COMPLICATIONS OF CIRRHOSIS

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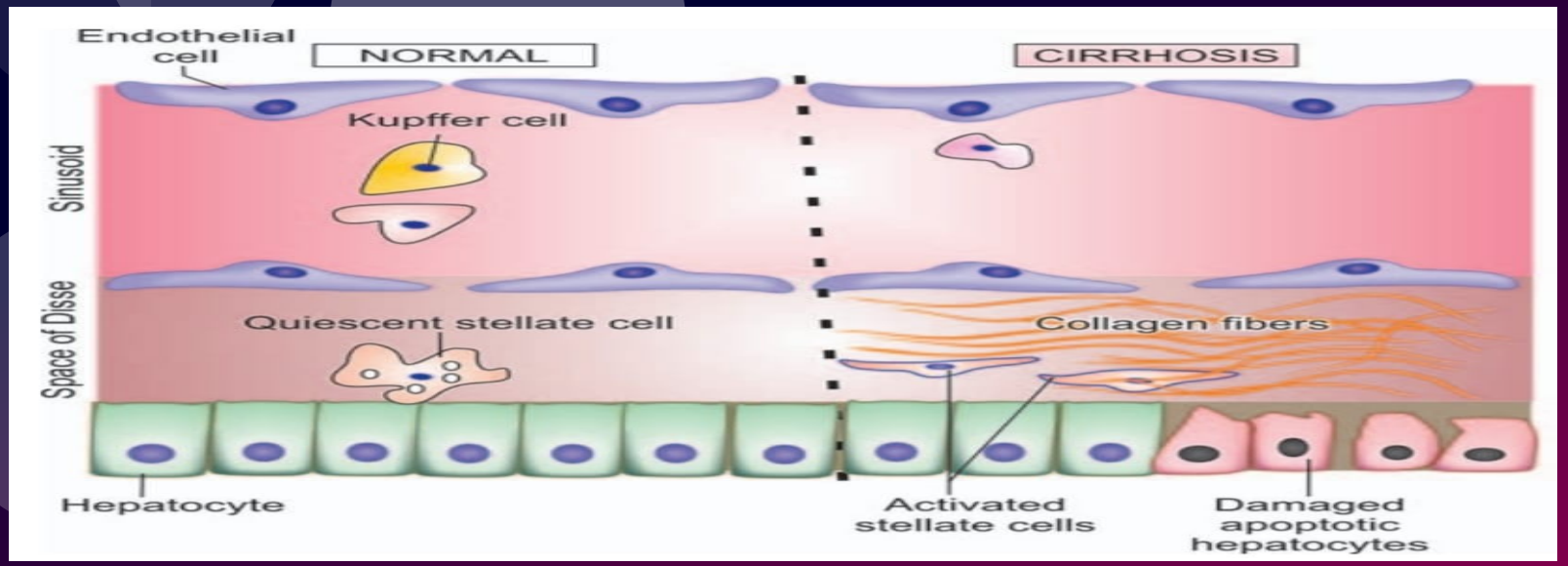
CIRRHOSIS

- End stage liver damage
- Cirrhosis is characterised by diffuse hepatic fibrosis and nodule formation.
- It is a diffuse process characterized by fibrosis and conversion of normal architecture to abnormal regenerating nodules.

PATHOGENESIS

Hepatocyte damage → Release of cytokines and chemokines → Activate stellate cells in the space of Disse



Transformed into highly fibrogenic with myocontractile Like property → Constrict sinusoidal vascular channel → Increased vascular resistance → Produce collagen → Fibrosis

CAUSES OF CIRRHOSIS

- Alcohol
- Chronic viral hepatitis (B or C)
- Non-alcoholic fatty liver disease
- Immune: primary sclerosing cholangitis, autoimmune liver disease
- Biliary: primary or secondary biliary cirrhosis, cystic fibrosis
- Genetic: haemochromatosis, α1antitrypsin deficiency, Wilson’s disease
- Chronic venous outflow obstruction
- Cryptogenic (unknown)

