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webinar series

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Hepatitis B Vaccine Issues

June 16, 2016

Advisory Committee on Immunization Practices (ACIP)

- The recommendations to be discussed are primarily those of the ACIP
  - composed of 15 experts in clinical medicine and public health who are not government employees
  - provides guidance on the use of vaccines and other biologic products to the Department of Health and Human Resources, CDC, and the U.S. Public Health Service

www.cdc.gov/vaccines/acip/

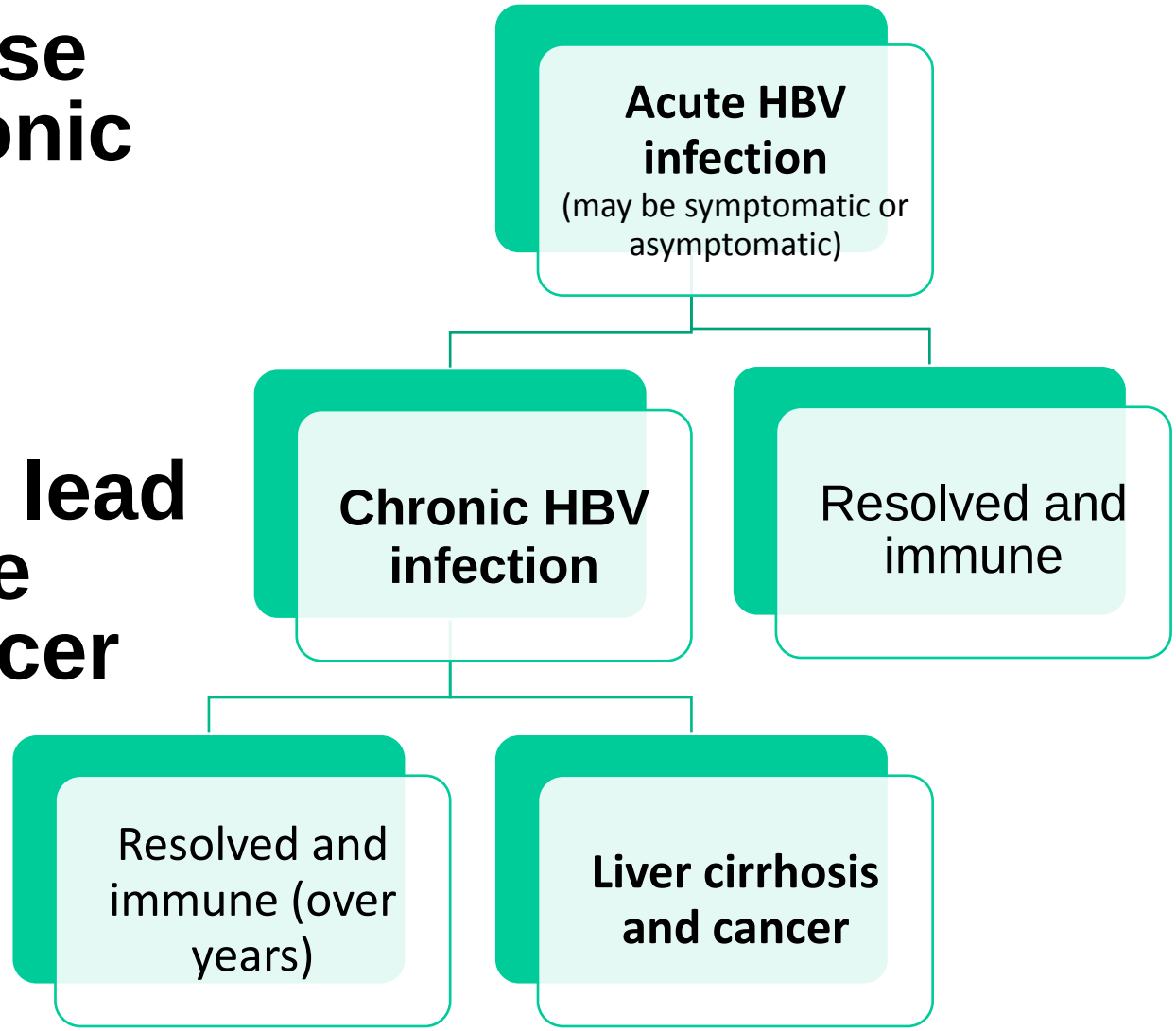
Background on Hepatitis B

- Hepatitis B is a liver infection caused by the hepatitis B virus (HBV)
- HBV is found in the blood and other body fluids of infected people (e.g., serum, semen, saliva, and vaginal secretions)
- Transmission occurs by contact with infected blood or other body fluid of an acutely or chronically infected person
  - in the U.S. the most commonly identified risk factors are sexual contact and injection drug use

