

جامعة  
الملك سعود  
King Saud University



# Liver Cirrhosis and its Complications

MED341

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# Objectives

- To understand cirrhosis, definition , causes and complications
- To know pathophysiology of cirrhosis complications
- To known how to approach patient with cirrhosis and its complications

# Spectrum of Liver Inflammation

Acute  
Hepatitis

Chronic injury  
e,g HBV, HCV ,  
NASH , AIH

Death  
Or  
Transplantation

Chronic hepatitis

Compensated  
Cirrhosis

Decompen  
sated  
cirrhosis

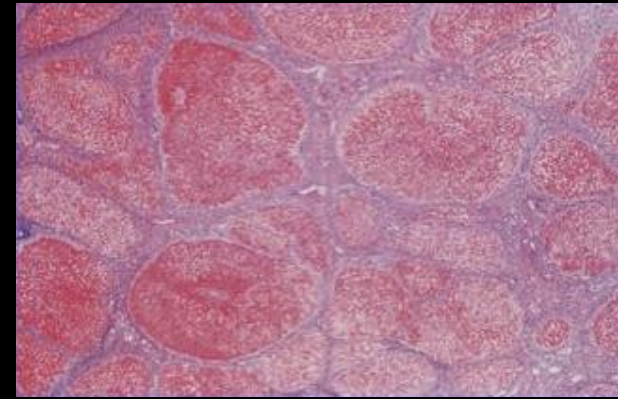
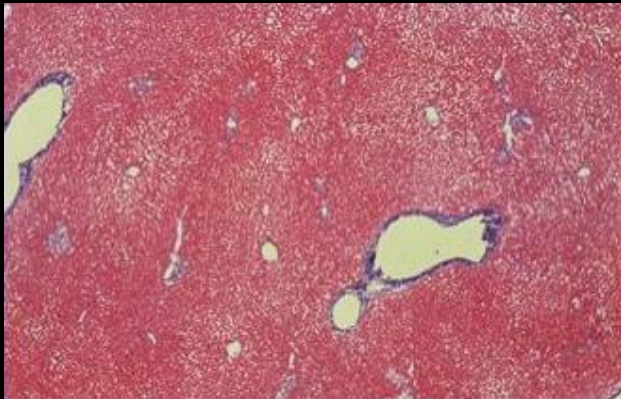
Cirrhosis  
complications;  
ascites, HE, HCC..etc

Progress (years)

Regression (some after Rx the cause )

Days -weeks

**Cirrhosis:** Late stage of chronic liver inflammation and fibrosis, in which liver parenchyma is distorted and replaced by fibrous tissue and regenerating nodules.

