Chapter 9

The Human Liver: Bridging Biological Function with Pathopharmaceutical Insights

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Abstract

The liver is the largest internal organ in the human body and is considered to be one of the most vital glands in human biology. The liver is involved in metabolism, detoxification, digestion and nutrient storage. This chapter will discuss the basic structure and function of the human liver, which includes its gross anatomy, microscopic anatomy, blood supply, nerve supply, and other vital physiological functions of the human liver. Moreover, some of the common diseases of the liver, which include metabolic dysfunction-associated steatotic liver disease, viral hepatitis, alcohol-associated liver disease, cirrhosis, and hepatocellular carcinoma, are also described in this chapter. The chapter will provide a brief description of the liver and its importance in human biology in a simple way.

Keywords: Anatomy of liver; Hepatocytes; Metabolism; Bile secretion; Detoxification; Liver disease.

1. Introduction

The liver is the largest visceral organ and the most complex gland in the human body. It plays a vital role in regulating metabolic processes, detoxifying harmful substances, producing bile, and maintaining nutritional balance. Almost all the nutrients that are absorbed from the digestive system pass through the liver via the portal vein. This enables the liver to change and regulate the concentration of these nutrients before they are circulated to the general circulation system [2]. This position enables the liver to act as a protective filter for the body.
The liver also plays a vital role in the body's immune system. Special cells in the liver filter out bacteria, toxins, and worn-out blood cells from the circulation system. The regenerative capacity of the liver also points to its physiological importance. Liver cells have the capacity to regenerate themselves even in the presence of considerable damage to the organ. This regenerative capacity is unique in human organs [1].

2. Gross Anatomy of the Human Liver

The liver is situated in the upper right part of the abdominal cavity. It is positioned beneath the diaphragm. The liver is covered by the rib cage. The liver is in close proximity to the stomach, duodenum, pancreas, and the right kidney. The weight of the liver in adults is 1.2-1.5 kg. The liver is soft in texture with a smooth surface and a sharp edge on the inferior surface [1].The liver is divided into *two lobes*: the right and left lobes, based on the presence of the *falciform ligament*. The right lobe is much larger than the left lobe. On the inferior surface, the liver is divided into the *caudate* and *quadrate lobes*. A thin fibrous capsule is present on the external surface of the

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liver. This capsule is known as *Glisson's capsule*. This capsule extends into the liver and supports the vessels and bile ducts [4].

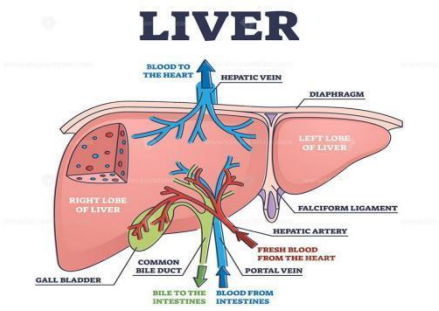
3. Blood Supply and Nerve Supply of the Liver

The liver is supplied with blood in a special way to meet the metabolic demands of the body. It receives oxygenated blood through the *hepatic artery* and nutrient-rich blood through the *portal vein*. About 70 to 75% of blood is supplied to the liver through the portal vein. Blood is removed from the liver through the *hepatic veins*, which open into the inferior vena cava [1]. The liver is supplied with *autonomic nerves* that regulate the blood flow, secretion, and metabolism of the liver through the sympathetic and parasympathetic nervous systems.

3.1 Microscopic Anatomy of the Liver

In microscopic anatomy, the liver is arranged in a series of plates of liver cells that radiate from a central vein. At the edge of these plates, known as hepatic lobules, there are portal triads that contain a branch of the hepatic artery, portal vein, and bile ducts [1].

The blood moves from the portal triads through the sinusoids to the central vein, where the liver cells are capable of removing the nutrients and detoxifying the harmful substances. At the same time, bile moves out of the liver cells through the bile canaliculi to the bile ducts [4].



3.2 Physiological Function of The Liver

Liver has a variety of physiological functions, which are vital for the body. During carbohydrate metabolism, the liver regulates the level of glucose present in the blood by storing the excess glucose in the form of glycogen and using it during the fasting period. It also converts glucose from other sources into the body for continuous supply [2]. This is done through the metabolism of other sources like fats and proteins into glucose. During protein metabolism, the liver is responsible for the synthesis of plasma proteins and the detoxification of ammonia into urea. Lipid metabolism is also carried out by the liver; it converts cholesterol into lipoproteins and bile salts [3].

3.3 Bile Secretion and Digestive Function

Bile is a *yellowish-green liquid* that is secreted by *hepatocytes*. Bile plays a vital role in the digestion and absorption of fat. Bile salts have the capability to *emulsify fat* to make it accessible to enzymes. Bile also plays a part in the absorption of *fat-soluble vitamins* and the elimination of waste products such as bilirubin [3].

3.4 Detoxification and Storage Functions

Detoxification of drugs, alcohol, and other harmful chemicals, including hormones, takes place in the liver, where the harmful chemicals are converted into water-soluble substances, which are then excreted from the body. The enzymes, such as *cytochrome P450*, play a role in detoxification as well [2]. Storage of vitamins and iron, such as ferritin, occurs in the liver, where vitamins like vitamin B12 are stored for long periods of time. In addition, the liver acts as a blood reservoir during emergency situations [1].

