Liver Cirrhosis and Complications

Objectives:

- To understand Cirrhosis definition, causes and complications
- To know the pathophysiology of Cirrhosis complications
- To know how to approach patients with Cirrhosis and its complications

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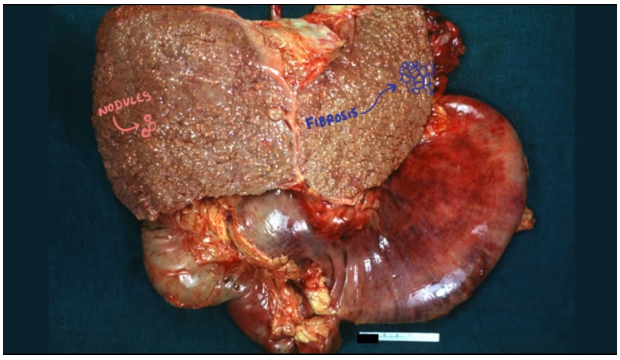
Resources: 436 slides, 435 team, Davidson, Kumar & Recall questions, Step Up to Medicine.

- Editing file
- Feedback

Liver Cirrhosis

Osmosis video

- **Cirrhosis:** Late stage of chronic liver inflammation and fibrosis, in which liver parenchyma is distorted and replaced by fibrous tissue and regenerating nodules (if no nodules present no cirrhosis is there). fibrous tissue replaces damaged or dead hepatocytes
- Chronic liver injury or Chronic hepatitis (caused by HBV, HCV, NASH, AIH) → Compensated Cirrhosis → Decompensated Cirrhosis → Death or liver transplantation .
- Explanation of the graph[1]



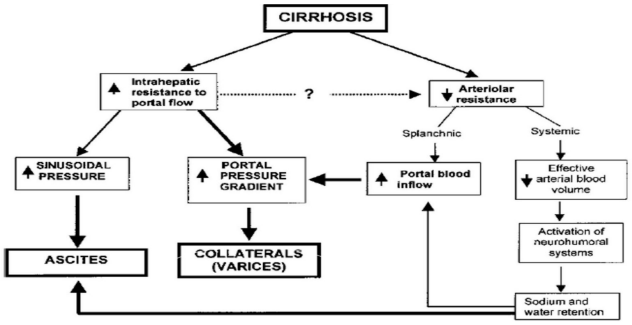


Figure 1. Pathogenesis of portal hypertension and its two main complications: varices and ascites.
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Explanation of figure 1 :

- Cirrhosis (Hepatocytes are totally replaced by nodules → resistance to blood flow into the liver → increase sinusoidal pressure → transudation of fluid → **ascites**.
- Also the pressure in portal system will increase and to bypass it venous **collaterals** will form in the abdomen and portosystemic shunts (blood shunts from portal veins to systemic veins) leading to **varices** which may rupture eg.esophageal varices, hemorrhoids.

-Splanchnic dilation leads to more portal blood inflow → more portal pressure → more collaterals → more varices.

-Systemic vasodilation → Low arteriolar resistance and third spacing (ascites,pleural effusion, Lower limb edema) results in intravascular depletion → **RAAS** system activated → more **Na/water** → more portal inflow → and the cycle repeats.

★ Histologic Staging: (Liver cirrhosis is diffuse disease affecting the whole liver)

★ Pathophysiology:

- Irreversible chronic injury of the hepatic parenchyma
- Extensive fibrosis - distortion of the hepatic architecture
- Formation of regenerative nodules
- Portal hypertension
  (Nodules formation and architecture distortion → resistance to blood flow → Portal hypertension)
- Vascular and humoral changes.

1

The distortion of liver anatomy causes (Cirrhosis):

A- Decreased sinusoidal blood flow through the liver → high resistance in portal circulation (portal hypertension) → this lead widespread manifestations, including (ascites, peripheral edema, splenomegaly, and varicosity of veins).

B- Hepatocellular failure that leads to impairment of biochemical functions, such as decreased albumin synthesis and decreased clotting factor synthesis.

The Sequence of how complication happened: Chronic inflammation in the end lead to cirrhosis that lead to portal hypertension then blood shunt to portosystemic circulation lead to decrease end diastolic volume that lead to decrease cardiac output lead to hypotension lead to activation of RAAS system lead to increased NA and water reabsorption lead to worsen ascites caused by portal hypertension and continuous in this cycle.

