

# Chapter 14

## Accessory Organs of the Small Intestine

### 14.1. The Pancreas

The pancreas has both an exocrine and an endocrine nature. These two functions are handled by histologically distinct regions of the pancreas. The exocrine pancreas accounts for the bulk of the parenchyma. The exocrine pancreas is punctuated by small, discrete islands of endocrine tissue called the Islets of Langerhans.

#### 14.1.1. The Exocrine Pancreas

##### a) Histology of the Exocrine Pancreas

**i) General Comments:** The exocrine portion of the pancreas is a compound acinar gland. It is composed of secretory acini deployed at the ends of a branching duct system. These ducts will eventually coalesce to form the Main Pancreatic Duct and the Accessory Pancreatic Duct (if present) which will drain into the lumen of the duodenum via the Hepatopancreatic Ampulla. Although the pancreas is retroperitoneal, there is a peritoneal component covering a portion of the pancreatic surface. Deep to the peritoneum will be a thin, incomplete capsule formed of dense irregular connective tissue. This capsule will extend into the pancreas as the Septa. These connective tissue septa will divide the pancreas into incomplete lobules of varying size. The secretory acinus of the pancreas is composed of pyramidal epithelial cells arranged around the terminus of an Intralobular/Intercalated Duct. These epithelial cells are joined to each other by junctional complexes on their lateral surfaces. They rest on a basement membrane which is rich in reticular fibers. The apical and basal portions of the acinar cells demonstrate two distinct staining patterns: The apical portion is acidophilic due to the presence of many membrane bound secretory vesicles containing digestive enzymes. The basal portion is basophilic due to the presence of abundant amounts of rough endoplasmic reticuli. The nucleus of the acinar cell is basally oriented.

##### ii) The Ducts of the Pancreas

a) Intralobular/Intercalated Ducts are composed of low simple cuboidal epithelium to typical simple cuboidal epithelium. These cells are easily distinguished from the acinar cells by their poorer staining.

b) Interlobular Ducts, which drain the intralobular ducts, are composed of a tall columnar epithelium. They travel through the septa. They increase in size as more ducts join them. The larger interlobular ducts will have a few argentaffin and goblet cells interposed among the columnar cells.

c) Main Pancreatic Duct/Duct of Wirsung is composed of stratified columnar epithelium lined by dense, collagenous, connective tissue. It travels the length of the pancreas and opens into a common passageway for the products of the pancreas and liver called the Hepatopancreatic Ampulla/Ampulla of Vater. The main pancreatic duct joins the Common Bile Duct to form the hepatopancreatic ampulla. The hepatopancreatic ampulla opens onto an elevation of the duodenal mucosa called the Duodenal Papilla. The

terminal portion of the main pancreatic duct (like the the common bile duct) will have longitudinally and circularly arranged smooth muscle which is part of the Sphincter of Oddi. The sphincter of Oddi controls the flow of digestive enzymes from the pancreas, gall bladder, and liver.

### **b) Functional Considerations**

The exocrine pancreas synthesizes a variety of digestive enzymes required for the breakdown of proteins, carbohydrates, fats, and nucleic acids including: trypsin, chymotrypsin, pancreatic amylase, procarboxypeptidase, proelastase, various lipases, deoxyribonuclease, and ribonuclease. These enzymes are stored in zymogenic granules, or secretory vesicles, in the apical portion of the acinar cells. Secretion of the pancreatic juice can be stimulated nervously or hormonally. Nervous stimulation is provided by the vagus nerve. Hormonal stimulation is provided by two hormones, both of which are produced by the duodenal mucosa:

- 1] Pancreozymin/Cholecystokinin - initiates the release of enzymes by the pancreas.
- 2] Secretin - initiates the release of an aqueous bicarbonate solution by the exocrine pancreas. This aqueous bicarbonate solution is the medium for the conveyance of the enzymes to the intestine. This aqueous bicarbonate solution also provides an alkaline environment to both neutralize stomach acids and to activate the pancreatic enzymes.

