TUTORIAL CLASS

PORTAL HYPERTENSION AND COPMPLICATIONS

DR AJAZ QADIR SENIOR RESIDENT MEDICINE, HIMSR

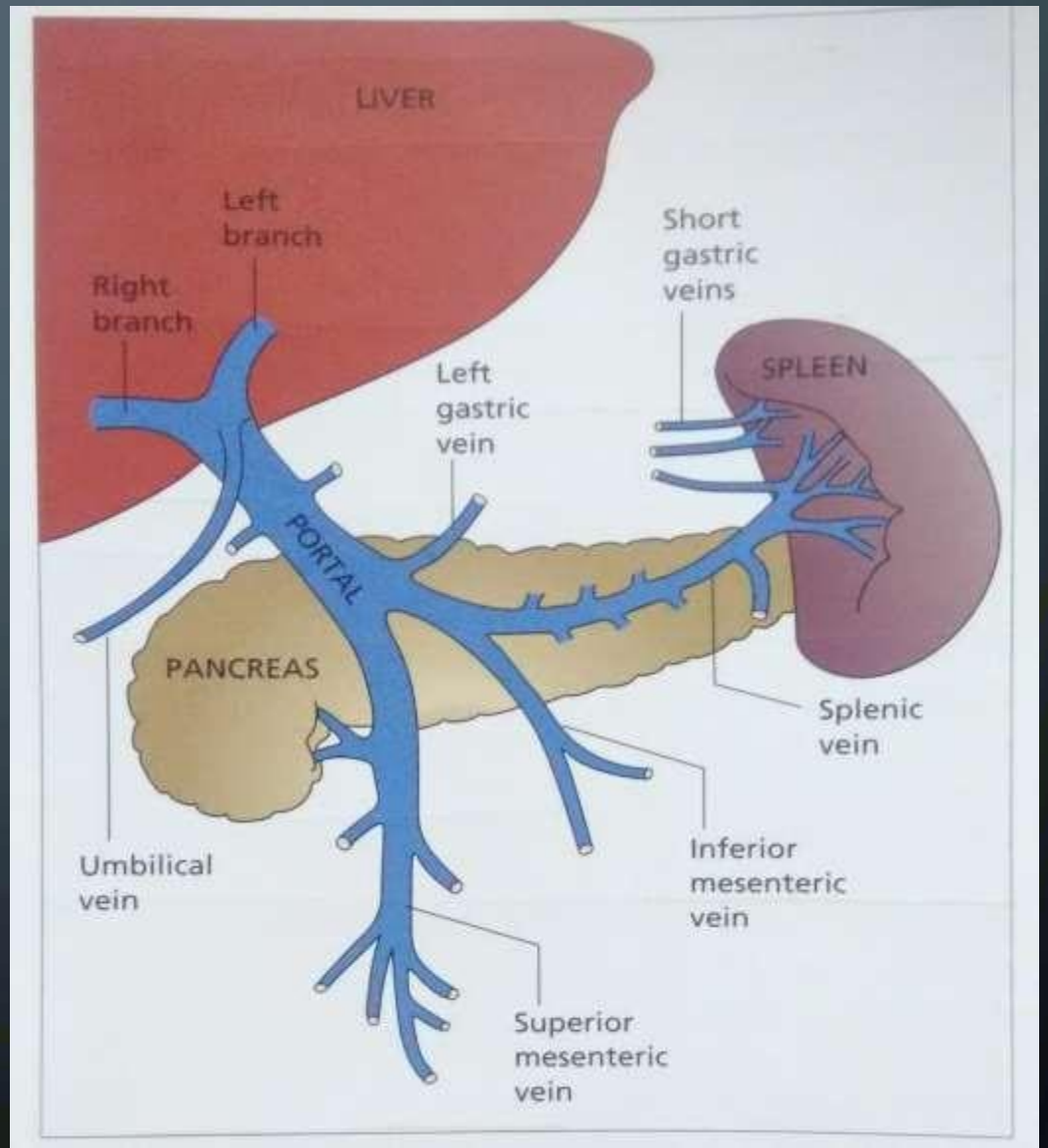
DEFINITION

- *Portal hypertension* is defined as the elevation of the hepatic venous pressure gradient to > 5 mmhg.
- Clinically significant portal hypertension is present when gradient exceeds 10 mmHg.
- Risk of variceal bleeding increases beyond a gradient of 12 mmHg.

MEASUREMENT OF PORTAL PRESSURE

- Hepatic venous pressure gradient (HVPG) is the difference between wedged hepatic venous pressure (WHVP) and free hepatic venous pressure (FHVP).
- Measurements are taken in the WHVP and FHVP positions by inflating and deflating the balloon in the tip of the catheter, introduced through internal jugular or femoral vein

ANATOMY OF PORTAL VENOUS SYSTEM



ANATOMY OF PORTAL VENOUS SYSTEM

- Portal vein is formed by the union of the superior mesenteric vein and the splenic vein just posterior to the head of the pancreas at the level of second lumbar vertebra
- Portal blood flow in man is about 1000 to 1200 ml/min

CLASSIFICATION AND CAUSES

- Prehepatic
  - Portal vein thrombosis
  - Splenic vein thrombosis
  - Massive spleenomegaly

CLASSIFICATION AND CAUSES

- Hepatic

1. Presinusoidal:

   schistosomiasis

   Congenital hepatic fibrosis

2. Sinusoidal:

   Cirrhosis of liver

   alcoholic hepatitis

3. Postsinusoidal:

   Hepatic sinusoidal obstruction (veno-occlusive syndrome)

CLASSIFICATION AND CAUSES

- Posthepatic
  - Budd-Chiari Syndrome
  - Inferior vena cava obstruction
  - cardiac causes:
    - Restrictive cardiomyopathy
    - Constrictive pericarditis
    - Severe congestive cardiac failure

PATHOPHYSIOLOGY

- The fundamental haemodynamic abnormality is an increased resistance to portal blood flow.
- Increased portal vascular resistance leads to gradual reduction in the flow of portal blood to the liver and simultaneously to the development of collateral vessels, allowing portal blood to bypass the liver and enter the systemic circulation directly.
- Collaterals develop when the pressure gradient between the portal and hepatic vein rises above a certain threshold, a process involves angiogenic factors.
- At the same time portal flow increases in the splanchnic bed due to splanchnic vasodilatation and increased cardiac output

PATHOPHYSIOLOGY

- Portal vascular resistance is increased in chronic liver disease.

Liver cell injury

↓

Stellate cell activation

↓

Stellate cells transform into myofibroblast

↓

De novo expression of specific smooth muscle protein alpha-actin

↓ Endothelin, NO Prostaglandins

Contraction of activated cells

↓

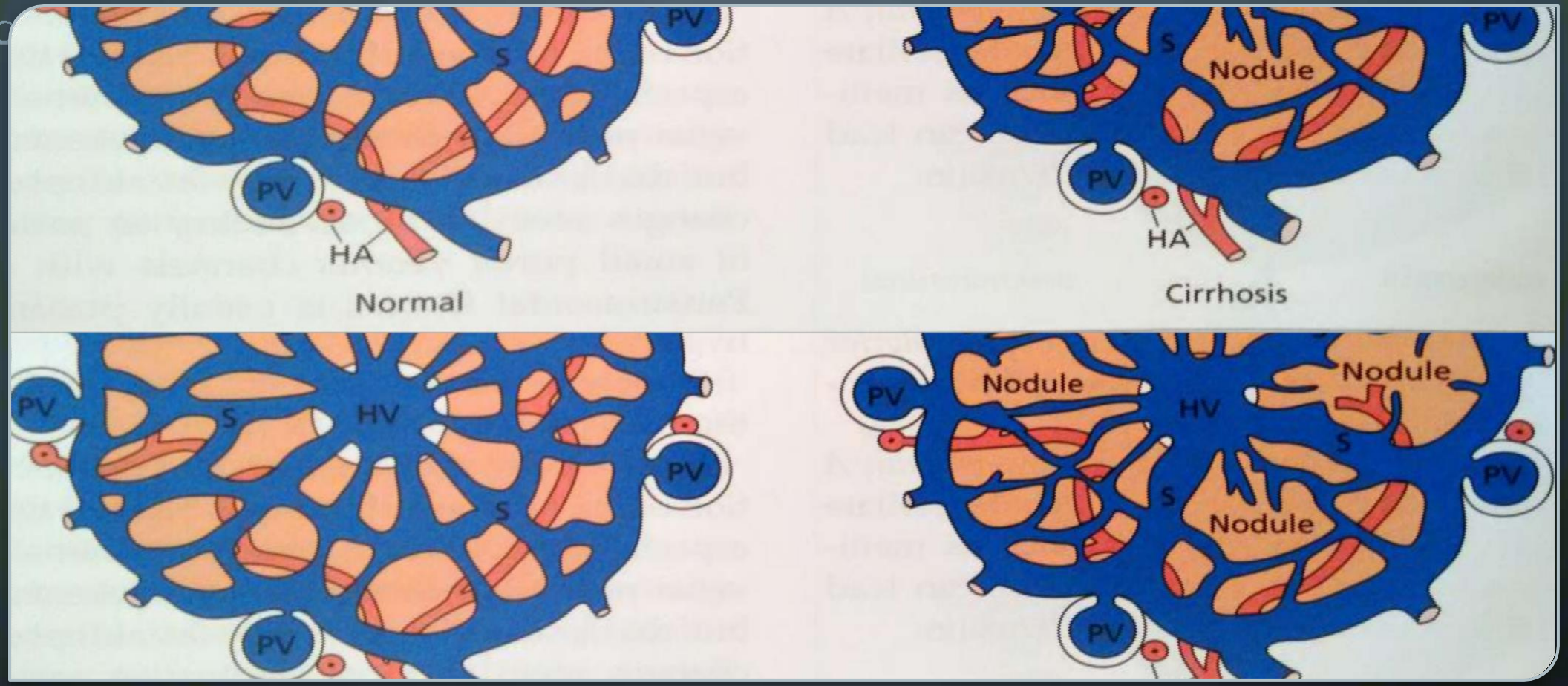
Abnormal blood flow pattern causing increased resistance

