Hepatitis B

Introduction

Hepatitis B virus (HBV) is a DNA virus. The outer surface of the virus contains the hepatitis B surface antigen (HBsAg). Other important antigenic components are hepatitis B core antigen (HBcAg), and hepatitis B early antigen (HBeAg). Chronic carriers have large amounts of surface antigen in their liver and blood and are HBsAg positive. They are more infectious if they are also early antigen (HBeAg) positive. Persons who are immune because they have recovered from HBV infection have core antibody (HBcAb) and surface antibody (HBsAb). Persons who are immune because of vaccination just have HBsAb, because vaccine is made from purified surface antigen.1

Neonates who catch HBV from their mothers are almost always asymptomatic. Following acute infection, 1 to 10% of those infected as adults and up to 90% of those infected as neonates remain persistently infected for many years, becoming chronic carriers.2 Chronically infected carriers of HBV are identified by the long-term presence (longer than 6 months) of circulating HBsAg. Vertical transmission of hepatitis B from a carrier mother to baby can be prevented in >90% by administration of hepatitis B vaccine and immunoglobulin to the baby within 72 hours of birth.3-7 In vaccinated infants, it is then thought that breast feeding offers no additional risk of transmission to the infant.8-10

Incidence

Hepatitis B prevalence in pregnant women in Sydney South West Area Health Service
January 2007 - November 2008, by hospital of delivery:

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Number of women tested</th>
<th>Number HBsAg positive</th>
<th>Rate/100 women</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPA</td>
<td>9452</td>
<td>112</td>
<td>1.2</td>
</tr>
<tr>
<td>Canterbury</td>
<td>2963</td>
<td>73</td>
<td>2.5</td>
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<tr>
<td>Bankstown-Lidcombe</td>
<td>3964</td>
<td>51</td>
<td>1.3</td>
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<td>Liverpool</td>
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</tr>
<tr>
<td>Fairfield</td>
<td>3685</td>
<td>114</td>
<td>3.1</td>
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</table>
Risk Factors

Routes of transmission include:
- Transmission of hepatitis B may result from percutaneous inoculation or mucosal contact with blood or sexual secretions from an HBsAg-positive individual.
- Transmission from infected mother to neonate (vertical transmission), usually occurring at or around the time of birth,
- Breastfeeding\textsuperscript{11}
- Child-to-child (horizontal) transmission, usually through contact between open sores or wounds,

Risk of vertical transmission to infant: in women with acute hepatitis B infection in pregnancy:
- 1\textsuperscript{st} trimester = \textasciitilde10% \textsuperscript{11}
- 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester = \textasciitilde75\% \textsuperscript{11}

The risk of vertical transmission is increased in infants of hepatitis BeAg positive mothers:
- HBsAg and HBeAg positive mothers = \textasciitilde71\%.\textsuperscript{3-6}
- HBsAg positive and HBeAg negative = \textasciitilde10\%.\textsuperscript{7}

Risk of infant becoming a hepatitis B carrier: is age dependent with more than 90\% of neonates who contract hepatitis B developing carrier status (Figure below).\textsuperscript{2}

Consequences

Effect of hepatitis B on pregnancy: Susceptible women who develop acute hepatitis B during pregnancy may have an illness indistinguishable from that in the general population. There have been reports of exacerbation of hepatitis and even fulminant hepatic failure in the peripartum period. The effect of chronic HBsAg carrier status is less clear with conflicting reports suggesting either hepatitis B infection in pregnancy is not associated with adverse pregnancy outcomes, or with gestational diabetes, antepartum haemorrhage and preterm delivery.

Effect on neonate: Infected neonates are almost invariably asymptomatic.

Long term consequences: Carriers of HBV are capable of transmitting the disease, though often remain asymptomatic and may not be aware that they are infected. Most of the serious complications associated with hepatitis B infection occur in HBV carriers. Chronic active hepatitis develops in > 20% of carriers, and up to 25% die prematurely of cirrhosis or hepatocellular carcinoma.

Diagnosis

Mother:

All pregnant women are screened for HBsAg in pregnancy. If HBsAg positive assess the stage of disease to determine infant’s risk of vertical transmission by determining:

- HB e status (HBeAg and anti-HBe)
- HBV DNA level (indicates amount of virus in bloodstream)

Infant:

- All infants born to HBsAg positive or HBeAg positive or HBV PCR positive mothers should have follow-up serology at 12 months including HBsAg – provide referral to GP.
- If HBsAg positive:
  - Perform LFTs, HBeAg
  - Refer for ongoing management:

Contact details:

<table>
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<tr>
<th></th>
<th>CHW</th>
<th>SCH</th>
<th>Kaleidoscope</th>
</tr>
</thead>
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<td>02 9382 1111</td>
<td>02 4921 3265</td>
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<td>Infectious Diseases</td>
<td>02 9845 3418</td>
<td>02 9382 1508</td>
<td>02 4921 4473</td>
</tr>
</tbody>
</table>

Interventions

Infection control – see infection control policy.

Prevention of Vertical transmission
1. Immunisation:

- **HBsAg positive mothers:**
  Infants of HBsAg positive mothers should receive within 12 hours (latest 48 hours) of birth:
  
  - H-B-VAX II (5µg/0.5ml), AND
  - Hepatitis B immunoglobulin (HBIG) (100 IU) AND
  - Combination hepatitis B vaccine at 2, 4 and 6 months of age.