## **14.1.2. The Endocrine Pancreas**

### **a) Histology of Endocrine Pancreas**

The endocrine pancreas is arranged into small spherical aggregates of cells known as the islets of Langerhans scattered amid the exocrine acini and ducts. The cells of the islets of Langerhans are arranged into compact, anastomizing cords. The islets of Langerhans use the blood stream, not ducts, to deliver their products. So the islets are extensively vascularized by fenestrated capillaries. The Cells of the Islets of Langerhans can hold several different types of cells, all of which are epithelial:

- i] Alpha Cells : Alpha cells typically represent 20% of the cell population in an islet. They produce the hormone glucagon.
- ii] Beta Cells: Beta cells typically represent 75% of the cell population in an islet. They produce the hormone insulin.
- iii] C Cells: These are clear staining cells lacking stainable granules. They may represent cells which have already released their products. They are low in number.
- iv] Delta Cells: Delta cells are also low in number making up about 5% of the cell population in an islet. Delta cells produce the hormone somatostatin which regulates nutrient homeostasis. Delta cells are identical in appearance to somatostatin producing argentaffin cells of the duodenum.
- v] There is an unnamed fifth type of cell in the islet which produces pancreatic polypeptide. They are located mostly in the periphery of the islets located in the head of the pancreas. Some individual pancreatic polypeptide producing cells are found throughout the exocrine tissue of this area. Pancreatic polypeptide is released in response to the ingestion of food. It stimulates the secretion of gastric enzymes and inhibits bile secretion and intestinal peristalsis.

### **b) Functional Considerations**

Glucagon and insulin exert a strong influence on carbohydrate metabolism, especially in adipose tissue, muscle, and the liver. Glucagon is released in response to a decrease in

blood-sugar levels. It stimulates glycogenolysis, the breakdown of glycogen to release glucose into the blood. Insulin is released in response to an increase in blood-sugar levels. It stimulates glucose to be stored as glycogen.

## **14.2. The Liver**

### **14.2.1. Basic Concepts**

The liver is a large glandular organ filling most of the right upper quadrant of the abdominopelvic cavity. It is immediately below the diaphragm and above the stomach. It serves to process nutrient-rich blood from the digestive tract, filter out harmful materials from this blood, and to produce Bile which will assist in the digestion of materials in the small intestine.

### **14.2.2. Histology of the Liver**

The liver has four incompletely separated lobes in humans. The lobes are invested with an extremely thin dense irregular connective tissue capsule called Glisson's Capsule. Glisson's capsule partially divides the four lobes. Visceral peritoneum covers portions of the liver and is external to Glisson's capsule where present. It covers all of the external liver except where the liver's c.t. capsule attaches to the epimysium of the diaphragm. The liver has a hilus called the Porta Hepatis for the passage of blood vessels and the bile carrying common hepatic duct. The liver receives a dual blood supply. It receives oxygen-rich blood from the hepatic artery. It receives nutrient rich blood from the hepatic portal vein which is the final portion of the hepatic portal system. The hepatic portal system is a system of blood vessels which carries nutrient-rich blood from the capillary beds servicing the digestive tube to the liver.

#### **a) Organization of the Parenchyma**

The liver's parenchyma is **not** divided up into discrete compartments or lobules by connective tissue partitions. Instead the hepatocytes are organized into anastomizing plates or laminae deployed about two axes serving as histological landmarks. These two axes are the Portal Triad and the Central Vein/Venule.

#### **b) The Portal Triad**

The portal triad consists of three structures: a branch of the Portal Vein, a branch of the Hepatic artery, and a branch of the Bile Duct. These three structures are bound together by a sheath of collagen called the Portal Canal which also contains small lymphatics and nerves. In a histological section an imaginary line can be drawn connecting these triads breaking the parenchyma up into hexagon shaped lobules.

*NB: This is one way, and the most common way, of breaking up the liver parenchyma.* In the center of each lobule is the central vein. The sinusoids are radially arranged within the lobule running from the portal triad to the central vein. The hepatocytes are arranged into plates between the sinusoids. The direction of blood flow in the liver lobule proceeds from the periphery to the center. The branches of the hepatic artery, found in each triad at each corner, deliver oxygen-rich blood to the sinusoids. Branches of the portal vein, also found at each corner, will deliver nutrient rich blood to the sinusoids. This blood will flow towards the center of the lobule delivering oxygen and nutrients to the cells and picking up wastes. The sinusoids will form an anastomizing network that allows blood from a few terminal portal veins and hepatic arterioles to perfuse a large network of sinusoids within the lobule. The sinusoids will carry blood to the center of the lobule where they are

drained by the central vein. The central vein runs along the long axis of the lobule; it is perpendicular to the sinusoids. The "central Vein" is really a venule. The central venules of neighboring lobules will join together and eventually form the Hepatic Vein which will exit the liver at the porta hepatis.

