Topic Page: Liver disease

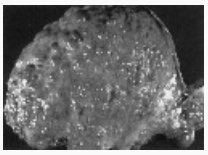


Image from: **Cirrhosis of the liver. The knobby...** in *The Cambridge Encyclopedia of Human Paleopathology*

Summary Article: **Liver Diseases (General)**
from *Encyclopedia of Global Health*

The liver is a vital organ in the body that plays a central role in human health including detoxification of ingested substances, lipid metabolism, and synthesis of blood clotting factors and important body proteins. The cells of the liver, hepatocytes, house thousands of chemical reactions every second in order to perform myriad functions that contribute to human health. As a central player in human physiology, the liver is involved in multiple interrelated body systems, and is subject to a variety of insults and mechanisms of disease.

EVALUATION OF LIVER DISEASE

Liver disease is classified according to the duration of abnormalities as either acute (<six months) or chronic (>six months). Evaluation of subjects with liver disease starts with basic laboratory blood tests. Elevation of molecules contained within the liver cell, the serum aminotransferases (AST and ALT) indicate injury to hepatocytes. Secondary to some insult, there is injury to the hepatocyte and these specific molecules can leak from the hepatocytes into the blood. The level of elevation in AST and ALT as well as their ratio may give some indication as to the possible inciting cause. For example, the ratio of blood AST to ALT is typically greater than 2 in alcoholic liver disease. In viral hepatitis, this ratio is characteristically less than one. Besides serum AST and ALT, other molecules can be studied to gain insight into liver disease. These include the enzyme alkaline phosphatase which is present in the liver, bone, and placenta. Elevations in serum alkaline phosphatase generally indicate obstruction of bile outflow from the liver, and concurrent elevation of alkaline phosphatase with elevation of liver enzymes suggests liver disease.

Besides the aforementioned tests of general injury to hepatic cells, other laboratory tests can help gain insight into the functional capacity of the liver. Bilirubin is a degradation product of hemoglobin that is carried in red blood cells. Breakdown and excretion of serum bilirubin involves processing in the liver, where broken-down bilirubin is processed (conjugated) and ultimately excreted. Elevated levels of unconjugated bilirubin can suggest a deficiency of the liver to take up and conjugate bilirubin, and elevated levels of conjugated bilirubin suggest deficiencies in excretion (possibly arising from mechanical obstruction).

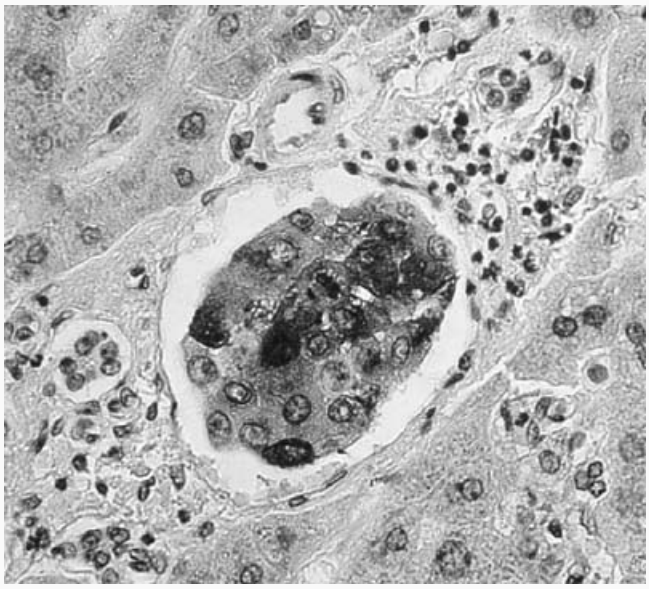
Tests are also available to evaluate the synthetic capabilities of the liver. Albumin, a blood protein that is critical for binding molecules in the blood and maintaining its oncotic pressure, is synthesized in the liver. A decrease in serum concentration of albumin, although not entirely specific for liver disease, may be seen in chronic liver disease. Proteins involved with blood coagulation and hemostasis are processed in the liver, and tests such as the prothrombin time (PT) and the corresponding international normalized ratio (INR) may be elevated in liver disease.

Aside from blood tests, evaluation of the liver also includes multiple imaging modalities that offer evaluation of the anatomy of the liver as well as the opportunity to possibly intervene when disease is present. Ultrasound of the liver is generally used to evaluate the biliary tree (predominant bile outflow tract of the liver) and evaluate for stones. Ultrasound can also detect large liver tumors and cysts. Advances in doppler ultrasonography can assess portal (liver-related) blood flow. Computerized

tomography and magnetic resonance imaging are now used to evaluate the substance of the liver (parenchyma) to delineate intra-liver anatomy. Endoscopic retrograde cholangiopancreatography (ERCP) can be done by a gastroenterologist or hepatologist with advanced training—in this procedure an endoscope is advanced through the digestive system to ultimately visualize the biliary tree. If gallstones or other material is present causing liver outflow blockage, stone extraction or stenting can be done to relieve obstruction. Magnetic resonance cholangiopancreatography provides for visualization of the biliary tree; however, therapeutic intervention as with ERCP is not possible.

