Approach to Management of Chronic Liver Disease

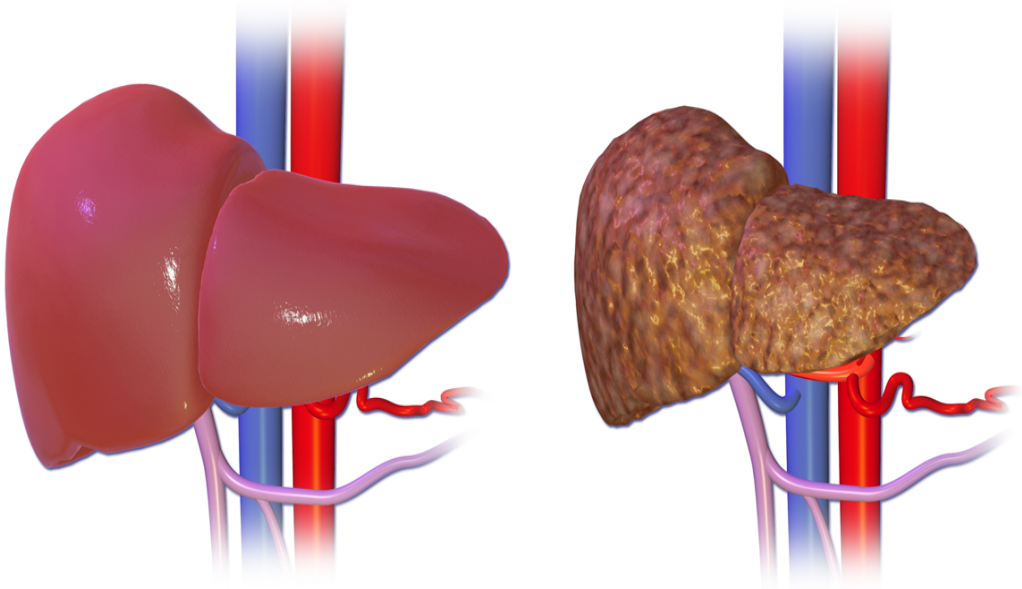
Mansour Altuwaijri, MBBS, MHSc

Assistant Professor & Consultant Gastroenterologist

Department of Medicine, College of Medicine & King

Khalid University Hospital, King Saud University

Medical City, King Saud University



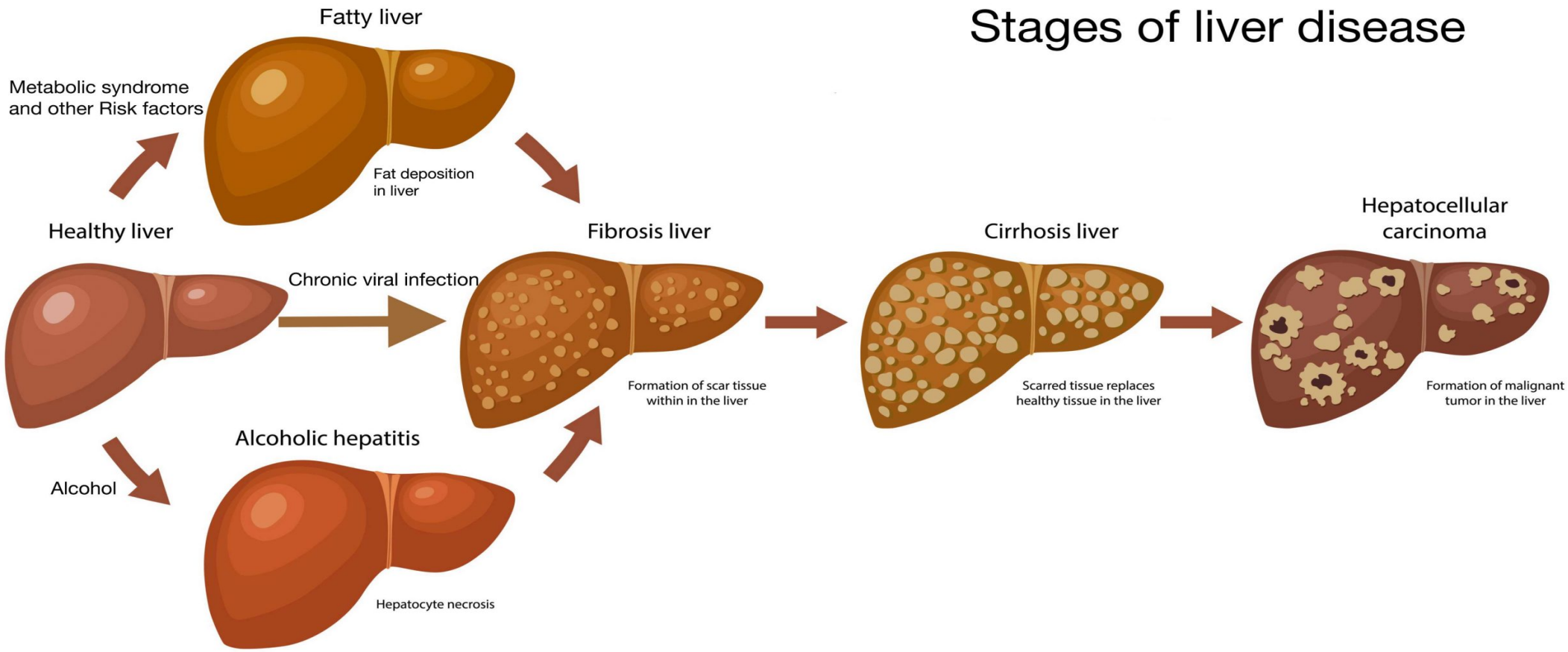
Normal Liver

Liver Cirrhosis

Objectives

- Stages of chronic liver disease (CLD).
- Common causes of CLD.
- Symptoms of CLD and Investigations.
- Common severity and prognosis classifications used in cirrhosis.
- Differentiate between compensated and decompensated cirrhosis
- Complications of chronic liver disease.
- Principles of management of CLD.

Stages of Liver Disease



What are the most common **causes** of cirrhosis?

Most common causes of cirrhosis are:

- **Chronic viral hepatitis (hepatitis B and hepatitis C)**
- **Alcoholic liver disease**
- **Nonalcoholic fatty liver disease**
- **Hemochromatosis**

Other causes?

Infections	**Hepatitis B, Hepatitis C**, Schistosomiasis
Toxins	**Alcohol**, Herbal
Metabolic	**Hemochromatosis**, Wilson's, Alpha-1 Antitrypsin deficiency, Amyloidosis, **NASH**
Autoimmune	Autoimmune Hepatitis, PSC, PBC
Vascular	Budd-Chiari Syndrome
Cardiac	Heart Failure (Congestive hepatopathy)

