LIVER CIRRHOSIS

Def: Clinically: any liver with sharp border & firm in consistency.

Pathologically: diffuse disease characterized by degeneration, regeneration nodules, fibrosis & loss of the hepatic architecture.

N.B: Bilharziasis is detected clinically as cirrhosis but pathologically, it is mere fibrosis.

Classification:

A. Aetiological classification:

1. Idiopathic, alcoholic cirrhosis.
2. Hemochromatosis.
3. Wilson's disease (hepatolenticular degeneration).
4. Biliary cirrhosis, post-hepatic cirrhosis.
5. Cardiac cirrhosis, iatrogenic (methotrexate & INH).
6. α 1- antitrypsin deficiency, malnutrition & congenital syphilis.

B. Morphological classification:

1. Micronodular cirrhosis (small nodules of the same size).
2. Macronodular cirrhosis (large nodules of variable sizes).
3. Mixed.

N.B: alcoholic cirrhosis is usually micronodular, while hepatitis cirrhosis is usually macronodular.

Clinical picture:

A. Compensated (latent) cirrhosis:

- Early in the disease, there is no important of liver functions.
- It is discovered accidentally during examination or by US of a different problem.

B. Decompensated (manifest) cirrhosis:

- Shrunken liver & splenomegaly.
- Manifestation of liver cell failure & portal hypertension.

C. Clinical picture of the cause.

D. Clinical picture of complication (as hepatoma).

Investigation:

1. Liver function test.
2. Investigation of portal hypertension.
3. Investigation of the cause.
4. Investigation of complication (for example, hepatoma is investigated by α – fetoprotein, US, CF & liver biopsy.
5. Biopsy: it is the surest diagnostic investigation.

Treatment:

1. Treatment of liver cell failure.
2. Treatment of portal hypertension.
3. Treatment of the cause.
4. Treatment of complication.
5. Antifibrotic drugs as: colchicine → increases collagen destruction.
   Penicillamine → decrease collagen synthesis.

Causes of liver cirrhosis

1. Alcoholic cirrhosis:
   - It depends on the duration more than the amount (needs 10 years or more).
   - Effect of alcohol on the liver: direct toxicity – nutritional deficiencies.
   - Pathology: micronodular cirrhosis + Mallory bodies (eosinophilic cytoplasmic bodies).
   - **Clinical picture**:
     - General picture of cirrhosis & liver cell failure.
     - History of chronic alcohol intake (alcoholism).
     - Acute alcoholic hepatitis (due to overdose) → sever pain & vomiting.
     - Chronic alcoholism:
       i. CNS: Korsakow syndrome (tremors, amnesia& confabulation).
       ii. Stomach: gastritis (morning nausea & vomiting).
       iii. Hand: dupuytren's contracure.
       iv. Face: flushing & bilateral parotid enlargement.
   - **Investigation**:
     - General investigation of cirrhosis.
     - Alcohol level in blood & IgA (elevated).
   - **Treatment**:
     - General measures used in treatment of cirrhosis.
     - Stop alcohol intake.
2. Hemochromatosis: (Bronzed bodies):
   - **Def**. Diffuse deposition of iron in the parenchymal tissue (hemosiderosis) associated with fibrotic changes & organ damage.
   - **Aetiology**:
     - Increased dietary intake (tonic& red wine) & absorption of iron due to increased mucosal block (apoferritin-ferritin system).
     - Parenteral iron used for treatment of anemia or repeated blood transfusion for treatment of chronic hemolytic anemia.
   - **Clinical picture**:
     - Skin: bronzed color.
     - Heart: cardiomyopathy, HF & arrhythmia.
     - Liver: cirrhosis.
     - Nerves: peripheral neuropathy.
     - Joints: arthropathy.
     - Endocrine glands:
       - Pancreas → D.M.
       - Deficiency of pituitary & suprarenal glands hormones.
       - Tests → atrophy, sterility & impotence.
   - **Cause of death**: sudden release of ferritin which is a strong VD → shock.
   - **Investigation**:
     - Increased serum (normally 125 µg/dl), increased iron saturation (normally 30%) & decreased total iron binding capacity (normally 400 µg/dl).
     - Liver biopsy.

Treatment:

- Decreasing dietary iron.
- Repeated venesection (we get rid of 250mg iron with every 100ml of blood.
- Desferroxamine (dysferal) → increase urinary excretion of iron.
- SHAM.

3. Wilson's disease (hepatolenticular degeneration) :

- **Def.** quantitative or qualitative deficiency of ceruoplasmin which is responsible for cooper carriage resulting in deposition of iron in tissues.
  - In quantitative deficiency: copper binds loosely to albumen & can easily leaven it.
  - In qualitative deficiency: there is decreased affinity of ceruoplasmin to copper.
- **Clinical picture:**
  - Liver cirrhosis.
  - Eye: cornea → Kayser Fleisher ring (green brown ring).
    Lens → sun flower cataract.
  - Kidney: Fanconi syndrome (renal tubular defect resulting in loss of amino acids, proteins, glucose, bicarbonates & potassium in urine.
  - Basal ganglia (lentiform nucleus): chorea & Parkinsonism.
- **Investigation:**
  - Decreased serum copper (normally 100 µg/dl).
  - Decreased serum ceruoplasmin).
  - Increased urinary copper excretion.
  - Increased liver content of copper.
- **Treatment:**
  - Copper chelating agents as penicillamine, 250 mg /day orally.
  - Potassium sulfide → prevents copper absorption.
  - Decreasing dietary copper.