WHAT CAUSE HEPATOCYTE DAMAGE

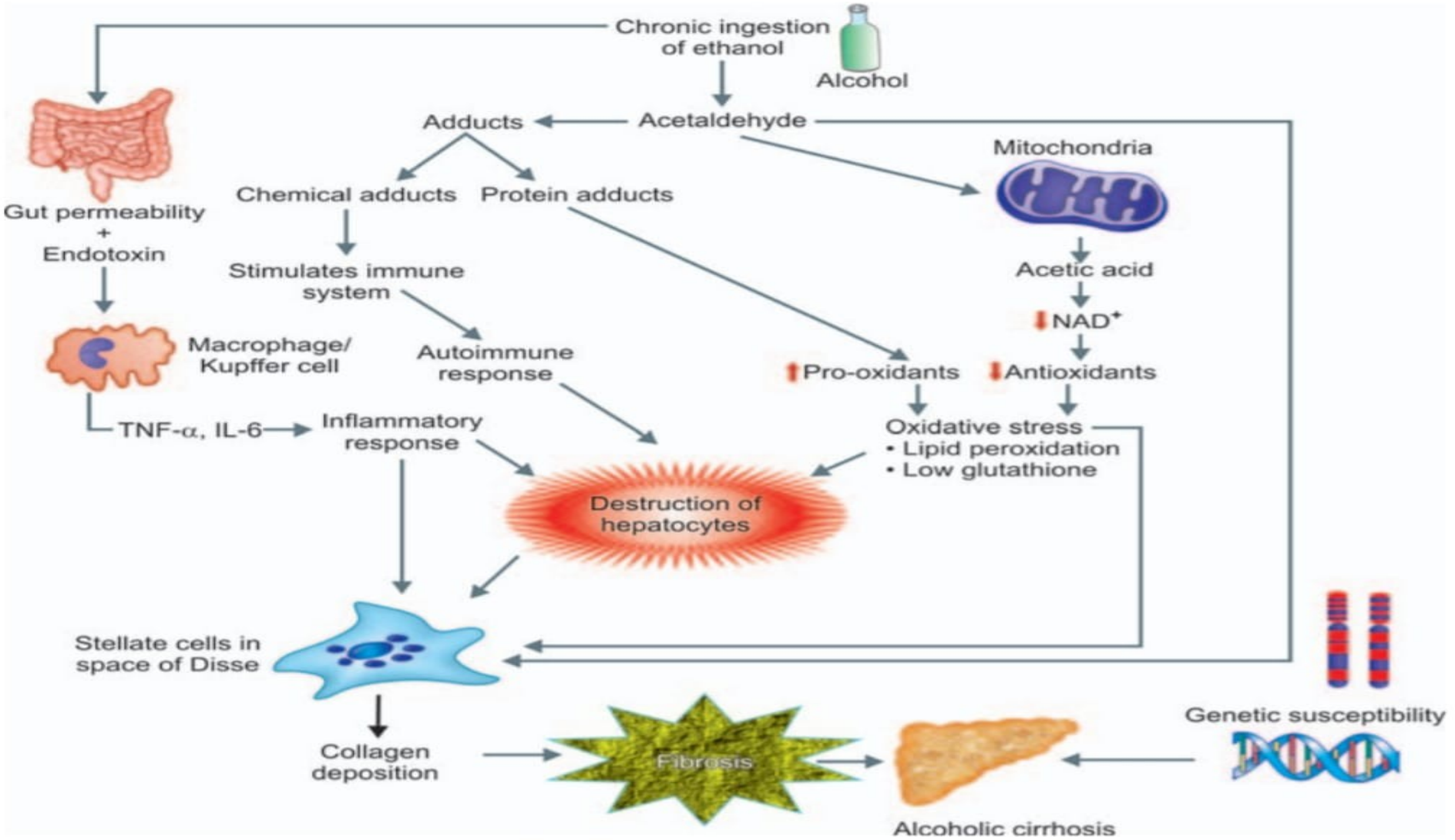


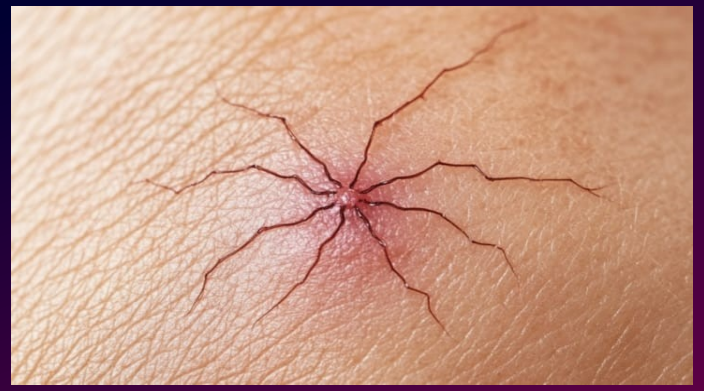
Fig. 19.13: Pathogenesis of alcoholic liver disease

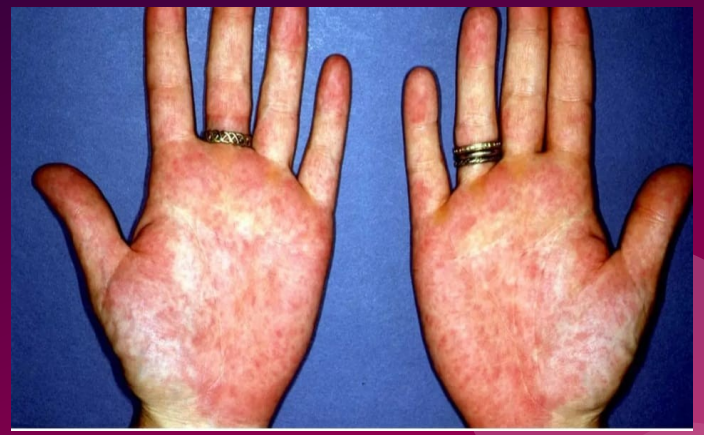
CLINICAL FEATURES

- Cirrhosis may be entirely asymptomatic
- Common symptoms include weakness, fatigue, muscle cramps, weight loss and non-specific digestive symptoms such as anorexia, nausea, vomiting and upper abdominal discomfort.

