

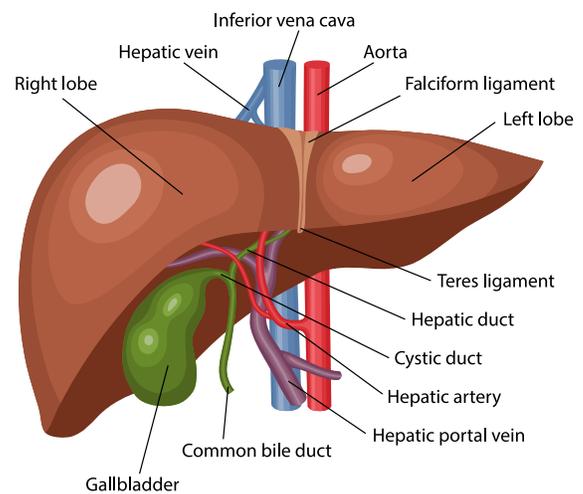
LABORATORY TESTS RELATED TO LIVER DISEASES AND CANCER

THE FUNCTIONS OF THE LIVER

The liver is the largest internal organ of the human body and is located in the upper quadrant of the abdomen on the right-hand side. One of the liver's primary functions is to regulate the levels of certain chemicals in the blood by producing, storing, and releasing bile (digestive fluid) and eliminating waste products. A gallon of blood passes through the liver every two and a half minutes and the liver regulates and processes nutrients and metabolizes (breaks down) chemical compounds (such as medicine).

The liver performs many other vital functions that help maintain homeostasis within the human body, which is the healthy equilibrium (a constant) maintained by the body, including producing vital blood components for clotting and metabolizing nutrients from intestinal blood flow.

Unlike any other organ in the body, the liver has two blood supplies. This is because there is a dual supply of blood from the portal vein and hepatic artery. The hepatic artery delivers blood from the abdominal aorta, whereas the portal vein directs venous blood from the GI system and other organs to the liver. This dual blood supply allows you to use your liver for a long time even if you lose parts of your liver to disease.



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THE HEPATITIS VIRUS

The hepatitis virus is an infection that results in inflammation and damage to the liver. There are multiple types of hepatitis, with a range of causes and effects. Hepatitis A and E usually result in short-term infections, and the body can eliminate the infection itself. In contrast, hepatitis B, C, and D can result in long-term infections since the human body cannot naturally defend against them effectively. Those types of hepatitis can become chronic, which can cause liver cancer, liver failure, or cirrhosis of the liver (see below).

HEPATITIS A is a liver infection caused by the hepatitis A virus (HAV). This type is found in the stool and blood of an infected person, and it is very contagious. Hepatitis A is usually a short-term infection and does not become chronic. There is a vaccine for Hepatitis A.

HEPATITIS B is a liver infection caused by the hepatitis B virus (HBV). This type is found in all body fluids of an infected person. Hepatitis B can begin as short-term, acute infections, but the virus can remain in the body long term and result in chronic and long-term. Chronic HBV may lead to cirrhosis and increase risk for liver cancer. There is a vaccine for Hepatitis B. Rarely, some patients with Hepatitis B may be eligible for liver transplants.

HEPATITIS C is a liver infection caused by the hepatitis C virus (HCV). This type is found in the blood of infected people. It can be spread to other individuals by sharing needles, personal care items, or injury via a sharp instrument. Hepatitis C can begin as short-term, acute infections, but the virus can remain in the body long term and result in chronic and long-term. Chronic HCV may lead to cirrhosis and increase risk for liver cancer. There are currently curative therapy regimens for Hepatitis C but some patients may require a liver transplant (most common reason for liver transplantation).

HEPATITIS D is a liver infection that is only active in people who have also been infected with the hepatitis B virus because the Hepatitis D virus is incomplete. Hepatitis D can make HBV infections worse. It is found in the blood and other bodily fluids. Hepatitis D can either be an acute, short-term infection or become a long-term, chronic infection; hepatitis D can lead to life-long liver damage and cirrhosis.

