

# **Management of patient with portal hypertension Management of patient with ascites**

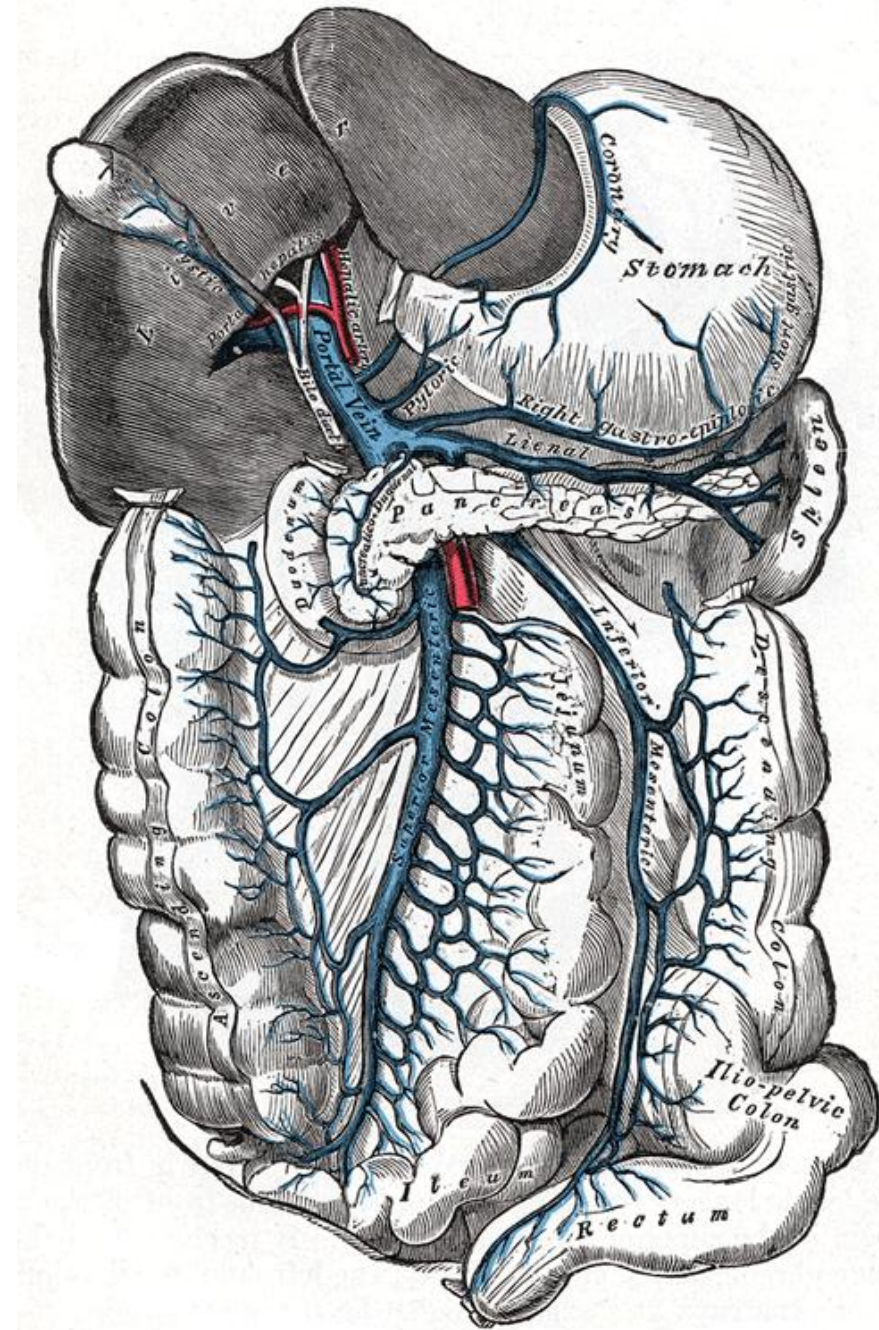
**STUDY MATERIALS FOR SELF-  
PREPARATION  
FOR VI COURSE STUDENTS**

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**Portal hypertension (PH)** is a clinical syndrome defined by a pathological increase in portal venous pressure (PVP)



# INTRODUCTION

- PH is elevated pressure in the portal vein
- It is caused most often by cirrhosis (in developed countries), schistosomiasis (in endemic areas), or hepatic vascular abnormalities
- Consequences include esophageal varices and portosystemic encephalopathy
- Diagnosis is based on clinical criteria, often in conjunction with imaging tests and endoscopy
- Treatment involves prevention of GI bleeding with endoscopy, drugs, or both and sometimes with portacaval shunting or liver transplantation

# DEFINITION

- PH is defined as a portal vein pressure greater than 10mmHg (250mm water column)
- Normal portal venous pressure is 5–10mmHg, which is sufficient to maintain a portal flow (13-24cm water column)
- Pressure in the portal vein of patients with PH exceeds 25cm water column

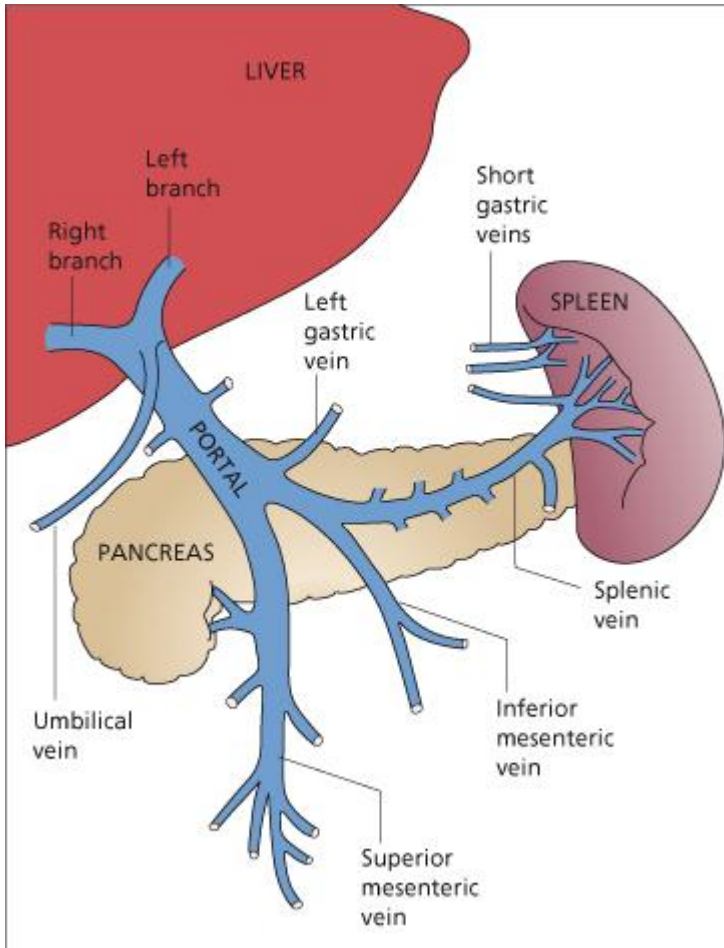
# HISTORY

- Hallion and Francois-Frank attempted the first PV pressure measurement in 1896 by inserting a cannula into the mesenteric vein of a dog and connecting it to a water manometer
- Direct measurement of portal pressure is invasive, inconvenient, and clinically impractical

# HISTORY

- In 1951, Myers and Taylor first described the measurement of wedged hepatic venous pressure (WHVP), which reflected sinusoidal pressure, an indirect measure of PV pressure
- Since then, the measurement of WHVP has been proven to be safe and closely correlated with the directly measured PVP
- Now widely used measurement of hepatic venous pressure gradient

# ANATOMY



- The portal venous system drains all blood from the abdominal GI tract, spleen, pancreas, and gallbladder back to the heart through the liver
- At the porta hepatis it divides into the right and left branches, which are segmentally distributed intrahepatically

# ANATOMIC CHARACTERISTICS OF PORTAL VENOUS SYSTEM

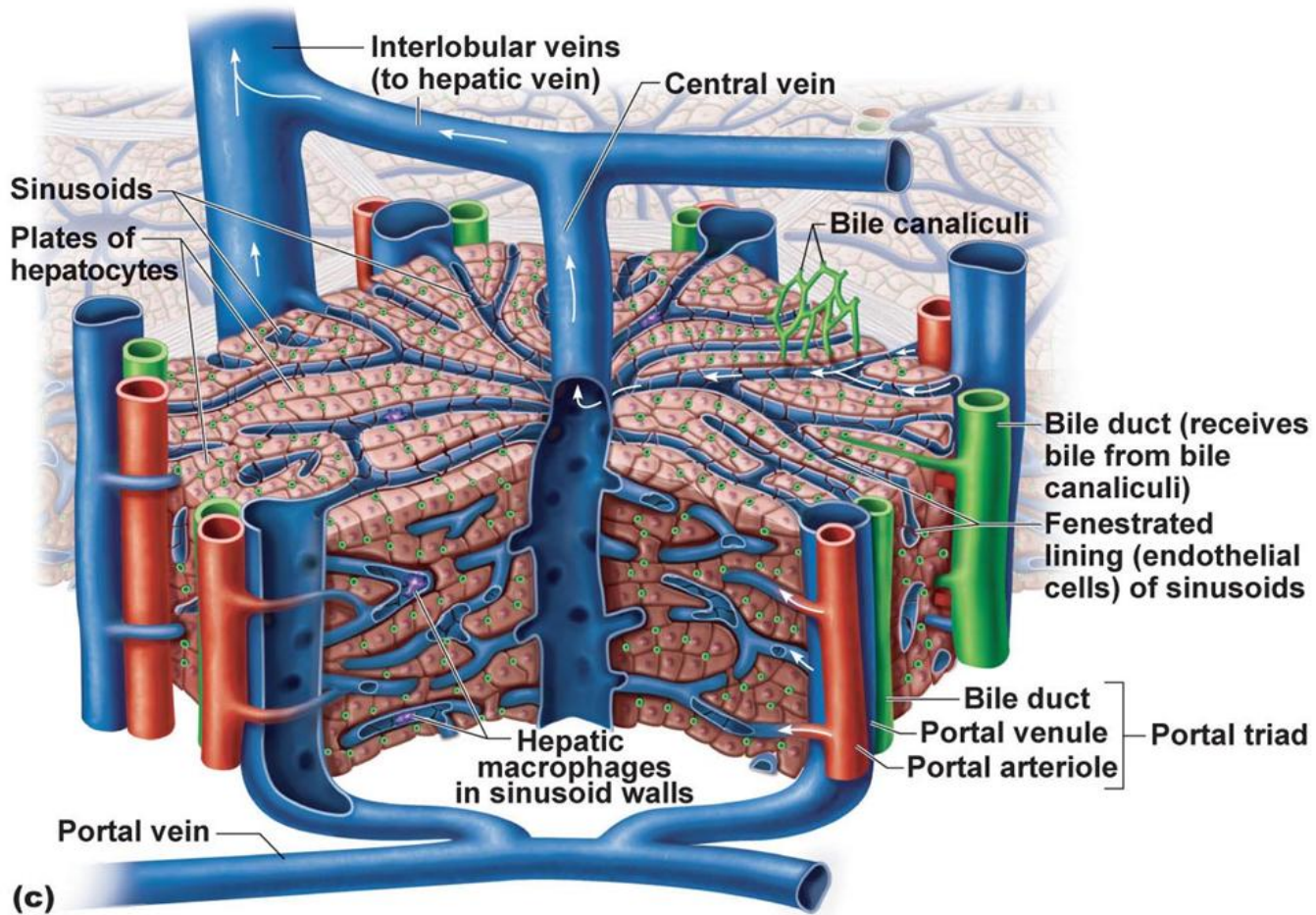
- The liver is a unique organ in that it has a dual blood supply: portal venous and hepatic arterial
- The PV is formed from the confluence of the superior mesenteric and splenic veins behind the neck of the pancreas and is 6 to 8 cm in length