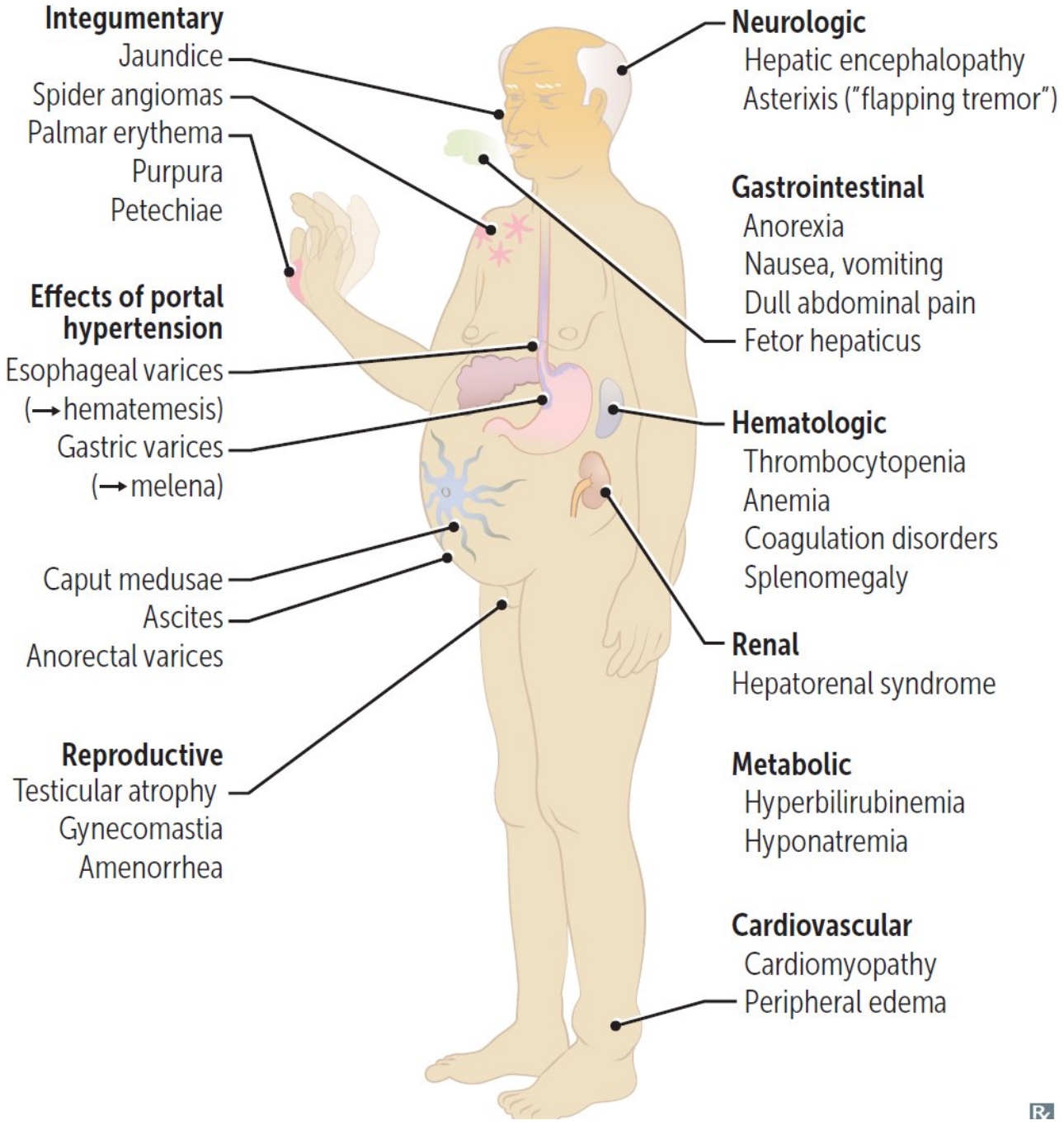
History?

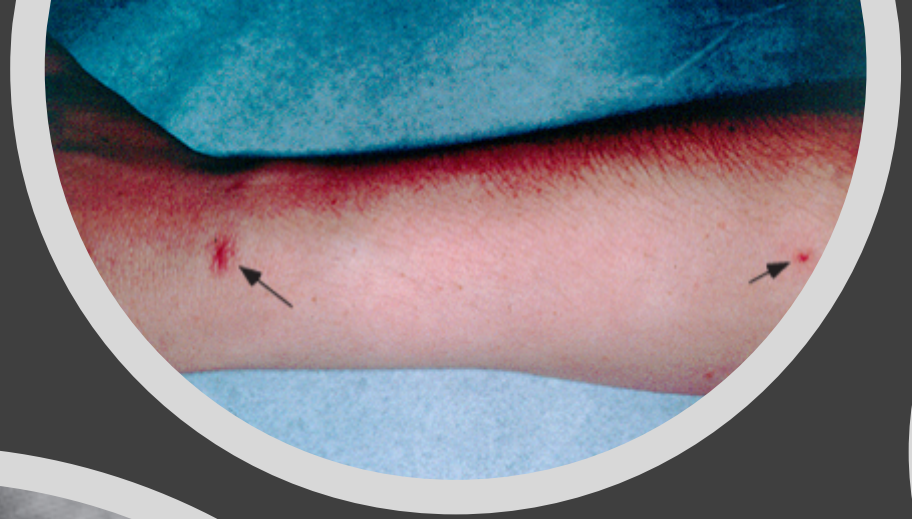
Alcoholic liver disease	History of alcohol abuse (duration, type and amount)
Chronic hepatitis B and C	IV drug use, sexual contact, tattoos and remote blood transfusion, family history
Primary sclerosing cholangitis (PSC)	Strong association with inflammatory bowel disease
Hereditary hemochromatosis	Family history of cirrhosis
Wilson disease	Family or personal history of cirrhosis at a young age, neurologic or psychiatric symptoms
Alpha-1 antitrypsin deficiency	Family or personal history of cirrhosis at a young age
Nonalcoholic fatty liver disease (NAFLD)	History of diabetes mellitus or metabolic syndrome
Autoimmune hepatitis	Associated with common autoimmune disorders, e.g. autoimmune thyroiditis, rheumatoid arthritis, type 1 diabetes mellitus, ulcerative colitis, celiac disease, SLE
Congestive hepatopathy	History of right-sided heart failure, constrictive pericarditis, mitral stenosis, tricuspid regurgitation, cor pulmonale, cardiomyopathy

What are the symptoms of CLD?

- Can be **compensated** or **decompensated** cirrhosis
- Can be **asymptomatic** or **symptomatic** cirrhosis
- Anorexia, weight loss, weakness, fatigue, muscle cramps, lower limb edema, diarrhea, easy bruisability, jaundice or pruritus
- Patients with decompensated cirrhosis may present with jaundice, pruritus, signs of **upper gastrointestinal bleeding** (hematemesis, melena, hematochezia), abdominal distension from **ascites**, or confusion due to **hepatic encephalopathy**.
- In women, amenorrhea or irregular menstrual bleeding].
- In men with cirrhosis may develop hypogonadism (impotence, infertility, loss of sexual drive, and testicular atrophy)

Clinical manifestations of Cirrhosis?





Clinical manifestations

Important Diagnostic Tests in Common Liver Diseases

Disease		Diagnostic Test
Hepatitis A (acute)		Anti-HAV IgM
Hepatitis B	**Acute**	HBsAg and anti-HBc IgM
	Chronic	HBsAg and HBeAg and/or HBV DNA
Hepatitis C		Anti-HCV and HCV RNA
Autoimmune hepatitis		ANA or ASMA, anti-LKM-ab, elevated IgG levels, and compatible histology
Primary biliary cholangitis		AMA, elevated IgM levels, and compatible histology
Primary sclerosing cholangitis		P-ANCA, cholangiography MRCP or ERCP
Nonalcoholic steatohepatitis		Ultrasound or CT evidence of fatty liver and compatible histology
α_1 Antitrypsin disease		Reduced α_{-1} antitrypsin levels
Wilson's disease		Decreased serum ceruloplasmin, increased urinary copper, increased hepatic copper level
Hemochromatosis		Elevated iron saturation and serum ferritin; genetic testing for HFE gene mutations
Hepatocellular cancer		Elevated α-fetoprotein level , CT or MRI with contrast

Investigations

Lab Test

- Moderately elevated aminotransferases (often with an AST:ALT ratio >1)
- Elevated ALP (2 to 3 times the ULN)
- Hyperbilirubinemia
- Thrombocytopenia
- Leukopenia/neutropenia
- Anemia
- Low serum albumin
- Prolonged PT/elevated INR*
- Hyponatremia
- Elevated serum creatinine

Radiology

- Small, nodular liver
- Ascites
- Hepatocellular carcinoma
- Portal/splenic/superior mesenteric vein thrombosis
- Portosystemic collaterals

Diagnostic confirmation

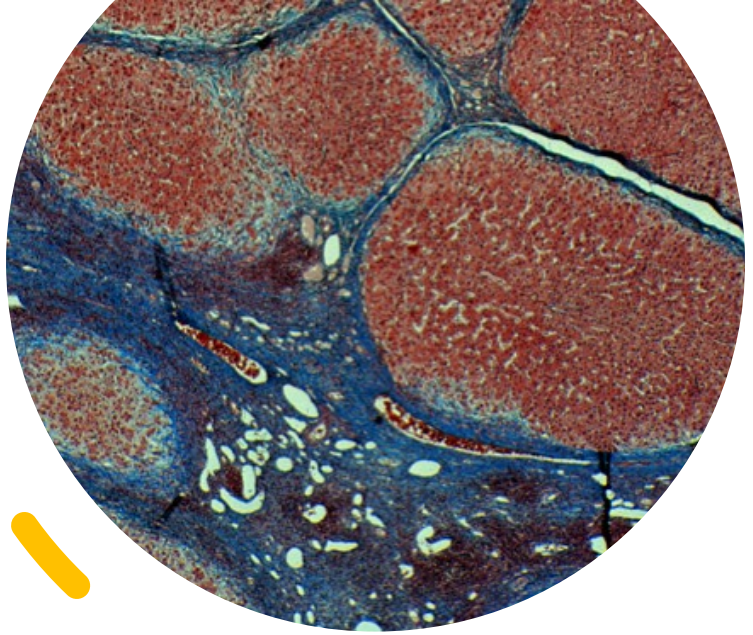
To confirm and support the clinical and radiologic manifestations if needed:

