Hepatitis B Overview

- **Serious**: Causes death from liver disease in up to 25% of those infected at birth.
- **Cancer related**: Liver cancer especially prevalent in areas of the world where hepatitis B is common.
- **Disease of refugees**: New arrival Southeast Asian refugees (1 out of 2 is immune, 1 out of 7 is a carrier, 1 out of 3 is susceptible).
- **Preventable**: Safe, effective, and affordable vaccination is available.

Geographic Distribution of Chronic HBV Infection

**HBsAg Prevalence**
- ≥8% - High
- 2-7% - Intermediate
- <2% - Low

Hepatitis B Incidence in U.S., 2001

- **Estimated incidence**: 78,000 cases/year
- **Reported cases**
  - Acute hepatitis B: 7,844

Transmission of HBV (1)

- **Concentration of HBV in various body fluids**
  - **High**: Blood, serum, wound exudates
  - **Medium**: saliva, semen, and vaginal secretions
  - **Low/not detectable**: urine, feces, sweat, tears, breastmilk
- **Perinatal – transplacental transmission, rare (2-5%)**
- **Sexual transmission – unprotected sex**
### Transmission of HBV (2)

- Percutaneous transmission – sharing of injection drug use equipment, needle stick injury, ear-piercing, body piercing, tattooing, inadequate sterilization of medical equipment, scarification
- Household and interhousehold transmission – less risk but significant - can occur in settings such as shared toothbrushes, razors, combs, washcloths

### Transmission of HBV (3)

- Passed from child to child by biting, shared objects, oozing cuts, impetigo, etc.
- Virus can exist on environmental surfaces for up to one week and remain infectious.
- Pre-chewing food for babies, or sharing food that has been chewed by someone else (chewing gum).

### Transmission of HBV (4)

- Institutionalized settings – risks of biting, sexual abuse
- More than 1/4 of acute cases have no readily identifiable risk factor
- Not spread by sneezing or coughing, sharing eating utensils.

### Risk Groups for HBV Infection (1)

- Immigrants/refugees from areas of high HBV endemicity (Asia, Pacific Islands, Sub-Saharan Africa, Amazon Basin, E. Europe, Middle East)
- Children born in U.S. to immigrants from areas of high HBV endemicity
- Alaska Natives and Pacific Islanders
- Household contacts and sex partners of people with chronic HBV infection

### Risk Groups for HBV Infection (2)

- People who have or who have had sexually transmitted diseases
- Heterosexuals with >1 sex partner in 6 months
- Men who have sex with men
- Users of illicit injectable drugs
- Health care workers in contact with blood

### Risk Groups for HBV Infection (3)

- Adopted children from mod/high-risk countries
- Hemodialysis patients
- Recipients of certain blood products
- Clients/staff at institutions for the developmentally disabled
- Inmates of long-term correctional facilities
### Hepatitis B Nomenclature and/or Lab Tests (1)

- **HBV**: Hepatitis B virus.
- **HBsAg**: Hepatitis B surface antigen. Marker of infectivity when found in serum.
- **anti-HBs**: Antibody to HBsAg. Marker of immunity when found in serum.
- **HBeAg**: Hepatitis B core antigen. No commercial test available for this.
- **anti-HBc**: Antibody HBeAg. Marker of past or current infection.

### Hepatitis B Nomenclature and/or Lab Tests (2)

- **IgM anti-HBc**: IgM is an antibody subclass of anti-HBc. Indicates recent infection with HBV (<4-6 mos.).
- **IgG anti-HBc**: IgG is a subclass of anti-HBc. Indicates "older" infection with HBV.
- **HBeAg**: Hepatitis B "e" antigen. Can only be present if HBsAg is positive. Marker of high degree of infectivity.
- **Anti-HBe**: Antibody to "e" antigen. May be present in infected or immune person.

### Hepatitis B Nomenclature and/or Lab Tests (3)

- **HBIG**: Hepatitis B immune globulin. Passively delivered antibody that provides "instant" protection against HBV.
- **HCC/PHC**: Hepatocellular carcinoma, primary hepatocellular carcinoma.
- **HDV**: Hepatitis D virus (the delta virus). Etiologic agent of delta hepatitis. Can cause infection only in the presence of HBV infection.

### Hepatitis B: Clinical Features

- Incubation period ranges from 45-180 days, average is 60-90 days
- Onset is insidious
- Clinical illness (jaundice): <10% for <5 yr olds 30%-50% for >5 yrs
- Acute case-fatality rate: 0.5%-1%
- Chronic infection: <5 yrs old, 30%-90% >5 yrs old, 2%-6%
- Premature mortality from chronic liver disease: 15%-25%

### Signs and Symptoms

- **Symptom**
  - there may be none
  - loss of appetite, malaise, nausea, vomiting, abdominal pain, arthralgias, myalgias
- **Signs**
  - there may be none
  - jaundice, fever, dark urine

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Acute Viral Hepatitis  
*Source: CDC*

<table>
<thead>
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<th>Year</th>
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<th>25-39</th>
<th>40+</th>
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<tr>
<td>1997</td>
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<td>1</td>
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Source: NNDSS

Interpretation of Hepatitis B Panel

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>antiHBc</th>
<th>antiHBe</th>
<th>IgM antiHBc</th>
<th>antiHBs</th>
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<td>negative</td>
<td>negative</td>
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<td>immune due to natural infection</td>
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</tr>
<tr>
<td>immune due to vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>acutely infected</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chronically infected</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>infected</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>four possible interpretations (see next slide)</td>
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</table>

Natural History

- Likelihood of becoming a carrier varies inversely with the age at which infection occurs.
- Pool of carriers in U.S. is 1-1.25 million persons.
- ~5000 persons die/yr. from HBV-related cirrhosis.

