# Recent Trends in Management of Hepatic syndromes

*An Essay*

Submitted for partial fulfillment of
Master Degree In Intensive care
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# Introduction

In health, the liver plays a central role in organism homeostasis. It plays a major role in metabolism, including glycogen synthesis and storage, gluconeogenesis, and protein and lipid metabolism. The liver is also responsible for the production of bile, plasma protein synthesis (including most clotting factors), and drug detoxification. Indeed, the liver has important interactions with every organ system ***(Huff Myer and Nemergnt, 2007).***

End-stage liver disease and its complications are leading causes of death among adults in Egypt and world wide, and thousands of patients await liver transplantation. The liver plays a central role in health and homeostasis and thus the diseased liver leads to many deleterious effects on multiple organ systems, including the pulmonary system, cardiovascular system, renal functions and central Nervous system ***(Anderson and Smith, 2005).***

Cirrhosis leads to a state of increased cardiac output, decreased systemic vascular resistance, and systemic hypotension, which may result in hepatic cardiomyopathy. In the gastrointestinal system, portal hypertension results in ascites and gastro esophageal varices. Hematologically, coagulopathy, and thrombocytopenia are commonly encountered. Hepatorenal syndrome and an over all decrease in renal function frequently complicate cirrhosis. In the central nervous system, cognitive dysfunction and hepatic encephalopathy may range from mild to severe. The pulmonary system is no exception, and the unique effects of liver disease on pulmonary function merits review ***(Ramsay, 2006).***

In recent years important achievement in management of complication of cirrhosis have been witnessed. This progress has been the consequence of a better understanding of their patho-physiology. Better delineation of clinical presentation, new diagnostic tools, and a critical reappraisal of available therapies are now in progress ***(Cordoba and Beatriz, 2008).***

## Aim of the work

To delineate the patho-physiology, clinical presentation, diagnostic procedures for liver cirrhosis, its subsequent syndromes and reviewing the most significant progress in therapeutic aspects for each syndrome.

## Review of contents:

- Anatomy and physiology of the liver.
- Patho-physiology of liver cirrhosis.
- Hepato cerebral syndrome.
- Hepato pulmonary syndrome
- Hepato renal syndrome.
- Hepato cardiac syndrome.

## Summary

## Arabic summary.

## Conclusion.

## References.

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالُوا سُبْحَانَكَ لا عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ العَلِيمُ الحَكِيمُ

صدق الله العظيم

**سورة البقرة آية (32)**

# To :

*My soul Brother*

Mohammed Abd El-Sabour Mansour

# Acknowledgment

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The liver plays a central role in health and homeostasis . Indeed, the liver has important interactions with every organ system, and thus the diseased liver leads to many deleterious effects on multiple organ systems, including the pulmonary system, cardiovascular system, renal functions and central nervous system ***(Anderson and Smith, 2005).***

Cirrhosis leads to a state of increased cardiac output, decreased systemic vascular resistance, and systemic hypotension, which may result in hepatic cardiomyopathy. Cirrhotic cardiomyopathy is the term used to describe a constellation of features indicative of abnormal heart structure and function in patients with cirrhosis. These include systolic and diastolic dysfunction, electrophysiological changes, and macroscopic and microscopic structural changes ***(Liu et al., 2002).***

In the gastrointestinal system, the normal liver has the ability to accommodate large changes in portal blood flow without appreciable alterations in portal pressure. Patients with cirrhosis demonstrate a combination of increased portal venous inflow and increased resistance to portal blood flow which results in portal hypertension. Portal hypertension results in ascites and potential formation of varices. High portal pressure may predispose patients to an increased risk of variceal hemorrhage. Other conditions that appear with increased incidence in patients with cirrhosis include peptic ulcer disease, and gallstones ***(Cordoba et al.,2004).***

Hepatorenal syndrome and an over all decrease in renal function frequently complicate cirrhosis. Hepatorenal syndrome (HRS) is the development of renal failure in patients with advanced chronic liver disease, occasionally fulminant hepatitis, who have portal hypertension and ascites ***(Nguyen et al., 2007).***