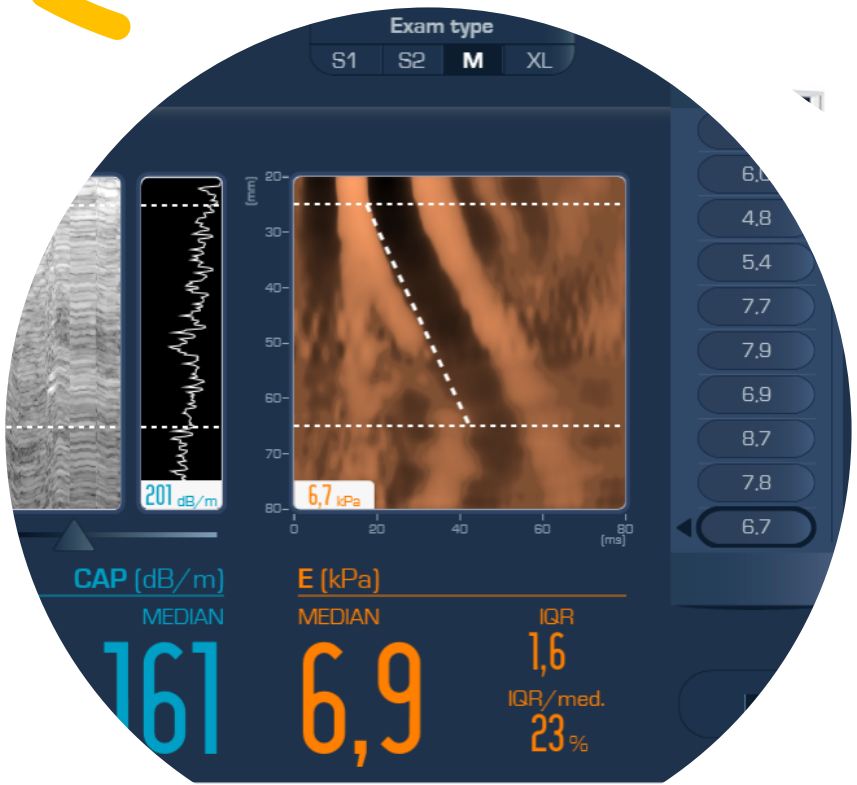
- **Invasive:**

  Biopsy (histopathology)

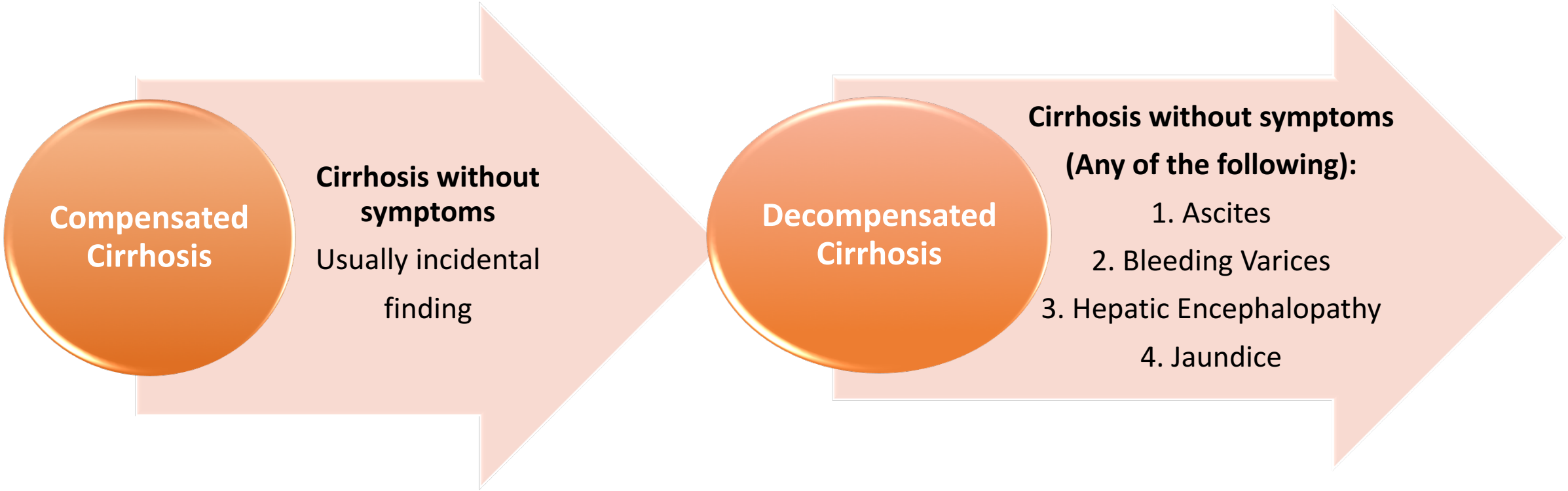
- **Noninvasive tests**

  Elastography (e.g fibroscan)





What is the course of cirrhosis?



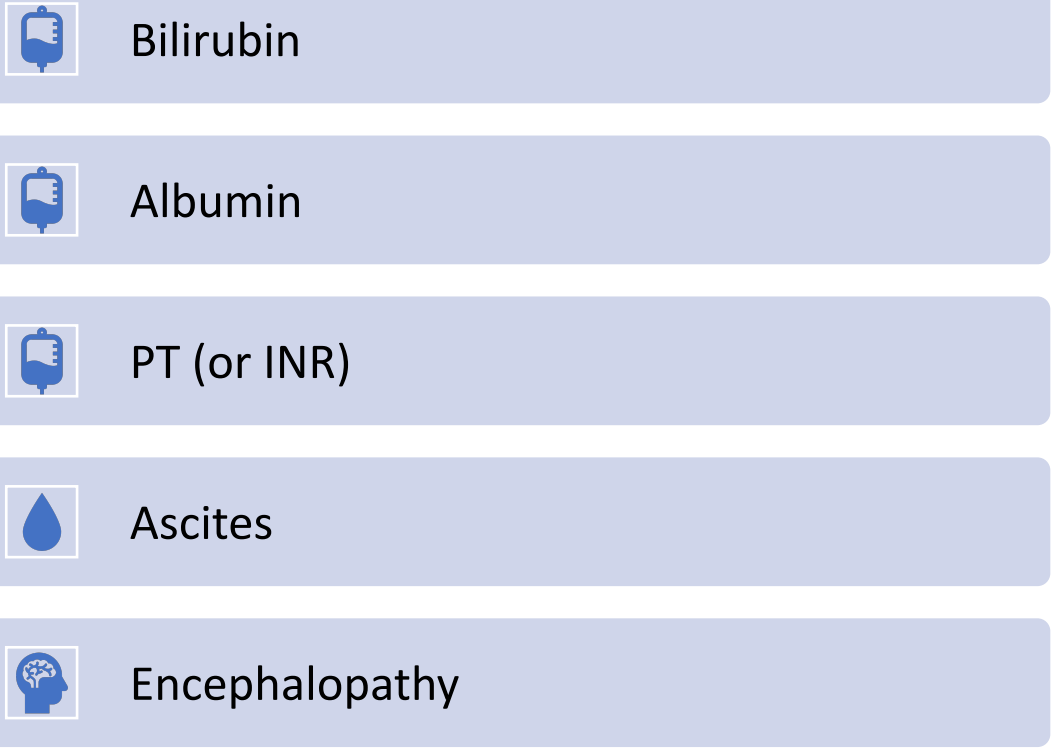
Severity & Prognosis of CLD

How to assess severity & prognosis of CLD?

- **Child–Pugh classification**
- MELD score (model for end-stage liver disease)

Child–Pugh classification

What are the 5 variables of Child–Pugh classification?