22.27 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





PROGNOSIS

- Cirrhosis is characterized into two prognostic groups: Compensated and Decompensated

Decompensated

- ascites, variceal bleeding, jaundice, encephalopathy
- median survival rate is around 2 years (variable)

Compensated

- period of non specific symptoms like flatulence, fatigue, anorexia
- relatively good prognosis with median survival more than 12 years

1. PORTAL HYPERTENSION

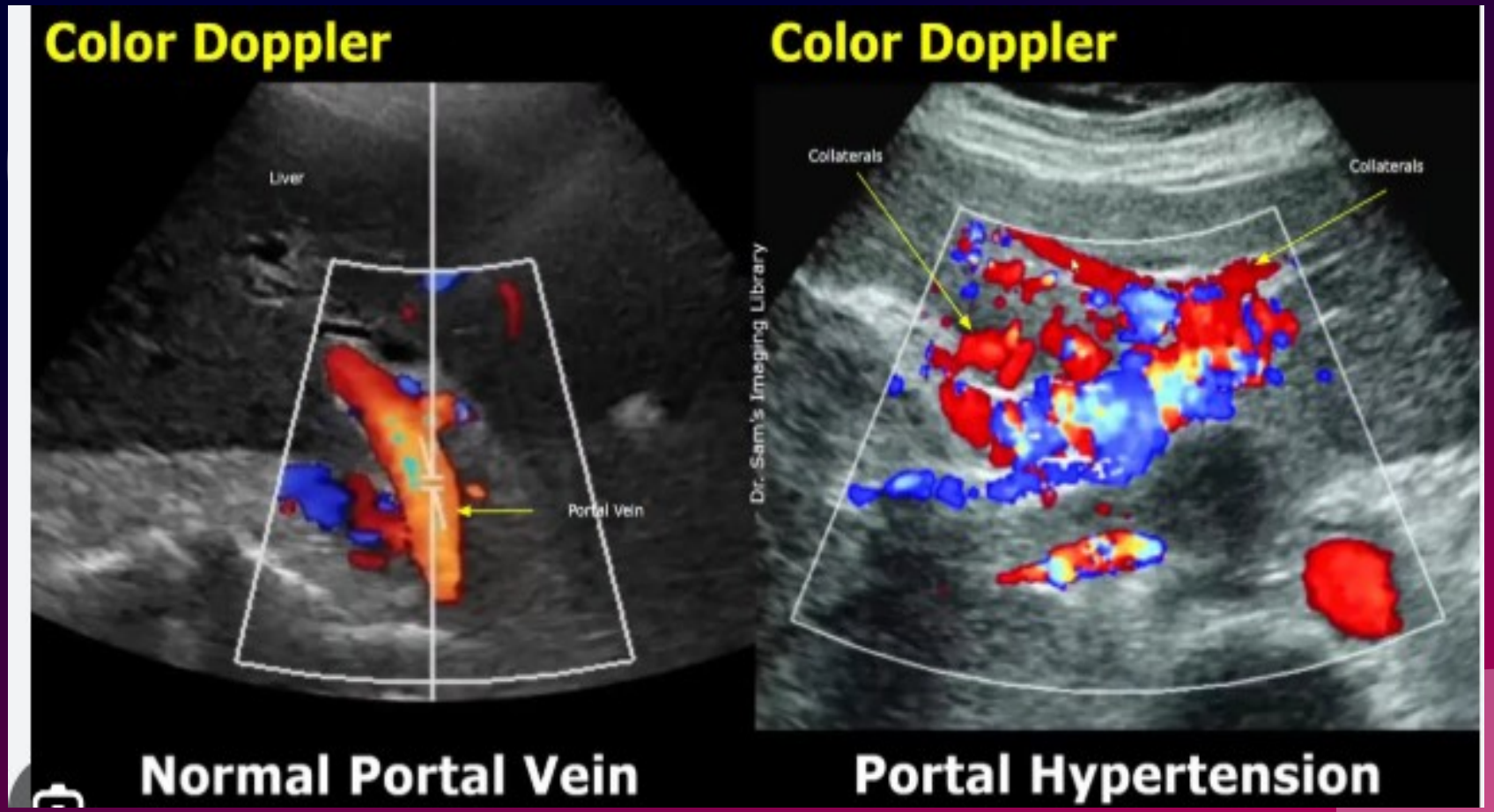
- Portal hypertension is characterised by prolonged elevation of the portal venous pressure (normally 5–6 mmHg).
- Clinically significant portal hypertension is present when the gradient exceeds 10 mmHg and risk of variceal bleeding increases over 12 mmHg.
- Cirrhosis causes 90% or more of portal hypertension in adults in developed countries.
- In cirrhosis and other conditions, there is obstruction to the portal venous flow by fibrosis, thrombosis and pressure by regenerative nodules.
- About 30-60% patients of cirrhosis develop significant portal hypertension.

CLINICAL FEATURES

- **Splenomegaly** is a cardinal finding. A diagnosis of portal hypertension is unlikely when splenomegaly cannot be detected clinically or by USS.
- Collateral vessels may be visible on the anterior abdominal wall and occasionally several radiate from the umbilicus to form a **caput medusae.**
- **Hematemesis** and **melena** due to variceal bleeding
- **Fetor hepaticus** due to portosystemic shunting.

