

Chapter 2

Development of Digestive Glands in Pigs

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2.1 Introduction

The digestive glands include the pancreas, liver, and the gallbladder. The pancreas plays a central role in the digestive system by synthesizing and secreting specific digestive enzymes, and thus has an integrative role for the absorption and metabolism of nutrients in the organism. The liver performs numerous physiological and metabolic functions for the pig's whole body, but the most important one is maybe metabolism of

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nutrients and toxins arising from digestion and/or absorption in the intestines. The pig's liver also produces bile, involved in lipid digestion. Bile is secreted into the intestinal system via the gallbladder. In pig, as in other mammals, the liver is involved in protein synthesis, toxin and hormone breakdown, vitamin storage as well as blood cell and blood component processing. The gallbladder is a small sac involved in bile storage. Bile is concentrated in the gallbladder. The gallbladder is located at the back of the liver. It is connected with the liver via the cystic duct and the hepatic bile duct.

2.2 Development of the Pancreas in Pigs

The pancreas is both an exocrine and an endocrine organ. Digestive enzymes are conducted via a duct system to the duodenum, and the endocrine products enter the blood directly. The bulk of the tissue in the pancreas is exocrine in nature.

The exocrine pancreas produces pancreatic juice, which contains enzymes, nonenzymatic proteins, and salts. These substances reach the duodenum via a single pancreatic duct in the pig (van den Borne et al. 2007). Enzymes able to digest proteins, carbohydrates, lipids, and nucleic acids, respectively, are produced in the acinar cells of the exocrine pancreas (Malagelada 1981; Pitchumoni et al. 1986). Electrolytes capable of neutralizing the acidic stomach contents and establishing the proper pH for enzymatic action are produced mainly in the intra-acinar and ductal cells (Schulz 1980). The islet cells of the endocrine pancreas produce hormones (e.g., insulin, glucagon) that regulate the utilization of the absorbed digestion products (Sitbon and Mialhe 1978; Christensen and Just 1988; Motyl et al. 1986; Malmlef et al. 1990). In the embryo, the pancreas develops as an outgrowth of the endoderm; the cell layer that delineates the primitive gut. Pancreatic progenitors derived from the endoderm form two buds (dorsal and ventral) which later fuse to form a single organ. Within these buds, the progenitor cells give rise, through a stepwise process, to endocrine, acinar, and duct cells.

The neonatal period is a very important developmental stage in the life of pig. The pancreas, an important digestive organ responsible for production of various hydrolytic enzymes, also shows a marked tissue mass gain (up to 80 %) during the first 2 postnatal days in newborn pigs (Widdowson and Crabb 1976; Tarvid et al. 1994).

In naturally suckled piglets, both body weight and pancreas weight increased with age. The pancreatic weight increased much faster than the body weight, particularly during the first postnatal day. The ratio of pancreas weight to body weight is significantly greater in 1-day and 3-day-old piglets than in newborn piglets. Mubira (1998) demonstrates that the pancreas growth is disproportionally faster than the body taken as a whole, the protein concentration in the pancreatic tissue is lower in 1- and 3-day-old than in the newborn piglets, The concentration of DNA in the pancreatic tissue remains unchanged with age and the total contents of protein and DNA increase progressively with age. Mubira (1998) also demonstrates that pancreatic lipase activity expressed either as per gram tissue weight, per milligram

protein or per milligram DNA is significantly lower in 1- and 3-day-old piglets when compared with newborn piglets, the enlargement of the acini is apparently due to an increase in the cell numbers although the difference among the three groups of animals in the number of cells per acinus did not reach a significant level and the size of the acinar cells did not change significantly with age.

However, the mechanisms responsible for this rapid pancreatic tissue growth are far from being completely understood, but are apparently related to colostrum ingestion since starved, water-fed, or formula-fed newborns show little changes (Tunthanathanich et al. 1992; Burrin et al. 1992). Further studies have shown that porcine colostrum contains a number of hormones and growth-promoting peptides, such as insulin, cortisol, epidermal growth factor (EGF), bombesin, and insulin-like growth factors-I and -II (IGF-I and -II) (Jaeger et al. 1990) and epithelial-like cells (Cera et al. 1987). The size of acinar cells decreased significantly in piglets fed 5 % lactose solution while it increased significantly in piglets fed porcine colostrum. The acinar cell mitotic index estimated from the incorporation rate of Brdu increased significantly in piglets fed either porcine colostrum or trypsinized porcine colostrums, the index being even greater in the trypsinized-colostrum group than in the colostrum group (Mubira 1998).

