Revised ACIP Hepatitis B (HepB) Vaccine Recommendations

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Division of Viral Hepatitis

Outline

- Overview
- Hepatitis B Virus (HBV) background, epidemiology, and prevention
- Existing HepB recommendations
- Revisions deliberated by Work Group

- **Overview**
- **Hepatitis B Virus (HBV) background, epidemiology, and prevention**
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Revised Statement

- **Single document with guidance for:**
  - HepB vaccination of infants, children, adolescents, and adults
  - Testing pregnant women for hepatitis B surface antigen (HBsAg), and, if positive, HBV DNA
  - HepB pre-vaccination and postvaccination serologic testing
  - HBV post-exposure prophylaxis (occupational and non-occupational exposures)

Revised Statement, cont.

- **Incorporates previously-published recommendations from:**
  - ACIP
  - CDC
- **Augmented with American Association for the Study of Liver Diseases (AASLD) recommendation 8A:** ***The AASLD suggests antiviral therapy to reduce the risk of perinatal transmission of hepatitis B in HBsAg-positive pregnant women with an HBV DNA level >200,000 IU/mL***

Terrault et al. Hepatology 2015.

Existing HepB Statements

A Comprehensive Immunization Strategy to Eliminate Transmission of HBV Infection in the U.S.: Recommendations of ACIP

Infants, Children, Adolescents (2005)

Adults (2006)

Existing HepB Statements, cont.

Diabetes (ACIP, 2011)

Health-care personnel (CDC, 2013)

Testing interval for infants (CDC, 2015)

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Hepatitis B Virus

- **Transmitted through percutaneous or mucosal exposure to infectious blood or body fluids**
- **Highly infectious; remains viable on environmental surfaces for at least 7 days**
  - Can be transmitted in the absence of visible blood

Bond et al. Lancet 1981.

Epidemiology of HBV in the U.S.

- **Nearly 3,000 cases of acute HBV infection reported to CDC in 2014**
  - Estimated 19,200 new cases considering under-ascertainment and underreporting
  - Estimated 952 perinatal infections annually
- **~850,000 persons with HBV infection**
  - Persons with chronic infection serve as the main reservoir for transmission
  - Imported chronic HBV infection accounts for ~95% of new U.S. cases

National Notifiable Diseases Surveillance System (NNDSS); Ko et al. JPIDS 2016; Roberts et al. Hepatology 2016; Mitchell et al. PLoS One 2011.

Reported Acute Hepatitis B

- Rate of reported acute HBV infections declined by 90.6% since recommendations for HepB vaccine first issued in 1982
- Rate fairly stable from 2010-2014, although increases occurred in some populations (e.g., whites aged 30-39 years reporting injection drug use in Kentucky, Tennessee, and West Virginia)

National Notifiable Diseases Surveillance System (NNDSS); Harris et al. MMWR 2016.

Incidence of Acute Hepatitis B, by Age Group — United States, 2000-2014

National Notifiable Diseases Surveillance System (NNDSS)

