Hepatitis B and Refugees: A Clinical Perspective

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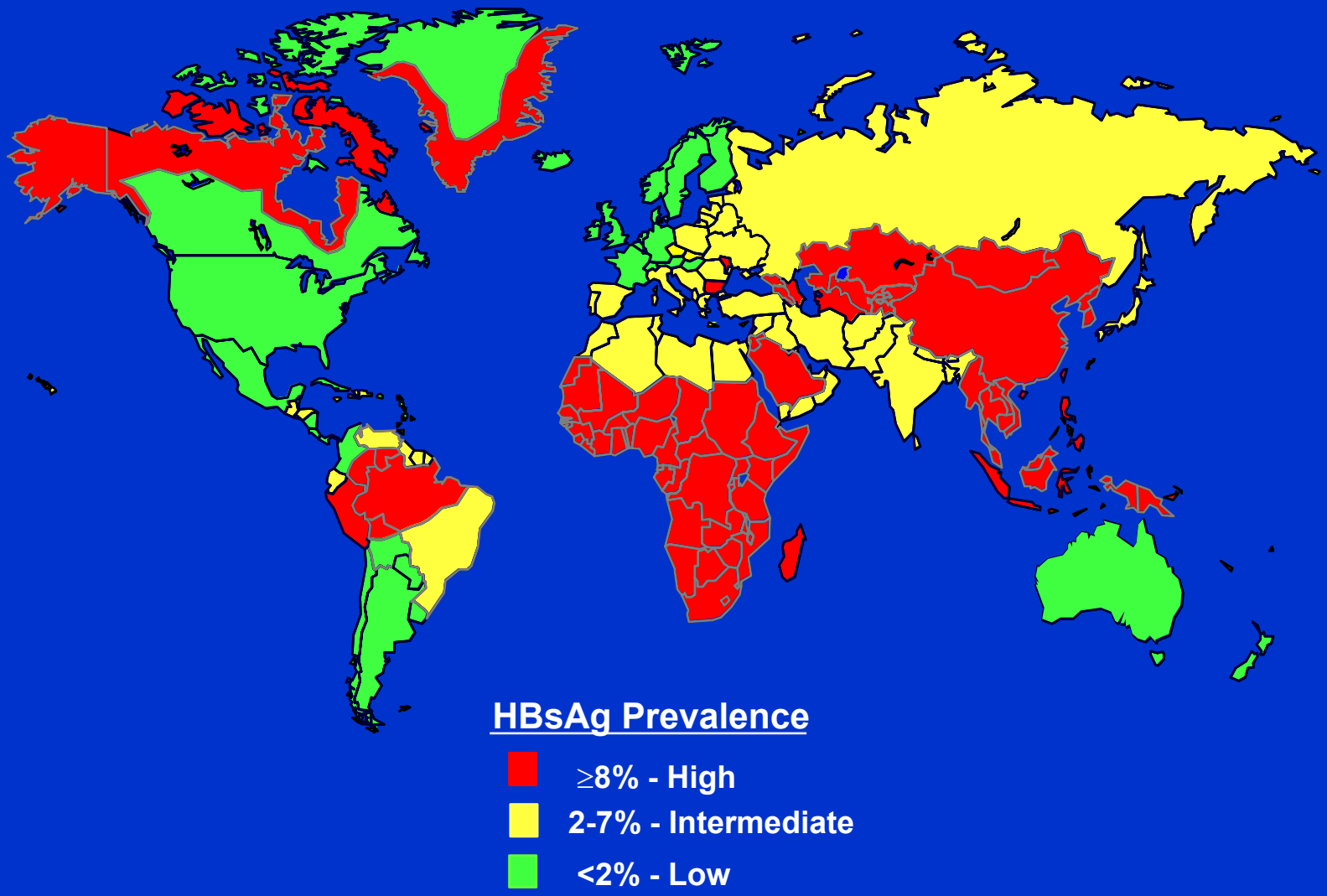
Hepatitis B Overview

- Serious: Causes death from liver disease in up to 25% of those infected at birth.
- Cancer related: Liver cancer especially prevalent in areas of 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



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

Prevalence of HBV Serologic Markers in Adults Throughout the World

- 2 billion people have hepatitis B serologic markers
- 350 million have chronic infection

Country	HBsAg + %	HBV marker + %
Ethiopia	11.0	70.0
Kenya	11.4	56.2
Nigeria	10.0	72.5
Namibia	14.0	87.5
Zaire	20.6	78.9
Liberia	7.6	61

Prevalence of HBV Serologic Markers in Adults Throughout the World (2)

