# Chapter 5
## The digestive system of the pig

*H.N. Lærke & M. S. Hedemann*

**This chapter deals with:**

- An overview of pigs' digestive tract
- A description of the essential digestive processes
- A description of the role of the digestive organs in digestion and absorption
- A discussion of animal and feed factors affecting the digestive capacity

## 1. Introduction

The digestive system of the pig is fundamentally similar to all other monogastric mammals, but the evolutionary development in size and digestive capacity reflects greatly the habitual diet. Pigs are true omnivores, but with a large fraction of the diet coming from plant material. As such they have a great capacity to digest enzyme degradable carbohydrates in the upper part of the gastro-intestinal tract, and a well-developed ecosystem in the large intestine to partly ferment and utilize fibrous material.

# 2. Anatomy of the digestive system

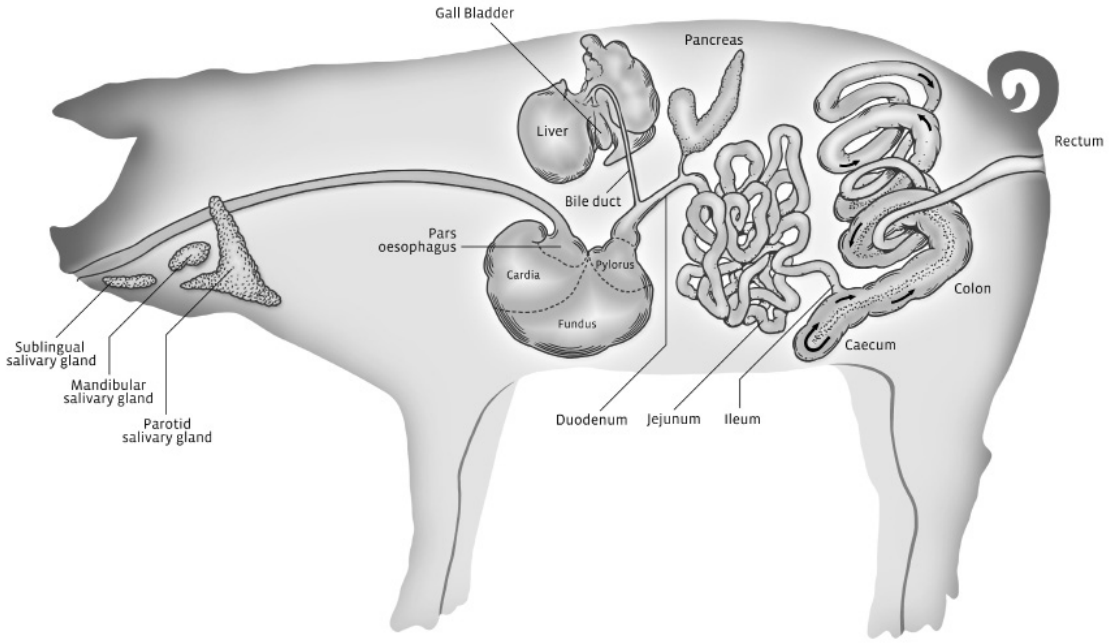


**Figure 5.1. Outline of the porcine digestive system (illustration by Mads Salicath).**

*2.1. Mouth and salivary glands*

The pig is born with 8 deciduous teeth, which increases to 32 with age. The full set of 44 permanent teeth is usually not fully acquired until 18 months of age. The permanent teeth consist of 3 pairs of incisors used for rooting, grasping and shearing food, 1 pair of canines, 4 pairs of premolars that coarsely grind the food, and finally 3 pairs of molars that crush the food into smaller particles.

The oral cavity is lined with a simple stratified squamous epithelium, which is keratinized in the areas where it is exposed to wear.

The muscular tongue, lips, cheek, and palate act together in the ingestion of food. Pigs have taste buds all over the oral cavity, but they are found in highest concentrations on the surface of the tongue.

Saliva is mainly secreted from three large glands; the parotid glands, the mandibular (also termed submaxillary) glands, and the sublingual glands. Major ducts from the parotid and mandibular glands transport saliva to the oral cavity, while the sublingual glands have multiple openings beneath the tongue. In addition, a number of small glands with a number of excretory ducts are present in the mouth. The parotid glands contain mainly serous cells, whereas the mandibular and sublingual glands contain both serous and mucus cells. Only the sublingual glands contain amylase. Serous saliva is thin and watery, while mucus saliva contains glycoprotein-rich mucins and is much thicker (viscous).

After leaving the mouth, feed enters the pharynx and oesophagus. The pharynx is long and narrow. The esophagus is short and covered with stratified squamous epithelium. Beneath the epithelium, a number of submucosal glands are located. Their function is to secrete mucin and bicarbonate, to neutralize luminal acid and protect the epithelium.

*2.2. The stomach*

The stomach of the pigs consists of a simple compartment that is divided into four functionally and structurally different regions (Figure 5.1). The pars oesophagea is a non-glandular extension of the esophagus into the proper stomach. Ulceration of the pars esophagea is a common phenomenon in pig production and develops from a complex interaction of dietary particle size, gastric fluidity, dietary carbohydrate content, and environmental stress factors. Recent studies have identified a hitherto uncultured spiral *Helicobacter* species *Helicobacter suis* sp. nov formerly described as *Candidatus Helicobacter suis*. The microorganism has been associated with ulceration of the non-glandular stomach and gastritis in pigs.

Next to the pars oesophagea is the glandular cardia that, in contrast to most other species, is very large and occupies approx. one third of the stomach luminal surface. The fundus, or proper gastric region, is located between the cardia and pylorus.

All three regions contain secretory glands located in so-called ‘gastric pits’ (Figure 5.2). Structurally, they are similar, but they contain different cell types. The major surface of the stomach and lining of the pits are covered with surface mucous cells that produce thick, tenacious mucus to protect the epithelium against injury from acid and grinding activity.

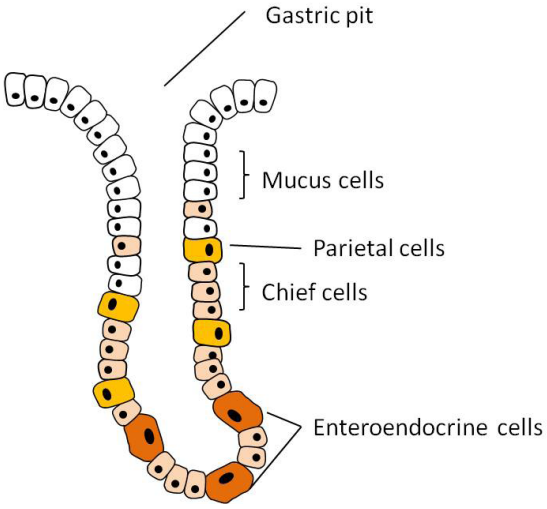


**Figure 5.2. Anatomical illustration of the gastric pit of the fundus.**

The gastric pits of the fundic mucosa contain HCl-producing parietal cells that are clustered in the neck of the gland. Distributed between these cells are mucous neck cells that produce thin mucus and proteases. As the only cells of the stomach lining, mucous neck cells divide and migrate either down into the gland or up into the pits and differentiate into any of the mature cell types. In the fundic region, pepsinogen-producing chief cells are located at the base of the fundic glands. In addition, the fundic mucosa also contain endocrine/paracrine somatostatin producing D cells, endocrine G cells producing gastrin, serotonin producing enterochromaffin (EC) cells, and histamine producing histamine-immunoreactive cells and mast cells.

The cardia and pyloric region (antrum) contain different cells types than in the fundic region. The cardiac glands have no chief cells, but have mucous cells that produce mucus, proteases and gastric lipase. The pyloric glands do contain mucous neck cells that produce mucus and proteases and zymogen producing chief cells, but contain no parietal cells. Furthermore, the pyloric glands

also contain gastrin producing G cells and somatostatin producing D cells, but the mucous cells are the dominant cells.

*2.2.1. Size and capacity of the stomach*

The weight of the stomach represents 0.5-0.8% of body weight in suckling pigs and between 1-1.3 % in growing pigs. In adult pigs, the stomach accounts for approximately 0.6% of total body weight. The capacity ranges from 30 ml in newborn piglets to approximately 3.5 l in slaughter pigs, and 5 l in adults. Under pressure the capacity increases to 8 and 12 l for slaughter and adult pigs, respectively. Numerous studies have shown that the bulk of the diet can influence the subsequent capacity of the stomach.

*2.3. The pancreas*

The pancreas is located in proximal duodenum. The body of the pancreas separates in two lobes with the centre surrounding the portal vein. A single pancreatic duct leaves the right lobe and enters the duodenum on a minor palpilla 12-20 cm distal to and separate from the bile duct entry, 20-25 cm from the pylorus.

The pancreas is a mixed endocrine and exocrine organ. The exocrine pancreas consists of the acinar cells and the duct system, representing more than 95% of the pancreas fresh weight (Figure 5.3). The acinar cells produce and store pancreatic enzymes and inactive zymogens, and when stimulated release them into the duct system for transport to the duodenum. Water, bicarbonate and other electrolytes of pancreatic juice are produced in centroacinar cells and cells of the intercalary and intralobular ducts.

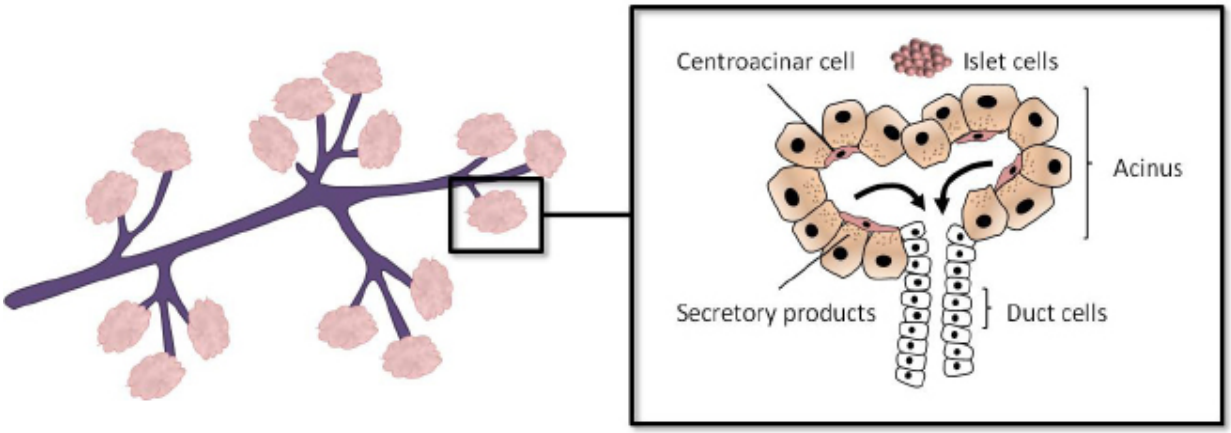


**Figure 5.3. The exocrine and endocrine cells of the pancreas.**

The endocrine part of the pancreas is restricted to the islets of Langerhans. The islets are distributed throughout the acinar exocrine tissue and contain glucagon producing alpha cells (15-20% of total islet cells), insulin and amylin producing beta cells (65-80%), somatostatin producing delta cells (3-10%), pancreatic polypeptide producing PP cells (3-5%), and possibly also ghrelin producing epsilon cells (<1%).

