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CHANGES IN THE MORPHOFUNCTIONAL AND HISTOLOGICAL STATE OF THE LIVER AS A RESULT OF INFLUENCING FACTORS

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ANNOTATION: In this article, we can obtain information about the structure and functions of the liver. Today, a number of efforts are being made to develop the field of medicine. We also review the opinions and scientific works of several researchers regarding the structure, functions, and histology of the functional units of the liver.

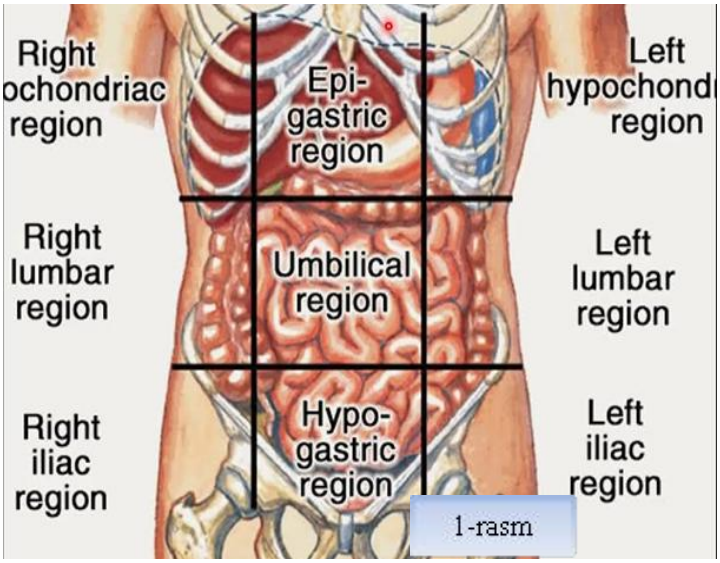
Keywords: Liver, liver structure, function, histomorphological units, lipogenesis.

Introduction

The liver is the primary metabolic organ in humans, performing numerous essential biological functions such as detoxification of the body, digestion, and the synthesis of proteins and biochemical substances necessary for growth. In humans, it is located in the upper right epigastric region of the abdomen, with one-third extending to the left side and two-thirds situated on the right (Figure-1). It lies beneath the diaphragm and is mainly protected by the lower right ribs.

Other metabolic roles include carbohydrate metabolism, hormone production, the conversion and storage of nutrients such as glucose and glycogen, and the breakdown of red blood cells. In both humans and animals, the liver participates in the digestion and absorption of food, and it stores fats and carbohydrates.

In humans, the liver is a complex and vital organ. It is the largest gland in the body (weighing 1200–2200 g). It is located in the abdominal cavity, beneath the diaphragm, under the right ribs and partially under the left ribs. It has a reddish-brown color, with a larger right lobe and a smaller left lobe. The transverse groove on the inferior surface of its central part is called the hepatic hilum or portal fissure. Through this region enter the hepatic artery, portal vein, and nerves, while the hepatic duct and hepatic veins exit. The hepatic duct joins the duct emerging from the gallbladder to form the common bile duct, which opens into the duodenum.



It remains unclear how the complete loss of liver function can be compensated long-term, but in the short term, liver dialysis techniques may be

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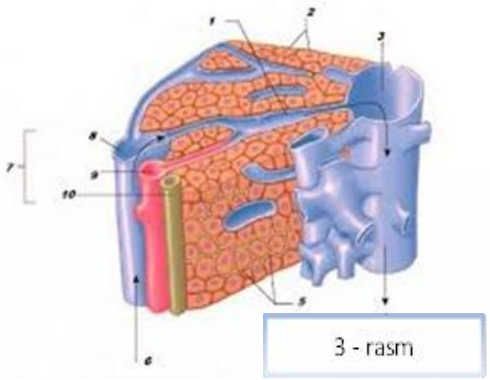
used. No artificial liver capable of providing long-term replacement has been developed. As of 2018, liver transplantation remains the only option for complete liver failure.

Macroscopic Anatomy

The liver is dark reddish-brown in color and consists of two lobes that differ in size and shape. The weight of the human liver is typically around 1.5 kilograms, and its width is approximately 15 centimeters. There is considerable individual variation; the standard reference range is 970–1860 grams for men and 600–1770 grams for women. It is the heaviest internal organ and the largest gland in the human body. The liver is located in the upper right quadrant of the abdominal cavity, beneath the diaphragm, to the right of the stomach, and above the gallbladder.

