Liver cirrhosis and it's complications

TUCOM
Dep. of Medicine
4th year
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Liver cirrhosis and it's complications

Learning objectives:

1. Define liver cirrhosis.
2. List the causes of liver cirrhosis.
3. Clarify the clinical features of liver cirrhosis.
4. Write a short notes about primary biliary cirrhosis, primary sclerosing cholangitis and haemochromatosis.
5. Identify the investigations of liver cirrhosis.
6. Summarize the treatment of liver cirrhosis.
7. List the complications of liver cirrhosis.
8. Review the following: portal hypertension and variceal bleeding, ascites in liver cirrhosis, spontaneous bacterial peritonitis, hepatic encephalopathy, hepatorenal syndrome and hepatopulmonary syndrome.

Liver cirrhosis

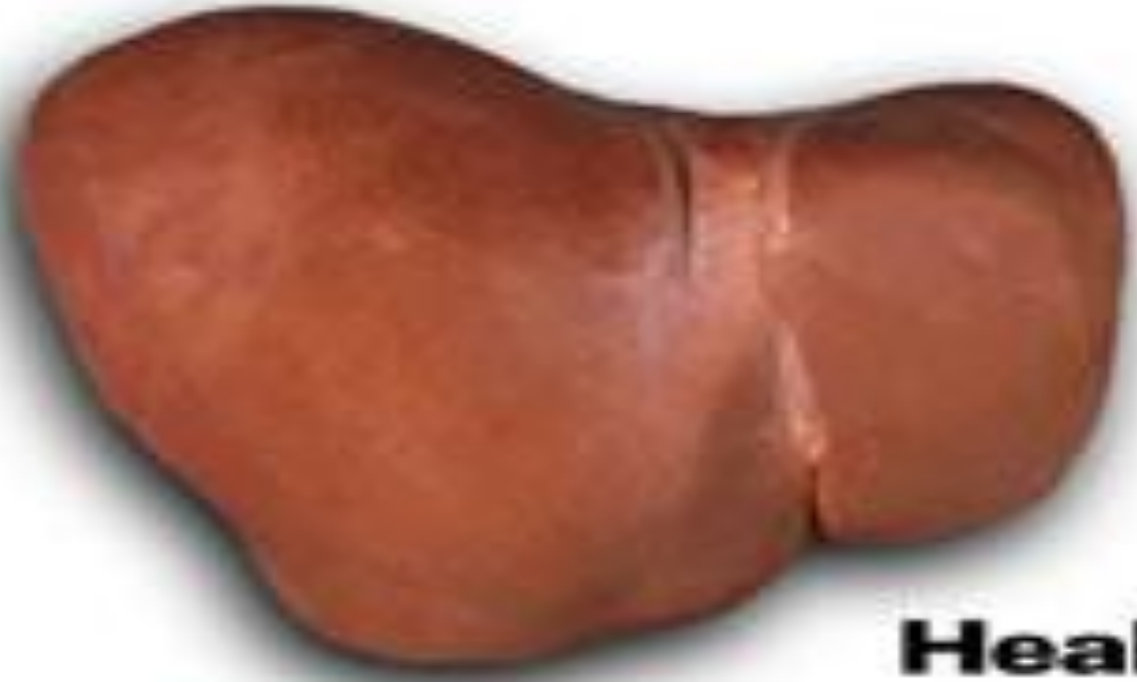
Liver cirrhosis: Is a slowly progressive, irreversible fibrous scarring and hepatocellular regeneration that leads to loss of normal hepatic lobular architecture, impaired hepatic function and disrupts the hepatic vasculature. Cirrhosis can be classified histologically into:

- Small (≤ 3 mm: *micronodular cirrhosis*)

A typical feature of alcoholic cirrhosis

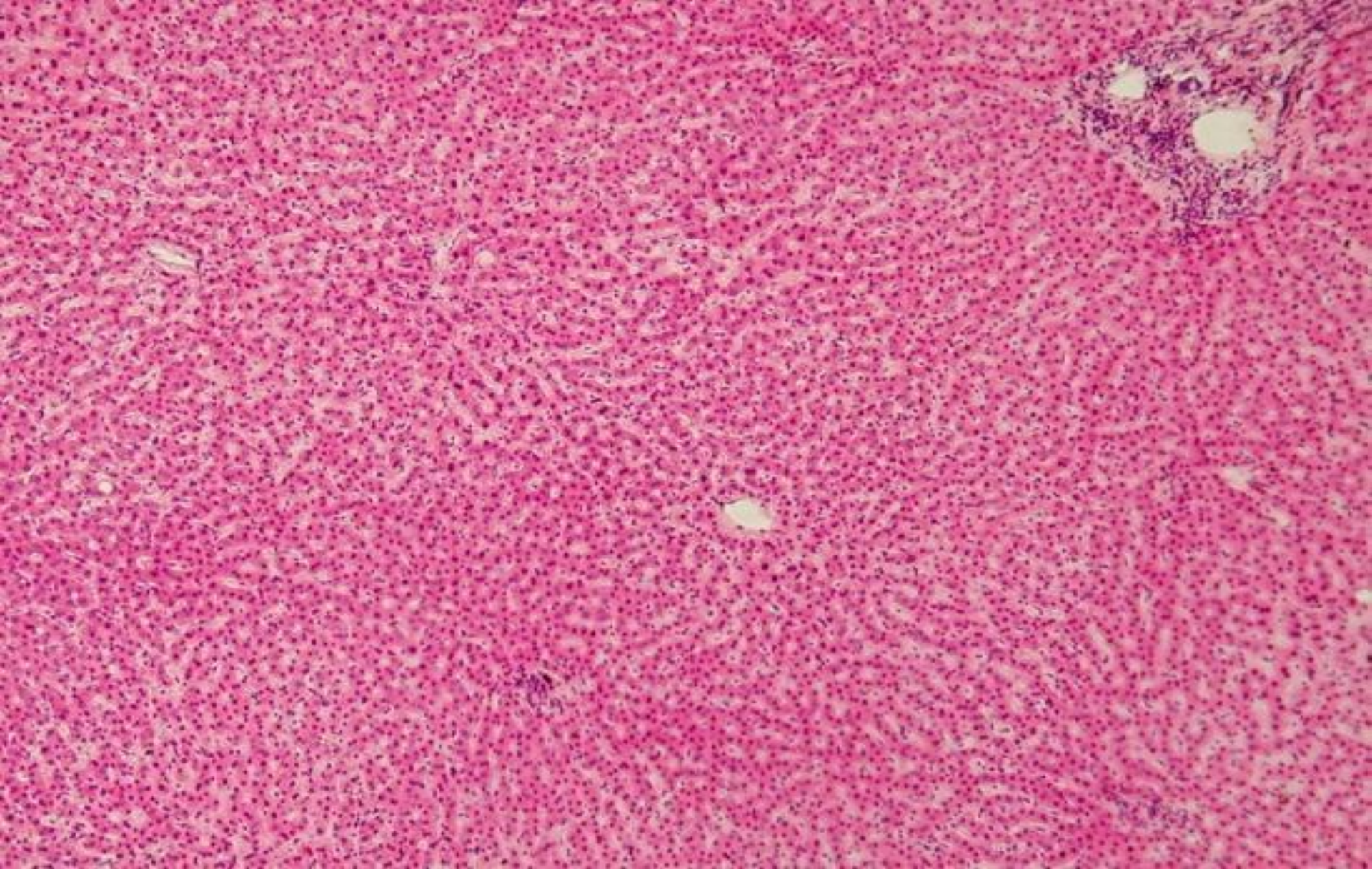
- Large (> 3 mm: *macronodular cirrhosis*)

Is more commonly seen as a sequelae to chronic active hepatitis

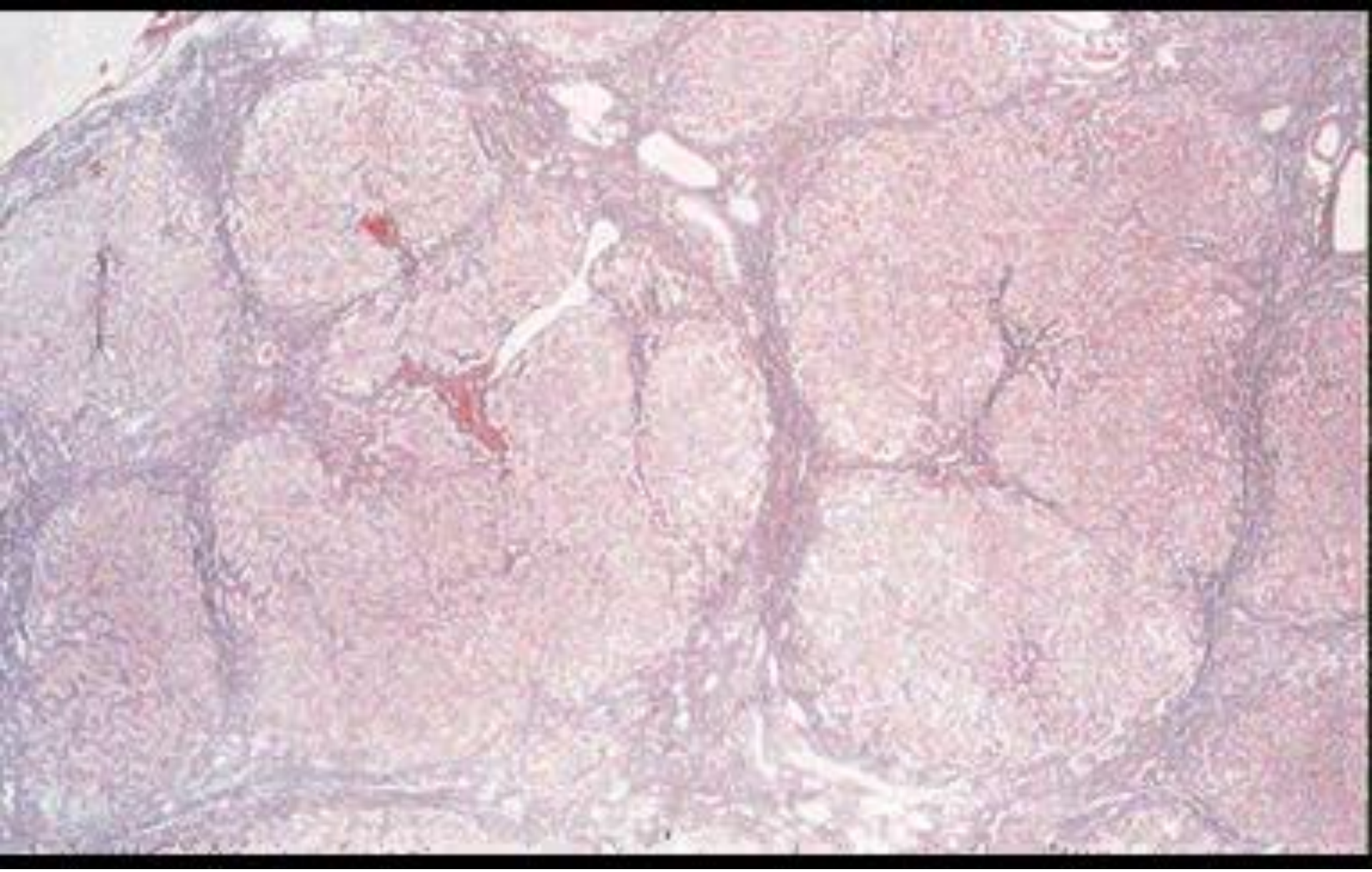


Healthy

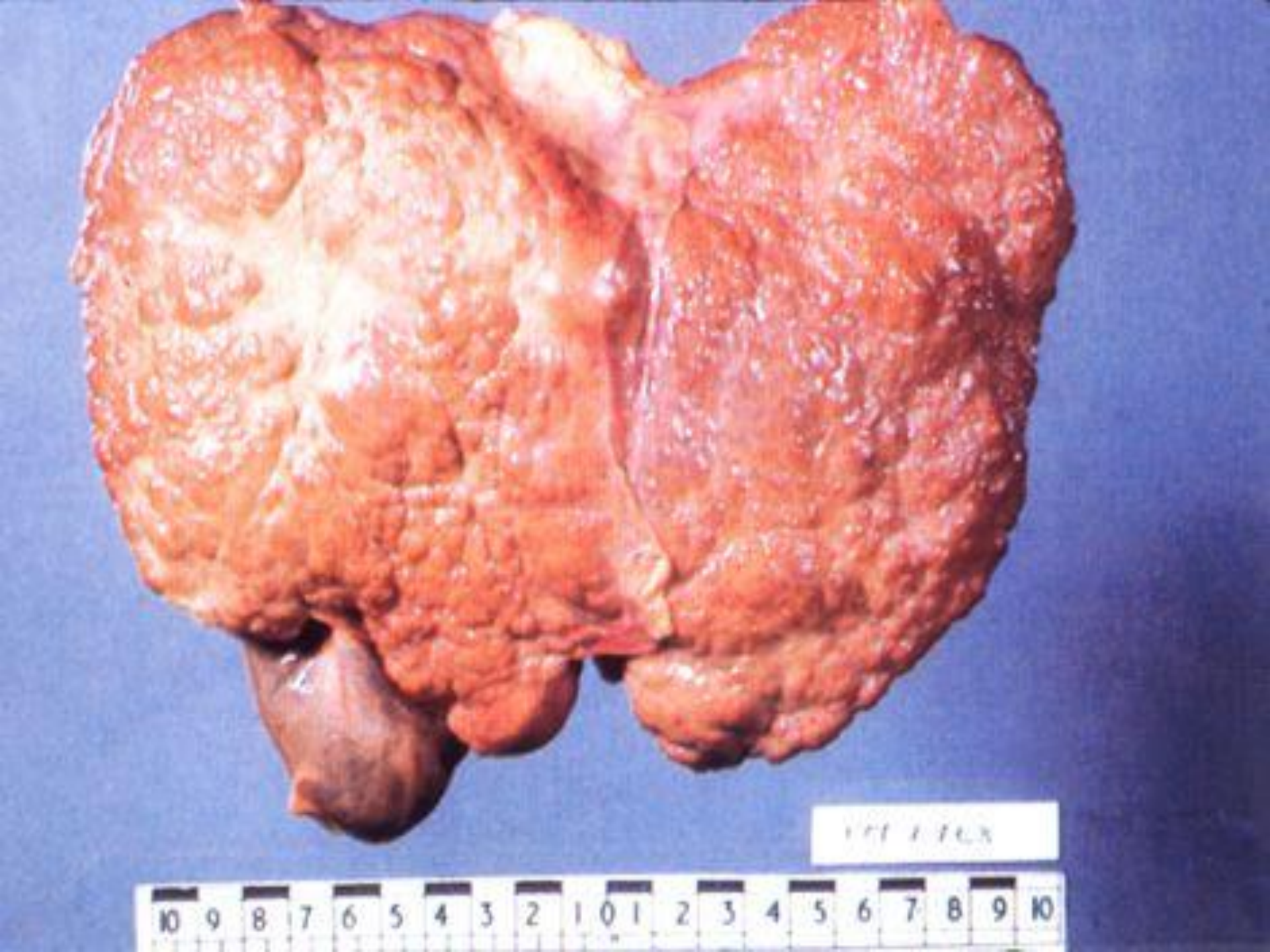
Cirrhosis



Normal liver. Columns of hepatocytes radiate from the portal tracts to the central veins. The portal tract contains a normal intralobular bile duct branch of the hepatic artery and portal venous radical.



Cirrhotic liver. The liver architecture is disrupted. The normal arrangement of portal tracts and hepatic veins is now lost and nodules of proliferating hepatocytes are broken up by strands of fibrous tissue forming cirrhotic nodules.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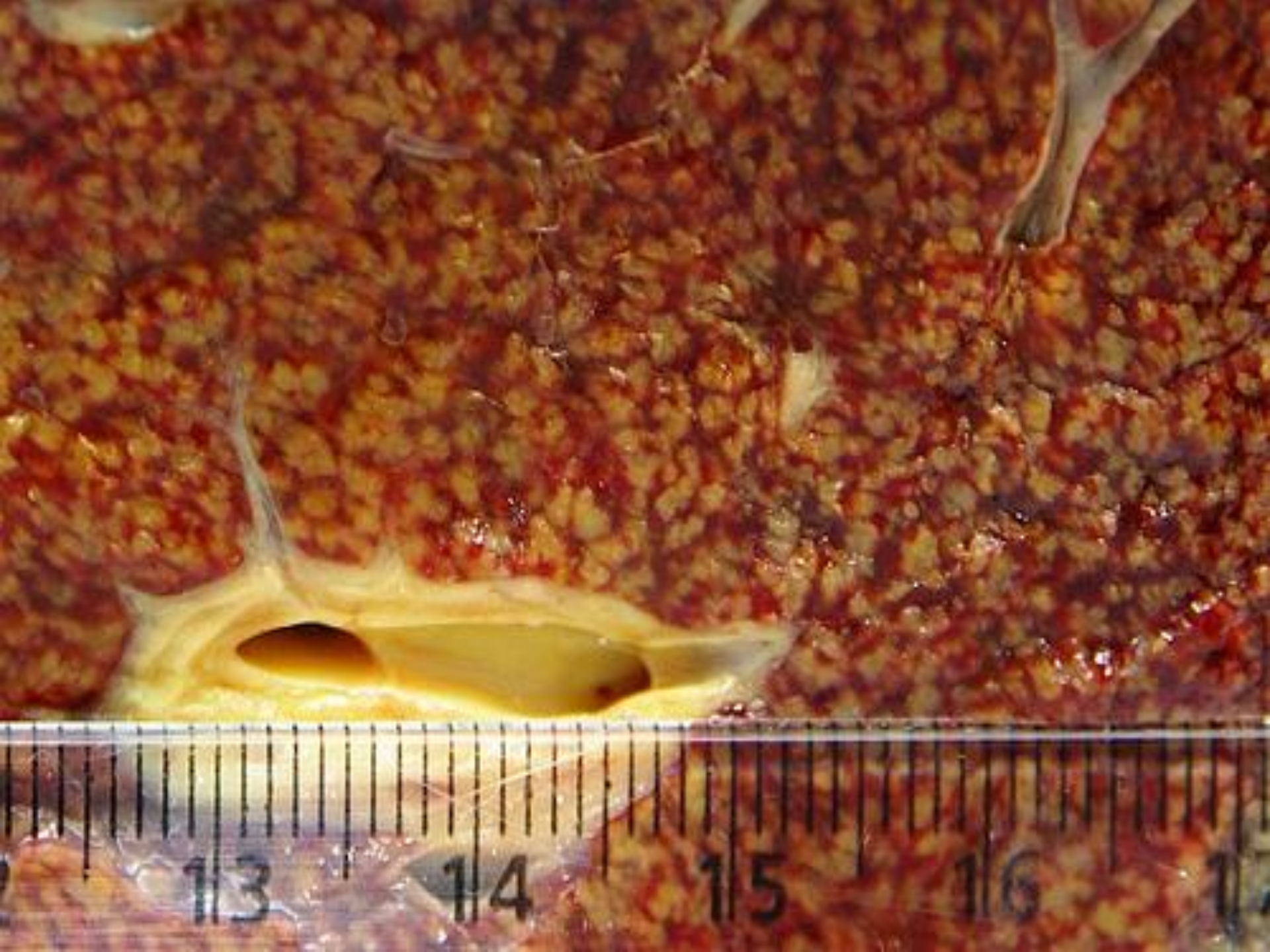
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METRIC
1
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Causes of liver cirrhosis

1. Alcohol
2. Chronic viral hepatitis B, D or C
3. Non-alcoholic fatty liver disease
4. Immune
    1. Primary sclerosing cholangitis
    2. Autoimmune liver disease
5. Biliary
    1. Primary biliary cirrhosis
    2. Cystic fibrosis
6. Genetic
    1. Haemochromatosis
    2. α_1-antitrypsin deficiency
    3. Wilson's disease
7. Cryptogenic (unknown)

- Hepatitis B virus is the major cause of cirrhosis in Asia and Africa.
- Alcoholic liver disease, Nonalcoholic fatty liver disease (NAFLD), and hepatitis C virus infection are the most common causes of cirrhosis in industrialized nations.

Primary biliary cirrhosis (PBC)

PBC Is an immune mediated, chronic, progressive cholestatic liver disease, which predominantly affects middle-aged women.

Clinical features: lethargy, arthralgia, pruritus, jaundice. Bone pain or fractures due to osteomalacia (fat-soluble vitamin malabsorption). Scratch marks, Xanthelasma, later on patients develops portal hypertension and liver failure.

Investigations: LFTs show a pattern of cholestasis. Hypercholesterolaemia. Antimitochondrial antibody is diagnostic. Liver biopsy shows a granuloma formation of the portal tracts, leading to progressive damage and eventually loss of the small and middle-sized bile ducts.