Natural History of Hepatitis B Virus (HBV) Infection

HBV can cause acute or chronic infection

Chronic HBV infection can lead to liver failure and liver cancer



Hepatitis B Virus Infection

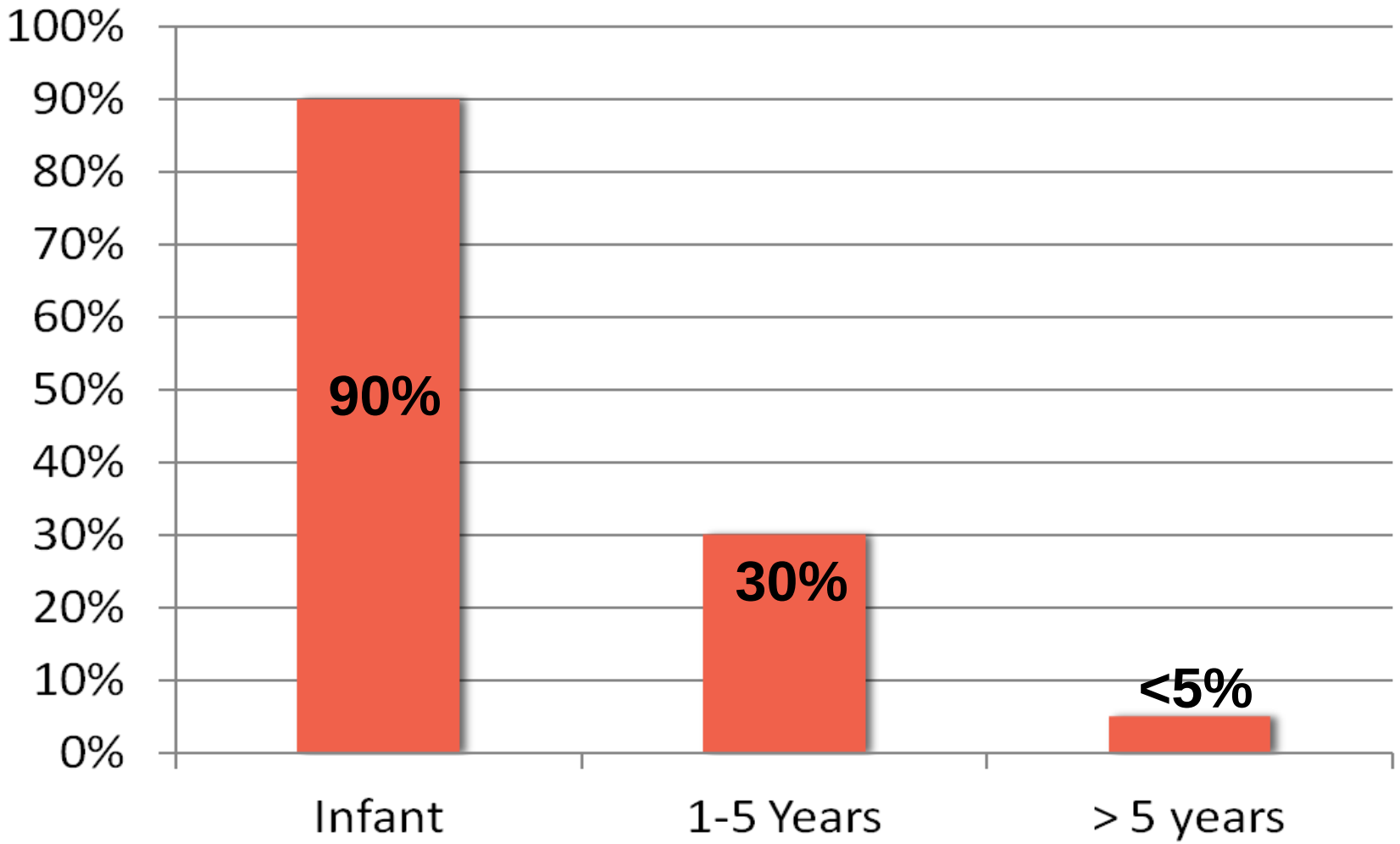
- **Established cause of chronic hepatitis and cirrhosis**
- **Human carcinogen - cause of up to 80% of hepatocellular carcinomas**
- **More than 240 million chronically infected worldwide (1-2 million in the U.S.)**
- **More than 780,000 deaths per year worldwide due to complications of hepatitis B infection (estimated 1,800 per year in the U.S.)**

