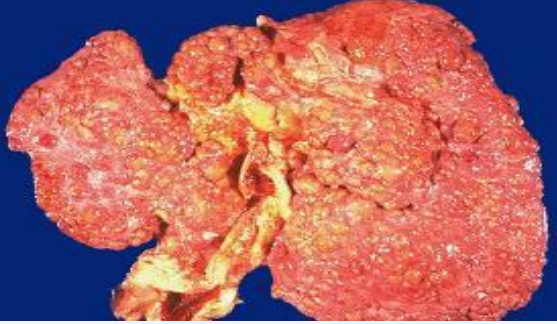

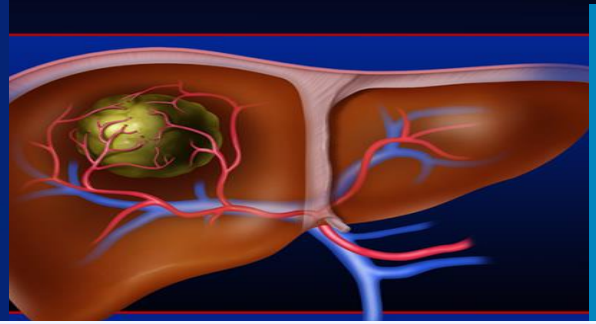

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# Liver Cirrhosis and its Complications

## MED341

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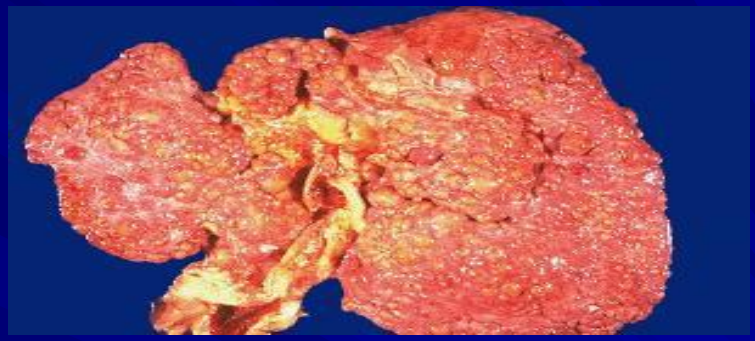
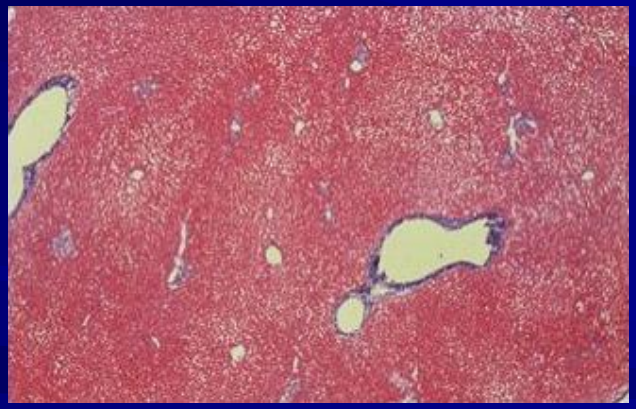
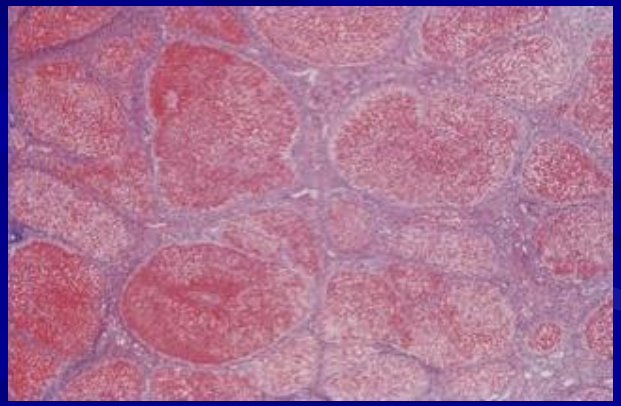
# Objectives

