Portal hypertension

Basic science - GI PMK

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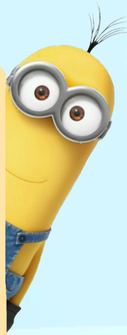
Outline

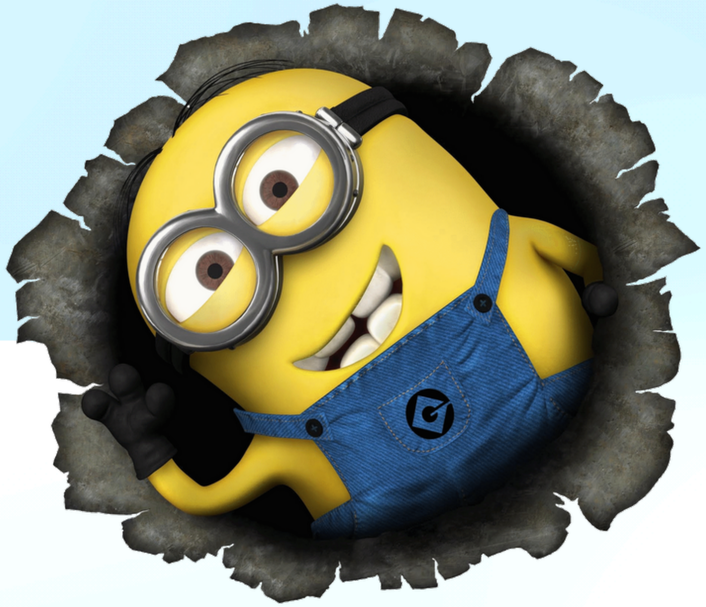
1. Anatomy
2. Pathophysiology
3. Etiology
4. Clinical manifestation
5. Diagnostic evaluation
6. Management

Portal hypertension

Defined as an elevation of portal blood pressure more than 5 mmHg



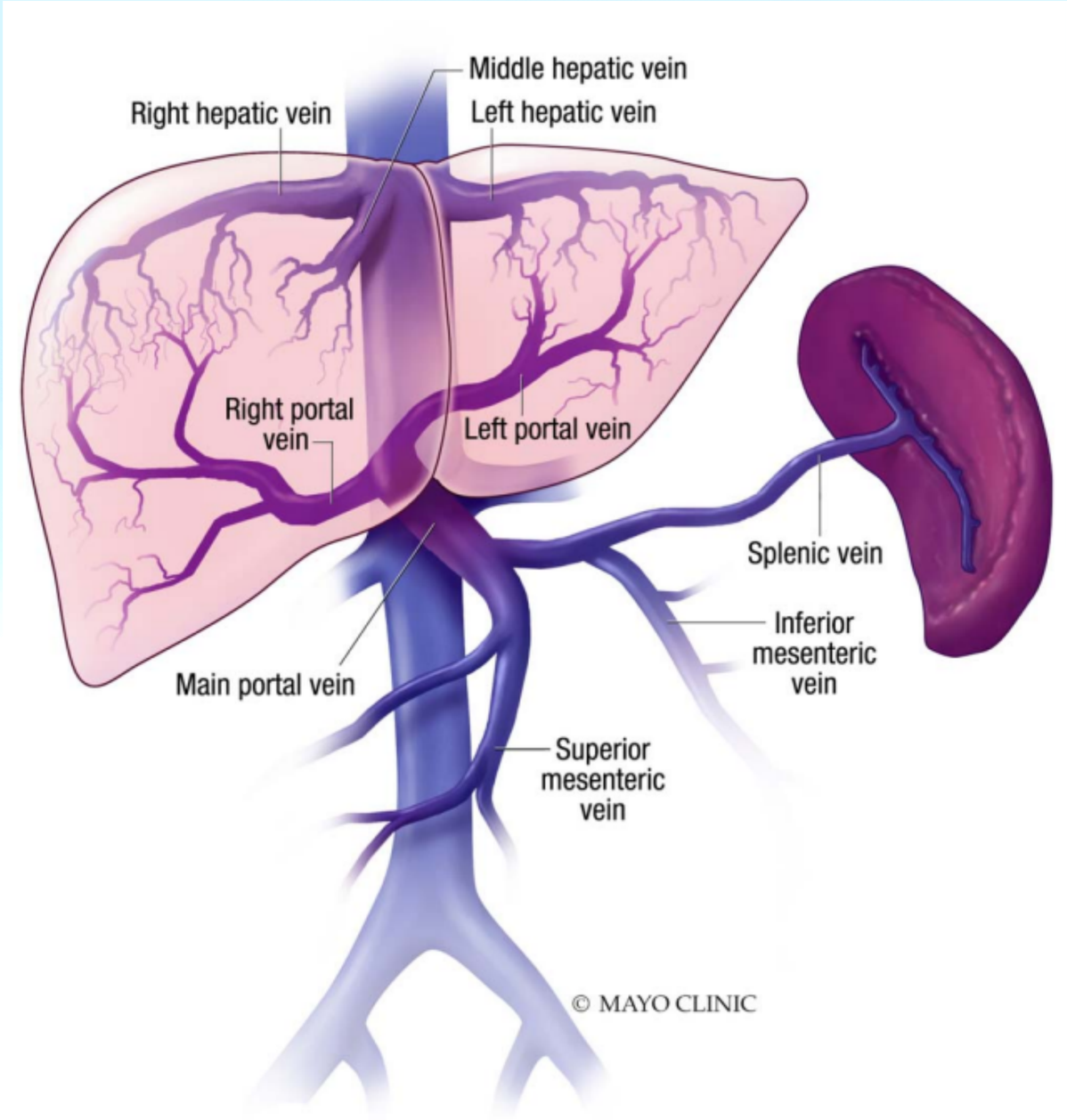
- One of the major causes of morbidity and mortality in children with liver diseases.
- High prevalence of cholangiopathies and cholestatic diseases in children, compared with adult.
- It’s a complication in a wide variety of pediatric liver disorders

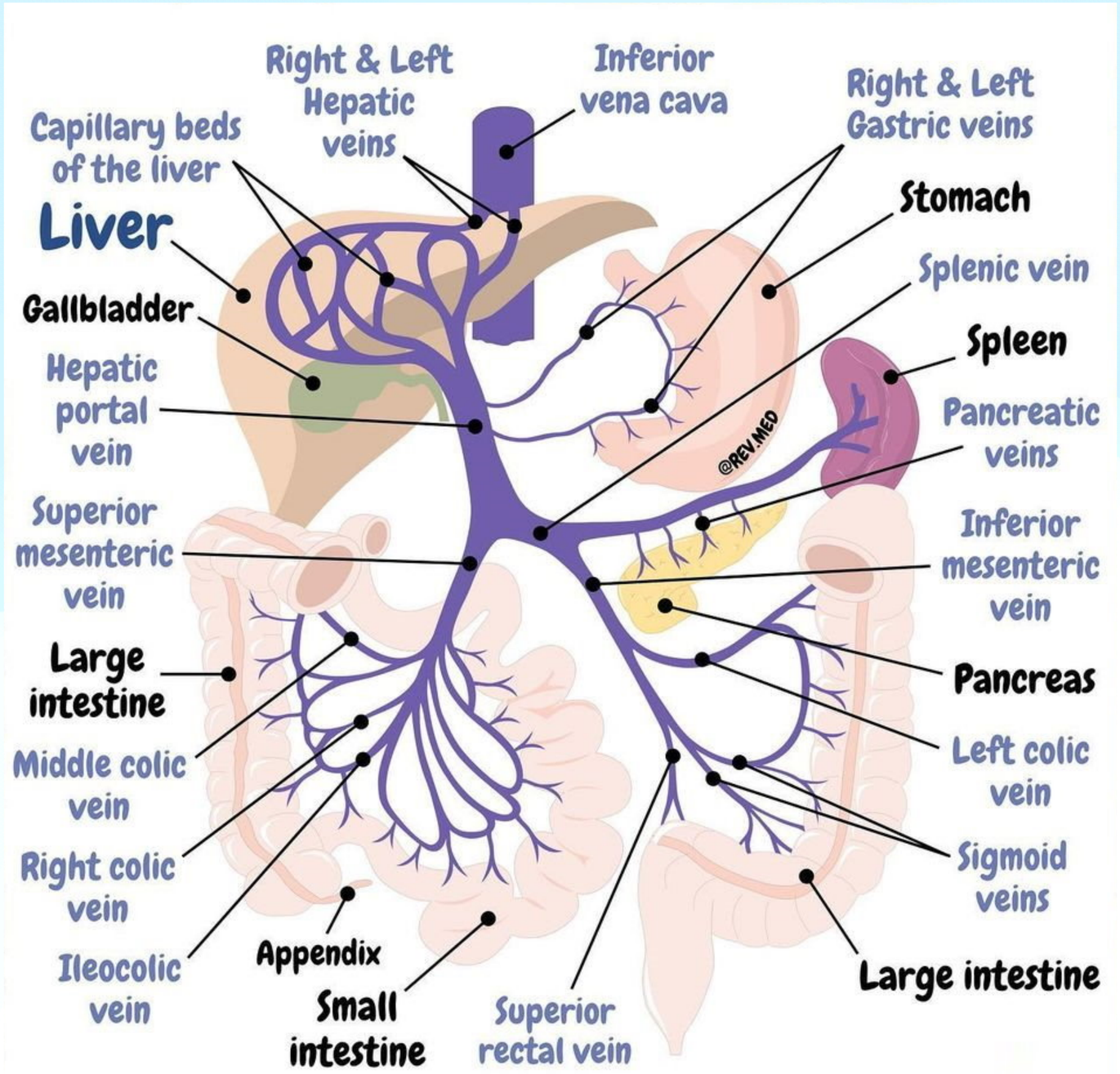


Anatomy

Portal venous system(PVS)

- PVS drains blood from the GI tract (except lower section of rectum), spleen, pancreas and gallbladder to the liver
- Originated from the mesentery of intestines & spleen and end in the hepatic sinusoids.
- Well-regulated blood flow in conjunction with very low resistance found in the portal system