*2.4. The liver and gallbladder*

The liver is thoroughly described in Chapter 13. Here, we will briefly describe its anatomy and function related to bile acid production and secretion.

Hepatocytes (liver cells) are plates or one-cell-layer thick cells that are bathed on both sides by hepatic sinoids and arranged radially around a central vein (Figure 5.4). The hepatic portal vein, a hepatic artery and an interlobular bile duct forms what is called ‘the portal triad’.

Blood from the portal vein and hepatic artery flows centrally in the hepatic sinoids, while bile produced by the hepatocytes drains into bile canaliculi and then through ducts of Hering to the interlobular bile ducts in the portal triad. The interlobular bile ducts further merge into larger intrahepatic ducts, which become the extrahepatic biliary system. This system includes the hepatic bile duct, which divides into a cystic duct connected to the gallbladder, and a common bile duct connecting to the duodenum. The bile duct enters the duodenum on a palpilla located 2-5 cm from the pylorus.

The bile secretion from the hepatocytes is constant, but bile is only released to the intestine when needed for lipid digestion. Hence, when little or no food is present in the duodenum, the Sphincter of Oddi is closed and bile is diverted from the bile duct to the gallbladder where the bile is concentrated. When food, particularly fat-rich food, enters the duodenum, the Spincter of Oddi is relaxed and the gall bladder contracts by a combination of neural and hormonal factors. Gut endocrine cells are stimulated to release CCK, while neural receptors located at the Spincter of Oddi in conjunction with the intramural plexus coordinate the bile duct and bladder peristalsis.

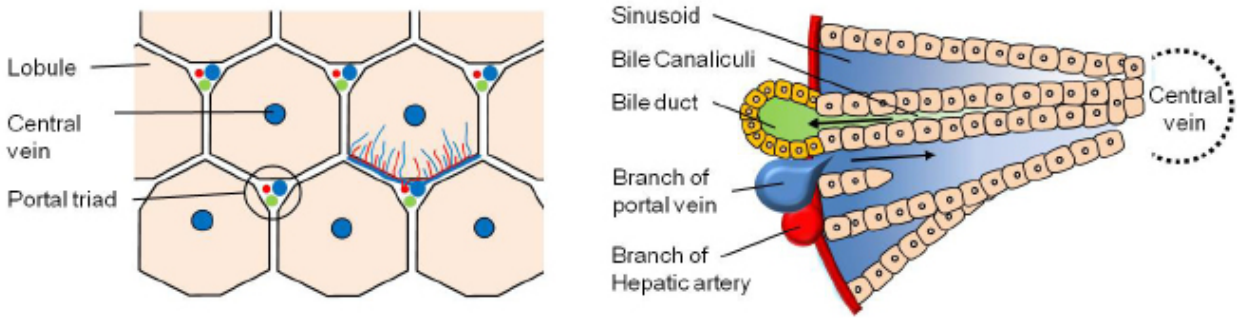


**Figure 5.4. Histological anatomy of the liver lobule and portal triad.**

*2.5. The small intestine*

The small intestine comprises the duodenum (4-4.5%), jejunum (88-91%) and ileum (4-5%). The proportion of duodenum in the neonate is similar to that of the adult, whereas the differentiation between jejunum and ileum is not clear. Although there are distinctive morphological features, the duodenum, jejunum and ileum share a lot of common features.

The small intestine consists of four major layers; the serosa, the muscularis, the submucosa and the mucosa (Figure 5.5). The serosa is the outermost layer of the intestinal wall. It has a squamous epithelium forming the mesentery that contains connective tissue, large blood vessels and nerves. The muscular layer contains two types of muscle fibres; an outer layer of longitudal muscles and an inner layer of circular muscles that are involved in gastrointestinal motility. The submucosa is a layer of connective tissue holding together the large blood and lymphatic vessels and neural complexes. The mucosa consists of three sublayers; the muscularis mucosa, the lamina propria and the epithelium. The muscularis mucosa consists of a longitudinal inner muscle and an outer muscle encircling the intestine and produce transient intestinal folds. The lamina propria consists of blood vessels, free lymphocytes and lymph nodes called Peyers patches, and neurons held together by connective tissue. It supports the structure and nourishes the epithelial layer. The epithelial layer consists of a single layer of epithelial cells. They cover the whole luminal surface of the intestine, which is severely folded by the formation of finger-like projections called villi, and at the base of these Crypts of Lieberkuhn, that are moat-like invaginations.

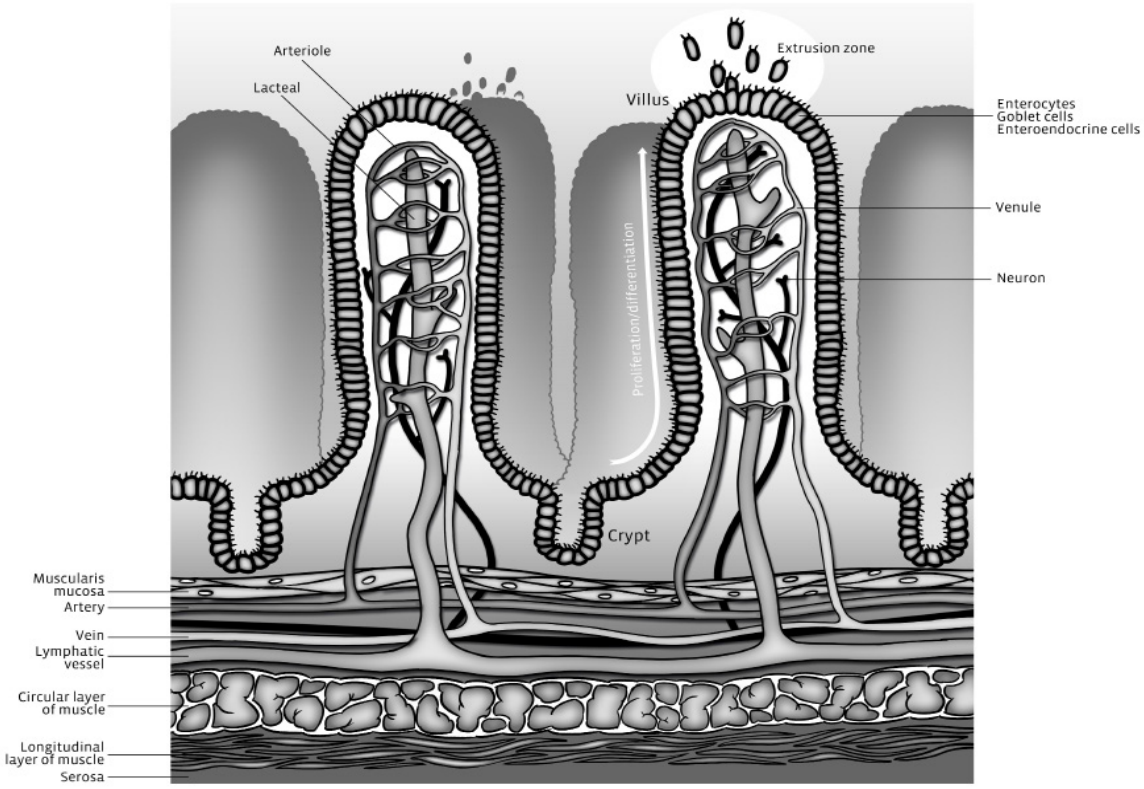


**Figure 5.5. Schematic presentation of the small intestinal wall (illustration by Mads Salicath).**

There are 3 types of epithelial cells on the villus surface: absorptive cells, goblet cells and enteroendocrine cells. They all originate from stem cells located near the base of the crypts. The entocytes migrate from the base to the tip of the villi and during migration, the enterocytes maturate. The digestive function (enzyme activity) begins as the enterocytes migrates over the basal third of the villi. The absorptive function starts to develop as they reach the upper to mid-level and continues to increase until they reach the top of the villi, where they are shed into the lumen. Hence, enterocytes at the surface of the villi are continuously renewed. Goblet cells are secreting viscous mucus, and are interspersed among the enterocytes. Goblet cells increase in number from the proximal jejunum to the distal ileum. Enteroendocrine cells are specialized endocrine cells of the gastrointestinal tract. They produce hormones such as secretin (S cells) and cholecystokinin (I cells).

The formation of villi increases the mucosal surface at least 5 times compared to a flat surface of equal size. Furthermore, the cell-surface of the enterocytes facing the lumen has an apical membrane forming microvilli (brush-border) that further enhances absorptive surface 14-40-fold. The microvilli have important digestive enzymes and other proteins attached. They extend into a jelly-like layer of glycoprotein known as the glycocalyx that covers the apical membrane. The remaining part of the enterocyte plasma membrane is called the basolateral membrane, referring to the base and side of the cell.

The length of villi increases from the duodenum to the mid-jejunum and then decreases again towards the terminal ileum. This reflects the various functions of the different segments of the small intestine.

Crypts also vary in size and composition along the intestine. They are deepest in the proximal small intestine (duodenum and jejunum) and shorter distally in the ileum. Paneth cells are located adjacent to stem cells at the base of the crypts. Their exact function is unknown but due to the

presence of lysozymes and defensins they most likely contribute to maintenance of the gastrointestinal barrier.

### *2.5.1. Size and capacity of the small intestine*

A range of studies have shown great similarity in length, volume, and weight of the different sections. At birth, the small intestine is about 2 m long and has a capacity of 72 ml. At weaning, it has more than tripled in length (6.5 m) and has a nine-fold higher capacity (650 ml). The small intestine of fully grown pigs is 16-21 m, weighs 2-2.5 kg and has a capacity of >20 l. Based on calculations of length and diameter, it has been calculated that the surface area of the mucosa of a newborn pig is 430 $cm^2$, while in 7-month-old pigs, it is 5.8 $m^2$. Whereas the small intestine accounts for approx. 4-5% of the weight of the animal during the suckling period, it decreases to 1.5% when reaching slaughter weight.

## *2.6. The large intestine*

The pig has a relatively short caecum and a long colon, consisting of an ascending, transverse and descending colon. The caecum is a cylindrical blind sac located at the proximal end of the colon. The caecum, the ascending and transverse colon and the proximal portion of the descending colon are arranged in a series of centrifugal and centripetal coils known as the spiral colon. The caecum and proximal part of the spiral colon have longitudinal muscular bands resulting in a series of pouches (haustra). The rectum is embedded in fat and is dilated to form ampulla recti just before ending at the anus.

The mucosa of the large intestine has no villi, but columnar epithelial cells with microvilli formed into straight tubular crypts. Numerous goblet cells secreting sulphated carbohydrate-protein complex intersperse the columnar cells to lubricate the colon. The rectum has a simple structure with columnar cells and only few goblet cells.

### *2.6.1. Size and capacity of the large intestine*

During the suckling period, the large intestine is small. From a weight of 10 g, a length of 0.8 m and a capacity of 40 ml at birth, it increases to 36 g, 1.2 m, and a capacity of 100 ml at 20 days of age. This corresponds approximately to 1.2% of body weight. After weaning and during the growing period, it grows dramatically (2-2.5% of body weight). At 100 kg, the weight has increased to 1.3 kg, the length to 5 m, and the capacity to approx. 10 l. Adult pigs have a large intestine weighing approx. 2.8 kg, with a length of 7.5 m and a capacity of 25 l.

