Elimination of Perinatal Transmission of Hepatitis B

Anitra P. Denson, MD, MPH
Perinatal Coordinator
HID/AIDS, Hepatitis, STD and TB Administration
DC Department of Health
Statement of Disclosure

• No financial relationships with any commercial interests
Agenda

- What is Hepatitis B, and how can it be prevented
- Epidemiology of Hepatitis B in the US
- Recommendations for screening and treatment
- Current reporting requirements and associated prevention activities
A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States
Hepatitis B

- Hepadnaviridae family
  - Surface antigen
  - Core antigen
  - Extracellular core antigen
  - Partially double-stranded DNA genome
Hepatitis B – Clinical Features

• Incubation period of 45-160 days (average 120 days)
• Non-specific prodrome
  • Fever, malaise, headache, myalgia
• At least 50% of infections are asymptomatic
• 1-2% of acutely infected persons progress to fulminant hepatitis

Question 1

• Compared to HIV, Hepatitis B Virus (HBV) is:
  • 1) More infectious
  • 2) Less infectious
  • 3) The same
  • 4) I have no idea.....
Question 1

• Compared to HIV, Hepatitis B Virus (HBV) is:
  • 1) More infectious
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  • 3) The same
  • 4) I have no idea.....
Hepatitis B – Worldwide Prevalence


Government of the District of Columbia HIV/AIDS, Hepatitis, STD, TB Administration
Hepatitis B – U.S.

- An estimated 800,000 – 1.4 million chronic HBV infections
- 5,000 – 8,000 become chronically infected every year

HBV in pregnant women

- The CDC estimates 25,600 birth to HBsAg positive women
- Perinatal HBV exposure can occur in utero or during delivery
- An estimated 952 perinatal HBV infections occur in the U.S.
- CDC estimates between 55-104 births to HBsAg positive women in DC

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
  - 10% of infants infected
  - 90% of infected infants become chronically infected

*in the absence of postexposure prophylaxis

Risk of chronic hepatitis by age

- Infant: 90%
- 1-5 Years: 30%
- > 5 Years: <5%
Hepatitis Prevention Strategy

**Strategy to Eliminate Hepatitis B Virus Transmission—United States**

- Prevent perinatal HBV transmission
- Routine vaccination of all infants
- Vaccination of children in high-risk groups
- Vaccination of adolescents
- Vaccination of adults in high-risk groups
Screening in Pregnancy
Question 2

• Which of the following women should be screened for HBV during her pregnancy?
• 1) 27y female, recently immigrated from Thailand
• 2) 32y female, history of HBsAg+ during a previous pregnancy
• 3) 20y female, born in the U.S.
• 4) 39y female, 3rd pregnancy, tested HBsAg- in previous pregnancies
• 5) All of the above
Question 2

• Which of the following women should be screened for HBV during her pregnancy?

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• 2) 32y female, history of HBsAg+ during a previous pregnancy

• 3) 20y female, born in the U.S.

• 4) 39y female, 3rd pregnancy, tested HBsAg- in previous pregnancies

• 5) All of the above
Recommendations for HBV screening during pregnancy

- A woman should be screened for HBV at the first prenatal visit for each pregnancy
- If she is unvaccinated and HBsAg-, she can be vaccinated during the pregnancy
- Repeat screen at delivery for women at high risk
- Screen at delivery if result of previous test is not available
# HBV Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Hepatitis B Surface Antigen</td>
</tr>
<tr>
<td></td>
<td>Acute or chronic infection</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Antibodies to HBsAg</td>
</tr>
<tr>
<td></td>
<td>Past infection OR post-vaccination</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Antibodies to HB core antigen</td>
</tr>
<tr>
<td></td>
<td>Acute, chronic or past infection</td>
</tr>
<tr>
<td>IgM HBc</td>
<td>IgM antibodies to HB core antigen</td>
</tr>
<tr>
<td></td>
<td>Acute or recent infection</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Hepatitis Be antigen</td>
</tr>
<tr>
<td></td>
<td>High-level HBV replication and viremia</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Antibodies to HBe</td>
</tr>
<tr>
<td></td>
<td>Acute, resolved, or chronic infection</td>
</tr>
<tr>
<td>HBV DNA</td>
<td>Hepatitis B Virus DNA</td>
</tr>
<tr>
<td></td>
<td>Active infection, acute or chronic</td>
</tr>
</tbody>
</table>
Interpreting the Results

<table>
<thead>
<tr>
<th>Patient</th>
<th>HBsAg</th>
<th>Anti-HBc</th>
<th>Anti-HBs</th>
<th>HBV DNA</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Neg</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td></td>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td><strong>Susceptible!</strong></td>
</tr>
<tr>
<td>2</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td>Neg</td>
<td>Past Infection</td>
</tr>
<tr>
<td>3</td>
<td>Neg</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Vaccinated</td>
</tr>
<tr>
<td>4</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Acute/Chronic</td>
</tr>
</tbody>
</table>
HBV Treatment During Pregnancy
To treat or not to treat...

