Chronic Liver Disease

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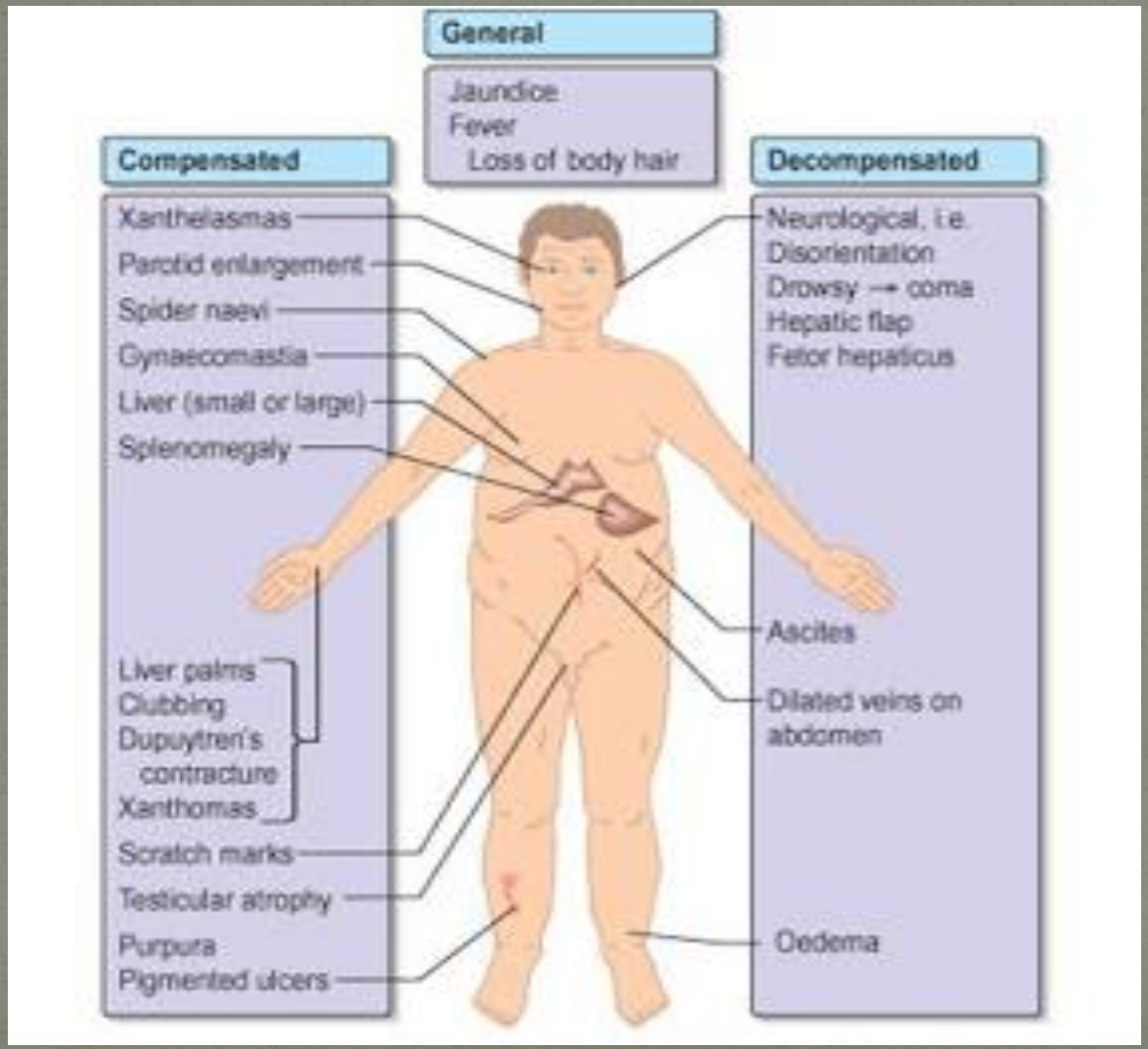
Symptoms of chronic liver disease

