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# Vaccines Against Varicella and Hepatitis B

Ch 13, 14 and 15

## Varicella Zoster Virus

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

## Varicella Pathogenesis

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- 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

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- 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

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- 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)

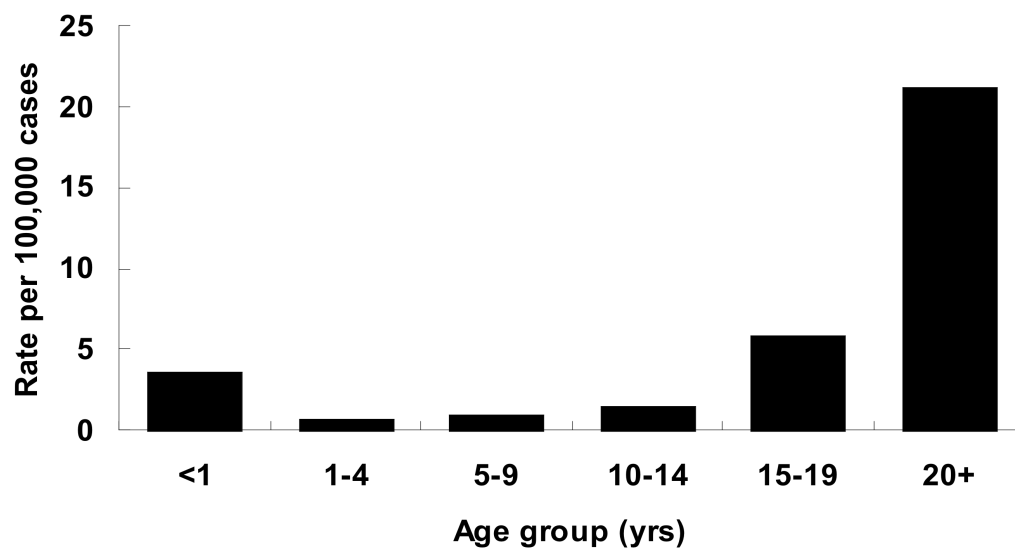
## Groups at Increased Risk of Complications of Varicella

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- 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

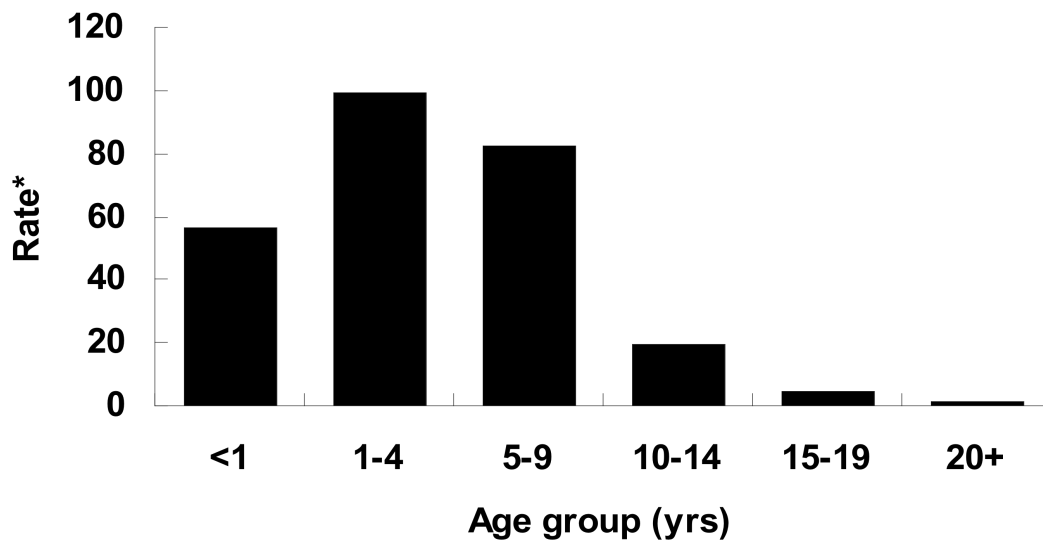
# Varicella Epidemiology

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- 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

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\*Rate per 100,000 population. National Health Interview Survey data