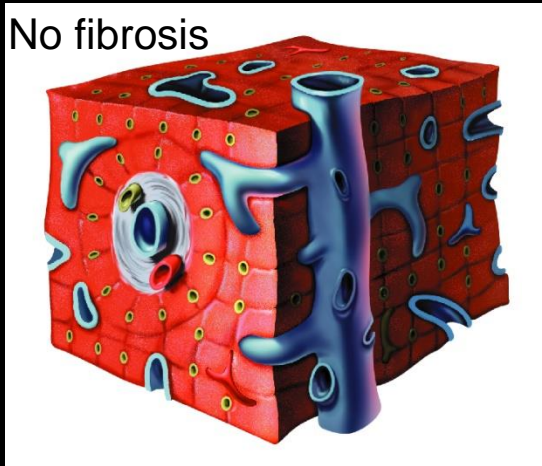


**NORMAL LIVER**

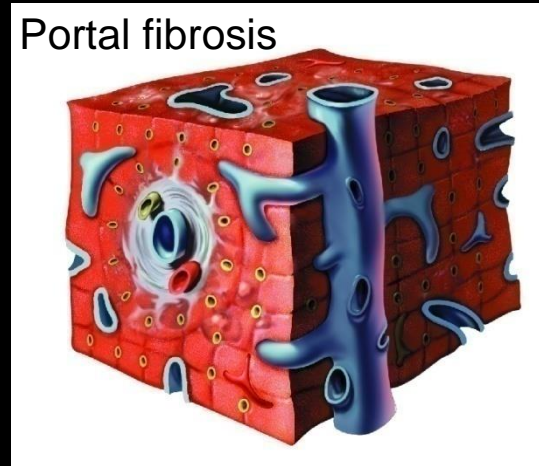
**CIRRHOTIC LIVER**

# Histologic Staging

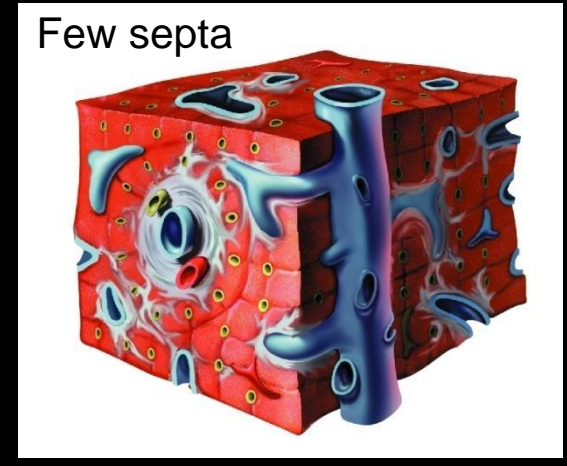
Stage 0



Stage 1



Stage 2



Stage 3



Stage 4



# Pathophysiology

- Irreversible chronic injury of the hepatic parenchyma
- Extensive fibrosis - distortion of the hepatic architecture
- Formation of regenerative nodules
- Portal hypertension
- Vascular and humoral changes

# Causes of Cirrhosis

## Commonest

- Viral (HBV+- HDV, HCV)
- NASH
- ASH

## Other causes

- Autoimmune  
(AIH, PBC, PSC)
- Metabolic & Hereditary  
WD, A1AT, HH
- Vascular  
BCS, HF
- Biliary  
SC
- Drugs
- Others (polycystic disease,  
granulomatous disease....)

How to approach patient  
with Cirrhosis?



- Symptoms
- Signs
- Lab
- Management

# Clinical manifestations

- No symptoms (Most patients in early cirrhosis)
- 

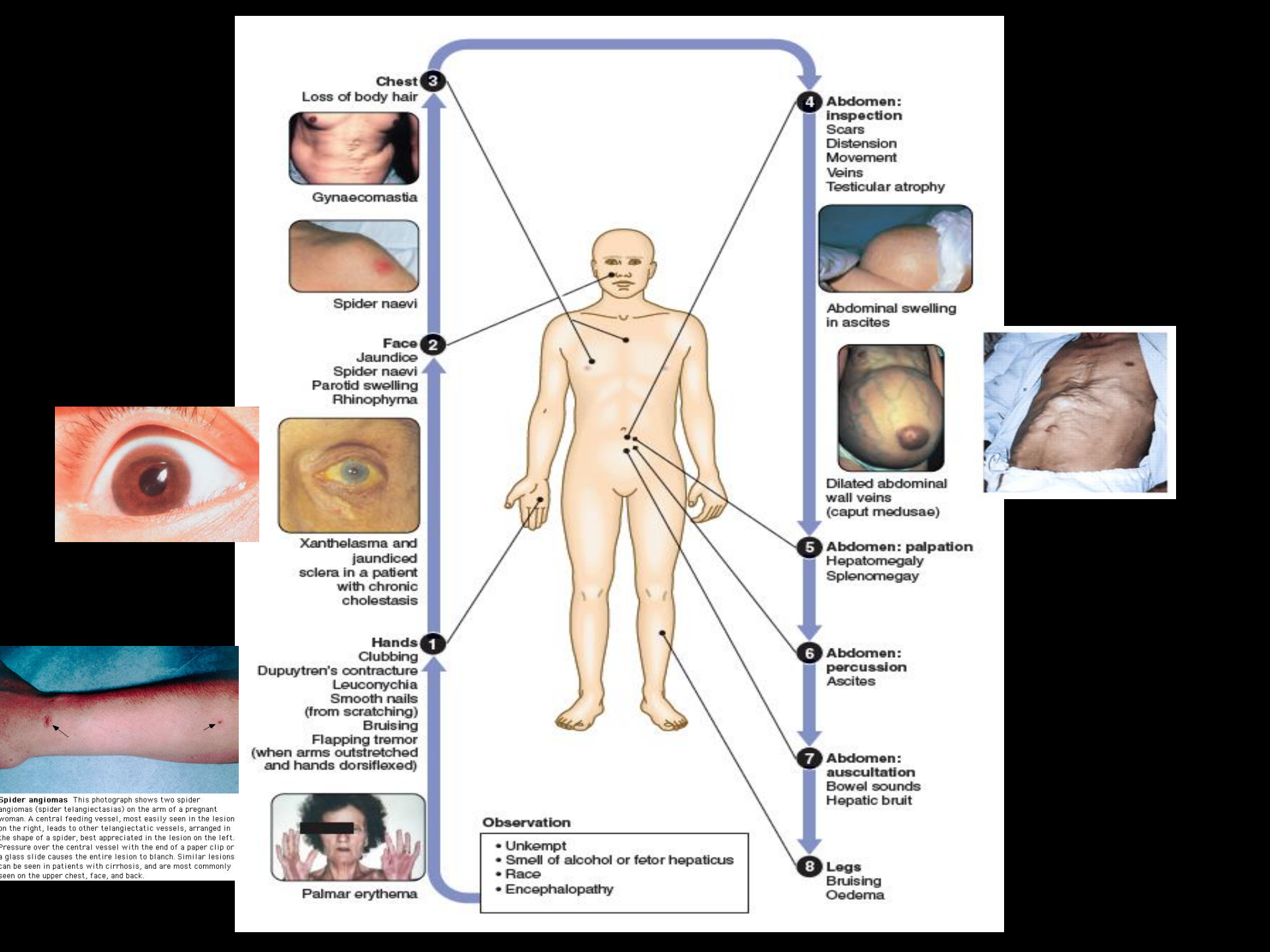
- Symptoms of cirrhosis (sometimes non-specific sx)
- Symptoms of decompensations (when liver start to fail.)