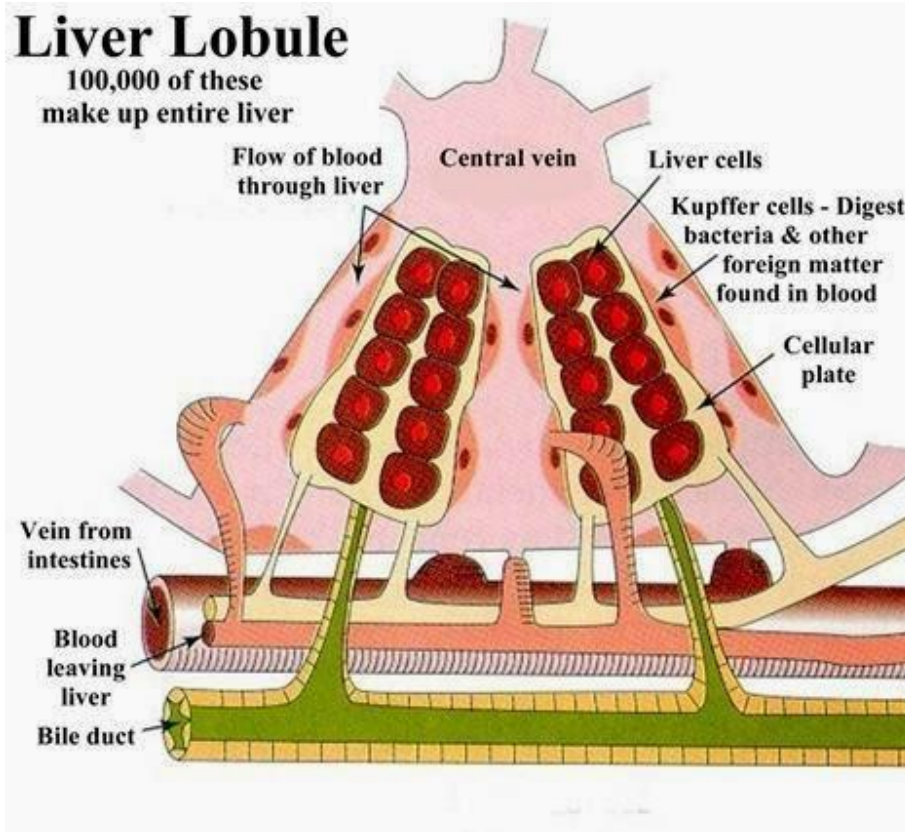
# ANATOMIC CHARACTERISTICS OF PORTAL VENOUS SYSTEM

- The tributaries of the PV connect with systemic venous system at the following sites:
- with the azygos vein and hemiazygos vein by coronary vein and esophageal plexus
- with middle and inferior haemorrhoid veins by inferior mesenteric vein and superior haemorrhoid vein
- with superior and inferior epigastric vein by obliterated umbilical vein and paraumbilical vein
- PV, SMV and IMV connect with IVC by retroperitoneal vein

# ANATOMY



# ANATOMY



- The internal structure of the liver is made of around 100,000 small hexagonal functional units known as lobules
- Each lobule consists of a central vein surrounded by 6 hepatic portal veins and 6 hepatic arteries
- These blood vessels are connected by many capillary-like tubes called **sinusoids**, which extend from the portal veins and arteries to meet the central vein like spokes on a wheel
- Each sinusoid passes through liver tissue containing 2 main cell types: Kupffer cells and hepatocytes

# ETIOLOGY

- Causes of PH may be divided into diseases **within the liver and diseases of the blood vessels outside the liver**
- With the exception of the rare splanchnic arteriovenous fistulas, all the conditions cause PH by producing obstruction to portal blood flow

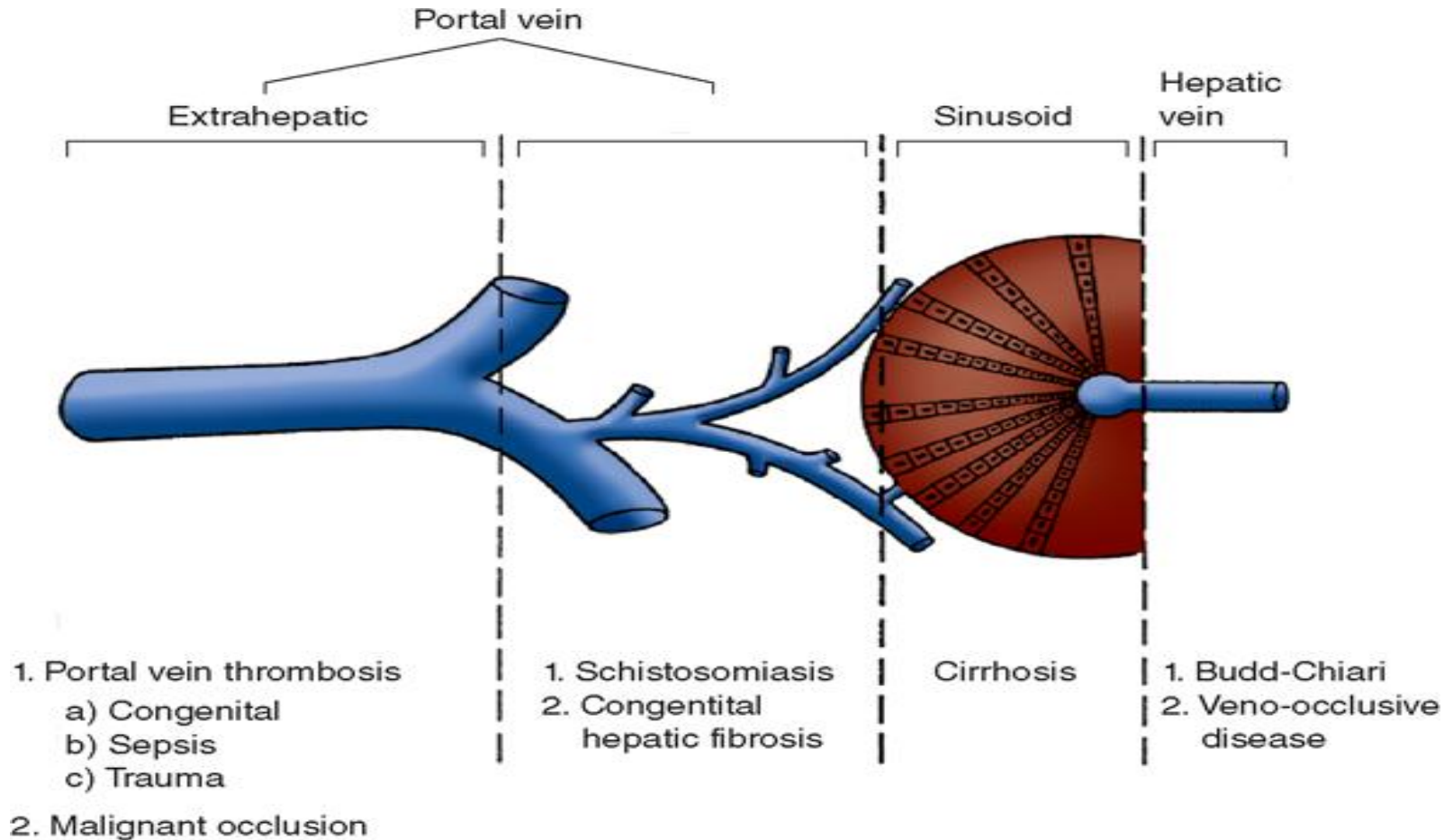
# ETIOLOGY

- The two most common causes of PH worldwide are **cirrhosis and hepatic schistosomiasis**
- In Western countries, PH is typically the result of cirrhosis, with noncirrhotic PH accounting for less than 10 percent of cases
- In other parts of the world, noncirrhotic PH due to causes such as schistosomiasis and PV thrombosis are the leading causes of PH

# CLASSIFICATION OF PH

- There are two separate and sometimes overlapping classification systems for the causes of PH, using either the liver or the hepatic sinusoid as the reference point
- The **former classifies** conditions into prehepatic, intrahepatic and posthepatic causes, **while the latter** divides conditions into presinusoidal, sinusoidal and postsinusoidal causes
- The clinical usefulness of this classification is in separating patients who have normal hepatocellular function from those who have hepatocellular damage

# CLASSIFICATION OF PH



Source: Zinner MJ, Ashley SW: *Maingot's Abdominal Operations*, 12th Edition: [www.accesssurgery.com](http://www.accesssurgery.com)

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# CLASSIFICATION OF PH

## Non-parenchymatous portal hypertension

1. *Prehepatic portal hypertension*
2. *Intrahepatic portal hypertension*

a. presinusoidal block

## Parenchymatous portal hypertension

- b. sinusoidal block
- c. postsinusoidal block

3. *Posthepatic portal hypertension*



# FORMS AND CAUSES OF PREHEPATIC PH

## **Congenital or postnatal**

1. Arterioportal fistulas  
= *hyperkinetic hypertension*
2. Atresia or hypoplasia of the portal vein
3. Thrombosis of the portal vein
  - encroachment of the postnatally obliterated umbilical vein on the portal vein
  - infection of the umbilical vein with phlebitis of the portal vein
4. Cruveilhier-von Baumgarten disease
5. Cavernous transformation of the portal vein

## **Acquired**

1. Thrombophlebitis or thrombosis of the portal vein
2. Compression of the portal vein
3. Cavernous transformation of the portal vein
4. Arterioportal fistulas  
= *hyperkinetic hypertension*
5. Compression or thrombosis of the splenic vein  
= *segmental portal hypertension*

# CAUSES OF PRESINUSOIDAL BLOCK IN INTRAHEPATIC PH

- **Congenital**

1. Rendu-Osler-Weber disease
2. Gaucher's disease
3. Cholangiodysplasia or congenital liver fibrosis (microcystic liver), congenital polycystic disease

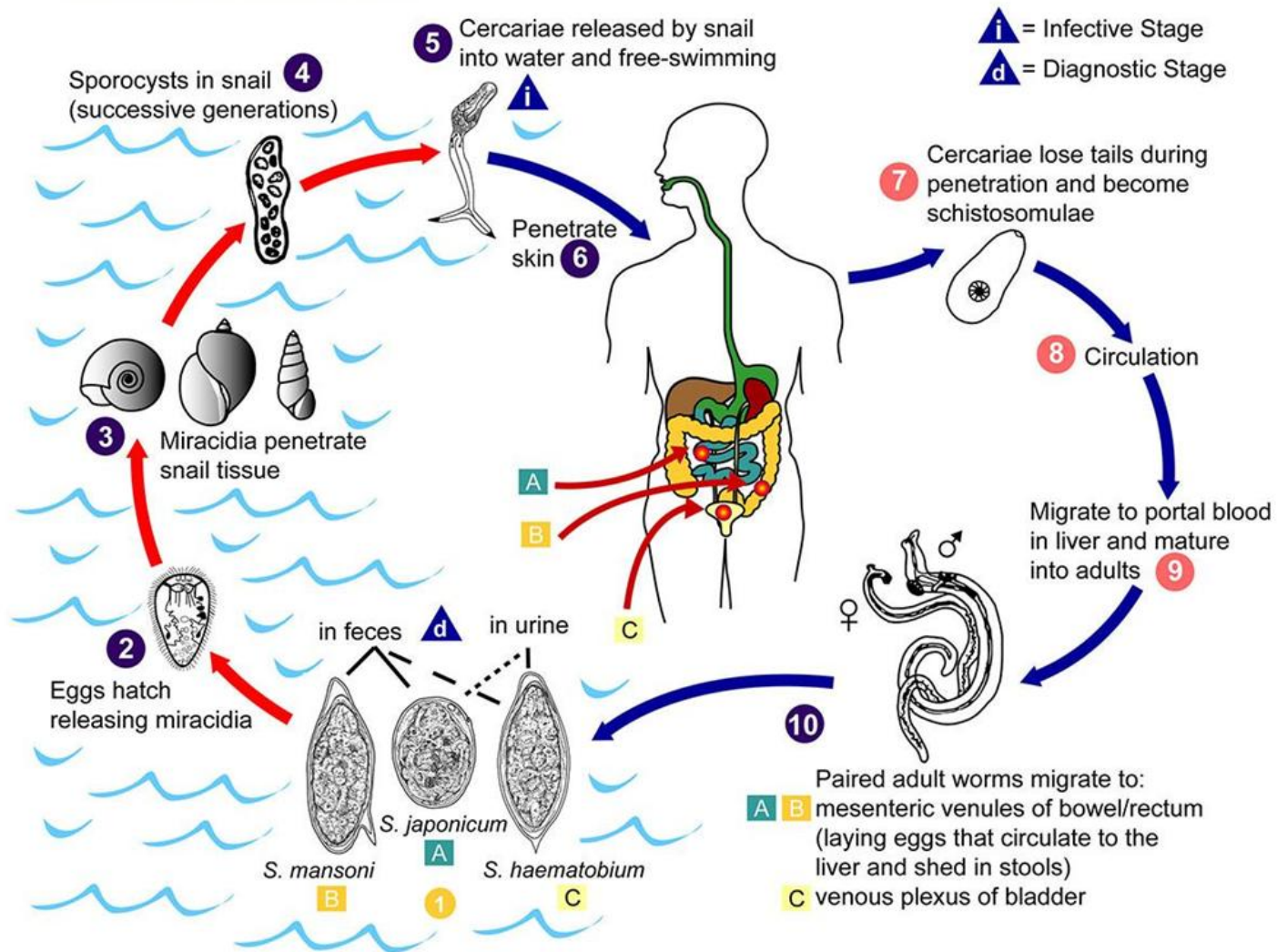
- **Acquired**

1. Thrombosis of the portal venous branches
2. Aneurysmal dilatation of the PV
3. Primary biliary cholangitis, primary sclerosing cholangitis
4. Sclerosing granulomas:  
schistosomiasis, sarcoidosis,  
tuberculosis
5. Myeloproliferative syndromes