Management:

- The hydrophilic bile acid, ursodeoxycholic acid (UDCA),

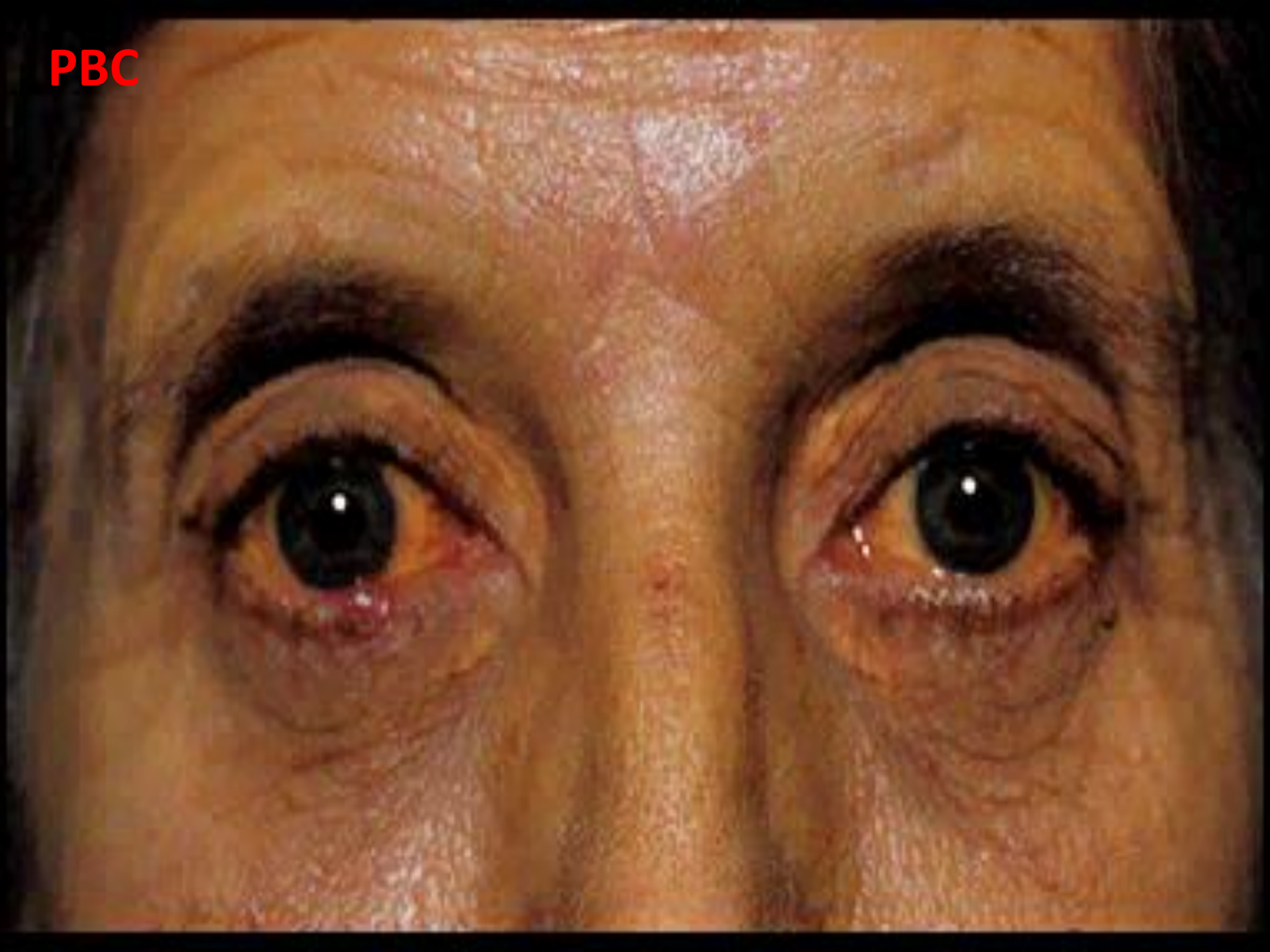
at a dose of 13–15 mg/kg/day improves bile flow, replaces toxic hydrophobic bile acids in the bile acid pool, and reduces apoptosis of the biliary epithelium, improves LFTs and slow down histological progression, it is the first-line treatment of PBC. Liver transplantation should be considered once liver failure has developed.

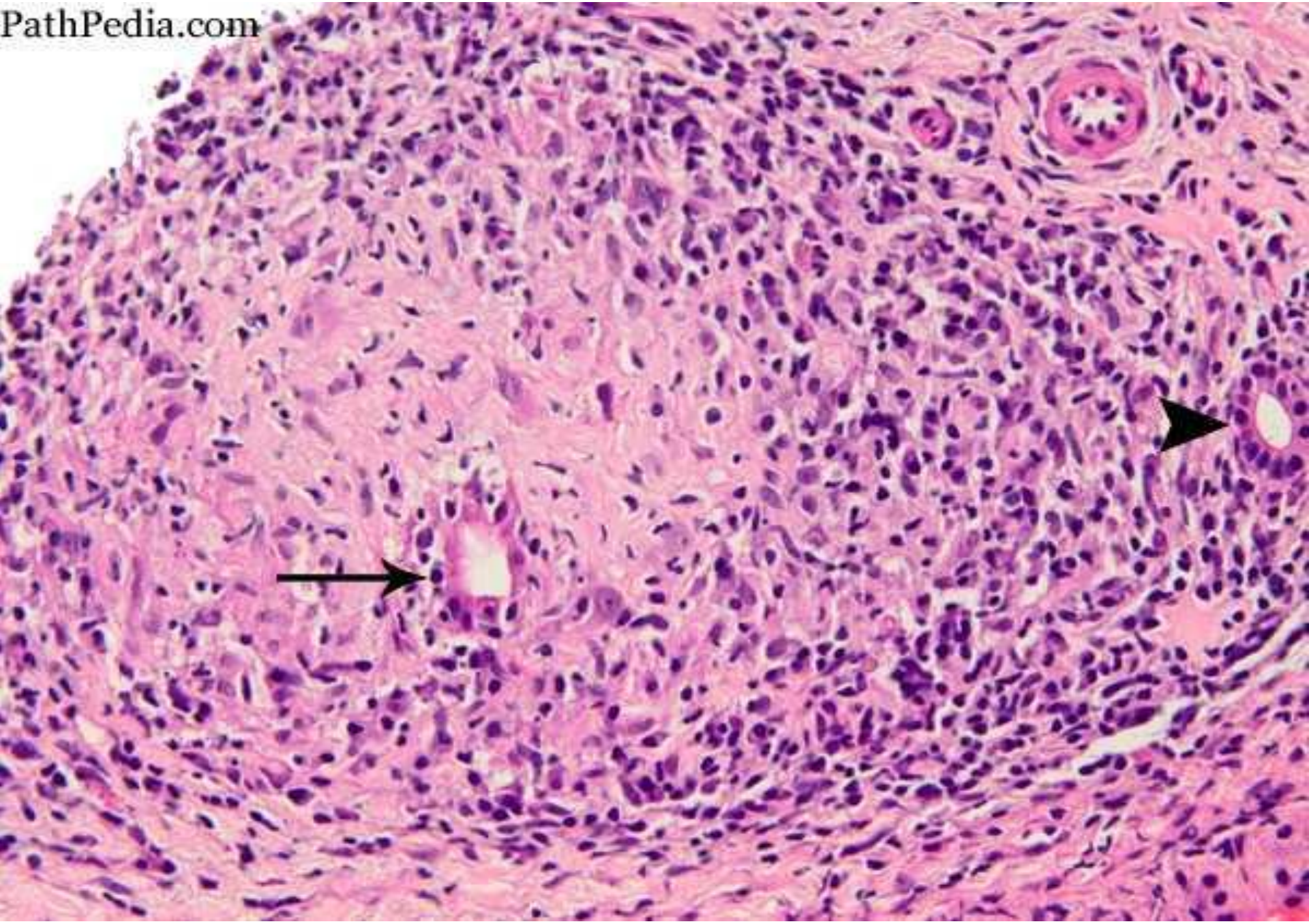
- Pruritus: First-line treatment is with the anion-binding resin colestyramine, which probably acts by binding potential pruritogens in the intestine and increasing their excretion in the stool. A dose of 4–16 g/day orally is used. The powder is mixed in orange juice and the main dose (8 g) taken before and after breakfast, when maximal duodenal bile acid concentrations occur.
- Osteopenia and osteoporosis are common, and treatment started with replacement calcium and vitamin D3. Bisphosphonates should be used if there is evidence of osteoporosis


Ursodeoxycholic Acid
300mg
Ursodeoxycholic Acid
Film-Coated Tablets
For oral use
WOCKHARDT
60 tablets


Cholestyramine
for Oral Suspension
USP
POWDER
PAR


Cholestyramine
for Oral Suspension
USP
PAR

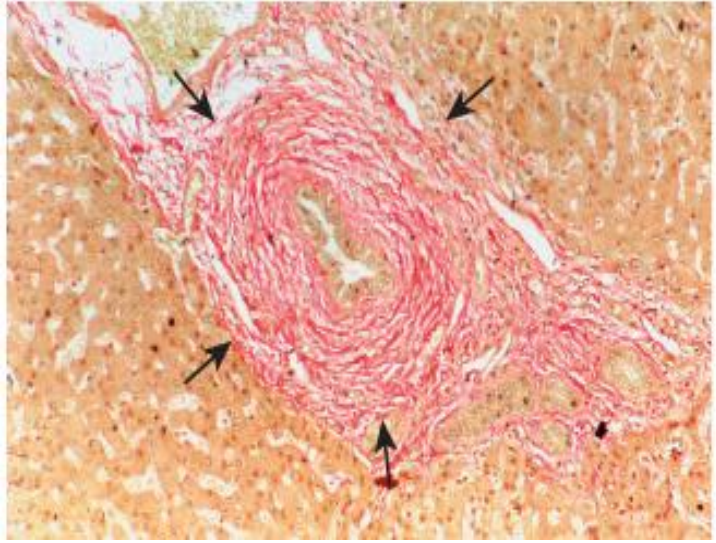

PBC

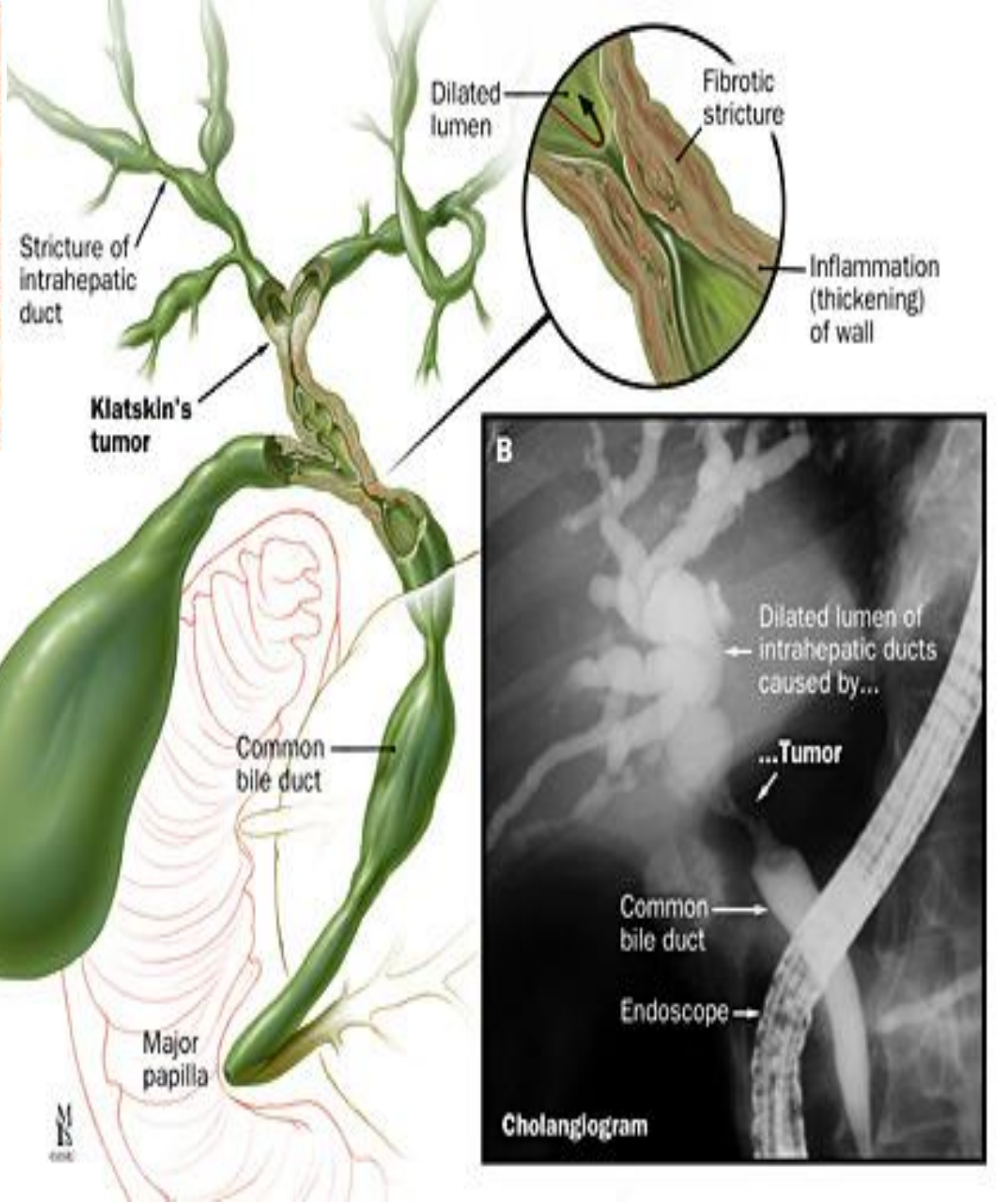


PBC portal tracts contain multiple granulomas

Primary sclerosing cholangitis: Is an autoimmune cholestatic liver disease caused by diffuse inflammation and fibrosis that involve the entire biliary tree and leads to the gradual obliteration of intrahepatic and extrahepatic bile ducts, and ultimately biliary cirrhosis, portal hypertension and hepatic failure. More common in young men. About two-thirds of patients have coexisting ulcerative colitis, Between 3% and 10% of patients with ulcerative colitis develop PSC. Cholangiocarcinoma develops in about 10-30% of patients during the course of the disease.

- Patient present with fatigue, jaundice, weight loss, right upper quadrant abdominal pain, pruritus and attacks of cholangitis.
- Investigations reveals a cholestatic pattern of LFTs. ERCP is usually diagnostic and may reveal multiple irregular stricturing and dilation. Histological appearances characteristic are periductal 'onion-skin' fibrosis and inflammation.
- Management: There is no cure for PSC, but management of cholestasis and its complications using UDCA. Broad-spectrum antibiotics (e.g. ciprofloxacin) should be given for acute attacks of cholangitis.




Dilated lumen
Fibrotic stricture
Inflammation (thickening) of wall
Stricture of intrahepatic duct
Klatskin's tumor
Common bile duct
Major papilla
B
Dilated lumen of intrahepatic ducts caused by...
...Tumor
Common bile duct
Endoscope
Cholangiogram

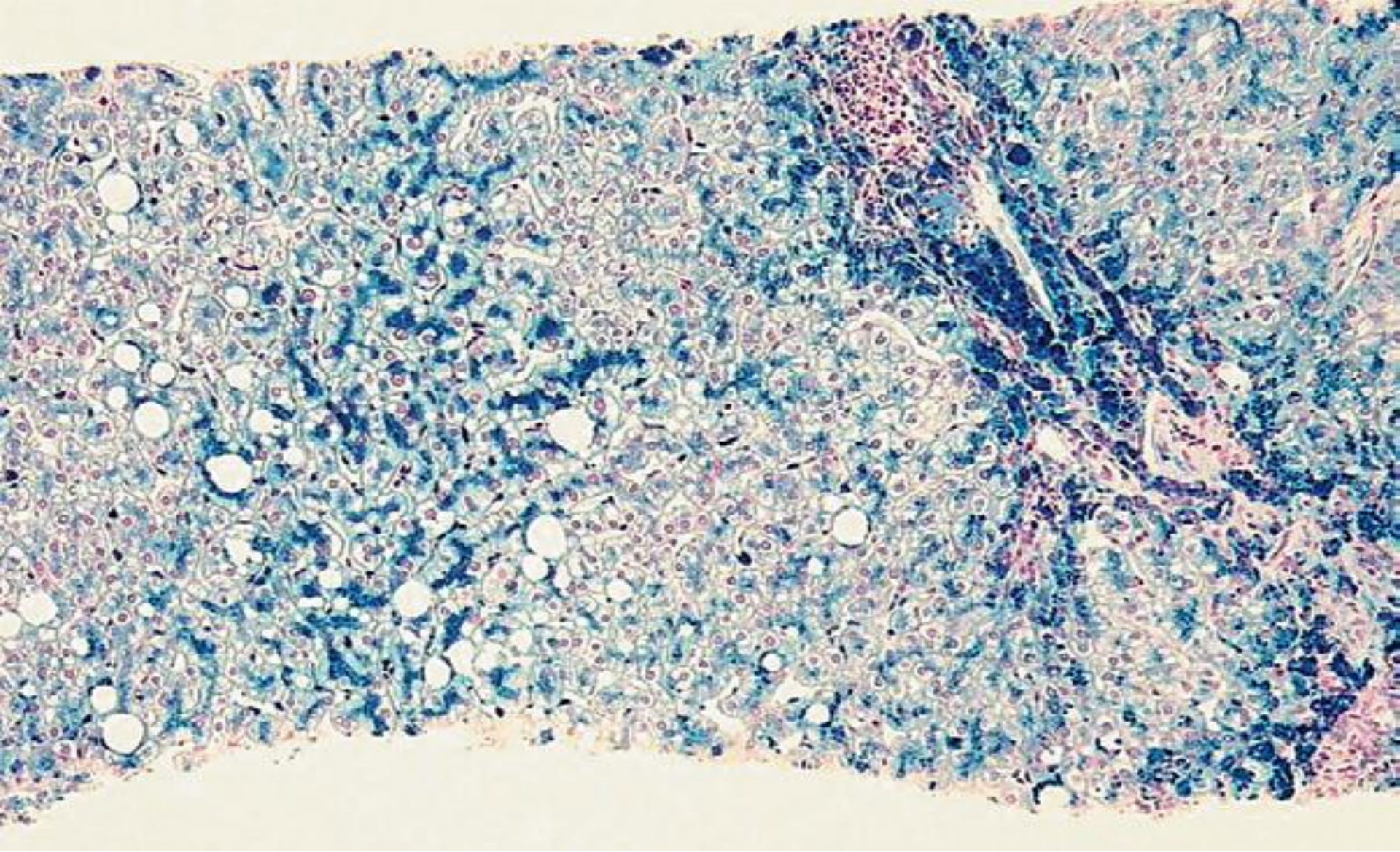
Haemochromatosis: Is a condition in which the amount of total body iron is increased; the excess iron is deposited in and causes damage to several organs including the liver. It may be primary or secondary to other diseases . Iron is deposited throughout the body and total body iron may reach 20-60 g (normally 4 g).

Hereditary haemochromatosis (HHC): is caused by increased absorption of dietary iron and is inherited as an autosomal recessive gene located on chromosome 6. Both the C282Y and the H63D mutations can be identified by genetic testing

Usually presents in men aged 40 years or over with features of hepatic cirrhosis (especially hepatomegaly), diabetes mellitus or heart failure. Arthropathy, Leaden-grey skin pigmentation due to excess melanin occurs, especially in exposed parts, axillae, groins and genitalia; hence the term 'bronzed diabetes'. Impotence, loss of libido, testicular atrophy and arthritis with chondrocalcinosis secondary to calcium pyrophosphate deposition are also common. Cardiac failure or cardiac dysrhythmia may complicate heart muscle disease.

Serum ferritin is greatly increased (greater than 1000 µg/L), the plasma iron is also increased, with a highly saturated plasma iron-binding capacity. The diagnosis is confirmed by liver biopsy, which shows heavy iron deposition and hepatic fibrosis which may have progressed to cirrhosis.

Treatment consists of weekly venesection of 500 ml blood (250 mg iron) until the serum iron is normal, this may take 2 years or more. The aim is to reduce ferritin to under 50 µg/L. Thereafter, venesection is continued as required to keep the serum ferritin normal.