The rapid pancreatic tissue growth in naturally suckling piglets is apparently related to ingestion of colostrum. Widdowson and Crabb (1976) found that rapid pancreatic growth would not occur if piglets were prevented from sucking and fed water only. Mubira (1998) study showed that pancreatic weight increased significantly in piglets bottle-fed porcine colostrum both in absolute and relative terms, but no increment was observed in the piglets bottle-fed lactose solution. All these observations indicate that colostrum may contain some trophic factors capable of stimulating pancreatic growth in newborn animals.

A number of growth-promoting peptides and hormones, such as EGF, IGF-I, IGF-II, bombesin, and insulin, have been found in the mammary gland secretions in pigs and in several other species (Jaeger et al. 1987; Donovan et al. 1994; Simmen et al. 1988; Read et al. 1984; Westrom et al. 1987). The concentration of these peptides is generally high in colostrum and often several fold greater than that in the maternal circulation (Donovan et al. 1994; Simmen et al. 1988; Read et al. 1984). There is evidence showing that these colostrum growth-promoting peptides are stable in the gastrointestinal lumen in suckling pigs (Shen and Xu 1996) and in suckling rats (Philipps et al. 1997) as it can be absorbed intact into the blood circulation in newborn pigs (Xu and Wang 1996) and in suckling rats (Thornburg et al. 1984). It has also been found in laboratory rodents that pancreatic cells possess specific receptors for EGF, IGF-I, and IGF-II (Potau et al. 1984; Korc et al. 1983; Williams et al. 1984). It was observed in an earlier study that newborn piglets fed infant milk formula supplemented with IGF-I or IGF-II had heavier pancreas and greater pancreatic RNA and DNA contents than did the control animals (Xu et al. 1994). Subcutaneous administration of bombesin and EGF stimulated pancreatic growth in rats (Papp et al. 1987; Dembinski et al. 1982) and EGF and insulin stimulated mouse pancreatic acinar cell growth in vitro (Logsdon 1986).

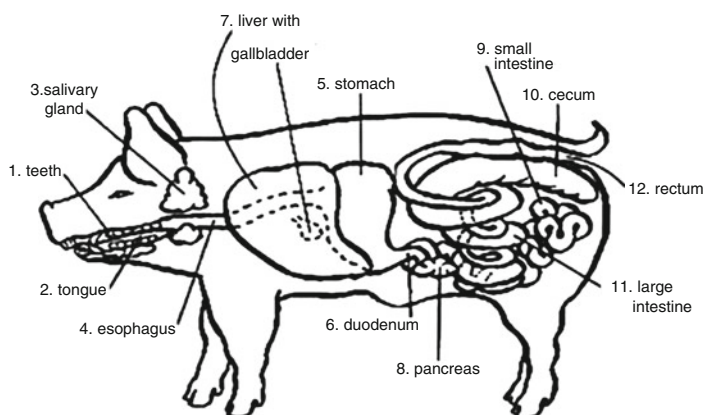


Fig. 2.1 The location of pig's liver and gallbladder

2.3 The Structure and Function of the Liver in Pigs

The liver is the largest internal organ, and the body's second largest, after the skin (Baruch 2000). The liver and its functions are referred to as the hepatic system, from the Greek word meaning liver. Schematically, liver metabolism can be partly view as the readjustment of molecules into a form usable by the pig's body tissues. In the case of toxins, liver metabolism converts poisonous molecules into less harmful molecules, finally eliminated into the urine.

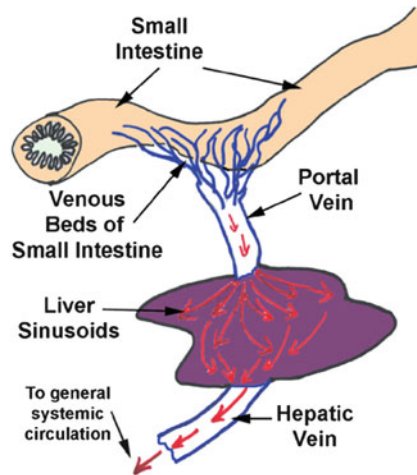
2.3.1 The Structure of the Liver

As shown in Fig. 2.1, the liver in pigs is located behind the diaphragm in the abdominal cavity, connected to the digestive system through the bile ducts, gallbladder, and duodenum. Blood supply to the liver is approximately 75 % from the venous system, directly from the intestines. Pig livers have four main lobes for filtering toxins and nutrients from the bloodstream: the right, left, caudate and quadrate. Bile ducts connect the lobes to the gallbladder, where excess bile is stored until needed.

