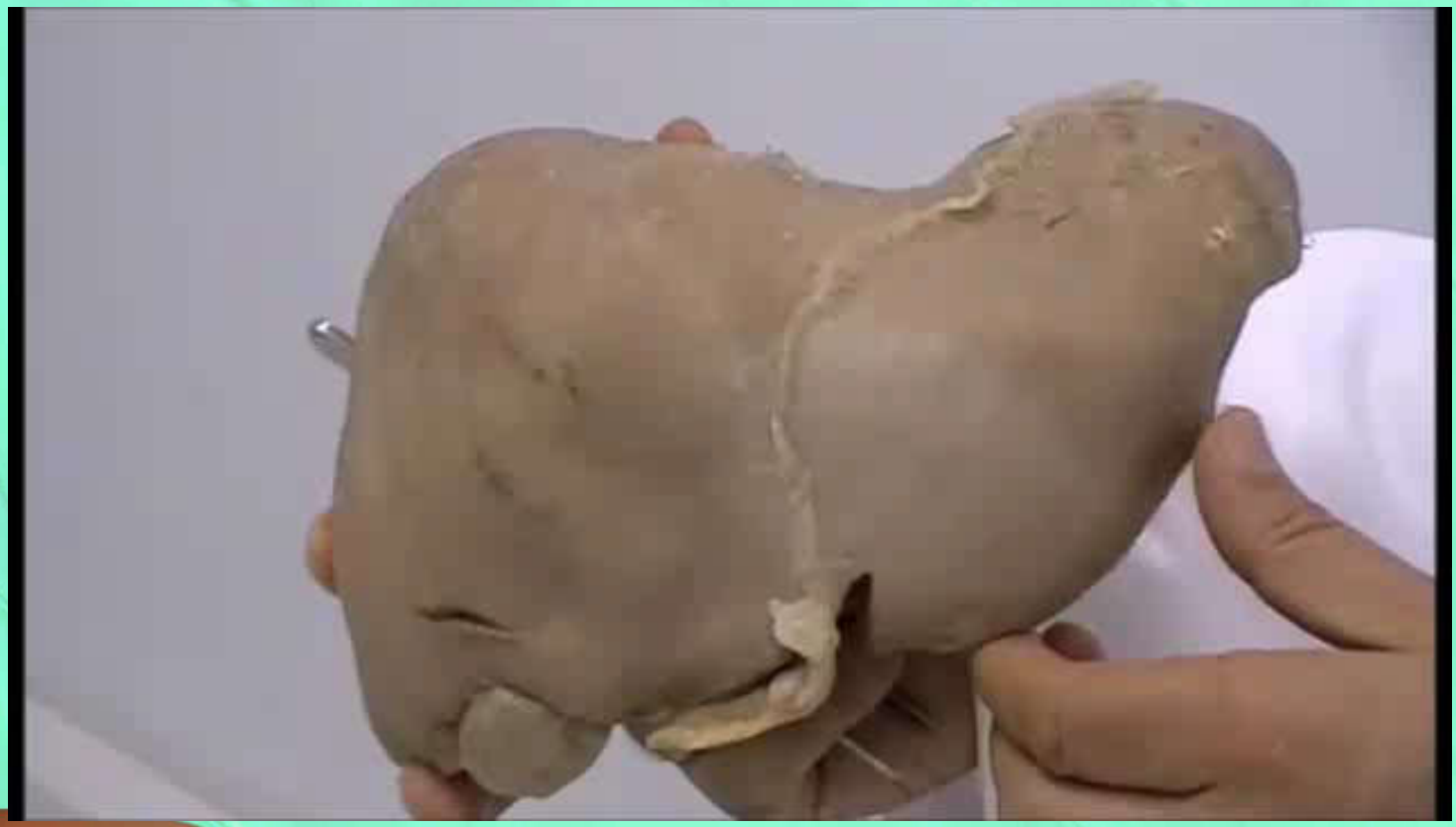
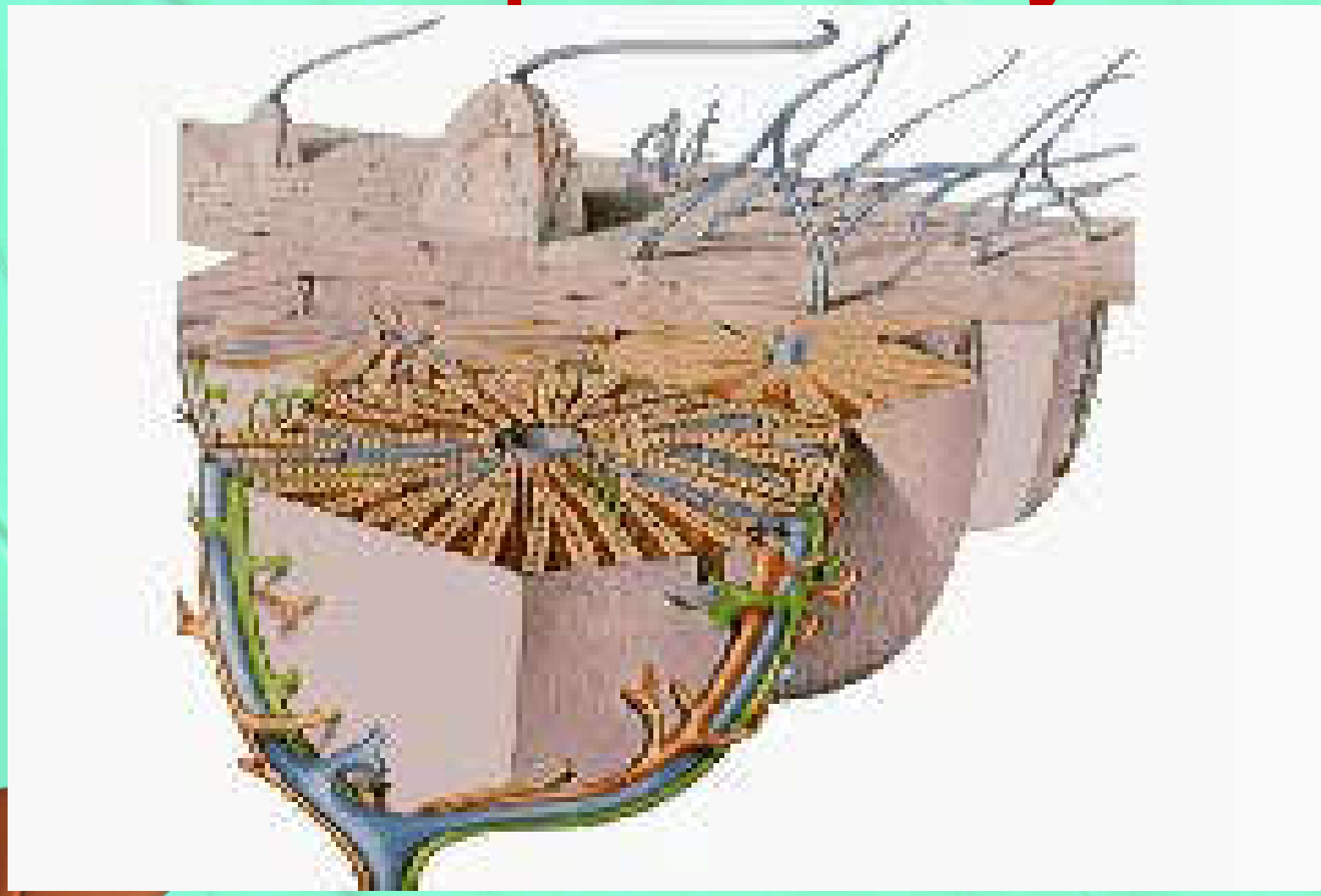
Common Pediatric Liver diseases

