Jaundice (icterus)

- Yellow discoloration of the sclera, skin, & mucous membranes is a sign of hyperbilirubinemia. Clinically apparent jaundice in children and adults occurs when the serum concentration of bilirubin reaches 2–3 mg/dL (34–51 μmol/L); the neonate may not appear icteric until the bilirubin level is > 5 mg/dL (85 μmol/L).

Cholestasis:

Definition:

1. It is increased serum conjugated bilirubin concentrations more than 20 % of total bilirubin.
2. It implies impairment of bile flow at any point from its formation in the hepatocyte to its excretion from the common bile duct.

Etiology:

It is classified as either **obstructive cholestasis** or **Hepatocelluar cholestasis.**

1. The obstructive cholestasis occurs when there is reduction in bile flow and retention of substances normally secreted in the bile (*mechanical* obstruction of bile flow).
2. Hepatocelluar cholestasis results from impairment of bile excretion (*functional* impairment of hepatic excretory function and bile secretion).

Diagnostic approach to conjugated Hyperiblirubinemia:

1. ***History and Physical examination:***

- Age and sex
- Family history of jaundice.
- History of maternal infection during pregnancy to exclude congenital infection**.**
- Child attending day-care center or nursery school (e.g. hepatitis A).
- History of blood transfusion.
- Jaundice: time of appearance, duration.
- Associated manifestations:
  i. Pruritis is commonly associated with obstructive jaundice.
  ii. Bleeding disorder is commonly associated with hepatic dysfunction.
  iii. Dark urine**,** Pale stools
  iv. Hepatomegaly, Hepatosplenomegaly
  v. Vomiting**,** abdominal distension, and pain or discomfort, tenderness and rash.
  vi. Abdominal mass.

2. ***Laboratory Investigations:***

a. Icreased total and direct bilirubin.
b. Complete blood picture shows: leukocytosis in sepsis.
c. Liver enzymes:
   i. Increased SGPT (ALT) and SGOT (AST).
   ii. Increased alkaline phosphatase more than 3 times the normal level in obstructive lesion.
   iii. Increased alkaline phosphatase less than 3 times than normal level in hepatocellular disease.
d. Increased serum cholesterol.
   i. More than 250 mg/dl in obstructive lesion.
   ii. Less than 250 mg/dl in hepatocellular disease.
e. Prolonged prothrombin time in hepatocellular disease.
f. Specific tests: to search for etiology

- T3, T 4 and TSH for cretinism
- Alpha one antitrypsin.
- HBsAg for hepatitis B
- Sweat chloride for cystic fibrosis.
- TORCH screening for congenital infection.
- Blood and CSF culture for sepsis.

. Ascites

Definition:

An accumulation of fluid in the peritoneal sac.

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

Clinical features:

1. Ascites may appear insidiously or may develop suddenly when hepatocelluar function is reduced e.g. by hemorrhage, shock and infection.
2. The symptoms of ascites include: Abdominal distension, abdominal pain and discomfort.
3. Clinically ascites can be detected by the following methods
   a. Abdominal percussion in knee-chest position which can detect minimal volume ascites.
   b. Shifting dullness which can detect moderate volume ascites.
   c. Transmitted thrill in cases of massive ascites.

Differential diagnosis:

Ascites should be differentiated from:

- Gases - Obesity - Abdominal cysts - Full urinary bladder

1- Liver function tests
   a. Usually shows impaired levels of transaminase
   b. Low plasma albumin
2- Abdominal ultrasongraphy to detect the degree as well as the cause of ascites.
3- Ascetic fluid tapping 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 (K+ preserve).
3. Therapeutic paracentesis (in severe cases).

Hepatitis

Definition:

It is an inflammatory process of the hepatocytes characterized by degeneration and regeneration with loss of hepatic architecture.

***Types*:**

1- Acute: less than six months duration. **2-** Chronic: more than six months.
Recently it's classified into:
a. Minimal hepatitis. b. Mild hepatitis.
c. Moderate hepatitis. d. Severe hepatitis.

***Etiology*:**

I. Infections**:**
1. Viral:
   a. Hepatotropic viruses e.g A, B, C, D, E, F, G, H viruses
   b. Non hepatotropic: infect the liver in the course of other **systemic illness:**
      - Epstein-Barr virus (EBV). - Cytomegalovirus (CMV).
      - Others: Coxsakie, ECHO, Rubella, Varicella & Measles viruses.
2. Bacterial:
   - As a part of generalized septicemia.
   .