↓ fibrogenesis

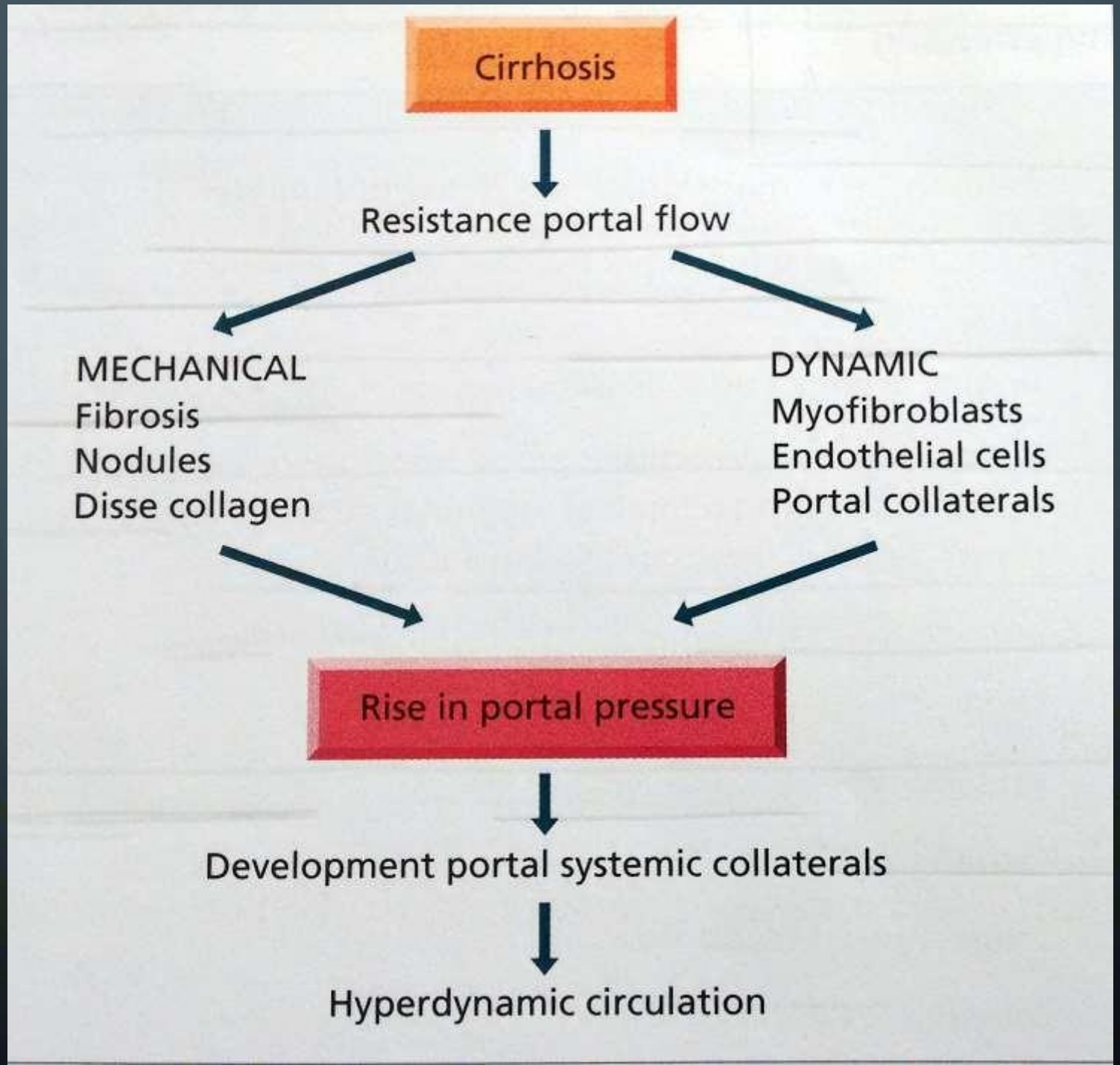
Increased resistance leads to portal hypertension

PATHOPHYSIOLOGY IN CIRRHOSIS

- Portal venous blood is diverted into collateral channels and some bypass the liver cells and is shunted directly into the hepatic venous radicles in fibrous septa.
- These portohepatic anastomosis develop from pre-existing sinusoids enclosed in the septa



- The regenerating nodules become divorced from their portal blood supply and are nourished by the hepatic artery.
- The obstruction to portal flow is partially due to nodules which compress hepatic venous radicles


Cirrhosis
Resistance portal flow
MECHANICAL
Fibrosis
Nodules
Disse collagen
DYNAMIC
Myofibroblasts
Endothelial cells
Portal collaterals
Rise in portal pressure
Development portal systemic collaterals
Hyperdynamic circulation

COLLATERAL CIRCULATION

- Normally 100 %of the portal venous blood flow can be recovered from the hepatic veins, whereas in cirrhosis only 13 %is obtained.
- The remainder enters collateral channels which form four main groups

COLLATERAL CIRCULATION

- ***Group I***: (At the cardia of stomach and at the anus)

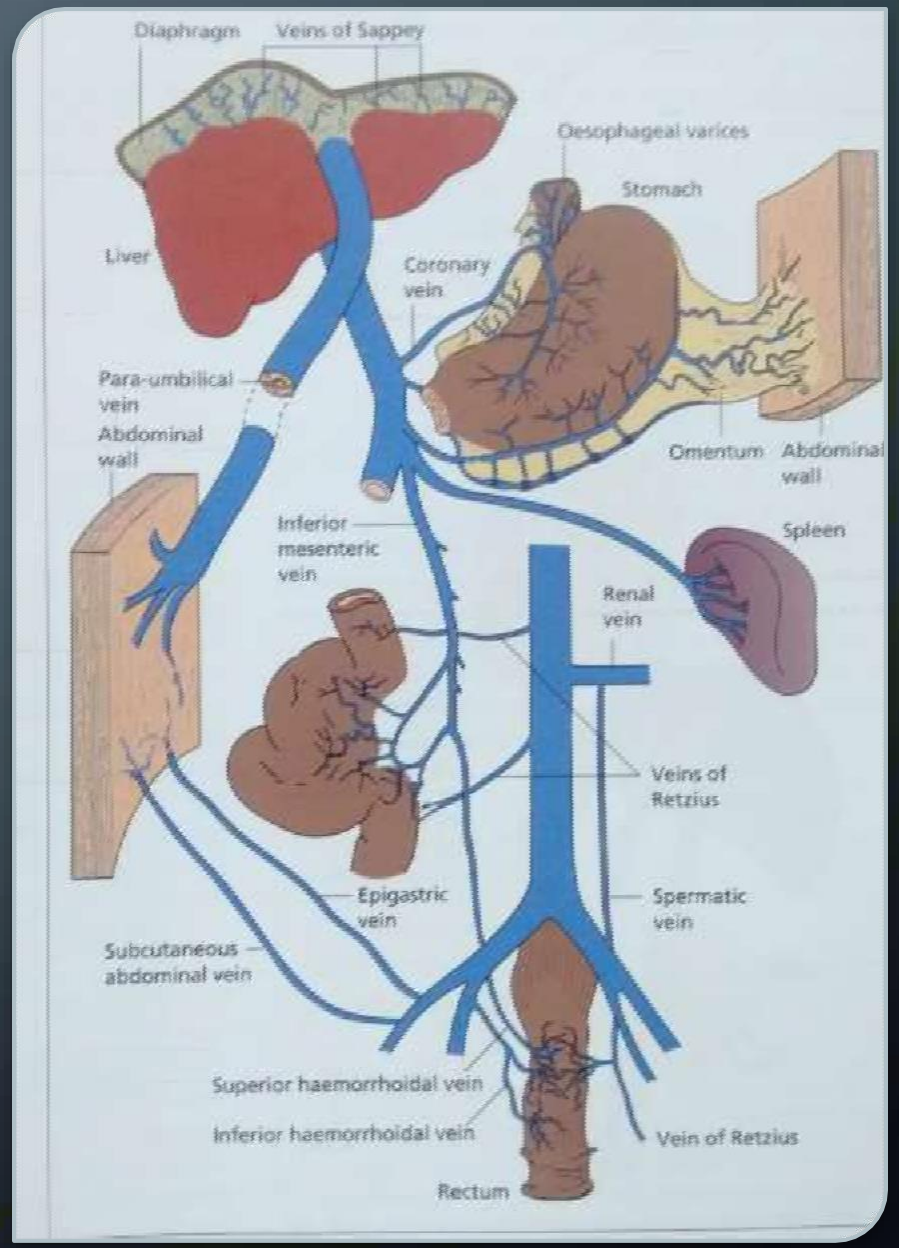
At the cardia of stomach

Portal System
- Left gastric vein
- Posterior gastric vein
- Short gastric veins

ANASTOMOSE

WITH

Caval system
- Intercostal veins
- Diaphragmo-esophageal vein
- Azygous minor veins



