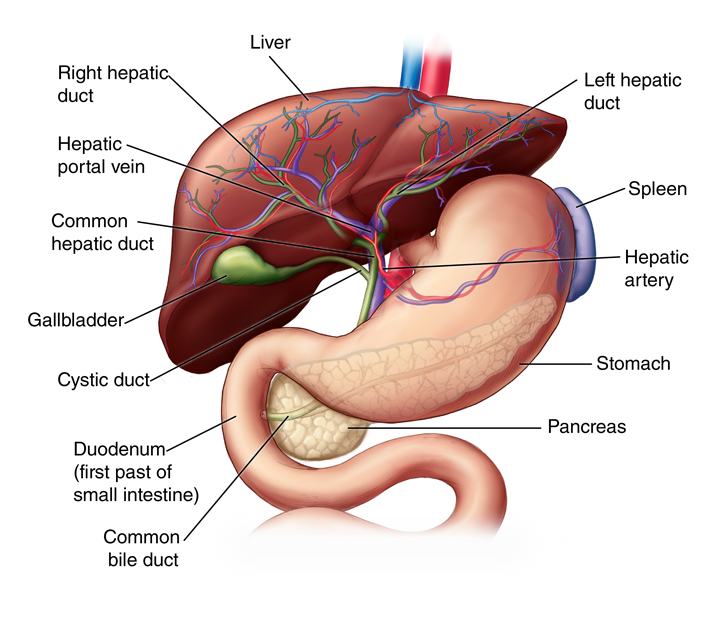
**Liver Disease and its identification**



The liver is located in the upper right-hand portion of the abdominal cavity, beneath the diaphragm, and on top of the stomach, right kidney, and intestines.

Shaped like a cone, the liver is a dark reddish-brown organ that weighs about 3 pounds.

There are 2 distinct sources that supply blood to the liver, including the following:

* Oxygenated blood flows in from the hepatic artery
* Nutrient-rich blood flows in from the hepatic portal vein

The liver holds about one pint (13%) of the body's blood supply at any given moment. The liver consists of 2 main lobes. Both are made up of 8 segments that consist of 1,000 lobules (small lobes). These lobules are connected to small ducts (tubes) that connect with larger ducts to form the common hepatic duct. The common hepatic duct transports the bile made by the liver cells to the gallbladder and duodenum (the first part of the small intestine) via the common bile duct.

Functions of the liver

The liver regulates most chemical levels in the blood and excretes a product called bile. This helps carry away waste products from the liver. All the blood leaving the stomach and intestines passes through the liver. The liver processes this blood and breaks down, balances, and creates the nutrients and also metabolizes drugs into forms that are easier to use for the rest of the body or that are nontoxic. More than 500 vital functions have been identified with the liver. Some of the more well-known functions include the following:

* Production of bile, which helps carry away waste and break down fats in the small intestine during digestion
* Production of certain proteins for blood plasma
* Production of cholesterol and special proteins to help carry fats through the body
* Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy) and to balance and make glucose as needed
* Regulation of blood levels of amino acids, which form the building blocks of proteins
* Processing of hemoglobin for use of its iron content (the liver stores iron)
* Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)
* Clearing the blood of drugs and other poisonous substances
* Regulating blood clotting
* Resisting infections by making immune factors and removing bacteria from the bloodstream
* *Clearance of bilirubin, also from red blood cells. If there is an accumulation of bilirubin, the skin and eyes turn yellow.*

When the liver has broken down harmful substances, its by-products are excreted into the bile or blood. Bile by-products enter the intestine and leave the body in the form of feces. Blood by-products are filtered out by the kidneys, and leave the body in the form of urine.

What is Heme?

If you’re a fan of the Impossible Burger, you may have heard about the magical ingredient that helps the plant-based patty taste so similar to beef: heme. The topic can be a bit confusing, since heme is not usually something, we see on ingredient lists — though if you eat meat, you’ve eaten your fair share of heme. Not to mention, your body produces its own heme. Heck, it might even be producing heme right now!

Heme is an essential molecule that contains iron, that is naturally found in fairly high concentrations in the blood of humans and other animals, and in much lower concentrations in plants. Heme is also what makes blood red, makes meat pink, and gives blood a subtle metallic flavor (which you can taste when eating meat, or if you’ve ever tasted your own blood, perhaps after accidentally biting your tongue). But most importantly, heme is “what makes meat taste like meat.”

Where does heme come from?

Heme is mostly found in human and animal blood, but many plants contain heme as well. One plant with a significant concentration of heme is the soybean, which contains leghemoglobin in its roots. For that reason, some chose soy (as well as yeast) to make its soy leghemoglobin, aka heme.

What is Bilirubin?

Bilirubin is a metabolite of heme, a compound that serves to coordinate iron in various proteins.

