Approach to Management of Chronic Liver Disease

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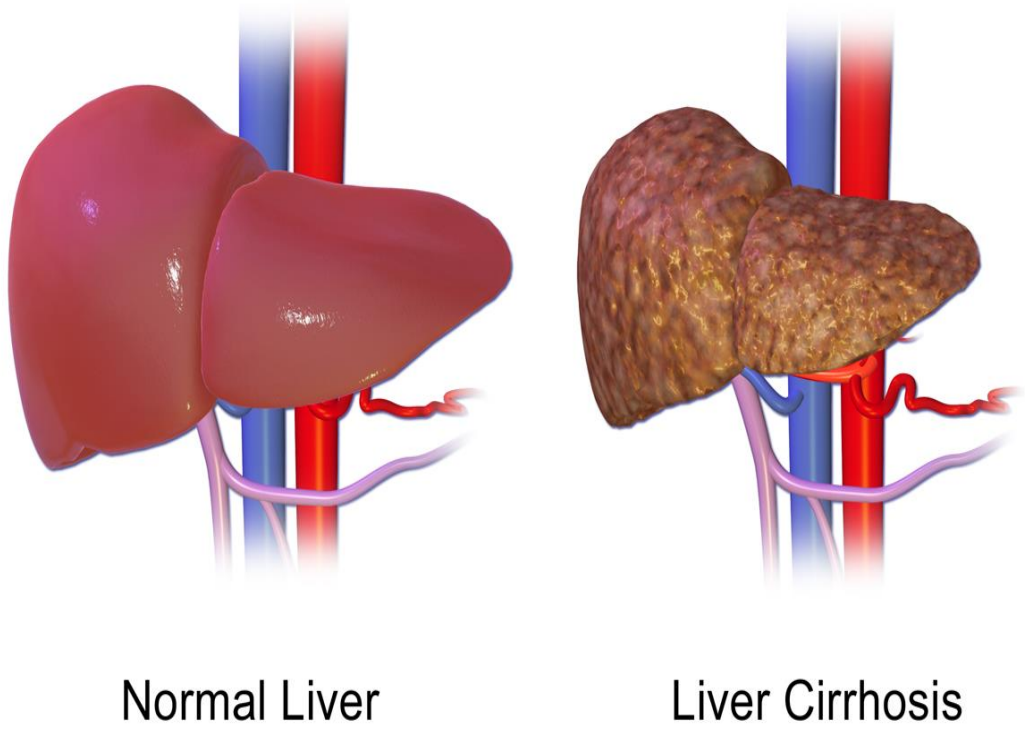


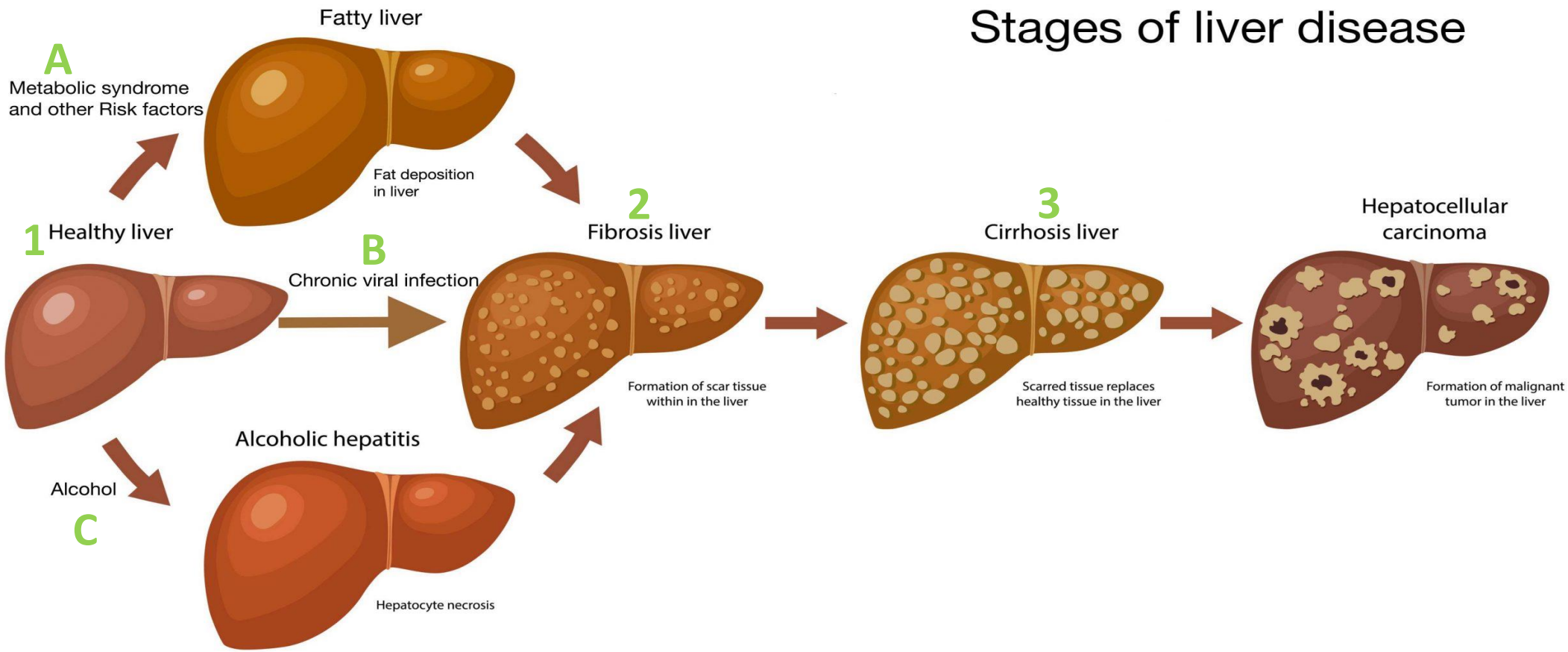
Normal Liver

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.
- I want you to know the **concepts: what is chronic liver disease, the complications and how to manage them.**

Stages of Liver Disease *Explanation in the next slide.*



Stages of Liver Disease

Liver disease does not start suddenly. First there is insult then continue progressing until end stage “cirrhosis”.

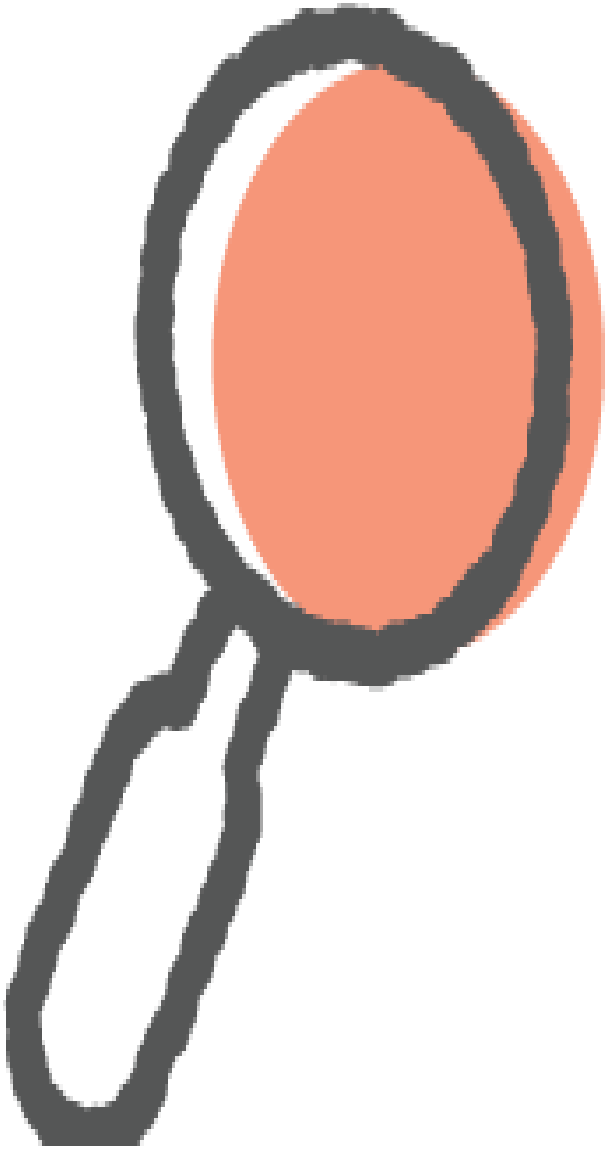
1. We start of with a healthy liver then many insults may occur that cause CLD:
   A. Patient might have **metabolic syndrome** (diabetes, obesity, etc..) which leads to accumulation/deposition of fat on the liver called **non-alcoholic fatty liver disease** (or non-alcoholic steatohepatitis “NASH”). The fat is an insult to the liver leading to inflammation then healing with scarring. Another cause of NASH is sudden weight loss.
   B. Patient might have a chronic **viral infection** (hepatitis **B or C**) which leads to inflammation and scarring.
   C. Patient who drink **alcohol** and it causes insult to the liver. This insult looks like fatty liver and so we call it **alcoholic fatty liver disease**. We classify it into alcoholic fatty liver or nonalcoholic fatty liver because they share similarities in terms of histology.
2. As the liver heals from the continuous insult and inflammation, **scars** / fibrosis are formed which replace the healthy tissue (replace normal hepatocyte) leading to cirrhosis. Cirrhosis is **irreversible.**
3. The cirrhotic liver becomes **stiff** and causes **backflow** of the blood in the portal vein leading to portal hypertension:
   - Loss of function. (Liver function includes clearing toxins and producing albumin & clotting factors: **10, 9, 7, 2**).
   - Splenomegaly (as the blood flows back through the splenic vein)
   - Esophageal varices (blood flows back through the esophageal veins).
   - And other complications (HCC, etc…)

