NORMAL BODY Microscopic Anatomy
Accessory Glands of the GI Tract, lecture 2

• Liver
• Gallbladder

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Objectives

By the end of this lecture, students will be able to:

• trace the flow of blood and bile within the liver

• describe the structure of the liver in regard to its functions

• indicate the major cell types of the liver and their functions

• distinguish the microanatomy of exocrine and endocrine function by the hepatocytes

• explain the functional organization of the gallbladder at the cellular level

(Lecture plan: overview of structure and function, then increasing resolution of microanatomy and cellular function)
Liver

October is “Liver Awareness Month” -- http://www.liverfoundation.org
Liver

- Encapsulated by CT sheath and mesothelium
- Lobes largely composed of hepatocytes in parenchyma
- Receives blood from small intestine and general circulation
Major functions of the liver

• Production and secretion of digestive fluids to small intestine (exocrine)
• Production of plasma proteins and lipoproteins (endocrine)
• Storage and control of blood glucose
• Detoxification of absorbed compounds
• Source of embryonic hematopoiesis
The liver lobule

- Functional unit of the parenchyma
- Delimited by CT septa, invisible in humans (pig is shown)
- Surrounds the central vein
- Bordered by portal tracts
Central vein, muralia and sinusoids
Parenchyma: Muralia and sinusoids

- Hepatocyte basolateral membrane faces sinusoidal lumen
- Bile canaliculi occur between adjacent hepatocytes
- Cords anastomose
Vascularization of the liver

- Receives veinous blood from small intestine via portal vein
- Receives freshly oxygenated blood from hepatic artery
- Discharges blood into vena cava via hepatic vein
Blood flow in the liver lobes

- flows in via the portal vein and hepatic artery
- oozes through the liver lobules to central veins
- flows out via the hepatic vein
Portal Tract (aka portal triad)

- Portal venule
- Hepatic arteriole
- Bile duct
- Lymph vessel
- Nerves
- Connective tissue
Figure 28–5  Diagram of hepatic structure. (From Gray’s Anatomy. London, Longman. After Prof. H. Elias.)
Central vein (a.k.a. terminal hepatic venule)

- At center of hepatic lobule
- Drains specialized capillaries called sinusoids
- Sinusoids flow through muralia (sheets/cords of hepatocytes)
Central vein - H&E
Fluid flow through the lobule

• Venous and arterial blood mix in the sinusoids
• Blood flows toward the central vein
• Bile is excreted into canaliculi
• Bile flows opposite to blood, toward portal tract
Functional units
- classic
- portal
- acinus

Junqueira et al., 1992
Zones of hepatocytes

- Zone 1 receives the most oxygen and food stuffs but also toxins
- Zone 3 receives secreted products of other zones
- Zones reflect patterns of liver damage
- Hepatocytes are capable of limited regeneration
- Repeated damage stimulates CT depos.
Intralobular biliary tree

- Bile canaliculi expand and contract with bile production
- No lining
- Drain into bile ductules (canals of Hering) lined with cuboidal epith.
- CoH drain into bile ducts, which exit at portal tract
Large bile ducts of the liver

- Interlobular bile ducts have cuboidal epithelium which becomes columnar near porta hepatis
- Dense CT sheath w/ smooth muscle forms as ducts get larger
- Lobar ducts join to form common hepatic duct
- CHD has columnar epithelium with microvilli, and all layers of GI tract except muscularis mucosae
- Joins cystic duct (to/from GB) to form common bile duct, which empties into duodenum
Major cells of the muralia and sinusoids

- hepatocytes
- endothelial cells
- Kupffer cells
- stellate cells
Space of Disse

- Between hepatocyte basolateral surface and sinusoidal endothelium
- About 1 μM deep
- Microvilli from hepatocytes project into SoD
- Endothelium has holes
- Plasma flows through
Fenestrated endothelium in sinusoid

(fenestrations organized into “sieve plates”)