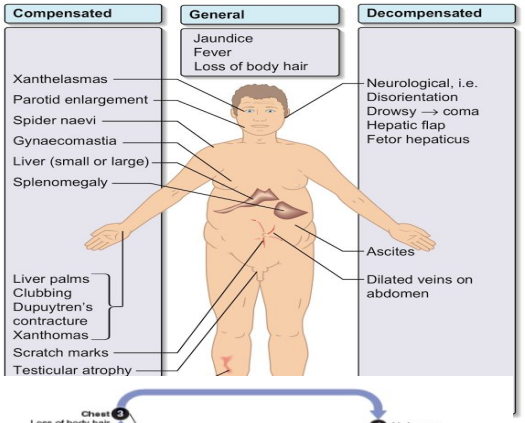
★ Aetiology First 3 are the commonest

Causes	Notes
Viral hepatitis (HBV and HCV)	• The **most common** cause worldwide HAV is not considered a cause because it does not lead to chronic liver injury
Alcoholic Steatohepatitis	• The most common cause in the western world • Like all drugs causing liver disease gives a **greater elevation in AST compared to ALT**. - may have xanthelasma because abnormality in lipid metabolism
Non-alcoholic Steatohepatitis	• Associated with Obesity, Diabetes, Hyperlipidemia, Corticosteroid use
Autoimmune hepatitis (AIH)	• Circulating auto-antibodies (antinuclear, smooth muscle, soluble liver antigen, Liver/kidney microsomal antibodies) (**ASMA**) **(ANA)** "Hypergammaglobulinemia" - may have xanthelasma because abnormality in lipid metabolism**.** - On histopathology: Rich plasma interface is a hallmark of AIH.
Primary Biliary Cirrhosis (PBC) (autoimmune)	• Progressive destruction of **intrahepatic bile ducts** causing cholestasis eventually leading to cirrhosis. • Affects women in 40s or 50s • Presents with pruritis with or without jaundice. In advanced disease there is xanthelasma (due to secondary hypercholesterolemia) • The most accurate blood test is Antimitochondrial antibody **(AMA)**
Primary Sclerosing Cholangitis (PSC) (autoimmune)	• Progressive obliterating fibrosis of **intra and extra hepatic ducts eventually leading to fibrosis** • More common in male than female • 75% or more occurs in association with IBD • The **most accurate test is Endoscopic retrograde cholangiopancreatography** not liver biopsy!
Alpha 1 antitrypsin deficiency	• Combination of liver disease and emphysema in young patient (under 40) who is non smoker

Wilson's disease	• Disorder of abnormally decreased copper excretion from the body because of a decrease in ceruloplasmin. Copper builds up in the liver, Kidney, Red blood cells and nervous system • Presents with : **Neurological symptoms**, coombs negative hemolytic anemia and renal tubular acidosis
Hemochromatosis	• Genetic disorder leading to **over-absorption of iron** in the duodenum • Presents with : Fatigue and joint pain, Erectile dysfunction in men and Amenorrhea in women, Skin darkening, Diabetes, Restrictive cardiomyopathy
Vascular	• Budd-Chiari syndrome, Heart failure, portal vein thrombosis • Hypoxic damage and necrosis of hepatocyte
Biliary	• Sclerosing Cholangitis
Drugs	• Methotrexate, acetaminophen toxicity

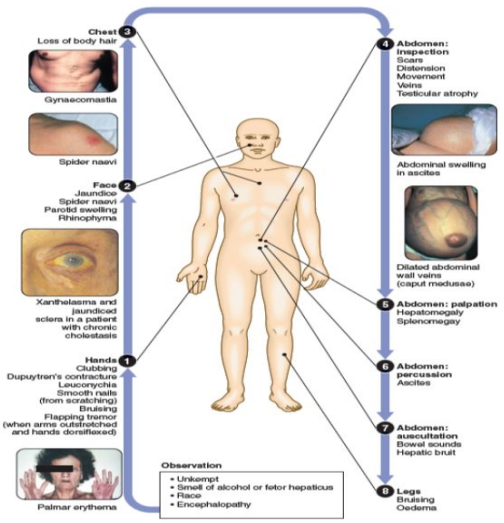
★ How to approach patient with cirrhosis?

- History
- Symptoms
- Signs
- Lab
- Radiology
- Management



★ Clinical Manifestations (Signs and Symptoms)[2]

- No symptoms (Most patients in early cirrhosis)
- Symptoms of cirrhosis (sometimes nonspecific symptoms) (in compensated)
- Symptoms of **decompensations** (when liver start to fail):
  1. Neurological disorientations (Hepatic encephalopathy)
  2. Ascites
  3. Dilated veins on abdomen and Variceal hemorrhage
  4. Hepatocellular carcinoma
  5. Pulmonary (Hepatopulmonary syndrome/Portopulmonary HTN)
  6. Jaundice and pruritus



Compensation:still do it is job

Compensated Cirrhosis: The liver is fibrosed but still maintain its function.

