Liver disease in children

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Objectives

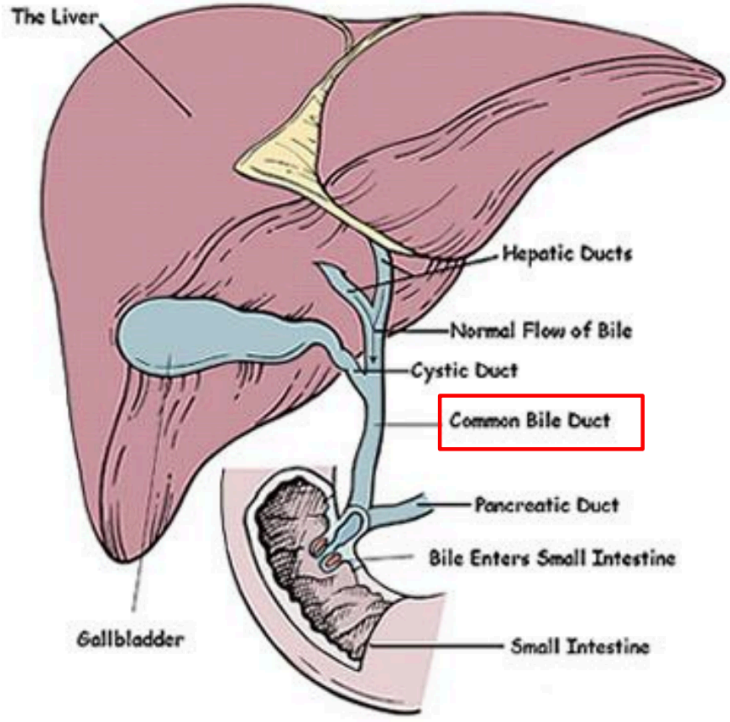
- To understand the anatomy & physiology of liver & biliary tree
- To be able to read & interpret the basics of liver function tests
- To be able to recognize the variable presentations of acute & chronic liver disease

- To know the most common conditions causing neonatal liver diseases & chronic liver diseases in children
- To know how to diagnose these conditions appropriately

PART - 1

NORMAL ANATOMY & PHYSIOLOGY OF THE LIVER

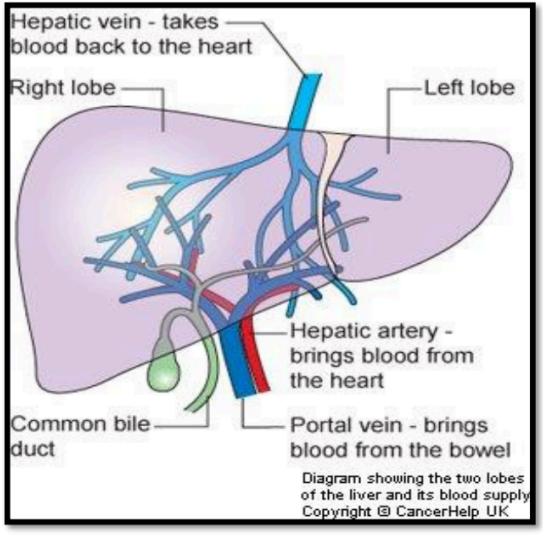
Liver anatomy

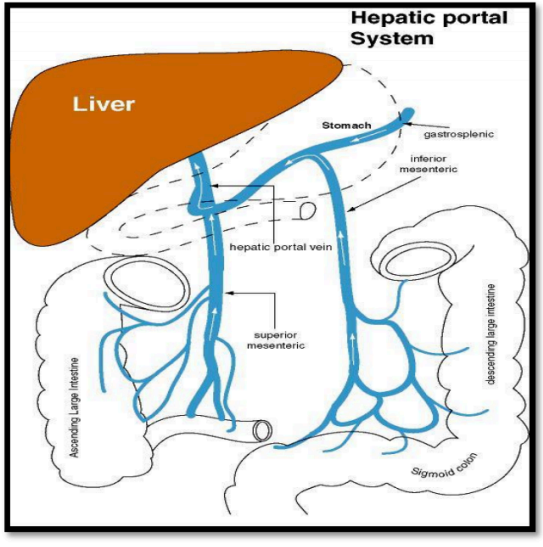


Liver blood supply

- Liver has **dual (bouble) Blood supply** resources ;
  - 70% from **portal** vein (**nutrients**)
  - 30% from **Hepatic** artery (**oxygenated** blood)

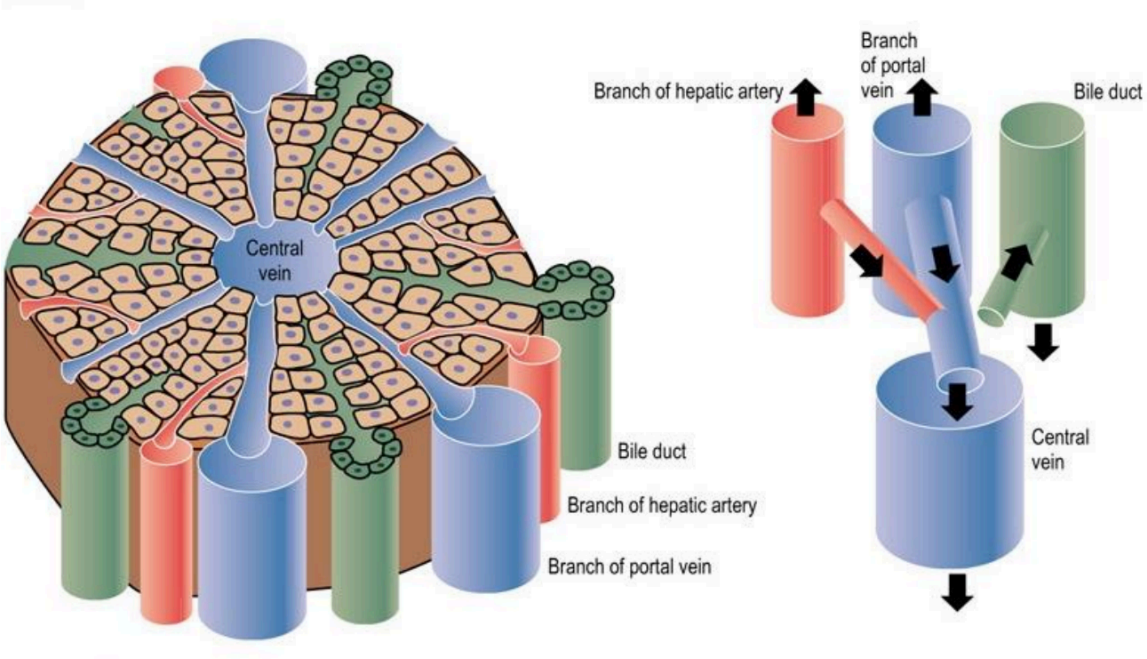
So liver is the least organ to be affected in case of shock, if you find that there is an insult to liver secondary to shock or hypotension this mean that the insult was severe enough to affect the organ that has double blood supply