N.B: nuts & chocolate are rich in copper.

4. Biliary cirrhosis:

- Aetiology: increased bile pigments in the liver due to biliary obstruction, either extrahepatic either extrahepatic or intrahepatic.

A. Extrahepatic obstruction:

1. From inside → by stones & ascaris.
2. From the wall → biliary atresia, stricture or tumor.
3. From outside → enlarged lymph nodes, cancer head of pancreas.

B. Intrahepatic obstruction:

Classification:

[1] 1ry biliary cirrhosis:

- **Aetiology:** immune disease & genetic role.
- **Pathology:** cirrhosis associated with injury & proliferation of bile ducts.
- **Incidence:** middle aged pre-menopausal females.
- **Clinical picture:**
  - Purities (50% of cases present with purities). It occurs months or years before jaundice.
  - Jaundice, liver cirrhosis (enlarged, firm with sharp border).
  - Splenomegaly.

- Skin: pigmentation, xanthoma & xanthelasma.
- Pale clubbing of fingers.
- Osteoporosis (that is why steroids are not used in treatment).

- **Investigation:**
  - Detection of autoantibodies as ANA, ASMA, anti-bile duct antibody & high IgM.
  - Alkaline phosphatase is elevated.
  - Liver biopsy is diagnostic.
- **Treatment:**
  - Immunosuppressive drugs as penicillamine.
  - Azathioprine.
  - Symptomatic relief of purities using cholestyramine.

[2] 2ry biliary cirrhosis:

- Chronic hemolytic anemia.
- Cholestatic viral hepatitis (Watson syndrome)
- Drugs:

Oral contraceptive.	Chlorpromazine.
Oral anticoagulants	PAS
Oral hypoglycemic	anabolic steroids

5. Post-hepatitis cirrhosis:

- **Aetiology:** usually following viral hepatitis B&C.
- **Pathology:**
  - Features of chronic active hepatitis.
  - Features of liver cirrhosis.
  - Ground glass appearance (specific for HBV).
  - +ve orcein stain.
- **Clinical picture**: the same as cirrhosis – history of infective hepatitis or chronic hepatitis.
- **Investigation**: as cirrhosis – viral hepatitis markers.
- **Treatment**: general measures for cirrhosis – treatment of chronic active hepatitis.

6. Cardiac cirrhosis:

- **Aetiology:** chronic venous congestion of the liver caused by:
  a. Right –sided heart failure.
  b. Tricuspid valve disease (either Stenosis or incompetence).
  c. Constrictive pericarditis.
  d. High IVC thrombosis.
  e. Budd – chiari syndrome.
  f. Veno- occlusive disease of the liver.
- **Clinical picture**:
  - Clinical picture of the cause.
  - Enlarged tender liver, soft then firm with sharp border.
  - Features of cirrhosis with appearance of portal hypertension before liver cell failure.

Budd-Chiari syndrome

- ⇨ Obstruction of large hepatic veins.
- ⇨ **Aetiology**:
  1. Thrombosis: (caused by clotting diseases as Polycythemia).
  2. Compression from outside by tumors or enlarged LNs.
- ⇨ **Clinical picture**:
  1. Acute stage: abdominal pain – vomiting – enlarged tender liver – ascites & mild jaundice.
  2. Chronic stage: features of liver cirrhosis.

Veno-occlusive disease of the liver

- ⇨ Obstruction of small intrahepatic veins.
- ⇨ Occurs in infants.
- ⇨ Caused by toxins.

7. Idiopathic (cryptogenic) cirrhosis:
   - Aetiology: unknown.
   - Investigation showed that 3% of cases are due to HBV infection (non-icteric attack).
   - Recent studies suggest that it is mostly (90%) due to HCV infection.

LIVER CELL FAILURE

Causes:

1. Liver cirrhosis.
2. Cholestasis.
3. Burns.
4. Hyperthermia.
5. Fulminant hepatitis.
6. Alcoholism.
7. Ray's syndrome.
8. Fatty liver of pregnancy.
9. Shock & hepatic artery legation.
10. Chemicals as halothane, INH, CCl_4 & rifampicin.

Clinical picture:

{1} Failure of health: loss of weight, weakness & easy fatigability.

{2} Cirrhotic liver: the liver is shrunken, firm with sharp border.

{3} Palpable spleen.

{4} Fever: causes:

a. Necrosis of the hepatocytes.

b. Failure of the liver to clear bacteria reaching it from the GIT & detoxify pyrogenic substance.

c. Spontaneous bacterial peritonitis.

Spontaneous bacterial peritonitis

Def.: bacterial infection of the peritoneal fluid in absence of known aetiology.

Incidence: 10% of cirrhotic patients.

Aetiology:

- It may be due to decreased anti-bacterial activity of peritoneal fluid.
- The causative organisms are E.Coli, Srtept. Fecalis, Staph. aureus, Gram – ve & opportunistic organism.

Clinical picture:

- Fever, abdominal pain & tenderness.
- Ascites resistant to treatment.
- Deterioration → hepatic encephalopathy.