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

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



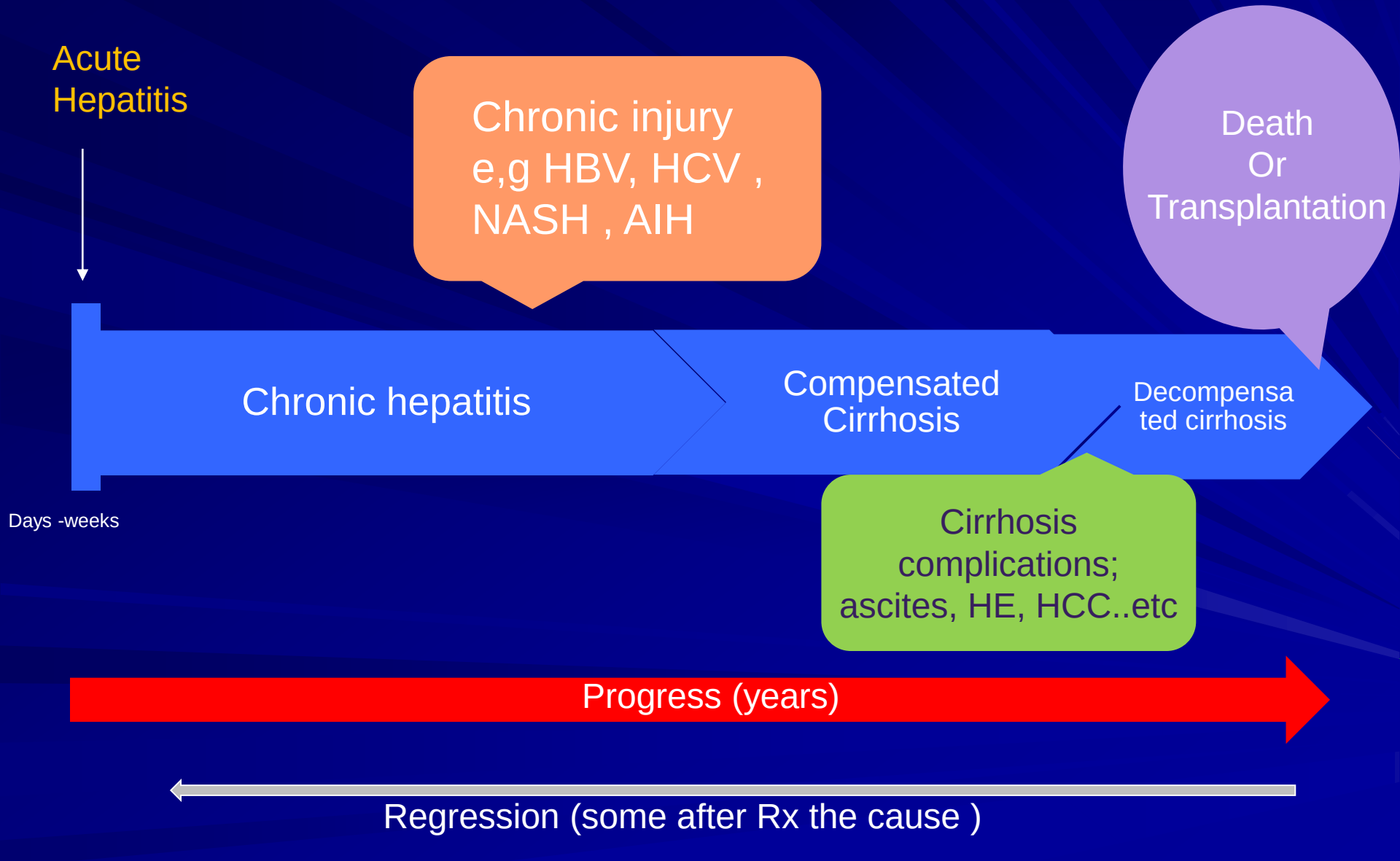




NORMAL LIVER

CIRRHOTIC LIVER

# Spectrum of Liver Inflammation



# 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

# How to approach patient with Cirrhosis?

- Symptoms
- Signs
- Lab
- Management

# Clinical manifestations

- No symptoms (Most patients in early cirrhosis)