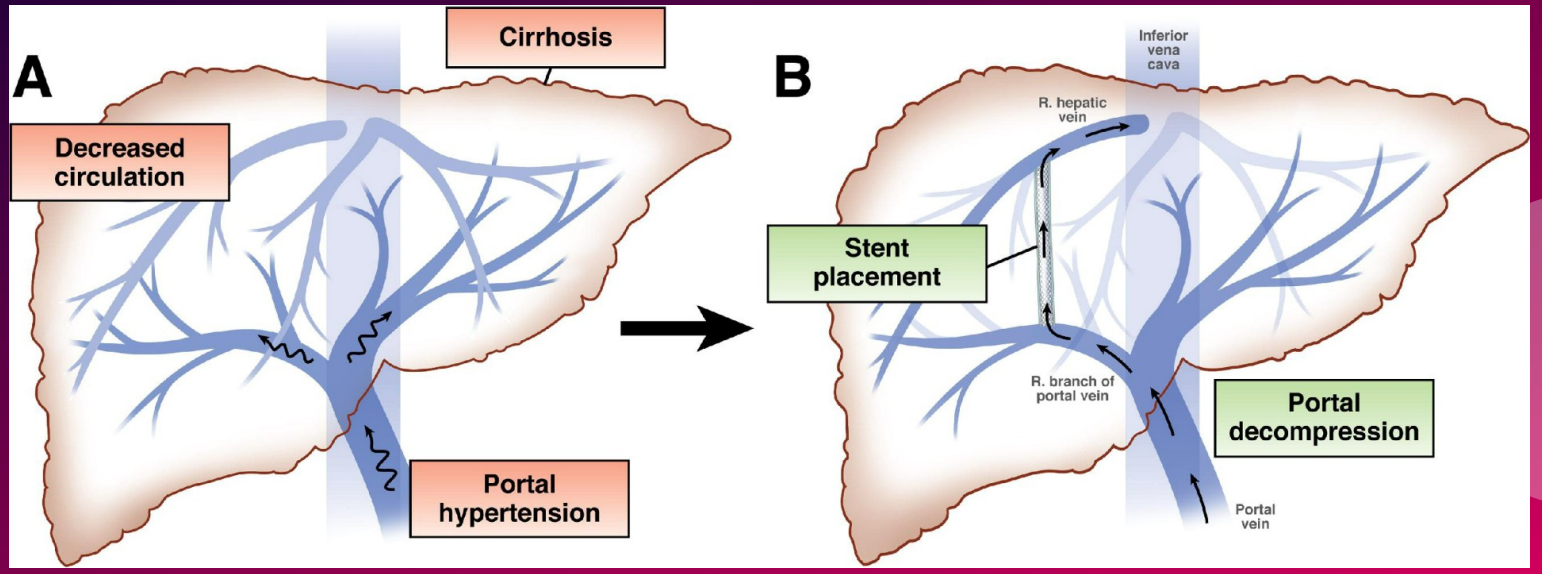
INVESTIGATIONS

- Upper GI Endoscopy : used to detect and to check periodically for varices.
- USG: dilated collaterals around gastroesophageal junction and splenic hilum, splenomegaly, dilated portal vein and splenic vein.
- CT and MRI angiography: can identify portal vein clot and hepatic vein patency.
- Blood tests : anemia and thrombocytopenia


Color Doppler
Liver
Portal Vein
Normal Portal Vein
Color Doppler
Collaterals
Collaterals
Dr. Sam's Imaging Library
Portal Hypertension

MANAGEMENT

- Reduction of portal pressure: Non-selective beta-blockers such as propranolol , nitrates
- TIPSS (transjugular intrahepatic portosystemic shunt): portal-systemic shunt placed through internal jugular vein percutaneously. It depresses the portal circulation.



