Vaccines Against Varicella and Hepatitis B
Ch 13, 14 and 15

Varicella Zoster Virus

• Herpesvirus (DNA)
• Primary infection results in varicella (chickenpox)
• Recurrent infection results in herpes zoster (shingles)
• Short survival in environment
Varicella Pathogenesis

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- Repeated episodes of viremia
- Multiple tissues, including sensory ganglia, infected during viremia

Varicella Clinical Features

- Incubation period 14-16 days (range 10-21 days)
- Mild prodrome for 1-2 days
- Rash generally appears first on head; most concentrated on trunk
- Successive crops over several days with lesions present in several stages of development
Herpes Zoster (Shingles)

- Reactivation of varicella zoster virus
- Can occur years or even decades after illness with chickenpox
- Generally associated with normal aging and with anything that causes reduced immunocompetence
- Lifetime risk of 20 percent in the United States
- Estimated 500,000-1 million cases of zoster diagnosed annually in the U.S
Varicella Complications

- Bacterial infection of skin lesions
- Pneumonia (viral or bacterial)
- Central nervous system manifestations
- Reye syndrome
- Hospitalization: 2-3 per 1,000 cases
- Death: 1 per 60,000 cases
- Postherpetic neuralgia (complication of zoster)

Groups at Increased Risk of Complications of Varicella

- Persons older than 15 years
- Infants younger than 1 year
- Immunocompromised persons
- Newborns of women with rash onset within 5 days before to 48 hours after delivery
Varicella Fatality Rate—United States, 1990-1994

*Deaths per 100,000 cases. Meyer et al, J Infect Dis 2000;182:383-90
Varicella Epidemiology

- Reservoir: Human
- Transmission: Airborne droplet
  Direct contact with lesions
- Temporal pattern: Peak in winter and early spring (U.S.)
- Communicability: 1-2 days before to 4-5 days after onset of rash
  May be longer in immunocompromised

Varicella Age-Specific Incidence
United States, 1990-1994

*Rate per 100,000 population. National Health Interview Survey data
Varicella in the United States

- Increasing proportion of cases are a result of breakthrough infection
- Outbreaks reported in schools with high varicella vaccination coverage
- Persons with breakthrough infection may transmit virus

Herpes Zoster

- 500,000 to 1 million episodes occur annually in the United States
- Lifetime risk of zoster estimated to be at least 20%
- 50% of persons living until age 85 years will develop zoster
Varicella-Containing Vaccines

- Varicella vaccine (either alone or w/ MMR)
  - approved for persons 12 months and older (only through 12 years for MMRV)
- Herpes zoster vaccine approved for persons 60 years and older

(these contain the same vaccine, just different concentrations)

Varicella Vaccine
Immunogenicity and Efficacy

- Detectable antibody
  - 97% of children 12 months-12 years following 1 dose
  - 99% of persons 13 years and older after 2 doses
- 70%-90% effective against any varicella disease
- 95%-100% effective against severe varicella disease
Varicella Breakthrough Infection

- Immunity appears to be long-lasting for most recipients
- Breakthrough disease much milder than in unvaccinated persons
- Recent evidence that risk of breakthrough infection increases with time since vaccination*


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Varicella Breakthrough Infection

- Retrospective cohort study of 115,000 children vaccinated in 2 HMOs during January 1995 through December 1999
- Risk of breakthrough varicella 2.5 times higher if varicella vaccine administered less than 30 days following MMR
- No increased risk if varicella vaccine given simultaneously or more than 30 days after MMR

*MMWR 2001;50(47):1058-61*
Varicella attenuation process

- Initial viral isolation from a child with varicella
- Adapted to human embryonic lung cell cultures
- Adapted to and propagated in embryonic guinea pig cell cultures
- Propagated in human diploid cell cultures (WI-38)
- Further passage in human diploid cell cultures (MRC-5) that are free of adventitious agents

Herpes Zoster Vaccine Efficacy

- Compared to the placebo group the vaccine group had:
  - 51% fewer episodes of zoster
  - Lower efficacy for older recipients
  - Less severe disease
  - 66% less postherpetic neuralgia
- Duration of immunity unknown

