2. SECRETIONS OF THE DIGESTIVE TRACT

SECRETORY GLANDS AND CELLS

The alimentary tract produces a large variety and quantity of substances which contribute to digesting the food, and protecting and regulating the functions of the digestive tract. All of these substances are secreted by either cells lining the digestive tract or by glands directly connected to the alimentary tract. Not only some of the regulatory substances are secreted into the lumen, but into the intracellular space, in order to reach circulation and then targeted tissues or directly in nearby cells (Fig. 2-1).

The type of secretion will also be related to the stage of digestion in which the food is found.

An example of the types of secretions by the oral cavity is presented in Fig. 2-4. The goblet cells, located throughout the digestive epithelium, produce significant amounts of mucus to protect the epithelium from physical damage but, most importantly, from the corrosive effects of acid especially in the stomach. There are varieties of enzyme secreting cells within the crypts of Lieberkühn. There are tubular glands in the stomach which contain Oxynctic or parietal cells capable of producing very strong hydrochloric acid (HCl) as well as peptic or chief cells which produce pepsinogen.

Examples of more complex glands are the salivary glands which produce a combination of enzymes, buffers and other fluids, the pancreas which secretes several enzymes and the liver which secretes among many things emulsifying agents to help in fat digestion.

In order to maintain some organization the secretions of the digestive tract will be discussed in sequence starting at the oral cavity and following the order in which they reach the digestive tract (Fig. 2-3).

The oral cavity

The first secretion into the digestive tract takes place in the oral cavity. There are three main types of salivary glands contributing to the production of saliva. These are the parotid, submandibular and sublingual glands, but also many small buccal glands contribute to the overall secretion (Fig. 2-4).
All salivary glands are comprised of multiple acini, which empty in collecting ducts before being secreted to the buccal cavity (Fig. 2-5).

Secretions differ for each type of salivary gland. Saliva contains a variety of protein compounds for different purposes and these changes are reflected in the secretion of each gland. Saliva also contains large amounts of fluids and ions, as well as bicarbonate (HCO₃⁻) for buffering purposes. The main component is a serous type of secretion which is based on an enzyme for the digestion of starches called ptyalin. This enzyme is an α-amylase. The other component of saliva is a mucus-like secretion that contains mucin which is a lubricant. This facilitates swallowing and protects buccal surfaces. While the parotid glands secrete only the enzyme containing type of saliva, the submandibular and sublingual glands secrete a combination of serous and mucus type of saliva. Finally, the buccal glands only produce mucus to protect the oral cavity. The saliva maintains a pH ranging from 6.0 to 7.0. This is the ideal pH for the maximal activity of the α-amylase.

As saliva leaves the acini there is a significant active absorption of Na⁺ and passive absorption of Cl⁻, and at the same time, the cells in the collecting ducts secrete K⁺ and HCO₃⁻. In other words, the composition of the secretion released by the cells of the acini is significantly different than that reaching the oral cavity. The reason for these changes is that the primary secretion more closely resembles the concentration of ions in extracellular fluid and, if these were maintained in the secreted saliva, the organism could fall into a serious ionic unbalance during periods of copious salivation.

Role of saliva. The role of saliva is multiple (Fig. 2-6). It lubricates the bolus with the fluid and the mucus, especially important in birds as it permits swallowing of fairly large pieces without physical damage to the throat and oesophagus. Saliva also contributes a significant amount of amylase for the digestion of carbohydrates as well as some lingual lipase which participates in lipid digestion.

Saliva also plays a role as an antibacterial agent by simply carrying away bacteria from the mouth, and having antibacterial compounds. Some of the compounds are the...
proteolytic enzymes (lysozyme) which digest bacteria. There are also antibodies, specific for oral bacteria. All these actions maintain the health of the oral cavity and the teeth of the animals.

The last role of saliva is thermoregulation. There are many animals that are not capable of sweating, dogs for example. These animals depend on the evaporation taking place over the tongue, oral cavity and respiratory tract to cool down the organism. This is easily observable when a dog is panting with the tongue hanging out. The dog evaporates large amounts of salivary fluids by rapidly passing air over the wet surfaces through very shallow and fast breathing. Other species such as horses and cows do not use saliva as a coolant, because they can cover the body with sweat that can then be evaporated. Mice and rats cannot pant or sweat, thus, they purposely use saliva to wet their fur in order to cool down.