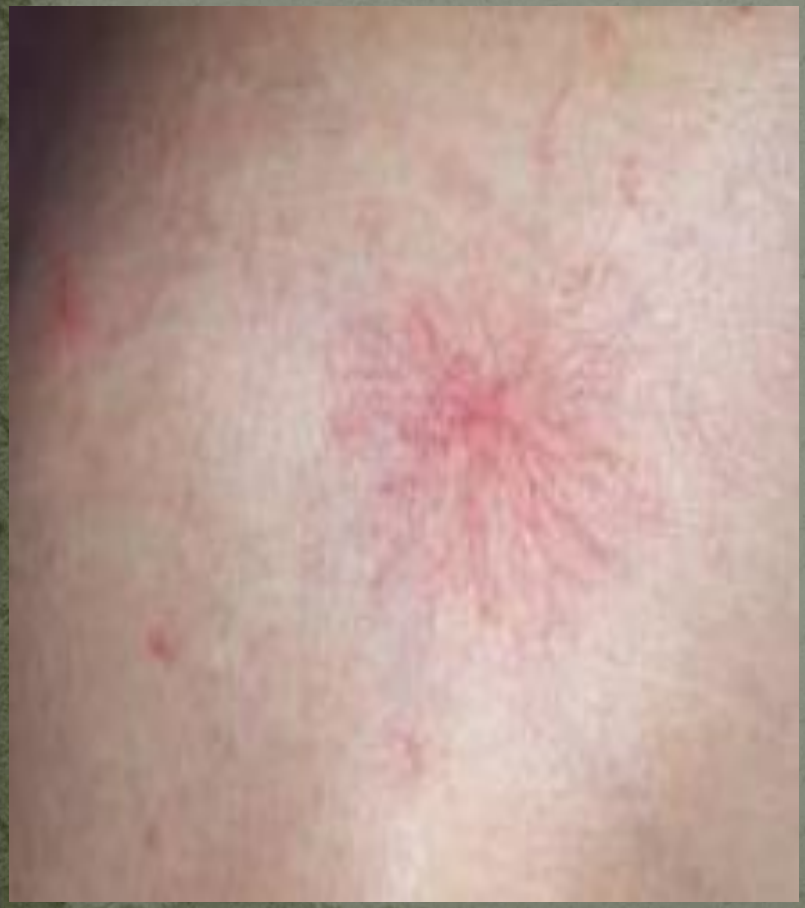
- Patients may be asymptomatic or complain of non-specific symptoms, particularly fatigue
- Right hypochondrial pain due to liver distension
- Abdominal distension due to ascites
- Ankle swelling due to fluid retention
- Hematemesis and melena from gastrointestinal hemorrhage
- Pruritus due to cholestasis
- Gynecomastia , loss of libido and amenorrhea due to endocrine dysfunction
- Confusion and drowsiness due to neuropsychiatric complications (portosystemic encephalopathy)