Antiviral Therapy in Chronic Hepatitis B Viral Infection During Pregnancy: A Systematic Review and Meta-Analysis

Findings

• Maternal Outcomes
  • Tenofovir, telbivudine and lamivudine all showed improved HBV DNA suppression compared to control
  • Telbivudine also showed improved ALT and higher rate of HBeAg loss
  • All treatment compared to control did not show any increase in postpartum hemorrhage rate, cesarean section rate

Findings

• Infant outcomes
  • Use of any antiviral in pregnant women reduced the likelihood of MTCT (RR=0.3)
  • Use of any antiviral reduced the risk of infant HBsAg+ by 13.4%
  • Use of any antiviral reduced the risk of + HBV DNA by 18.7%
  • No statistical difference on reports of congenital malformations rate, prematurity rate or Apgar scores

Treatment During Pregnancy

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.

Quality/Certainty of Evidence: Low
Strength of Recommendation: Conditional

Treatment During Pregnancy

- Antiviral therapy should be started at 28-32 weeks of gestation
- Treatment can be discontinued from birth to 3m postpartum
- Tenofovir – Category B
- Telbivudine – Category B
- Lamivudine – Category C

### Summary of Treatment Recommendations


<table>
<thead>
<tr>
<th>American Association for the Study of Liver Diseases</th>
<th>Antiviral therapy is suggested to reduce the risk of perinatal transmission of HBV in HBsAg-positive pregnant women with HBV DNA levels &gt;200,000 IU/mL.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality/Certainty of Evidences Low</td>
<td>The use of antiviral therapy is not recommended to reduce the risk of perinatal transmission of HBV in HBsAg-positive pregnant women with HBV DNA levels ≤200,000 IU/mL.</td>
</tr>
<tr>
<td>Strength of Recommendation: Conditional</td>
<td></td>
</tr>
<tr>
<td>World Health Organization</td>
<td>In HBV-monoinfected pregnant women, the indications for treatment are the same as for other adults, and TDF is recommended.</td>
</tr>
<tr>
<td>European Association for the Study of the Liver</td>
<td>No recommendation was made on the routine use of antiviral therapy to prevent mother-to-child HBV transmission as a result of the current limited and low-quality evidence base.</td>
</tr>
<tr>
<td></td>
<td>Tenofovir, lamivudine, or TDF (as a potent FDA Pregnancy Category B agent) may be used for the prevention of perinatal and intrapartum HBV transmission in the last trimester of pregnancy in HBsAg-positive women with high levels of viremia (serum HBV DNA &gt;6-7 log10 IU/mL).</td>
</tr>
<tr>
<td>Evidence Grade: B1</td>
<td></td>
</tr>
<tr>
<td>Asian-Pacific Association for the Study of the Liver</td>
<td>In pregnant women with chronic HBV infection who need antiviral therapy, TDF is the drug of choice for most infected during the first through third trimesters of pregnancy. TDF is a Pregnancy Category B drug with adequate safety data in HIV-positive women and has the least chance of viral resistance.</td>
</tr>
<tr>
<td>Evidence Grade: B1</td>
<td>For the reduction of risk of mother-to-child transmission that occurs during the perinatal period, the use of short-term maternal nucleoside analogues starting from 28 to 32 weeks of gestation is recommended using either TDF or telbivudine for those mothers with HBV DNA levels &gt;6-7 log10 IU/mL.</td>
</tr>
<tr>
<td>Evidence Grade: B2</td>
<td>Breastfeeding is discouraged during maternal nucleoside analogue treatment. For those with alanine transaminase flares detected during the treatment period, continuation of antiviral treatment according to maternal liver disease status may be indicated.</td>
</tr>
<tr>
<td>Evidence Grade: B2</td>
<td></td>
</tr>
</tbody>
</table>

**Note:**
- FDA, US Food and Drug Administration; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; TDF, tenofovir disoproxil fumarate.
Management During Delivery

• For the mother
  • No prenatal care/unknown HBsAg status
  • TEST, TEST, TEST!