Very recently, bilirubin has been shown to possess important functions as an antioxidant, but it also serves simply as a means to excrete unwanted heme, derived from various heme-containing proteins such as hemoglobin, myoglobin, and various P450 enzymes.

Bilirubin and its metabolites are also notable for the fact that they provide color to the bile and stool, as well as, to a lesser extent, the urine.

Bilirubin derives from two main sources. The majority (80%) of the bilirubin formed in the body comes from the heme released from senescent red blood cells. The remainder originates from various heme-containing proteins found in other tissues, notably the liver and muscles.

Can excess of Bilirubin is harmful?

It is important for the body to be able to excrete bilirubin as it is potentially toxic. Excessive levels of bilirubin in the bloodstream can lead to accumulation of bilirubin in the brain due to its ability to cross the blood–brain barrier, a condition known as kernicterus (meaning “yellow-stained nucleus”) and cause certain diseases.

The development of this condition impairs brain function by mechanisms that are not well-understood, but it can be fatal if left untreated. Bilirubin is also notable for its yellow coloration.

Accumulation of this substance in the blood is the basis for jaundice, or a yellow discoloration of the skin and eyes which is a common symptom of liver diseases. Thus, measurement of bilirubin in the plasma can be a useful marker of such conditions.

Direct Bilirubin

**Does this test have other names?**

**Conjugated bilirubin**

**What is this test?**

This test looks for bilirubin in your blood or urine.

Bilirubin is a substance made when your body breaks down old red blood cells. This is a normal process. Bilirubin is also part of bile, which your liver makes to help digest the food you eat.

A small amount of bilirubin in your blood is normal. Healthy adults make 250 to 350 milligrams (mg) of bilirubin each day.

Bilirubin that is bound to a certain protein (albumin) in the blood is called unconjugated, or indirect, bilirubin. Conjugated, or direct, bilirubin travels from the liver into the small intestine. A very small amount passes into your kidneys and is excreted in your urine. This bilirubin also gives urine its distinctive yellow color.

This test is usually done to look for liver problems, such as hepatitis, or blockages, such as gallstones.

**Why do I need this test?**

You may need this test if your liver doesn't seem to be working the way it should. Signs and symptoms include:

* Jaundice, or yellowing of your skin and whites of your eyes
* Dark-colored urine
* Nausea
* Vomiting
* Fatigue
* Pain or swelling in the belly

You may also have this test if you drink a lot of alcohol on a regular basis. Drinking too much alcohol can damage the liver over time, so you may have this test to check for signs of possible liver damage.

You may also need this test if your healthcare provider suspects that you may have:

**Hepatitis**. Your liver can become inflamed for different reasons, including excessive drug or alcohol use and infection from hepatitis viruses. Inflammation of the liver is called hepatitis. When liver cells are damaged from hepatitis, the liver may release both indirect and direct bilirubin into the bloodstream. This causes higher levels.

**Gallstones**. The bile duct is a tube that carries bile to the small intestine. Bilirubin or cholesterol can form stones that block the duct. This causes bilirubin—mostly direct bilirubin—to rise in your bloodstream.

**Inflammation of the bile duct**. Higher levels of direct bilirubin in your bloodstream may stem from inflammation in the tube that carries bile to the small intestine.

**What other tests might I have along with this test?**

Your healthcare provider is likely to order this test as part of a liver panel, or group of related liver tests. When your liver is damaged, liver enzymes may leak into your blood. Your provider may order blood tests for these enzymes, such as:

Alkaline phosphatase, or ALP

Aspartate transaminase, or AST

Alanine transaminase, or ALT

Your healthcare provider may also order a test to check the levels of liver proteins like albumin.

**What do my test results mean?**

Test results may vary depending on your age, gender, health history, the method used for the test, and other things. Your test results may not mean you have a problem. Ask your healthcare provider what your test results mean for you.

***Results are given in milligrams per deciliter (mg/dL). Direct Bilirubin: Normal results of the blood test range from 0 to 0.3 mg/dL in adults. Total bilirubin: 0.1 to 1.2 mg/dL (1.71 to 20.5 µmol/L)***

If your results on the blood test are higher, bilirubin may also show up in your urine. Bilirubin is not present in the urine of normal, healthy individuals.

Results that are higher may mean that you have a liver problem, hepatitis, or gallstones.

Higher levels may also mean that you have:

* Septicemia, an infection in the bloodstream commonly known as blood poisoning
* Sickle cell anemia
* Certain cancers or tumors
* Certain rare inherited diseases
* Scarring of the bile ducts

If your results show low levels of bilirubin, your healthcare provider usually will not monitor them.

What is the relationship between Heme, Total Bilirubin, Direct Bilirubin and Indirect Bilirubin?