**Regulation of salivation.** Salivation is regulated by multiple factors (Fig. 2-7). Parasympathetic stimulation is one of the mechanisms that trigger salivation. Taste and texture of food on the tongue, mouth and pharynx trigger the salivatory nuclei situated between the medulla and the pons. The taste of some compounds, such as sour ones is recognized as powerful triggers of salivation. The smell of pleasing food increases salivation, while the smell of unpleasant food inhibits salivation. Salivation can also be triggered through classical conditioning as demonstrated by Pavlov. Sympathetic stimulation, although not a powerful stimulator, does cause salivation.

### Volume and composition

The volume of saliva produced depends on the species and the diet (Fig. 2-8). A mature pig can produce close to one liter of saliva per day while a mature cow can produce between 100-200 liters per day. In the case of ruminants the saliva plays an important role in buffering the acids generated in the fermentation process, which means has a high content of bicarbonate and phosphate.

**Salivary volume and composition**

- **Daily volume ranges widely**
  - 1 litre in an adult pig
  - 100-200 L in the adult cow

- **Ruminants have saliva high in bicarbonate and phosphate**
  - Needed to buffer fermentation acids

### The stomach

**Functional anatomy.** In monogastrics, the entrance to the stomach is through the oesophagus and immediately adjacent to it is the oesophageal gland region. As it can be seen in figure 2-9, this is followed by the cardiac glandular region and the fundic glandular region. All these areas make up close to 80% of the stomach area. The pyloric glandular region which empties in the duodenum covers the remaining 20% of the area.
Gastric secretions. In the stomach there are many mucus cells covering surfaces and pits. These cells produce thick mucus, alkaline in nature, which protects the tissue from the acid content (Fig. 2-10, 2-11).

**Gastric secretions**
- Surface and pits covered with mucus cells
  - Produce thick protective mucus
  - Alkaline in nature
- Within the pits are tubular glands
  - Oxyntic or gastric glands
  - Pyloric glands
- Produce slightly different secretions depending on region

**Pyloric glands**
- Similar to gastric glands
- Have few chief cells
- Almost no parietal cells
- Mainly mucus cells
  - Like neck cells secrete some pepsinogen
  - Mucus lubricate food passage
  - Protect stomach from digestive enzymes
- Endocrine cells secreting gastrin

**Figure 2-10. Production of different secretions by the stomach**

**Figure 2-11. Production of mucus in the stomach**

Within the pits there are tubular glands which depending in their position within the stomach, can be either oxyntic, also known as gastric, or pyloric.

The oxyntic glands are located mainly in the cardiac and fundic glandular region and produce HCl, pepsinogen, intrinsic factor and mucus. The pyloric glands are located in the pyloric glandular region and produce mucus, pepsinogen and gastrin (Fig. 2-12).

A drawing of the typical distribution of cells within a gastric gland is presented in figure 2-13 and the details of the structure of an Oxyntic cell are shown in figure 2-14.

**Figure 2-13. Secretions produced by the gastric or oxyntic gland**

These glands secrete slightly different proportions of each compound depending on the area of the stomach in which they are located. Pyloric glands have similar structure to gastric glands but having fewer chief cells, and almost no parietal or oxyntic cells; therefore, they produce little or no HCl.

Pyloric glands contain mucus and endocrine cells. The mucus cells, as the mucus neck cells, produce mostly mucus to protect the stomach by coating it and the passage towards the duodenum by lubricating it. These cells also
produce some pepsinogen. The endocrine cells produce gastrin, a hormone that regulates gastric secretions.

**Gastrin secretion.** Gastrin is secreted by the G (gastrin) cells of the pyloric glands (Fig. 2-15) in response to the presence of proteins (usually meat). Gastrin is secreted into the lumen of the stomach. With the help of the movements by the walls of the stomach, the contents mix and distribute in such a way that gastrin gets in contact with the enterochromaffin-like cells in the body of the stomach.

