Liver cirrhosis

Definition:

Diffuse liver disease characterized by degeneration (hepatocellular necrosis), regeneration nodules, fibrosis and loss of lobular architecture.

Causes:

- Chronic viral hepatitis (B,C,D).
- Autoimmune hepatitis.
- Alcoholic cirrhosis
- Metabolic :NAFLD; Wilson's disease, hemochromatosis and alpha 1 anti-trypsin deficiency.
- Cholestasis (chronic): If prolonged, it may be end by biliary cirrhosis as PBC
- Heart failure and constrictive pericarditis may lead to hepatic fibrosis ("cardiac cirrhosis")

Pathophysiology :

- **Pathogenesis**

- The hallmark of cirrhosis is the development of scar tissue that separate hepatocyte nodules, which eventually replace the entire liver architecture.
- The principle cell involved in pathogenesis of fibrosis is hepatic stellate cell , which lie in space of Disse. In resting state, it has intracellular droplets containing vitamin A (retinoid droplet) & they express desmin (a filament protein present in muscles).
- Following hepatic injury, activation of hepatic stellate cell is done

➢ Results of activation

1-Proliferation of stellate cell by platelet derived growth factor.

2-Chemotaxis (can migrate toward cytokine chemoattractant “to site of inflammation”).

3-Fibrogenesis by activated satellate cell which converted into myofibroblast like which produce high-density matrix in the sub endothelial space, resulting in “capillarization” of the hepatic sinusoid.

4-Contraction to sinusoids with significant microvascular changes occur (dilated peribiliary plexus, venous branches around cirrhotic nodules & arterio portal anastomosis as well as flattening of hepatic veins. These micro vasculature changes are important in the development of intrahepatic shunting & portal hypertension).

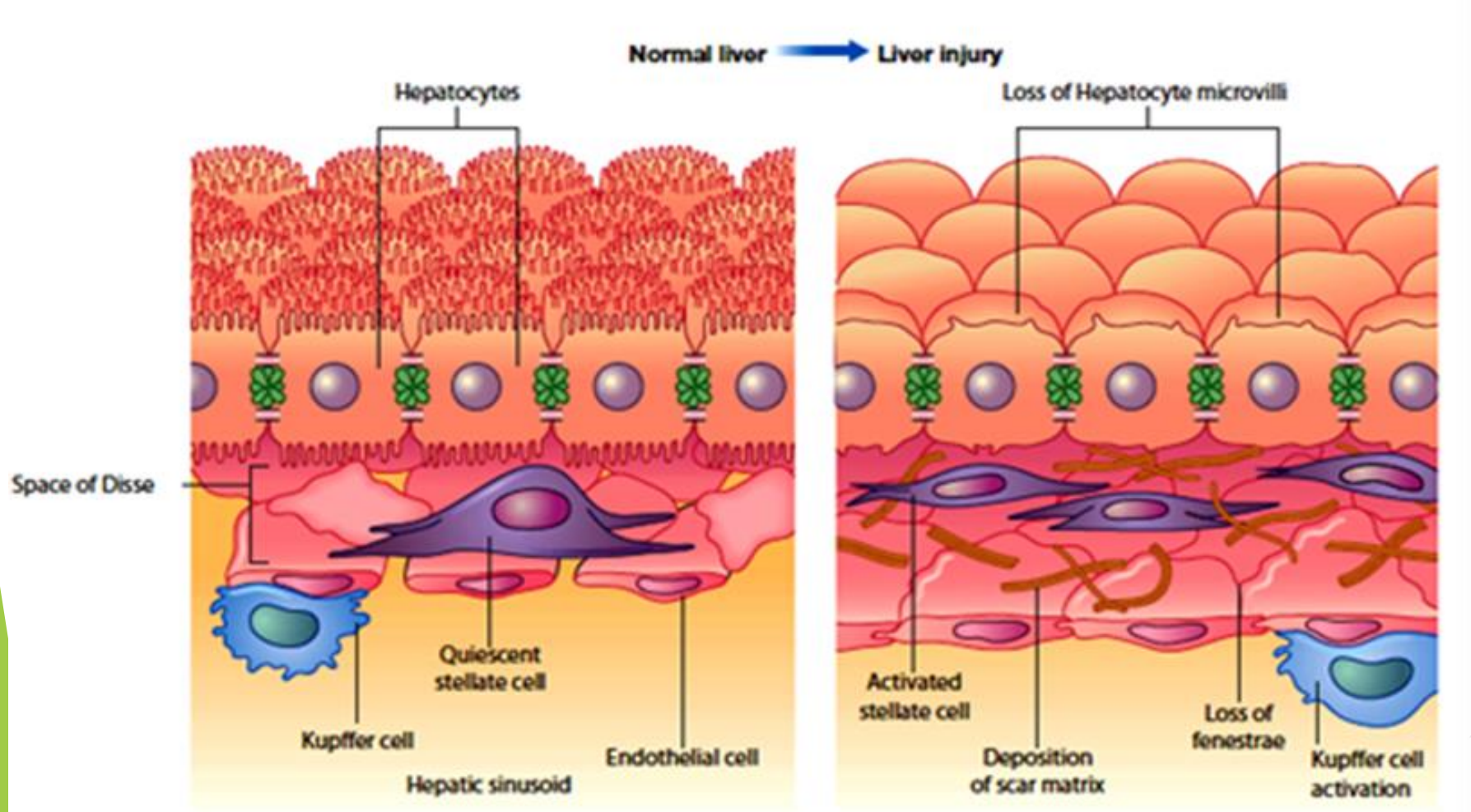
5-Matrix degradation (i.e. replacement of non-fibrilar collagen “fine” by fibrilar collagen “tough” for new septa formation).