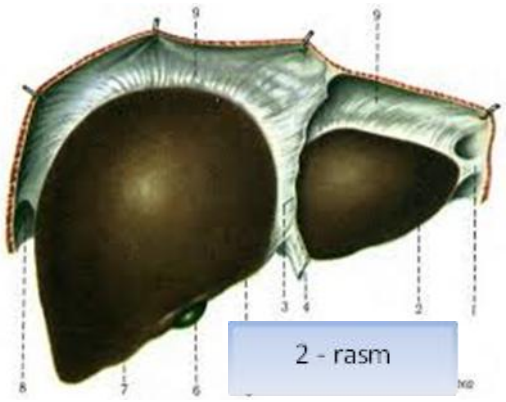
The liver is supplied by two major blood vessels: the hepatic artery and the portal vein. The portal vein carries nutrient-rich blood from the entire gastrointestinal tract, as well as from the spleen and pancreas. These vessels branch into small capillaries called liver sinusoids, which then lead to the hepatic lobules. Hepatocytes are the functional units of the liver. Each lobule consists of millions of hepatocytes (Figure 2), which serve as the primary metabolic cells.


3 - rasm

The lobules are interconnected by a thin, dense, irregular fibroelastic layer of connective tissue that extends from the fibrous capsule covering the liver, called Glisson's capsule—named after the British physician Francis Glisson. This tissue spreads throughout the liver along with the vessels, ducts, and nerves at the hepatic hilum. Except for a small bare area, the entire surface of the liver is covered with a serous membrane derived from the peritoneum, which adheres firmly to the underlying Glisson's capsule.

Microscopic Anatomy

From a microscopic perspective, each liver lobe consists of hepatic lobules. The lobules are approximately hexagonal in shape and are composed of plates of hepatocytes and sinusoids that radiate from the central vein toward the imaginary perimeter of the interlobular portal triads (Figure 3). The central vein drains blood from the lobule and eventually joins the hepatic vein, which carries blood out of the liver. The characteristic structural feature of a lobule is the portal triad located at each corner. The portal triad consists of a branch of the hepatic artery, a branch of the portal vein, and a bile duct. On liver ultrasonography, the triad can be visualized as the "Mickey Mouse sign": the head represents the portal vein, while the hepatic artery and bile duct form the "ears."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The liver is the central biochemical laboratory of the body, performing a wide range of vital functions; without the liver, neither humans nor animals can survive. The liver produces 600–

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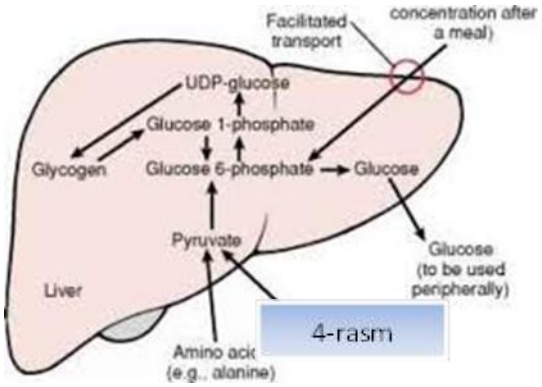
700 grams of bile per day, playing an essential role in digestion and the absorption of nutrients from the intestine. It participates in the metabolism of proteins, fats, and carbohydrates. Additionally, it detoxifies harmful substances formed during metabolism or entering the body from external sources, thereby fulfilling a protective function.



Special stellate cells of the liver are capable of phagocytosis and antibody production. The liver also serves as a reservoir for blood. During embryonic development, it participates in hematopoiesis and hemoglobin formation. Up to one-fifth of the total blood volume of the body can be stored in the liver's vessels. Excess water in the blood is partially filtered by the liver and contributes to the formation of bile and lymph.

The liver continuously produces bile and releases it through its bile ducts; the flow of bile into the duodenum begins during food intake and continues until the stomach is emptied. At other times, the sphincter of the common bile duct contracts and closes its opening. When bile produced by the liver enters the gallbladder, it becomes more concentrated and darker because water and certain other substances are absorbed through the gallbladder wall into the bloodstream.