Right & Left Hepatic veins
Inferior vena cava
Right & Left Gastric veins
Capillary beds of the liver
Liver
Stomach
Splenic vein
Gallbladder
Spleen
Hepatic portal vein
Pancreatic veins
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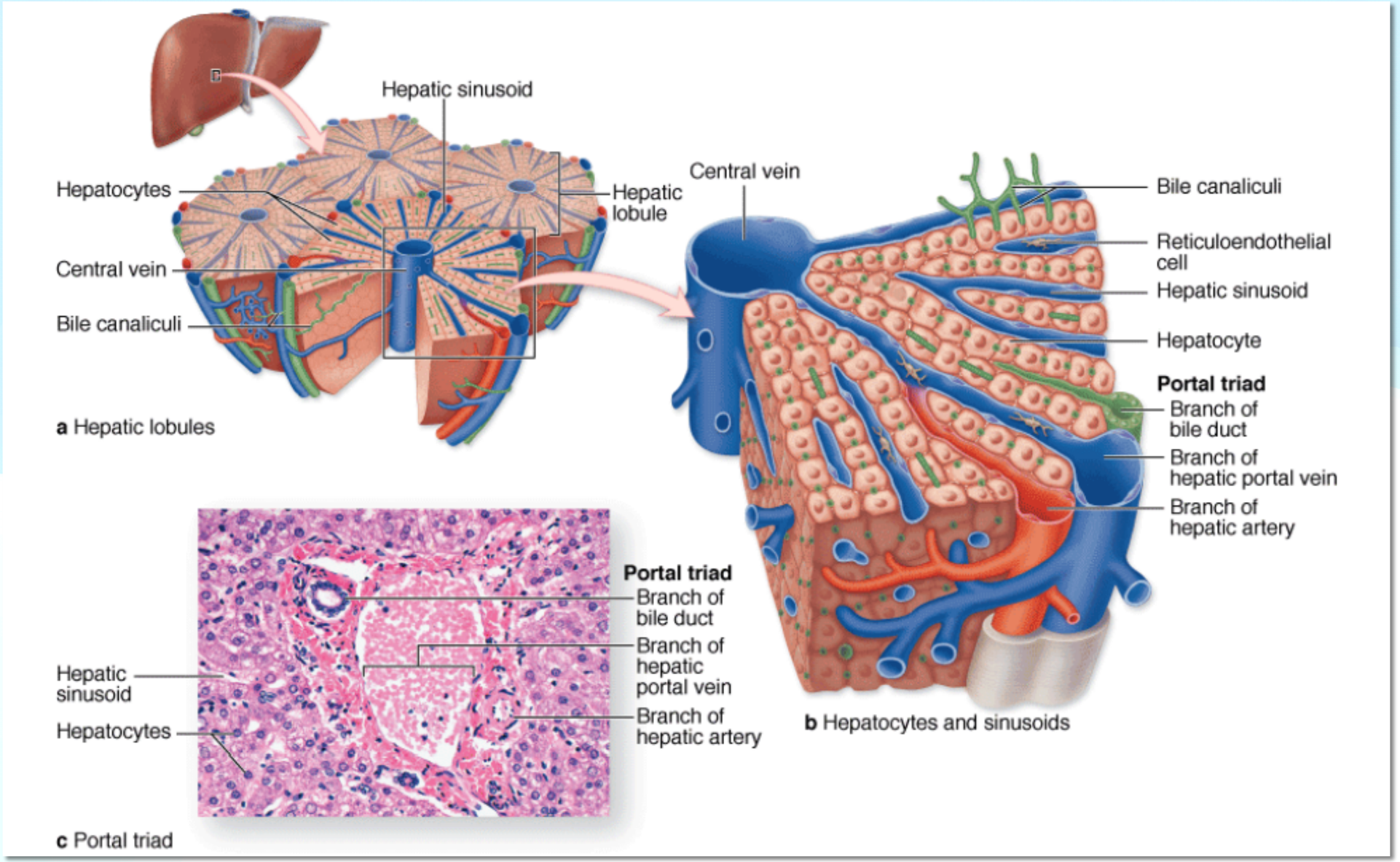
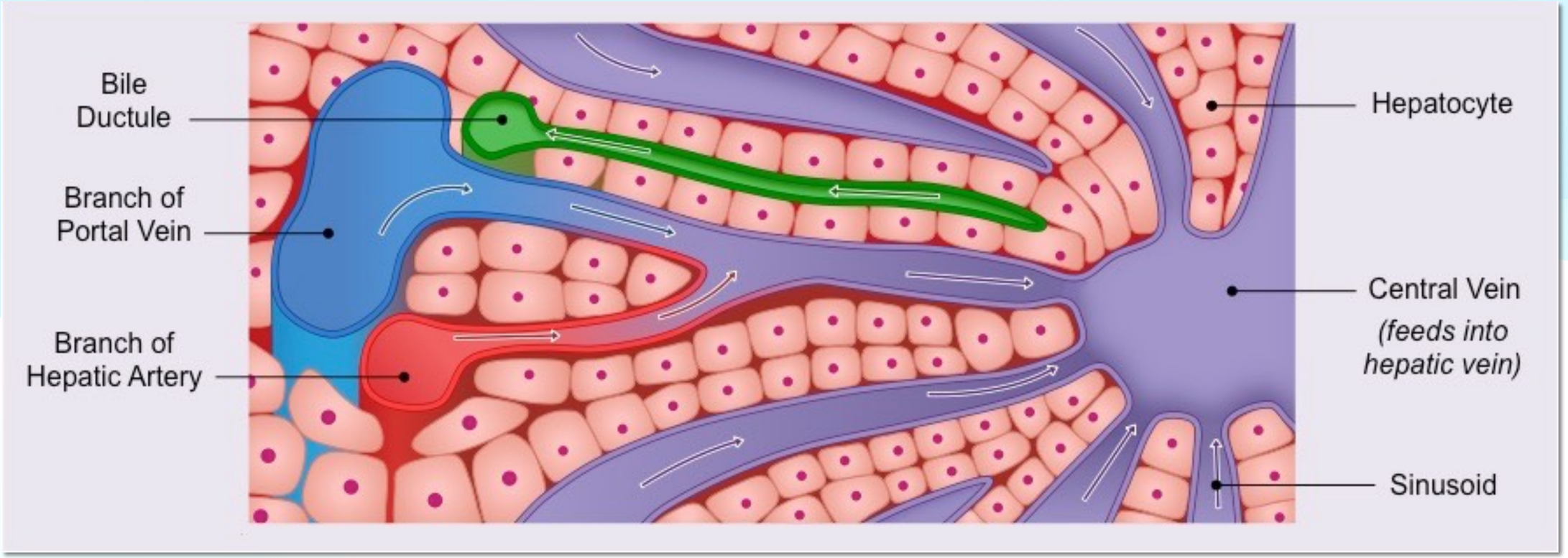
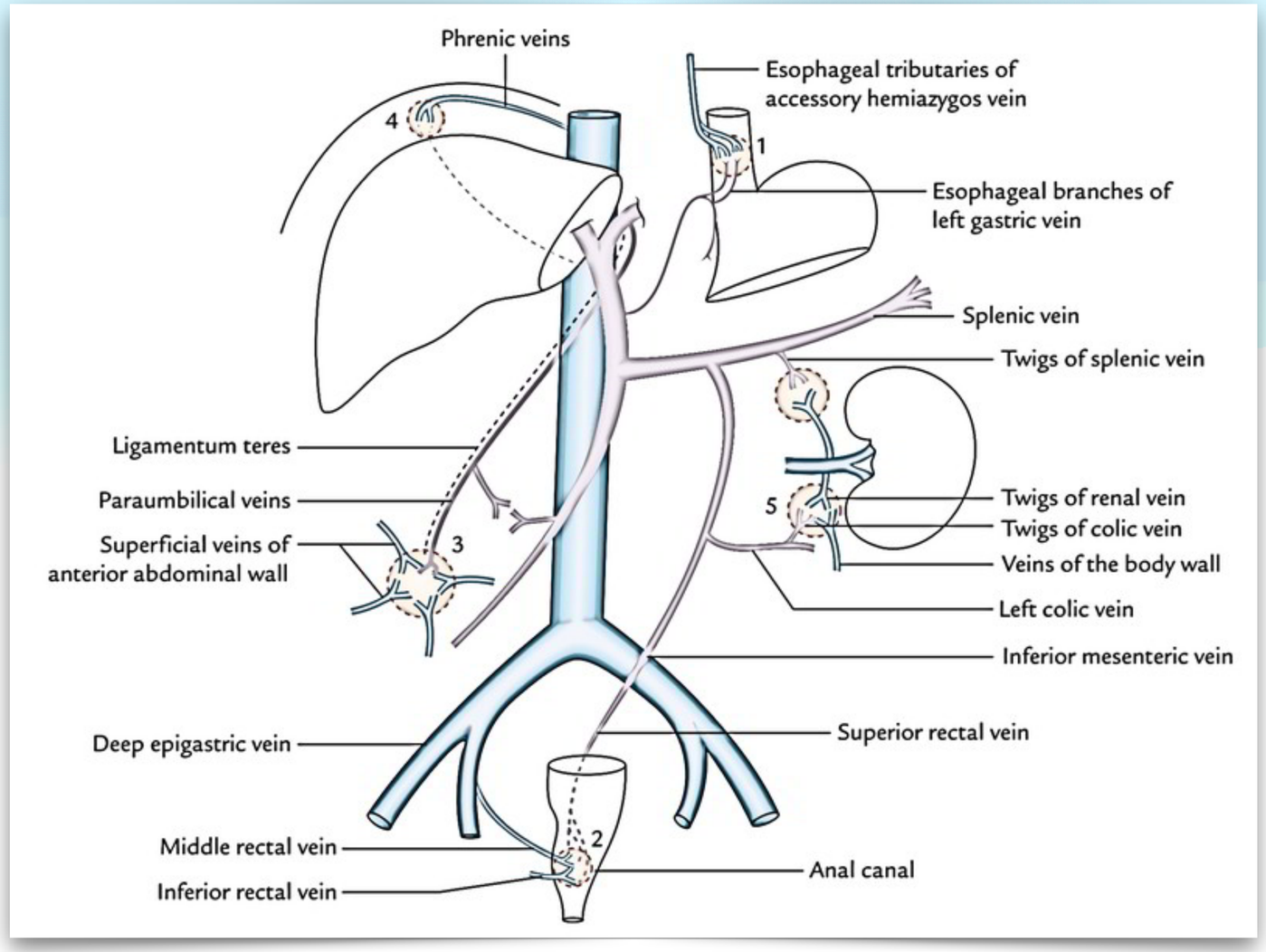
Superior mesenteric vein
Inferior mesenteric vein
Large intestine
Pancreas
Middle colic vein
Left colic vein
Right colic vein
Sigmoid veins
Ileocolic vein
Appendix
Small intestine
Superior rectal vein
Large intestine

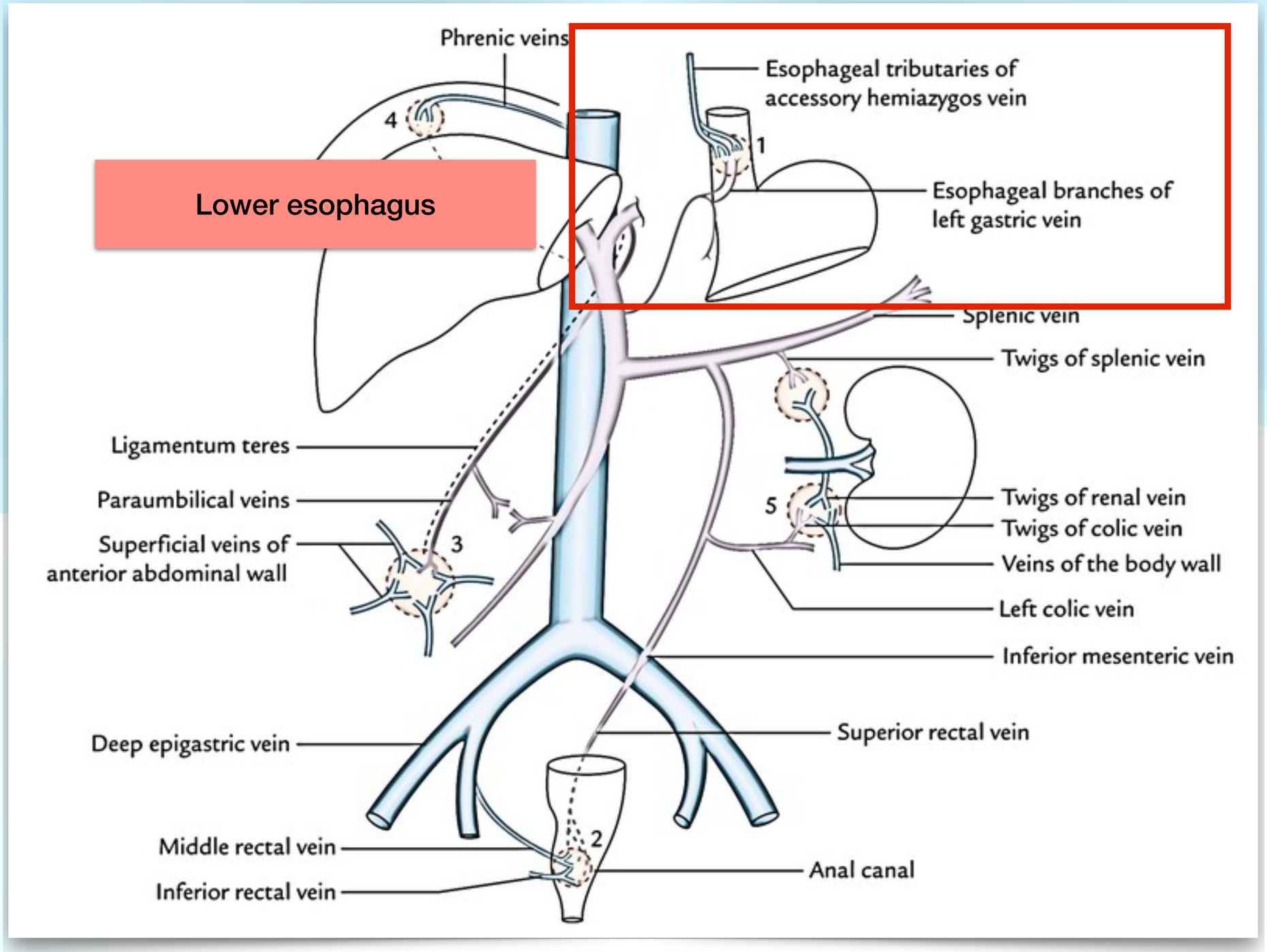

Hepatic sinusoid
Hepatocytes
Hepatic lobule
Central vein
Bile canaliculi
a Hepatic lobules
Central vein
Bile canaliculi
Reticuloendothelial cell
Hepatic sinusoid
Hepatocyte
Portal triad
Branch of bile duct
Branch of hepatic portal vein
Branch of hepatic artery
b Hepatocytes and sinusoids
Portal triad
Branch of bile duct
Branch of hepatic portal vein
Branch of hepatic artery
Hepatic sinusoid
Hepatocytes
c Portal triad

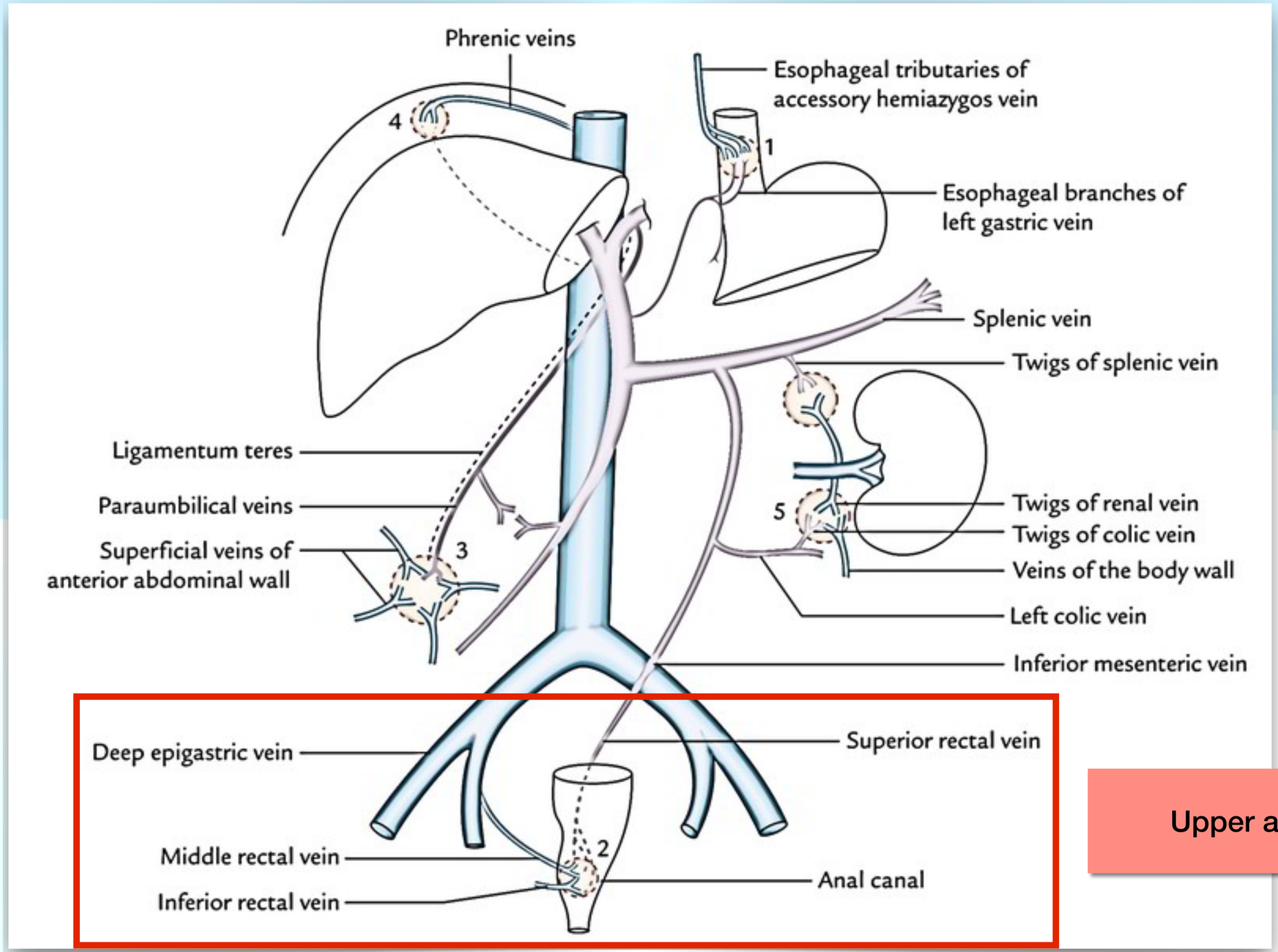

Bile
Ductule
Branch of
Portal Vein
Branch of
Hepatic Artery
Hepatocyte
Central Vein
(feeds into
hepatic vein)
Sinusoid