HEPATITIS E is a liver infection that is caused by the hepatitis E virus (HEV). This type is found in an infected person's stool. It is caused by ingesting tiny, microscopic portions from drinking water that have been contaminated with feces. Hepatitis E is self-limited and is usually a short-term infection and does not become chronic.

ALCOHOLIC HEPATITIS is a liver condition caused by individuals who heavily drink over an extended time. However, it does also occur rarely in people who do not drink heavily. Alcoholic hepatitis can be an acute form of liver disease with variable severity. Chronic alcoholic hepatitis leads to cirrhosis and liver failure. Alcoholic hepatitis is the second most common reason for liver transplant.

AUTOIMMUNE HEPATITIS is a liver condition that occurs when the human body's immune system damages the liver cells with inflammation. If untreated, it can cause cirrhosis of the liver or liver failure. It is thought that autoimmune hepatitis results from a genetic disorder as it is found more often in female patients. Autoimmune hepatitis is a long-term chronic liver disease.

Virus	Transmission	Incubation*
Hepatitis A	Blood, stool	Range: 15–50 days (Average: 28 days)
Hepatitis B	All bodily fluids	Range: 60–150 days (Average: 90 days)
Hepatitis C	Primarily blood	Range: 2 weeks–6 months (Average: 2 weeks–3 months)
Hepatitis D	Parenteral, sexual, perinatal	Range: 45–160 days (Average: 90 days)
Hepatitis E	Fecal-oral especially waterborne	Range: 2–10 weeks (Average: 5–6 weeks)

**Incubation is the specific amount of time it takes for a person to experience the physical symptom of disease after being exposed to the virus.*

OTHER LIVER DISEASES AND CONDITIONS

CIRRHOSIS OF THE LIVER

Cirrhosis is a late-stage result of liver disease, where healthy liver tissue is overtaken by scarred tissue. Several liver diseases and conditions can cause liver cirrhosis, such as chronic alcohol abuse and chronic viral hepatitis. Cirrhosis is the injury of healthy liver cells leading them to cell death and inflammation; cell repair is initiated, leading to scar tissue and non-functional liver cells by blocking blood flow.

HEMOCHROMATOSIS

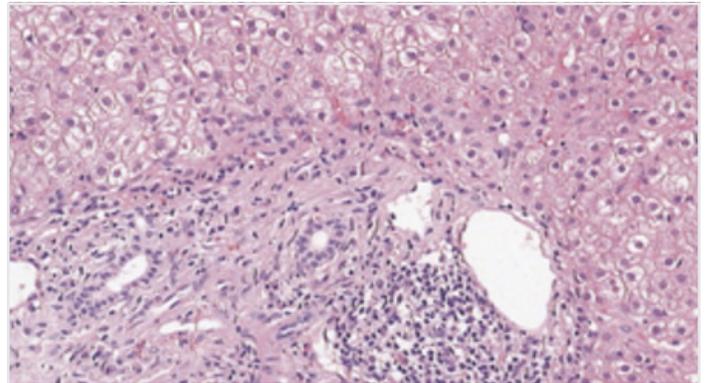
Hemochromatosis is a hereditary disorder that causes your body to absorb too much iron from the contents you consume. The excess iron is stored in the body's organs, especially the liver. Too much iron can be dangerous, leading to liver disease, heart problems, and diabetes. The genes which cause hemochromatosis are inherited, but only a minority of individuals ever develop serious issues.

LIVER FAILURE

Liver failure occurs when your liver is not functioning correctly to perform its basic functions, such as excreting toxins. Annually, in the U.S. alone, 30 million individuals suffer from liver disease and more than 8,000 Americans received liver transplants in 2017. Many different diseases and infections can lead to liver failure: hepatitis B and hepatitis C, non-alcoholic fatty liver disease, alcohol abuse, and hemochromatosis.