3- Protozoal: e.g amoebic hepatitis.

II. Drugs and Toxins:

- Anti T.B. e.g Isoniozid - Antimetabolites - Anticonvulsant (valporic acid)
- Irradiation - Chloropromazin - Total parenteral nutrition
- Carbontetrachloride - Halothane

III. Immunological Disorders:

1- As apart of : SLE & JRA

2- Isolated auto immune hepatitis (lipoid hepatitis)

IV. Metabolic Causes:

- Alpha antitrypsine deficiency - Galactosemia - Tyrosinemia
- Hemosiderosis - Wilson disease

V. Vascular Causes

- Hepatic vein thrombosis. - Hepatic artery thrombosis

VI. Tumors:

- Primary: hepatoma or hepatoblastoma
- Secondary: neuroblastoma, lymphoma, leukemia

Viral Hepatitis

1. Hepatitis A

***Mode of transmission*: fecal - oral route.**

Incubation period:

1. 15 - 45 days (average 4 week).
2. The virus is excreted in stool during the first few weeks of infection, prior to the onset of symptoms.

Clinical picture:

1- Prodromal stage: (1-2 weeks) (pre-Icteric)
- Headache, anorexia, malaise.
- Nausea, vomiting, lethargy. This phase can be passed unnoticed by the parents.

2- Icteric phase: (2-3 weeks), characterized by:
- Jaundice - Dark urine.
- Abdominal pain - Soft, enlarged, tender liver.

3- Convalescence phase: (1-2 weeks)
- After which the child becomes nearly normal.

- In endemic areas 30 - 80 % of children acquire subclinical or anicteric infection in the first few years of life.
- Typical infection presents with:
  - Anorexia - Nausea - Vomiting
  - Fever - Abdominal discomfort
  - Irregular bowel motions for a few days - Dark urine & scleral jaundice.

Laboratory diagnosis:

1. Liver function tests:
   a. Raised serum level of direct & indirect bilirubin.
   b. Urine contains both bilirubin (dark color) & Urobilinogen.
   c. Marked elevation of serum transaminases (ALT & AST).
   d. Increase in serum levels of alkaline phosphatase & 5 nucleotidase.
2. IgM Anti- HAV is detected at the onset of the symptoms and disappears within 4 months while IgG anti-HAV appears at 8 weeks and persists for life

Complications:

1. **Acute fulminant hepatitis:**
   a. It is a rare condition with massive destruction of the liver cells.

b. It is presented clinically by persistent vomiting, disorientation, encephalopathy, bleeding tendency, edema and ascites.

2. **Aplastic anemia:**
   a. Is a very rare complication, it is transient but may be fatal.
   b. It is due to bone marrow depression.
   c. Death is usually due to serious infection resulting from depressed immunity.
3. **Prolonged Cholestatic syndrome:**
   a. The patient becomes intensely pruritic and jaundiced.
   b. It is due to hepatocyte edema which may cause element of obstruction.

Treatment:

1. There is no specific therapy for acute viral hepatitis,
2. Most children are managed at home except if liver cell failure is suspected.
3. Balanced diet with low fat intake should be given.

Prevention:

1. Period of infectivity: Contagious for about 7 days before and 7 days after the onset of jaundice.
2. Period of isolation from school: Patient should be excluded from school and child care centers, from the appearance of dark color urine and appearance of jaundice till 7 days after.
3. Careful hand washing after changing diapers and before preparation of food.
4. Fly control.
5. Intramuscular immunoglobulin may be indicated in pre and post exposure.
6. Hepatitis A vaccine is now available to be given to children older than two years of life. Contacts are immunized with immunoglobulin or the vaccine.

2. Hepatitis B

Mode of transmission:

1. **Perinatal transmission (vertical transmission)**
   - Infection appears to be due to contact with a mother's infected blood at the time of delivery.
   - Transplacental transmission is rare.
2. **Parenteral**: In patient receiving blood transfusion or blood products, renal dialysis, dental care and through contaminated syringe and needles.
3. **Child to child transmission**: It may occur through biting of insects, drooling and shared chewing gums.

***NB*:** *Although HBV was detected in breast milk of infected mother there is no role of breast milk in transmitting the infection.*

Incubation period: HBV has long incubation period (45-160 days).