6- Retenoid loss.

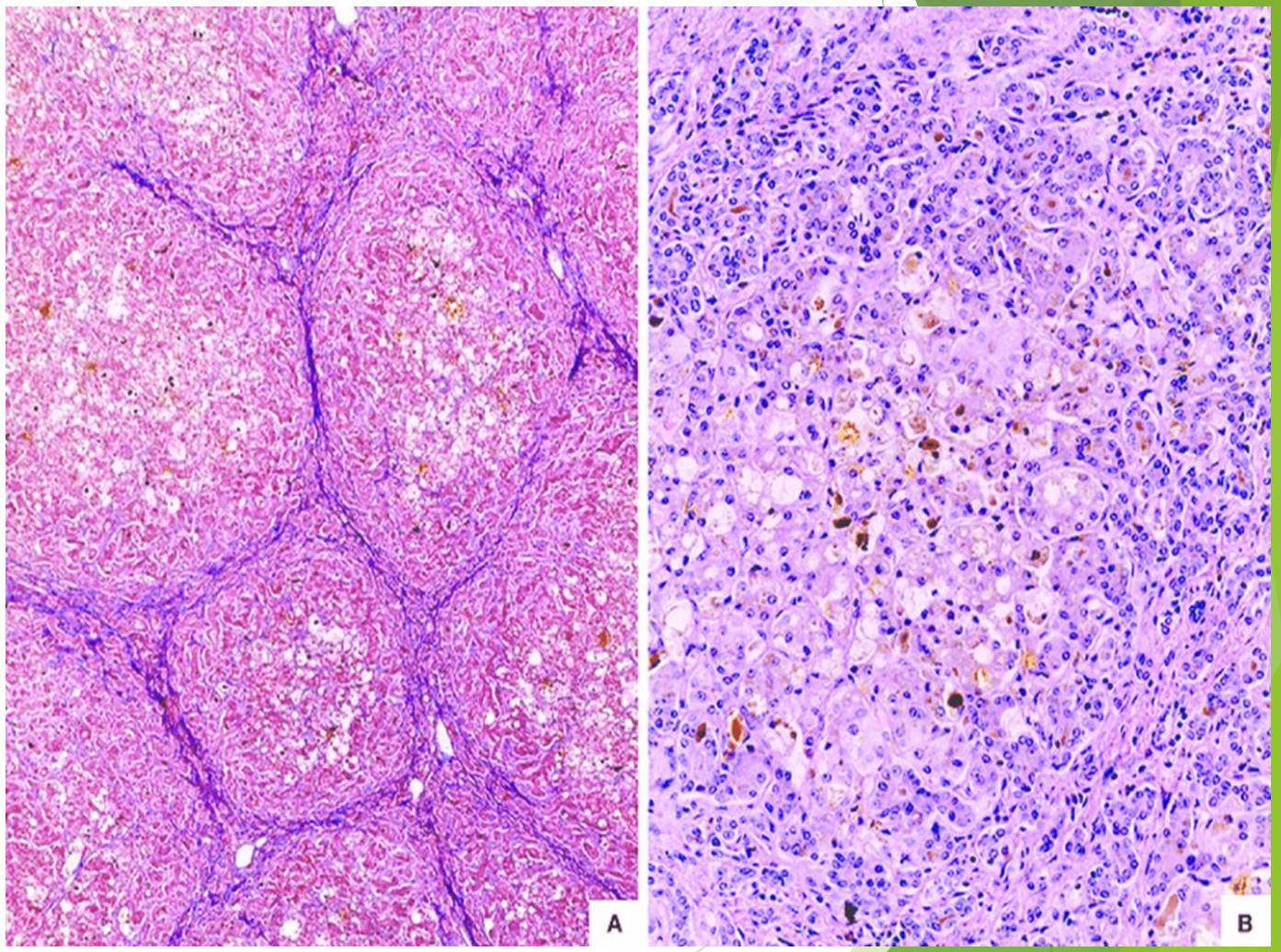
7-WBCs chemoattraction & cytokine release