6. Toxically induced hepatoportal sclerosis/periportal fibrosis: arsenic, vinyl chloride monomers, insecticides (particularly with copper sulphate), cytostatics (methotrexate, 6-mercaptopurine), cyanamide
7. Collagenoses
8. Haemoblastoses (e.g. mastocytosis)
9. Lymphoblastoses
10. Wilson's disease
11. Haemochromatosis
12. Malignant diseases
13. Liver adenoma
14. Nodular regenerative hyperplasia
15. Partial nodular transformation
16. Idiopathic (non-cirrhotic) presinusoidal block

# PRESINUSOIDAL BLOCK IN INTRAHEPATIC PH

## Schistosomiasis



# PRESINUSOIDAL BLOCK IN INTRAHEPATIC PH SCHISTOSOMIASIS



# CAUSES OF A SINUSOIDAL BLOCK IN INTRAHEPATIC PH

## 1. Storage of substances

- fatty liver
- acute fatty liver in pregnancy
- amyloidosis
- glycogenosis type III
- Gaucher's disease
- Niemann-Pick disease
- $\alpha$ 1-antitrypsin deficiency

## 2. Hepatotoxins

- alcoholic hepatitis
- vitamin A
- vinyl chloride, methotrexate

## 3. Severe parenchymal loss

- acute viral hepatitis
- acute liver failure
- malaria

## 4. Peliosis hepatitis

## 5. Chronic hepatitis

## 6. Regenerative nodes in cirrhosis

## 7. Formation of nodes

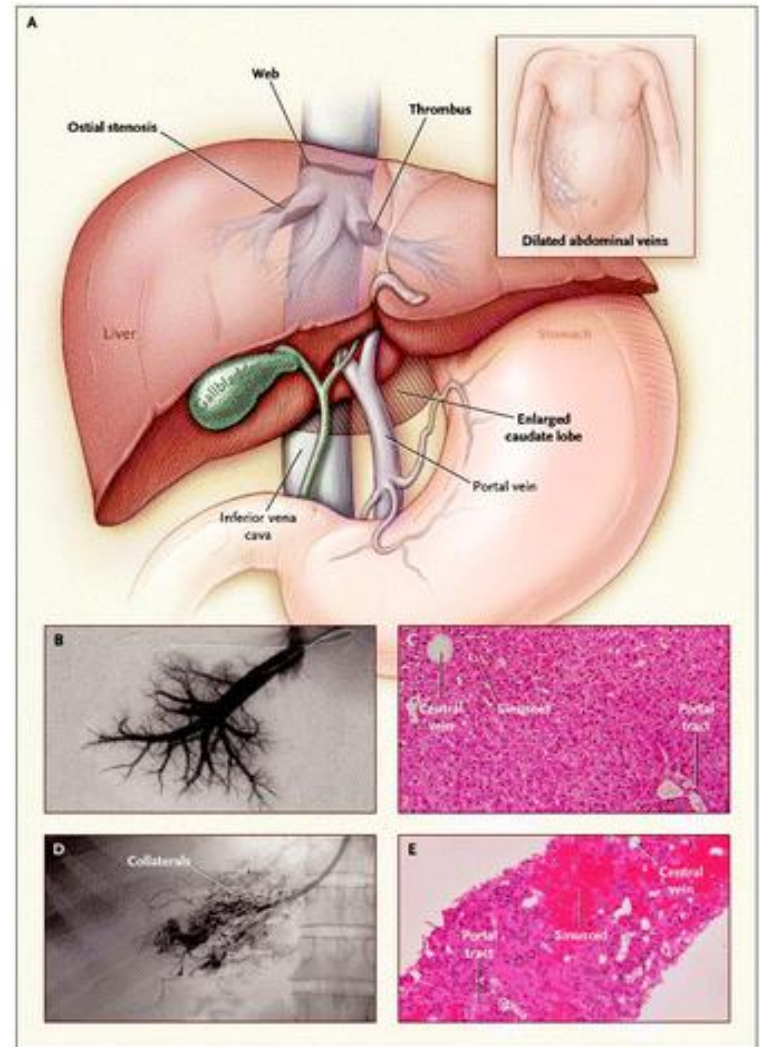
## 8. Cirrhosis

# CAUSES OF A POSTSINUSOIDAL BLOCK IN INTRAHEPATIC PH

1. Liver cirrhosis (e.g. Wilson's disease, haemochromatosis)
2. Budd-Chiari syndrome
  - Stuart-Bras syndrome (veno-occlusive disease, radicular form)
    - pyrrolizidine alkaloids contraceptives
    - cytostatic agents anabolic agents
    - immunosuppressants exposure to X-rays
    - thorocontrast
  - Chiari's disease (obliterative hepatic endophlebitis, truncal form)
3. Alcoholic hepatitis
4. Alcoholic central hyaline sclerosis
5. Partial nodular transformation of the liver

# POSTSINUSOIDAL PH

- **Budd–Chiari syndrome** is the least common cause of PH, but may be reversible if identified and treated early
- It is a congestive hepatopathy caused by blockage of hepatic veins. This syndrome occurs in 1/100 000 in the general population
- Hypercoagulable state could be identified in 75% of the patients



# CAUSES OF POSTHEPATIC PH

## Heart

1. Right heart insufficiency
2. Constrictive pericarditis
3. Tricuspid valve incompetence
4. Idiopathic dilative cardiomyopathy

## Inferior vena cava

1. Membranous obstruction
2. Anomaly
3. Thrombosis
4. Tumours
5. Nephrotic syndrome
6. Polycythaemia vera

## Hepatic veins

1. Anomaly
2. Chiari's syndrome
3. Tumours
4. Amoebic abscess



# PATHOPHYSIOLOGY OF PH

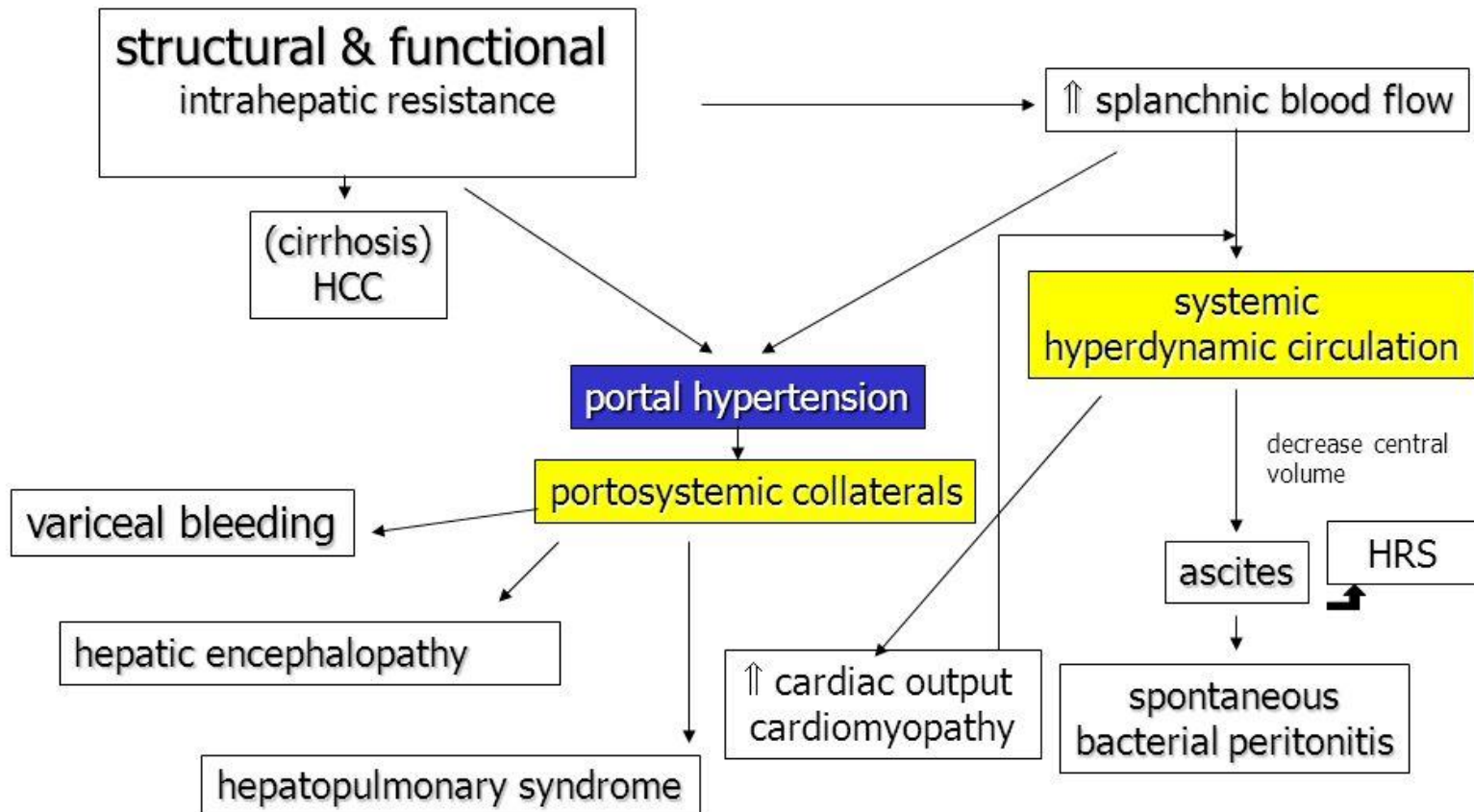
- The major theories have been the ‘backward’ and the ‘forward’ flow theories:
  - backward theory postulates that all consequences of PH result from obstruction to portal venous flow
  - forward flow theory postulates that increased inflow to the portal venous system (usually because of splenomegaly) causes the changes that lead to the clinical findings of PH
- Current evidence indicates that both theories contribute to the pathophysiology

# PATHOPHYSIOLOGY OF PH

- In the resting state, the PV carries about 75% of total hepatic blood flow and provides 1/2 of the liver's O<sub>2</sub> supply
- The PV is valveless; thus, pressure in the portal system depends on the product of input from blood flow in the portal vein and total hepatic resistance to outflow

# PATHOPHYSIOLOGY OF PH

## PORTAL HYPERTENSION: pathophysiological sequelae



# PATHOPHYSIOLOGY OF PH

- Splenomegaly with hypersplenism: the spleen may be enlarged and may result in the secondary hypersplenism including anemia, leukopenia (WBC < 3000/mm<sup>3</sup>) and thrombocytopenia
- Ascites develops in association with severe hepatocellular damage and is a manifestation of hepatic decompensation