Enterocromaffin-like cells secrete histamine into the deep gastric glands, thus reaching the parietal cells that then release HCl. The HCl mixes with the stomach contents lowering the pH (Fig. 2-16).

**Pepsinogen secretion.** Pepsinogen is secreted principally by the peptic or chief cells and in smaller quantities by the mucus neck cells of the gastric glands. The presence of acetylcholine from the vagus nerve or from the enteric nervous system, as much as the stimulation from stomach acid regulate the release of pepsinogen (Fig. 2-17).
A feedback mechanism blocks gastrin production by G cells and reduces HCl production by parietal cells when there is a low pH. Low pH also inhibits the enteric nervous system reflex, thus reducing the release of pepsinogen by acetylcholine stimulation (Fig. 2-18).

Feedback control by acid

- If pH reaches 3 or below
- G cells are blocked
  - Do not secrete gastrin
  - Further acid production is reduced
- Acid inhibits enteric nervous reflex
  - Reduces pepsinogen secretion

Figure 2-18. Regulation of stomach pH

Phases of gastric secretions

All gastric secretions can be triggered in one or more of three phases, a cephalic, a gastric, and an intestinal phase (Fig. 2-19).

During the cephalic phase the stimulation of gastric secretion is mediated through inputs generated by the sight, the smell and the taste of food. The response is enhanced when the appetite of the animal is high. The stimulation mediated through the cephalic phase is responsible for about 20% of the secretions resulting from a meal.

The gastric phase is activated when the food enters the stomach and directly activates local enteric system nervous reflex; the mechanism for the release of gastrin, which in turn promotes gastric secretion and a vagal reflex, which further supports gastric secretions. These stimuli are maintained for as long as there is food in the stomach and are responsible for a further 70% of the total secretions associated with a meal.

The food entering the duodenum, now called chyme, stimulates further gastrin secretion and, through this mechanism, known as the intestinal phase, the last 10% of the gastric secretion is accounted for.

At the time that the chyme enters the small intestine it triggers both, the intestinal phase of gastric secretion and the reverse enterogastric reflex. This reflex is conveyed by the myenteric nervous system; the extrinsic sympathetic and vagus nerves are responsible for inhibiting stomach secretion (Fig. 2-20).

The pancreas

The next organ contributing secretions to the digestive process is the pancreas, as shown in figure 2-3. This organ has a similar glandular design to the salivary gland, but the secretions are different (Fig. 2-21).
The cells in the acini secrete digestive enzymes (Fig. 2-22) responsible for the digestion of proteins, carbohydrates and fats while the ducts and ductules are responsible for the production of large amounts of sodium bicarbonate, which neutralizes acidity from the chyme (Fig. 2-23). All these secretions are released into the pancreatic duct before reaching the duodenum. A difference from the salivary glands, the pancreas has the Islets of Langerhans where the hormone insulin is produced to help in glucose metabolism. This hormone is secreted into the circulation which contribute to the digestion of proteins fats and carbohydrates (Fig. 2-23).

The pancreas produces a significant number and quantity of digestive enzymes, which contribute to the digestion of proteins fats and carbohydrates (Fig. 2-23).

Pancreatic secretions

- Similar structure as salivary glands
  - Enzymes secreted by acini
  - Large volume sodium bicarbonate secreted by ductules and ducts
- Drain into hepatic duct
- Contain Islets of Langerhans
  - Produce hormones (insulin and others)
  - Secreted to circulation

Figure 2-21. Characteristics of pancreatic secretions

Pancreatic enzymes

- Contain enzymes for proteins, carbohydrates and fat
  - Proteins
    - Trypsin, chymotrypsin, nuclease, carboxypeptidases, elastases
  - Carbohydrates
    - Pancreatic amylase
  - Lipids
    - Pancreatic lipase, cholesterol esterase and phospholipase

Figure 2-22. Enzymes produced by the pancreas

To help protein digestion the pancreas secretes trypsin, which is the most abundant, chymotrypsin, carboxypeptidases, nuclease and elastases. All these enzymes are secreted as inactive proenzymes called trypsinogen, chymotrypsinogen, procarboxypeptidase, pronuclease and proelastase, respectively.