Chronic Hepatitis B

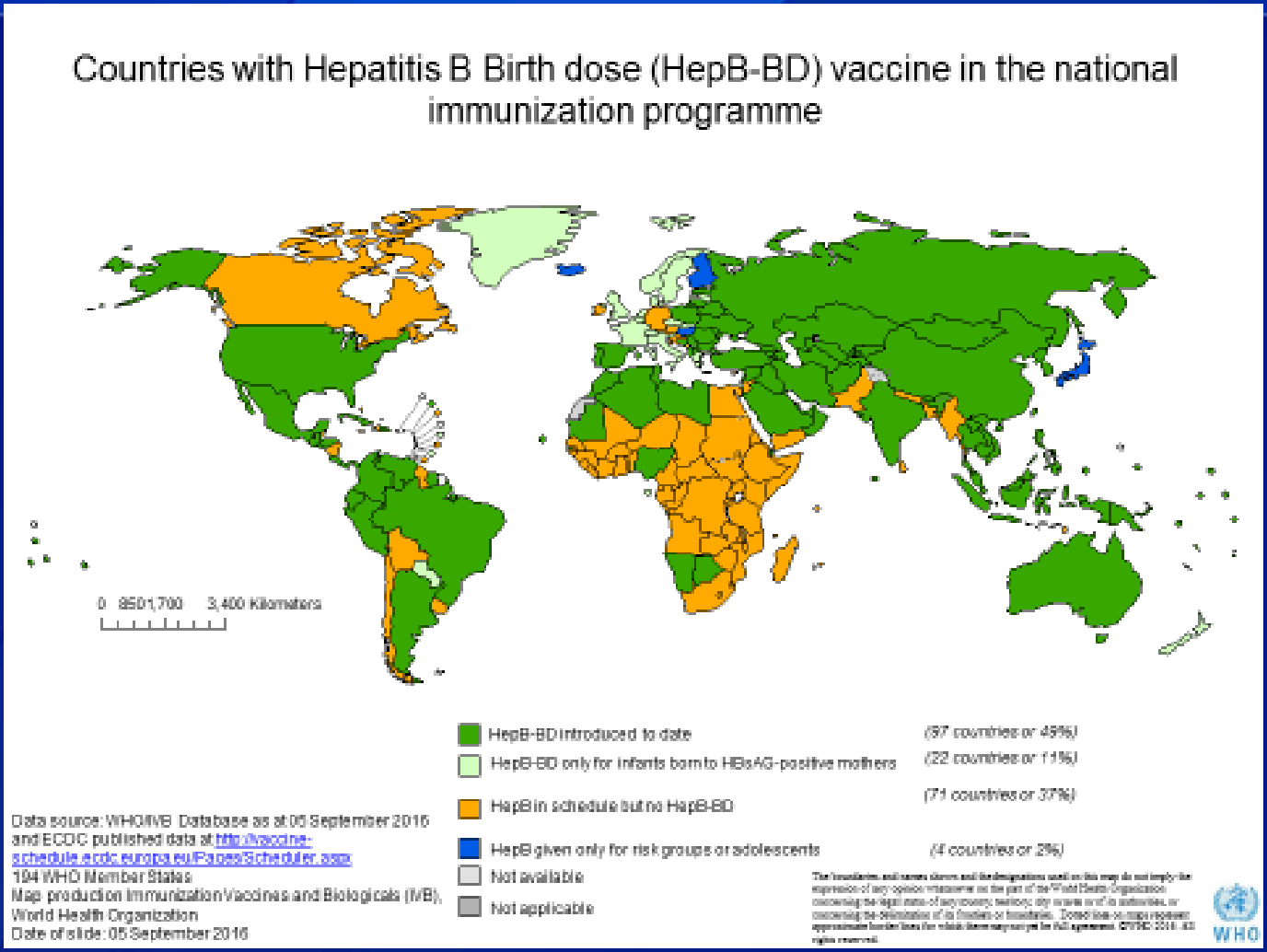
- **Chronic HBV infection develops in approximately:**
  - 90% of infected infants
  - 30% of infected children aged <5 years
  - <5% of infected persons aged ≥5 years
- **Risk of premature death from cirrhosis/liver cancer with chronic HBV infection**
  - ~25% if infected during childhood
  - ~15% if infected after childhood

Mast et al. MMWR 2005; Goldstein et al. Int J Epidemiol 2005.

Perinatal HBV Infection

- **Primarily from mucosal exposure to infected blood and other body fluids during delivery**
- **Without post-exposure prophylaxis, perinatal HBV infection develops in:**
  - ~90% of infants born to mothers who are HBsAg-positive/hepatitis B e antigen (HBeAg)-positive
  - 5-20% of infants born to mothers who are HBsAg-positive/HBeAg-negative

Nelson et al. JPIDS 2014; Mast et al. MMWR 2005.



WHO recommends all infants receive their first dose of HepB vaccine as soon as possible after birth, preferably within 24 hours

WHO Hepatitis B Vaccines Position Paper. Weekly Epidemiological Record 2009.

Efficacy of Post-exposure Prophylaxis for Preventing Perinatal HBV Transmission

- **HepB vaccine alone is 75% effective in preventing perinatal HBV transmission**
  - Hepatitis B immune globulin (HBIG) alone 71% effective
- **Combined efficacy 94%**

Beasley et al. Lancet 1983; Lee et al. BMJ 2006.

Assessment of Serologic Evidence of Protection

- Antibody to hepatitis B surface antigen (anti-HBs) ≥10mIU/mL measured 1-2 months after HepB vaccine series corresponds to vaccine-induced protection
- Protection lasts 30 years or longer among immunocompetent vaccine responders

Leuridan et al. CID 2011; Bruce et al. JID 2016.

HepB Vaccine Seroprotection

- 3-dose vaccine series results in protective anti-HBs (≥10 mIU/mL) in 98% of healthy infants and 90-95% of healthy children and adults aged <40 years
- Lower seroprotection associated with prematurity, advanced age, diabetes, obesity, chronic illness, smoking

Schillie et al. Vaccine 2012; Mast et al. MMWR 2006.

