Medicine TEAM 437

MED437 KING SAUD UNIVERSITY

Liver cirrhosis & complications

Objectives :

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

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Resources :

- 437 slides | Slightly Different Than 436 Slides
- Teamwork 436 & 435
- Doctor notes | Dr. Khalid AlSwat & Dr.Nahlah Azzam
- Oxford Clinical Medicine

Liver cirrhosis

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

- The final stage of any chronic liver inflammation End stage
- Irreversible in its advanced stages If we detect it in an early stage, it could be reversed

Chronic liver injury (Chronic hepatitis) → Compensated Cirrhosis → Decompensated Cirrhosis → Death or liver transplantation

First inflammation causes long term obstruction and fibrosis. With time, hepatocyte regenerate in nodules (new hepatocyte forming group) ➟ with chronic inflammation and fibrosis deposit it ends with cirrhosis

Pathophysiology

A- Decreased sinusoidal blood flow through the liver (vasoconstriction) → 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.

- complication happen after cirrhosis develop
- Even after cirrhosis the liver can maintain the function for 5-10 years ➟ compensated cirrhosis
  80% will survive 10 years

Aetiology

◦Hep A and E are acute infections, therefore not risk factors
◦HDV can appear with HBV causing it to be more aggressive

Viral hepatitis (B and C)

Alcoholic Steatohepatitis

Non-alcoholic Steatohepatitis

Drugs

Biliary

Hemochromatosis

Primary Sclerosing Cholangitis (autoimmune)

Wilson's disease

Autoimmune hepatitis

Primary Biliary Cirrhosis (autoimmune)

Alpha 1 antitrypsin deficiency

Vascular

history

Presenting symptoms x	Past and drug history	Past and drug 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 - Hemochromatosis - 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	Facial features	Chest wall features	Abdominal features
● Clubbing ● Leukonychia(LowAlbumin) ● Palmarerythema (bc of high Estrogen) ● Bruising (bc of Thrombocytopenia) ● Cholesteroldeposits ● Dupuytrencontracture ● Cyanosis(inpatientswith hepatopulmonary syndrome).	● Musclewasting ● Telangiectasia ● Bruising (bc of Thrombocytopenia) ● Parotidgland swelling ● Jaundicedsclera ● Xanthelasma	● Gynecomastia in men (bc of high Estrogen) ● Telangiectasia (Spider naevi)	● Collateral ● Bruising (bc of Thrombocytopenia) ● Hepatomegaly ● Splenomegaly ● Abdominaldistension ● Hepaticbruit ● LossofsecondarySexual hair and testicular atrophy in men. (bc of high Estrogen)

Clinical manifestations (Signs and symptoms)

- No symptoms (Most patients in early cirrhosis)
- Symptoms of cirrhosis (sometimes nonspecific symptoms)
- 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)**

Investigations

Lab tests	
LFTs	● Moderately elevated aminotransferases (often with an AST:ALT ratio >1) ● Elevated ALP (2 to 3 times the ULN[1])
CBC	Thrombocytopenia Leukopenia/neutropenia Anemia
Liver function	Prolonged prothrombin time/elevated INR and Low serum albumin
Hyperbilirubinemia / Hyponatremia / Elevated serum creatinine	

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

Confirm the diagnosis

Biopsy (Gold standard)

Noninvasive tests :

1- Serum score systems

2- Elastography (e.g fibroscan)-

Fibroscan :it's the best when there is no cirrhosis at all or a very severe one.

Assess severity and prognosis of liver disease

Important: memorize only the parameters not numbers

1- Child-Turcotte-Pugh score or Child Criteria (CPT score)

Points	1	2	3
Encephalopathy	None	Minimal	Advanced (coma)
Ascites	Absent	Controlled	Refractory
Bilirubin (μmol/L)	<34	34–51	>51
Albumin (g/L)	>35	28–35	<28
Prothrombin (sec)*	<4	4–6	>6

*Difference between the patient and the control. Differences of 4 to 6 seconds correspond approximately to a prothrombin ratio of ~50 to 40% of normal.