As shown in Figure 5.6, the large intestine grows more slowly than the small intestine in the initial period after birth. On the other hand, the large intestine continues to grow for months even after the growth of the small intestine has stalled, resulting in a lower ratio of small intestinal-to-large intestinal weight. The more rapid growth in length of the small intestine compared to the large intestine in the suckling period reflects the fact that the diet during suckling is highly nutritious and provides no residues to the colon, while after weaning and later in life, pigs are fed diets that are more fibrous and less digestible.

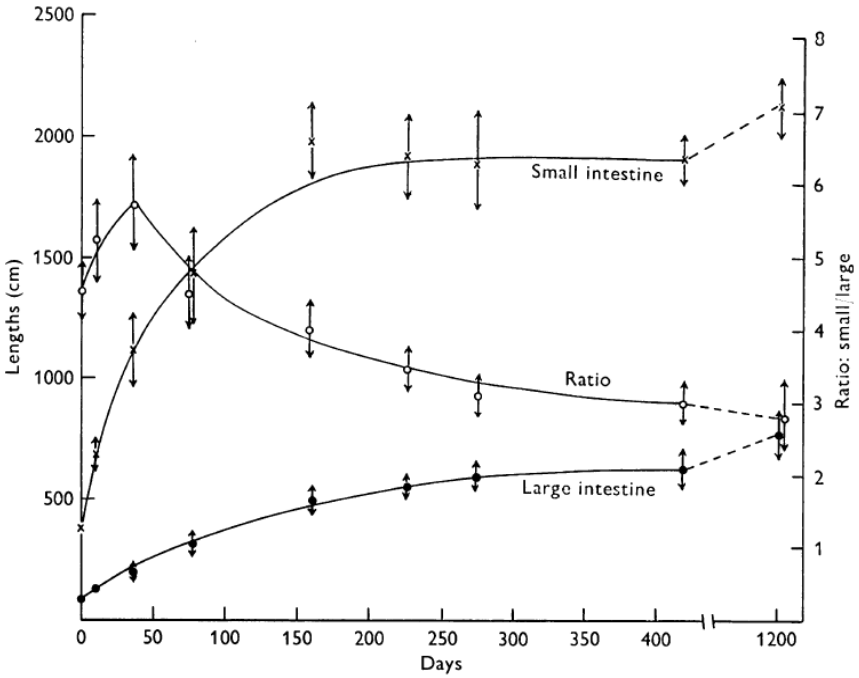


**Figure 5.6. Length of the small (x) and large intestine (black dots) of pigs at different ages, and the ratio (white dots) between them [14]. Reprinted with permission from John Wiley & Sons Ltd.**

# 3. Function of the digestive organs

*3.1.Salivary secretion*

Saliva contains a mixture of water (99%), inorganic salts, mucins, and α-amylase. In addition, to provide protection against diseases, it also contains lysozyme that breaks down the polysaccharide walls of many kinds of bacteria and immunoglobulin A, which play a critical role in mucosal immunity. Saliva moistens the food, lubricates the esophagus, and initiates the digestion of starch. However, the activity of salivary α-amylase is low. Hence, although α-amylase is secreted in the oral cavity, starch digestion is not believed to be of quantitative importance here, as the time spent in the mouth is too short. Some digestion may on the other hand take place in the proximal part of the stomach prior to acidification with gastric juice. Salivary secretion is stimulated by external cognitive or sensory stimuli (cephalic stimulation) as a response to expectation of food, but also directly to physical and/or chemical stimulation in the mouth. The volume and total activity increases with increased feeding level.

From a quantitative point, salivary α-amylase is not considered important as the ratio of total salivary amylase to total pancreatic amylase is only about 1:250,000 in the postprandial phase (0-5 hours after feeding).

*3.2. Gastric secretion*

Gastric juice is a clear and slightly viscous fluid. The major constituents in gastric juice are shown in Table 5.1.

| **Table 5.1.** Major constituents in gastric juice, their origin and physiological function. | | |
|---|---|---|
| Constitient | Origin | Function |
| HCl | Pareíetal cells | Regulating pH |
| Mucin | Mucous cells | Lubricating anf protecting the mucosal surface |
| Pepsin A | Chief cells | Protein digestion |
| Gastricin | Chief cells | Protein digestion |
| Chymosin and Pepsin B | Chief cells | Milk clotting and protein digestion |
| Lipase | Chief cells | Triglyceride digestion |

HCl is secreted by the parietal cells. However, HCl is not produced within the parietal cell because it would destroy the cell. Both $H^+$ and $Cl^-$ are independently transported from the parietal cell to the stomach lumen. Hydrogen ions are generated from the dissociation of carbonic acid that is produced by the enzyme carbonic anhydrase acting upon $CO_2$ and $H_2O$. $H^+$ is then transported to the stomach lumen through a proton pump ($H^+/K^+$-ATPase). As hydrogen ions are secreted, bicarbonate anions accumulate in the cell. To counterbalance this accumulation, $HCO_3^-$ is exchanged for Cl- at the basolateral membrane. The $K^+$ cations that accumulate within the cells are released back into the lumen in combination with $Cl^-$ anions.

HCl plays two important roles in gastric juice. Firstly, it facilitates protein digestion. HCl denaturates dietary protein thereby exposing peptide bonds to proteolytic enzymes. In addition, HCl activates pepsinogen to pepsin and provides a medium of low pH that ensures optimal activity of the enzyme. Secondly, the low pH provides a non-specific defence mechanism because it inhibits microorganisms from proliferating in the gastric lumen and causing damage to the gastrointestinal tract.

Four types of proteases have been found in the gastric juice of pigs (Table 5.1). They are all secreted as inactive zymogens (proenzymes that are activated in the lumen) to avoid self-digestion of the cells. The zymogens are activated in the lumen at an acidic pH below 5 or by active pepsin A. Pepsin A is the predominant gastric protease in adult pigs followed by gastricsin. They have strong proteolytic activity at pH 2-3. Pepsin digests approx. 10-15% of dietary protein before it is inactivated in the small intestine. In suckling piglets, chymosin is the predominant protease. It has potent milk clotting activity at pH around 6. Milk clotting is important in suckling animals: it prolongs the passage time of milk along the gastrointestinal tract and enables thorough digestion and absorption of milk nutrients.

Apart from pepsinogen, the chief cells of the cardiac region of the pig stomach also secrete minor amounts of gastric lipase. This enzyme hydrolyses medium- and long-chain triglycerides and plays a role in the hydrolysis of triglycerides in the stomach of the young pig. However, at 4 weeks of age the total activity of gastric lipase is only 1/600 of the lipase activity in the pancreas.

Mucin secreted by the mucous neck cells of the gastric glands constitutes a major component of the viscous mucus layer. This layer protects the stomach epithelium from the acid conditions and grinding activity present in the lumen.

### *3.2.1. Regulation of gastric secretion*

Gastric acid secretion is regulated by gastrin, histamine, and acetylcholine that stimulates while somatostatin inhibits acid secretion (Figure 5.7).

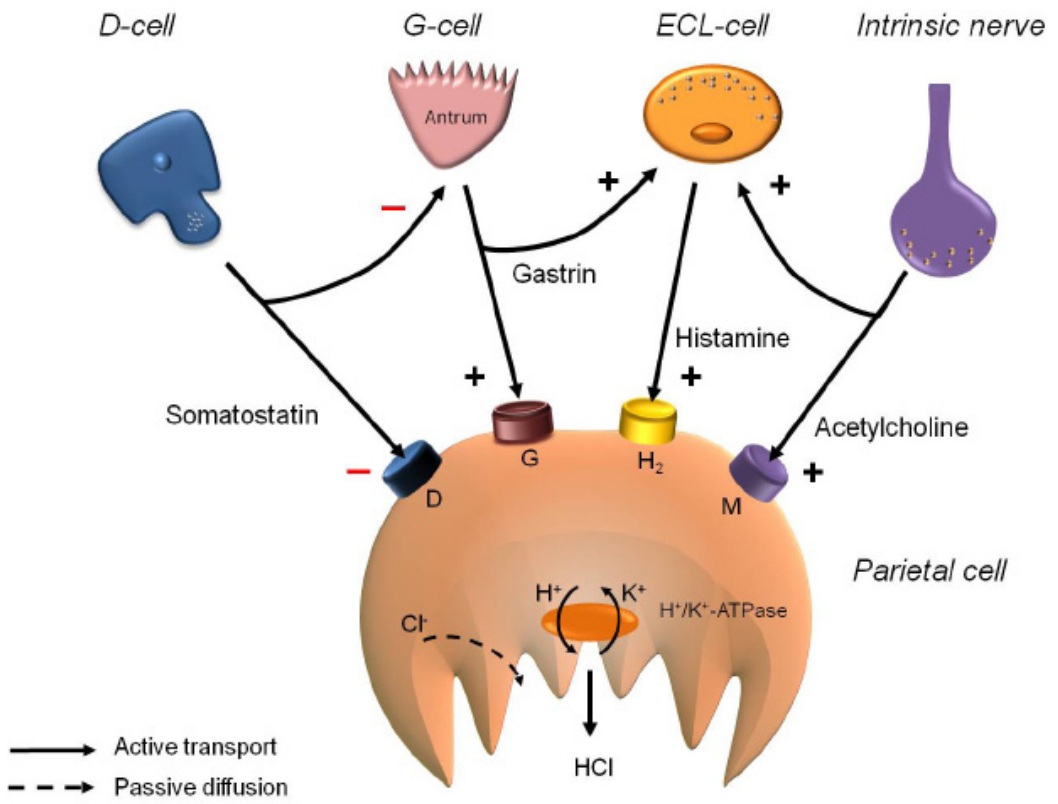


**Figure 5.7. Regulatory pathways that control HCl secretion from parietal cells.**

Gastrin is produced by G cells in the antral mucosa. The production and release of gastrin is stimulated by feed compounds, mainly small peptides and amino acids, and by nervous reflexes activated by gastric distension when food enters the stomach. Gastrin is secreted into the blood stream and acts on the parietal cells via a G receptor. Histamine is an amplifying substance in acid secretion. Histamine is produced by local mast cells and enterochromaffin-like cells (ECL) and acts on parietal cells in a paracrine fashion. Acetylcholine is a neural transmitter produced by cholinergic neurons. Acetylcholine is released as response to activation of stretch receptors. The secretion of hydrochloric acid is most efficient when all three regulators are present. Gastric acid secretion is controlled by a feedback mechanism. When pH is 3 or below, acid secretion diminishes and gastrin release is blocked. The acidity prevents amines from diffusing into G cells and activates hormone secretion. Furthermore, acid in the lumen causes D cells to release somatostatin. Somatostatin inhibits the parietal cells from secreting acid and G cells from releasing gastrin.

The regulatory mechanisms that control pepsinogen secretion are much less researched, but it is generally believed that pepsinogen secretion is under same regulatory influences as acid secretion.

The gastric secretory activity can be divided into three phases: cephalic, gastric, and intestinal. The anticipation of food stimulates gastric acid secretion. This is controlled by the central nervous system and is called the cephalic phase. The cephalic phase lasts for minutes and prepares the stomach for the entry of food. The gastric phase begins when food enters the stomach. It lasts for hours and accounts for two thirds of the gastric secretions. During the gastric phase, acid and pepsinogen secretion is increased. When digesta enters the duodenum, the intestinal phase initiates. This phase functions to decrease gastric motility and to reduce the secretion of gastric acid and pepsinogen. The intestinal phase lasts for hours.

