Complications of Liver Cirrhosis

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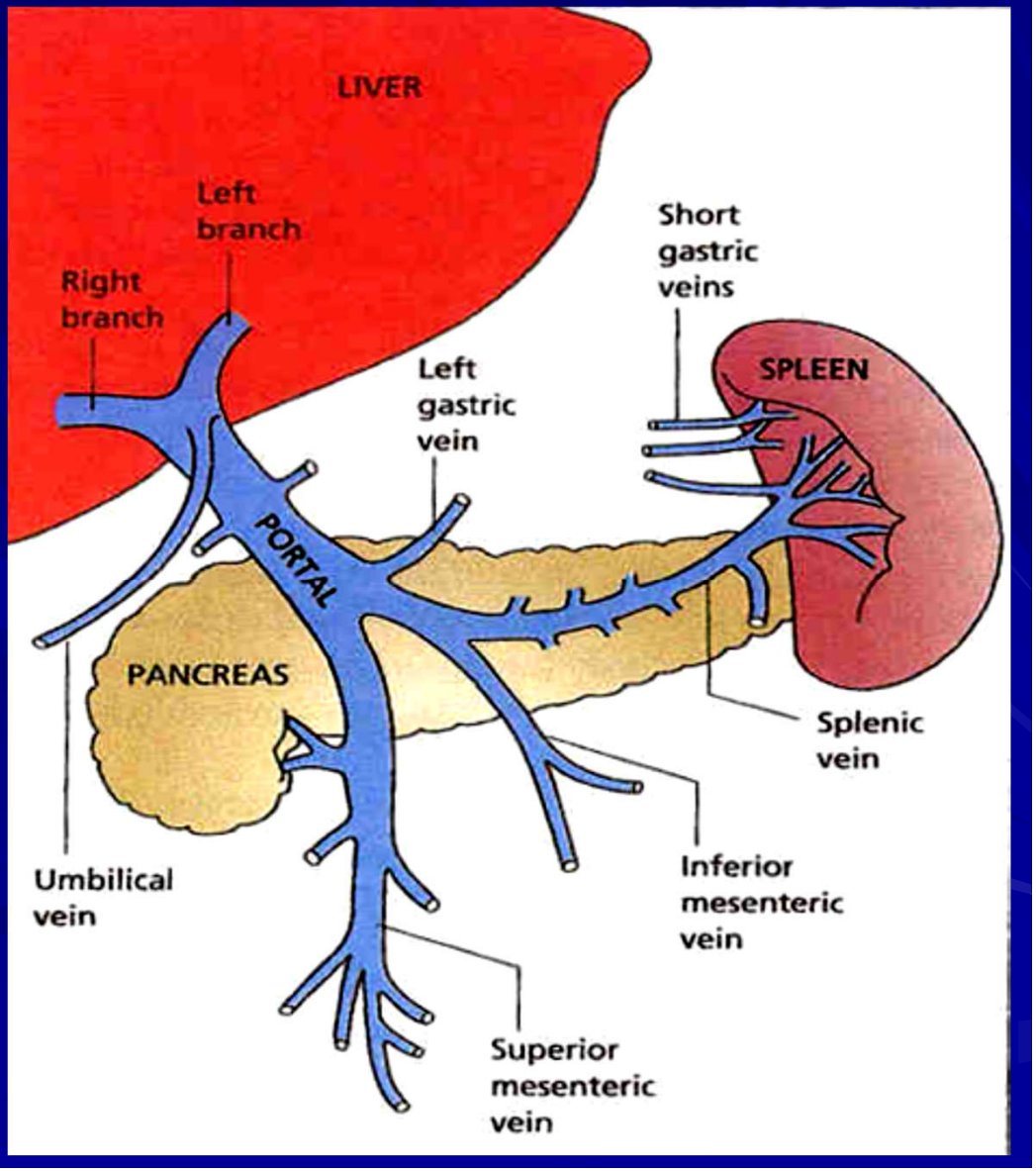
Complications of LC

- Portal hypertension and gastrointestinal hemorrhage
- Ascites
- Portosystemic encephalopathy
- Renal failure (hepatorenal syndrome)
- Hepatopulmonary syndrome
- Hepatocellular carcinoma
- Bacteremia, infections
- Malnutrition

Portal Hypertension

Anatomy of the portal venous system

- The portal vein is formed by the union of the superior mesenteric and splenic veins.
- The pressure within it is normally 5-8 mmHg.