Anatomy and physiology

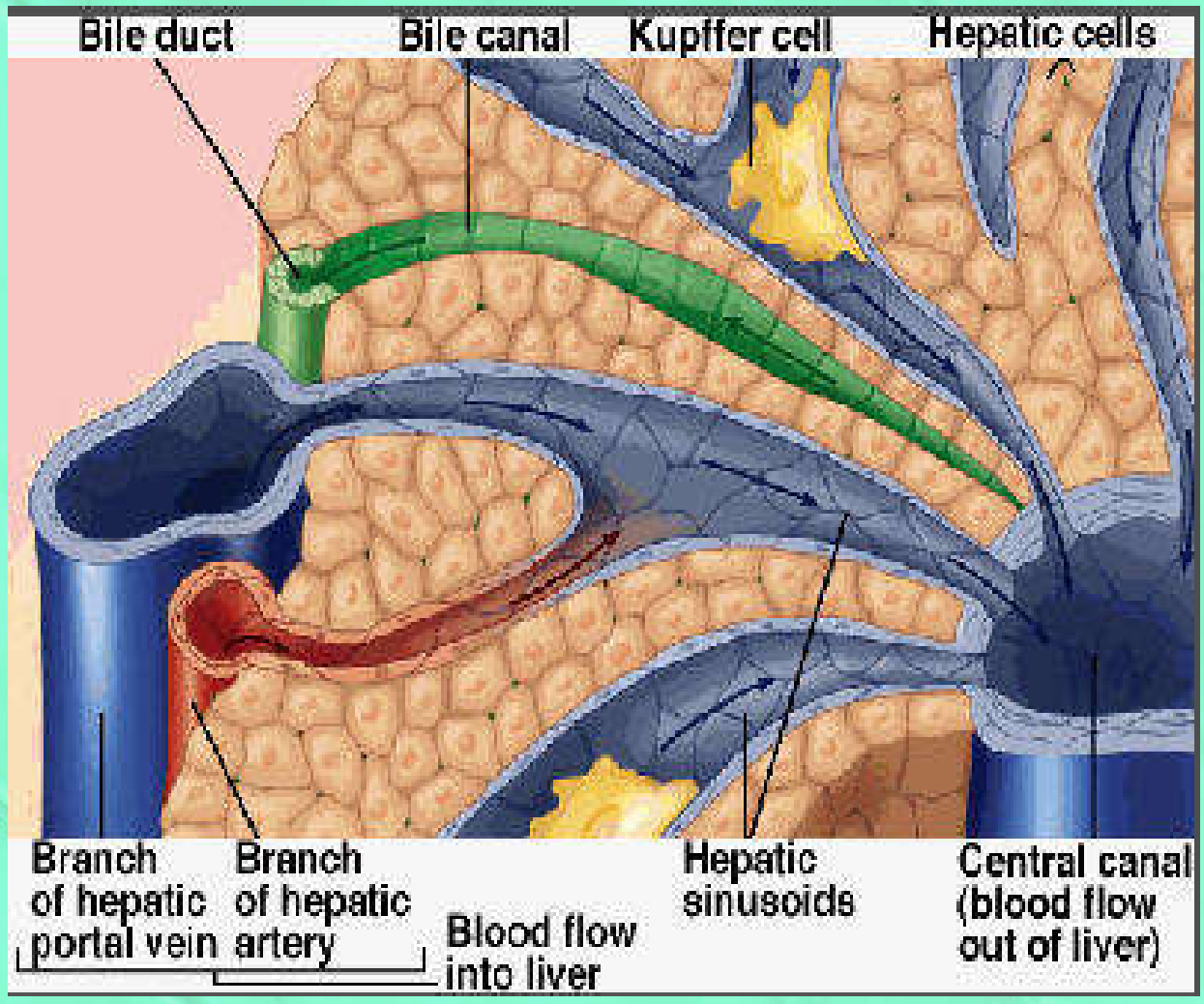
Gross Anatomy



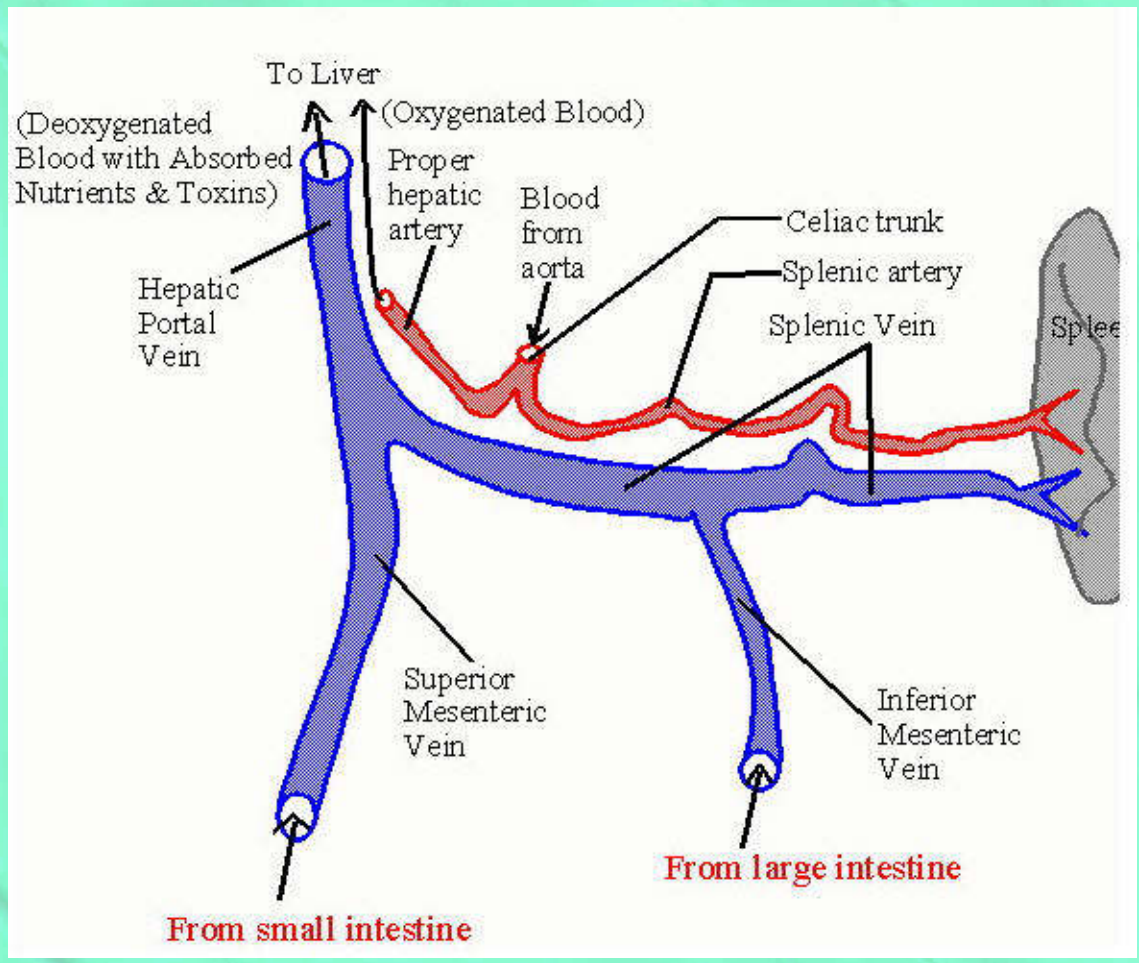
Microscopic anatomy



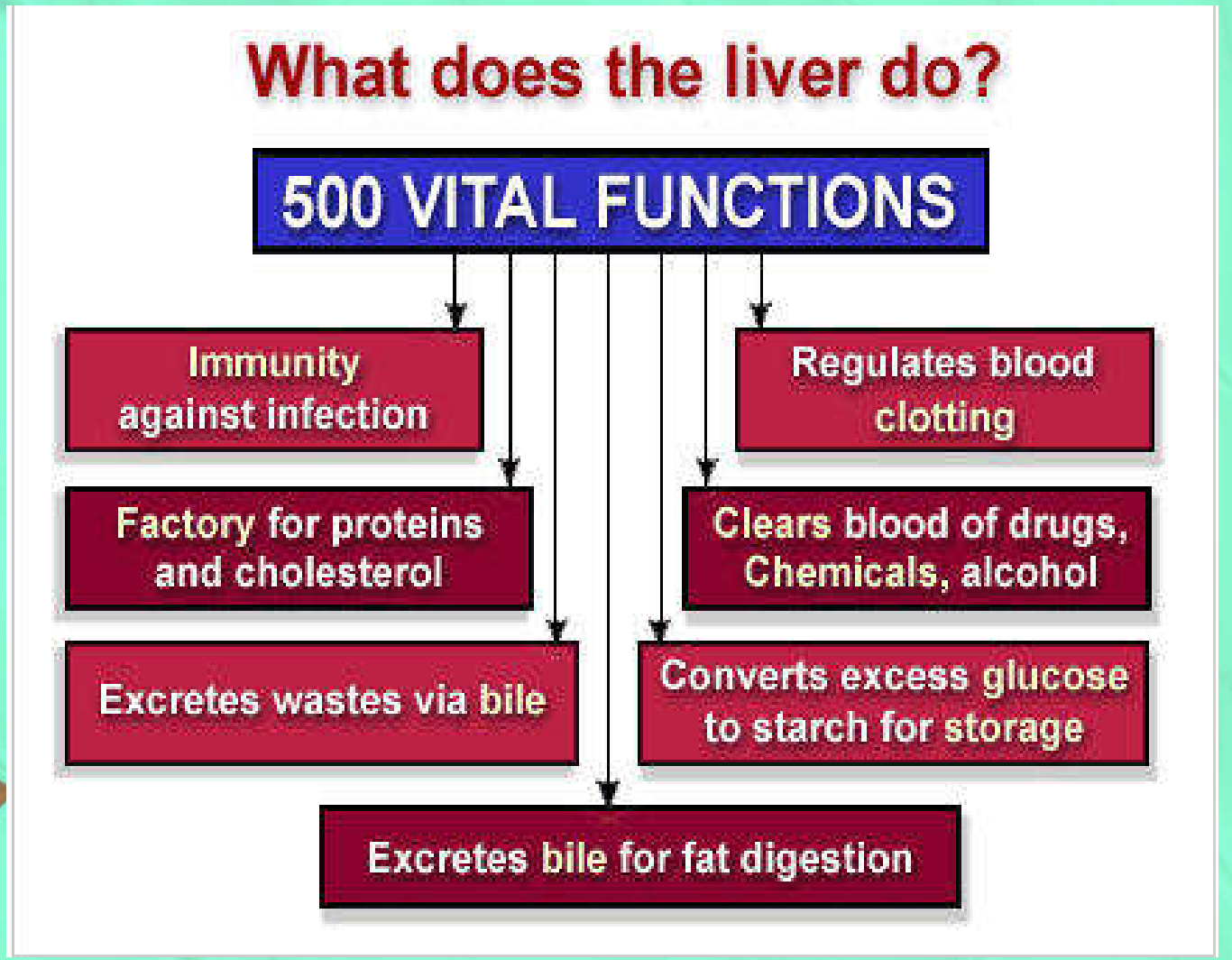
Hepatic circulation



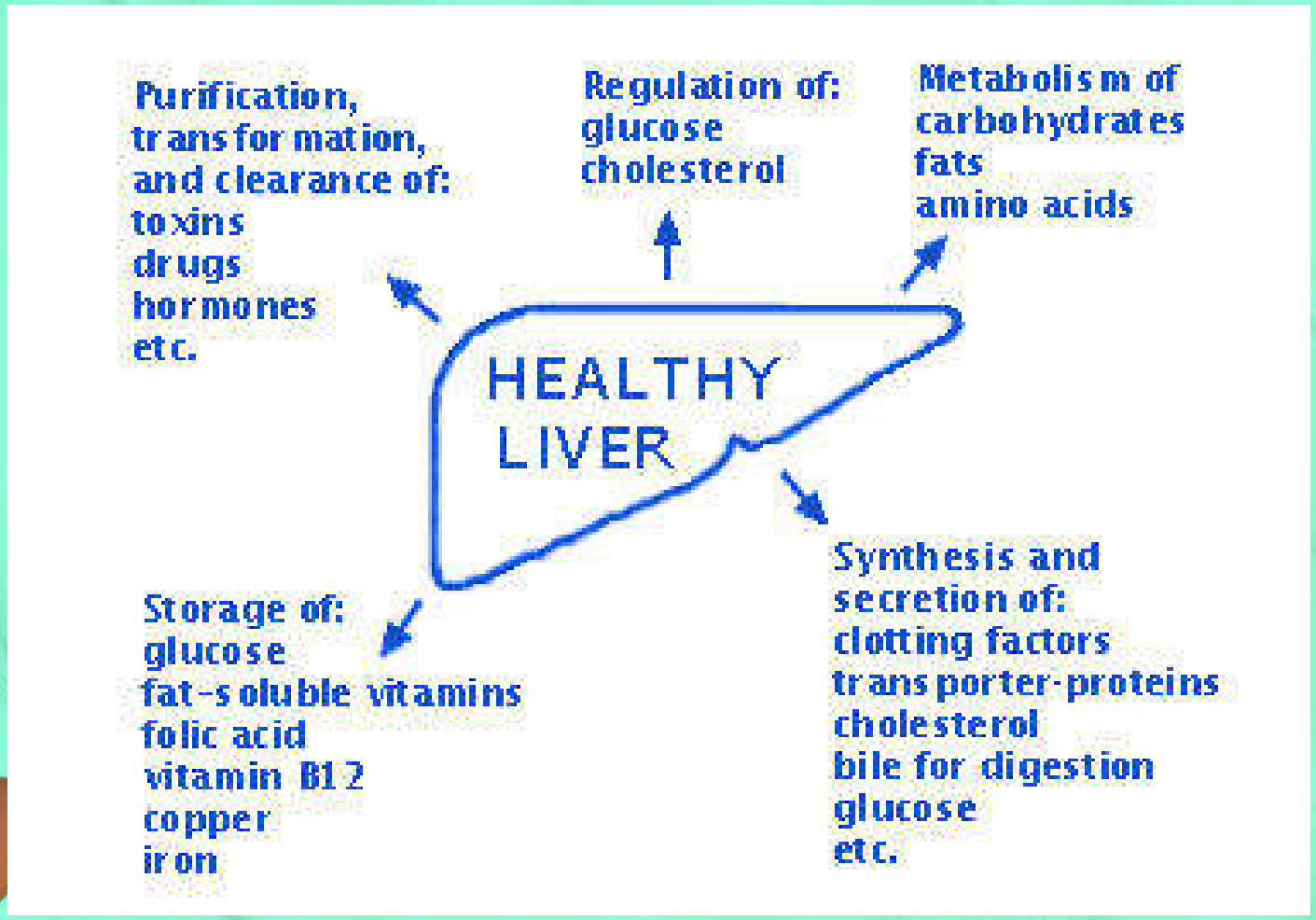
Portal circulation



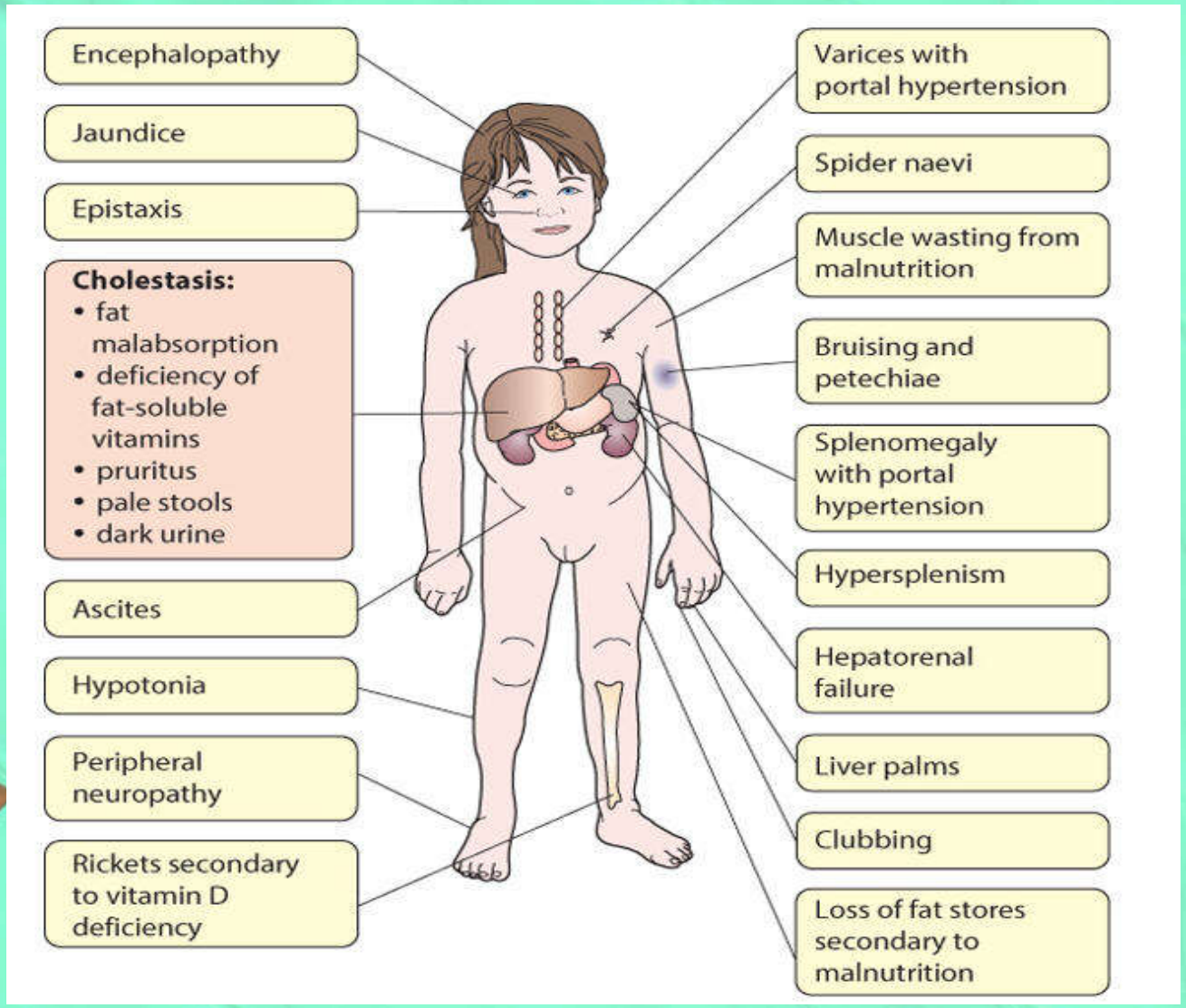
Liver functions



Liver functions



Manifestation of liver disease



Assessment of liver diseases

I-liver function tests

- **Bilirubin**
- Bilirubin in urine(Obstructive jaundice,Hepatocelluar jaundice)
- Serum bilirubin its normal value 0.8- 1.2 mg/dl

- unconjugated bilirubin it is raised in (hemolytic anemia,hepato- biliary jaundice)

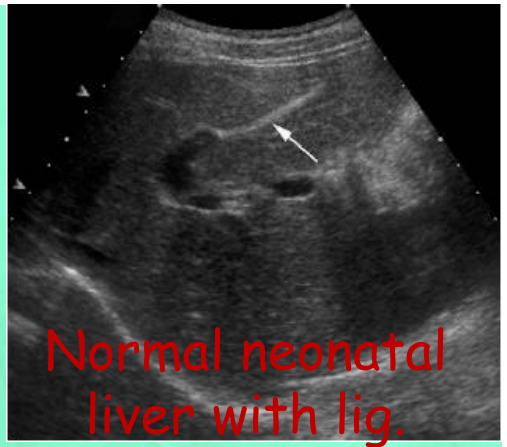
-conjugated bilirubin is raised in obstructive jaundice

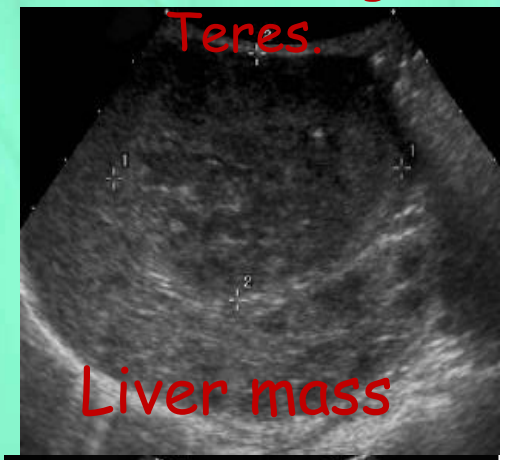
- Urobilinogen in urine it is increased in(Hepatocelluar jaundice,hemolytic anemia)

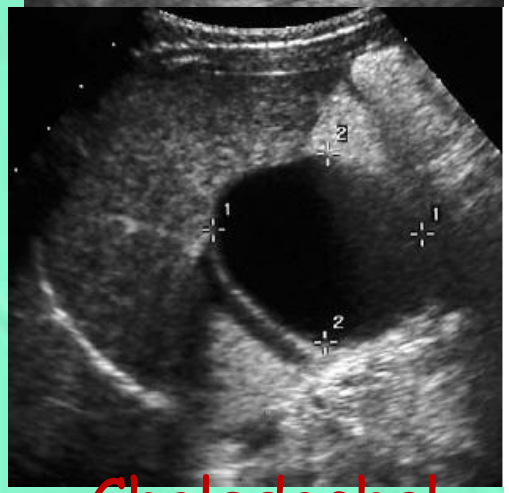
- **Alanine aminotransferase (ALT)** normal value is 5-45U/L
- **Aspartate transaminase (AST)** normal value 15-55U/L