Investigation:

- Leucocytosis.
- Aspiration of peritoneal fluid → 250 WBC_s / mm^3.
- Culture of the peritoneal fluid.

Treatment: 3rd generation cephalosporins as cefotaxime (calforan).

{5} Foetor hepaticus:

- Normally, bacteria in the colon act proteins producing methyl mercaptan, indicant & skatol which pass through the portal vein to the liver where they are detoxified.
- In liver cell failure, these substances pass unchanged through the liver or bypass it through porto-systemic shunts.
- Foetor hepaticus is a bad mouth odour described as aromatic sweetish & highly fecal or rotten moth or open grave.
- It increased by constipation & decreased by defecation or antibiotics.

{6} Cardiovascular manifestations:

- Hyperdynamic circulation: due to anemia & increased vasodilator substances (decreased destruction in the liver).
- Hypovolemic shocks: due to increased VD substances, ascites, tapping of ascites → splanchnic shock.
- Central cyanosis (hepatopulmonary syndrome) due to:
  - Portopulmonary shunts.
  - Pulmonary A-V shunts (due to increased VD substances).
  - Ascites → basal collapse of the lungs.
  - Interstitial pulmonary fibrosis (due to decreased lung perfusion) & V/P unequality (Ventilation / Perfusion).

{7} Hematological manifestations:

- Anemia : 3 types may occur:
  1. Microcytic hypochromic: due to iron deficiency from bleeding.
  2. Normocytic normochromic: due to bone marrow suppression & hypersplenism
  3. Microcytic hyperchromic: due to deficiency of vit. B_{12}.
- Bleeding : due to:
  1. Decreased synthesis of clotting factors in the liver (prothrombin, fibrinogen, factors V, VII, IX & X).
  2. Platelet disorder: thrombocytopenia (due to hypersplenism) &/or thromboasthenia (platelets are coated by abnormal globulin from ESR).

{8} Hepatorenal syndrome:

- Def. acute functional renal failure in patient with chronic liver disease.
- Aetiology:
  1. Decreased blood volume due to ascites, tapping of ascites diuretics & massive VD.
  2. Decreased release of quinine, bradykinins & PG_s by the kidney →increase perglomerular resistance → VC of afferent arterioles.

- Investigation: renal function test.
- Prognosis: bad with about 80% mortality.
- Treatment: treatment of liver cell failure & acute renal failure.

{9} Hepatocellular jaundice:

- Orange yellow - Dark urine & pale stool.

{10} Ascites: causes :

- **Hypoalbuminemia**:
  - Due to decreased synthesis of albumin in liver.
  - Normal albumin level is 4-5 gm/dl.
  - Ascites threshold is < 3gm / dl.
- **Portal hypertension**:
  - Alone, it can't produce ascites.
  - With hypoalbuminemia it leads to localization of the transudate to areas drained by portal vein.
- **Lymphorrhewa**:
  - It occurs in post-sinusoidal obstruction.
  - There is increased lymph production → dilated lymphatics on the surface of the liver with extravasation of lymph into the peritoneal cavity (weeping liver)
- Salt & water retention: due to increased production & decreased destruction of ADH & aldosterone.
- **Other causes**: associated tuberculosis peritonitis, malignant peritonitis, spontaneous bacterial peritonitis or liver malignancy.

{11} Skin manifestations:

- Pallor due to anemia. Pruritus & pigmentation.
- Purpura due to thrombocytopenia.
- Paper money skin → numerous small vessels scattered in random fashion.
- Palmer Erythema → Erythema in the heads of metacarpals, thenar & hypothenar eminences with central pallor.
- Spider naevi → dilated arterioles with radiating capillaries, present in areas drained by the SVC (above the nipple), compression of the central arteriole by the head of a pin result in blanching of radiating capillaries.
- Skin manifestations of vitamin deficiency.

⇨ Other causes of palmer Erythema & spider naevi:

- Rheumatoid arthritis – thyrotoxicosis – pregnancy - Steroids – old age.

{12} Nails manifestation:

- Spooning: due to iron deficiency anemia.
- Leuconychia: white nails due to hypoalbuminemia.
- Clubbing of fingers: more common with primary biliary cirrhosis.

{13} Endocrine changes:

- **Gonadal dysfunction**:

In males (feminization)	In females (defeminization)
Gynecomastia	Breast atrophy
Feminine distribution of suprapubic hair.	Decreased libido
Loss of axillary hair.	Amenorrhea & sterility
Decreased libido, impotence & testicular atrophy	Decreased 2ry sex characters

- **Glucose metabolism**:
  - Hypoglycemia: occurs in (fulminant hepatitis-late cirrhosis-hepatic tumors).
  - Post-prandial hyperglycemia: due to decreased liver uptake of glucose & insulin resistance.
  - Diabetes mellitus: occurs in hemochromatosis & primary biliary cirrhosis.
- **Growth hormone**: normal or increased level but no growth as the diseased liver can't produce somatomedins which are essential for the action of GH.
- **Thyroid hormone**:in liver cell failure, there is decreased conversion of T_4 to T_3.

