Hepadnaviridae
Hepatitis B

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Electron micrograph of serum containing hepatitis B virus after negative staining.
Hepatitis B

- Hepadnaviridae family
  - DNA virus
  - Double-shelled particles
    - Outer lipoprotein envelope (surface Ag)
    - Inner viral nucleocapsid (core)
  - seven genotypes
  - four major subtypes.
  - All HBV subtypes share one common antigenic determinant - "a."
  - Thus, antibodies to the "a" determinant confer protection to all HBV subtypes

Diagrammatic representation of the hepatitis B virion and the surface antigen components

EM of Hepatitis B virion
Viral Hepatitis – Clinical Classification

"Infectious"

Enterically transmitted

"NANB"

Parenterally transmitted

others – F, G

"Serum"

Viral hepatitis
Introduction

- Primary infection of liver
- Divided into six types: A, B, C, D, E, G
- Type F: transfusion associated hepatitis, a mutant (HBx) of HBV.
- All are RNA virus except HBV which is a DNA virus.
# Viral Hepatitis Overview

## Types of Viral Hepatitis

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<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
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</thead>
<tbody>
<tr>
<td><strong>Source of virus</strong></td>
<td>feces</td>
<td>blood/ blood-derived body fluids</td>
<td>blood/ blood-derived body fluids</td>
<td>blood/ blood-derived body fluids</td>
<td>feces</td>
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<td><strong>Route of transmission</strong></td>
<td>fecal-oral</td>
<td>percutaneous permucosal</td>
<td>percutaneous permucosal</td>
<td>percutaneous permucosal</td>
<td>fecal-oral</td>
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<tr>
<td><strong>Chronic infection</strong></td>
<td>no</td>
<td>yes</td>
<td>yes</td>
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<tr>
<td><strong>Prevention</strong></td>
<td>pre-exposure immunization</td>
<td>pre/post-exposure immunization</td>
<td>blood donor screening; risk behavior modification</td>
<td>pre/post-exposure immunization; risk behavior modification</td>
<td>ensure safe drinking water</td>
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</tbody>
</table>
A, B, Cs of Viral Hepatitis

• **A**
  – fecal-oral spread: hygiene, drug use, men having sex with men, travelers, day care, food
  – vaccine-preventable

• **B**
  – sexually transmitted – 100x more infectious than HIV
  – blood-borne (sex, injection drug use, mother-child, and health care)
  – vaccine-preventable

• **C**
  – blood borne (injection drug use primarily)
  – 4-5 times more common than HIV
  – NOT vaccine-preventable!
Acute Hepatitis – Clinical Symptoms

Asymptomatic > Symptomatic > Fulminant Liver Failure > Death

Symptoms (if present) are the same, regardless of cause (e.g., A, B, C, other viruses, toxins)

- Nausea, vomiting
- Abdominal pain
- Loss of appetite
- Fever
- Diarrhea
- Light (clay) colored stools
- Dark urine
- Jaundice (yellowing of eyes, skin)

Pre-icteric stage

Icteric stage
Structure of HBV

- Hepadnaviridae family
- 42 nm DNA virus with an outer envelope and inner core

Nucleocapsid / Core (HBcAg, HBeAg)
Circular DNA: partly double stranded
Envelope (HBsAg)
DNA polymerase
Structure of HBV

- Exists in 3 different forms in serum of infected individuals:
  1. Spherical particle – 22nm, most abundant
  2. Tubular or filamentous particle – 22nm
  3. Dane particle – 42nm, few in no, double walled spherical structure, true infectious form of HBV.
Hepatitis B Antigens

• Hepatitis B surface antigen (S): HBs Ag – the envelope protein – detectable in blood

• Hepatitis B core antigen (HBcAg) – not detectable in blood.

• Hepatitis B e antigen (HBeAg) - Detectable in blood during active viral multiplication, generally at the same time as HBsAg
Hepatitis B – Clinical Features

- **Incubation period:** long Average 60-90 days
  Range 45-180 days
- Fever is not prominent
- 90-95% with acute hepatitis recover within 1-2 months of onset.
- Mortality in about 0.5-2% of cases.
- 1-10% develop chronic infection.
Outcome of HBV Infection

Infection

Asymptomatic

Resolved Immune

Asymptomatic

Chronic infection

Cirrhosis Liver cancer

Resolved Immune

Chronic infection

Symptomatic acute hepatitis B

Cirrhosis Liver cancer
Epidemiology

- Natural infection occurs only in humans.
- Virus maintained in carriers.
- Largest carrier pool in China followed by India.
- Carrier – a person with detectable HBsAg in blood for more than 6 months.
- Carrier state is more common in males.
- Carriers - two types:
  1. Super carriers – high titre HBsAg, along with HBeAg, DNA polymerase and HBV in circulation, with elevated transaminases.
  2. Simple carriers – low infectivity & low titres of HBsAg.
Epidemiology

