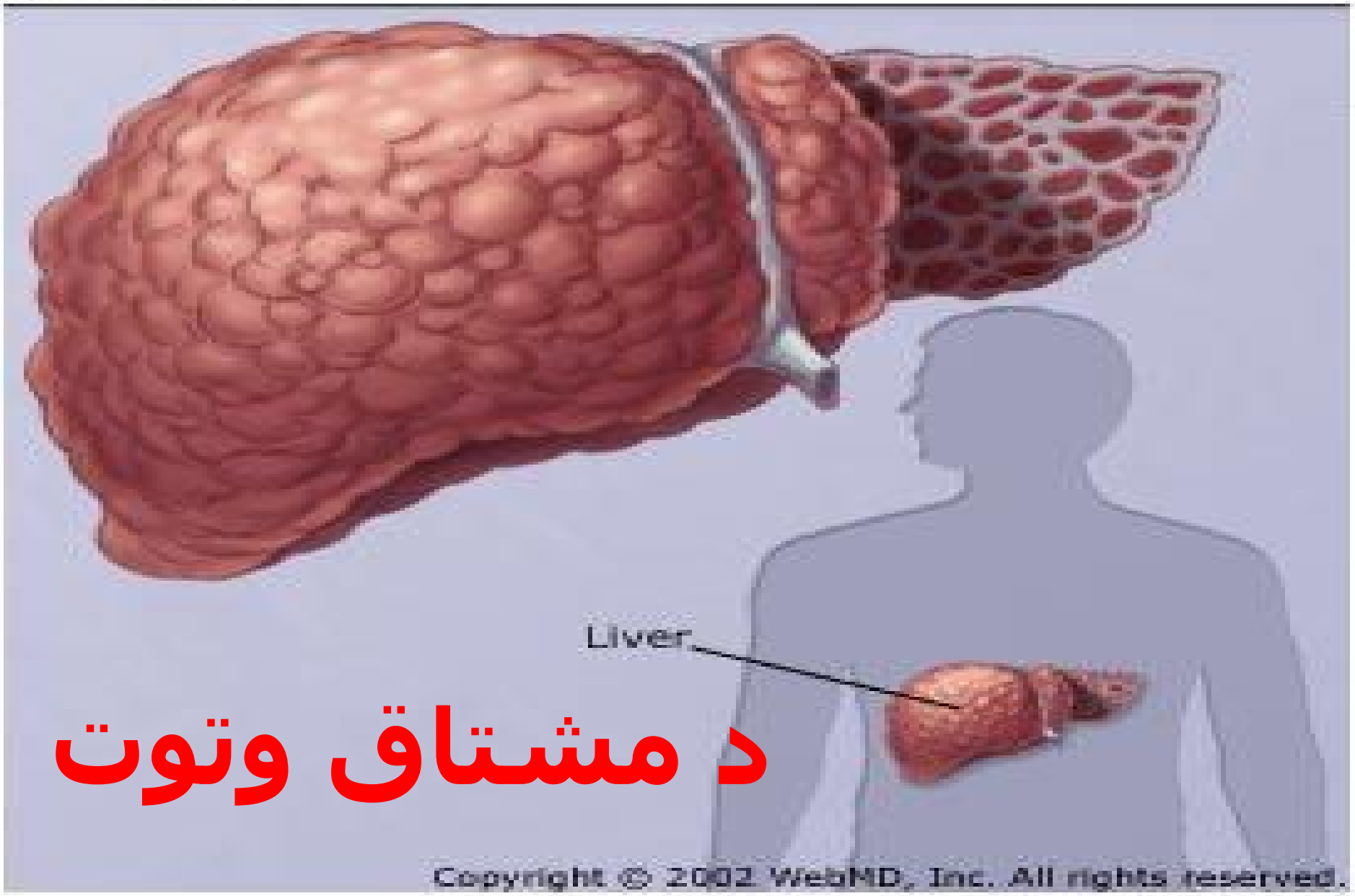
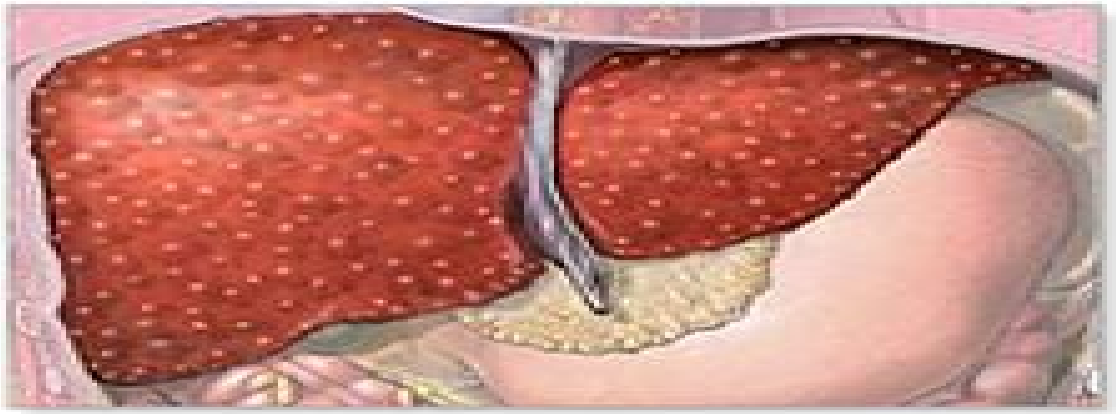
Cirrhosis