Clinical manifestations:

1. Infection tends to be more insidious, and might last longer than HAV infection.
2. Asymptomatic carrier is more common.
3. Acute infection presented with:
   a. Jaundice, dark color urine, anorexia, nausea, malaise.
   b. Hepatomegaly splenomegaly.
   c. Extrahepatic manifestations as:
   - Papular skin eruption - Arthralgia - Glomerulonephritis
   - Aplastic anemia - Polyarthritis
4. Chronic hepatitis may present with:
   a. Chronic active hepatitis
   b. Cirrhosis
   c. Hepatocellar carcinoma in adult

Laboratory diagnosis:

1. **Liver function tests**:
   The first clinical evidence of infection is elevation of ALT. which begin to rise before the prodromal symptoms appears
2. **Hepatitis markers:**

- The serological pattern of HBV is differ depending on either the patient is a carrier or acute or chronic case.
- Routine screening for HBV requires at least two serological markers:
- HBsAg which indicate infection and HBeAg which indicate high infectivity.
- HBcAb (IgM) is detected early in the disease & is replaced after many months by IgG. Evaluation is important because it differentiates between the carrier and acute and chronic patient.

Complications:

1. Persistent infection
   a. Following acute infection, approximately 5% of infected individuals fail to eliminate the virus completely and become persistently infected.
   b. Those who are at particular risk include:
      i. Babies and young children.
      ii. Immuno-compromised patients
      iii. Males > females.
2. Chronic hepatitis which can leads to cirrhosis
3. Acute fulminant hepatitis with encephalopathy, coagulopathy and cerebral edema. Rare; accounts for 1% of infections.
4. Aplastic anemia
5. Hepatocelluar carcinoma on top of cirrhosis

Prevention:

1. Hepatitis B vaccine is now included in the first year compulsory vaccination program worldwide.
2. Hepatitis B immunoglobulins (0.5 ml) should be given soon after delivery to babies whom mothers are HBsAg positive together with vaccine.
3. Proper screening of blood and blood products to eliminate all blood-borne viruses.

Prognosis:

1. Recovery may be complete.
2. The child may remain as a symptomatic carrier.
3. Chronic course for months or years**.**

3. Hepatitis C

Etiology:

- HCV was previously known as non-A non-B hepatitis.
- There are many genotypes (1, 2, 3, 4) and phenotypes (a, b, c, d, e,…) of each genotype.
- The most common genotypes in Egypt are 1 and 4 and phenotype a & c.

Mode of transmission:

1. Post-transfusion: with repeated transfusion of blood and blood products.
2. Intravenous drug, needle prick exposure, hemodialysis, organ transplant.
3. Perinatal transmission is uncommon & transplacental transmission not proved until now.

Incubation period:

The incubation period is 7 - 9 weeks.

Clinical picture:

1. The clinical pattern of the acute infection is usually similar to that of other hepatitis.
2. Acute HCV infection is usually mild and may be asymptomatic but fulminant liver failure may occur with poor prognosis.
3. HCV is the most likely hepatitis virus to cause chronic infection (in about 25 % of the patients).
4. Chronic HCV infection may be associated with extra-hepatic manifestations, including:
   - Cutaneous Vasculitis - Peripheral neuropathy - Cerebritis
   - Membrano-proliferative glomerulonephritis - Nephrotic syndrome

Complications:

- Fulminant hepatitis (low risk) - Chronic hepatitis (high risk)
- Hepatocelluar carcinoma is lower than HBV**.**

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Prevention:

1. There is no available vaccine against HCV.
2. Proper screening of blood and blood products to eliminate all blood-borne viruses.
3. **Hygienic care in :-**
   a. Dentistry (sterilization of all equipment , using disposable instrument to every person)
   b. Using disposable syringe for injection.
   c. Careful hygienic measure during shaving.
   d. Delivery by caesarian section for mothers with hepatitis C.

-Chronic Hepatitis

Etiology:

1. Chronic infection with HBV, HDV or HCV.
2. Autoimmune chronic hepatitis.
3. Metabolic diseases as Wilson disease & α- 1- antitrypsin.
4. Drug-induced as isonicotinic acid hydrazine (INH), rifampicin.
5. Chronic inflammatory bowel disease particularly ulcerative colitis.

Clinical Picture:

Chronic hepatitis may start as an acute hepatitis, which fails to resolve within 3 - 6 months or as an insidiously progressing liver disease, or might be accidentally diagnosed in an asymptomatic child. The liver is usually enlarged and firm, and the spleen may be also enlarged and firm. Jaundice, bleeding tendency, palmar erythema, spider naevi and ascites may be present.