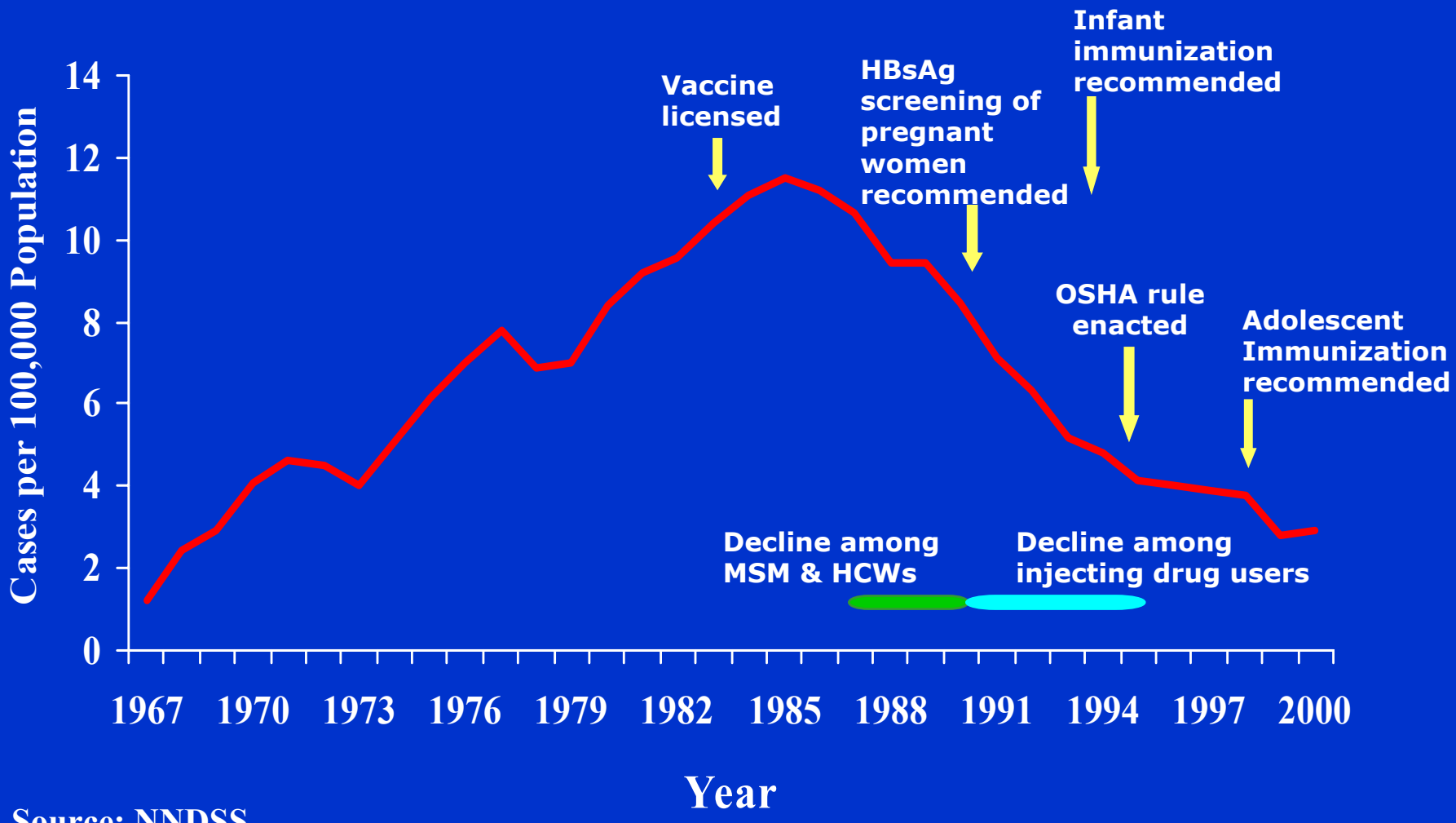
Country	HBsAg + %	HBV marker + %
Singapore	5 - 6	n/a
Chinese	10 -15	
Aboriginal (Aust)	5 - 25	n/a
Maori (New Zea)	10 -12	
Korean	12	
Burmese	8 -10	
Indonesian	5	
Indian	5 -15	
Japanese	1 - 3	
Aust/NZ (Ang-Sax)	0.1	

Source: *Gut* 1996: 38 (suppl. 2)

Hepatitis B Incidence in U.S., 2001

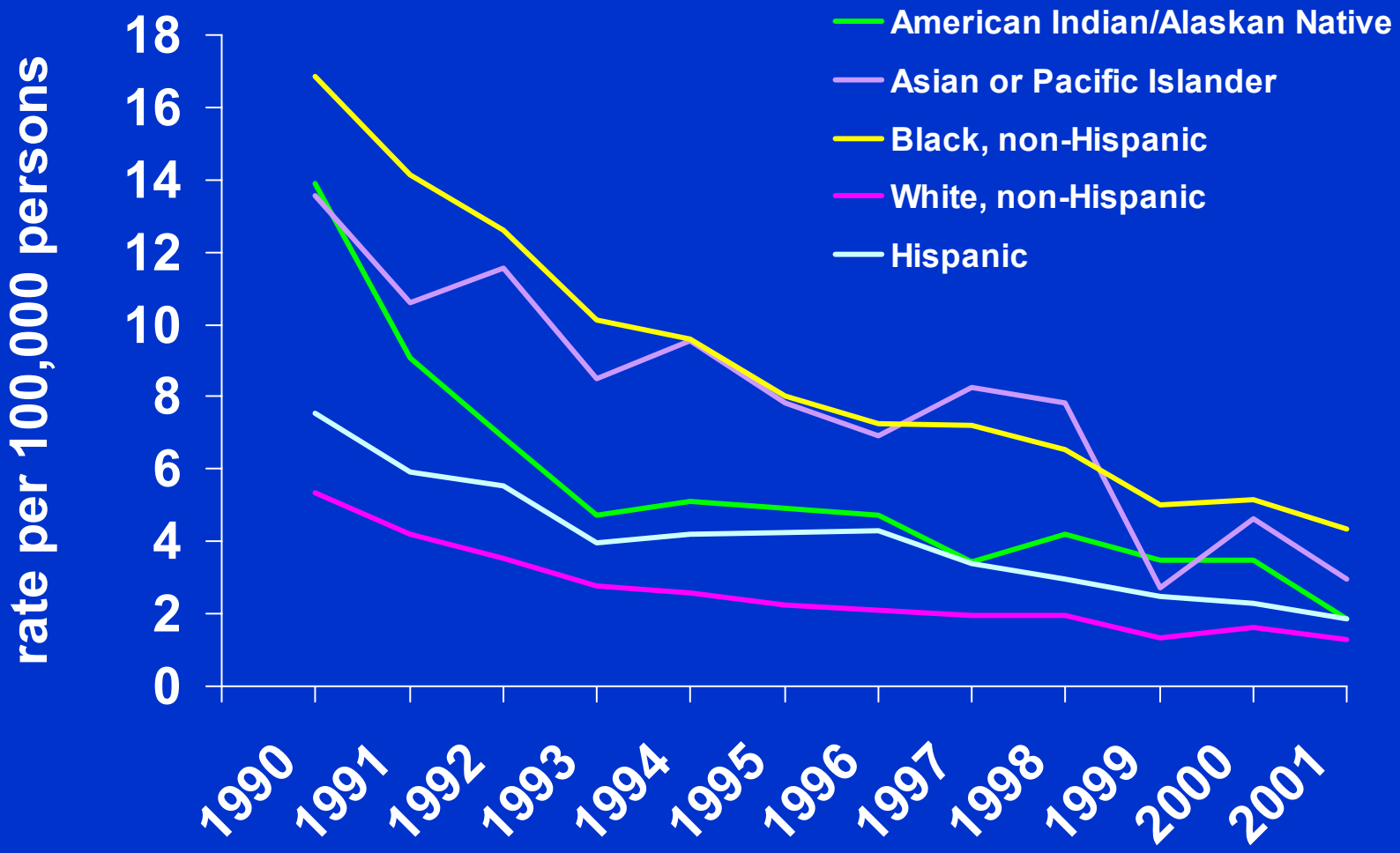
- Estimated incidence
  - 78,000 cases/year
- Reported cases
  - Acute hepatitis B: 7,844