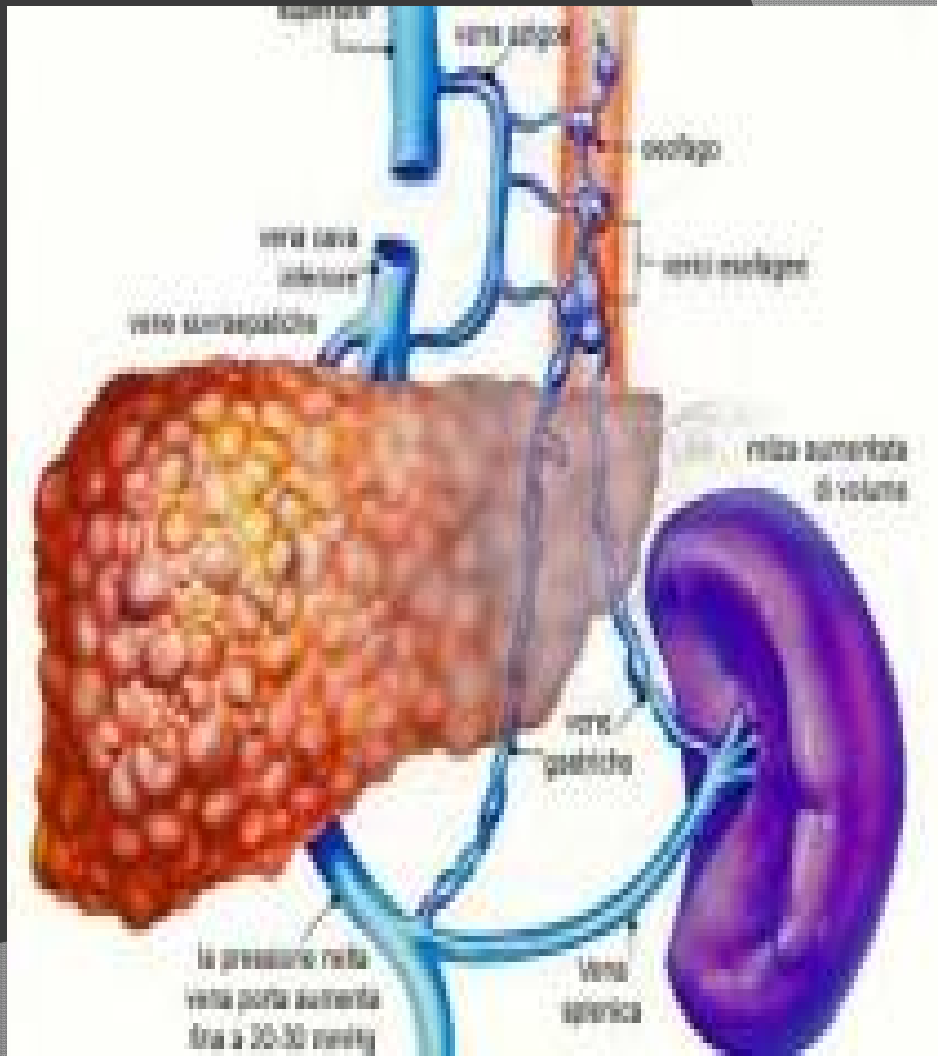


- It is a common disease characterized by diffuse hepatic fibrosis and nodule formation.
- It can occur at any age, has significant morbidity.
- the most common causes of cirrhosis are chronic viral hepatitis and prolonged excessive alcohol consumption.



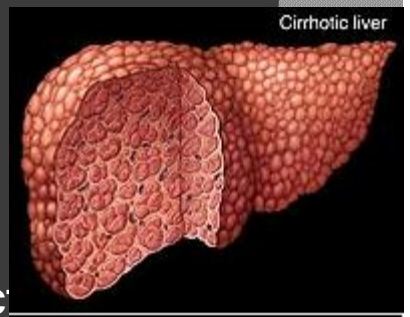
Causes of cirrhosis

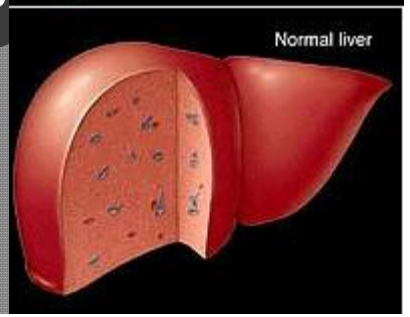
- Alcohol
- Chronic viral hepatitis (B or C)
- Non-alcoholic fatty liver disease
- Immune
  - Primary sclerosing cholangitis
  - Autoimmune liver disease
- Biliary
  - Primary biliary cirrhosis
  - Secondary biliary cirrhosis
  - Cystic fibrosis
- Genetic
  - Haemochromatosis
  - Wilson's disease
  - α_1-antitrypsin deficiency
- Cryptogenic (unknown-15%)
- Chronic venous outflow obstruction



Pathophysiology

- The cardinal feature of cirrhosis is an increase in fibrous tissue, progressive and widespread death of liver cells, and inflammation leading to loss of the normal liver architecture.
- Following liver injury, stellate cells in the space of Disse are activated by cytokines produced by Kupffer cells and hepatocytes. This transforms the stellate cell into a myofibroblast-like cell, capable of producing collagen, pro-inflammatory cytokines and other mediators which promote hepatocyte damage and cause tissue fibrosis .
- Destruction of the liver architecture causes distortion and loss of the normal hepatic vasculature with the development of portosystemic vascular shunts and the formation of nodules.
- Cirrhosis evolves slowly over years to decades, and normally continues to progress even after removal of the aetiological agent (e.g. abstinence from alcohol, venesection in haemochromatosis).
- Cirrhosis can be classified histologically into two types:
- *Micronodular cirrhosis*, characterised by small nodules
- about 1 mm in diameter and seen in alcoholic cirrhosis.
- *Macronodular cirrhosis*, characterised by larger nodules
- of various sizes. Areas of previous collapse of the liver architec
- are evidenced by large fibrous scars.