- **ALK (**Alkaline transferase **): elevated in cholestasis and bone disease.**
- **GGT : differntiate cholestasis from bone disease**
- **Serum albumin** level may be decreased in cirrhosis.
- **Prothrombin time and concentration** (cirrhosis, hepatic failure, obstructive jaundice and bleeding disorders.)
- **Serum immunoglobulins** may be elevated in CID

II-Imaging of the liver

- **Liver ultrasound**
- Diffuse liver disease; cirrhosis, metabolic disease, hepatic periportal bilharzial fibrosis and fatty liver
- Biliary channel patency, choledocal cyst and gallstones
- Patency and diameter of portal vein
- Focal lesions, liver abscess
- Ascites and subphrenic abscess.







- **CT scan**

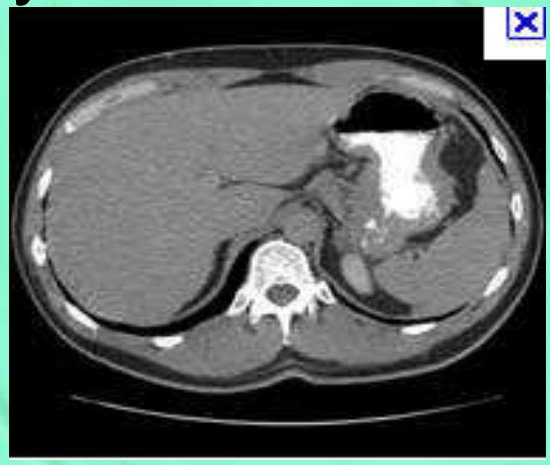
Focal lesion, cyst or other lesions

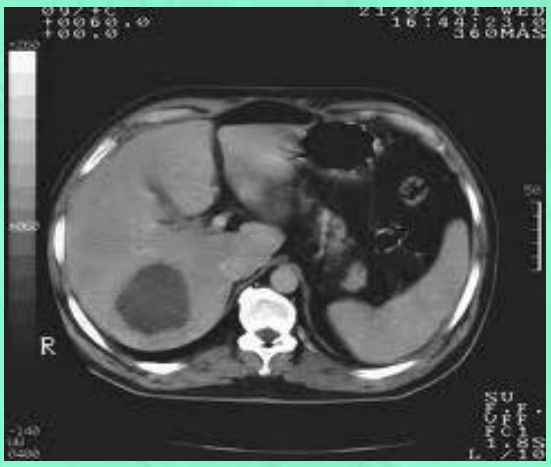
- **Magnetic resonance imaging (MRI)**

Shows patency of biliary tree, focal lesion.

- **Cholangiography**

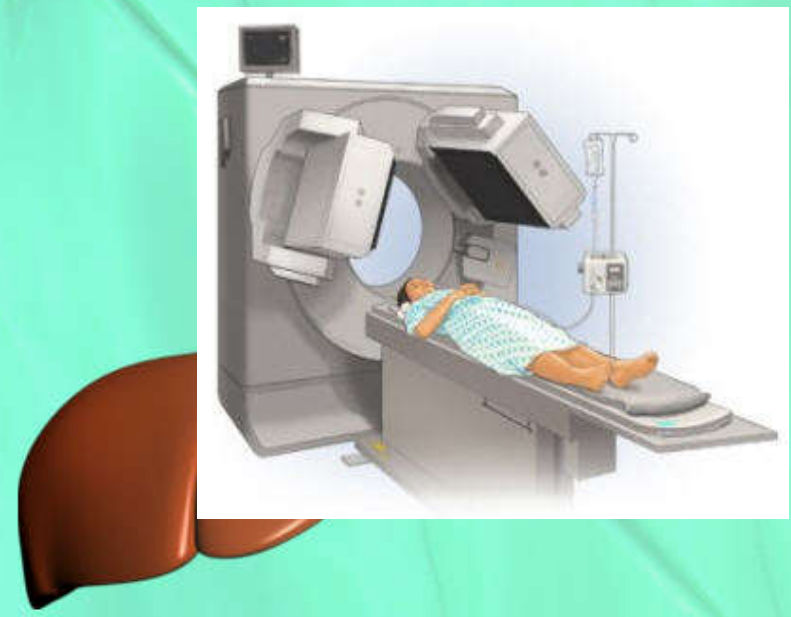
Direct visualization of intrahepatic and exctrahepatic biliary tree.