In fibrosis, hepatocytes which normally don’t synthesize type III &type IV collagen may produce them. The increased collagen disrupts the hepatic architecture & converts sinusoids to capillaries, so impeding metabolic exchange through basement membranes between liver cells & the blood and causing portal hypertension.

Hepatic liver cells and the hepatic sinusoid in normal and injured liver.



Regeneration nodules



Clinical picture

A- (Compensated cirrhosis): Discovered accidentally

B- (Decompensated cirrhosis):(ascites, variceal bleeding, encephalopathy, or jaundice).

1- Manifestation of liver cell failure (parenchymal):

The onset of symptoms is usually insidious with development of fatigue, muscle cramps, and weight loss.

- **Anorexia** is usually present and may be extreme, with associated reduced muscle strength and exercise capacity.

- Abdominal pain may be present and is related either to hepatic enlargement and stretching of Glisson capsule or to the presence of ascites

- Hormonal disturbances including menstrual abnormalities (usually amenorrhea), erectile dysfunction, loss of libido, sterility, and gynecomastia.

- -Weight loss occurs in advanced cirrhosis (Spider man appearance).

- **Skin manifestations:** consist of spider telangiectasias (invariably on the upper half of the body), palmar erythema and Dupuytren contractures specially in alcoholic cirrhosis. Evidence of vitamin deficiencies (glossitis and cheilosis) is common. Itchy skin due to increased bilirubin and bile salts, Ecchymotic patches due to thrombocytopenia
- **Jaundice**
- **Ascites**, pleural effusions, peripheral edema.
- **Encephalopathy**: day-night reversal, asterixis, tremor, dysarthria, delirium, drowsiness, and ultimately coma
- **Fever** is present in up to 35% of patients and usually reflects associated alcohol-associated hepatitis, spontaneous bacterial peritonitis, or another infection.

2-Manifestation of portal hypertension :

- **Hematemesis** is the presenting symptom in 15–25% due to development of esophageal varices as a result of portal hypertension .
- **Splenomegaly** usually present.

C- Specific features related to the cause of cirrhosis.