Pathophysiology

- Portal venous pressure above 10-12 mmHg
- Mainly due to increased portal vascular resistance and to a lesser extent to increased portal blood flow.
- Leads to development of collaterals between the portal and systemic veins.

The main sites of collaterals are:

- **At the gastro-esophageal junction between:**

The Lt gastric, short gastric veins (portal) and azygos minor, intercostal veins forming esophageal and gastric varices

- **At The rectum between:**

  Superior hemorrhoidal vein (portal) and inferior, middle hemorrhoidal veins (systemic) forming rectal varices

- ***At the anterior abdominal wall between :***

  Paraumbilical veins (portal) and superior, inferior epigastric veins (systemic) forming caput medusae.

- ***Between splenic vein and Lt renal vein.***

- ***Where abdominal viscera come in contact with the diaphragm or retroperitoneal tissues.***

Causes of portal hypertension

Portal hypertension can be classified according to the site of obstruction:

1. Prehepatic – due to blockage of portal vein before the liver as in:

   - portal vein thrombosis (due to neonatal sepsis, inherited prothrombotic conditions)

   - splenic vein thrombosis

2. Intrahepatic – due to distortion of the liver architecture:

- presinusoidal (e.g. in schistosomiasis)
- sinusoidal (in all causes of cirrhosis).
- postsinusoidal (as in veno-occlusive disease, Budd-Chiari syndrome)

3. Posthepatic – due to venous blockage outside the liver (rare) as in:

- right-sided heart failure
- constrictive pericarditis.
- IVC obstruction

Clinical features

- May be asymptomatic.
- Presenting features may include:

1. Splenomegaly
2. Features of chronic liver disease
3. Hematemesis or melena.
4. Ascites
5. Encephalopathy.

Investigations

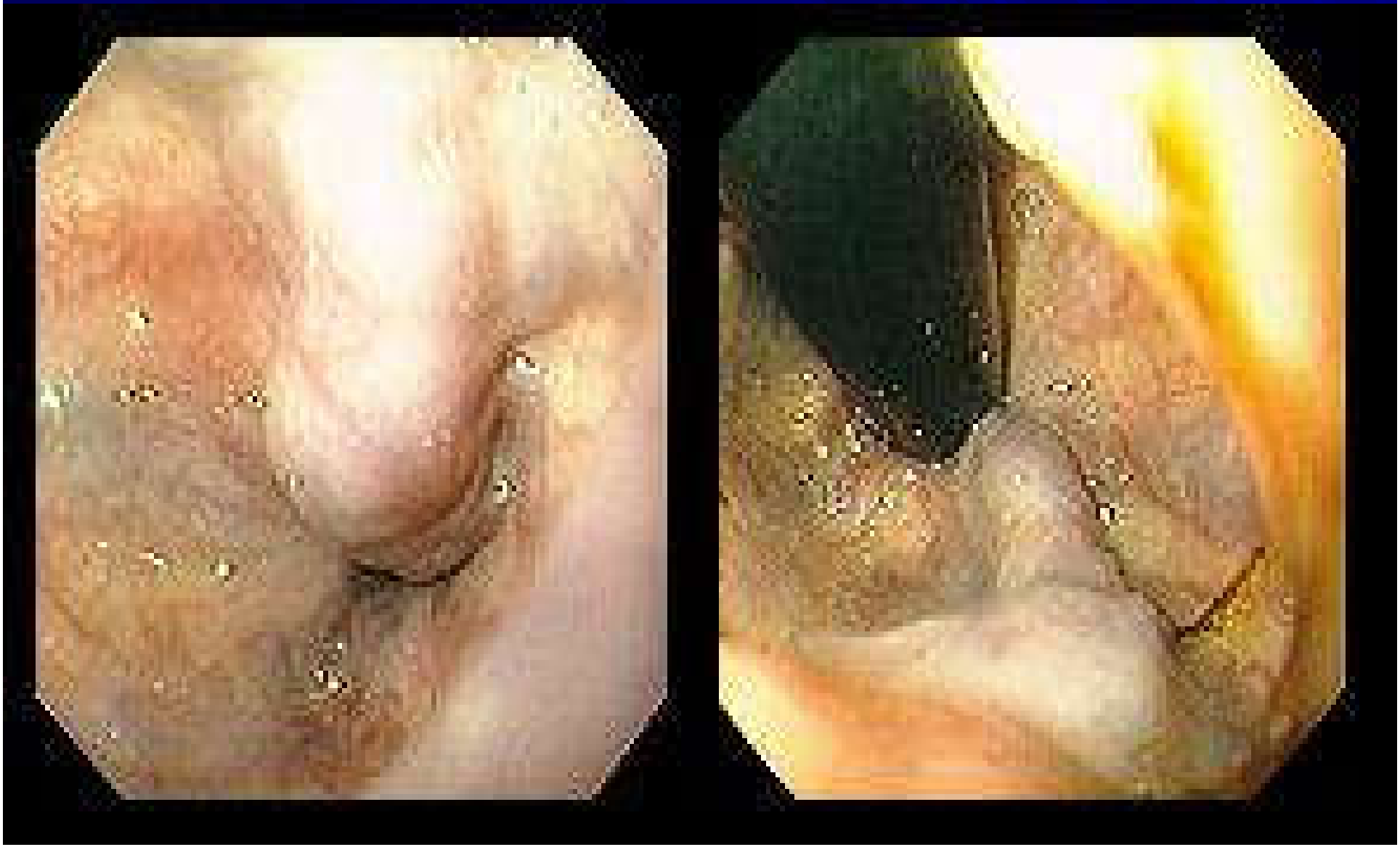
- Endoscopy
- Abdominal US or CT scan
- Doppler US
- MRI and MRA
- Direct portal pressure measurement.

NB: The most common complication of portal hypertension is the development of varices: esophageal v, gastric v, rectal v, portal hypertensive gastropathy, colorectal v & colopathy

Diagnosis of gastroesophageal varices

- History: hematemesis, melena
- Physical examination
- US examination of abdomen
- Endoscopy

Esophageal Varices on EGD



Management

1. Initial Management of active bleeding

- General management

1. Assessment and monitoring of vital signs
2. Two IV lines, blood samples to type and cross match for blood transfusion
3. Hb, prothrombin time, urea, creatinine, electrolytes, liver biochemistry and blood cultures.
4. Start prophylactic antibiotics – third generation cephalosporins, e.g. cefotaxime

