Hepatitis B and Hepatitis B Vaccine

Epidemiology and Prevention of Vaccine-Preventable Diseases

National Immunization Program
Centers for Disease Control and Prevention
Revised January 2006

Hepatitis B

• Epidemic jaundice described by Hippocrates in 5th century BCE
• Jaundice reported among recipients of human serum and yellow fever vaccines in 1930s and 1940s
• Australia antigen described in 1965
• Serologic tests developed in 1970s

Hepatitis B Virus

• Hepadnaviridae family (DNA)
• Numerous antigenic components
• Humans are only known host
• May retain infectivity for at least 1 month at room temperature

Hepatitis B Virus Infection

• >300 million chronically infected worldwide
• Established cause of chronic hepatitis and cirrhosis
• Human carcinogen—cause of up to 80% of hepatocellular carcinomas

Note to presenters:
Images of vaccine-preventable diseases are available from the Immunization Action Coalition website at http://www.vaccineinformation.org/photos/index.asp
**Hepatitis B Clinical Features**
- Incubation period 60-150 days (average 90 days)
- Nonspecific prodrome of malaise, fever, headache, myalgia
- Illness not specific for hepatitis B
- At least 50% of infections asymptomatic

**Hepatitis B Complications**
- Fulminant hepatitis
- Hospitalization
- Cirrhosis
- Hepatocellular carcinoma
- Death

**Chronic Hepatitis B Virus Infection**
- Chronic viremia
- Responsible for most mortality
- Overall risk 10%
- Higher risk with early infection

**Risk of Chronic HBV Carriage by Age of Infection**

**Hepatitis B Epidemiology**
- **Reservoir** Human
- **Transmission** Bloodborne
  Subclinical cases transmit
- **Communicability** 1-2 months before and after onset of symptoms
  Chronic carriers

**Hepatitis B Perinatal Transmission***
- If mother positive for HBsAg and HBeAg
  - 70%-90% of infants infected
  - 90% of infected infants become chronically infected
- If positive for HBsAg only
  - 5%-20% of infants infected
  - 90% of infected infants become chronically infected

*in the absence of postexposure prophylaxis
Global Patterns of Chronic HBV Infection

• High (>8%): 45% of global population
  – lifetime risk of infection >60%
  – early childhood infections common

• Intermediate (2%-7%): 43% of global population
  – lifetime risk of infection 20%-60%
  – infections occur in all age groups

• Low (<2%): 12% of global population
  – lifetime risk of infection <20%
  – most infections occur in adult risk groups

HBV Disease Burden in the United States*

New infections  78,000/yr
Current carriers   >1 million
New carriers    >5,000/yr
Death           5,000/yr

*2001 estimates

Risk Factors for Hepatitis B

CDC Sentinel Sites. 2001 data.

Hepatitis B Virus Infection by Duration of High-Risk Behavior

Hepatitis B—United States, 1978-2005*

Age of Infection of Acute and Chronic Hepatitis B Virus Infection

CDC Sentinel Sites. 1989 data.
**Strategy to Eliminate Hepatitis B Virus Transmission—United States**

- Prevent perinatal HBV transmission
- Routine vaccination of all infants
- Vaccination of children in high-risk groups
- Vaccination of adolescents
- Vaccination of adults in high-risk groups

**Hepatitis B Vaccine**

1965 Discovery of Australian antigen
1973 Successful HBV infection of chimpanzees
1981 Licensure of plasma-derived vaccine
1986 Licensure of recombinant vaccine
1991 Universal infant vaccination
1996 Universal adolescent vaccination

**Hepatitis B Vaccine**

- Composition: Recombinant HBsAg
- Efficacy: 95% (Range, 80%-100%)
- Duration of Immunity: >15 years
- Schedule: 3 Doses
- Booster doses not routinely recommended

**Hepatitis B Vaccine Formulations**

- Recombivax HB (Merck)
  - 5 mcg/0.5 mL (pediatric)
  - 10 mcg/1 mL (adult)
  - 40 mcg/1 mL (dialysis)
- Engerix-B (GSK)
  - 10 mcg/0.5 mL (pediatric)
  - 20 mcg/1 mL (adult)

**Protection* by Age Group and Dose**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Infants**</th>
<th>Teens and Adults***</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16%-40%</td>
<td>20%-30%</td>
</tr>
<tr>
<td>2</td>
<td>80%-95%</td>
<td>75%-80%</td>
</tr>
<tr>
<td>3</td>
<td>98%-100%</td>
<td>90%-95%</td>
</tr>
</tbody>
</table>

* Anti-HBs antibody titer of 10 mIU/mL or higher
** Preterm infants less than 2 kg have been shown to respond to vaccination less often
*** Factors that may lower vaccine response rates are age >40 years, male gender, smoking, obesity, and immune deficiency

**Recommended Dose of Hepatitis B Vaccine**

<table>
<thead>
<tr>
<th>Infants and children &lt;11 years of age</th>
<th>Recombivax HB Dose (mcg)</th>
<th>Engerix-B Dose (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mL (5)</td>
<td>0.5 mL (10)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adolescents 11-19 years</th>
<th>0.5 mL (5)</th>
<th>0.5 mL (10)</th>
</tr>
</thead>
</table>

| Adults >20 years                      | 1.0 mL (10)              | 1.0 mL (20)          |
Hepatitis B Vaccine
Long-term Efficacy

- Immunologic memory established following vaccination
- Exposure to HBV results in anamnestic anti-HBs response
- Chronic infection rarely documented among vaccine responders

Hepatitis B Vaccine
Routine booster doses are NOT routinely recommended for any group