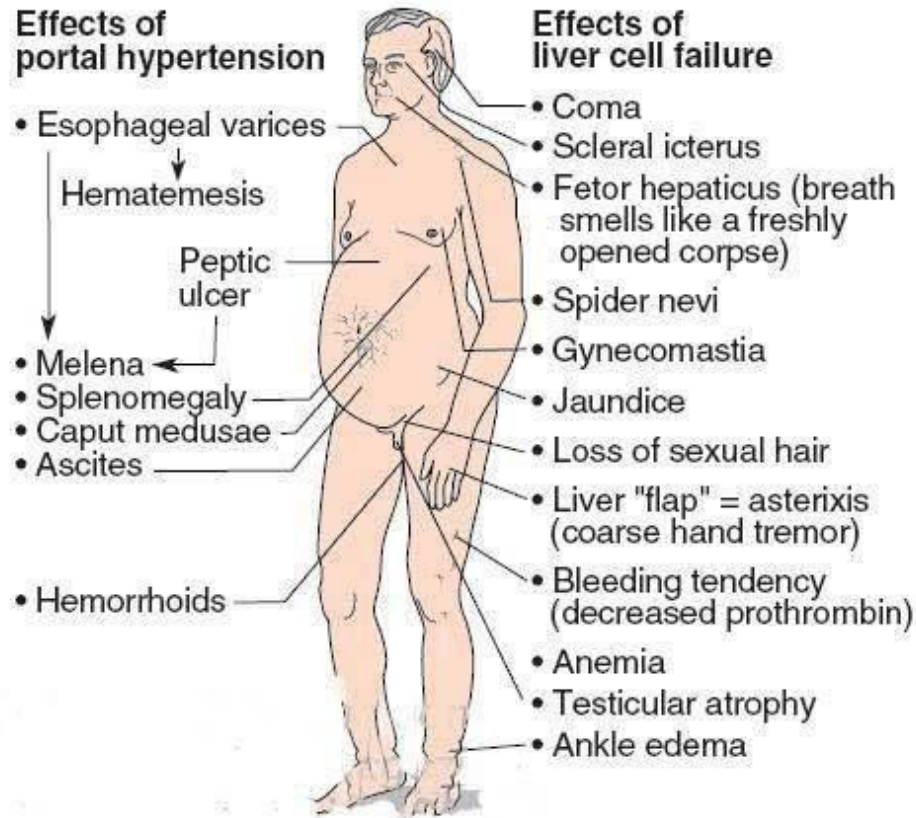
# ANAMNESIS

- The main anamnestic details given by the patient are related to various targeted questions:
  - existence of a liver disease
  - existence of extrahepatic diseases
  - alcohol abuse
  - medication
  - consumption of tea containing alkaloids
  - tarry stools, haematemesis, bleeding tendency, thrombophilia
  - visits to tropical regions (malaria, etc.)
  - oedema, abdominal pain

# CLINICAL PRESENTATION

- PH is often asymptomatic until complications develop
- **Clinical manifestations of PH include:**
  - splenomegaly
  - abdominal wall collateral vessels
  - thrombocytopenia
  - spider angiomas
  - gynecomastia in a patient with cirrhosis
  - complications of PH

# CLINICAL PRESENTATION



**Presentation of cirrhosis/portal hypertension.**

# CLINICAL PRESENTATION

## Caput medusae

- **Periumbilical veins** themselves can become engorged as well
- **Caput medusae** are engorged epigastric veins around the umbilicus that are seen in the setting of PH





# CLINICAL PRESENTATION

## Complications of PH include:

- Variceal hemorrhage
- Portal hypertensive gastropathy
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome
- Hepatic hydrothorax
- Hepatopulmonary syndrome
- Portopulmonary hypertension
- Cirrhotic cardiomyopathy
- Hepatic encephalopathy
- Ascites

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Variceal veins and hemorrhage

- **Variceal veins and hemorrhage:** patients with variceal hemorrhage typically present with hematemesis and/or melena
- If the bleeding is severe, there may be signs of hemodynamic instability

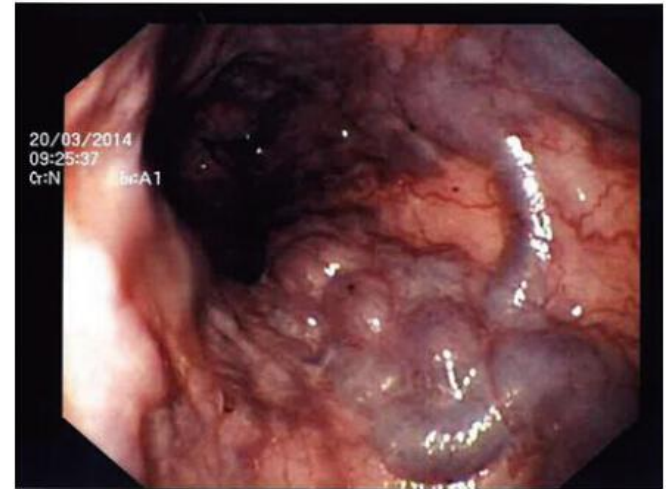
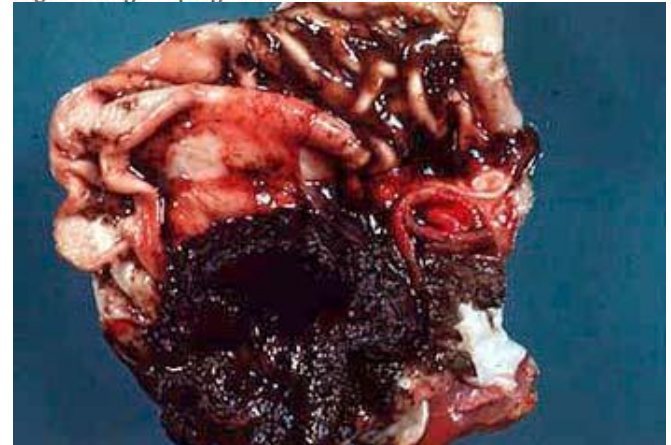


Figure 1 Large esophageal varices at EGD.



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

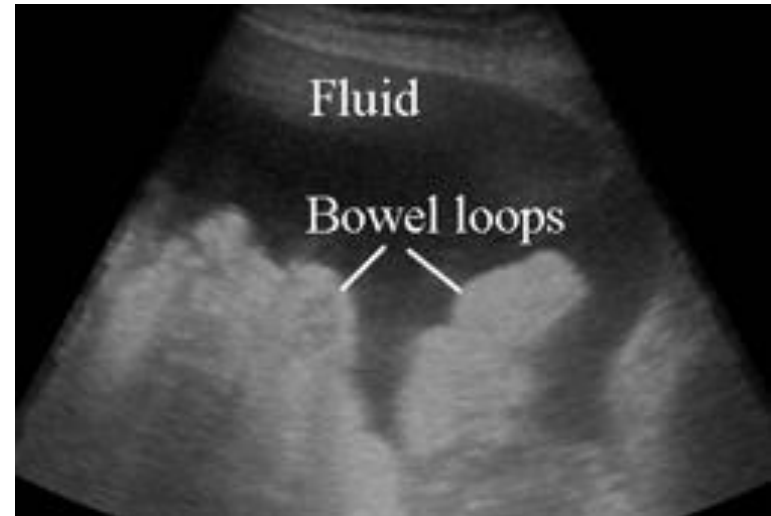
## Portal hypertensive gastropathy

- **Portal hypertensive gastropathy (PHG):** while extremely common in patients with PH, is an **uncommon** cause of significant bleeding in these patients
- When PHG is the sole cause of bleeding, there is diffuse mucosal oozing with no other lesions such as varices to account for the gastrointestinal bleeding and anemia
- The mucosa is friable, and bleeding presumably occurs when the ectatic vessels rupture
- The severity of gastropathy is related to the level of portal pressure, the level of hepatic vascular resistance, and the degree of reduction in hepatic blood flow

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Spontaneous bacterial peritonitis

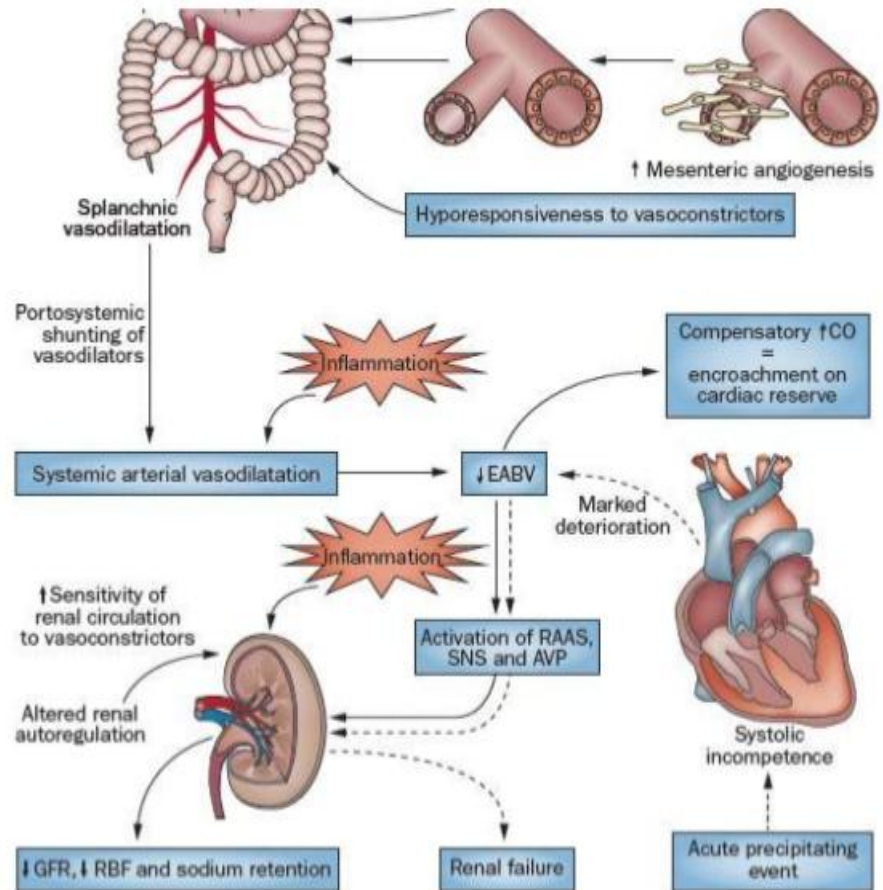
- **Spontaneous bacterial peritonitis:**
  - fever, abdominal pain
  - abdominal tenderness
  - altered mental status
  - Some patients are asymptomatic and present with only mild laboratory abnormalities
- The new onset of renal failure should prompt an investigation for spontaneous bacterial peritonitis



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Hepatorenal syndrome

- **Hepatorenal syndrome** refers to the development of renal impairment in the setting of cirrhosis
- Arterial vasodilatation in the splanchnic circulation, which is triggered by PH, appears to play a central role in the hemodynamic changes and the decline in renal function in hepatorenal syndrome



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Hepatorenal syndrome

- **Hepatorenal syndrome (HRS)** is a serious complication of liver cirrhosis with critically poor prognosis
- **Clinically HRS can be divided into types 1 and 2**
- **Type 1 HRS** is characterised by a rapid and progressive impairment of renal function as defined by a doubling of the initial serum creatinine to a level higher than 221  $\mu\text{mol/L}$  in less than 2 weeks; the GFR is usually below 20 mL/min; the median survival time is less than 2 weeks and practically all patients die within 8–10 weeks after the onset of renal failure
- **Type 2 HRS** is characterised by a subtler course with initial serum creatinine levels less than 221  $\mu\text{mol/L}$ ; the main clinical consequence of type 2 HRS is diuretic-resistant ascites; patients have a longer median survival time of approximately 6 months

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Hepatorenal syndrome

### International Ascites Club's Diagnostic Criteria of HRS

#### Major criteria

- Chronic or acute liver disease with advanced hepatic failure and PH
- Low GFR: serum creatinine  $>133 \mu\text{mol/L}$  or 24h creatinine clearance  $<40 \text{ mL/min}$
- Absence of shock, ongoing bacterial infection or treatment with nephrotoxic drug
- Absence of gastrointestinal or renal fluid losses
- No sustained improvement in renal function following diuretic withdrawal and expansion of plasma volume with 1.5 L of isotonic saline
- Proteinuria  $<0.5 \text{ g/d}$  and no ultrasonographic evidence of obstructive uropathy or parenchymal renal disease

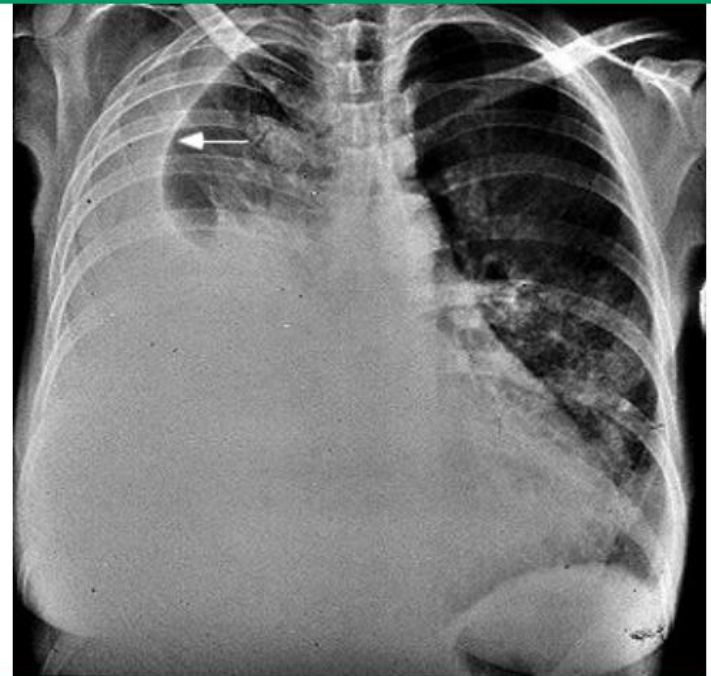
#### Additional criteria

- Urine volume  $<0.5 \text{ L/d}$
- Urine sodium  $<10 \text{ mmol/L}$
- Urine osmolality  $>$  plasma osmolality
- Urine red blood cells  $<50$  high power field
- Serum sodium concentration  $<130 \text{ mmol/L}$