### **c) The Hepatocyte**

The primary cellular constituent of the liver is the Hepatocyte which makes up about 80% of the cellular population. The hepatocytes are in close association with a duct system for the secretion and delivery of Bile. The hepatocytes are in close association with a sinusoid system for the secretion of substances into the blood. This association with the sinusoids also allows for the recovery of nutrients arriving from the digestive tract through the hepatic portal system. The hepatocytes store these nutrients and will release them into the blood as needed. Ex; glucose is stored as glycogen, fats are stored as triglycerides. Hepatocytes will synthesize most of the circulating plasma proteins, detoxify many lipid-soluble poisons, and remove certain waste products from the blood. The hepatocyte is a polyhedral cell with a central, often polyploid nucleus. On average 65% of the hepatocyte population is mononucleated but 35% are binucleated. Rough endoplasmic reticuli are abundant in these cells and accounts in part for the basophilic nature of these cells. Smooth endoplasmic reticuli are also abundant.

The ultrastructural relationship between the hepatocyte and the sinusoidal endothelium is designed to maximize the easy exchange of substances between the hepatocytes and the blood. The sinusoidal endothelium is discontinuous with open fenestrations. A Perisinusoidal Space/Space of Disse separates the endothelium from the hepatocytes.

Plasma freely percolates through the sinusoidal endothelium into the perisinusoidal space. The perisinusoidal space contains plasma but the formed elements can not enter due to the size of the sinusoidal fenestrae. This allows for liver cells to receive nutrients and to dispense substances into circulation. The perisinusoidal space contains only a few reticular fibers, an incomplete or even absent basal lamina, and short microvilli which project into the space from the hepatocytes. The lining of the hepatic sinusoids consists of two cell types: The more abundant cell is the endothelial cells which form a discontinuous lining. These endothelial cells are flat and have dense nuclei. The stellate shaped Kupffer Cells guard the fenestrae of the sinusoids. Kupffer cells are stellate shaped cells having vesicular nuclei. Kupffer cells are macrophage which line the liver sinusoids. They phagocytize bacteria and foreign particulate matter, assist in the secretion of bilirubin, and assist in the conservation of iron from deteriorating erythrocytes. They filter the blood perfusing the liver. They are involved in the metabolism of hemoglobin recovered from senescent erythrocytes. They produce bilirubin and store iron in the cytoplasm as hemosiderin. Bilirubin is released into circulation and retrieved by the hepatocytes which conjugate it and excrete it in the bile.

Another cell associated with the sinusoids is the Lipocyte. Lipocytes are fat storing cells. They will also store the fat soluble vitamin vitamin A. Lipocytes are found in small numbers within the perisinusoidal spaces.

### **14.2.3. The Flow of Bile**

The intralobular passageways which carry bile from it's point of origin to the bile ducts at the periphery of the lobule are the Bile Canaliculi. The walls of the bile canaliculus is composed of the indented cell membranes of contiguous hepatocytes. Tight junctions along the lateral walls of the adjacent hepatocytes form an impermeable seal along the

length of the bile canaliculus. This structural arrangement segregates bile flow from blood flow. Bile flow is opposite to blood flow going towards the periphery of the lobule. So a bile canaliculus is, in essence, the space between two plates of hepatocytes into which bile is secreted by the hepatocytes. At the periphery of the lobule the bile canaliculus joins with the small Terminal Bile Ductules/Cholangioles. The terminal bile ductules have a lining of low simple cuboidal epithelium. The terminal bile ductules will often have short extensions called the Canals of Hering. Their walls are lined by a simple squamous epithelium. The canals of Hering will extend into the lobule and carry bile from the bile canaliculi into the terminal bile ductule proper. The terminal bile ductules will empty into larger vessels called Interlobular Bile Ducts. Interlobular bile ducts are lined by a simple cuboidal epithelium. These are the bile duct branches found in the portal triad. Interlobular bile ducts drain into the Portal Canals. Portal canals are lined by a simple columnar epithelium. Portal canals will drain into the Right and Left Bile Ducts which will drain into the Common Hepatic Duct which drains the entire liver.