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

Most common causes of cirrhosis are (these constitute 80-90% of cases):

- **Chronic viral hepatitis (hepatitis B and hepatitis C) –** could be most common.
- **Alcoholic liver disease**
- **Nonalcoholic fatty liver disease** – becoming more common now in KSA.
- **Hemochromatosis** – more in the western countries

Other causes?



Infections	**Hepatitis B, Hepatitis C**, Schistosomiasis (infection goes to the liver causing infestation and periportal inflammation may end up with cirrhosis).
Toxins	**Alcohol**, Herbal (very important and dangerous can cause acute liver failure)
Metabolic	**Hemochromatosis** (iron overload), Wilson's (copper accumulation), Alpha-1 Antitrypsin deficiency, Amyloidosis, **NASH** (non-alcoholic steatohepatitis)
Autoimmune	Autoimmune Hepatitis, PSC (primary sclerosing cholangitis), PBC (primary biliary sclerosis)
Vascular	Budd-Chiari Syndrome
Cardiac	Heart Failure (Congestive hepatopathy): when there is heart failure blood goes back into the IVC then into the liver leading to congestion.

History?

Understand the concept of it.
These are hints that give you indication of underlying cause through history.

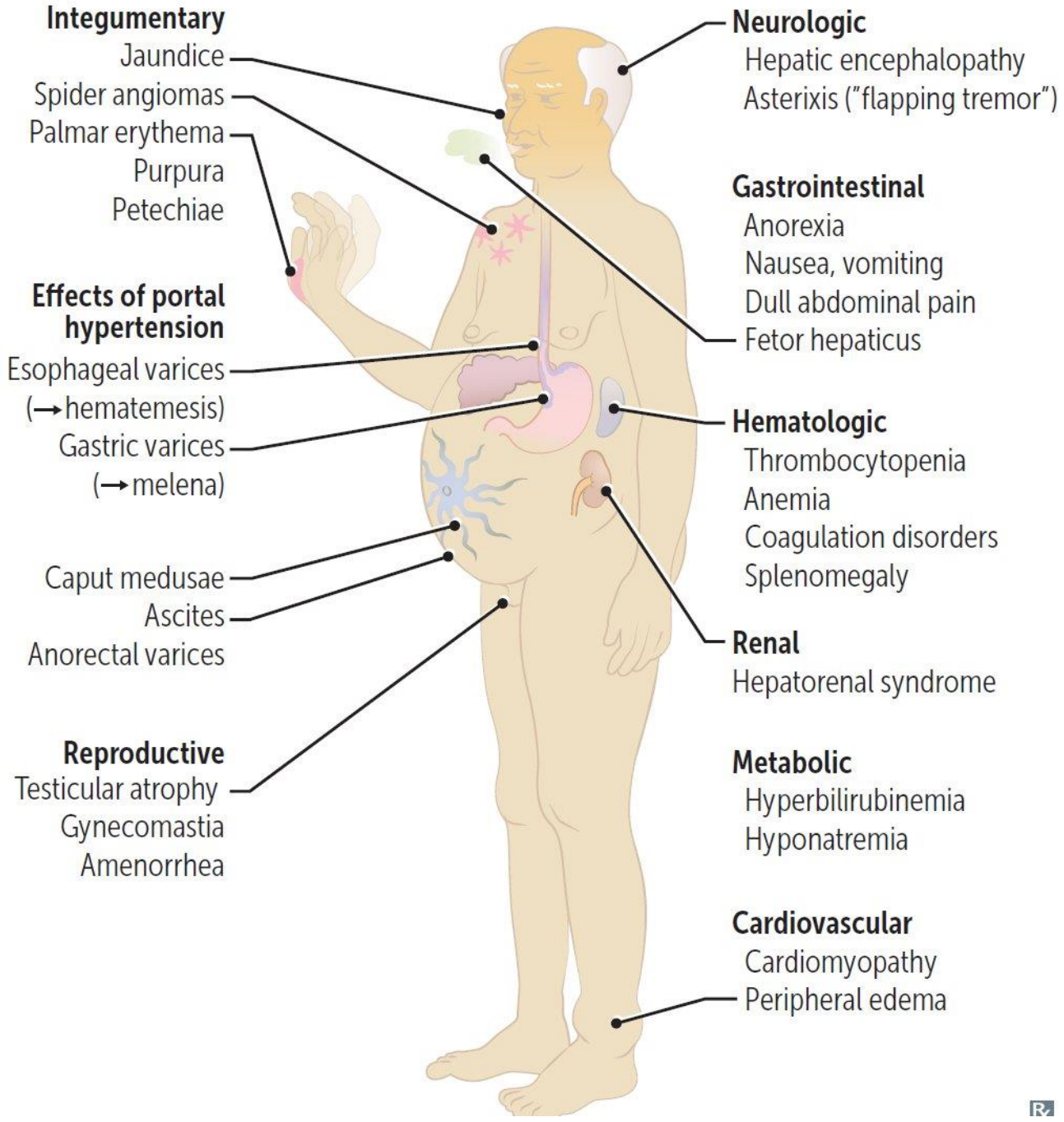
Alcoholic liver disease	History of alcohol abuse (duration, type and amount) you have to dig deep in the history and ask about the alcohol use.
Chronic hepatitis B and C	IV drug use, sexual contact, tattoos and remote blood transfusion, family history, vertical transmission, nail polishing (especially in females, need to use own equipment)
Primary sclerosing cholangitis (PSC)	Strong association with inflammatory bowel disease (UC or CD)
Hereditary hemochromatosis	Family history of cirrhosis
Wilson disease	Family or personal history of cirrhosis at **a young age** with jaundice, neurologic or psychiatric symptoms (may even affect speech)
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 (association not causation) 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** (functioning) or **decompensated** (not functioning so will have complications) cirrhosis.
- Can be **asymptomatic** (when compensated) or **symptomatic** (when decompensated) cirrhosis.
- Possible symptoms (not all need to be present): anorexia, weight loss, weakness, fatigue, muscle cramps, lower limb edema, diarrhea, easy bruisability (b/c not producing clotting factors: 10, 9, 7, 2), jaundice or pruritus (itching from bilirubin deposition in skin)
- 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**. You need to know the complications.
- In women, amenorrhea or irregular menstrual bleeding.
- In men with cirrhosis may develop hypogonadism (impotence, infertility, loss of sexual drive, and testicular atrophy).