COLLATERAL CIRCULATION

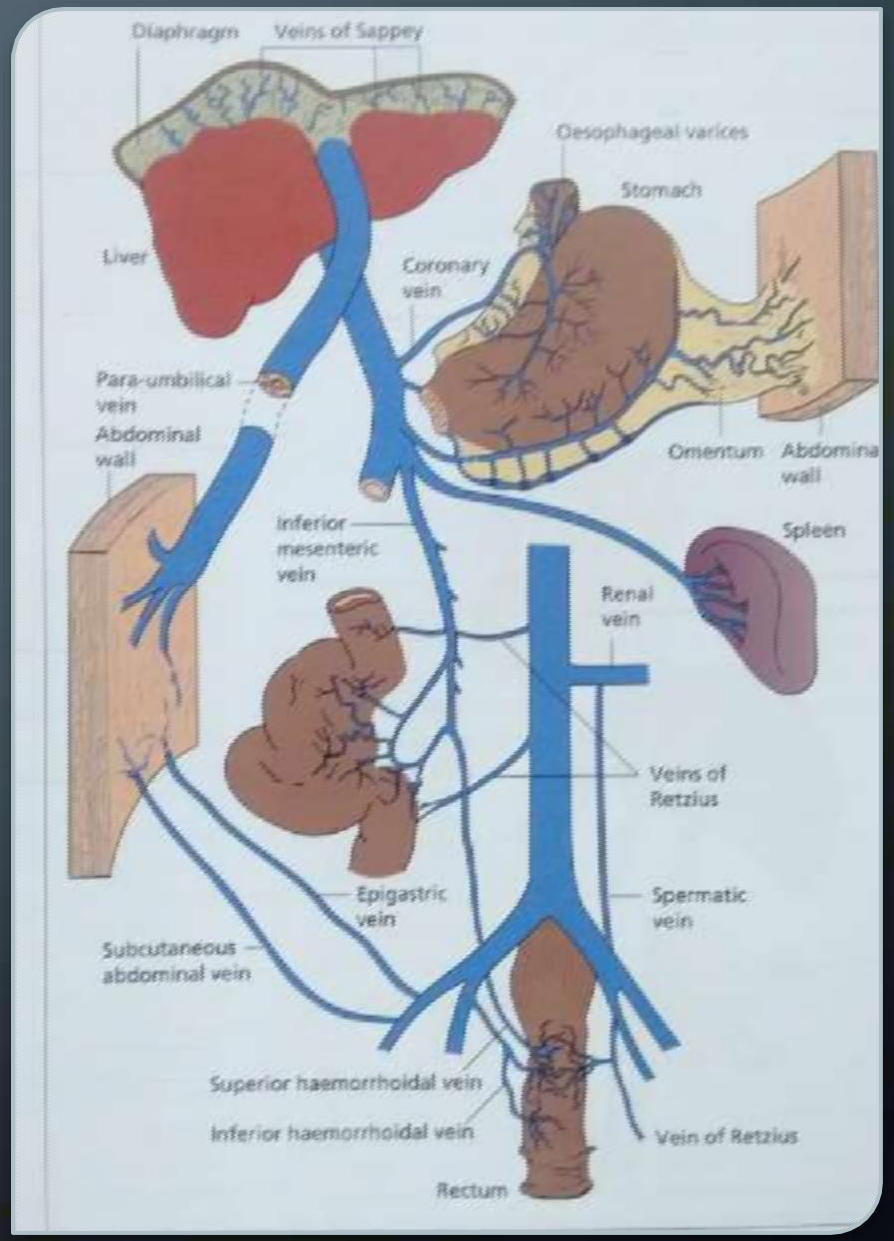
- ***Group I:***

At the anus

Portal system — Superior haemorrhoidal vein

Anastomose with

Caval system — Middle haemorrhodal vein; Inferior Haemorrhoidal vein

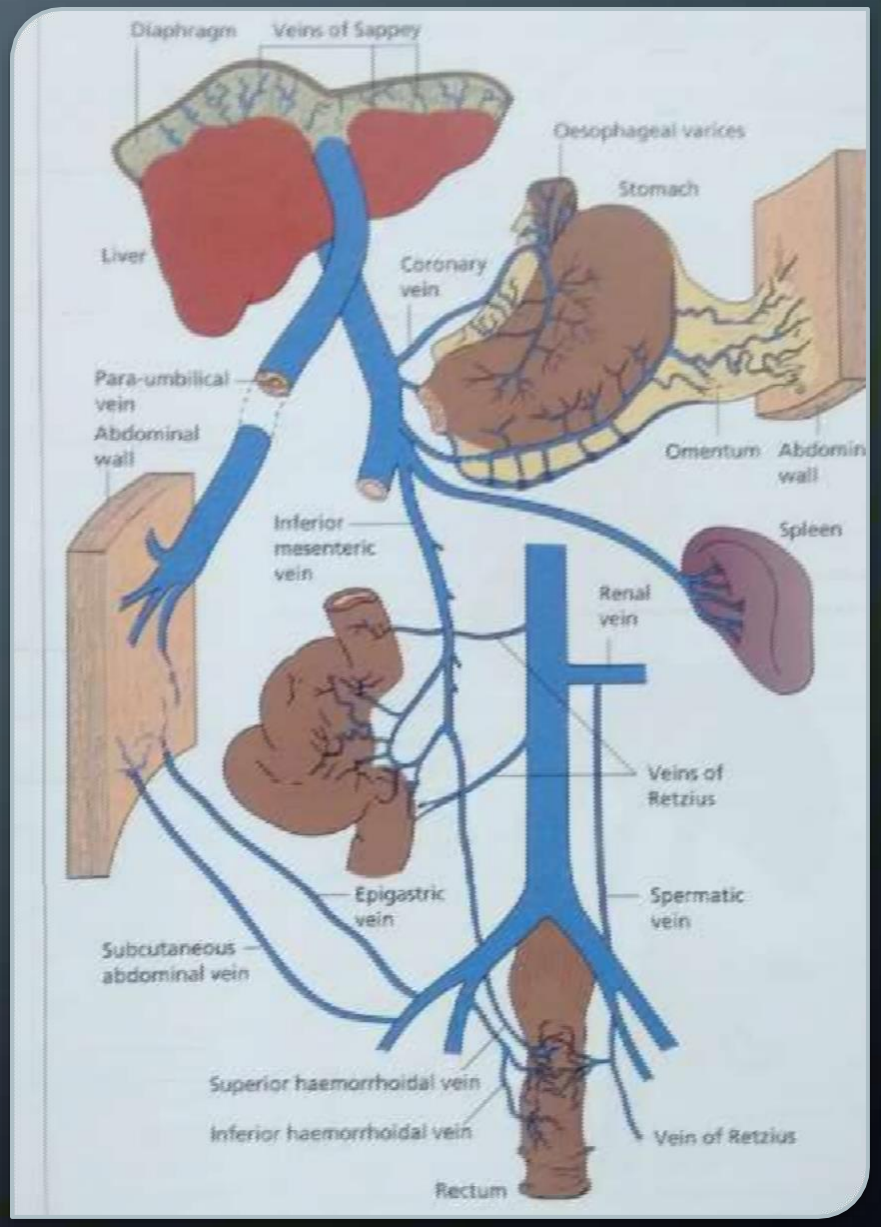


COLLATERAL CIRCULATION

- ***Group II:***

  At the umbilicus.

  In the falciform ligament through the paraumbilical veins anastomosing with superficial abdominal veins

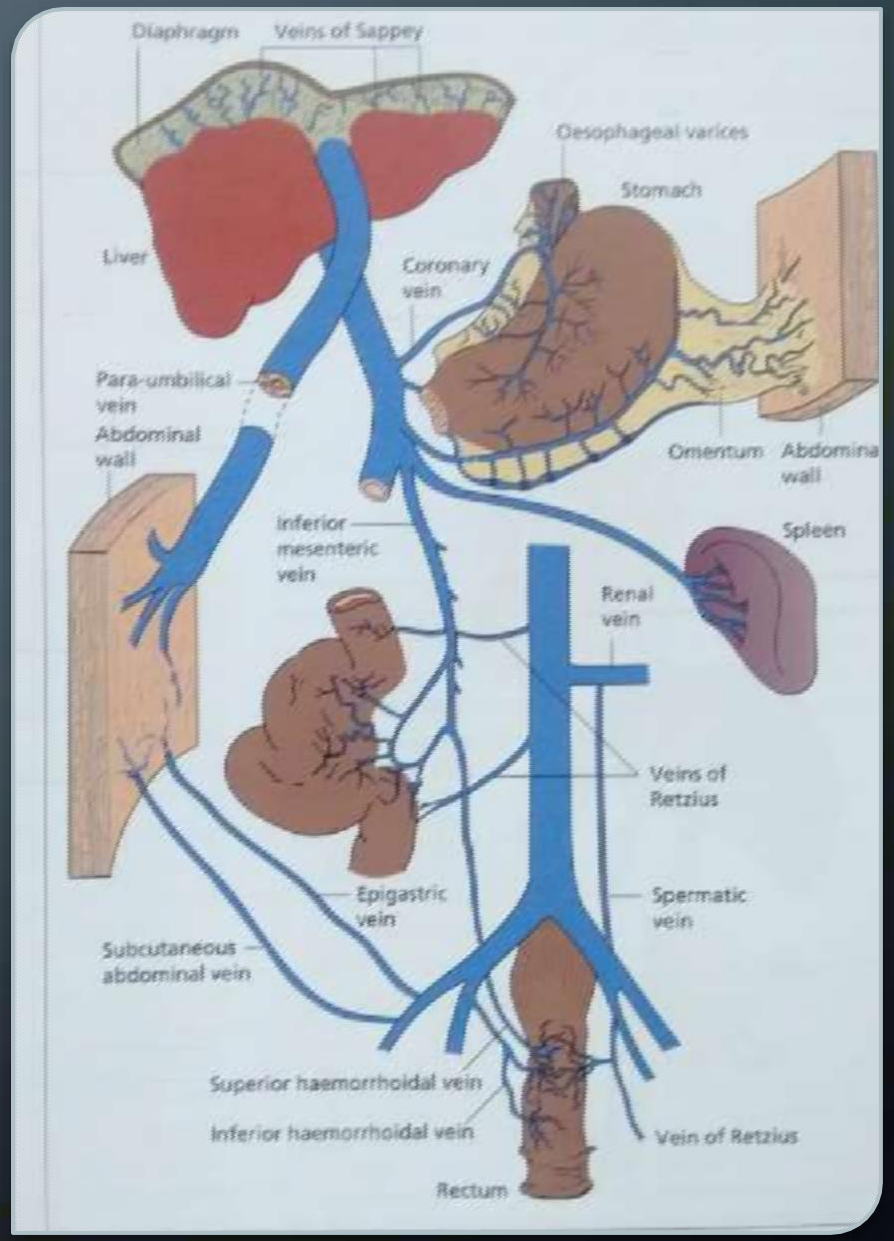


COLLATERAL CIRCULATION

- ***Group III:***

Where the abdominal organs are in contact with retroperitoneal tissues or adherent to abdominal wall.