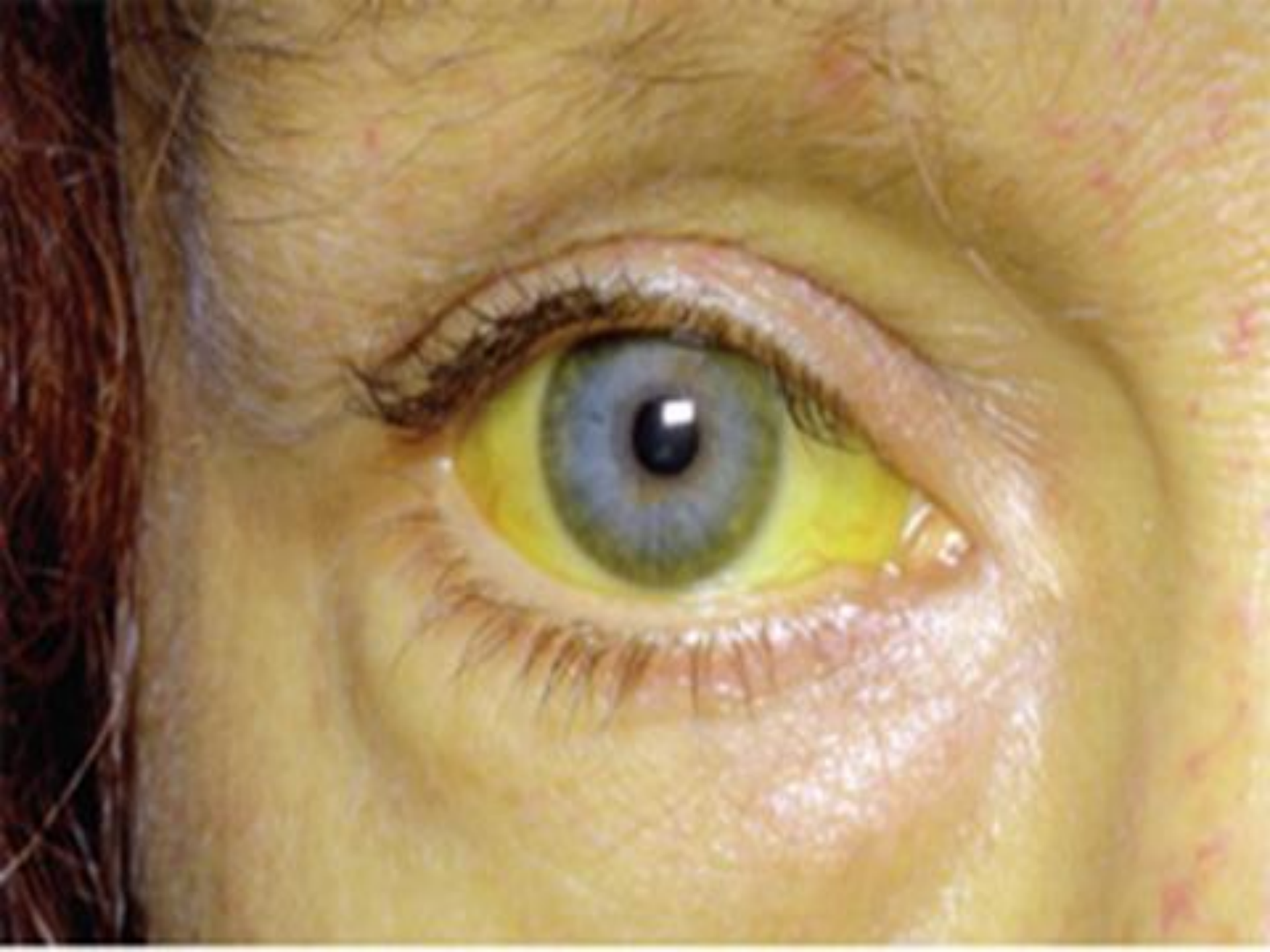


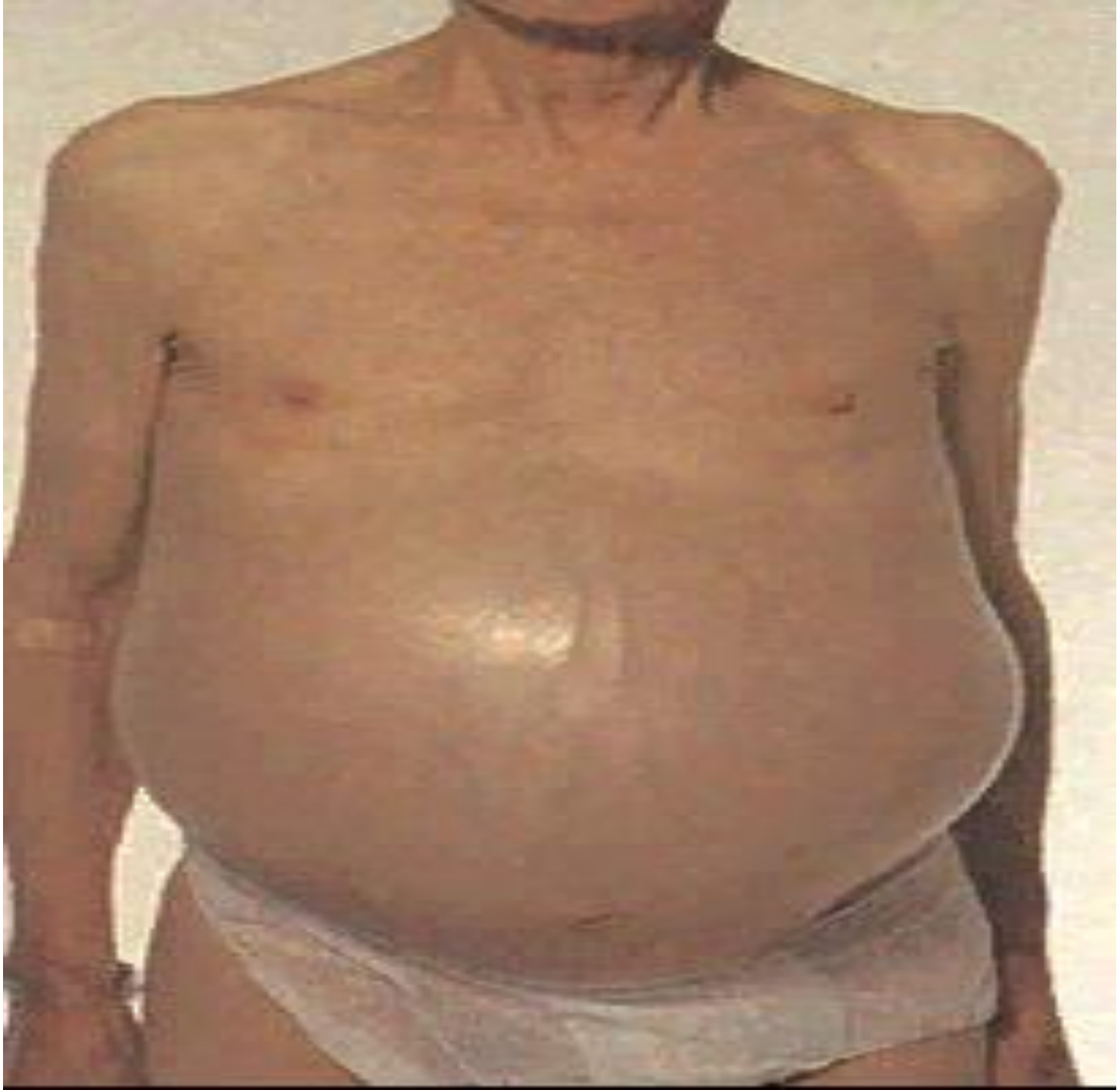
Liver histology: haemochromatosis. This Perls stain shows accumulating iron within hepatocytes, which is stained blue. There is also accumulation of large fat globules in some hepatocytes (macrovesicular steatosis). Iron also accumulates in Kupffer cells and biliary epithelial cells.

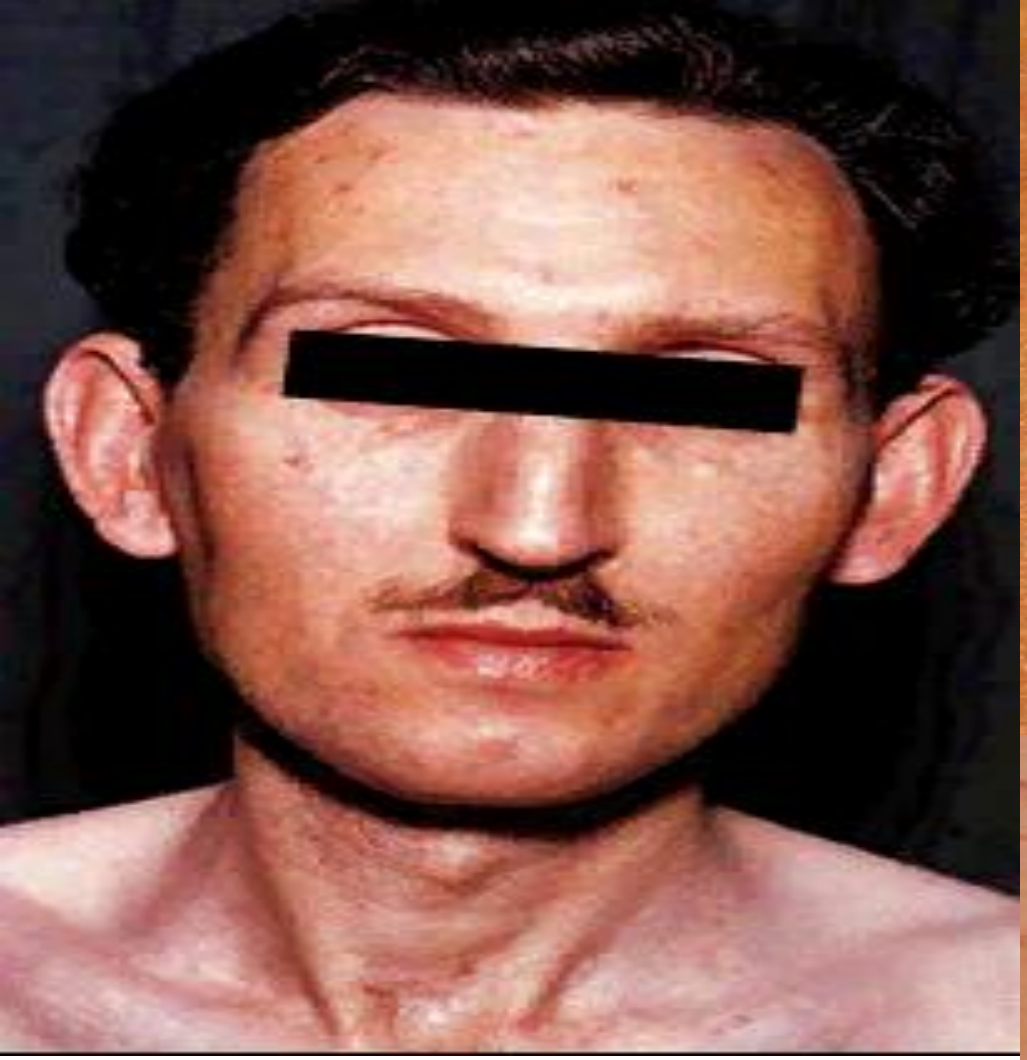
Clinical features of liver cirrhosis

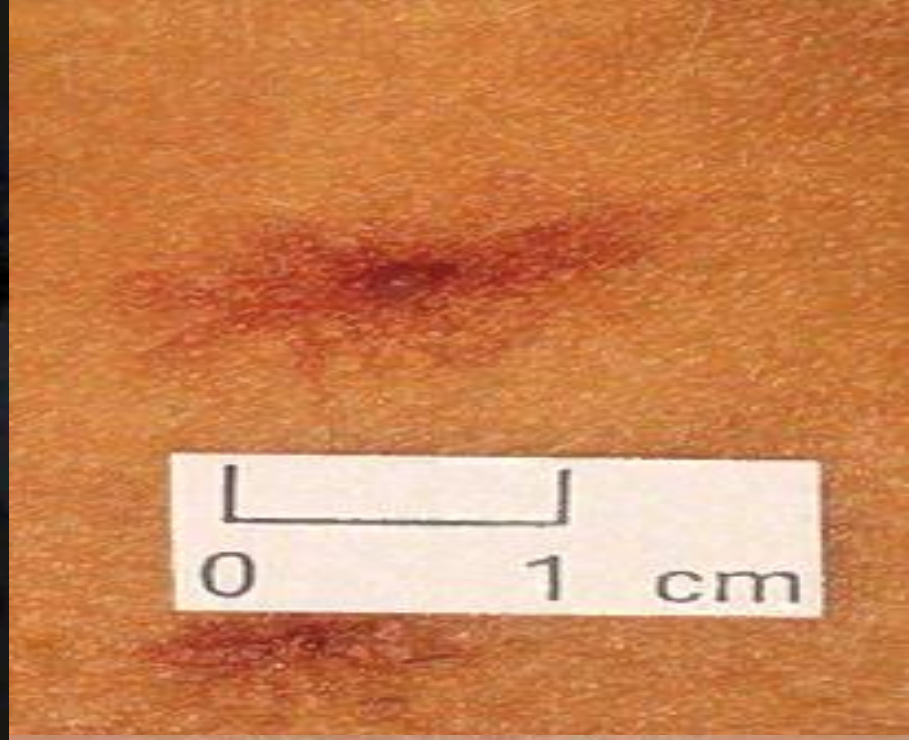
- **Hepatomegaly:** especially in alcoholic liver disease and haemochromatosis. **Small size liver** noticed in viral hepatitis or autoimmune liver disease. The liver is often hard, irregular and non-tender.
- **Jaundice**
- **Ascites**
- **Circulatory changes**
  - Spider telangiectasia, palmar erythema, cyanosis
- **Endocrine changes**
  - Loss of libido, hair loss
  - Men: gynaecomastia, testicular atrophy, impotence
  - Women: breast atrophy, irregular menses, amenorrhea

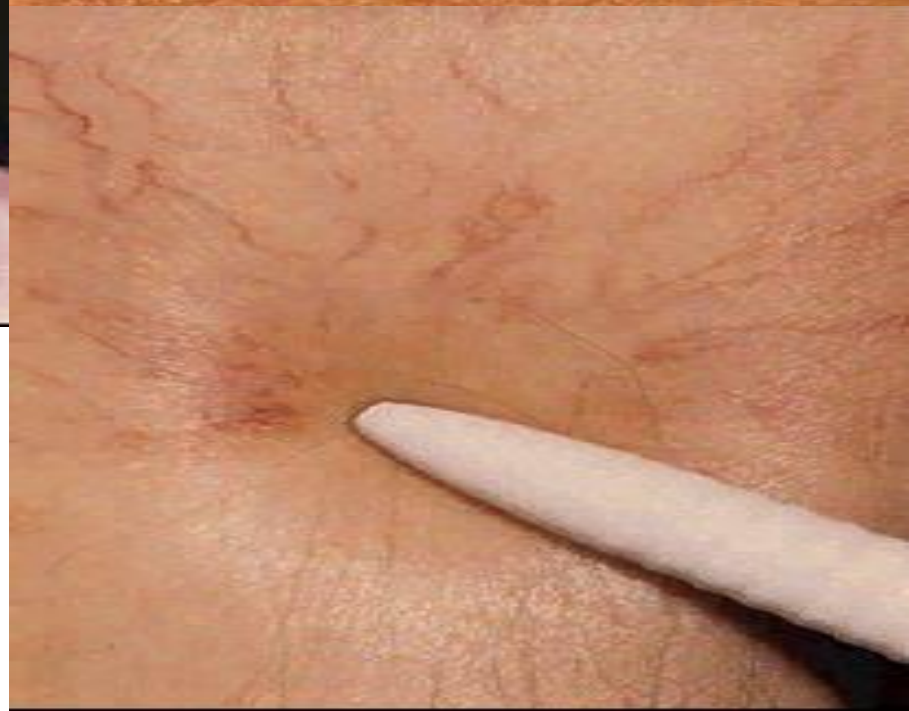
- **Hemorrhagic tendency**
  - Bruises, purpura, epistaxis, menorrhagia
- **Portal hypertension**
  - Splenomegaly, collateral vessels (caput medusa), variceal bleeding (oesophageal, gastric and rectal varices), fetor hepaticus.
- **Hepatic (portosystemic) encephalopathy**
- **Other features**
  - Pigmentation, digital clubbing, duputryn's contracture, Pruritus.
- **Features of chronic liver failure (decompensated cirrhosis):** Worsening synthetic liver function, prolonged PT and low albumin. Hepatic encephalopathy. Ascites. Spontaneous bacterial peritonitis. Hepatorenal failure.