This is the histological pic of the hepatocyte, it's hexagonal. all the functions of the liver happens inside the hepatocytes then all secretions from hepatocyte goes to the canaliculi (the green one) then the canaliculi they form the bile duct. the blue one is the portal veins that will compine to form the central vein which will descend to inferior vena cava to the heart

Liver Histology



Liver FUNCTIONS

Synthetic Function

1- **Glucose** Glocuse storage + convert glycogen to glucose in case of fasting

2- **Plasma proteins:** (albumin, globulins, Clotting factors)

3-Lipids: cholesterol and lipoproteins

4- **Bile salts** Imp to fat absorption

Detoxification and excretion

1- Bilirubin

2- Ammonia convert to to urea (urea cycle) then get excreted with urine

3-Drug metabolites

4- Cholesterol

Storage Function

1- **Glucose→ Glycogen**

2- **Vitamins** A, D, E, K and B_{12}

What are the liver function markers?

Liver enzymes # LFTs

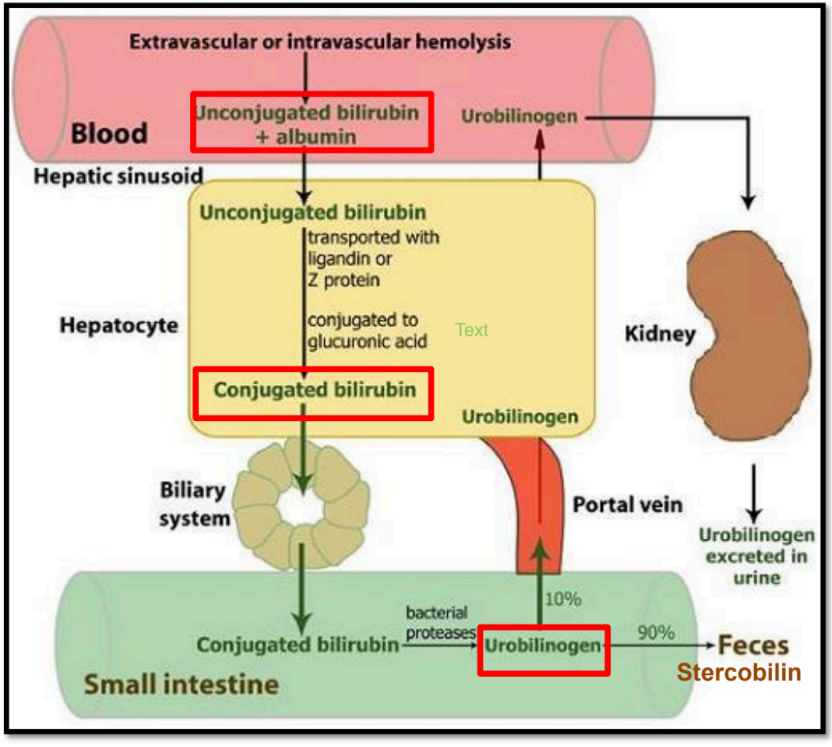
- **Enzymatic markers:**
  - ALT (more specific)
  - AST comes from different sources like RBCs, small bowel, muscle diseases
  - ALP can come from bone (that's why it's high in growing kids and pregnant ladies cuz it comes from placenta)
  - GGT (more specific)

- **Synthetic function markers:**
  - Glucose
  - Bilirubin
  - Bile acids
  - Albumin, Globulins
  - Clotting factors (PT &PTT)
  - Urea (from NH3 & AAs)

Bilirubin metabolism

This is very very important graph

2- The clinical importance of this pathway is when we have an obstruction in the biliary system so the bile or bilirubin will not go down to the bowel this will make the stool color pale or acholic because the bilirubin didn't meet the bacteria inside the colon thus didn't gave the normal color of the stool.
in pediatrics we think of mechanical obstruction like stone or biliary atresia



1- RBCs half-life is about 20 days then it breakdown into different component one of them is the unconjugated bilirubin (fat soluble), it needs to be carried out by albumin inside the blood then it will be taken to the liver. inside the liver, it comes conjugated (water soluble) then it goes to biliary system to the small bowel to the large bowel where it meet the normal flora which convert conjugated bilirubin into urobilinogen. 90% of urobilinogen will go through colon then stool and this what will give the stool its normal color. while 10% of urobilinogen will go to the enterohepatic circulation to be reabsorbed and then get excreted through the kidney.

Hyperbilirubinemia: (important numbers)

- Hyperbilirubinemia (HB) **biochemically** = **TSB > 1.5 mg/dl** (26 mmol/l)

Total serum bilirubin

multiplied by 17 to convert to mmol

- Jaundice become **clinically** evident if total **SBL > 5 mg/dl** (86 mmol/l)

Serum bilirubin level

- Conjugated HB: if **cong. Billi. > 20** % of the total Bili (mcq)

Direct

Very important to remember!

Hyperbilirubinemia

- Conjugated/Direct HB ⇔ Liver disease

- Unconjugated/Indirect HB is mostly non-liver related (RBC hemolysis-- Muscle disease)
  EXCEPTIONS: Indirect hyperbilirubinemia but they're coming from a liver source
  - Criglar Najjar syndrome
  - Gilbert syndrome

Causes of un-conjugated HB (MCQs)

How to differentiate? breast feeding jaundice is related to the feeding itself it happens in the first few days of life because the mother doesn't have enough milk so the child get little bit dehydrated and become jaundice while the breast milk jaundice is caused by the component of the milk itself it has some component that delay the conjugation process & it usually occur late around 1-2 weeks of life. both of them are benign and we can stop feeding for 1-2 days to confirm diagnosis and then we tell the mother to continue feeding the baby normally.