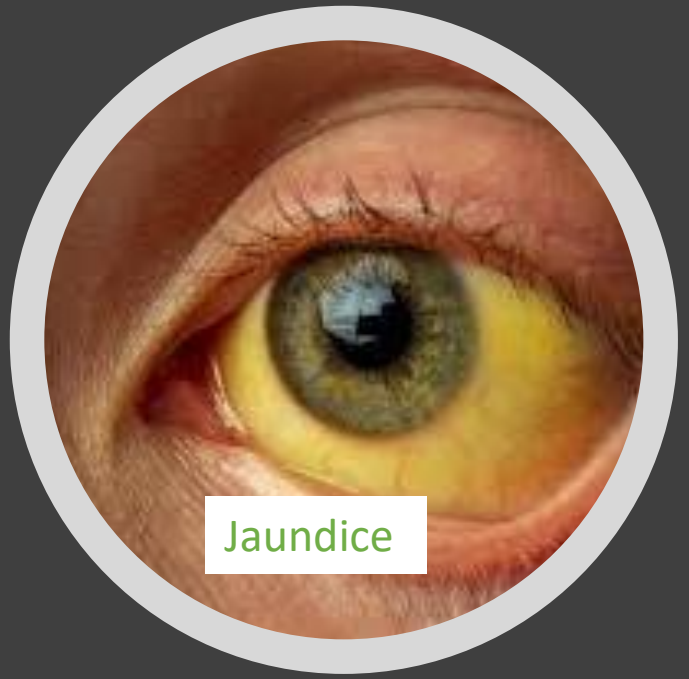
Clinical manifestations of Cirrhosis?

This picture summarizes the findings. You have to **know it** and keep it in your mind.



Clinical manifestations


Spider angiomata


Jaundice


Dupuytren's contractures


Lower limb edema


Ascites

Important Diagnostic Tests in Common Liver Diseases
(work up for patient with elevated liver enzymes)

Disease		Diagnostic Test
Hepatitis A (acute)		Anti-HAV IgM (remember IgM → acute, while IgG → previous infection)
Hepatitis B	**Acute**	HBsAg and anti-HBc IgM
	Chronic	HBsAg and HBeAg and/or HBV DNA → also used to screen pre-op.
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* -> to assess functionality not working
- Hyponatremia
- Elevated serum creatinine -> b/c of third spacing of fluid leads to renal problems “pre-renal”.

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:**

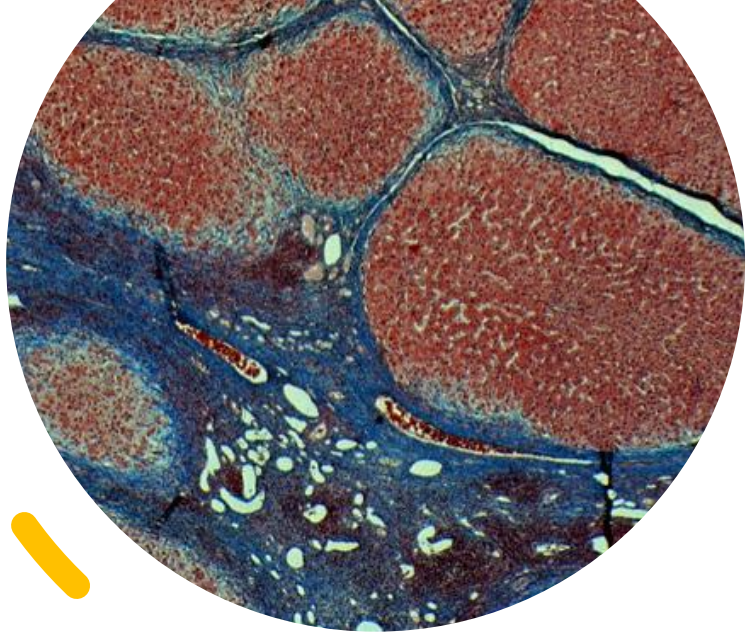
  Biopsy (histopathology)

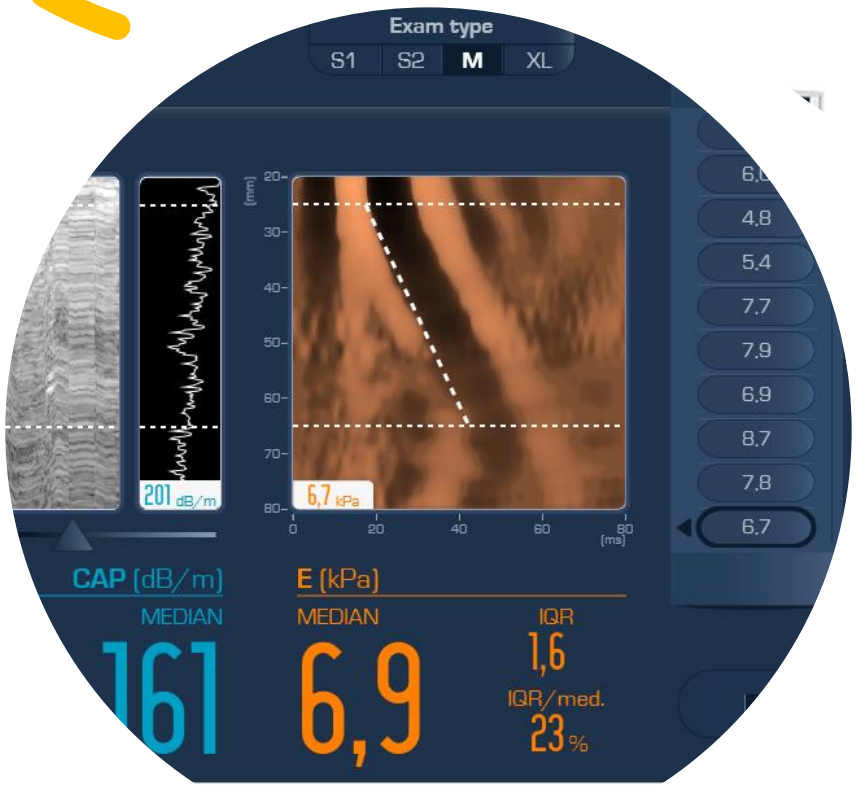
  Rarely done, if there it is helpful.

- **Noninvasive tests**

  Elastography (e.g fibroscan)

  Like US probe put on the liver and assess elasticity and fibrosis.





What is the course of cirrhosis?

Compensated Cirrhosis

Cirrhosis without symptoms

Usually incidental finding

Decompensated Cirrhosis

Cirrhosis with symptoms

(Any of the following):

1. Ascites
2. Bleeding Varices
3. Hepatic Encephalopathy
4. Jaundice

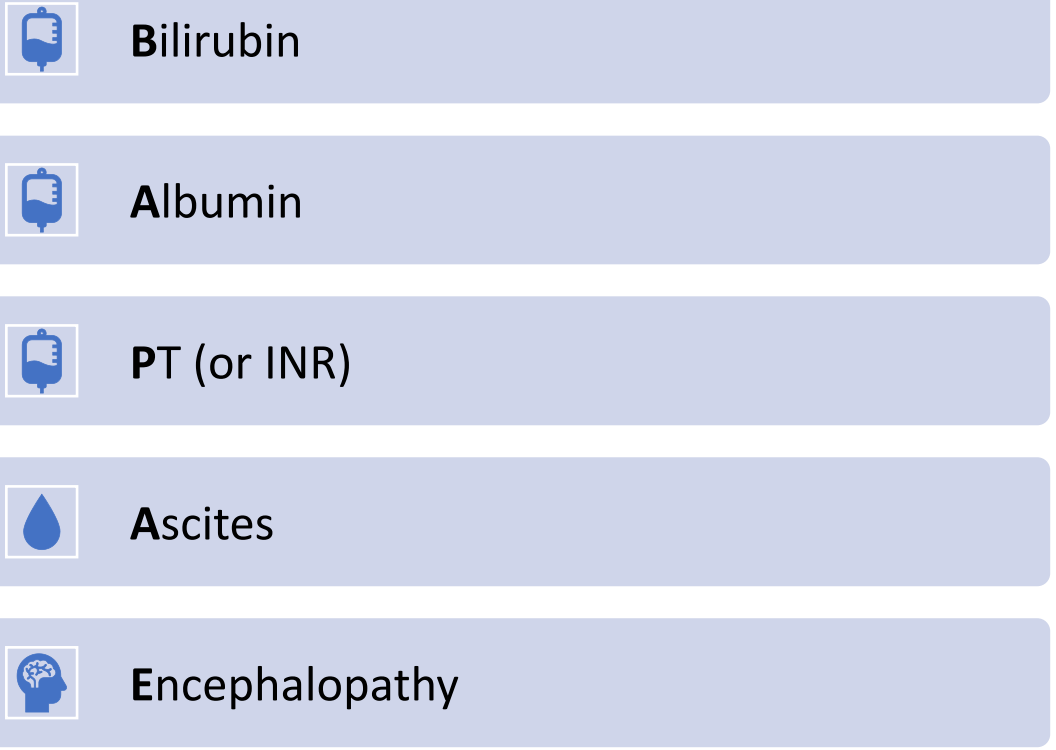
Severity & Prognosis of CLD (Important!)