(Continuing) Microscopic and Functional Aspects of the Liver

All substances absorbed from the digestive system enter the bloodstream and reach the liver, where some are used to build complex molecules while others are broken down. For example, amino acids arriving with the blood are used to synthesize blood proteins such as albumins, globulins, and others. Several substances—including fructose, galactose, lactose, and glycerol—are converted to glucose in the liver (Figure 4), which is then transformed into glycogen. Glycogen is stored in hepatocytes and, when the body requires increased energy, it is reconverted into glucose and released into the bloodstream.

The liver also participates in pigment metabolism; hemoglobin is broken down there, and bilirubin is formed and rendered water-soluble. The liver synthesizes lipids, which are transported by the blood to various organs and tissues to participate in metabolic processes. Cholesterol, prothrombin, and heparin are also synthesized in the liver. Some substances carried to the liver by the blood may be harmful to the body. Detoxification or partial excretion of these substances via bile is a major function of the liver. For example, toxic substances such as lead, arsenic, and others are retained in the liver and later excreted from the body in the form of harmless organic compounds, often protein-bound. Ammonia produced during protein breakdown, as well as some uric acid, is converted into urea in the liver and eliminated from the body through urine (urea is less toxic and more soluble).When excessive toxic substances accumulate in the body (for example, in chronic digestive diseases or alcoholism), liver functions become impaired, which leads to severe illnesses. Liver diseases include acute and chronic inflammatory processes as well as parasitic infections.Liver tissue infiltrations include amyloidosis, glycogenesis, fatty degeneration, granulomatosis, and lymphomas.Functional liver disorders include Gilbert syndrome, Dubin-Johnson syndrome, and Crigler–Najjar syndrome.Intrahepatic biliary diseases include cholangitis, inflammatory processes of the bile

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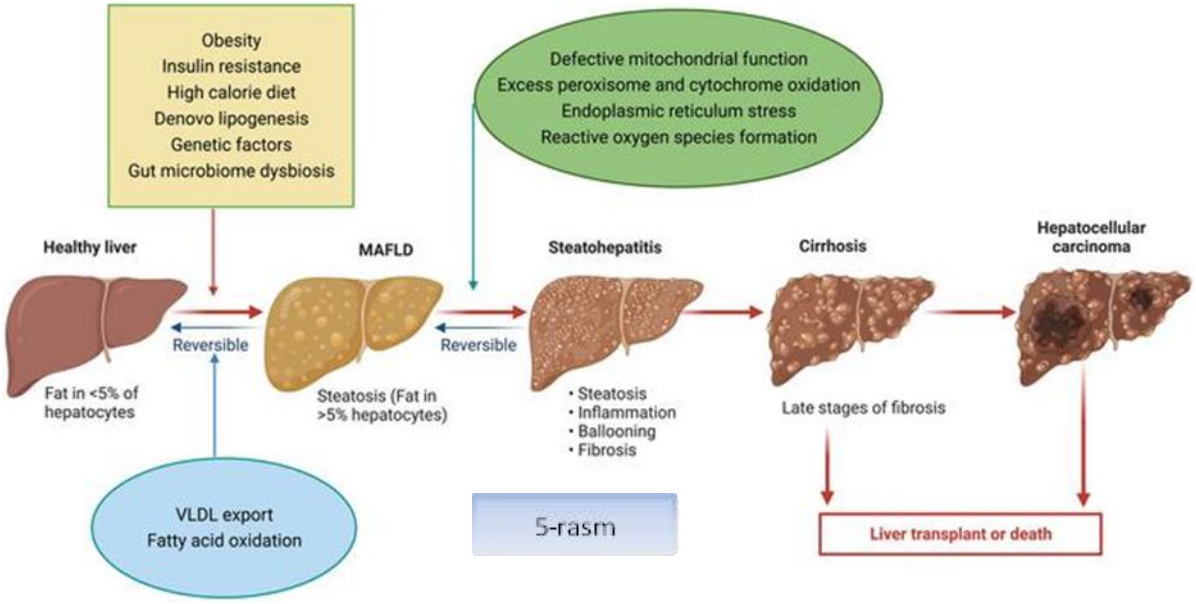

ducts, and gallstone disease leading to obstruction and scarring of the tissues.
Disturbances in hepatic blood supply include hepatic vein thrombosis, congestion due to heart failure, development of cirrhosis, and arteriovenous shunts.

