



A REVIEW: LIVER DISORDERS AND TREATMENTS

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Abstract: Liver is the most complex and important organs in the human body. A total loss of liver function leads to death within minutes. Liver is the largest gland in the body. It weighs about 1.5 kg (3 to 4 pounds), lies immediately under the diaphragm, and occupies most of the right hypochondrium and part of the epigastrium. the common disorders of the liver include cirrhosis, viral hepatitis, alcoholic liver disease, hemochromatosis, and liver cancer. Liver transplantation is often the best option for either liver cancer or cirrhosis. There is an extreme shortage in the number of donor organs available, and there are restrictions on who can receive liver transplants. Due to these problems, alternatives are constantly being sought. Some of the primary areas of research involve gene therapy, xenotransplants, and bioartificial livers.

Key words- Liver, liver functions, liver diseases, liver treatments.

Introduction:

Liver: The liver is among the most complex and important organs in the human body. Its primary function is to control the flow and safety of substances absorbed from the digestive system before distribution of these substances to the systemic circulatory system. A total loss of liver function leads to death within minutes.

Location and size of liver: The liver is the largest gland in the body. It weighs about 1.5 kg (3 to 4 pounds), lies immediately under the diaphragm, and occupies most of the right hypochondrium and part of the epigastrium.

Liver lobes and lobules: The liver consists of two lobes separated by the falciform ligament. The left lobe forms about one sixth of the liver, and the right lobe makes up the remainder. The right lobe has three parts designated as the right lobe proper, the caudate lobe and the quadrate lobe. Each lobe is divided into numerous lobules by small blood vessels and by fibrous strands that form a supporting framework for them. The hepatic lobules are the anatomical

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units of the liver, are tiny hexagonal or pentagonal cylinder about 2 mm high and 1 mm in diameter. A small branch of the hepatic vein extends through the center of each lobule. Around this central vein, in plates or irregular walls radiating outward, are arranged the hepatic cells. On the outer corners of each lobule, several sets of tiny tubes branches of the hepatic artery, of the portal vein and of the hepatic duct are arranged. From these, irregular branches of the interlobular veins extend between the radiating plates of hepatic cells to join the central vein. Minute bile canaliculi are formed by the spaces around each cell that collect bile secreted by the hepatic cells.

Blood enters a lobule from branches of the hepatic artery and portal vein. Arterial blood oxygenates the hepatic cells, whereas blood from the portal system passes through the liver for inspection. Sinusoids in the lobule have many reticuloendothelial cells (mainly kupffer cells) along their lining. These phagocytic cells can remove bacteria, worn RBCs, and other particles from the blood stream. Ingested vitamins and other nutrients to be stored or metabolized by liver cells enter the hepatic cells that form radiating walls of the lobule. Dissolved toxins in the blood are also absorbed into hepatic cells, where they are detoxified. Blood continues along sinusoids to a vein at center of the lobule. Such central, intralobular vein eventually lead to the main hepatic veins that drain into the inferior vena cava. Bile formed by hepatic cells passes through canaliculi to the periphery of the lobule to join small bile duct.

Bile Ducts: The small bile ducts within the liver join to form two larger ducts that emerge from the undersurface of the organ as the right and left hepatic ducts. These immediately join to form one hepatic duct. The hepatic duct merges the cystic duct from the gallbladder, forming the common bile duct, which opens into the duodenum.¹⁻²

Liver Functions

The liver has four essential functions:

- 1) Synthesis of many proteins that circulate in the blood.

These include albumin, coagulation factors, alpha1-antitrypsin, very low density, and many others.

- 2) Stores nutrients for later use, liver balances the supply of nutrients with demand. For example, the liver stores glucose as glycogen, and converts it back to glucose as needed. If the supply of glycogen is depleted, the liver can also synthesize glucose from amino acids, lactate, and glycerol, although this is less efficient than break down glycogen into glucose. Additionally, the liver metabolizes fatty acids, cholesterol, amino acids. The liver both synthesizes cholesterol and remove it from circulation. Liver also synthesize non-essential amino acids when needed by the body.

- 3) Detoxification and elimination of toxic substances.

Toxins are detoxified by the liver's ability to metabolize lipophilic compounds. These compounds enter the liver sinusoids and then the area of disse.

- 4) Production of bile.

Bile acts as a detergent, and breaks fats down into smaller components so they can be digested in the small intestine. Bile also provides a way for the liver to remove wastes, including bilirubin, cholesterol, and toxins. Bile is formed in the biliary canaliculi, which drain into the interlobular bile ducts. These ducts then merge with other ducts, forming large intermediate ducts, which eventually merge into the right and left hepatic ducts, which themselves merge into the common hepatic duct, which merges with the cystic duct from the gallbladder, finally forming the common bile duct, which empties into the small intestine.³

Liver Diseases and Treatments: One way to classify liver disorders is by their duration. A chronic disorder lasts for more than 6 months; a

subacute disorder lasts for 3 to 6 month; while an acute disorder occurs over a period less then 3 months. A very severe disorder that leads to liver failure within 6 weeks is termed fulminant. Some of the common disorders of the liver include cirrhosis, viral hepatitis, alcoholic liver disease, hemochromatosis, and liver cancer.