How to assess severity & prognosis of CLD?

- We have multiple scoring systems. Why do we use them? To know the severity or prognosis.
- **Child–Pugh classification** very important and commonly used.
- **MELD score** (model for end-stage liver disease) we use it to assess the pt for liver transplant.

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)

- I don’t want you to memorise the numbers, just understand where they came from. And how we make up Child A, B, C.
- First look for ascites and score.
- Then check the bilirubin and albumin levels and score accordingly. Example if pt bilirubin level is 2.5 mg/dL we give them a score of 2.
- PT and INR are interchangeable so only use **ONE**. Usually **we use the INR**. This table is from an old study so it shows PT, but converted to INR now.
- Finally assess for encephalopathy.
- Add up the scores and identify class:
  - Class A: 5 – 6 points
  - Class B: 7 – 9 points
  - Class C: 10 – 15 points

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%.

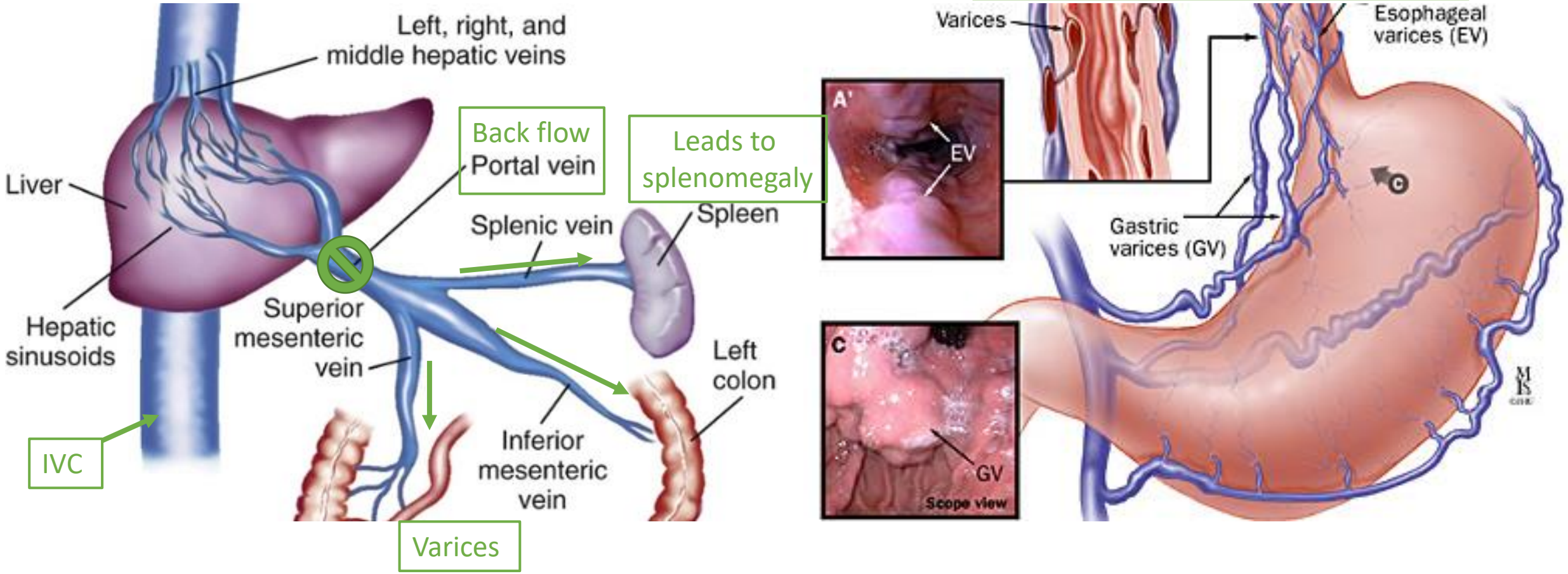
INR: international normalized ratio.

What are the common complications of Cirrhosis?

- **Variceal hemorrhage**
- **Ascites**
  - Spontaneous bacterial peritonitis (infection/bacteria in ascites fluid from translocation of gut bacteria into ascites)
  - Hepatic hydrothorax
  - Hepatorenal syndrome
- **Hepatocellular carcinoma (HCC)**
- **Hepatic encephalopathy**
- Pulmonary
  - Hepatopulmonary syndrome
  - Portopulmonary hypertension