NON-ALCOHOLIC FATTY LIVER DISEASE

Non-alcoholic fatty liver disease is an umbrella term for a range of liver conditions affecting a group of individuals who drink little to no alcohol. NAFLD is a phenomenon of excess lipid (the molecular term for fat) deposited in liver cells. The damage of NAFLD is similar damage to that caused by alcohol. NAFLD is more common in the western world, in the United States, affecting about 1 quarter of the population.



UNDER THE MICROSCOPE

This is an image of the liver tissue under the microscope stained with hematoxylin & eosin (routine). Most of the image is of liver cells ("fried egg" appearance). At the bottom center there is a "portal triad" which consists of a bile duct, a vein, and an artery. Normally, only these three structures are seen; however, this patient has moderately active viral Hepatitis C infection; therefore, inflammation (the clusters of dark blue cells) are present.

LIVER CANCER

Liver cancer is cancer that begins in the cells of your liver. There are several types of liver cancer. The most common form of liver cancer is hepatocellular carcinoma, which often occurs in individuals with chronic liver disease, such as cirrhosis caused by hepatitis B and hepatitis C. Another less common type of liver cancer is intrahepatic cholangiocarcinoma, which forms in the bile ducts, an organ that aids in digestion. Hepatoblastomas, a rare childhood cancer, originates in the cells of the liver. A few factors increase the risk of liver cancer, including chronic infection, hepatitis B, hepatitis C, or alcoholic cirrhosis.

LABORATORY TESTS RELATED TO LIVER DISEASES AND CANCER*

**Please note that reference ranges are set by individual laboratories for their specific populations and vary accordingly. Therefore, a discussion of your specific testing results with your healthcare provider is recommended.*

ALBUMIN: This test measures albumin levels, a protein that the liver makes and is in blood. Albumin is the main protein of blood plasma, and it helps bind other minerals and hormones. Albumin is responsible for keeping fluid inside blood vessels, transporting certain molecules, and providing nourishment to the tissues. Albumin levels will increase or decrease depending on the patient's condition. This test is important because low albumin levels indicate malnutrition, liver disease, or an inflammatory disease. High albumin levels can indicate acute infections, burns, and stress from surgery or a heart attack. Typical reference ranges are 3.4 to 5.4 g/dL.

ALKALINE PHOSPHATASE (ALP): This test measures the ALP in your blood, an enzyme found in several tissues throughout the body, mainly in the liver and bones. This test is important because elevated ALP levels are commonly present in liver disease, bile obstruction, gallbladder disease, or bone disorders. Typical reference ranges for adults are between 50-70 mg/dL.

ALANINE AMINOTRANSFERASE (ALT): This test measures the amount of ALT in your blood, an enzyme found mainly in the liver and kidney cells. This test is important because high levels of ALT show early detection of liver disease. Typical reference ranges for adults are between 8-20 U/L.

ASPARTATE AMINOTRANSFERASE (AST): This test measures AST levels in your blood, an enzyme found throughout the body, specifically in the heart and the liver. When liver muscles are injured, it releases high levels of this enzyme, making this a helpful test for identifying liver-damage. Typical reference ranges for adults are between 8-20 U/L.

ASK YOUR DOCTOR

- What is the course of action based on my lab results?
- What are all my treatment options?
- What are the signs and symptoms I should look out for during or after receiving treatment?
- Why do you recommend this particular treatment option?
- What lab tests and which results indicate successful treatment?
- What are the markers we are monitoring? What are the levels we are hoping for? What happens if the markers are higher than we would like to see?
- Are there additional tests that could be used to understand my disease and prognosis better?

ALPHA-FETO PROTEIN (AFP): This test is used to determine the amount of alpha-fetoprotein in women in their second trimester of pregnancy. This protein is generated in the liver of a fetus that is still developing and goes through the placenta into the mother's blood. AFP can be elevated in diseases such as hepatitis and cirrhosis. Typical reference ranges for pregnant adults are below 10 ng/mL.