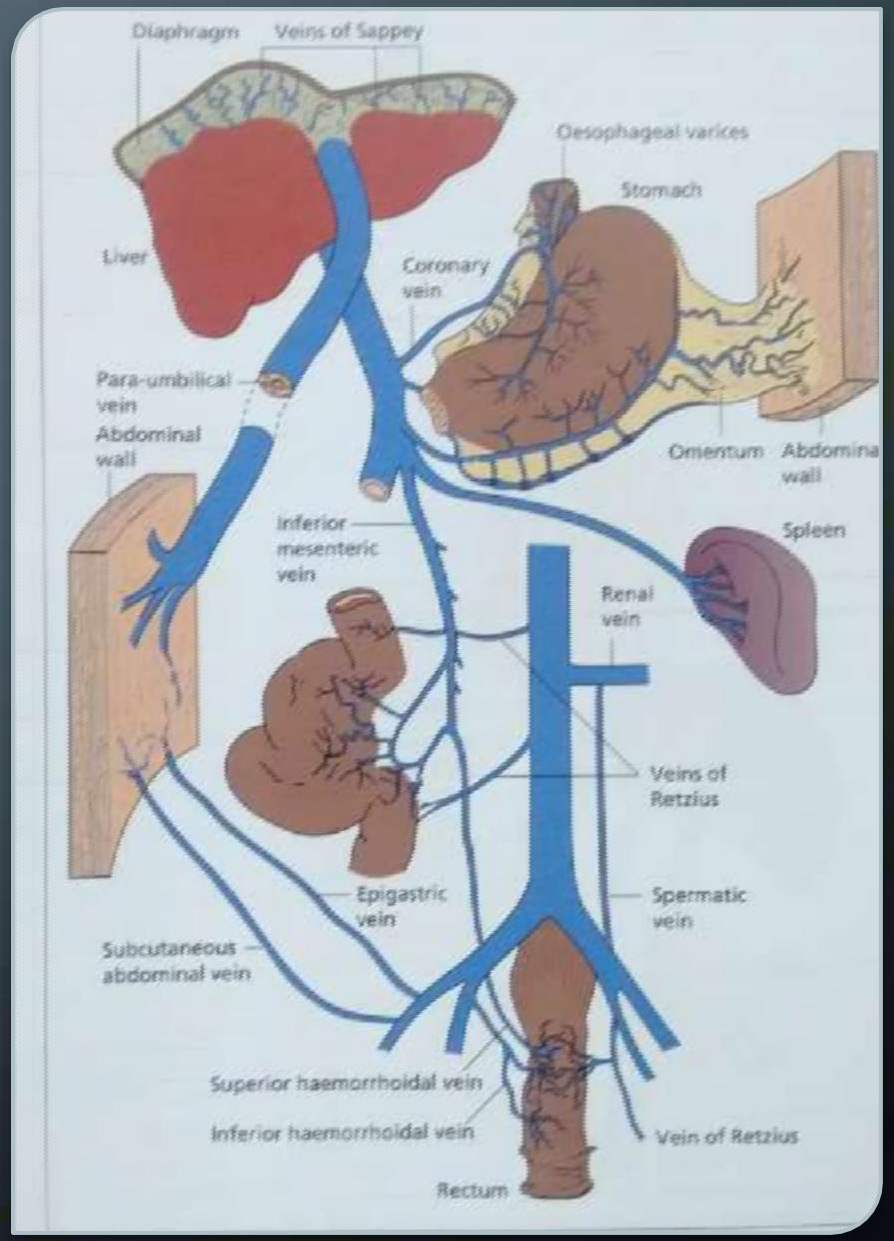
These collaterals run from liver to diaphragm and in spleenorenal ligament and omentum.



COLLATERAL CIRCULATION

- ***Group IV:***

Portal venous blood is carried to the left renal vein through blood entering directly from the splenic vein.



ASCITES IN PORTAL HYPERTENSION

★ Factors involved in the pathogenesis of ascites

- Increased portal pressure with vasodilation of splanchnic arterial system.
- Sodium retention due to activation of the raas due to hyperaldosteronism, causing fluid accumulation and expansion of ecf
- Sodium retention is also the consequence of a homeostatic response caused by underfilling of arterial circulation secondary to splanchnic vasodilatation.
- Increased production of splanchnic lymph.
- Hypoalbuminaemia.

CLINICAL FEATURES

- History:

  Cirrhosis is the commonest cause.

  Past abdominal infectious conditions, is important in extrahepatic portal vein thrombosis.

  Inherited or acquired thrombotic conditions drugs like sex hormones predispose to portal and hepatic vein thrombosis.

  Haematemesis is the commonest presentation.

  Melaena without haematemesis may result from bleeding varices

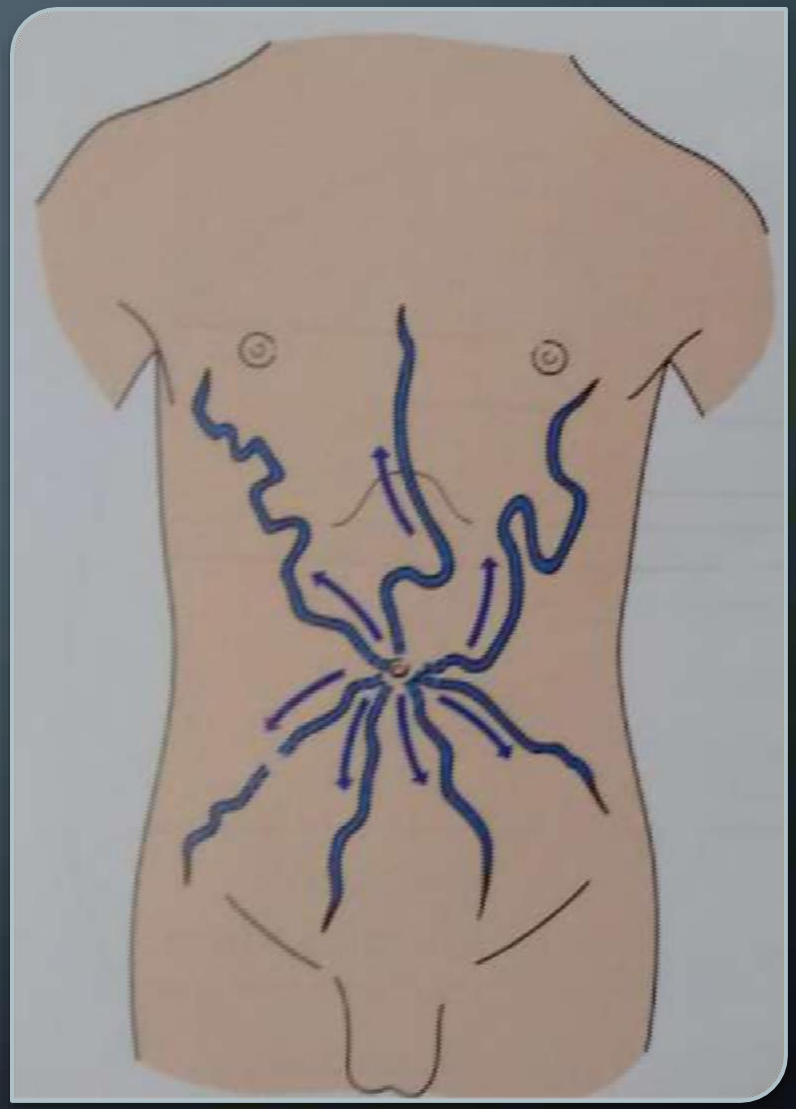
CLINICAL FEATURES

- Abdominal wall veins:

  Prominent collateral veins radiating from umbilicus are termed caput medusa.

  A venous hum may be heard usually in the region of xiphoid process or umbilicus.

- Spleenomegaly (Mild to moderate)
- Ascites
- Anorectal varices
- Fetor hepaticus



DIAGNOSIS OF PORTAL HYPERTENSION

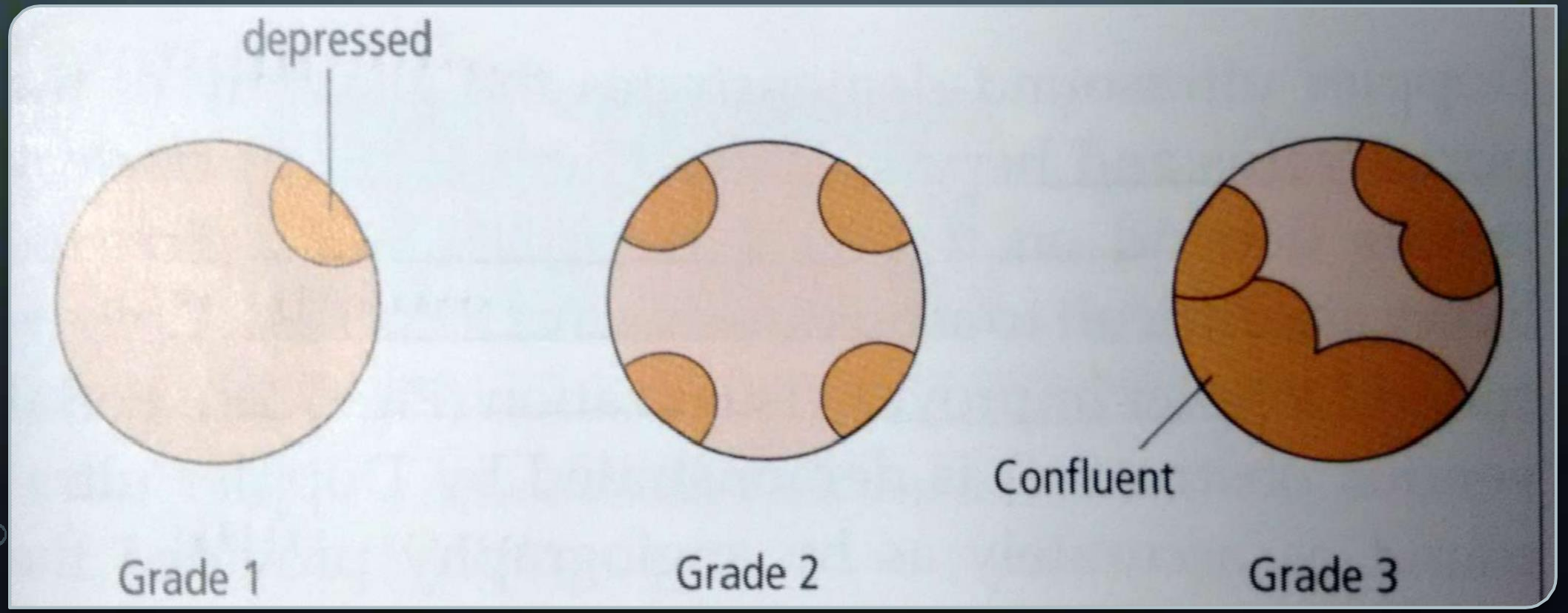
- Imaging :
  - Ultrasonography
  - Doppler Ultrasonography
  - CT Contrast arterioportography
  - MR angiography

COMPLICATIONS

- Variceal bleeding
- Congestive gastropathy
- Hypersplenism
- Ascites
- Iron deficiency anaemia
- Renal failure
- Hepatic encephalopathy