{14} Hepatic encephalopathy:

- **Def.** it is a state of brain inhibition in a patient with chronic liver disease.
- **Pathogenesis**: bacteria in the colon act on proteins producing toxic substances which pass unchanged through the liver or bypass it through porto-systemic shunt → CNS → encephalopathy.
- **These toxic substances include**:
  1. Ammonia: it combines with α-ketoglutamic producing glutamine which interferes with kreb's cycle.
  2. Revised ammonia.
  3. False chemical transmitters: tyramine & octapamine reach the brain & act instead of dopamine & adrenaline.
  4. Hypoglycemia.
  5. Increased aromatic & decreased branched amino acids: normally branched amino acids (as valine, leucine & isoleucine) pass the BBB (blood prain barrier), but when they are used as a source of energy, aromatic amino acids (as tryptophan & phenylalanine) enter the brain & act as false neurotransmitters.
  6. Lipids → increased short-chain fatty acids inhibit the reticular formation in the brainstem.
  7. hypokalemia: due to increased aldosterone & use of diuretics leading to:
     - Increased production of ammonia by the kidney & facilitates its entry into the brain.
     - It decreases glucose entry to the brain cells.
  8. Increased GABA which is an inhibitory neurotransmitter.
  9. Benzodiazepines act on the receptors of GABA producing similar effect → contraindicated in liver cell failure.
- **Precipitating factors**:
  1. Increased ammonia: high protein intake – hemorrhage – GI bleeding – transfusion of stored blood – tissue destruction (trauma – surgery).
  2. Hypokalemia: use of diuretics – tapping of ascites – vomiting & diarrhea.
  3. Drugs: morphine & Benzodiazepines – diuretics – ammonium chloride.
- **Clinical picture**: pass in 2 stages:
  1. Precoma:
     - Personality changes: alternating crying & laughing – childish facies – disorientation to time, place & persons – defecation & urination in unsuitable places.
     - Apathy with slow response to questions.
     - Speech is slow, slurred & monotonus.

- Inverted sleep rhythm.
- Tachycardia due to respiratory alkalosis.
- Flapping tremors (asterixis).

2. Coma:
   - Irritable coma, sweating, + ve Babiniski sign.
   - No tremors, dilated pupils, hyperventilation.
   - Exaggerated deep reflexes.

- **Investigation**:

1. Blood picture: anemia
   - Anemia.
   - Leucopenia (due to bone marrow suppression & hypersplenism). Leucocytosis may occur in infections.
   - Thrombocytopenia, prolonged bleeding time.
2. Liver function test: bilirubin, ALT, AST, serum albumin, alkaline phosphatase & prothrombin time.
3. Ammonia level in the blood (normally 0.8 – 1 µg/ml).
4. CSF glutamine level.
5. EEG.
6. Liver biopsy to confirm the diagnosis, detect the cause & complications.

Treatment of liver cell failure

[I] Treatment of the cause.
[II] Correction of the precipitating factors.
[III] Treatment of ascites.
[IV] Treatment of hepatic encephalopathy.

Treatment of ascites

1. **Bed rest:** to decrease metabolites handled by the liver & increase renal perfusion.
2. **Diet:**
   - Salt restriction (< 0.5 gm /day), fluid balance.
   - Increase protein intake to correct hypoalbuminemia (should restricted if manifestations of encephalopathy develop).
   - Plenty of carbohydrate as source of energy.
   - Plenty of vitamins to support the liver.
3. **Follow up:** by daily recording of urine output & body weight.
4. **Diuretics:**
   - Indication: failure of diet regimen to control ascites (failure to decrease body weight > 1kg in the 1st 4 days).
   - Dose:
     - Start with spironolactone 25 mg/6 hours to be increased to 100 mg/6 hours.
     - If refractory add frusemide 40 – 80 mg / day.
   - Side effects:
     - Spironolactone: gynecomastia.
     - Frusemide: hypokalemia, so give it with Spironolactone or give KCl.
   - Precautions: the rate of ascites fluid reabsorption should be limited to 700 – 900 ml/day.

5. **Increasing the osmotic pressure of plasma: by:**
   - Salt-free albumin (human albumin) →improve ascites but very expensive & of short half life.
   - Dextran - Plasma transfusion.

6. **Tapping of ascites:**
   - **indications**:
     - Relief of dyspnea & pressure syndrome.
     - Diagnostic of the cause of ascites.
     - To decrease pressure on the renal vein to give chance for diuretics to act.
     - To give antibiotics (in infection) or cytotoxic drugs (in malignancy).
   - **Amount:**
     - Partial tapping: 1000 cc.
     - Complete tapping: 5 – 10L (proteins are to be replaced by salt-free albumin 6 gm /L removed).
   - **Site:**
     - Mc Burney's point on the left side.
     - Midway between the umbilicus & symphysis pubis.
   - **Complications:**
     - Pain, hemorrhage & infection.
     - Shock, either neurogenic (due to pain) or splanchnic (due to sudden VD of the splanchnic blood vessels).
     - Injury of the abdominal organs as urinary bladder.
     - May precipitate hepatic encephalopathy due to hypokalemia & increased absorption of ammonia.
     - Repeated tapping may cause hypoalbuminemia.
7. **Treatment of terminal ascites**:
   - **Le veen shunt:**
     - It is a tube with one way valve connecting the peritoneal cavity to the jugular veins.
     - Complications: hypervolemia – pulmonary edema – septicemia – DIC.
   - **Denever shunt:** it has an additional valve to control the rate of flow of the peritoneal fluid.
   - **Ultra filtration & re-infusion.**

N.B: treatment of refractory ascites: bed rest, salt restriction & shunt operation.