Haemolysis ; will be discussed in different lecture

- **COOMB +ve:**
  - ABO incompt., Rh incompt
  - Autoimmune
  - Drug-induced HA
- **COOMB - ve;**
  - RBC membrane defects- Hbpathy- Enzyme defects
  - HUS

Non- haemolysis;

1- Breast feeding/Milk Jaundice

2- Criglar Najjar syndrome

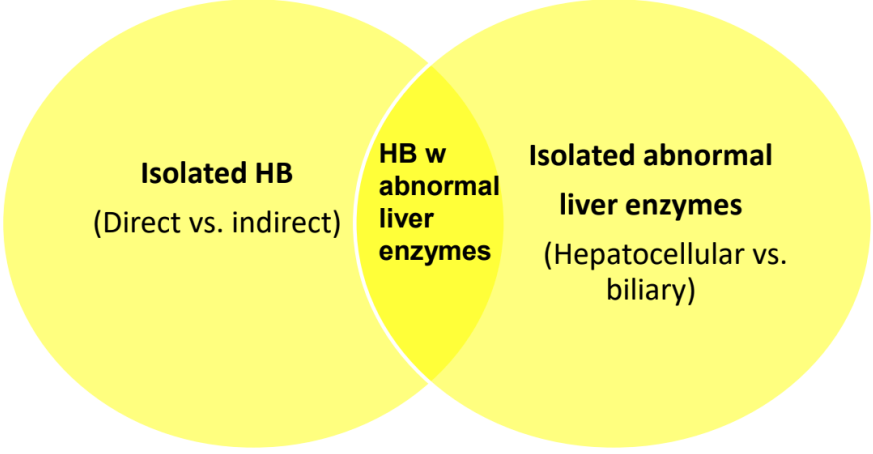
3- hypothyroidism

when the baby have hypothyroidism he will be a very slow feeder > dehydrated > indirect hyperbilirubinemia. In addition, thyroxine is very important hormone in the conjugation process of the bilirubin

4- Gilbert syndrome

Biochemical Patterns of liver diseases

- Isolated **Hyperbilirubinemia** (HB)
- Isolated **abnormal liver enzymes** (w/t HB)
- **Both** (Hyperbilirubinemia with abnormal liver enzymes)



They need continuous phototherapy (more than 17hr/day) which can be done in the first few months of life but after that it will be difficult. in very elevated levels they need exchange transfusion & plasmapheresis to remove excess bilirubin from the blood. at the end, the only cure for these kids is liver transplantation although their liver is working fine except for this enzyme. so we don't remove all liver we only do axillary liver transplant (take a small portion of liver from adult donor & connect it to patient's liver)

Isolated Hyperbilirubinemia

	Disease	Defect	Manifestations	TREATMENT
Indirect	**Gilbert's syndrome** Present at childhood - adolescent	**Mutation in UGT1A1** (< 30% of the normal activity) of the enzyme UGT1A1	Mild jaundice during **stress** Fasting, sick	None
	Crigler-Najjar syndrome type 1 In infants	**Mutation in UGT1A1** (absent activity)	**Sever** jaundice (risk for **kernicterus**) Permanent CNS insult	PhtoTx Exchange Tf Liver Tp
	Crigler-Najjar syndrome type 2 In infants Milder form	**Mutation in UGT1A1** (< 10% of the normal activity)	Mild-mod jaundice	Phonoparbitone This will induce enzyme activity
	Direct HB Both benign, present after delivery			
	Dubin-Johnson syndrome	MRP2 receptor mutation (impair **transport** process across canalicular membrane)	Neonatal cholestasis – no symptoms	None
	Rotor syndrome	OTP1B1 & OTP1B3 mutation (affect **reuptake** of cong.Billi by hepatocytes)	Neonatal cholestasis – no symptoms	None

Patterns for liver diseases:

1*) Cholestatic or obstructive* bile duct injury

GGT /ALP > AST/ALT

2) *Hepatocellular or liver cell inj*ury:

ALT/AST > GGT/ALP

3) Mixed: Mostly

- There is often considerable overlap between injury types in a patient who has liver disease.

QUESTIONS FROM PART 1

PART-2

Liver disease in children

Liver disease in children

- **Variable : age dependant**
  - **Infants:** Biliary atresia (BA), Neonatal hepatitis, metabolic liver disease, genetic disorders (progressive familial intraheptaic cholestasis (PFIC)

  - **Older children = adults liver diseases:**
    Viral Hepatitis**,** Wilson disease, Auto-immune hepatitis, ect…

- **The main presenting** symptoms of liver disease is **jaundice**
- **Any jaundice after 2 weeks of age should be investigated (MCQ)**

Cholestatic liver disease

- **Cholestasis → chole= bile Stasis=stagnation**
- The obstruction of bile flow either:
  - **Mechanical block** (biliary atresia, stones…) or
  - **Functional block** (cellular **receptor** & **transporter** levels):eg: progressive familial intrahepatic cholestasis (PFIC)

Very common cause of cholestasis in pediatric in our country

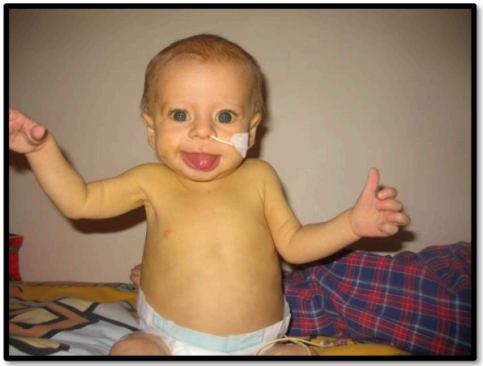
- **Cholestasis is characterized by an accumulation of compounds that cannot be excreted through the bile**
  - Conjugated/direct bilirubin→ jaundice (Cholestasis # jaundice)
  - Enzymes (GGT/ALP>ALT/AST)→ high liver enzymes in serum
  - Bile salts→ itchiness It could be severe enough to do liver transplant (severe itchiness > cry all night > not able to sleep > mother\father not sleeping & not going to work > very difficult social life
  - Cholestrol→ xanthomas

Get deposited under the skin

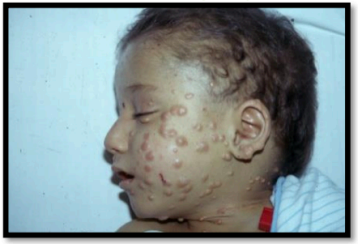
Presentation of cholestasis

- **Jaundice** (accumulation of conjugated bilirubin)
- **Pale stool (Acholic stool)… Why?? (MCQ)** obstruction > bilirubin won't meet the normal bacteria in the colon > won't form the urobilinogen > won't have the normal stool color
- **Dark and foamy urine** (bile salts in the urine)
- **Pruritis** (accumulation of bile salts under the skin)
- **Xanthomas depositions** (accumulation of cholestrol[Fat] in the skin)
- **Hepatomegaly +/- Splenomegaly** (Portal HTN, Storage disease, infiltrative process)
- **Failure to thrive (FTT)/** poor weight gain
- **Incidental lab finding**

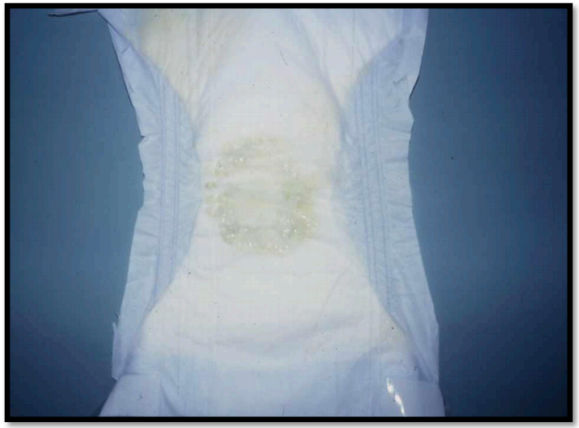
Signs of cholestatic liver disease



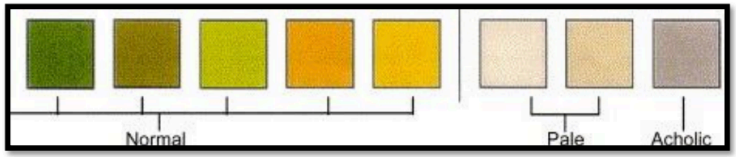
Jaundiced + abdominal distention (ascites) + muscle wasting + failure to thrive that's why we put NG tube to feed him