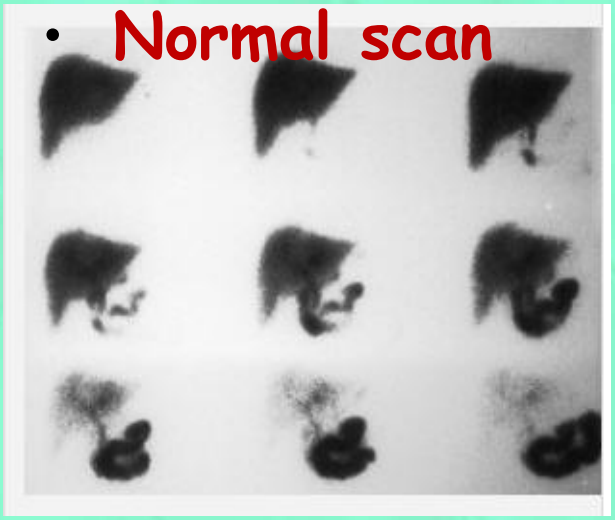


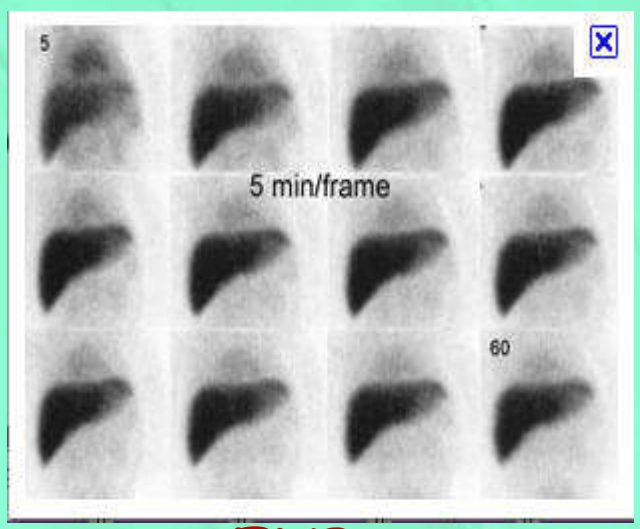
Rdioisotopic scanning

- it display liver size, morphology, focal lesions and biliary excretion.



- Normal scan





EHBA

III-Liver biopsy and histopathological examination,

it is the key for diagnosis of most liver disease.

Some aspects of neonatal cholestasis

- Prolonged neonatal jaundice caused by liver disease is a conjugated hyperbilirubinemia and it usually accompanied by Pale stool,Dark urine,Bleeding tendency and Failure to thrive.
- Impairment of bile flow from its formation to its excretion(from the bile duct)

Conjugated hyperbilirubinemia : (> 20% of total bilirubin)

Bile buct obstruction:

- Biliray atresia.
- Choledochal cyst.

Neonatal hepatitis :

- Idiopathic neonatal hepatitis.
- Congenital infection (TORCH).
- Inborn error of metabolism : galactosemia, tyrosinemia (type 1), alpha-one antitrypsin deficiency.
- TPN.
- Cystic fibrosis.

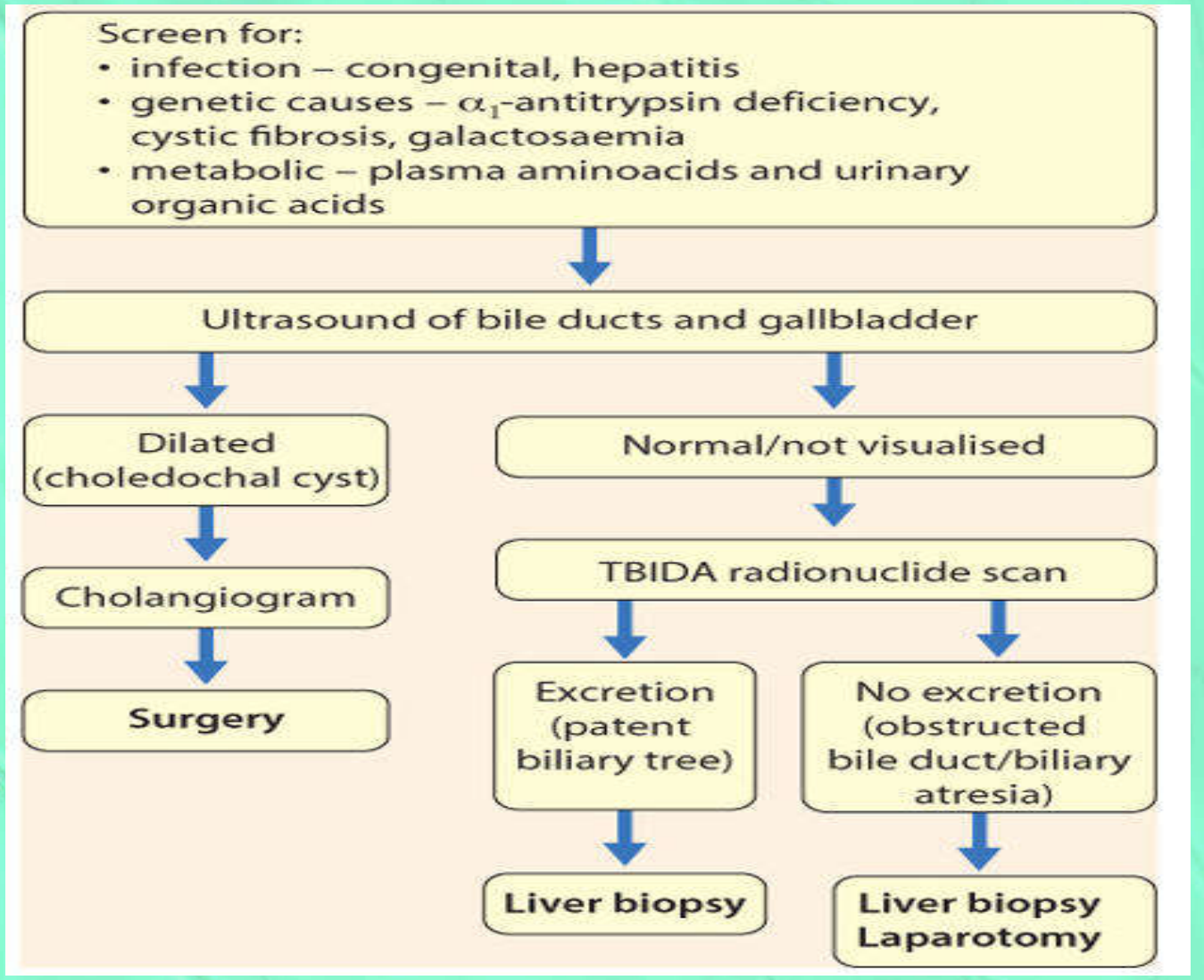
What is the diagnosis?

This child was breast fed, he became markedly jaundiced on the third day of life. At 5 weaks of age he presented with poor feeding, and vomiting as well as a history of bruising on the forehead and shoulders. His urine had become dark and stools intermittently pale. Hb 8.8 gm/ dl

Plt 380,000 PT prolonged

Bilirubin 18 mg/dl direct 11.5 mg/dl

Evlauation of neonatal conjugated hyperbilirubinemia :



Choledochal cyst:

- Cystic dilatation of the extrahepatic biliary system.
- 25 % present in infancy with cholestasis.
- Diagnosis is established through ultrasonography or isotope scanning.
- Treatment is surgical

Hepatitis A

- RNA virus, spread by feco-oral contamination.
- Incubation period: 15-40 days.(average 4 wks)
- Usually occurs in outbreaks.
- May be asymptomatic, but the majority have mild illness.
- Nausea, vomiting, abdominal pain, lethargy, vomiting, jaundice, and dark urine.

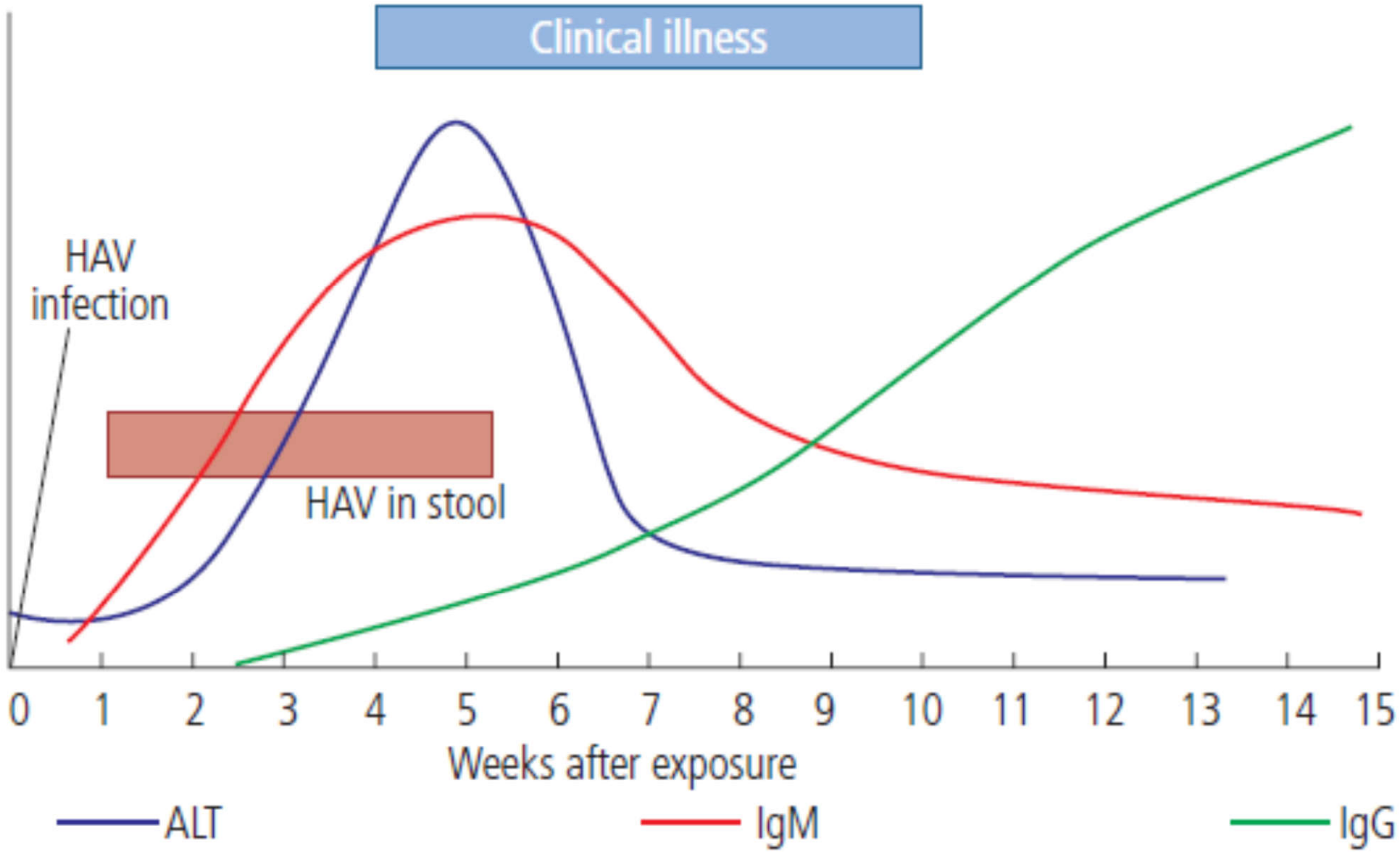
Hepatitis A

- Examination : tender hepatomegaly.
- Resolve clinically and biochemically in 2-4 weeks.
- Chronic liver disease does not occur.
- Most serious complication is fulminant hepatitis and acute liver cell failure.
- Some may develop prolonged cholestatic hepatitis (which is self limiting)
- Diagnosis : IgM antibodies in patient`s serum.