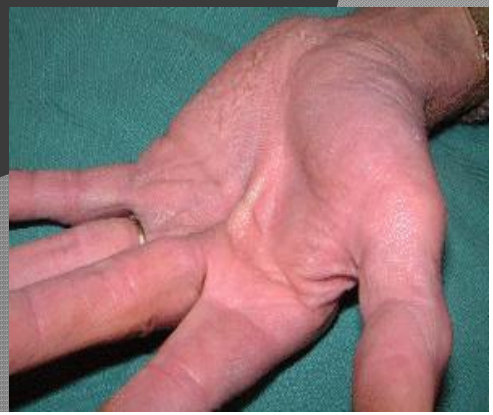


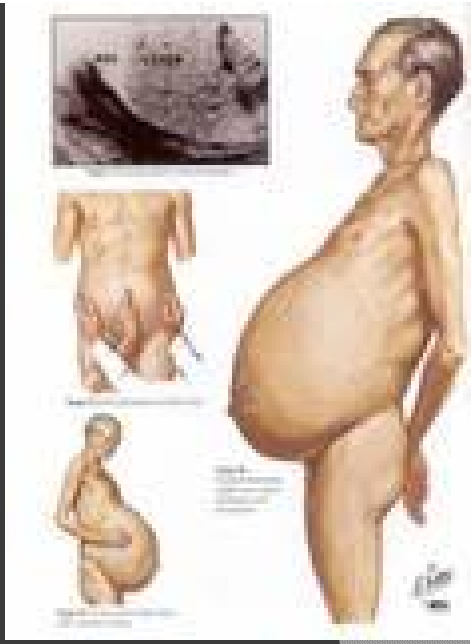


Clinical features of hepatic cirrhosis

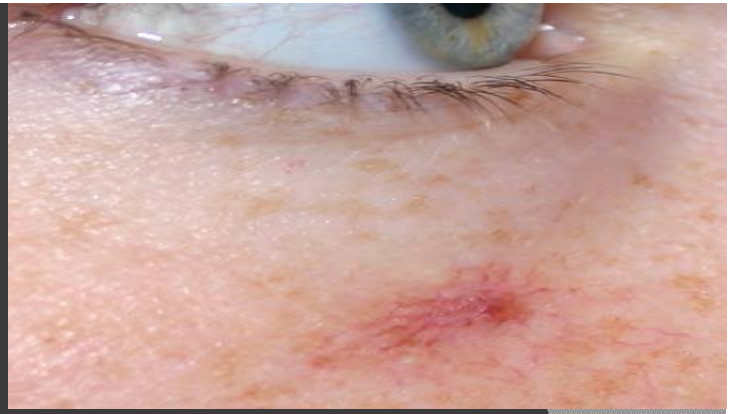
Hepatomegaly (although liver may also be small)

- **Jaundice**
- **Ascites**
- **Circulatory changes**
  - **Spider telangiectasia, palmar erythema, cyanosis**
- **Endocrine changes**
  - **Loss of libido, hair loss**
  - **Men: gynaecomastia, testicular atrophy, impotence**
  - **Women: breast atrophy, irregular menses, amenorrhoea**
- **Haemorrhagic tendency**
  - **Bruises, purpura, epistaxis**
- **Portal hypertension**
  - **Splenomegaly, collateral vessels, variceal bleeding**
- **Hepatic (portosystemic) encephalopathy**
- **Other features**
  - **Pigmentation, digital clubbing,**
  - **Dupuytren's contracture**

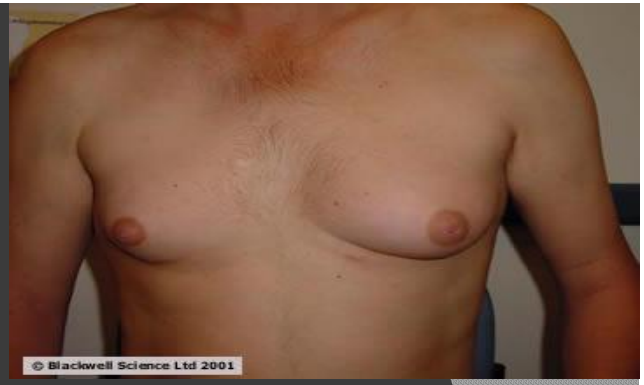




- Asymptomatic presentation common and the diagnosis is made incidentally at ultrasound or at surgery.
- Others present with isolated hepatomegaly, splenomegaly or signs of portal hypertension .
- When symptoms are present, they are often non-specific and include weakness, fatigue, muscle cramps, weight loss, anorexia, nausea, vomiting and upper abdominal discomfort .
- Hepatomegaly is common when the cirrhosis is due to alcoholic liver disease and haemochromatosis.
- A reduction in liver size is especially common if the cause of cirrhosis is viral hepatitis or autoimmune liver disease. The liver is often hard, irregular and non-tender.