- Prevalence of hepatitis carriers - varies in different countries

1. **High endemicity**: carrier rate >8% as in SE Asia, China, parts of S. America

2. **Intermediate**: 2 to 7% as in ME Asia, India, S. Asia

3. **Low endemicity**: <2% as in Western Europe, N. America, Australia
HBV Modes of Transmission

- Sexual
- Parenteral
- Perinatal
### Concentration of HBV in Various Body Fluids

<table>
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<tr>
<th>High</th>
<th>Moderate</th>
<th>Low/Not Detectable</th>
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<tr>
<td>blood</td>
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<td>serum</td>
<td>vaginal fluid</td>
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<td>wound exudates</td>
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Risk Factors Associated with Transmission of HBV

- **IV drug abuse** — HBV transmission is four times more common than HIV
- **Transfusion or transplant from infected donor**
- **Occupational exposure to blood** - Mostly needle sticks
- **Iatrogenic** — dialysis, unsafe injection practices (reuse of needles/syringes, contaminated multiple dose medication vials), dental procedures, blood bank
Risk Factors Associated with Transmission of HBV

• **Transmission from Carrier mothers**
  - by contact of maternal blood with the skin & mucosa of the fetus during birth
  - Very high (60-90%) if the mother is HBeAg +ve and low (5-15%) if negative

• **High risk Sexual behaviour**
  Multiple sex partners, homosexuals & those diagnosed with STDs like HIV, gonorrhea etc
Laboratory Diagnosis

- **Serology** – specific diagnosis, demonstration of serological markers

- **HBV DNA levels** – indicator of viral replication & great infectivity
  - measured by PCR, DNA:DNA hybridization.

- **Histopathology** – ground glass appearance of infected hepatocytes due to HBsAg.
Acute Hepatitis B Virus Infection with Recovery

Typical Serologic Course

- **Symptoms**
- **HBeAg**
- **anti-HBe**
- **Liver enzymes**
- **Total anti-HBc**
- **IgM anti-HBc**
- **HBsAg**
- **anti-HBs**

### Week 0-100

- **Titer**
- **Weeks after Exposure**

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**Liver enzymes**

- **HBeAg**
- **anti-HBe**
- **Total anti-HBc**
- **IgM anti-HBc**
- **HBsAg**
- **anti-HBs**
Progression to Chronic Hep. B Virus Infection
Typical Serologic Course

- IgM anti-HBc
- Total anti-HBc
- HBsAg
- HBcAg
- HBeAg
- anti-HBe

Time (Weeks after Exposure)

Weeks after Exposure
<table>
<thead>
<tr>
<th>Virus/Antibody markers</th>
<th>Interpretation</th>
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<td><strong>HBsAg</strong></td>
<td><strong>HBeAg</strong></td>
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Reduce or Eliminate Risks for Acquiring HBV Infection

• Screening and testing donors of blood, organs, and tissues
• Virus inactivation of plasma-derived products
• Risk-reduction counselling and services
  – Obtain history of high-risk drug and sex behaviors
  – Provide information on minimizing risky behavior, including referral to other services
  – Vaccinate against hepatitis A and/or hepatitis B
• Infection control practices
• Blood and body fluid precautions
Passive Immunisation

• Hyperimmune hepatitis B immune globulin (HBIG) given soon after exposure to infection
• 300-500 IU I.M., single dose
• Prepared from human volunteers with high titres of anti-HBs
• Also given to protect patient from severe recurrent HBV infection following liver transplantation
• Protects against illness & carrier state, may not prevent infection.
New Vaccine

• Special vaccine containing all antigenic components (S, Pre S1 & Pre S2) of HBsAg.

• Gives greater seroconversion.
Post Exposure Prophylaxis (PEP)

• For non immune persons exposed to HBV:
  1. Percutaneous or mucosal exposure to HBsAg +ve blood
  2. Sexual exposure to HBsAg +ve person
  3. Perinatal exposure of an infant to HBsAg +ve mother.

• PEP includes HBIG + full course of Hep B vaccine.
Baby Shots for Hepatitis B
if the mother has Hepatitis B

Birth

Hepatitis B Vaccine + H-BIG

1 - 2 months old

Hepatitis B Vaccine

6 months old

Hepatitis B Vaccine
If you have never had hepatitis B, you can get 3 shots . . .

Hepatitis B can be prevented!

. . . and get long lasting protection.
Treatment

- Supportive care
- Therapy
  1. IFN alpha 2b – mimics cells natural defense mechanisms
  2. Adeovir Dipivoxil – inhibits HBV DNA polymerase, chronic hepatitis
  3. Lamivudine – inhibits reverse transcriptase