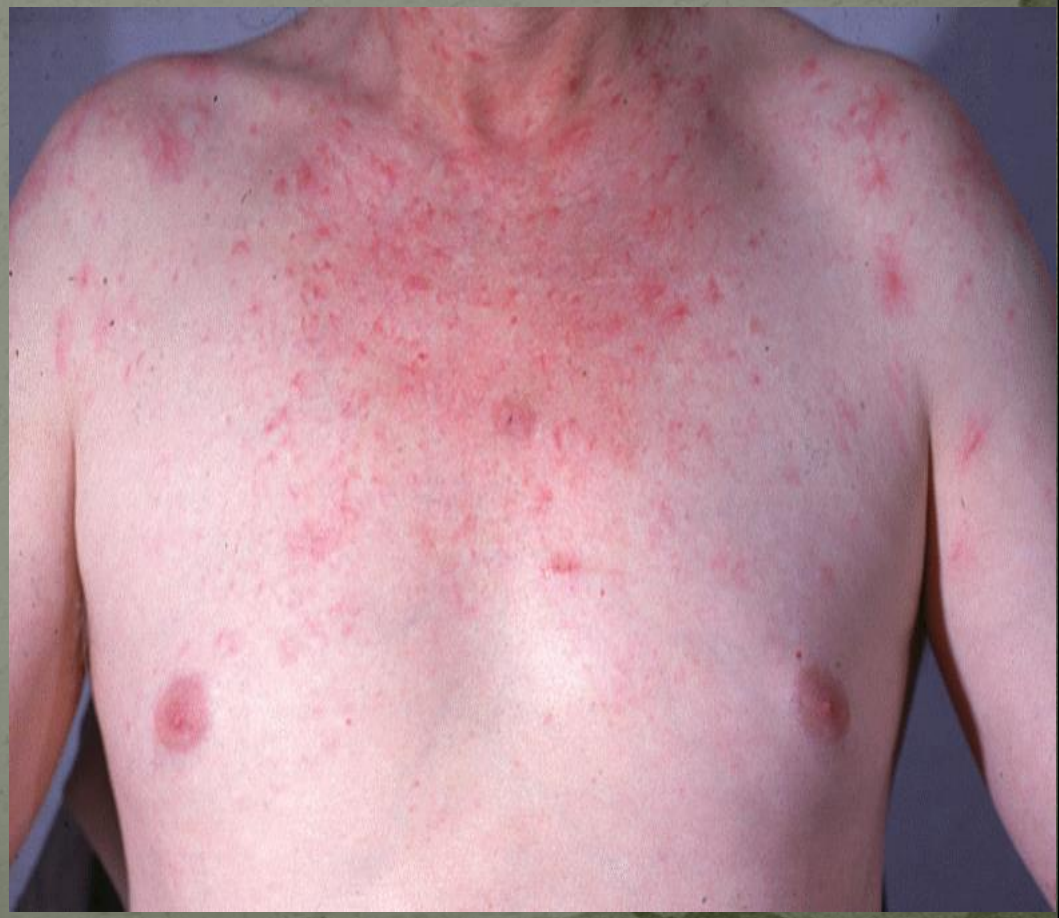
Signs of chronic liver disease



SPIDER NEVI

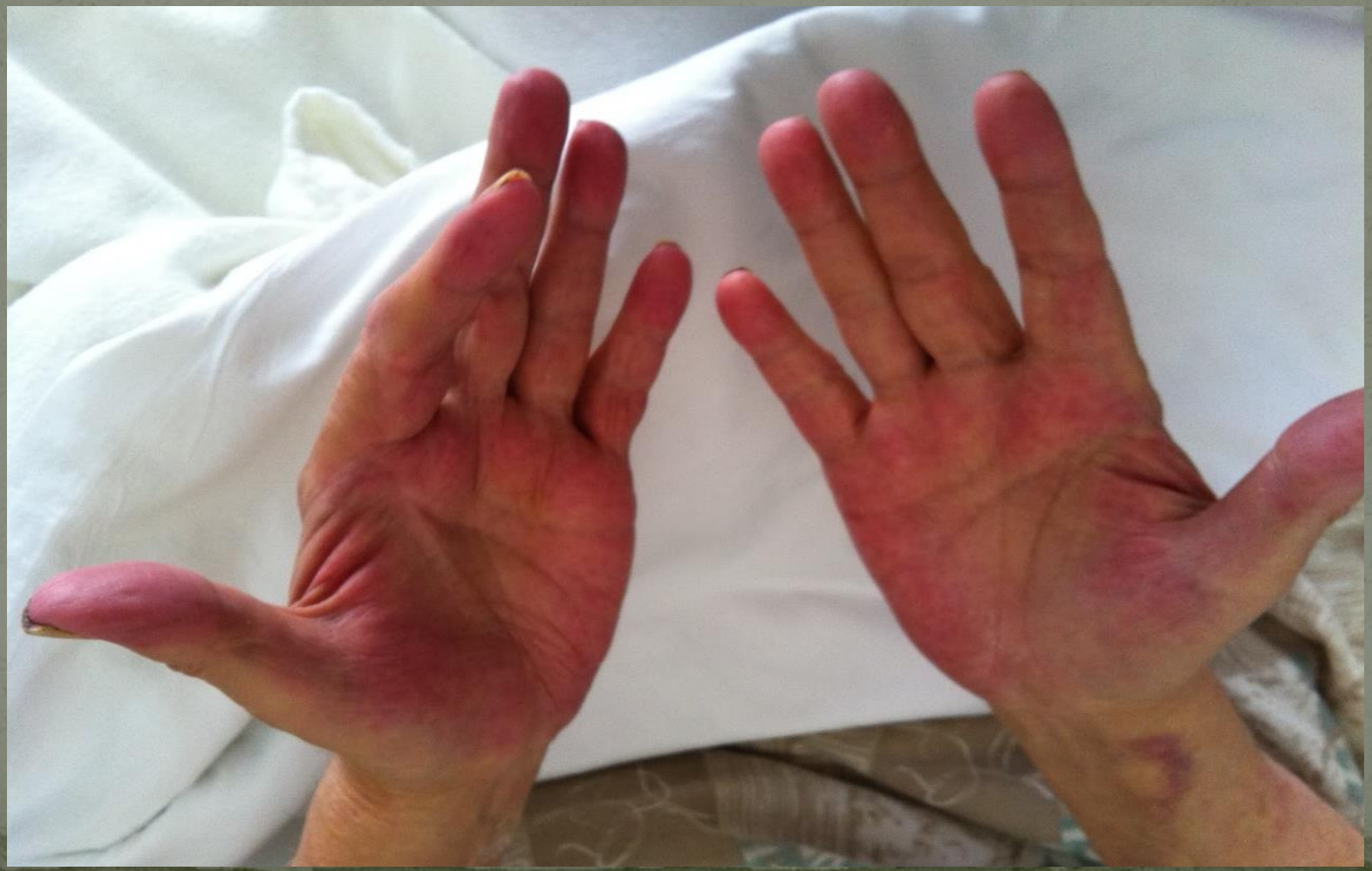
- Telangiectasias that consist of a central arteriole with radiating small vessels. They are found in the distribution of the superior vena cava (above the nipple line)