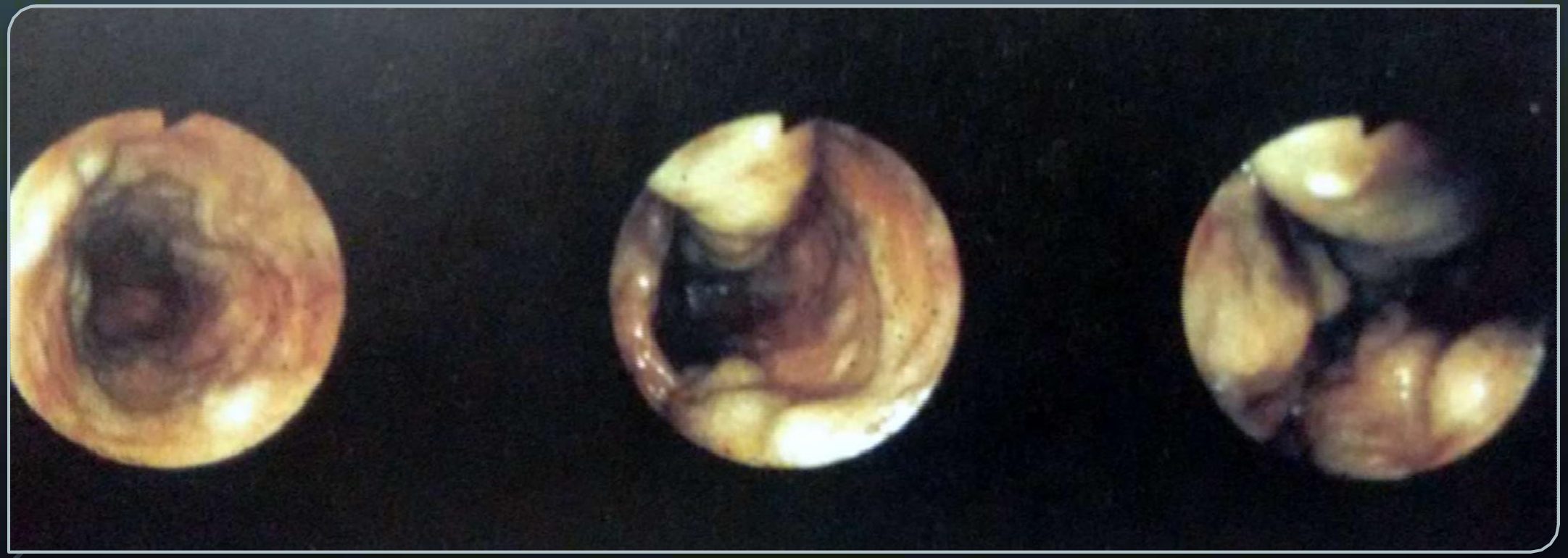
DIAGNOSIS OF VARICES

- Endoscopy is the best screening test to detect varices.



DIAGNOSIS OF VARICES

- Endoscopy is the best screening test to detect varices.



MANAGEMENT OF ACUTE VARICEAL BLEED

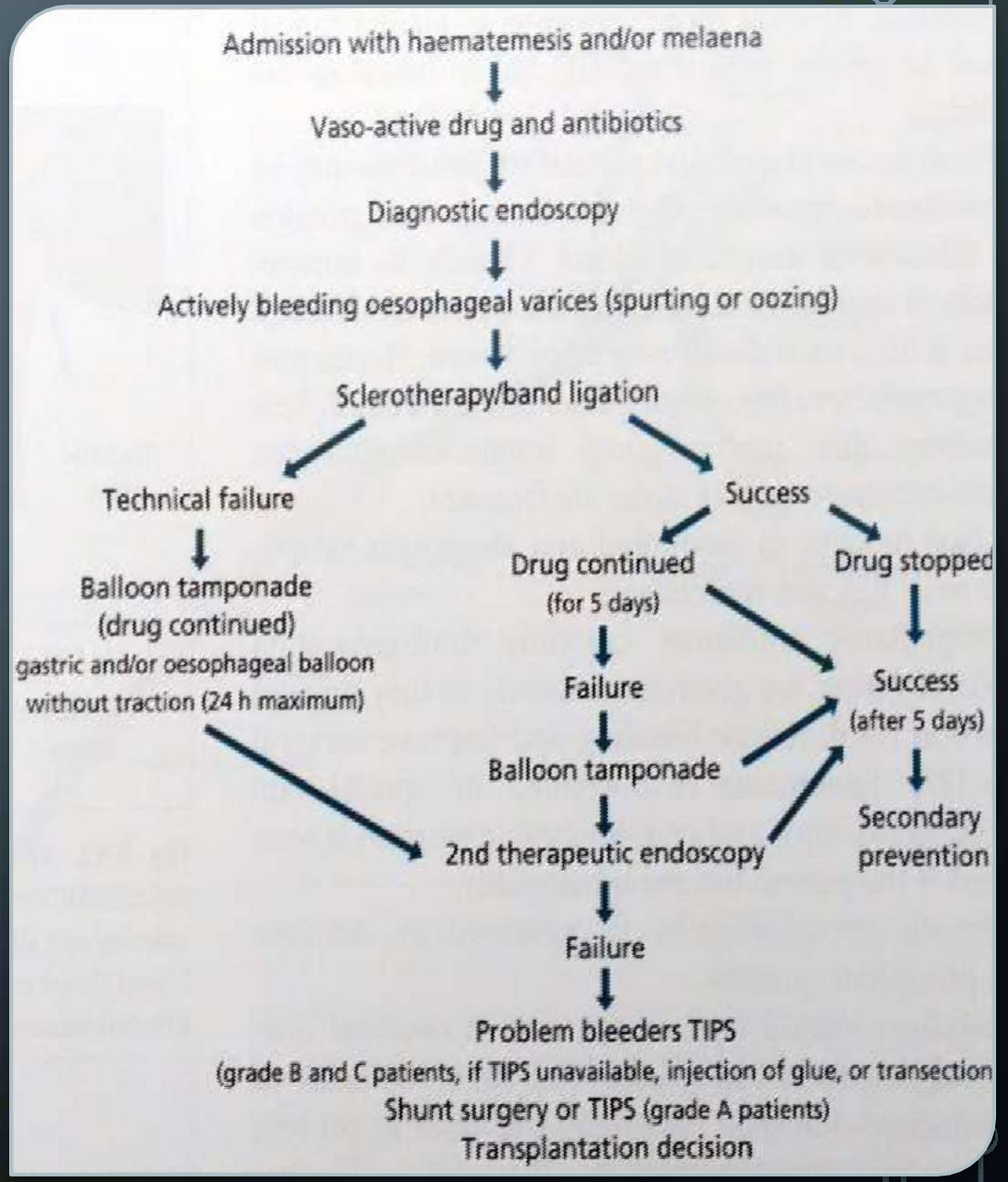
- Diagnostic endoscopy is performed first.
- Haemodynamic monitoring is done.
- Fresh frozen plasma, vitamin K & platelet transfusion if necessary given to prevent further worsening of coagulation.
- Hepatic encephalopathy is prevented by giving lactulose.
- Therapeutic options available are:

  Vasoactive drugs Endoscopic

  sclerotherapy Variceal banding

  Sengstaken-Blakemore tube

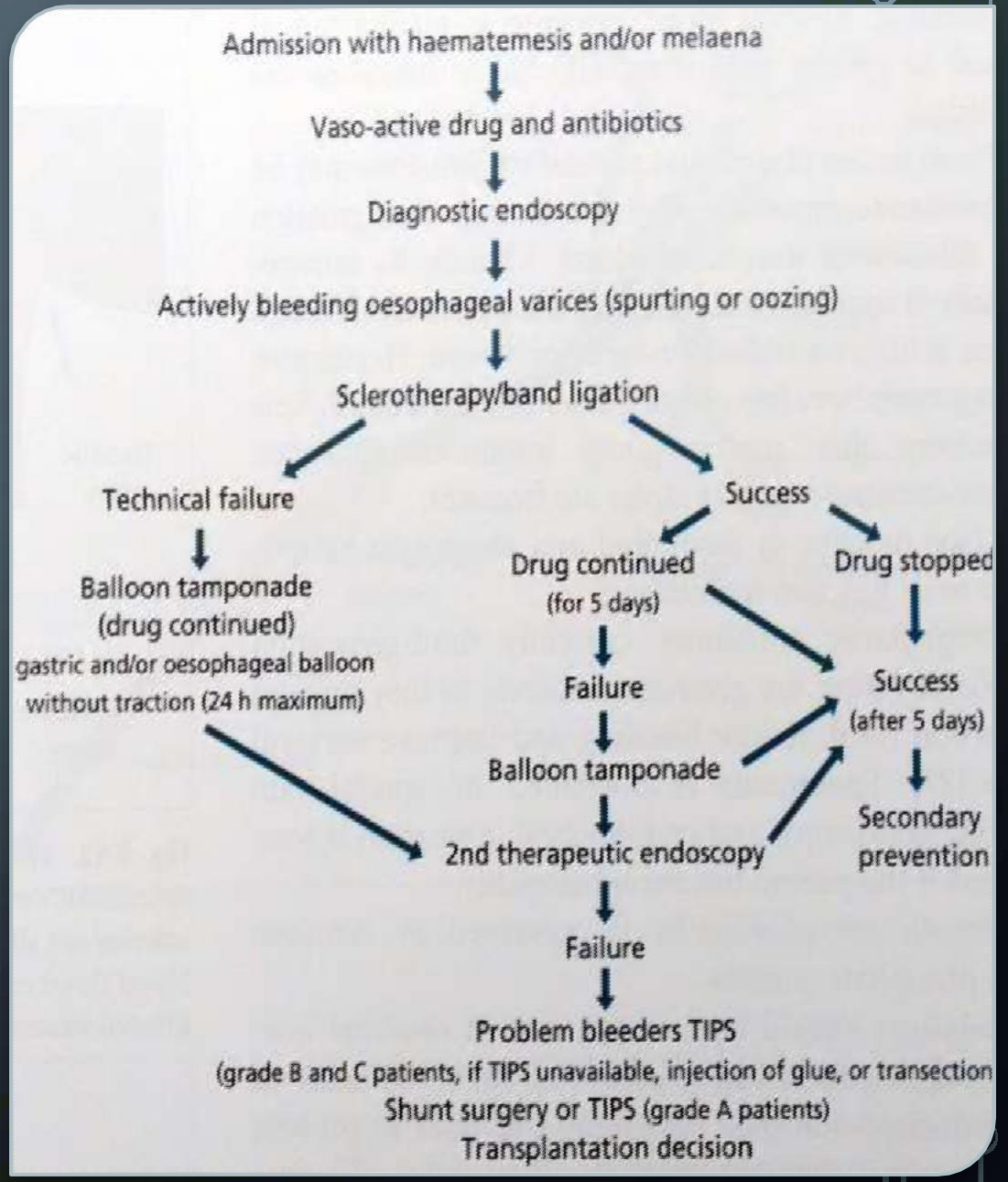
  TIPS (Trasnjugular Intrahepatic Porto-systemic stenting)