Testing for Anti-HBs and Protection

- **Anti-HBs after HepB vaccine series wanes over time**
  - Measurable anti-HBs can drop to <10 mIU/mL
- **Even when anti-HBs decreases to <10 mIU/mL, breakthrough HBV infection uncommon in immunocompetent vaccine responders**

Middleman et al. Pediatrics 2014; Leuridan et al. CID 2011.

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Strategy to Eliminate HBV Transmission in the U.S.

- **Screen all pregnant women for HBsAg**
  - Prophylaxis (HepB vaccine and HBIG) within 12 hours of birth for all infants born to HBsAg-positive women
- **Universal vaccination of all infants beginning at birth (before hospital discharge) as a safety net**
- **Routine vaccination of previously unvaccinated children and adolescents aged <19 years**
- **Vaccination of adults at risk for HBV infection, including those requesting protection from HBV without acknowledgment of a specific risk factor**

Mast et al. MMWR 2005; Mast et al. MMWR 2006.

Identification of HBV-infected Pregnant Women

- **All pregnant women should be tested routinely for HBsAg during an early prenatal visit**
  - Testing should occur in each pregnancy, even if the woman has been previously vaccinated or tested

HepB Vaccine and HBIG Schedule for Newborn Infants

Maternal HBsAg status	Infant birth weight	
	≥2,000 grams	<2,000 grams
Positive	HepB vaccine and HBIG within 12 hrs of birth	HepB vaccine and HBIG within 12 hrs of birth; birth dose not counted as part of vaccine series
Unknown	HepB vaccine within 12 hrs of birth	HepB vaccine and HBIG within 12 hrs of birth; birth dose not counted as part of vaccine series
Negative	HepB vaccine before hospital discharge	Delay first dose of HepB vaccine until age 1 month or hospital discharge

Permissive Language to Delay Birth Dose

- **"On a case-by-case basis and only in rare circumstances, the first dose may be delayed until after hospital discharge for an infant who weighs ≥2,000 grams and whose mother is HBsAg-negative"**
  - Physician's order to withhold birth dose
  - Copy of the original maternal HBsAg-negative laboratory report on chart
  - Administer by age 2 months
  - Do not delay if high risk situation

Vaccine Series Completion and Postvaccination Serologic Testing

- **HepB vaccine series completed at age 6 months for infants born to HBsAg-positive/unknown mothers, age 6-18 months for infants born to HBsAg-negative mothers**
- **Postvaccination serologic testing (anti-HBs and HBsAg) at age 9-12 month, or 1-2 months after the final dose of the vaccine series if delayed, for infants born to HBsAg-positive mothers**
  - Revaccination (3-dose), followed by repeat postvaccination serologic testing, for infants with anti-HBs <10mIU/mL

Children and Adolescents not Previously Vaccinated

- **HepB vaccination recommended for all children and adolescents aged <19 years**
  - Those not previously vaccinated should be vaccinated routinely at any age with an appropriate dose and schedule

Adults Recommended for HepB Vaccination

- **Persons at risk for infection by sexual exposure**
  - e.g., sex partners of HBsAg-positive persons, men who have sex with men
- **Persons at risk for infection by percutaneous or mucosal exposure to blood**
  - e.g., injection-drug users, health-care and public safety workers, persons with end-stage renal disease, adults with diabetes
- **Others**
  - e.g., international travelers to regions with high or intermediate HBV endemicity, persons with chronic liver disease, persons with HIV infection
- **All persons seeking protection from HBV infection**

Settings in Which all Adults Recommended for HepB Vaccination

- Sexually transmitted disease treatment facilities
- HIV testing and treatment facilities
- Facilities providing drug-abuse treatment and prevention services
- Health-care settings targeting services to injection-drug users
- Correctional facilities
- Health-care settings targeting services to men who have sex with men
- Chronic-hemodialysis facilities and end-stage renal disease programs
- Institutions and nonresidential day care facilities for developmentally disabled persons

Pre-vaccination Serologic Testing

- **Vaccination of persons who are immune to HBV infection (due to past infection or vaccination) does not increase risk for adverse events**
  - Pre-vaccination serologic testing might reduce costs by avoiding vaccination of persons who are already immune

Pre-vaccination Serologic Testing, cont.