Xanthomas - Alagille syndrome



Pale stool (Acholic stool)



Stool card given to parents in countries common with cholestatic liver disease like east Asia in order to bring the baby to the hospital & have early diagnosis to avoid irreversible liver damage

Evaluation of infants with cholestatic liver disease

- **STEP1: Confirm the presence of cholestasis**
  (Clinically: jaundice, acholic stool, pruritis, **& lab:** direct hyperbilli**)**

  + high GGT

- **STEP 2: Rule out surgical obstruction** such as Biliary atresia, Choledocal cyst and GB stones **(Abdm US)** Normal? go to step 3

  Gallbladder

- **STEP 3: Investigate the treatable medical conditions:**
  - **Infections:** UTI, TORCH infections
  - **Endocrine**: hypothyrodism, panhypopituitarism
  - **Metabolic** disorders (Galactosemia, Tyrosenemia)

  the bacteria will secret some toxins that will affect the conjugation process, easy to treat with antiviral/antibacterial therapy

- **STEP 4: Further studies for other causes (genetic/metabolic)**

Hepato-cellular liver disease

- Necrosis of hepatocytes following a **viral, ischemic or toxic insult** to the liver will cause primarily an elevation of enzymes found within the hepatocyte (ALT and AST)

- In hepatocellular disease, the serum levels of GGT and AP do not rise to the same degree as the aminotransferases (in general)

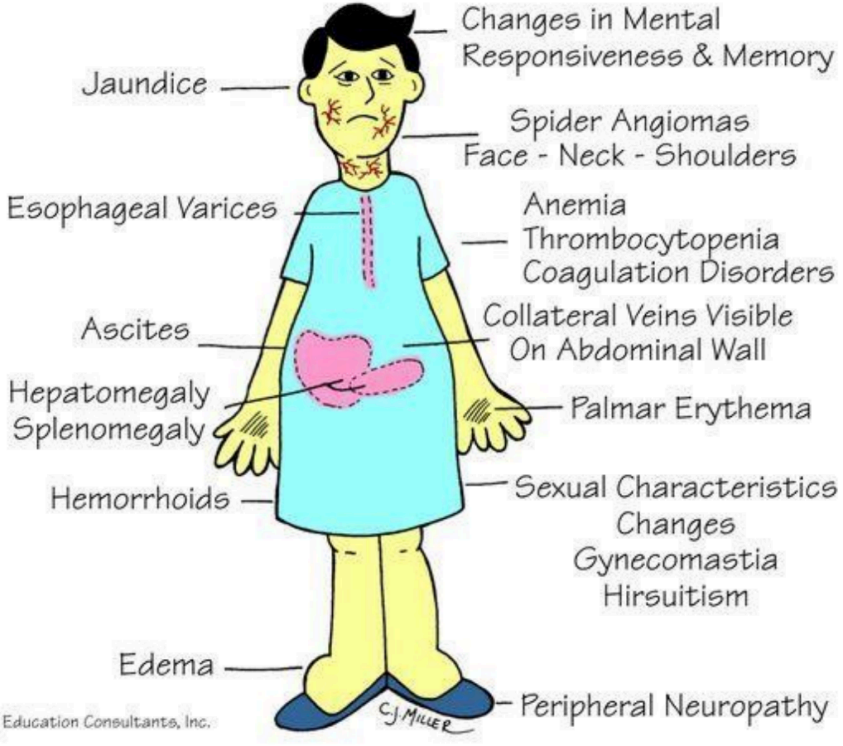
Chronic hepatitis

- **Definition:**
  - an inflammatory condition of the liver in which the biochemical and histologic abnormalities persist for more than 6 months from any disease.

- **Chronic hepatitis in children can be caused by:**
  viral infection (Hep B & C); autoimmune process; hepatotoxic drugs; or metabolic, or systemic disorders

- Can progress to CLD if the primary disease not treated well

CIRRHOSIS:
LATER CLINICAL MANIFESTATIONS



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Causes of liver disease in ***neonates & infants*** *(both types)*

- Cholestatic disorders
  - —Biliary atresia
  - —Choledochal cyst
  - —Paucity of intrahepatic bile ducts (eg, Alagille syndrome)
  - —Progressive familial intrahepatic cholestasis syndromes (Byler disease and syndrome)
  - —Benign recurrent intrahepatic cholestasis
  - —Caroli disease and syndrome
  - —Inspissated bile (S/P hemolytic disease)
  - —Cholelithiasis

- Viral hepatitis or other infectious diseases in the neonate
  - —Cytomegalovirus
  - —Herpes simplex virus/herpes zoster virus/human herpesvirus 6
  - —Epstein-Barr virus
  - —Parvovirus B19
  - —Rubella
  - —Reovirus—type 3
  - —Adenovirus
  - —Enterovirus
  - —Bacterial sepsis/urinary tract infection
  - —Syphilis
  - —Tuberculosis
  - —Toxoplasmosis

- Idiopathic neonatal hepatitis and mimickers
  - —Cystic fibrosis
  - —Alpha 1-antitrypsin deficiency
  - —Hypopituitarism/hypothyroidism
  - —Neonatal iron storage disease

Causes of liver disease in neonates & infants

للاطلاع

- Metabolic disease
  - —Disorders of peroxisomal function (Zellweger syndrome)
  - —Disorders of bile acid metabolism
  - —Disorders of urea cycle (arginase deficiency)
  - —Disorders of amino acid metabolism (tyrosinemia)
  - —Disorders of lipid metabolism (Niemann-Pick type C/Gaucher/Wolman)
  - —Disorders of carbohydrate metabolism (galactosemia, fructosemia, type IV glycogen storage disease)

- Toxic/pharmacologic injury (eg, acetaminophen, total parenteral nutrition, hypervitaminosis A)

- Tumors (intra- and extrahepatic)

QUESTIONS from part 2

PART-3

SPECIFIC LIVER DISEASES IN INFANTS

Imp in real life & MCQs

Biliary Atresia (BA)

- Biliary atresia is an **obstructive disease** of the **biliary tree** (mainly extra-hepatic) secondary to idiopathic inflammatory/autoimmune process??

