### Hepatotrophic viruses

**Definition**

Viruses causing hepatitis are either:

1. Hepatotropic viruses as HAV, HBV, HCV, HDV, HEV, HFV, HGV, TTV
2. Other viruses as Epstein Barr virus, CMV, Yellow fever

<table>
<thead>
<tr>
<th>MOT</th>
<th>HAV</th>
<th>HBV</th>
<th>HCV</th>
<th>HDV</th>
<th>HEV</th>
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<tbody>
<tr>
<td><strong>Oral-fecal</strong></td>
<td><strong>Blood-borne route</strong></td>
<td><strong>Blood-borne route</strong></td>
<td><strong>Blood-borne route</strong></td>
<td><strong>Oral-fecal</strong></td>
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<tr>
<td><strong>Anal-oral sex.</strong></td>
<td>• Blood, • tattoos, Sexually Vertical</td>
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**Natural history**

- Predominantly a benign self limited disease
- Usually full recovery without a residual hepatic damage
- No chronicity
- No carrier state
- Rarely (0.1%) acute liver failure occurs and has mortality of 70%
- Immunity is life long due to persistence of HAV – IgG

**In absence of Hep D**

- Prognosis is good but less favourable than HAV
- Complete recovery in 905 of adult and 30% of children
- The remaining pass to chronic hepatitis or carrier state
- Acute liver failure occurs in 1% of cases
- Presence of HDV worsen the prognosis

**Active immunization**

1. Inactivated HAV vaccine
2. Travelers to high risk areas
3. Children
4. Food handlers
5. Lab workers
6. Hemophiliacs
7. Patient on hemodialysis
8. Gay
9. Injecting drug users
10. Person with multiple sex partners
11. Sex partners of drug user

**Passive immunization**

Immunoglobulins to contacts with HAV patient within 2 weeks of exposure (with the 1st dose of the vaccine) and give a protection for 6 months or attenuate the virus to a sub clinical form

**Active immunization**

HBV vaccine which is recombinant yeast derived vaccine containing HbsAg, should be given to

1. Infants,
2. High risk group as contacts of HBV carriers
3. Health care workers
4. Hemophiliacs
5. Patient on hemodialysis
6. Gay
7. Injecting drug users
8. Person with multiple sex partners
9. Sex partners of drug user

Given intra – deltoid at 0,1,6 months schedule

**Prevention**

**Active immunization**

- Although the prognosis is more aggressive than HAV, it is good in males and non pregnant ladies with full recovery
- In pregnant ladies, 20 – 40% develops acute liver failure with very bad prognosis but no chronicity and no carrier state

### Nb

- Vertical transmission is common in HBV than HCV.
- Sexual transmission is common in HBV. HBV is present in all body secretions.
### Acute hepatitis

#### Definition
Is an acute inflammation of liver of less than 6 months duration

#### Causes

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<tr>
<td><strong>1.</strong></td>
<td><strong>Viral hepatitis</strong>&lt;br&gt;a) Hepatotropic viruses: more than 95% of viral cause&lt;br&gt;b) Non-hepatotropic viruses:</td>
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<td><strong>2.</strong></td>
<td>Herpes S, CMV, Epstein-Barr, yellow fever virus, adenoviruses</td>
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<td><strong>3.</strong></td>
<td>Non viral infections: toxoplasma, Leptospiros, Q fever</td>
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<td><strong>4.</strong></td>
<td>Alcohol</td>
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<td><strong>5.</strong></td>
<td>Toxins: Amanita toxin in mushrooms, carbon tetrachloride</td>
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#### Clinical feature (classical)

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<tr>
<td><strong>Prodromal phase</strong>&lt;br&gt;Pre – icteric phase&lt;br&gt;- It starts by non specific gastrointestinal or influenza like symptoms&lt;br&gt;- Usually this phase is &lt; 1 week, but may be several weeks or few hours and the main symptoms are fever, anorexia malaise&lt;br&gt;- Clinically there may be right hypochondrial dull achning pain, soft and tender liver and a soft spleen in 10% of cases</td>
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<td><strong>Icteric phase</strong>&lt;br&gt;- It last 1 – 3 weeks, but it is shorter in HAV than HBV&lt;br&gt;- By the onset of jaundice, fever drops and the general condition improves especially in HAV</td>
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<td><strong>Post icteric</strong>&lt;br&gt;Convalescent phase&lt;br&gt;- It starts by disappearance of jaundice and continuous until full clinical recovery&lt;br&gt;- Although the enzymes become normal but there may be fatigue, depression and probably anorexia</td>
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#### Clinical feature (atypical)

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<td><strong>Acute anicteric hepatitis</strong>&lt;br&gt;It may occur with any type, but more common with HCV and with HAV in children and can progress to chronic liver disease according to the type of the virus</td>
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<td><strong>Acute cholestatic hepatitis</strong>&lt;br&gt;It is common with HAV and indicates intra – hepatic cholestasis with raised direct s. bilirubin and ALP with less marked aminotransferase elevation. Urine become dark and stool caly – colored with pruritus.&lt;br&gt;- Prognosis is good</td>
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<tr>
<td><strong>Acute liver failure</strong>&lt;br&gt;It can occur with all types but is common with HEV in pregnant with 50% mortality and alcoholism favor its occurrence with HCV. HBV and HEV may contribute together with other new viruses</td>
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<tr>
<td><strong>Immune complex hepatitis</strong>&lt;br&gt;Patients develop a syndrome like serum sickness during the icteric phase due to the rapid formation of antibody before disappearance of antigen with antigen – antibody reaction leading to fever, rash, migratory arthritis in big joints and glomerulonephritis.&lt;br&gt;- It may occur with any type, but more common with HCV and with HAV</td>
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#### Investigation