Hepatitis B by Year, United States, 1966 - 2000



Source: NNDSS

Hepatitis B by Race/Ethnicity, 1990-2001



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

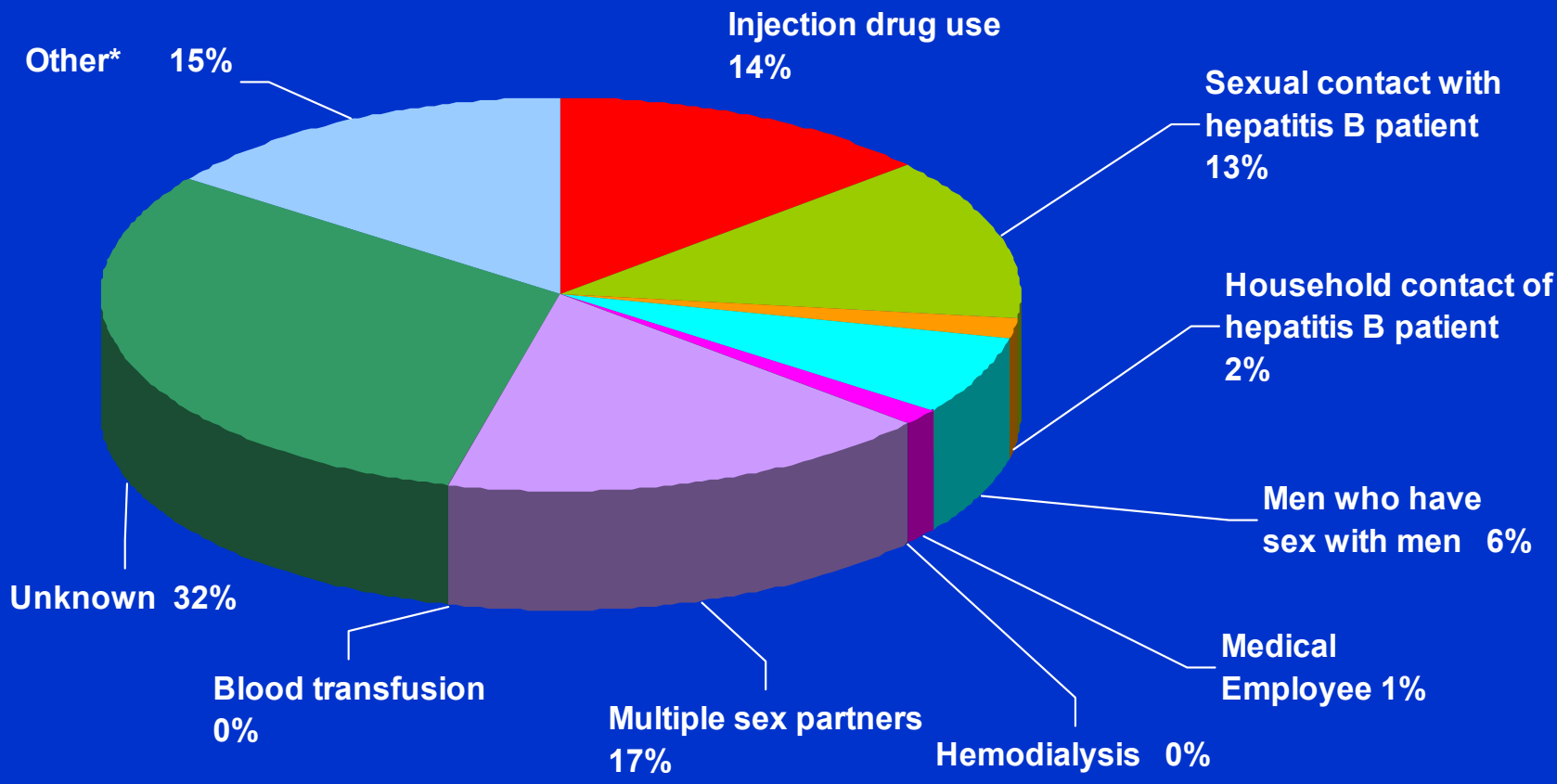
Risk Groups for HBV Infection (2)