### *3.3. Pancreatic exocrine secretion*

The primary function of the exocrine pancreas is to provide digestive enzymes for the digestion of the major nutrients, and neutralize the acidic chyme entering the duodenum from the stomach to allow the pancreatic enzymes to function.

Pancreatic juice is a clear, colourless liquid that contains salts, bicarbonate, and enzymes. It has a pH of 8.2-8.6, and is secreted continuously. A basal secretion is observed between the meals and ingestion of a meal stimulates the secretion for 3-7 hours depending on the frequency of feeding. The average flow of pancreatic juice is 1-6 ml/hour/kg. The flow is dependent on the composition of the diet, the frequency of feeding, and the age of the animal.

Two methods are used to collect pancreatic juice in pigs. A small catheter is placed in the pancreatic duct and a small T cannula or catheter is inserted into the duodenum for return of collected pancreatic juice, or pancreatic juice is collected from an isolated duodenal pouch in which the pancreatic duct enters. The cannula in the pouch may be connected to a re-entrant duodenal cannula. Both methods may disturb the regulatory mechanisms of pancreatic secretion and it has been shown that the daily volume of pancreatic juice secreted is higher when a catheter is placed in the pancreatic duct of the pigs.

#### *3.3.1 Regulation of pancreatic secretion*

The main regulatory pathways that control exocrine pancreatic secretion are the hormones secretin and cholecystokinin (CCK) and nervous stimulation.

Acinar, centroacinar, and duct cells have receptors for secretin, CCK, and acetylcholine. When these binding sites are occupied, the cells are stimulated to secrete, but maximum secretion is observed when all receptors are occupied. Secretin is secreted by the endocrine S cells in the mucosa of the proximal small intestine. Secretin is released in response to acid or fatty acids in the duodenal lumen and it stimulates release of bicarbonate by pancreatic duct cells. CCK is released into the blood stream in response to the presence of amino acids, peptides, and fatty acids in the duodenal lumen. CCK is secreted by I cells in the proximal small intestine and it stimulates the secretion of digestive enzymes by the acinar cells. Acetylcholine, released by nerve endings near the pancreatic cells, stimulates secretion. The neurons are stimulated to release acetylcholine by impulses from the enteric nervous system or through the vagus nerve. The sight and smell of food induces vagal responses leading to pancreatic secretion. This is the cephalic phase of pancreatic secretion analogous to the cephalic phase of gastric secretion described previously. Distension of the stomach also causes vagovagal reflexes (gastrointestinal reflex circuits where afferent and efferent fibres of the vagus nerve coordinate responses to gut stimuli) stimulating pancreatic secretion, which is the gastric phase of pancreatic secretion. When digesta enters the duodenum it evokes a large increase in the rate of pancreatic secretion and the intestinal phase involves both endocrine as well as neuronal stimuli. The distention of the duodenum produces enteric nerve impulses that lead to the release of acetylcholine. The endocrine (hormonal) part of the intestinal phase occurs in response to the chemical stimulation, digestion products of protein and fat stimulates the release of CCK and the low pH of the digesta stimulates the release of secretin.

The exocrine pancreatic secretion is controlled by a feedback mechanism. Diversion of pancreatic juice from the duodenum increases pancreatic secretion. It has been suggested that trypsin is the main component in this feedback regulation as reintroduction of pancreatic juice or infusion of trypsin, but not amylase into the duodenum markedly decreased pancreatic secretion. Furthermore, ingestion of raw soybeans containing trypsin inhibitor increases pancreatic secretion. There is strong evidence that this feedback regulation is linked with the release of CCK. Enterostatin, a pentapeptide released from procolipase when it is activated by trypsin in the duodenal lumen, may play a role in the feedback mechanism as well. Intraduodenal infusion of enterostatin has been shown to inhibit pancreatic enzyme secretion. In the ileum, exposure of the gut mucosa to especially fat and carbohydrates activates the ileal brake. The ileal brake is a distal to proximal feed-

back mechanism to control transit of a meal through the gastrointestinal tract in order to optimize nutrient digestion and absorption. The ileal brake reduces gastric acid secretion, pancreatic enzyme secretion, and bile acid secretion.

### *3.4 Pancreatic secretory enzymes*

#### *3.4.1. α -amylase*

Pancreatic α-amylase hydrolyses starch (from plant sources) and glycogen (from animal sources). Starch is composed of amylose, a linear polymer of glucose that is linked by α-1,4 glycosidic bonds and amylopectin, a branched polymer of glucose that contains both α-1,4 glycosidic bonds and α-1,6 glycosidic bonds. α-amylase cleaves the interior α-1,4 glycosidic bonds of starch. During the lifetime of the enzyme-substrate complex amylase hydrolyses starch by multiple attacks through cleavage of several bonds. The major products of starch hydrolysis are maltose, isomaltose, maltotriose, sugars composed of two or three glucose units, and α-limit dextrins, oligosaccharides of 5-0 glucose residues containing both α-1,4 and α-1,6 glycosidic bonds. For more information regarding digestion of starch, see Chapter 8.

#### *3.4.2. Lipases*

Pancreatic juice contains three lipolytic enzymes: lipase, phospholipase A2, and carboxyl ester hydrolase, and a protein cofactor, colipase. Lipase is secreted as a fully active enzyme and is the most important enzyme in the digestion of fat. Lipase hydrolyses triglycerides, the most abundant lipid in the diet, and diglycerides and the products are free fatty acids and monoglycerides. Lipase is strongly inhibited by bile salts in the duodenum and the protein cofactor colipase is the only agent known to counteract this inhibition. Colipase is secreted as a zymogen, procolipase, which requires cleavage by trypsin to become active. Phospholipase A2 splits fatty acids from phospholipids. It is secreted as an inactive zymogen that requires activation by trypsin. Carboxyl ester hydrolase, also known as carboxyl ester lipase and cholesterol ester hydrolase, has an unusually broad substrate specificity; it hydrolyses mono-, di-, and triglycerides, cholesterol- and retinol esters, and lysophosphatidylglycerols. However, the main physiological function probably is to hydrolyse retinol- and cholesterol esters. For more information on digestion of fat, see Chapter 10.

#### *3.4.3. Proteases*

The major proteolytic enzymes secreted by the exocrine pancreas are listed in Table 5.2. All proteolytic enzymes are secreted as inactive zymogens to protect the gland from autodigestion.

**Table 5.2.** Proteolytic enzymes secreted by the exocrine pancreas.

| Enzyme | Action | Precursor | Activator |
|---|---|---|---|
| Trypsin | Endopeptidase | Trypsinogen | Emterokinase, trypsin |
| Chymotrypsin | Endopeptidase | Chymotrypsinogen | Trypsin |
| Elastase | Endopeptidase | Proelastase | Trypsin |
| Carboxypeptidase A | Exopeptidase | Procarboxypeptidase A | Trypsin |
| Carboxypeptidase B | Exopeptidase | Procarboxypeptidase B | Trypsin |

The activation of the proteolytic enzymes is initiated by the activation of trypsin by enterokinase, an intestinal brush-border enzyme. Trypsin then activates all other zymogens as well as trypsinogen. Trypsin is an endopeptidase meaning that it breaks proteins at internal points along the amino acid chain, it specifically cleaves peptide bonds on the carboxyl side of basic amino acids (lysine and arginine). The catalytic activity of chymotrypsin is directed towards peptide bonds involving the carboxyl groups of tyrosine, tryptophan, phenylalanine and leucine. Elastase cleaves on the carboxyl side of aliphatic amino acids (alanine, leucine, isoleucine, valine, and glycine). The carboxypeptidases are zinc-containing metalloenzymes. They are exopeptidases meaning that they remove a single amino acid from the carboxyl-terminal end of proteins and peptides. Quantitative aspects of protein digestion are thoroughly described in Chapter 9.

### *3.4.4. Pancreatic secretion and dietary composition*

The content in the pancreatic tissue and in pancreatic juice of the major digestive enzymes, proteases, amylase, and lipase, changes in proportion to the dietary content of their respective substrates, protein, carbohydrates, and fat. The physiological significance of this adaptation is unknown as the pancreas normally synthesizes and secretes a ten-fold excess of digestive enzymes.

The level and source of protein affect the synthesis and secretion of proteolytic enzymes. The trypsin and chymotrypsin activities increase as the protein content of the diet increase, with chymotrypsin showing the most sensitive response.

The level of fat and the fatty acid composition regulate the synthesis and secretion of lipolytic enzymes. When the amount of fat increases, lipase secretion from the exocrine pancreas increases. Furthermore, there are indications that fatty acids with differing chain length stimulate the pancreatic secretion in the order C18:1>C12:0>C8:0. In addition, the degree of saturation may affect the output of the exocrine pancreas.

The effect of carbohydrates on exocrine pancreatic secretion has to be divided into the effect of starch and the effect of non-starch polysaccharides (NSP) and dietary fibre (DF). There is convincing evidence that the secretion of α-amylase adapts to the starch content in the diet. Increasing the amount of starch in the diet elicits an increased secretion of α-amylase. Several studies have been performed in order to elucidate the response of the exocrine pancreas to NSP and DF. The studies differ with respect to feed intake, feeding regimen, body weight, and the method used to collect pancreatic juice. Furthermore, the definition of DF differs between the studies making comparisons difficult. Hence, it is not possible to draw a conclusion on the effect of NSP and DF on exocrine pancreatic secretion.

### *3.5. Bile secretion*

Bile has pH of 7.4-7.9 and contains bile salts, phospholipids, and cholesterol, which sums up to a total lipid content of 0.6-0.7%. It also contains sodium, potassium, chloride, bicarbonate, mucus and bile pigments, of which the latter are endogenous waste products.

Both bile salts and phospholipids play an important role in the digestive function, and the molar ratio of total phospholipid to total bile salts is 1:10.1. The bile salts aid emulsification and absorption of lipids.

Bile acids are de novo synthesized in the liver by conversion of cholesterol to primary bile acids by the action of 7a-hydroxylase (CYP7A1), also called the neutral pathway, or by the acidic (alternate) pathway in which the cholesterol side chain is hydroxylated by CYP27 followed by hydroxylation of the sterol nucleus by the action of CYP7B1. The bile acid synthesis is completed in the hepatocyte perixisomes, where the bile acids are conjugated with either glycine or taurine. As example, see the synthesis of conjugated hyocholate in Figure 5.8.

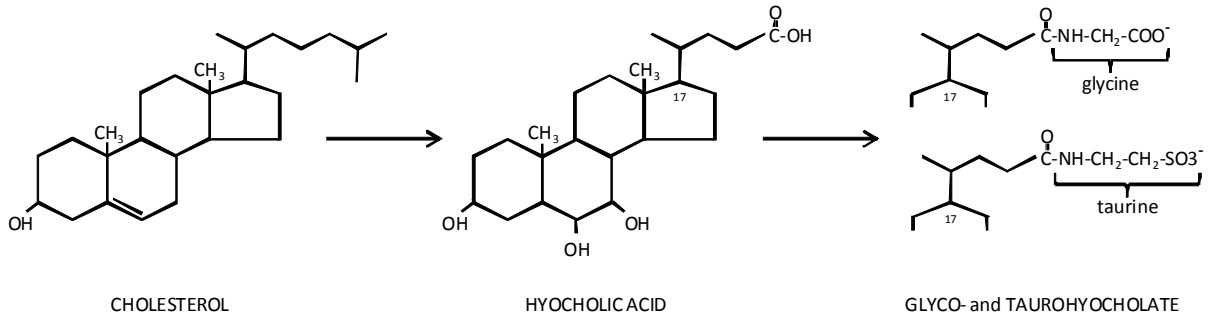


**Figure 5.8. Formation of conjugated bile salts from cholesterol.**

In contrast to most mammals that mainly produce cholic acid (CA) and chenodeoxycholic acid (CDCA) from cholesterol, the domestic pig is different in that it produces almost no CA. Instead, it produces hyocholic acid (HCA) in amounts equal to that of CA in other mammals.