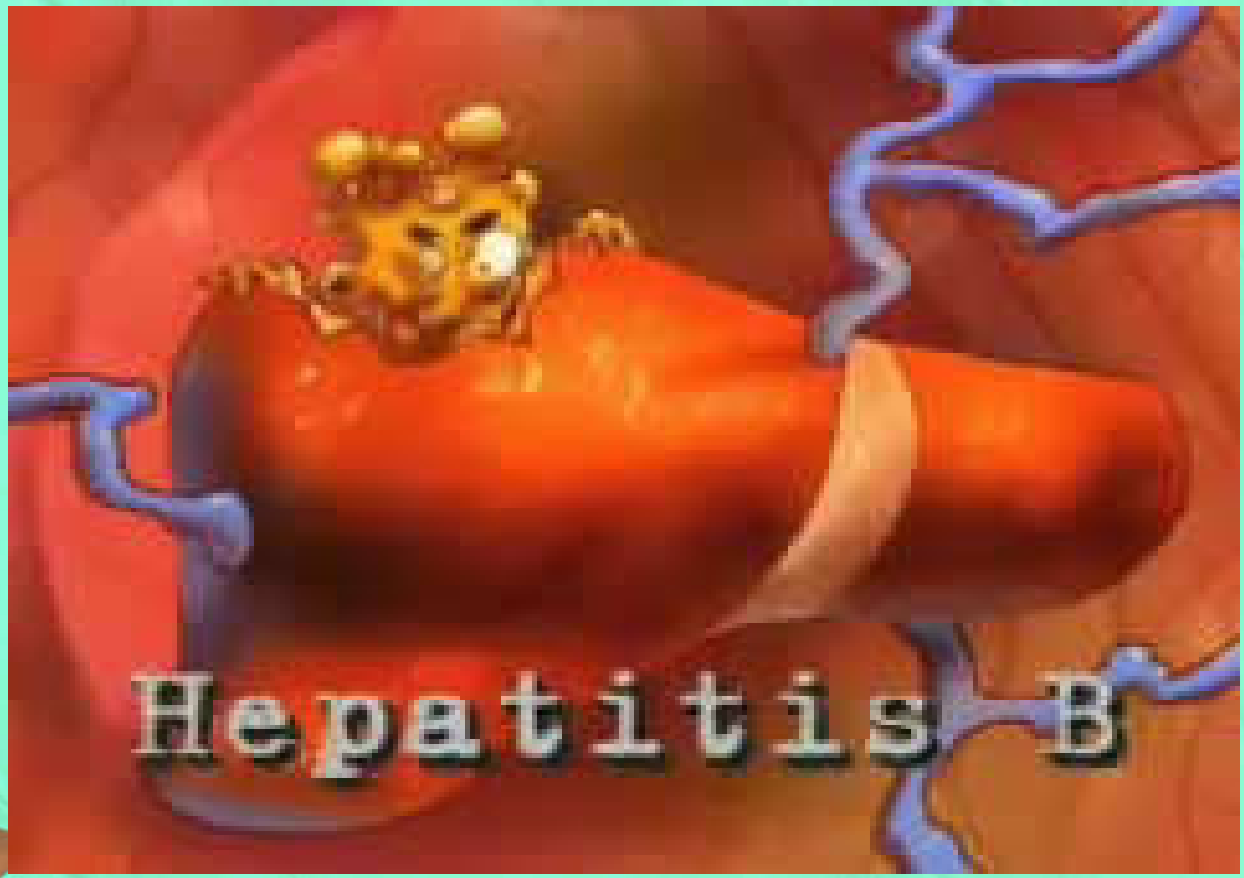
Hepatitis A

- Prophylaxis :
  - PT is contagious for 7 days before & 7 days after onset of jaundice
  - Good hygiene.
  - IVIG after exposure: 80-90% effective.
  - HAV (Vaccine) : after exposure or when travelling to endemic area.
  - Children > 12 months with CLD : 2 doses HAV 6 months apart.
- Treatment:
  - No specific treament.
  - Bed rest.
  - Symptomatic.

Time course of hepatitis A virus (HAV) infection.



Hepatitis B



Hepatitis B

- DNA virus.
- Important cause of acute and chronic liver diseases.
- Transmitted by:
  - Prenatally from carrier mother.
  - Blood transfusion.
  - Blood components.
  - Needle stick injuries.
- Incubation period : 6 weeks : 6 months.

Hepatitis B

- Clinically:
  - Asymptomatic.
  - Classical features of acute hepatitis.
  - 1-2 % develop fulminant hepatitis.
  - 5-10 % become chronic carriers, which may progress to cirrhosis and carcinoma
- Diagnosis:
  - HBs Ag
  - Anti HBc IgM
  - HBe Ag

Hepatitis B

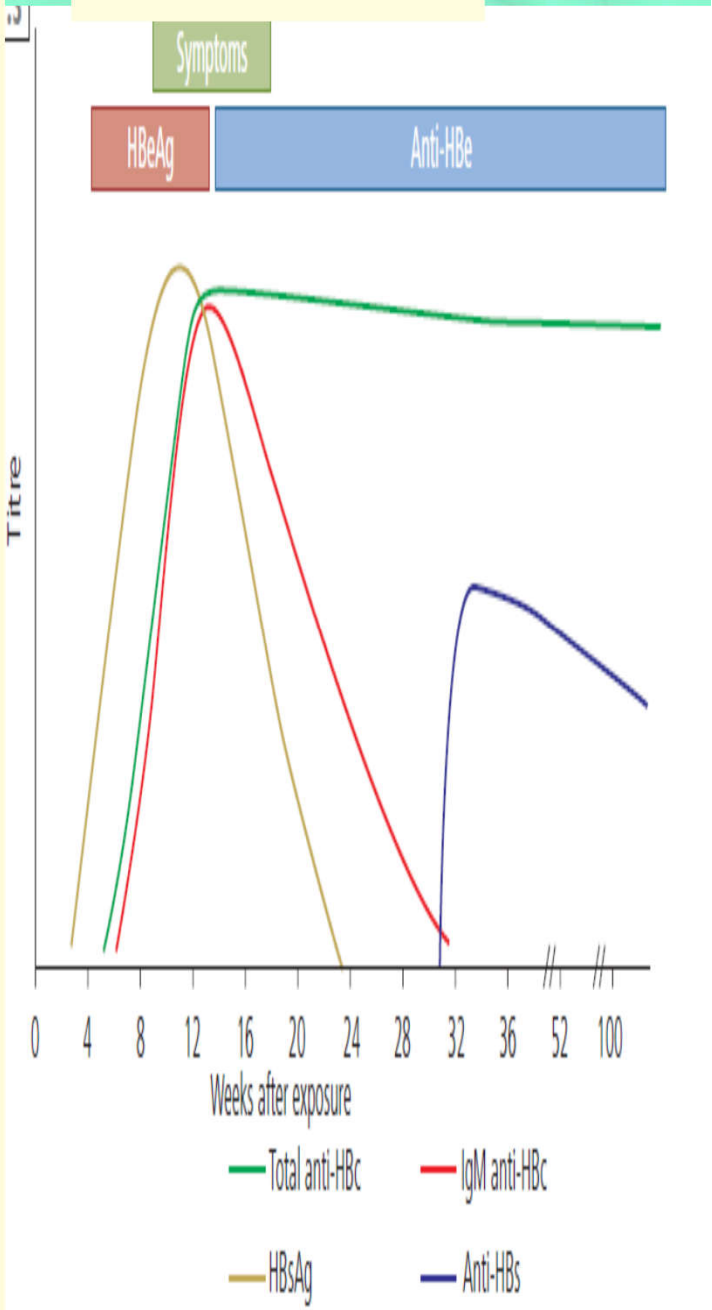
- Treatment:
  - Acute hep. B: needs no specific treatment.
  - Chronic hep. B:
    - Alpha interferon 3 times/week for 6 months.
    - Lamivudine for children > 2 years.
    - Adefovir for children > 12 years.
  - Fulminant hepatitis: liver transplantation.

Hepatitis B

- Prophylaxis:
  - Hepatitis B vaccine.
  - Post exposure:
    - Hepatitis B vaccine
    - HBIG
    - Combination.
    - As soon as possible after exposure up to 7 days.
    - Neonates with HBsAg +ve mothers : HBIG plus HB vaccine.

Test	Antigen/antibody	Interpretation
HBsAg	Hepatitis B surface antigen	Detection of acute or chronic infection Used in HBV vaccine development Transient identification of serum HBsAg can be seen after a recent vaccination
Anti-HBs	Antibody to HBsAg	Identifies who has resolved infection with HBV Positive in immune, vaccinated individuals
HBeAg	Hepatitis B e antigen	Detects HBV infection with increased risk of transmitting HBV
Anti-HBe	Antibody to HBeAg	Detects HBV infection with decreased risk of transmitting HBV
Anti-HBc	Antibody to HBV core antigen	Detects acute, resolved, or chronic HBV infection Not present after immunization
IgM anti-HBc	IgM antibody to HBV core antigen	Identifies acute or recent HBV infections
HBV DNA by PCR	Amplified HBV DNA	Detects virus in blood or liver tissue Indicates ongoing infection

Hepatitis B virus (HBV) markers



Hepatitis C

Hepatitis C

- RNA virus.
- Reponsible for most cases of post-transfusion hepatitis.
- Children at risk: Hemophilia, hemoglobinopathies.
- Vertical tranmission from mother may occur but rare.
- Clinically:
  - Acute hepatitis is rare.
  - Chronic hepatitis occurs in 50% of infected patients, and may progress to cirrhosis and hepatocellular carcinoma after many years.