Bake Another Pie At Eleven

What are the classes of Child–Pugh classification?

- **class A** (well-compensated disease)
- **class B** (significant functional compromise)
- **class C** (decompensated disease)

Child-Pugh classification of severity of cirrhosis

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time			
Seconds over control	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

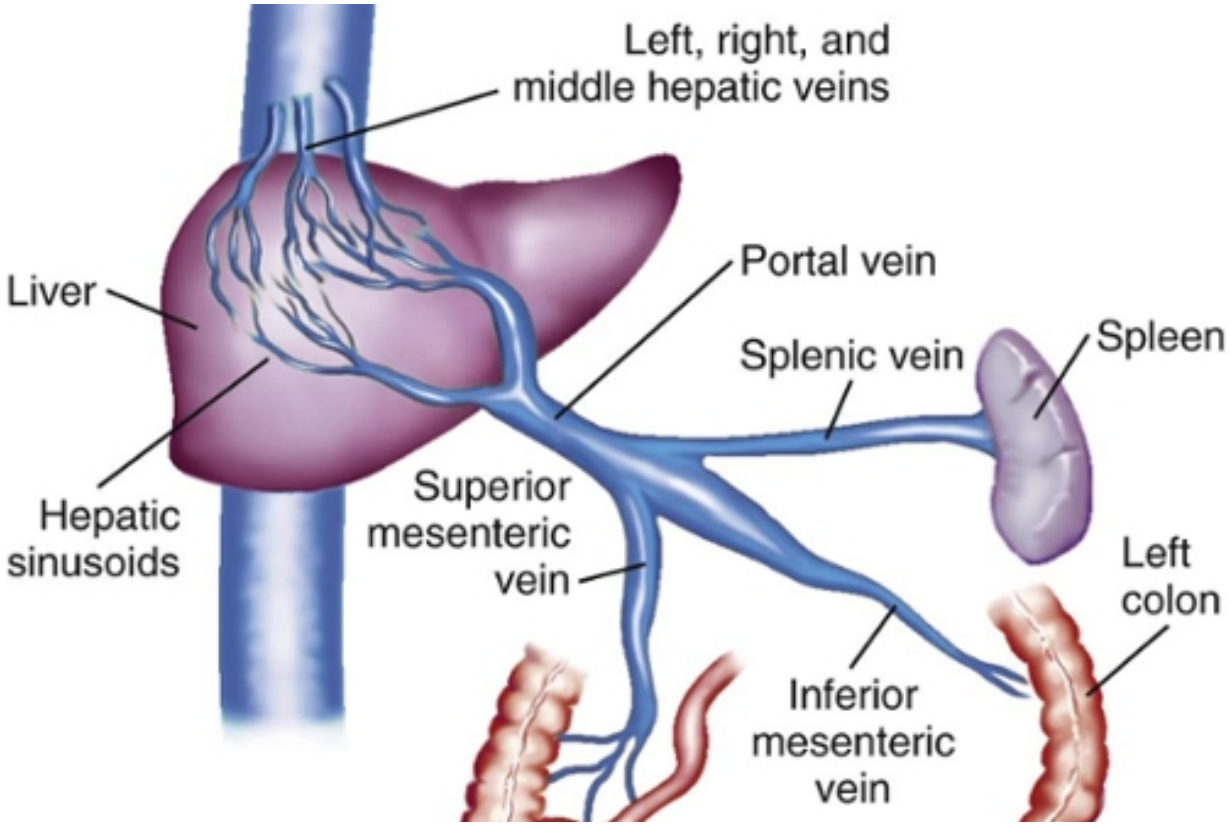
Modified Child-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Turcotte-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease); 7 to 9 is class B (significant functional compromise); and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two-year patient survival: class A: 100 and 85%; class B: 80 and 60%; and class C: 45 and 35%.

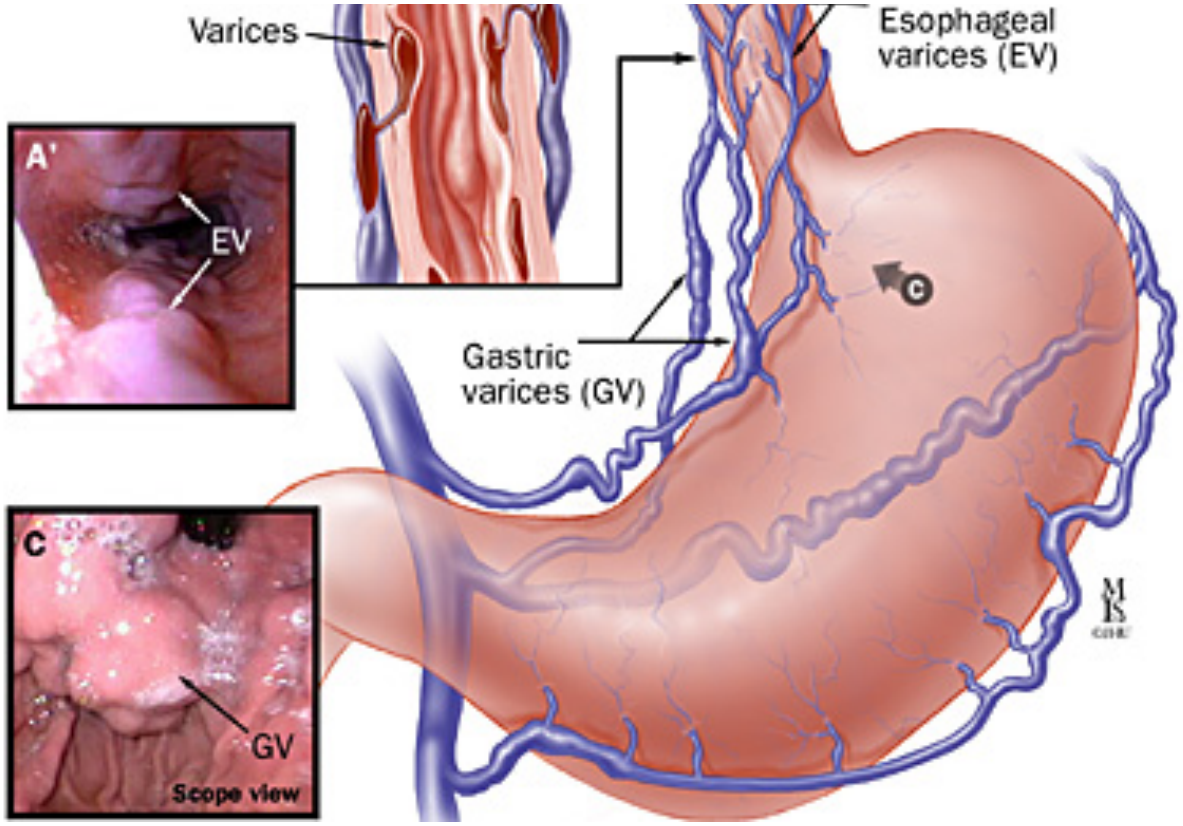
INR: international normalized ratio.

What are the common complications of Cirrhosis?