In pigs, almost all bile acids are glyco-conjugated (93%), which is in contrast to many other species. In chickens, rats, dogs and sheep, bile acids are almost entirely tauro-conjugated, while other species conjugate with both taurine and glycine (e.g. cattle 49:51, humans 26:74).

Bile acids are mainly found in the form of Na-salts as the transport proteins pumping the bile acids in and out of the cells (mucosal cells and hepatocytes) are sodium-dependent.

When excreted from the gallbladder into the intestine, a majority of the conjugated primary bile salts are reabsorbed by the apical sodium dependent bile acid transporter (ASBT) expressed on the luminal surface of mucosal cells in the distal small intestine.

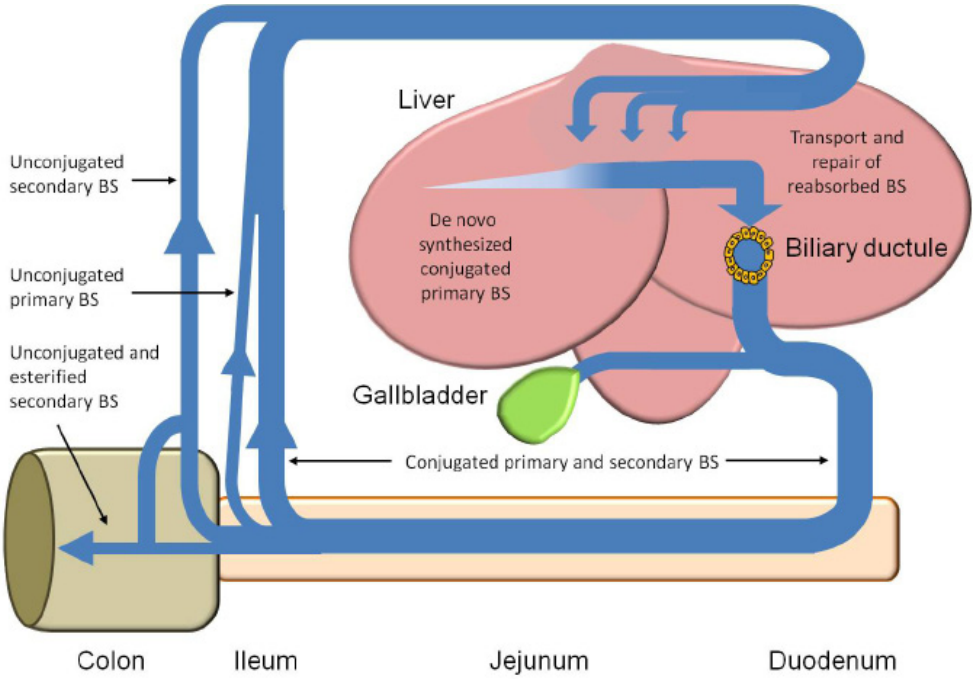


**Figure 5.9. Synthesis and enterohepatic circulation of bile salts.**

However, some of the bile salts are deconjugated to free bile salts and may be further converted to secondary bile salts, e.g. by dehydroxylation to deoxycholic acid (DCA) and hyodeoxycholic acid (HDCA) by the microflora in the distal small intestine and colon. By deconjugation and dehydroxylation, the hydrophobicity and pKa of the bile salts increase, thereby permitting recovery via passive absorption across the colonic epithelium.

Hence, along with de novo synthesized bile salts and reabsorbed primary bile salt, these unconjugated primary and secondary bile salts are transported to the liver via the portal vein, reconjugated and then again excreted in bile. This recirculation of bile salts is termed entero-hepatic circulation, and is a mechanism to cope with the demand of bile acids, which by far exceeds the capacity for production.

As a result, bile collected from the gallbladder or the small intestine will contain a mixture of primary and secondary bile salts (approx. half of each in Figure 5.10), but the exact ratio will depend on dietary composition as particularly high-fibre feed will lead to higher faecal excretion and less reabsorption of secondary bile salts.

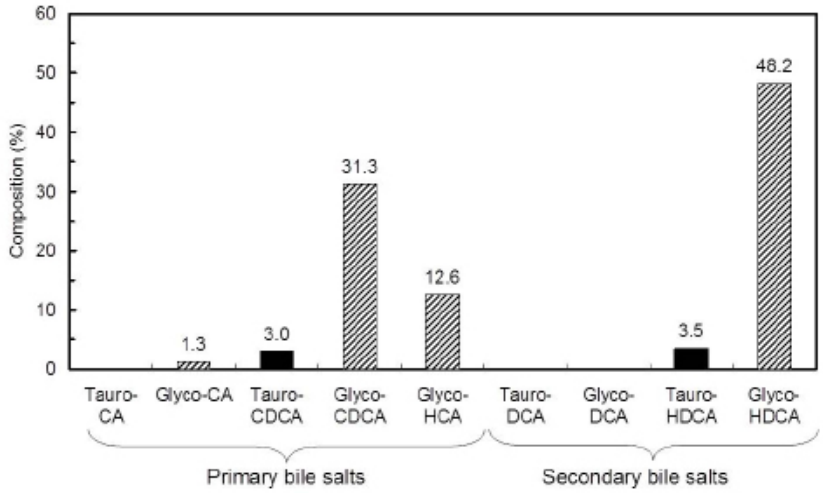


**Figure 5.10. Molar composition (%) of bile salts in bile of pigs. (Abbreviations: CA, cholic acid, CDCA, chenodeoxycholic acid; HCA, hyocholic acid; HDCA, hyodeoxycholic acid. (Adapted from [1].)**

As already mentioned, phospholipids also play an important role in the digestion and absorption of lipids. The phospholipids of porcine bile is entirely in the form of phosphatidyl choline, dominated by the 16:0-18:2 diacyl forms (59.6%), followed by 16:0-18:1 (18.4%) and 18:0-18:2 (15.9%).

Bile flow has been measured in a range of studies with different cannulation techniques and diets. The total bile flow over 24 hours has been measured to be in the range 30-60 ml/kg body weight in growing pigs (Table 5.3) and influenced by diet.

Inclusion of wheat bran increase both bile secretion and concentration of bile acids in the bile, and short term-studies have shown immediate responses to change in diet and continuing increases in flow and concentration for days after addition of the fibre.

| **Table 5.3.** Bile flow (ml/kg/24 hours) in pigs | | | | |
|---|---|---|---|---|
| Technique | Weight, kg | Diet | Flow, ml/kg | Reference* |
| Simple bile duct cannulation without control of the Sphincter of Oddi | 60 | | 38 | [10] |
| | 45 | | 46 | [7] |
| | 42 | 2, 10 or 20% lard | 47-53 | [7] |
| Re-entrant bile duct cannulation | 25-30 | Traditional European diet | 48 | [17] |
| | 25-30 | Semi-synthetic** | 30 | [17] |
| Bile duct cannulation with re-entrant cannula in duodenum | 43 | Wheat/fishmeal | 35 | [15] |
| | 43 | Wheat/fishmeal + 40% wheat bran | 59 | [15] |

*) For full reference see [12]. **) starch, sucrose, casein, maize oil and cellulose.

Increasing fat content of the diet induce only a modest increase in bile flow, but a dramatic increase in bile acid secretion and a moderate increase in phospholipid and cholesterol output when increasing the fat content from 2 to 10%. A further increase in fat content to 20% of the diet does not lead to further increase in bile acid flow, while phospholipid and cholesterol output continue to increase. The composition of the lipids in the diet (degree of saturation) does not appear to influence the rate of bile acid and phospholipid secretion, but the secretion of cholesterol increases.

Another important aspect of bile secretion is the removal of degradation of red blood cell turnover. In the Kupffer cells of the liver (but also in phagocytes, spleen and bone marrow), heme is converted into biliverdin (green colour) then further to bilirubin. The bilirubin is transported to hepatocytes for conjugation, and then in conjugated form secreted in the bile, where it is responsible for its green/yellow colour. When excreted to the intestine, conjugated bilirubin is converted by the gut microflora to urobilinogen, then further to urobilin and stercobilin and finally excreted in faeces, giving it its characteristic brown colour. Some of the urobilinogen is reabsorbed from the gut and excreted by the kidney as urobilin, which is responsible for the yellow colour of urine.

### *3.6. Small intestinal digestion and absorption*

#### *3.6.1. Digestion of carbohydrates*

The luminal phase of carbohydrate digestion applies only to starches and the enzyme involved is α-amylase secreted from the pancreas. Starch hydrolysis products (maltose, isomaltose, maltotriose, and α-limit dextrins) and dietary disaccharides (sucrose and lactose) are digested in the membranous phase by digestive enzymes that are a structural part of the intestinal surface membrane.

All polysaccharides are hydrolysed to monosaccharides prior to absorption (Figure 5.11). Six different oligosaccharidases performing this hydrolysis are located on the brush border membrane of the enterocyte. They are lactase (EC 3.2.1.23), trehalase (EC 3.2.1.28), and four maltases. The maltases are classified as isomaltase (EC 3.2.1.10), sucrase (EC 3.2.1.48), and two forms of glucoamylase (EC 3.2.1 3). Lactase is specific for lactose that is cleaved into glucose and galactose. Trehalase cleaves trehalose into two glucose units. Isomaltase hydrolyses the α-1,6 linkages in isomaltose. Sucrase specifically hydrolyses sucrose, but it has a general capability to hydrolyse α-1,4 linkages. Sucrase and isomaltase exist as one single polypeptide chain and is often referred to as sucrase-isomaltase. The enzyme complex is capable of hydrolyzing α-limit dextrins into its monosaccharidic units. Glycoamylase actively hydrolyses both α-1,4 and α-1,6 glycosidic bonds and hence is capable of hydrolyzing both α-limit dextrins, maltose, isomaltose, and maltotriose. Maltase (EC 3.2.1.20) catalyses the same reactions, and the enzyme is also referred to as maltase-glucoamylase.