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Hepatic hydrothorax

- **Hepatic hydrothorax** is defined as the presence of a pleural effusion in a patient with cirrhosis and no evidence of underlying cardiopulmonary disease
- It results from the movement of ascitic fluid into the pleural space through defects in the diaphragm and is usually right-sided
- The negative intrathoracic pressure generated during inspiration favors the passage of fluid from the peritoneal to the pleural space
- Patients usually present with:
  - shortness of breath
  - cough
  - hypoxemia
  - and/or chest discomfort



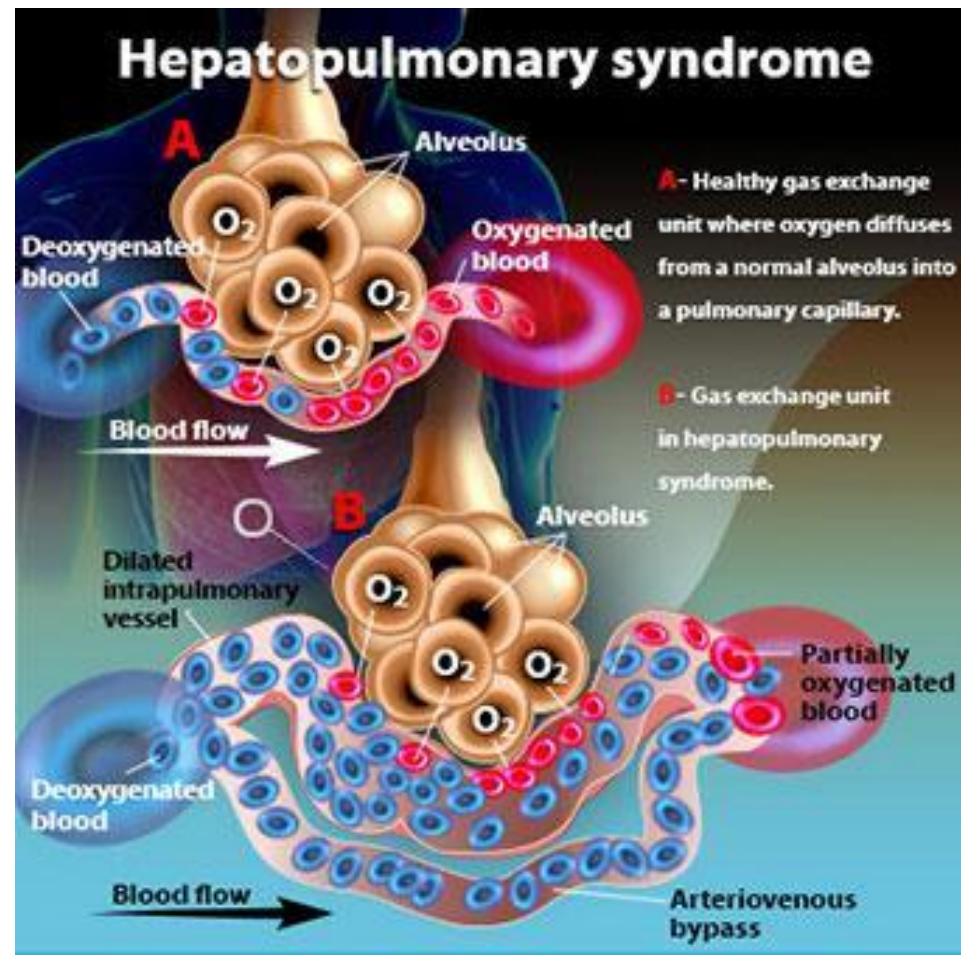
Large right sided pleural effusion forming typical meniscoid arc (arrow) in patient with advanced liver cirrhosis.  
*Courtesy of Paul Stark, MD.*



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Hepatopulmonary syndrome

- **Hepatopulmonary syndrome** is defined as the triad of liver disease, pulmonary gas exchange abnormalities leading to arterial deoxygenation, and evidence of intrapulmonary vascular dilatations
- The clinical features are the consequences of both hepatic and pulmonary dysfunction
- More than 80 percent of patients present with symptoms of liver disease; the remainder experience dyspnea as their initial symptom
- Hypoxia is a common finding
- The prognosis associated with HPS is poor



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Portopulmonary hypertension

- **PH-associated pulmonary hypertension (portopulmonary hypertension)** refers to the presence of pulmonary hypertension in patients with PH
- Patients may present with:
  - fatigue
  - dyspnea
  - peripheral edema
  - chest pain
  - syncope

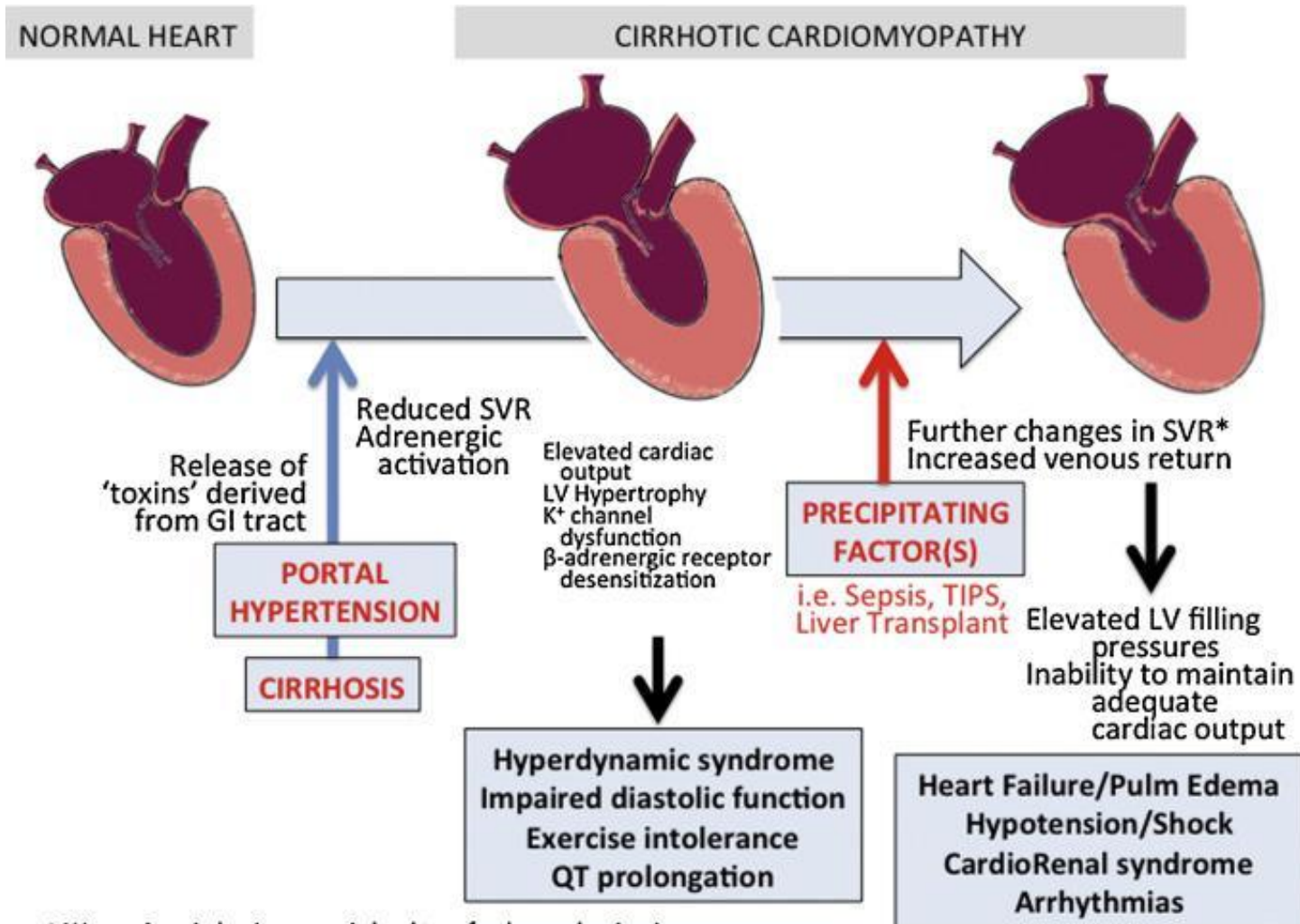
# CLINICAL MANIFESTATIONS ASSOCIATED WITH THESE COMPLICATIONS

## **Cirrhotic cardiomyopathy**

- **Cirrhotic cardiomyopathy** is defined by chronic cardiac dysfunction in the setting of cirrhosis
- It is characterized by decreased contractile responsiveness to stress or altered diastolic relaxation with electrophysiologic abnormalities
- It is thought to be related to both PH and cirrhosis

# CLINICAL MANIFESTATIONS ASSOCIATED WITH THESE COMPLICATIONS

## Cirrhotic cardiomyopathy



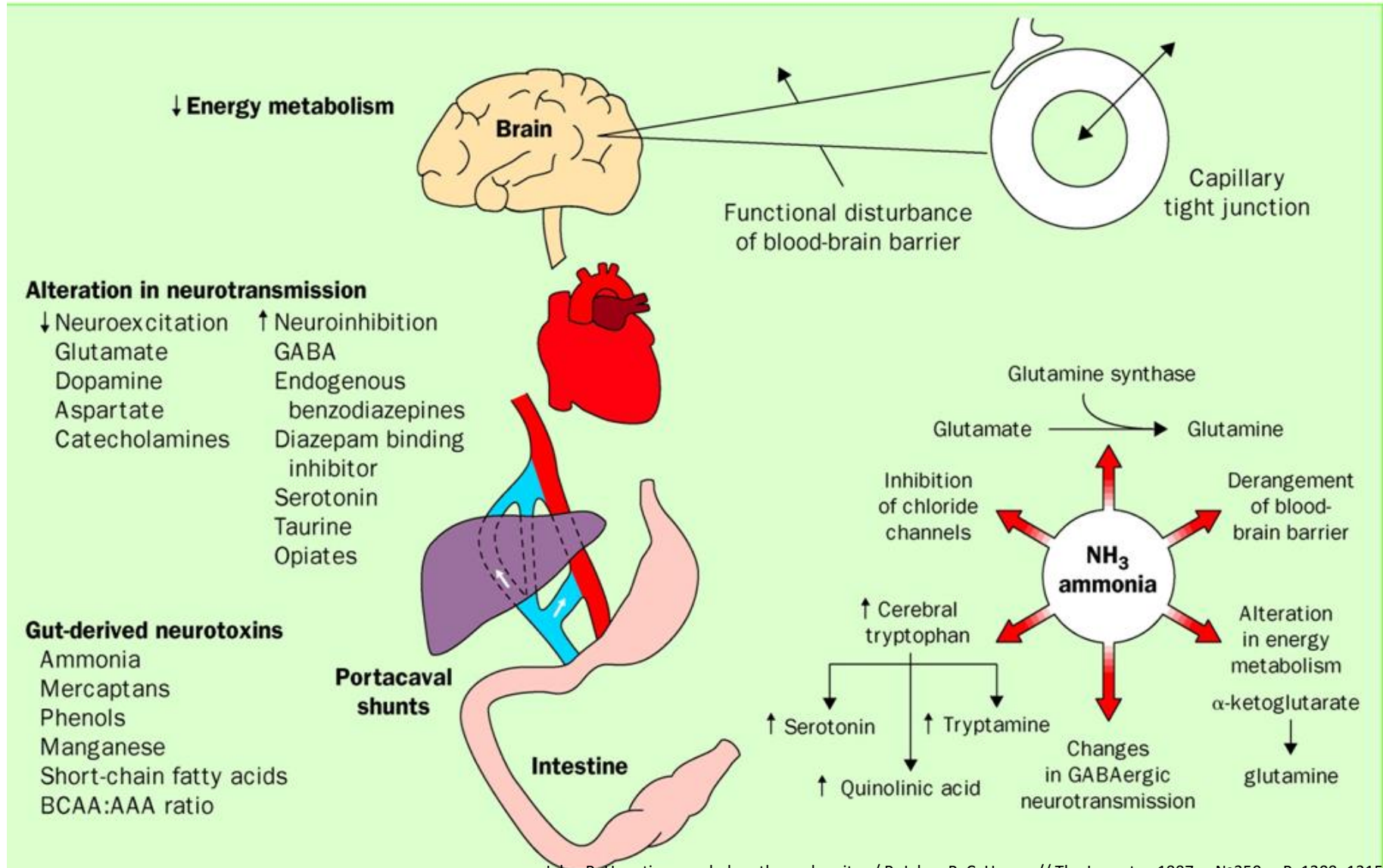
\* Worsening cirrhosis or sepsis lead to a further reduction in Systemic Vascular Resistance (SVR), whereas a rapid increase in SVR is seen after liver transplant.