2. ASCITES

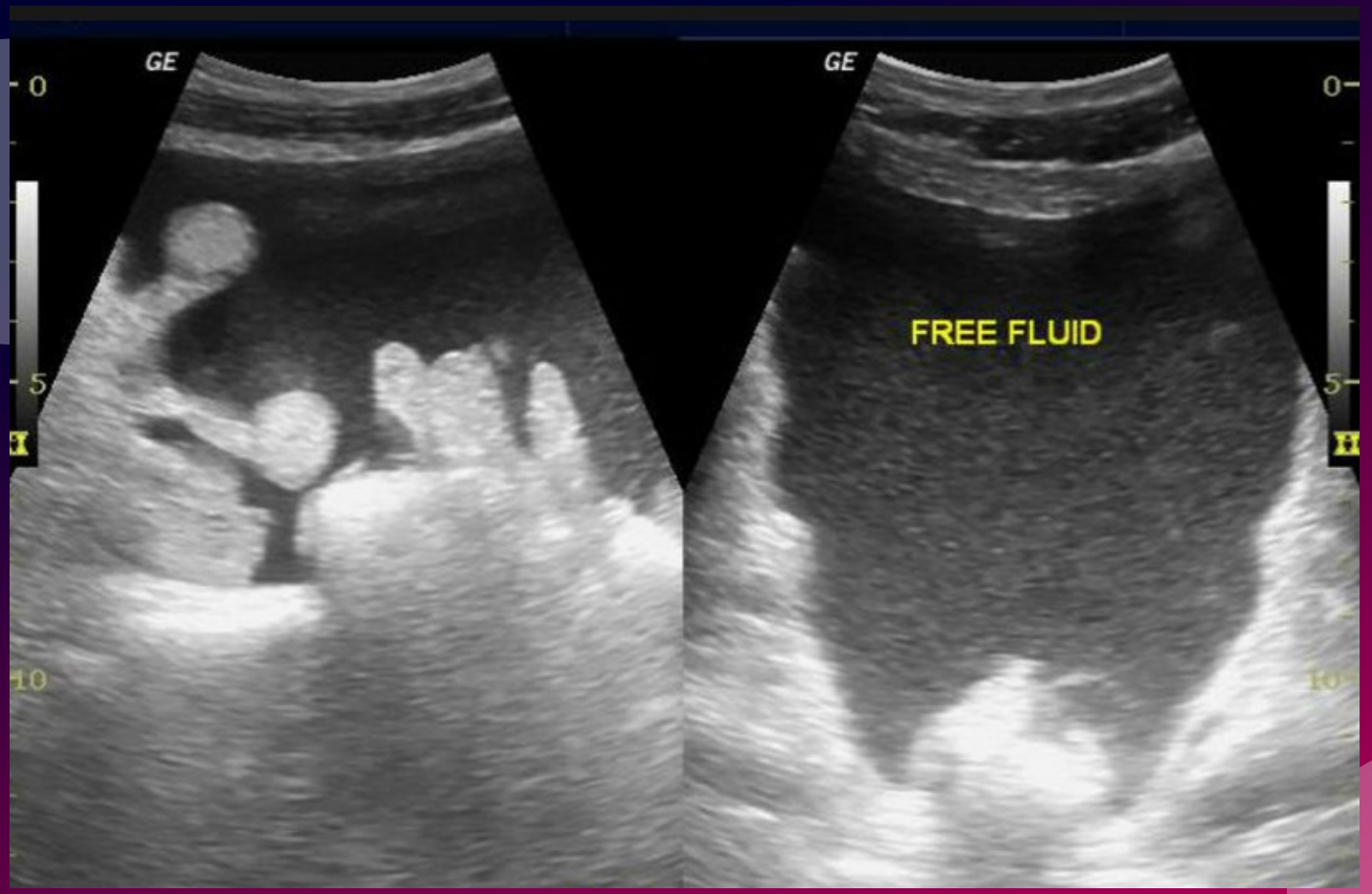
- The accumulation of excess fluid in the peritoneal cavity
- Ascites usually becomes clinically detectable when at least 500 mL have accumulated
- Appearance of fluid: clear, straw coloured or light green
- The fluid is transudative , has less than 5g/dl of protein content and specific gravity of about 1.01.

CLINICAL FEATURES

- Abdominal distension, abdominal pain, loss of appetite, shortness of breath, nausea, vomiting, pedal edema
- Fullness in the flanks, fluid thrill, flank dullness, shifting dullness, spider angioma, palmar erythema.
- Other signs include everted umbilicus, divarication of the recti, scrotal oedema and dilated abdominal veins

INVESTIGATIONS

- USS is the best means of detecting ascites.
- Paracentesis may point to the underlying cause.
- Serum-ascites albumin gradient (SAAG) : >1.1 g/dL due to portal hypertension


GE
0
5
10
GE
FREE FLUID
0
5
10

MANAGEMENT

- Sodium restriction
- Diuretics : Spironolactone is the drug of choice
- Transjugular intrahepatic portosystemic stent shunt (TIPSS)
- Paracentesis

3. VARICEAL BLEEDING

- Bleeding usually occurs from varices near the gastro-oesophageal junction or in the stomach.
- The mortality from bleeding oesophageal varices is about 45% in those with advanced liver disease.

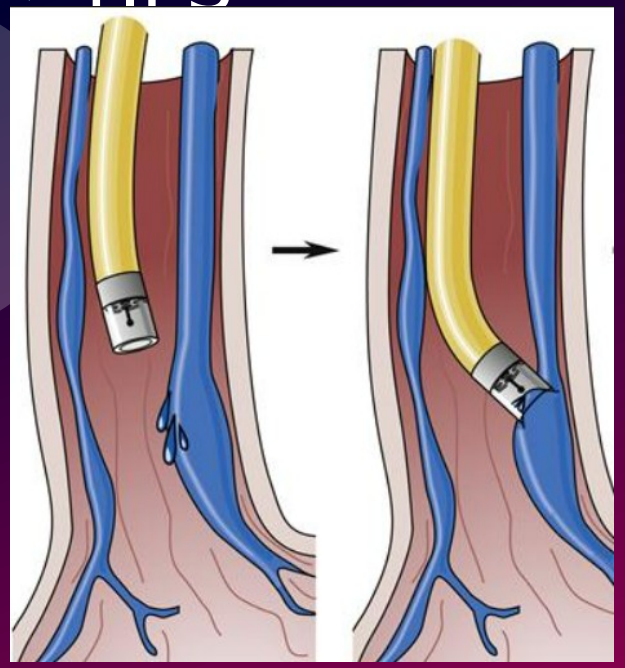
DIAGNOSIS :

