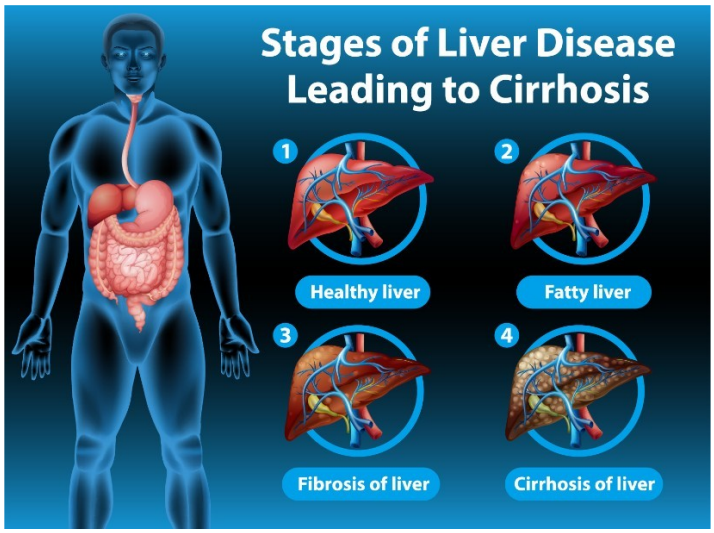
NR507 Edapt Week 5 Liver Cirrhosis

Introduction to Liver Cirrhosis



Cirrhosis of the liver is a condition characterized by the progressive scarring of liver tissue, typically resulting from long-term liver inflammation and injury. This scarring can lead to impaired liver function and potentially serious complications. Chronic liver diseases such as hepatitis C, hepatitis B, and long-term alcohol abuse are common causes of cirrhosis.

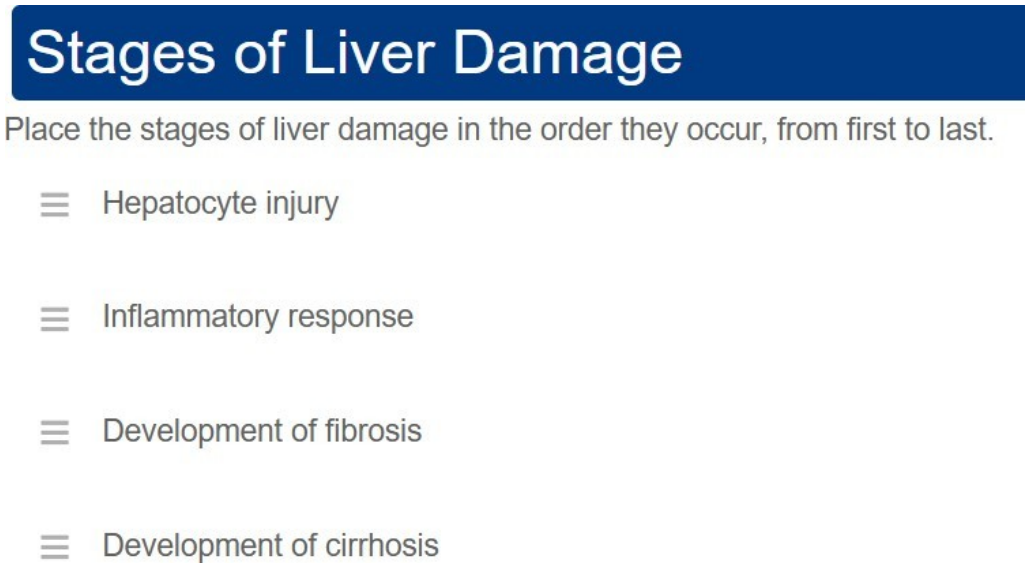
Liver Functions

Drag the functions of the liver to the box on the right.

Functions	Functions of the Liver
Metabolism	Metabolism
Detoxification	Detoxification
Produce insulin	
Store nutrients	Store nutrients
Produce bile	Produce bile
Store bile	
Filter blood	Filter blood

The liver is involved in the metabolism of carbohydrates, proteins, and fats; detoxification of harmful substances; storage of vitamins, minerals, and glycogen; production of bile for digestion; and filtration of blood.