- **Variceal hemorrhage**
- **Ascites**
  - Spontaneous bacterial peritonitis
  - Hepatic hydrothorax
  - Hepatorenal syndrome
- **Hepatocellular carcinoma (HCC)**
- **Hepatic encephalopathy**
- Pulmonary
  - Hepatopulmonary syndrome
  - Portopulmonary hypertension

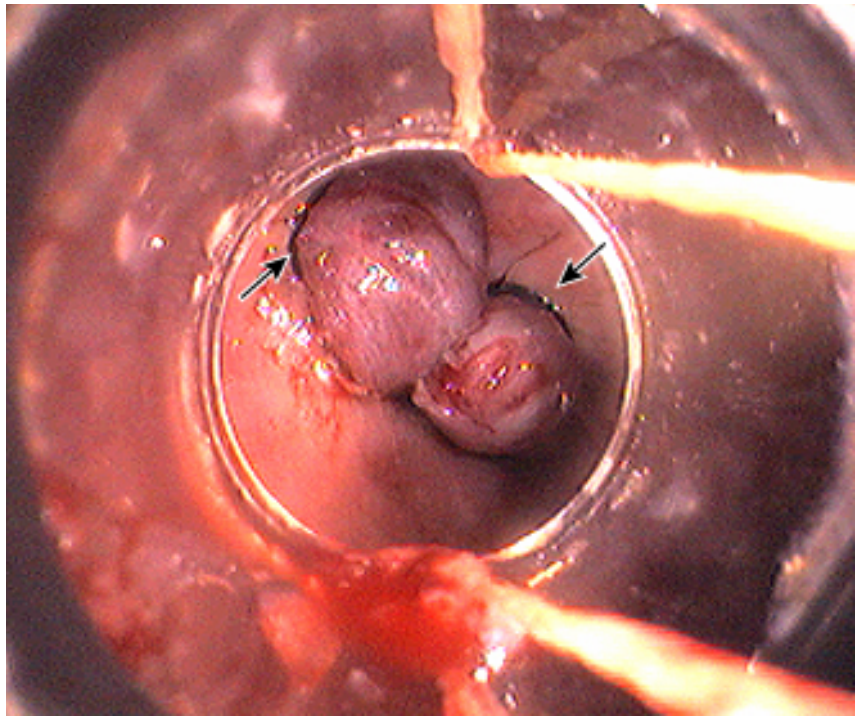
Portal hypertension

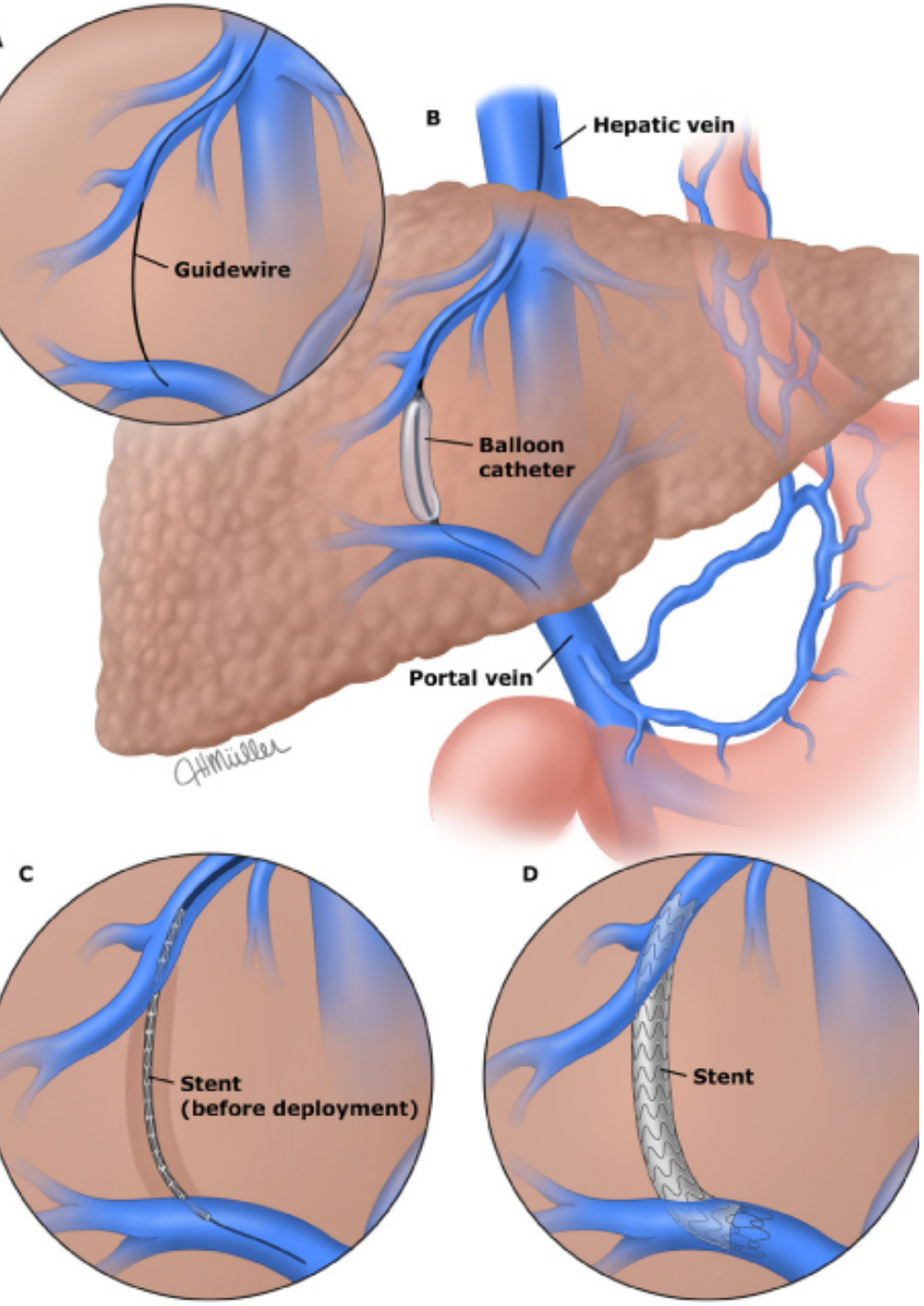




What is the management Variceal Bleeding?

1. Endoscopic treatment
2. Octereotide
3. Antibiotics





What if endoscopic therapy fails?

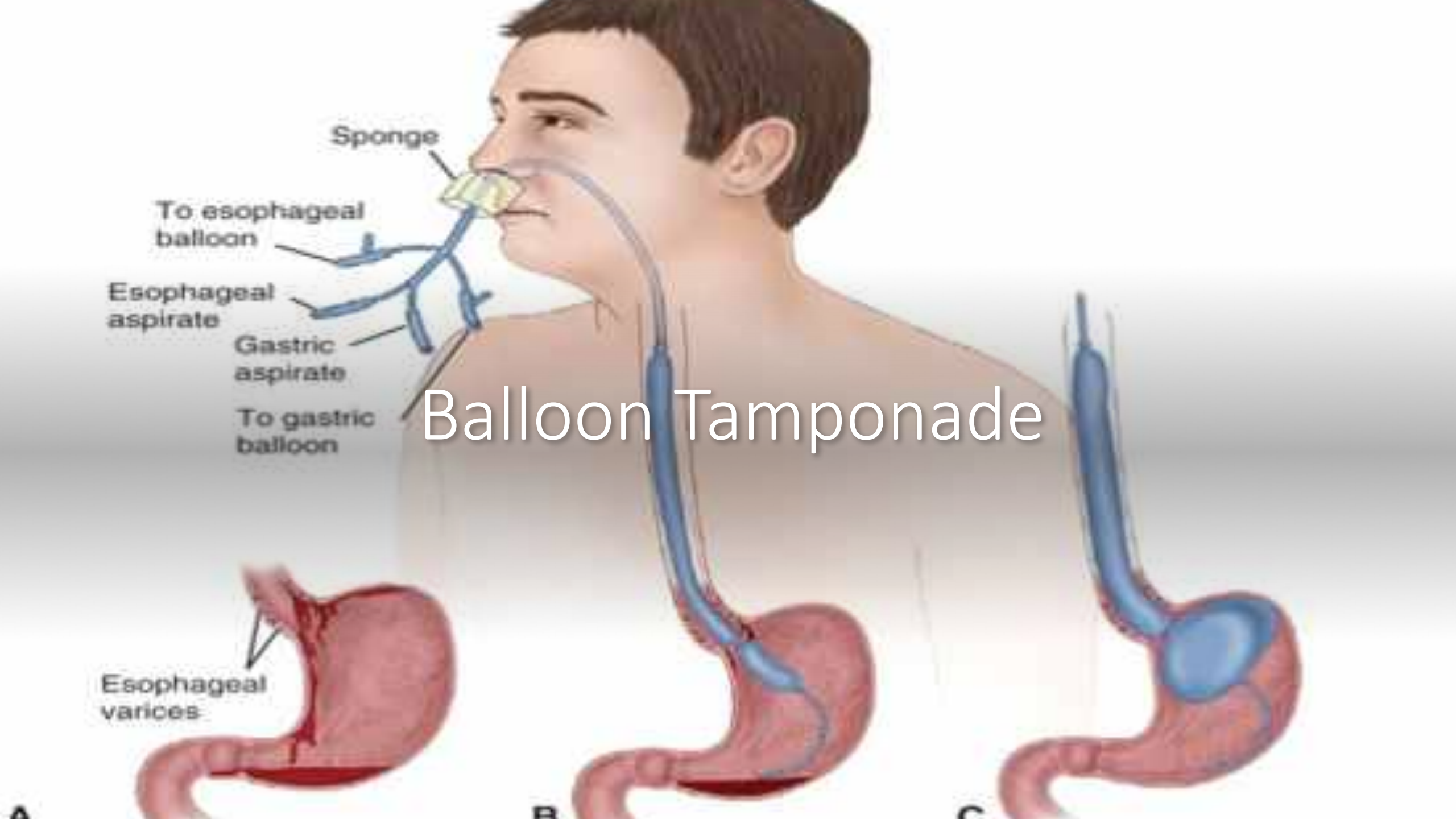
- TIPS (Transjugular Intrahepatic Portosystemic Shunt)
- Balloon Tamponade
- Surgery