Decompensated Cirrhosis: The liver is extensively fibrosed for prolonged time that can't maintain its function and start to go for liver failure.

[2] Majority of chronic hepatitis and compensated liver cirrhosis are ASYMPTOMATIC and pass unnoticed until their first presentation with complications: decompensated , portal HTN, HCC. these complications are beyond treatment and our only option is transplant.

★ History: When taking history, look for the risk factors because there is usually no symptoms.

Presenting symptoms	Past and drug history	Family history	Social history
1-Asymptomatic mainly **2-Nonspecific constitutional symptoms ,** such as fatigue, weakness, and weight loss, etc.) **3-Symptoms of decompensation** -abdominal distension due to ascites and hepatomegaly, -coffee-ground vomitus and black stool (melena) secondary to GI hemorrhage -altered mental status in hepatic encephalopathy -lower extremity swelling -jaundice, and pruritus. -Many patients come with **HCC** as the first presentation. **Other less common symptoms:** respiratory (pulmonary hypertension, hepatic hydrothorax..)	- History of liver disease (all chronic liver disease can lead to cirrhosis) - Surgery and dental - Metabolic syndrome - Drugs: Methotrexate, amiodarone , amoxicillin /clavulanate etc..)	- Wilson - Hemochromaosis - Apha-antitrypein - Viral hepatitis	Risk-taking behaviors: - IV drug use, sexual contact, and tattoos. - Alcohol (amount type duration) - Travel history?

★ Clinical Features

Hand and nail features:	Facial features	Chest wall features	Abdominal features
• Clubbing • Leukonychia (Low Albumin) • Palmar erythema (bc of high Estrogen) • Bruising (bc of Thrombocytopenia) • Cholesterol deposits • Dupuytren contracture • Cyanosis (in patients with hepatopulmonary syndrome).	• Muscle wasting • Telangiectasia • Bruising (bc of Thrombocytopenia) • Parotid gland swelling • Jaundiced sclera • Xanthelasma	• Gynecomastia in men (bc of high Estrogen) • Telangiectasia (Spider naevi)	• Collateral • Bruising (bc of Thrombocytopenia) • Hepatomegaly • Splenomegaly • Abdominal distension • Hepatic bruit • Loss of secondary Sexual hair and testicular atrophy in men. (bc of high Estrogen)

★ Investigations

1. Lab Test

LFTs:

- **Moderately** elevated aminotransferases (often with an AST:ALT ratio >1)
  A very early sign of advanced cirrhosis is reversed AST:ALT ratio (no more hepatocytes to produce ALT which is normally more than AST)
  ALT more specific than AST because AST found in myocardium and skeletal muscle cells
- Elevated ALP (2 to 3 times the ULN[3])

CBC:

- Thrombocytopenia (platelet will be low due to hypersplenism)
- Leukopenia/neutropenia (also because of hypersplenism)
- Anemia
  The pathogenesis of abnormal hematological indices (HIs) in cirrhosis is multifactorial and includes portal hypertension-induced sequestration, alterations in bone marrow stimulating factors, viral- and toxin-induced bone marrow suppression and consumption or loss,Abnormalities in HIs are associated with an increased risk of complications including bleeding and infection.

Liver function:

- Prolonged prothrombin time/elevated INR*, and Low serum albumin* (are the best indicators of liver function)

Hyperbilirubinemia* / Hyponatremia* / Elevated serum creatinine* (***With advanced disease**)

Increase in unconjugated **bilirubin** and decrease in conjugated **bilirubin** because liver fail to do function .
patients with cirrhosis may develop **hyponatremia** due to either hypovolemia (example: loss of extracellular fluid due to diuretics) or hypervolemia (expanded extracellular fluid volume due to the inability of the kidneys to excrete solute-free water proportionate to the amount of free water ingested)

Hyponatremia due to salt/water retention

2. Radiology

Mild to moderate disease	With advanced disease
1. Surface nodularity	1. Small nodular liver, eg.liver span reduced to 7cm
2. Increased echogenicity (ultrasound)	2. Ascites
3. Atrophy of the right lobe	3. Hepatocellular carcinoma
4. Hypertrophy of the caudate or the left lobes	4. Portal, splenic, superior, mesentric vein thrombosis
	5. Portosystemic collateral
	6. Splenomegaly

\+ **Investigate the cause of cirrhosis**

[3] Upper limit of normal

So you have positive History, Lab results (revered AST:ALT ratio , thrombocytopenia , hypo-albumina, hyponatremia, High bilirubin) and Ultrasound showed Nodular liver. That is not enough to confirm, you need:

Confirm the Diagnosis:

- **Invasive:**
  1- Biopsy (Histology): Gold standard. To confirm the replacement by nodules and fibrosis.
- **Noninvasive tests :**
  1- Elastography (e.g fibroscan): measure liver elasticity and gives you grade.
  2- Serum score systems
  If patient has manifestation of decompinasiate eg: (Advanced cases, HCC) we do not need to confirm the diagnosis.