In the central nervous system, cognitive dysfunction and hepatic encephalopathy may range from mild to severe. Hepatic encephalopathy is a frequent and serious complication of cirrhosis that carries prognostic implications ***(Cordoba and Beatriz,2008).***

The pulmonary system is no exception. Cirrhosis is associated with two unique entities that affect the pulmonary vasculature: hepatopulmonary syndrome and portopulmonary hypertension ***(Ramsay, 2006).***

Hepatopulmonary syndrome, which is found in approximately 20% of patients awaiting liver transplantation, refers to the triad of hepatic dysfunction, hypoxemia, and intrapulmonary vascular dilations, and responds well to liver transplantation. In portopulmonary hypertension, cirrhosis and portal hypertension lead to pulmonary arterial hypertension, portopulmonary hypertension has been considered a contraindication for transplantation. Currently, patients must have mild to moderate pulmonary hypertension to be considered for transplantation, and may still require long-term therapy with vasodilators to prevent right-ventricular failure and, consequently, failure of the newly transplanted liver allograft ***(Huffmyer and Nemergut,2007).***

Specific medical therapies may be applied to many liver diseases in an effort to diminish symptoms and to prevent or forestall the development of cirrhosis. Examples include prednisone and azathioprine for autoimmune hepatitis, interferon and other antiviral agents for hepatitis B and C, phlebotomy for hemochromatosis, ursodeoxycholic acid for primary biliary cirrhosis, and trientine and zinc for Wilson disease ***(Ahboucha et al.,2004).***

These therapies become progressively less effective if chronic liver disease evolves into cirrhosis. Once cirrhosis develops, treatment is aimed at the management of complications as they arise. Certainly variceal bleeding, ascites, and hepatic encephalopathy are among the most serious complications experienced by patients with cirrhosis. However, attention also must be paid to patients' chronic constitutional complaints ***(Merion,2004).***

Liver transplantation has emerged as an important strategy in the management of patients with decompensated cirrhosis. Patients should be referred for consideration of liver transplantation after the first signs of hepatic decompensation ***(Lewis et al.,2007).***

Contraindications for liver transplantation include severe cardiovascular or pulmonary disease, active drug or alcohol abuse, malignancy outside the liver, sepsis, or psychosocial problems that might jeopardize patients' abilities to follow their medical regimens after transplant. The presence of HIV in the bloodstream also is a contraindication to transplant. However, successful liver transplantations are now being performed in patients with no detectable HIV viral load due to antiretroviral therapy. Additional clinical study is required before liver transplantation can be offered routinely to such patients ***(Teh et al.,2007).***

***Aim of Essay:***

1. To delineate the patho-physiology, clinical presentation, diagnostic procedures for liver cirrhosis and its subsequent syndromes .
2. To review the most significant progress in therapeutic aspects for each syndrome used in intensive care unit .

The liver is the largest organ of the human body, weighs approximately 1500 g, and is located in the upper right corner of the abdomen. The organ is closely associated with the small intestine, processing the nutrient-enriched venous blood that leaves the digestive tract ***(MacSween et al.,2002).***

The liver performs over 500 metabolic functions, resulting in synthesis of products that are released into the blood stream(e.g. glucose derived from glycogenesis, plasma proteins, clotting factors and urea), or that are excreted to the intestinal tract (bile). Also, several products are stored in liver parenchyma (e.g. glycogen, fat and fat soluble vitamins) ***(Wanless ,1999).***

Almost all blood that enters the liver via the portal tract originates from the gastrointestinal tract as well as from the spleen, pancreas and gallbladder. A second blood supply to the liver comes from the hepatic artery, branching directly from the celiac trunc and descending aorta. The portal vein supplies venous blood under low pressure conditions to the liver, while the hepatic artery supplies high-pressured arterial blood. Since the capillary bed of the gastrointestinal tract already extracts most $O_2$, portal venous blood has a low $O_2$ content. Blood from the hepatic artery on the other hand, originates directly from the aorta and is, therefore, saturated with $O_2$. Blood from both vessels joins in the capillary bed of the liver and leaves via central veins to the inferior caval vein ***(Saxena et al.,1999).***