APPROACH TO PATIENT WITH LIVER DISEASES

Approaching patients with liver disease often involves a combination of the aforementioned labs and imaging modalities. When these are completed, more specific serum laboratory tests may be pursued to establish a diagnosis; this is often combined with a liver biopsy in which a sample of liver tissue is obtained via a needle, and the obtained specimen is studied by a pathologist using microscopy. The term *hepatitis* is a nonspecific term and generally means inflammation of the liver; this can be secondary to viruses, autoimmune phenomenon, drugs, and a variety of other causes. Once diagnosis is established, therapy can be directed at the specific causative agents. Regardless of etiology, consistent and unaddressed insult to the liver can lead to a final pathway of permanent fibrosis and scarring, referred to as cirrhosis. The treatment of liver diseases in the 21st century centers on managing liver disease to prevent onset of cirrhosis and the attendant risk of hepatic failure. Once liver disease has progressed to the point of cirrhosis and hepatic failure, management is more focused on addressing the common comorbid conditions seen in patients with advanced liver disease including infection, edema, bleeding, and encephalopathy (altered mental status).



A cluster of cancer cells with brown-staining cytoplasm is pictured within a portal tract of the liver

VIRAL HEPATITIS

At the present time, there are currently five identifiable forms of viral hepatitis: A, B, C, D, and E. These viruses are considered hepatotropic, meaning that the liver is the primary site of infection where viral replication and cellular damage occur. Other viruses such as Epstein-Barr virus (EBV) and cytomegalovirus (CMV) can also affect the liver. As Dr. Kenneth Sherman explains, “All hepatitis viruses can cause acute infection, which is defined as the presence of clinical, biochemical, and serologic abnormalities for up to six months. Hepatitis A and E are cleared from the body within six months and

do not cause persistent infection for a longer period. In contrast, hepatitis B, C, and D can lead to chronic infection, which is more likely to be associated with the development of cirrhosis. An increased risk of primary hepatocellular carcinoma occurs in patients who are chronically infected with hepatitis B, C, and D." Management for the acute phase of viral hepatitis is generally supportive with a focus on symptom-related management, serum profiles are drawn to try and identify a specific virus, and liver enzymes are followed over time. Treatment strategies exist and are consistently being refined to treat chronic infection with hepatitis B and C.

ALCOHOLIC LIVER DISEASE

The consumption of alcohol exerts a direct toxic effect on the liver. The spectrum of damage to the liver is highly variable and the amount of alcohol necessary to create permanent damage to the liver is also variable. In general, with consumption of alcohol there is mild elevation in serum aminotransferases and deposition of fat into the liver. This condition, known as "fatty liver," can be seen in people with moderate alcohol consumption and is largely reversible with alcohol cessation. As Abittan explains, "Daily consumption of alcohol amounting to >45gm/day is associated with progressive liver injury." With large episodes of alcoholic consumption, an acute hepatitis picture can develop. Treatment of alcoholic liver disease is centered on maintenance of absolute abstinence from alcohol.

NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease in the United States. As Dr. Lisker-Melman describes, "The spectrum of histologic forms include hepatic steatosis (fat deposition), steatosis with nonspecific inflammation, and nonalcoholic steatohepatitis (NASH). NASH is characterized by steatosis, inflammation, necrosis, and fibrosis. Approximately 25 percent of patients with NASH progress to cirrhosis over a 10- to 15-year period." At present, no established treatment is available for NAFLD.

METABOLIC LIVER DISEASE

A variety of genetic metabolic disorders can lead to liver disease. These include Wilson's disease, hereditary hemochromatosis, and alpha 1-antitrypsin deficiency. Wilson's disease is an inherited disorder in which there are abnormalities in the body's processing of the compound copper; this disorder leads to abnormal copper deposition in the liver with resultant damage. Treatment for this disorder includes treatment with copper-chelating agents. Liver transplantation is curative in progressive disease. Hereditary hemochromatosis is an inherited disorder in which there is abnormal absorption of iron in the intestine. There is excessive iron absorption and deposition into various organs including the liver. Therapy consists of phlebotomy (blood drawing) to deplete serum iron. Alpha 1-antitrypsin deficiency is a disorder in which a specific enzyme necessary in the lung and liver is not produced at an adequate level. Patients develop liver disease as well lung disease, generally early-on-set emphysema.