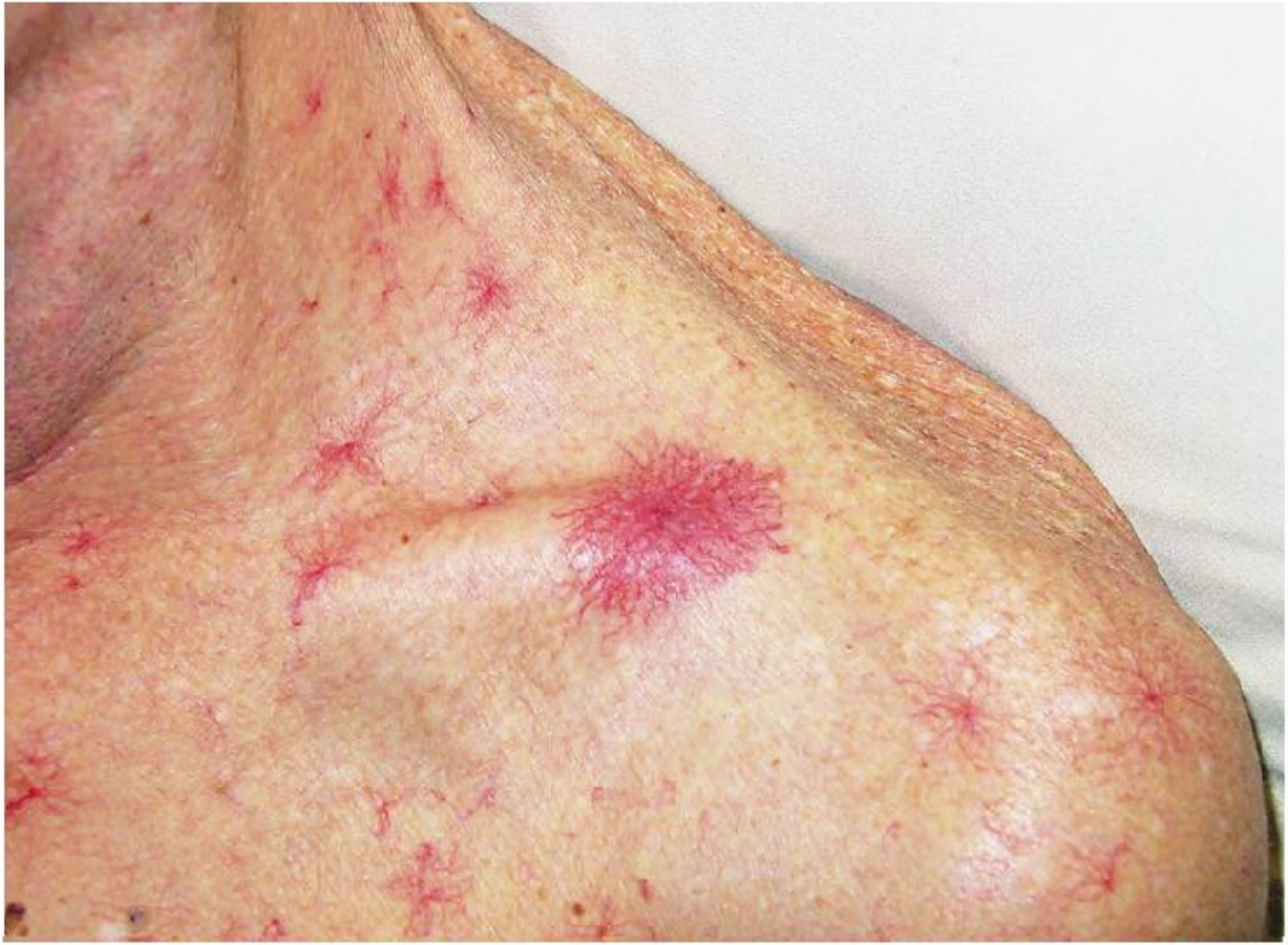


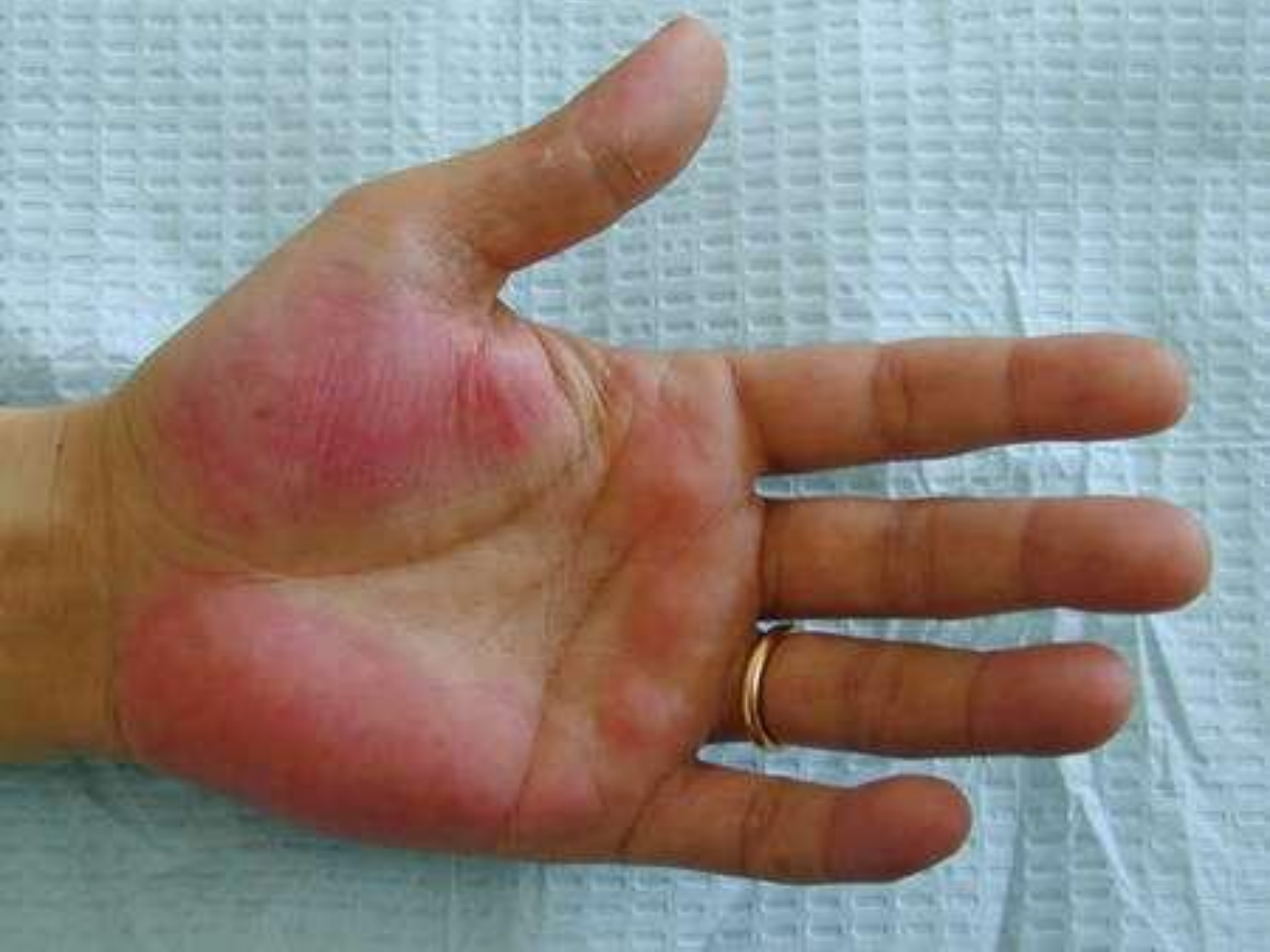


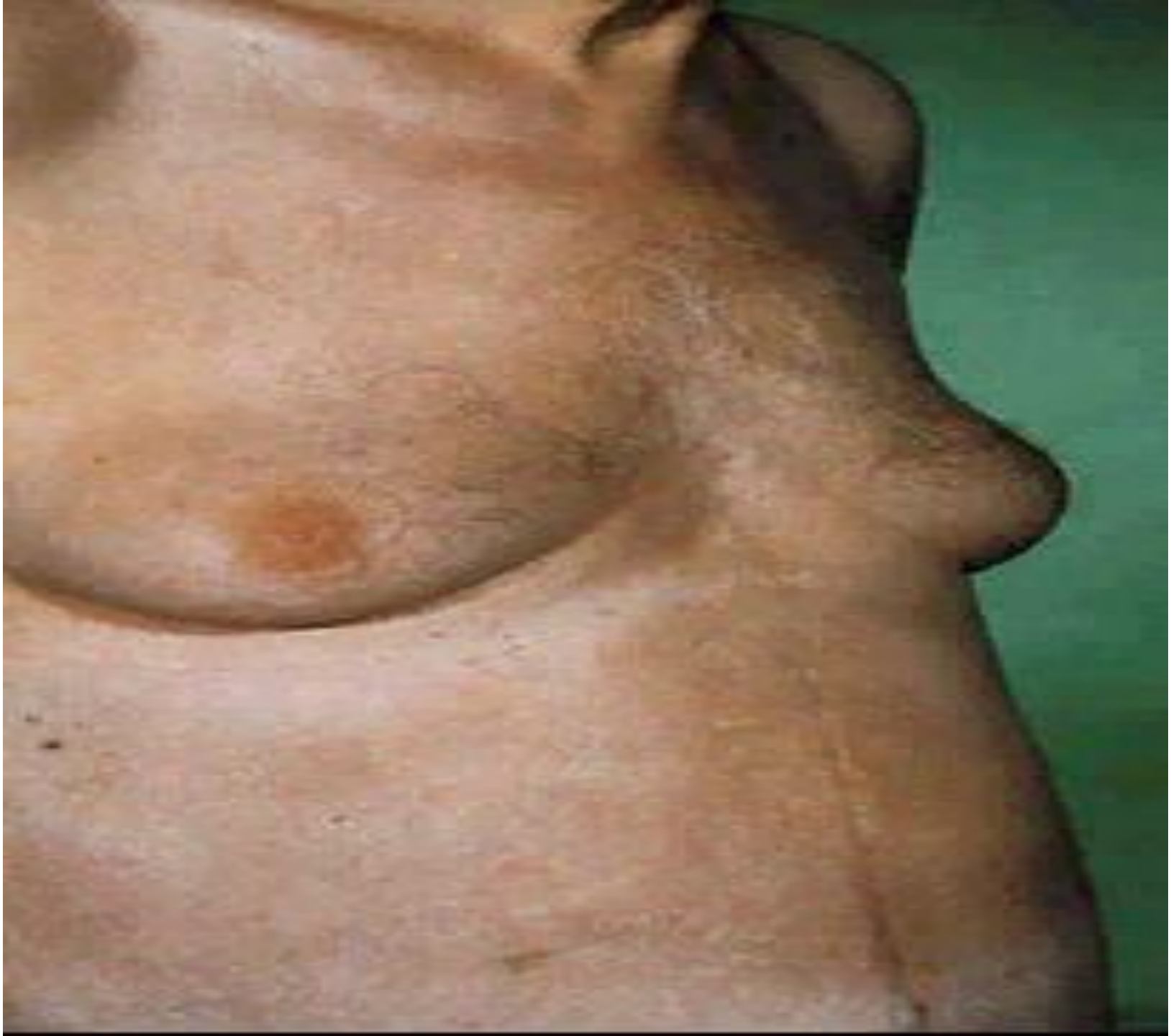


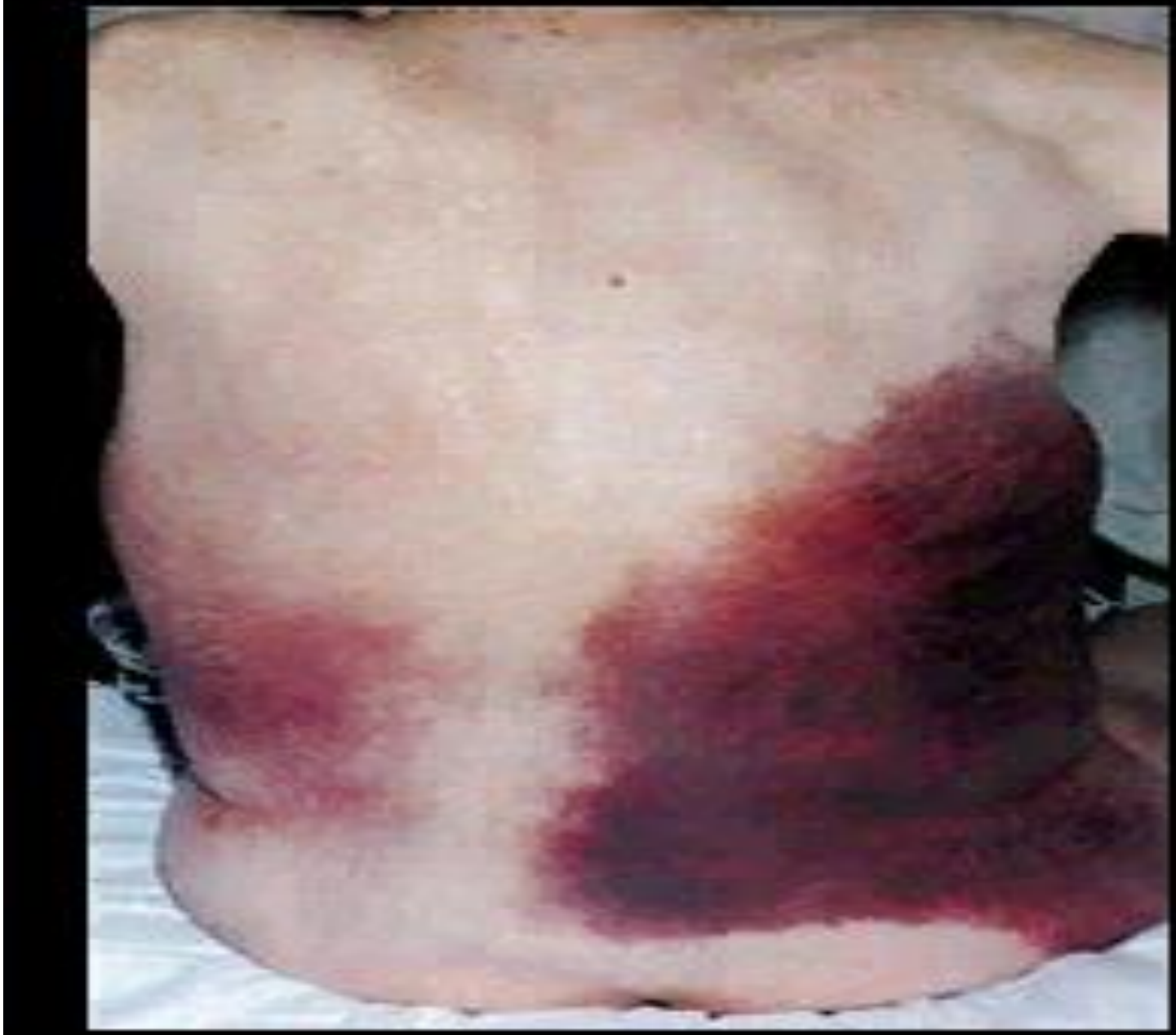


Spider telangiectasias occur and comprise a central arteriole (which occasionally raises the skin surface), from which small vessels radiate. They vary in size from 1 to 2 mm in diameter, are usually found only above the nipples, and can occur early in the disease.

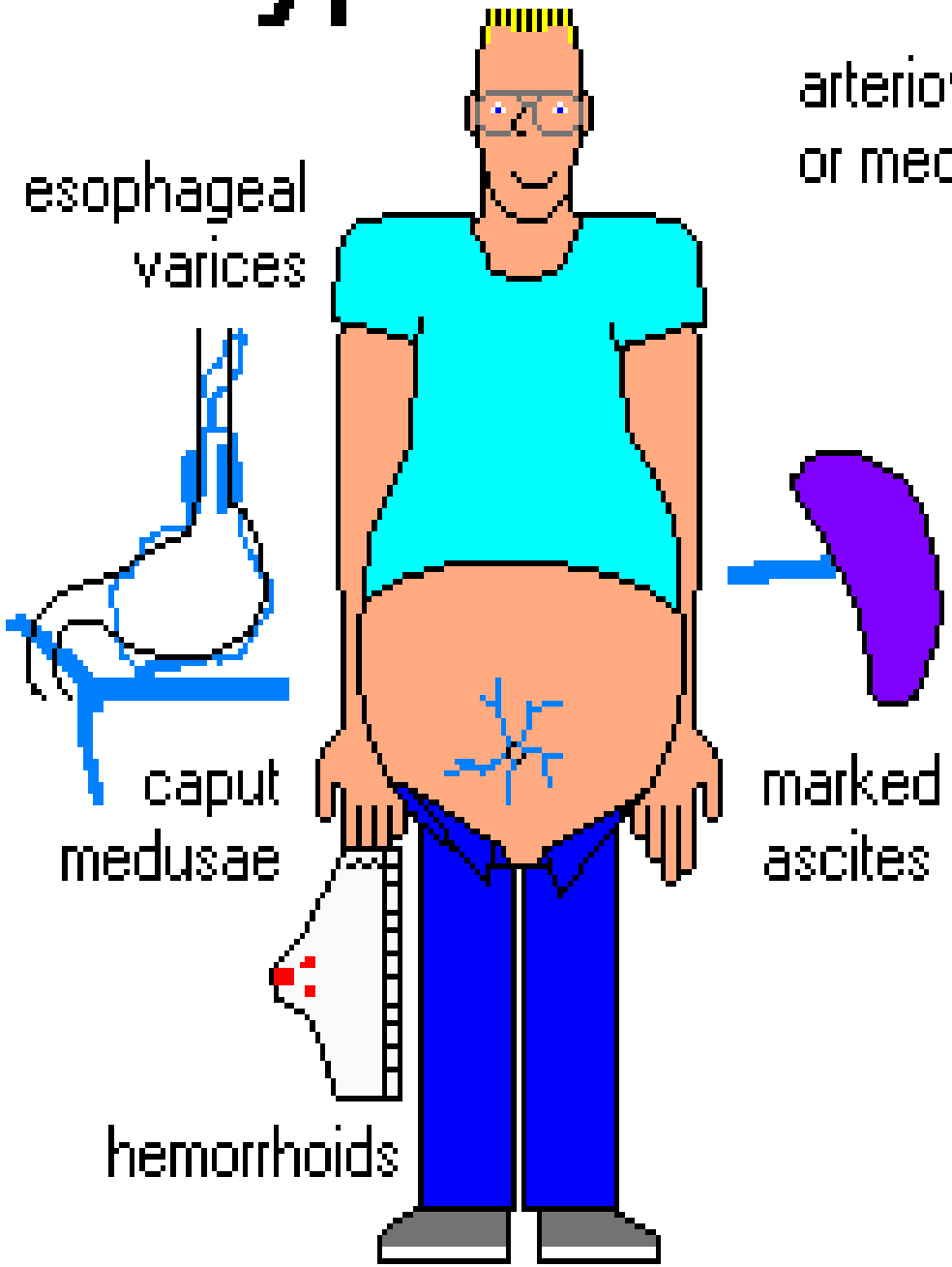








Portal Hypertension



arteriovenous shunting and/
or mechanical obstruction

esophageal
varices

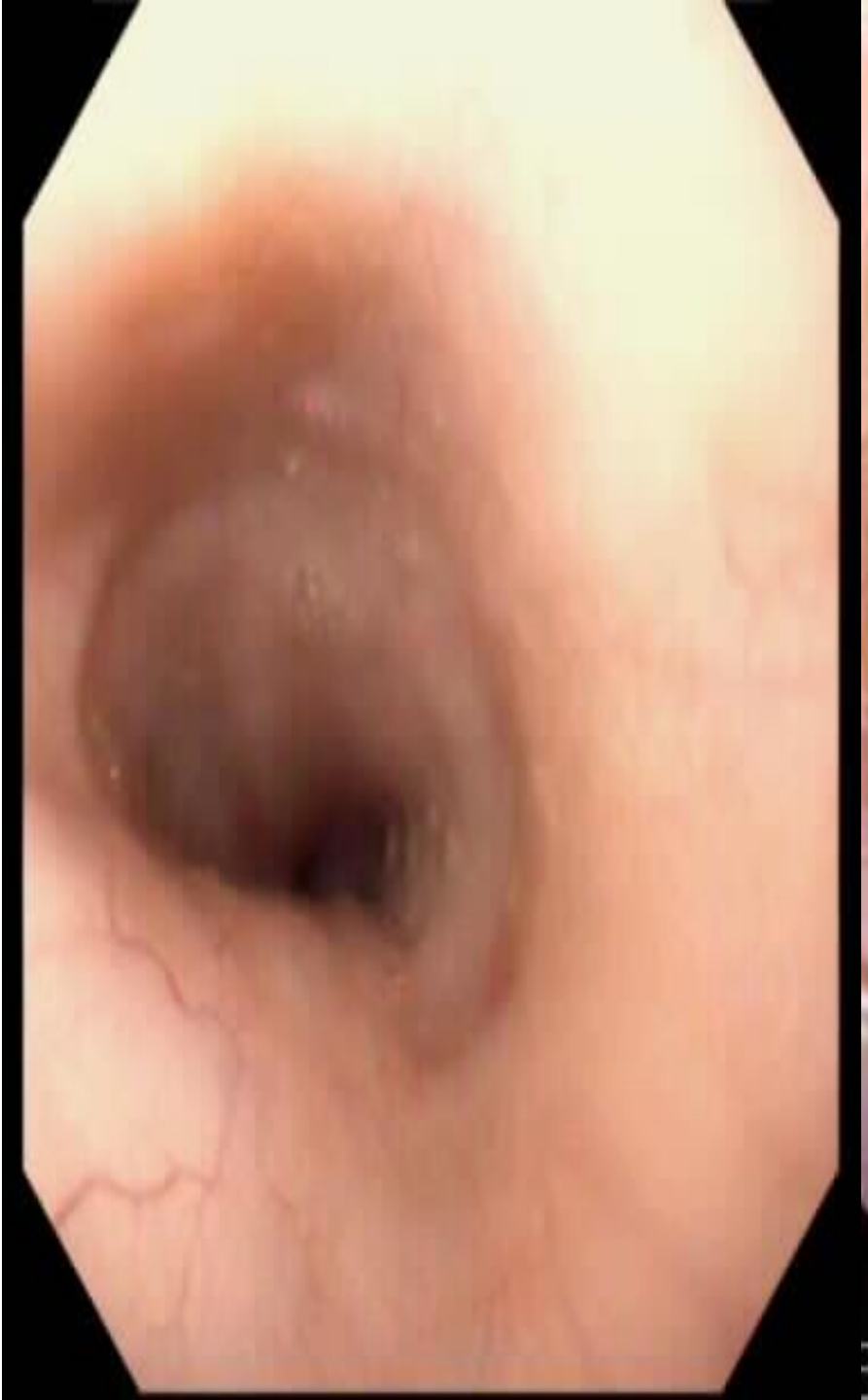
hypersplenism:
-- moderate anemia
-- neutropenia
-- thrombocytopenia

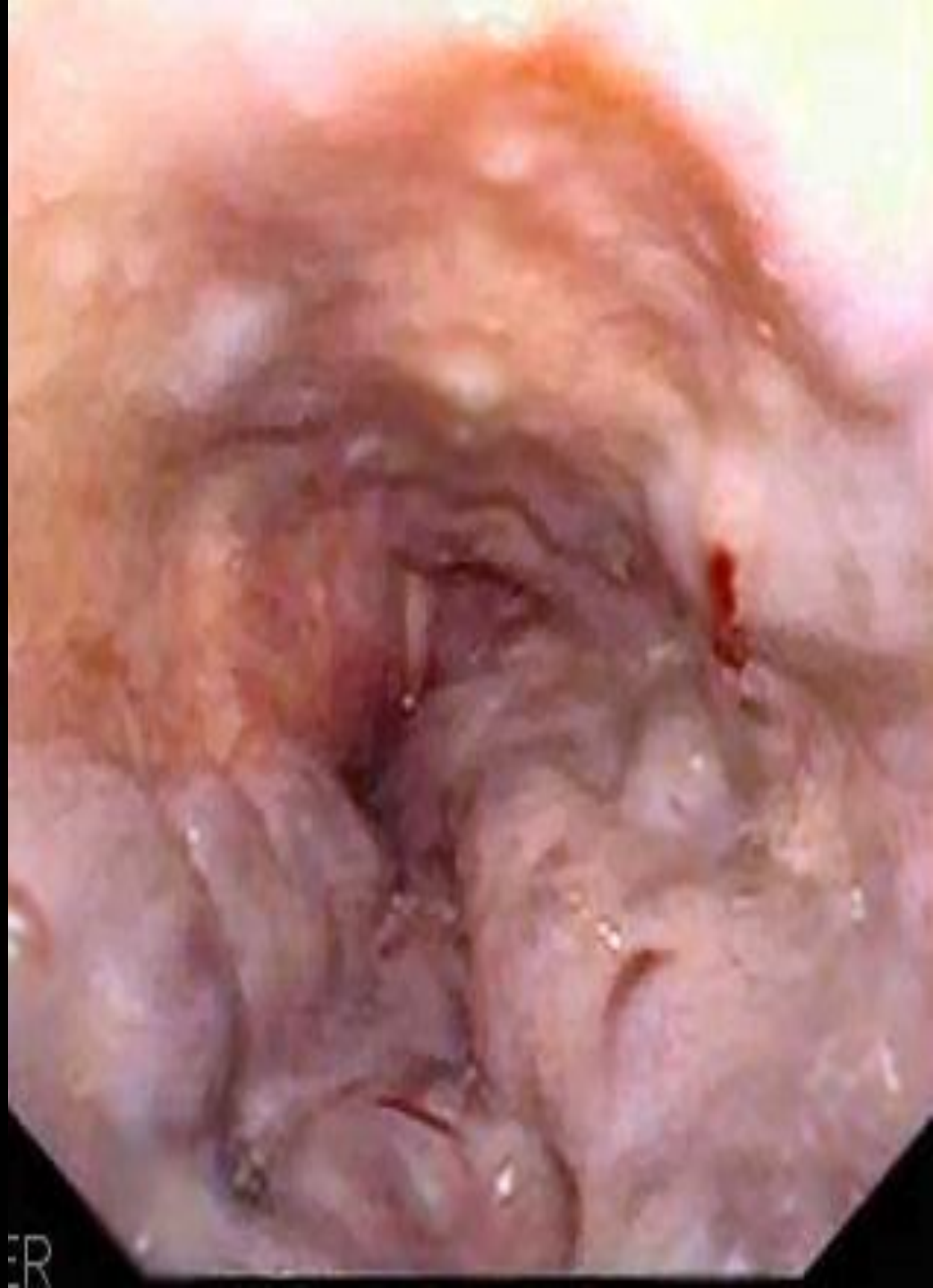
caput
medusae

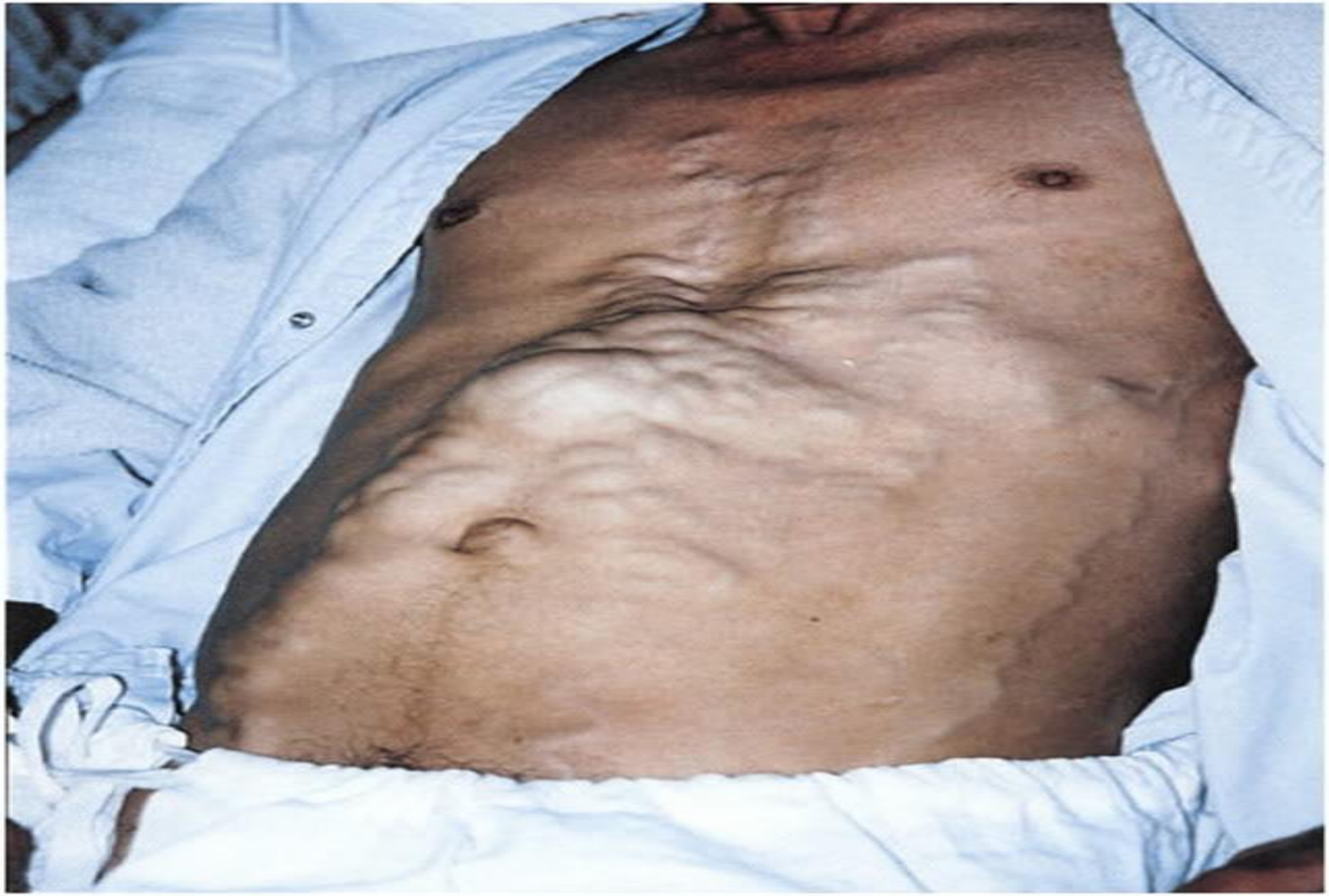
marked
ascites

hemorrhoids

Of course,
liver failure and
its signs are often
present as well.

