LIVER OF THE HORSE

The liver of the horse is situated obliquely in the cranial abdomen in contact with the diaphragm. It lies entirely within the intrathoracic part of the abdominal cavity, the greater part (about three-fifths) of it to the right of the median plane.
There is no gall bladder associated with the liver of the horse, hence there is no cystic duct.

The liver is the largest gland in the body and performs an astonishingly large number of tasks that impact all body systems. One consequence of this complexity is that hepatic disease has widespread effects on virtually all other organ systems.

There are three fundamental roles of the liver:

1. **Vascular functions**, including formation of lymph and the hepatic phagocytic system.
2. **Metabolic achievements** in control of synthesis and utilization of carbohydrates, lipids and proteins.
3. **Secretory and excretory functions**, particularly with respect to the synthesis of secretion of bile.

The latter is the only one of the three that directly affects digestion - the liver, through its biliary tract, secretes bile acids into the small intestine where they assume a critical role in the digestion and absorption of dietary lipids. However, understanding the vascular and metabolic functions of the liver is critical to appreciating the gland as a whole.

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**The Hepatic Vascular System**

The circulatory system of the liver is unlike that seen in any other organ. Of great importance is the fact that a majority of the liver's blood supply is venous blood.

**Hepatic Blood Volume and Reservoir Function**

The liver receives approximately 30% of resting cardiac output and is therefore a very vascular organ. The hepatic vascular system is dynamic, meaning that it has considerable ability to both store and release blood - it functions as a reservoir within the general circulation. In the normal situation, 10-15% of the total blood volume is in the liver, with roughly 60% of that in the sinusoids. When blood is lost, the liver dynamically adjusts its blood volume and can eject enough blood to compensate for a moderate amount of hemorrhage. Conversely, when vascular volume is acutely increased, as when fluids are rapidly infused, the hepatic blood volume expands, providing a buffer against acute increases in systemic blood volume.

**Architecture of Hepatic Tissue**

The liver is covered with a connective tissue capsule that branches and extends throughout the substance of the liver as septae. This connective tissue tree provides a scaffolding of support and the highway which along which afferent blood vessels, lymphatic vessels and bile ducts traverse the liver.

**Formation of Lymph in the Liver**

Approximately half of the lymph formed in the body is formed in the liver. Due to the large pores or fenestrations in sinusoidal endothelial cells, fluid and proteins in blood flow freely into the space between the endothelium and hepatocytes (the "space of Disse"), forming lymph.

**The Hepatic Phagocytic System**

The liver is host to a very important part of the phagocytic (phagocyte - A cell, such as a white blood cell, that engulfs and absorbs waste material, harmful microorganisms, or other foreign bodies in the bloodstream and tissues.) system. Lurking in the sinusoids are large numbers of a type of tissue macrophage known as the **Kupffer cell**. Kupffer cells are actively phagocytic and represent the main cellular system for removal of particulate materials and microbes from the circulation.
The Biliary System
The biliary system is a series of channels and ducts that conveys bile - a secretory and excretory product - from the liver into the lumen of the small intestine.

Secretion of Bile and the Role of Bile Acids In Digestion
Bile is a complex fluid containing water, electrolytes and a battery of organic molecules including bile acids, cholesterol, phospholipids and bilirubin that flows through the biliary tract into the small intestine.

There are two fundamentally important functions of bile in all species:
- Bile contains bile acids, which are critical for digestion and absorption of fats and fat-soluble vitamins in the small intestine.
- Many waste products, including bilirubin, are eliminated from the body by secretion into bile and elimination in feces.

In species with a gallbladder (man and most domestic animals except horses and rats), further modification of bile occurs in that organ. The gall bladder stores and concentrates bile during the fasting state. Typically, bile is concentrated five-fold in the gall bladder by absorption of water and small electrolytes - virtually all of the the organic molecules are retained.

Secretion into bile is a major route for eliminating cholesterol. Free cholesterol is virtually insoluble in aqueous solutions, but in bile, it is made soluble by bile acids and lipids like lethicin.

Role of Bile Acids in Fat Digestion and Absorption
Their amphipathic nature enables bile acids to carry out two important functions:

- **Emulsification of lipid aggregates**: Bile acids have detergent action on particles of dietary fat which causes fat globules to break down or be emulsified into minute, microscopic droplets. Emulsification is not digestion per se, but is of importance because it greatly increases the surface area of fat, making it available for digestion by lipases, which cannot access the inside of lipid droplets.
- **Solubilization and transport of lipids in an aqueous environment**: Bile acids are lipid carriers and are able to solubilize many lipids by forming micelles - aggregates of lipids such as fatty acids, cholesterol and monoglycerides - that remain suspended in water. Bile acids are also critical for transport and absorption of the fat-soluble vitamins.

Role of Bile Acids in Cholesterol Homeostasis
Hepatic synthesis of bile acids accounts for the majority of cholesterol breakdown in the body. This route for elimination of excess cholesterol is probably important in all animals, but particularly in situations of massive cholesterol ingestion.

Enterohepatic Recirculation
Large amounts of bile acids are secreted into the intestine every day, but only relatively small quantities are lost from the body. This is because approximately 95% of the bile acids delivered to the duodenum are absorbed back into blood within the ileum. Venous blood from the ileum goes straight into the portal vein, and hence through the sinusoids of the liver.

