UPDATE HEPATITIS B IMMUNIZATION

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Discolosures

• No disclosures
• I will mention non licensed hepatitis B vaccine
Goals of Presentation

- Understand the epidemiology of hepatitis B virus (HBV) infection in the US
- To review screening recommendations for pregnant women for HBV infection
- To discuss the importance of the birth dose
- To understand the impact of infant and childhood hepatitis B vaccination programs in Alaska and the USA
- To discuss new recommendations for the administration of hepatitis B vaccine in adults
- To review data from Alaska Study on how long protection from hepatitis B vaccine lasts in adults and children
Pop Quiz

35 y.o. Mother who was born in the Philippines and came to US at age 5 who is negative for HBsAg. She is married to a US born Caucasian male. All of her children have been vaccinated against HBV. Her provider tells her that since she is HBsAg-negative she would suggest waiting until the baby is 2 months old to start hepatitis B vaccine. The mother is a stay at home mom.

a) The child is at not risk of HBV infection in the 1st 2 months of life and this is perfectly acceptable option
b) The child is at a remote risk of HBV infection but the risk benefit ratio of vaccination allows the option to delay vaccine
c) This child could conceivable be at risk for HBV infection
d) A very low risk of autism makes it a smart decision to refer vaccination
If anti-HBs (-) and at high risk consider vaccination of the pregnant woman during pregnancy or postpartum.

HBV Screening Algorithm for Pregnant Women

HBsAg and anti-HBs tests

- HBsAg (-)
  - If anti-HBs (-) and at high risk consider vaccination of the pregnant woman during pregnancy or postpartum
- HBsAg (+)
  - Order additional tests:
    - ALT
    - HBeAg, anti-HBe
    - HBV DNA level
  - HBeAg (+) or HBV DNA >20,000 IU/mL or ALT elevated:
    - Refer to specialist immediately during pregnancy
  - HBeAg (-) or HBV DNA <2,000 IU/mL or ALT normal:
    - Refer to specialist or primary care provider postpartum

*New norms establish elevated ALT as ≥19 IU/L for women, ≥30 IU/L for men

Recommend screening of all household and sexual contacts

- HBsAg (-) Anti-HBs (-)
  - Vaccinate
- HBsAg (-) Anti-HBs (+)
  - Immune (No follow-up required)
- HBsAg (+)
  - Primary care provider to evaluate and monitor

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Apuzzio J, et al. The Female Patient 2012;37(5):30-4
Acute Hepatitis B Virus Infection with Recovery

Weeks after Exposure
Acute Hepatitis B Virus Infection with Progression to Chronic Infection

- IgM anti-HBc
- Total anti-HBc
- HBsAg
- Acute (6 months)
- Chronic (Years)
- HBeAg
- anti-HBe
- IgM anti-HBc
Primary Modes of HBV Transmission by Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Primary Mode of Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>• Perinatal</td>
</tr>
<tr>
<td>Early childhood</td>
<td>• Unsafe injections</td>
</tr>
<tr>
<td></td>
<td>• Inapparent parenteral*</td>
</tr>
<tr>
<td>Late childhood, adolescence, adulthood</td>
<td>• Unsafe injections</td>
</tr>
<tr>
<td></td>
<td>• Sexual</td>
</tr>
<tr>
<td></td>
<td>• Injection drug use</td>
</tr>
</tbody>
</table>

* From family member to child or child to child, through inapparent exposure to HBV infected blood from open cuts
Rates of Symptomatic and Chronic HBV by Age at Infection

<table>
<thead>
<tr>
<th>Age at Infection</th>
<th>Symptomatic HBV Infection</th>
<th>Chronic HBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 year</td>
<td>&lt; 1 %</td>
<td>90%</td>
</tr>
<tr>
<td>1 – 5 years</td>
<td>5 – 15%</td>
<td>25 - 50%</td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>20 – 50%</td>
<td>6 – 10%</td>
</tr>
</tbody>
</table>

McMahon BJ, J Infect Dis 1985;151:599
Hyams KC. Clin Infect Dis 1995;20:992
2 Modes of HBV Transmission in Infancy and Early Childhood

- “Vertical” .... from infected mother during pregnancy or delivery (perinatal infections)
- “Horizontal”.... from infected household member or close contact
Perinatal Transmission