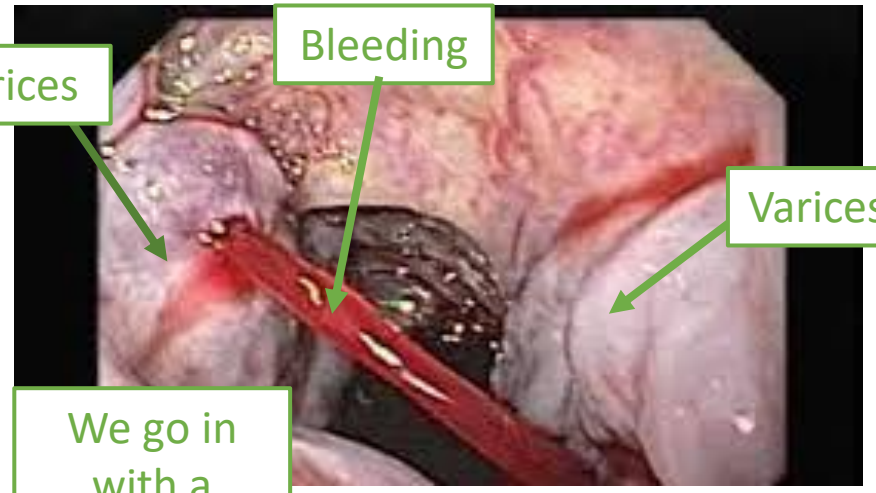
Portal hypertension

Varices are varicose veins of the esophagus but they bleed

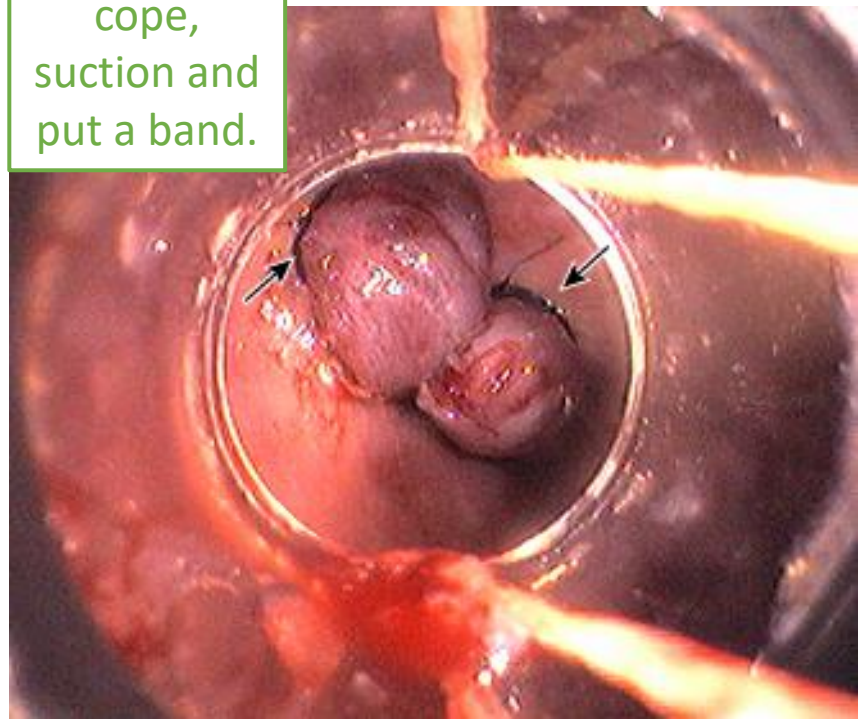


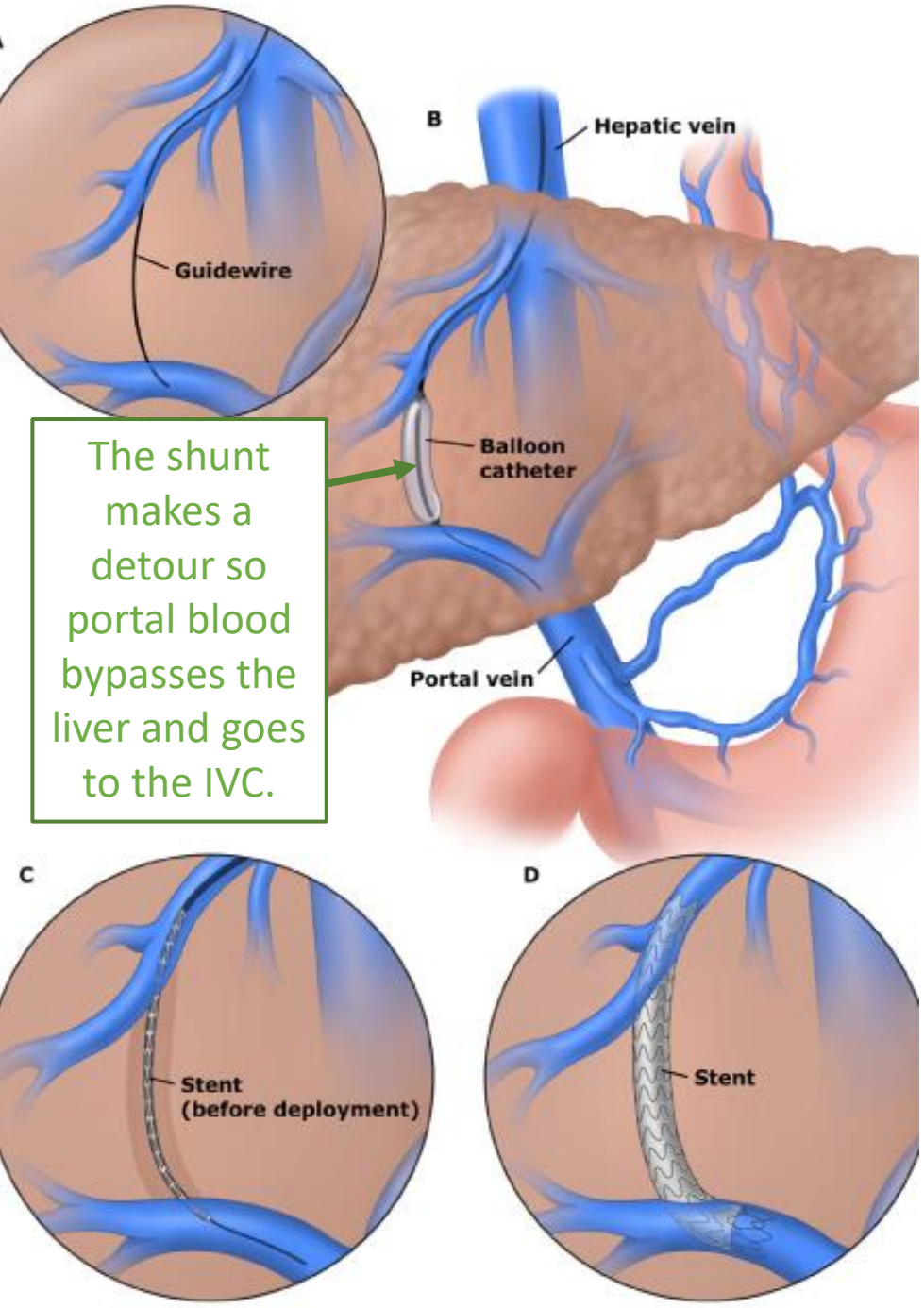
What is the management Variceal Bleeding? **We do all them together**

1. **Endoscopic treatment**(this is a hyperlink to watch the video on youtube) **= banding**
2. **Octereotide** -> decreases portal pressure which decreases the varices
3. **Antibiotics** -> we give antibiotics b/c we found pts that come in with cirrhosis and bleeding present with infection in the hospital (UTI, SBP) so we give antibiotic for 5 days.



We go in with a cope, suction and put a band.





The shunt makes a detour so portal blood bypasses the liver and goes to the IVC.

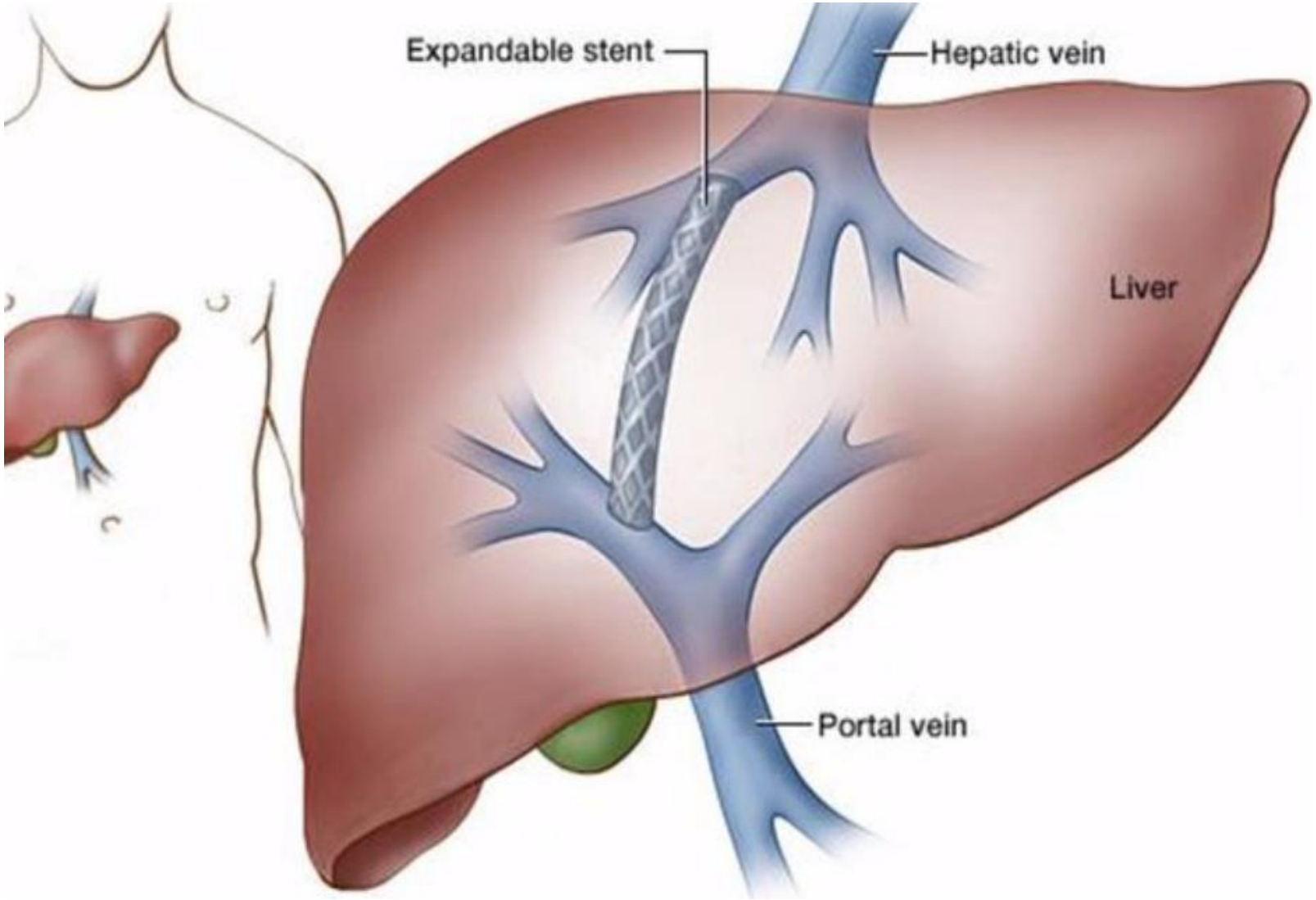
What if endoscopic therapy fails?

- TIPS (Transjugular Intrahepatic Portosystemic Shunt) – see the picture for explanation.
- Balloon Tamponade
- Surgery

When is TIPS also indicated?