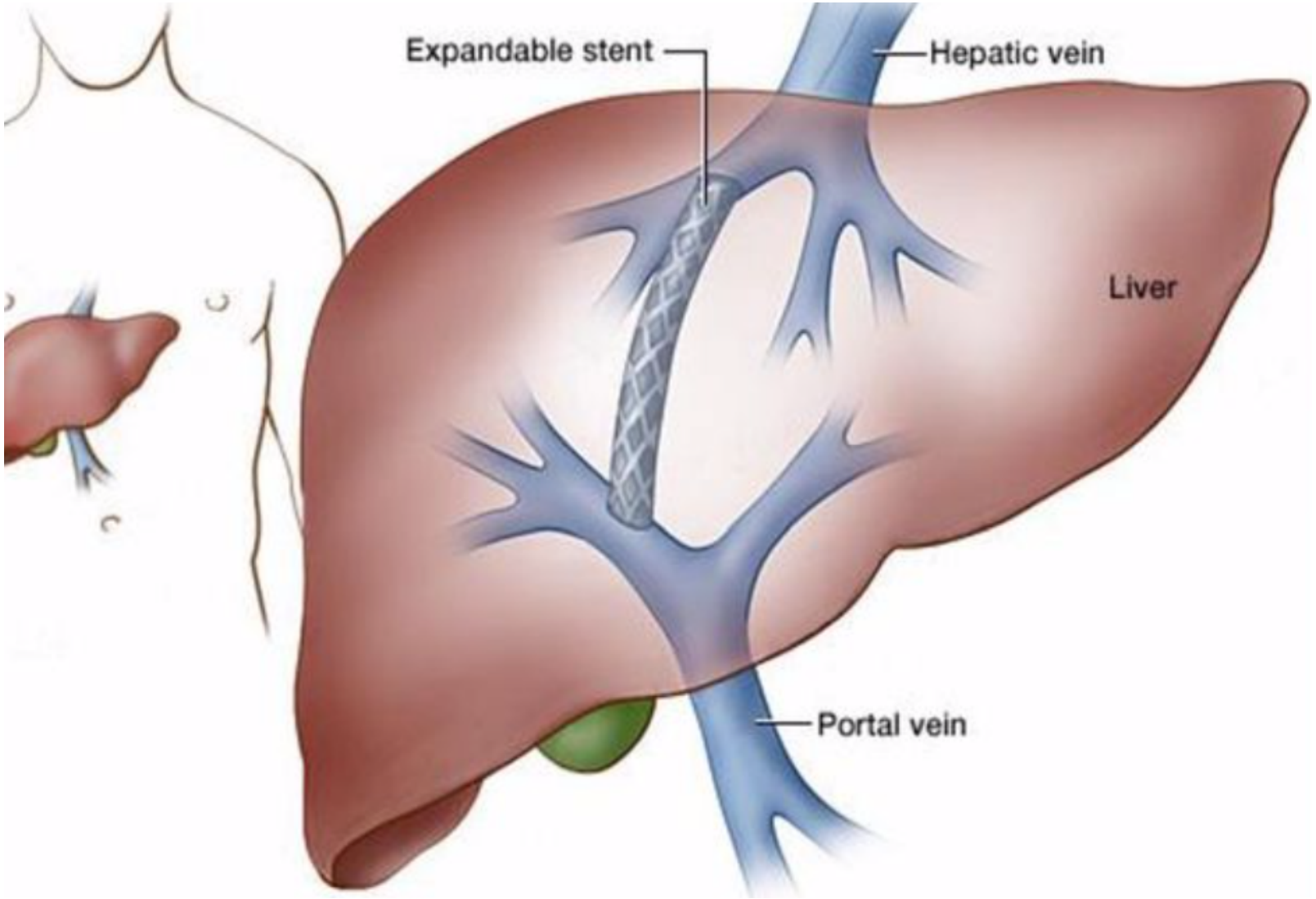
When is TIPS also indicated?

- TIPS is indicated in:

1. Refractory Ascites
2. Uncontrolled variceal bleeding (Esophageal, Gastric)

Balloon Tamponade



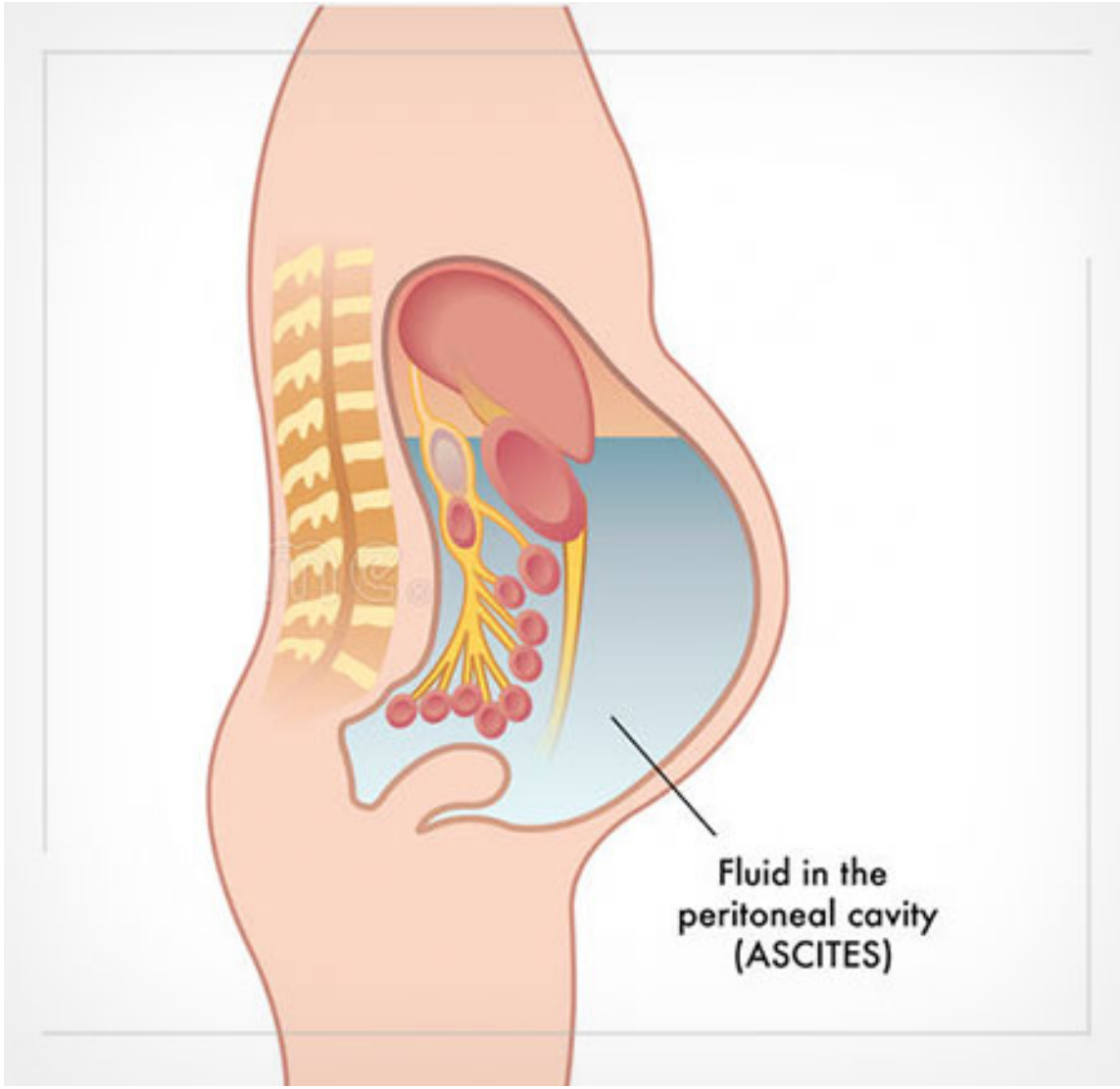


TIPS

TRANSJUGULAR
INTRAHEPATIC
PORTOSYSTEMIC SHUNT

Ascites

- Accumulation of fluid within the peritoneal cavity
- 1500 ml of fluid must be present before flank dullness is detected.
- Shifting dullness
- If no flank dullness is present less likely ascites (< 10%).
- Ascites:
    - 85% of due to cirrhosis
    - 15% other causes



Rule of thumb: Any ascites needs to be tapped (when possible) to determine the cause of ascites

Ascitic Fluid Analysis

Routine tests on ascetic fluid:

1. Cell count and differential
2. Albumin
3. Total protein

Other *optional* tests: glucose, LDH, Gram stain, cultures and amylase…etc.