# History

Presenting symptoms	Past and drug History	Family history	Social history
<p>1-Asymptomatic</p> <p>2-Nonspecific constitutional symptoms, such as fatigue, weakness, and weight loss, etc.)</p> <p>3-Symptoms of decompensation</p> <ul style="list-style-type: none"> <li>-abdominal distension due to ascites and hepatomegaly,</li> <li>-coffee-ground vomitus and black stool (melena) secondary to GI hemorrhage</li> <li>-altered mental status in hepatic encephalopathy</li> <li>-lower extremity swelling</li> <li>-jaundice, and pruritus.</li> </ul> <p>Other less common symptoms: respiratory (pulmonary hypertension, hepatic hydrothorax..)</p>	<p>History of liver disease (all chronic liver disease can lead to cirrhosis)</p> <p>Surgery and dental</p> <p>Metabolic syndrome</p> <p>Drugs (MTX, amiodarone, amoxicillin/clavulanate etc..)</p>	<p>Wilson</p> <p>Hemochromatosis</p> <p>Alpha-antitrypsin</p> <p>Viral hepatitis</p>	<p>Risk-taking behaviors: IV drug use, sexual contact, and tattoos.</p> <p>Alcohol (amount type duration)</p> <p>Travel</p>

# Clinical Features

Hand and nail features:	Facial features	Chest wall features	Abdominal features
Clubbing	Muscle wasting	Gynecomastia in men	Collateral
Leukonychia	Telangiectasia	Telangectasia	Bruising
Palmar erythema	Bruising		Hepatomegaly
Bruising	Parotid gland swelling		Splenomegaly
Cholesterol deposits	Jaundiced sclerae		Abdominal distension
Dupuytren contracture	Xanthelasma		Hepatic bruit
Cyanosis (in patients with hepatopulmonary syndrome).			Loss of secondary Sexual hair
			Testicular atrophy in men.



**3 Chest**

Loss of body hair  
Gynaecomastia



**2 Face**

Jaundice  
Spider naevi  
Parotid swelling  
Rhinophyma



Xanthelasma and jaundiced sclera in a patient with chronic cholestasis

**1 Hands**

Clubbing  
Dupuytren's contracture  
Leuconychia  
Smooth nails (from scratching)  
Bruising  
Flapping tremor (when arms outstretched and hands dorsiflexed)



Palmar erythema

**4 Abdomen: inspection**

Scars  
Distension  
Movement  
Veins  
Testicular atrophy



Abdominal swelling in ascites



Dilated abdominal wall veins (caput medusae)