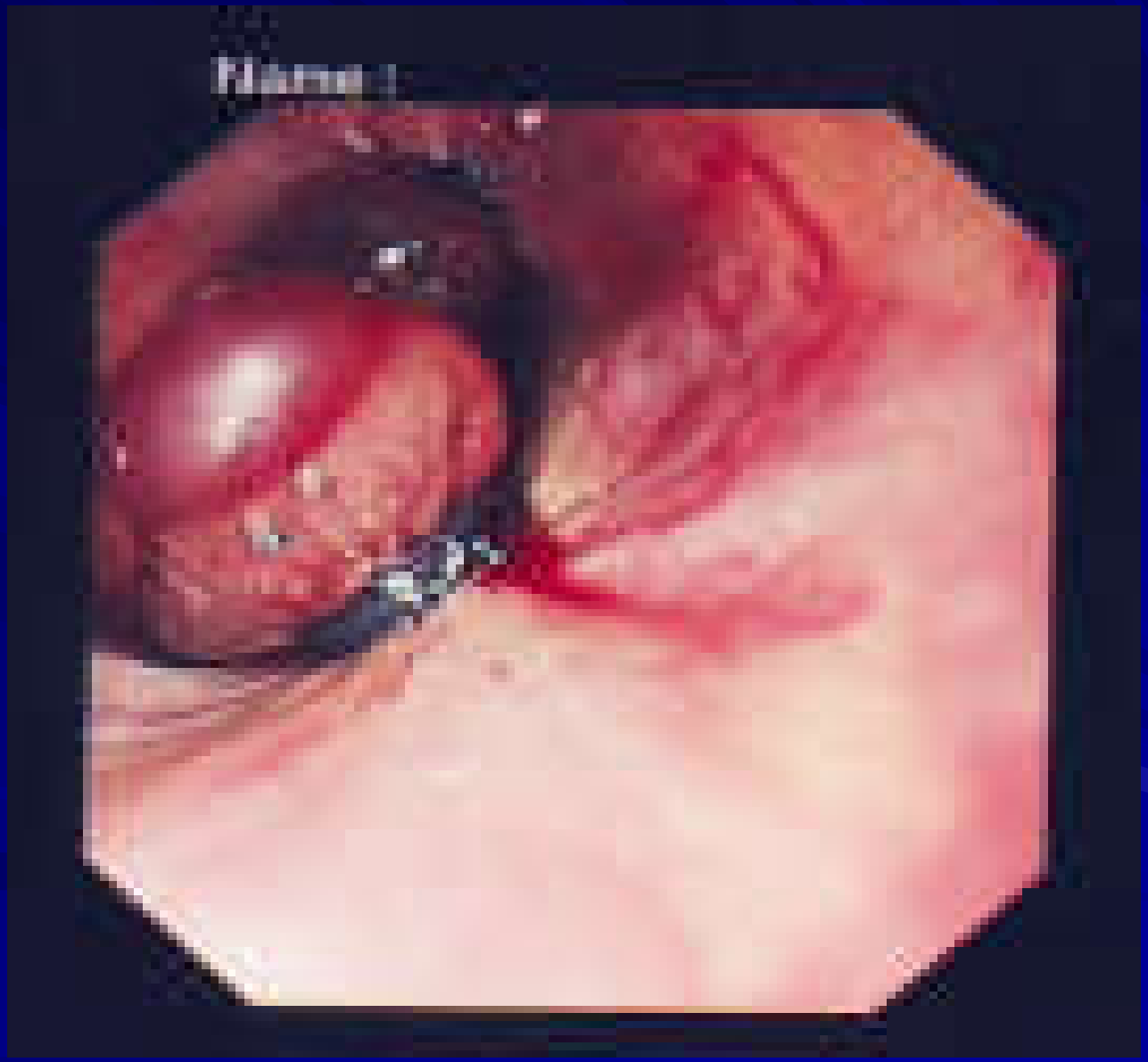
- Resuscitation

1. Monitoring of general condition of the patient - pulse and blood pressure, observation of any new bleeding.
2. Restore blood volume with plasma expanders or, if possible, blood transfusion

2. Urgent endoscopy

- Endoscopy should be performed once the patient is hemodynamically stable usually within 2-12 hours.
- *Injection sclerotherapy or variceal banding*