- Mild haemolysis may occur due to hypersplenism
- Palmar erythema can be seen early in the disease
- Spider telangiectasias occur and comprise a central arteriole, from which small vessels radiate. They vary in size from 1 to 2 mm in diameter, are usually found only above the nipples, and can occur early in the disease. One or two small spider telangiectasias can be found in about 2% of healthy people and can occur transiently in greater numbers in the third trimester of pregnancy, but otherwise they are a strong indicator of liver disease.
- Florid spider telangiectasia, gynaecomastia and parotid enlargement are most common in alcoholic cirrhosis.
- Pigmentation is most striking in haemochromatosis and in any cirrhosis associated with prolonged cholestasis.
- Pulmonary arteriovenous shunts also develop, leading to hypoxaemia and eventually to central cyanosis, but this is a late feature.



- Endocrine changes are noticed more readily in men, who show loss of male hair distribution and testicular atrophy. Gynaecomastia is common and can be due to drugs such as spironolactone.
- Easy bruising becomes more frequent as cirrhosis advances.
- Epistaxis is common and sometimes severe; it can mimic upper gastrointestinal bleeding if the blood is swallowed.
- Splenomegaly and collateral vessel formation are features of portal hypertension, which occurs in more advanced disease .
- Evidence of hepatic encephalopathy also becomes increasingly common with advancing disease.
- Non-specific features of chronic liver disease include clubbing of the fingers and toes. Dupuytren's contracture is traditionally regarded as a complication of cirrhosis, but the evidence for this is weak.
- *Chronic liver failure develops when the metabolic capacity of the liver is exceeded.* It is characterised by the presence of encephalopathy and/or ascites. The term 'hepatic decompensation' or 'decompensated liver disease' is often used when chronic liver failure occurs.

Complications

1- Bruising and bleeding resulting from decreased production of coagulation factors.

2- Jaundice

3- Itching (pruritus) because of bile salt products deposited in the skin.

4- Hepatic encephalopathy

5- Hepatocellular carcinoma.

6- Portal hypertension

7- Ascites

8- Esophageal varices

9- immune system dysfunction, leading to infection

10- Hepatorenal syndrome - has a very high mortality (over 50%).

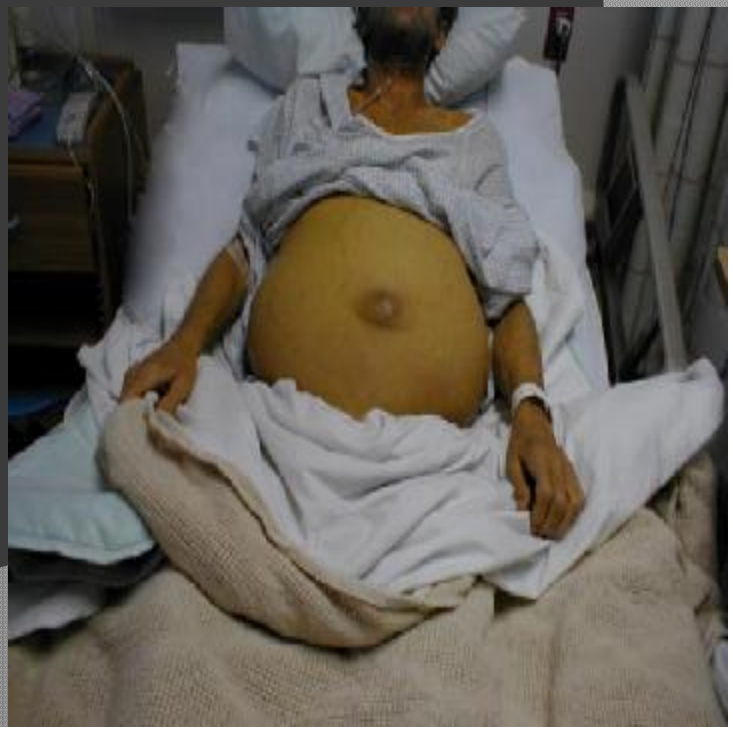
11- Hepatopulmonary syndrome - blood bypassing the normal lung circulation (shunting), leading to cyanosis and dyspnea (shortness of breath), characteristically worse on sitting up.