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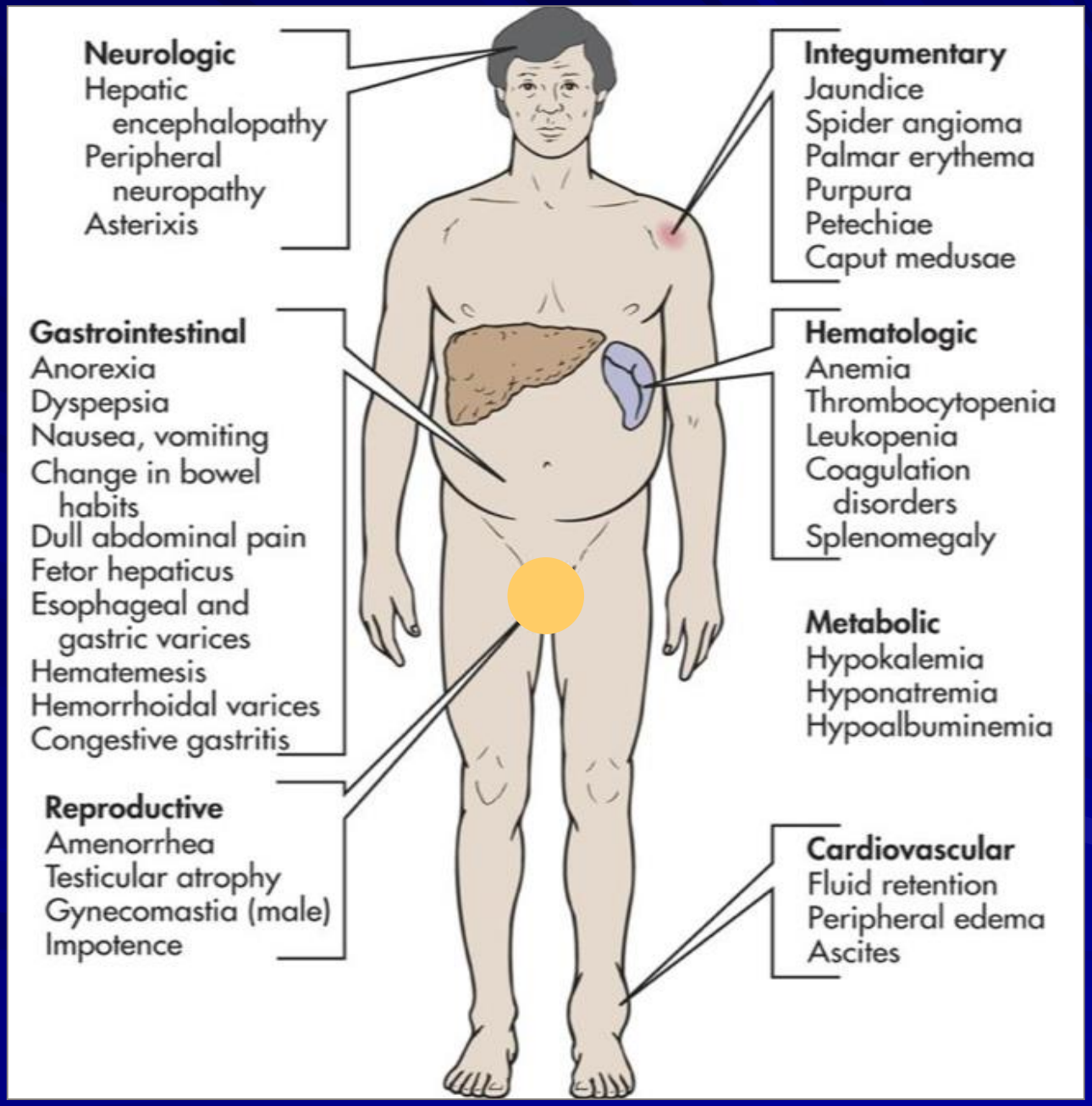
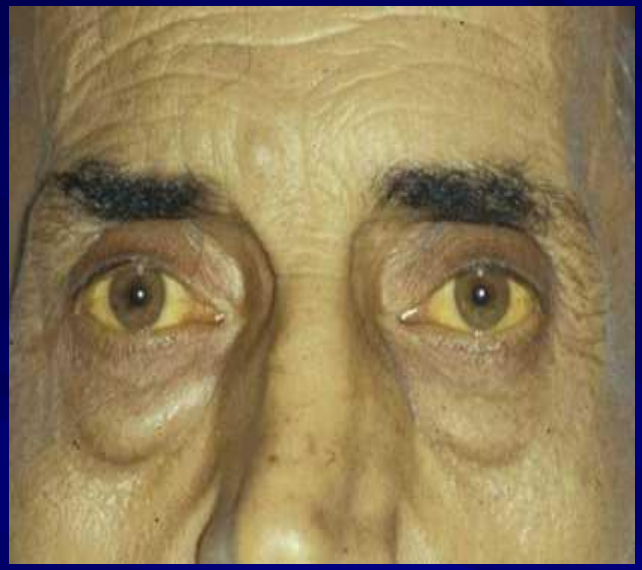
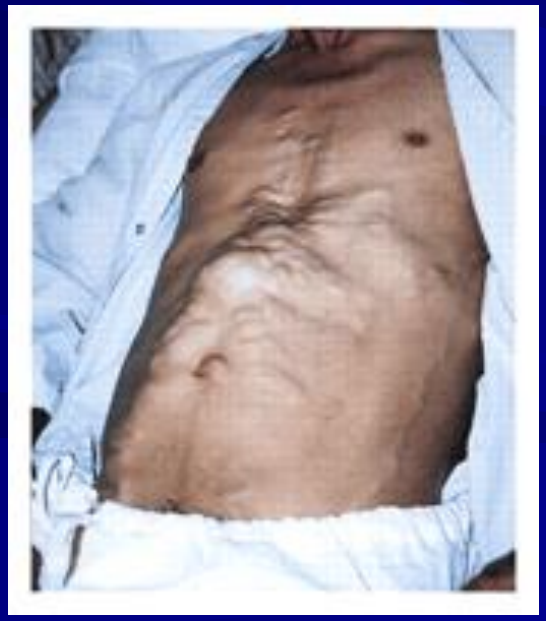