*NEJM* 2005;352(22):2271-84.
Varicella Vaccine Recommendations
Children

- Routine vaccination at 12-15 months of age
- Routine second dose at 4-6 years of age
- Minimum interval between doses of varicella vaccine for children younger than 13 years of age is 3 months (otherwise 4 weeks)

Herpes Zoster Vaccine*

- Approved for a single dose among persons 60 years and older
- May vaccinate regardless of prior history of herpes zoster (shingles)
- Persons with a chronic medical condition may be vaccinated unless a contraindication or precaution exists for the condition

*provisional recommendations as of January 2007
Varicella Immunity*

- Written documentation of age-appropriate vaccination
- Laboratory evidence of immunity or laboratory confirmation of disease
- Born in the United States before 1980
- Healthcare provider diagnosis or verification of varicella disease
- History of herpes zoster based on healthcare provider diagnosis

*provisional recommendations as of January 2007

Varicella Vaccine Adverse Reactions

- Local reactions (pain, erythema)
  - 19% (children)
  - 24% (adolescents and adults)
- Rash – 3%-4%
  - may be maculopapular rather than vesicular
  - average 5 lesions
- Systemic reactions not common
Herpes Zoster Vaccine
Adverse Reactions

- Local reactions - 34% (pain, erythema)
- No serious adverse reactions identified

Varicella-Containing Vaccines
Contraindications and Precautions

- Severe allergic reaction to vaccine component or following a prior dose
- Immunosuppression
- Pregnancy
- Moderate or severe acute illness
- Recent blood product
Varicella-Containing Vaccines
Use in Immunocompromised Persons

- Most immunocompromised persons should receive varicella-containing vaccines
- Varicella vaccine may be administered to persons with isolated humoral immunodeficiency
- Consider varicella vaccination for HIV-infected children with CD4% of 15% or higher

Varicella-Containing Vaccine
Storage and Handling

- Store frozen at 5°F (-15°C) or lower at all times
- Store diluent at room temperature or refrigerate
- Discard if not used within 30 minutes of reconstitution
Hepatitis B

• Epidemic jaundice described by Hippocrates in 5th century BC
• 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 more than 7 days at room temperature
Hepatitis B Virus Infection

- More than 350 million chronically infected worldwide
- Established cause of chronic hepatitis and cirrhosis
- Human carcinogen—cause of up to 80% of hepatocellular carcinomas

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 5%
- 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

HBV Disease Burden in the United States*

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>New infections</td>
<td>78,000/yr</td>
</tr>
<tr>
<td>Current carriers</td>
<td>&gt;1 million</td>
</tr>
<tr>
<td>New carriers</td>
<td>&gt;5,000/yr</td>
</tr>
<tr>
<td>Death</td>
<td>5,000/yr</td>
</tr>
</tbody>
</table>

*2001 estimates
Risk Factors for Hepatitis B

Gay men

IV drug users

Heterosexual, multiple partners

Unknown

Other

16%

5%

16%

IV drug users

Gay men

MSM

24%

Hepatitis B Virus Infection by Duration of High-Risk Behavior

Percent infected

0 20 40 60 80 100

Years at Risk

0 3 6 9 12 15

IV drug user

HCWs

Homosexual men

Heterosexual

MMWR 2006;55(RR-16):6-7
Strategy to Eliminate Hepatitis B Virus Transmission—United States

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

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

- Composition: Recombinant HBsAg
- Efficacy: 95% (Range, 80%-100%)
- Duration of Immunity: >20 years
- Schedule: 3 Doses
- Booster doses not routinely recommended

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
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

Postvaccination Serologic Testing

- Not routinely recommended following vaccination of infants, children, adolescents, or most adults
- Recommended for:
  - chronic hemodialysis patients
  - other immunocompromised persons
  - persons with HIV infection
  - sex partners of HBsAg+ person
  - infants born to HBsAg+ women
  - certain healthcare workers
Postvaccination Serologic Testing

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

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></td>
<td></td>
</tr>
<tr>
<td>Severe systemic reactions</td>
<td>1%</td>
<td>0.4%-6%</td>
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<tr>
<td></td>
<td>rare</td>
<td>rare</td>
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