12- Portopulmonary hypertension: increased blood pressure over the lungs as a consequence of portal hypertension.

13- Portal gastropathy : which refers to changes in the mucosa of the stomach in patients with portal hypertension, and is associated with cirrhosis severity.

Features of chronic liver failure

- **Worsening synthetic liver function**
  - **Prolonged prothrombin time**
  - **Low albumin**
- **Jaundice**
- **Portal hypertension**
- **Variceal bleeding**
- **Hepatic encephalopathy**
- **Ascites**
  - **Spontaneous bacterial peritonitis**
  - **Hepatorenal failure**

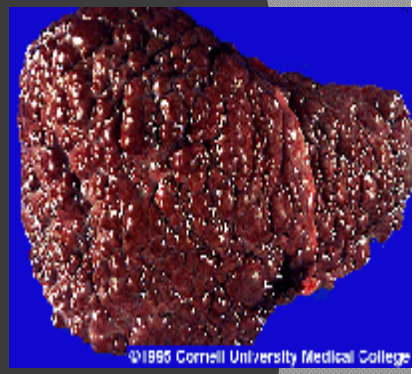


Diagnosis

() The gold standard for diagnosis of cirrhosis is a liver biopsy

() Lab findings:

Aminotransferases - AST and ALT are moderately elevated, with AST > ALT. However, normal aminotransferases do not preclude cirrhosis.



Alkaline phosphatase - usually slightly elevated.

Gamma-glutamyl transferase : Typically much higher in chronic liver disease from alcohol.

Bilirubin - may elevate as cirrhosis progresses.

Albumin - levels fall as the synthetic function of the liver declines

Prothrombin time - increases since the liver synthesizes clotting factors.

Globulins - increased due to shunting of bacterial antigens away from the liver to lymphoid tissue.

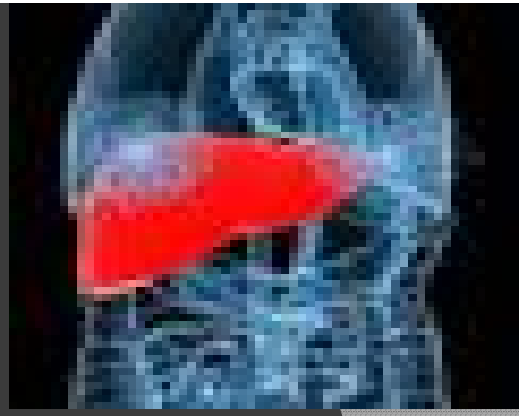
hyponatremia due to inability to excrete free water resulting from high levels of ADH and aldosterone.

- *thrombocytopenia* - due to both congestive splenomegaly as well as decreased thrombopoietin from the liver.
- *Leukopenia and neutropenia* - due to splenomegaly.
- *Coagulation defects* - the liver produces most of the coagulation factors and thus coagulopathy correlates with worsening liver disease.
- Serology for hepatitis viruses,
- autoantibodies (ANA, anti-smooth muscle, anti-mitochondria, anti-LKM)
- Ferritin and transferrin saturation (markers of iron overload), copper and ceruloplasmin (markers of copper overload)
- Alpha 1-antitrypsin
- *Ultrasound* is routinely used in the evaluation of cirrhosis, Ultrasound may also screen for hepatocellular carcinoma, portal hypertension and Budd-Chiari syndrome (by assessing flow in the hepatic vein).
- A new type of device, the FibroScan (transient elastography), uses elastic waves to determine liver stiffness . The FibroScan is much faster than a biopsy (usually last 2.5–5 minutes) and is completely painless.
- abdominal CT and liver/bile duct MRI (MRCP).
- Endoscopy

managment

- **This includes treatment of the underlying cause, maintenance of nutrition and treatment of complications , Chronic liver failure due to cirrhosis can be treated by liver transplantation.**
- **Management of ascites**