- TIPS is indicated in:

1. Refractory Ascites (when you can't manage it even after giving them everything)
2. Uncontrolled variceal bleeding (Esophageal, Gastric)



TIPS

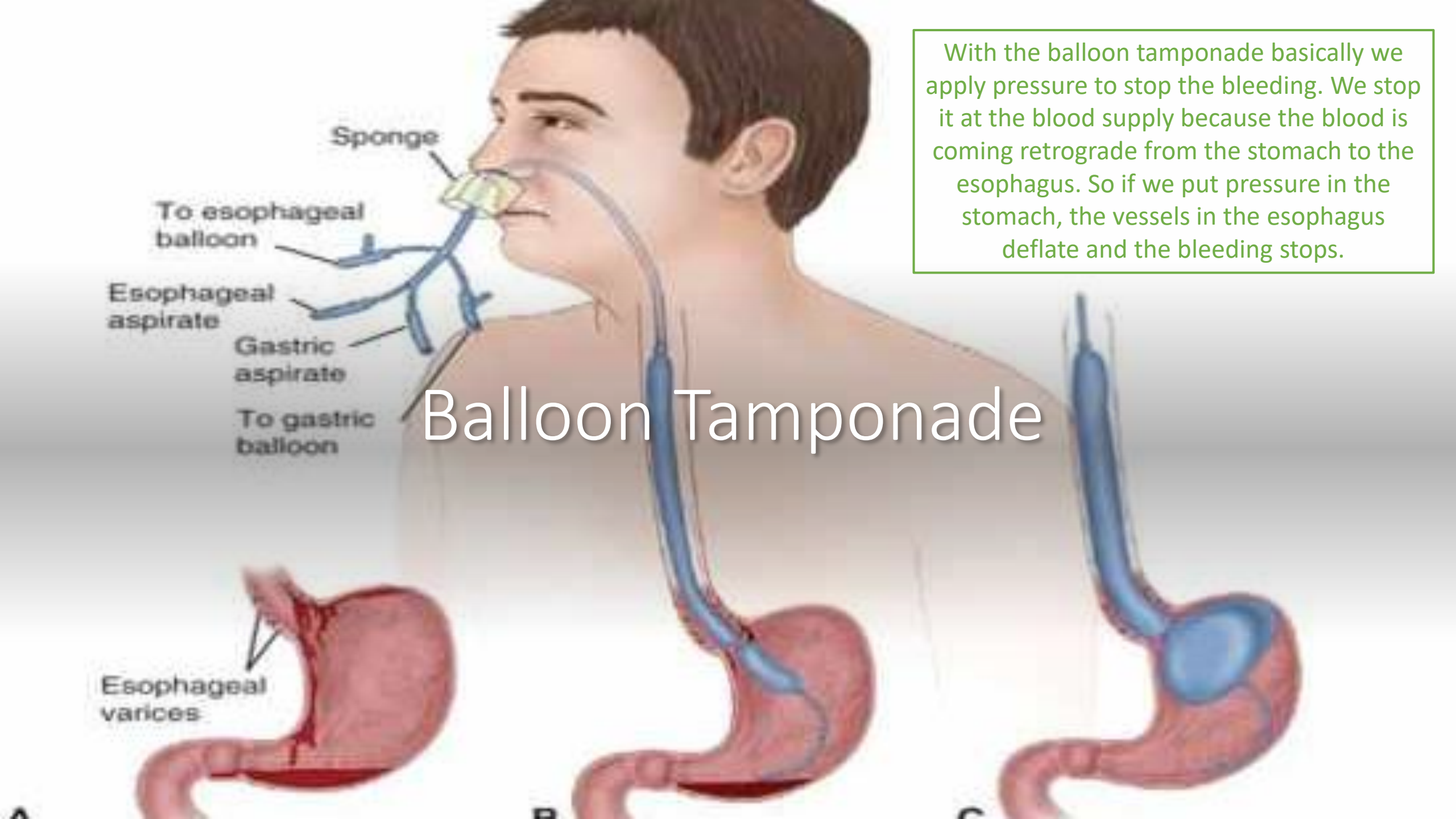
TRANSJUGULAR (enter through jugular)

INTRAHEPATIC (in the liver)

PORTOSYSTEMIC (porto- from portal vein , systemic – to the systemic circulation IVC.

SHUNT/stent

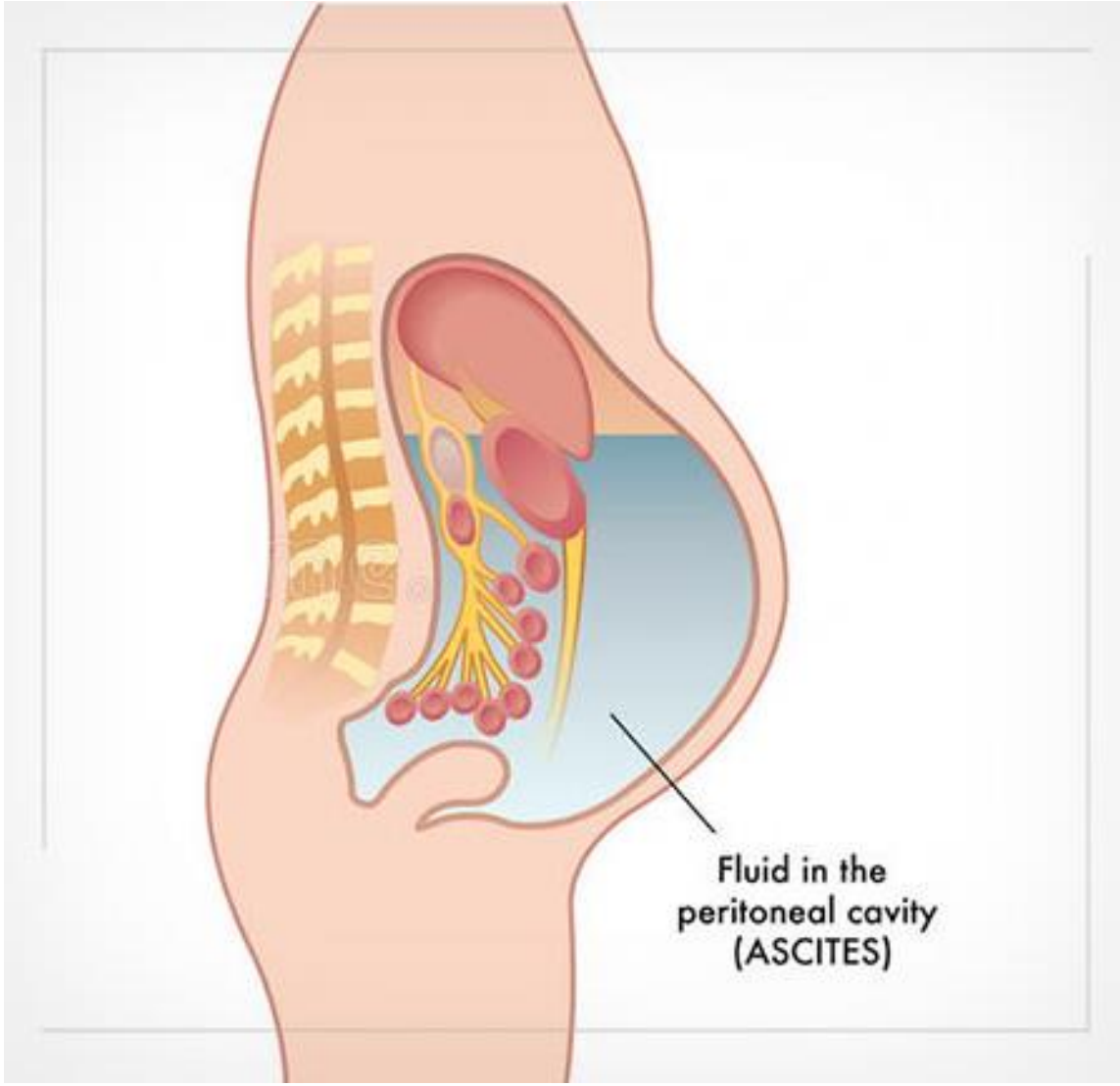
Balloon Tamponade



With the balloon tamponade basically we apply pressure to stop the bleeding. We stop it at the blood supply because the blood is coming retrograde from the stomach to the esophagus. So if we put pressure in the stomach, the vessels in the esophagus deflate and the bleeding stops.

Ascites

- Accumulation of fluid within the peritoneal cavity,
- 1500 ml of fluid must be present before flank dullness is detected clinically.
- 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 and if there is infection!

Ascitic Fluid Analysis

Routine tests on ascetic fluid:

1. Cell count and differential (see WBC + RBC)
2. Albumin
3. Total protein

Other *optional* tests: glucose*, LDH, Gram stain*, cultures* and amylase…etc.
*to see if there is infection

How to evaluate the cause of ascites?