For carbohydrate digestion the pancreas produces pancreatic amylase and, for lipids it produces pancreatic lipase, cholesterol esterase and phospholipase. The reason for proenzymes is to protect the pancreatic tissue from digestion, before the proenzymes reach the duodenum.

The pancreas also produces trypsin inhibitor. This mechanism works well because trypsin is the enzyme which activates all the other proteolytic proenzymes as can be seen in figure 2-24. The activation of trypsinogen to trypsin is carried out by an enzyme produced by enterocytes called enterokinase or by trypsin itself.

Regulation of pancreatic secretions

The regulatory mechanisms to control pancreatic secretion involve three different possible stimuli (Figs. 2-25, 2-26).

As it happens in the stomach for gastric secretion, acetylcholine secreted by the parasympathetic vagus nerve and by cholinergic nerves from the enteric nervous system
can also stimulate pancreatic secretions. In particular, the enzymes produced by the acinar cells are stimulated by acetylcholine.

Cholecystokinin produced by duodenal and upper jejunal mucosa in response to entrance chyme from the stomach, also stimulates acinar cells to produce digestive enzymes.

**Regulation of pancreatic secretion**

- **Three main stimuli**
  - Acetylcholine (acinar cells)
    - Parasympathetic vagus
    - Cholinergic nerves in enteric nervous system
  - Cholecystokinin (acinar cells)
    - Duodenal and jejunal mucosa (food)
  - Secretin (tubular cells)
    - Duodenal and jejunal mucosa (acid)

Secretin, also produced by duodenal and upper jejunal mucosal cells, is secreted in response to the increased acidity found in chyme coming from the stomach; and, it triggers the production of buffers by the tubular cells of the pancreas.

**Phases of pancreatic secretions**

As it was the case with gastric secretions, the pancreatic secretions are also produced in three very similar phases, a cephalic, a gastric and an intestinal phase (Fig. 2-27).
duodenum and upper jejunum the production of cholecystokinin and secretin will trigger the production of significant amounts of enzymes by the acinar and buffers by duct cells of the pancreas. The hormone secretin is produced as the prohormone prosecretin and released into the small intestine, where the acidity of the chyme stimulates its secretion and, activates the hormone to secretin to be absorbed into circulation. Through circulation secretin reaches the pancreas and stimulates the production of bicarbonate, which neutralizes the acidity in the small intestine. This process will take place when the chyme has a pH of 4.5 or less.

The liver
The secretory function of the liver is limited to the production of a detergent-like substance, bile (Fig. 2-28).

### Liver secretion

- **Bile is the main product**
  - An 80 Kg animal secretes about 600-1000 mL of bile
- **Produced by hepatocytes**
- **Secreted into duodenum, or**
- **Stored in gallbladder**
  - Concentrated form

This detergent which serves to emulsify fat material is produced by the hepatocytes and in an 80 kg animal may be as much as 600-100 mL per day. The bile also contributes to absorption of digested fat products and serves as a carrier for circulatory waste, which once it is secreted into the small intestine, is not reabsorbed and it is eventually discarded with the faeces (Fig. 2-29).

### Bile production
The production of bile is an ongoing process. The secretions of the hepatocytes are collected by the bile canaliculi, located between hepatocytes in the hepatic plates, and transported towards the interlobular septa until it joins the terminal bile ducts. These ducts eventually empty in the hepatic duct and common bile duct and, if the body is required to digest fat, the bile can be emptied directly into the duodenum or, if not, can be routed towards the gallbladder via the cystic duct. The capacity of the gallbladder is only about 60 mL in a 90 kg animal but it can store the bile production of about 12 hours of 450 mL of bile by concentrating the bile, through absorption of water and electrolytes by the gallbladder mucosa.