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)

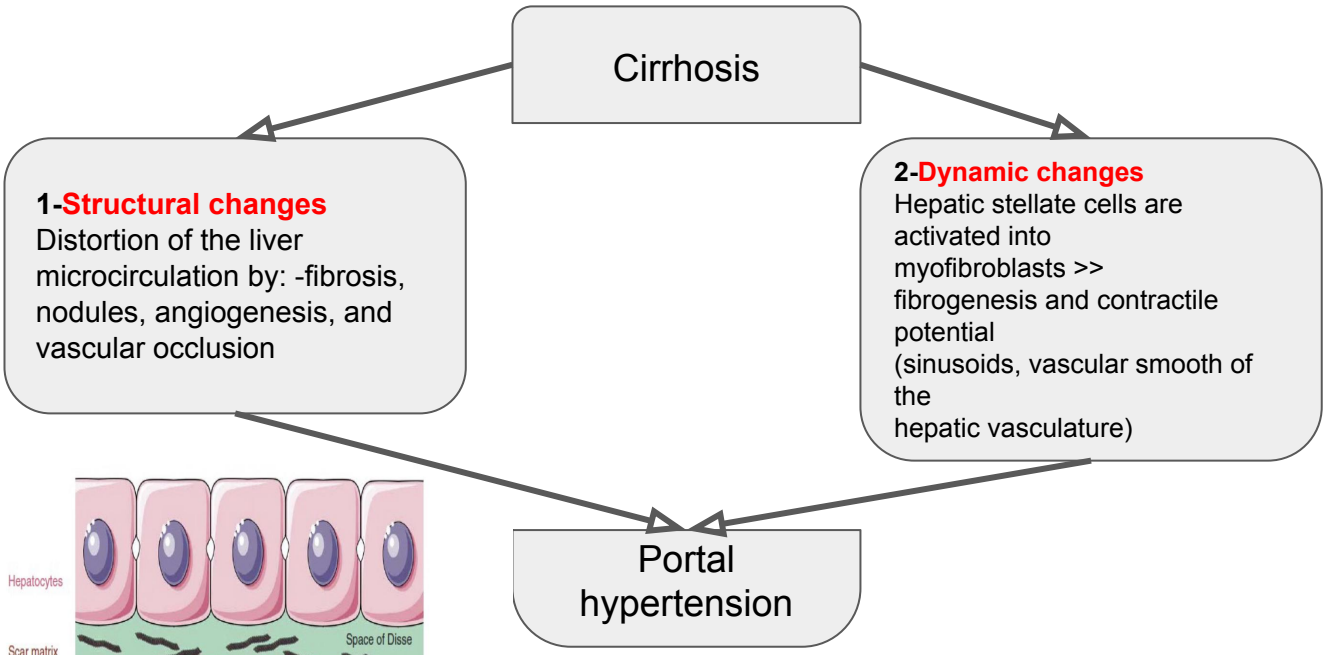
3.8	11.2	9.6
Serum bilirubin	INR	Serum creatinine

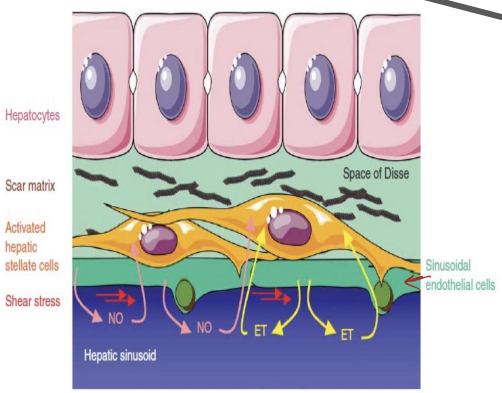
+6.4

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

Portal hypertension is the begging and requirement for most cirrhosis complications