- 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

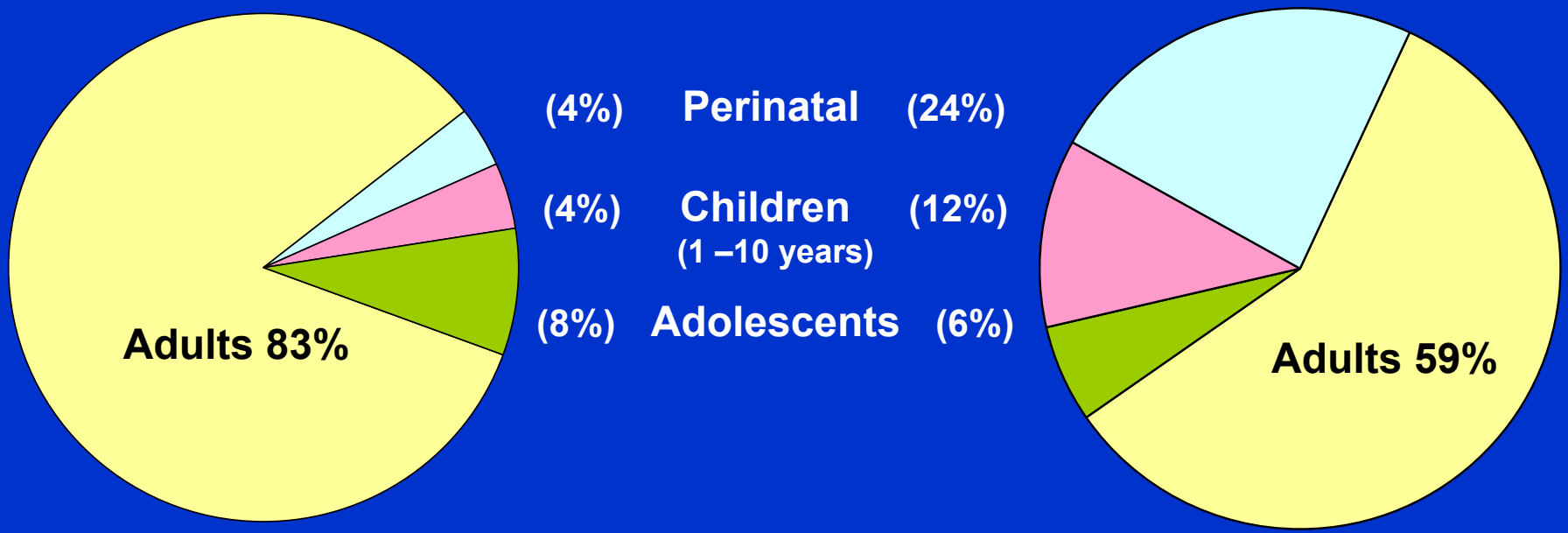
Risk Factors Associated with Reported Hepatitis B, 1990-2000, United States



Source: NNDSS/VHSP

*Other: Surgery, dental surgery, acupuncture, tattoo, other percutaneous injury

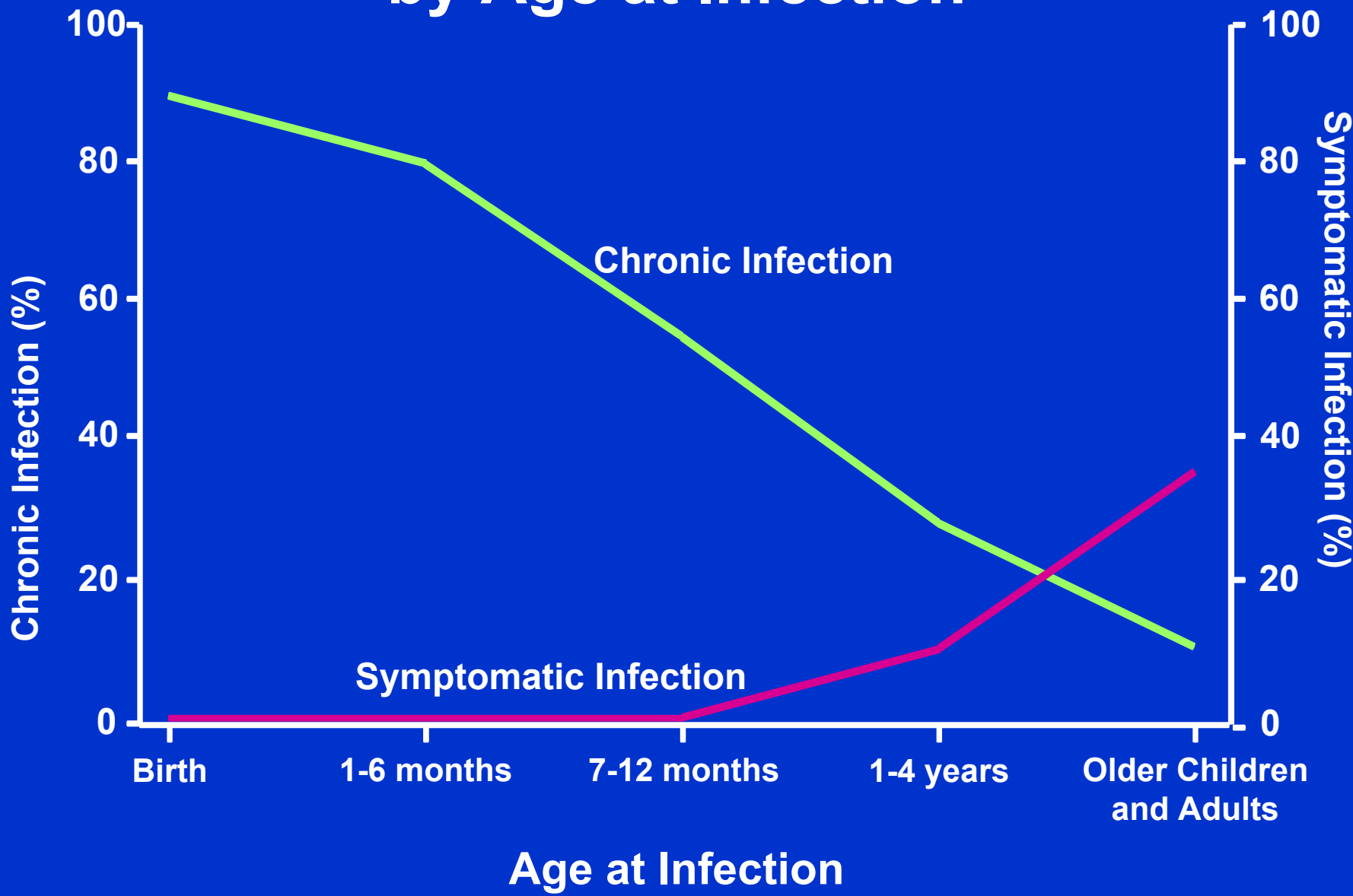
Age at Acquisition of Acute and Chronic HBV Infection United States, 1989 Estimates