MANAGEMENT OF ACUTE VARICEAL BLEED

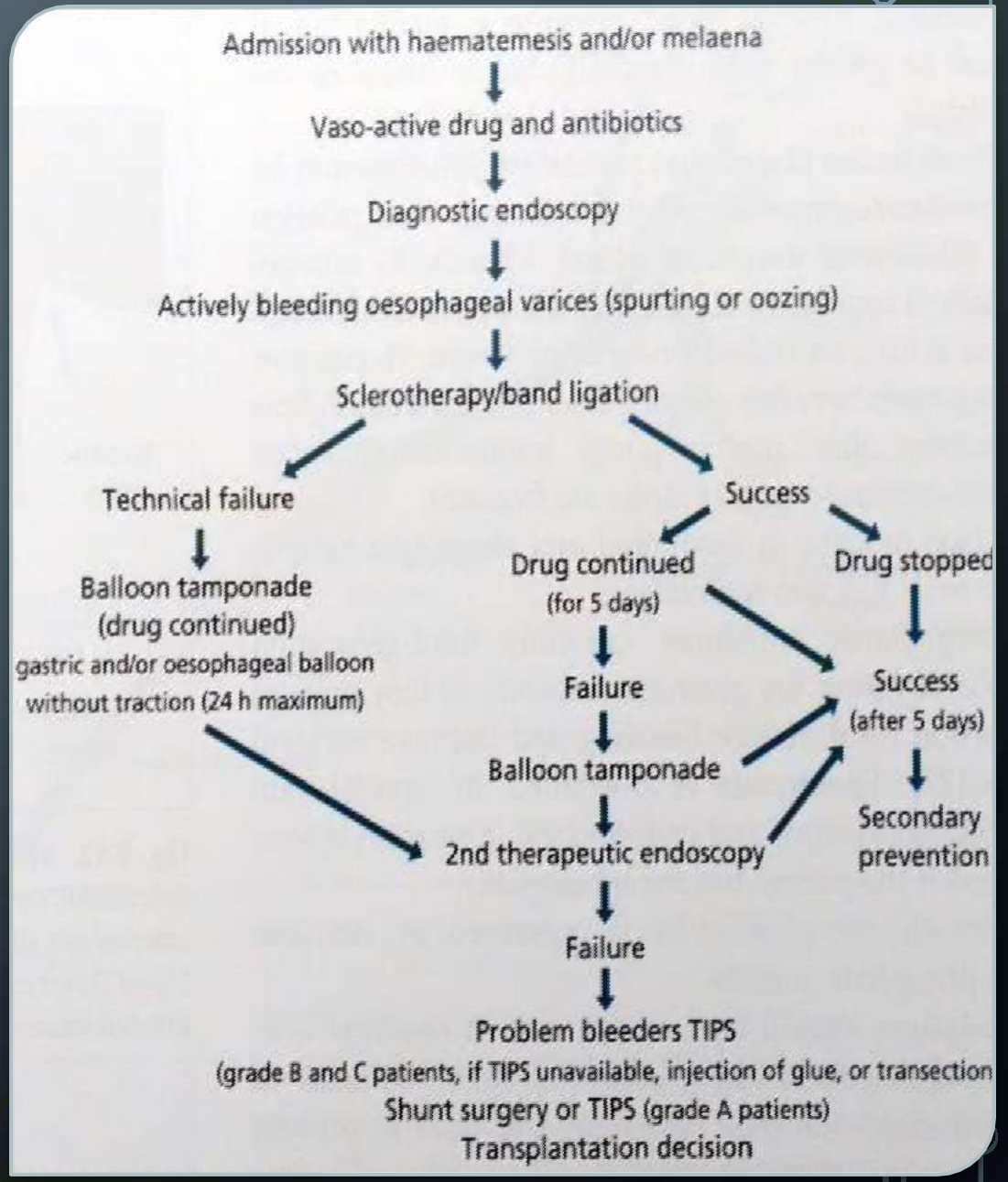
- ***Vasoactive drugs***:

1. Vasopressin &Terlipressin. Both lower portal venous pressure by constriction of splanchnic arterioles.
2. Somatostatin: in addition to constriction of splanchnic arterioles, it inhibits splanchnic vasodilatory peptides like glucagon.
3. Octreotide.



MANAGEMENT OF ACUTE VARICEAL BLEED

- The combination of immediate use of a vasoactive drug and endoscopic banding ligation or sclerotherapy is the therapeutic gold standard for acute treatment of bleeding varices

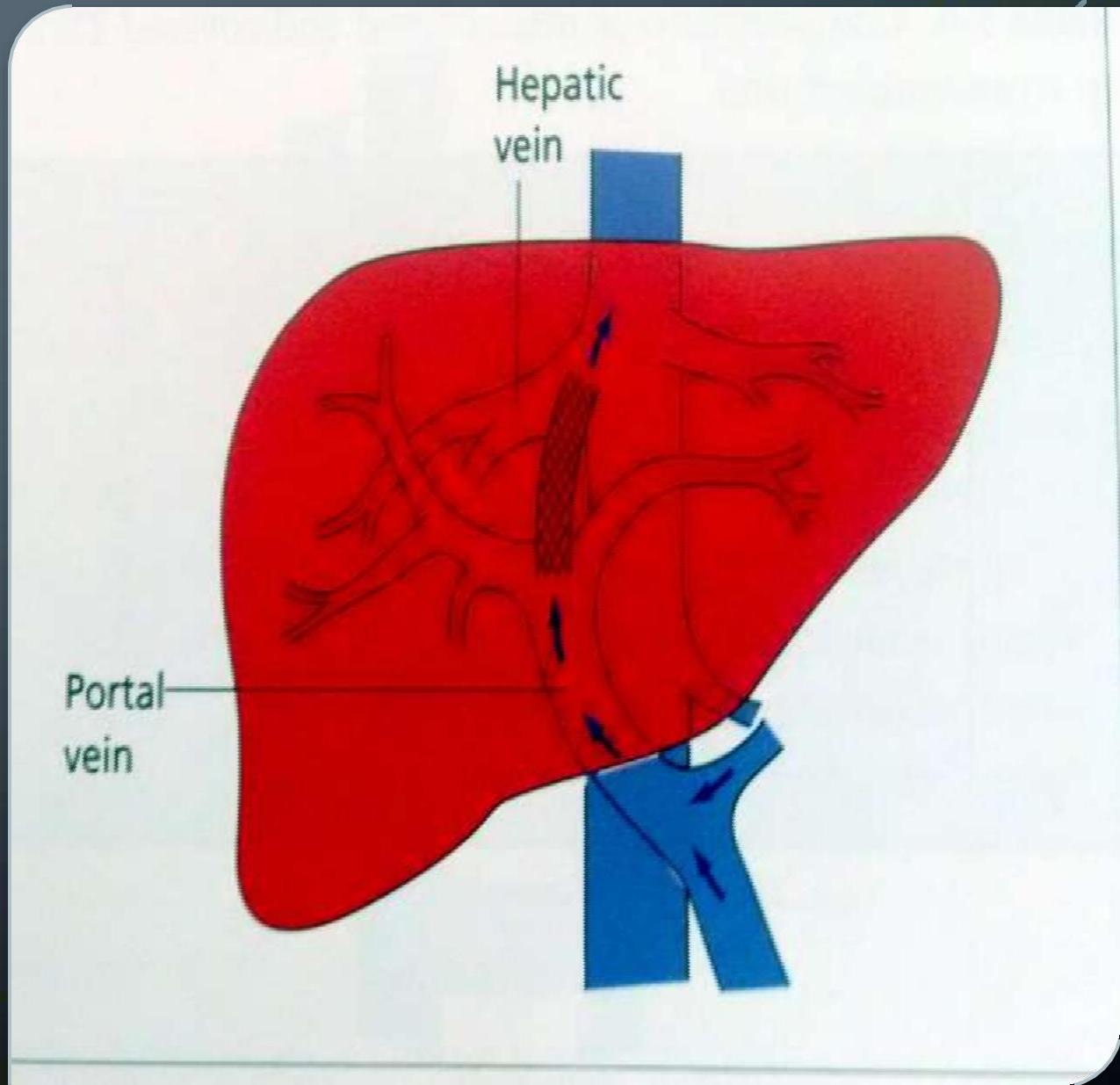


MANAGEMENT OF ACUTE VARICEAL BLEED

- ***TIPS :***

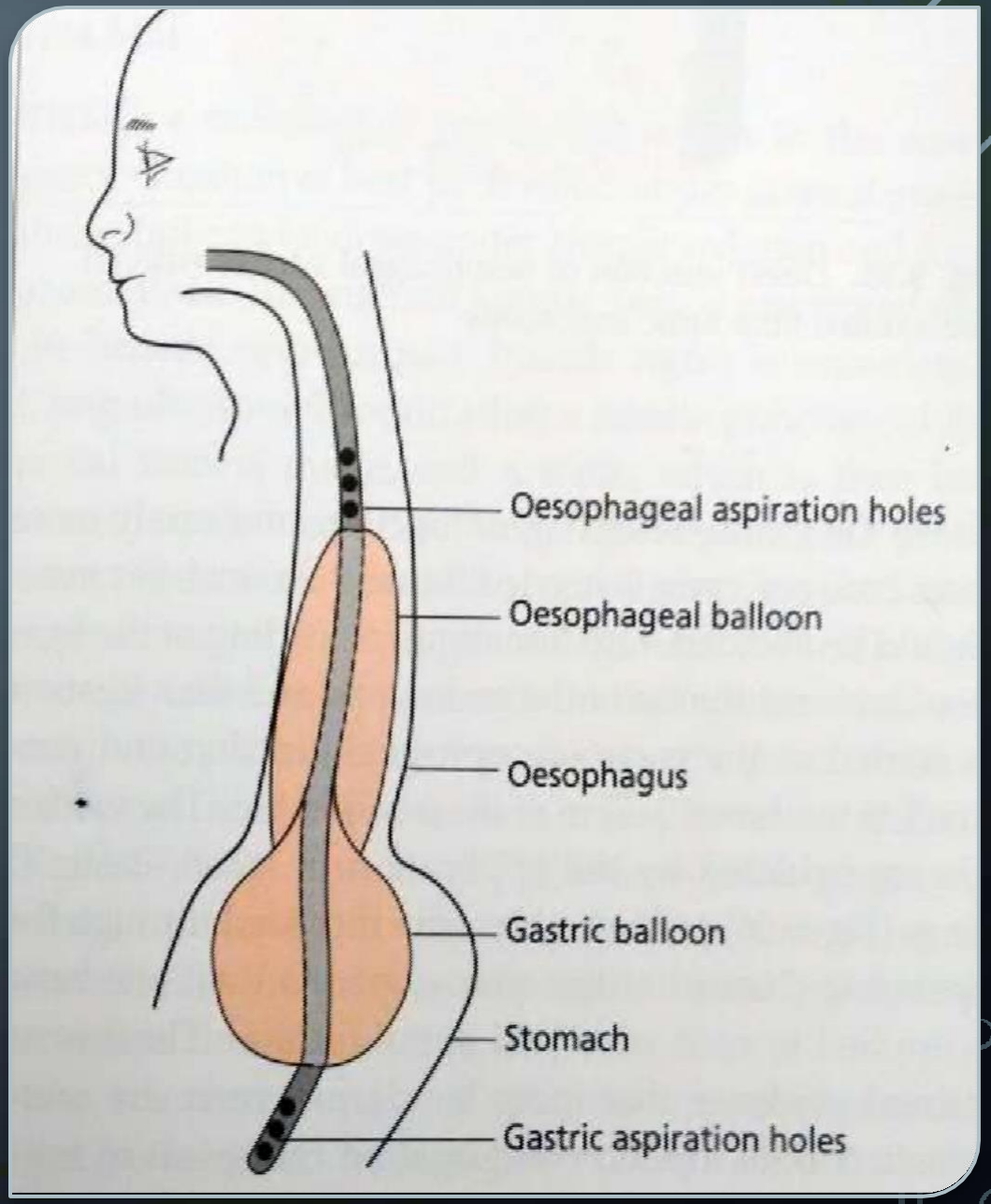
An expandable metal stent is inserted between portal vein and hepatic vein producing an intrahepatic portosystemic shunt