★ Assess Severity and Prognosis of Liver Disease:

- Assessing the severity will help us to know the prognosis, also help the physician to evaluate the need of liver transplant.

1- Child-Turcotte-Pugh score or Child Criteria (CPT score) Has clinical and laboratory parameters

Table 3-1 Child–Pugh Classification to Assess Severity of Liver Disease			
POINTS	**1**	**2**	**3**
Ascites	Absent	Slight	Moderate
Bilirubin	<2.0 mg/dL (<34.2 micromol/L)	2.0–3.0 mg/dL (34.2-51.3 micromol/L)	>3.0 mg/dL (>51.3 micromol/L)
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4
PT (seconds over control) or INR ratio	<4	4 to 6	>6
	<1.7	1.7–2.3	>2.3
Albumin	>3.5 g/dL (>35 g/L)	2.8–3.5 g/dL (28-35 g/L)	<2.8 g/dL (<28 g/L)

- **Class A—5 to 6 points total** (least severe liver disease), 100-85% 2-year survival high percentage of survival mean cirrhosis do not mean death in all time .
- **Class B—7 to 9 points total** (moderate severe liver disease), 80-60% 2-year survival
- **Class C—10 to 15 points total** (severe liver disease), 45-35% 2-year survival. If it was above 40 © we don't do biopsy because of risk of bleeding.

2- 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

أهم شي تعرفون يعتمد على ايش (Creatinine Serum+INR+Bilirubin)

★ Management:

Cirrhosis is irreversible and frequently progress. Management is that of complications seen in decompensated cirrhosis. Correcting the underlying cause, venesection for haemochromatosis, abstinence from alcohol for alcoholic cirrhosis, may halt the progression of liver disease

Common complications of cirrhosis:

Complications of liver failure
(note the mnemonic **AC, 9H**)
- **A**scites
- **C**oagulopathy
- **H**ypoalbuminemia
- Portal **H**ypertension
- **H**yperammonemia
- **H**epaticencephalopathy
- **H**epatorenal syndrome
- **H**ypoglycemia
- **H**yperbilirubinemia/jaundice
- **H**yperestrinism
- **H**epatocellularcarcinoma

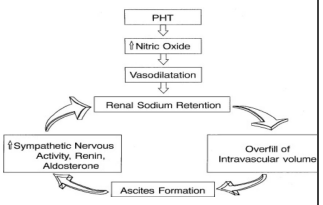
Complications happens when liver fail to compensate (Decompensated Cirrhosis)

- Variceal hemorrhage (separate lecture)
- Ascites (most common complication of cirrhosis)
    - Asictes +- refractory ascites
    - Spontaneous Bacterial Peritonitis
- Hepatic hydrothorax
- Hepatorenal syndrome
- Hepatocellular carcinoma
- Hepatic Encephalopathy
- Pulmonary:
    - Hepatopulmonary syndrome
    - Portopulmonary HTN

Female's doctor: What I need you to focus more : Ascites, Encephalopathy, HCC , SAAG diagnostic values

Complications of liver cirrhosis :

1. Ascites



- VERY important complication **with poor prognosis They die within 1-2 years**
- Accumulation of fluid in the peritoneal cavity. First step in development of ascites is the presence of significant portal HPN.
- 85% of ascites is due to cirrhosis, and 15% have other causes.
- Poor prognosis (unless Liver Tx)
- Two-year survival of patients with ascites is approximately 50%
- (increased hydrostatic pressure) and hypoalbuminemia (reduced oncotic pressure). In cirrhosis peripheral arterial vasodilation leads to reduction in effective blood volume with activation of the sympathetic nervous system and renin-angiotensin system > Promoting salt and water retention

Causes (DDx):	Transudate	Exudate
	• Portal hypertension (most common) • Cardiac failure	• Cancer • Infections • Nephrotic syndrome. • Pancreatitis
Examination	• 1.5 L of fluid must be present before flank dullness is detected. More specific than shifting. • Shifting dullness[4]	

[4] 83% sensitivity and 56% specificity in detecting ascites.