## Gross anatomy

The liver possesses three surfaces, superior, inferior and posterior. A sharp, well-defined margin divides the inferior from the

superior in front; the other margins are rounded ***(MacSween et al.,2002).***

The superior surface is attached to the diaphragm and anterior abdominal wall by a triangular or falciform fold of peritoneum, the falciform ligament, in the free margin of which is a rounded cord, the ligamentum teres (*obliterated umbilical vein*). The line of attachment of the falciform ligament divides the liver into two parts, termed the right and left lobes, the right being much the larger ***(Saxena et al.,1999).***

The inferior and posterior surfaces are divided into four lobes by five fossæ, which are arranged in the form of the letter H. The left limb of the H marks on these surfaces the division of the liver into right and left lobes; it is known as the left sagittal fossa**,** and consists of two parts, viz., the fossa for the umbilical vein in front and the fossa for the ductus venosus behind. The right limb of the H is formed in front by the fossa for the gall-bladder**,** and behind by the fossa for the inferior vena cava**;** these two fossæ are separated from one another by a band of liver substance, termed the caudate process**.** The bar connecting the two limbs of the H is the porta (*transverse fissure*); in front of it is the quadrate lobe, behind it the caudate lobe ***(MacSween et al.,2002).***

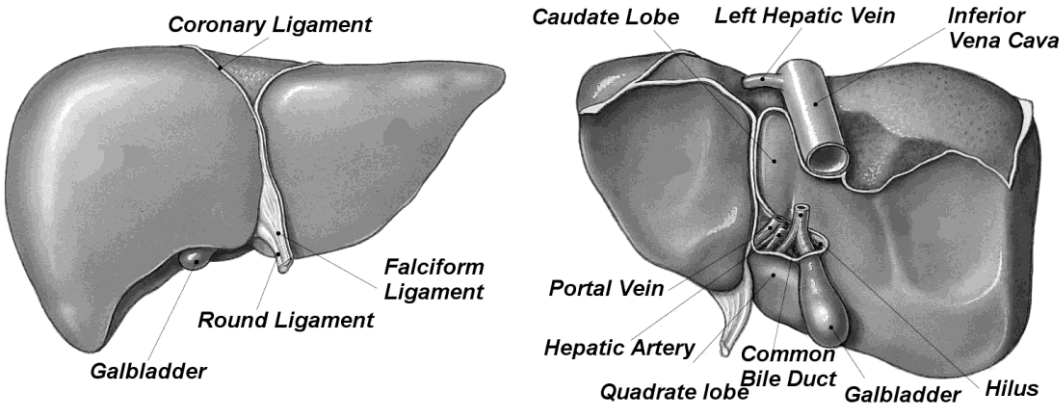


***Figure 1: The liver***

## Basic liver architecture

The major blood vessels, portal vein and hepatic artery, lymphatics, nerves and hepatic bile duct communicate with the liver at a common site, the hilus. From the hilus, they branch and rebranch within the liver to form a system that travels together in a conduit structure, the portal canal ***(Wanless, 1999).***

From this portal canal, after numerous branching, the portal vein finally drains into the sinusoids, which is the capillary system of the liver. Here, in the sinusoids, blood from the portal vein joins with blood flow from end-arterial branches of the hepatic artery.Once passed through the sinusoids, blood enters the collecting branch of the central vein, and finally leaves the liver via the hepatic vein ***(MacSween et al., 2002).***

The hexagonal structure with, in most cases, three portal canals in its corners draining into one central vein, is defined as a lobule . The lobule largely consists of hepatocytes (liver cells) which are arranged as interconnected plates, usually one or two hepatocytes thick. The space between the plates forms the sinusoid ***(Ludwig,1972).***

A more functional unit of the liver forms the acinus. In the acinus, the portal canal forms the center and the central veins the corners. The functional acinus can be divided into three zones: 1)the periportal zone, which is the circular zone directly around the portal canal, 2)the central zone, the circular area around the central vein, and 3) a midzonal area, which is the zone between the periportal and pericentral zone ***(Ishak and Sharp, 2002).***