Approach is taken through internal jugular vein



MANAGEMENT OF ACUTE VARICEAL BLEED

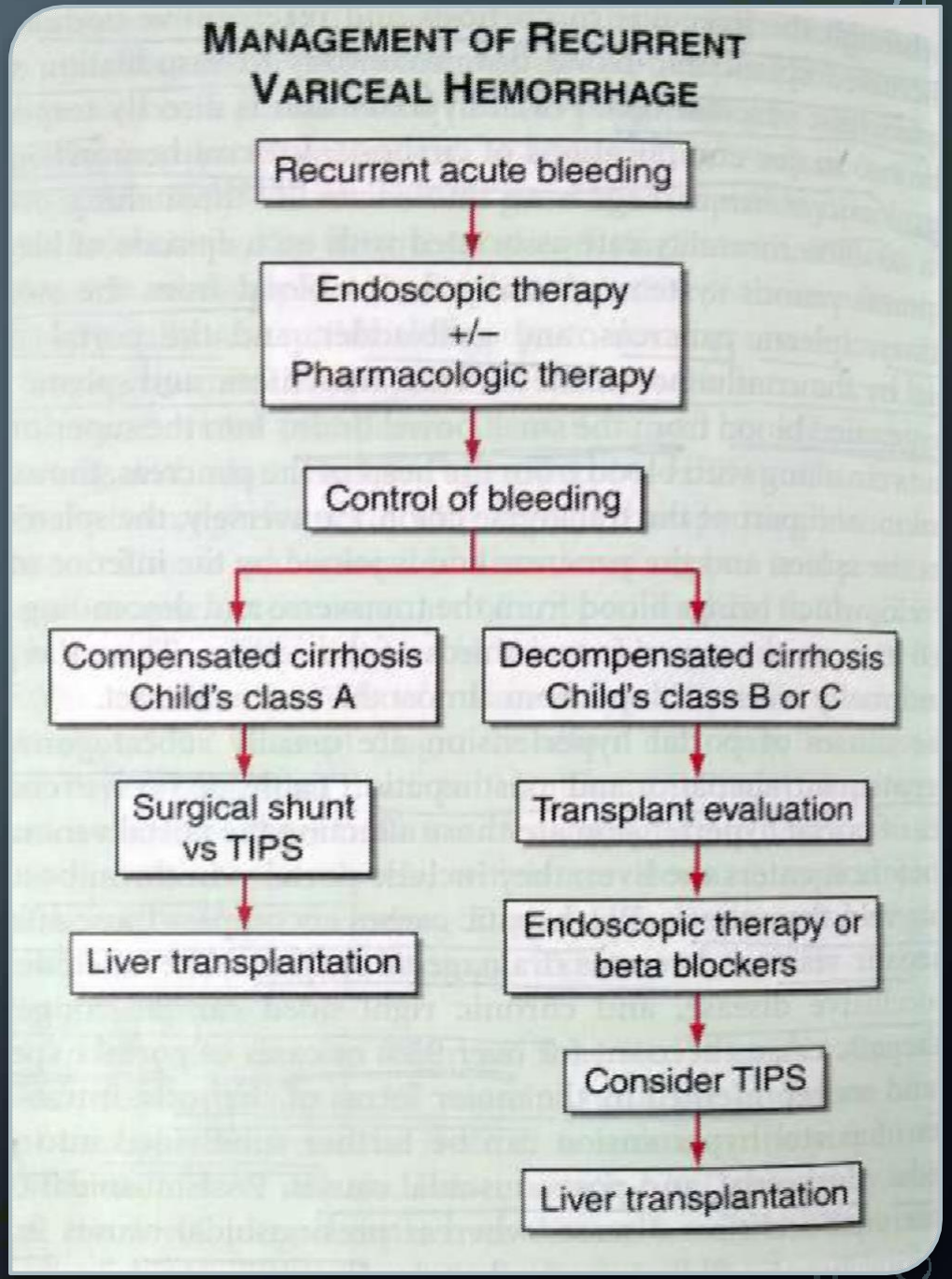
- Use of **Senstaken-Blakemore tube** has decreased now a days, with use of vasoactive drugs, sclerotherapy and TIPS.



MANAGEMENT OF RECURRENT VARICEAL BLEED

Group designation	A	B	C
Serum bilirubin* (mg/dL)	Below 2.0	2.0–3.0	Over 3.0
Serum albumin (g/dL)	Over 3.5	3.0–3.5	Under 3.0
Ascites	None	Easily controlled	Poorly controlled
Neurological disorder	None	Minimal	Advanced coma
Nutrition	Excellent	Good	Poor: 'wasting'

*1 mg = 17 µmol/L.



SECONDARY PREVENTION OF VARICEAL BLEEDING

- Beta-blockers are used as secondary measuere to prevent recurrent variceal bleeding.
- Propranolol or nadolol is effective in reducing portal venous pressure.
- Administration of these drugs at doses that reduce the heart rate by 25 %has been shown to be effective in the primary prevention of variceal bleeding.

HEPATIC ENCEPHALOPATHY

Definition

- It is a state of disordered CNS function, resulting from failure of liver to detoxify toxic agents because of hepatic insufficiency and porto-systemic shunt.
- It represents a reversible decrease in neurologic function.
- It occurs most often in patients with cirrhosis but also occur in acute hepatic failure.

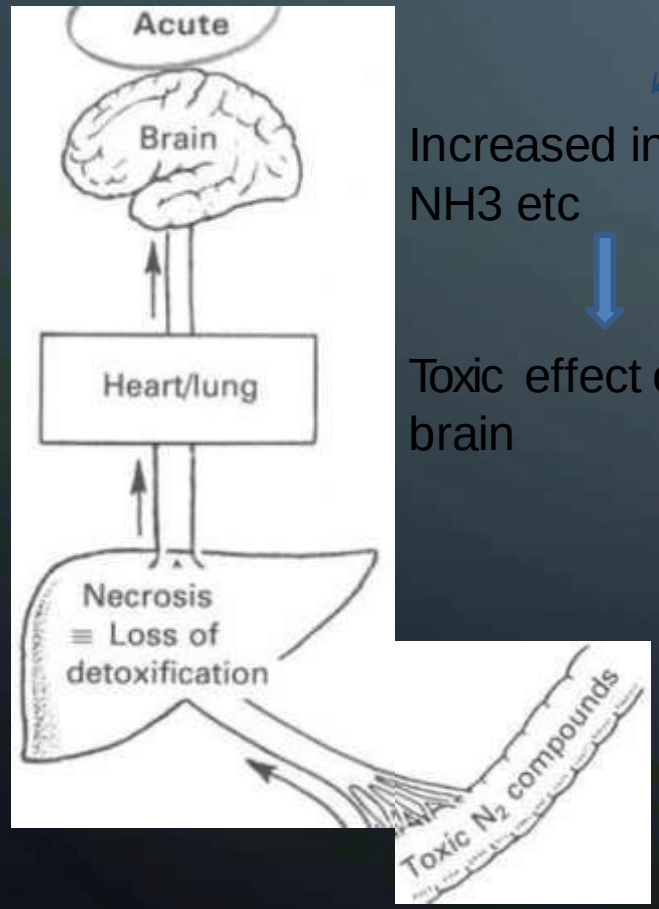
Pathogenesis

- Ammonia formed by protein breakdown in GIT
- Liver → liver dysfunction (abnormal) → NH3 → Passes BBB → Hepatic encephalopathy.
- Other factors:
- Increase sensitivity to glutamine & GABA (inhibitory neurotransmitter)
- Increase circulating levels of endogenous benzodiazepines.