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- If no Flank dullness is present less likely ascites (<10%)

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<tr><td>Investigation</td><td colspan="2">Diagnostic aspiration of ascitic fluid should be carried out in any new ascites</td></tr>
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Routine:
1. Cell count and differential
2. Albumin and total protein “To measure SAAG”

Optional (when there is suspicion of infection):
1. Gram stain and culture
2. Glucose
3. Lactate dehydrogenase
4. Amylase to exclude pancreatic ascitis

Unusual:
1. AFB smear (Not sensitive) and culture (higher sensitivity)
2. Cytology
3. Triglyceride
4. Bilirubin

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Other tests:
Depends on the clinical scenario:
- Secondary peritonitis:

LDH, and glucose: Spontaneous bacterial peritonitis (SBP) from Secondary ascetic fluid CEA (Carcinoembryonic antigen) > 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)

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<tr><td>Management
Depends on the cause!
So the most important thing is to treat underlying cause</td><td>Initial treatment of ascites</td><td>Treatment of refractory ascites ~10%</td></tr>
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Stepwise approach:

1. Dietary salt restriction (< 88 meq or 2000 mg/day)
2. Diuretics (most successful regime is combination of Spironolactone and Furosemide)

Spironolactone blocks RAAS which is activated in cirrhosis. We give laxatives if pt. Has lower limb eodema.

➔ Monitor electrolytes and kidney function
- Discontinue non-steroidal anti-inflammatory drugs as they worsen liver function!
- Rx of underlying cause
- Evaluation for liver transplantation

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Ascites that is :
- Unresponsive to sodium restricted diet and high dose diuretic treatment[5],
- Development of clinically significant complications of diuretics[6]

1. Serial therapeutic paracenteses (Ascites tap) + intravenous infusion of albumin if draining > 5L fluid
2. Transjugular intrahepatic portosystemic shunt (TIPS)
3. Liver transplantation
4. Peritoneovenous shunt

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[5]400 mg per day of spironolactone and 160 mg per day furosemide

[6] 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

★ Classification of ascites by the Serum Albumin-Ascites Gradient (SAAG):

MOST IMP part in the lecture (we advise you to know all the causes in the next table)

High albumin gradient (SAAG>=1.1g\dL) **Transudate 90%**	Low albumin gradient (SAAG<1.1g\dL) **Exudate 10%**
> OR = 1.1 → portal HTN related ascites. Causes of portal HTN: • **Cirrhosis** • Heart failure / Constrictive pericarditis • Alcoholic hepatitis • Budd chiari • Massive hepatic metastases In case of Portal HTN and Heart disease	**< 1.1 → Non portal HTN ascites** (Local causes) • Peritoneal carcinomatosis • Lymphoma. • Peritoneal tuberculosis • Pancreatitis • Serositis • Nephrotic syndrome decreased serum albumin lead to decreased oncotic pressure Local causes

★ Complications of ascites:

Spontaneous bacterial peritonitis:

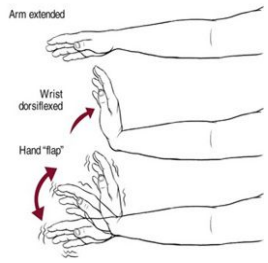
- Infection of ascitic fluid (spontaneous means without perforation = idiopathic cause).
- Usually gram negative, the 3 most common isolates: (**E.Coli**), **klebsiella**, **s.pneumoniae**.
- **Presentation:** variable (Fever, abdominal pain, abdominal tenderness , altered mental status) maybe all, some or none present. "None" of the symptoms above is the most common presentation. They mostly present with -worsening of their condition/ascites. -Encephalopathy. Here you must suspect SBP.
- **Diagnosis:** Ascitic fluid cell count → PMN count (>250 cells/mm3) (I want you to remember this number along with SAAG values) and a positive ascitic fluid bacterial culture.
- **Treatment:**
  - Cefotaxime or a similar third generation cephalosporin IV covers 95% of flora including common organism (treatment of choice for suspected SBP).
  - Albumin when: severe cases to reduce mortality and renal failure. **Creatinine** >1 mg/dL, **BUN** > 30 mg/dL, total **bilirubin** >4 mg/dL

2. Hepatic encephalopathy important

- Hepatic encephalopathy is a reversible brain dysfunction caused by liver insufficiency and portosystemic shunts.
- Occurs with advanced hepatocellular disease either chronic (Cirrhosis) or acute (Fulminant) it is also present in patient following surgical or TIPS shunts.
- It manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma.
- **Pathophysiology Different mechanisms:**
- Liver can't compensate for proteins intake, so there will be production of ammonia from these proteins by the action of gut microbiota. This ammonia will go to the blood -> BBB -> step 3,4.