- It leads to gradual fibrosis and ultimate obliteration of the biliary tract → biliary cirrhosis → liver failure→ **infant death within 2 years If not treated (surgery or liver transplantation)**

- **The most frequent indication worldwide for liver transplantation among infants and children (NOT in KSA)**

In KSA, metabolic and genetic disorders are more common and most common is the progressive familial intraheptaic cholestasis (PFIC) but for your exam choose biliary atresia

BA - Diagnosis

- **Clinical presentation**:
  - It presents with **signs of cholestasis** (jaundice, acholic stool, pruritis, FTT) in the **first 2-6 weeks of life (MCQ)**

- **Abdominal US:** rule out other causes of biliary obstruction (choledochal cyst, GB stones…)

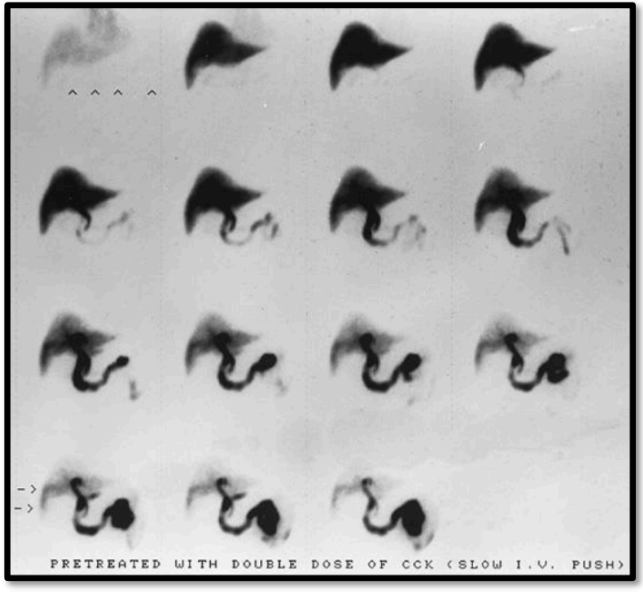
  congenital anomaly that affect the biliary system

- **Hepato-biliary scintography = nuclear scan (HIDA scan):**
  - shows good uptake of tracer and then NO excretion into the intestine, even 24 hours later (next slide)

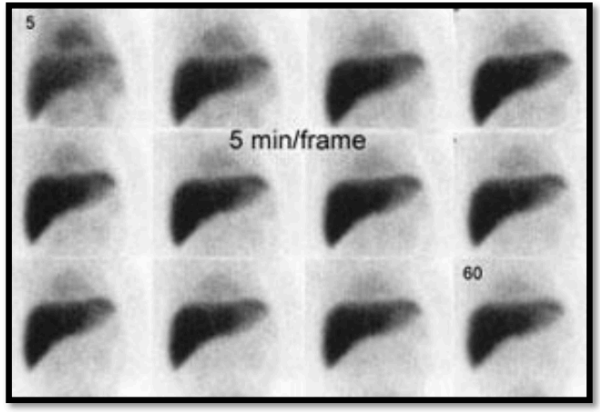
نحقن ماده نيوكلير وناخذ صوره كل ١٠-٥ دقايق، الابتيك يكون ممتاز لكن ما يكون فيه اكسكريشن وهذا ابنورمال

ماصرنا نستخدمه موجود فقط بالكتب لان ماراح يفيدنا بشيء لما يكون فيه بيل ستول معناته غالباً راح نشوف ابستركشن وش الجديد

Hepato-biliary scintigraphy (HIDA scan)



NORMAL HIDA SCAN



HIDA scan in BA patient

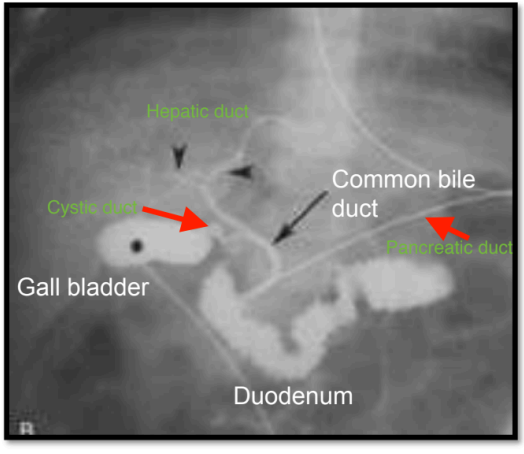
BA - Diagnosis

- **A liver biopsy:**
  - confirms the diagnosis by revealing characteristic findings (proliferation of the interlobular bile ducts, periportal fibrosis, and bile plugs in canaliculi and ductules) مو مهم تعرفون الفيتشرز

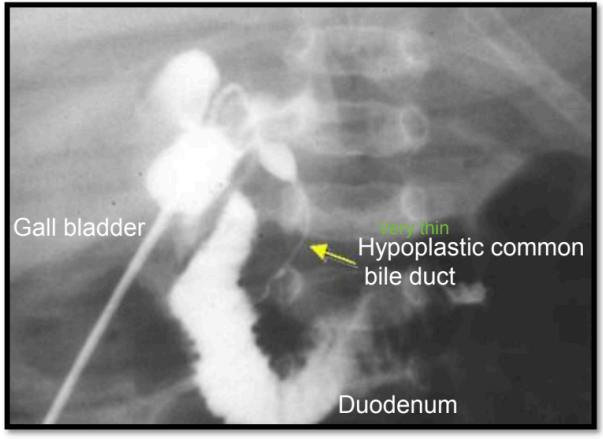
- *Definitive diagnosis* is confirmed by **Intra-operative cholangiogram**

The surgeon will insert a catheter inside the gallbladder through the skin then they inject a dye that goes from the gallbladder to the cystic duct > biliary system shows you clear hepatic duct & common bile duct CBD & pancreatic duct > small bowl. this is the normal pathway but in patients with biliary atresia (see next slide)

Definitive diagnosis is confirmed by Intra-operative cholangiogram



Normal study

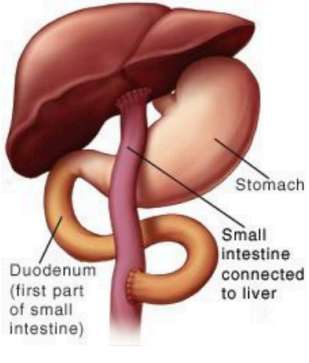


Abnormal study
(hypoplastic common bile duct)

This confirm the diagnosis > take child directly to the OR > Kasai procedure

BA Management

- **Surgical correction (Kasai procedure or porto-entero-stomy) :**
  liver Small bowl Connection
  removing the blocked bile ducts and gallbladder and replacing them with a segment of child's own small intestine
  Or hepato-entero-stomy
- Should be done before 2 months of age (MCQ)
  - after this age, there is increased risk of fibrosis & subsequent cirrhosis→ decrease the chance for surgery success)
- **Liver transplantation** if:
  - Kasai failed, or
  - Late presentation (> 3 months) or
  - Decompensated liver disease