**5 Abdomen: palpation**

Hepatomegaly  
Splenomegaly

**6 Abdomen: percussion**

Ascites

**7 Abdomen: auscultation**

Bowel sounds  
Hepatic bruit

**8 Legs**

Bruising  
Oedema

**Observation**

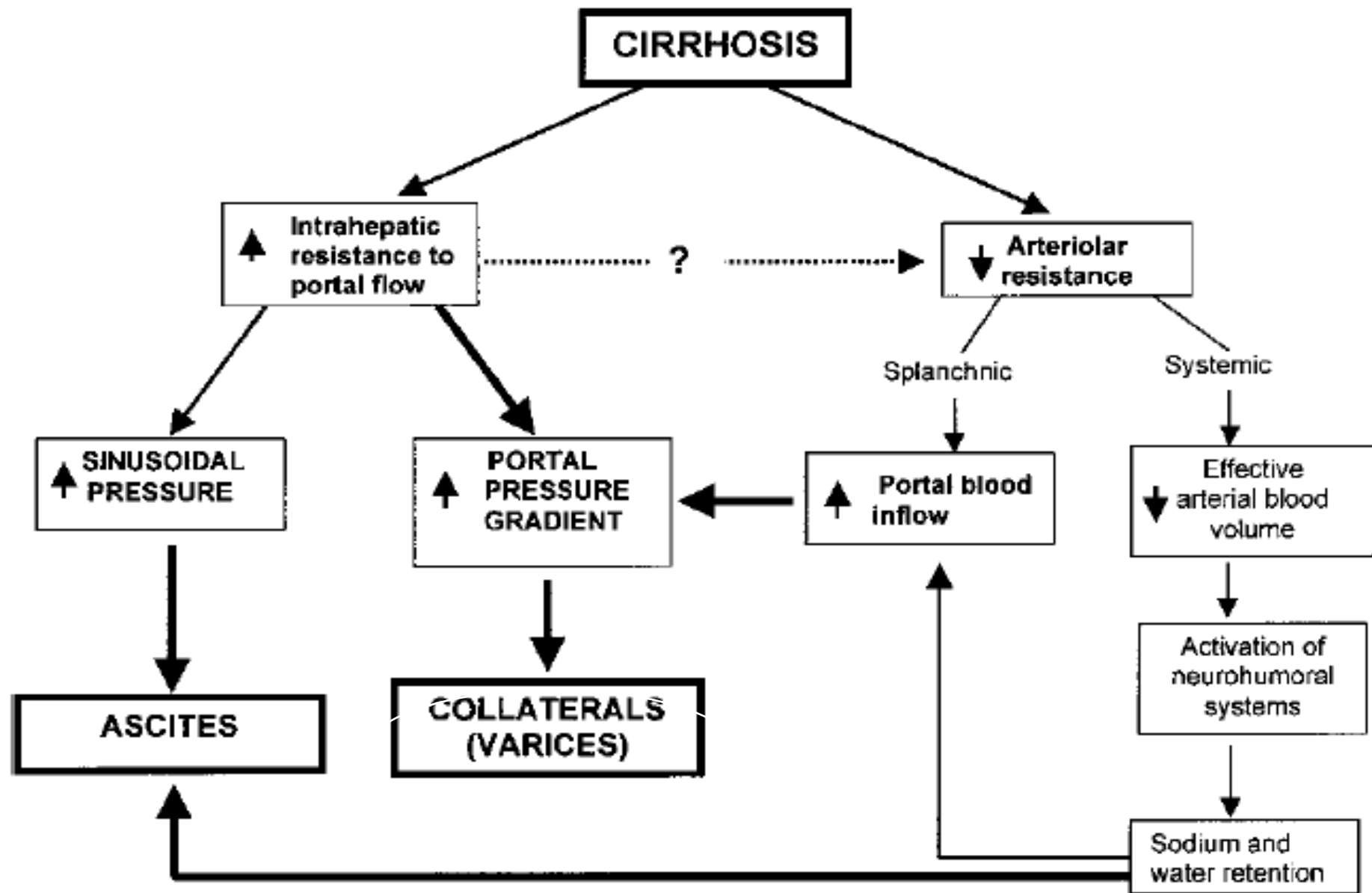
- Unkempt
- Smell of alcohol or fetor hepaticus
- Race
- Encephalopathy



**Spider angiomas** This photograph shows two spider angiomas (spider telangiectasias) on the arm of a pregnant woman. A central feeding vessel, most easily seen in the lesion on the right, leads to other telangiectatic vessels, arranged in the shape of a spider, best appreciated in the lesion on the left. Pressure over the central vessel with the end of a paper clip or a glass slide causes the entire lesion to blanch. Similar lesions can be seen in patients with cirrhosis, and are most commonly seen on the upper chest, face, and back.

# Common Cirrhosis Complications

- Variceal hemorrhage
- Ascites
  - Ascites +/- refractory ascites
  - Spontaneous Bacterial Peritonitis
  - Hepatic hydrothorax
  - Hepatorenal syndrome
- Hepatocellular carcinoma
- Hepatic Encephalopathy
- Pulmonary
  - Hepatopulmonary syndrome
  - Portopulmonary HTN



**Figure 1.** Pathogenesis of portal hypertension and its two main complications: varices and ascites.

# Investigations in cirrhosis

Lab Test	Radiology
Moderately elevated aminotransferases (often with an AST:ALT ratio >1)	Surface nodularity
Elevated ALP (2 to 3 times the ULN)	Increased echogenicity (ultrasound)
<b>Thrombocytopenia</b>	Atrophy of the right lobe
Leukopenia/neutropenia	Hypertrophy of the caudate or left lobes
Anemia	Small, nodular liver*
<u>Low serum albumin*</u>	Ascites*
Prolonged prothrombin time/elevated INR*	Hepatocellular carcinoma*
<b>Hyperbilirubinemia*</b>	Portal/splenic/superior mesenteric vein thrombosis*
Hyponatremia*	Portosystemic collaterals*
Elevated serum creatinine*	