BILIRUBIN: This test measures the amount of bilirubin in the blood, a waste product produced by the breakdown of heme, a component of hemoglobin found in red blood cells. The liver processes bilirubin to remove it from the body. This test is important because levels of bilirubin assess a person's liver function. Typical reference ranges for are 0.1-1.2 mg/dL.

GAMMA-GLUTAMYL TRANSPEPTIDASE (GGT): This test is used to determine the level of the enzyme gamma-glutamyl transferase (GGT) in the blood. The enzyme is usually found in multiple organs but has an incredibly high concentration in the liver. This test is important because increased levels of GGT indicate liver disease. Typical reference ranges for adults are between 9-48 U/L.

LACTATE DEHYDROGENASE (LDH): This test is used to determine the amount of lactate dehydrogenase (LDH) in some bodily fluids and the blood. LDH is an enzyme utilized for energy production and is located in many cells throughout the body. The most increased levels of LDH are found in the liver, lungs, kidney, blood cells, heart, and muscles. This test is important because when LDH levels are increased, it indicates cell damage throughout the body. Typical reference ranges for adults are between 105-333 IU/L.

TOTAL PROTEIN: This test measures the amount of albumin and globulin, which are both proteins, in the blood. A total protein test is utilized during a patient's regular health checkup. It can also be used if a person is experiencing unexplained weight loss, tiredness, or any related liver or kidney disease symptoms. This test is important because albumin and all other proteins in the blood may decrease with severe liver disease; this test will help indicate whether or not there is liver disease. Typical reference ranges for adults are between 6.0- 7.8 g/dL.

PROTHROMBIN TIME (PT): This test is used to assess whether an individual can form blood clots correctly. The test can calculate the number of seconds it takes for a clot to form in the blood once specific reagents are added. The PT test is usually used along with a partial thromboplastin time test (PTT). Combined, these tests help determine the function of coagulation factors. This test is important because it helps determine if the liver is correctly making the blood coagulation factors produced mainly by the liver; a prolonged PT may indicate the severity of liver damage. Typical coagulation time for adults is between 11-15 seconds.

PARTIAL THROMBOPLASTIN TIME (PTT): This test is used to help evaluate a person's ability to form blood clots. It measures how many seconds it takes for a person to form a clot. This test is important because when the blood vessel or walls are injured, a process called the coagulation cascade begins to stop bleeding; this test measures how long it takes for the bleeding to stop. Typical coagulation time for adults is between 25-40 seconds.

LIVER BIOPSY is a procedure in which a needle is inserted into the liver to withdraw a tiny amount of tissue so a pathologist can examine it under a microscope. This procedure is done when liver damage is suspected but a definitive diagnosis cannot be made with blood tests.. Since liver biopsies are invasive, it is only done when other tests are inconclusive.

AUTOIMMUNE ANTIBODIES

When the immune system functions normally, it produces responses, which protect the body against harmful invasions from foreign substances like bacteria, parasites, and cancerous cells. These responses can include specific immune cells and/or antibodies. Autoimmune disease occurs when immune responses go against the body's normal constituents and begin harming the natural immunological response.

LABORATORY TESTS RELATED TO AUTOIMMUNE ANTIBODIES

ANTINUCLEAR ANTIBODY (ANA): The test is used to help diagnose if a person is positive for an autoimmune disorder that affects many tissues and organs. It is important to note that a positive ANA test does not diagnose one particular disease, but it does indicate a potential autoimmune disorder. This test is important because it helps to narrow down to a specific autoimmune disease such as Lupus or Sjogren's, affecting the liver. A positive ANA test means that autoantibodies are present.