Collateral circulation

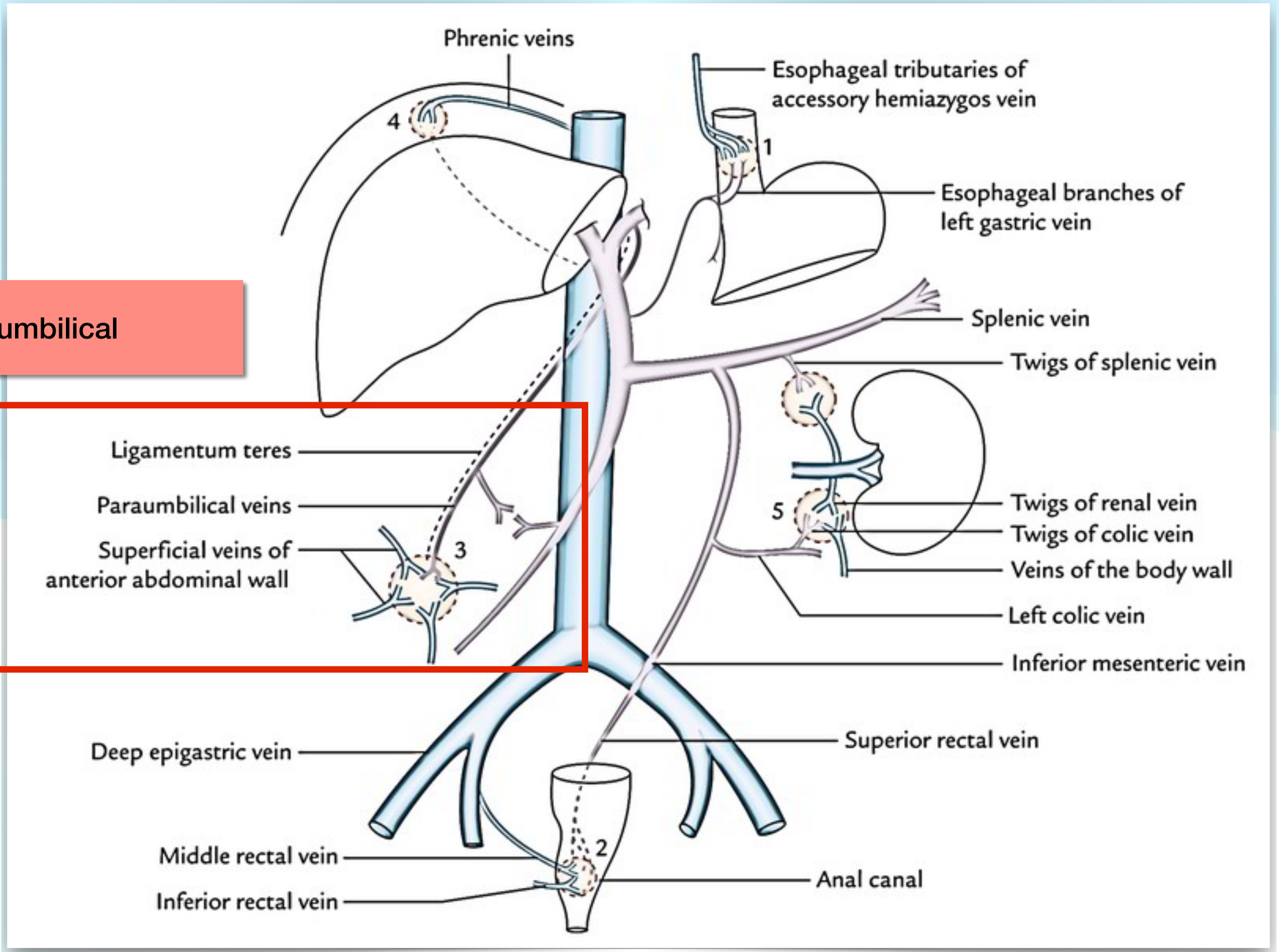
- When the portal circulation is obstructed >> collateral circulation develops to carry portal blood into systemic system
- The number of collateral channels depends on the severity and duration of portal hypertension



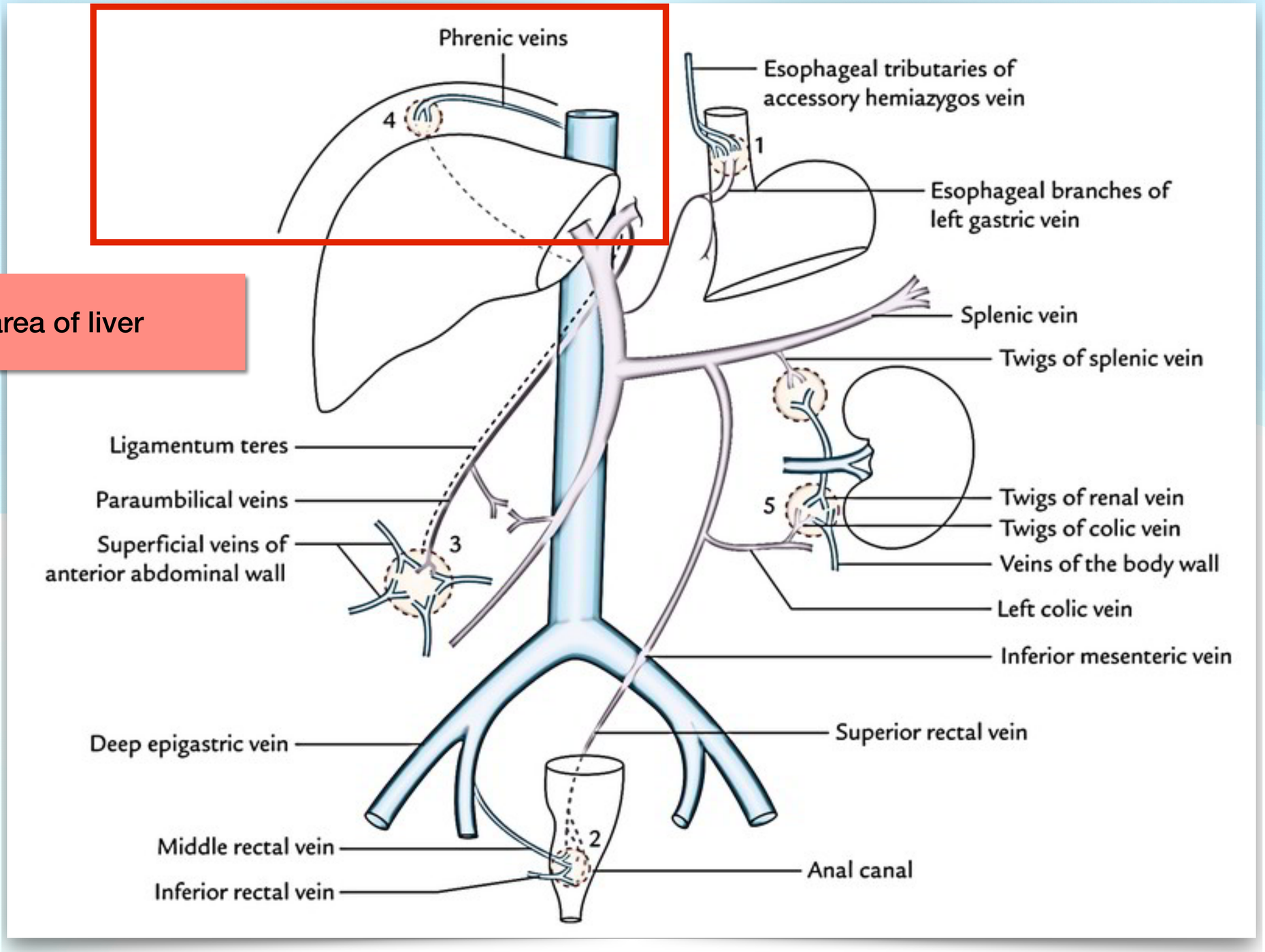

Lower esophagus
Phrenic veins
Esophageal tributaries of accessory hemiazygos vein
Esophageal branches of left gastric vein
Splenic vein
Twigs of splenic vein
Ligamentum teres
Paraumbilical veins
Superficial veins of anterior abdominal wall
Twigs of renal vein
Twigs of colic vein
Veins of the body wall
Left colic vein
Inferior mesenteric vein
Deep epigastric vein
Superior rectal vein
Middle rectal vein
Inferior rectal vein
Anal canal
1
2
3
4
5

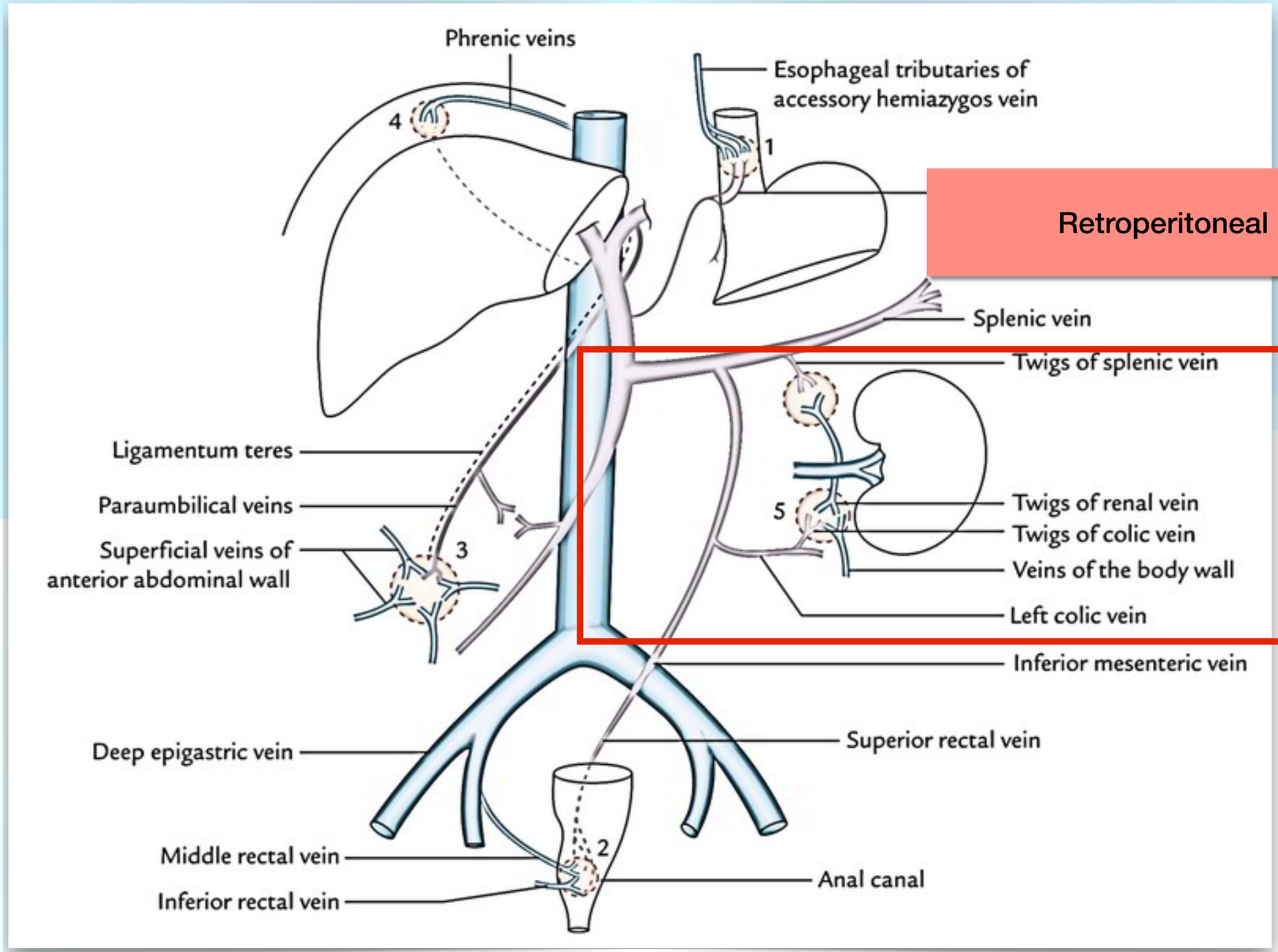

Phrenic veins
Esophageal tributaries of accessory hemiazygos vein
4
1
Esophageal branches of left gastric vein
Splenic vein
Twigs of splenic vein
Ligamentum teres
Paraumbilical veins
Superficial veins of anterior abdominal wall
3
5
Twigs of renal vein
Twigs of colic vein
Veins of the body wall
Left colic vein
Inferior mesenteric vein
Deep epigastric vein
Superior rectal vein
Middle rectal vein
Inferior rectal vein
2
Anal canal
Upper anal canal