Bilirubin is an orange-yellow pigment, a waste product primarily produced by the normal breakdown of heme. Heme is a component of hemoglobin, which is found in red blood cells (RBCs). Bilirubin is ultimately processed by the liver so that it can be removed from the body. This test measures the amount of bilirubin in the blood to evaluate a person's liver function or to help diagnose anemias caused by RBC destruction (hemolytic anemia).

RBCs normally degrade after about 120 days in circulation. Bilirubin is formed as the liver breaks down and recycles aged red blood cells.

Two forms of bilirubin can be measured or estimated by laboratory tests:

* **Unconjugated bilirubin** is formed when heme is released from hemoglobin. It is carried by proteins to the liver. In the liver, sugars are attached (conjugated) to bilirubin to form conjugated bilirubin.
* **Conjugated bilirubin** enters the bile and passes from the liver to the small intestines, where it is further broken down by bacteria and eventually eliminated in the stool. Thus, the breakdown products of bilirubin give stool its characteristic brown color. Normally, the level of conjugated bilirubin in the blood is very low.

The bilirubin test is included in the comprehensive metabolic panel (CMP) and the liver panel, which are often used as general health screenings.

Usually, an initial test measures the total bilirubin level (unconjugated plus conjugated bilirubin).

If the total bilirubin level is increased, the laboratory can use a second test to detect water-soluble forms of bilirubin, called "direct" bilirubin. The direct bilirubin test provides an estimate of the amount of conjugated bilirubin present.

**Subtracting the direct bilirubin level from the total bilirubin level helps estimate the "indirect" level of unconjugated bilirubin.**

*A small amount (approximately 250 to 350 milligrams, or about 4 milligrams per kilogram of body weight) of bilirubin is produced daily in a normal, healthy adult. Most bilirubin (70%-90%) comes from damaged or degraded RBCs, with the remaining amount coming from the bone marrow or liver. Normally, small amounts of unconjugated bilirubin are released into the blood, but almost no conjugated bilirubin is present.*

*If the bilirubin level increases in the blood, a person may appear jaundiced, with a yellowing of the skin and/or whites of the eyes. The pattern of bilirubin test results can give the healthcare practitioner information regarding the condition that may be present.*

***Adults and children***

*Total bilirubin that is mainly unconjugated (indirect) bilirubin may be increased when:*

*There is an unusual number of red blood cells (RBCs) being broken down and destroyed (e.g., hemolytic or pernicious anemia, blood transfusion reaction). The liver is unable to process bilirubin (i.e., with liver disease such as cirrhosis or inherited problems)*

*You have a relatively common inherited condition called Gilbert syndrome, due to low levels of the enzyme that produces conjugated bilirubin*

*If conjugated (direct) bilirubin is elevated more than unconjugated (indirect) bilirubin, there typically is a problem associated with decreased elimination of bilirubin by the liver cells. Some conditions that may cause this include:*

* *Viral hepatitis (hepatitis A, hepatitis B, hepatitis C)*
* *Drug reactions*
* *Alcoholic liver disease*

*Conjugated (direct) bilirubin is also elevated more than unconjugated (indirect) bilirubin when the liver is able to process bilirubin but there is blockage of the bile ducts. This may occur, for example, with:*

* *Gallstones present in the bile ducts*
* *Tumors*
* *Scarring of the bile ducts*

Rare inherited disorders that cause abnormal bilirubin metabolism such as Rotor, Dubin-Johnson, and Crigler-Najjar syndromes, may also cause increased levels of bilirubin.

*Low levels of bilirubin are generally not a concern and are not monitored.*

***Newborns***

Increased total and unconjugated bilirubin levels are relatively common in newborns in the first few days after birth. This finding is called "physiologic jaundice of the newborn" and occurs because the newborn's liver is not mature enough to process bilirubin yet. Usually, physiologic jaundice of the newborn is temporary and resolves within a few days to two weeks.

However, if the bilirubin level is critically high or increases rapidly, the healthcare practitioner will diagnose the cause so appropriate treatment can be started as soon as possible.

Increased bilirubin levels may result from the accelerated breakdown of red blood cells due to:

* Blood type incompatibility between the mother and her newborn, causing hemolytic disease of the newborn (HDN)
* Certain congenital infections
* Lack of oxygen (hypoxia)
* Diseases that can affect the liver

In most of these conditions, only unconjugated (indirect) bilirubin is increased.

A rare (about 1 in 12,000 births) but life-threatening congenital condition called biliary atresia can cause increased total and conjugated bilirubin levels in newborns. This condition must be quickly diagnosed and treated, usually with surgery, to prevent serious liver damage that may require liver transplantation within the first few years of life. Some children may require liver transplantation despite early surgical treatment.

Reference Links:

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