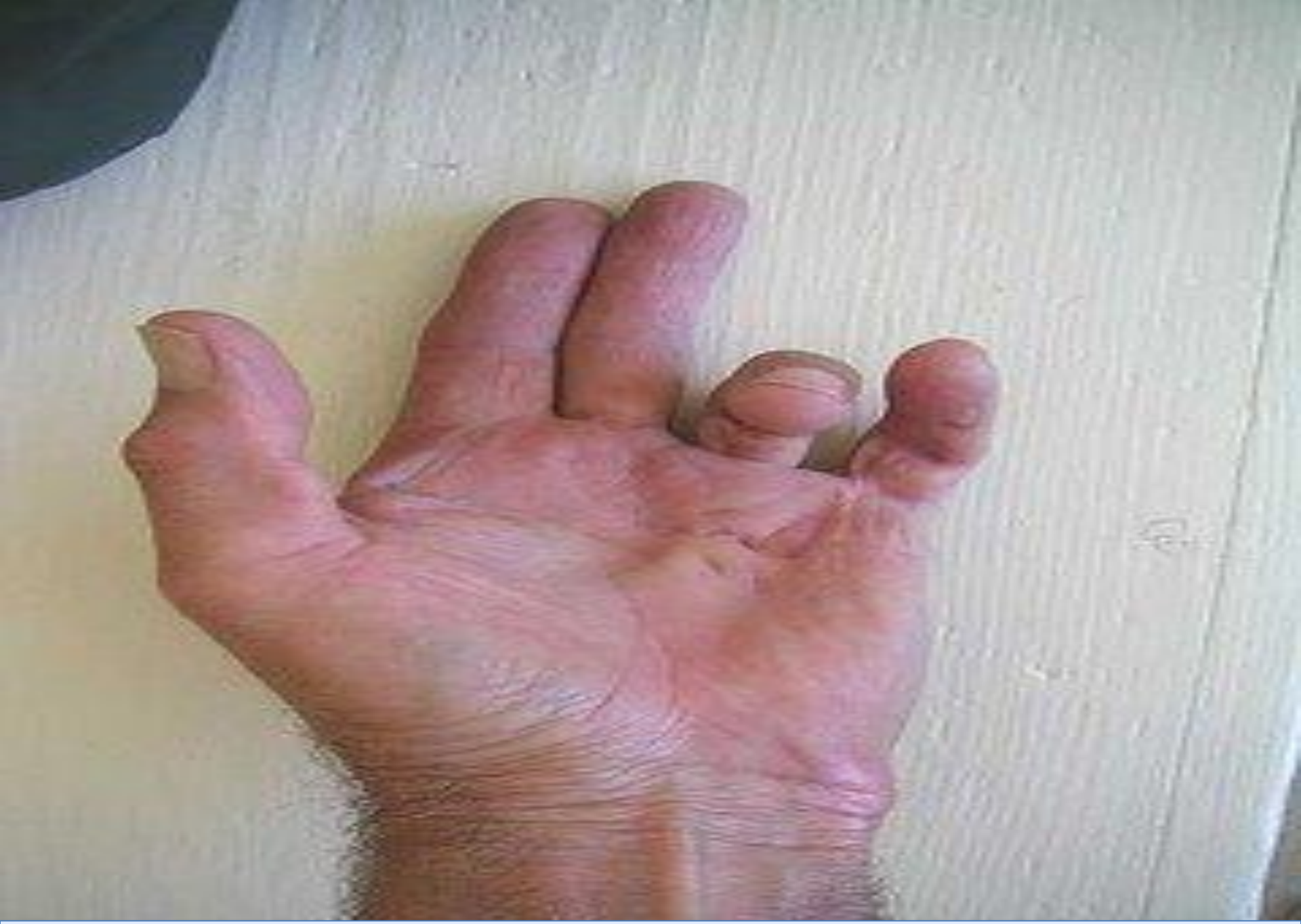




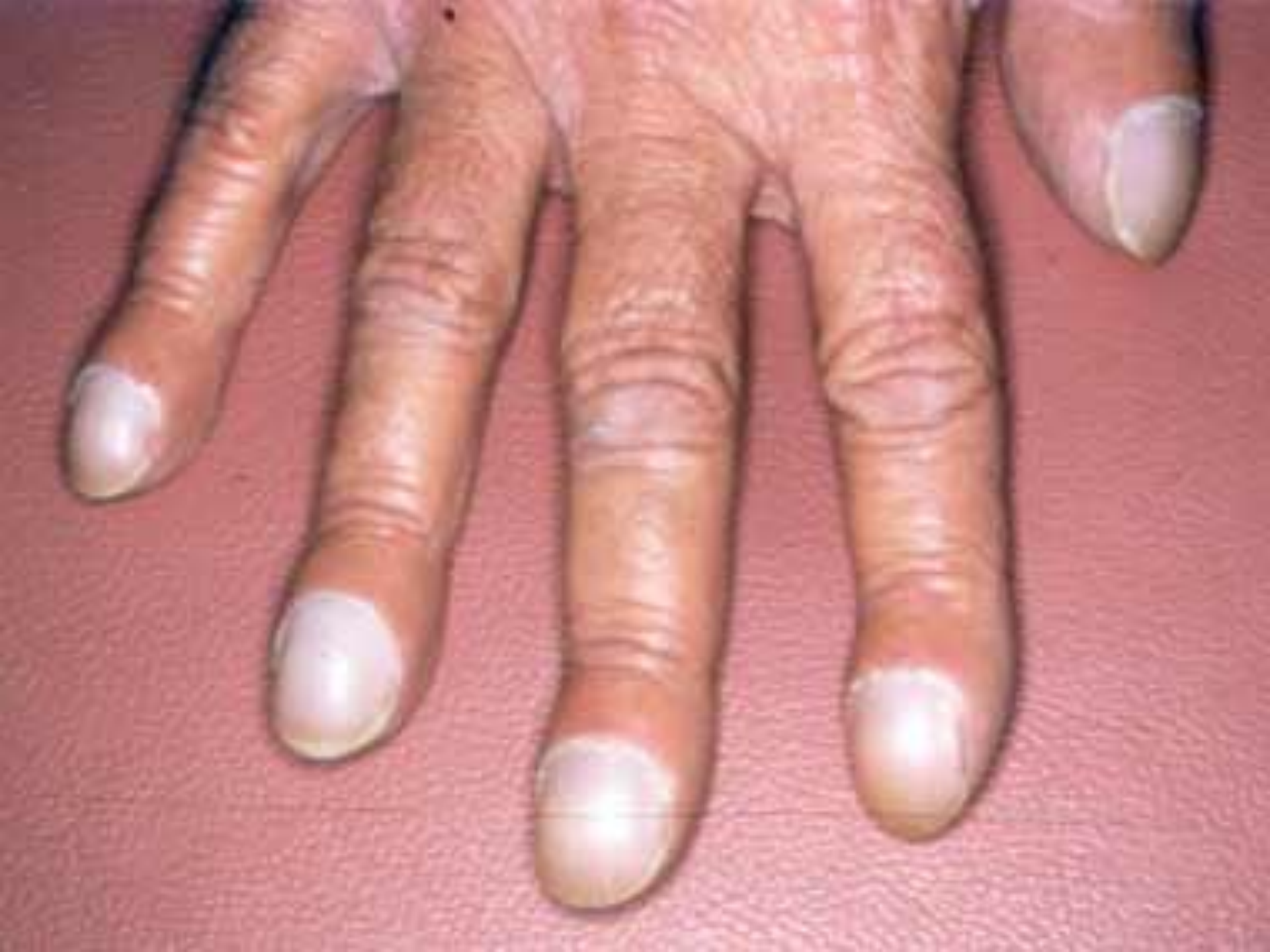


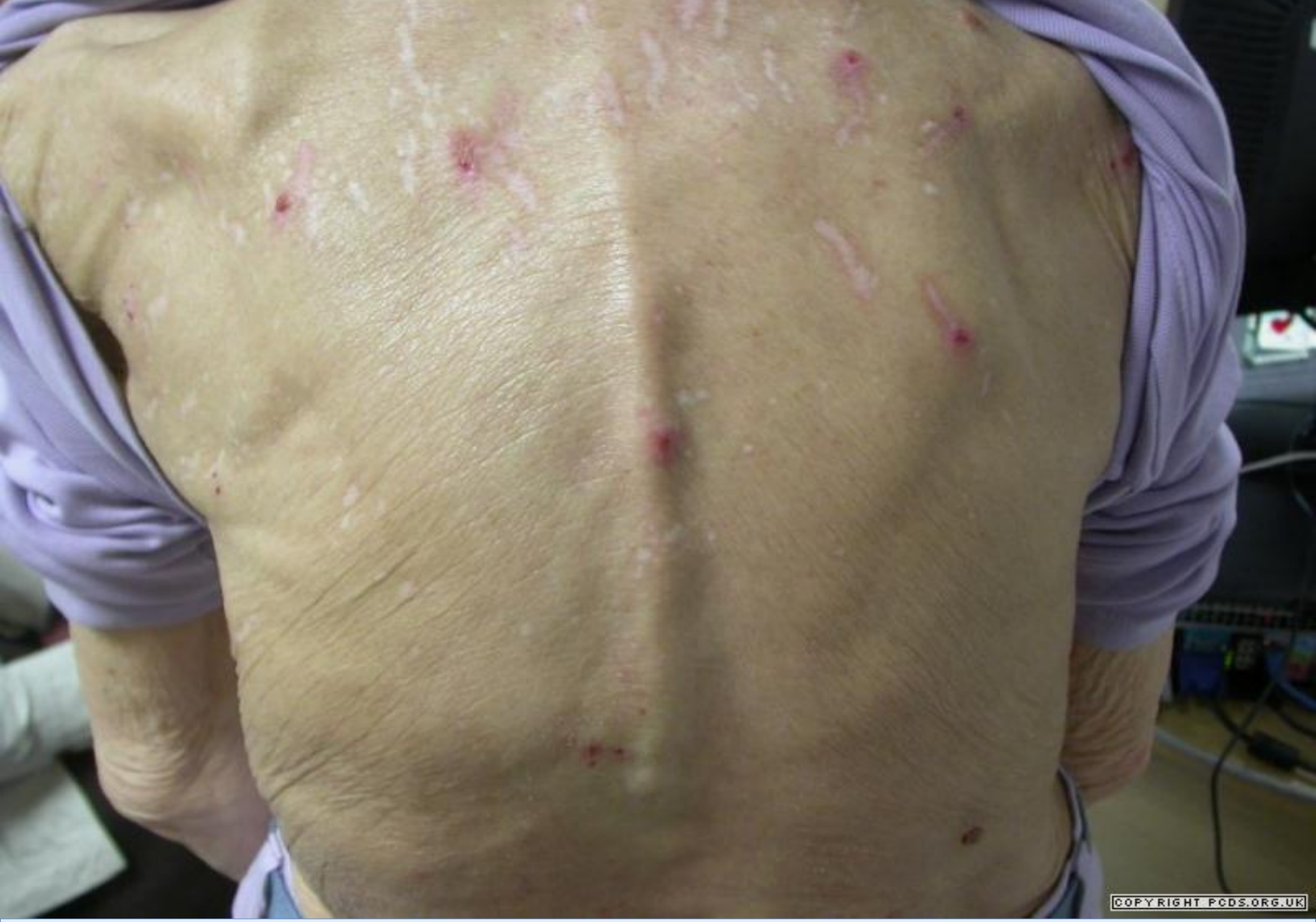
Caput medusae is the appearance of distended and engorged paraumbilical veins, which are seen radiating from the umbilicus across the abdomen.

The name *caput medusae* ("head of Medusa"): is a Latin word referred to the cap of Medusa, who had venomous snakes in place of hair.



Duputryn's contracture





Pruritus: the patient scratched and excoriate areas of skin that can be reached.

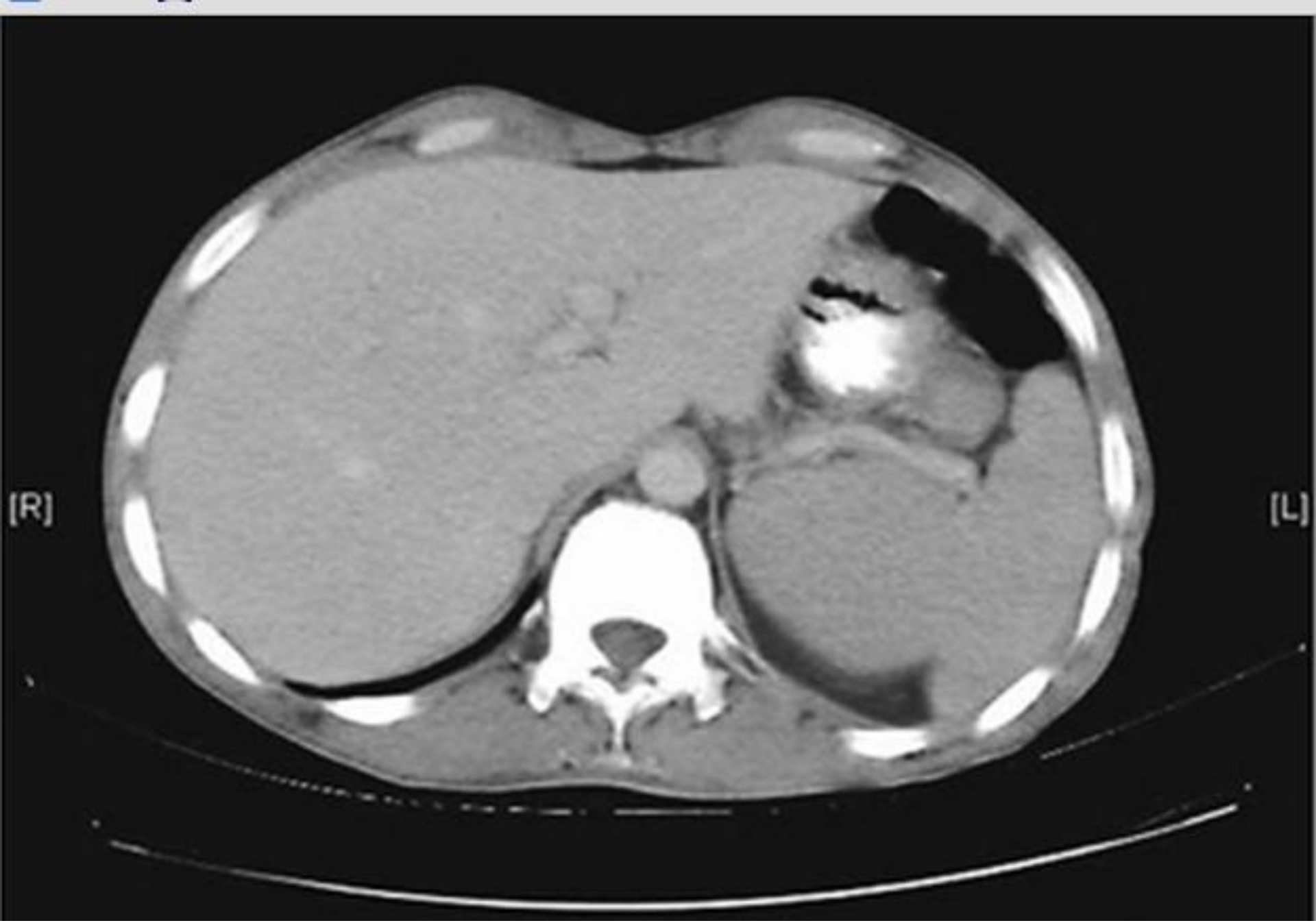
Investigations

A-Laboratory Features:

- **Hepatocellular dysfunction:** (Hypoalbuminemia and prolonged PT), hyperbilirubinemia, low blood urea and elevated ammonia levels.
- **Portal hypertension:** Thrombocytopenia and leukopenia.
- **Anemia:** Hypersplenism or GI bleeding.

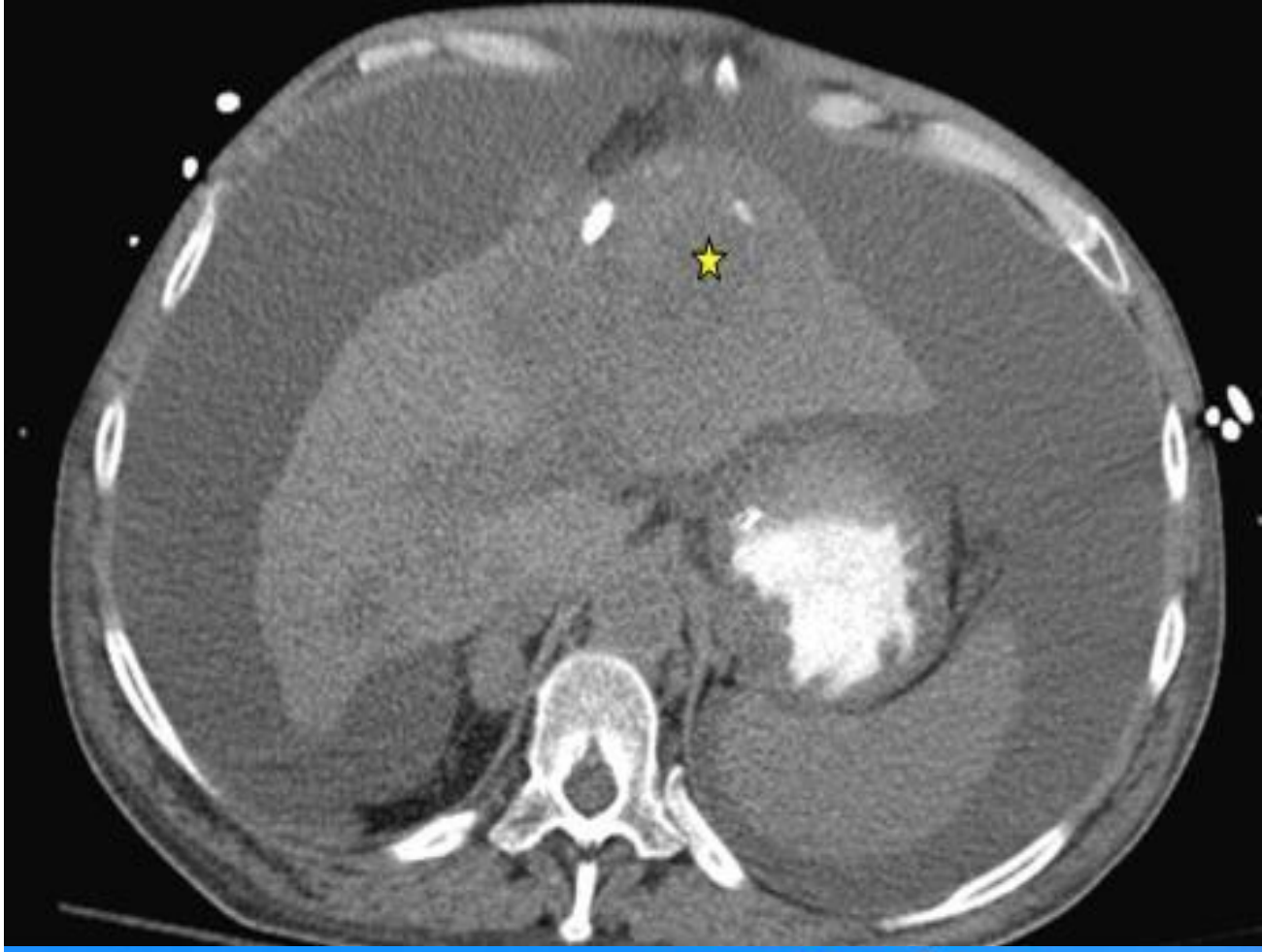
B- Radiologic features: includes U/S of abdomen with or without Doppler of the portal and hepatic venous vessels. CT or MRI: which show liver atrophy with nodular surface and features of portal hypertension.

C- liver biopsy: no need in the presence of clinical and laboratory features but may be considered when the cause of liver disease is doubtful.



Normal liver on CT scan, with smooth liver contours, normal size of spleen.