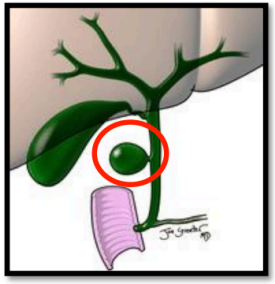
Choledocal cyst

DDx of biliary atresia

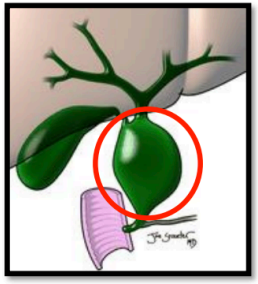
- Cystic dilatation of the biliary tree at different levels → **obstructive picture** Diagnosed with US

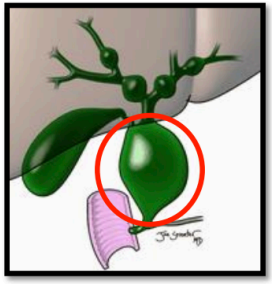
Same as biliary atresia

- Present with cholestasis picture, abdominal mass or asymptomatic, biliary stones or biliary carcinoma in adults



only we resect the cyst





here we have to resect the whole section

- Treatment: surgical excision

Alpha-1 Antitrypsin deficiency

- A-1 AT is a **protease inhibitor** (inhibit elastase, trypsin) → protect lung from neutrophil elastase destruction

الجسم في حاله هدم وبناء، فإذا ماتت خلايا الرئتين يفرز الجسم elastase, trypsin عشان يهضمها ويحللها بالتالي يتخلص منها. فلازم يكون فيه توازن بينها وبين الالفا انتي تربسن لان لما يكون عندي دفشنسي يصير فيه دستركشن للرئه ويصير عندهم emphysema

but in liver it's total different mechanism, the problem is the accumulation of Pi ZZ

- **A-1 AT deficiency cause:**
  - Liver disease (children or adults)
  - Emphysema lung disease (mainly seen in adults)

Autosomal Recessive

- **AR disease** (rare in our community) Genetic mutation
  - Pi MM→ Pi ZZ →form abnormal A-1 AT protein→ **failed excretion from liver (trapped)** → cholestatic liver disease

Accumulate

Alpha-1 Antitrypsin deficiency

- **Dx:**
  - A-1 AT level, phenotyping (pi ZZ) and
  - confirmed with Liver biopsy (seen in special stain)
  - Genetics

- **Treatment: supportive**

- **Prognosis:** varies (improve over time ….> chronic liver disease

Neonatal Hepatitis

Conditions that is not diagnosed

فقط عشان تعرفونها لو شفتوها في الكتب لكن بالكتب الجديدة ما صاروا يستعملونها

مصطلح قديم، قديماً مع قله الدياقنوستك مودالتيز كان كثير من الاشياء اللي مايعرفون يشخصونها يسمونها Neonatal Hepatitis الان مع التطور صارت الاشياء اللي كنا نسميها Neonatal Hepatitis صار لها تشخيص

- “Idiopathic" neonatal hepatitis = **an <u>aetiology has not been identified</u>**

- The list **gets smaller overtime** (new advancement in diagnostic modalities = more genetic & metabolic causes are discovered daily)

- Management of these infants involves supportive measures till specific cause found

?? Questions PART 3

Part 4

SPECIFIC LIVER DISEASES IN OLDER CHILDREN

Liver disease in older children = adults !!

We will focus on hepatitis & Wilson disease
the rest is FYI

- **Infectious** (Viral, Bacterial, Protozoal)
- **Toxic/medications** (drugs, TPN)
- **Ischemia** (CR arrest, hypotention)
- **Metabolic disorders** (CHO, FAT, Amino Acids)
- **Autoimmune:** AIH
- **Genetics;** Wilson disease
- **Vascular** (thrombosis)
- **Infiltrative/Malignancy** (leukemia, primary liver tumours)

Acute hepatitis

- Five primarily viruses: hepatitis A, B, C, D, and E
- The clinical presentation of viral hepatitis varies with the pathogen (**hepato-cellular injury**→ mixed)
- **HEPATITIS A: (MCQs)**
- ***Presentation:***
  - ***flu-like illness*** , Anorexia, fever, vomiting, abdominal pain, darkening of the urine, **following ingestion of contaminated food or contact with infected patient (**oral-fecal route **)**

كلما كان الطفل اكبر كلما كان الجاوندس اوضح

- Hepatitis A is often an-icteric (no jaundice) in young children (<5 y) and frequently is unrecognized

HEPATITIS A

- **Diagnosis** of acute infection is based on the presence of anti-HAV IgM antibody in serum (MCQ)

- The disease typically is **self-limited** in children and often is clinically not clear In very verry rare cases, they can present with fulminant hepatic failure with severe necrosis to the hepatocyte and all the liver cells are destroyed & the only cure is liver transplant

- No chronic carrier state is identified (full recovery or rarely death from fulminant liver failure)

- **Treatment** is supportive (IVF, Antipyretics)

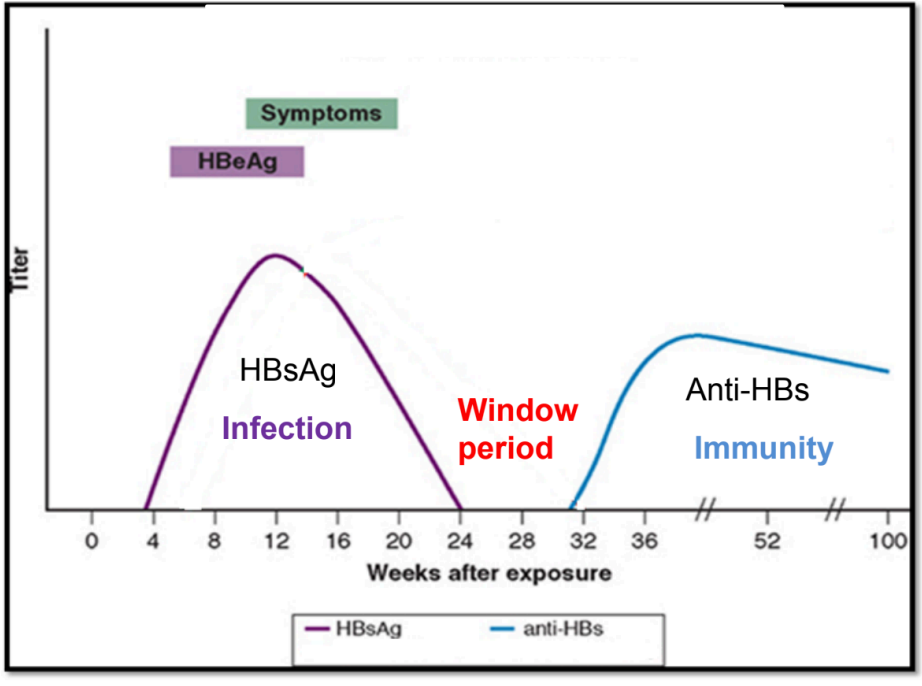
- **Prevention**: Hep. A vaccine: 2 doses (18 ms & 24 months)