1. Neurotoxin (ammonia) liver convert ammonia to urea in urea cycle . if the liver is abnormal ammonia accumulation and affects brain .
2. Blood-to-brain transport of neurotransmitter
3. Activation of inhibitory (gamma-aminobutyric acid, serotonin) neurotransmitter systems
4. Impairment of excitatory (glutamate, catecholamines) neurotransmitter systems
5. Enhanced neural inhibition

- **Clinical features:** Flapping tremor is a specific clinical finding in advanced liver disease.



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

Precipitants of hepatic encephalopathy caused by:	Treatment
1. **Drugs** eg. Benzodiazepine, narcotics, alcohol 2. **Increased ammonia production, absorption or entry into the brain:** high protein intake[7], Gastrointestinal bleeding, Infection (Most common), Electrolyte disturbances such as hypokalemia, Constipation[8](Most common), Metabolic alkalosis, 3. **Dehydration:** Vomiting, Diarrhea, Hemorrhage, Diuretics, Large volume paracentesis 4. **Portosystemic shunts:** Radiographic or surgically placed shunts, Spontaneous shunts 5. **Vascular occlusion:** Hepatic or portal vein thrombosis 6. **HCC**	**The aims of management is to identify and treat any precipitating factors and to minimize absorption of ammonia:** 1. Lactulose First line of treatment[9] (trap ammonia and decrease its absorption) 2. Antibiotics to reduce the number of bowel organisms and hence production of ammonia (Rifaximin or metronidazole) 3. Oral BCAAs and LOLA 4. Maintenance of nutrition with adequate calories and protein is initially restricted

[7] The liver is unable to digest the proteins, proteins induce gut bacterial growth -> production of ammonia by bacteria , this ammonia will travel to the brain
[8] With constipation the bacteria is trapped in the gut so more ammonia will accumulate in the body
[9] Most common precipitant patients come with is constipation that is why Lactulose is the first line management.

- Female's doctor : 3,4,5,6 : Just understand the concept. You don't need to know it in detail

3. Hepatorenal syndrome

Development of **functional** acute kidney injury in a patient who usually **has advanced liver disease** either cirrhosis or alcoholic hepatitis. Marked peripheral vasodilatation leads to fall in systemic vascular resistance and effective hypovolemia. This in turn results in vasoconstriction of the renal circulation with markedly reduced renal perfusion. Poor prognosis.(pre-renal)

Diagnosis By exclusion[10]	• **Type I:** rapid, aggressive. Acute renal failure due to cirrhosis progress in days. They die without liver transplant • **Type II :** slow, less aggressive ○ **present as:** azotemia, oliguria, hyponatremia, hypotension,low urine sodium < 10 mEq/L.
Treatment	• It is acute renal failure due to liver cirrhosis, so it is reversed with liver transplant. • Correct underlying cause • Albumin • Vasoconstrictors of splanchnic vessels (Terlipressin, octreotide, midodrine, epinephrine) • HD (Hemodialysis) • Liver Transplantation

4. Portopulmonary Syndrome

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

5. 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 like pores.
- Commonly Rt side
- **Dx**: Reveals a **transudative fluid** and Serum to fluid albumin gradient greater than 1.1
- Management similar to ascites (drain, albumin, diuretics)

[10] Majority of azotemia is not due to HRS

6. Hepatopulmonary syndrome (HPS)

Triad:

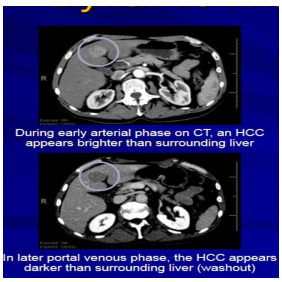
1. Liver disease (liver disease, portal hypertension, or portosystemic shunts)
2. Increased alveolar-arterial gradient while breathing room air
3. Evidence for intrapulmonary vascular abnormalities, referred to as intrapulmonary vascular dilatations (shunting)

➔ Mild hypoxemia is common

➔ In severe disease patients are breathless on standing

7. Hepatocellular carcinoma (Hepatoma) HCC

- Patients with chronic liver disease or cirrhosis have a markedly increased risk of developing hepatocellular carcinoma. Poor prognosis (median survival is only 6-20 months)
- Incidence in compensated cirrhosis is ~3%/year, 25-30% in 10 y.
- Other aetiological factors include **aflatoxin(toxin produced by Aspergillus which found in food contaminated with aflatoxin like Nut,milk and cheese) ,androgenic steroids and contraceptive pills and vinyl chloride (found in plastic).**