Risk of Becoming Chronically Infected with HBV

- 2% - 6% of older children and adults
- 20% - 50% of children <5 yrs
- 85% - 90% of infants infected at birth

Treatment for HBV

- Three FDA-licensed treatment options available for adults in the United States
  - interferon alfa-2b (IntronA), recombinant administered subcutaneously qd or 3x/wk
  - lamivudine (Epivir-HB) administered by mouth qd
  - adefovir dipivoxil (Hepsera) administered by mouth qd

Consult a liver specialist to assist in determining whether your patient is a treatment candidate.

Monitoring HBsAg+ Patients

- Discuss monitoring with a liver specialist having much experience in managing viral liver diseases.
  - Annual physical exam.
  - Blood work every 6-12 mos.
  - Liver biopsy?
  - Liver ultrasound or CT scan every 6-12 mos.
  - "fetoprotein (AFP) every 6-12 mos.
- Education of patient about disease.
Management of Family Members of HBsAg+ Patients

- Test all family members with hepatitis B panel (HBsAg, antiHbc, antiHBs)
- For those susceptible, vaccinate
- For susceptible sex partner(s), test after 3 doses to be sure s/he converts to antiHBs+
- Education of family members

Hepatocellular Carcinoma – HCC (1)

- HBV leads to liver cancer
  - epidemiologic correlation in many populations
  - risk for HCC is 12-300 times greater in HBsAg+ persons
  - HBV DNA is incorporated into DNA of hepatoma cells
- Incidence
  - peak incidence is in 40-60 yr olds
  - in Taiwan, #1 cause of death for men >40 yrs
  - 0.25-1 million deaths/year in the world
  - over 1500 persons die/yr in the U.S. from HCC
  - HCC is 3-4x more common in HBsAg+ men than women

Hepatitis B Prevention (1)

- Hepatitis B Immune Globulin (HBIG)
  - provides temporary passive protection
  - indicated in certain postexposure settings
- Hepatitis B Vaccine
  - vaccinate all children 0-18 years of age
    - infant schedule: birth dose preferred (0, 1-2, 6), (0, 1-4, 6-18)
      - Schedule if using monovalent vaccine followed by Comvax ® (0, 2, 4, 12)
    - children/teens: (0, 1, 6), (0, 1-2, 4) (0, 1, 6-12) or (0, 12, 24) month schedule. There is also a two-dose schedule for 11-15 year olds using Recombivax HB ® only. This schedule is 0, 4-6 months.

Hepatitis B Prevention (2)

- Hepatitis B Vaccine (continued)
  - Vaccinate all high-risk individuals
    - Adult schedule (0, 1-2, 6)
    - Testing can be done if concern that patient has been previously infected, but do not delay administering first dose of vaccine until a later visit; test, then give first dose.
- Hepatitis B Prenatal Testing
  - Test EVERY pregnant woman during every pregnancy for HBsAg, even if she has been immunized against hepatitis B or is chronically infected.
  - Send a copy of the original lab report to the hospital.

Hepatitis B Prevention (3)

- Hepatitis B Prenatal Testing
  - Test EVERY pregnant woman during every pregnancy for HBsAg, even if she has been immunized against hepatitis B or is chronically infected.
  - Send a copy of the original lab report to the hospital.

Childhood or Adult Schedule

#### Recommended dosages of hepatitis B vaccines *

<table>
<thead>
<tr>
<th>Vaccine brand</th>
<th>Age group</th>
<th>Dose</th>
<th>Volume</th>
<th># Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engerix-B</td>
<td>0-11 years, 5 years and older</td>
<td>10µg</td>
<td>0.5 ml</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>0-11 years, 6 years and older</td>
<td>10µg</td>
<td>1.0 ml</td>
<td>3</td>
</tr>
<tr>
<td>Recombivax HB (Merck &amp; Co.)</td>
<td>0-11 years</td>
<td>10µg</td>
<td>1.0 ml</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0-11 years, 6 years and older</td>
<td>10µg</td>
<td>1.0 ml</td>
<td>2</td>
</tr>
</tbody>
</table>

* The schedule for hepatitis B vaccination is flexible and varies. Consult the AAFP statement on Hepatitis B (11/91), AAP’s 2000 Red Book, or the package insert for details.