Treatment of hepatic encephalopathy

1. **Proteins:**
   - Diet:
     - Protein restriction.
     - Excess carbohydrates as source of energy & to prevent protein breakdown.
     - Diet rich in potassium as organic juice.
   - Hemorrhage: repeated enema – control GI bleeding.
2. **Bacteria:**
   - Antibiotics: neomycin 1gm 4 times /day – streptomycin 2 gm / day.
   - Lactulose: it is alternative to neomycin.

     It consists of 2 parts: **lactose**: osmotic laxative, **lactic acid**: changes PH of the colon making it unsuitable for bacterial growth.

3. **Ammonia:**
   - Glutamic acid: combines with ammonia.
   - Arginine- sorbitol:
     - Arginine + ammonia → urea (harmless).
     - Sorbitol → fructose → support the liver.
4. **CNS: L-dopa** → dopamine – Bromocryptine.
5. **Supportive treatment**:
   - Care of bowel & bladder.
   - Care of respiration.
   - Avoid bed sores by changing the position of the patient regularly & using air mattresses.

AMOEBIC DYSENTRY
AMOEBIC LIVER ABSCESS

HEPATITIS

Causative agent: the vegetative form of Entamoeba histolytica.

Route of infection: oral → intestine → portal vein → liver.

Pathology:

1. Hepatitis: diffuse enlargement with foci of necrosis caused by the proteolytic enzymes of the Entamoeba histolytica.
2. Acute abscess:
   - Foci of necrosis coalesce forming an abscess with shaggy necrotic wall.
   - Content: chocolate brown necrotic material (tomato juice or Anchovy sauce).
3. Chronic abscess:
   - Usually single abscess with thick wall & smooth lining.
   - Site: usually in the upper part of the right lobe of the liver.

N.B: amoebic liver abscess is more common in the right lobe of the liver because of the stream line theory: E.histolytica infects the right colon → portal vein → right branch → right lobe of the liver.

Clinical picture:

Symptoms:

A. General symptoms: fever with rigors – headache – malaise & sweating.

B. Local symptoms:
   - Pain in the right hypochondrium (dull-aching, stabbing or throbbing).
   - It is referred to the back, right shoulder or lower chest.
   - It increases by coughing or straining.

C. Lung symptoms: symptoms of plural & lung affection as cough & expectoration of tomato juice.

Signs:

A. General symptoms: fever with earthy look.

B. Local symptoms:
   - Enlarged tender liver.
   - Marked tenderness of the lower ribs & intercostal spaces.

- Rarely, jaundice may be seen, if appeared it is obstructive (due to obstruction of big bile ducts by abscess).
- Lately, there is edema over the chest wall & liver

C. Lung symptoms:

- Signs of empyema.
- Signs of lung abscess.
- Pleural rub, effusion & consolidation (basal).

Complications:

1. 2ry bacterial infection → pyrogenic abscess.
2. Chronisty.
3. Rupture & spread:
   a. Upward: subphrenic abscess – pleural effusion &empyema – lung abscess – pericarditis.
   b. Downward: peritonitis – fistula formation – with other organs.
   c. To the skin: Cutaneous amoebiasis (of poor prognosis).
   d. To the blood: other organs (brain, lungs).

Investigations:

1. For amoeba:
   a. Stool analysis → vegetative form or cyst form.
   b. Sigmoidoscopy → may show amoebic ulcers (flask-shaped ulcers with healthy mucosa in between).
   c. Immunological tests: FAT (fluorescent antibody technique) – CFT (complement fixation test) – ELIZA.
2. For the liver:
   a. Leucocytosis (PNL).
   b. Liver function tests.
   c. X-ray → raised right copula of the diaphragm.
   d. US, CT & isotopic scanning.
3. Other tests:
   a. Therapeutic test: give Antiamoebic drugs as metronidazole & detect response.
   b. Diagnostic aspiration of the abscess guided by US → aspirate is anchovy sauce fluid.

Treatment:

1. Bed rest & good nutrition.
2. Medical treatment :
   a. Emetine hydrochloride:
   - Dose: 60 mg / day IM for 10 days.
   - Side effects: CVS → hypotension & arrhythmia.
     GIT upset.
     CNS → peripheral neuritis.

   b. Dehydroemetine: as emetine hydrochloride but less effective & less toxic.
   c. Metronidazole (flagyl):
   - Dose: 500 mg / t.d.s. orally for 10 days.
   - It is very effective & safe.
   - Side effects: metallic taste.

d. Tinidazole:
- Dose: 2 gm /day for 5 days.
- It is effective & safe as metronidazole.

e. Chloroquine:
- 500 mg twice daily for 2 days then , 250mg twice daily for 21 days.
- Side effects: corneal opacity – retinopathy.

f. Antibiotics to prevent & treat 2ry bacterial infection.

g. Analgesics & vitamins.

h. Furamide: it eradicates bowel infection (dose 500 mg t.d.s for 10 days).