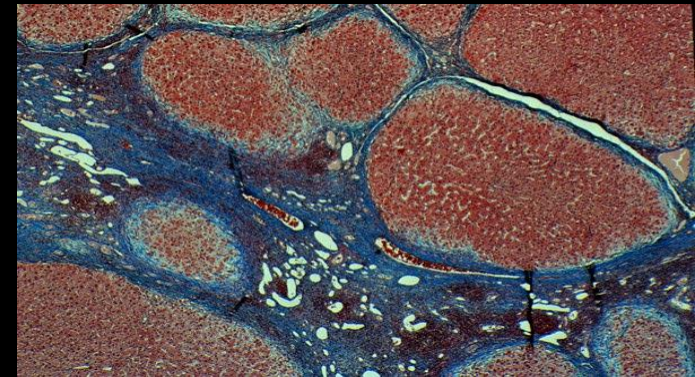
\* With advanced disease



# Diagnosis confirmation?

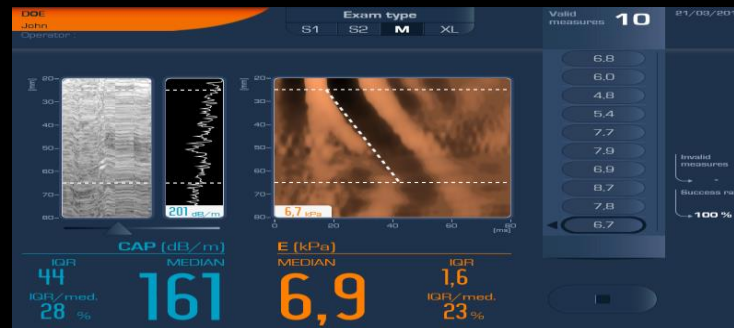
*To confirm and support the clinical and radiologic manifestations if needed*

## 1-Biopsy (histology)



## 2-Noninvasive tests

- Serum score systems
- Elastography (e.g fibroscan)



# How to assess severity & prognosis?

☐ Child–Turcotte–Pugh score or Child Criteria (CPT score)...see table

☐ MELD score

(model for end-stage liver disease)

- MELD = 3.8[serum bilirubin (mg/dL)] + 11.2[INR] + 9.6[serum creatinine (mg/dL)] + 6.4

☐ others

# CPT score for classification of Cirrhosis severity

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)
PT (Seconds over control) or INR	<4 <1.7	4 to 6 1.7 to 2.3	>6 >2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