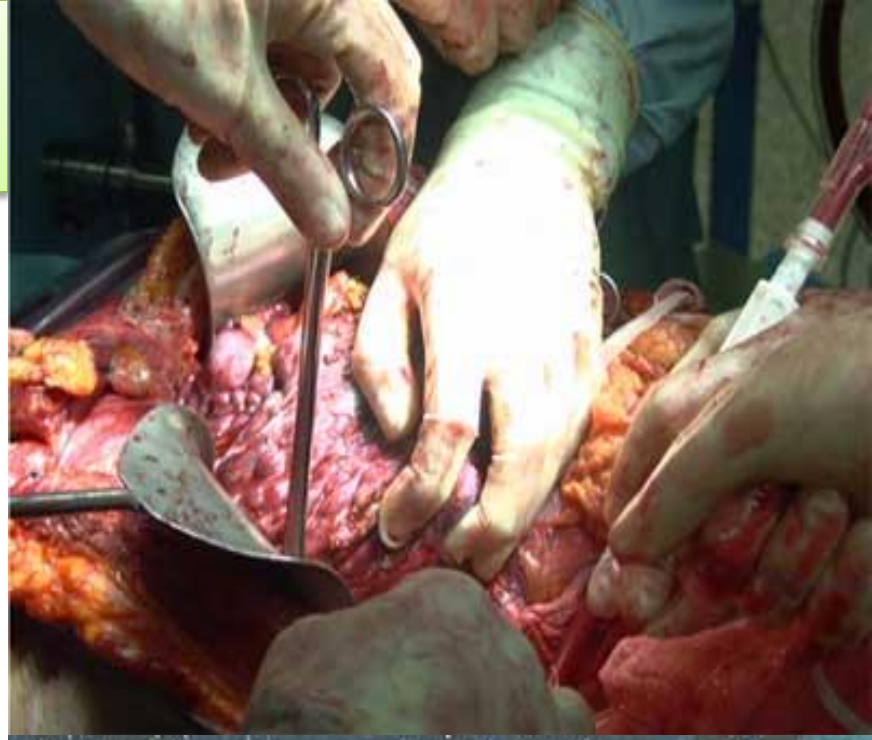
CT image of upper abdomen revealing cirrhotic liver with a large mass in left hepatic lobe (star) and massive ascites

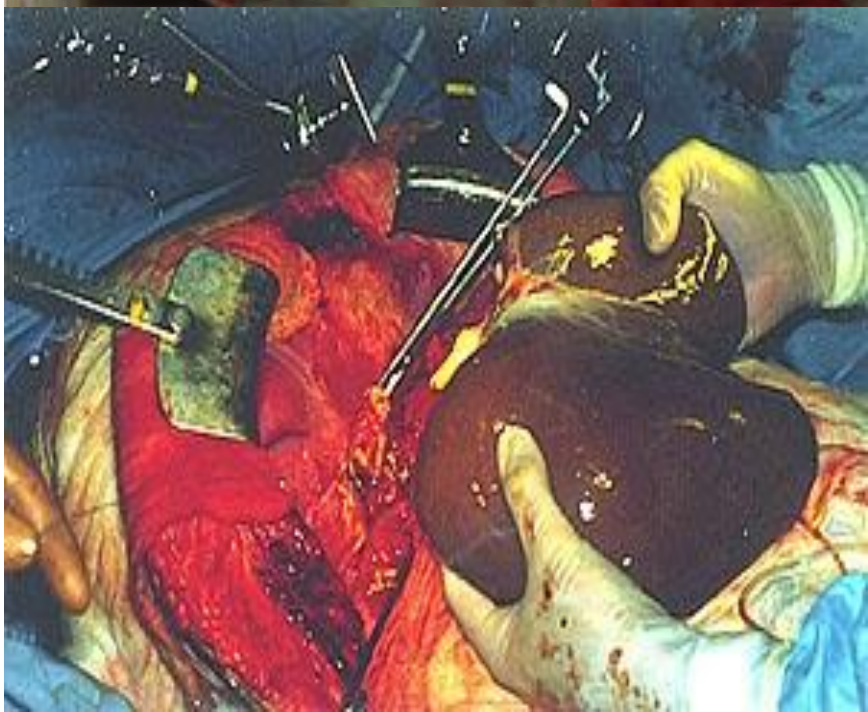


Cross-section of liver showing green-yellow hepatocellular carcinoma in left hepatic lobe (star).

Treatment of liver cirrhosis

- Treatment of any known cause
- The maintenance of nutrition
- Treatment of the complications of cirrhosis
- Endoscopy should be performed to screen for esophageal varices and repeated every 2 years.
- Regular surveillance for hepatocellular carcinoma
- Liver transplantation: accounts for about three-quarters of all liver transplants





Prognosis: Child-Pugh classifi. of prognosis in cirrhosis

	1	2	3
Encephalopathy	None	Mild	Marked
Bilirubin (µmol/l)	< 34	34-50	> 50
Albumin (g/l)	> 35	28-35	< 28
Prothrombin time (seconds prolonged)	< 4	4-6	> 6
Ascites	None	Mild	Marked

Child-Pugh grade	Hepatic deaths (%)
< 7 = Child's A	43
7-9 = Child's B	72
> 9 = Child's C	85

Major complications of liver cirrhosis

A. Hepatocellular dysfunction and portal hypertension, which may result in:

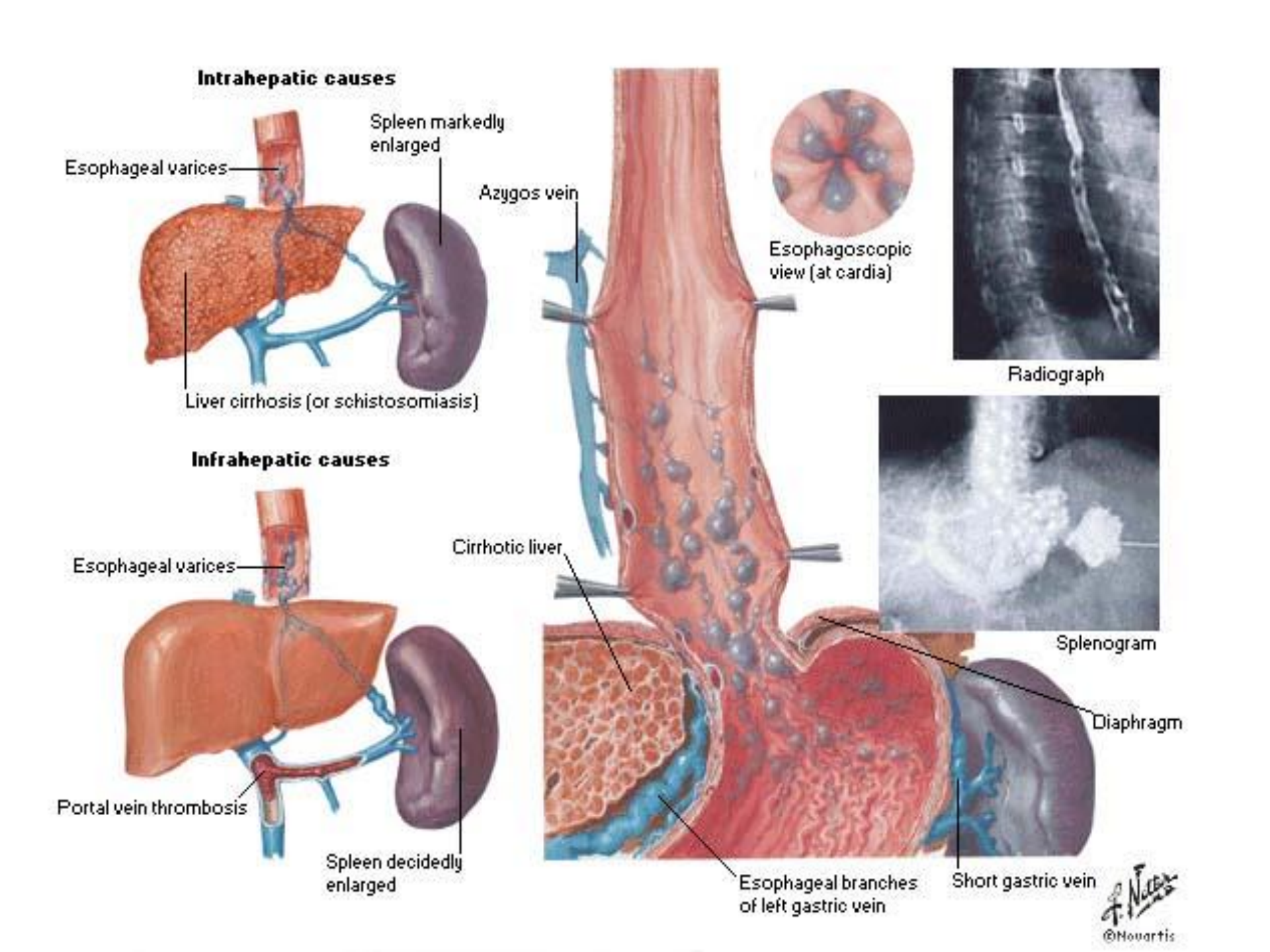
1. Variceal hemorrhage
2. Ascites, which can be further complicated by spontaneous bacterial peritonitis
3. Hepatic encephalopathy
4. Hepatorenal syndrome
5. Hepatopulmonary syndrome

B. Hepatocellular carcinoma

Portal hypertension

- Prolonged elevation of the portal venous pressure above 12 mmHg (normally 5- 6 mmHg).
- Increase in intrahepatic vascular tone → increased resistance to portal venous flow → an increase in portal venous pressure → development of collateral vessels, allowing portal blood to bypass the liver and enter the systemic circulation directly especially in the distal oesophagus, stomach and rectum, in the anterior and abdominal wall.
- Splenomegaly is a cardinal finding.
- Hypersplenism is common: Thrombocytopenia
- Collateral vessels around the umbilicus to form a caput medusae. Rarely, give a venous hum on auscultation

- Oesophageal and gastric varices can be a source of severe bleeding. Rectal varices also cause bleeding and are often mistaken for haemorrhoids.
- Fetor hepaticus results from portosystemic shunting of blood, which allows mercaptans to pass directly to the lungs.
- Ascites occurs as a result of renal sodium retention
- Diagnosis: is often made clinically. Increased wedged hepatic venous pressure (WHVP). This is an indirect measurement of portal vein pressure. endoscopy to determine whether gastro-oesophageal varices are present.
- The management of portal hypertension is largely focused on the prevention and/or control of variceal haemorrhage.


Intrahepatic causes
Esophageal varices
Spleen markedly enlarged
Liver cirrhosis (or schistosomiasis)
Infrahepatic causes
Esophageal varices
Portal vein thrombosis
Spleen decidedly enlarged
Azygos vein
Cirrhotic liver
Esophagoscopic view (at cardia)
Radiograph
Splenogram
Diaphragm
Esophageal branches of left gastric vein
Short gastric vein
©Novartis

Variceal hemorrhage

- Commonly arises from oesophageal varices located within 3–5 cm of the gastrooesophageal junction, or from gastric varices. Predisposing factors: big size varices, endoscopic variceal features such as red spots and stripes, high portal pressure, liver failure and taking aspirin or NSAIDs.
- Endoscopy is mandatory to determine the size ,site of varices, and source of bleeding. To introduce some therapeutic options.

Management:

A- Management of acute variceal bleeding:

1- The priority in acute bleeding is to restore the circulation with blood and plasma. prophylactic broad-spectrum antibiotics, such as oral ciprofloxacin or intravenous cephalosporin. Prophylactic acid suppression with proton pump inhibitors

2- Pharmacological reduction of portal venous pressure: Terlipressin is a synthetic vasopressin analogue. It reduces portal blood flow and/or intrahepatic resistance and hence reduces portal pressure. It reduces mortality in the setting of acute variceal bleeding.

3- Banding ligation and sclerotherapy: Band ligation involves the varices being sucked into a cap placed on the end of the endoscope, allowing them to be occluded with a tight rubber band. The occluded varix subsequently sloughs with variceal obliteration. Band ligation has fewer side effects than, and has largely replaced, sclerotherapy, a technique in which varices are injected with a sclerosing agent.

4- Balloon tamponade: This technique employs a Sengstaken–Blakemore tube possessing two balloons that exert pressure in the fundus of the stomach and in the lower oesophagus respectively. Additional lumens allow material to be aspirated from the stomach and from the oesophagus above the oesophageal balloon. This technique may be used in the event of life-threatening haemorrhage if early endoscopic therapy is not available or is unsuccessful.

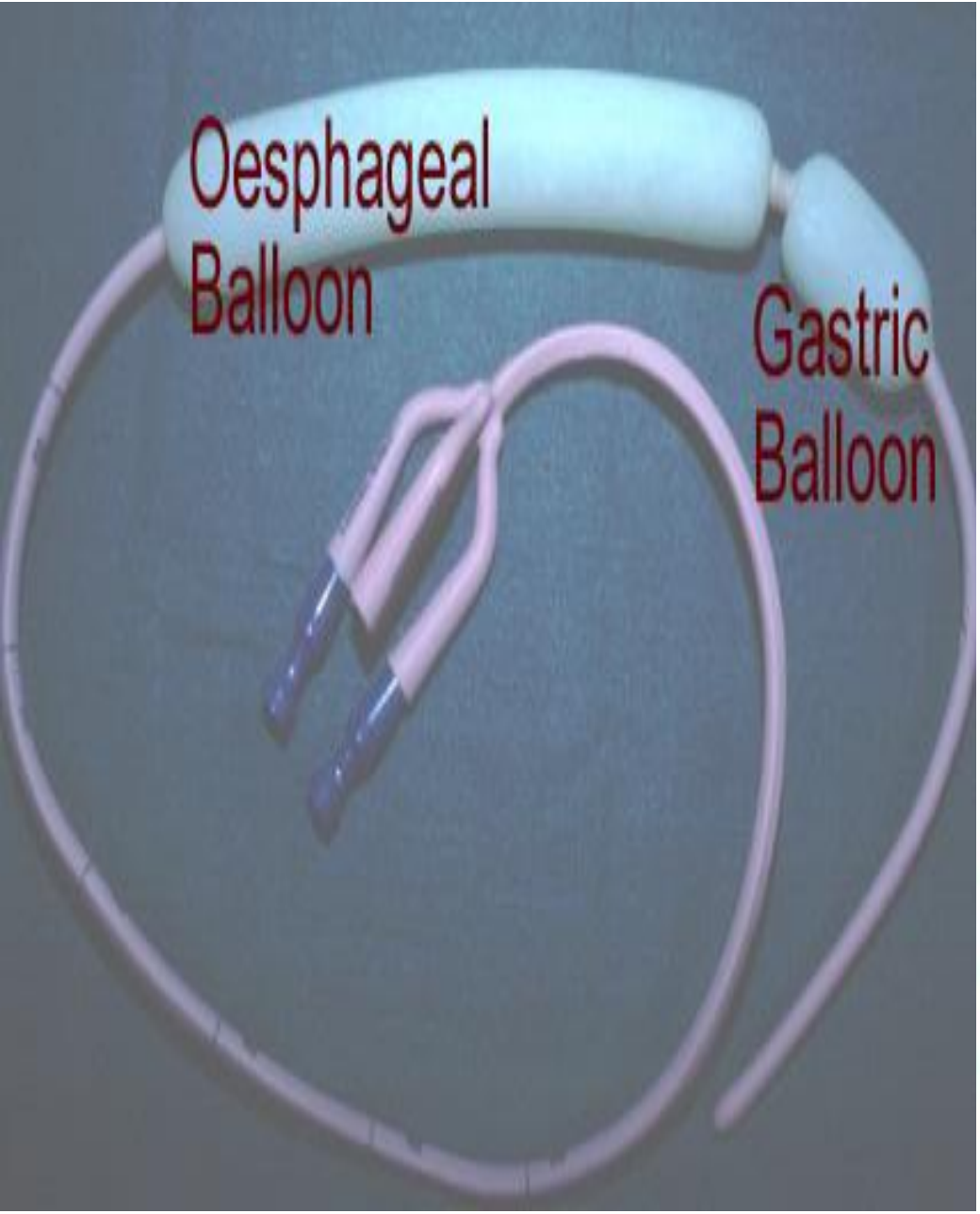
5- TIPSS: This technique uses a stent placed between the portal vein and the hepatic vein within the liver to provide a portosystemic shunt and therefore reduce portal pressure. It is carried out under radiological control via the internal jugular vein.

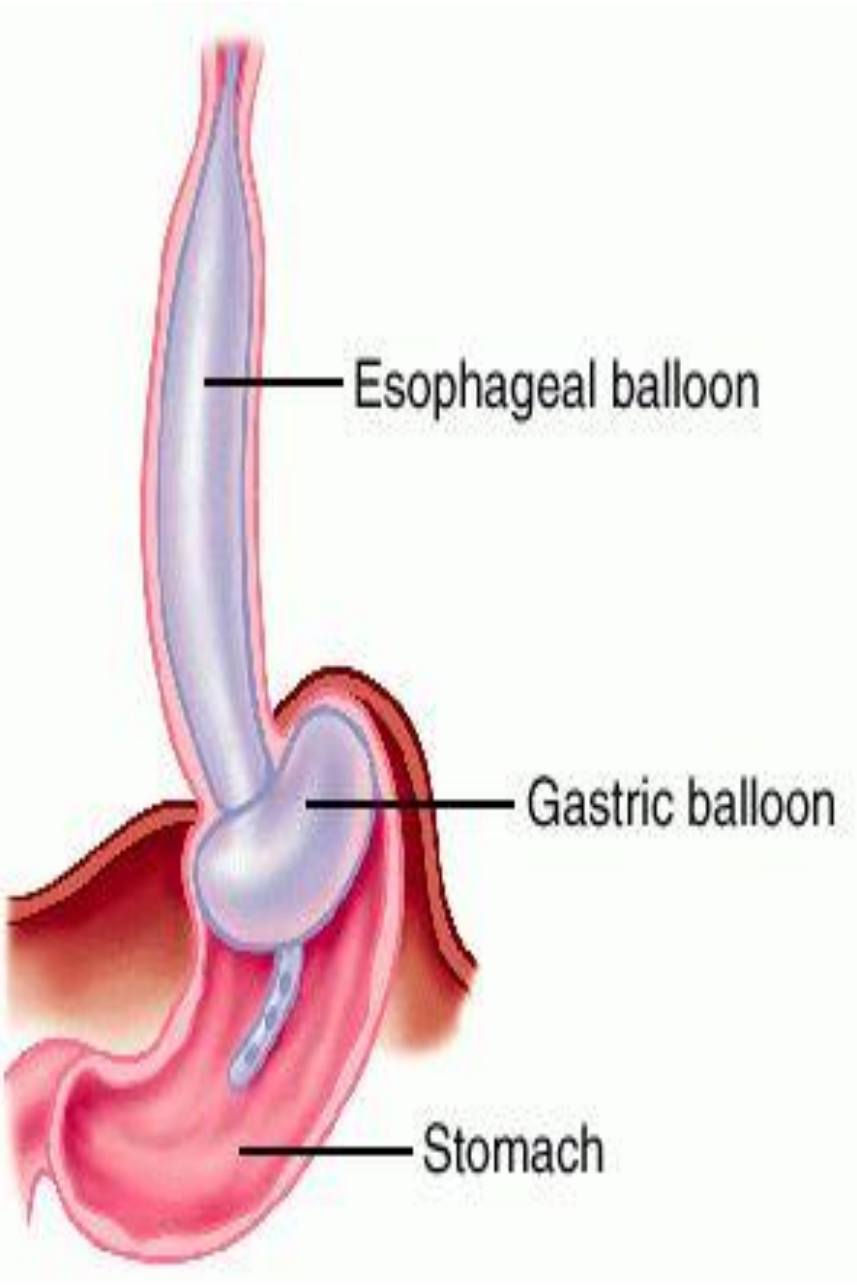
6- Portosystemic shunt surgery. Surgery prevents recurrent bleeding, but carries a high mortality and often leads to encephalopathy.

7- Oesophageal transection. Rarely, surgical transection of the varices may be performed as a last resort when bleeding cannot be controlled by other means, but operative mortality is high.