Varix Banding



3. Other measures

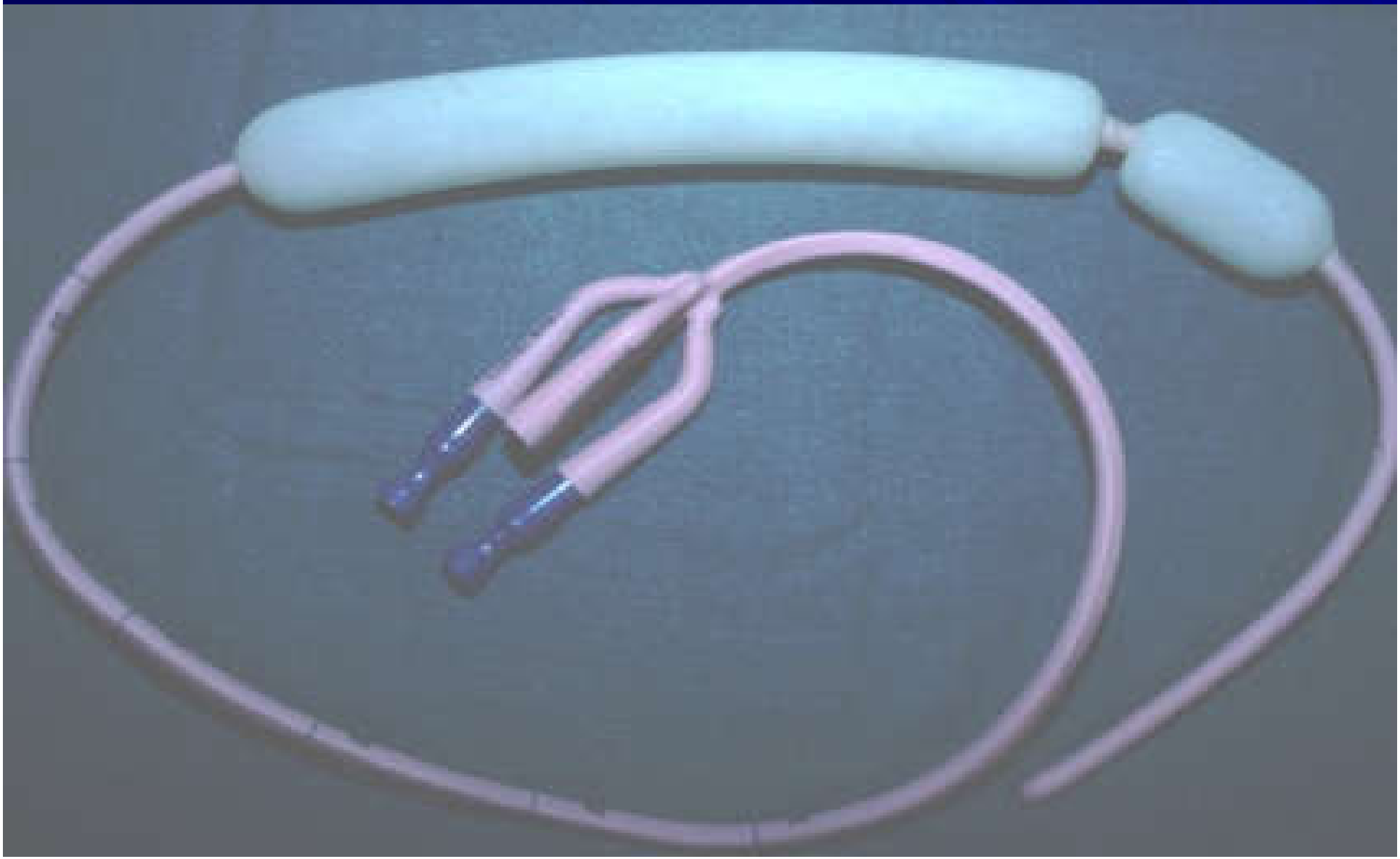
*A- **Vasoconstrictor therapy***

- Whilst waiting for endoscopy and in combination with endoscopic techniques.
- To restrict portal inflow by splanchnic arterial constriction.
- Includes terlipressin, somatostatin, octreotide. Care in patients with ischemic heart disease.