Score	Class	1-2 Year survival
5-6	A	100-85%
7-9	B	80-60%
10-15	C	45-35%

# ASCITES



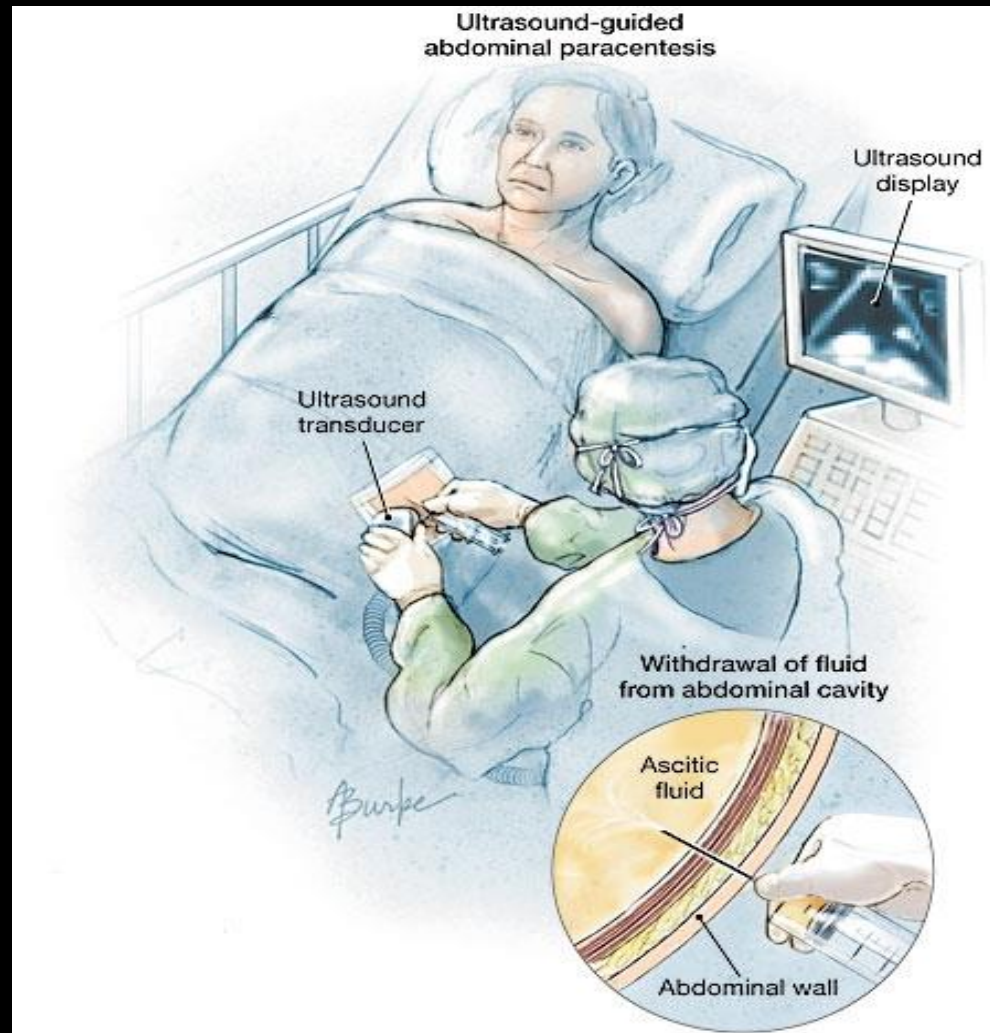
# Ascites

- Accumulation of fluid within the peritoneal cavity
- 1,500 mL of fluid must be present before flank dullness is detected.
- Shifting dullness: 83% sensitivity and 56% specificity in detecting ascites.
- If no flank dullness is present less likely ascites (< 10%).
- Ascites:
  1. 85% of due to cirrhosis
  2. 15% other causes

# Ascites

- Most common complication of cirrhosis
- First step in development of ascites is the presence of significant portal HPN
- Poor prognosis (unless Liver Tx)
  - Two-year survival of patients with ascites is approximately 50%

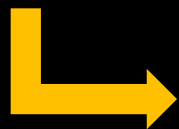
Any new ascites should be tapped and analyzed!



# Ascitic Fluid Analysis

ROUTINE	OPTIONAL (WHEN THERE IS SUSPICION OF INFECTION)	UNUSUAL	UNHELPFUL
Cell count and differential	Culture in blood culture bottles	AFB smear and culture	pH
Albumin	Glucose	Cytology	Lactate
Total protein	Lactate dehydrogenase	Triglyceride	Cholesterol
	Amylase	Bilirubin	Fibronectin
	Gram's stain		Glycosaminoglycans

Abbreviation: AFB, acid-fast bacteria. \*Adapted from Runyon.<sup>17</sup> Reprinted with permission from Saunders Elsevier.



Measure **SAAG**



# Serum-to-Ascites Albumin Gradient (SAAG)

## High SAAG $\geq 1.1$ g/dL

- Cirrhosis
- Heart failure/constrictive pericarditis
- Alcoholic hepatitis
- Budd chiari
- Massive hepatic metastases

## Low SAAG $< 1.1$ g/dL

- Peritoneal carcinomatosis
- Peritoneal tuberculosis
- Secondary peritonitis
- Pancreatitis
- Serositis
- Nephrotic syndrome

# Initial treatment of ascites

- 1-Dietary sodium restriction
  - Limiting sodium intake to 88 meq (2000 mg) per day
- 2-Diuretics (most successful therapeutic regimen is the *combination* of Spironolactone and Furosemide)
  - Monitor electrolytes and kidney function
- Discontinue non-steroidal anti-inflammatory drugs
- Rx of underlying cause
- Evaluation for liver transplantation

# Refractory Ascites



- ~10%

Ascites that:

- Unresponsive to sodium-restricted diet and high dose diuretic treatment

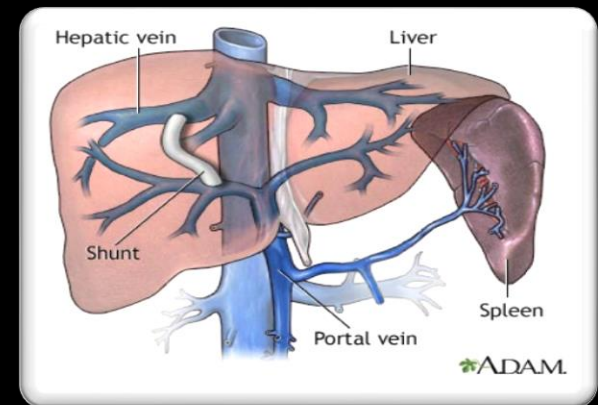
(400 mg per day of spironolactone and 160 mg per day furosemide), or