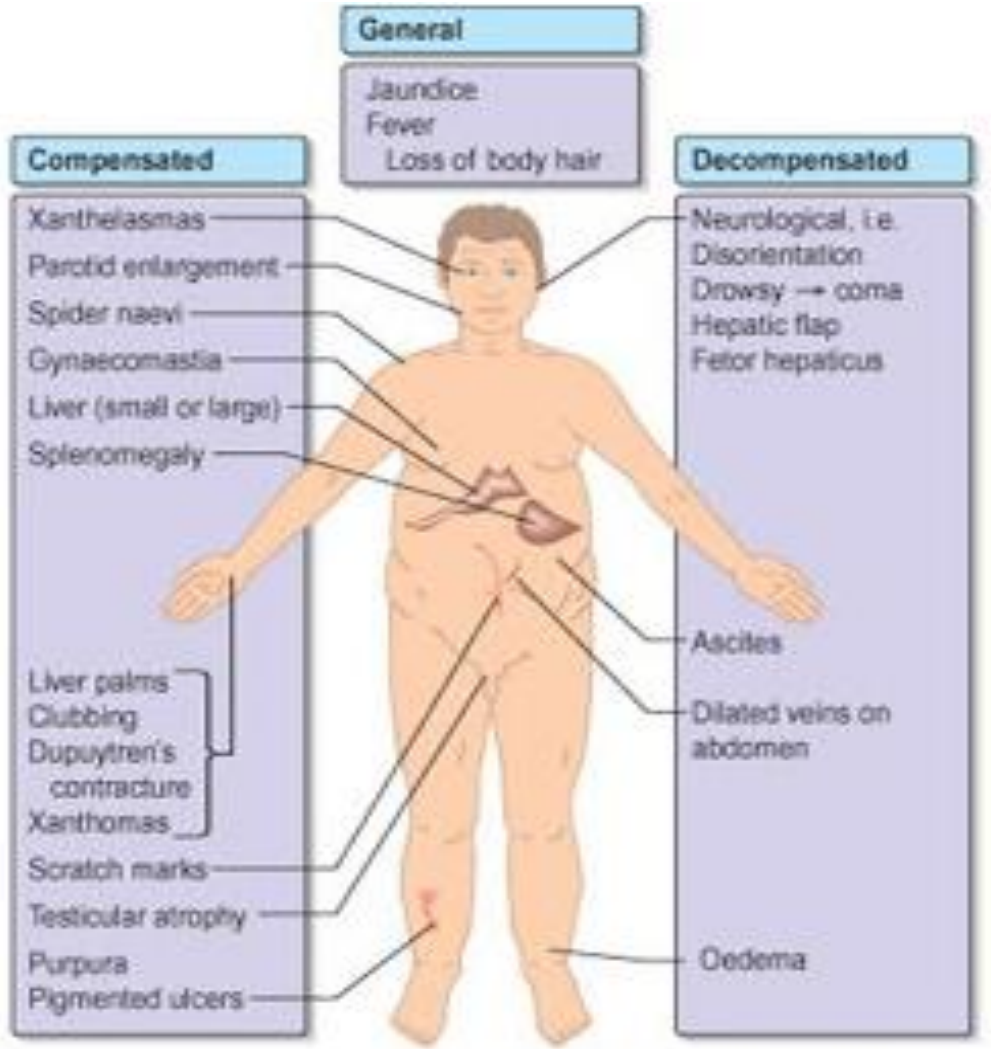
D- Complications:

- Hepatocellular carcinoma,
- Hepatorenal and
- Hepatopulmonary syndrome

Complications

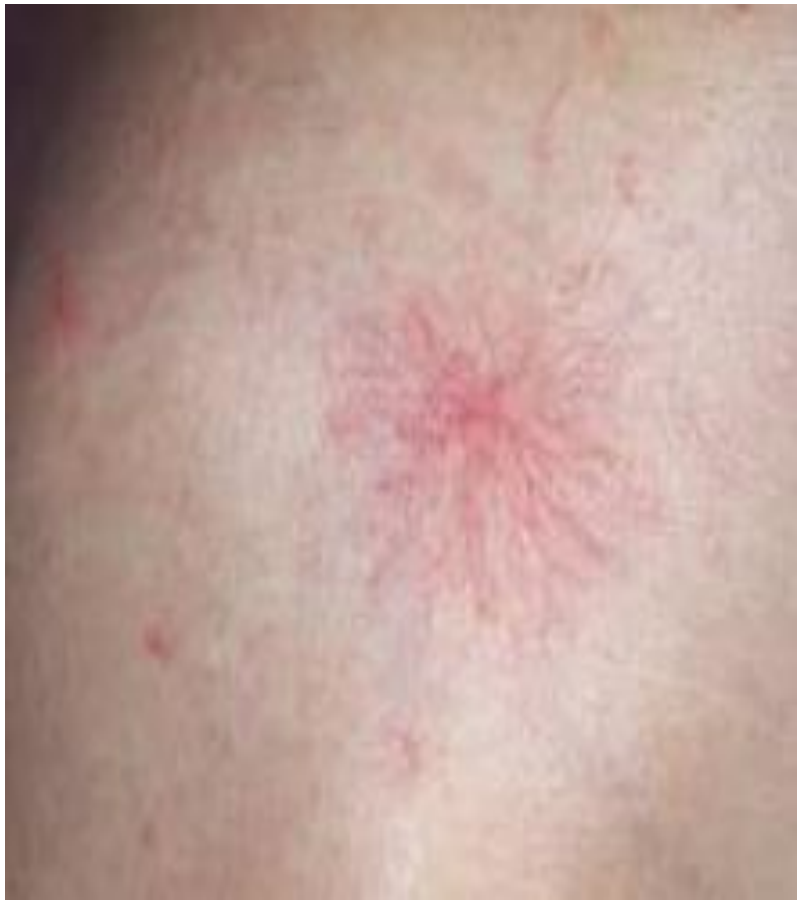
- Portal hypertension
- Variceal bleeding
- Ascites
- Portosystemic encephalopathy
- Spontaneous bacterial peritonitis
- Renal failure (hepatorenal syndrome)
- Hepatopulmonary syndrome
- Primary hepatocellular carcinoma