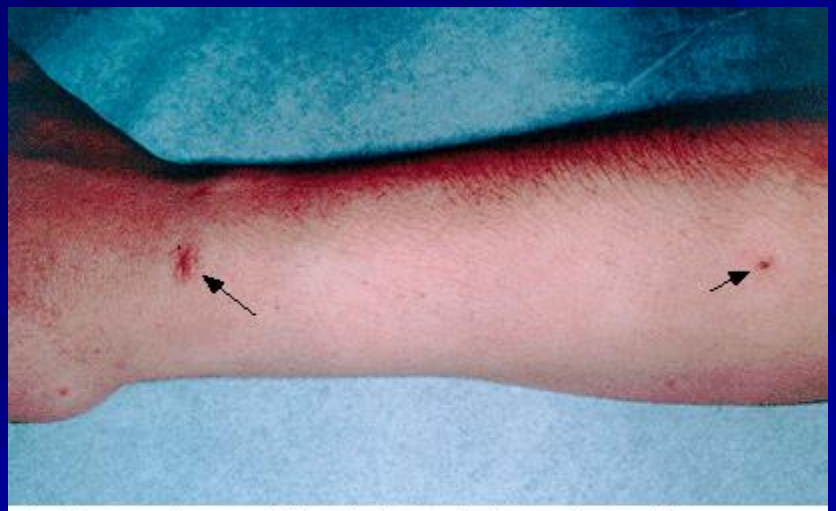
- Symptoms of cirrhosis (sometimes non-specific sx)
- Symptoms of decompensations (when liver start to fail.)