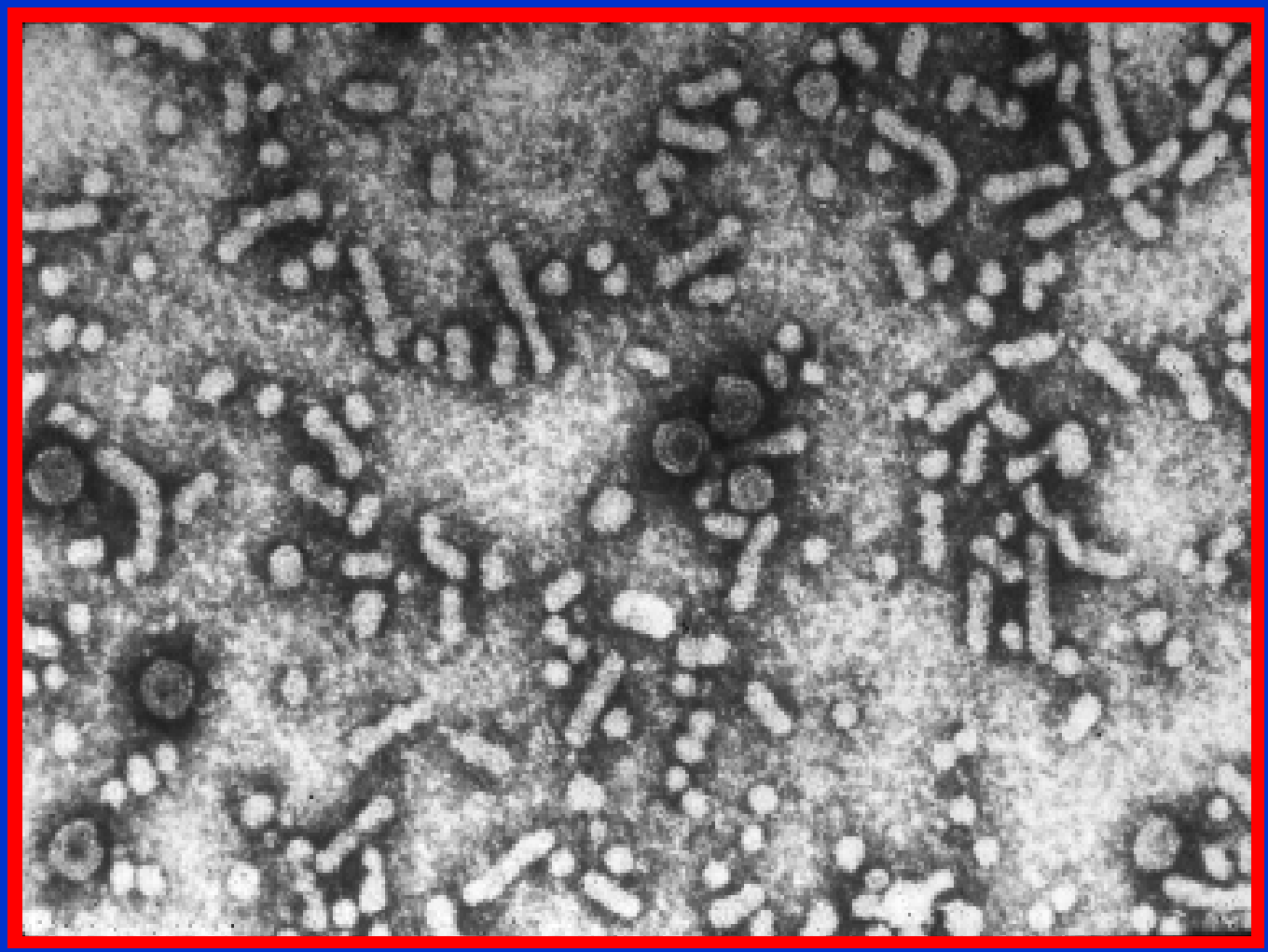
Acute HBV Infections

Chronic HBV Infections

Outcome of Hepatitis B Virus Infection by Age at Infection



Hepatitis B Virus



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.
- **HBcAg**: Hepatitis B core antigen. No commercial test available for this.
- **anti-HBc**: Antibody HBcAg. 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%