How to evaluate the cause of ascites?

Measure **SAAG** (Serum Albumin-Ascetic Gradient)

SAAG = ***S***erum ***A***lbumin – ***A***scetic ***A***lbumin

SAAG

≥ 1.1 g/dl PORTAL HYPERTENSION	<1.1 g/dl NON PORTAL HYPERTENSION
Chronic Liver disease	Nephrotic syndrome
Budd-Chiari Syndrome	Peritoneal Tuberculosis
Congestive heart failure	Pancreatitis
	Peritoneal carcinomatosis

Protein ≥ 2.5 g/dl	Protein <2.5 g/dl	Protein ≥ 2.5 g/dl	Protein <2.5g/dl
Congestive heart failure	Chronic Liver disease	Pancreatitis TB	Nephrotic Syndrome
Budd-Chiari Syndrome		Cancinomatosis	

How do we treat ascites?

1. Salt Restriction (< 2g/day)
2. Diuretics (Furosemide and Spironolactone)
3. Paracenthesis +/- albumin
4. TIPS

Spontaneous Bacterial Peritonitis (SBP)

How do we diagnose SBP?

- Ascitic fluid polymorphonuclear leukocyte (PMN) (neutrophils) count ≥ 250 cells/mm^3
- Usually one organism (gram negatives) - E-coli or klebsiella
- *If multiple organisms think of secondary peritonitis*

- **How to treat SBP?**
  1. Antibiotics
  2. Albumin

Hepatic encephalopathy (HE)

What is Hepatic encephalopathy (HE)?

HE is a reversible syndrome of impaired brain function occurring in patients with advanced liver disease

HE is characterized by cognitive deficits and impaired neuromuscular function (from disorientation & asterixis to coma)

What are the common precipitants of HE?

- **Drugs** (*benzodiazepines*, narcotics or *alcohol*)
- **Increased ammonia production, absorption or entry into the brain** (excess dietary intake of protein, *GI bleeding, infection*, electrolyte disturbances such as hypoK, *constipation* or metabolic alkalosis)
- **Dehydration** (e.g. vomiting, diarrhea, hemorrhage or diuretics)
- **Vascular occlusion** (i.e. hepatic or portal vein thrombosis)
- **Hepatocellular carcinoma (HCC)**

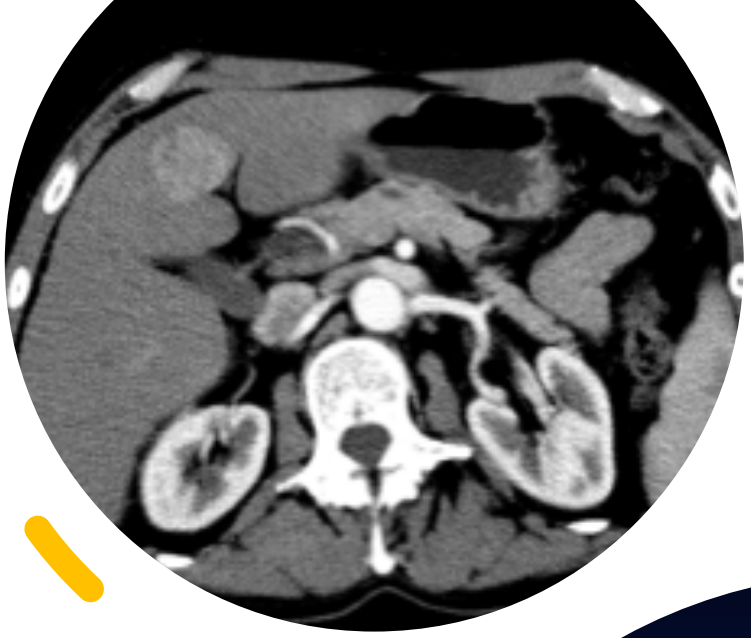
Treatment of HE

IDENTIFY and **TREAT** **precipitating factors** for HE

Lactulose is the first choice (or rifaximin: non-absorbable antibiotic)