Hepatitis C

- Diagnosis:
  - Anti HCV (3rd generation ELIZA)
  - PCR
- Prevention:
  - No vaccine.
  - IVIG is not effective.
  - No scalp monitoring during delivery.
  - CS of mothers with high titres.
- Breast feeding is generally allowed unless there is bleeding nipple.

Hepatitis C

- Treatment of chronic Hepatitis C:
  - Alpha interferon plus ribavirin.
  - Pegylated interferon not studied well in children.
  - HCV Polymerase inhibitors(Sofosbuvir)
  - Saftey &efficacy not established in children
  - Liver transplantation in end stage liver disease.

Hepatitis D (Delta agent)

- Defective RNA virus.
- Depend on hepatitis B for its replication.
- May cause acute exacerbation of chronic hep. B.

Hepatitis E

RNA virus.

- Enterally transmitted, mostly by contaminated water.

Acute liver cell failure

Massive hepatic necrosis with subsequent loss of liver functions with or without encephalopathy. Uncommon but associated with high mortality.

Causes:

- Infections(Viral infection e,g hepatitis viruses A, B, C, non hepatitis viruses CMV,EBV,Adenovirus)
- Poisoning:(Paracetamol, INH, Halothane, Amanita phalloides (poisonous mashroom).
- Metabolic:(Wilson disease, tyrosinemia)
- Autoimmune hepatitis(primary or secondary).
- Reye`s syndrome.

Malignancy(infiltration)

Clinically

-Jaundice (Rye`s syndrome is anicteric) - Coagulopathy.
- Hypoglycemia. -Electrolyte disturbance. -Fetor hepaticus.
- Encephalopathy: early alternate irritability and confusion, drowsiness, finally coma.

Complications: -Cerebral edema. - Hemorrhage. -Sepsis. - Pancreatitis.

Diagnosis -Bilirubin may be normal in early stages.
- Transaminases: markdly elevated (10-100 times).
- Defective coagulation (PT,PTT.INR).
-Plasma ammonia: elevated.
- Blood glucose: may be low.

Management:

- PICU.
- Maintain normal blood glucose (IV glucose).
- Central line with close monitoring of fluids and electrolytes.
- Preventing sepsis with broad spectrum antibiotics.
- Preventing hemorrhage: Vit K, FFP. ,He-blocking drugs,PPI
- Controll hyperammonemia(Oral neomycin /metronidazole,Oral lactulose., Enema)
- N-acetylcysteine.
- Mannitol for cerebral edema.
- Mechanical ventilation for comatosed patients.
- Hemodialysis. Liver transplantation.

Some aspects of pediatric chronic liver diseases (CLD)

Clinical presntation:

- Acute hepatitis. -Hepatosplenomegally.
- Cirrhosis. -Portal hypertension.-Lethargy and malnutrition.

Causes:

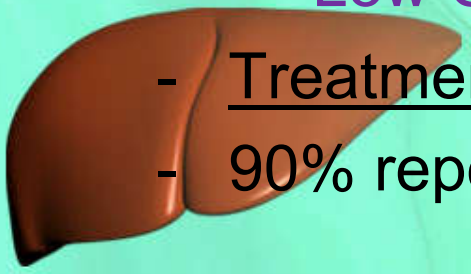
- Chronic hepatitis:((Post viral hepatitis B,C, ….Autoimmune hepatitis.,Drugs. Inflammatory bowel diseases. Primary sclerosing cholangitis.)
- Wilson disease > 3 years.
- Alpha-1-antitrypsin deficincy.
- Cystic fibrosis.
- Secondry to: Neonatal liver disease. Or Bile duct obstruction

Autoimmune hepatitis

- The mean age 7-10 years.
- More common in girls.
- Clinically:
  - Acute hepatitis.
  - Fulminant hepatic failure.
  - With autoimmune manifestations; arthritis, skin rash, nephritis, hemolytic anemia, SLE.
- Diagnosis:

  -SMAs -ANAs - LKMs

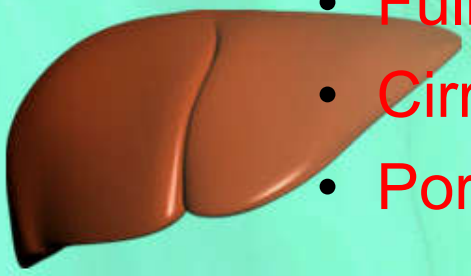
  - Low C4 -Typical histopathological picture.



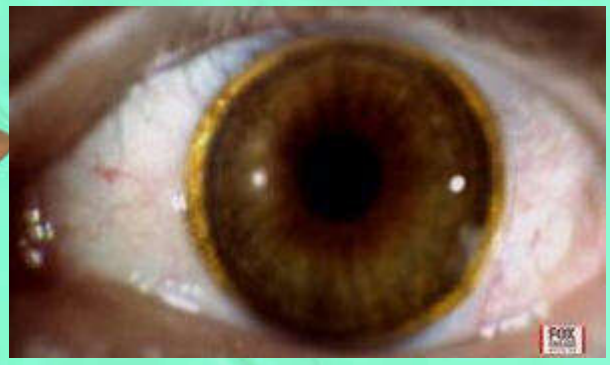
- Treatment:
- 90% repond to prednisolone and azathioprine

Wilson disease

- AR disorder (chromosome 13).
- Reduced synthesis of ceruloplasmin (copper binding protein).
- Accumulation of copper in liver, kidney, brain, and cornea.
- Rare in children less than 3 years.
- Hepatic presentation is more likley
- clinically:
  - Acute hepatitis.
  - Fulminat hepatitis.
  - Cirrhosis.
  - Portal hypertension.



- Neuropsychatric features : 2nd decade.
  - Deterioration of school performance.
  - Behavioral changes.
  - Tremors and dysarthria.
- Renal tubular dysfunctions with vit.D Res. Rickets.
- Kayser-Fleischer ring: Not before 7 years.



Wilson disease

- Diagnosis:

  Low serum ceruloplasmin.

  Low serum copper.

  Excess urine copper.

  Confirmesd by Increased hepatic copper,or gene mutation

- Treatment:

  Penicillamine.

  Zinc to lower copper absorption.

  Pyridoxine to prevent peripheral neuropathy.

  Liver transplantation.(acute liver failure or en stage liver disease)

Congenital hepatic fibrosis

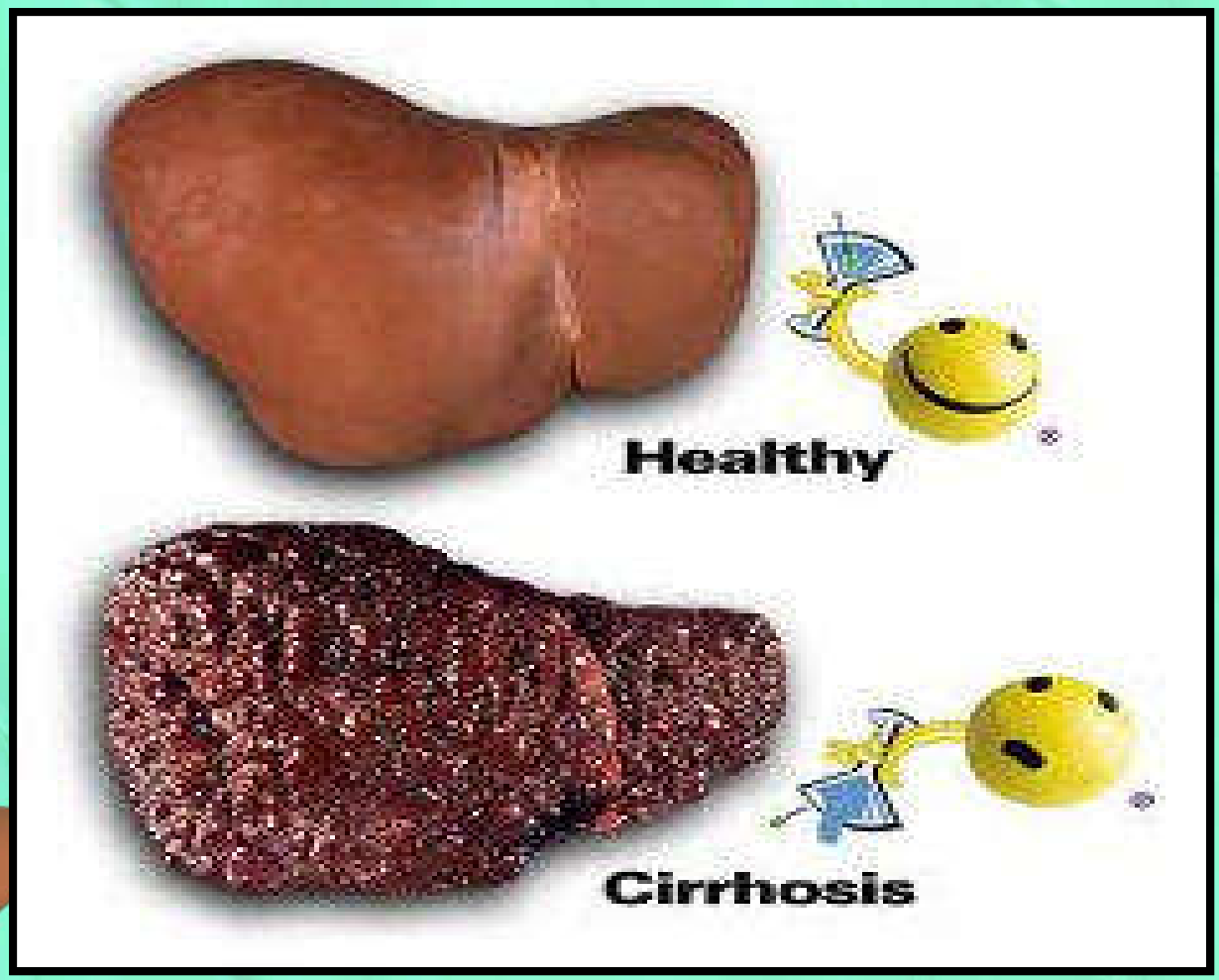
- presents in children over 2 years old with Hepatosplenomegaly, abdominal distension and portal hypertension.
- Renal disease may coexist.
- liver function tests are normal in the early stage.
- Liver histology shows large bands of hepatic fibrosis containing abnormal bile ductules.
- The consequent portal hypertension causes bleeding from varices.