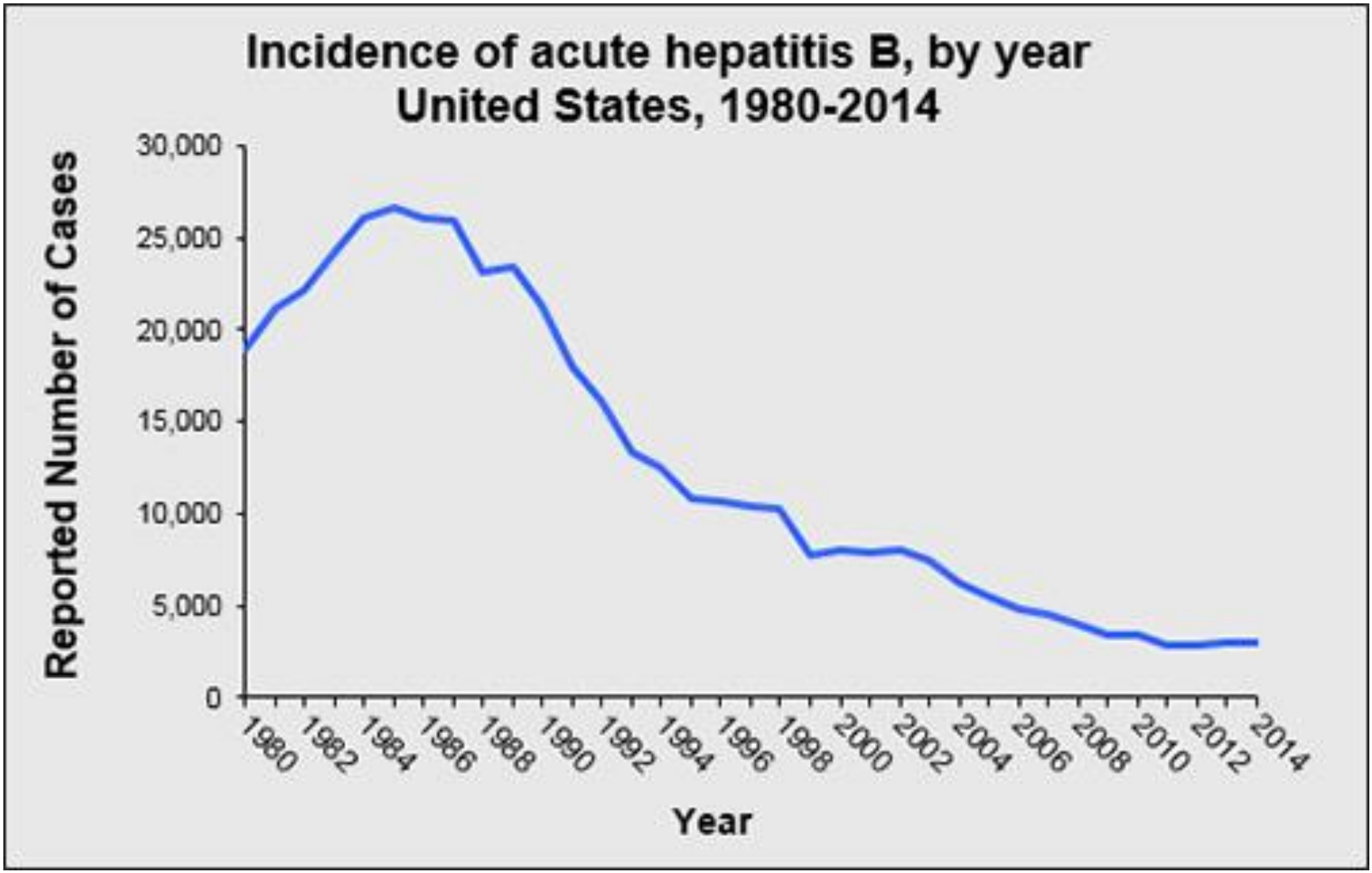
World Health Organization data, 2015

Perinatal Hepatitis B Transmission

- An infant can acquire HBV from:
  - an infected mother (transmitted at birth)
  - a chronically infected member of the household
- In the absence of post-exposure treatment up to 90% of infants born to an HBsAg positive woman will be infected