Neurologic
Hepatic encephalopathy
Peripheral neuropathy
Asterixis
Integumentary
Jaundice
Spider angioma
Palmar erythema
Purpura
Petechiae
Caput medusae
Gastrointestinal
Anorexia
Dyspepsia
Nausea, vomiting
Change in bowel habits
Dull abdominal pain
Fetor hepaticus
Esophageal and gastric varices
Hematemesis
Hemorrhoidal varices
Congestive gastritis
Hematologic
Anemia
Thrombocytopenia
Leukopenia
Coagulation disorders
Splenomegaly
Metabolic
Hypokalemia
Hyponatremia
Hypoalbuminemia
Reproductive
Amenorrhea
Testicular atrophy
Gynecomastia (male)
Impotence
Cardiovascular
Fluid retention
Peripheral edema
Ascites







**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 *(separate lecture)*
- Ascites
  - Asictes +- refractory ascites
  - Spontaneous Bacterial Peritonitis
  - Hepatic hydrothorax
  - Hepatorenal syndrome
- Hepatocellular carcinoma
- Hepatic Encephalopathy
- Pulmonary
  - Hepatopulmonary syndrome
  - Portopulmonary HTN

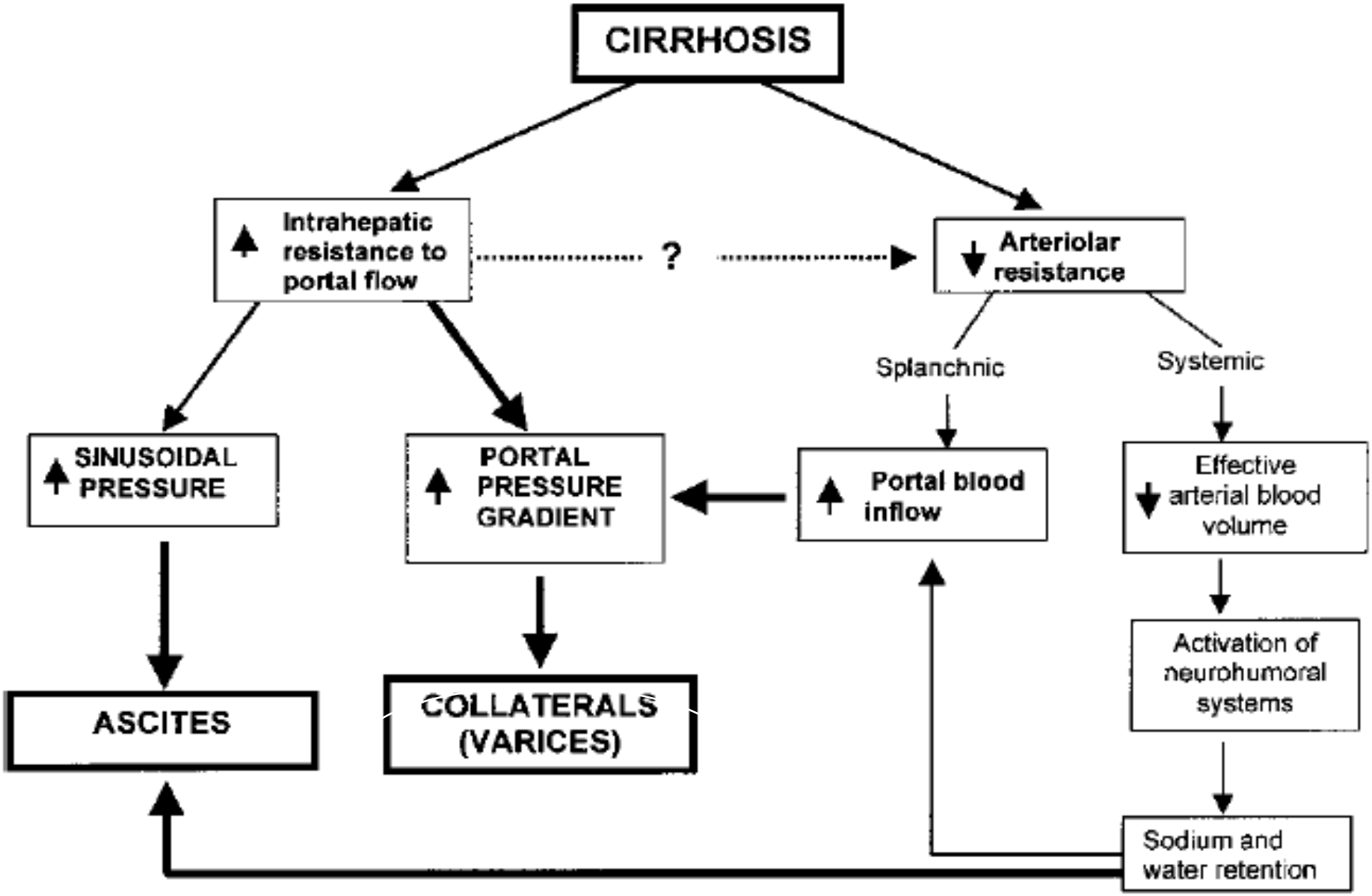



**Figure 1.** Pathogenesis of portal hypertension and its two main complications: varices and ascites.

# Investigations in cirrhosis

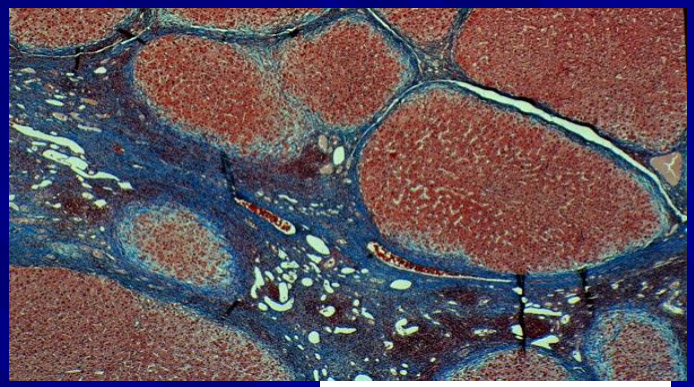
| Lab Test | Radiology |
|---|---|
| Moderately elevated aminotransferases (often with an AST:ALT ratio >1) | Surface nodularity |
| Elevated ALP (2 to 3 times the ULN) | Increased echogenicity (ultrasound) |
| **Thrombocytopenia** | Atrophy of the right lobe |
| Leukopenia/neutropenia | Hypertrophy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

+ Investigations of the cirrhosis Cause

** With advanced disease*

# Diagnosis confirmation?

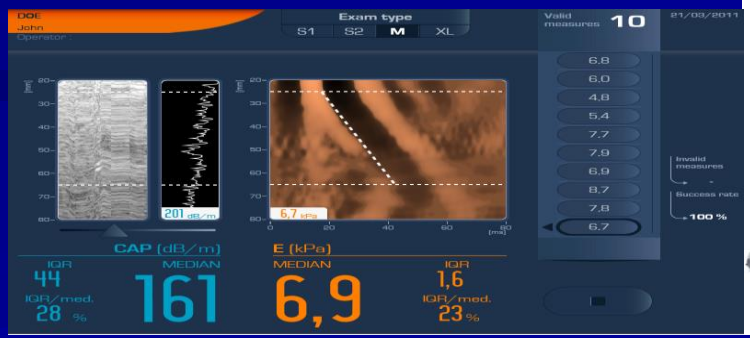
*To confirm and support the clinical and radiologic manifestations if needed*



1-Biopsy (histology)

2-Noninvasive tests

- ❑Serum score systems
- ❑Elastography (e.g fiobroscan)