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Hepatic encephalopathy

- **Hepatic encephalopathy (HE)** defined as a disturbance in central nervous system function because of hepatic insufficiency
- HE is a reversible state that occurs in patients with liver disease or portosystemic shunts
- HE is a hallmark of deteriorating liver function, and patients should be assessed early for liver transplantation
- Suspect in any liver disease patient presenting with mental changes
- HE is usually preceded by precipitating events

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS HE (pathogenesis)



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## HE (precipitating events)

- **Electrolyte imbalance**
  - Diuretics
  - Vomiting
  - Diarrhoea
- **Gastrointestinal bleeding**
  - Oesophageal and gastric varices
  - Gastroduodenal erosions
- **Constipation**
  - Dietary protein overload
- **Infection**
  - Spontaneous bacterial peritonitis
  - Urinary
  - Chest
- **Drugs**
  - Alcohol withdrawal
  - Benzodiazepines
  - Barbiturates
  - Analgesics
  - Other sedatives

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## HP (clinical presentation)

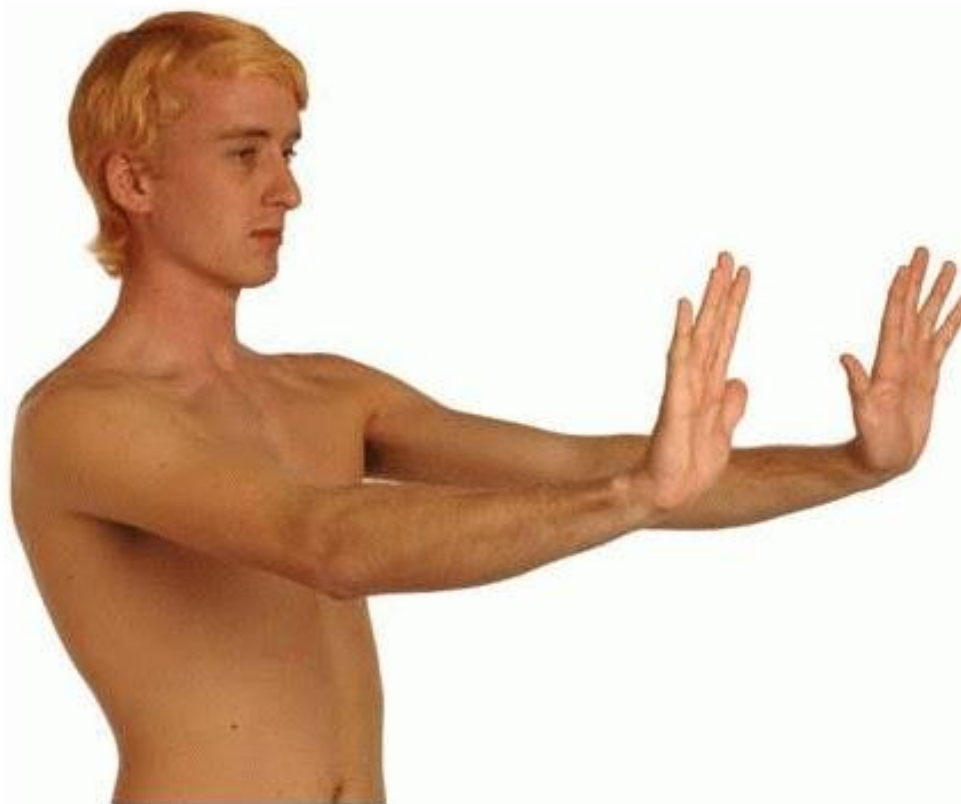
- **The typical features of HP include:**
  - impaired consciousness (drowsiness)
  - monotonous speech
  - flat affect (asterixis)
  - metabolic tremor
  - muscular incoordination
  - impaired handwriting
  - fetor hepaticus
  - upgoing plantar responses
  - hypoactive or hyperactive reflexes
  - decerebrate posturing



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## HE (clinical presentation)

### Asterixis



Ask the patient to stretch out their hands in front of them with the hands dorsiflexed at the wrists and fingers outstretched and separated. The patient should hold that position for at least 15 seconds. If flap is present, the patient's hands will move in jerky, irregular flexion/extension at the wrist and MCP joints. The flap is nearly always bilateral. May be subtle and intermittent.

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS HE

## THE WEST HAVEN CRITERIA OF ALTERED MENTAL STATE IN HE

- **Stage 0.** Lack of detectable changes in personality or behavior. Asterixis absent.
- **Stage 1.** Trivial lack of awareness. Shortened attention span. Impaired addition or subtraction. Hypersomnia, insomnia, or inversion of sleep pattern. Euphoria or depression. Asterixis can be detected.
- **Stage 2.** Lethargy or apathy. Disorientation. Inappropriate behavior. Slurred speech. Obvious asterixis.
- **Stage 3.** Gross disorientation. Bizarre behavior. Semistupor to stupor. Asterixis generally absent.
- **Stage 4.** Coma.

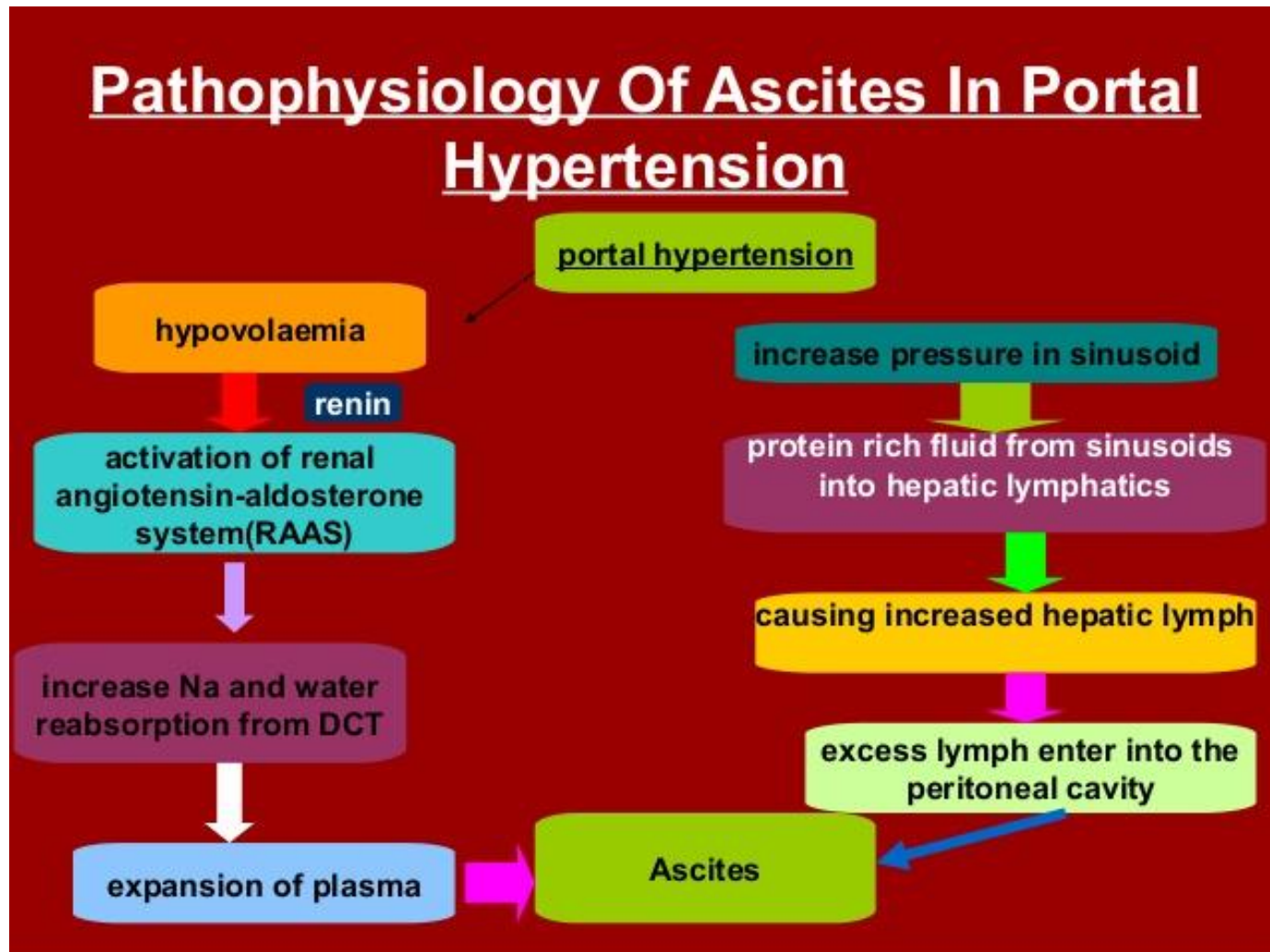
# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Ascites

- **Ascites** can be recognized by the wide protuberance of the abdomen with moderate bulging of the abdominal flanks and spreading of the navel
- Examination by percussion produces **tympanic intestinal resonance** in the upper area and typical **dullness in the flanks**
- Small ascites (about 1 litre) is determined in the **knee-elbow position**, whereby dullness is detected in the lower abdominal region
- The **fluctuation wave** is an impressive sign: a short hard surge of the fluid swell against the palpating hand is virtually conclusive

# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Ascites (pathophysiology)



# CLINICAL MANIFESTATIONS ASSOCIATED WITH COMPLICATIONS

## Ascites

- Patients with **ascites** typically report:
- progressive abdominal distension that may be painless or associated with abdominal discomfort
- Also may complain:
  - weight gain
  - shortness of breath
  - early satiety
  - dyspnea resulting from fluid accumulation and increased abdominal pressure



# DIAGNOSIS

- **Past history** of chronic alcoholism, hepatitis, complicated biliary disease, or exposure to hepatotoxins should lead one to include cirrhosis in the differential diagnosis
- **Nonspecific complaints** such as weight loss, malaise, and weakness
- **Underlying chronic liver disease** on physical examination are spider angiomas, palmar erythema, testicular atrophy, and gynecomastia
- A palpable spleen in association with these signs suggests PH
- Signs of hepatic functional decompensation or advanced PH, such as jaundice, ascites, palpation of a firm irregular liver edge, dilated abdominal wall veins, impairment of mental status or the presence of asterixis (liver flap)

# DIAGNOSIS

## Laboratory tests

### Blood test:

- anemia, leukopenia and thrombocytopenia (bleeding, nutritional deficiencies, etc)
- coagulation may also be impaired

# DIAGNOSIS

## Laboratory tests

### Liver function test will reveal:

- Serum albumin is often declined (which is a reliable index of chronic liver disease)
- Elevation of hepatocellular enzymes (aspartate aminotransferase and alanine aminotransferase)
- High level of total bilirubin (which are also indicators of hepatocellular damages)
- Hepatitis serology should be obtained in most patients with cirrhosis (HBV,HCV)
- All newly diagnosed cirrhotic patients should be screened for hepatocellular carcinoma by determination of  $\alpha$ -fetoprotein level



# DIAGNOSIS

## Laboratory tests

Table 1 Diagnostic tests, suggested etiology, and current treatment for the most frequent forms of liver cirrhosis in adult patients

Abnormal test(s)	Etiology	Treatment
$\gamma$ GT (high), MCV (high)	Alcohol	Abstinence
HBsAg, HEV-DNA, HBe-IgM, HDV-RNA (positivity)	HBV + Delta virus infection	Interferon $\alpha$ -2b, nucleoside (Lamivudine, Telbivudine, Entecavir) and nucleotide (Adefovir, Tenofovir) analogues
HCV-RNA (positivity)	HCV infection	Interferon plus ribavirin
$\gamma$ GT (high), alkaline phosphatase (high), AMA (positivity)	Primary biliary cirrhosis	Ursodeoxycholate
ANA, ASMA, LKM (positivity)	Autoimmune hepatitis	Prednisone, azathioprine
Ferritin (high), transferrin saturation index (> 45%), liver iron content (high), HFE gene mutation for hereditary hemochromatosis (C282Y, H63D)	Hemochromatosis	Phlebotomy, deferoxamine
Ceruloplasmin (low), serum (low) and 24 h urine copper excretion (high)	Wilson's disease	D-penicillamine, zinc
HDL-cholesterol (low), glucose (high), triglycerides (high)	NAFLD/NASH	Low caloric diet, exercise, drugs lowering insulin-resistance

AMA: Anti-mitochondrial antibody; ANA: Antinuclear antibody; ASMA: Anti-smooth-muscle antibody;  $\gamma$ GT:  $\gamma$ -glutamyltransferase; HBV-DNA: Hepatitis B virus DNA; HCV-RNA: Hepatitis C virus RNA; HBsAg: Hepatitis B surface antigen; HDL: High density lipoprotein; HDV-RNA: Hepatitis delta virus RNA; LKM: Liver kidney microsomes; MCV: Mean corpuscular volume; NASH: Nonalcoholic steatohepatitis; NAFLD: Nonalcoholic fatty liver disease.

