the type of cells lining the mucosa is simple columnar epithelium, it secretes mucus and bicarbonate, and it has goblet cells in the gland. Paneth’s cells are located in base and the gland, but these cells are not found in villi. They secret immunoglobulins and lysozymes (antibodies) and it protects the flora of small intestines. Stem cells are basal and their function is the regeneration of other cells, there’re also enteroendocrine cells (like stomach, here is enteroendocrine cells and stem cells).

So these are the differences between villi and the gland (important).

Note: each absorptive cell has 3000 microvilli.

In duodenum, villi have leaf-like appearance. On the other hand, in jejunum and ileum villi have finger-like projections.

Duodenum has Brunner's glands in submuacosa and its villi have leaf-like appearance.

Jejunum has plicae cirulares, it’s prominent.

Ileum has Peyer's patches, they are lymphatic nodules found in lamina propria and can be found in submucosa.

Paneth’s cells have specialized stain, they are found in the base of the gland, it secretes lysozymes (anti-bacterial) and it controls intestinal flora. M (microfold) cells are located between the basement membrane of mucosa (from muscularis mucosa) till the surface; it interrupts the base and extends to the surface. These cells contain lymphocytes and macrophages that engulf the bacteria and foreign bodies inside the cytoplasm and send an image (copy) of these bacteria and foreign bodies to lymphocytes so it can produce antibodies (these cells are
important for immunity; as GI tract is the passage for anything you eat, so bacteria and foreign bodies might enter into the GI tract, these cells do filtration by lymphocytes).

Some figures of small intestines:

Do not forget to study the slides and take a look at their figures, good luck.

A special dedication to Asem Abu-Gamar.