# How to asses 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

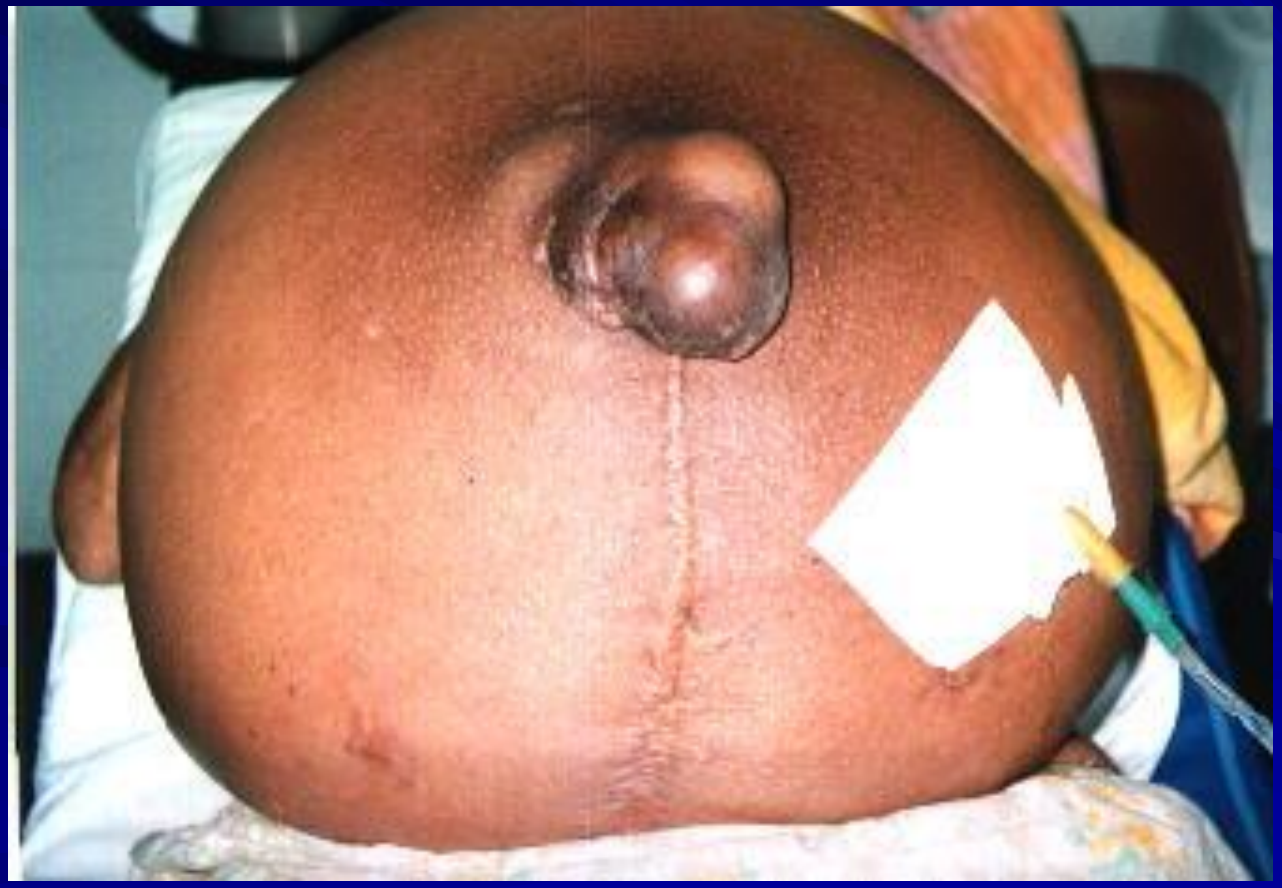
- others

# 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 | 4 to 6 | >6 |
| | <1.7 | 1.7 to 2.3 | >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

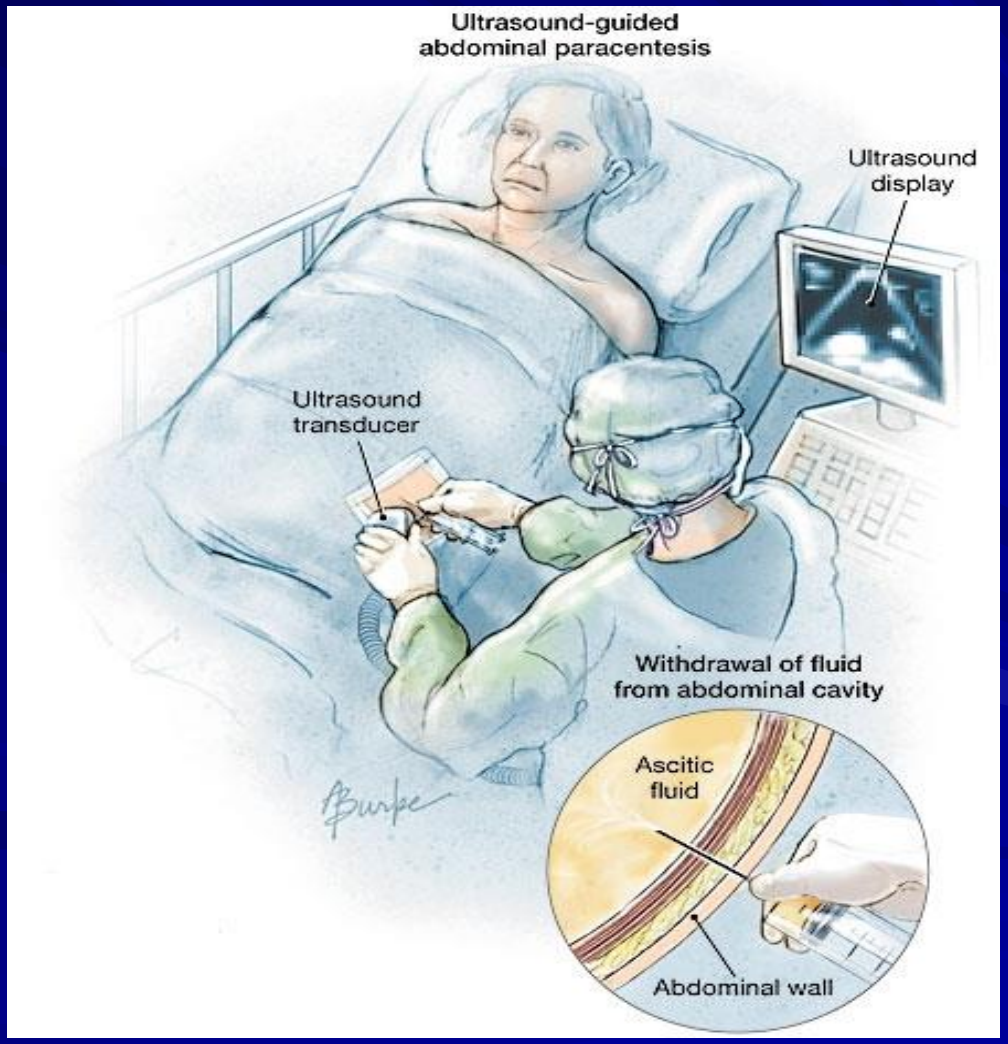
- Accumulation of fluid within the peritoneal cavity
- 1,500 mL of fluid must be present before flank dullness is detected.
- Shifting dullness: 83% sensitivity and 56% specificity in detecting ascites.
- If no flank dullness is present less likely ascites (< 10%).
- Ascites:
  1. 85% of due to cirrhosis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