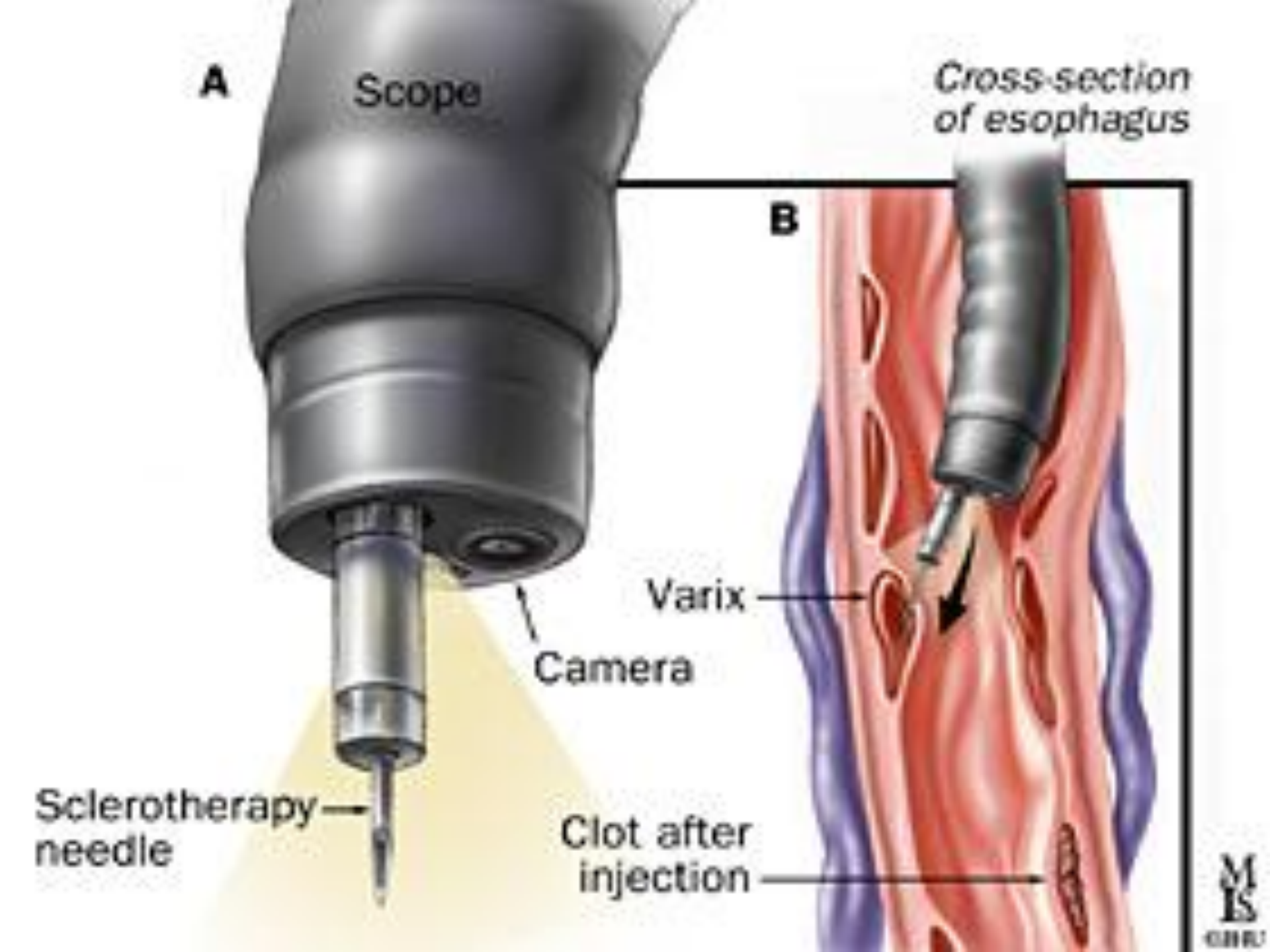
B- Secondary prevention of variceal bleeding

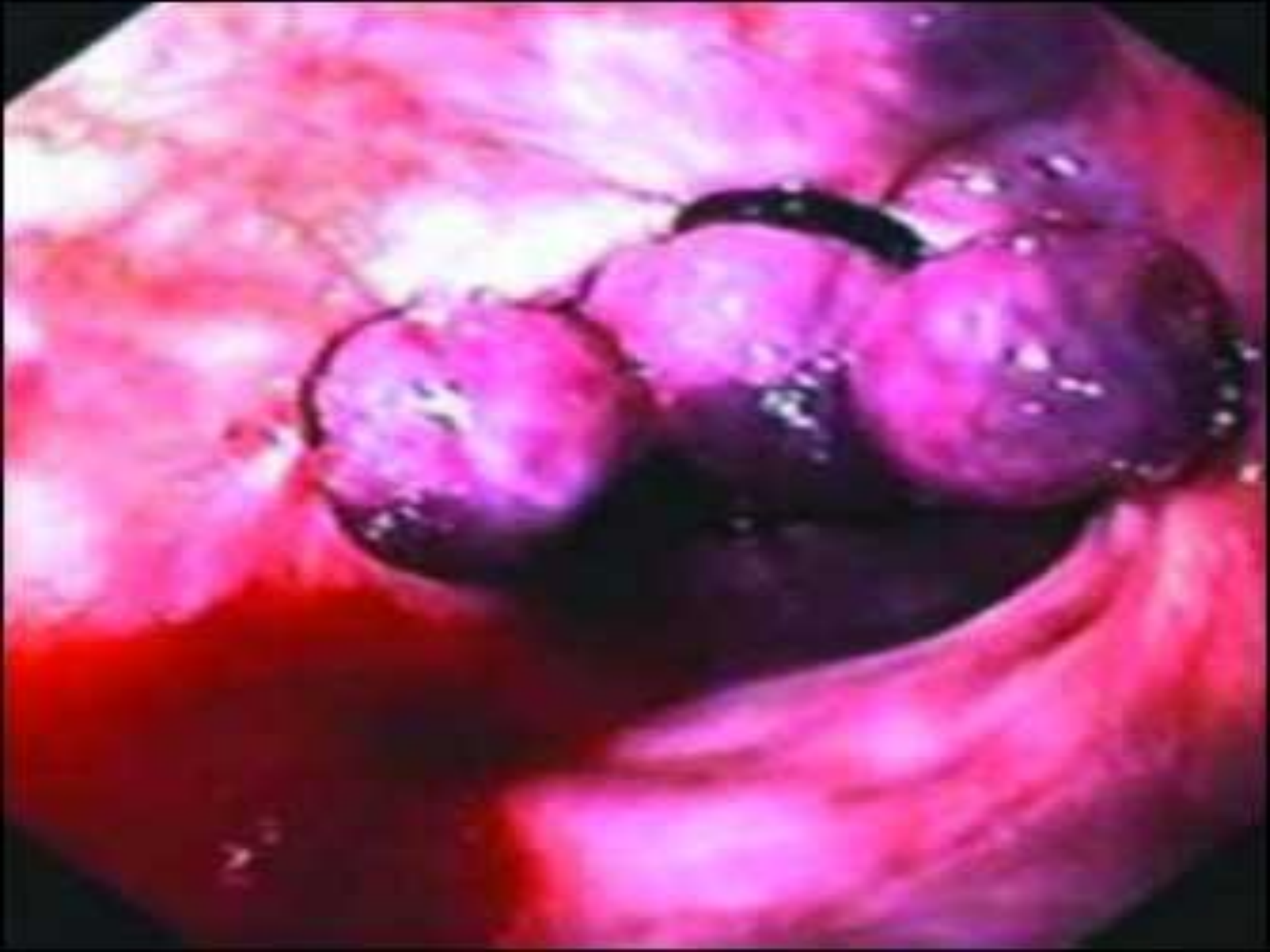
1. Beta-blockers
2. Oesophageal banding programme with repeated sessions of therapy at 1- to 2-week intervals until the varices are obliterated.
3. TIPSS may also be considered in this setting.

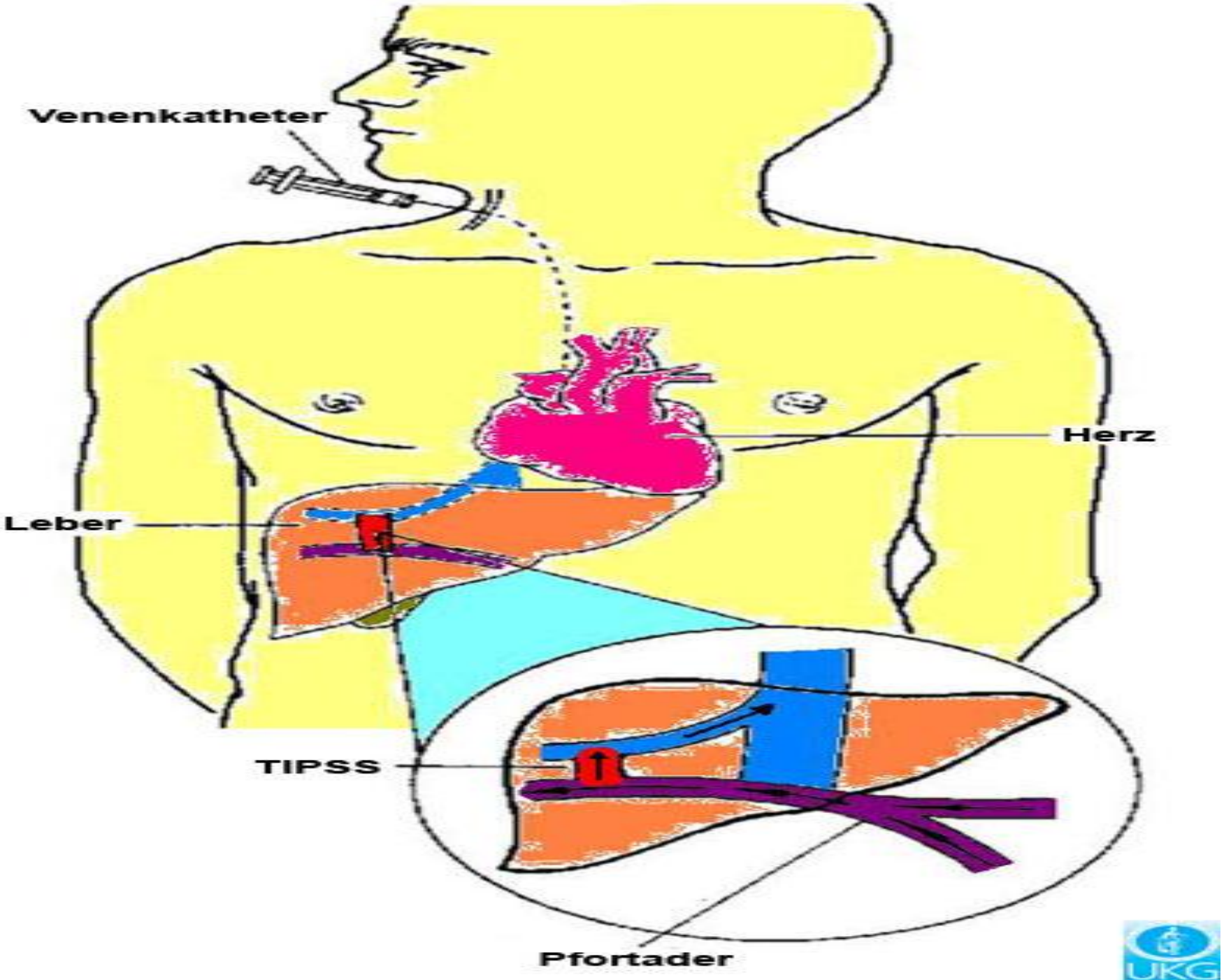


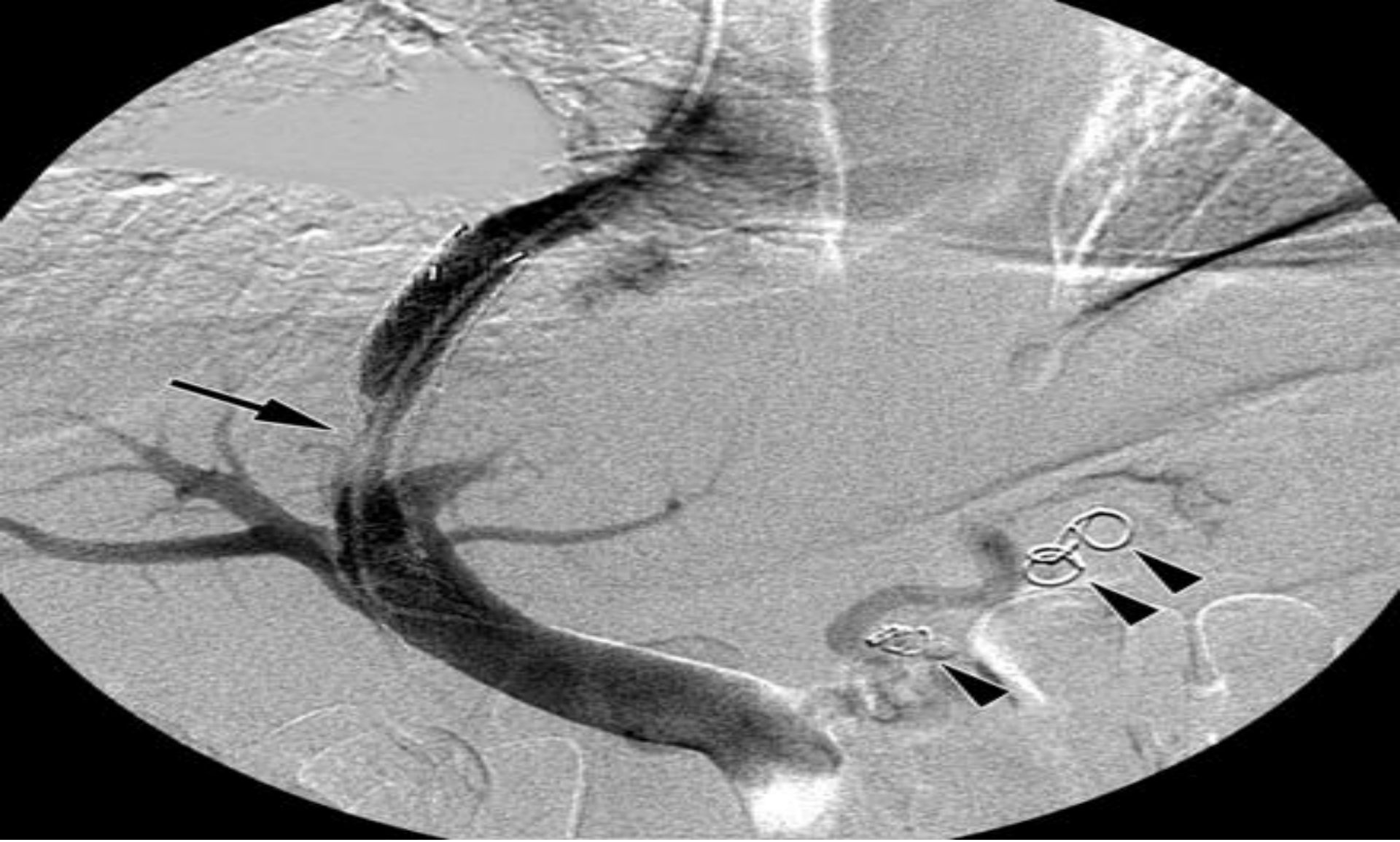


Sengstaken Blakemore catheter obtain temporary hemostasis by direct compression of the varices


A
Scope
Cross-section
of esophagus
B
Varix
Camera
Sclerotherapy
needle
Clot after
injection




Venenkatheter
Herz
Leber
TIPSS
Pfortader



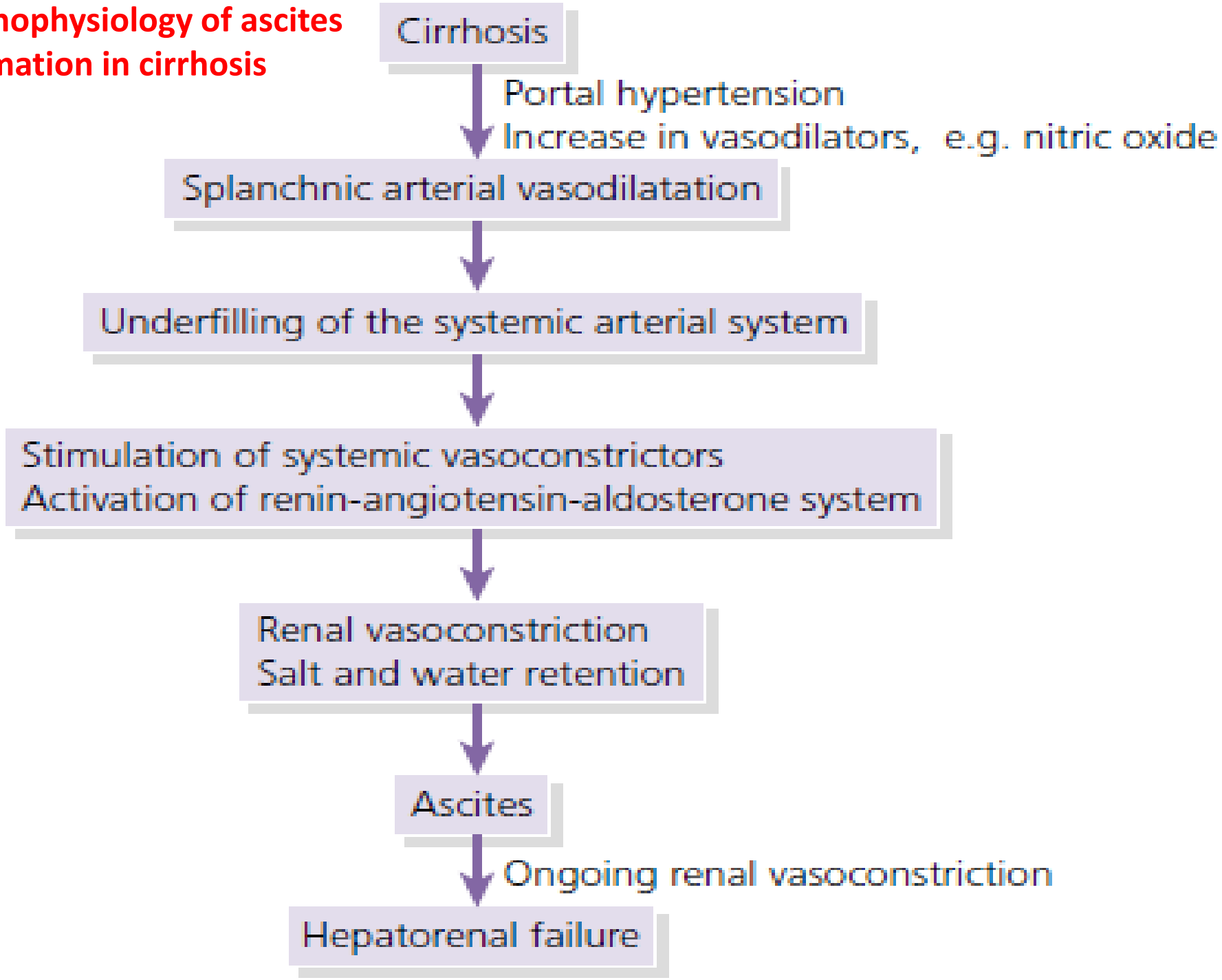
Transjugular intrahepatic portosystemic shunt (TIPS) procedure because of variceal bleeding unresponsive to pharmacologic and endoscopic treatment. Portogram shows clearly visible narrow segment (*arrow*) of portosystemic shunt. Coils (*arrowheads*) placed to occlude esophageal varices.

Ascites

- Accumulation of excess fluid in the peritoneal cavity
- Clinically detectable when it is greater than 500 ml
- Cirrhosis is the most common cause of ascites
- A high serum-ascites albumin gradient (>1.1 g/dL) signifies portal hypertension

Pathogenesis in cirrhosis: Splanchnic vasodilation mediated by vasodilators, mainly nitric oxide (*overflow theory*) that lead to fall in systemic arterial pressure. This leads to activation of the renin-angiotensin system with secondary aldosteronism, increased sympathetic nervous activity and increased atrial natriuretic hormone secretion. These lead to renal sodium and water retention to normalize arterial pressure (*underflow theory*).

Pathophysiology of ascites formation in cirrhosis



Serum-ascites albumin gradient or gap (SAAG)

SAAG = (albumin concentration of serum) - (albumin concentration of ascitic fluid).

SAAG >=1.1g/dL

1. Cirrhosis
2. Alcoholic hepatitis
3. CHF
4. Constrictive pericarditis
5. Budd – Chiari syndrome

SAAG <1.1g/dL

1. Peritoneal carcinomatosis
2. Peritoneal TB
3. Pancreatitis
4. Serositis
5. Nephrotic syndrome
6. Bowel obstruction / infarction / perforation

Management:

1- Bed rest: can improve ascites as the upright position can result in activation of the rennin- angiotensin system, reduced glomerular filtration rate and sodium excretion.

2- Sodium and water restriction: Daily sodium intake to 100 mmol/day (2 g/d). No add salts to their food and avoid processed foods. Drugs containing relatively large amounts of sodium, and those promoting sodium retention such as non-steroidal anti-inflammatory drugs (NSAIDs), must be avoided.

3- Diuretic drugs: Spironolactone (100-400 mg/day) is the drug of choice. Some also require powerful loop diuretics, e.g. furosemide. Patients who do not respond to doses of 400 mg spironolactone and 160 mg furosemide are considered to have **Refractory ascites.**

4- Paracentesis: is the first-line treatment of refractory ascites. Paracentesis to dryness is safe, provided the circulation is supported with an intravenous colloid such as human albumin (6–8 g per litre of ascites removed, usually as 100 mL of 20% human albumin solution (HAS) for every 1.5–2 L of ascites drained) or another plasma expander.

5- TIPS and shunts urgery: is a recognised treatment of refractory ascites. It is alternative to large-volume paracentesis, but can aggravate encephalopathy

6- Peritoneo-venous shunt: Is a long tube with a non-return valve running subcutaneously from the peritoneum to the internal jugular vein in the neck, which allows ascitic fluid to pass directly into the systemic circulation. Insertion of these shunts is now rare.