- 1) **Cirrhosis** is a widespread and progressive chronic liver condition in which hepatocyte activity is depressed due to excessive amounts of fibrous scar tissue inhibiting blood flow. This blood flow obstruction can cause portal hypertension, which leads to additional complications, including shunting of vens around the liver. Other complications of portal hypertension include swollen veins in the esophagus and accumulation of fluid in the abdomen. Other potential complications of cirrhosis include bleeding problem, kidney disorders, osteoporosis, and liver cancer. The only treatment options are to treat the condition that caused the cirrhosis, and liver transplantation.
- 2) The term **hepatitis** refers to inflammation of the liver. Hepatitis can have several causes, the most common being viruses or alcoholism. Viral hepatitis comes in several forms, the most common being hepatitis B (40%), hepatitis A (32%), and hepatitis C. HVB and HVC are spread by the blood, and can become chronic conditions, which can lead to cirrhosis. A vaccine has been developed for HVB, which has helped control its spread. HVC often becomes chronic, and thus can be life threatening. Viral hepatitis has several treatment options, which frequently have undesirable side effects. Interferon is used for treating HBV and HCV. Interferons are so named because they interfere with viral replication. The body makes interferon naturally, but supplementing this with synthetically made interferon can sometimes be beneficial against viral hepatitis. However, the selection criteria for who should use

interferon are quite stringent, attesting to downsides of this therapy. Additionally, interferon is available by injection only, and is quite expensive. Newer forms of antiviral therapy exist, but interferon is still the most common.

- 3) **Alcoholic liver disease** comes in 3 major varieties: alcoholic fatty liver, alcoholic hepatitis, and alcoholic cirrhosis. All 3 can occur alone or even together in the same patient. The primary form of treatment is abstinence from drinking alcohol.
 - a) **Fatty liver** is the most common, and the least harmful. It can occur within days of moderate to heavy drinking. Fat accumulates in the cytoplasm of liver cells, causing the liver to swell, sometimes to large proportions. Fatty liver often has no symptoms, and can disappear as quickly as it appears.
 - b) **Alcoholic hepatitis** is inflammation of the liver, and can exist as either acute or chronic conditions. Symptoms can vary greatly, from asymptomatic to severe fever, nausea, and abdominal pain. Acute hepatitis can often cause death, and the chronic form often leads to cirrhosis. On the bright side, alcoholic hepatitis is also potentially reversible, if recovery occurs and the patient abstains from drinking.
 - c) **Alcoholic cirrhosis**, like all forms of cirrhosis, is often life threatening. The disease is characterized by regenerative nodules of hepatic tissue completely surrounded by fibrous scar tissue. The scar tissue grows faster than liver cells can regenerate, and the growing network of scar tissue inhibits blood flows. Once cirrhosis develops, the risk of liver cancer elevates substantially, even if the patient abstains from drinking for several years.
- 4) **Hemochromatosis** is a condition in which too much iron is contained in the body. It is the most common genetic disease. Chronic hemochromatosis can lead to cirrhosis, cancer, impotence and heart problems. Iron

damages the body through its promotion of oxidation, increasing the level of free radicals in the body. Harmful levels of iron can be accumulated in body simply by eating too of the wrong foods and supplements. The human body uses approximately 1 to 2 milligrams of iron daily. However, the average diet contains between 10 and 20 milligrams of iron. In hemochromatosis, the body cannot absorb iron as effectively, and also cannot detect when iron levels are too high. This excess iron is then absorbed into the body's organs, particularly the liver. Hemochromatosis is treated by lowering the level of iron in the body. The most common method is via phlebotomies. A phlebotomy is purposefully removing blood from the body. Diet is also very important to patients with hemochromatosis. Iron needs to be kept to a minimum, as well as alcohol and medications that may do further damage to the liver.

- 5) **Liver cancer.** Liver tumors are not always malignant. One type of benign tumor is Hemangioma, which is a non-malignant tumor filled with blood. Treatment is not necessary for these tumors. Malignant fall into two major categories: Metastatic and primary liver tumors. A metastatic tumor is a malignant growth whose primary growth site is someplace other than the liver. The liver is a frequent target of metastatic cancers, as it is the primary filter of venous blood from several organs, such as the colon. The prognosis for patients with metastatic liver cancer is typically poor; most patients die within 1 year of diagnosis. The most common primary liver malignant cancer is hepatocellular carcinoma (HCC). HCC is one of the most common cancers in the world. Hepatitis C often leads to cirrhosis, and cirrhosis often leads to primary liver cancer. Liver tumors can be detected and identified using a combination of blood tests, imaging studies, and liver

biopsies. As with metastatic liver tumors, the prognosis for patients with primary liver cancer is quite poor. Liver cancer is treated most often with surgery, where the tumor is cut out of the liver. Large section of the liver can be removed and liver will often be able to regenerate itself to its previous full size. Unfortunately, this does not work for patients with cirrhosis. In that case, a liver transplant is the best option.⁴⁻⁷

Advanced Treatment of Liver Disease: Liver transplantation is often the best option for either liver cancer or cirrhosis. There is an extreme shortage in the number of donor organs available, and there are restrictions on who can receive liver transplants. Due to these problems, alternatives are constantly being sought. Some of the primary areas of research involve gene therapy, xenotransplants, and bioartificial livers.

1) Scientists have found that they can reduce and even reverse the amount of fibrosis that occurs in damaged livers by controlling the level of a gene named HGF (hepatocyte growth factor) in rats. If this can be extended to humans, it would obviously have enormous benefits.

2) Xenotransplants are being pursued for replacements of all types of organs. Several companies have developed breeds of transgenic animals that would present less of an immunological barrier than the xenotransplants used in the past. For example, Ximerex, inc is developing hybrid that consist of pig livers partially repopulated with human cells. Baboon livers have already been transplanted into humans, although with poor success thus far.

3) Bioartificial livers are also being developed. Currently, these are most often used to bridge the gap while waiting for a liver transplant. For example, the Hepat Assist Liver Support System employs a hollow-fiber membrane bioreactor containing 7×10^9 cryopreserved porcine hepatocytes along with associated equipment to provide temporary liver functionality. In one study using the HepatAssist system (which is now in phase III

clinical trials), 30 day patient survival rates improved to 90% compared to a normal level of 50-60%.⁸⁻¹²

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