Hepatocytes extract bile acids very efficiently from sinusoidal blood, and little escapes the healthy liver into systemic circulation. Bile acids are then transported across the hepatocytes to be resecreted into canaliculi. The net effect of this enterohepatic recirculation is that each bile salt molecule is reused about 20 times, often two or three times during a single digestive phase.
It should be noted that liver disease can dramatically alter this pattern of recirculation - for instance, sick hepatocytes have decreased ability to extract bile acids from portal blood and damage to the canalicular system can result in escape of bile acids into the systemic circulation. Assay of systemic levels of bile acids is used clinically as a sensitive indicator of hepatic disease.

**Biliary Excretion of Waste Products: Elimination of Bilirubin**
The liver is well known to metabolize and excrete into bile many compounds and toxins, thus eliminating them (usually) from the body. Examples can be found among both endogenous molecules (steroid hormones, calcium) and exogenous compounds (many antibiotics and metabolites of drugs). A substantial number of these compounds are reabsorbed in the small intestine and ultimately eliminated by the kidney.

One of the most important and clinically relevant examples of waste elimination via bile is that of bilirubin. Additionally, the mechanisms involved in elimination of bilirubin are similar to those used for elimination of many drugs and toxins. Bilirubin is a useless and toxic breakdown product of hemoglobin, which also means that it is generated in large quantities. In the time it takes you to read this sentence aloud, roughly 20 million of your red blood cells have died and roughly 5 quintillion (5 \times 10^{15}) molecules of hemoglobin are in need of disposal.

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**Metabolic Functions of the Liver**
Hepatocytes are metabolic superachievers in the body. They play critical roles in synthesizing molecules that are utilized elsewhere to support homeostasis, in converting molecules of one type to another, and in regulating energy balances. If you have taken a course in biochemistry, you probably spent most of that class studying metabolic pathways of the liver. At the risk of damning by faint praise, the major metabolic functions of the liver can be summarized into several major categories:

**Carbohydrate Metabolism**
It is critical for all animals to maintain concentrations of glucose in blood within a narrow, normal range. Maintenance of normal blood glucose levels over both short (hours) and long (days to weeks) periods of time is one particularly important function of the liver. Hepatocytes house many different metabolic pathways and employ dozens of enzymes that are alternatively turned on or off depending on whether blood levels of glucose are rising or falling out of the normal range.

Two important examples of these abilities are:
- Excess glucose entering the blood after a meal is rapidly taken up by the liver and sequestered as the large polymer, glycogen (a process called glycogenesis). Later, when blood concentrations of glucose begin to decline, the liver activates other pathways which lead to depolymerization of glycogen (glycogenolysis) and export of glucose back into the blood for transport to all other tissues.
- When hepatic glycogen reserves become exhausted, as occurs when an animal has not eaten for several hours, do the hepatocytes give up? No! They recognize the problem and activate additional groups of enzymes that begin synthesizing glucose out of such things as amino acids and non-hexose carbohydrates (gluconeogenesis). The ability of the liver to synthesize this "new" glucose is of monumental importance to carnivores, which, at least in the wild, have diets virtually devoid of starch.
Fat Metabolism
Few aspects of lipid metabolism are unique to the liver, but many are carried out predominantly by the liver. Major examples of the role of the liver in fat metabolism include:

- The liver is extremely active in oxidizing triglycerides to produce energy. The liver breaks down many more fatty acids that the hepatocytes need, and exports large quantities of acetoacetate into blood where it can be picked up and readily metabolized by other tissues.
- A bulk of the lipoproteins are synthesized in the liver.
- The liver is the major site for converting excess carbohydrates and proteins into fatty acids and triglyceride, which are then exported and stored in adipose tissue.
- The liver synthesizes large quantities of cholesterol and phospholipids. Some of this is packaged with lipoproteins and made available to the rest of the body. The remainder is excreted in bile as cholesterol or after conversion to bile acids.

Protein Metabolism
The most critical aspects of protein metabolism that occur in the liver are:

- Deamination and transamination of amino acids, followed by conversion of the non-nitrogenous part of those molecules to glucose or lipids. Several of the enzymes used in these pathways (for example, alanine and aspartate aminotransferases) are commonly assayed in serum to assess liver damage.
- Removal of ammonia from the body by synthesis of urea. Ammonia is very toxic and if not rapidly and efficiently removed from the circulation, will result in central nervous system disease. A frequent cause of such hepatic encephalopathy in dogs and cats are malformations of the blood supply to the liver called portosystemic shunts.
- Synthesis of non-essential amino acids.

Hepatocytes are responsible for synthesis of most of the plasma proteins. Albumin, the major plasma protein, is synthesized almost exclusively by the liver. Also, the liver synthesizes many of the clotting factors necessary for blood coagulation.

The Pancreas: Introduction

As chyme (pre-digested, acidified mass of food that passes from the stomach into the small intestine) floods into the small intestine from the stomach, two things must happen:

- acid must be quickly and efficiently neutralized to prevent damage to the duodenal mucosa
- macromolecular nutrients - proteins, fats and starch - must be broken down much further before their constituents can be absorbed through the mucosa into blood

The pancreas plays a vital role in accomplishing both of these objectives, so vital in fact that insufficient exocrine secretion by the pancreas leads to starvation, even if the animal is consuming adequate quantities of high quality food.

In addition to its role as an exocrine organ, the pancreas is also an endocrine organ and the major hormones it secretes - insulin and glucagon - play a vital role in carbohydrate and lipid metabolism. They are, for example, absolutely necessary for maintaining normal blood concentrations of glucose.