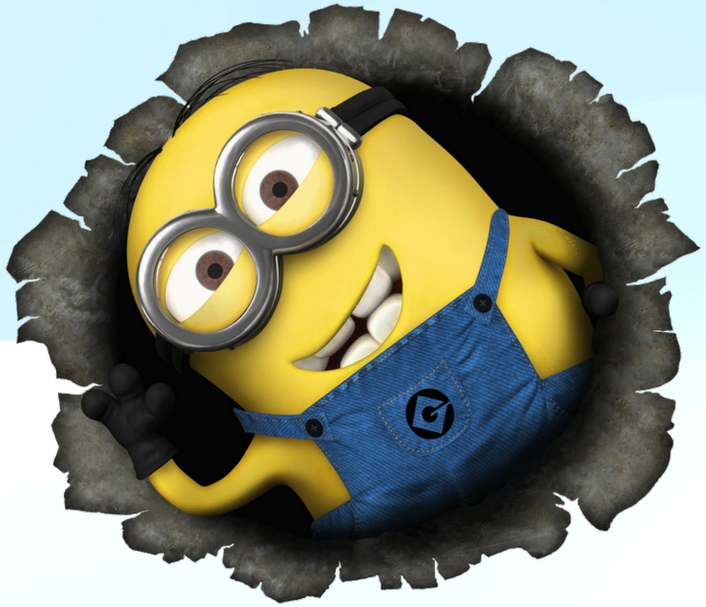
Paraumbilical



Bare area of liver




Phrenic veins
Esophageal tributaries of accessory hemiazygos vein
4
1
Retroperitoneal
Splenic vein
Twigs of splenic vein
Ligamentum teres
Paraumbilical veins
Superficial veins of anterior abdominal wall
3
5
Twigs of renal vein
Twigs of colic vein
Veins of the body wall
Left colic vein
Inferior mesenteric vein
Deep epigastric vein
Superior rectal vein
Middle rectal vein
Inferior rectal vein
2
Anal canal



Pathophysiology

Increase intrahepatic vascular resistance

Increase portal pressure

Increase splanchnic blood flow

Opening of pre-existing blood vessels

Angiogenesis

Portosystemic collateral vessels formation

Esophageal varice

Hepatic encephalopathy

Sepsis

Increase intrahepatic vascular resistance

- The portal and hepatic venous systems are low-resistance systems in healthy individuals.
- Common causes : vascular lumen compromised , alteration of vascular tone

Vascular lumen compromised

Blood Flow: $\Delta P = Q*R$ or $Q = \Delta P/R$

Q = flow (mL/min)
Δ P = pressure gradient (mm Hg)
R = resistance (mm Hg/mL/min)

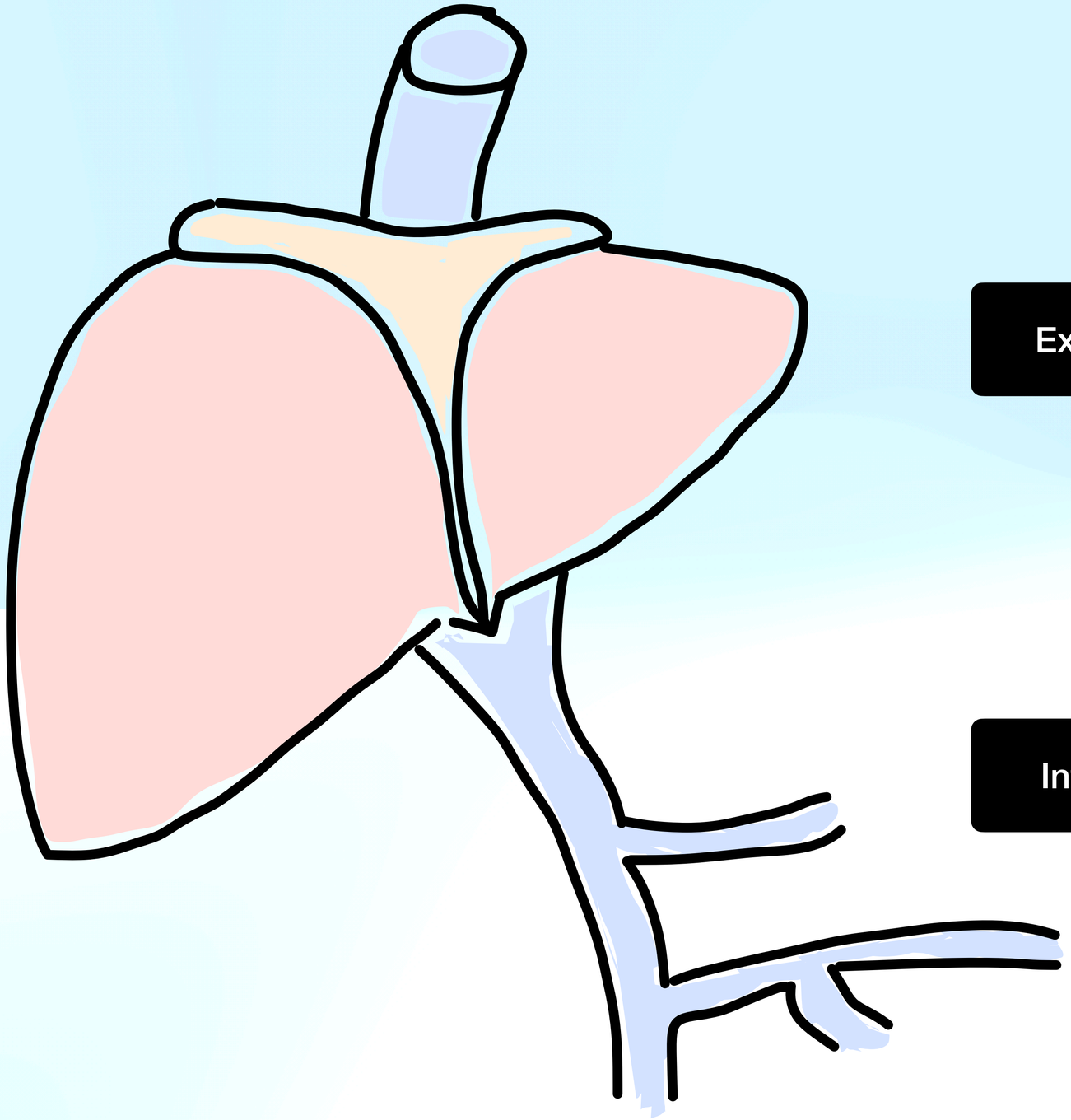
Resistance to Blood Flow

Poiseuille equation

$$R = \frac{8\eta L}{\pi r^4}$$

R = resistance
η = viscosity of blood
L = length of blood vessel
r^4 = radius of blood vessel raised to the fourth power

If radius decreases by one half,
resistance increases by 16-fold (= 2^4)!!!



Post-hepatic

Extra-hepatic

Pre-hepatic

Intra-hepatic

Extrahepatic cause

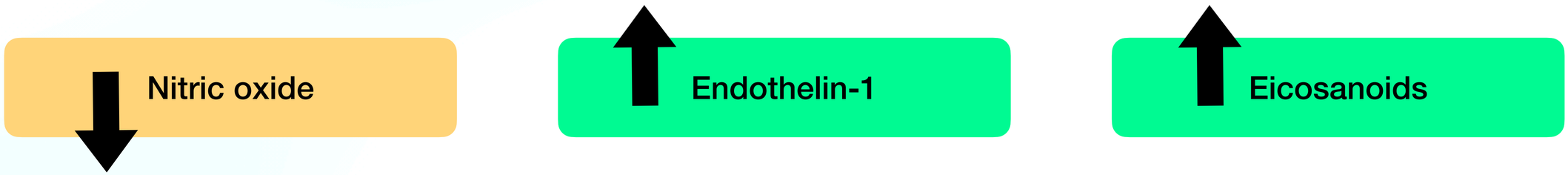
- Compromised vascular lumen from obstruction (mass, thrombosis)

Intrahepatic cause

- Vary mechanisms : Impingement to intrahepatic portal venue lumen, hepatocyte swelling / hyperplasia, portal tract inflammation / fibrosis
- One of the major clinical differences from extra hepatic causes : present of on-going hepatocellular injury
- In biliary tract diseases : portal venue compromised

Alteration of vascular tone

- In most type of liver disease, vasoactive substances may play important role in regulating intrahepatic resistance to blood flow.



Increase splanchnic blood flow

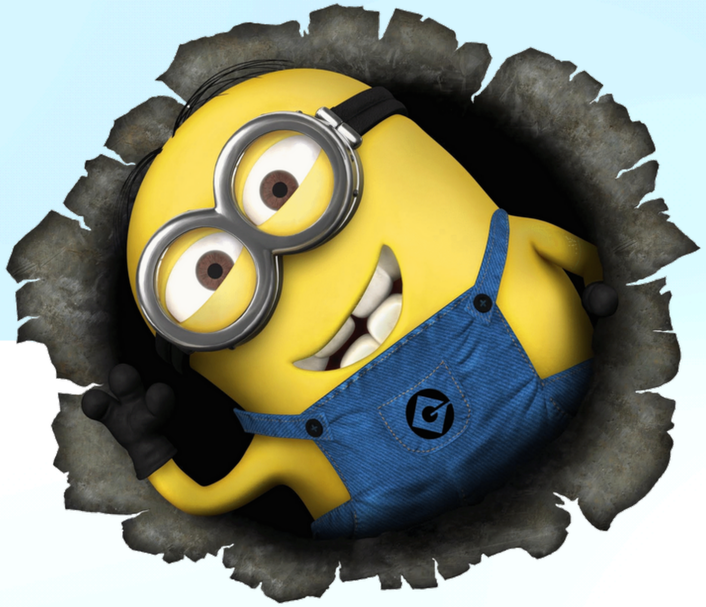
Increase production of vasodilators → Hyperdynamic circulation

- ↑ Cardiac output
- ↓ Splanchnic arteriolar tone
- ↓ Splanchnic vascular vasoconstrictor

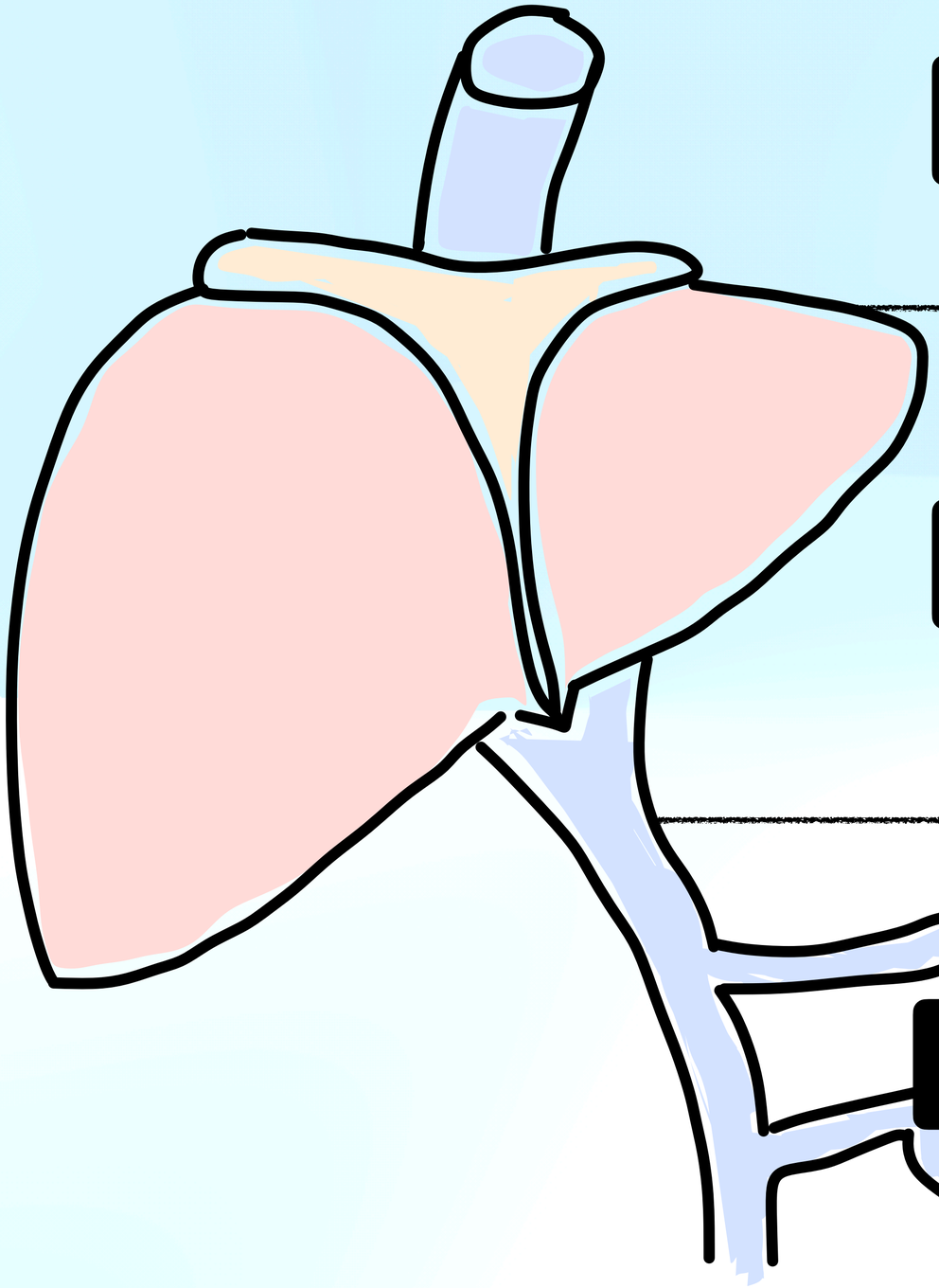
} ↑ Portal inflow

Enhanced angiogenesis

- Vascular endothelial, placental and platelet-derived growth factors are increased in cirrhosis
- Angiogenesis >> Increases blood return to liver and in the periphery it may open up portosystemic collaterals