- Transmission from infected mother to infant
  - Predominantly occurs in HBV genotype C
- Occurs through percutaneous and permucosal exposure to mother’s blood
- Usually occurs during birth
- *In utero* transmission rare: accounts for ~5% of perinatal infections
- HBV **not** transmitted by breastfeeding
Risk of Perinatal HBV Transmission by HBeAg Serostatus of Mother

<table>
<thead>
<tr>
<th>Serostatus of Mother</th>
<th>% Infants Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg Positive</td>
<td>85% - 100%</td>
</tr>
<tr>
<td>HBeAg Positive</td>
<td></td>
</tr>
<tr>
<td>HBsAg Positive</td>
<td>5% - 30%*</td>
</tr>
<tr>
<td>HBeAg Negative</td>
<td></td>
</tr>
</tbody>
</table>

Depends on level of HBV DNA
Perinatal HBV Infection in the USA

• According to a report in 2010 by the Institute of Medicine, an estimated 1,000 infants in the US per year develop chronic hepatitis B infection:
  • 2 primary reasons are:
    • Lack of screening of mother for HBsAg
    • Failure to give birth dose, especially when mother has not been previously screened. >90% of HBV transmission can be prevented by giving the birth dose followed by completing immunization schedule
  • Other reasons included:
    • Very high HBV DNA viral load in mother (> 10 log copies/ml)
      • Antiviral prophylaxis of mother may prevent this from occurring
    • Failure to give HBIG post delivery
HBV in the Environment

- Stable in environment for at least 7 days
- Present in absence of visible blood
- Transmission via contaminated objects
Horizontal HBV Transmission during Early Childhood (0 - 5 Years)

- Contact with HBV in body fluids (blood, serum, saliva) from infected household members (including mother) or contact with contaminated surfaces
- Transmission via breaks in skin, e.g., injuries or dermatitis, or via mucosal exposures, e.g., sharing tooth brushes
- HBV resistant to drying, alcohol; remains stable on environmental surfaces for ~ 7 days
- Pre-exposure vaccination starting at birth is best prevention of horizontal HBV transmission

Bancroft WH J Infect Dis 1977;135:79
Beasley RP J Infect Dis 1983;147:85
Changing Patterns of U.S. Immigration 1820-2004

*Projected based on 2001-2004 data

Source: Yearbook of Immigration Statistics, 2004
Recombinant Hepatitis B Vaccine Efficacy (VE) among Infants Born to HBsAg, HBeAg-Positive Women by Vaccine Type and Dosage

<table>
<thead>
<tr>
<th>Country</th>
<th>HBI G</th>
<th>Hepatitis B Vaccine Efficacy Without and With HBIG Ages 0, 1, 6 months</th>
<th>Other Dosages &amp; Schedules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burma Thailand</td>
<td>No</td>
<td>MSD 5 ug</td>
<td>59%-79%</td>
</tr>
<tr>
<td>Thailand</td>
<td>GSK 10 ug</td>
<td>92%</td>
<td>95%</td>
</tr>
<tr>
<td>Thailand USA</td>
<td>Yes</td>
<td>MSD 5 ug</td>
<td>88%-97%</td>
</tr>
<tr>
<td>Thailand Taiwan</td>
<td>GSK 10 ug</td>
<td>100%</td>
<td>89%-98%</td>
</tr>
</tbody>
</table>

Hepatitis B Vaccines

- Available since 1981
- Composed of HBsAg adsorbed to aluminum hydroxide
- Elicits development of neutralizing antibodies to HBsAg (anti-HBs) which confer protection from infection
- Plasma-derived and recombinant formulations
Administration of Hepatitis B Vaccine

- Typically given as a three dose series
  - Four dose series used routinely in Alaska because of combination DTaP-HepB-IPV (Pediarix)
  - Schedule flexible
    - 0,1-2,6 month schedule most commonly used
- Microgram dose varies by manufacturer and age of recipient
- Vaccines can be used interchangeably if given at dose recommended by manufacturer
Four Doses of Hepatitis B Vaccine vs. Three Doses

- Excellent protection (>95%) is provided with 4 doses of hepatitis B vaccine
- A fourth dose does not improve seroconversion rate but would provide higher level of anti-HBs post vaccination series
- Unfortunately, well conducted randomized controlled studies comparing 3 to 4 doses of vaccine are not available
- There is absolutely no harm to getting a fourth dose of hepatitis B vaccine for either an infant or an adult
  - However, extra doses for adults are not needed; documentation of receiving 3 doses of vaccine at any time is sufficient
Hepatitis B Vaccine Safety