Four lobes are surrounded by a capsule of fibrous connective tissue called Glisson's capsule. The Glisson's capsule in turn is covered by the visceral peritoneum (tunica serosa), except where the liver adheres directly to the abdominal wall or other organs. The parenchyma of the liver is divided into lobules, which are incompletely partitioned by septa from Glisson's capsule (Ekataksin and Wake 1991). The parenchyma within the lobules is supported only by fine reticular fibers (which are discernible only with special preparations).

The blood vessels supplying the liver (portal vein and hepatic artery) enter at the hilum (or porta hepatis), from which the common bile duct (carrying bile secreted by the liver) and lymphatic vessels also leave (Fig. 2.2).

Fig. 2.2 The liver's structure and anatomical placement



Within the liver sinusoids, the oxygen-poor but nutrient rich blood from the portal vein mixes with the oxygenated blood from the hepatic artery. From the sinusoids, the blood enters a system of veins which converge to form the hepatic veins. The hepatic veins follow a course independent of the portal vessels and enter the inferior vena cava. Liver cells, or hepatocytes, are large polygonal cells, usually tetraploid and often binucleate in the adult (Sen and Jalan 2005). Each nucleus has two or more nucleoli. The average life span of liver cells is 5 months. They contain abundant rough endoplasmic reticulum and mitochondria, large deposits of glycogen and lipid droplets of various sizes, and several small elaborate Golgi complexes. They also contain many peroxisomes, a variable amount of smooth endoplasmic reticulum and lysosomes (Vega 2004). In standard histological preparations, liver cells usually appear vacuolated because the glycogen and lipids are removed during processing. Liver cells are capable of considerable regeneration when liver substance is lost (Harada et al. 2009).

2.3.2 The Function of the Liver

The liver is extremely versatile, having both endocrine and exocrine functions. Liver is involved in numerous metabolic activities and acts as a storage depot. The list below is an attempt to categorize its numerous and diverse activities.

2.3.2.1 Blood Supply

As mentioned above, the liver receives a dual blood supply. The hepatic portal vein provides the majority of the incoming blood, the rest coming from the hepatic artery. The blood from the portal vein has already supplied the small intestine, pancreas, and spleen, and is largely deoxygenated. It contains nutrients and noxious

materials absorbed in the intestine. The blood from the hepatic artery supplies the liver with oxygen. Because the blood from the two sources intermingles as it perfuses the liver cells, these cells must carry out their many activities under low oxygen conditions that most cells would not be able to tolerate.

2.3.2.2 The Protein and Lipid Synthesis

The liver synthesizes a number of proteins, as suggested by its abundant rER and Golgi. One of the most important of these is albumins (responsible for several functions including colloid osmotic pressure), the protein parts of several kinds of lipoproteins, nonimmune alpha and beta globulins, prothrombin, and numerous glycoproteins, including fibronectin. These proteins are considered as endocrine secretions because they are released directly from the liver cells into the blood supply. The liver also synthesizes cholesterol and the lipid portion of lipoproteins. The enzymes for these activities are found in the sER.

2.3.2.3 Metabolic Functions

The liver is involved in a wide range of metabolic activities. Among its major metabolic functions are gluconeogenesis (the formation of glucose from non-carbohydrate precursors), and the deamination of amino acids. In addition to the proteins listed above, the liver also releases a number of other products directly into the blood as endocrine secretions. These include products of carbohydrate metabolism, e.g., glucose released from stored glycogen, and modified secretions from other organs, e.g., triiodothyronine (T3).

2.3.2.4 Storage of Metabolites

Liver cells store large deposits of glucose in the form of glycogen, which can be stained by the periodic acid-Schiff or PAS procedure. They also store lipids in the form of droplets of varying sizes. The latter can be revealed with Sudan staining after tissue fixation. The removal of these materials in routine preparations gives liver cells a foamy or vacuolated appearance. Lysosomes within hepatocytes may be a normal storage site for iron, in a form of a ferritin complex. Excessive amounts of iron may accumulate in cells as an unusable yellowish-brown pigment called hemosiderin, a partly denatured form of ferritin. Liver lysosomes also contain pigment granules (lipofuscin) and partially digested cytoplasmic organelles. The liver also stores vitamins, especially vitamin A, which is transported from the liver to the retina to be used in the formation of visual pigments. Most of the vitamin A is not stored in the hepatocytes, however, but in special fat-storing cells, called Ito cells, within the sinusoids. Ito cells also store the other three fat-soluble vitamins, D, E, and K, as well as vitamin B12.