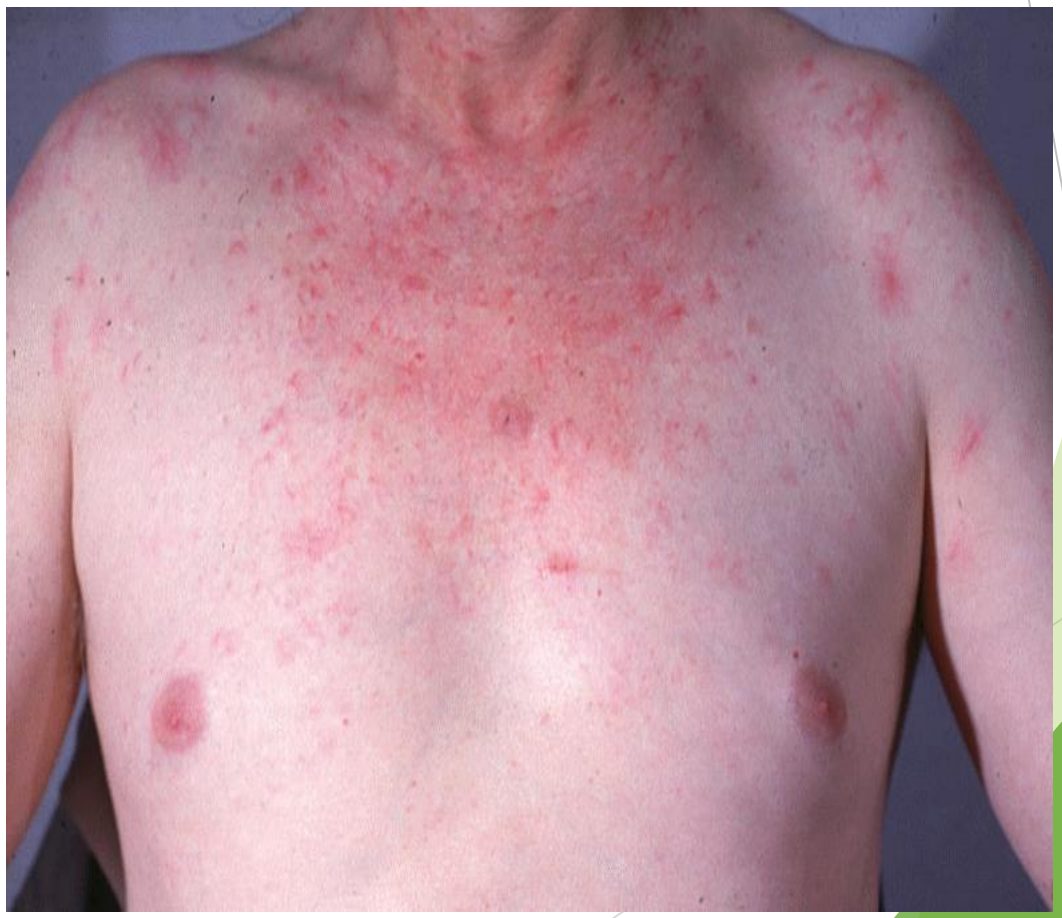
Signs of chronic liver disease



SPIDER NEVI

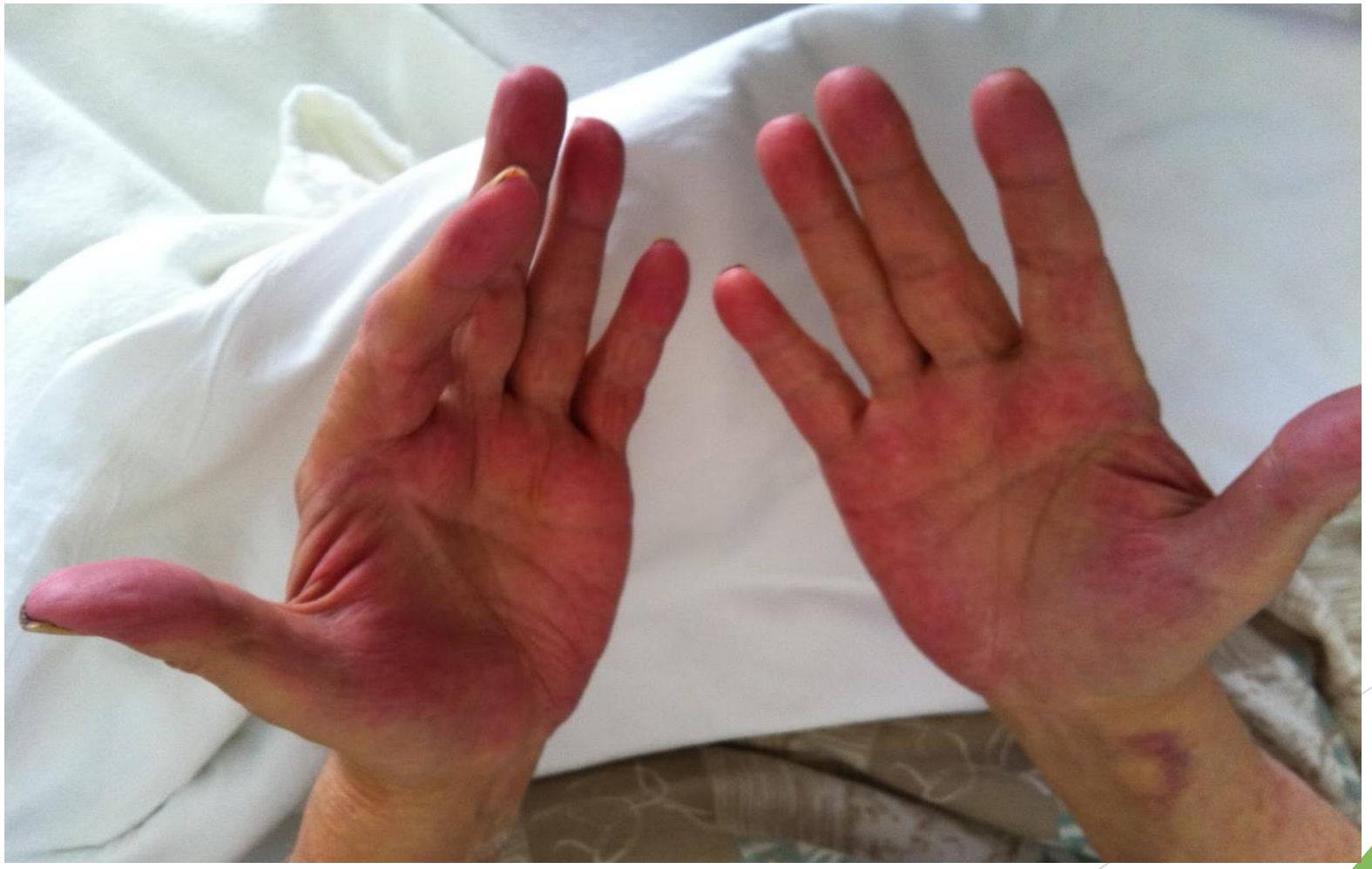
- Telangiectasias that consist of a central arteriole with radiating small vessels. They are found in the distribution of the superior vena cava (above the nipple line)