Liver cirrhosis and portal hypertension

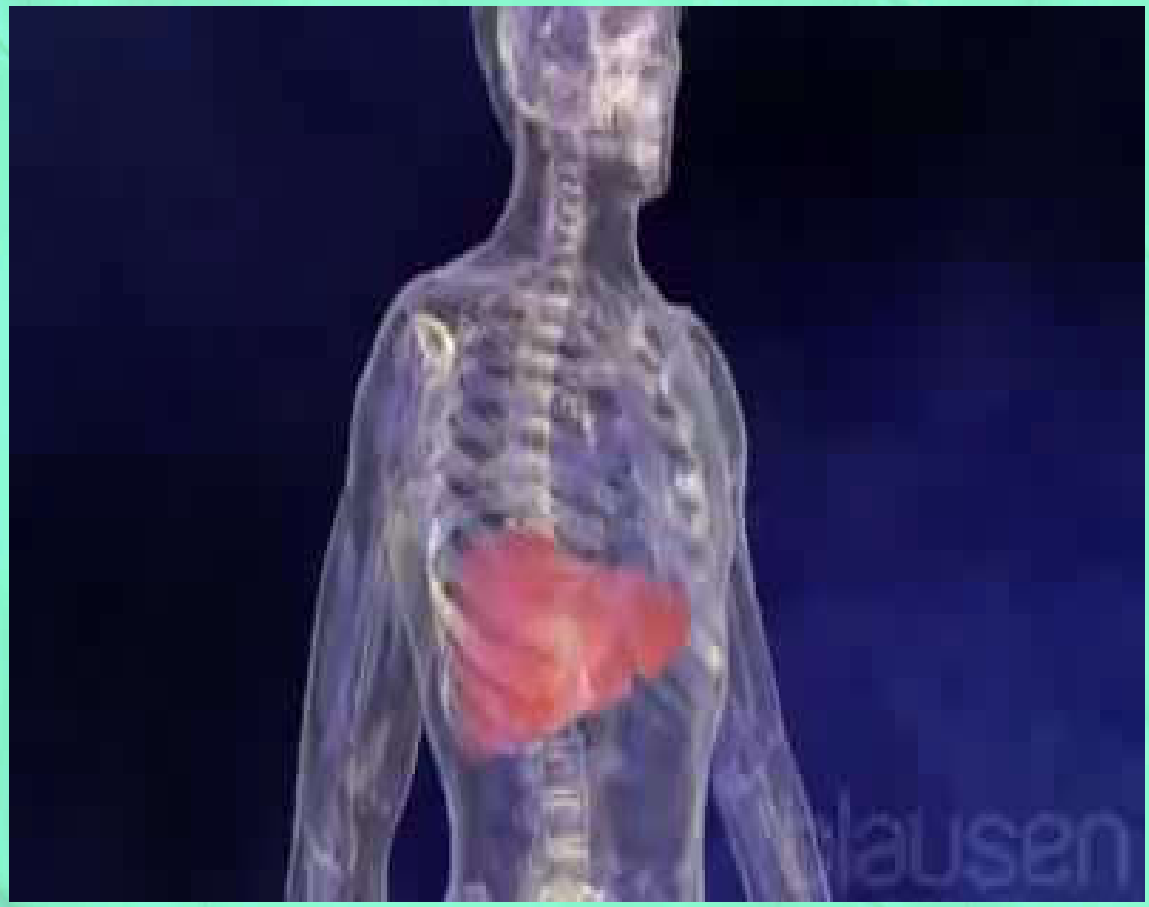
Liver cirrhosis

- Pathological term indicates degeneration of liver cell, extensive fibrosis with regenerative nodules resulting in loss of normal architecture of hepatic nodules
- Micronodular,, Macronodular& Mixed forms
- Secondary to long standing hepatocellular disease , biliary obstruction. Or Hereditary diseases(Galactosaemia, Wilson disease or α -1-antitrypsin deficiency
- Clinically: depend on :
  - Degree of diminished liver functions.
  - Development of portal hypertension.
- Hepatocellular carcinoma may develop.

Liver cirrhosis



Liver cirrhosis



Clinical picture

Compensated cirrhosis

- The disease may be asymptomatic
- The patient has mild pyrexia., malnutrition and FTT
- Circulatory changes: palmar erythema and hyperkinetic circulation.
- Firm enlargement of the liver and spleen are helpful
- Portal hypertension with portosystemic collaterals.
- Slight increase in serum transaminases.

Decompensated cirrhosis

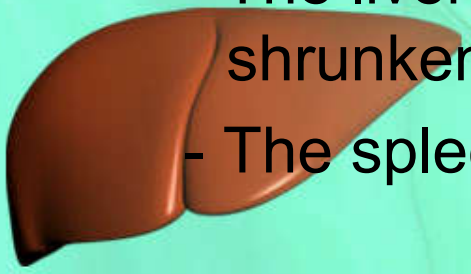
The major events are liver failure and portal hypertension

other features include:

- Appearance of jaundice in patients with post-necrotic cirrhosis.
- Ascites and development of peripheral edema.

Hepatic encephalopathy and fetor hepaticus on the exhaled breath.

- Spontaneous bruising and epistaxis
- Low grade fever without infection , Clubbing of fingers, sparse body hair, vascular spiders and palmar erythema .
- The liver may be enlarged with firm regular edge, or shrunken
- The spleen may be palpable.



Investigations

- **LFTs:** ↑ serum bilirubin & transaminases
- **Hematologic changes**

-Anemia.,leucopenia&thrombocytopenia

-The prothrombin time is prolonged.

- **Ultrasonic scanning** *(*Shows liver size, abnormal liver texture and features of portal hypertension.
- **Endoscopy:**
- **Liver biopsy*:***

may give a clue to etiology and activity. It reveals hepatocyte necrosis, nodule and new collagen formation

Complications

- Portal hypertension and Ascites.
- **Hepatic encephalopathy**
- **Endocrinal changes.**
- **Hyperdynamic circulation.**
- **Bleeding diathesis.**
- Impaired fat metabolism.
- Renal failure.
- Impaired hepatic metabolism of drugs and hormones.
- Increased susceptibility to infection.

Management of liver cirrhosis

- Minimize further liver damage by treating the cause if possible.
- Prevent or reduce complications
- Diet: high-caloric low-protein diet. A protein intake should be reduced to 0.5 gm/kg/day. Vegetable proteins may be less likely to precipitate encephalopathy than animal proteins.
- Supplementation of fat soluble vitamin
- Liver transplantation may be life saving

Causes of portal hypertension

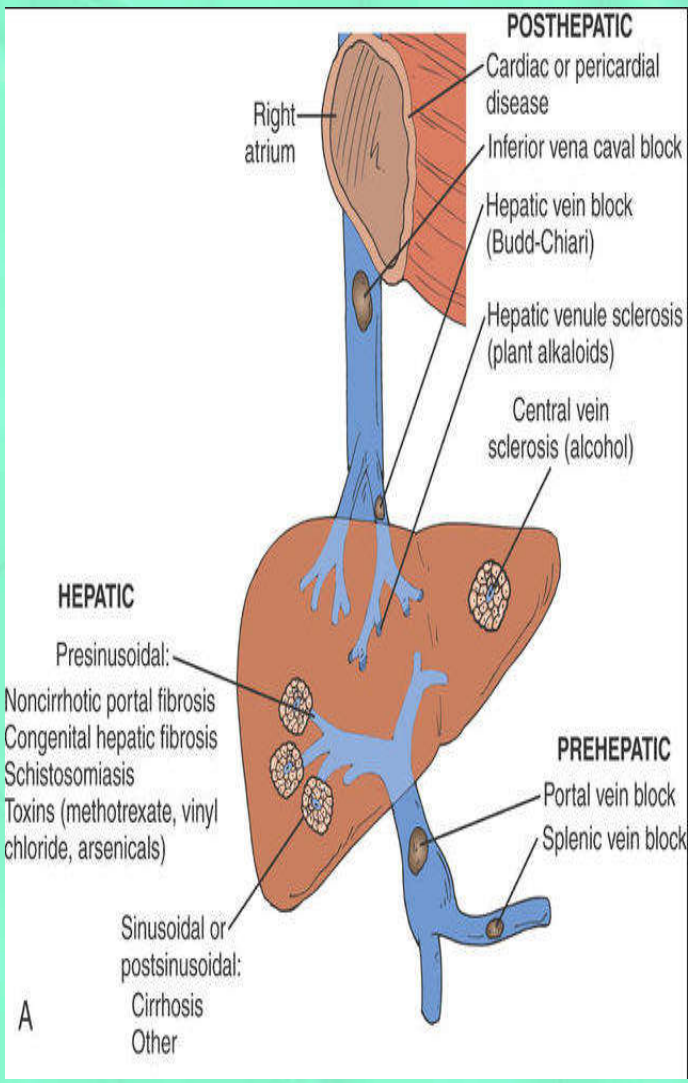
- **Prehepatic** due to:

- Portal vein thrombosis

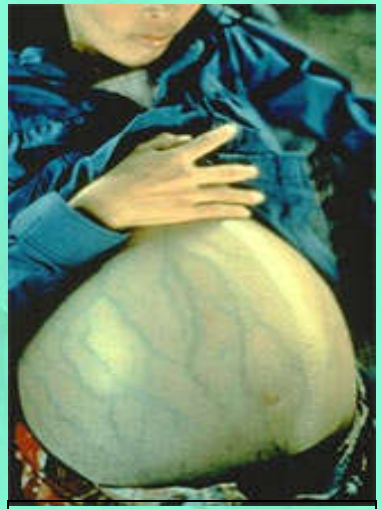
& Splenic vein thrombosis

-Idiopathic

- **Intrahepatic**
  - -Presinusoidal (portal fibrosis)
  - -Sinusoidal (as in cirrhosis)
  - -Post sinusoidal as in veno-occlusive disease.
- **Posthepatic** (suprahepatic) IVC block, constrictive pericarditis,….

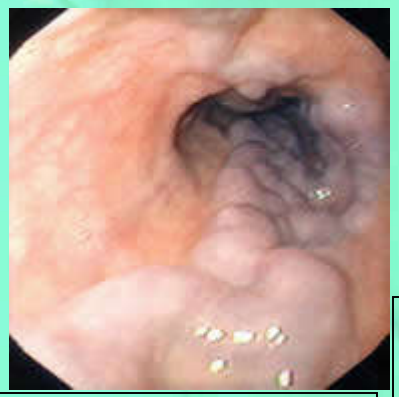


signs, symptoms and lab findings associated with **portal hypertension**

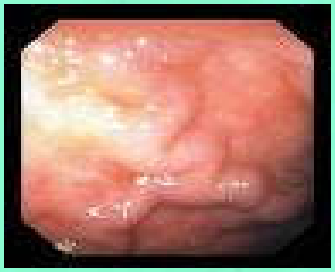


Ascites

Caput medusa



Esophageal varices (UGI bleeding)



Rectal varices

Hemorrhoids (LGI bleeding)

Hypersplenism

Splenomegaly

Thrombocytopenia

Diagnosis

Confirmation of portal vein obstruction by ultrasound

Confirmation of varices by endoscopy -Liver biopsy.

Management of PH

By treatment of the underlying cause whenever possible.

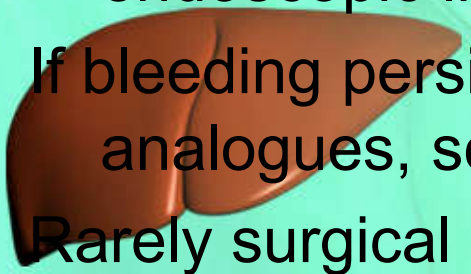
Bleeding esophageal varices are treated by Acute bleeding is treated conservatively with blood transfusions and H_2-blockers (e.g. ranitidine) or omeprazole. vitamin K administration.