- **HBsAg negative mothers:**
  
  - All infants should receive a birth dose of thiomersal-free monovalent hepatitis B vaccine (H-B-VAX II 5µg/0.5ml), followed by doses given in combination vaccine (Infanrix hexa (DTPa-hepB-IPV-Hib) at 2, 4 and 6 months. Preterm infants born at <32 weeks gestation and/or <2000g birth weight are advised to receive an extra dose of hepatitis B vaccine at 12 months. Routine vaccination reduces risk of infection in high risk communities (available patient analysis: Hep BAg positive = RR 0.12, 95% CI 0.03, 0.44). A recent RCT demonstrated 100% seroconversion by 6 months of infants receiving either hepatitis B vaccine at birth, 6 and 14 weeks, or 6,10 and 14 weeks. A universal birth dose is given to prevent vertical transmission from a carrier mother (recognising that there may be errors or delays in maternal testing, reporting, communication or appropriate response), and prevent horizontal transmission in the first months of life from a carrier among household or other close contacts. The birth dose should be given as soon as the baby is physiologically stable, and preferably within 24 hours of birth.

Notes regarding immunisation:

- If hepatitis B vaccine and immunoglobulin has not been given at birth, it is recommended that H-B-VAX II AND Hepatitis B immunoglobulin be given as soon as possible up to 7 days. There is good evidence that hepatitis B vaccine and immunoglobulin are still effective up to at least 3 days of age. Trials of hepatitis B immunoglobulin before hepatitis B vaccine was available have reported an effect of this treatment given at 0, 3 and 6 months.
- If an infant has missed the birth dose and is aged 8 days or older, a catchup schedule is not required. A primary course of a hepatitis B-containing combination vaccine should be given at 2, 4 and either 6 or 12 months of age (provided the mother is HBsAg negative).

Preterm babies

- Preterm babies do not respond as well to hepatitis B-containing vaccines as term babies.
- For babies at <32 weeks' gestation or <2000g birth weight, give vaccine at birth, 2, 4 and 6 months of age and give a booster at 12 months of age. [note updated guidelines advising on a dose of H-B Vax II for all infants at birth].

2. **Mode of delivery:** Caesarean section is not advocated for delivery of infants born to HBsAg positive mothers. In infants who received both hepatitis B vaccine and immunoglobulin at birth, observational data report that mode of delivery does not influence vertical transmission rate to infants of hepatitis (forceps 7.3%; vacuum extraction 7.7% and caesarean section 6.8%). In infants who only received hepatitis B vaccine, infants born by vaginal delivery (24.9%) were at higher risk of hepatitis B infection compared with infants delivered by caesarean section (10%).

3. **Breast feeding:** Hepatitis B DNA and HBsAg may be detected in breast milk. However, there is no evidence that breast feeding is a risk factor for hepatitis B infection if the infant has received hepatitis B
vaccination and immunoglobulin. It is our policy to advise avoidance of breast feeding if the mother is HBsAg positive and has bleeding or cracked nipples.

4. General advice:
If a child does have hepatitis B, the family should be educated to practice ‘blood awareness’ (link: Hepatitis B parent information sheet). This means being alert to the potential presence of blood from your infected child (eg from a wound or a bite) and knowing how to deal with it.

What we do at RPA

All women should be screened for HBsAg in pregnancy. HBsAg positive women should have additional screening to determine risk of infection for the newborn including HBeAg and anti-HBeAb, and HBV DNA level.

All infants: receive H-B-VAX II (5µg/0.5ml) preferably within 12 hours after birth (latest 48 hours). If not given at birth, may be given up to 7 days of age. Subsequent doses of combination vaccine are given at 2, 4 and 6 months of age by the GP.

Infants of HBsAg positive mothers:

- Receive -B-VAX II (5µg/0.5ml), AND
- Hepatitis B immunoglobulin (HBIG) (100 IU) preferably within 12 hours after birth (latest 48 hours). If not given at birth, may be given up to 7 days of age.
- Subsequent doses of combination vaccine are given at 2, 4 and 6 months of age by the GP.
- All infants born to HBsAg positive or HBeAg positive or HBV DNA positive mothers should have follow-up serology at 12 months including HBsAg – provide referral to GP.

Preterm infants: For babies at <32 weeks’ gestation or <2000g birth weight, give vaccine at birth, 2, 4 and 6 months of age and give a booster at 12 months of age.

Key Points

| All women should be screened for HBsAg in pregnancy. | 2b3, 20, 23, 32, 33 |
| Without immunisation, over 70% of infants born to HBsAg positive and HBeAg positive mothers will themselves develop Hepatitis B infection. | 2b3 |
| Without immunisation, approximately 5 to 10% of infants born to HBsAg positive but HBeAg negative mothers will themselves develop Hepatitis B infection. | 2b3 |
All infants born to HBsAg positive mothers should receive hepatitis B vaccination and immunoglobulin within 12 hours of birth. There is evidence of some benefit even as late as 7 days from birth.  

There is no evidence that breast feeding is a risk factor for hepatitis B infection if the infant has received hepatitis B vaccination and immunoglobulin.

Caution should be exercised if there is bleeding or cracked nipples in a Hep BsAg positive woman.

All infants born to HBsAg positive or HBeAg positive or HBV DNA positive mothers should have follow-up serology at 12 months including HBsAg – provide referral to GP.

References


A/Prof David Osborn
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