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

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

SAAG (very important you have to memorise it)

≥ 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

Then we look at the **protein** to further differentiate between the causes:

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 Low b/c the liver is not producing	Pancreatitis TB	Nephrotic Syndrome Low b/c losing protein in urine
Budd-Chiari Syndrome		Cancinomatosis	

How do we treat ascites?

1. Salt Restriction (< 2g/day)

2. Diuretics (Furosemide [given to reduce potassium side effects of spironolactone] and Spironolactone)

3. Paracenthesis +/- albumin - if you exceed a certain amount you give albumin replacement.

4. TIPS

Spontaneous Bacterial Peritonitis (SBP)

How do we diagnose SBP?

- Do paracentesis and asses ascitic fluid polymorphonuclear leukocyte (**PMN**) (neutrophils) count **≥ 250 cells**/mm^3
- Usually **one** organism (gram negatives) - E-coli or klebsiella , others: enterococcus, pseudomonas (mnemonic: KEEPs)
- *If **multiple** organisms think of secondary peritonitis* (perforation of colon and bacteria enters the ascites)

- **How to treat SBP?** (we use **both**)
  1. Antibiotics
  2. Albumin – it reduces mortality in SBP.

Hepatic encephalopathy (HE)

What is Hepatic encephalopathy (HE)?

Just understand what it means, don't memorise.

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

Accumulation of ammonia b/c liver can't convert it to ammonium.

HE is characterized by cognitive deficits (patient sleepy or disoriented) and impaired neuromuscular function (from disorientation & asterixis* to coma)

*Asterixis occurs because there is milliseconds of sleep pattern in the brain b/c of accumulation of toxins.

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 (eating more meat), *GI bleeding,* ***infection***, electrolyte disturbances such as hypoK, ***constipation*** *(very important cause!)* or metabolic alkalosis)
- **Dehydration**, like in elderly pts (e.g. vomiting, diarrhea, hemorrhage or diuretics – more than prescribed)
- **Vascular occlusion** (i.e. hepatic or portal vein thrombosis)
- **Hepatocellular carcinoma (HCC)**

Treatment of HE

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

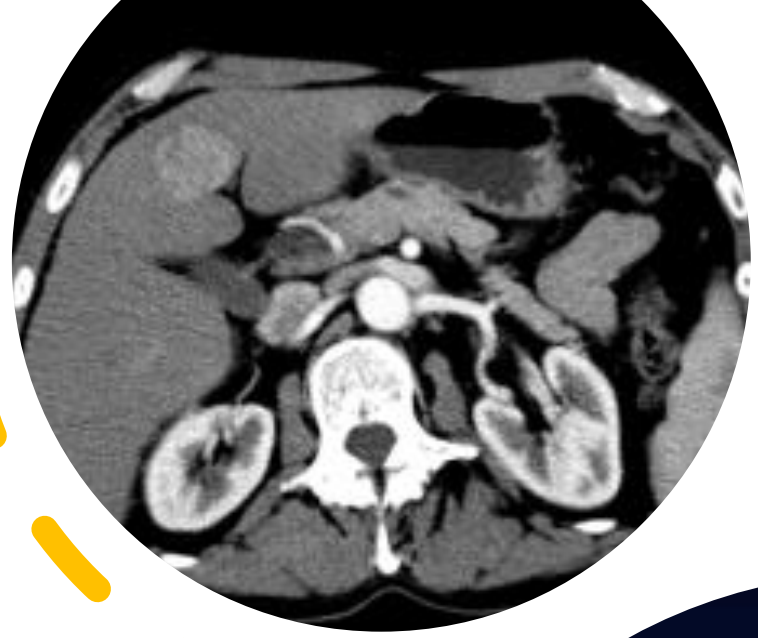
Lactulose is the first choice (or rifaximin: non-absorbable antibiotic so only act in gut)

Lactulose is a laxative that draws ammonia out (يطلعه).
Pts start to pass at least 3 bowel movements per day, and once they pass stool and ammonia leaves the body they start waking up and concentrating and talking to you.

Tests to diagnose HCC

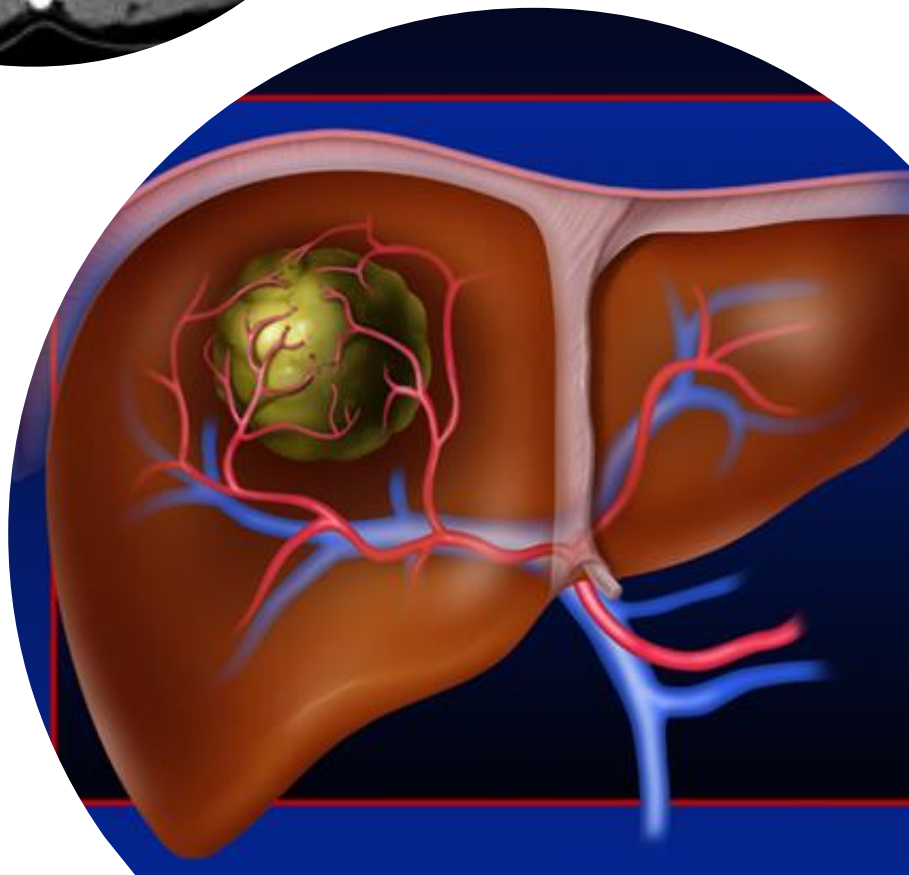
- Blood tests (AFP) you can use this but Us is the most important one.
- Radiology (most important)
- Biopsy (not routinely done)

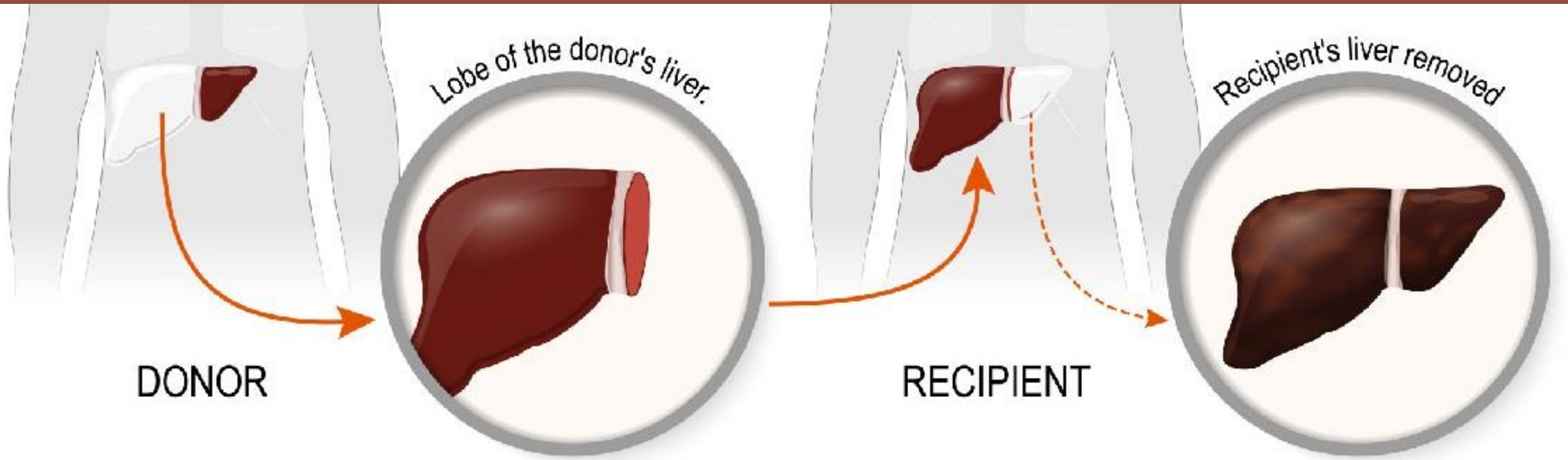
Rule of thumb: any patient with cirrhosis need US every 6 months to screen for HCC!!!