- Development of clinically significant complications of diuretics

, e.g., encephalopathy, serum creatinine greater than 2.0 mg/dL, serum sodium less than 120 mmol/L, or serum potassium greater than 6.0 mmol/L

# Management Lines

- Serial therapeutic paracenteses (LVP)  
+albumen (if draining > 5 L of fluid).
- Liver transplantation
- Transjugular intrahepatic portosystemic stent-shunt (TIPS)
- Peritoneovenous shunt



# Spontaneous Bacterial Peritonitis (SBP)

- Infection of ascitic fluid
  - the 3 most common isolates: Escherichia coli, Klebsiella pneumoniae, and Streptococcal pneumoniae
- Clinical manifestations: (all, some, sometimes-none)
  - Fever
  - Abdominal pain
  - Abdominal tenderness
  - Altered mental status

# SBP

- The diagnosis is established by
  - PMN count ( >250 cells/mm<sup>3</sup>)
  - A positive ascitic fluid bacterial culture

## Rx

- Antibiotics:

Cefotaxime or a similar ***third-generation cephalosporin*** -treatment of choice for suspected SBP; it used to cover 95% of the flora including the common organisms

- Albumin

# Hepatorenal syndrome

## **Acute renal failure (Functional) – usually Cirrhosis with ascites**

- Dx by exclusion (NB: minority of azotemia is not due HRS)
- 2 types
  - Type I: rapid, aggressive
  - Type II : slow, less aggressive
- Rx
  - Correct underlying cause
  - Albumin
  - Vasoconstrictors (Terlipression, octeriotide, midodrine, epinephrine)
  - HD
  - Liver Tx

# Hepatic Hydrothorax

- Pleural effusion in a patient with cirrhosis and no evidence of underlying cardiopulmonary disease.
- 5-10% of cirrhosis patients.
- Cause: movement of ascitic fluid into the pleural space through defects in the diaphragm.
- Commonly Rt side
- Dx
  - reveals a transudative fluid
  - serum to fluid albumin gradient greater than 1.1
- Management similar to ascites



# Hepatopulmonary syndrome (HPS)

Triad:

- Liver disease (liver disease, portal hypertension, or portosystemic shunts)
- Increased alveolar-arterial gradient while breathing room air
- Evidence for intrapulmonary vascular abnormalities, referred to as intrapulmonary vascular dilatations (shunting)

-Mild hypoxemia is common w/o HPS (ascites)

# Portopulmonary HTN

- Refers to the presence of pulmonary hypertension in the coexistent portal hypertension
- Prevalence in cirrhotic patients is approximately 2%
- Diagnosis:
  - Suggested by echocardiography
  - Confirmed by right heart catheterization

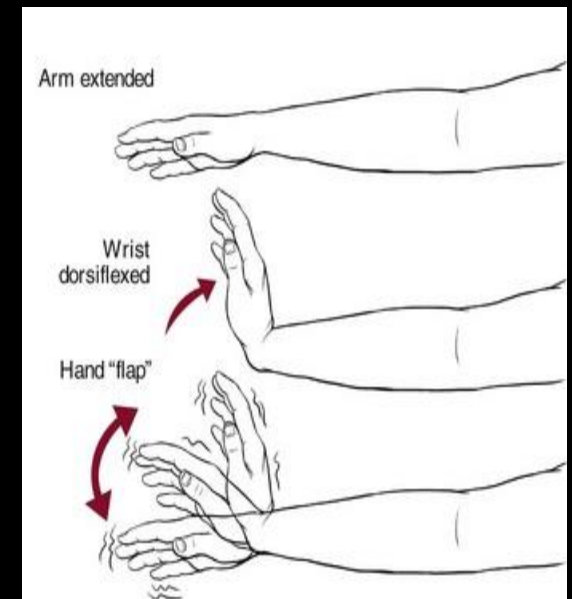
# Hepatic encephalopathy (HE)

# Definition of HE

- Hepatic encephalopathy is a brain dysfunction caused by liver insufficiency and/or PSS
- It manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma.