Hepatitis B

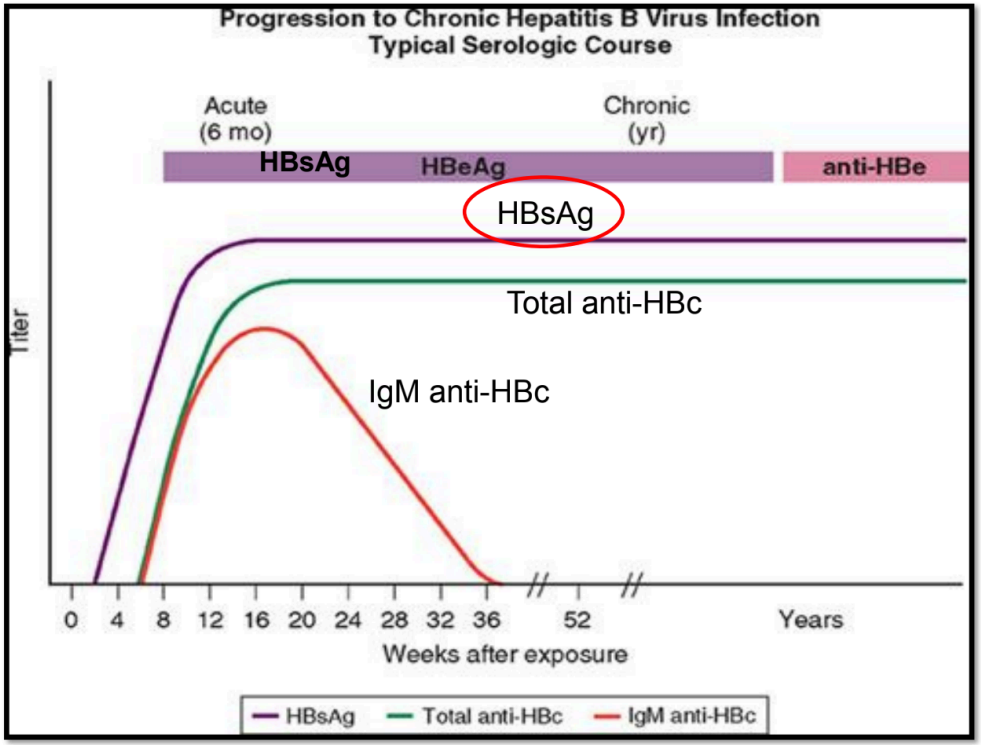
- Hepatitis B virus (HBV) infection can cause both acute and chronic hepatitis
- It can progress to cause **cirrhosis and hepatocellular carcinoma** if not treated (take long time to happen)
- **Risk of transmission:** primarily **vertical** (mother to baby during delivery) in children or via contaminated blood + other risk factors..
- **Diagnosis**: Hepatitis B surface antigen **(HBsAg)**
- **Chronic HBV infection** is associated with the persistence of HBsAg and HBV DNA for **> 6 moths**

نعطي الجسم فرصه يتخلص منه، لو قعد اكثر من ٦ شهور فهذا كرونك وصعب يروح من نفسه

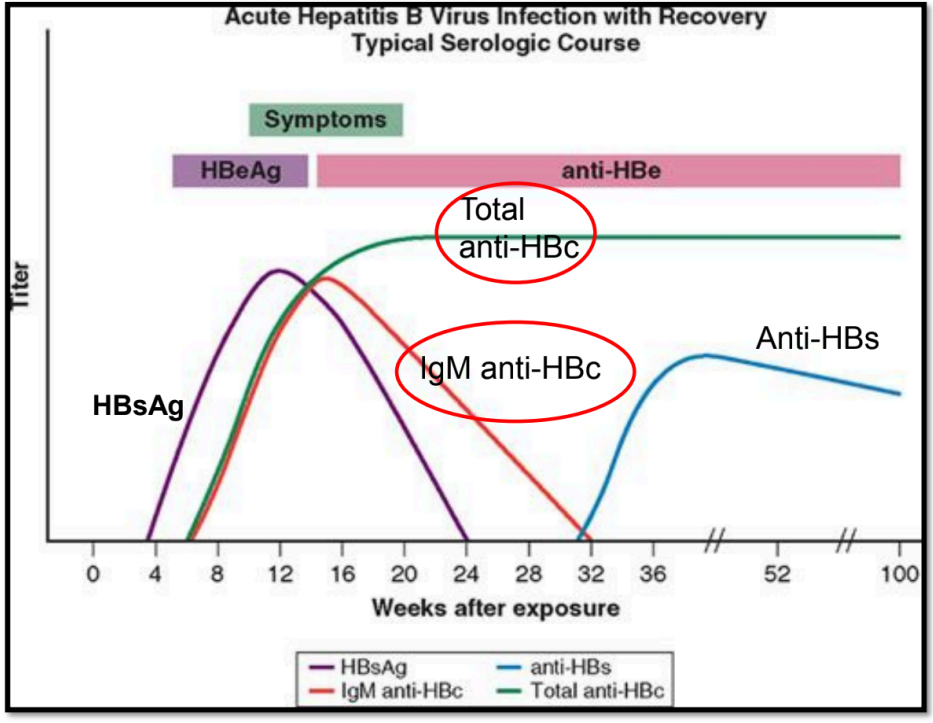
HBV serology markers



Chronic hepatitis



HBV serology markers.. recovery



Hepatitis B serological markers

Imp to your future, USMLE.. etc

* HBsAg => Hepatitis B surface antigen

* Anti-HBs => Hepatitis B surface antibody

* Anti-HBc => hepatitis B core antibody

* IgM Anti-HBc => IgM antibody to hepatitis B core antigen

* HBeAg => Hepatitis B e antigen

* HBeAb => Hepatitis B e antibody

HBsAg **anti-HBc** **anti-HBs**	negative negative negative	Susceptible
HBsAg **anti-HBc** **anti-HBs**	negative positive positive	Immune due to natural infection
HBsAg **anti-HBc** **anti-HBs**	negative negative positive	Immune due to hepatitis B vaccination
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive positive negative	Acutely infected
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive negative negative	Chronically infected
HBsAg **anti-HBc** **anti-HBs**	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

HBsAg => +ve => Infection
If it was:
IgM Anti-HBc => acute infection
IgG Anti-HBc => chronic infectior

Anti-HBs => +ve => Immunity

How to differentiate when Anti-HBs is +ve whither it's previous infection or got vaccinated? (both have -ve HBsAG & +ve Anti-HBs)