- **Pre-vaccination serologic testing recommended for household, needle-sharing, or sex contacts of HBsAg-positive persons; persons born in regions of high HBV endemicity; and HIV-positive persons**
  - Pre-vaccination serologic testing might be cost effective for injection drug users, incarcerated persons, men who have sex with men, and persons born in regions of intermediate HBV endemicity
- **First vaccine dose should typically be administered immediately after collection of blood for serologic testing**

Postvaccination Serologic Testing

- **Serologic testing for immunity not recommended after routine vaccination of infants, children, adolescents, and adults**
- **Postvaccination serologic testing recommended for:**
  - Infants born to HBsAg-positive mothers
  - Health-care personnel
  - Chronic hemodialysis patients
  - HIV-infected and other immunocompromised persons
  - Sex partners of HBsAg-positive persons
- **Testing recommended 1-2 months after the final dose of the vaccine series (at age 9-12 months for infants)**
  - Revaccination recommended if anti-HBs <10 mIU/mL

Post-Exposure Prophylaxis for HBV: Occupational Exposures

	Source patient HBsAg status	
HCP vaccination and response status	Positive	Negative
Unvaccinated	HBIG x1, initiate vaccination	Initiate vaccination
Previously vaccinated		
Known responder	No prophylaxis	No prophylaxis
Known non-responder		
After 3 doses	HBIG x1, initiate revaccination	Initiate revaccination
After 6 doses	HBIG x2 (separated by 1 month)	No prophylaxis

Post-Exposure Prophylaxis for HBV: Non-Occupational Exposures

	Management	
Exposure	Unvaccinated person	Vaccinated person
HBsAg-positive source	HepB vaccine series and HBIG	HepB dose
Source with unknown HBsAg status	HepB vaccine series	No prophylaxis

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Work Group Supports Testing HBsAg-Positive Pregnant Women for HBV DNA

- **Identifies infants at greatest risk for perinatal HBV infection**
  - AASLD suggests maternal antiviral therapy to reduce the risk of *perinatal* transmission when maternal HBV DNA >200,000 IU/mL
- **Prioritizes women for referral for HBV management and therapy**

Work Group Supports Postvaccination Serologic Testing for Infants whose Mother's HBsAg Status Remains Unknown Indefinitely

- **For example, when infant surrendered confidentially and anonymously shortly after birth**
  - All 50 states have some form of safe-haven law to reduce risk of infant abandonment
  - Medical data on infants safely-surrendered lacking

Work Group Deliberated over Removal of Permissive Language for Birth Dose after Hospital Discharge

Existing language

For all medically stable infants weighing ≥2,000 grams at birth and born to HBsAg-negative mothers, the first dose of vaccine should be administered before hospital discharge. Only single-antigen HepB vaccine should be used for the birth dose.

On a case-by-case basis and only in rare circumstances, the first dose may be delayed until after hospital discharge for an infant who weighs ≥2,000 grams and whose mother is HBsAg-negative.

Revised language (proposed)

For all medically stable infants weighing ≥2,000 grams at birth and born to HBsAg-negative mothers, the first dose of vaccine should be administered within 24 hours of birth. Only single-antigen HepB vaccine should be used for the birth dose.