## Grading system for hepatic encephalopathy

Grade	Mental status	Asterixis	EEG
I	Euphoria/depression	Yes/no	Usually normal
	Mild confusion		
	Slurred speech		
	Disordered sleep		
II	Lethargy	Yes	Abnormal
	Moderate confusion		
III	Marked confusion	Yes	Abnormal
	Incoherent		
	Sleeping but arousable		
IV	Coma	No	Abnormal



# Pathophysiology of HE

## Different mechanisms

- Neurotoxin (ammonia)
- Blood-to-brain transport of neurotransmitter
- → activation of inhibitory (gamma-aminobutyric acid, serotonin) neurotransmitter systems
- → impairment of excitatory (glutamate, catecholamines) neurotransmitter systems
- enhanced neural inhibition

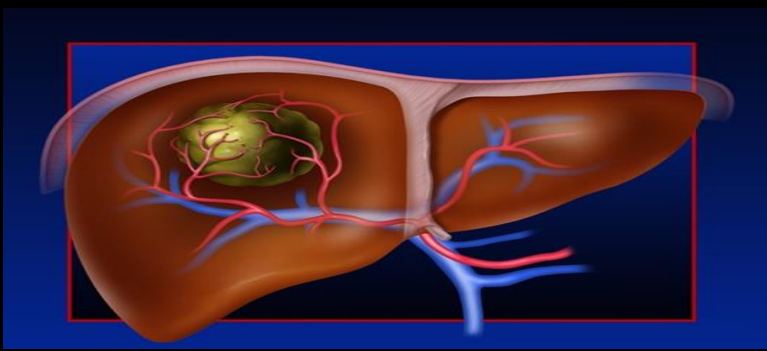
# Precipitants of hepatic encephalopathy in patients with cirrhosis

- **Drugs**
  - Benzodiazepines
  - Narcotics
  - Alcohol
- **Increased ammonia production, absorption or entry into the brain**
  - Excess dietary intake of protein
  - Gastrointestinal bleeding
  - Infection
  - Electrolyte disturbances such as hypokalemia
  - Constipation
  - Metabolic alkalosis
- **Dehydration**
  - Vomiting
  - Diarrhea
  - Hemorrhage
  - Diuretics
  - Large volume paracentesis
- **Portosystemic shunting**
  - Radiographic or surgically placed shunts
  - Spontaneous shunts
- **Vascular occlusion**
  - Hepatic vein thrombosis
  - Portal vein thrombosis
- **HCC**

# Rx

- Identify and treat precipitating factors for HE
- Lactulose is the first choice for treatment
- Other medications:  
Rifaximin, Metronidazole, Oral BCAAs and LOLA





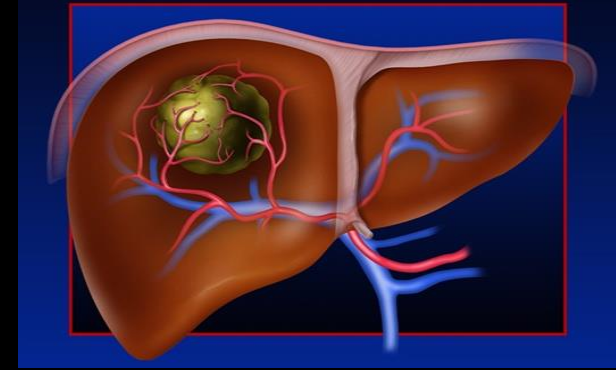
# Hepatocellular Carcinoma (HCC)

- Patients with cirrhosis have a markedly increased risk of developing hepatocellular carcinoma
- Incidence in compensated cirrhosis is ~3%/year
- 25-30% in 10 y.

# Tests to diagnose HCC

- Blood tests (AFP)
- Radiology (**most important**)
- Biopsy

# HCC Diagnosis: Dynamic Imaging



During early arterial phase on CT, an HCC appears brighter than surrounding liver



In later portal venous phase, the HCC appears darker than surrounding liver (washout)

- HCCs are hypervascular
- Tumor blood supply:
  - 100% hepatic artery
- Liver parenchymal blood supply:
  - 30% hepatic artery
  - 70% portal vein
- Dynamic imaging (MRI, CT) follows tumor density with time after IV contrast bolus
  - Requires both arterial enhancement and washout

# HCC Rx options

Options (depends of the stage)

- Surgical (resection, liver transplantation)
- Ablation (radiofrequency (RFA), or alcohol injection)
- Embolization (TACE; trans-arterial chemoembolization or TARE: trans-arterial radio-embolization)
- Chemotherapy
- Palliative

# Liver Transplantation

- Liver transplantation is the definitive treatment for patients with decompensated cirrhosis
- Depends upon the severity of disease, quality of life and the absence of contraindications

# HCC Surveillance

- Screening recommendations:
  - Radiology for HCC surveillance Q6 months for all cirrhosis patients

# Other recommendations

## Avoidance of Superimposed Insults

- Avoidance of:
  - Alcohol
  - Acetaminophen
  - Herbal medications

## Vaccinations

All cirrhotic should be vaccinated to:

- Hepatitis A and B
- Pneumococcal vaccine
- Influenza vaccination

Thank You