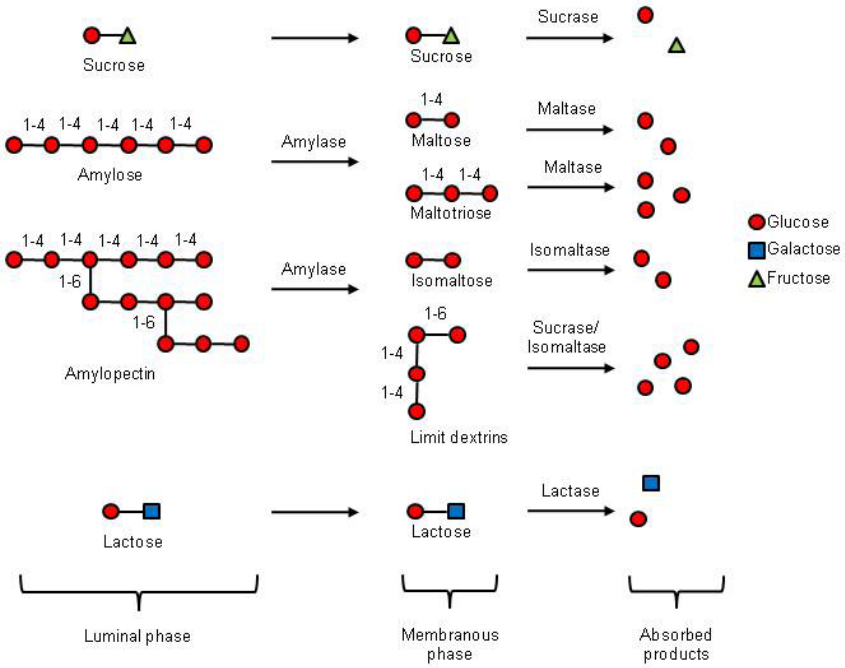


**Figure 5.11. Digestion of starch and dietary saccharides.**

Each of the oligosaccharidases has a characteristic distribution curve along the small intestine. The activity of lactase and trehalase is highest in the proximal part of the intestine (at 10-20% of the intestinal length), whereas the activity of the maltases is maximum mid-way along the small intestine.

The monosaccharides are absorbed either by active transport of facilitated diffusion. Three carrier proteins (GLUT2, GLUT5, and SGLT1) have been identified in the pig. GLUT5 is responsible for fructose transport through the apical membrane. The transport is independent of $Na^+$ and energy, but fructose can only move down its concentration gradient. Apical glucose and galactose uptake occurs via the SGLT1 symporter. The sugars are cotransported with two molecules of $Na^+$ and, as $Na^+$ and the sugars are moved in the same direction, it is a symporter. This transport is energy dependent as it requires $Na^+$ to be pumped out of the cell by the $Na^+/K^+$-ATPase in the basolateral membrane. The sugars move out of the cell at the basolateral membrane by facilitated diffusion mediated by GLUT2.

*3.6.2. Digestion of protein*

Proteins are made up of 20 amino acids that can be combined in an infinite number of ways. This is reflected in the number of enzymes taking part in the luminal digestion of protein; four proteases from the stomach and five from the exocrine pancreas.

The products of the luminal digestion of protein are free amino acids and oligopeptides of varying length. The oligopeptides are further digested by peptidases on the brush border membrane of the enterocytes. About 20 different peptidases have been identified. They are classified as endopeptidases, aminopeptidases, carboxypeptidases, and dipeptidases according to their hydrolytic properties. Some of the brush border peptidases are found in the cytoplasm of the enterocytes as well where they digest absorbed di- and tripeptides before they are transported into the blood circulation.

Petidases are generally present along the whole length of the small intestine except for the most proximal part of the duodenum. Maximum activity has been observed in the distal part of the jejunum and the proximal part of the ileum.

Free amino acids, di- and tripeptides are absorbed by the enterocytes through active transport. So far, transport systems for neutral, cationic, anionic, and imino acids have been identified in the porcine small intestine. Short chain peptides are transported across the brush border membrane by a transport protein named PEPT1. PEPT1 is an $H^+$/peptide symporter with the capability to transport essentially every possible di- or tripeptide. However, at present it is unknown to what extent peptide transport contributes to overall absorption of amino acids from the gastrointestinal tract. Intracellularly, peptides may be hydrolysed to free amino acids.

Transport of amino acids through the basolateral membrane is facilitated through various transport systems as well. Dipeptides may be transported through the basolateral membrane, too; this transport is linked to $H^+$ transport and is energy-dependent.

*3.6.3. Digestion of fat*

Fats, or lipids, have limited solubility in water, the major medium in which digestion occurs. To overcome this problem the lipid digestion and absorption is divided into four phases: 1) emulsification; 2) hydrolysis; 3) micelle formation; and 4) absorption (Figure 5.12).

The emulsification process starts in the stomach by the physical contractions of the gastrointestinal wall and is continued in the duodenum where bile acids are added. During emulsification the fat globules are broken down to fine lipid particles that form a stable suspension in the water-based environment.

The hydrolysis of the lipids, primarily triglycerides, takes place at the oil-water interface. Pancreatic lipase is inhibited by bile salts at the surface, but this inhibition is reversed by colipase that binds to the micelle and clears the surface of bile constituents and allows lipase to get access to the underlying triglycerides. The hydrolytic products, free fatty acids and monoglyceride, and the other dietary lipid compounds combine with bile salts to form water-soluble micelles.

Lipid absorption occurs primarily in the jejunum, but the process of lipid absorption is incompletely understood. The micelles come close to the unstirred water layer along the brush border membrane. The uptake of lipid compounds across the apical membrane involves both passive diffusion and carrier mediated active transport by special fatty acid binding proteins.

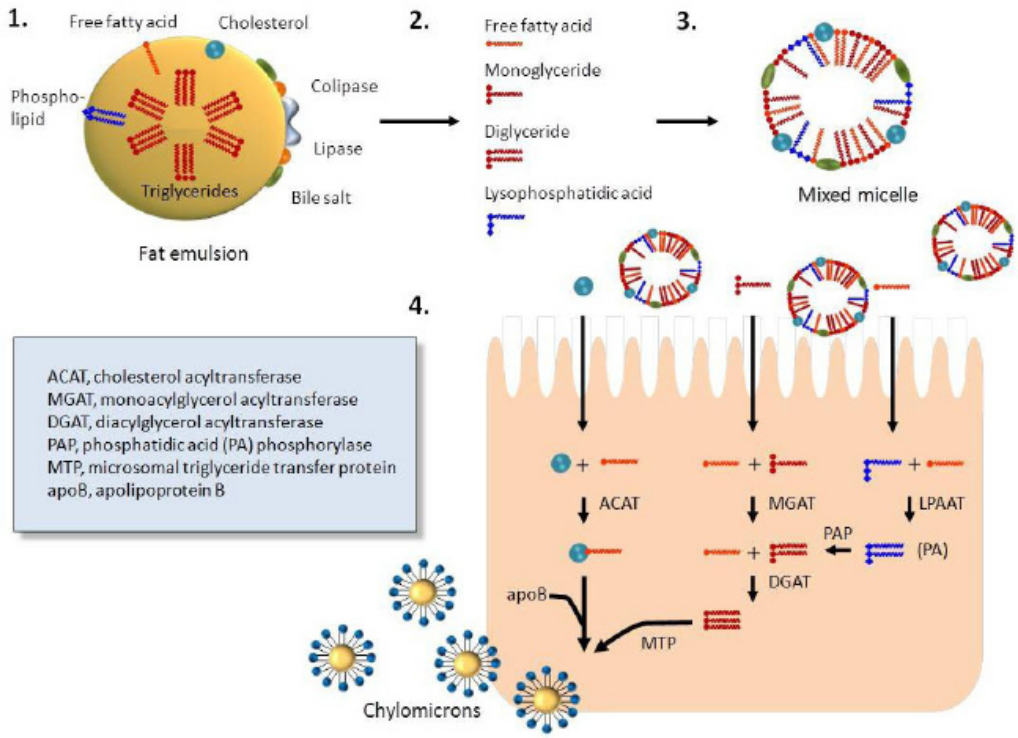


**Figure 5.12. Digestion and absorption of lipids.**

After entering the enterocyte, free fatty acids and monoglycerides are reesterified to form triglycerides and phospholipids. These are then packed with cholesterol and intracellular apolipoproteins to form chylomicrons for transport out of the cell across the basolateral membrane to the lacteal, a lymphatic capillary. The lacteals merge to form lymphatic vessels that transport fat to the thoracic duct.

*3.6.4. Small intestinal secretion*

Brunner's glands, which are located in the submucosa on the part above the sphincter of Oddi, produce bicarbonate containing alkaline secretion, which protects the duodenum from the acidic content of chyme, provides an alkaline condition for the intestinal enzymes and lubricates the intestinal walls. The secretion from Brunner's glands increases upon feeding and it is mediated by neurohormonal stimuli.

The goblet cells secrete mucin, which is a good lubricant. The mucus blends into the glycocalyx and forms a viscous layer. The glycocalyx, the mucus layer, and the unstirred water layer form a diffusion barrier that nutrients must pass before entering the enterocytes. Furthermore, the mucus layer protects the epithelium from potentially noxious intraluminal substances and may prevent the binding of intraluminal bacteria to the epithelial cells. Mucin is continuously secreted from the goblet cells. When exposed to a secretagogue, goblet cells undergo an accelerated secretory event. A wide range of agents can alter mucin output (e.g. cholinergic agents, neuropeptides and hormones, and toxins), and dietary components like non-digestible carbohydrates and milk peptides have also been shown affect the intestinal mucus layer.

Apart from the secretions from Brunner's glands and the goblet cells, the mucosa of the small intestine is an important secretory tissue as well. It is difficult to measure the amount and composition of the intestinal juice due to the simultaneous processes of secretion and absorption, but it has

been estimated in 70 kg pigs that 6 l of intestinal juice is secreted containing 15 g N. The amount of endogenous N entering the lumen of the small intestine from gastric juice, bile, pancreatic juice, and intestinal juice is estimated to be 21.57 g N in 30-50 kg pigs [2].

### *3.7. Large intestinal digestion and absorption*

The cells of the large intestine have no digestive enzymes as in the small intestine, but the large intestine is the major site of absorption of fluids and electrolytes, and a very active site of microbial digestion of undigested feed residues, endogenous secretions, sloughed mucosal cells etc.

#### *3.7.1. Large intestinal secretion and absorption*

The ileum and proximal colon secrete large amounts of alkaline fluid to facilitate microbial digestion. A substantial amount of the water and associated electrolytes are reabsorbed along the colon, particularly in the first 40%. The water absorption is a passive process coupled to active transport of the electrolytes. In 40 kg pigs fed a cereal/fish meal based diet, 3.2 l of water is absorbed in the colon. Compared to this, only 1 l is absorbed in pigs fed a refined semi-purified casein based diet. Hence, within the first one-third of the colon the dry matter content increases from 13 to 20% and in the remainder two-thirds up to 25%.

The small intestine is the most important site for both vitamin and mineral absorption, but the large intestine is particularly important to the absorption of vitamin K, biotin, and the electrolyte minerals (sodium, chloride, and potassium). Hence, different minerals are absorbed at different sites. Calcium and P are absorbed in the first half of the small intestine, sodium in the ileum and the colon, Mg only in the colon, and K is absorbed in all regions of the digestive tract. For more information regarding vitamin and mineral metabolism, see Chapters 11 and 12.

Absorption of short fatty acids (SCFA) produced by the microflora in the caecum and colon by fermentation of undigested feed residues and endogenous component (sloughed cells, mucins, enzymes bile components etc.) is a major function of the large intestine. The flux of SCFA across the colonic epithelia cell depends on the age of the animal and composition of the diet. Furthermore, SCFA are the far most important fuel (60-70% of the energy supply) for the colonic mucosa, and butyrate is the preferred fuel for colonic epithelial growth and proliferation. SCFA absorbed for the colon are taken by the mesenteric veins and transported via the portal vein to the liver. For further information on colonic fermentation, see Chapters 7 and 8.