Insulin is produced by the pancreas. Bile is stored in the gallbladder.



Liver damage often begins with injury to hepatocytes, the liver cells responsible for various metabolic functions. This injury triggers an inflammatory response, leading to the accumulation of immune cells and cytokines in the liver. Chronic inflammation can then stimulate the activation of hepatic stellate cells, which are responsible for producing collagen and other extracellular matrix proteins, leading to the development of fibrosis. If the underlying cause of liver damage persists, fibrosis can progress to cirrhosis, characterized by extensive scarring and disruption of liver architecture.

Enlargement of the liver is common in chronic liver disease, including cirrhosis, and may be palpable on physical examination. Accumulation of fluid in the abdominal cavity is a common complication of liver cirrhosis and can be assessed through physical examination and imaging studies. Enlargement of breast tissue in males can occur due to hormonal imbalances associated with liver dysfunction. Gastrointestinal bleeding, particularly from esophageal varices, is a serious complication of liver cirrhosis and can manifest as bloody or tarry stools (melena).

While hypertension can be associated with chronic liver disease, it is not typically a direct consequence of liver cirrhosis. It may be more related to other comorbidities or underlying causes of liver disease, such as obesity or alcohol misuse.

Normal Physiology of the Liver

Physiology of the Liver

Metabolism: The liver metabolizes carbohydrates, fats, and proteins, converting them into energy or storing them for later use. It also converts ammonia, a byproduct of protein metabolism, into urea, which is excreted in urine.

Detoxification: The liver detoxifies substances such as drugs, alcohol, and metabolic waste products. It breaks down these substances into less harmful forms that can be excreted by the body.

Synthesis: The liver synthesizes proteins like albumin, which helps maintain osmotic pressure in the blood, and clotting factors like fibrinogen and prothrombin, which are necessary for blood coagulation.

Storage: The liver stores important nutrients such as glucose, vitamins A, D, K, and B-12, and minerals such as iron and copper.

Immune function: Kupffer cells in the liver are part of the immune system, which help to remove bacteria and other pathogens from the blood.

Bile production: The liver produces bile, a substance that helps in the digestion and absorption of fats in the small intestine.

Blood filtration: The liver receives blood from the hepatic portal vein, which carries nutrients from the digestive system, and the hepatic artery, which carries oxygenated blood. The liver filters this blood, removing toxins and processing nutrients before it returns to the heart.

Regeneration: The liver has a remarkable ability to regenerate. Even if a significant portion of the liver is removed or damaged, it can regenerate to its original size, assuming there is no underlying chronic liver disease.

Pathophysiology of Liver Cirrhosis

Liver cirrhosis is characterized by the progressive loss of liver function due to chronic liver damage. This damage leads to the formation of scar tissue, which replaces healthy liver tissue and disrupts the liver's normal structure and function. Early diagnosis and management of underlying liver diseases are crucial in preventing the progression of cirrhosis.

Hepatocyte Injury and Death: Chronic liver damage caused by factors such as alcohol abuse, viral hepatitis, or nonalcoholic fatty liver disease leads to the death of hepatocytes (liver cells). This ongoing injury triggers an inflammatory response.

Inflammation and Fibrosis: In response to hepatocyte injury, inflammatory cells, such as macrophages and lymphocytes, infiltrate the liver. These cells release cytokines and growth factors that promote the activation of hepatic stellate cells, which are responsible for producing collagen and other proteins that form scar tissue (fibrosis). Fibrosis initially helps repair the liver but can become excessive and lead to cirrhosis.