Hepatitis B Vaccine
Routine Infant Schedule

<table>
<thead>
<tr>
<th>Dose+</th>
<th>Usual Age</th>
<th>Minimum Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary 1</td>
<td>Birth</td>
<td>- - -</td>
</tr>
<tr>
<td>Primary 2</td>
<td>1-2 months</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Primary 3</td>
<td>6-18 months*</td>
<td>8 weeks**</td>
</tr>
</tbody>
</table>

* infants who mothers are HBsAg+ or whose HBsAg status is unknown should receive the third dose at 6 months of age
** at least 16 weeks after the first dose
+ an additional dose at 4 months is acceptable if the clinician prefers to use a combination vaccine that contains hepatitis B vaccine

Third Dose of Hepatitis B Vaccine

- Minimum of 8 weeks after second dose, and
- At least 16 weeks after first dose, and
- For infants, at least 24 weeks of age

Preterm Infants

- Birth dose and HBIG if mother HBsAg positive
- Preterm infants <2,000 grams have a decreased response to vaccine administered before 1 month of age
- Delay first dose until chronologic age 1 month if mother HBsAg negative

COMVAX

- Hepatitis B-Hib combination
- Use when either antigen is indicated
- Cannot use <6 weeks of age
- May be used in infants whose mothers are HBsAg positive or status is unknown
Pediarix

- DTaP – Hep B – IPV combination
- Approved for 3 doses at 2, 4 and 6 months
- Not approved for booster doses
- Licensed for children 6 weeks to 7 years of age

Pediarix

- May be used interchangeably with other pertussis-containing vaccines if necessary
- Can be given at 2, 4, and 6 months to infants who received a birth dose of hepatitis B vaccine (total of 4 doses)
- May be used in infants whose mothers are HBsAg positive or status unknown

Hepatitis B Vaccine

Adolescent Vaccination

- Routine vaccination recommended through age 18 years
- Integrate into routine adolescent immunization visit
- Flexible schedules

Hepatitis B Vaccine

Adolescent and Adult Schedule

<table>
<thead>
<tr>
<th>Dose</th>
<th>Usual Interval</th>
<th>Minimum Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary 1</td>
<td>---</td>
<td>- - -</td>
</tr>
<tr>
<td>Primary 2</td>
<td>1 month</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Primary 3</td>
<td>5 months</td>
<td>8 weeks*</td>
</tr>
</tbody>
</table>

*third dose must be separated from first dose by at least 16 weeks

Alternative Adolescent Vaccination Schedule

- Two 10 mcg doses of Recombivax HB separated by 4-6 months
- Approved only for adolescents 11-15 years of age
- Only applies to Merck hepatitis B vaccine

Adult Hepatitis B Vaccine Candidates

- Men who have sex with men
- Heterosexual with multiple partners
- Persons diagnosed with an STD
- Prostitutes
- Injection drug users
- Inmates of long-term correctional facilities
- Persons receiving hemodialysis
- Healthcare workers
**Other Hepatitis B Vaccine Candidates**

- Staff of institutions for developmentally disabled
- Alaska Natives, Pacific Islanders
- Immigrants/refugees*
- Adoptees, orphans, unaccompanied minors*
- Household members and sex partners of HBV carriers
- Extended travel to areas of high endemicity
- Recipients of certain blood products

*from countries of high or intermediate HBV endemnicity

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**Twinrix**

- Combination hepatitis A vaccine (pediatric dose) and hepatitis B (adult dose)
- Schedule: 0, 1, 6 months
- Approved for persons ≥18 years

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**Prevaccination Serologic Testing**

- Not indicated before routine vaccination of infants or children
- May be considered when vaccinating adolescents in groups with high rates of HBV infection
  - Alaska Natives
  - Pacific Islanders
  - Children of immigrants from endemic countries
  - Family members of HBV carriers

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**Postvaccination Serologic Testing**

- Not routinely recommended following vaccination of infants, children, adolescents, or most adults
- Recommended for:
  - Hemodialysis patients
  - Infants born to HBsAg+ women
  - Sex partners of HBsAg+ person
  - Immunodeficient persons
  - Certain healthcare workers

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**Postvaccination Serologic Testing**

Healthcare workers who have contact with patients or blood should be tested for antibody after vaccination

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**Management of Nonresponse to Hepatitis B Vaccine**

- Complete a second series of three doses
- Should be given on the usual schedule of 0, 1 and 6 months
- Retest 1-2 months after completing the second series
**Persistent Nonresponse to Hepatitis B Vaccine**

- <5% of vaccinees do not develop anti-HBsAg after 6 valid doses
- May be nonresponder or "hyporesponder"
- Check HBsAg status
- If exposed, treat as nonresponder with postexposure prophylaxis

**Prevention of Perinatal Hepatitis B Virus Infection**

- Begin treatment within 12 hours of birth
- Hepatitis B vaccine (first dose) and HBIG at different sites
- Complete vaccination series at 6 months of age
- Test for response at 9-18 months of age

### Hepatitis B Vaccine Adverse Reactions

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Infants and Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain at injection site</td>
<td>13%-29%</td>
<td>3%-9%</td>
</tr>
<tr>
<td>Mild systemic complaints (fatigue, headache)</td>
<td>11%-17%</td>
<td>0%-20%</td>
</tr>
<tr>
<td>Temperature ≤99.9°F (37.7°C)</td>
<td>1%</td>
<td>0.4%-6%</td>
</tr>
<tr>
<td>Severe systemic reactions</td>
<td>rare</td>
<td>rare</td>
</tr>
</tbody>
</table>

### Hepatitis B Vaccine Contraindications and Precautions

- Severe allergic reaction to a vaccine component or following a prior dose
- Moderate or severe acute illness

**National Immunization Program Contact Information**

- Telephone: 800.CDC.INFO
- Email: nipinfo@cdc.gov
- Website: www.cdc.gov/nip