• For the mother
  • Known HBsAg positive
  • Chronic Hep B is not an indication for C-section
Management During Delivery

- Infant – HBsAg negative mom
  - No need for HBIG
  - Hep B vaccine given at birth

- Infant – HBsAg positive mom
  - HBIG
  - Hep B vaccine

- Infant – Unknown HBsAg status
  - Hep B vaccine
  - HBIG can be given up to 7 days after delivery once mother status is documented
Infant Management – HBsAg+

- All infants born to HBsAg+ mothers should receive both vaccine and HBIG
- For infants <2000 gm, the first Hep B vaccine dose should not be counted in the 3 dose vaccine series
- Complete post-vaccine serology testing (9-12m of age)
Infant Management – HBsAg -

- Infant should receive birth dose within 12 h
- For infants <2000gms wait until 1m of age
- Post-vaccine serology testing at 9-12m
Infant Management – Unknown HBsAg

- ≥2000 grams
  - Hep B vaccine within 12 hours of delivery
  - Verify mother’s status, if HBsAg+ give HBIG within 7 days of delivery
- <2000 grams
  - Hep B vaccine within 12 hours of delivery
  - If mother’s status isn’t documented, give HBIG within 12 hours of delivery
  - Infant will still require 3-dose Hep B vaccine

- Post-vaccine serology testing at 9-12m
Post-exposure prophylaxis

• 85-95% effective with Hep B vaccine and HBIG
• >90% of term infants develop protective antibody levels
• Uninfected infants who do not develop protective levels, repeat vaccine series

DOH Prevention Activities
Report the Pregnancy!!

- Pregnancy in HBsAg+ women is a reportable condition in the District
- Report form available online
Pregnancy Reporting

Patient Information

Last Name  First Name  DOB
Address
City  State  Zip Code
Phone Number  Emergency Contact:  Phone:

Race  American Indian/Alaska Native  Asian  Black or African American  Native Hawaiian or Other Pacific Islander  White  Unknown
Ethnicity:  Hispanic/Latino  Not Hispanic/Latino  Unknown

DIAGNOSIS:  HIV  Hepatitis B  Hepatitis C  HSV  Syphilis  Other
(Please attach a copy of all lab reports)

Linkage to Care

Is the patient engaged in obstetrical care?  Yes  No  EDD:
Is the patient engaged in specialist care?  Yes  No  N/A  Date of Diagnosis:
Is the patient currently on treatment for the above diagnosis?  Yes  No
If yes, what medications?
Case management

- Identify infants requiring case management
- Reminder system for Hep B vaccine
- Document Hep B vaccine doses in DOCIIS
- Verify post-vaccine serology testing (PVST)
- http://doh.dc.gov/page/PerinatalHepB
Working with Providers

• Make sure providers and hospitals are aware of the most recent recommendations
• Verify that there are policies and procedures in place to ensure timely dosing for all infants in the District
• Case management of infants to ensure timely vaccine dosing and PVST where appropriate
Hospital Policy

• All birthing hospitals should:
  • Implement policy and procedures to administer the recommended Hepatitis B vaccine birth dose
  • Implement standing orders for administration of Hep B vaccine as part of routine care of all medically stable infants weighing ≥2000gm at birth
  • Follow national recommendations for prophylaxis of all newborn infants born of HBsAg+ women and to those whose status is unknown
  • Ensure a copy of the original lab report from mother’s HBsAg screening test is placed in the infant’s chart, or is available
Hepatitis B Birth Dose Honor Roll

- Recognition by the Immunization Action Coalition (IAC) for achieving
  - At least a 90% vaccination rate
  - Written policies, procedures and protocols for implementing the universal Hepatitis B vaccine birth dose
- Apply at www.immunize.org
Other Perinatally transmitted infections

- HIV – 1\textsuperscript{st} and 3\textsuperscript{rd} trimester screening
- Syphilis – recent increase in congenital syphilis in the country
- Hepatitis C – future consideration
Summary recommendations

- The CDC and the U.S. Preventative Services Task Force (USPSTF) recommend:
  - Screening all pregnant women for HBsAg at the first prenatal visit
  - For HBsAg+ women, test for HBeAg, HBV DNA, ALT
  - Screening women with unknown status or at higher risk when admitted for delivery
  - Administering HBIG and Hep B vaccine within 12 hours of birth for infants born to mothers who are HBsAg+
  - Administering HBV vaccine within 12 hours of birth for infants born to mothers with unknown HBV status; HBIG within 7 days if indicated
  - Providing information about HBV for pregnant women with HBV and educating about importance of vaccination series for infant and PVST
  - Referral to case management
Questions???