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<tr>
<td><strong>HAV</strong></td>
<td>1. ALT (SGPT), AST (SGOT) may reach high level&lt;br&gt;2. S. bilirubin, ALP moderately elevated in classical type and markedly in the cholestasis type&lt;br&gt;3. Dx of virus → HAV Ab IgM&lt;br&gt;4. Recovery is monitored by appearance of HAV Ab IgG</td>
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<tr>
<td><strong>HBV</strong></td>
<td>1. ALT, AST are increased but not as high with HAV&lt;br&gt;2. Dx of virus → HbsAg, HB cab (IgM) (marker during window phase) or both&lt;br&gt;3. HbsAg → detected in both acute and chronic hepatitis&lt;br&gt;4. Hbe Ag to Hbe ab / HbsAg to HbsAb → improvement&lt;br&gt;5. Persistent HbsAg &gt; 6 months indicates chronicity&lt;br&gt;6. Cases with HBV should be examined for the possibility of associated HDV by examination for HDV ab or HDV RNA by PCR</td>
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<td><strong>HCV</strong></td>
<td>1. Serum ALT may rise rapidly and then fall rapidly, may rise and remained elevated and may fluctuate over weeks or months&lt;br&gt;2. S. bilirubin and ALP may or may not rise&lt;br&gt;3. Detection of HCV RNA by PCR is the only means to diagnose acute HCV because HCV ab may take several months to appear and by time they appear, the acute stage is over the most cases</td>
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<tr>
<td><strong>HDV</strong></td>
<td>Cases with HBV should be examined for the possibility of associated HDV by examination for HDV ab or HDV RNA by PCR</td>
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<tr>
<td><strong>HEV</strong></td>
<td>1. Serum aminotransferases are increased + HEV ab IgM is diagnostic&lt;br&gt;2. Recovery is monitored by appearance of HEV ab IgG</td>
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#### Diagnosis

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<td><strong>Clinical suspicion &amp; Hx of exposure to HEV within 2-12 w.</strong>&lt;br&gt;Development of jaundice in previously healthy patients. (Dx of virus → HEV Ab IgM)&lt;br&gt;Acute elevation of liver enzymes 10-20 fold with or without elevation of Sr. bil 2-8 w after exposure.&lt;br&gt;Detectable Sr. HCV-RNA 1-2 w after exposure.&lt;br&gt;HCV-Ab seroconversion 8-8 w after infection (window phase) but may be delayed up to 6 months.&lt;br&gt;HCV-Ab is less reliable than HCV-RNA in early detection of acute infection.</td>
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#### Treatment
- Etiological tt: There is no specific treatment for acute viral hepatitis (except for acute HCV).
- Moderate bed rest is advised for symptomatic patients but absolute bed rest is not advisable
1. **Diet**
   - Diet should be a good mixed nutritious and not just honey or CHO as some still believe,
   - Even fat is not contra indicated if the patient can tolerate without dyspepsia.
   - So the patient should be given any food he desires in the time he likes

2. **Liver supportive drugs** as silimarine are unproven value but not allowable

3. Excess vitamins are better avoided and corticosteroids may be dangerous as they increase the risk of relapse and chronicity

4. Urosodeoxycholic acid is effective in cholestatic type of HAV

In acute liver failure liver transplantation is recommended because of high mortality

In summary, 4 NOs have come out of the recent research

1. No for absolute bed rest
2. No for dietary restriction
3. No for corticosteroids
4. No for unnecessary drug (often metabolized in liver)

**Drug induced hepatitis**

- In acute HCV current data suggest that treatment with interferon-based regimens during acute HCV infection can augment the rate of sustained virologic clearance beyond which might be expected from later treatment in the chronic phase.
- HCV-RNA showed be assed 3 months after onset of symptoms, if still positive (viral clearance can occur in 20% of cases) conventional interferon 5 MU S.C. daily for 4 weeks followed by 5 MU three times weekly for 20 more weeks can give 98% viral clearance.
- Recently, pegylated interferon can be given for only 12 weeks.
- But in cases infected via a transfusion and those with asymptomatic acute HCV (as in accidental needle pricking); chronic infection appears to be high in such patients, potentially warranting immediate treatment upon diagnosis.

More than 900 drugs have been implicated in causing liver injury and it is the most common reason for a drug to be withdrawn from the market.

Drug induced liver injury is responsible for 50% of all acute liver failures.

**Mechanisms of hepatic injury:**
1. Mitochondrial damage which releases excessive amount of oxidants which in turn injures hepatic cells.
2. Activation of some enzymes in the cytochrome P-450 system lead to oxidative stress.
3. Injury to hepatocyte and bile duct cells lead to accumulation of bile acid inside liver. This promotes further liver damage.

**Types of drug reaction:**
- **Type A hepatitis**
  - Hepatotoxicity: dose dependent as in the case of acetaminophen overdose.
  - Examples: Acetaminophen, Allopurinol, Amiodarone, NSAIDS

- **Type B:** idiosyncrasy occurs without warning and does not have a clear dose-response as in Troglitazone.

<table>
<thead>
<tr>
<th>Type of injury</th>
<th>ALT</th>
<th>ALP</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Hepatocellular</td>
<td>&gt; 2 fold rise</td>
<td>Normal</td>
<td>Acetaminophen, Allopurinol, Amiodarone, NSAIDS</td>
</tr>
<tr>
<td>Cholestatic</td>
<td>Normal</td>
<td>&gt; 2 folds rise</td>
<td>Anabolic steroid, Chlorpromazine, Erythromycin, Hormonal contraception</td>
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<tr>
<td>Mixed</td>
<td>&gt; 2 folds rise</td>
<td>&gt; 2 folds rises</td>
<td>Enalapril, Carbamazepine, Sulfonamide, Phenytin</td>
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