Risk of Developing Chronic Hepatitis B by Age at Infection





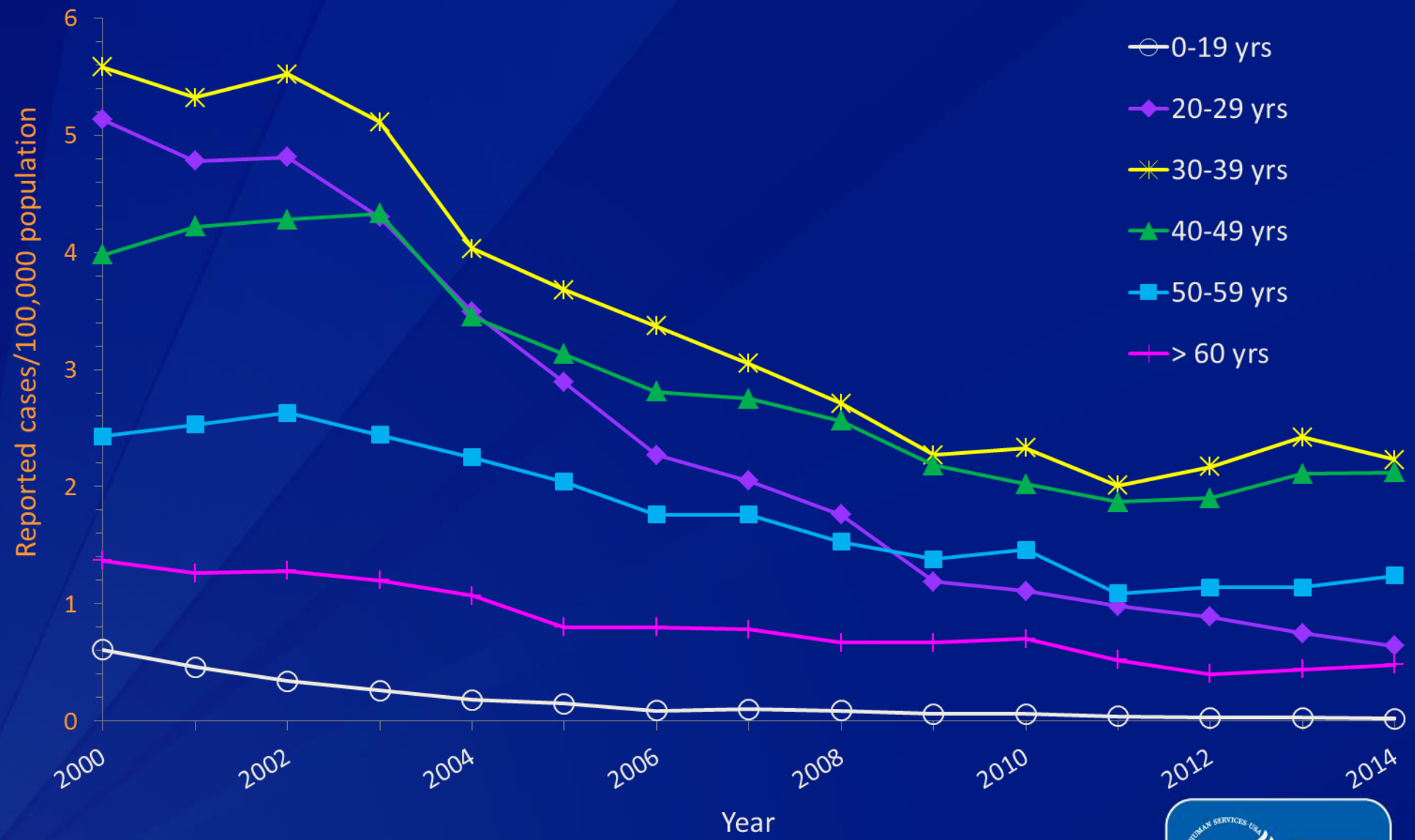
www.cdc.gov/hepatitis/statistics/index.htm

HBV Disease Burden in the United States

- Prevaccine era
  - estimated 300,000 persons infected annually, including 24,000 infants and children
- 2014
  - 2,953 reported acute cases
  - estimated 19,200 cases (range, 11,000-47,100) based on under-reporting
  - estimated 800 perinatal infections

www.cdc.gov/hepatitis/statistics/index.htm

Figure 3.2. Incidence of acute hepatitis B, by age group — United States, 2000–2014



Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)

Hepatitis B Vaccine

- Contains recombinant HBsAg
- Intramuscular administration only
- Usual schedule: 0, 1, 6 months
- Variant schedules are acceptable (0, 1, 4 months, 0, 2, 4 months, 0, 1, 2, 12 months)
- No less than 16 weeks between doses 1 and 3
- Duration of immunity more than 20 years

MMWR 2013;62(RR-10):1-19

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)**

Recommended Dose of Hepatitis B Vaccine

	Recombivax HB	Engerix-B
	Dose (mcg)	Dose (mcg)
Infants and children <11 years of age	0.5 mL (5)	0.5 mL (10)
Adolescents 11-19 years	0.5 mL (5)	0.5 mL (10)
Adults ≥20 years	1.0 mL (10)	1.0 mL (20)

Hepatitis B Vaccine Administration Errors

- If less than an age-appropriate dose is given (0.5 mL to a person ≥20 years)
  - if the error is discovered while the person is still in the office give another 0.5 mL dose immediately
  - if the error is discovered later give a full age-appropriate dose
- If more than an age-appropriate dose is give (1.0 mL to a person <20 years)
  - count the dose
  - continue the schedule as usual

CDC personal communication

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
- Upper limit of duration of protection is not known – at least 20 years

Hepatitis B Vaccine

Routine booster doses are <u>NOT</u> routinely recommended for any group, including healthcare providers

Hepatitis B Vaccine
Routine Infant Schedule

Dose+	Usual Age	Minimum Interval
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 and 24 weeks of age

+an additional dose at 4 months is acceptable if the clinician prefers to use a combination vaccine that contains hepatitis B vaccine

Why a Birth Dose?