Pathway of Liver Damage Progression

Injury → Hepatitis → Fibrosis → Cirrhosis → Liver cancer (Figure 5).The most common type of liver injury is hepatitis. Hepatitis is inflammation of the liver cells. Inflammation is a universal bodily response to tissue damage and aims to isolate the affected area and eliminate pathogenic agents such as bacteria. Hepatitis may be acute or chronic.Acute hepatitis develops rapidly, and if the harmful factor is removed, the liver can fully recover without complications.
If the inflammatory process lasts for six months or more and becomes chronic, fibrotic tissue gradually replaces dead hepatocytes. Fibrosis is the replacement of normal liver tissue with connective tissue fibers. As in the healing of any injury, scar tissue forms at the site of liver damage. This tissue is firm and rich in collagen, elastin, and other components usually found in the extracellular matrix. Scar tissue cannot perform the functions of normal hepatocytes. Fibrosis may develop rapidly or progress over a long period. The final stage of fibrosis is cirrhosis.

Liver Cirrhosis

Cirrhosis is a chronic, irreversible disease in which the parenchymal tissue of the liver is replaced with fibrous connective tissue or stroma. A cirrhotic liver may be enlarged or shrunken, abnormally dense, and nodular. In various situations, the disease progresses to its terminal stage within 2–4 years, causing severe pain, suffering, and eventually death.

Liver Cancer

The surviving hepatocytes attempt to repair the damage and begin to divide actively. However, along with other contributing factors, this process often leads to the development of liver cancer.

Physiological Importance of the Liver

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The liver is involved in digestion, detoxifies harmful substances entering the body through food, water, or air, and plays a major role in metabolism. Bile produced by the liver participates in digestion and stimulates the motility of the intestines. All essential nutrients pass through the liver and are processed there. Additionally, the liver synthesizes many plasma proteins and serves as a reservoir for a large amount of blood, which can be released into circulation during hemorrhagic shock.

In the modern world, humans are exposed to the adverse effects of environmental pollution and often experience stressful working conditions, neglecting their health. Food products widely purchased by the public frequently contain pesticides, nitrates, insecticides, harmful preservatives, dyes, heavy metal salts, and other toxic substances. Furthermore, uncontrolled medication use, chronic stress, depression, unhealthy habits, poor sleep, and improper diet weaken the body's defense mechanisms and impair liver function. The liver serves as the natural filter of the body.

Excessive consumption of carbohydrate-rich, fatty, and protein-rich foods leads to the formation and accumulation of lipids in the liver.

Numerous studies have shown that free sugars (i.e., monosaccharides and disaccharides) can increase de novo lipogenesis (DNL) in the liver, resulting in excessive lipid accumulation and the development of hepatic steatosis (Sources: Sanders, Acharji & Walker; Hudgins, Parker & Levin).
Additionally, research has demonstrated that when mice are fed diets high in carbohydrates, lipids, and proteins, significant fat accumulation occurs in their livers. It should also be emphasized that similar changes are observed in healthy humans: after consuming high-carbohydrate, high-fat, and high-protein meals, noticeable alterations in liver morphology occur after a certain period. These findings indicate the potential harmful role of excess carbohydrates, fats, and proteins in the development of hepatic steatosis.

Starchy carbohydrates are polysaccharides that require more steps for digestion and breakdown compared to free sugars. However, because they lack the intense taste stimulation of free sugars, they are often consumed in excess unintentionally. Moreover, since starchy carbohydrates constitute a major component of daily diets, their consumption tends to be long-term. Therefore, we hypothesize that prolonged consumption of high-starch carbohydrates may exert effects similar to those of free sugars (Sources: Antunes, Godoy & de Almeyda-Souza; Myette-Côté, Durrer & Neudorf).

Thus, these dietary factors play a significant role in altering the morphofunctional state of the liver and contribute to the increasing prevalence of liver-related diseases in modern times.

Conclusion

In conclusion, the importance of the liver for the human body is evident. The liver performs a protective function in the human organism. Exposure to harmful substances, various unhealthy habits, irregular daily eating patterns, and disordered diets contribute to the increase in modern diseases and the progression of illnesses. To reduce the risk of diseases and maintain health, it is essential to follow a balanced diet, avoid harmful behaviors, and pay attention to personal hygiene.

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