Balloon tamponade by use of sengestaken tube to stop bleeding

Endoscopic injection of sclerosing solutions (sclerotherapy, endoscopic ligation by elastic rubber bands

If bleeding persists, octreotide infusion, vasopressin analogues, sclerotherapy or band ligation may be effective.

Rarely surgical excision and portosystemic shunt surgery.



Ascites

An accumulation of fluid in the peritoneal cavity

Etiology

1.**Transudate:**

(Heart failure,Nephrotic syndrome,Liver cirrhosis, Constrictive pericarditis)

2.**Exudate**:

(Peritonitis,Tuberculosis,Malignancy e.g. neuroblastoma,Polyserositis)

3**.Haemorrhagic**

(Trauma,Bleeding tendency,Malignancy

4.**Biliary**

(Spontaneous perforation of common bile duct.,Post operative,Congenital obstruction)

5.**Chylous** (Malignant infiltration,Thoracic duct obstruction,Traumatic)

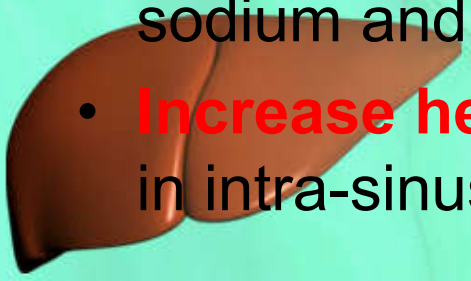
Pathogenesis of ascites in hepatic cirrhosis:

Two main factors in liver disease favor the development of ascites :

- **Hypoalbuminemia**: lowers plasma osmotic pressure, allowing the transfer of fluid into the tissue spaces and hence into the peritoneal cavity.
- **Intra-hepatic vascular obstruction**: leads to increased portal venous pressure.

The above mechanisms lead to

- **accumulation of fluid in peritoneal cavity (ascites)**, → reduced plasma volume and so reduced glomerular filtration. → **increased aldosterone** and retention of sodium and water leads more ascites.
- **Increase hepatic lymph formation** due to the increase in intra-sinusoidal pressure this adds to the ascites.



Laboratory diagnosis

1-liver function test

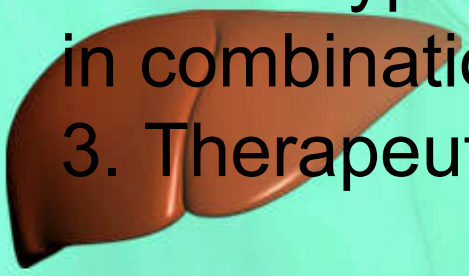
- Usually shows impaired levels of transaminase
- Low plasma albumin

2- Abdominal ultrasonography to detect the degree of ascites

3- Ascetic fluid tabbing for chemical and cytological examination.

Treatment of ascites

1. Sodium restriction
2. Diuretics: used cautiously because they may lead to hypovolemia. Furosemide can be used in combination with spironolactone.
3. Therapeutic paracentesis: in severe cases.



Spontaneous bacterial peritonitis

- This should always be considered if there is undiagnosed fever, abdominal pain, tenderness or an unexplained deterioration in hepatic or renal function.
- A diagnostic paracentesis should be performed.
- Treatment is with broad-spectrum antibiotics

Hepatic encephalopathy

- This is precipitated by gastrointestinal haemorrhage, sepsis, sedatives, renal failure or electrolyte imbalance.
- It is difficult to diagnose in children as the level of consciousness may vary throughout the day.
- Infants present with irritability and sleepiness.
- Older children present with abnormalities in mood, sleep rhythm, intellectual performance and behaviour.

Management of children with chronic liver disease

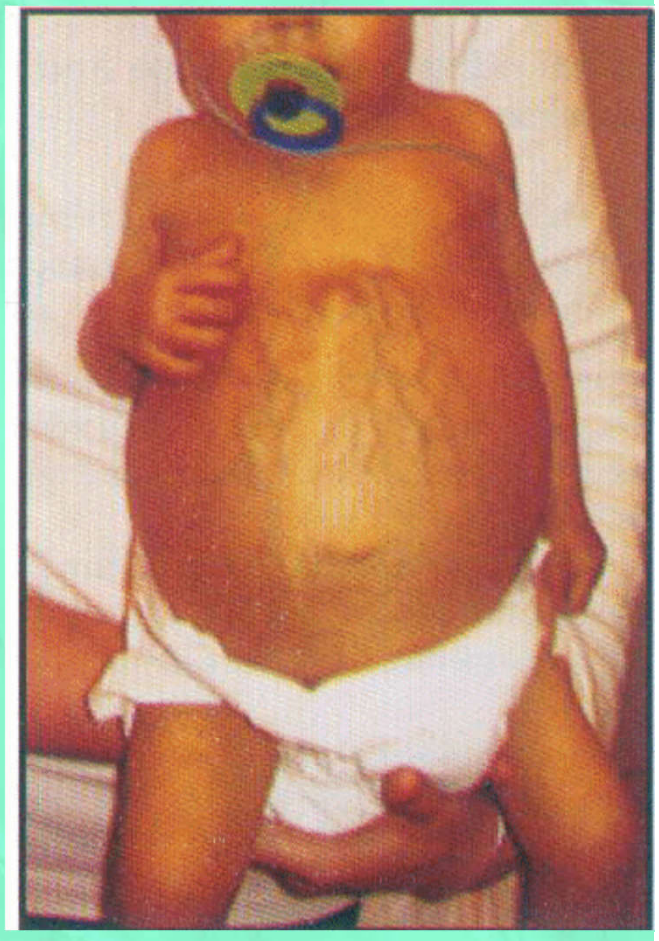
- Nutrition: High-caloric low-protein diet
- Fat soluble vitamins. **Vitamin. K,A ,E &D.**
- Pruritus. cholestyramine, ursodeoxycholic acid,
- Encephalopathy.

- ttt precipitating factor -Protein restriction.
- reduce ammonia reabsorption Neomycin/ metronidazole

VENO-OCCLUSIVE DISEASE

Veno-occlusive disease is an intrahepatic obstruction of hepatic veins by thrombotic lesions, which results in a *postsinusoidal portal hypertension.* The cause is unknown, but ingestion of herbal hepatotoxins may be responsible.

Clinical diagnosis depends on the presence of hepatomegaly, rapidly developing ascites and dilated abdominal wall veins in a malnourished child between the ages of 1- 4 years. Jaundice is usually mild or absent and spleen is not enlarged. Prognosis is generally bad as most cases deteriorate and die within several months of onset. Some cases may live longer and develop liver cirrhosis.



Treatment

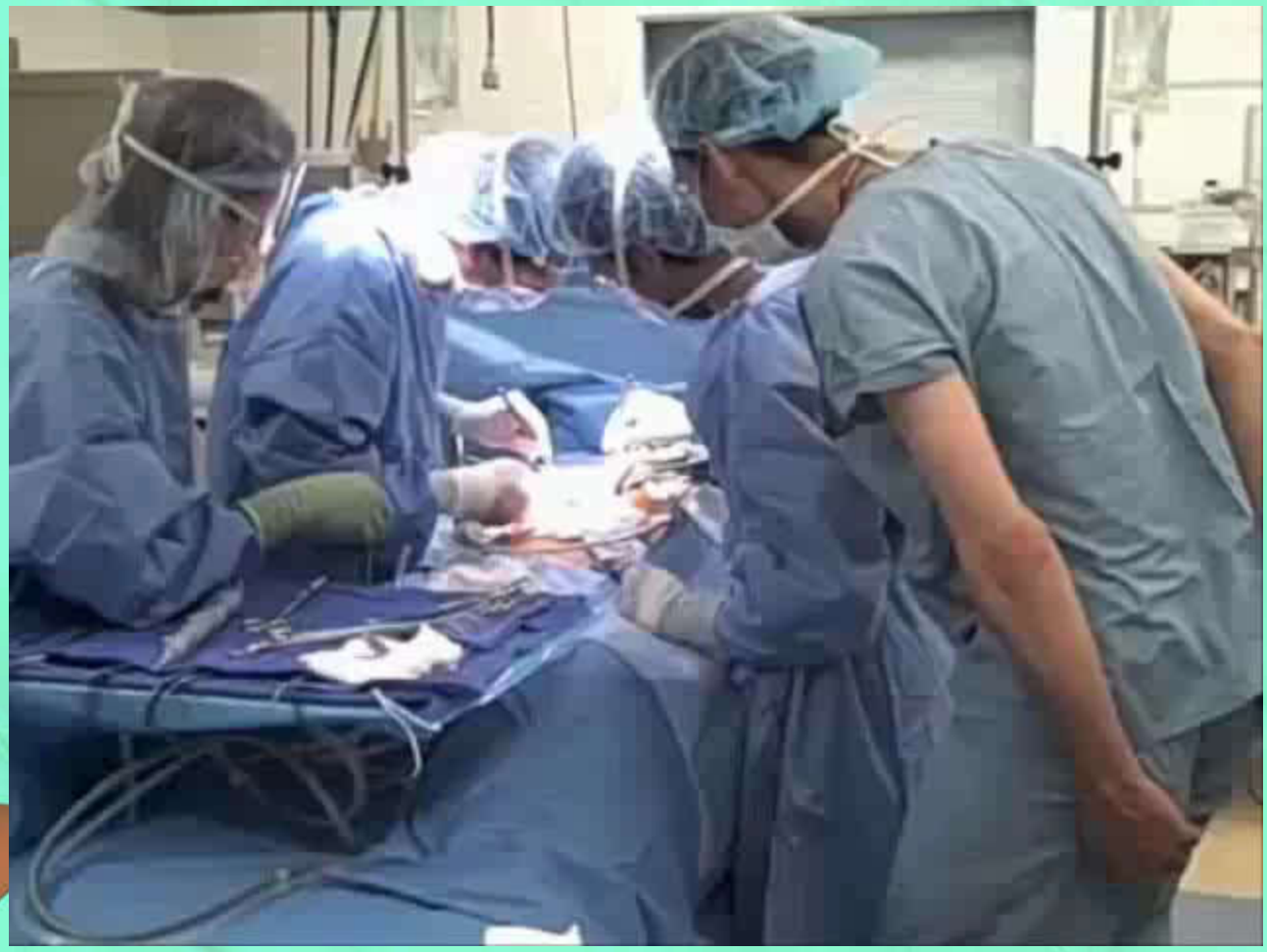
- There is no specific therapy, but avoiding toxic alkaloids in herbal infusions is prophylactic.
- High protein, low salt diet and vitamins.
- Diuretics
- Plasma and low salt albumin.
- Steroids may be tried in some cases.
- Tapping of Ascites.

Liver transplantation

- Severe malnutrition unresponsive to intensive nutritional therapy
- Recurrent complications (bleeding varices,resistant ascites)
- Failure of growth and development
- Poor quality of life.

Most children receive part of an adult's liver, which is either reduced to fit the child's abdomen (reduction hepatectomy) or split (shared between an adult and child).

Liver transplantation



Thank you!!