7- Liver transplantation

CAUSES OF ASCITES

Common causes

- Malignant disease
  - Hepatic
  - Peritoneal
- Cardiac failure
- Hepatic cirrhosis

Other causes

- Hypoproteinaemia
  - Nephrotic syndrome
  - Protein-losing enteropathy
  - Malnutrition
- Hepatic venous occlusion
  - Budd-Chiari syndrome
- Pancreatitis
- Lymphatic obstruction
- Infection
  - Tuberculosis
  - Spontaneous bacterial peritonitis
- Rare
  - Meigs' syndrome
  - Vasculitis
  - Hypothyroidism
  - Renal dialysis

Ascitic fluid: appearance

- Cirrhosis: clear, straw-coloured or light green
- Malignant disease: bloody
- Infection: cloudy
- Biliary communication: heavy bile staining
- Lymphatic obstruction: milky-white (chylous)

Useful investigations

- Total albumin (plus serum albumin)
- Amylase
- White cell count
- Cytology
- Microscopy and culture

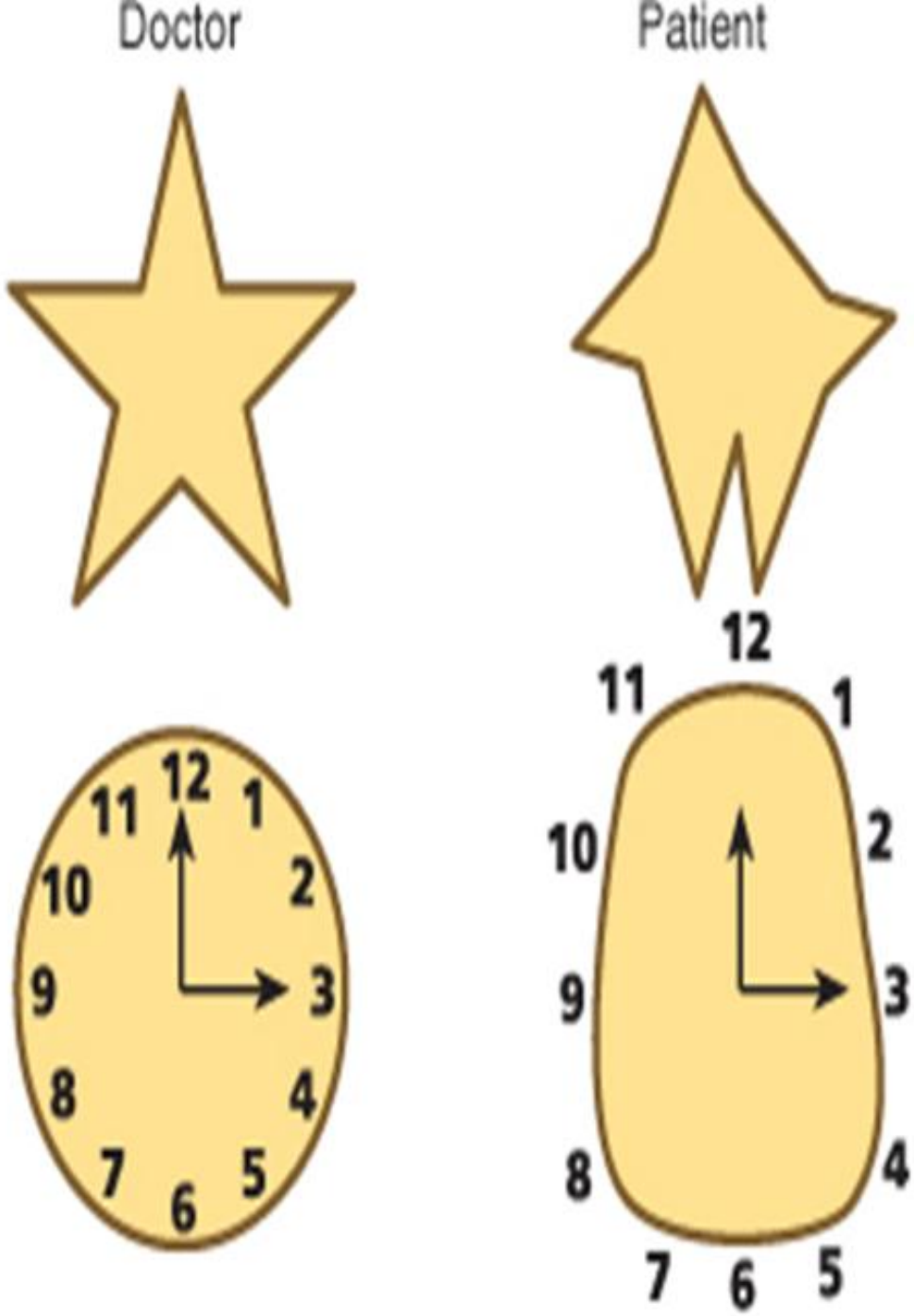
Spontaneous bacterial peritonitis

- Infection of ascitic fluid in a patient with obvious features of cirrhosis and ascites. ***Escherichia coli*** is the organism most frequently found.
- **Presented** with abdominal pain, rebound tenderness, absent bowel sounds and fever
- Diagnostic paracentesis show cloudy fluid, and an **ascites neutrophil count above 250 × 10^6/L**. Ascitic fluid culture for detection of organisms.
- **Treatment** should be started immediately with broad spectrum antibiotics, such as cefotaxime or piperacillin/ tazobactam).
- **Prophylactic** norfloxacin 400 mg/day indicated in recurrent SBP, an ascitic fluid total protein concentration <1 g/dL, or active gastrointestinal bleeding.

Hepatic encephalopathy

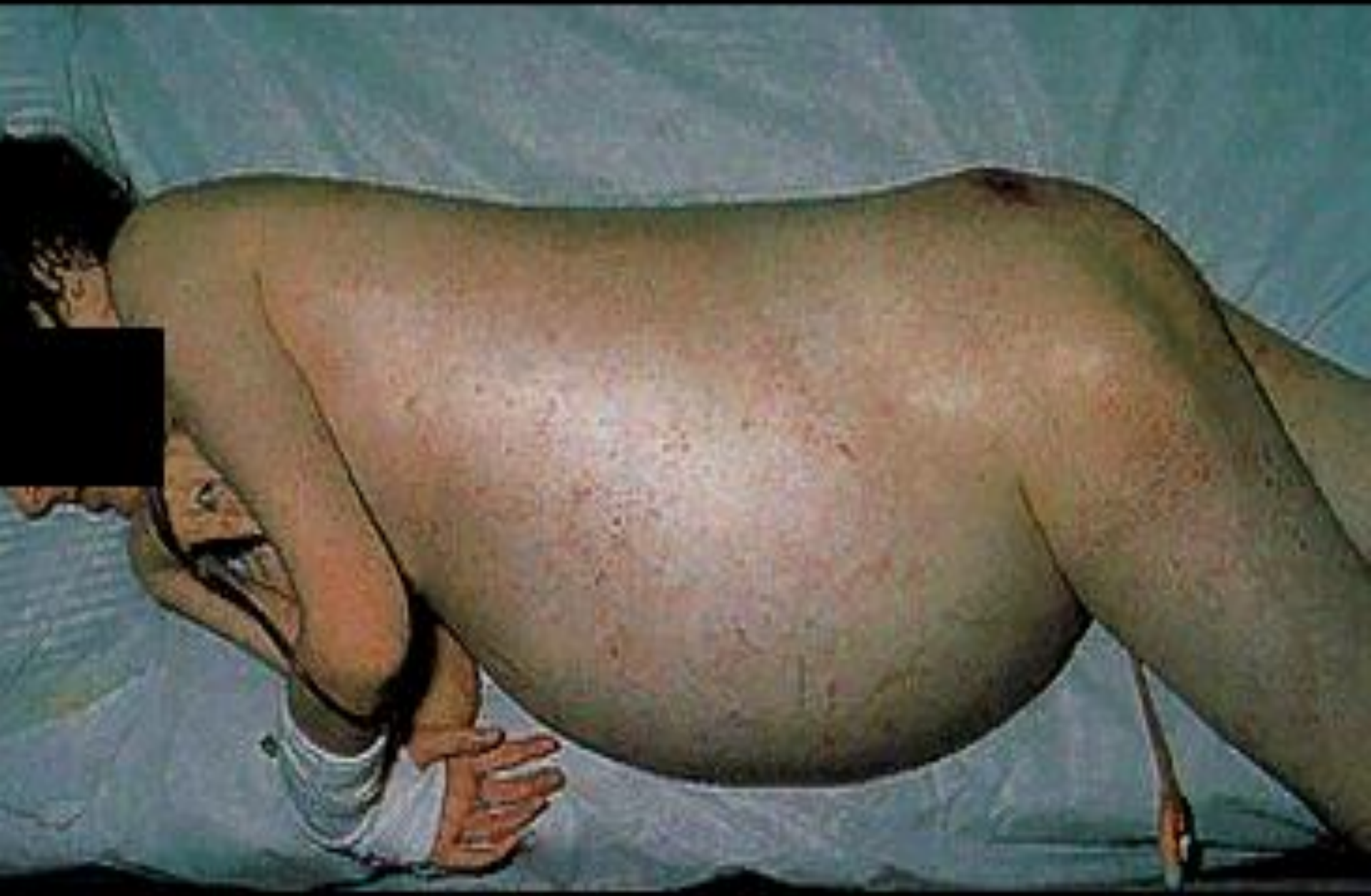
- A neuropsychiatric syndrome that may complicate advanced liver disease.
- Extensive portosystemic collateral formation (*shunting*).
- Inadequate hepatic removal of nitrogenous compound like **ammonia, γ-aminobutyric acid, octopamine, amino acids, mercaptans and fatty acids.** Which pass through portosystemic shunting to CNS, lead to brain dysfunction and cerebral oedema.
- **Examination:** Disturbed consciousness, fetor hepaticus, flapping tremor (asterixis) , constructional apraxia, hyper-reflexia and bilateral extensor plantar responses. The degree of encephalopathy can be graded from 1 to 4, depending on these features, and this is useful in assessing response to therapy.

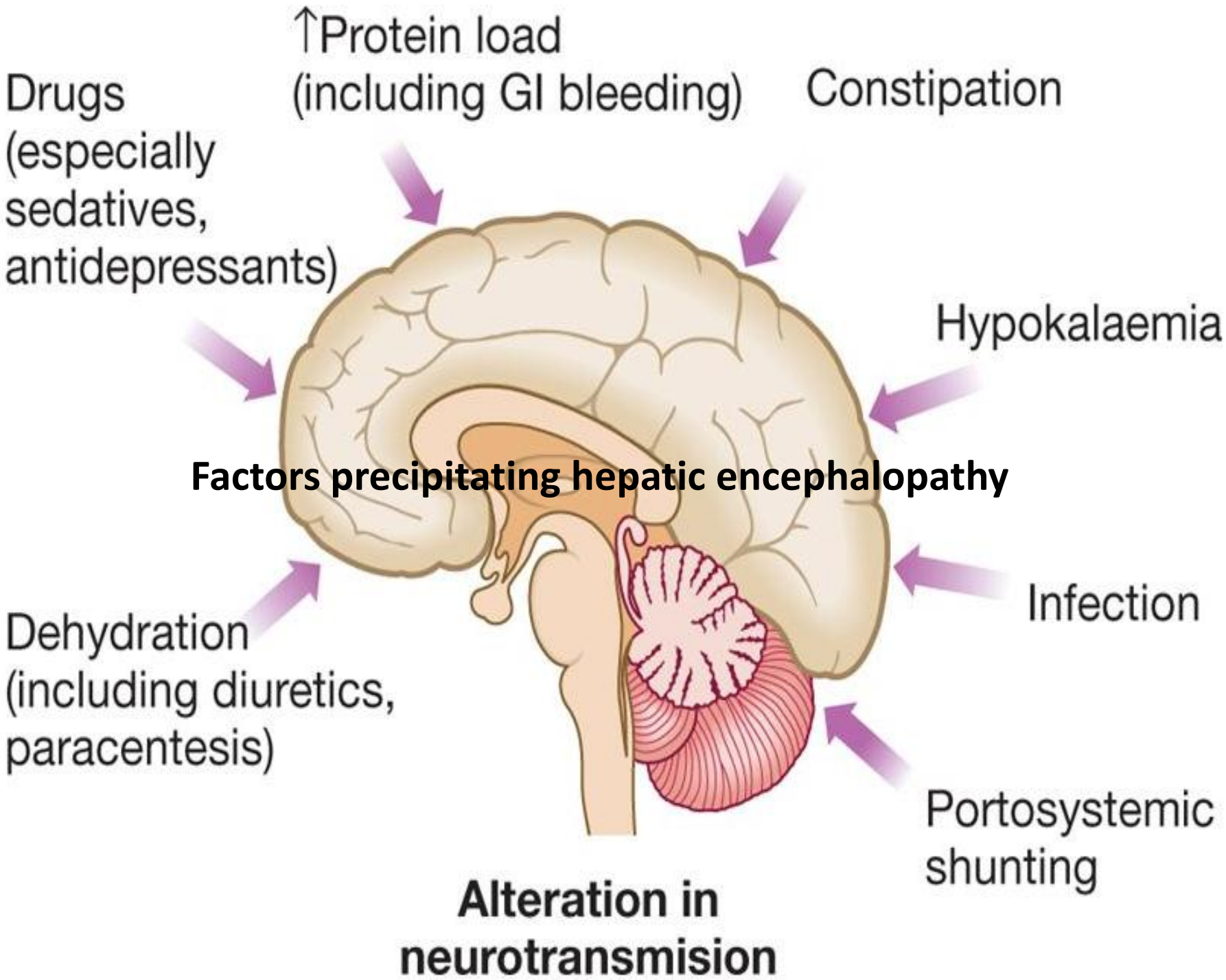
Constructional apraxia in encephalopathy. Drawing stars and clocks may reveal marked abnormality.



Clinical grading of hepatic encephalopathy

Clinical grade	Clinical signs
Grade 1	Poor concentration, slurred speech, disordered sleep rhythm
Grade 2	Drowsy, occasional aggressive behavior, lethargic
Grade 3	Marked confusion, gross disorientation
Grade 4	Unresponsive to voice, unconscious





Factors precipitating hepatic encephalopathy

Treatment:

- If the patient is in a **coma**, supportive measures: airway protection, fluid balance, nutrition support
- Identify and remove any possible **precipitant**: correct electrolyte disturbances, stop drugs especially opiates, benzodiazepines and diuretics.
- Actively seek and treat any **infection**
- **Lactulose** (15–30 mL 3 times daily) is increased gradually until the bowels are moving twice daily. It produces an osmotic laxative effect, reduces the pH of the colonic content, thereby limiting colonic ammonia absorption.
- **Rifaximin** (400 mg 3 times daily) is a well tolerated, non-absorbed antibiotic that acts by reducing the bacterial content of the bowel and has been shown to be effective. Alternative to it are neomycin and metronidazole.
- **Liver transplantation** indicate in chronic or refractory encephalopathy

Hepatorenal syndrome

Functional renal failure complicated advanced liver disease .

Two types:

Type I rapidly progressive renal failure bad prognosis.

Type II more slowly better prognosis.

Treatment:

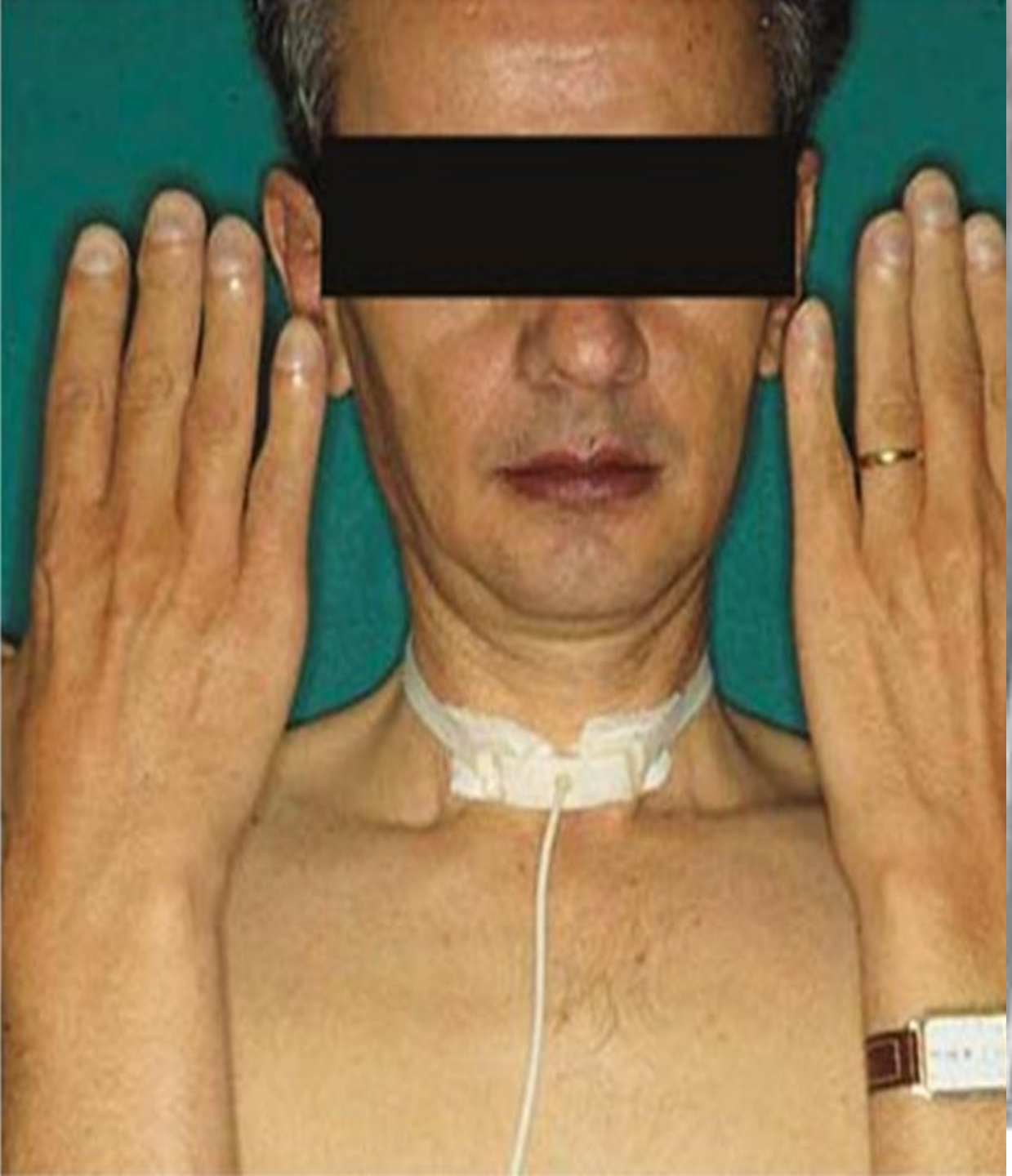
- Correction of plasma volume depletion
- Vasopressin
- TIPSS
- Liver transplantation

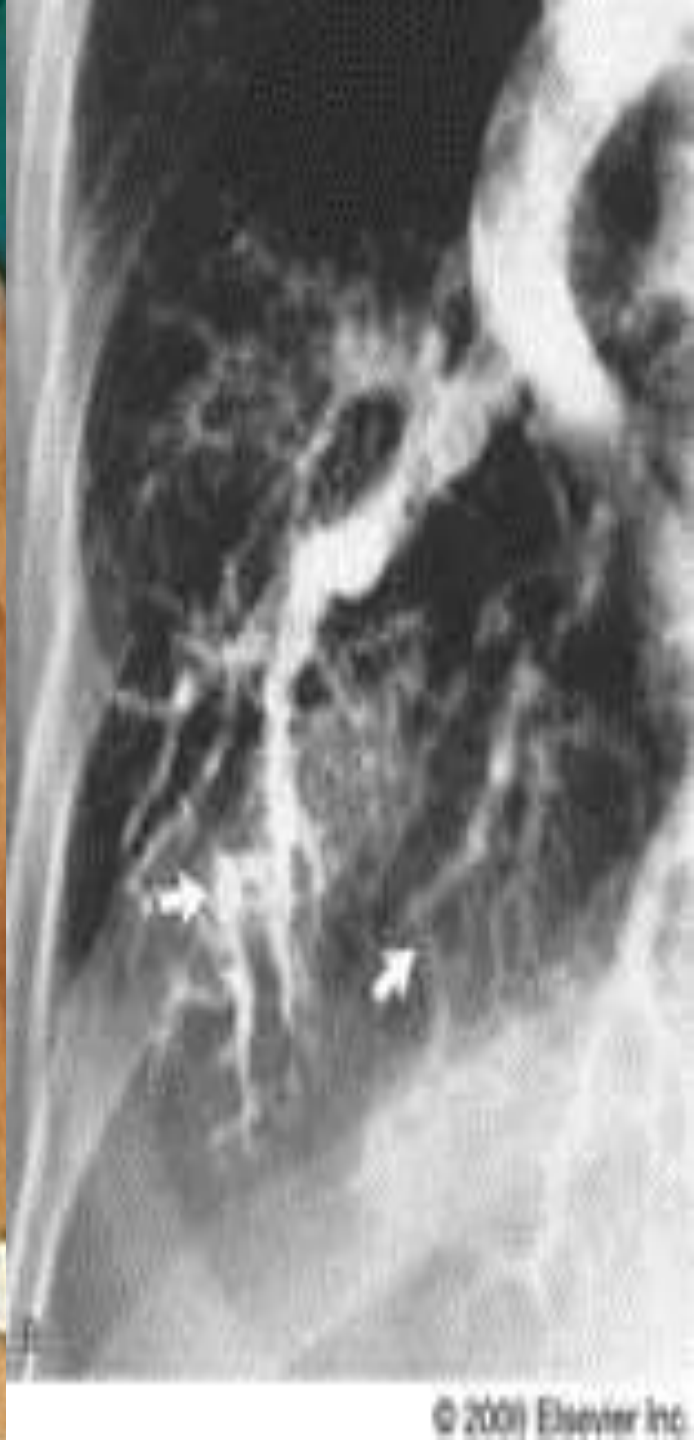
Hepatopulmonary syndrome

- Characterised by hypoxemia, intrapulmonary vascular dilatation and chronic liver disease with portal hypertension.
- **Clinical features:** Digital clubbing, cyanosis, spider naevi and a characterized by reduction in arterial oxygen saturation on standing.

Treatment:

- No proven medical therapy exists
- Oxygen
- Liver transplantation





Quiz

A 50 years old female came to your clinic with 7 months history of malaise, anorexia, arthralgia, and jaundice. Her investigations reveals bilirubin 200 µmol/l, ALT 250 iu/l, Alk Ph 105 iu/l, s. albumin 29 g/l.

What is your differential diagnosis from this history?

She has past medical history of thyroiditis and DM. further investigation show elevated IgG level. ANA and anti-smooth muscle Abs were positive, serological test for hepatic viruses were negative. Liver biopsy showed mononuclear infiltrate of the portal and periportal areas, plasma cells and fibrosis, iron and copper stains were negative.

What is your diagnosis now? What is your treatment?

She discontinue her medication (steroid + azathioprine) and return to your clinic with abdominal distension and ankle swelling over the last few weeks. She feels generally tired and lethargic.

What other features would you looks for?

She tell you that she has poor appetite, and has weight loss. She bruises easily with cutaneous signs of chronic liver disease, ascites and peripheral edema on examination. There is no meleana on rectal examination.

What is the final diagnosis?

Thanks