- Hepatitis B vaccine administered to millions of infants, children and adults worldwide
- Side effects rare
- Anaphylaxis estimated to occur in 1 per 600,000 doses administered
- No scientific data linking hepatitis B vaccine and
  - multiple sclerosis
  - other autoimmune diseases
  - Autism
Summary of Rationale for Universal Birth Dose of Hepatitis B Vaccine

- Prevents most vertical HBV transmission to infants born to HBsAg-positive women, and
- Provides “safety net” for infants whose mother’s status unknown or uncertain at delivery
- Prevents horizontal HBV infection during childhood regardless of HBsAg-status of mother & contacts
- First dose at birth results in higher rates of on-time completion of hepatitis B series, other vaccines*

Figure 3.1. Reported number of acute hepatitis B cases — United States, 2000–2011

Source: National Notifiable Diseases Surveillance System (NNDSS)
Figure 3.2. Incidence of acute hepatitis B, by age group — United States, 2000–2011

Source: National Notifiable Diseases Surveillance System (NNDSS)
Figure 3.4. Incidence of acute hepatitis B, by race/ethnicity — United States, 2000–2011

Source: National Notifiable Diseases Surveillance System (NNDSS)
Incidence Symptomatic Hepatitis B in Alaska Native Peoples 1981-2008

- CDC/HIS Vaccine Demonstration Program begins in 16 villages of Yukon Kuskokwim Delta
- Statewide Program begins-all susceptibles immunized: pregnant women screened/infants HBvax + HBIG
- begin universal newborns immunization
Number of HBsAg-positive Alaska Native Children Under 20 Years of Age: 1988-2008

Figure 2.

No. HBsAg Positive

% HBsAg+

Year


0 50 100 150 200 250 300 350 400 450 500

0.0% 0.2% 0.4% 0.6% 0.8% 1.0% 1.2% 1.4%
HCC in Alaska Natives <20 years of age

P value for trend = 0.002

Hepatology 2011;54:801-7
Does Hepatitis B Vaccine Provide Long-term Protection from HBV Infection?

• Persons fully vaccinated in child or adulthood who respond is protected from subsequently acquiring acute symptomatic hepatitis B and developing the chronic carrier state for at least 30 years after vaccination

• Infants who respond to hepatitis B vaccine are also protected for up to 20 years, though anti-HBs is likely to have disappeared and they may not respond to a booster dose

  • Cellular immunity likely provides long-term protection
    • Breakthrough infections are reported to not result in symptomatic infection or lead to chronic carrier stage
    • Recent study shows persons exposed after blood transfusion to HBV who were vaccinated had rapid development of innate immunity
    • Infants in Taiwan who received an incomplete vaccination series starting at birth had decrease risk of subsequent acute hepatitis and HCC compared to unvaccinated infants
Outbreaks of Hepatitis B Virus Infection among Persons with Diabetes with Blood Glucose Monitoring, 1990-2012

No. Outbreaks Reported to CDC

Year

0 1 2 3 4 5 6 7


Hospital (2)
Nursing Home (8)
Assisted Living Facility (16)
Transmission of Hepatitis B Virus (HBV) during Blood Glucose Monitoring

Infected with HBV

Indirect person to person contact transmission

Infected with HBV

Blood contaminated equipment/supplies (includes no visible blood); HBV infectious for >7 days
Pop Quiz

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Pop Quiz

- Correct Answer:
  - c) This child could conceivable be at risk for HBV infection
  - WHY?
    - There is a large extended family most of whom were born in the Philippine Islands
    - Mom is getting pressure to bring baby over to see relatives in the Philippine Islands when the baby is 4-6 weeks old
  - What could the provider do if she does not want to give the birth dose?
    - Investigate all family members and friends from mom’s family to make sure they were screened and vaccinated and urge no contact with any members found to be HBsAg+
    - Tell her she absolutely cannot go the Philippine Islands now.
    - Strict isolation for mother and child till child is 8 weeks old and gets 1st dose of vaccine.
Hepatitis B: What Hospitals Need to Do to Protect Newborns