## Varicella in the United States

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- 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

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- 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\*

\*Chavez et al. *New Eng J Med* 2007;356:1121-9

## 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

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- 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\*

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- 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\*

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- 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

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- 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

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

## Varicella-Containing Vaccines Contraindications and Precautions

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- 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

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- 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

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- 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

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- 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

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- 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**

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- 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**

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- 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

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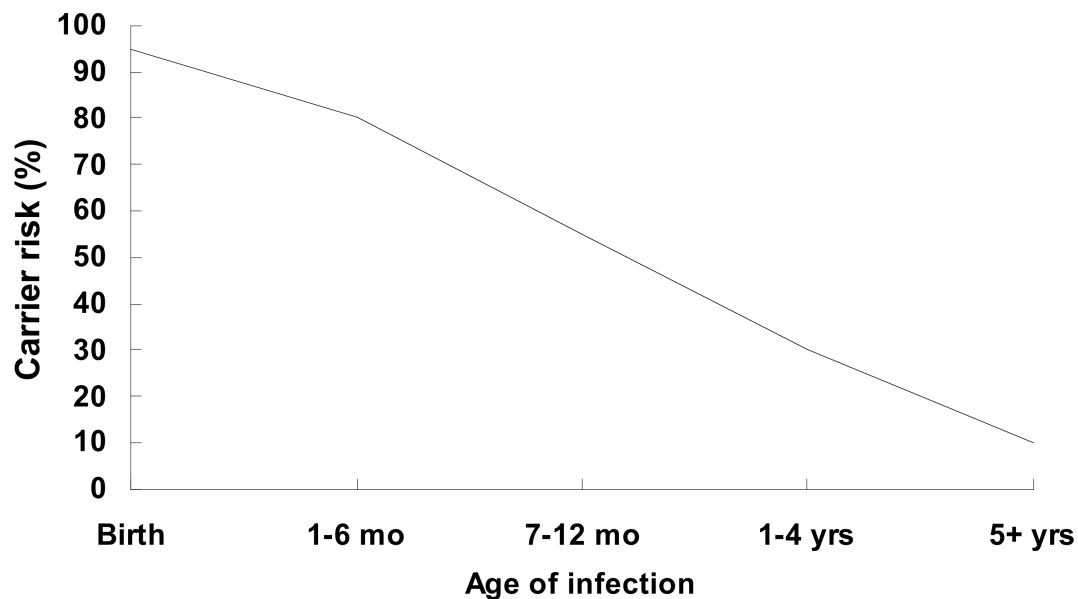
- Fulminant hepatitis
- Hospitalization
- Cirrhosis
- Hepatocellular carcinoma
- Death

## Chronic Hepatitis B Virus Infection

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- 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\*

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- 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**

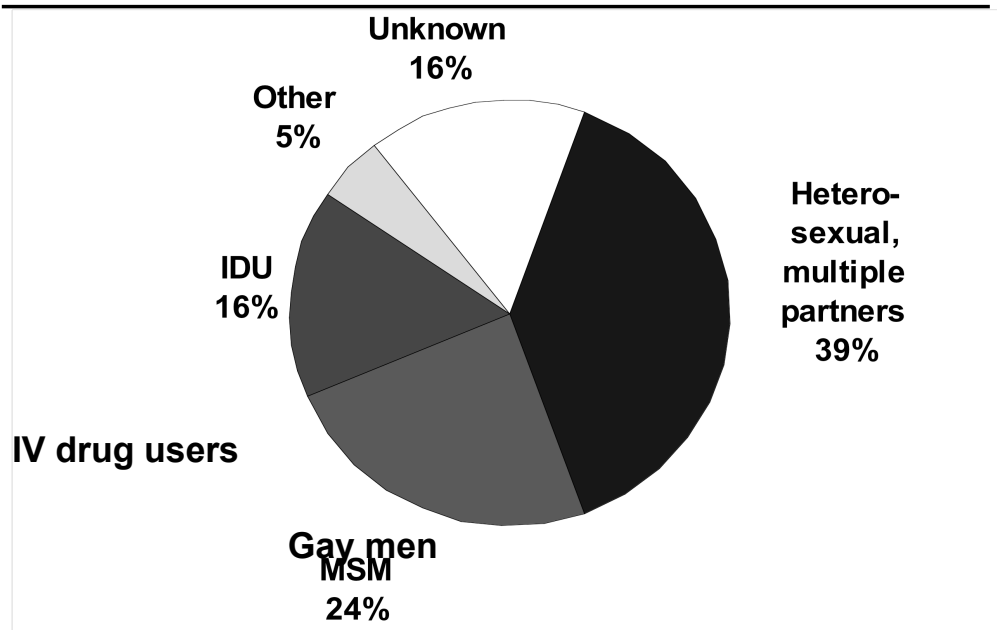
## HBV Disease Burden in the United States\*