## 4. Passage of digesta along the gut

Regulation of digesta flow through gastrointestinal motility is an important factor for digestion and absorption. Furthermore, in mature animals, gastrointestinal motility is synchronised with exocrine biliary excretion, pancreatic flow of liquid, enzymes, and bicarbonate, with gastro-duodenal pH, plasma levels of gut hormones (pancreatic polypeptide, motilin and gastrin), and mesenteric blood flow. This apparent synchronisation is evidently of major importance for an optimal digestion and absorption process, and coordination between absorption of nutrients and motility has been observed. This pulsatility and synchronisation between the various physiological functions of the gastrointestinal tract is postulated to represent gastrointestinal homeostasis.

#### *4.1.1. Gastrointestinal motility*

The motility of the gut can be measured at three different levels; transit of intraluminal contents, mechanical activity, i.e. contraction or pressure gradients, or by the myoelectrical activity. The myoelectrical activity is the basis for the mechanical activity, which in turn will influence the flow (mixing and propelling) of digesta.

The proximal stomach primarily serves as food storage area with little mixing activity, but weak continuous contractions gently propel contents to the distal stomach. As the stomach gradually empties, tension of the wall increases and directs food towards the distal part.

The antrum is characterised by intense electrical activity starting from the mid stomach and migrating towards the pylorus. The function of the distal stomach is to grind, mix and propel food towards the pylorus. When the antral waves approach the pylorus, it constricts and allows only small particles to pass to the duodenum. Large particles are ground and ejected back into the antrum.

The motility of the stomach is under neuro-hormonal control. Anticipation of food will lead to vagal stimulation of gastric motility (cephalic activity), and the activity is increased by sensory receptors when food enters the stomach. Gut hormones play a complex role in gastric motility. Gastrin, produced in G-cells located in the antrum, and ghrelin appear to stimulate gastric motility, CCK and GLP-1 inhibit gastric motility, whereas the effects of secretin and GIP under physiological conditions are unclear.

Delivery of food from the stomach to the small intestine must match the rate of digestion and absorption. Therefore gastric emptying is regulated by reflexes, and receptors for these reflexes are located in the duodenum, where they are activated by low pH, high osmolarity, and the presence of fat.

The motility of the small intestine is characterised by two distinctive phases; the digestive and interdigestive phase. In the digestive phase, motility is characterised by non-propulsive (segmentation) contractions that mainly aid to mix digesta with the secretions, and propulsive activity that moves digesta forward along a short distance.

In the interdigestive phase, motility consists of a regular pattern comprising a quiescent phase, where there is very little muscle contraction or flow of gut contents. This is followed by a phase where contractions mix the gut contents and propel them forward. Finally, an activity front with intense muscular contraction obliterates the lumen and prevents backflow of the gut contents. This migrating motor complex (MMC) has a house-keeping function that promotes bacterial clearance of the gut and maintains intestinal homeostasis. In suckling pigs the pattern is more irregular than in adult pigs, which probably relates to immaturity of the enteric nervous system or the extrinsic modulating systems.

The ileo-caecal sphincter is a circular muscle located at the junction of the small and large intestine that prevents backflow of caecal contents into the ileum.

The motility pattern in the colon is completely different from that of the small intestine. Segmentation contractions form sacculations known as hausta, which mix the colonic content. Peristaltic contractions facilitate the movement of digesta through the colon. As a counteracting mechanism, antiperistaltic contractions (retropulsion) propagate digesta towards the ileum, which impede the movement of digesta, and force accumulation of material in the proximal part of the colon. This serves to allow for efficient absorption of water and electrolytes and extends the time for microbial fermentation. Mass movements or giant migrating contractions often involve the entire large intestine and provide a major force for defecation.

*4.1.2. Transit time*

The time it takes for the digesta to travel through the gut varies with the age of the animal and the diet. Many different methods and calculation procedures have been used, making comparisons among studies difficult. Fluid leaves the stomach faster than solid particles, which are selectively retained according to their size. Large particles (>2 cm) have a long transit time due to retention in the stomach. Feed stays in the stomach for 0-6 hours or even longer in adult pigs. The transit time

in the small intestine varies from less than 2 up to 6 hours, while 70-85% of the time spent on passing the intestine is in the caecum and colon, where the digesta stays for 20-43 hours.

In growing pigs fed different diets, it has been demonstrated that the mean retention time (MRT) averaged 1, 4 and 38 hours in the stomach, small intestine and large intestine, respectively, leading to a total transit time of 43 hours. While increasing the insoluble fibre content in the diet had no effect on retention time in the stomach, it decreased the retention time of both the liquid and solid phases in the small intestine and tended to decrease the retention time in the large intestine as well. In other studies, total transit times in growing pigs varied in the interval 24-75 hours. Comparative studies have revealed sows have a doubling in mean retention time (81 hours) compared to growing and finishing pigs, and that transit time was highly variable in sows.

## 5. Factors affecting digestive capacity

### *5.1. Development in enzyme activity from birth to weaning*

The secretion of digestive enzymes from the gastrointestinal tract undergoes major changes at birth when the nutrition changes from parenteral (via blood) to enteral (via gut) nutrition and again at weaning when the diet is changed from sow's milk to solid feed.

#### *5.1.1. Enzymes in the salivary glands and the gastric mucosa*

α-amylase is present in the salivary glands at birth. The amount of α-amylase in the gland per unit body weight increases up to 3 weeks of age. In older pigs, the amount of α-amylase in the gland per unit body weight decreases.

The gastric acid secretion is low at birth, probably due to immaturity of many of the parietal cells, and increases rapidly during the first week of life as parietal cell size and number increase. A positive linear relationship between maximal acid output and body weight has been observed from birth to 5-6 weeks of age. However, the gastric acid secretory capacity developed more rapidly in pigs fed creep feed or weaned to solid feed.

The ontogeny of the four gastric proteases displays a clear link between their characteristics and the nutrition of the pig. Chymosin is the major gastric protease at birth. The primary function of chymosin is to clot milk without further proteolytic breakdown of peptide bonds. In the week following birth, the tissue concentration of prochymosin declines quite rapidly, but it remains the dominant zymogen until 3-4 weeks of age. At 2 months of age, chymosin activity is no longer detectable. Only traces of pepsinogen A are found in the fundic mucosa at birth. The concentration increases gradually until 3 weeks of age, and a more rapid increase is observed thereafter. Pepsinogen A becomes the predominant zymogen in the fundic tissue from 4-5 weeks of age. The developmental pattern of progastricsin is similar to that of pepsinogen A. The concentration of pepsinogen B in the fundic tissue is low at birth. It increases from 1 week of age to 3-5 weeks of age, and then it plateaus at a lower level. In addition to age, access to solid feed before weaning and weaning to solid feed has a stimulatory effect on the capacity of the stomach to secrete proteases.

The activity of gastric lipase in the cardiac mucosa is increasing from birth to weaning. At weaning, an instant increase in the activity of gastric lipase is observed and the activity remains at this level through the post-weaning period (up to 8 weeks of age). Due to a very low activity of gastric lipase compared to the activity of pancreatic lipase after weaning, the importance of gastric lipase to the lipid digestion is probably low in adult pigs.

#### *5.1.2. Pancreatic secretory enzymes*

The development of the different enzymes in the pancreas is regulated by age, age and bodyweight at weaning, the physical and chemical composition of the pre- and post-weaning diets,

or by interactions between several of these factors. Studies on the ontogeny of pancreatic enzymes have been performed either in pancreatic tissue obtained from slaughtered animals or using surgically modified piglets with a permanent catheter in the pancreatic duct. Studies of the tissue concentration of pancreatic enzymes allow only one measurement for each animal, whereas the continuous secretion can be observed in the surgically modified piglets. However, studies on surgically modified piglets are very difficult to perform and only a limited number of studies have been performed.

The secretion of pancreatic juice can, obviously, only be studied in surgically modified animals. Prior to weaning, the secretion of pancreatic juice is low (0.5 ml/kg/hour) and suckling does not affect the pancreatic outflow. After weaning, the basal secretion of pancreatic juice increases (1-2 ml/kg/hour) and ingestion of solid feed stimulates the juice outflow (4 ml/kg/hour). In growing pigs, the outflow of pancreatic juice is between 1 and 6 ml/kg/hour depending on body weight, feed composition, and feeding regimen or an interaction between these factors.

The activity of trypsin in the pancreatic tissue remains constant from the first week of life until weaning. Weaning causes a transient decrease in the trypsin activity, but one week post-weaning the activity in the pancreatic tissue is equal to that observed at weaning. During the following weeks, the trypsin activity in the pancreatic tissue increases, and 3 weeks post-weaning the activity of trypsin is 2.5 times higher than at weaning. When the secretion of trypsin is studied in piglets adapted for continuous collection of pancreatic juice, no decrease in trypsin outflow is observed. On the contrary, the secretion of trypsin increases during the first 5 days post-weaning. The low activity of trypsin in the pancreatic tissue immediately post-weaning may be a reflection of the fact that the stores in the pancreatic tissue are depleted.

Chymotrypsin activity increases up to weaning. The activity decreases dramatically at weaning, and it takes 2-4 weeks to recover to levels similar to those observed prior to weaning. There are no data on the secretion of chymotrypsin in the immediate post-weaning period.

The activity of amylase in the pancreatic tissue is extremely low at birth. The activity is increased 1.5-5-fold up to weaning followed by a decrease in the week following weaning and a recovery to levels equal to or greater than those immediately before weaning during the subsequent 2-4 weeks. The activity of amylase is inducible by the level of starch in the diet. This has been observed in suckling piglets where increased intake of creep feed was paralleled by an increased amylase activity in the pancreatic tissue. Also, in chronically fistulated piglets, increases in both the basal and the postprandial output of amylase were observed post-weaning.

A relatively large increase in the activity of pancreatic lipase is observed from birth to weaning. This is probably an effect of age. Furthermore, sow milk contains a high concentration of lipid, and the amount of milk and the lipid content increase during the first 3-4 weeks of lactation, which stimulates synthesis and secretion of lipase. The activity of lipase in pancreatic tissue declines abruptly at weaning and remains low for two weeks post-weaning. Again, these results differ somewhat from those observed in piglets adapted for continuous collection of pancreatic juice. In these pigs, the preprandial secretion of lipase did not change after weaning, while postprandial outputs of lipase increased after weaning.

*5.1.3. Brush border membrane enzymes*

The activity of the carbohydrases in the brush border of enterocytes in the small intestine develops in two different directions. Lactase, which cleaves lactose, undergoes a marked decrease in activity between the second and fifth weeks of life. This is the result of both a genetic inherent reduction of the activity and due to the loss of substrate. Maltase, but not sucrase, is present in the small intestine of fetal and newborn pigs, and sucrase is present in week-old pigs. From one week of age, the activity levels of both maltase and sucrase increase quite rapidly. Weaning has significant effects on the development of the carbohydrases. In weaned pigs, the activity levels of sucrase, maltase, and lactase are significantly lower than those in suckling pigs of similar age. From two

weeks post-weaning onwards, the activity levels of the carbohydrases, with the exception of lactase, continue to increase up to 200 days of age.