# DIAGNOSIS

## Hepatic venous pressure gradient (HVPG)

- The HVPG is measured to approximate the gradient in pressure between the PV and the inferior vena cava (IVC)
- It can quantify the degree of PH due to sinusoidal resistance to blood flow (the most common cause of PH)
- A normal HVPG is between 1 and 5 mmHg
- PH is present if the HVPG is  $\geq 6$  mmHg
- **PH typically becomes clinically significant when the HVPG is  $\geq 10$  mmHg**, at which point varices may develop
- Once the HVPG is  $\geq 12$  mmHg, patients are at risk for variceal bleeding and the development of ascites
- The portal pressure gradient can also be determined by direct measurement of the pressure in the portal vein and IVC, but it is associated with a risk of intraperitoneal bleeding, so it is rarely used

# DIAGNOSIS

## HVPG Technique

- **The HVPG is calculated by subtracting the free hepatic venous pressure (FHVP, which reflects intra-abdominal pressure) from the wedged hepatic venous pressure (WHVP, which reflects portal venous pressure)**
- These values are obtained by hepatic vein catheterization. The WHVP is typically obtained by balloon occlusion of the hepatic vein, though it can also be estimated by wedging the catheter in the end tributaries of a hepatic vein. The balloon occlusion technique estimates the pressure from a larger portion of the liver than is obtained if the catheter is wedged in an end tributary.
- After giving the patient light conscious sedation (eg, midazolam), a balloon-tipped catheter is introduced through the right jugular vein, often under ultrasound guidance. The catheter is advanced through the right atrium into the IVC and then into the right hepatic vein using fluoroscopic guidance. Alternatively, the femoral or antecubital veins can be used to for venous access.
- To obtain the FHVP, the catheter is maintained in the hepatic vein 2 to 4 cm from its take off from the IVC. Typically, the difference in pressure between the IVC (measured at the hepatic vein ostium) and hepatic vein is  $\leq 1$  mmHg. A difference  $> 1$  mmHg suggests incorrect placement of the catheter (too deep into the hepatic vein). Pressure in the right atrium cannot be used to approximate the FHVP.
- To obtain the WHVP, the hepatic vein is occluded by inflating the balloon at the tip of the catheter. A small amount of contrast dye (5 mL) is injected to confirm that the hepatic vein is occluded. If it is occluded, there should be no reflux of the dye above the balloon, and it should not washout via communications with other hepatic veins. Veno-venous communications may lead to washout of the contrast. These communications are rare in cirrhosis, though they are commonly seen in idiopathic portal hypertension. The pressure should not be recorded until a stable value is obtained, which often takes 45 to 60 seconds.
- **Once the FHVP and WHVP are determined, the HVPG is calculated by subtracting the FHVP from the WHVP.**

<https://www.uptodate.com/contents/portal-hypertension-in-adults>

[https://www.facebook.com/groups/InternalMedKhNU/?multi\\_permaLinks=1964266770524319&notif\\_t=group\\_activity&notif\\_id=1505473376187426](https://www.facebook.com/groups/InternalMedKhNU/?multi_permaLinks=1964266770524319&notif_t=group_activity&notif_id=1505473376187426)

# DIAGNOSIS

## HVPG: Prognostic implications

**Prognostic implications of HVPG thresholds** — The risk of developing complications of PH and mortality rates increase as HVPG values increase. Various HVPG thresholds have been noted to have prognostic significance among patients with cirrhosis:

- In patients with compensated cirrhosis:
  - HVPG 10 mmHg: Development of gastroesophageal varices, development of hepatocellular carcinoma, decompensation after surgery for hepatocellular carcinoma
  - HVPG 12 mmHg: Variceal bleeding
  - HVPG 16 mmHg: First clinical decompensation in patients with varices, mortality
- In patients with decompensated cirrhosis:
  - HVPG 16 mmHg: Variceal rebleeding, mortality
  - HVPG 20 mmHg (in patients with active variceal hemorrhage): Failure to control active variceal hemorrhage, low one-year survival
  - HVPG 22 mmHg: Mortality in patient with alcoholic cirrhosis and acute alcoholic hepatitis
  - HVPG 30 mmHg: Spontaneous bacterial peritonitis

# DIAGNOSIS

## HVPG: Contraindications and limitations

- Limitation of the HVPG is that the WHVP is a measure of pressure within the hepatic sinusoids
- As a result, pre-sinusoidal causes of portal hypertension may be associated with a normal FHVP, WHVP, and HVPG.
- HVPG may be normal with post-sinusoidal causes of portal hypertension that increase pressure both in the hepatic vein and in the sinusoids. However, in this situation, both the FHVP and the WHVP will be abnormal
- If pre-sinusoidal portal hypertension is suspected and the HVPG is normal, direct measurement of the pressure in the PV and IVC can be obtained to determine the portal perfusion gradient. Direct measurement is performed using transhepatic or transvenous catheterization of the portal vein.
- A relative contraindication to HVPG measurement is an allergy to iodinated contrast. This can be overcome by using carbon dioxide in place of contrast when confirming balloon occlusion. In patients with a history of cardiac arrhythmias, care should be taken when moving the catheter in the right atrium.
- **Patients with thrombocytopenia or an elevated international normalized ratio may require platelets or fresh frozen plasma, respectively, prior to performing an HVPG measurement.**

# DIAGNOSIS

## HVPG: Complications

- Complications with HVPG measurement are uncommon and typically are related to local injury at the venous access site
- Arrhythmias, which are usually transient, may be seen as the catheter is moved within the right atrium
- **Associated procedures** — other procedures that can be performed at the same time as HVPG measurement include transjugular liver biopsy, measurement of hepatic blood flow and **indocyanine green clearance**, and wedged hepatic retrograde portography using carbon dioxide.

# DIAGNOSIS

## Ultrasonography

- Findings on transabdominal ultrasound with Doppler imaging may support a diagnosis of portal hypertension, but lack sensitivity
- **Findings that may be seen in patients with PH include (1):**
  - Ascites
  - Splenomegaly
    - Dilation of the splenic vein (>10 mm)
  - Nodular liver
  - Portal flow mean velocity <12 cm/second
  - Inversion of flow in the PV
  - Portosystemic collaterals (patent-paraumbilical vein, splenorenal collaterals, dilated left and short gastric veins)
  - Portal vein diameter >13 mm
  - Decreased or no respiratory variation in splenic and superior mesenteric vein diameter
  - Portal/splenic/superior mesenteric vein thrombosis

# DIAGNOSIS

## Ultrasonography

- **Findings that may be seen in patients with PH include (2) :**
  - Dilation of the ventricular coronary vein (>6 mm)
  - Reduction of blood flow velocity less than 10 cm/sec
  - Restricted respiratory modulation of the vascular width of up to 3 mm (increase on inspiration and decrease on expiration) regarding the PV and more particularly the splenic vein and the superior mesenteric vein
  - Decrease in width of the lumen by more than 50% on exhalation = absence of PH
  - Stasis of the gallbladder and gastric walls
  - Recanalization of the umbilical vein
  - Cavernous transformation of the portal vein



# DIAGNOSIS

## Transient elastography

- **Transient elastography** using ultrasound is a noninvasive method for detecting hepatic fibrosis
- Studies are also looking at it as an option for noninvasively diagnosing portal hypertension
- Studies have reported areas under the receiver operating characteristic (AUC) curve of 0.77 to 0.99 for transient elastography predicting portal hypertension, with variable optimal liver stiffness cutoff values (13.6 to 34.9 kPa (Kilopascal))
- It has been suggested that a value  $<13.6$  kPa can be used to rule out portal hypertension, whereas a value  $\geq 21.1$  kPa can be used to rule it in
- Values between 13.6 and 21.1 kPa are considered to be indeterminate

# DIAGNOSIS

## Liver Biopsy

- Percutaneous liver biopsy is a useful technique for establishing the cause of cirrhosis and for assessing activity of the liver disease. It should not be done when either coagulopathy or moderate ascites is present
- Laparoscopic biopsy reduces the false-negative rate for diagnosing cirrhosis as compared with blind biopsy techniques

# DIAGNOSIS

## Ascitic fluid tests

### Required

- Macroscopic appearance (strawcoloured, turbid, bloody, chylous)
- Cell count and differential
- Albumin
- Total protein
- Culture in blood culture bottles
- Gram's stain

### Optional

- Glucose (for secondary peritonitis)
- LDH (for secondary peritonitis)
- Amylase (for pancreatic ascites)
- AFB smear and tuberculosis culture
- Adenosine deaminase (for tuberculosis)
- Cytology (for malignant ascites)
- Triglycerides
- Bilirubin
- pH, lactate (for bacterial peritonitis)

# DIAGNOSIS

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

$$\text{SAAG} = [\text{albumin}]_{\text{serum}} - [\text{albumin}]_{\text{ascites}}$$

### High gradient ( $\geq 11$ g/L)

Low total protein

- Cirrhosis
- Metastases
- Alcoholic hepatitis
- Fulminant hepatic failure

Normal total protein

- Congenital hepatic fibroblast
- Hepatic vein thrombosis
- Constrictive pericarditis
- Veno-occlusive disease
- Myxedema

### Low gradient ( $\leq 11$ g/L)

- Peritoneal carcinomatosis
- Tuberculous peritonitis
- Pancreatic ascites
- Biliary ascites
- Nephrotic syndrome
- Serositis or collagen vascular disease

# DIAGNOSIS

## Further

- Diagnosis of the underlying liver disease
- Estimation of functional hepatic reserve
- Definition of portal venous anatomy and hepatic hemodynamic evaluation
- Identification of the site of upper gastrointestinal hemorrhage, if present

# DIAGNOSIS

## Hepatic functional reserve

**Table 2 Child-Pugh scoring system for liver cirrhosis and related indication priority for transplantation<sup>[20]</sup>**

<b>Score</b>	<b>1</b>	<b>2</b>	<b>3</b>
Bilirubin (mg/dL)	< 2	2-3	> 3
Prothrombin time (INR)	< 4 sec. (< 1.7)	4-6 sec. (1.7-2.3)	> 6 sec. (> 2.3)
Albumin (g/dL)	> 3.5	3.5-2.8	< 2.8
Ascites	Absent	Mild	Severe
Encephalopathy	Absent	Mild	Severe

The Child-Pugh score is given by the sum of the score (1 to 3) of each of the five parameters. A score of 6 or lower defines the patient as class A, 7 to 9 as class B, and 10 or higher as class C.