Removal of Permissive Language for Delaying Birth Dose

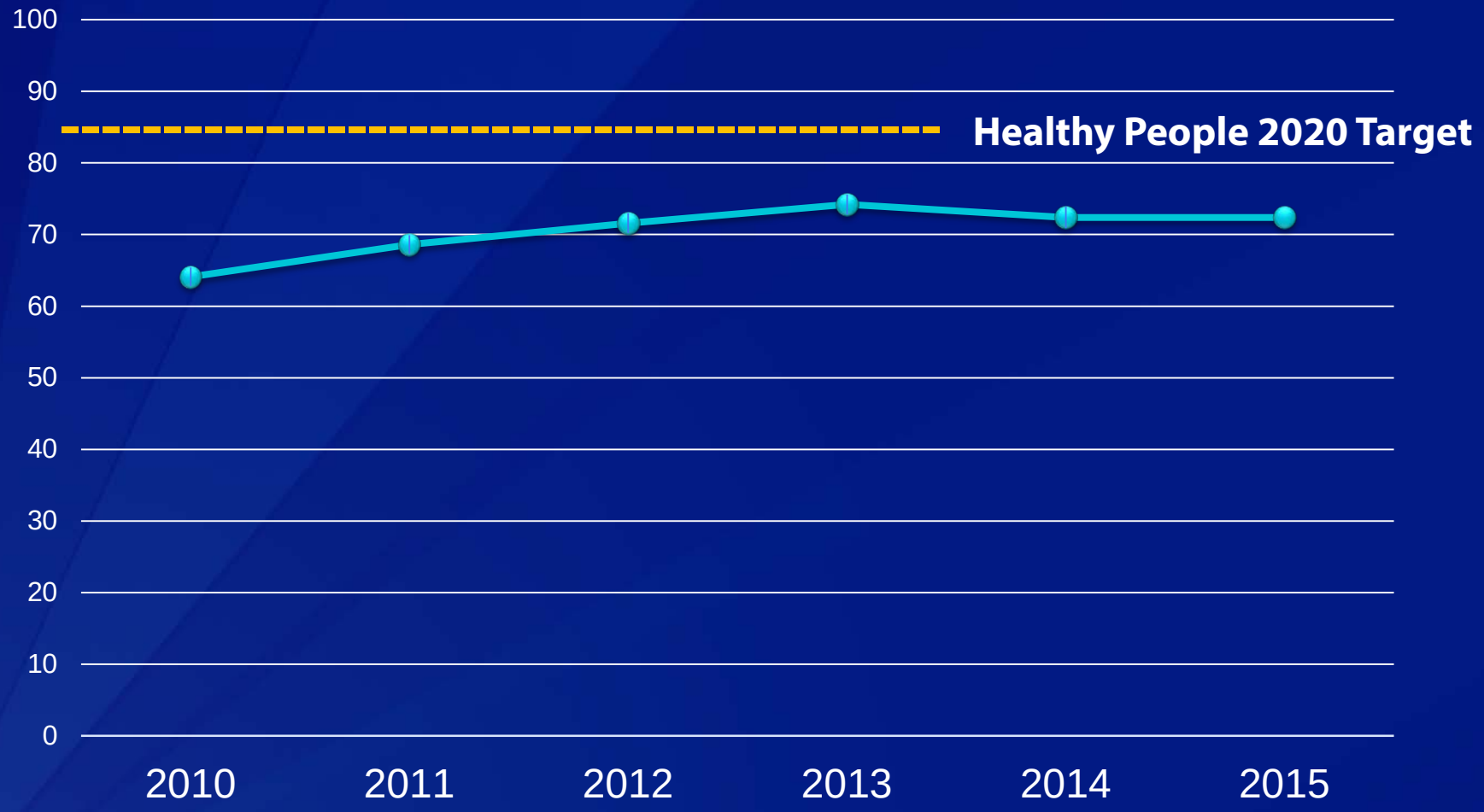
- **Infants born to HBsAg-positive mothers in British Columbia, 1984-1989 (n=770)**

Age at first dose (days)	Proportion of participants (%)	Infection rate per 1,000	P-value
1-3	96	47	<0.001
4-7	2	0	
8-61	1	222	
≥62	1	333	

- **aOR for increase in infection with increasing age at 1st dose: 4.3 (95% CI, 2.2-8.4)**

Marion et al. Am J Epidemiol 1994.

HepB Birth Dose* Coverage — National Immunization Survey, 2010-2015



*One dose by 3 days

Removal of Permissive Language for Delaying Birth Dose

- **Universal birth dose prior to hospital discharge serves as a safety net to prevent HBV transmission for infants not identified due to errors in:**
  - Maternal HBsAg testing
  - Transcription of maternal HBsAg test results
  - Reporting maternal HBsAg test results
- **Work Group consensus not reached**

Work Group Supports Providing Examples of Chronic Liver Disease

- **Examples include, but are not limited to, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and liver function tests >2 times the upper limit of normal**
  - ≥3-dose HepB vaccine coverage among adults aged ≥19 years with chronic liver conditions (2014): 29.8% (95% CI, 23.9-36.5)

Williams et al. MMWR 2016.

CDC Program Supports Explicit Recommendation for HepB Vaccine for Persons with HCV Infection

- **Increasing incidence of HBV and HCV infections**
  - Young, non-urban adults who inject drugs
  - East of Mississippi River (e.g., Kentucky, Tennessee, West Virginia)
- **Risk for liver disease progression**
  - Multiplicative risk for hepatocellular carcinoma with HBV/HCV co-infection

Zibbell et al. MMWR 2015; Harris et al. MMWR 2016; Bell et al. Acta Gastroenterol Belg 2000.; Oh et al. BMC Cancer 2012.

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Discussion & Vote

Does ACIP approve removing the permissive language for the HepB vaccine birth dose to be administered after hospital discharge?

Does ACIP recommend HepB birth dose within 24 hours of birth for infants weighing ≥2,000 grams born to HBsAg-negative mothers?

Does ACIP approve the revised HepB statement?