### Role of bile

- Bile acids help emulsify fat particles
- Support absorption of digested fat
- Help neutralize acid
- Serve to discard waste, toxins
  - Bile pigments, bilirubin

### Composition and recycling
Bile contains water, bile salts, bilirubin, cholesterol, fatty acid, lecithin, as well as Na+, K+, Ca2+, Cl- and HCO3-. Most of these materials are continuously recycled. It is estimated that 94% of the secreted bile salts are reabsorbed by the small intestine. Half of it re-enters the mucosa of the upper small intestine by diffusion and the rest is actively transported by the distal ileum. Once in circulation, they reach the liver through the portal system and there they are absorbed by the hepatocytes and secreted towards the canaliculi for further service. This recirculation is called the enterohepatic circulation (Fig. 2-30).
Regulation of liver secretions
The emptying process of the gallbladder is by rhythmical contractions of its wall and the relaxation of the sphincter of Oddi which closes the common bile duct at the point of entry into the duodenum. This is achieved by cholecystokinin at the same time as the stimulation of the pancreas for production of enzymes. The secretion is also supported by acetylcholine from the vagus and the enteric nervous system (Fig. 2-31).

Regulation of bile secretion
- **Cholecystokinin**
  - Released from duodenal mucosa
    - Stimulates gallbladder contraction
    - Relaxation of sphincter of Oddi
  - Supported by acetylcholine
    - From vagus and enteric nervous system

Figure 2-31. Regulation of bile secretion by cholecystokinin

The hormone secretin stimulates not only bicarbonate secretion by the pancreatic ducts, but it also stimulates sodium bicarbonate production by the bile ducts, thus, increasing the volume of bile produced for several hours following a meal. During the process of concentrating the contents of the gallbladder much of the fluid and electrolytes are removed, but the quantity of bile salts, cholesterol and lecithin does not change. Cholesterol in bile does not serve any known purpose and it is believed to be there as a result of the synthesis of bile salts. Cholesterol is very insoluble in water so it has to be carried by the bile salts. If the concentration is too drastic, there is a chance that cholesterol precipitates in the gallbladder forming gallstones, which may also be produced by other imbalances.

The small intestine
Secretions of the small intestine. Located at the start of the duodenum between the pylorus and the papilla of Vater, where the common hepatic duct joins the duodenum, are found the Brunner’s glands. These glands are responsible for production of highly alkaline mucus to neutralize the acidity in the chyme. The stimulus to secrete it is the presence of chyme and the vagal simulation which also controls absorption of the products of digestion.

Between the villi, throughout the intestine are small depressions or pits called crypts of Lieberkühn. These crypts contain some goblet cells, which produce mucus to protect the villi’s surface and the enterocytes. The enterocytes within the crypt secrete large volumes of water and electrolytes. Enterocytes in the villi in turn absorb large amounts of water, electrolytes, as well as, nutrients. The fluid secreted by the enterocytes is highly alkaline and is derived from extra cellular fluid.

This liquid is reabsorbed in the villi, but while in the lumen of the GIT it serves to provide a watery environment close to the cells that permits the gastric secretions. Secretin also stimulates Brunner’s glands (Fig. 2-32).

Secretions of the small intestine
- **Brunner’s glands**
  - At beginning of duodenum
  - Between pyloro and papilla of Vater
  - Secrete highly alkaline mucus
    - Tactile stimulation of mucosa
    - Vagal stimulation
    - Secretin
- **Crypts of Lieberkühn**
  - Throughout the small intestine
  - Contain some Goblet cells
    - Secrete mucus to protect surface
  - Mainly enterocytes
    - Secrete large volumes of water and electrolytes

Figure 2-32. Secretions of the small intestine

Although not secreted, the enterocytes produce and exteriorize a variety of digestive enzymes which will participate in the last steps of digestion (Fig. 2-33). The role of each will be discussed in the next section dealing with digestion.
The stimulation of the secretory activity by the small intestine is mainly the physical presence of chyme. This may be mediated through enteric reflexes which also promote motility. The only endocrine regulation of small intestine secretion is done by secretin and cholecystokinin in a similar manner as they stimulate secretions in other organs (Fig. 2-34).

The large intestine

Secretions of the large intestine. The large intestine has the same crypts of Lieberkühn but there is no villi. In the crypts there are no significant enzymes so the only predominant type of cells are mucus ones (Fig 2-35). The rate of mucus secretion is regulated by the amount of intestinal content and its purpose is to protect the intestinal walls from physical excoriation and from the large amount of bacterial present in feces. Mucus also helps to bind fecal material.