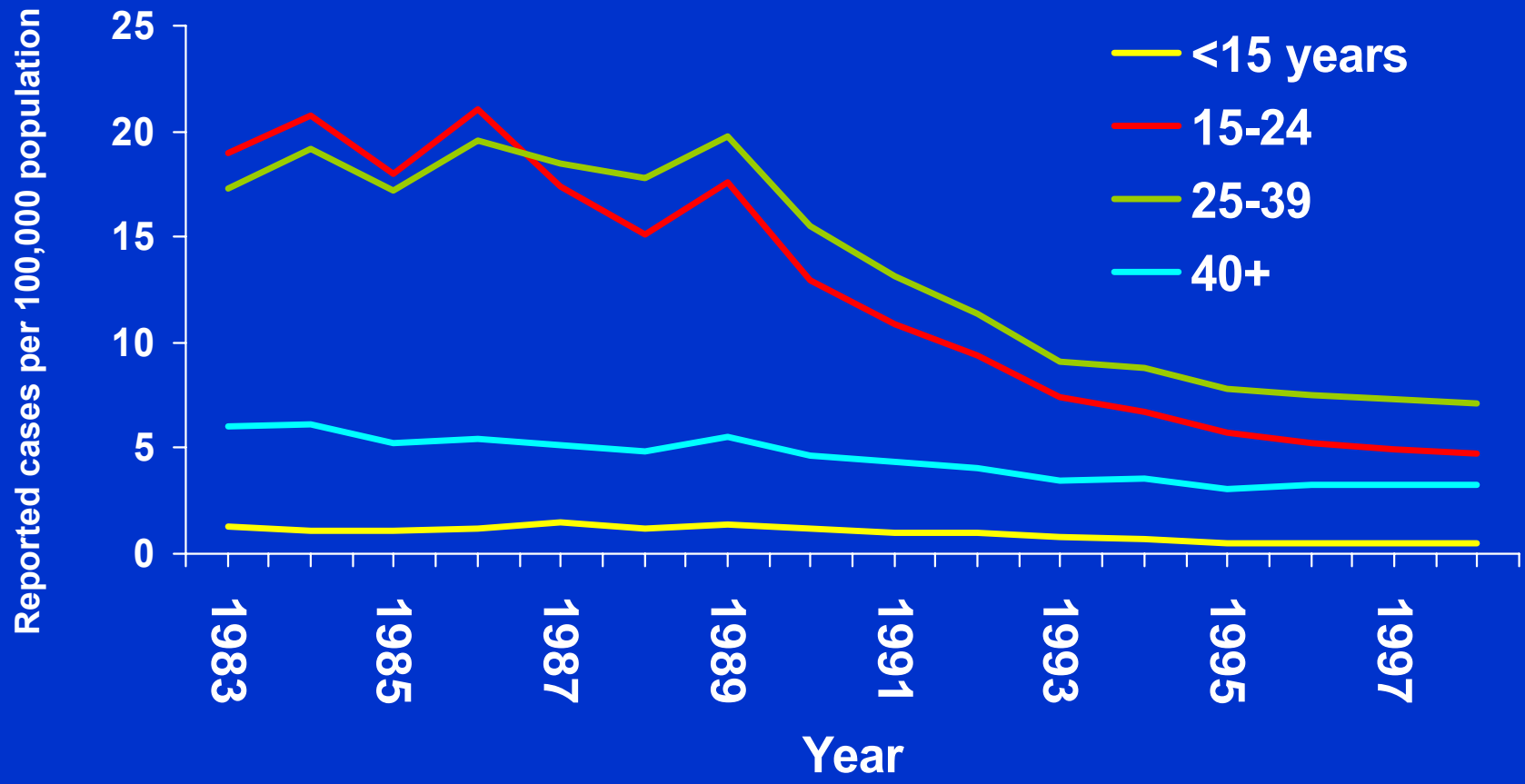
Acute Viral Hepatitis

Source: CDC

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

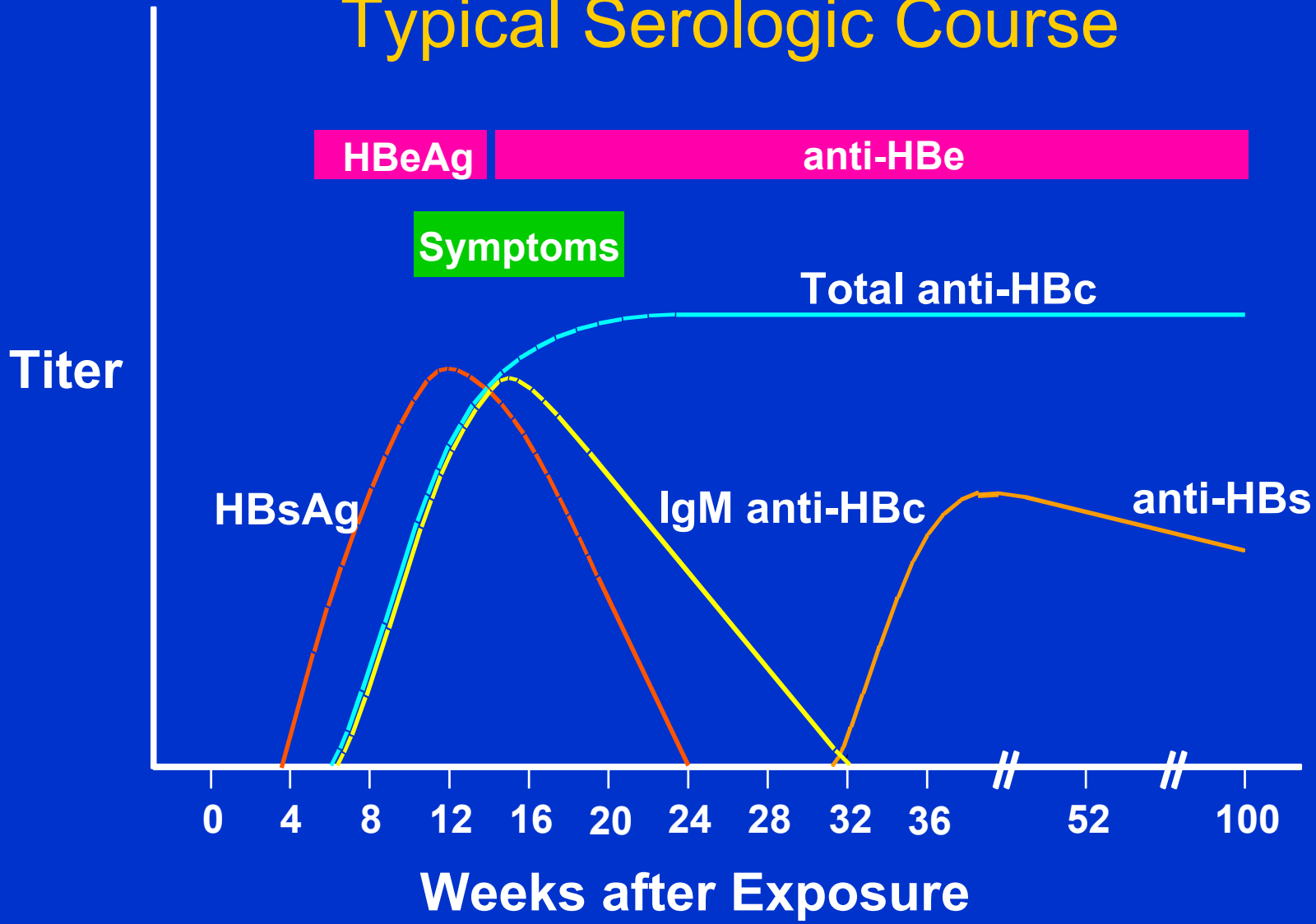
Reported Cases of Hepatitis B, by Age, U.S., 1983-1998