Møller S et al .Scand J Gastroenterol. 2015

Common complications of 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

- Once a patient develops liver failure and complication, they are considered to have Decompensated Cirrhosis
- 50% will survive 2 years

complications of 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

Cirrhosis leads to **portal hypertension**, subsequently there will be splanchnic vasodilation and congestion. Cirrhotic patients immunity is usually weak, which leads to bacterial infection and the bacteria mainly cause vasodilation by endotoxin from bacterial translocation.
This will reduce the effective vascular circulation which will trigger retention and compensatory mechanism (eg.ascites)

complications of cirrhosis

Causes (DDx):

Transudate	Exudate
● Portal hypertension (most common)	● Cancer
● Cardiac failure	● Infections
	● Pancreatitis
	● Nephrotic syndrome.

Examination

- 1.5 L of fluid must be present before flank dullness is detected. M ore specific than shifting.
- Shifting dullness[4]
- If no Flank dullness is present less likely ascites (<10%)

Investigation

Routine:

1. Cell count and differential
2. Albumin and total protein **"To measure SAAG"**

The first step in managing patient with ascites is analyzing the fluid by tapping
Why?
1-to determine etiology
2-to rule out infections

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

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)

Management

Initial treatment of ascites

Stepwise approach:

1. **Dietary salt restriction** Dietary sodium intake and diuretics are effective in 90% of patients
   (< 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

Treatment of refractory ascites ~10%

Ascites that is :

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

Serial therapeutic paracenteses (Ascites tap) + intravenous infusion of albumin if draining > 5L fluid

Transjugular intrahepatic portosystemic shunt (TIPS)

Liver transplantation Peritoneovenous shunt

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

Subtract serum to ascites, never divide

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:

the commonest infection in cirrhotic patient are :
1-ascitic infections
2-UTI

- 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

- 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. (mainly ammonia but not present in all patients)
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.

Precipitants of hepatic encephalopathy caused by:	Treatment
1. **Drugs eg. Benzodiazepine, narcotics, alcohol** 2. **Increased ammonia production, absorption or entry** 7 **into the brain: high protein intake , Gastrointestinal bleeding, Infection (Most common), Electrolyte disturbances such as hypokalemia, Constipation8(Most common), Metabolic alkalosis,** 3. **Dehydration: V omiting, 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 treatment9 (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

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) the main problem is renal vasoconstriction ➟ renal impairment

Diagnosis By exclusion 10	● **Type l:** rapid, aggressive. Acute renal failure due to cirrhosis progress in days. They die without liver transplant ● **Type ll :** 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 so we give patient vasoconstrictors, to stop splanchnic vasodilation caused by cirrhosis and break the cycle ➟ decrease renal vasoconstriction

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)

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

7. Hepatocellular carcinoma (Hepatoma) HCC

incidence is higher in : viral hepatitis, fatty liver

- 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:

- 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

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

Chronic liver injury or Chronic hepatitis → Compensated Cirrhosis → Decompensated Cirrhosis → Death or liver transplantation.

-Aetiology
Most common: NASH, ASH, viral hepatitis (HBV,HCV)

Other: autoimmune hepatitis, PBC,PSC, alpha1 antitrypsin deficiency, WD, hemochromatosis, drugs.

-Investigations:
Lab tests:

- LFT
- CBC
- Prolonged prothrombin time
- INR
- Hyperbilirubinemia
- Serum albumin