- **The primary goal of administering hepatitis B vaccine at birth is to protect babies from chronic HBV infection**
- **Approximately 25% of infants with perinatal HBV infection will die prematurely as a result of complications of cirrhosis or liver cancer**

Effectiveness of Hepatitis B Vaccine Starting at Birth

- **Post-exposure prophylaxis of infants born to infected women is 85–95% effective when started within 12 hours of birth**
  - **post-exposure prophylaxis: hepatitis B vaccine + hepatitis B immune globulin (HBIG) at birth, completion of hepatitis B vaccine series, post-vaccination testing for response at 9-12 months of age***
- **Hepatitis B vaccination starting at birth even without HBIG will prevent transmission of the infection in 70–95% of infants born to chronically infected women**

***Or 1–2 months after the final dose of the HepB vaccine series if completion of the series is delayed. *MMWR* 2015:64:1118-20**

The Opportunity To Prevent Perinatal Hepatitis B Virus Infection

- Hospitals have an opportunity to protect the future health of infants born in their facilities
  - each year in the U.S., an estimated 25,000 infants are born to mothers who are infected with HBV, and not all of their infants receive post-exposure prophylaxis
  - some infants are first exposed shortly after birth to HBV by household members or caretakers who have chronic HBV infection
- Most infants can be protected if hospitals routinely provide a birth dose of hepatitis B vaccine to all newborn infants

The Problem

- **Many infants in the United States are not receiving the birth dose of hepatitis B vaccine**
  - **In 2014 only 72% of U.S. infants received hepatitis B vaccine within 3 days of birth**
  - **States' coverage rates varied between 48% and 88% (81% in MO)**
- **There is room for improvement in protecting newborn infants in every state**

2014 National Immunization Survey.
***MMWR* 2015;64:897-904**

Why Should All Newborns Receive a Birth Dose of Hepatitis B Vaccine

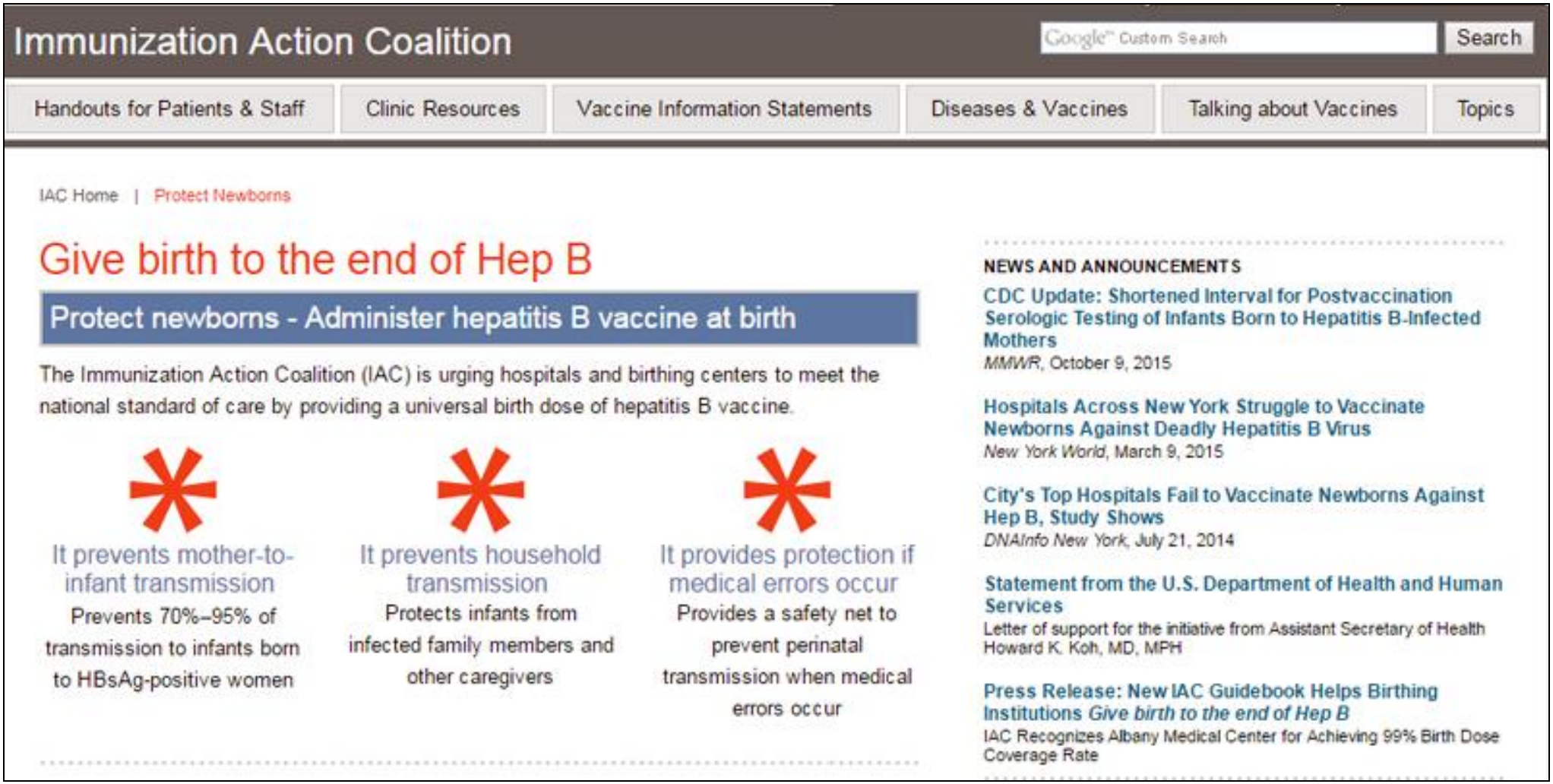
- **Prevents mother-to-infant transmission:** Prevents 70–95% of infection among infants born to HBsAg-positive women
- **Prevents household transmission:** Protects infants from infected family members and other caregivers
- **Protects when medical errors occur:** Provides a safety net to prevent perinatal HBV infection when medical errors occur