Etiology



Post-hepatic

- Budd-Chiari syndrome
- Right sided heart failure
- IVC obstruction

Intra-hepatic

- Liver cirrhosis
- Veno-occlusive disease
- Congenital hepatic fibrosis

Pre-hepatic

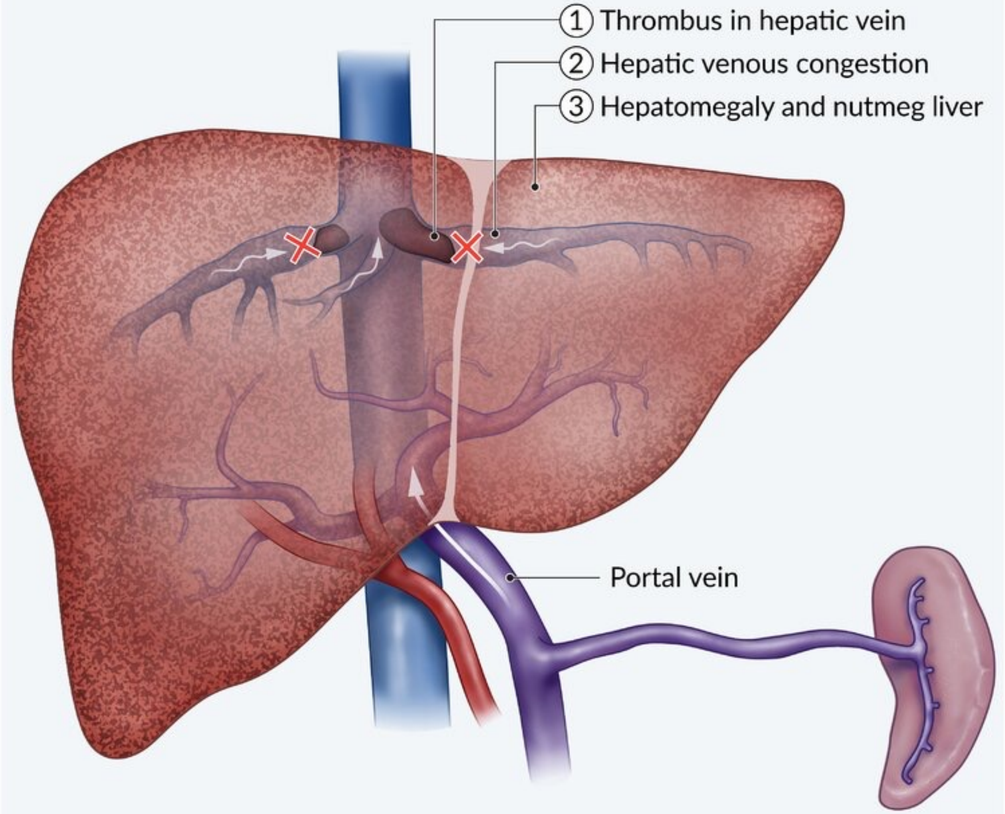
- Portal vein thrombosis ; EHPVO
- Splenic vein thrombosis

Anatomic level	Disorder
Extrahepatic disorders	Venous obstruction Splenic vein thrombosis Portal vein thrombosis/cavernous transformation Budd–Chiari syndrome Inferior vena cava obstruction
Intrahepatic disorders	Biliary tract disease Extrahepatic biliary atresia Cystic fibrosis Choledochal cyst Sclerosing cholangitis Intrahepatic cholestasis syndromes Alagille syndrome Byler disease Bile duct hypoplasia Congenital hepatic fibrosis Caroli disease
Hepatocellular disease	Autoimmune hepatitis Hepatitis B and C Wilson disease α_1-antitrypsin deficiency Glycogen storage type IV Toxins Ethanol Methtrexate 6-mercaptopurine
Miscellaneous	Chronic congestive heart failure Arteriovenous fistula Splenomegaly Vitamin A Arsenic Vinyl chloride Miscellaneous Histiocytosis X Venoocclusive disease Schistosomiasis Gaucher disease Hepatoportal sclerosis Peliosis Idiopathic portal hypertension

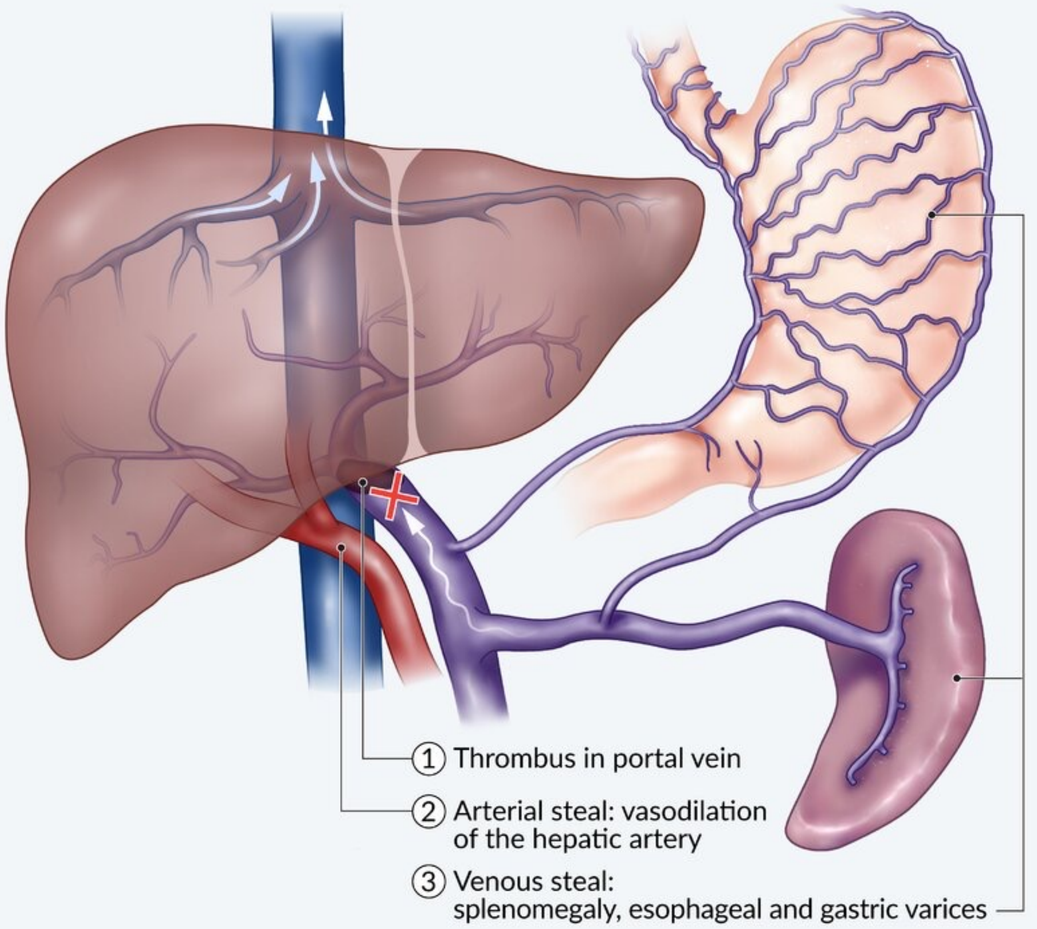
Budd-Chiari syndrome

- Obstruction to hepatic veins anywhere between the efferent hepatic veins and the entry of IVC into the right atrium.
- Hepatic venous outflow obstruction from
    - Thrombosis of hepatic veins (Hypercoagulable states)
    - Compression / Invasion of hepatic veins (Tumor, Infection, trauma)
- Hepatic venous congestion >> increase sinusoidal pressure >> congestive hepatopathy

Budd-Chiari syndrome



Portal vein thrombosis



Cirrhosis

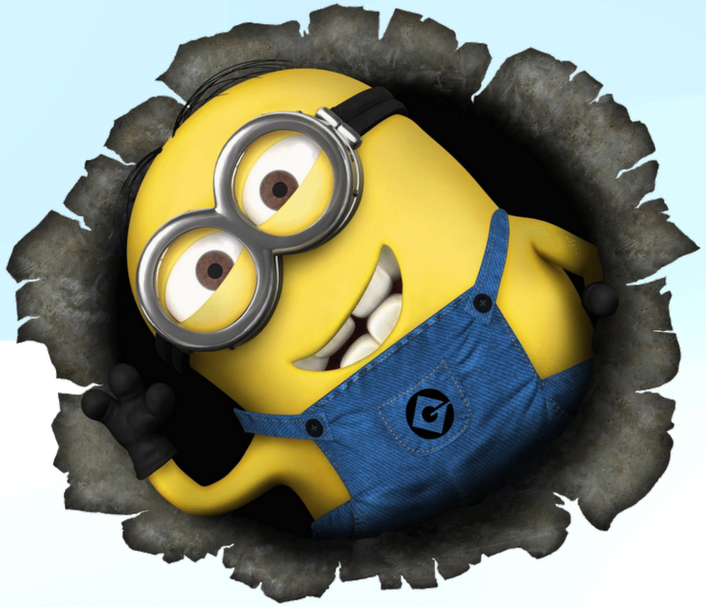
- The most common cause of portal hypertension in children
- Numerous causes of cirrhosis such as Biliary atresia, Autoimmune hepatitis, Chronic viral hepatitis and metabolic liver diseases
- Fibrosis obstructs portal venous return >> increase portal pressure

Veno-occlusive disease

- Most common cause of hepatic vein obstruction in children
- Occlusion of the centrilobular venules or sub lobular hepatic veins
- Risk factors :
    - HSCT
    - Chemotherapy patients (Azathioprine, mercaptopurine, thioguanine)

Portal venous thrombosis

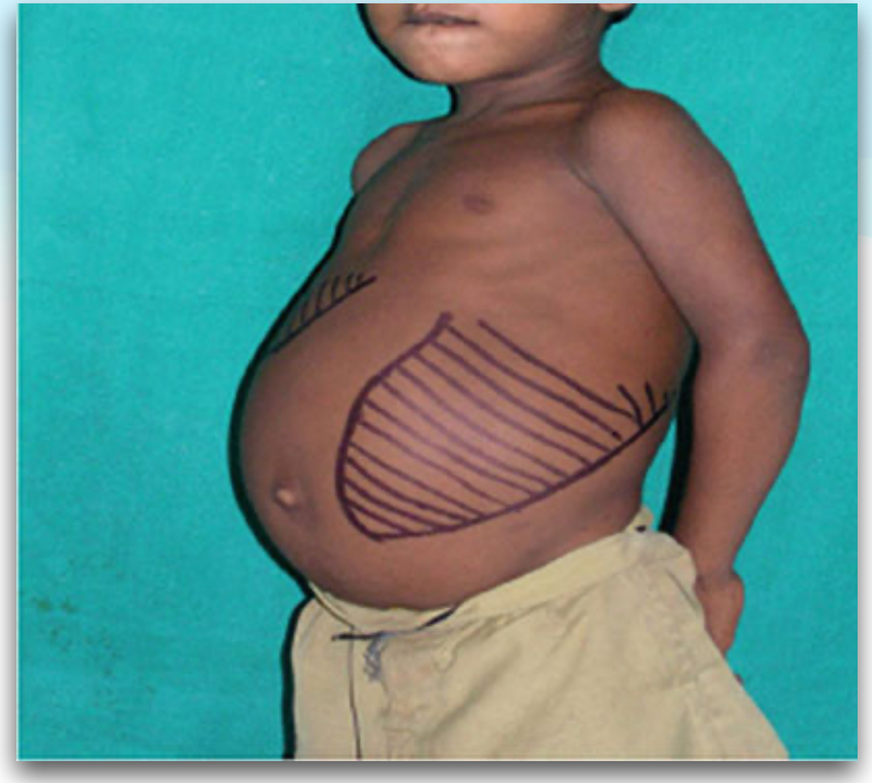
- Most common cause of extra hepatic portal hypertension.
- The obstruction can occur at any level of portal vein.
- Risk factors :
    - Neonatal umbilical vein catheterization, omphalitis, trauma
    - In older children ; Intra-abdominal infection, Inflammatory bowel disease or biliary infection
    - Hypercoagulable states