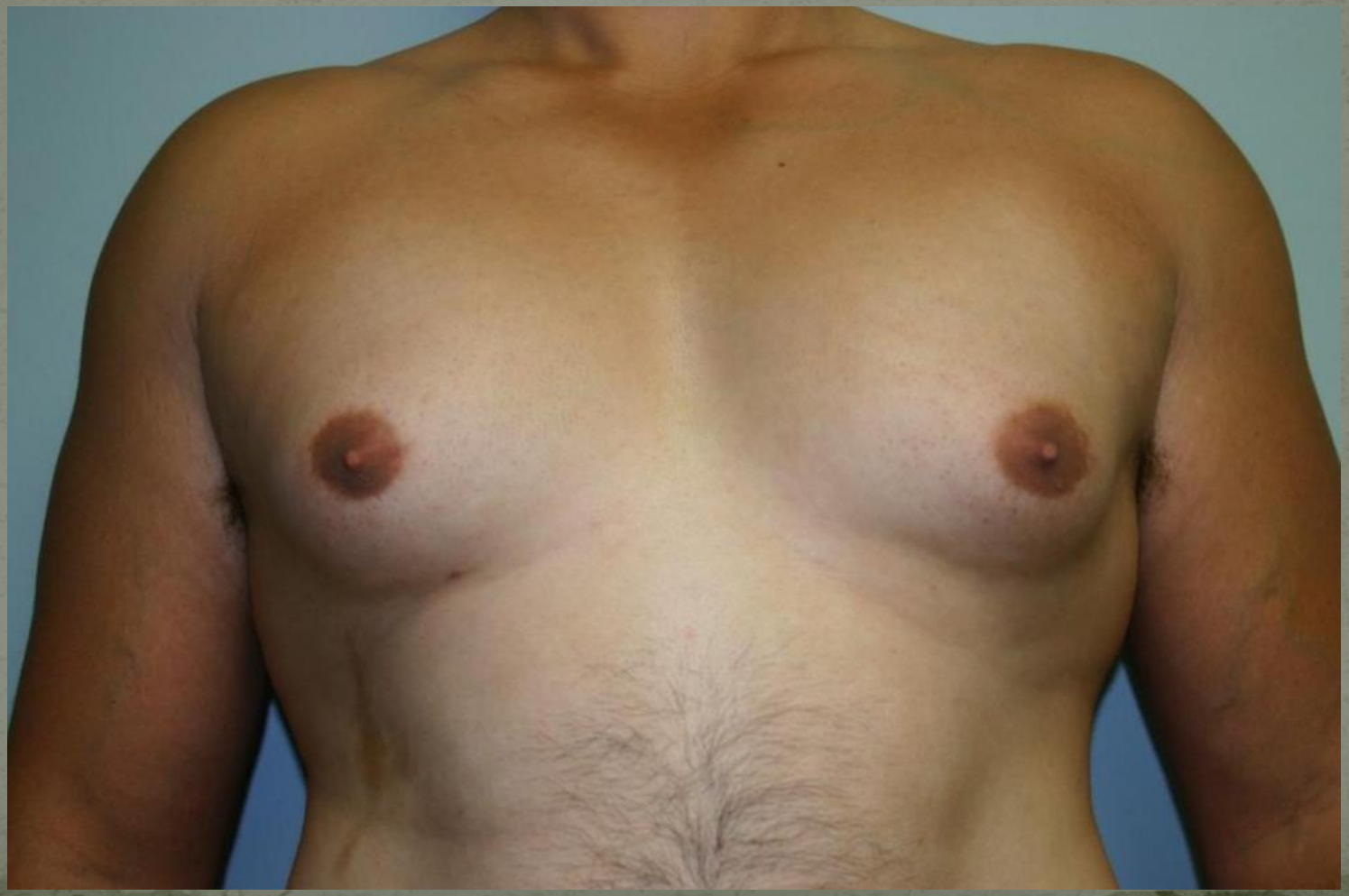
PALMAR ERYTHEMA

- A non-specific change, indicative of a hyperdynamic circulation

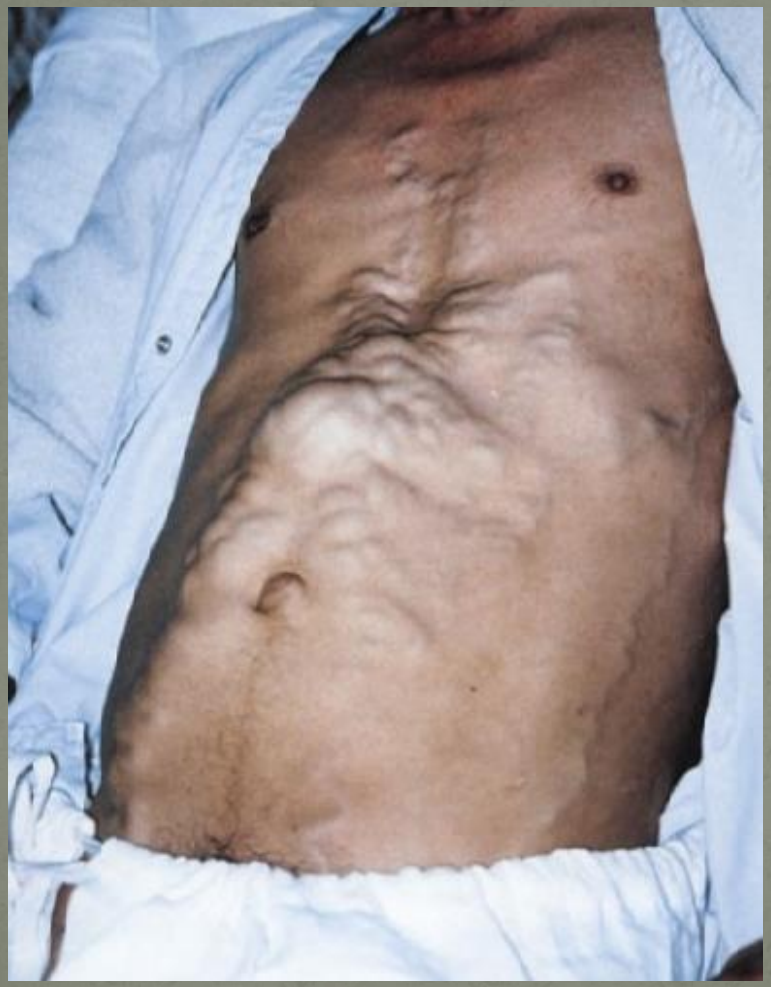


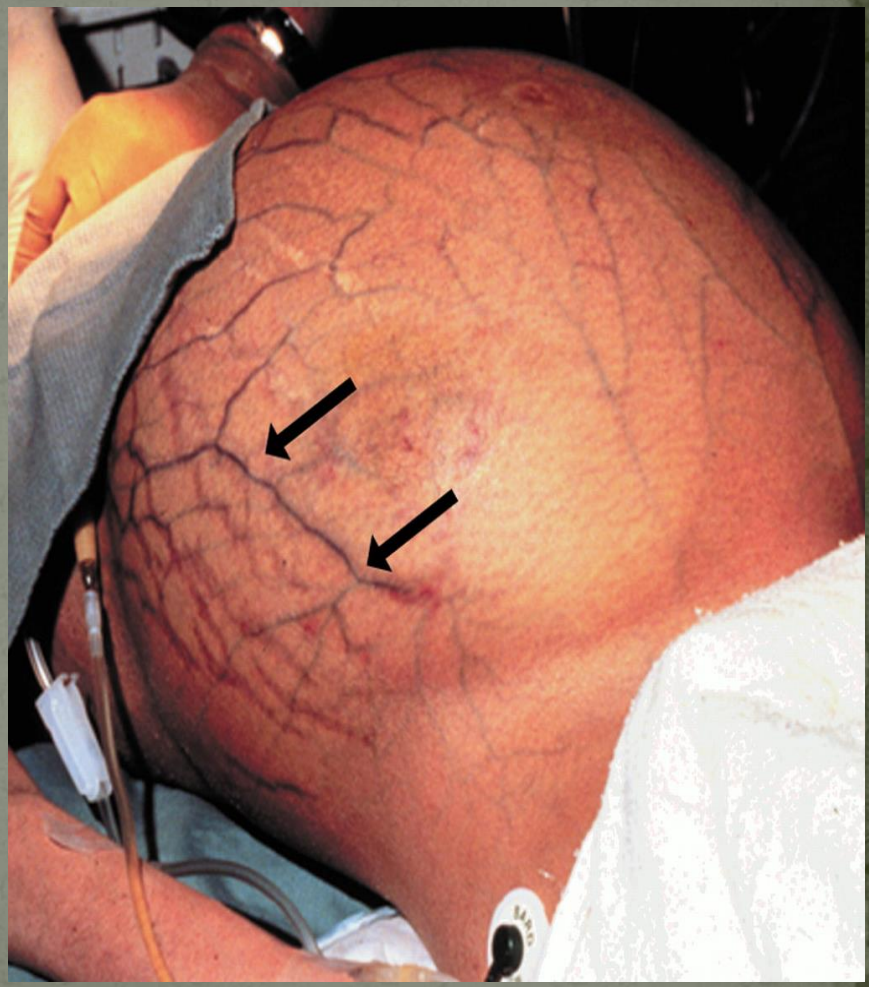
DUPUYTREN'S CONTRACTURE

GYNECOMASTIA



CAPUT MEDUSA





Liver Cirrhosis

- Cirrhosis results from the necrosis of liver cells followed by fibrosis and nodule formation
- The liver architecture is diffusely abnormal and this interferes with liver blood flow and function
- This derangement produces the clinical features of portal hypertension and impaired liver cell function
- Alcohol is the most common cause in the West, but viral infection is the most common cause world-wide

- Cirrhosis is characterised by diffuse hepatic fibrosis and nodule formation. It is the most common cause of portal hypertension.
- Worldwide, the most common causes are chronic viral hepatitis, prolonged excessive alcohol consumption and NAFLD, but any condition leading to persistent or recurrent hepatocyte injury may lead to cirrhosis
- Cirrhosis may also occur in prolonged biliary injury, as is found in primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC) and post-surgical biliary strictures.
- Persistent impairment of venous return from the liver, Budd–Chiari syndrome and cardiac hepatopathy, can also result in cirrhosis

- Hepatomegaly is common when the cirrhosis is due to alcoholic liver disease or haemochromatosis.
- Progressive hepatocyte destruction and fibrosis gradually reduce liver size as the disease progresses in other causes of cirrhosis.
- The liver is often hard, irregular and non-tender.