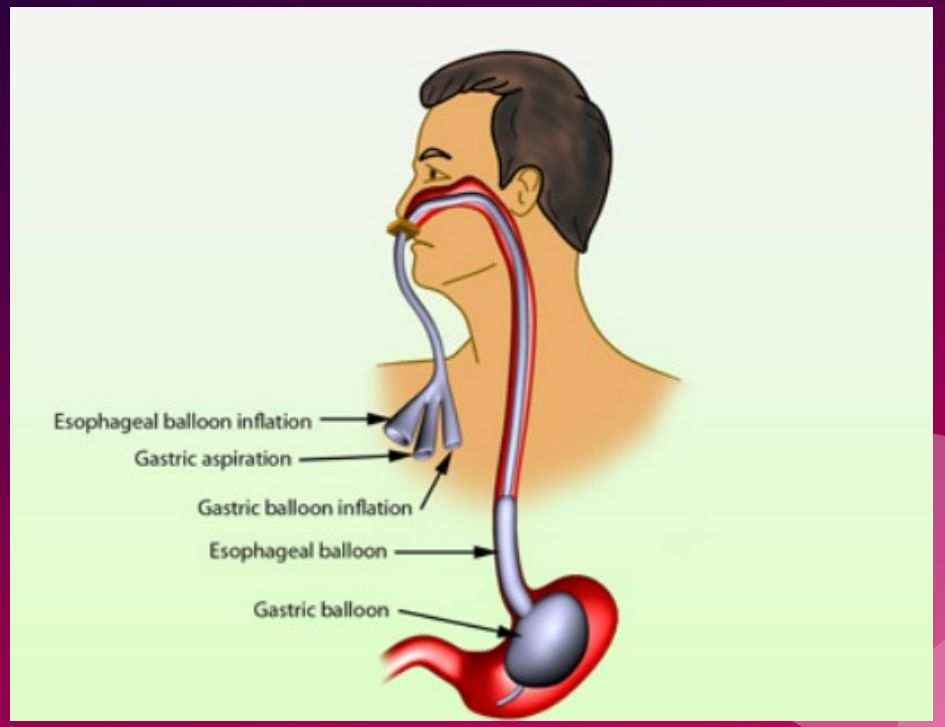
- Hematemesis: “coffee ground” appearance, Melena.
- Hyperactive bowel sounds and an elevated blood urea and low hemoglobin suggest upper GI bleeding.
- Significant variceal bleed: pallor, tachypnea, tachycardia, and hypotension.
- Nasogastric tube lavage reveals fresh or altered blood in the stomach.
- Upper GI endoscopy can confirm the diagnosis.

MANAGEMENT OF ACUTE VARICEAL BLEEDING

- All patients with cirrhosis and GI bleeding should receive prophylactic broad-spectrum antibiotics such as ciprofloxacin.
- Pharmacological reduction of portal venous pressure : Terlipressin
- Diagnostic endoscopy with banding or sclerotherapy
- Variceal banding : varices are sucked up into an endoscope accessory and occluded with a tight rubber band
- Sclerotherapy: varices are injected with a sclerosing agent to obliterate them

- Balloon tamponade: Sengstaken-Blakemore tube with two balloons which exert pressure in the fundus of the stomach and in the lower oesophagus respectively when inflated. Oesophageal balloon compresses oesophageal varices.
- TIPS





4. HEPATIC ENCEPHALOPATHY

- Hepatic encephalopathy is a neuropsychiatric syndrome caused by liver disease
- Precipitating causes include trauma, drugs, infection, protein load (including GI bleeding) and constipation.
- Liver failure and portosystemic shunting of blood are two important factors underlying hepatic encephalopathy

13.7 Clinical grading of hepatic encephalopathy

Clinical grade	Clinical signs
Grade 1	Poor concentration, slurred speech, slow mentation, disordered sleep rhythm
Grade 2	Drowsy but easily rousable, occasional aggressive behaviour, lethargic
Grade 3	Marked confusion, drowsy, sleepy but responds to pain and voice, gross disorientation
Grade 4	Unresponsive to voice, may or may not respond to painful stimuli, unconscious

CLINICAL FEATURES

- Alteration of sleep cycle is an early symptom
- Confusion, restlessness, drowsiness, disorientation, stupor seen in severe cases

Examination

- A flapping tremor (asterixis).
- Inability to perform simple mental arithmetics
- Inability to draw objects such as a star (constructional apraxia)
- Hyper-reflexia.
- Bilateral extensor plantar responses

INVESTIGATIONS

- Serum ammonia level
- EEG shows diffuse slowing of the normal alpha waves with eventual development of delta waves
- Serum electrolytes, urea, creatinine, glucose, etc
- Brain imaging (CT or MRI) is required if stroke is suspected

MANAGEMENT

- Lactulose (15–30 mL 3 times daily) produces an osmotic laxative effect
- Rifamixin(400 mg 3 times daily) reduces the bacterial content of the bowel.
- Dietary protein restriction is no longer recom mended

5. SPONTANEOUS BACTERIAL PERITONITIS

- Most common bacterial infection with cirrhosis
- Translocation of bacteria from intestine into ascites
- Causative organism: Escherichia coli (most common)
- Presents with complaints of abdominal pain or fever with obvious features of cirrhosis and ascites.
- High rate of acute kidney injury and mortality

INVESTIGATIONS:

- Paracentesis and blood culture
- Ascitic fluid may show cloudy fluid and neutrophil count of >250 x 10^6/L
- Blood culture positive for causative organism

TREATMENT

- Cefotaxime or Piperacillin/Tazobactam
- Prophylaxis with Norfloxacin (400 mg/day), ciprofloxacin (750 mg/week) or cotrimoxazole (960 mg/day).

