VIRAL HEPATITIS

(By Dr. S. UMA DEVI M.D)

Viral hepatitis specifically refers to a primary infection of the liver by one of the five etiologically associated viruses (the number is now believed to be seven including type F and G).

These five types of hepatitis include:

**TYPE A:** Synonyms: infectious hepatitis, epidemic jaundice, short incubation period hepatitis

**Type B:** Serum or transfusion hepatitis

**TYPE C:**

**TYPE D:** caused by defective virus; has no independent existence; depends on HBV: drug abusers are prone for it.

**TYPE E:** Epidemically prone, enterically transmitted.

**Method of transmission**
- **Hepatitis A and E:** feco oral
- **Hepatitis B:** via 1) contaminated blood 2) Contaminated syringes/needles 3) unsafe sex 4) transplacental
- **Hepatitis C and D:** Thr’ contaminated syringes, thr’ blood and blood products

**HAV versus HAB virus infection**

**Similarities:** Both infections are similar in clinical picture

**Differ in**
1. Incubation period
2. Route of entry
3. Immunity conferred
4. Onset

**CLINICAL PICTURE (USUAL CLINICAL PICTURE)**

**TYPE A AND TYPE B**
1. Prodromal period 1 week (flu like picture)
2. Icteric phase 2 weeks (jaundice, tender hepatomegaly)
3. Convalescent period 3 wks
4. Biochemical recovery later (after 6 months)

<table>
<thead>
<tr>
<th>DIFFERENTIATING FEATURES</th>
<th>TYPE A</th>
<th>TYPE B</th>
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<tbody>
<tr>
<td>Age</td>
<td>Increased susceptibility in adults</td>
<td>Transfusion of contaminated blood Contaminated syringes/needles Unsafe sex Transplacental</td>
</tr>
<tr>
<td>Entry route</td>
<td>Oral</td>
<td>Contaminated syringes/needles</td>
</tr>
<tr>
<td>Incubation period</td>
<td>15 to 30 days</td>
<td>60 to 100 days</td>
</tr>
<tr>
<td>Onset</td>
<td>Acute</td>
<td>insidious</td>
</tr>
<tr>
<td>Immunity</td>
<td>Life long, no recurrence</td>
<td>Life long in 95%</td>
</tr>
<tr>
<td>Course of illness</td>
<td>Self limiting</td>
<td>Proneness in alcoholics</td>
</tr>
<tr>
<td>--------------------------</td>
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</tr>
<tr>
<td>Carrier state</td>
<td>No</td>
<td>--</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Liver cancer</td>
<td>No</td>
<td></td>
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<tr>
<td></td>
<td>Yes</td>
<td>Yes</td>
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</table>

(.MNEMONICS for Differentiating features-AEIOU-Age,entry,incubation.onset course)

**What are the unusual modes of presentation of hepatitis A?**
1. Fulminant hepatitis
2. Pronounced cholestasis simulating obstructive jaundice

**FIG 1. Sequence of serological markers in acute hepatitis A**

**What is fulminant hepatitis?**
Severe hepatitis with massive hepatic necrosis resulting in hepatic coma and death. Occurs in 0.5 to 1% of viral hepatitis (type A to E)
Other causes: drugs and toxins, Shock, CAH, Bud-chiari, Wilsons syndrome, Baterial, parasitic

**What is an-icteric hepatitis?**
Jaundice is not clinically evident but tender hepatomegaly +
These patients usually suffer from CAH etc

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**HBV Hepatitis**

**Etiology:**
Hepatitis B virus
Hepatitis B is 50 -100 times more infective than HIV.

Antigens of HBV:
- Surface antigen—HBS Ag
- Core antigen---HBCAg  (enclosed by outer coat of HBs Ag
- HB E Ag -----Additional antigen found in some cases along withHBSAg
  - HBE Ag is specific for HBV.

ANTIBODIES
- For HBS Ag-  Anti HBSAg
- FOR HBCAg-AntiHBCAg
- For HBEAg-Anti HBE Ag

Lab diagnosis of Hepatitis B
Depends on many serological markers
**SIX---** HBS Ag- and  Anti HBSAg
  - HBCAg-AntiHBCAg
  - HBEAg-Anti HBE Ag

How are serological markers useful?
1. To know the stage of the disease
2. Degree of infectivity
3. Prognosis
4. Immune status of the patient

1. Stage of the disease
HBS AGg appears first and then the anti HBC antibody
So, if HBS AGg is present and Anti HBC is absent it means very early infection in non vaccinated

2. Infectivity of the patient
Presence of antigen HBE correlates with abundance of Dane particles in circulation
Such situation indicatesincreased risk of transmission of HBV infection via various routes

3. Prediction of development of carrier state
Persistance of HBS Ag at 3rd month and persistence of HBS Ag at 6th month,
               Indicates carrier state

4. Prediction of recovery
Presence of antibodies againstHBE i.e. presence of antiHBE indicates recovery is under way.
25% of adults chronically infected in childhood, later die from cirrhosis or liver cancer.