24.30 Features of chronic liver failure

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

24.28 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 cholangitis
  - Secondary biliary cirrhosis
  - Cystic fibrosis
- Genetic:
  - Haemochromatosis
  - Wilson's disease
  - Alpha-1-antitrypsin deficiency
- Cryptogenic (unknown – 15%)
- Chronic venous outflow obstruction
- Cardiac hepatopathy with chronic hepatic congestion
- Any chronic liver disease

Pathology

- The characteristic features of cirrhosis are regenerating nodules separated by fibrous septa and loss of the normal lobular architecture within the nodules
- Two types of cirrhosis have been described:
- Micronodular cirrhosis. Regenerating nodules are usually less than 3 mm in size and the liver is involved uniformly.
- This type is often caused by ongoing alcohol damage or biliary tract disease
- Macronodular cirrhosis. The nodules are of variable size and normal acini may be seen within the larger nodules
- This type is often seen following chronic viral hepatitis
- A mixed picture with small and large nodules is sometimes seen

Investigations

Severity assessment

- Liver function: Serum albumin and prothrombin time are the best indicators of liver function
- Liver biochemistry: This can be normal, depending on the severity of cirrhosis. In most cases there is at least a slight elevation in the serum ALP and serum aminotransferases. In decompensated cirrhosis all biochemistry is deranged
- Serum electrolytes: A low sodium indicates severe liver disease due to a defect in free water clearance or to excess diuretic therapy
- Serum creatinine: An elevated concentration > 130 μmol/ L is a marker of worse prognosis
- Serum α-fetoprotein: If > 200 ng/mL is strongly suggestive of the presence of a hepatocellular carcinoma

Investigation

Cause assessment

This can be determined by:

- viral markers
- serum autoantibodies
- serum immunoglobulins
- iron indices and ferritin
- copper, ceruloplasmin
- α1-antitrypsin
- Serum copper and serum α1-antitrypsin should always be measured in young cirrhotics.
- Total iron-binding capacity (TIBC) and ferritin should be measured to exclude hereditary hemochromatosis

Imaging

Ultrasound examination.

- This can demonstrate changes in size and shape of the liver. Fatty change and fibrosis produce a diffuse increased echogenicity
- In established cirrhosis there may be marginal nodularity of the liver surface and distortion of the arterial vascular architecture. The patency of the portal and hepatic veins can be evaluated
- It is useful in detecting hepatocellular carcinoma

CT scan

- Shows hepatosplenomegaly, and dilated collaterals. Contrast-enhanced scans are useful in the detection of hepatocellular carcinoma.

Endoscopy

- Performed for the detection and treatment of varices

MRI

- Useful in the diagnosis of benign tumors

Liver Biopsy

- This is usually necessary to confirm the severity and type of liver disease
- Special stains are required for iron and copper, and various immunocytochemical stains can identify viruses, bile ducts and angiogenic structures
- Chemical measurement of iron and copper is necessary to confirm diagnosis of iron overload or Wilson's disease
- Adequate samples in terms of length and number of complete portal tracts are necessary for of chronic viral hepatitis

Management

- Management is that of the complications seen in decompensated cirrhosis
- Patients should have 6-monthly ultrasound to detect the early development of a hepatocellular carcinoma as all therapeutic strategies work best with small single tumors
- Treatment of the underlying cause may arrest or occasionally reverse the cirrhotic changes
- The only dietary restriction is to reduce salt intake
- Alcohol, aspirin and NSAIDs should be avoided

Course and Prognosis

- This is extremely variable, depending on many factors, including the aetiology and the presence of complications
- Development of any complication usually worsens the prognosis
- In general, the 5-year survival rate is approximately 50%, but this also varies depending on the aetiology and the stage at which the diagnosis is made
- There are a number of prognostic classifications based on modifications of Child's grading (A, B and C) and the model for end-stage disease (MELD), based on serum bilirubin, creatinine and INR, which is widely used as a predictor of mortality in patients awaiting liver transplantation.