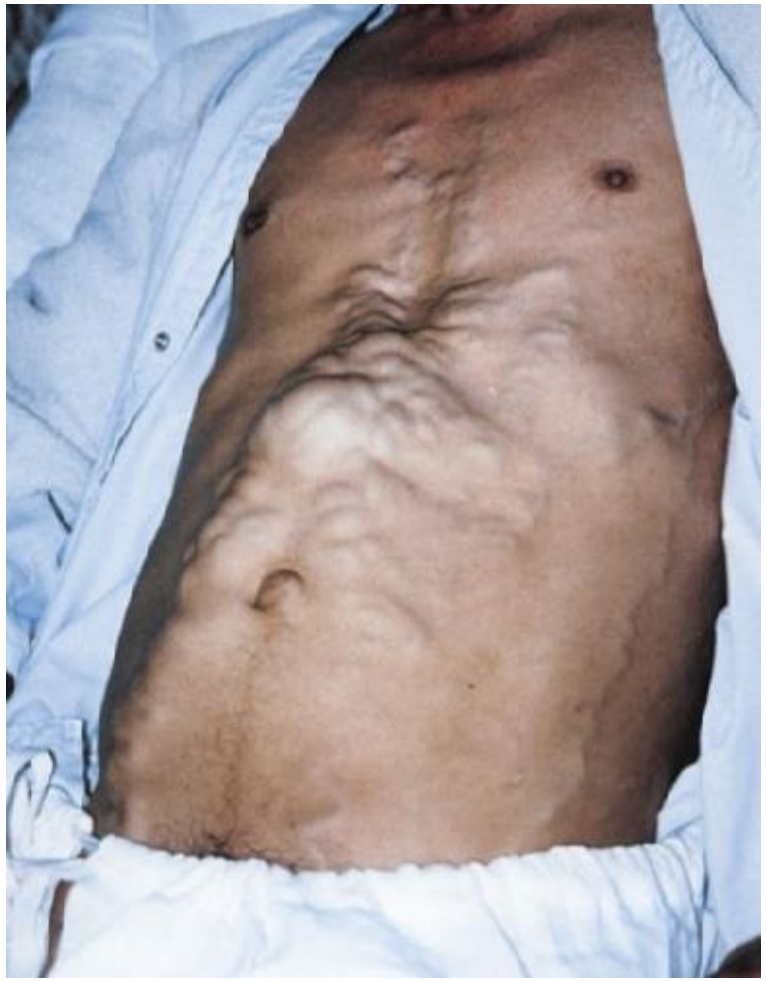
PALMAR ERYTHEMA

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



DUPUYTREN’S CONTRACTURE

CAPUT MEDUSA



Diagnosis

A- Diagnosis of liver cirrhosis

1- Suggestive:

- Sonar (echogenicity, irregular borders & prominent caudate lobe).
- C.T. scan. .

B-To assess function & complications:

- Laboratory Findings : CBC, L.F.T, PT, PTT, INR ,KFT.

-Upper G.I.T endoscopy

Triphasic CT and dynamic MRI for detecting HCC

N.B: once cirrhosis developed, screening for HCC must be done every 6 months using ultrasound and AFP.