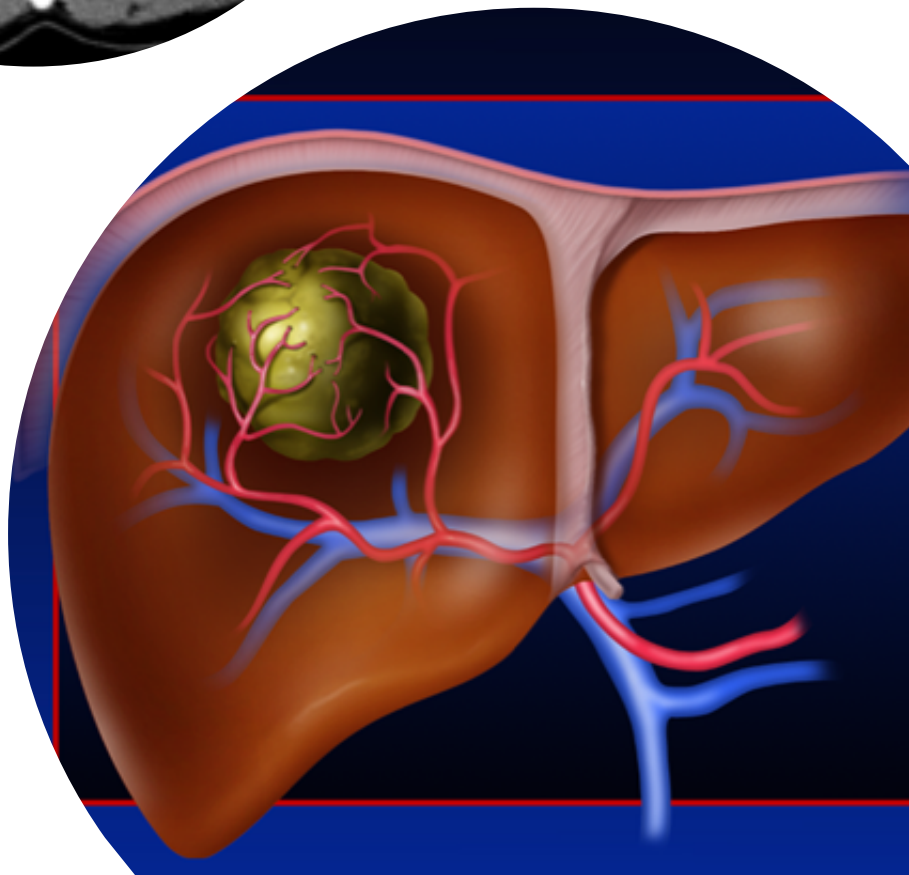
Tests to diagnose HCC

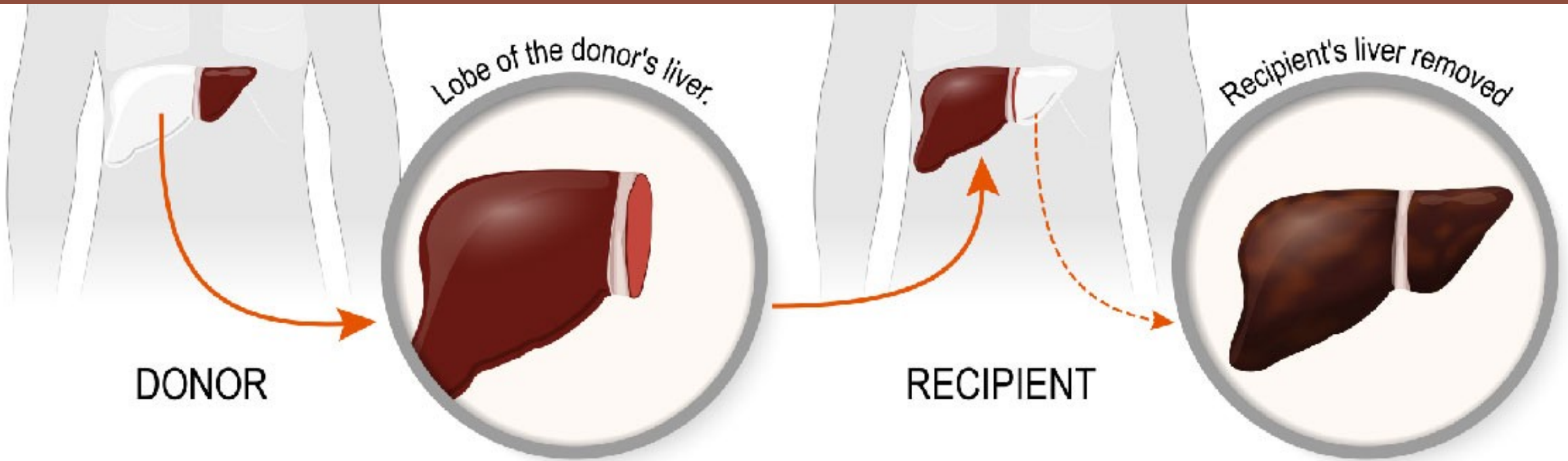
- Blood tests (AFP)
- Radiology (most important)
- Biopsy (not routinely done)



Treatment options for HCC

- Surgical (resection or liver transplantation)
- Ablation
- Embolization
- Chemotherapy
- Palliative



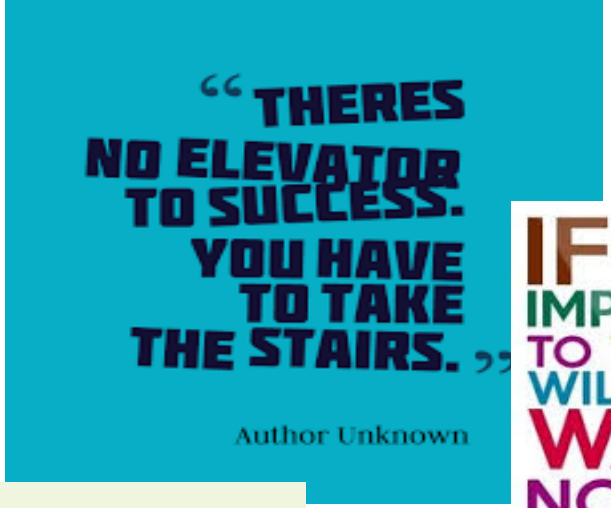


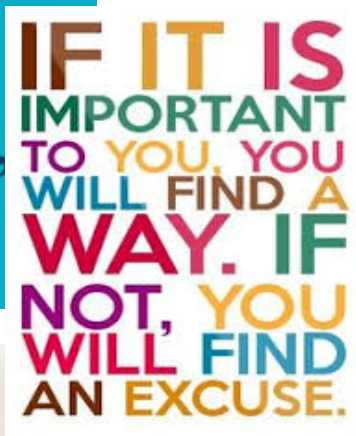
Liver Transplantation

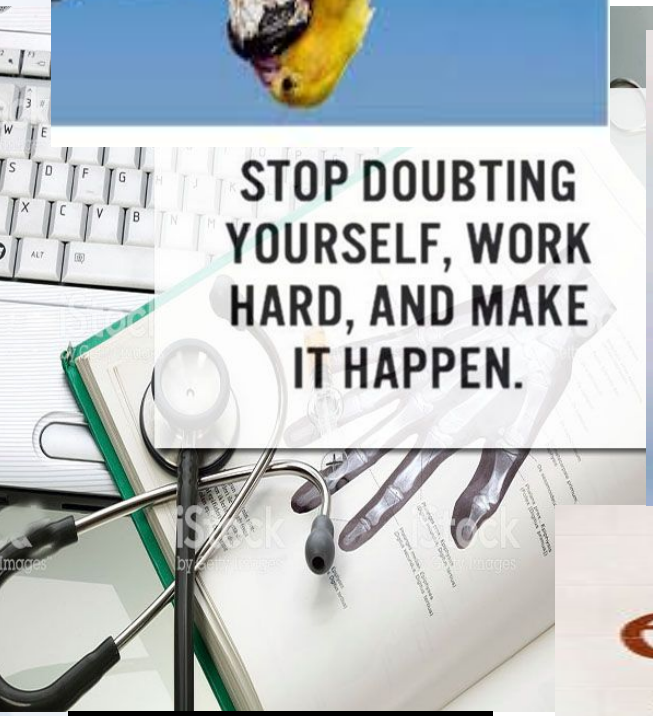
Liver transplantation is the definitive treatment for patients with cirrhosis

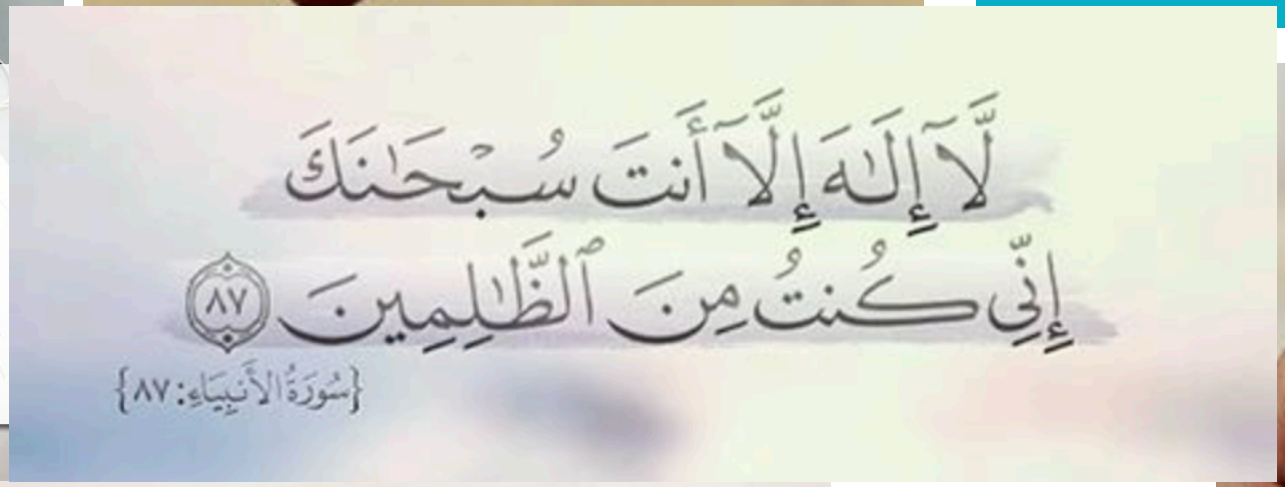
Summary & important points

- Determine the cause of CLD and treat if possible, Prevent further insult (Vaccinations, avoid hepatotoxic medications & Alcohol), Prevent and treat complications.
- Most common ***complications*** of CLD are: **Variceal bleeding, Ascites, Hepatic encephalopathy, HCC.**
- **Assess severity** using **Child-Pugh classification** (5 variables: Bilirubin, PT(or INR), Albumin, Ascites, Encephalopathy), OR **MELD**
- SBP is ***diagnosed*** when **neutrophils** (not total WBC) count in ascitic fluid is ≥ 250 cells/mm^3 and ***treated*** with antibiotics and albumin
- **Treat precipitants** of HE and give **Lactulose**
- ***Screen* for HCC** with liver imaging **every 6 months** (in patient with cirrhosis)
- Liver **transplantation** is the **definitive treatment** for patients with cirrhosis









IT'S NEVER TOO LATE