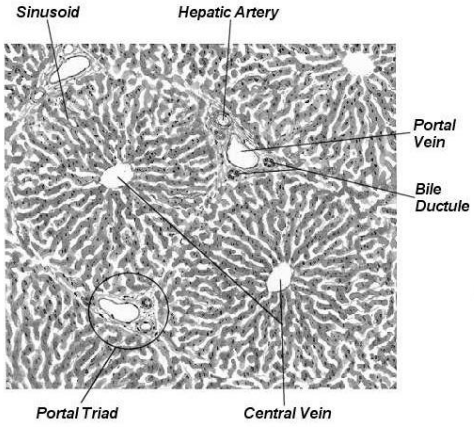


*Figure 2:The liver lobule with portal canals (hepatic artery, portal vein and bileduct), sinusoids and collecting central veins.*

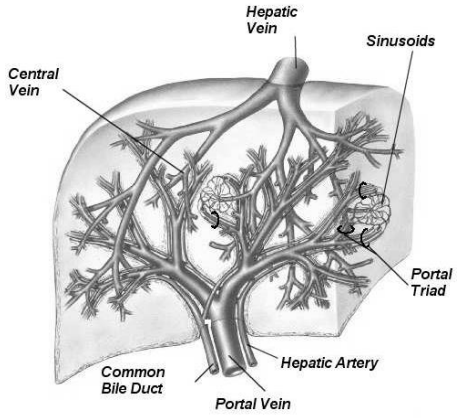


*Figure 3: Network of branching and rebranching blood vessels in the liver.*

## Sinusoids

Sinusoids are the canals formed by the plates of hepatocytes. They are approximately 8-10*mc*m in diameter and comparable with the diameter of normal capillaries. They are orientated in a radial direction in the lobule. Sinusoids are lined with endothelial cells and Kupper cells, which have a phagocytic function ***(MacSween et al.,2002).***

Plasma and proteins migrate through these lining cells via so-called fenestrations(100-150 nm) into the Space of Disse, where direct contact with the hepatocytes occurs and uptake of nutrients and oxygen by the hepatocytes takes place. On the opposite side of the hepatocyte plates are the bile canaliculi situated (1 *mc*m diameter) ***(Wanless ,1999).***

Bile produced by the hepatocytes empties in these bile canaliculi and is transported back towards the portal canal into bile ductiles and bile ducts, and finally to the main bile duct and gallbladder to become

available for digestive processes in the intestine. The direction of bile flow is opposite to the direction of the blood flow through the sinusoids ***(Saxena et al.,1999).***

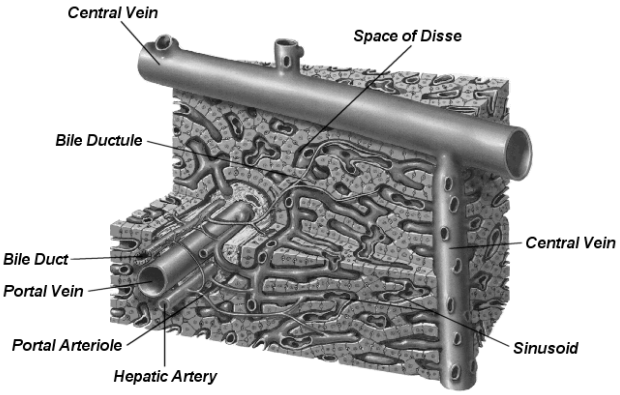


Figure 4: ***Detailed view of the liver sinusoidal structure.***

## Liver functions

Removing and excreting body wastes and hormones as well as drugs and other foreign substances is one of important function of the liver,These substances have entered the blood supply either through production by metabolism within the body or from the outside in the form of drugs or other foreign compounds. Enzymes in the liver alter some toxins so they can be more easily excreted in urine ***(McCuskey,1994).***

Synthesizing plasma proteins, including those necessary for blood clotting Most of the 12 clotting factors are plasma proteins produced by the liver. If the liver is damaged or diseased, it can take longer for the body to form clots. Other plasma proteins produced by the liver include albumin which binds many water-insoluble substances and contributes to osmotic pressure, fibrogen which is key to the clotting process, and certain globulins which transport substances such as cholesterol and iron ***(Gumucio et al.,1994).***

Producing immune factors and removing bacteria, helping the body fight infection The phagocytes in the liver produce acute-phase proteins in response to microbes. These proteins are associated with the