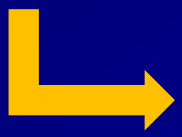
# Any new ascites should be tapped and analyzed!



# 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.[17] Reprinted with permission from Saunders Elsevier.*



**Measure SAAG**

# Serum-to-Ascites Albumin Gradient (SAAG)

**High SAAG ≥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

# Other tests

Depends on the clinical scenario:

- Secondary peritonitis:
  - LDH, and glucose: SBP from Secondary
  - ascetic fluid CEA(>5 ng/mL OR ALP >240 (gut perforation)

- Cytology for peritoneal carcinomatosis : The sensitivity 96.7% if 3 samples (from different paracentesis procedures)

- AFP: the sensitivity of smear of ascetic fluid for mycobacteria approaches zero; the sensitivity of fluid culture for mycobacteria is approximately 50% (better results from PCR AND BIOPSY)

# 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

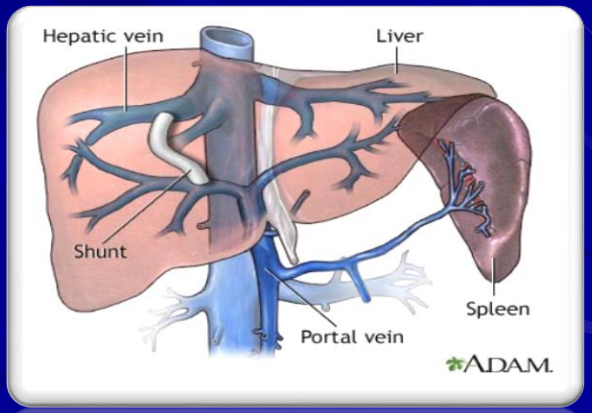
(400 mg per day of spironolactone and 160 mg per day furosemide), or

- 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 portasystemic stent-shunt (TIPS)
- Peritoneovenous shunt



# Spontaneous Bacterial Peritonitis (SBP)

- Infection of ascitic fluid

  -the 3 most common isolates: E 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/mm3)
  - 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; when
  - creatinine >1 mg/dL
  - BUN >30 mg/dL
  - total bilirubin >4 mg/dL

# 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 |

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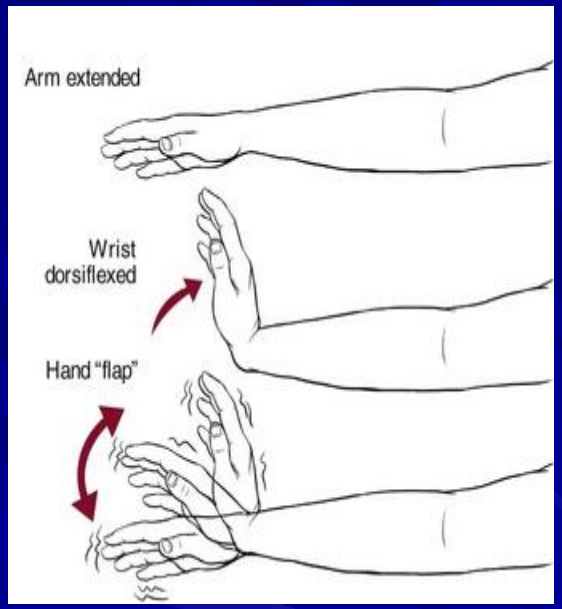