Kupffer cells

- reside in the sinusoidal lumen
- mononuclear phagocytic cells
- destroy particulate debris, including old RBCs
Hepatic stellate cell

- reside between hepatocytes and endothelium
- many long cellular processes
- major source of fat and vitamin A storage
- major effector of hepatic fibrogenesis
The hepatic stellate cell undergoes “activation” in response to liver injury

- accumulation at injury site
- contraction
- release of cytokines
- massive synthesis of collagen and other ECM molecules
Alcohol’s potential effects on liver microanatomy

- Fat uptake, cytoskeletal disorganization and death of hepatocytes
- Fibrous tissue upon repeated attempts at regeneration
- Impaired circulation from disrupted lobules and acini
Hepatocytes perform both exocrine and endocrine functions

- Exocrine - secretion of bile
- Bile aids in the digestion of fats in SI
- Bile is composed of water, bile salts, bilirubin, cholesterol

- Endocrine - secretion of plasma proteins, lipoproteins and glucose
- Responsive to insulin and glucagon
Hepatocytes secrete endocrine and exocrine products into different compartments

- Endocrine secretions across the basolateral membrane, into the plasma in the space of Disse
- Exocrine secretions across the apical membrane into the bile canaliculus
- Tight junctions seal apical from basolateral membrane
Hepatocyte organelles

- **Peroxisomes (P)** - oxidation: gluconeogenesis, metabolism of alcohol, lipids, etc.
- **SER** - degrades and conjugates toxins/drugs and makes cholesterol and lipid moieties
- **RER** - synthesizes proteins
- **Lysosomes (L)** - organelle turnover, iron storage?
- **Glycogen granules (G)** - reservoir for glucose
- **All the usual suspects** also present: nucleus, mitochondria (M), golgi, etc.
Endocrine functions of hepatocytes

- Glucose and AA’s absorbed from SoD
- Glucose to glycogen cycle in SER
- Proteins synthesized in RER
- Secreted into SoD
Glycogen storage in rat liver:
A. fasted 2 hr.        B. fasted 21 hr.
Bile production and recycling by the hepatocyte

90% of bile acids are recirculated

10% of bile acids are synthesized de novo

Synthesis of cholic acid and conjugation with glycine and taurine

Bile acids reabsorbed in the intestines
Bilirubin

- breakdown product of hemoglobin
- formed by mononuclear phagocytic system
- taken up as insoluble form (toxic)
- processed in SER
- secreted in water-soluble form in bile
Gallbladder

- Adjoins posterior aspect of liver
- Hollow, pear-shaped
- Functions to store and concentrate bile (< 100 mL in humans)
- Contraction stimulated by cholecystokinin
- CCK released by SI mucosa in response to fats

http://www.cancer.gov/types/gallbladder
Gallbladder - mucosal folds
Gallbladder- lumenal surface
Layers of the Gallbladder

- Mucosa
- Muscularis externa
- Adventitia of CT
- Serosa of mesothelium covers free surfaces
- NB - no muscularis mucosae or submucosa
Gallbladder mucosa

- Tall columnar epithelial cells with microvilli
- Epithelial cells secrete small amounts of mucous
- Lamina propria is highly vascularized
Concentration of bile

- Na pumped to intercellular space at lateral membranes
- Water follows
- Water and Na diffuse in from lumen - microvilli increase area
- Water flows into CT (large arrows) and is reabsorbed
- Bile volume decreased
Gallstones

Summary

**Liver**
- Blood flows from portal tracts to central vein
- Bile flows from canaliculi to portal tract
- Parenchymal cell is hepatocyte. Stellate, Kupffer and fenestrated epithelial cells also key.
- Substances taken up from plasma flowing through Space of Disse in sinusoids to central veins
- Endocrine secretions into plasma
- Exocrine secretions into bile canaliculi

**Gallbladder**
- Like muscularized flask for holding and concentrating bile.
- Interior surface lined with tall columnar epithelial cells with microvilli
- Bile concentrated by sodium pumping out of the epithelial cells into lamina propria – water follows, reducing bile volume.