Perinatal Hepatitis B Management Errors

- Ordering the wrong hepatitis B screening test
- Misinterpreting or mistranscribing the hepatitis B test results
- Failing to communicate the HBsAg test results to or within the hospital
- Not giving hepatitis B vaccine to infants born to mothers of unknown HBsAg status within 12 hours of birth
- Not giving prophylaxis to an infant even when the mother's HBsAg-positive status is documented

All birthing hospitals should Implement policies and procedures to administer the recommended universal hepatitis B vaccine birth dose, ensuring that every newborn infant receives hepatitis B vaccine at birth, or no later than hospital discharge.

MMWR 2005;54(RR-16) www.cdc.gov/mmwr/PDF/rr/rr5416.pdf



www.immunize.org/protect-newborns/

Hepatitis B Vaccine
Adolescent and Adult Schedule

Dose	Usual Interval	Minimum Interval
Primary 1	---	- - -
Primary 2	1 month	4 weeks
Primary 3	5 months	8 weeks*

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

Interruption of the Hepatitis B Vaccine Series

- **It is not necessary to restart the series or add doses if the hepatitis B vaccine series is interrupted, regardless of the interval since the last dose**

MMWR 2013;62(RR-10):1-19

Adults at Risk for HBV Infection

- **Sexual exposure**
  - **sex partners of HBsAg-positive persons**
  - **sexually active persons not in a long-term, mutually monogamous relationship***
  - **persons seeking evaluation or treatment for a sexually transmitted disease**
  - **men who have sex with men**

***persons with more than one sex partner during the previous 6 months**

Adults at Risk for HBV Infection

- **Percutaneous or mucosal exposure to blood**
  - **current or recent IDU**
  - **household contacts of HBsAg-positive persons**
  - **residents and staff of facilities for developmentally disabled persons**
  - **healthcare and public safety workers with risk for exposure to blood or blood-contaminated body fluids**
  - **persons with end-stage renal disease**
  - **persons with diabetes mellitus**

***MMWR* 2006;55(RR-16):6-8**

Adults at Risk for HBV Infection

- Others groups
  - international travelers to regions with high or intermediate levels (HBsAg prevalence of 2% or higher) of endemic HBV infection
  - persons with HIV infection

MMWR 2006;55(RR-16):6-8

Prevaccination Serologic Testing

- Not indicated before routine vaccination of infants, children, and most adolescents and adults
- Recommended for
  - all persons born in Africa, Asia, the Pacific Islands, and other regions with HBsAg prevalence of 2% or higher
  - household, sex, and needle-sharing contacts of HBsAg-positive persons
  - men who have sex with men
  - injection drug users

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+ persons
  - infants born to HBsAg+ women
  - healthcare personnel

Hepatitis B Evidence of Immunity for Healthcare Personnel (HCP)

- **Written documentation of a properly spaced 3-dose series of hepatitis B vaccine, *and***
- **Confirmation of immunity (antibody to hepatitis B surface antigen [anti-HBs] ≥10 mIU/mL) 1 to 2 months after the third dose**
- **CDC recommends that HCP have <u>both</u> documentation of vaccination and a positive anti-HBs**
- **HCP lacking documentation of vaccination should be considered unvaccinated**

***MMWR* 2013;62(RR-10):1-19**

The "New" Hepatitis B Serology Issue: HCP Vaccinated as Infants or Adolescents

- Routine hepatitis B vaccination of infants was first recommended in 1991
- Catch-up vaccination of adolescents recommended in 1995
- Vaccination coverage among 19-35 month-old children first exceeded 90% in 2000
- The oldest cohorts vaccinated as infants are now in their early 20s
- Routine serologic testing of infants is not recommended (except if mother is HBsAg positive)