Investigations	 • **Blood tests** (Alpha Fetoprotein AFP) • **Radiology** (most important) ○ Dynamic CT and MRI (See tumor density with time after IV bolus contrast. Requires both arterial enhancement and washout). ○ Tumors blood supply is always arterial Vs liver parenchymal blood supply is 70% from portal vein. ○ Triphasic (high resolution) CT imaging : 1-without contrast 2- post IV injection: early arterial phase 3-delayed portal venous phase. ○ In triphasic CT scan t will show Characteristic Enhancement, i.e. hyperdensity (light up) on the arterial phase followed by washout on the portal/venous phase (because it is not supplied by the portal vein). ○ HCC are Hypervascular: the tumor Receives blood 100% from the Hepatic artery. Liver parenchymal blood supply = 30% hepatic artery, 70% portal vein. • **Biopsy** only performed when there is diagnostic doubt as there is risk of tumor seeding in the percutaneous needle biopsy tract.
Treatment	**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) 1. Liver Transplantation is the only option in latestages 2. Surgical resection considered only in early stages 3. Ablation (alcohol, RFA, Microwave) 4. Transarterial chemoembolization or Radioembolization (injection of a chemotherapeutic agent and lipiodol into the hepatic artery) 5. Systemic therapy: oral chemo e.g. sorafenib (very limited role) 6. Palliative

★ Liver Transplantation: Video

- 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 varices:** Upper Gl endoscopy every 2 years and then less if varices develop
- **Avoidance of Superimposed Insults**
    1. Alcohol
    2. Acetaminophen
    3. Herbal medications
- **Vaccinations** (All cirrhotic should be vaccinated to)
    1. Hepatitis A and B
    2. Pneumococcal vaccine
    3. Influenza vaccination

Summary

Liver cirrhosis		
Definition	Late stage of chronic liver inflammation and fibrosis, in which liver parenchyma is distorted and replaced by fibrous tissue and regenerating nodules	
Progression	Chronic liver injury or Chronic hepatitis → Compensated Cirrhosis → Decompensated Cirrhosis → Death or liver transplantation.	
Most common Aetiology	• Viral hepatitis (HBV & HCV) • Alcoholic Steatohepatitis • Non-alcoholic Steatohepatitis	
Investigations	• **Lab tests:** ○ LFT ○ CBC ○ Prolonged prothrombin time	○ INR ○ Hyperbilirubinemia ○ Serum albumin • **Radiology**
Confirm the Diagnosis	**Invasive:** 1- Biopsy	**Noninvasive tests:** 1- Elastography 2- Serum score systems
Severity of Liver Disease	• Child-Turcotte-Pugh score • MELD score	