Clinical features

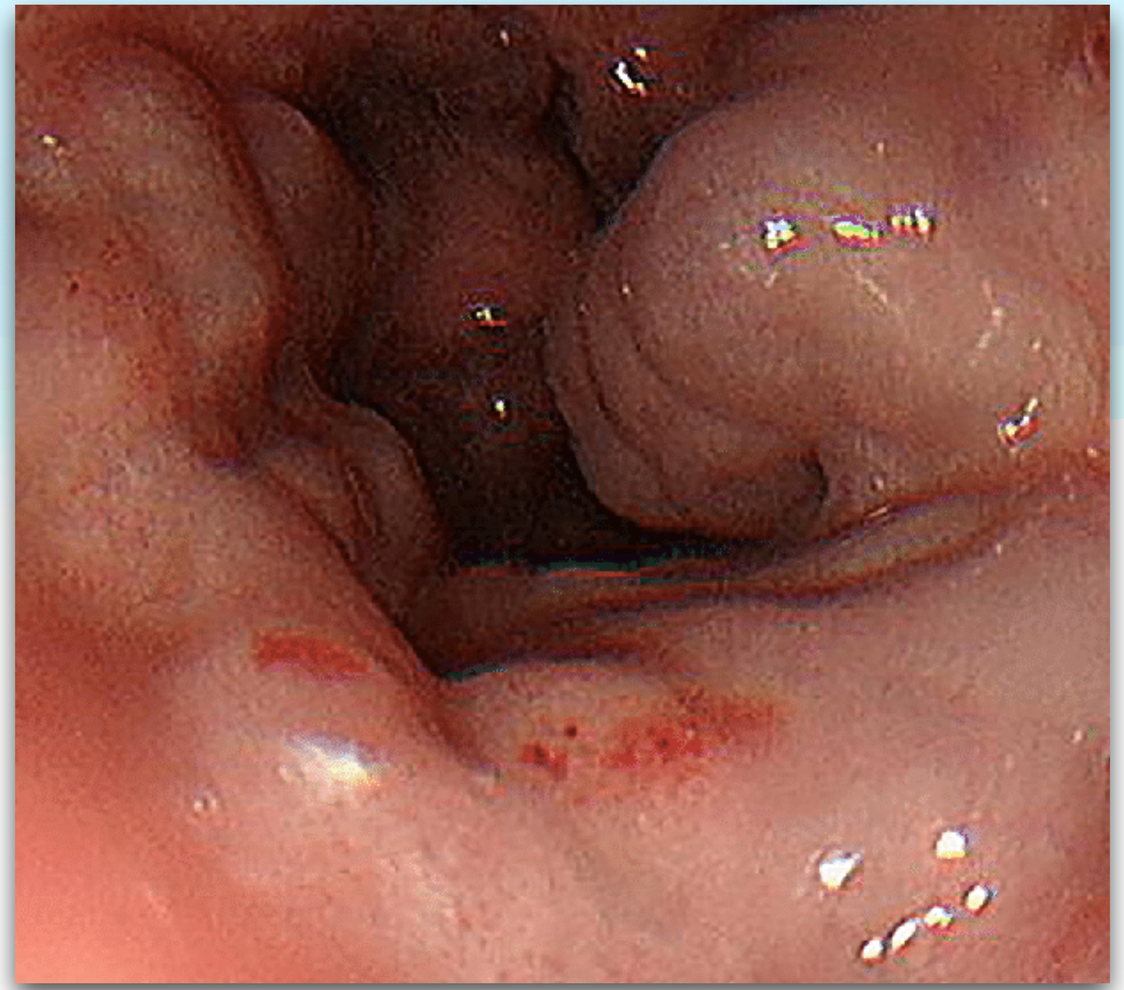
Sign of portal hypertension

- Variceal bleeding
- Splenomegaly
- Ascites



Variceal bleeding

- Most common from esophageal varices
- The risk of a first bleeding in children with cirrhosis is 22%
- In children with biliary atresia, 15-25% have bleeding on long-term follow-up
- Age onset of first bleeding depend on etiology.
- Precipitating factor such as fever, respiratory tract infection and aspirin use.



Splenomegaly

- Most common presentation
- If combination with gastrointestinal bleeding >> Suspected portal hypertension
- Spleen size is not relate to portal pressure

Ascites

- 7-21% in children with portal hypertension
- Increased portal pressure drive fluids out of intravascular space into the peritoneum

Clinical

Post-hepatic (Budd-Chiari syndrome)

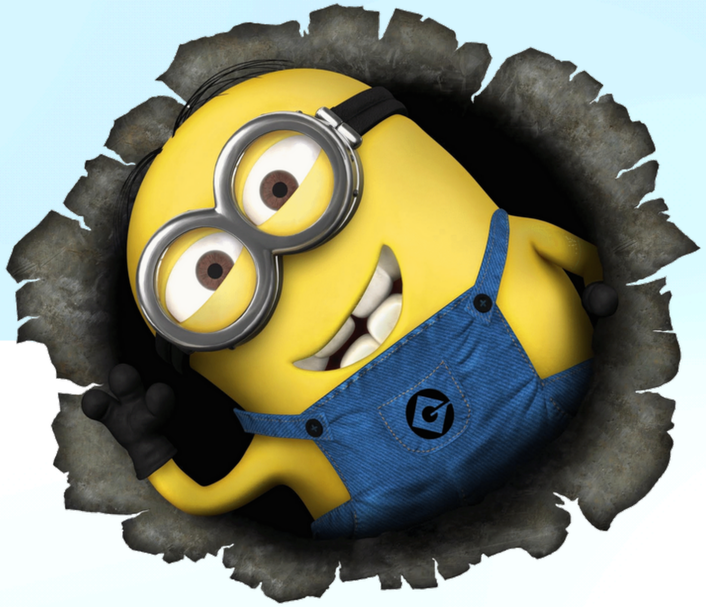
- Splenomegaly + Hepatomegaly
- Massive ascites
- Lab : thrombocytopenia, abnormal LFT, coagulopathy

Intra-hepatic (Liver cirrhosis)

- Splenomegaly +- Hepatomegaly
- Sign of chronic liver disease
- Lab : thrombocytopenia, abnormal LFT, coagulopathy

Pre-hepatic (EHPVO)

- Splenomegaly
- Lab : thrombocytopenia, normal LFT



Diagnostic evaluation

History taking - Physical examination

- Portal hypertension should be suspected in any child with significant gastrointestinal hemorrhage or unexplained splenomegaly.
- The combination of gastrointestinal hemorrhage and splenomegaly is highly suggestive of portal hypertension until proven otherwise.
- Physical examination should be assess to sign of chronic liver disease
- Abdominal ascites >> difficult to assess by physical examination in some children (incoorporation)

Investigation

- CBC
- LFT
- Coagulogram
- Portal pressure >> rarely direct assessed as a quantitative measurement
    - Indirect method : HVPG (Hepatic venous pressure gradient) ; available in adult

Ultrasonography

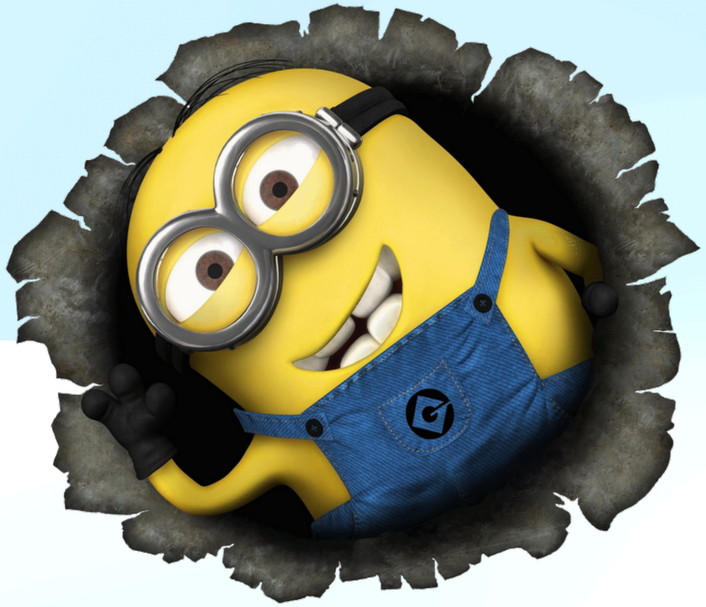
- Ultrasound with doppler flow examination >> investigation of choice
- Non-invasive, Inexpensive but depend on skill/experience of operator
- Important information : Hepatic size and echogenicity along with modularity features, spleen size, Ascites
- Doppler >> vessel diameter, direction of blood flow in the vessel and echogenic material in the vessel

Liver and spleen stiffness

- Non-invasive tool for diagnosis fibrosis
- In adult, Liver stiffness has been assessed in hepatocellular disease but in children it has been undertaken in very different diseases
- Liver-based assessment of liver stiffness may be useful in identifying children with clinical features of portal hypertension
- Spleen stiffness is not as well characterized.

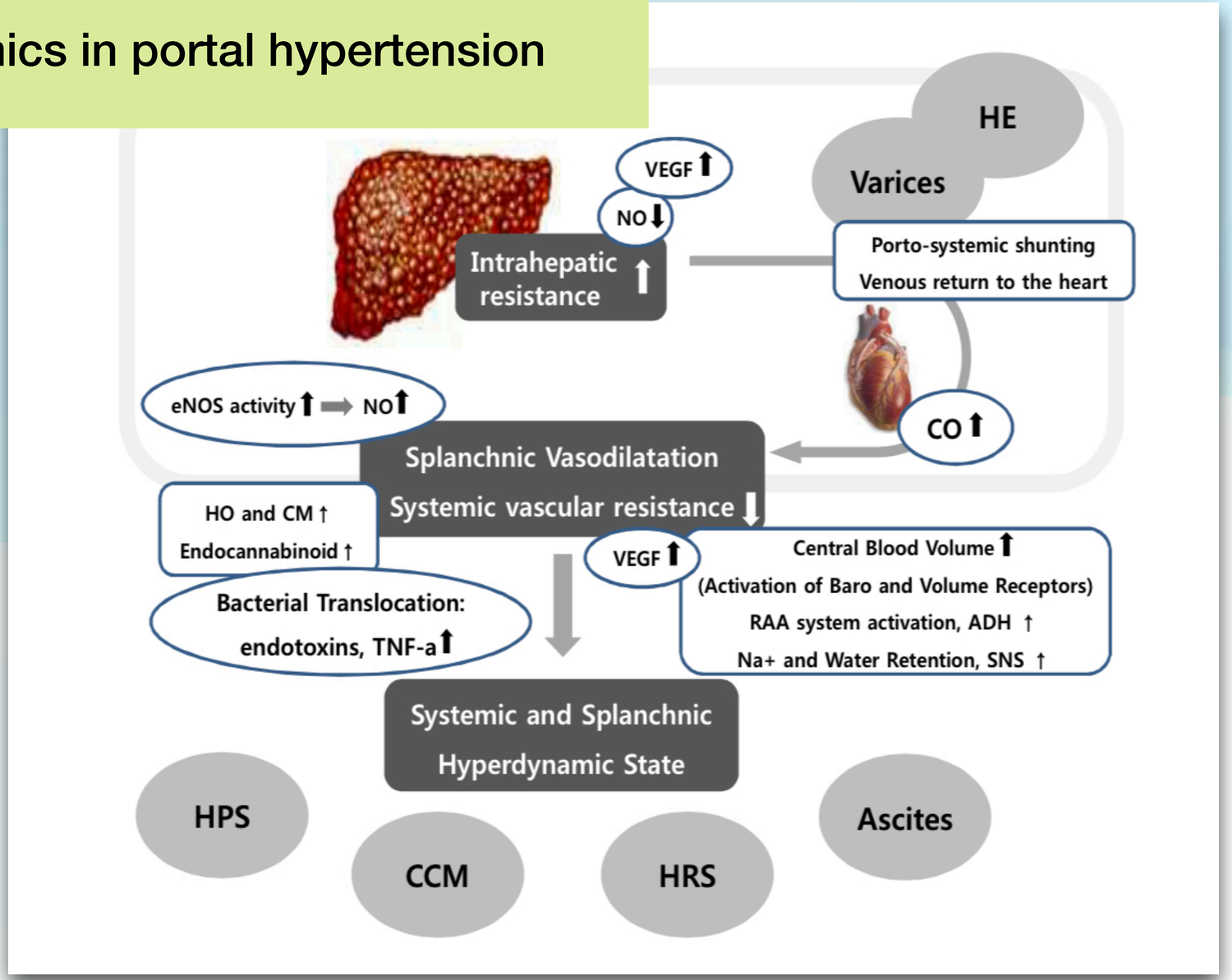
Endoscopy

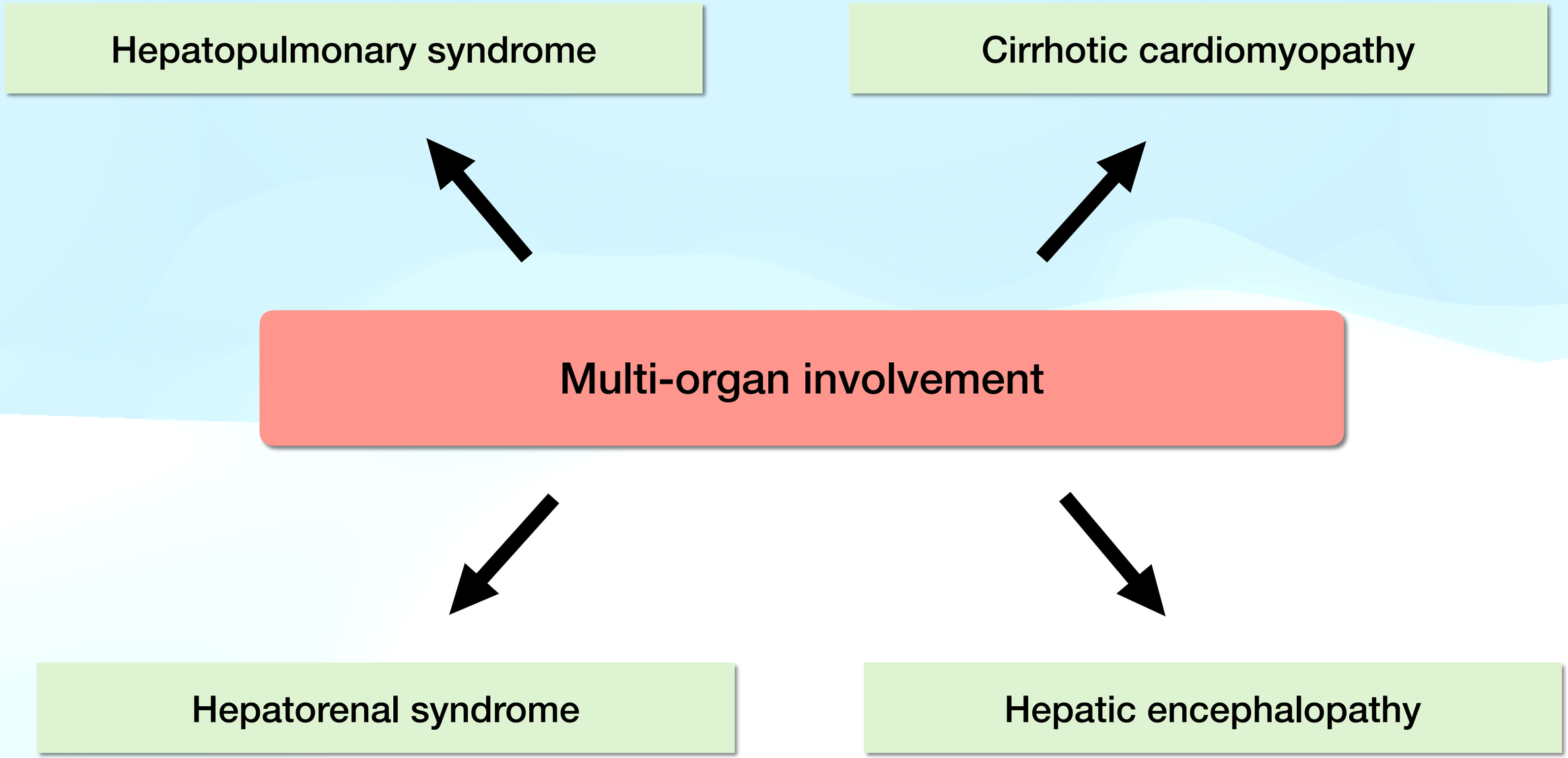
- Flexible fiberoptic endoscopy >> most reliable method for detecting esophageal varices and identifying source of gastrointestinal bleeding.
- Useful in case gastrointestinal hemorrhage with sign of chronic liver disease
- Endoscopic appearance of varies >> can be predictive risk of recurrent bleeding.