MMWR 2013;62(RR-10):1-19

Hepatitis B Vaccination

- **95% of healthy infants will achieve seroprotection against hepatitis B 1 to 2 months after a complete 3-dose series**
- **By 18 years after vaccination approximately 84% of persons vaccinated at younger than 1 year of age will not have detectable anti-HBs**

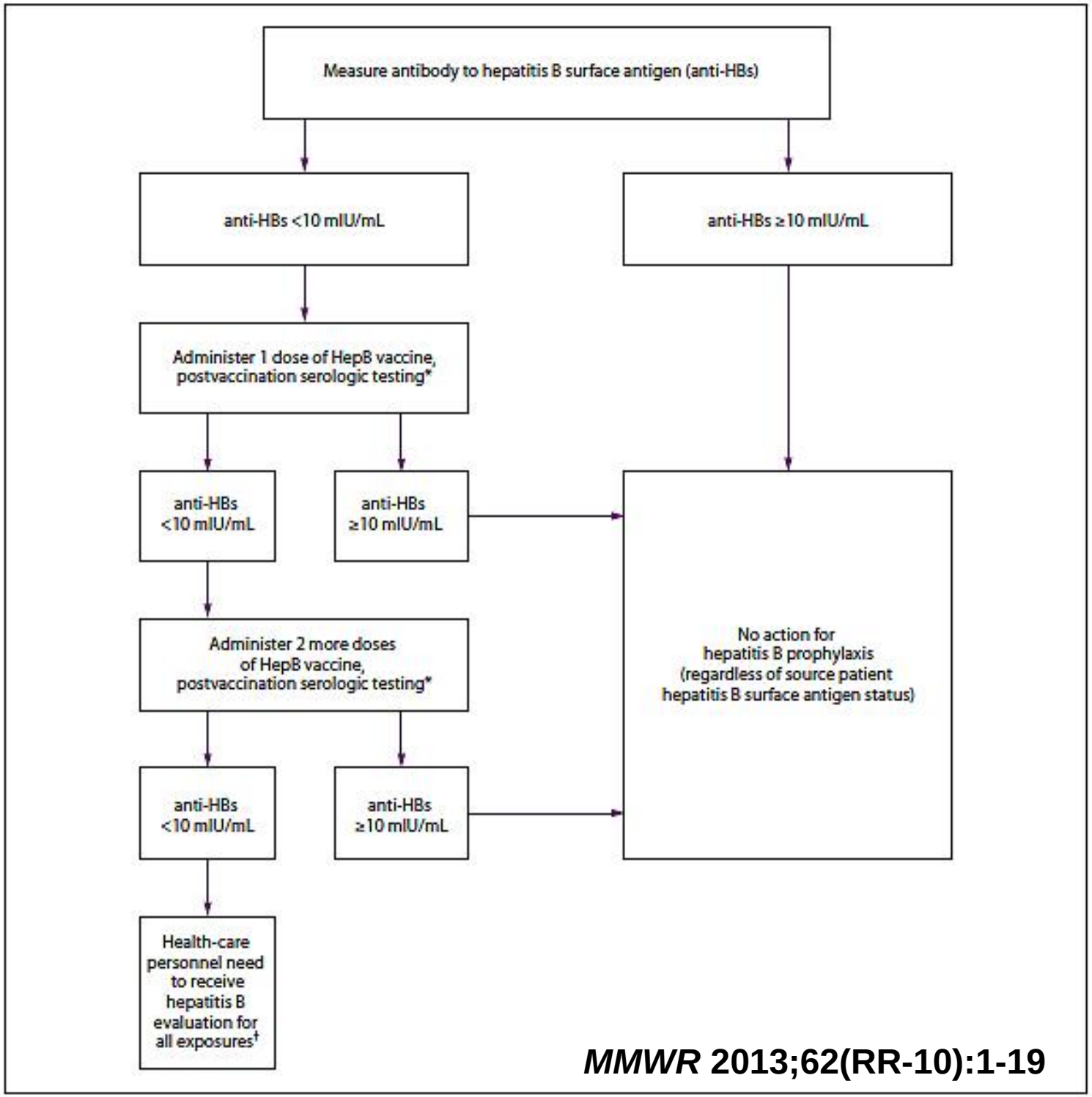
***MMWR* 2013;62(RR-10):1-19**

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 62 / No. 10
December 20, 2013

CDC Guidance for Evaluating Health-Care Personnel for Hepatitis B Virus Protection and for Administering Postexposure Management

***MMWR* 2013;62(RR-10):1-19**

FIGURE 6. Pre-exposure evaluation for health-care personnel previously vaccinated with complete, ≥3-dose HepB vaccine series who have not had postvaccination serologic testing*