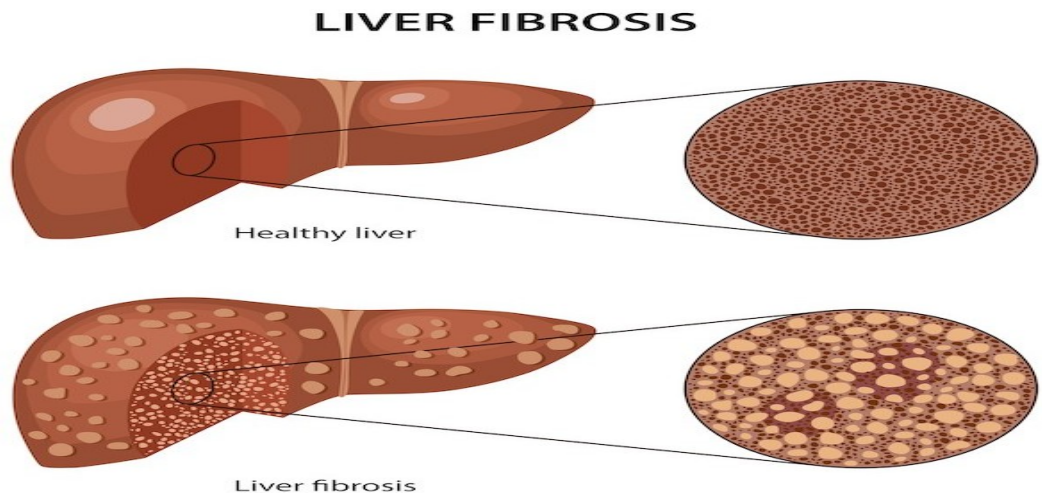
Nodules Formation: As fibrosis progresses, the liver develops regenerative nodules surrounded by fibrous tissue. These nodules disrupt the normal architecture of the liver and impair its function.

Portal Hypertension: The formation of scar tissue and nodules disrupts blood flow through the liver, leading to increased pressure in the portal vein (portal hypertension). Portal hypertension can cause complications such as varices (enlarged veins in the esophagus or stomach), ascites (fluid buildup in the abdomen), and hepatic encephalopathy (brain dysfunction due to liver failure).

Hepatic Dysfunction: As cirrhosis progresses, the liver's ability to perform its normal functions, such as metabolizing nutrients, detoxifying harmful substances, and producing proteins, is impaired. This can lead to complications such as jaundice (yellowing of the skin and eyes due to bilirubin buildup), coagulopathy (impaired blood clotting), and hypoalbuminemia (low levels of albumin in the blood).

Hepatocellular Carcinoma: Chronic inflammation and regenerative processes in cirrhosis may contribute to the development of hepatocellular carcinoma, a type of liver cancer.

Fibrosis



Liver fibrosis is the process by which excessive scar tissue forms in the liver in response to chronic liver injury. It is a precursor to cirrhosis and is characterized by the accumulation of extracellular matrix proteins, primarily collagen, in the liver tissue.

Initiation: Liver fibrosis is often initiated by chronic liver injury caused by various factors such as viral hepatitis (e.g., hepatitis B or C), alcohol abuse, nonalcoholic fatty liver disease (NAFLD), autoimmune hepatitis, or other conditions that lead to persistent liver inflammation and damage.

Inflammatory Response: In response to liver injury, inflammatory cells, such as macrophages and lymphocytes, are recruited to the site of injury. These cells release cytokines and growth factors that promote hepatic stellate cell (HSC) activation.

Activation of Hepatic Stellate Cells: HSCs are normally inactive cells in the liver that store vitamin A. In response to liver injury, HSCs become activated and transform into myofibroblast-like cells. Activated HSCs are the primary source of collagen and other extracellular matrix proteins in liver fibrosis.

Extracellular Matrix Deposition: Activated HSCs produce excessive amounts of collagen and other proteins, including fibronectin and laminin, that form the extracellular matrix. This matrix accumulates in the liver tissue, leading to the formation of scar tissue.

Progression to Cirrhosis: If the underlying liver injury persists, the process of fibrosis can progress to cirrhosis, characterized by extensive scarring and nodular regeneration of the liver tissue. Cirrhosis is associated with significant liver dysfunction and complications.

Liver fibrosis may be reversible if the underlying cause of liver injury is treated or removed. If left untreated, fibrosis can progress to cirrhosis, which is associated with a higher risk of liver failure, portal hypertension, hepatocellular carcinoma, and other serious complications.

Complications of Cirrhosis