3. Aspiration of the abscess:
   a. Indication: cases not respond to medical treatment.
   b. It is guided by US using wide bore needle.
4. Surgical treatment:
   a. Indication:

left lobe abscess.	Multiple abscesses.
Large abscess.	Absent response to aspiration.
2ry bacterial infection.	Thick pus not suitable for aspiration

HEPATIC TUMORS

Classification:

1. Benign: of no clinical importance.
2. Malignant:
   a. 1ry: originates from:
      i. Hepatocytes → hepatocellular carcinoma (hepatoma).
      ii. Bile canaliculi → cholangioma & cholangiocarcinoma.
      iii. Blood sinusoids → hemangioma & hemangiocarcinoma.
   b. 2ry:
      i. More common than 1ry tumors.
      ii. Arises from the GIT, chest, breast & prostate.
      iii. Umbilicated → with areas of central necrosis.

HEPATOCELLUAR CARCINOMA HEPATOMA

Incidence:

- It is the commonest 1ry malignant tumor of the liver.
- Age: > 40 years.
- More common in males (male: female ratio is 3: 1).

Predisposing factors:

- Chronic infection with HBV & HCV.
- Liver cirrhosis specially if due to alcoholism & hemochromatosis.
- Aflatoxin: toxin produced by aspergillus falvus fungus which grows on stored grains specially in hot humid condition.
- Benign tumors as adenoma.
- Massive immunodeficiency & cytotoxic drugs.
- Contractive pills → increase adenoma only & cause focal nodular hyperplasia.

Clinical picture:

- May be asymptomatic & discovered accidentally.
- Deterioration of cirrhotic patient.
- Pain or lump in the right hypochondrium.
- Liver cell failure.
- Portal hypertension due to portal vein thrombosis.
- Para-malignant syndrome → distal manifestations of the tumor without metastases due to production of hormone-like substance :
    - Painful gynecomastia.
    - Hypercalcemia, hyperlipidemia & hyperthyroidism.
    - Hypoglycemia.
- Metastatic manifestation:
    - Direct → malignant ascites.
    - Lymphatic → spread to the axillary & mediastinal LNs.
    - Blood → spread to the lungs, bones & brain.
- Liver:
    - Palpation: enlarged, hard, tender & nodular liver.
    - Auscultation: friction rub (due to perhepatitis) & arterial rub (as the tumor is highly vascular).
- Malignant ascites, jaundice may be seen.
- Loss of weight, anorexia, fever & cachexia.

Investigation:

1. Laboratory:
    - Hepatitis B markers may be +ve.
    - A-fetoprotein: elevated in 50 – 80 % of cases > 2000 ng /dl.
    - Elevated alkaline phosphatase.
    - Elevated ferritin.
    - Increased vit. B_{12} binding protein.
2. Radiological:
    - Abdominal US, CT & MRI.
    - Chest X-ray for metastases.
    - Portal venograhpy, IVC venograhpy.
    - Barium swallow & barium meal to show tumor extension.
    - Aspiration of the ascetic fluid & examination.
    - Liver biopsy guided by US → the surest diagnostic method.

Treatment:

1. Prophylaxis:
    - Prevention of HBV & HCV infection - Avoiding aflatoxins.
2. Curative treatment:
    - Surgical resection: occasionally needed for small encapsulated tumor affecting one lobe → partial lobectomy.
    - Chemotherapy: it causes remission in one third of patients:
        - Adriamycin 60 mg / m^2 surface area / week for 3 doses- side effects → heart failure in normal heart.
        - 5-flurouracil.

- Catheterization of hepatic artery and chemotherapy or embolization by gel foam.
- Percutaneous injection of ethanol into the tumor → necrosis.
- Liver transplantation:
  - Results are unsatisfactory.
  - Immunosuppressive drugs given to prevent rejection favour recurrence & metastases.

Prognosis:

- Usually bad.
- Average survival time 1 – 2 years.
- Shortened by chemotherapy.

PORTAL HYPERTENSION

Def.: Elevation of portal venous pressure above normal.

The normal level is 7-10 mm Hg or 100 – 200 mm H_2O.

If exceeds 15 mm Hg or 150 mm H_2O → portal hypertension.

Causes:

1. Pre-hepatic (infra-hepatic):
   - Increased blood viscosity: Polycythemia – dehydration.
   - Increased portal blood flow: due to arterial-portal vein fistula before the portal vein enters the liver.
   - Portal vein obstruction before entering the liver due to:
     - Congenital narrowing of portal vein.
     - Compression from outside by cancer head of pancreas, hepatocellular carcinoma or enlarged LNs at porta hepatic.
     - Thrombosis:
       - Infection of the umbilicus in neonates which may spread to the portal vein through the para-umbilcial vein.
       - Abdominal infection & septicemia → portal thrombophlebitis.
       - Post-splenectomy → decreased sequestration of platelets & RBCs.
       - Splenic vein thrombosis.
2. Intra-hepatic:
   - Pre-sinusoidal: obstruction of the portal vein branches inside the liver:
     - Schistososmiasis → peri-portal fibrosis.
     - Congenital hepatic fibrosis (fibrosis of the portal traces).
     - Lymphoma, leukemia & sarcoidoisis → infiltration of the portal tracts by abnormal cells.
     - Toxins → arsenic.
   - Sinusoidal: obstruction of liver sinusoids due to cirrhosis.
   - Post-sinusoidal: obstruction of small intra-hepatic veins due to veno-occlusive disease.
3. Post-hepatic (supra-hepatic): obstruction of the venous blood flow from the liver to the right heart:
   - Bedd-chiari syndrome (hepatic vein obstruction).
   - High I.V.C obstruction (above the level of the hepatic vein).