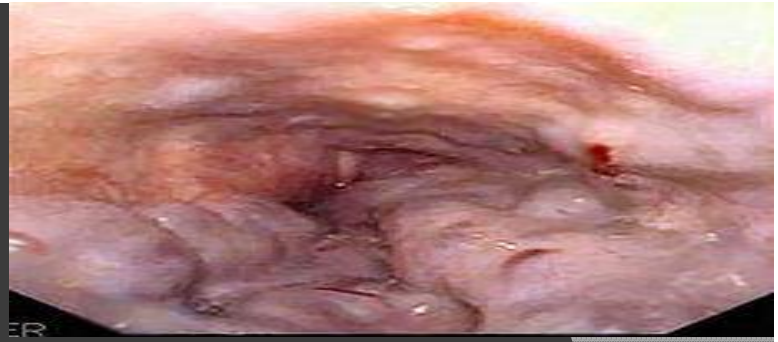
Hepatorenal syndrome



- **This occurs in 10% of patients with advanced cirrhosis complicated by ascites. There are two clinical types; both are mediated by renal vasoconstriction due to underfilling of the arterial circulation.**

Type 1 hepatorenal syndrome **is characterised by progressive oliguria, a rapid rise of the serum creatinine and a very poor prognosis (without treatment, median survival is less than 1 month). There is usually no proteinuria, a urine sodium excretion below 10 mmol/day and a urine/plasma osmolarity ratio of > 1.5. Treatment consists of albumin infusions in combination with terlipressin and is effective in about two-thirds of patients. Haemodialysis should not be used routinely because it does not improve the outcome. Patients who survive should be considered for liver transplantation.**

Type 2 hepatorenal syndrome **usually occurs in patients with refractory ascites, is characterised by a moderate and stable increase in serum creatinine, and has a better prognosis.**



Varices and hepatocellular carcinoma surveillance

- Once the diagnosis of cirrhosis is made, endoscopy should be performed to screen for oesophageal varices and ultrasound performed to check for hepatocellular carcinoma .

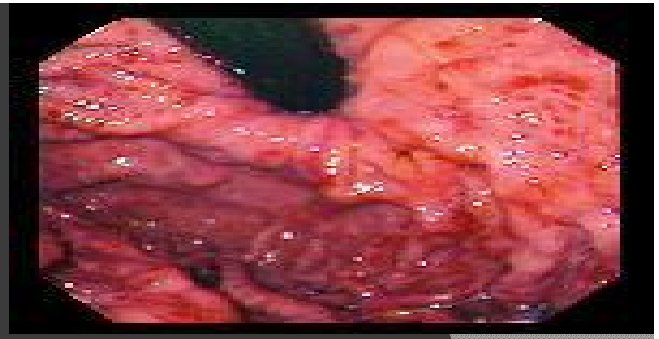
Prognosis

- The overall prognosis in cirrhosis is poor.
- Many patients present with advanced disease and/or serious complications that carry a high mortality.
- Overall, only 25% of patients survive 5 years from diagnosis
- The prognosis is more favourable when the underlying cause of the cirrhosis can be corrected, as in alcohol misuse, haemochromatosis and Wilson's disease.

Poor prognosis occur in:

- Deteriorating liver function
- jaundice
- ascites
- encephalopathy
- Increasing bilirubin
- falling albumin (or an albumin concentration < 30 g/L)
- marked hyponatraemia (< 120 mmol/L)
- prolonged prothrombin time

Congestive gastropathy



() Long-standing portal hypertension causes chronic gastric congestion recognisable at endoscopy as multiple areas of punctate erythema ('snake skin gastropathy').

() Rarely, similar lesions occur more distally in the gastrointestinal tract. These areas may become eroded, causing bleeding from multiple sites.

() Acute bleeding can occur, but repeated minor bleeding causing iron-deficiency anaemia is more common. Anaemia may be prevented by oral iron supplements but repeated blood transfusions can become necessary.

() Reduction of the portal pressure using propranolol 80-160 mg/day is the best initial treatment. If this is ineffective, a TIPSS procedure can be undertaken.

CIRRHOSIS
Later Clinical Manifestations