Complication

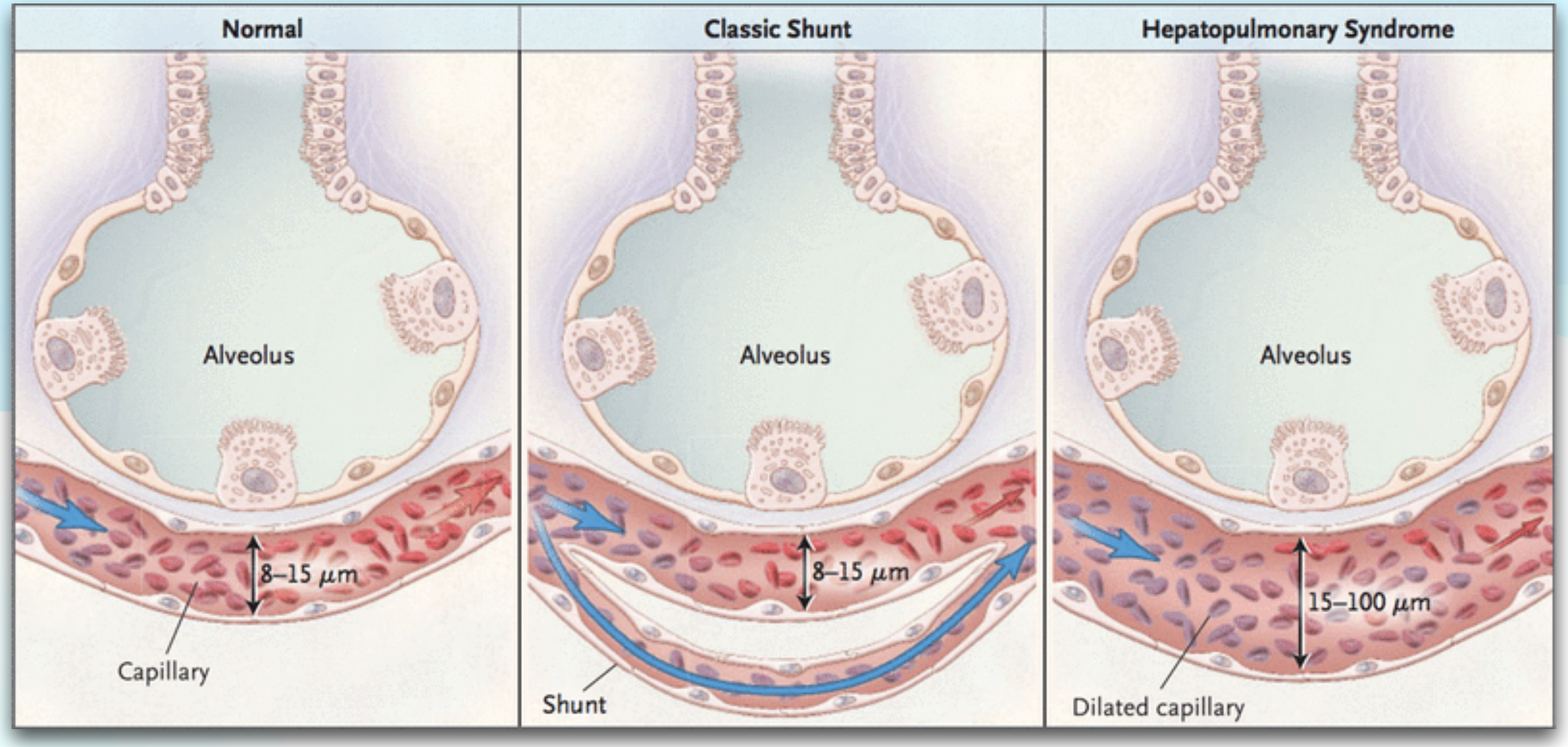
Hemodynamics in portal hypertension



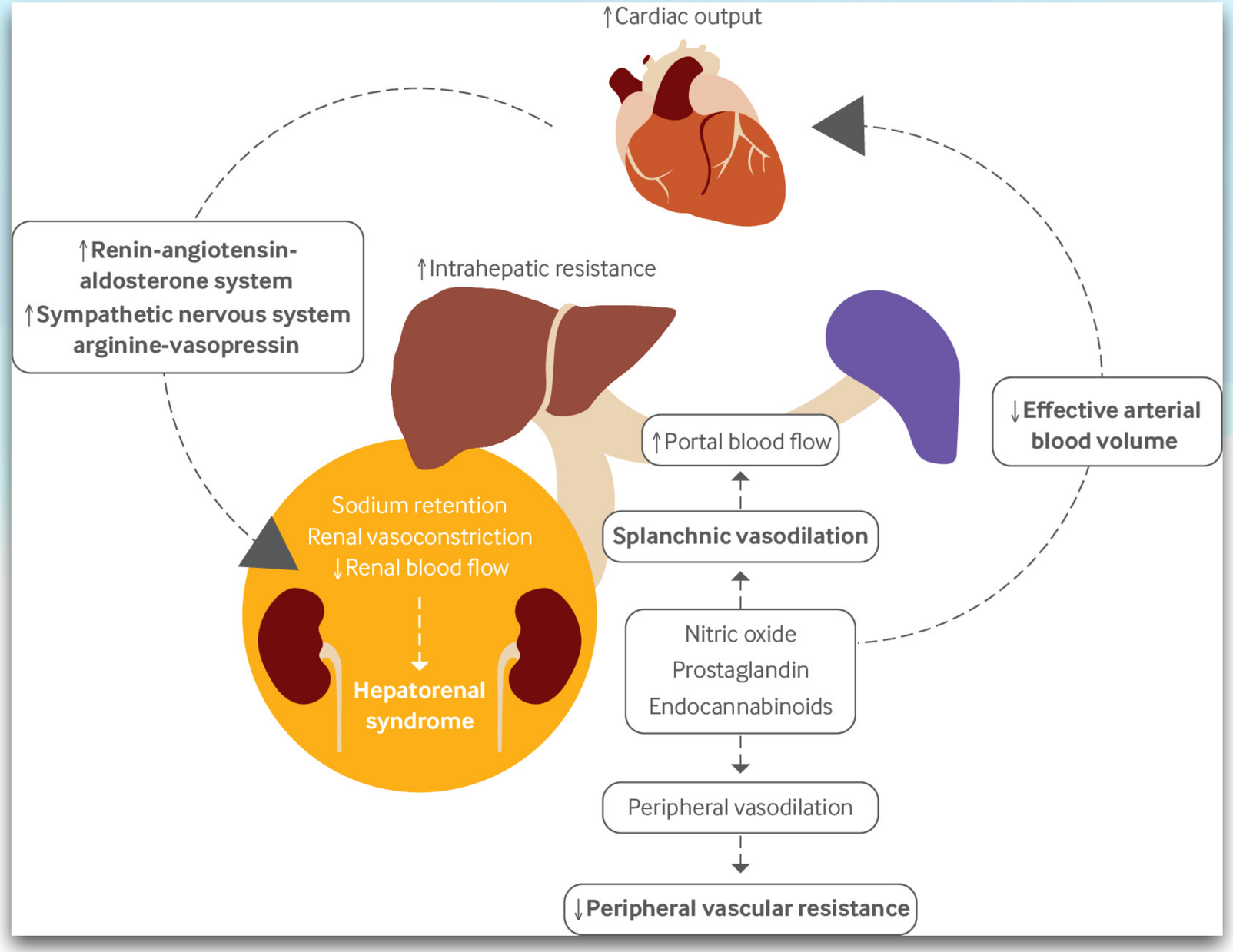

Hepatopulmonary syndrome
Cirrhotic cardiomyopathy
Multi-organ involvement
Hepatorenal syndrome
Hepatic encephalopathy

Hepatopulmonary syndrome

- Intrapulmonary right to left shunt (VQ mismatch) >> Systemic desaturation
- Associated with orthodeoxia
- Vasoactive substance related with hyper dynamic circulation (NO, Endothelin-1)
- Early asymptomatic
- Late manifestation : Shortness of breathing, exercise intolerance and clubbing finger
- Early detection by agitated saline echocardiography


Normal
Alveolus
8–15 μm
Capillary
Classic Shunt
Alveolus
8–15 μm
Shunt
Hepatopulmonary Syndrome
Alveolus
15–100 μm
Dilated capillary

Hepatorenal syndrome

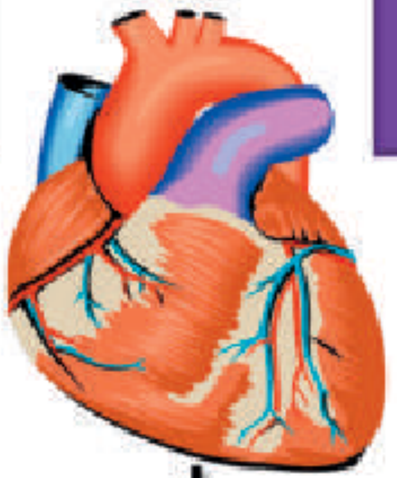


Cirrhotic cardiomyopathy

- Pathogenesis is multifactorial ; decreases beta-adrenergic receptor signal transduction, cardiomyocyte cellular membrane dysfunction and increased activity of cardio-depressant substances
- Usually silent or mild symptom ; But it can overt heart failure by stress from liver transplantation or trans jugular intrahepatic portosystemic shunt insertion.

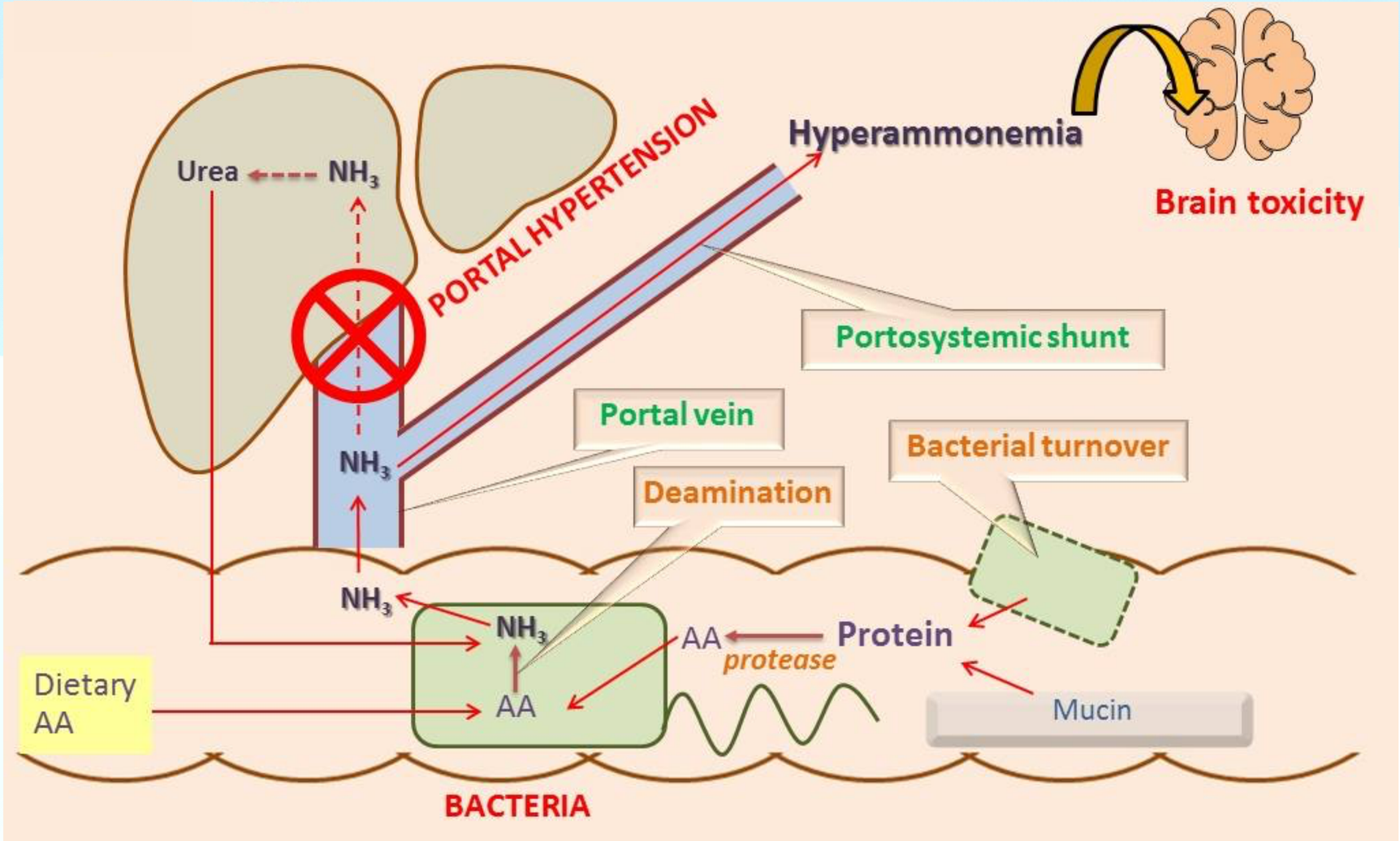
Structural changes
– enlarged cardiac chambers (especially left atrium)
– increased myocardial mass