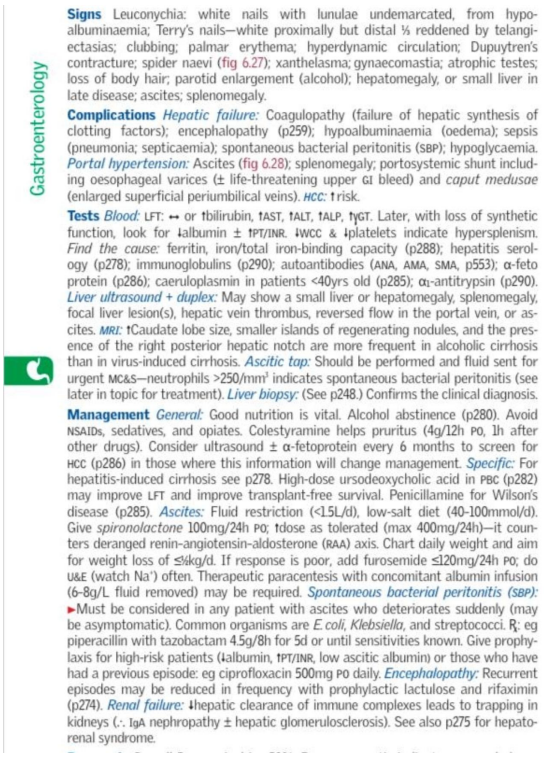
Radiology

-Confirm the Diagnosis :
Invasive: 1- Biopsy

Noninvasive tests:
1- Elastography
2- Serum score systems

-Severity of Liver Disease:

- Child-Turcotte-Pugh score
- MELD score



Gastroenterology

Signs Leuconychia: white nails with lunulae undemarcated, from hypoalbuminaemia; Terry's nails—white proximally but distal ⅓ reddened by telangiectasias; clubbing; palmar erythema; hyperdynamic circulation; Dupuytren's contracture; spider naevi (fig 6.27); xanthelasma; gynaecomastia; atrophic testes; loss of body hair; parotid enlargement (alcohol); hepatomegaly, or small liver in late disease; ascites; splenomegaly.

Complications *Hepatic failure:* Coagulopathy (failure of hepatic synthesis of clotting factors); encephalopathy (p259); hypoalbuminaemia (oedema); sepsis (pneumonia; septicaemia); spontaneous bacterial peritonitis (SBP); hypoglycaemia. *Portal hypertension:* Ascites (fig 6.28); splenomegaly; portosystemic shunt including oesophageal varices (± life-threatening upper GI bleed) and *caput medusae* (enlarged superficial periumbilical veins). *HCC:* ↑risk.

Tests *Blood:* LFT: ↔ or ↑bilirubin, ↑AST, ↑ALT, ↑ALP, ↑γGT. Later, with loss of synthetic function, look for ↓albumin ± ↑PT/INR. ↓WCC & ↓platelets indicate hypersplenism. *Find the cause:* ferritin, iron/total iron-binding capacity (p288); hepatitis serology (p278); immunoglobulins (p290); autoantibodies (ANA, AMA, SMA, p553); α-feto protein (p286); caeruloplasmin in patients <40yrs old (p285); α_1-antitrypsin (p290). *Liver ultrasound + duplex:* May show a small liver or hepatomegaly, splenomegaly, focal liver lesion(s), hepatic vein thrombus, reversed flow in the portal vein, or ascites. *MRI:* ↑Caudate lobe size, smaller islands of regenerating nodules, and the presence of the right posterior hepatic notch are more frequent in alcoholic cirrhosis than in virus-induced cirrhosis. *Ascitic tap:* Should be performed and fluid sent for urgent MC&S—neutrophils >250/mm³ indicates spontaneous bacterial peritonitis (see later in topic for treatment). *Liver biopsy:* (See p248.) Confirms the clinical diagnosis.