Source: NNDSS

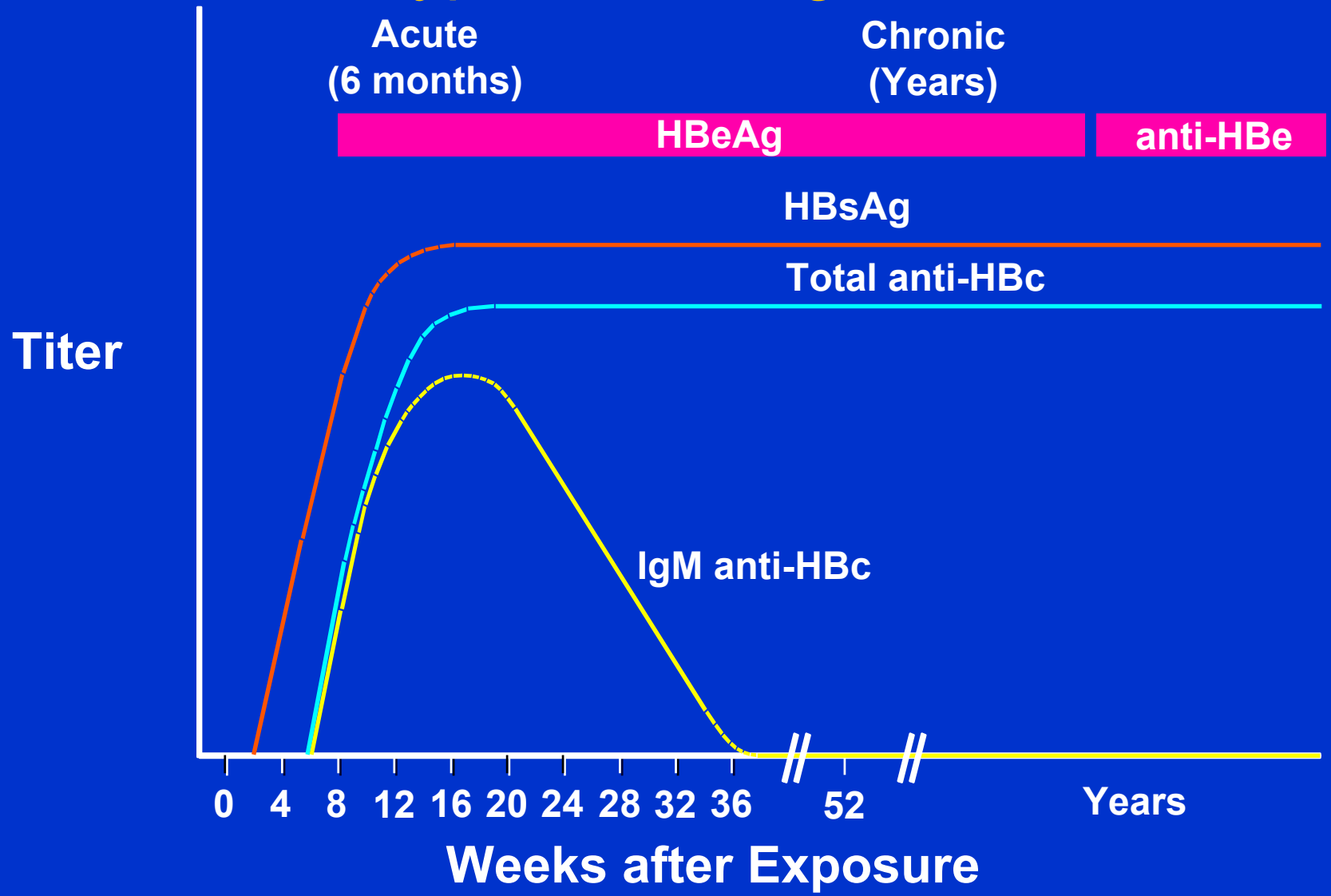
Acute HBV Infection with Recovery

Typical Serologic Course



Progression to Chronic HBV Infection

Typical Serologic Course



Interpretation of Hepatitis B Panel

HBsAg	negative	
antiHBc	negative	susceptible
antiHBs	negative	
HBsAg	negative	
antiHBc	positive	immune due to natural infection
antiHBs	positive	
HBsAg	negative	
antiHBc	negative	immune due to vaccine
antiHBs	positive	
HBsAg	positive	
antiHBc	positive	acutely infected
IgM antiHBc	positive	
antiHBs	negative	
HBsAg	positive	
antiHBc	positive	chronically
IgM antiHBc	negative	infected
antiHBs	negative	
HBsAg	negative	
antiHBc	positive	four possible interpretations
antiHBs	negative	(see next slide)

Four possible interpretations of isolated antiHBc positive

1. May be recovering from acute HBV infection.
2. May be distantly immune and test not sensitive enough to detect very low level of anti-HBs in serum.
3. May be susceptible with a false positive anti-HBc.
4. May be undetectable level of HBsAg present in the serum and the person is actually a carrier.