***MMWR* 2013;62(RR-10):1-19**

Hepatitis B Vaccine and HCP

- **Management of HCP who have written documentation of a complete series of hepatitis B vaccine doses in the past who were not tested for antibody response following the vaccination series and who now test negative for anti-HBs**
  - **administer 1 dose of hepatitis B vaccine then test for anti-HBs 1 to 2 months later**
  - **if positive (anti-HBs ≥10 mIU/mL) the person is immune and nothing else needs to be done**

***MMWR* 2013;62(RR-10):1-19**

Management of Nonresponse to Hepatitis B Vaccine

- For persons who remain seronegative after the "booster" dose
  - complete a second series of three doses (i.e., 2 more doses)
  - use the usual schedule of 0, 1 and 6 months
  - may use a compressed schedule (0, 1, 4 months)
  - retest for anti-HBs 1 to 2 months after completing the second series

MMWR 2013;62(RR-10):1-19

Hepatitis B Revaccination

- **47% of 3-dose series recipients without protective antibody levels after a primary vaccination series develop vaccine-induced seroprotection after one additional dose of hepatitis B vaccine**
- **69% of initial nonresponders will develop seroprotection after 3 revaccination doses**

***Am J Prev Med* 1998;15:1-8**

Persistent Nonresponse to Hepatitis B Vaccine

- Less than 5% of vaccinees do not develop anti-HBs after 6 valid doses
- May be nonresponder or "hyporesponder"
- ACIP does not recommend revaccination with more than 3 doses (i.e., more than 6 total doses)
- Check HBsAg and anti-HBc status if not already done
- If exposed, treat as nonresponder with HBIG postexposure prophylaxis

MMWR 2013;62(RR-10):1-19

TABLE 2. Postexposure management of health-care personnel after occupational percutaneous and mucosal exposure to blood and body fluids, by health-care personnel HepB vaccination and response status

Health-care personnel status	Postexposure testing		Postexposure prophylaxis		Postvaccination serologic testing†
	Source patient (HBsAg)	HCP testing (anti-HBs)	HBIG*	Vaccination	
Documented responder§ after complete series (≥3 doses)	**No action needed**				
Documented nonresponder¶ after 6 doses	Positive/unknown	—**	HBIG x2 separated by 1 month	—	No
	Negative	**No action needed**			
Response unknown after 3 doses	Positive/unknown	<10mIU/mL**	HBIG x1	Initiate revaccination	Yes
	Negative	<10mIU/mL	None		
	Any result	≥10mIU/mL	**No action needed**		
Unvaccinated/incompletely vaccinated or vaccine refusers	Positive/unknown	—**	HBIG x1	Complete vaccination	Yes
	Negative	—	None	Complete vaccination	Yes

Abbreviations: HCP = health-care personnel; HBsAg = hepatitis B surface antigen; anti-HBs = antibody to hepatitis B surface antigen; HBIG = hepatitis B immune globulin.

* HBIG should be administered intramuscularly as soon as possible after exposure when indicated. The effectiveness of HBIG when administered >7 days after percutaneous, mucosal, or nonintact skin exposures is unknown. HBIG dosage is 0.06 mL/kg.

† Should be performed 1–2 months after the last dose of the HepB vaccine series (and 4–6 months after administration of HBIG to avoid detection of passively administered anti-HBs) using a quantitative method that allows detection of the protective concentration of anti-HBs (≥10 mIU/mL).

§ A responder is defined as a person with anti-HBs ≥10 mIU/mL after ≥3 doses of HepB vaccine.

¶ A nonresponder is defined as a person with anti-HBs <10 mIU/mL after ≥6 doses of HepB vaccine.

** HCP who have anti-HBs <10mIU/mL, or who are unvaccinated or incompletely vaccinated, and sustain an exposure to a source patient who is HBsAg-positive or has unknown HBsAg status, should undergo baseline testing for HBV infection as soon as possible after exposure, and follow-up testing approximately 6 months later. Initial baseline tests consist of total anti-HBc; testing at approximately 6 months consists of HBsAg and total anti-HBc.

***MMWR* 2013;62(RR-10):1-19**

Hepatitis B Serologic Testing

- **HCP who have written documentation of a complete 3 (or more) hepatitis B vaccine series AND subsequent postvaccination anti-HBs level of 10 mIU/mL or higher are considered to be immune**
- **Immunocompetent persons have long-term protection against HBV infection and do not need further periodic testing to assess anti-HBs levels**

***MMWR* 2013;62(RR-10):1-19**

Resources

- General Recommendations on Immunization. *MMWR* 2011;60(RR-2):1-61
- Immunization of Healthcare Workers. *MMWR* 2011;69(RR-7):1-45
- CDC Guidance for Evaluating Health-Care Personnel for Hepatitis B Virus Protection and for Administering Postexposure Management. *MMWR* 2013;62(RR-10):1-19
- Immunization Action Coalition www.immunize.org