### **14.3. The Gall Bladder**

Since the liver is continuously producing bile and bile is only needed when food has been ingested the gall bladder serves to store and to concentrate bile until it is needed. To facilitate this the gall bladder is distensible and contractible. Because it does not produce its own products the gall bladder is not organized like the pancreas or liver as a secretory organ. The gall bladder is a small, pear shaped organ located in a depression on the inferior surface of the right hepatic lobe. It will release bile into the Cystic Duct which will join the common hepatic duct to form the common bile duct.

#### **14.3.1. The Histology of the Gall Bladder**

The gall bladder's histology more closely resembles that of the digestive tube than that of the other accessory organs. It is not principally epithelial or organized into lobes and lobules. Instead it is a hollow organ with tunics making up its walls.

The lumen of the gall bladder is lined by a Tunica Mucosa. The tunica mucosa is arranged into folds, called Rugae, which will be lost as the gall bladder fills with bile. The epithelium of the tunica mucosa is a simple columnar type. These columnar cells have central, elongate nuclei. Their apical surface have microvilli. These microvilli increase surface area for the better absorption of water from bile so as to concentrate the bile. The mucosa lacks glands except in the neck of the gall bladder where invaginations of the epithelium will extend into the lamina propria forming simple tubuloacinar glands. The lamina propria of the tunica mucosa is a loose connective tissue. The tunica mucosa of the gall bladder does not have a true muscularis mucosa. Instead it has a Muscular Lamina. The muscular lamina consists of irregularly anastomizing bundles of smooth muscle separated by dense connective tissue rich in collagen, elastic, and reticular fibers. External to muscular lamina is the Perimuscular Layer. The perimuscular layer is a relatively thick connective tissue layer external to the tunica mucosa. The perimuscular layer is a dense irregular connective tissue consisting mostly of collagen fibers and some elastic fibers. It will also have fibroblasts and a variable number of adipocytes. Lymphatics and blood vessels will traverse the perimuscular layer on their way to the mucosa. The outermost layer of the gall bladder is a Tunica Serosa. The perimuscular layer is covered, for the most part, by the same visceral peritoneum covering the liver.

#### **14.3.2. The Duct System of the Gall Bladder**

The neck of the gall bladder connects to the cystic duct. The cystic duct joins with the common hepatic duct to form the common bile duct. The common bile duct joins with the main pancreatic duct to form the hepatopancreatic ampulla. The walls of the common bile duct will be lined by a tall simple columnar epithelium and will include scattered bundles of smooth muscle. The smooth muscle bundles are not prominent until the terminus of the duct near the duodenum. Here the smooth muscle component is well developed to form the sphincter of Oddi. The sphincter of Oddi is located around the terminus of the common bile duct and often around the terminus of the main pancreatic duct. The sphincter of Oddi prevents the flow of bile into the common bile duct when the stomach is empty. This causes the bile to back up the cystic duct into the gall bladder for storage. The sphincter of Oddi is composed of circular and longitudinal smooth muscle. It generally consists of four parts:

- a) Sphincter Choledochus - an annular sheath around the common bile duct. Its contraction prevents bile flow.
- b) Sphincter Pancreaticus - an annular sheath around the terminus of the main pancreatic duct. Its contraction prevents the flow of pancreatic juice.
- c) Sphincter Ampullae - an annular sheath around the opening of the hepatopancreatic ampulla.
- d) Fasciculi Longitudinales - a longitudinally arranged smooth muscle. It facilitates the flow of bile when contracted.

### **14.3.3. Functional Aspects of Bile**

Bile is an aqueous solution composed of pigments such as biliverdin and bilirubin, water, salts, lecithin, and cholesterol. Bile salts emulsify fats to increase their solubility. Bile salts will often be reabsorbed by the small intestine to be used again. Bile is stored in a concentrated form in the bladder due to the ability of its epithelium to absorb water and inorganic salts.

### **14.3.4. Hormonal Control of the Gall Bladder**

The hormones secretin and cholecystokinin/pancreozymin are released from the duodenal mucosa. This release is stimulated by the presence of fatty substances in the chyme entering the duodenum from the stomach. Cholecystokinin/pancreozymin activates contraction of the gall bladder which causes it to release bile. It also induces the relaxation of the sphincter of Oddi. Secretin acts on the bile ducts causing them to release a watery bicarbonate solution that mixes with, and dilutes, the bile.