2.3.2.5 Detoxification and Inactivation of Noxious Substances

The liver is, after the gastrointestinal tract, the first organ to receive metabolic substrates and nutrients from the intestine, but it is also the first to receive any toxic substances, for instance carcinogens or drugs that have been ingested. The sER of liver cells contains enzymes involved in the degradation and conjugation of toxins (in addition to those responsible for synthesizing cholesterol and the lipid portion of lipoproteins). Under conditions of challenge by drugs, toxins or metabolic stimulants, the sER becomes the predominant organelle. Stimulation by one drug, e.g., alcohol, enhances its ability to detoxify some other compounds. On the other hand, some toxins can get metabolized by the liver to even more damaging compounds.

2.4 The Structure and Function of the Gallbladder in Pigs

The gallbladder is one of the most dispensable organs in mammal. The gallbladder is a small sac and is the storage depot for bile. Bile is only concentrated in the gallbladder. The gallbladder is located at the back part surface of the liver (Fig. 2.1). It is connected with the liver via the cystic duct and the hepatic bile duct. Together they form the common bile duct, which leads into the small intestine.

2.4.1 The Structure of the Gallbladder in Pigs

The gallbladder is a tubular organ. Its tunica mucosa is a very regular simple columnar epithelium, with no goblet cells or glands. The deep folds in the bottom of the mucosa, which are often cut in cross section, sometimes look like “glands,” but they have no secretory activity. There is a scanty lamina propria, and a thin tunica muscularis. There is no muscularis mucosae, and this is one of the “landmarks” for this organ. The gallbladder is only partially covered by a fold of peritoneum; its opposite side is seated in a pocket in the surface of the liver. Bile ducts carry bile to the gall bladder for temporary storage.

The low magnification image above shows the walls of the gallbladder (Fig. 2.3). They vary in height depending on how full the bladder is. At higher magnification, the nature of the gallbladder epithelium is revealed: a simple columnar form, containing no goblet cells. Though these cells do have a few microvilli on their free surfaces, they cannot be considered as real brush borders. There is no muscularis mucosae in these structures, and the tunica muscularis is stringy and scanty with collagen fibers. Since it has only the function of squirting bile into the duct that carries it to the duodenum, it appears little developed.

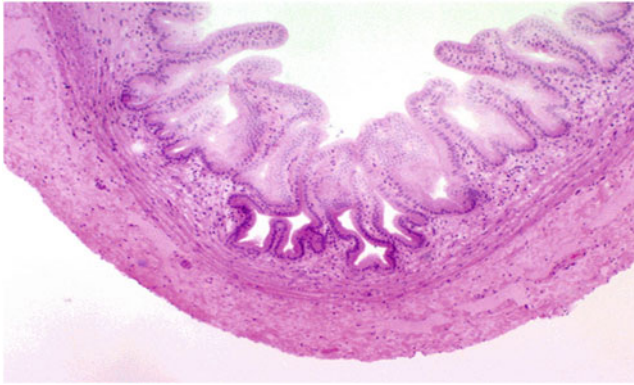


Fig. 2.3 The wall of the gallbladder at the low magnification image

2.4.2 The Function of the Gallbladder in Pigs

Bile is continuously formed in bile canaliculi in the liver hepatocytes, where it is collected and secreted into the hepatic bile duct. Bile is a complex fluid containing water, electrolytes, and a battery of organic molecules including bile acids (water-soluble derivatives of cholesterol), cholesterol, phospholipids, and bilirubin (McMaster and Elman 1926). The rate of bile fluid secretion is dependent on the circadian rhythm of the animal.

Bile is the exocrine secretion of the liver, released into ducts which eventually form the common hepatic duct. It, in turn, unites with the cystic duct from the gallbladder to form the common bile duct which enters the duodenum.

Bile contains bile salts, also called bile acids, which are important in emulsifying the lipids of the digestive tract, thereby promoting easier digestion by lipases and absorption. Bile salts are largely recycled between the liver and gut.

Bile also contains cholesterol and phospholipids, and another function of bile salts is to keep them in solution. Cholesterol and phospholipids serve as metabolic substrates for other cells and as precursors for components of cell membranes and steroid hormones. They are largely reabsorbed in the gut and recycled.

Bile also contains pigments, which detoxify bilirubin, the breakdown product of hemoglobin from aging and of abnormal red blood cells destroyed in the spleen. The detoxified bilirubin, mainly in the form of bilirubin glucuronide, is eliminated through the feces (and gives them their color). Failure of the liver to absorb bilirubin, or to conjugate it to its glucuronide, or to secrete the bilirubin glucuronide, may result in jaundice. Finally, bile contains electrolytes (largely reabsorbed in the gut). The latter maintain bile as an isotonic fluid.

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Nutritional and Physiological Functions of Amino Acids
in Pigs

Blachier, F.; Wu, G.; Yin, Y. (Eds.)

2013, IX, 307 p., Hardcover

ISBN: 978-3-7091-1327-1