By Anti-HBc
Vaccinated => -ve Anti HBc
Infected (natural immunity) => +ve Anti-HBc

HBeAG => +ve => high infectivity
HBeAb => +ve => low infectivity

Treatment

- **Prevention:**
- **newborn of Hep BsAg-positive mothers (MCQ):**
  - **Passive immunization**: **Hep. B Immunoglobulins** (within 12 hrs of birth)
  +
  - **Active immunization: Hep. B Vaccine after birth** (within 7 days after birth, then at 1 month & 6 months)

- Rx for older children: antiviral meds
  - ??? Wait & observe (spontaneous recovery, new better antiviral meds with less side effects)

Hepatitis C

- Hepatitis C virus (HCV) causes acute hepatitis, which **progresses to chronic disease (End-stage liver disease can occur in up to 10 %)**

- Risk of transmission similar to hepatitis B

- **Diagnosis** is based on the detection of
  - persistently elevated anti-HCV antibodies (above 18 ms of age)
  - **confirmed** by PCR for HCV RNA-active infection

Why? because below 18 months we will find the mother's anti-HCV antibodies in the baby's blood but if we find it after 18 months then it's for sure the baby's antibodies not the mother

Hepatitis C

- **Treatment**:
  - Spontaneous viral clearance from acute infections can occur in pediatrics (15-56%)
- antiviral Rx (new generation, > 95% effective)
- **Prophylaxis**: no vaccine yet

Hepatitis D Not important

- Hepatitis D virus (HDV) infection occurs only in patients who have HBV infection
- Associated primarily with intravenous drug abuse
- HDV usually aggravates liver disease in a patient who has hepatitis B and always should be considered in those who have particularly aggressive HBV disease

Hepatitis E

- Hepatitis E virus (HEV) occurs in epidemics in parts of the world that have poor sanitary conditions
- It can be a particularly devastating disease in pregnant women can cause abortion

Viral hepatitis.. summary

	Hepatitis A virus (HAV)	Hepatitis B virus (HBV)	Hepatitis C virus (HCV)	Hepatitis D virus (HDV)	Hepatitis E virus (HEV)
Viral genome	RNA	DNA	RNA	RNA	RNA
Transmission	Faecal-oral route	Blood and other body fluids	Blood	Blood and other body fluids	Faecal-oral route
Incubation period	14–28 days	30–180 days	14 days –6 months	HDV requires HBV for replication	14–70 days
Diagnosis	• Anti-HAV-specific AB • HAV RNA	• HBV surface protein • Anti-HBV-specific AB	• Anti-HCV-specific AB • HCV RNA	• Anti-HDV-specific AB • HDV RNA	• Anti-HEV-specific AB • HEV RNA
Possible chronic infection	No	Yes	Yes	Yes	Yes
Vaccine	Yes	Yes	No	No	Yes (in China only)

AB, antibody; DNA, deoxyribonucleic acid; RNA, ribonucleic acid

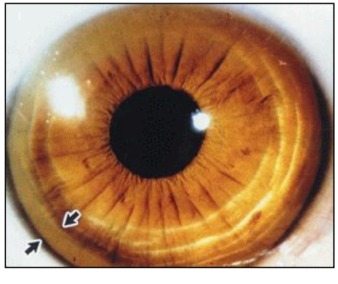
Wilson disease (a must to know)

Multisystem disease

- AR disorder
- caused by a defect in biliary copper **excretion**

- **Excessive copper accumulation (multi-systems):**
  - **liver** → leads to cirrhosis
  - **Other organs**: cornea, kidneys, and brain, resulting in extra-hepatic manifestations of the disease

Cloudiness Nephropathy Psychosis & depression



- Wilson disease SHOULD be included in the differential diagnosis of any child who presents with liver disease, neurologic abnormalities, behavioural changes (treatable condition)

That's why it's very important condition to be excluded

Wilson disease

- Wilson disease may present as ***fulminant hepatic failure***, usually in association with a ***hemolytic crisis*** due to the toxic effect of copper on red blood cells.

- **Definitive diagnosis** requires evaluation of:
  - 24-hour urinary copper excretion **and**
  - copper quantification in liver tissue obtained by biopsy
  - Genetic test (useful in asymptomatic children of 1st degree relatives)

Bind to the copper

- **Therapy** is **chelating** therapy of the copper with **penicillamine**, which allows for its excretion into the urine (early diagnosis = better prognosis)

AIH Autoimmune hepatitis

- AIH is a hepatic inflammation associated with the presence of circulating **autoantibodies against liver cells** in the absence of other recognized causes of liver disease
- Other autoimmune diseases may coexist, including: thyroiditis, DM

- **Dx:**
  - **High transaminases +**
  - **High autoimmune markers (anti SMA, KLM)**
  - **High serum gamma globulin concentrations**
  - **Liver biopsy**

- Rx: Immunosuppressive medications e.g.: steroids….

Ischemic hepatitis

It have double blood supply so it heal faster

- Ischemic hepatitis results from **shock (eg, dehydration), asphyxia, cardio-respiratory arrest, or seizures**.
- The disorder is due to hypotension/hypoperfusion to the liver
- Typically, aminotransaminases are elevated in the absence of other markers of severe liver disease.
- Ischemic hepatitis may resemble infectious hepatitis, but it is distinguished easily by rapidly decreasing aminotransaminases levels in the days following the initial insult without increasing coagulopathy or hyperbilirubinemia.

Infiltrative disorders

- **Infiltrative disorders** of the liver are observed with leukemia, lymphoma, and neuroblastoma (*more common than primary liver tumers*)
- **Primary liver tumors**: Hepatoblastoma, hepatocarcinoma, and hemangioendothelioma
- **Presentation:** hepatomegaly or abdominal distension or mass
- Serum alpha-fetoprotein levels usually are elevated.
- Dx by CT scan or MRI
- Surgical excision of a solitary tumor or radiation/chemotherapy is the treatment of choice.

THE END

QUESTIONS

TABLE 6. Miscellaneous Physical Findings Associated With Liver Disease

Infants
• Microcephaly: congenital cytomegalovirus, rubella, toxoplasmosis
• Characteristic facies: arteriohepatic dysplasia (Alagille syndrome)
• Cataracts: galactosemia
• Retinal pigmentation and posterior embryotoxon: Alagille syndrome
• Abnormal auscultation of lungs: cystic fibrosis
• Neuromuscular abnormalities (tremors, flaccidity): lipid storage disease, Wilson disease, disorders of oxidative phosphorylation
Children
• Pruritus: chronic cholestasis
• Hemangiomas: hemangiomatosis of the liver
• Kayser-Fleischer rings: Wilson disease
• Glossitis: cirrhosis
• Enlarged kidneys: congenital hepatic fibrosis or polycystic disease
• Arthritis and erythema nodosum: liver disease with chronic inflammatory bowel disease
• Arthritis, acne, fatigue: autoimmune hepatitis