B- Balloon tamponade

- To control bleeding if endoscopic therapy or vasoconstrictor therapy has failed, unavailable, contraindicated or if there is severe hemorrhage.
- Complications include:
- Aspiration pneumonia,
- Esophageal rupture and
- Mucosal ulceration,
- The procedure is very unpleasant for the patient.

Sengstaken Tube



C- Emergency surgery

- This is used when other measures fail particularly, if the bleeding is from gastric fundal varices.

- TIPS
- Esophageal transection and acute portosystemic shunt surgery are rarely performed nowadays.

Prevention of recurrent variceal bleeding

1- Non-selective beta-blockade:

- Propranolol in a dose sufficient to reduce resting pulse rate by 25% or as long as tolerable.
- Nadolol tab.
- Carvedilol (alpha and beta blocker) is recently introduced.

2- Endoscopic treatment.

- Between 30% and 40% of varices return per year.
- Banding is superior to sclerotherapy (not used nowadays).

3- Transjugular portosystemic stent shunt.

Used if endoscopic or medical therapy fails.

4- Surgical procedures

- *Surgical portosystemic shunting* is associated with an extremely low risk of rebleeding, but produces significant encephalopathy.
- *Liver transplantation* is the best option when there is poor liver function.

Ascites

Causes of ascites divided according to the type of ascitic fluid:

Straw-coloured

- Cirrhosis
- Congestive cardiac failure
- Constrictive pericarditis
- Meigs' syndrome
- Hepatic vein obstruction (Budd-Chiari syndrome)
- Hypoproteinemia, (e.g. nephrotic syndrome)
- Malignancy
- Infective: Tuberculosis, following perforation, SBP
- Chronic pancreatitis

Chylous

- Obstruction of main lymphatic duct (e.g. by carcinoma) – chylomicrons are present
- Cirrhosis (occasional)

Hemorrhagic

- Malignancy
- Ruptured ectopic pregnancy
- Abdominal trauma
- Acute pancreatitis

Pathogenesis

1- Sodium and water retention:

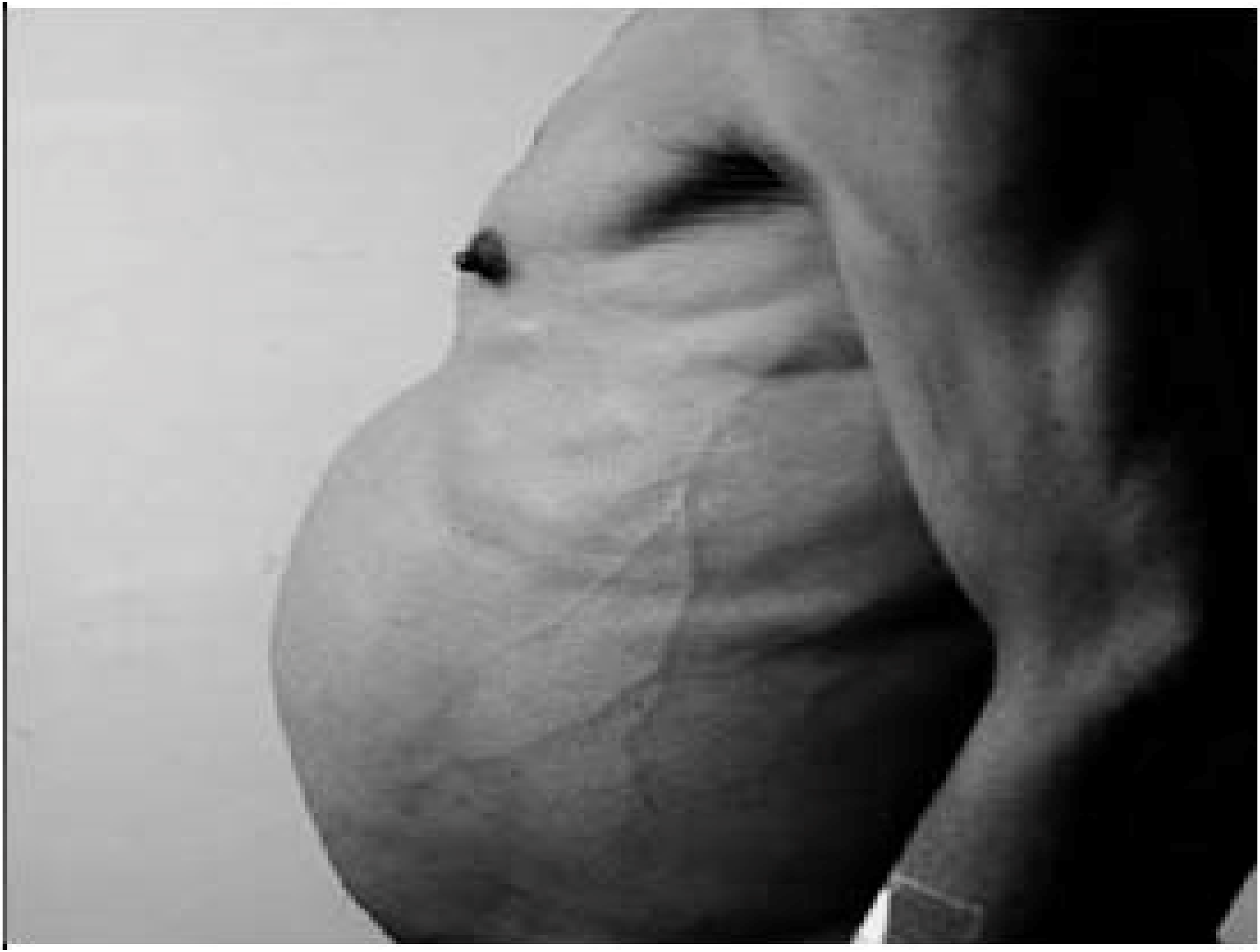
- Nitric oxide, atrial natriuretic peptide and prostaglandins are potent vasodilators that increase in liver cirrhosis.
- They produce peripheral arterial vasodilatation and consequent reduction in the effective blood volume.

2- Portal hypertension :

- Exerts a local hydrostatic pressure → increased hepatic and splanchnic production of lymph and transudation of fluid into the peritoneal cavity.

3- Low serum albumin

- Further contributes by a reduction in plasma oncotic pressure.



Clinical features

- Abdominal swelling
- Respiratory distress.
- Shifting dullness.
- Peripheral edema.
- Pleural effusion (usually on the right side)

Investigations

Diagnostic aspiration:

- Cell count: A neutrophil count above 250 cells /mm3 is indicative SBP.
- Bacterial stain and culture: for bacteria and acid-fast bacilli.
- Protein: > 3 gm /dL suggests an exudate.
- Cytology: for malignant cells.
- Amylase: to exclude pancreatic ascites.

Abdominal Ultrasound

Classification of ascites by the serum-albumin ascites gradient (SAAG)

High albumin gradient SAAG ≥ 1.1 g/dL	Low albumin gradient SAAG < 1.1 g/dL
Liver cirrhosis Alcoholic hepatitis Congestive heart failure Massive liver metastases	Peritoneal carcinomatosis Peritoneal TB Pancreatitis Serositis Nephrotic syndrome
Portal hypertension or heart failure	**Peritoneal or kidney disease**

Treatment

- Treat the underlying disease
- Rest
- Salt restriction (< 2 gm /day)
- Diuretics: Aldosterone inhibitor (spironolactone) or loop diuretic
- Paracentesis
- Peritoneal ultrafilteration
- Shunts (TIPS)
- Liver transplantation

Spontaneous bacterial peritonitis (SBP)

- Infection of ascitic fluid
- Usually gram negative (E.Coli, *Klebsiella* and enterococci)
- Mortality is high
- Suspected in patients with ascites and clinical deterioration
- Diagnosis: ascitic tap → PMN >250 cell /cmm
- Treatment: third generation cephalosporin IV
- Occurs in approximately 8% of cirrhotics with ascites.
- Recurrence is common (70% within a year) and an oral quinolone, e.g. norfloxacin, ciprofloxacin is used to prevent it.