Child-Pugh classification of cirrhosis[2]

Factor	Units	1	2	3
Serum bilirubin	µmol/L mg/dL	<34 <2.0	34-51 2.0-3.0	>51 >3.0
Serum albumin	g/L g/dL	>35 >3.5	30-35 3.0-3.5	<30 <3.0
Prothrombin time	Second prolonged INR	0-4 <1.7	4-6 1.7-2.3	>6 >2.3
Ascites		None	Easily controlled	Poorly controlled
Hepatic encephalopathy		None	Minimal	Advanced

Child-Pugh class assignment[2]

Total Points	Class	Liver Status
5-6	A	Compensated
7-9	B	Decompensated
10-15	C	Decompensated

Complications

- Portal hypertension
- Variceal bleeding
- Ascites
- Portosystemic encephalopathy
- Spontaneous bacterial peritonitis
- Renal failure (hepatorenal syndrome)
- Hepatopulmonary syndrome
- Primary hepatocellular carcinoma

Portal Hypertension

- The portal vein is formed by the union of the superior mesenteric and splenic veins
- The pressure within it is normally 5–8 mmHg with only a small gradient across the liver to the hepatic vein
- As portal pressure rises above 10–12 mmHg, the compliant venous system dilates and collaterals occur within the systemic venous system
- The main sites of the collaterals are at the gastro-oesophageal junction, the rectum, the left renal vein, the diaphragm, the retroperitoneum and the anterior abdominal wall via the umbilical vein
- The collaterals at the gastro-oesophageal junction (varices) are superficial in position and tend to rupture
- Rectal varices are found frequently (30%) and can be differentiated from hemorrhoids, which are lower in the anal canal
- The microvasculature of the gut becomes congested giving rise to portal hypertensive gastropathy and colopathy, in which there is punctate erythema and sometimes erosions, which can bleed

Portosystemic Encephalopathy

- This is a chronic neuropsychiatric syndrome secondary to cirrhosis
- Encephalopathy is potentially reversible
- In cirrhosis, the portal blood bypasses the liver via the collaterals and the toxic metabolites pass directly to the brain to produce the encephalopathy
- Many toxic substances may be causative factors, including ammonia, free fatty acids, mercaptans and accumulation of false neurotransmitters (octopamine) or activation of the γ-aminobutyric acid (GABA) inhibitory neurotransmitter system
- Ammonia is produced by intestinal bacteria breaking down protein

Factors precipitating portosystemic encephalopathy

- High dietary protein
- Gastrointestinal hemorrhage
- Constipation
- Infection, including spontaneous bacterial peritonitis
- Fluid and electrolyte disturbance due to diuretic therapy or paracentesis
- Drugs (e.g. any CNS depressant)
- Portosystemic shunt operations, TIPS
- Any surgical procedure
- Progressive liver damage
- Development of hepatocellular carcinoma

Clinical Features

- The patient becomes increasingly drowsy and comatose
- Chronically, there is a disorder of personality, mood and intellect, with a reversal of normal sleep rhythm
- The patient may be irritable, confused, disoriented and has slow slurred speech
- General features include nausea, vomiting and weakness
- Convulsions are very rare
- Signs include fetor hepaticus (a sweet smell to the breath) and a coarse flapping tremor called asterixis
- Decreased mental function

Treatment

- Identify and treat the possible precipitating cause
- Give purgation and enemas to empty the bowels of nitrogenous substances
- Lactulose (10–30 mL three times daily) is an osmotic purgative that reduces the colonic pH and limits ammonia absorption
- Maintain nutrition with adequate calories
- Antibiotics (e.g. metronidazole)

Hepatorenal Syndrome

- occurs typically in patients with advanced cirrhosis and almost normal renal histology
- It is sometimes precipitated by vigorous diuretic therapy, NSAIDs, diarrhea, paracentesis, and infection, particularly spontaneous bacterial peritonitis
- The initiating factor is thought to be extreme peripheral vasodilatation, possibly due to nitric oxide, leading to an extreme decrease in the effective blood volume and hypotension
- This activates the homeostatic mechanisms, causing a rise in plasma renin, aldosterone, norepinephrine and vasopressin, leading to vasoconstriction of the renal vasculature
- Diuretic therapy should be stopped and intravascular hypovolemia corrected, preferably with albumin.
- Liver transplantation is the best option

Thank You