**PREVENTION OF HEPATITIS B INFECTION**

- **Active immunization** with Hepatitis B vaccine containing HBSAg
- **Passive immunization** with hyper immune serum with hepatitis immunoglobulin (HBIG)

**TYPES OF VACCINE**

(hepatitis B vaccine is 92% effective)

- Plasma derived
- Yeast derived

Dose and schedule of vaccine - (Plasma derived)
3 doses - 0, 1st mth and 6th month parenteral

**HBV vaccination is indicated in whom?**
1. Health care workers
2. Doctors and nurses in dialysis unit and hemophilia centers
3. Immuno deficient patients
4. Spouses of patients with acute hepatitis and spouses on carriers of HBV.

**What is NON A, Non B virus?**
2 important types
1. Blood born Non A Non B virus infection caused by hepatitis C
2. Water born Non A Non B caused by Hepatitis E virus (HEV)

Features of **Hepatitis C** infection

- Incubation period: 50 days
- Route of infection: parenteral - 90% post transfusional
- Carrier state is described

**DELTA HEPATITIS - HDV**

Features
- Causes HDV hepatitis
- HDV is a defective virus; cannot exist independently.
- It requires HBV for multiplication and transmission

**Two types of infection of HDV**

1. Coinfection - infection simultaneous with HBV
2. Super infection - infecting a patient already infected with HBV

**Summary**

<table>
<thead>
<tr>
<th><strong>HEPATITIS TYPE</strong></th>
<th><strong>MAIN METHODS OF TRANSMISSION</strong></th>
<th><strong>COMMON OUTCOME</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A (HAV, infectious hepatitis)</td>
<td>Contamination of food, etc. with fecal matter from infected person</td>
<td>Often resolves completely after 4 to 8 weeks; usually does not become chronic</td>
</tr>
<tr>
<td>B (HBV, serum hepatitis)</td>
<td>Contaminated blood transfusions; shared needles associated with intravenous drug use</td>
<td>Often less favorable than type A; can be fatal in 10 to 10% of cases in the elderly and after blood transfusions; can become chronic in 10 to 15% of cases</td>
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</tbody>
</table>
C (HCV, hepatitis C)  
| Shared needles or contaminated blood transfusion; sexual transmission rate low but possible | Irregular course; patient is often asymptomatic for years; can lead to chronic hepatitis |

D (delta agent)  
| This virus is closely associated with HBV | Exists only concurrent with hepatitis B; causes extremely severe symptoms; may be an important cause of hepatitis worldwide |

**Investigations in Acute Hepatitis**

Urine – Bilirubin  
Total count - low with neutropenia  
SGOT and SGPT are raised - levels can go to 400-4000IU/L  
Serum bilirubin raised  
Prothrombin time normal -12 sec. If markedly prolonged indicates severe liver damage.

**Other viruses causing Hepatitis**

EB virus  
Cytomegalovirus  
Coxasackie virus  
Yellow fever  
Herpes simplex  

**Other infectious agents causing Hepatitis**

Leptospirosis  
Toxoplasmosis

**CHRONIC HEPATITIS**

Any hepatitis lasting 6mths or longer showing chronic and persistent liver damage.

**Histological classification of Chronic hepatitis**

Chronic persistent hepatitis (CPH)  
Chronic lobular hepatitis (CLH)  
Chronic active hepatitis (CAH)

**Chronic persistant and chronic lobular hepatitis**

- Usually follow Acute hepatitis B or C  
- Both may be  
  - asymptomatic or  
  - cause vague symptoms, have no clinical signs (Smtms Hepatomegaly)  
  - Persistantly high transaminase value

Chronic persistant hepatitis (syn Portal hepatitis) portal mononuclear inflammation  
Chronic lobular hepatitis-diffuse lobular inflammation  
Lobular spotty inflammation-resembles resolving acute viral hepatitis
CHRONIC ACTIVE HEPATITIS
Serious condition, progress to hepatic cirrhosis, hepatic malignancy
Histologically fibrosis present with inflammation
Other organs affected—Thyroid, eye, kidney, blood vessels—Thyroiditis, corneal ulcerations, membrano proliferative glomerulo nephritis, vasculitic syndromes and sometimes also arthritis, pulmonary fibrosis.