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
    - also licensed for use in children
  - lamivudine (Epivir-HB) administered by mouth qd
  - adefovir dipivoxil (Hepsera) administered by mouth qd

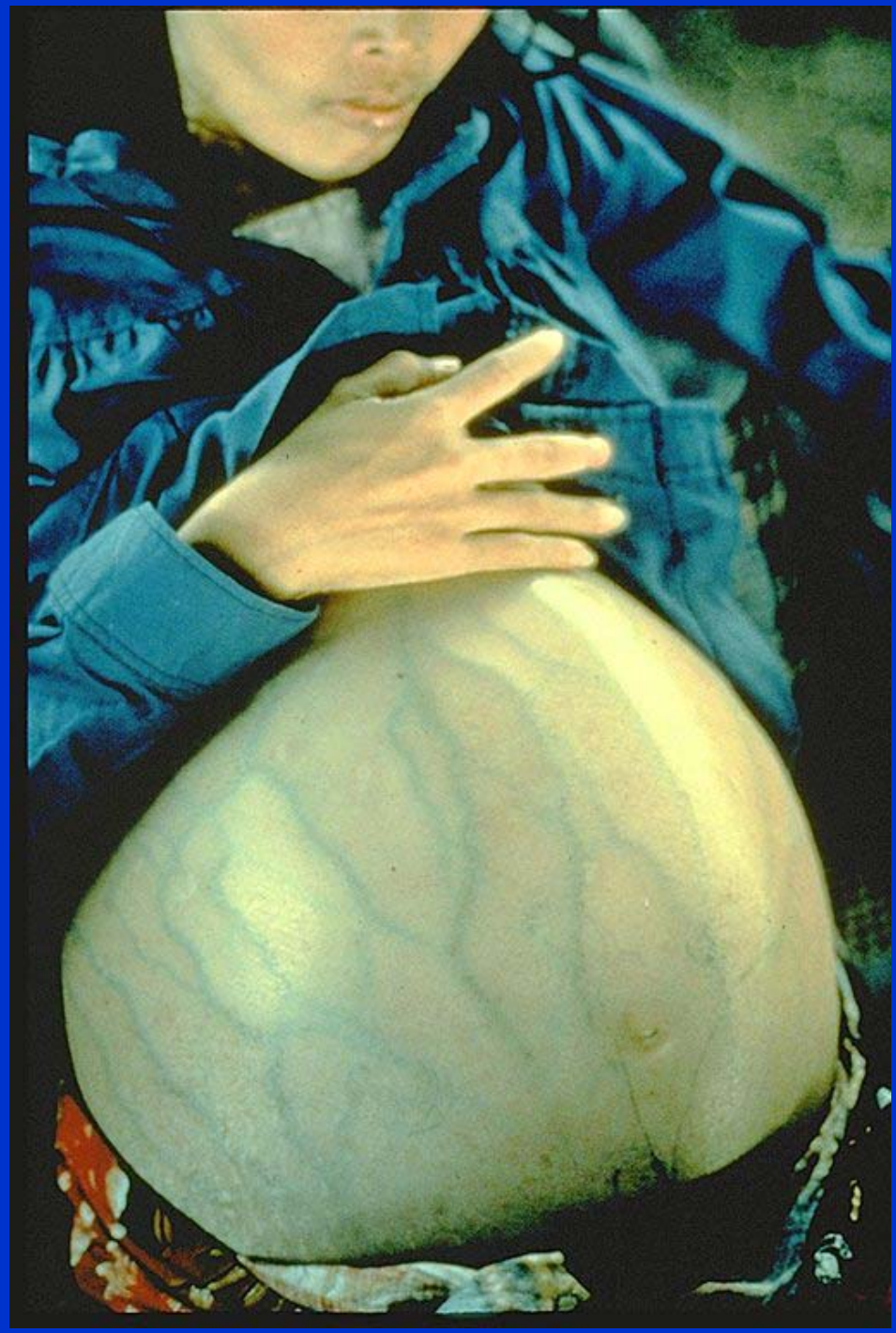
Consult a liver specialist to assist in determining whether your patient is a treatment candidate.

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.
  - αfetoprotein (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



This Khmer woman died of hepatoma, four months after arriving in a refugee camp in Thailand.

Source: Patricia Walker, MD

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

HCC (2)

- 5-year survival rate for hepatoma is 2.3%.
- Previously, only therapy that appeared to improve survival was resection of small asymptomatic tumors (5-year survival with surgery is 25%).
- Newer modalities of treatment are seeing some success.
  - radiologically based radio frequency ablation
  - chemo embolization
  - ethanol injection
- Transplantation in combination with above also occurring. Long-term follow-up data on the effectiveness of these treatments is not yet available.
- Important to screen every 6-12 mos for small lesions so new treatment modalities may be considered.
- Hepatitis B vaccine is the first vaccine to prevent cancer.

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.

Childhood or Adult Schedule

Never start the series over!

Never! Never! Never!

Recommended dosages of hepatitis B vaccines *				
Vaccine brand	**Age group**	**Dose**	**Volume**	**# Doses**
Engerix-B (GSK)	0-19 years	10 µg	0.5 ml	3
	20 years and older	20 µg	1.0ml	3
Recombivax HB (Merck & Co.)	0-19 years	5 µg	0.5 ml	3
	11-15 years	10 µg	1.0 ml	2
	20 years and older	10 µg	1.0 ml	3

* The schedule for hepatitis B vaccination is flexible and varies. Consult the ACIP 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 formulation) 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/1.0ml 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

Vaccination and antibody response status of exposed workers	Treatment		
	Source HBsAg positive	Source HBsAg negative	Source unknown or not available for testing
Unvaccinated	HBIG x 1 and initiate HB vaccine series	Initiate HB vaccine series	Initiate HB vaccine series
Previously vaccinated			
Known responder	No treatment	No treatment	No treatment
Known non-responder*	HBIG X 1 and initiate revaccination or HBIG X 2	No treatment	If known high risk source, treat as if source were HBsAg positive
Antibody response unknown	Test exposed person for anti-HBs 1. If adequate, no treatment is necessary. 2. If inadequate*, administer HBIG x 1 and vaccine booster.	No treatment	Test exposed person for anti-HBs 1. If adequate, no treatment is necessary. 2. If inadequate*, administer vaccine booster and recheck titer in 1-2 months.

* A non-responder is a person with inadequate levels of serum antibody to HBsAg (I.e., 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

Elimination of Hepatitis B Virus Transmission: United States

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.

References: Harmonized Childhood Immunization Schedule

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

Remember…

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