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

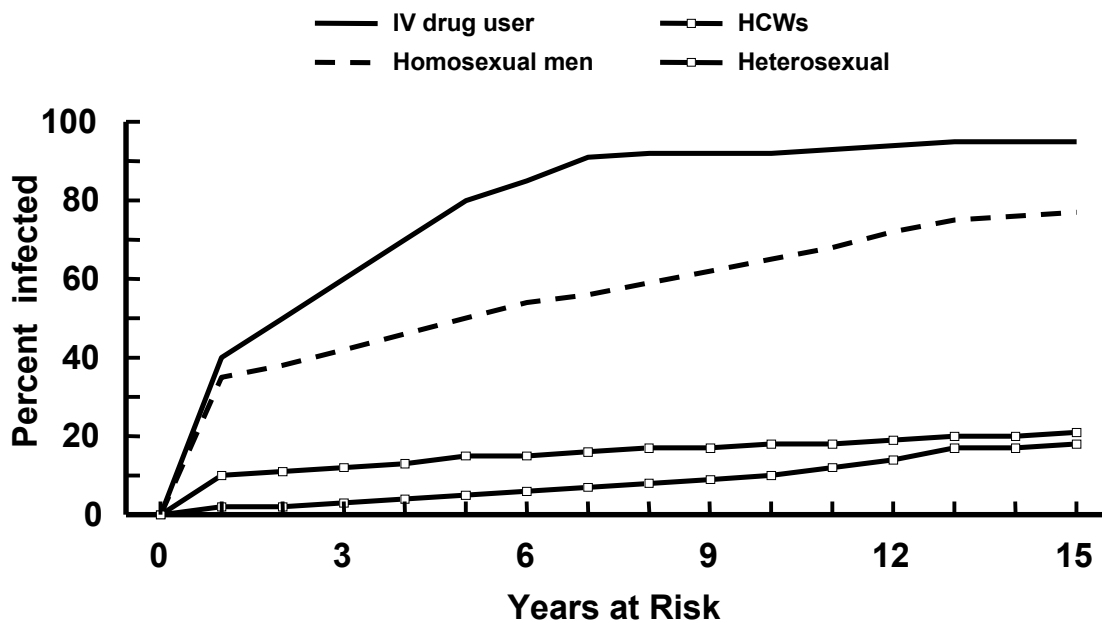
**\*2001 estimates**

# Risk Factors for Hepatitis B



MMWR 2006;55(RR-16):6-7

# Hepatitis B Virus Infection by Duration of High-Risk Behavior



## 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

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- 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

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<u>Dose+</u>	<u>Usual Age</u>	<u>Minimum Interval</u>
Primary 1	Birth	- - -
Primary 2	1- 2 months	4 weeks
Primary 3	6-18 months*	8 weeks**

\* 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

Dose	Infants**	Teens and Adults***
1	16%-40%	20%-30%
2	80%-95%	75%-80%
3	98%-100%	90%-95%

\* **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

	<u>Adults</u>	<u>Infants and Children</u>
Pain at injection site	<b>13%-29%</b>	<b>3%-9%</b>
Mild systemic complaints (fatigue, headache)	<b>11%-17%</b>	<b>0%-20%</b>
Temperature $\leq 99.9^{\circ}\text{F}$ ( $37.7^{\circ}\text{C}$ )		
Severe systemic reactions	<b>1%</b>	<b>0.4%-6%</b>
	<b>rare</b>	<b>rare</b>