Management *General:* Good nutrition is vital. Alcohol abstinence (p280). Avoid NSAIDs, sedatives, and opiates. Colestyramine helps pruritus (4g/12h PO, 1h after other drugs). Consider ultrasound ± α-fetoprotein every 6 months to screen for HCC (p286) in those where this information will change management. *Specific:* For hepatitis-induced cirrhosis see p278. High-dose ursodeoxycholic acid in PBC (p282) may improve LFT and improve transplant-free survival. Penicillamine for Wilson's disease (p285). *Ascites:* Fluid restriction (<1.5L/d), low-salt diet (40-100mmol/d). Give *spironolactone* 100mg/24h PO; ↑dose as tolerated (max 400mg/24h)—it counters deranged renin-angiotensin-aldosterone (RAA) axis. Chart daily weight and aim for weight loss of ≤½kg/d. If response is poor, add furosemide ≤120mg/24h PO; do U&E (watch Na^+) often. Therapeutic paracentesis with concomitant albumin infusion (6-8g/L fluid removed) may be required. *Spontaneous bacterial peritonitis (SBP):* ▶Must be considered in any patient with ascites who deteriorates suddenly (may be asymptomatic). Common organisms are *E coli, Klebsiella,* and streptococci. Rx: eg piperacillin with tazobactam 4.5g/8h for 5d or until sensitivities known. Give prophylaxis for high-risk patients (↓albumin, ↑PT/INR, low ascitic albumin) or those who have had a previous episode: eg ciprofloxacin 500mg PO daily. *Encephalopathy:* Recurrent episodes may be reduced in frequency with prophylactic lactulose and rifaximin (p274). *Renal failure:* ↓hepatic clearance of immune complexes leads to trapping in kidneys (∴ IgA nephropathy ± hepatic glomerulosclerosis). See also p275 for hepatorenal syndrome.

Oxford: clinical medicine

Complications of liver cirrhosis		
1. Ascites: Accumulation of fluid in the peritoneal cavity		
Investigation	Routine: 1. Cell count and differential 2. Albumin and total protein To measure SAAG	
Management	1. Dietary salt restriction 2. Diuretics (most successful is Spironolactone and Furosemide combination)	
Refractory ascite	1. Unresponsive to sodium restricted diet and high dose diuretic treatment, 2. Development of clinically significant complications of diuretics	
SAAG	High albumin gradient (SAAG>=1.1g\dL) ● Cirrhosis / Alcoholic hepatitis ● Heart failure / Constrictive pericarditis.	Low albumin gradient (SAAG<1.1g\dL) ● Peritoneal carcinomatosis ● Lymphoma. ● Nephrotic syndrome
Complications	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	
2.Hepatic encephalopathy: Hepatic encephalopathy is a reversible brain dysfunction caused by liver insufficiency and portosystemic shunts. **(Flapping tremor)**		
Pathophysiology	Neurotoxin (ammonia) → cross BBB → Activation of inhibitory neurotransmitter systems→ Impairment of excitatory neurotransmitter systems → Enhanced neural inhibition	
Precipitants	• Drugs • Increased ammonia • Dehydration	• Portosystemic shunts • Vascular occlusion • HCC
Treatment	● Lactulose (decrease absorption of ammonia) ● Rifaximin or metronidazole (decrease GI bacteria that produce ammonia)	
3.Hepatorenal syndrome: Development of functional acute kidney injury in a patient who usually has advanced liver disease either cirrhosis or alcoholic hepatitis		
4.Portopulmonary Syndrome: the presence of pulmonary hypertension in the coexistent portal hypertension		
5.Hepatic Hydrothorax: Pleural effusion in a patient with cirrhosis and no evidence of cardiopulmonary disease		
6.Hepatopulmonary syndrome (HPS) **Triad of :** Liver disease , Increased alveolar-arterial gradient , Evidence for intrapulmonary vascular abnormalities		
7. Hepatocellular carcinoma (Hepatoma) HCC		
Investigation	● 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	

Questions

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. Palmar 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

1D
2E (alcoholic liver is cause of increase MCV)
3E
4C

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

8-what the most common complication of liver cirrhosis?
A- ascites
B- hepatopulmonary syndrome
C- hepatorenal syndrome
D- hepatic hydrothorax

9- serum to ascites albumin gradient of 2g/dL means?
A- pancreatitis
B-ascites
C- serositis
D- nephrotic syndrome

5C (bc her history is related to AIH and prednisolone is steroid immunosuppressive therapy)
6C
7A
8A
9B