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<thead>
<tr>
<th>HISTOLOGY</th>
<th>CPH</th>
<th>CAH</th>
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<tbody>
<tr>
<td>Prognosis</td>
<td>Good</td>
<td>poor</td>
</tr>
<tr>
<td>Liver cell necrosis</td>
<td>Minimal</td>
<td>Extensive and progressive</td>
</tr>
<tr>
<td>Signs of fibrosis</td>
<td>Nil</td>
<td>Extensive</td>
</tr>
<tr>
<td>Progression to cirrhosis</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Infiltration of inflammatory cells</td>
<td>Confined to portal tract</td>
<td>Extends beyond portal tract into lobule</td>
</tr>
<tr>
<td>Piecemeal necrosis</td>
<td>Absent</td>
<td>present</td>
</tr>
<tr>
<td>Bridging necrosis</td>
<td>Absent</td>
<td>present</td>
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Piecemeal necrosis:
- This the hallmark of Chronic active hepatitis
- Extension of portal infiltration into hepatic lobules
- Extension of limiting plate into hepatic cells
- These cells (zone1) are surrounded by connective tissue forming “Rosettes”

Bridging necrosis
Necrosis and subsequent fibrous septa extend from portal zone to portal zone or portal zone to central vein.

Etiology of chronic hepatitis
Viral—hepatitis virus—B, C, D.
Drugs—Methy dopa, INH,
Wilson,
Autoimmune (Lupoid)
Alpha1 antitrypsin deficiency

Clinical presentation of Chronic hepatitis
Usually with jaundice
Some present with complications of cirrhosis
Extra hepatic features in HBV and autoimmune etiology
- are immune complex mediated.

Treatment of CAH
Most promising treatment—alpha interferon in HBeAg/HBV Dna positive patients
morphologic features of both acute and chronic hepatitis

Diagrammatic representations of the morphologic features of acute and chronic hepatitis. Bridging necrosis (and fibrosis) is shown only for chronic hepatitis; bridging necrosis may also occur in acute hepatitis (not shown).

http://cueflash.com

TREATMENT OF VIRAL HEPATITIS
1. Suppovtive therapy for self limiting hepatitis like HAV
2. INTERFERON Most promising treatment-alpha interferon in HBeAg/HBV DNA positive patients
3. Anti viral drugs
   Hepatitis B Lamivudin
   Ribaverin for Hepatitis C

AUTO IMMUNE HEPATITIS

Cause: autoimmune
Clically ;
Jaundice and
extra hepatic manifestations like arthritis, Glomerulo nephritis, poly arteritis
May have hepato splenomegaly
Lab test: Anti smooth muscle antibody ANA.

Etiology of Various types of Hepatitis arranged in alphabetical order

**hepatitis A** a self-limited viral disease of worldwide distribution, usually transmitted by oral ingestion of infected material but sometimes transmitted parenterally; most cases are clinically inapparent or have mild flu-like symptoms; any jaundice is mild.

**anicteric hepatitis** viral hepatitis without jaundice.

**hepatitis B** an acute viral disease transmitted primarily parenterally, but also orally, by intimate personal contact, and from mother to neonate. Prodromal symptoms of fever, malaise, anorexia, nausea, and vomiting decline with the onset of clinical jaundice, angioedema, urticarial skin lesions, and arthritis. After 3 to 4 months most patients recover completely, but some may become carriers or remain ill chronically.

**hepatitis C** a viral disease caused by the hepatitis C virus, commonly occurring after transfusion or parenteral drug abuse; it frequently progresses to a chronic form that is usually asymptomatic but that may involve cirrhosis.

**cholangiolic hepatitis**
**cholestatic hepatitis**
1. inflammation of the bile ducts of the liver associated with obstructive jaundice.
2. hepatic inflammation and cholestasis resulting from reaction to drugs such as estrogens or chlorpromazines.

**hepatitis D, delta hepatitis** infection with hepatitis D virus, occurring either simultaneously with or as a superinfection in hepatitis B, whose severity it may increase.

**hepatitis E** a type transmitted by the oral-fecal route, usually via contaminated water; chronic infection does not occur but acute infection may be fatal in pregnant women.

**enterically transmitted non-A, non-B hepatitis** (ET-NANB).

**hepatitis G** a post-transfusion disease caused by Hepatitis G virus, ranging from asymptomatic infection to fulminant hepatitis.

**infectious hepatitis**

**infectious necrotic hepatitis** black disease
A fatal disease of sheep, sometimes of humans in US and Australia due to clostridium Novyi marked by necrotic areas in the liver.

**lupoid hepatitis** chronic active hepatitis with autoimmune manifestations.

**neonatal hepatitis** hepatitis of uncertain etiology occurring soon after birth and marked by prolonged persistent jaundice that may progress to cirrhosis.

**non-A, non-B hepatitis** a syndrome of acute viral hepatitis occurring without the serologic markers of hepatitis A or B, including hepatitis C and hepatitis E.
**posttransfusion hepatitis**  viral hepatitis, now primarily hepatitis C, transmitted via transfusion of blood or blood products, especially multiple pooled donor products such as clotting factor concentrates.

**serum hepatitis**

**transfusion hepatitis**  post transfusion hepatitis

**viral hepatitis**  Hepatitis A,B,C,D and E.

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