- Right ventricular failure & tricuspid incompetence.
- Pericardial effusion & constrictive pericarditis.

Pathology & clinical picture:

Items	Pathology	Clinical picture
GIT	Gastrointestinal congestion	Dyspepsia, constipation,distension & malabsorption
Liver	➢ Supra-hepatic causes → congested. ➢ Hepatic → cirrhosis. ➢ Infra-hepatic → free.	➢ Enlarged, tender & pulsating. ➢ Cirrhotic → sharp border & firm in consistency.
spleen	➢ Enlarged due to reticulo-endothlia hyperplasia & back pressure. ➢ Its size depends on: 1. The degree of portal hypertension. 2. Age (old →fibrosis→not huge). 3. Collaterals.	➢ Dragging pain in the left hypochondrium. ➢ Pressure on the surrounding organs. ➢ Pancytopenia due to hypersplenism: 1. ↓RBCs → anemia. 2. ↓WBCs → infections. 3. ↓Platelets→ bleeding tendency.
	N.B: splenomegaly is slight in supra-hepatic causes & may not be enlarged in cases of supra-hepatic obstruction.	
Ascites	➢ Portal hypertension alone can't cause ascites but it increases the capillary filtration pressure → localization of ascites in the peritoneal cavity. ➢ Ascites in cirrhosis usually indicates liver cell failure.	➢ Signs of increased intra-abdominal pressure. ➢ + Ve shifting dullness. ➢ Dilated veins on the anterior abdominal wall. ➢ If tense ascites → fluid thrill.

Collaterals: they are caused by dilatation of the porto-systemic anastomoses.

site	Portal	Systemic part	Clinical picture
Oesophageal-gastric junction	Oesophageal branch of the left gastric & short gastric veins.	Lower oesophageal veins	Oesophageal varices associated with hematemesis or melena.
Rectoanal junction	Superior rectal vein	Middle & inferior rectal veins	Bleeding piles
Along the falciform ligament	Para-umbilcial veins	Superficial vein of the anterior abdominal wall	Caput medusa & venous hum on the epigastrium
Abdomen	Abdominal viscera	Veins of the abdominal wall & retroperitoneal structure.	Usually silent
lungs	Right branch of the portal vein	IVC	Porto-pulmonary shunts → cyanosis.

Investigation:

1. Detection of oesophageal & gastric varices: this indicates the presence of portal hypertension:
   a. Barium swallow → regular rounded fixed smooth filling defects or longitudinal furrows in the oesophagus.
   b. Endoscopy used for:
      Diagnosis of early varices — grading of varices
      Detection of signs of impending rupture — detection of active bleeding
      Treatment → sclerotherapy.
2. Visualization of the portal system (dilated portal vein & presence) of shunts indicates portal hypertension: US & CT scan.
3. Estimation of portal vein pressure: Wedged hepatic venous pressure.
4. Evaluation of the liver:
   - Liver function test & liver biopsy.
5. Evaluation of the patent:
   - Blood picture, chest X-ray & ECG.
   - Urine & stool analysis.

Treatment of portal hypertension:

1. Treatment of oesophageal varices.
2. Treatment of hepatic encephalopathy.

OESOPHAGEAL VARICES

Def. Dilated tortuous veins, located at the lower third of the oesophagus & upper part of the stomach. They are an example of porto-systemic shunts.

Causes: as portal hypertension.

Clinical picture:

1. Clinical picture of portal hypertension.
2. Clinical picture of oesophageal varices:
   - May be silent but should be searched for in every patient with cirrhosis by Barium swallow & endoscopy.
   - Anemia due to repeated mild bleeding.
   - Rupture varices →hematemesis, melena & may be shock before attacks of hematemesis, the patient feels anorexia, nausea & metallic taste.
   - Rupture varices is precipitated by:
   1. Explosion →sudden increase of the portal pressure as during exertion, straining, coughing & lifting heavy objects.
   2. Erosion due to:
      - Ingestion of hard food.
      - Increased acidity of the stomach.
      - Drugs as NSAIDs.
      - Hepatotoxic drugs.
      - Organophosphorus compounds.

Investigation: as portal hypertension.

