# 69: THE LIVER and GALL BLADDER

The liver is the largest gland in the body. A gland is defined as something that secretes one or more substances that are useful to the body. As we will see, the liver is the ultimate gland, as it secretes more different types of chemicals than any other gland in the body. The liver of an average-sized adult weighs about 3 pounds (1.5 kg). Human livers are the same color as those chicken livers you see in the grocery store (a reddish brown) and have a rubbery texture.

Both the liver and the stomach lie right below the diaphragm. In the last drawing we saw that the diaphragm has three holes in it: for the inferior vena cava, the descending aorta, and the esophagus. The esophagus leads to the stomach, and we will learn more about it in the next lesson. Both the inferior vena cava and the descending aorta connect to the liver. The aorta brings oxygen-rich blood into the liver. The blood that the vena cava transports into the heart is low in oxygen but it is rich in nutrients, as we will see.

The blood supply to the liver comes from two sources: from the descending aorta, as we just mentioned, and also from veins called the **hepatic portal veins**. (Words that begin with "hep" or "hepa" always have something to do with the liver. "Hepatic portal" might be translated as "doorway in the liver.") The blood in the hepatic portal veins comes from several sources: from the spleen, the pancreas, the stomach, and the intestines. Basically, all of the blood from the abdominal cavity (everything below the diaphragm) comes into the liver through these portal veins. This means that before any nutrients from food are distributed to the body, they must go through the liver first. The liver keeps track of how much sugar and fat are in the blood and will do its best to prevent an overload of either one. For example, if the glucose level in the blood is too high, the liver can start catching and storing the extra glucose molecules, putting them into long strings called **glycogen**. (We also find glucose stored as glycogen in muscle tissue.) About 5 percent of the liver's weight is glycogen.

Between meals, your liver is constantly checking the blood's glucose level and when it begins to fall below about 70 grams per deciliter (a deciliter is one tenth of a liter) the liver will begin to break down some of the glycogen and turn it back into glucose, and release it into the blood. If the liver runs out of stored glycogen and the body still needs more glucose, the liver cells will begin turning amino acids into glucose. Ultimately, all forms of energy (sugar, fats, proteins) must be converted into glucose so that it can be fed into the Krebs cycle and then into the Electron Transport Chain. If the liver runs out of space to store glucose as glycogen, it will then begin turning the glucoses into triglycerides and send them out into the body to be picked up by adipose cells that will store them as fat. The process can go the other way, too, as the liver can turn protein and fat into glucose. This is how carnivores who eat only protein and fat survive. Their livers convert the protein and fat into glucose. This process is called **gluconeogenesis**. ("Gluco" = sugar, "neo" = new, "genesis" = to make) In the process of turning aminos into glucose, the nitrogen part of the amino acid must be discarded, as there isn't any nitrogen in either sugars or fats. The nitrogen from the amino acid is discarded as a molecule of $NH_3$, ammonia, a substance that is very poisonous to the body. But the liver has a way to deal with ammonia—it quickly turns it into a molecule of urea, which still contains that nitrogen but is much less poisonous. The urea can safely float around in your blood until it reaches the kidneys where it will be filtered out and then sent out of the body with the urine.

The liver can also turn sugars and fats into amino acids. There are still those 6 "essential" amino acids that your liver can't make and that you must get from your diet, but the rest can be manufactured by liver cells. If you eat too much of one kind of amino and not enough of another, the liver has enzymes that know how to transform one amino into another. Pretty amazing!

Another major function of the liver is to produce **bile**. Bile is a liquid made of water, bile salts (also called bile acids), cholesterol and phospholipids. Bile acts very much like the dish soap you use to cut the grease on your dirty dishes. Bile "emulsifies" fats, meaning it breaks them up into very small pieces. Each tiny bit of fat is surrounded by phospholipids that have their water loving heads facing outwards so that the fat molecules can travel safely in the blood. (The job of the salts/acids is to act as a surfactant.)

The gall bladder is the storage area for bile. When fatty foods reach the **duodenum** (the first part of the small intestine, pronounced either *du-ODD-den-um* or *du-oh-DEE-num*), chemical signals are sent to the gall bladder telling it to release some bile. (In people who have had their gall bladder removed, the bile just flows directly from the liver into the duodenum.)

Other functions of the liver include making and transporting cholesterol using "shuttles" called LDL and HDL. The LDL's are the delivery system taking cholesterol out to the cells. The HDL's are involved in collecting leftovers and returning them to the liver for recycling. (Doctors tells us we want more HDL's than LDL's.) The liver also stores iron (Fe) and fat-soluble vitamins: A, D, E K, plus B12.

A microscopic view of the liver shows that it is made of individual units called **lobules**. Each lobule is approximately in the shape of a hexagon. At the center is a **central vein** that will eventually lead into the hepatic vein that goes up into the inferior vena cava. At each vertex of the hexagon you find a **triad** of three vessels: 1) a hepatic artery, 2) a portal vein, and 3) a **bile canaliculi** (tiny canal). The hepatic arteries contain blood that came in from the descending aorta so they are rich in oxygen. The portal veins contain blood that came in from the veins in the stomach and intestines so they are rich in nutrients. Both the hepatic arteries and the portal veins lead into the central vein. (As with all other blood vessels in the body, they are made of endothelial cells.) The fluid in the bile canaliculi comes from all the surrounding cells, and goes out through larger and large bile vessels until it reaches the **bile duct**. The large "common" bile duct connects to both the gall bladder and the duodenum.

The blood from these tiny portal veins and hepatic arteries joins together in a space called the **sinusoid**. On the walls of this sinusoid space, macrophages called **Kupffer cells** crawl around looking for bacteria to destroy or red blood cells that need to be recycled. It is in the Kupffer cells that hemoglobin is broken down into heme and globin.

The large cells (that are not endothelial cells) are called **hepatocytes**. The hepatocytes have three notable features: 1) a large amount of smooth ER, 2) microvilli (that look like fringe), and 3) occasionally a double nucleus. When cells have more DNA than normal, this is called **polyploidy**. Why many liver cells are polyploid is not yet fully understood. Notice the bile canaliculi between the cells. The hepatocytes do numerous jobs including breaking down toxins such as alcohol, making and monitoring glucose, fats and amino acids (as we've already mentioned), making clotting factors for the clotting cascade (from lesson 38), making blood proteins such as albumen, and making all the immune system proteins that begin with "C" (C-reactive protein and C1 through C9, from lesson 48).

The space between the hepatocytes and the endothelial cells is called the **space of Disse**. Plasma from the blood leaks out into this space, interacts with the hepatocytes along their microvilli, then drains into the lymph system. Stellate cells live in this space; they store vitamins and make the collagen network that holds all the lobule cells in place.