Treatment options for HCC

- Surgical (resection or liver transplantation)
- Ablation
- Embolization – go into vein and inject material which embolizes and strangulate the cancer.
- Chemotherapy
- Palliative





Liver Transplantation

Liver transplantation is the **definitive treatment** for patients with cirrhosis.

You can stabilize the patient and get him to compensate and monitor them, but you still need to refer them to liver transplant team so that if someday he decompensates, they already know the case.

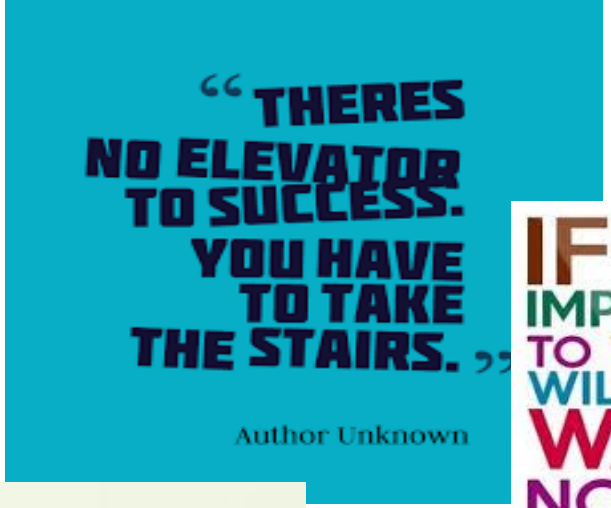
These are the important concepts that you have to understand them and memorise them.

Summary & important points

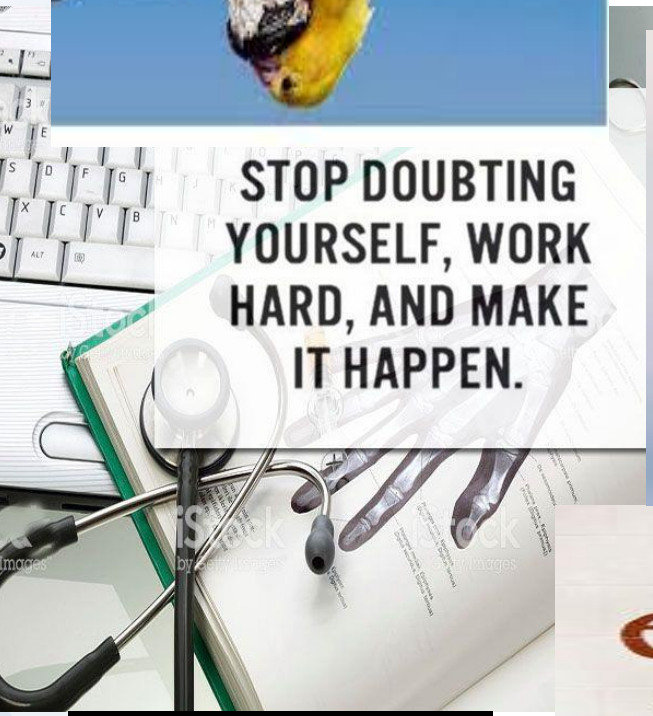
- Determine the cause of CLD and treat if possible (so if pt has NASH try to control DM, obesity etc..), Prevent further insult (Vaccinations, avoid hepatotoxic medications & alcohol), Prevent and treat complications.
- Most common ***complications*** of CLD are: **Variceal bleeding, Ascites, Hepatic 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.

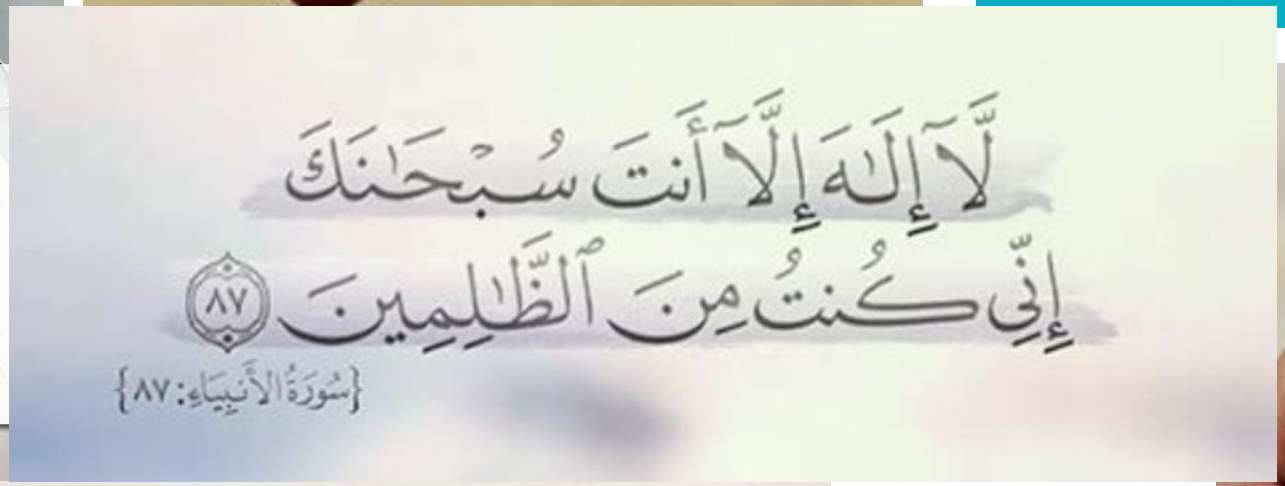

Where there's a will, There's a way!


وتوكل على الله
وكفى بالله وكيلا


“THERES NO ELEVATOR TO SUCCESS. YOU HAVE TO TAKE THE STAIRS.”
Author Unknown


IF IT IS IMPORTANT TO YOU, YOU WILL FIND A WAY. IF NOT, YOU WILL FIND AN EXCUSE.


STOP DOUBTING YOURSELF, WORK HARD, AND MAKE IT HAPPEN.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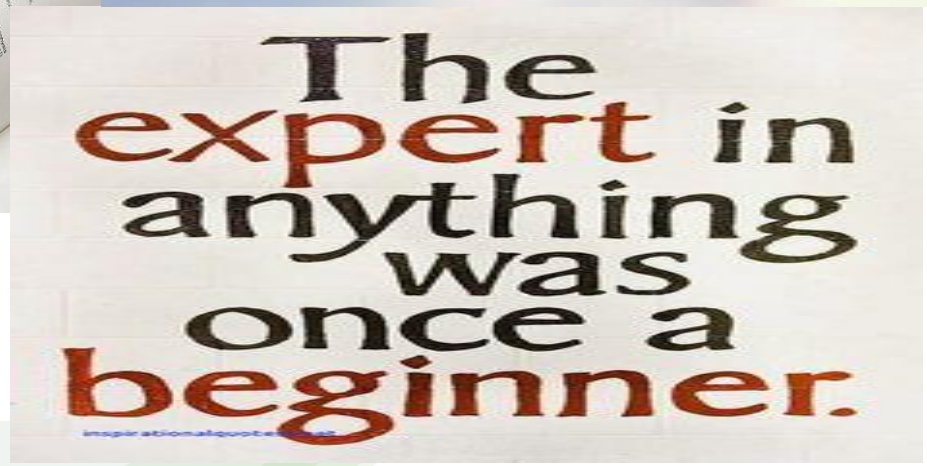
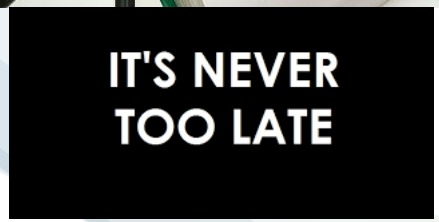
I can't do it


The expert in anything was once a beginner.


CHANGE


A MISTAKE IS SUCCESS IN PROGRESS


IT'S NEVER TOO LATE