- Anemia: is present in up to 75% of patients. It may be normocytic anemia of chronic disease or due to acute variceal hemorrhage or hypersplenism; microcytic in chronic blood loss due to portal gastropathy; macrocytic due to Vit B12 or folate deficiency.

- - Leukocytic count may be low, reflecting hypersplenism, or high, suggesting infection

- - Thrombocytopenia, the most common cytopenia in cirrhotic patients, is secondary to alcohol-induced marrow suppression, sepsis, folate deficiency, or splenic sequestration

- **C- To find cause**
- -Viral markers (HBsAg, HCV Ab.), auto antibodies & Fe, Cu level

Liver Biopsy

- Widely replaced by the use of ultrasound and fibroelastography along with serologic testing
- Performed 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

TABLE 11.1 ■ Etiology and Diagnostic Evaluation of the Common Causes of Cirrhosis

Etiology	Diagnostic Evaluation
Infection	
Hepatitis B	HBsAg, anti-HBs, anti-HBc, HBV DNA
Hepatitis C	Anti-HCV, HCV RNA
Hepatitis D	Anti-HDV
Toxins	
Alcohol	History, AST/ALT ratio, IgA level, liver biopsy
Cholestasis	
Primary biliary cholangitis	AMA, IgM level, liver biopsy
Secondary biliary cirrhosis	MRCP, ERCP, liver biopsy
Primary sclerosing cholangitis	MRCP, ERCP, liver biopsy
Autoimmune	
Autoimmune hepatitis	ANA, IgG level, smooth muscle antibodies, liver-kidney microsomal antibodies, liver biopsy
Vascular	
Cardiac cirrhosis	Echocardiogram, liver biopsy
Budd-Chiari syndrome	CT, US, MRI/MRA
Sinusoidal obstruction syndrome	History of offending drug use, liver biopsy
Metabolic	
Hemochromatosis	Iron studies, *HFE* gene mutation, liver biopsy
Wilson disease	Serum and urinary copper, ceruloplasmin, slit-lamp eye examination, liver biopsy
Alpha-1 antitrypsin deficiency	Alpha-1 antitrypsin level, protease inhibitor type, liver biopsy
NASH	History, risk factors (obesity, diabetes mellitus, hyperlipidemia), liver biopsy
Cryptogenic	Exclude NASH, celiac disease, drugs

AMA, Antimitochodrial antibodies; *anti-HBc,* antibody to hepatitis B core antigen; *anti-HBs,* antibody to hepatitis B surface antigen; *anti-HCV,* antibody to hepatitis C virus; *anti-HDV,* antibody to hepatitis D virus; *AST,* aspartate aminotransferase; *ALT,* alanine aminotransferase; *CT,* computed tomography; *ERCP,* endoscopic retrograde cholangiopancreatography; *HBsAg,* hepatitis B surface antigen; *IgA,* immunoglobulin A; *IgM,* immunoglobulin M; *MRCP,* magnetic resonance cholangiopancreatography; *MRA,* magnetic resonance angiography; *MRI,* magnetic resonance imaging; *NASH,* nonalcoholic steatohepatitis; *US,* ultrasonography.

treatment

A- Treatment of liver cell failure and portal hypertension.

-Liver transplantation in appropriate candidates is curable

B-Treatment of the cause if curable: Ex. hemochromatosis & Wilson.

C-Treatment of decompensation consequence or complications

1. Ascites and edema 2- Bleeding varices.

3-. Spontaneous bacterial peritonitis 4-. Hepatorenal syndrome

5. Hepatic encephalopathy

6-Hepatopulmonary syndrome Long-term oxygen therapy is recommended for severely hypoxemic patients.

7- Hepatocellular carcinoma

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

Poor Prognostic Indicators in Cirrhosis

Blood tests

- Low albumin (< 28 g/L)
- Low serum sodium (< 125 mmol/L)
- Prolonged prothrombin time > 6 seconds above normal value
- Raised creatinine > 130 µmol/L

Clinical

- Persistent jaundice
- Poor response to therapy
- Ascites
- Variceal hemorrhage
- Neuropsychiatric complications developing with progressive liver failure
- Small liver
- Persistent hypotension


Thank You!