<table>
<tr><th colspan="3">Complications of liver cirrhosis</th></tr>
<tr><td colspan="3">1. Ascites: Accumulation of fluid in the peritoneal cavity</td></tr>
<tr><td>Investigation</td><td colspan="2">Routine:
1. Cell count and differential
2. Albumin and total protein To measure SAAG</td></tr>
<tr><td>Management</td><td colspan="2">1. Dietary salt restriction
2. Diuretics (most successful is Spironolactone and Furosemide combination)</td></tr>
<tr><td>Refractory ascites</td><td colspan="2">1. Unresponsive to sodium restricted diet and high dose diuretic treatment,
2. Development of clinically significant complications of diuretics</td></tr>
<tr><td>SAAG</td><td>High albumin gradient (SAAG>=1.1g\dL)
● Cirrhosis / Alcoholic hepatitis
● Heart failure / Constrictive pericarditis.</td><td>Low albumin gradient (SAAG<1.1g\dL)
● Peritoneal carcinomatosis
● Lymphoma.
● Nephrotic syndrome</td></tr>
<tr><td>Complications</td><td colspan="2">Spontaneous bacterial peritonitis: Infection of ascitic fluid,
Diagnosis: Ascitic fluid cell count → PMN count (>250 cells/mm3) & a positive ascitic fluid culture
Treatment: Cefotaxime + Albumin</td></tr>
<tr><td colspan="3">2.Hepatic encephalopathy: Hepatic encephalopathy is a reversible brain dysfunction caused by liver insufficiency and portosystemic shunts. (Flapping tremor)</td></tr>
<tr><td>Pathophysiology</td><td colspan="2">Neurotoxin (ammonia) → cross BBB → Activation of inhibitory neurotransmitter systems → Impairment of excitatory neurotransmitter systems → Enhanced neural inhibition</td></tr>
<tr><td>Precipitants</td><td>● Drugs
● Increased ammonia
● Dehydration</td><td>● Portosystemic shunts
● Vascular occlusion
● HCC</td></tr>
<tr><td>Treatment</td><td colspan="2">● Lactulose (decrease absorption of ammonia)
● Rifaximin or metronidazole (decrease GI bacteria that produce ammonia)</td></tr>
<tr><td colspan="3">3.Hepatorenal syndrome: Development of functional acute kidney injury in a patient who usually has advanced liver disease either cirrhosis or alcoholic hepatitis.</td></tr>
<tr><td colspan="3">4.Portopulmonary Syndrome: the presence of pulmonary hypertension in the coexistent portal hypertension</td></tr>
<tr><td colspan="3">5.Hepatic Hydrothorax: Pleural effusion in a patient with cirrhosis and no evidence of cardiopulmonary disease.</td></tr>
<tr><td colspan="3">6.Hepatopulmonary syndrome (HPS)
Triad of : Liver disease , Increased alveolar-arterial gradient , Evidence for intrapulmonary vascular abnormalities</td></tr>
<tr><td colspan="3">7. Hepatocellular carcinoma (Hepatoma) HCC</td></tr>
<tr><td>Investigation</td><td colspan="2">● Blood tests (Alpha Fetoprotein AFP)
● Radiology: Dynamic CT and MRI (See tumor density with time after IV bolus contrast. Requires both arterial enhancement and washout)
● Biopsy</td></tr>
</table>

Examine Yourself !! (from 435)

1. A 67-year-old man presents feeling unwell and complaining of general malaise. He mentions a long history of alcohol abuse and his past medical history shows deranged liver function tests. Which of the following clinical signs does not form part of chronic liver disease?

A. Finger clubbing B. Palmer erythema C. Spider naevia D. Koilonychia E. Jaundice

2. You see a 56-year-old man in your clinic with suspected alcoholic liver disease. Liver function tests reveal a bilirubin of 36iu/L, AST of 150iu/L, ALT 75iu/L and ALP 100iu/L. Which of the following blood test parameters would support a diagnosis of alcoholic-related liver disease?

A. Normal mean cell volume (MCV) B. Low MCV C. Normal mean cell haemoglobin (MCH) D. Low MCH E. Raised MCV

3. A 47-year-old man presents complaining of weight gain, on examination there is an abdominal distension with a fluid thrill. Which of following is not a cause of ascites secondary to venous hypertension?

A. Congestive heart failure B. Cirrhosis C. Constrictive pericarditis D. Budd–Chiari syndrome E. Nephrotic syndrome

4. A 56-year-old man, diagnosed with emphysema, presents with a one-month history of jaundice and ascites. Your registrar suspects that this patient may have liver disease as well, after examination and investigations the patient has liver cirrhosis. Select the most likely cause of his condition ?

A. AIH B. HBV or HCV C. α1-antitrypsin deficiency D. Alcoholic hepatitis E. None

5. You see a 56-year-old woman who presents with a two-month history of jaundice. Associated symptoms include lethargy and polyarthralgia. Her LFTs reveal a bilirubin of 46iu/L, AST 200, ALT 175, ALP 104. On examination, the patient is jaundiced and has finger clubbing. There are several spider naevi on the front and back of the trunk. Her abdomen is soft and there is a smooth hepatomegaly. Prior to her onset of symptoms, the patient has been fit and well. Viral serology is normal and anti-soluble liver antigen (SLA) is detected. You decide to start this patient on treatment. The most appropriate treatment is?

A. Liver transplantation B. Methotrexate C. Prednisolone D. Cyclosporin E. Antivirals

6. Which of the following is sign for hepatic encephalopathy ?

A. Clubbing nails. B. Testicular atrophy C. flapping tremor D.Jaundice E.None

7. A patient on your ward is diagnosed with hepatocellular carcinoma. You are asked to perform a tumour marker level on this patient. Which of the following tumour markers are elevated in hepatocellular carcinoma?

A. α-fetoprotein B. Carcinoembryonic antigen (CEA) C. CA15-3 D. HcG E. CA125

1 D / 2 E (alcoholic liver is cause of increase MCV) / 3 E / 4 C / 5 C (bc her history is related to AIH and prednisolone is steroid immunosuppressive therapy) / 6 C / 7 A