# Pathophysiology of HE

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

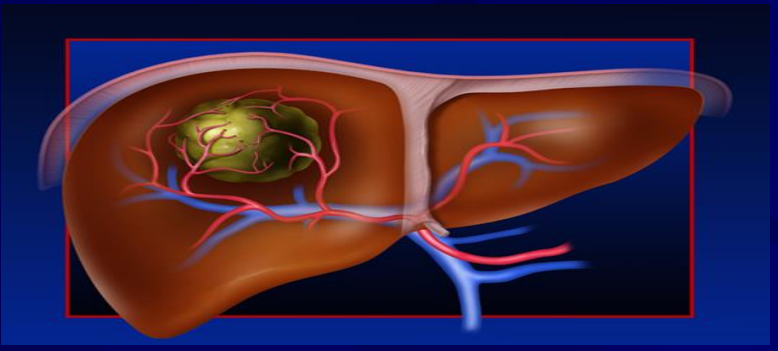
- **Drugs**
  - Benzodiazepines
  - Narcotics
  - Alcohol
- **Increased ammonia production, absorption or entry into the brain**
  - Gastrointestinal bleeding
  - Infection
  - Electrolyte disturbances such as hypokalemia
  - Constipation
  - Metabolic alkalosis
- **Dehydration**
  - Vomiting
  - Diarrhea
  - 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, and others



# Hepatocellular Carcinoma (HCC)

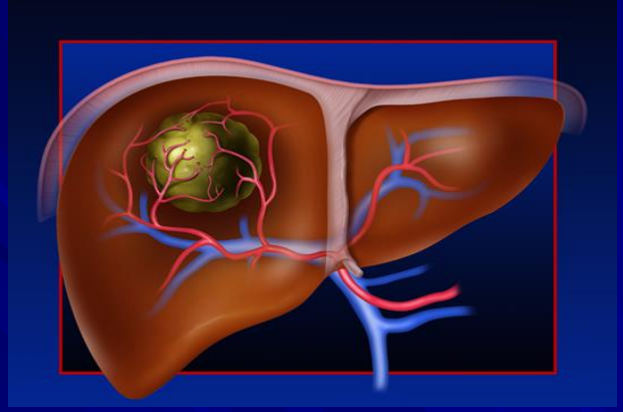
- Patients with cirrhosis have a markedly increased risk of developing hepatocellular carcinoma

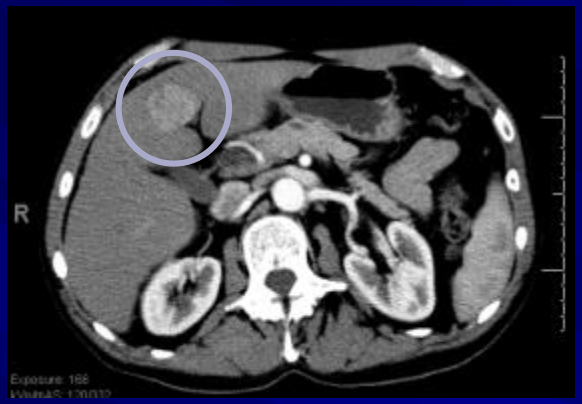
- Incidence in compensated cirrhosis is ~3%/year
- 25-30% in 10 y.

# Tests to diagnose HCC

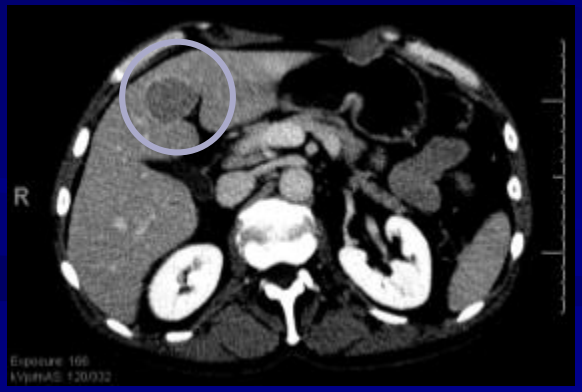
- Blood tests (AFP)
- Radiology (most important)
- Biopsy

# 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

# Staging and Treatment of HCC

- Rx depends on several factors, including:
  - the stage of the tumor + stage of liver disease
- Different scoring systems
- Famous system(Barcelona Clinic Liver Cancer Staging Classification (BCLC)
- Rx Options:

1-Liver Transplantation
2-Resection
3-Ablation (alcohol, RFA, Microwave etc…)
4-Transarterial chemoembolization or Radioembolization
5-Systemic therapy (oral chemo eg sorafenib)

# 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

# General Recommendations for all cirrhotic patients

## HCC Surveillance

US for HCC surveillance Q6 months for all cirrhosis patients

## Endoscopy screening for varies

Upper GI endoscopy every 2 years and then less if varices develop

## Avoidance of Superimposed Insults

Avoidance of:

- Alcohol
- Acetaminophen
- Herbal medications

## Vaccinations

- Hepatitis A and B
- Pneumococcal vaccine
- Influenza vaccination

Thank you