Treatment:

1. Silent varices:
   - **A. Medical treatment:**
     - β-blockers to decreases the cardiac output.
     - Somatostatin → mesenteric VC.
     - Nitrites → portal VD.
     - Verapamil to decrease the hepatic resistance.
   - **B. Sclerotherapy:** peri-variceal injection of a sclerosant material as ethanolamine oleate → fibrosis around the wall of the blood vessels.
   - **C. Surgical treatment:** only if splenectomy is indicated → Hassab operation → splenectomy & devascularization of the stomach except the right gastroepiploic vessels.
2. Bleeding varices:
   - **A. Hospitalization & bed rest.**
   - **B. Anti-shock measures:**
     - Fresh blood transfusion as it contains clotting factors & doesn't contain ammonia.
     - Bed rest & warmth.
   - **C. Vitamin K** to correct hypoprothrombinemia.
   - **D. IV Cimetidine (H_2 blockers):** to prevent stress ulcers as 20% of patients has ulcers due to increased gastrin hormone which is not metabolized in the liver.
   - **E. Sedation:** better avoided but if necessary, use diazepam or oxazepam but not morphine as it is metabolized in the liver.
   - **F. Endoscopy:** to define the site of hemorrhage & sclerotheraby :
     - Complication:

Pain, perforation.	Fibrosis, mediastinitis.
Pericarditis	pericardial effusion
Pleurisy	pleural effusion

Paraplegia (as it may cut the blood supply of the spinal cord.

   - **G. Medical treatment:**
     - **<u>Vasopressin:</u>**
       - Action: mesenteric arteriolar VC.
       - Dose: 20 unit in 200 ml glucose 5% over 20 minutes, it may be repeated every 4 – 6 hours.
       - Side effects:
         - Vasoconstriction causing blanching of the shin & hypertension.
         - Abdominal pain, colic, vomiting & diarrhea.
         - If used during pregnancy → abortion.
       - Contraindications:
         - Coronary heart disease - Cerebrovascular disease -
         - Hypertension & pregnancy.

- **Glypressin:**
  - Advantages over vasopressin: selectivity of action on mesenteric blood vessels only.
  - Dose: 2 mg IV. 1mg may be given every 6 hours with maximum 1 mg for the next 24 hours.
- **Somatostatin:** action: as glypressin – dose: 5 μg IV.
- **Octreotide:** it is a synthetic analogue of somatostatine given SC.

H. Sungestaken-Blakemore tube:

- **Consist of 3 lumens & 2 balloons:**
  - 2 balloons: gastric (inflated by 100 ml H_2O).
    Oesophageal (inflated by 40 mm Hg air).
  - 3 lumens one for gastric aspiration & feeding.
    One for inflation of the gastric balloon.
    One for inflation of the oesophageal balloon.
- **Indications:** sever attack of hematemesis with no available blood transfusion.
- **Action:** porto-systemic disconnection by the gastric balloon.
- The tube is left in place for 24 hours:
  - If bleeding stops → deflated & left in place for another 24 hours.
  - If bleeding continues → reinflate the tube & do injection sclerotherapy.
- **Complication:**

Oesophageal ulceration & rupture	asphyxia
Inhalation pneumonia	pressure necrosis.

I. Emergency operation:

- Variceal legation (devascularization).
- Oesophageal transection (using staple gun).
- Portocaval shunt.

J. Transjugualr intrahepatic portosystemic shunt (TIPSS): a special device is introduced through the jugular vein to the liver then a stent is put to connect the hepatic & portal veins.

K. Transhepatic variceal sclerosis: a catheter is introduced through the liver to the portal vein → left & short gastric vein are catheterized & injected by gel foam.

L. Injection of tissue adhesive (glue) as histoacryl blue.

M. Band legation: a rubber band is used to strangulate the varices & stop bleeding → necrosis & fall down.

3. Between attacks:

A. Medical treatment: β-blockers as propranolol are used to :

- Inhibit the heart (β_1 effect) → decrease the cardiac output.
- Produce mesenteric arterioles VC (β_2 effect).

B. Attack of varices:

- Sclerotherapy: monthly till varices disappear then follow up.
- Use of tissue adhesives.
- Band legation & vasoligation.
- Tuner's operation: gastro-oesophageal venous disconnection.
- Modified Tuner's operation: gastro-oesophageal venous disconnection + partial gastrectomy.

C. Elective surgery: shunt operation to decrease the portal BP:

- Portocaval shunt:

Precautions:

Repeated bleeding	fair liver function.
No ascites	serum albumin> 3gm /dl
Serum bilirubin < 1.5 mg/dl	

Complications:

Hepatic encephalopathy	HCF
DM	edema & ascites
Hemochromatosis	DU.

- Warren's operation: distal spleno-renal shunt vein thrombosis.

ASCITES

Def.: accumulation of fluid in the peritoneal cavity.

Causes:

A. Transudate:

1. Causes of portal hypertension.
2. General hypoalbuminemia (as part anasarca):
   a. Nephritic syndrome.
   b. Nutritional edema.
   c. Sever heart failure.

B. Exudates: due to local peritoneal causes as:

A. Tuberculous peritonitis:

- Occurs in young age.
- Abdomen is tender & rigid ± doughy.
- Spleen is not felt.
- Toxemia of TB (1ry or 2ry).
- May → adhesion & int. obstruction.

B. Malignant ascites:

- Massive hemorrhagic & rapidly reaccumulating.
- Malignant cells on aspiration.
- Abdominal mass may felt after tapping.
- ± Nodules around the umbilicus.

C. Pseudomyxoma peritonii:

- Rupture mucocele of the appendix (+ + +).
- Rupture mucocele of the gall bladder.
- Pseudomuconium cystadenoma of the ovary.

C. Chylous ascites: due to thoracic duct obstruction caused by LNs, tumors or filariasis.

- Features :

Color: milky white. Rich in fats

Clears on addition of ether. Stains orange with Sudan III.