6. HEPATORENAL SYNDROME

- Renal dysfunction due to severe renal vasoconstriction due to underfilling of the arterial circulation.
- Type 1 hepatorenal syndrome (HRS-AKI) : Characterised by progressive oliguria, a rapid rise of the serum creatinine and a very poor prognosis.
- Type 2 hepatorenal syndrome(HRS-NAKI): Characterised by moderate and stable increase in serum creatinine, and has a better prognosis.
- The renal failure in the hepatorenal syndrome is reversible with improvement in hepatic function.
- Diagnosis of hepatorenal syndrome should be made only after excluding other causes producing concomitant damage to both the organs, circulatory failure

MANAGEMENT

- Identifying and treating precipitating factors
- Diuretics and beta blockers should be prevented.
- Nephrotoxic drugs (vasodilators, NSAIDS) should be stopped.
- Volume replacement to treat fluid loss/deficits
- IV albumin infusion in combination with Terlipressin
- TIPSS

7. HEPATOCELLULAR CARCINOMA

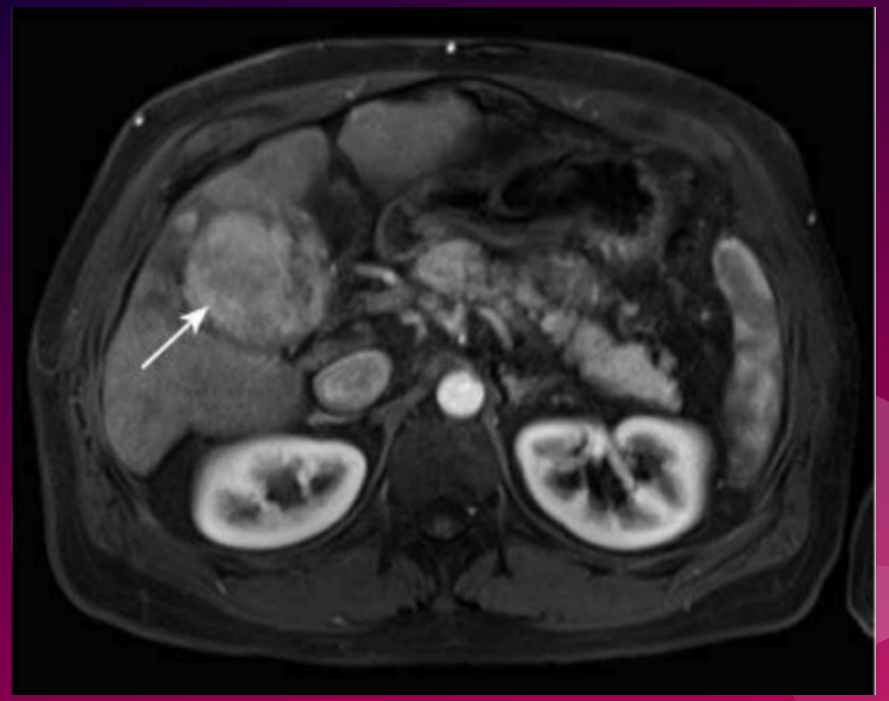
- Hepatocellular carcinoma (HCC) is the most common primary liver tumour.
- Cirrhosis is present in 75–90% of individuals with HCC and is an important risk factor.

CLINICAL FEATURES

- _In patients with cirrhosis, HCC may cause variceal haemorrhage, increasing ascites or deterioration in jaundice
- Other symptoms include weight loss, anorexia and abdominal pain.
- Examination may reveal hepatomegaly or a right hypochondrial mass.