SMOOTH MUSCLE ANTIBODY (SMA): Smooth muscle antibodies (SMA) are autoantibodies, which are proteins produced by the body's immune system. These antibodies can recognize and attack their own actin, a protein found in smooth muscle and many other tissues, especially the liver. This test detects the amount (titer) of SMA in the bloodstream. This test is important because it helps narrow down to liver disease. Tests for actin antibodies detect more cases of autoimmune hepatitis but, in some studies, give more *false-positive* results than tests for smooth muscle antibodies.

ANTI-LKM-1: Liver kidney microsome type 1 (anti-LKM-1) antibodies are autoantibodies that target their enzyme called cytochrome P450 2D6 (CYP2D6), a protein mainly found in liver cells. The development of anti-LKM-1 antibodies is associated with type 2 autoimmune hepatitis. This test detects and measures the amount of anti-LKM-1 in the blood. This test is important because it helps diagnose autoimmune hepatitis and differentiate between type 1 and type 2 autoimmune hepatitis.

LIVER TRANSPLANTS

The liver is the only organ in the body that regenerates or grows back. An individual needs a liver transplant once their liver is no longer functioning adequately. This person is then said to be in liver failure. When a compatible donor for a liver is available, a person needing a new liver can undergo liver transplantation.

There are two types of liver transplants: cadaveric and live donor (partial). Cadaveric transplants occur with donations from deceased or brain-dead donors. Live organ transplants are when a small portion of a liver is removed from a live donor and transplanted into the recipient's body. The section of the transplanted liver will regenerate and grow, creating a full new liver. The decision of whether a patient needs a cadaveric or partial liver transplant is related to age, body size, and availability.

LABORATORY TESTS INVOLVED IN LIVER TRANSPLANTS

Before a liver transplant, it is important to prep by conducting a few lab tests to ensure the transplant recipient is a good candidate. The following tests are essential to assess the eligibility and compatibility for a liver transplant.

BLOOD CROSSMATCHING: This is a test performed before transplantation to help assess whether the donor organ will be compatible with the recipient based on compatibility of blood. The purpose of crossmatching is to ensure that the recipient is a good candidate for the transplant. A positive crossmatch results in the recipient's antibodies attacking the donor's, which means the liver is not suitable for transplant. A negative crossmatch means that the recipient's antibodies do not attack the donor's, which means the liver is eligible for transplant.

HUMAN LEUKOCYTE ANTIGEN (HLA): HLA testing assesses the genes and antigens people have inherited. Testing is also done for anti-HLA antibodies that could cause the transplant to fail. The purpose of this test is to align a donor up with the recipient to make sure that they have matching antigens to increase the chance of a successful transplant.

DONOR-SPECIFIC ANTIBODY (DSA): Elevated DSA levels may indicate that a form of rejection occurs involving the patient's antibodies against the donor's liver. Additional support for a diagnosis of rejection can be obtained from the examination of a liver transplant biopsy.

BLOOD TYPE COMPATIBILITY:

		Donor's Blood Type							
		0-	0+	B-	B+	A-	A+	AB-	AB+
Patients' Blood Type	AB+	x	x	x	x	x	x	x	x
	AB-	x		x		x		x	
	A-	x				x			
	A+	x	x			x	x		
	B+	x	x	x	x				
	B-	x		x					
	0+	x	x						
	0-	x							

MEET LAUREL & CLAUDETTE



After a generous and life-saving donation of her son AJ's liver, Claudette (right) meets Champion Laurel (left).

After a 25-year career as a nurse, Laurel was familiar with the role laboratory professionals and pathologists play in healthcare. When she was diagnosed with hepatitis C in 1990, that familiarity became personal. Laurel received a liver transplant in 2011 after Claudette donated her son's organs after he suddenly passed away at age 18. Laurel and Claudette met years later, and Laurel tries to honor AJ's life through living hers.

To learn more and to watch a video about Laurel and Claudette, go to www.ascp.org/patients

“Without pathologists and laboratory specialists, I don’t know if I would be here. Without that knowledge base that they provide, I don’t know where I’d be.”