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4. Diseases

4.1 Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Etiology and Pathogenesis: MASLD represents the hepatic manifestation of metabolic syndrome and is caused mainly by insulin resistance, obesity, and type 2 diabetes mellitus [5]. It is defined as the presence of hepatic steatosis of at least 5% and at least one metabolic risk factor, such as hypertension and hyperlipidemia, without the presence of other factors like excessive alcohol use [7]. The disease can range from simple steatohepatitis to Metabolic Dysfunction-Associated Steatohepatitis (MASH), which involves hepatocellular damage and lobular inflammation [7].

Diagnostics and Management: The Fibrosis-4 (FIB-4) index is the recommended initial diagnostic tool for assessing the risk of advanced hepatic fibrosis [8]. Although the definitive diagnostic tool for the disease remains liver biopsy, non-invasive tests (NITs) like Vibration-Controlled Transient Elastography (VCTE) have been gaining popularity as a monitoring tool [8]. The management strategy for the disease involves weight loss of 7-10% due to lifestyle modifications, which have been found to improve steatohepatitis [5]. The management also includes Resmetirom, a thyroid hormone receptor-β selective agonist for the treatment of advanced hepatic fibrosis, and GLP-1 receptor agonists like Semaglutide for the management of associated conditions like obesity and diabetes [5].

4.2 Chronic Viral Hepatitis (HBV and HCV)

Etiology and Pathogenesis: The etiology of chronic hepatitis is due to infection with the Hepatitis B (HBV) and Hepatitis C (HCV) viruses, both of which cause chronic necroinflammatory changes and can

result in cirrhosis [6, 9]. HBV is a DNA virus, and the virus integrates into the genome, whereas HCV is an RNA virus [9]. The cumulative risk for hepatocellular carcinoma (HCC) is high due to immunologic destruction of hepatocytes[9].

Diagnostics and Management: Diagnosis is established through serological markers (HBsAg for HBV; anti-HCV for HCV) followed by quantitative PCR to determine viral load [9]. Management of HBV focuses on lifelong suppression of viral replication using nucleos(t)ide analogues like *Tenofovir (TDF/TAF)* or *Entecavir* [7]. For HCV, the standard of care is the use of pan-genotypic Direct-Acting Antivirals (DAAs) like *Sofosbuvir/Velpatasvir*, which can achieve a Sustained Virologic Response (SVR) in over 95% of patients after 8–12 weeks of therapy [6].

5. Alcohol-Associated Liver Disease (ALD)

Etiology and Spectrum: ALD is caused by excessive and prolonged consumption of ethanol, leading to mitochondrial damage and oxidative stress through its metabolite, acetaldehyde [9]. ALD includes a variety of conditions from alcoholic steatosis, acute hepatitis, and chronic cirrhosis [9]. ALD is increasingly becoming a major risk factor for death from liver disease, especially with malnutrition and sarcopenia in its late stages.

Diagnostics and Management: ALD is diagnosed based on a history of excessive ethanol consumption and raised liver enzyme levels, such as an AST/ALT ratio > 2:1 and raised levels of GGT enzyme [9]. Disease severity is often determined based on MELD scores and Maddrey Discriminant Function [10]. Abstinence from alcohol is considered the only cure for ALD, as it is the only intervention that completely stops disease progression [10]. Corticosteroids, such as

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Prednisolone, may be considered for reducing mortality rates among patients suffering from severe acute hepatitis [10].

5.1 Cirrhosis and Hepatocellular Carcinoma (HCC)

Etiology and Malignancy: Cirrhosis is the end-stage of chronic liver inflammation, where 80–90% of HCC cases arise within a cirrhotic environment [9]. HCC is currently the third leading cause of cancer-related mortality globally [11]. Transformation into malignancy involves complex molecular changes, often in the setting of portal hypertension and regenerative nodules [9, 12].

Diagnostics and Management: Surveillance for HCC in cirrhotic patients is recommended every six months using ultrasound and Alpha-fetoprotein (AFP) [12]. Diagnosis is confirmed via multiphasic CT or MRI using *LI-RADS* criteria [11]. Treatment follows the *BCLC staging system:* early-stage tumors are managed with surgical resection, thermal ablation, or liver transplantation [12]. For advanced-stage disease (BCLC C), systemic combination immunotherapies, specifically *Atezolizumab plus Bevacizumab*, have become the first-line standard of care, significantly improving overall survival compared to older tyrosine kinase inhibitors [11, 13].

6. Conclusion

The human liver is an essential organ in the human body and plays a vital role as the main hub for metabolism, detoxification, and immune defense. The complex gross and microscopic anatomy of the human liver enables it to filter nutrients and harmful substances before they enter the human body. Moreover, the liver's remarkable regenerative capacity makes it a vital organ for human survival. In addition to its vital roles in the human body, the liver's remarkable regenerative capacity makes it a vital organ for human survival.

However, the human liver is vulnerable to various severe health problems, ranging from metabolic disorders such as MASLD to infections such as viral hepatitis and alcoholic liver diseases. If not properly managed in the early stages, the human liver is vulnerable to severe end-stage cirrhosis and liver cancer. It is vital for the students and future medical practitioners to understand the vital relationship between the human liver and metabolic balance in the human body.

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