Pathogenesis (acute & chronic)

The basic cause is same in both forms but the mechanism is somewhat different

Diminished detoxification of toxic intestinal nitrogenous compounds

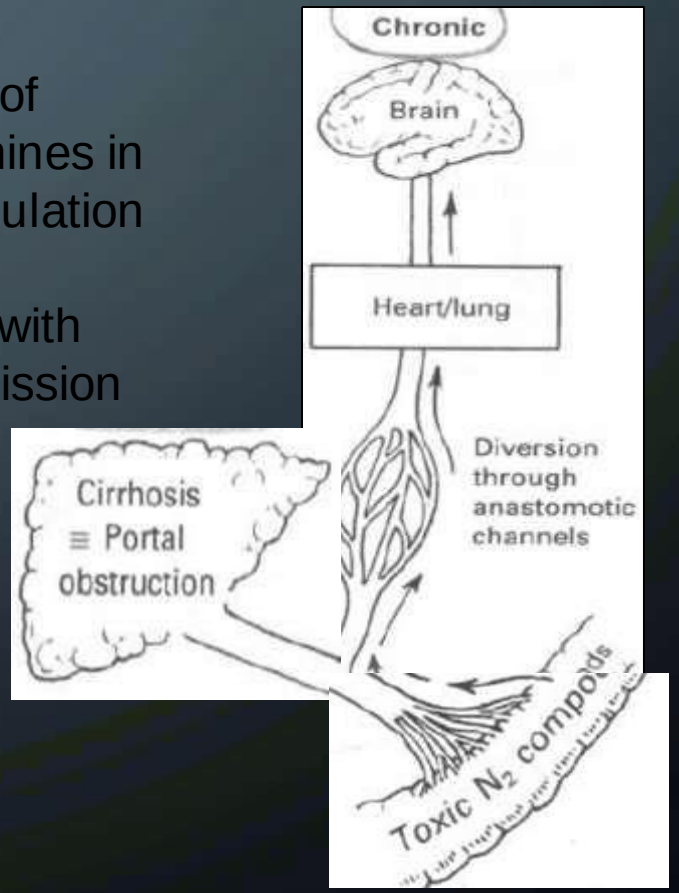


Increased in blood NH3 etc

Toxic effect on brain

Appearance of abnormal amines in systemic circulation

Interference with neurotransmission



Causes

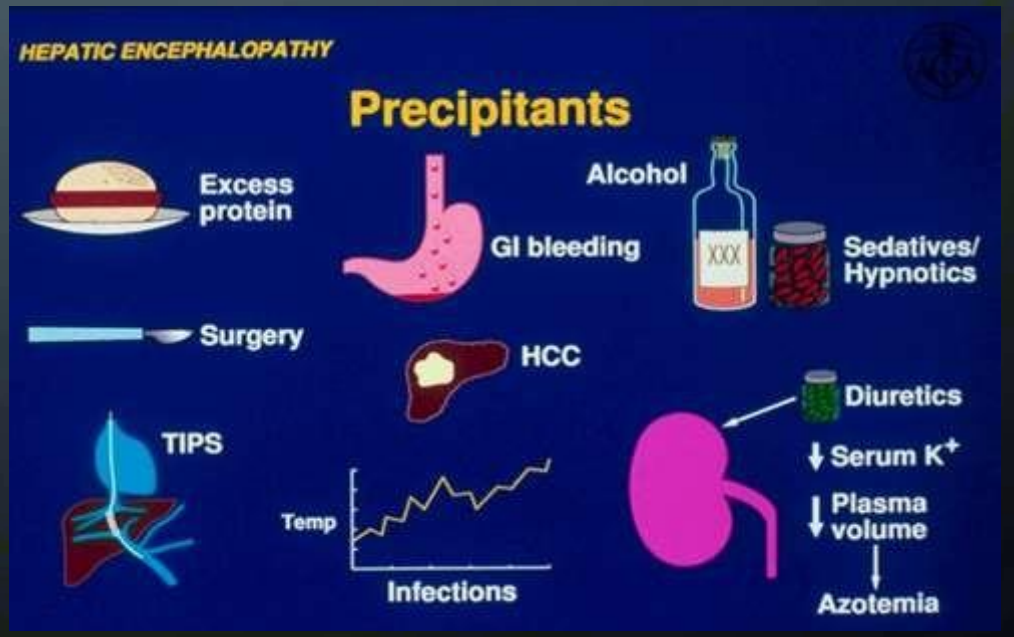
- **Chronic parenchymal liver disease:**
- Chronic hepatitis.
- Cirrhosis.

- **Fulminating hepatic failure:**
- Acute viral hepatitis.
- Drugs.
- Toxins e.g. Wilson's Disease, CCL4.

- Surgical Portal-systemic anastomoses, - portacaval shunts, or Transjugular intrahepatic portal-systemic shunting [TIPS]).

Precipitating Agents

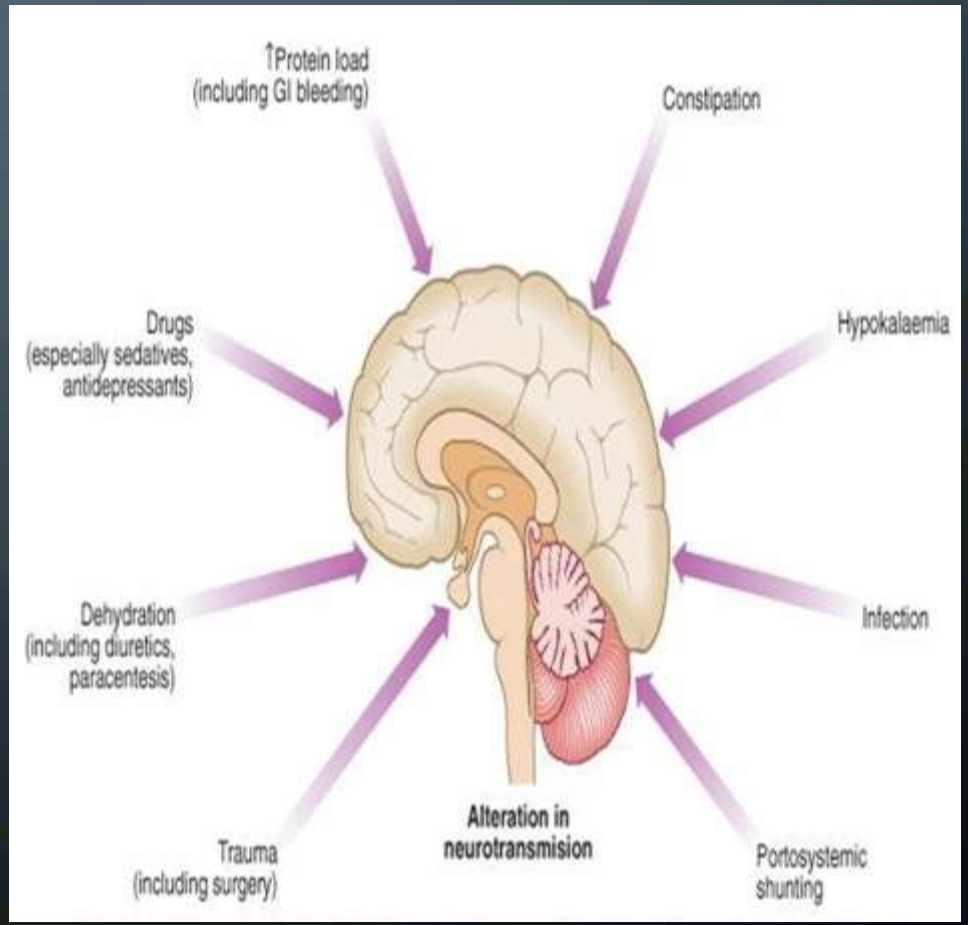
- (A) Increase Nitrogen Load
  - (a) Constipation.
  - (b) Gastro intestinal bleeding.
  - (c) Excess dietary intake of protein & fatty acids.
  - (d) Azotemia.



Precipitating Agents

- (B) Infections & Trauma (Surgery)
- (C) Electrolyte & Metabolic imbalance

- Hypokalemia.
- Alkalosis.
- Hypoxia.
- Hyponatremic.



Clinical features according to grading

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

West-Haven criteria for HE: OHE

Stage	Consciousness	Intellect and behaviour	Neurological findings
0	Normal	Normal	Normal examination; if impaired psychomotor testing, then MHE
1	Mild lack of awareness	Shortened attention span; impaired addition or subtraction	Mild asterixis or tremor
2	Lethargic	Disoriented; inappropriate behaviour	Obvious asterixis; slurred speech
3	Somnolent but arousable	Gross disorientation; bizarre behaviour	Muscular rigidity and clonus; Hyper-reflexia
4	coma	Coma	Decerebrate posturing

Investigation

- **Diagnosis is usually made clinically**

- Routine Investigations - CBC, LFTS, Electolytes, Urea, Creatinine, Prothrombin time, Albumin , A/G ratio.

- Elevation of blood ammonia.

- EEG (Electroencephalogram)

- CSF & CT Scan – Normal.

TREATMENT

- Hospitalize the patient.
- Maintain ABC.
- Identify and remove the precipitating factors.
- Iv fluid dextrose ,saline.
- Stop Diuretic Therapy.
- Correct any electrolyte imbalance.
- Ryle tube feeding & bladder catheterization.
- Reduce the ammonia (NH3) Load.
- Diet – Restriction of protein diet.
  High glucose diet.
- Treat Constipation by Laxatives.

Lactulose

- Lactulose 15-30ml X 3 – 4 times a day- result aims at 2-4 stools/day.
- Rectal use is indicated when patient is unable to take orally.
- 300ml of lactulose in 700ml of saline or sorbitol as a retention enema for 30 – 60 min.
- May be repeated 4 – 6 hours.

Treat the GIT & other Infections

Antibiotics:

- Rifaximin
- Broad spectrum antibiotic, recently approved in humans for HE.
- Negligible systemic absorption.
- Shown to decrease hospitalizations and length of stay as compared to lactulose in humans.
- DOSE: 550 mg orally B.I.D

- **Metronidazole :** 250mg orally T.D.S
- **Neomycin :** 0.5 – 1 g orally 6 or 12 hours for 7 days.
- Side effects: Ototoxicity, nephrotoxicity.
- **Vancomycin :** 1 g orally B.I.D

DIET

- With held dietary protein during acute episode if patient cannot eat.
- Oral intake should be 60 – 80 g/day as tolerated.
- Vagetable protein is better tolerated than meat protein.
- G.I.T bleeding should be controlled
- 120ml of magnesium citrate by mouth or NG tube every 3 – 4 hours until stool free of blood.

Stimulation of metabolic ammonia metabolism:

- **Sodium benzoate**
- 5 g orally twice a day.

- **L-ornithine-L-aspartate**
- 9 g orally thrice a day.

- **L-acyl-carnitine aspartate**
- 4 g orally daily.

- **Zinc sulphate**
- 600mg/day in divided doses.

Correct amino acid metabolic imbalance

- Infusion or oral administration of BCAA
  (branched-chain amino acid)
- Its use is unnecessary except in patient who are intolerant of standard protein supplements.

GABA/BZ complex antagonist:

- Flumazenil (particularly if patient has been given banzodiazepines)
- Opiods & sedatives should be avoided.

Acarbose

- α – glucosidase inhibitor.
- Under study.

- Other Therapies:

- Prebiotics & probiotics.
- Extracorporeal albumin dialysis (MARS)
- Liver transplant.

THANK YOU