AUTOIMMUNE

As Dr. Albert Czaja explains, "Autoimmune hepatitis is an unresolving inflammation of the liver of unknown cause that is characterized by hepatitis, autoantibodies, and hypergammaglobulinemia (an increase in immunoglobulins—protective molecules in blood serum). Autoimmune hepatitis mainly affects women and is generally diagnosed during the fourth decade." Specific antibody tests exist to evaluate for autoimmune hepatitis. Treatment options for autoimmune hepatitis are being refined but generally involve the use of steroids to decrease inflammation. Variants of autoimmune hepatitis include primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). Both of these disorders

are associated with the occurrence of inflammatory bowel disease.

VASCULAR DISEASE

The liver constitutes 5 percent of body weight in adults and receives 20 percent of cardiac output via the hepatic artery and portal vein. Abnormalities in blood inflow or outflow can cause severe liver dysfunction acutely. Budd-Chiari syndrome results from obstruction of the venous outflow tract (the hepatic veins) from any etiology, including mechanical obstruction or thrombosis (blood clot). Most patients require decompression of the hepatic veins to preserve liver function. Other vascular-related insults to the liver include ischemic hepatitis or “shock liver” in which blood flow to the liver is compromised transiently with resultant dysfunction. In patients with congestive heart failure, inability of the heart to pump blood forward results in backup of blood flow on the venous return side and congestion of the liver with blood (congestive hepatopathy). In these instances treatment of the underlying vascular or cardiac disorder leads to a return of normal liver function.

DISEASE TREATMENT

The treatment of liver disease depends upon the specific cause of dysfunction. Treatment can range from supportive and symptomatic relief in the instance of an acute viral hepatitis to emergent surgery or liver transplantation in the event of an acute vascular event. In general, consistent liver injury, regardless of etiology leads to permanent damage and cirrhosis. With cirrhosis and decreased hepatic function come a variety of comorbid conditions that must be discussed when dealing with generally advanced liver disease.

As aforementioned, the liver plays a critical role in detoxifying the blood, forming important blood proteins, and synthesizing clotting factors. When the liver fails secondary to progressive disease these protective functions are lost and the result is improper clearance of toxins, lack of important blood proteins, and the propensity for bleeding secondary to diminished clotting factors. Patients with advanced liver disease often have mental status changes (encephalopathy) secondary to their inability to clear blood toxins.

Serum levels of toxins such as ammonia may be elevated in patients with hepatic encephalopathy; however, altered mental status is likely multifactorial and does not correlate well with serum levels of ammonia. The lack of important blood proteins such as albumin results in decreased oncotic pressure of the blood, and as a result, fluid that would normally remain in blood vessels transposes into soft tissues. The result is body-wide swelling (anasarca). Of particularly concern is swelling in the abdomen (ascities); fluid in abdomen is a nidus for infection.

This infection is named spontaneous bacterial peritonitis and carries a high mortality in patients with liver disease. Treatment includes diuretics (promoters of urination) to manage swelling and prompt antibiotic therapy when infections develop. The issue of bleeding is twofold in patients with liver disease: (1) there is a decrease in clotting factors that predispose to bleeding and (2) cirrhosis creates portal hypertension and, as a result, there is backflow of blood into vessels that are generally not designed to handle that volume. These vessels are called varices and can rupture in the esophagus or stomach. Management of liver disease in general attempts to manage the dangerous complications of infection and bleeding.

SEE ALSO:
Alcoholism; Cirrhosis; Encephalopathy; Hepatitis; Liver Cancer.

BIBLIOGRAPHY

- C. S. Abittan, “Alcoholic Liver Disease,” Clinical Perspectives in Gastroenterology (v.2/1, 1999).
- A. J. Czaja, “Frequency and Nature of the Variant Syndromes of Autoimmune Liver Disease,” Hepatology (v.28, 1998).
- M. Lisker-Melman, “Liver Diseases,” Washington Manual of Medical Therapeutics, 31st ed. (Lippincott, Williams, and Wilkins, 2004).

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Seetharam, A. (2008). Liver diseases (general). In Y. Zhang, *Encyclopedia of global health*. Thousand Oaks, CA: Sage Publications. Retrieved from https://search.credoreference.com/content/topic/liver_disease

Chicago

Seetharam, Anil. "Liver Diseases (General)." In *Encyclopedia of Global Health*, by Yawei Zhang. Sage Publications, 2008. https://search.credoreference.com/content/topic/liver_disease

Harvard

Seetharam, A. (2008). Liver diseases (general). In Y. Zhang, *Encyclopedia of global health*. [Online]. Thousand Oaks: Sage Publications. Available from: https://search.credoreference.com/content/topic/liver_disease [Accessed 27 May 2019].

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