Hepatic Encephalopathy

- Reversible impairment of neurological function secondary to liver disease
- Acute: seen with acute liver failure
- Acute on chronic: in established cirrhosis

Pathogenesis

- The mechanism is unknown.
- 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 are suggested as:

- *Ammonia,* free fatty acids, mercaptans, false neurotransmitters
- Activation of GABA system.
- Increased aromatic AA and reduced branched-chain AA (valine, leucine and isoleucine).

Factors precipitating portosystemic encephalopathy

- High dietary protein
- Gastrointestinal haemorrhage
- Constipation
- Infection, including spontaneous bacterial peritonitis
- Fluid and electrolyte disturbance
- Diuretic therapy or paracentesis
- Drugs (e.g. CNS depressants)
- Portosystemic shunt operations,
- Progressive liver damage
- Development of hepatocellular carcinoma

Clinical features

- Chronically, there is a disorder of personality, mood and intellect, with reversal of sleep rhythm.
- The patient is irritable, confused, disoriented and has slow slurred speech.
- Coma occurs as the encephalopathy becomes more marked, but there is hyperreflexia and increased tone.

Signs include:

- Fetor hepaticus
- Flapping tremor (asterixis)
- Constructional apraxia (the patient is unable to draw a five-pointed star)
- The ability to join numbers and letters with a pen within a certain time is prolonged

Drawing Tests

Normal

Patient

Investigations

- EEG: may show characterestic delta waves.
- Visual evoked responses also detect subclinical encephalopathy.
- Arterial blood ammonia is occasionally useful in the differential diagnosis of the cause of the coma and to follow the course of encephalopathy.

Management

- Identify and remove the possible precipitating cause.
- Restriction of protein intake.
- Give purgation and enemas to empty the bowels of nitrogenous substances.
- Lactulose (10-30 mL three times daily) is an osmotic purgative and reduces the colonic pH and limits ammonia absorption.

- Antibiotics for eradication of bacterial flora: Rifaximin or metronidazole. Neomycin is less commonly used.
- L-ornithine L-aspartate: decrease blood amonia
- Benzodiazepine antagonists e.g. flumazenil
- Liver transplantation.

Hepatorenal Syndrome

- The renal failure is described as 'functional'.
- The hepatorenal syndrome occurs typically in a patient with advanced cirrhosis with jaundice and ascites.
- Advanced cases may progress beyond the 'functional' stage to produce an acute tubular necrosis.
- The initiating factor is thought to be extreme peripheral vasodilatation possibly due to nitric oxide, leading to decrease in the effective blood volume and hypotension .

- This activates the hemostatic 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.
- IV vasoconstrictors
- Liver transplantation is the best option.
- The overall prognosis is poor.

Hepatopulmonary syndrome

- Hypoxemia occurring in patients with advanced liver disease.
- It is due to intrapulmonary vascular dilatation with no evidence of primary pulmonary disease.
- The patients have features of cirrhosis with cyanosis, with more severe disease are breathless on standing (platypnea).

- Transthoracic Echo may show intrapulmonary shunting
- CT pulmonary angiography
- Arterial blood gases confirm the arterial oxygen desaturation.
- These changes are improved with liver transplantation.

Hepatocellular carcinoma
HCC

- HCC is common in areas of HCV and HBV prevalence.
- Symptoms and signs are usually non-specific.
- Diagnosis by imaging tests, AFP measurement and occasionally liver biopsy.
- Screening with periodic imaging and AFP is indicated in all cirrhotic patients.

Large Hepatocellular Carcinoma


Thank you