The pattern of distribution of the brush border carbohydrases alters with age in piglets. The activity of sucrase, isomaltase, and glucoamylase is low and uniformly distributed along the small intestine in 3-week-old suckling piglets. The distribution gradually approaches the adult pattern, and by 8 weeks of age the pattern has close similarities to the adult pattern. The distribution of lactase does not alter, whereas the activity of trehalase increases in the proximal region during the period 3-8 weeks of age.

The development of the brush border peptidases is much less investigated. The overall trend for the activity of peptidases in suckling pigs is that the activity is high at birth and decrease with age and the activities are lower at 5 weeks of age than during the first week of life. Weaning has been shown to further reduce the peptidase activity of the brush border enterocytes, but from day 5 post-weaning the enzymatic activity levels increase. In general, knowledge about the development of the peptidases after weaning is limited, but it is assumed that they develop similarly as is true for the carbohydrases (except lactase).

The activity of the peptidases is highest in the medial and distal parts of the small intestine in the suckling pig. At weaning the activity declines, particularly in the distal part, and during the immediate post-weaning period (days 1-9 post-weaning) the activity is similar throughout the small intestine. It is not known when the distribution pattern of the peptidases approaches the adult pattern.

### *5.2. Feed factors affecting digestibility*

In this section, different dietary factors that may impede or enhance the digestive processes are briefly described. For further information regarding effect on nutritive value, see the specific chapters regarding carbohydrates (Chapter 8), proteins (Chapter 9), fat (Chapter 10), minerals (Chapter 11), and vitamins (Chapter 12).

#### *5.2.1. Antinutritional factors*

Many types of feedstuffs contain antinutritional factors (ANF) such as insoluble fibre, lignin, glucosinolates, tannins, and lectins. They reduce nutrient digestibility and increase endogenous protein losses, e.g. by increased intestinal mucus secretion. The presence of high levels of ANF can cause substantial reductions in protein and amino acid digestibilities. From a health perspective, young pigs with a less mature digestive system are more susceptible to ANF, but ANF may also lead to growth depression in older animals. In plant breeding, great efforts have been made to reduce the level of ANF to improve nutrient digestibility, particularly regarding protein-rich feedstuffs such as in the pulses (peas, soy bean, and Faba bean), but heat-treatment is mostly employed to destroy some of the ANF.

##### *5.2.1.1. Dietary fibre*

Dietary fibres of plant feed material are restrictors of energy density, feed intake and nutrient bioavailability. Dietary fibres are part of the cell walls enclosing the nutrients, and their physicochemical properties (physical presence, water binding capacity and viscosity) may induce increased endogenous losses of nitrogen through increased secretions of enzymes, mucus, sloughed epithelial cells, and microbial protein. On the other hand, dietary fibre may help maintaining gut health, reducing the incidence of gastric ulcers, pathogenic intestinal diseases and increase satiety and welfare of sows (see Chapter 8 for details).

##### *5.2.1.2. Trypsin inhibitors*

Protease inhibitors cause enlargement of the pancreas, increasing size of the acinar cells, and increased secretion of digestive enzymes. Hence, growth depression appears to be caused by endogenous loss of amino acids in form of hyper secretion of enzymes, which diverts amino acids

from synthesis of body protein to losses in faeces. Soybeans are the most concentrated source of trypsin inhibitors, where they are located in the cotyledon, but they are also found in peas. Protease inhibitors make up 0.2–10.0% of total seed protein of beans of various species, but contents are found in peas, field beans and other grain legumes that are 5–20 times lower than in soy beans. Protease inhibitors can be inactivated by heat-processing or removed by fractionation, and the extent of inactivation depends on the initial level, particle size, and processing conditions. In properly processed products, up to 80% of the trypsin inhibitor activity is inactivated. More extensive heating, which would destroy all inhibitor activity, will adversely affect protein digestibility and quality.

*5.2.1.3. Tannins*

Tannins are water-soluble polyphenolic compounds that precipitate proteins, lower the activity of digestive enzymes, may damage the mucosa, reduce the digestibility of protein, carbohydrates, and minerals, and exert systemic toxic effects. Reduced protein digestibility caused by tannin-containing feeds is ascribed largely to interactions between either tannins and dietary proteins, or tannins and exocrine and mucosa-associated digestive enzymes, or both. Similar to trypsin inhibitors, tannins also cause enlargement of the pancreas. Tannins are classified into hydrolysable tannins that are readily hydrolysed and condensed tannins that are resistant to hydrolysis. Both types exhibit the ability to complex and precipitate proteins. Condensed tannins are most commonly found in dicotyledonous plants, where they are mainly present in the testa of coloured seeds. Certain varieties of world-wide important crops, such as sorghum, millet, barley, and a number of beans (field beans and Faba beans) and peas may contain considerable amounts of tannins.

*5.2.1.4. Lectins and saponins*

Lectins are carbohydrate binding glycoproteins found in various pulses. They are resistant to digestion in the gastrointestinal tract, which allows them to bind to membrane glycosyl groups of the mucosal cells lining. This damages the epithelial cells leading to increased loss of gut epithelial cells and increased loss of endogenous protein. They reduce the activity of the brush border enzymes, and depress nutrient absorption. They also increase the production of mucins and can lead to loss of plasma proteins to the intestinal lumen, which in turn reduces protein digestibility and retention. Furthermore, they can modulate the bacterial flora and immune state of the digestive tract. They can also promote enlargement and/or atrophy of key internal organs and tissues and alter the hormonal and immunological status.

Lectins (haemagglutinins) are typically measured according to their ability to agglutinate erythrocytes although this binding is not a physiological concern. Peas of different varieties have a lectin content of approx. one tenth of that in soybeans.

Saponins are bitter-tasting ANFs of lucerne that reduce palatability, feed intake and rate and efficiency of weight gain.

*5.2.1.5. Phytate*

Phytic acid is naturally occurring in seeds, nuts and cereal grains, where it functions as a store of mineral nutrients and inositol to be used during germination. Phytate contains negatively charged phosphate groups, and can chelate several nutritionally essential minerals in the gastrointestinal tract, making them less bioavailable. Phytic acid is typically found as salts of mono- and divalent cations, collectively known as phytate associated to protein globules. Some digestive enzymes such as α-amylase, alkaline phosphatase, carboxypeptidases, and aminopeptidases require metal cofactors, such as zinc or calcium for full activity, and chelation of these metals may impair their activity. Phytate may also bind directly to proteins directly or indirectly via a cation bridge. Phytate is heat-stable and is not destroyed by heat processing, whereas endogenous phytase present in the seeds will be destroyed. Soaking, fermentation, or germination will, on the other hand, expose the phytic acid to endogenous, bacterial, or yeast phytases and reduce phytate levels in the feed.

### *5.2.2. Milling and heat-treatment*

The purpose of milling feed is to aid the digestion process by breaking the plant cells, thereby increasing substrate surface and enhancing accessibility for the digestive enzymes to attack cell contents. Generally, reducing particle size will increase digestibility. However, reducing particles size may have negative consequences for gut health.

Thermal processing (steam flaking, extrusion, boiling, autoclaving, micronization) of plant feedstuffs gelatinizes starch, which increases its digestibility. Heating will also burst plant cell walls, which increases accessibility for the digestive enzymes. Heating destroys some the antinutritional factors (trypsin inhibitors) and make some of the dietary fibres more fermentable for the intestinal microflora. However, excessive heating (particularly under dry and alkaline conditions) will promote formation of Maillard products (a reaction between reducing sugars and amino acids) that reduce the amino acid digestibility. Heating will also destroy endogenous phytase present in the feed.

### *5.2.3. Exogenous enzymes*

Feed enzymes degrading cell wall polysaccharides have mainly been used for weaners to enhance digestibility. These animals are more susceptible to the impairment of digestion (encapsulation of nutrients and viscosity) than older animals. Enzymes are available for increasing the small intestinal digestibility of cereal based feed stuffs (β-glucanase, xylanase, protease) and sources of vegetable protein such as soybeans, rapeseed, sunflower seed and legumes (protease and α-galactosidase). Phytase can be added to pig feed to increase the digestibility of phosphorus and the minerals, which it is chelating. This enzyme is relevant not only for piglet feed, but for the entire production chain.

## 6. Summary

This chapter provided an overview of the digestive system and described, in qualitative terms, the processes involved in the assimilation of food. The role of the gut microflora is described in Chapter 6, and in Chapters 8, 9, 10, 11 and 12, quantitative aspects of digestion and metabolism of nutrients are thoroughly described.

## 7. References


1. **Alvaro, D., Cantafora, A., Attili, A.F., Corradini,,S.G., Deluca,C., Minervini,G., Dibiase,A. & Angelico,M.** (1986) Comparative Biochemistry and Physiology B-Biochemistry & Molecular Biology 83, 551-554.

2. **Bock,. H.-D., Eggum, B.O., Low, A.G., Simon, O. & Zebrowska, T.** (1989) Protein Metabolism in Farm Animals: Evaluation, Digestion, Absorption, and Metabolism. VEB Deutscher Landwirtschaftsverlag, Berlin, and Oxford University Press, Oxford and New York.

3. **Clemens, E.T., Stevens, C.E. & Southworth, M.** (1975) Journal of Nutrition, 105: 759-768.

4. **Cranwell, P.D.** (1995) Development of the neonatal gut and enzyme systems. In: The neonatal pig. Development and survival, Varley, M.A. (Ed.), CAB International, Wallingford, UK.

5. **Cunningham, J.G. & Klein, B.G.** (2007) Textbook of Veterinary Physiology 4th edition. Elsevier Science. ISBN10: 1416036105.

6. **Johnson, L.R.** (2006) Physiology of the gastrointestinal tract. Volume 2, 4th ed. Elsevier.

7. **Juste, C., Corring, T. & Breant, P.** (1979) Annales de Biologie Animale Biochimie Biophysique, 19, 79-90.

8. **Juste C., Demarne. Y. & Corring, T.** (1983) Journal of Nutrition, 113, 1691-1701.

9. **Kidder, D.E. & Manners, M.J.** (1978) Digestion in the pig, Bristol : Scientechnica, ISBN 0856080225.

10. **Laplace, J.P. & Ouaissi, M.A.** (1977) Annales de Zootechnie, 26, 595-613.

11. **Latymer, E.A., Low, A.G., Fadden, K., Sambrook, I.E., Woodley, S.C. & Keal, H.D.** (1990) Archives of Animal Nutrition, 40, 667-680.

12. **Lewis, A.J. & Lee Southern, L.** (2001) Swine Nutrition, 2nd ed., CRC Press Taylor & Francis N.Y.. ISBN:0-8493-0696-5.

13. **Low, A.G. & Partridge, I.G.** (1980) Current concepts of digestion and absorption in pigs. ISBN 0-7084-0167-8.

14. **McCance** (1974) Journal of Anatomy, 117, 475-479.

15. **Payne D., Juste C., Corring, T. & Février, C.** (1989) Nutrition Reports International 40, 761-771.

16. **Pond, W.G. & Mersmann, H.J.** (2001) Biology of the domestic pig. Ithaca, NY: Comstock Publishing Associates, Cornell University Press. ISBN-100801434688.

17. **Sambrook, I.E.** (1981) Journal of the Science of Food and Agriculture, 32, 781-791.

18. **Warner, A.C.I.** (1981) Nutritional Abstract Review B51: 780-820.