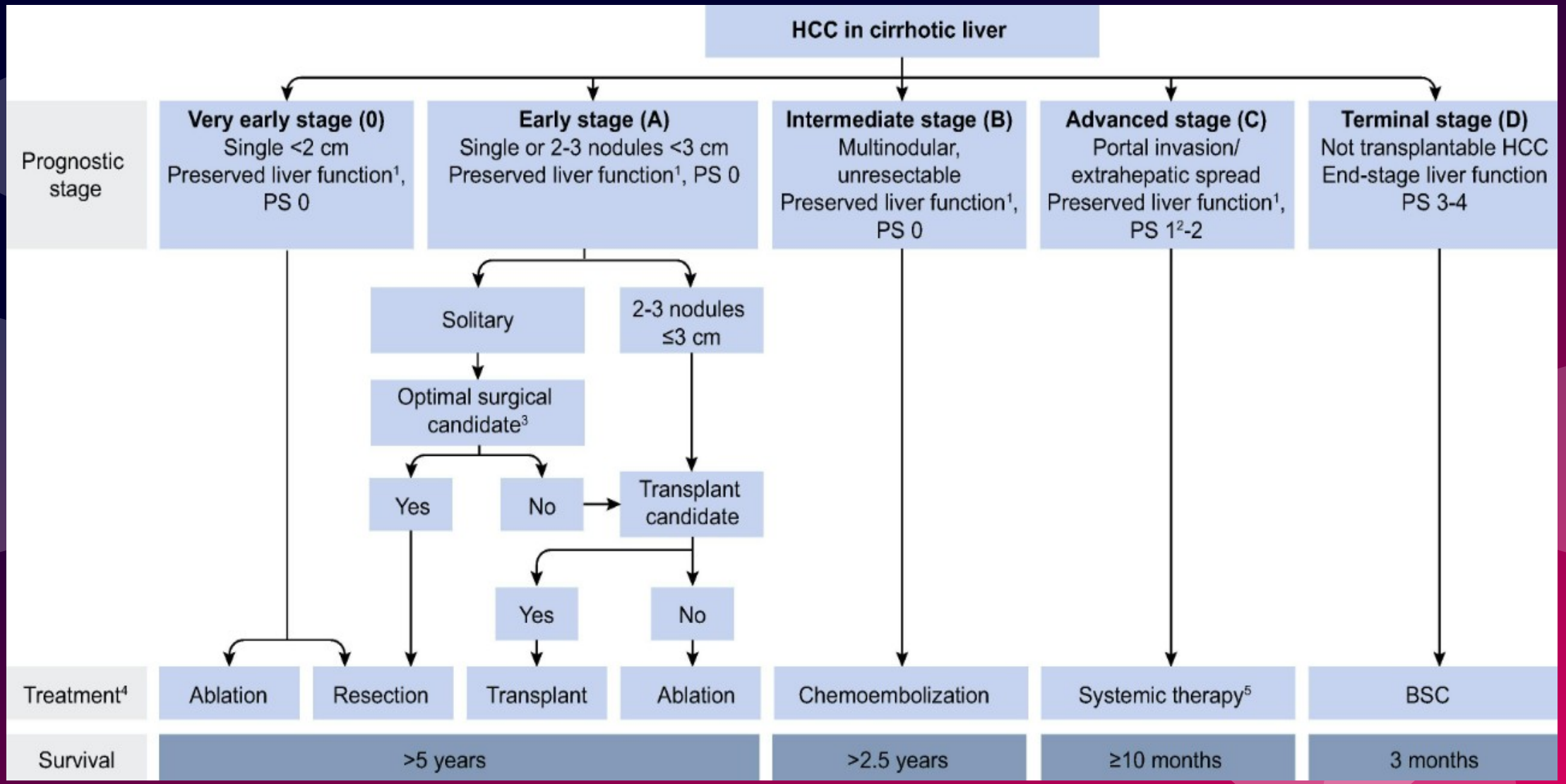
INVESTIGATIONS

- AFP is produced by 60% of HCCs
- Ultrasound: will detect focal liver lesions as small as 2–3 cm, also show evidence of portal vein involvement and features of coexistent cirrhosis
- Liver biopsy: can be done for histological confirmation



MANAGEMENT

- Hepatic Resection
- Liver Transplantation
- Percutaneous Ablation : Percutaneous ethanol injection into the tumour
- Chemo-embolisation: Hepatic artery embolisation with Gelfoam and doxorubicin


HCC in cirrhotic liver
Prognostic stage
Very early stage (0)
Single <2 cm
Preserved liver function[1], PS 0
Early stage (A)
Single or 2-3 nodules <3 cm
Preserved liver function[1], PS 0
Intermediate stage (B)
Multinodular, unresectable
Preserved liver function[1], PS 0
Advanced stage (C)
Portal invasion/ extrahepatic spread
Preserved liver function[1], PS 1[2]-2
Terminal stage (D)
Not transplantable HCC
End-stage liver function
PS 3-4
Solitary
2-3 nodules ≤3 cm
Optimal surgical candidate[3]
Yes
No
Transplant candidate
Yes
No
Treatment[4]
Ablation
Resection
Transplant
Ablation
Chemoembolization
Systemic therapy[5]
BSC
Survival
>5 years
>2.5 years
≥10 months
3 months

8. HEPATOPULMONARY SYNDROME

- Arterial hypoxaemia in a patient with cirrhosis without significant lung disease.
- Due to intrapulmonary shunting and significant ventilation-perfusion mismatch.
- Clinical symptoms: finger clubbing, spider angioma, platypnea

DIAGNOSIS

- Demonstrating hypoxemia, no evidence of significant lung disease, and shunt on bubble echocardiography

TREATMENT

- Oxygen supplementation, liver transplantation

OTHER COMPLICATIONS OF CIRRHOSIS

- Chronic relapsing pancreatitis
- Gallstones usually of pigment type, are seen twice more frequently in patients with cirrhosis
- Infections are more frequent in patients with cirrhosis due to impaired phagocytic activity of reticuloendothelial system.
- Haematologic derangements such as bleeding disorders and anaemia due to impaired hepatic synthesis of coagulation factors and hypoalbuminaemia
- Endocrine disorders : gynecomastia , testicular atrophy in males and amenorrhea in females

REFERENCE

- Davidson’s Essentials of Medicine
- Robbins and Cotran Pathological Basis of Disease 9th Edition
- Textbook of Pathology Harshmohan 6th Edition

THANK YOU