# DIAGNOSIS

## Special examinations

### Endoscopy

- In the nonbleeding cases, the manifestation of varices may be observed, The risk of the first variceal bleed may be predicted from:
  - variceal size
  - «red color signs»
- In the massive bleeding cases, it is a very useful procedure to determine the site and the cause of upper gastrointestinal hemorrhage

# DIAGNOSIS

## Special examinations

### Computerized Tomography (CT)

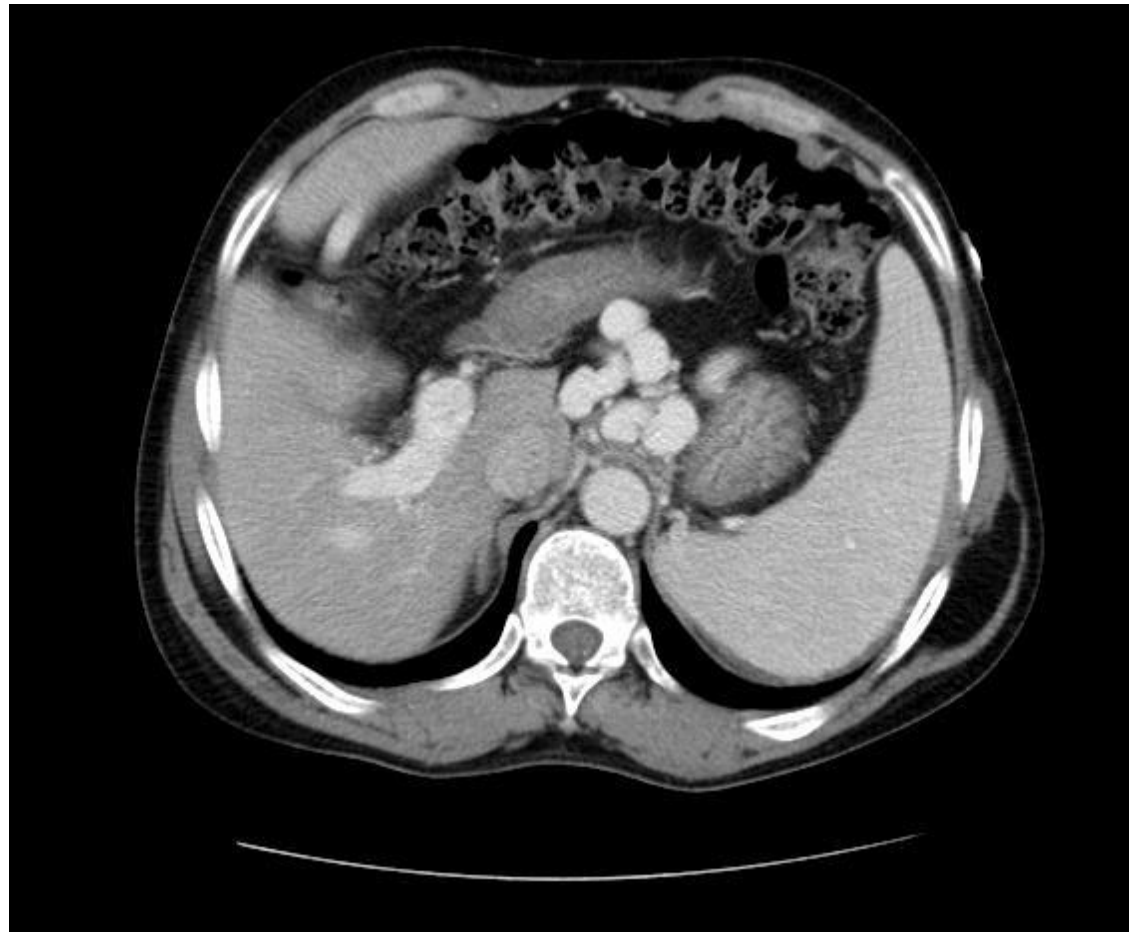
- CT scan is not affected by patients body habitus or the presence of bowel gas
- Compared with ultrasound scan, CT is more effective
- With improvement of spiral CT scan and 3-dimensional angiographic reconstructive techniques, portal vasculature may be visualized more accurately



# DIAGNOSIS

## Special examinations

### Computerized Tomography (CT)



# DIAGNOSIS

## Special examinations

### Barium swallow

- To demonstrate the presence of esophageal varices
- Esophageal varices may be recognized as a tortuous, worm-like appearance of the mucosa on a barium swallow
- The three key variables that are predictive of variceal bleeding are Child class, variceal size, and the presence and severity of red wale markings (indicative of epithelial thickness)

# TREATMENT

- Treatment is directed at the cause of PH
- The goals of pharmacotherapy are to reduce mortality and morbidity, and prevent complications associated with acute bleeding related to PH
- Pharmacologic therapy for PH includes the use of vasoconstrictors and vasodilators
- Beta-blockers are used to provide primary and secondary prophylaxis
- The vasoconstrictors somatostatin and octreotide are used to treat acute bleeding in patients with PH before performing endoscopy
- Vasodilators such as isosorbide mononitrate reduce intrahepatic vascular resistance without decreasing peripheral or portal-collateral resistance

# TREATMENT

**There are three aims or problems requiring treatment by surgical procedure:**

- Esophageal varices and variceal bleeding
- Splenomegaly with hypersplenism
- Ascites

**Among these conditions, treatment of bleeding, esophageal varices is the most important aspect of the therapy of portal hypertension**

# TREATMENT

## Esophageal varices: Pharmacologic therapy

TABLE 3. Management of Patients With Moderate/Large Varices That Have Not Bled

Therapy	Recommended Dose	Therapy Goals	Maintenance/Follow-up
Propranolol	<ul style="list-style-type: none"> <li>• 20-40 mg orally <i>twice</i> a day</li> <li>• Adjust every 2-3 days until treatment goal is achieved</li> <li>• Maximal daily dose:               <ul style="list-style-type: none"> <li>○ 320 mg/day in patients without ascites</li> <li>○ 160 mg/day in patients with ascites</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Resting heart rate of 55-60 beats per minute</li> <li>• Systolic blood pressure should not decrease &lt;90 mm Hg</li> </ul>	<ul style="list-style-type: none"> <li>• At every outpatient visit make sure that heart rate is on target</li> <li>• Continue indefinitely</li> <li>• No need for follow-up EGD</li> </ul>
Nadolol	<ul style="list-style-type: none"> <li>• 20-40 mg orally <i>once</i> a day</li> <li>• Adjust every 2-3 days until treatment goal is achieved</li> <li>• Maximal daily dose:               <ul style="list-style-type: none"> <li>○ 160 mg/day in patients without ascites</li> <li>○ 80 mg/day in patients with ascites</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Resting heart rate of 55-60 beats per minute</li> <li>• Systolic blood pressure should not decrease &lt;90 mm Hg</li> </ul>	<ul style="list-style-type: none"> <li>• At every outpatient visit make sure that heart rate is on target</li> <li>• Continue indefinitely</li> <li>• No need for follow-up EGD</li> </ul>
Carvedilol	<ul style="list-style-type: none"> <li>• Start with 6.25 mg <i>once</i> a day</li> <li>• After 3 days increase to 6.5 mg twice-daily</li> <li>• Maximal dose: 12.5 mg/day (except in patients with persistent arterial hypertension)</li> </ul>	<ul style="list-style-type: none"> <li>• Systolic arterial blood pressure should not decrease &lt;90 mm Hg</li> </ul>	<ul style="list-style-type: none"> <li>• Continue indefinitely</li> <li>• No need for follow-up EGD</li> </ul>
EVL	<ul style="list-style-type: none"> <li>• Every 2-8 weeks until the eradication of varices</li> </ul>	<ul style="list-style-type: none"> <li>• Variceal eradication (no further ligation possible)</li> </ul>	<ul style="list-style-type: none"> <li>• First EGD performed 3-6 months after eradication and every 6-12 months thereafter</li> </ul>

Any of these four therapies can be used, but current data do not support the use of combination therapy.

# TREATMENT

## Esophageal varices: Pharmacologic therapy

TABLE 4. Vasoactive Agents Used in the Management of Acute Variceal Hemorrhage

Drug	Recommended Dose	Duration
Octreotide (SMT analogue)	Initial IV bolus of 50 micrograms (can be repeated in first hour if ongoing bleeding) Continuous IV infusion of 50 µg/hr	2-5 days
Vasopressin	Continuous IV infusion: 0.2-0.4 U/min; can be increased to 0.8 U/min It should always be accompanied by IV nitroglycerin at a starting dose of 40 µg/min, which can be increased to a maximum of 400 µg/min, adjusted to maintain a systolic blood pressure 90 mm Hg.	24 hours
SMT	Initial IV bolus 250 µg (can be repeated in the first hour if ongoing bleeding) Continuous IV infusion of 250-500 µg/h	2-5 days
Terlipressin (VP analogue)	Initial 48 hours: 2 mg IV every 4 hours until control of bleeding Maintenance: 1 mg IV every 4 hours to prevent rebleeding	2-5 days

Only one of these four agents should be used.

Abbreviations: IV, intravenous; SMT, somatostatin; VP, vasopressin.

The immediate goal of therapy in these patients is to control bleeding, to prevent early recurrence (within 5 days) and prevent 6-week mortality, which is considered, by consensus, the main treatment outcome

# TREATMENT

## Esophageal varices: Endoscopic therapy

- **Endoscopic therapy** is with sclerotherapy, banding ligation or a combination of both
- Endoscopic treatment of varices gained acceptance in the 1970s with the advent of flexible endoscopy
- In the 1990s endoscopic banding was introduced and has largely replaced sclerotherapy
- Obliteration of varices with either technique requires several sessions, but studies suggest that banding requires less sessions, has a lower complication rate and that the rebleeding rate at two years is 30% to 35% and is significantly lower with banding
- Mortality is not significantly different between sclerotherapy and banding

# TREATMENT

## Esophageal varices: Decompression

- Radiologic shunt is by a transjugular intrahepatic portal systemic shunt (TIPS) and has become a popular method to treat variceal bleeding in the 1990s, especially in the acute setting
- TIPS are introduced through the right internal jugular vein, catheterization of a main hepatic vein, transparenchymal catheterization of the portal vein, and serial dilation of the track until large enough to insert a stent. Once placed the stent is dilated sufficiently to reduce the portal systemic gradient below 12 mmHg
- Absolute contraindications to placement are rightsided heart failure, severe liver failure and polycystic liver disease. Relative contraindications such as hepatic tumors, encephalopathy and hepatic or portal vein thrombosis are judged individually. Complications of TIPS include acute stent thrombosis, hemobilia, stent migration and others related to angiography in general



# TREATMENT

## Hepatorenal Syndrome

- **Use of renal vasodilators (dopamine and prostaglandin analogues) was abandoned due to side effects and lack of adequate data confirming the benefits**
- **In most studies, vasoconstrictors were given in combination with albumin, with improved efficacy**
- Administration of terlipressin (0.5–2 mg/4–6h intravenously) is associated with an improvement in renal function in about 60% of the patients and the incidence of ischaemic side-effects is about 10%
- Somatostatin analogues (octreotide), and alpha-adrenergic agonists (midodrine and noradrenaline) have also been used
- Midodrine (7.5–12.5 mg/8 hr orally) is found to be effective and is often used as a first-line treatment since the cost of terlipressin is high and it may not be available in some countries

# TREATMENT

## HE

- Identify the precipitating factors
- Stop diuretics
- Empty bowels of nitrogen containing content
  - Control bleeding
  - Protein-free diet
- Lactulose ( $\beta$ -galactosidofructose) and lactitol ( $\beta$ -galactosidosorbitol)
- Antibiotics: rifaximin; other: neomycin (an aminoglycoside), metronidazole (for anaerobes only), paromomycin, and oral vancomycin
- Maintain energy, fluid, and electrolyte balance
- Increase dietary protein slowly with recovery

# TREATMENT

## Liver transplantation

- **Liver transplantation** has changed the management of PH in the 1990s
- The occurrence of ascites and encephalopathy with variceal bleeding may indicate advanced liver disease and if the patient has no contraindications, liver transplantation may be indicated
- However, if the patient has adequate liver function, treatment should be directed at the variceal bleeding: liver transplantation is reserved for patients with end stage liver disease
- Shortage of donor organs dictates that recipients may wait for transplantation for an extended period of time
- During this period, patients with portal hypertension and variceal bleeding may need treatment that bridges them to transplantation such as endoscopic therapy or TIPS

# TREATMENT

## Ascites

- 1. Dietary sodium** restriction: two grams (88 mmol) of sodium per day is appropriate for most patients
- 2. Fluid restriction** is not needed unless the patient has hyponatremia
- 3. Diuretic therapy:** spironolactone is the drug of choice, 100 mg - starting dose; furosemide, starting dose 40 mg

# TREATMENT

## Ascites

### Therapeutic Paracentesis

- Hemodynamic changes, hyponatremia, and azotemia may occur after removal of 4 L to 15 L of fluid, requiring administration of a plasma expander, usually albumin
- Albumin, 6 g to 8 g, should be given per liter of fluid removed for paracentesis greater than 5 L

# TREATMENT

## Ascites

### Monitoring

- Twice weekly, renal function and serum electrolytes should be monitored during dose adjustment
- Target weight loss should be 1 kg to 2 kg a day if peripheral edema is present but only 0.5 kg a day in patients without edema

**THE END**