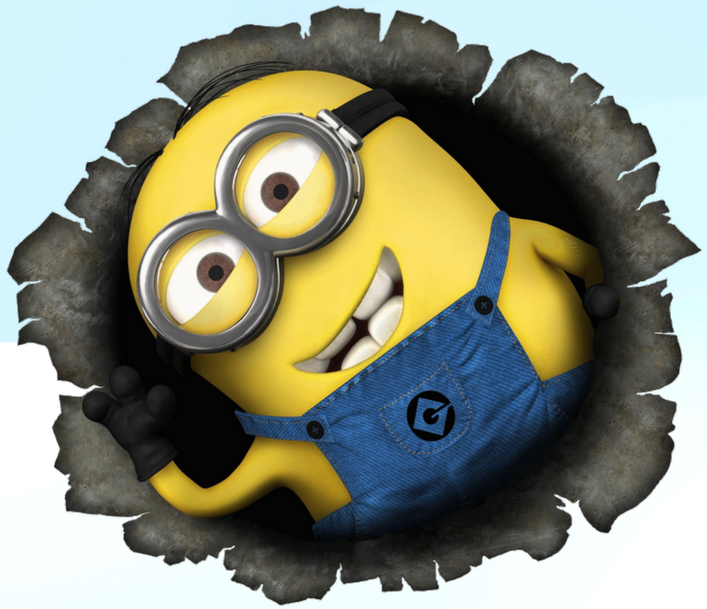
«Electrical» changes
– prolonged QT interval
– abnormal chronotropic response
– electromechanical uncoupling



Functional changes
– impaired increased cardiac output with exercise or other stimuli
– resting LVEF <55% (rare)
– diastolic dysfunction
– ↑ BNP/NT-proBNP

Hepatic encephalopathy





Management

Acute variceal hemorrhage

Long-term management

Acute vatical hemorrhage

- Primary assessment (ABC)
- Volume replacement : isotonic crystalloid solution
- PRC transfusion (keep Hb 7-9 g/dL)
- NG tube insertion (assess severity of bleeding)
- Correction of coagulopathy (Vitamin K, FFP, Platelet transfusion)
- Monitor ongoing blood loss (vital signs, serial Hct, urine output)
- Antibiotic prophylaxis (High risk fatal infectious complication)

*** Beware of fluid overload in portal hypertension

Acute variceal hemorrhage

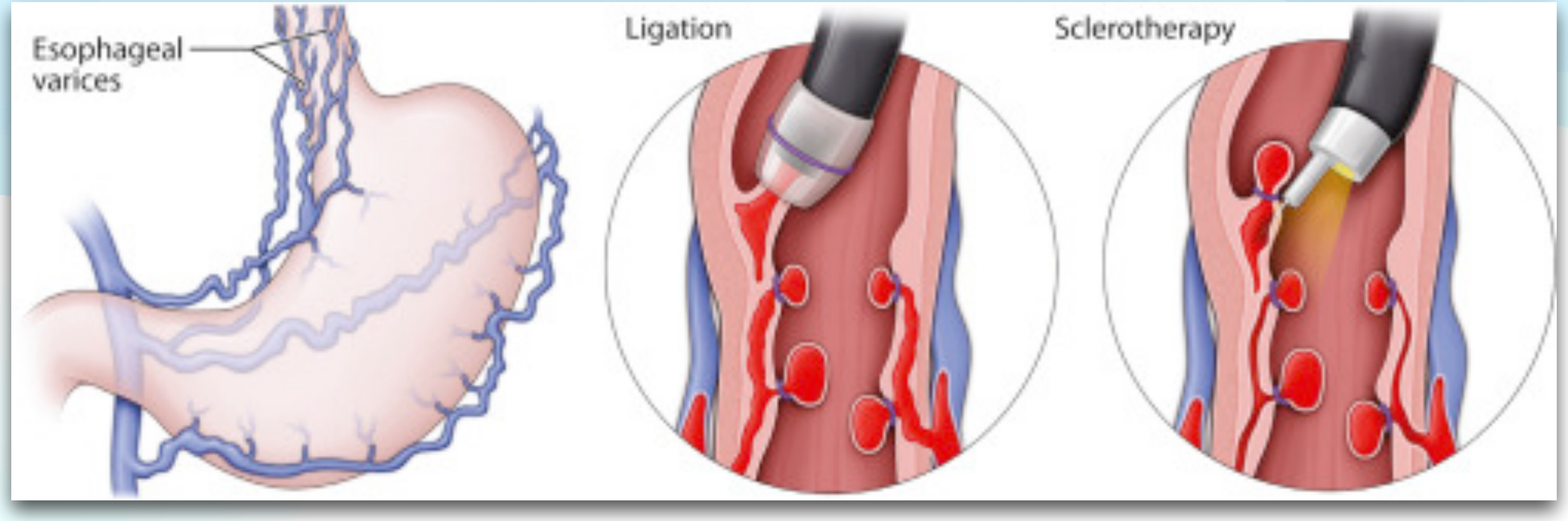
Vasoactive agents

Vasopressin, Somatostatin and analogue (Octeotride)

- Reduced splanchnic blood flow >> decrease portal blood flow
- Somatostatin & analogue less side effects than vasopressin
- Dose: Octeotride 1-2 mcg/kg (max 100 mcg) IV bolus then 1-2 mcg/kg/hr (max 250 mcg/hr) continuous IV infusion
- SE : bradycardia, hyperglycemia

Acute variceal hemorrhage

Endoscopic therapy



EVL

EVS

Acute variceal hemorrhage

Endoscopic therapy

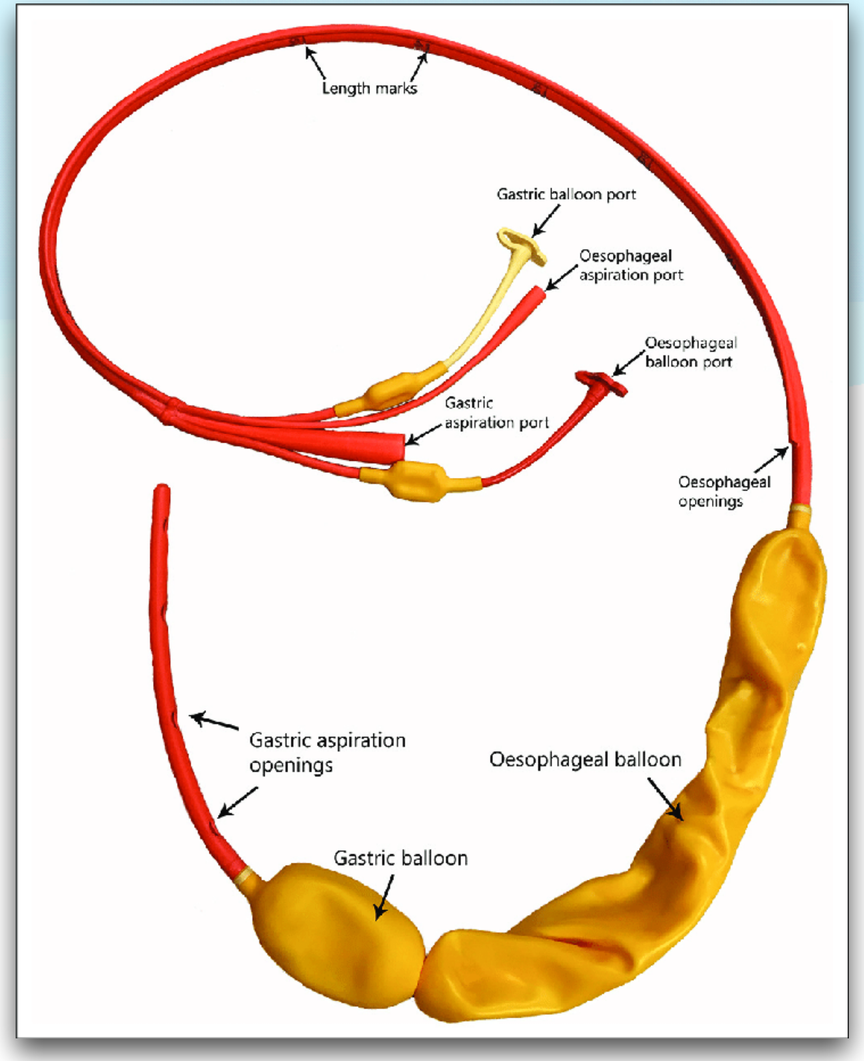
Sheffield Scoring System

History taking
Significant pre-existing condition: 1
Presence of melaena: 1
History of large amount of hematemesis: 1
Clinical assessment
HR > 20 (from mean HR for age): 1
Prolonged CRT: 4
Laboratory findings
Hb drop > 20 g/L : 3
Management and resuscitation
Need for fluid bolus: 3
Need for blood transfusion (Hb < 80 g/L): 6
Need for other blood product: 4
Total score: 24
Cut-off: 8 (> 8 considered as threshold for intervention)

Acute variceal hemorrhage

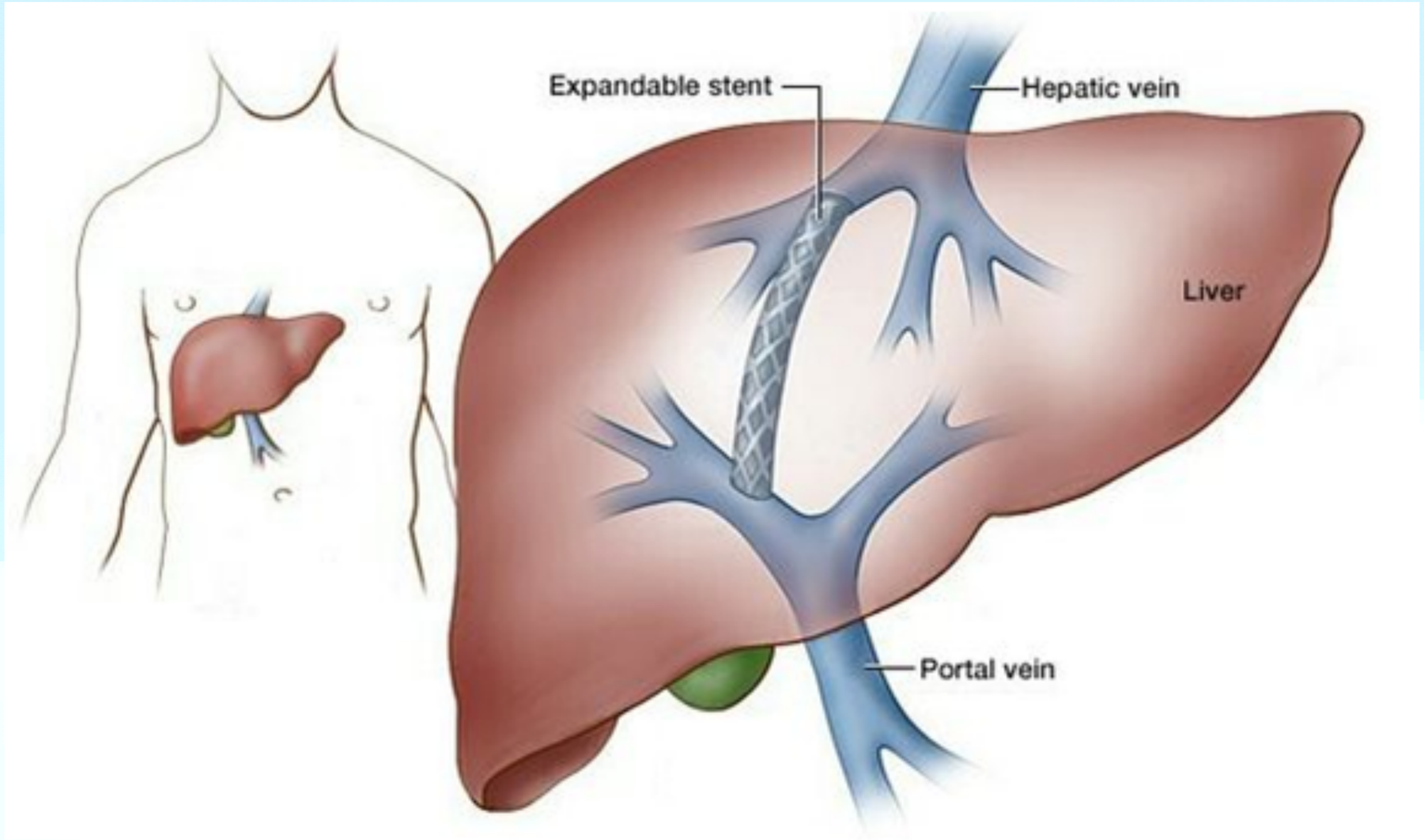
Sengstaken-Blakemore tube (SSBT)

- Temporary treatment
- Balloon tamponade
- If remove SSBT >> re-bleeding 30-60%
- Complication : Pressure necrosis, airway obstruction, aspiration



Long-term management

- Propanolol
  - Non-selective beta-adrenergic antagonist
  - Dose : 2-8 mg/kg/day
- Endoscopic therapy every 2-4 wk (eradicate varices)
- If refractory vatical bleeding or hypersplenism consider ;
    - TIPS (Transjugular intrahepatic portosystemic shunt)
    - Surgical shunt



TIPS (Transjugular intrahepatic portosystemic

Take home message

Thank you for your attention