Note: For adult dialysis patients: the Engerix-B dose required is 40µg (2.0ml) (use the adult 20µg/ml formulations on a schedule of 0, 1, 2, and 6 months). For Recombivax HB, a special formulation for dialysis patients is available. The dose is 40µg/2 ml and it is given on a schedule of 0, 1, and 6 months.
Prevention Schedule for Infants of HBsAg-POSITIVE Mothers

- HBIG 0.5 ml IM within 12 hrs. of birth.
- Dose #1 of Hep B vaccine in the opposite thigh within 12 hrs. of birth.
- Dose #2 of Hep B vaccine at 1-2 mos.
- Dose #3 of Hepatitis B vaccine at 6 mos.
- Testing for antiHBs and HBsAg 9-15 mos.
  - If negative for both, repeat the series and test 1–2 months later!

Schedule for infants of mothers with UNKNOWN HBsAg status

- Test mother for HBsAg in hospital ASAP.
- If mother's test is positive, give HBIG ASAP (within 7 days of birth).
- Give dose #1 of Hep B vaccine within 12 hrs. of birth. DO NOT DELAY THIS DOSE waiting for the lab result.
- Dose #2 of Hep B vaccine at 1-2 mos.
- Dose #3, follow dosing schedule based on mother's HBsAg status.

Schedule for infants with HBsAg-NEGATIVE mothers

- Dose #1 recommended to be given at birth.
- Dose #2 can be given at 1-4 mos. of age
- Dose #3 at 6-18 mos. of age
  - Final dose should NOT be given before age 6 mos.
  - May also give monovalent hepatitis B #1 at birth followed by 3 does of Comvax® at 2, 4, and 12-15 mos., or 3 doses of Pediarix® at 2, 4, and 6 mos.

Dosing schedule for older children and teens (NOT INFANTS)

- **Rule #1**: There must be at least 4 wks. between dose #1 and dose #2.
- **Rule #2**: There must be at least 8 wks. between dose #2 and dose #3.
- **Rule #3**: There must be at least 4 mos. between dose #1 and dose #3.
- **Rule #4**: No matter how delayed dose #2 or #3 is, do not start the series over again.
- **Suggested spacing options**: 0, 1-2, 4-6 mos.; 0, 2, 12 mos.; 0, 12, 24 mos.

Dosing Schedule for Adults

- 0, 1, 6 month interval is standard for HCWs
  - Space dose #1 and #2 four wks. apart
  - Space dose #2 and #3 five mos. apart
- Alternative schedules 0, 2, 4; 0, 1, 4
- Never re-start the series if dosing was delayed. Continue from where you left off.
- Use a 1" or 1.5" needle. If obese, use 2".
- Injection must be intramuscular in deltoid.

Recommended post-exposure prophylaxis for exposure to HBV

<table>
<thead>
<tr>
<th>Source exposed to infection of unknown status</th>
<th>Treatment if post-exposure prophylaxis given</th>
<th>Treatment if post-exposure prophylaxis not given</th>
<th>Treatment if post-exposure prophylaxis not given but HBsAg positive available for testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Previously vaccinated</td>
<td>None</td>
<td>None</td>
<td>According to individual risk assessment</td>
</tr>
<tr>
<td>Known non-responder*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Known responder</td>
<td>Initiates vaccine series</td>
<td>Initiates vaccine series</td>
<td>None</td>
</tr>
<tr>
<td>Previously vaccinated and unvaccinated</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Known responders and unvaccinated</td>
<td>Initiates vaccine series</td>
<td>Initiates vaccine series</td>
<td>None</td>
</tr>
</tbody>
</table>

* A non-responder is a person with inadequate levels of serum antibody to HBsAg (e.g., anti-HBs <10 mIU/mL).

Source: MMWR, June 29 2001, vol 50, RR-11, p22
Elimination of Hepatitis B Virus Transmission: United States

Objectives
• Prevent chronic HBV Infection
• Prevent chronic liver disease
• Prevent primary hepatocellular carcinoma
• Prevent acute symptomatic HBV infection

Strategy
• Prevent perinatal HBV transmission
• Routine vaccination of all infants
• Vaccination of children in high-risk groups
• Vaccination of adolescents
  • all unvaccinated children at 11-12 years of age
  • “high-risk” adolescents at all ages
• Vaccination of adults in high-risk groups

AAP, AAFP, and ACIP Recommend Hepatitis B “Catch-up”
• Give hepatitis B vaccine to all children 0-18 y.o.
• “Providers should make special efforts” to catch-up children (of parents) from moderate/high risk endemic areas.

Remember…
You should never start the hepatitis B vaccine series over again, no matter how long each dose is delayed!

References
Deborah L. Wexler, MD
Executive Director
Immunization Action Coalition
www.immunize.org

References
CDC. Recommended childhood immunization schedule- U.S., Jan-Dec 1998 MMWR 1998; 47:10-1
CDC. Recommended childhood immunization schedule- U.S., Jan-Dec 1998 MMWR 1999; 48:14-5
CDC. Recommended childhood immunization schedule- U.S., Jan-Dec 1998 MMWR 2000; 49:36-7