Management of Blood-Borne Viruses in the Neonate

Alison M Kesson

Infectious Diseases and Microbiology

alison.kesson@health.nsw.gov.au

Hepatitis B virus

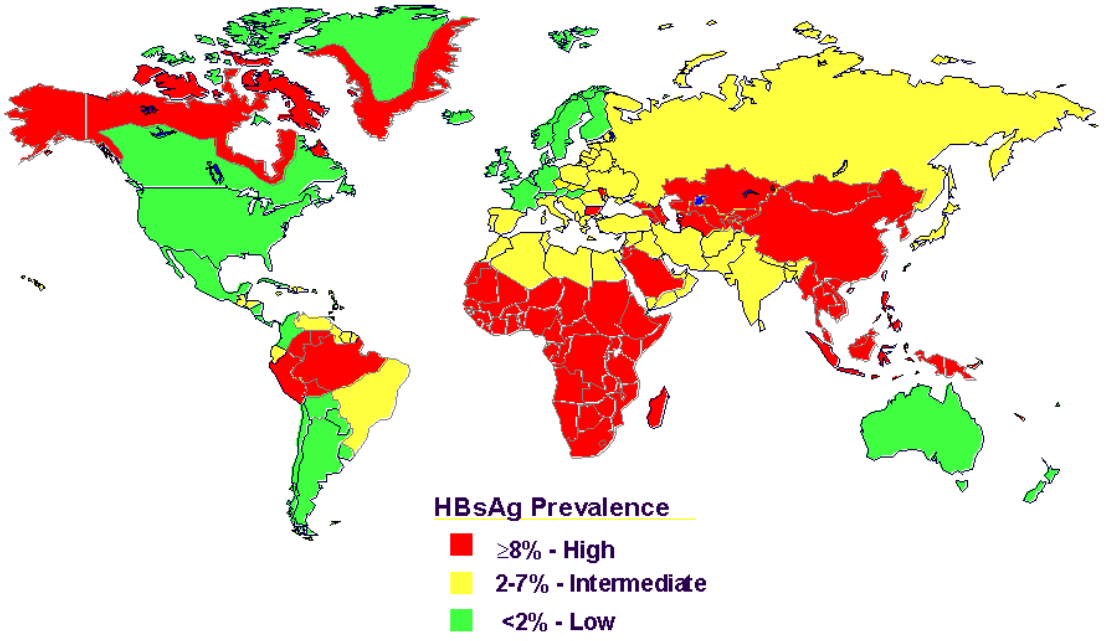
What is Hepatitis B?

- Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus.
- It is a major global health problem and one of the most serious types of viral hepatitis.
- It can cause chronic liver disease and puts people at high risk of death from cirrhosis of the liver and liver cancer.

Epidemiology

- Worldwide, an estimated two billion people have been infected with the hepatitis B virus (HBV), and more than 240 million have chronic (long-term) liver infections - carriers.
- About 15-25% of adults who become chronically infected during childhood later die from liver cancer or cirrhosis.
- Approximately 600,000 die annually
- Carriage rates
  - N America; W Europe; Australasia 0.5%
  - Mediterranean; S America; E Europe 2-7%
  - Africa; SE Asia 8-20%

Geographic Distribution of Chronic HBV Infection



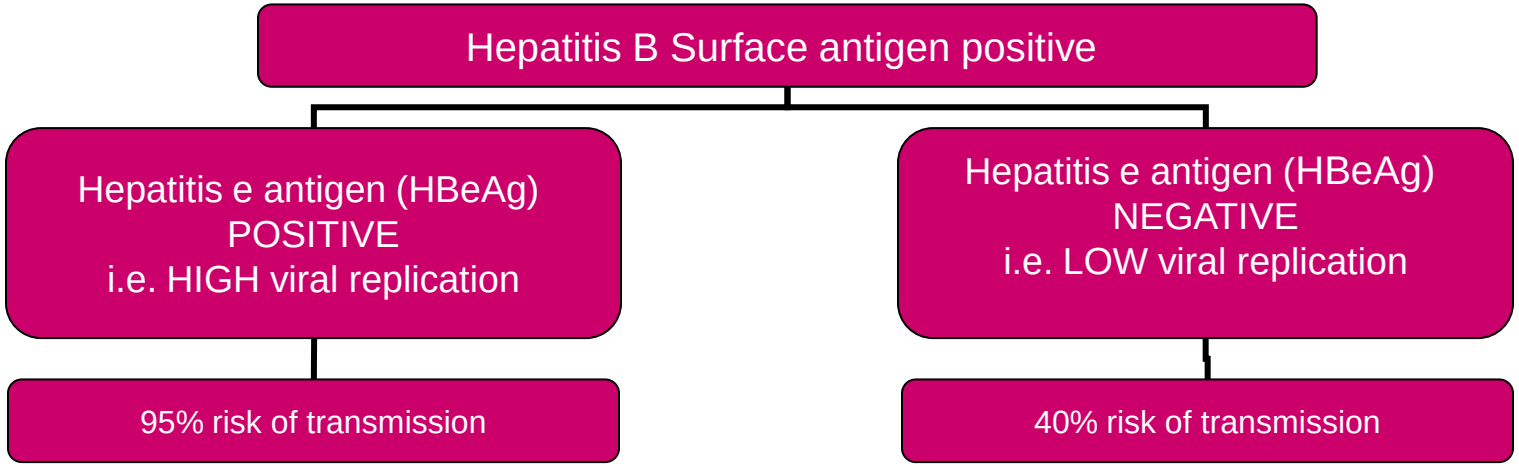
Prevalence in Australia varies between ethnic groups.
High in Aboriginal and Asian born populations

The problem

- Hepatitis B virus (HBV) infection in a pregnant woman poses a serious risk to her infant at birth.

- Without postexposure immuno-prophylaxis, approximately 40% of infants born to HBV-infected mothers in first world countries will develop chronic HBV infection, approximately one-fourth of whom will eventually die from chronic liver disease.

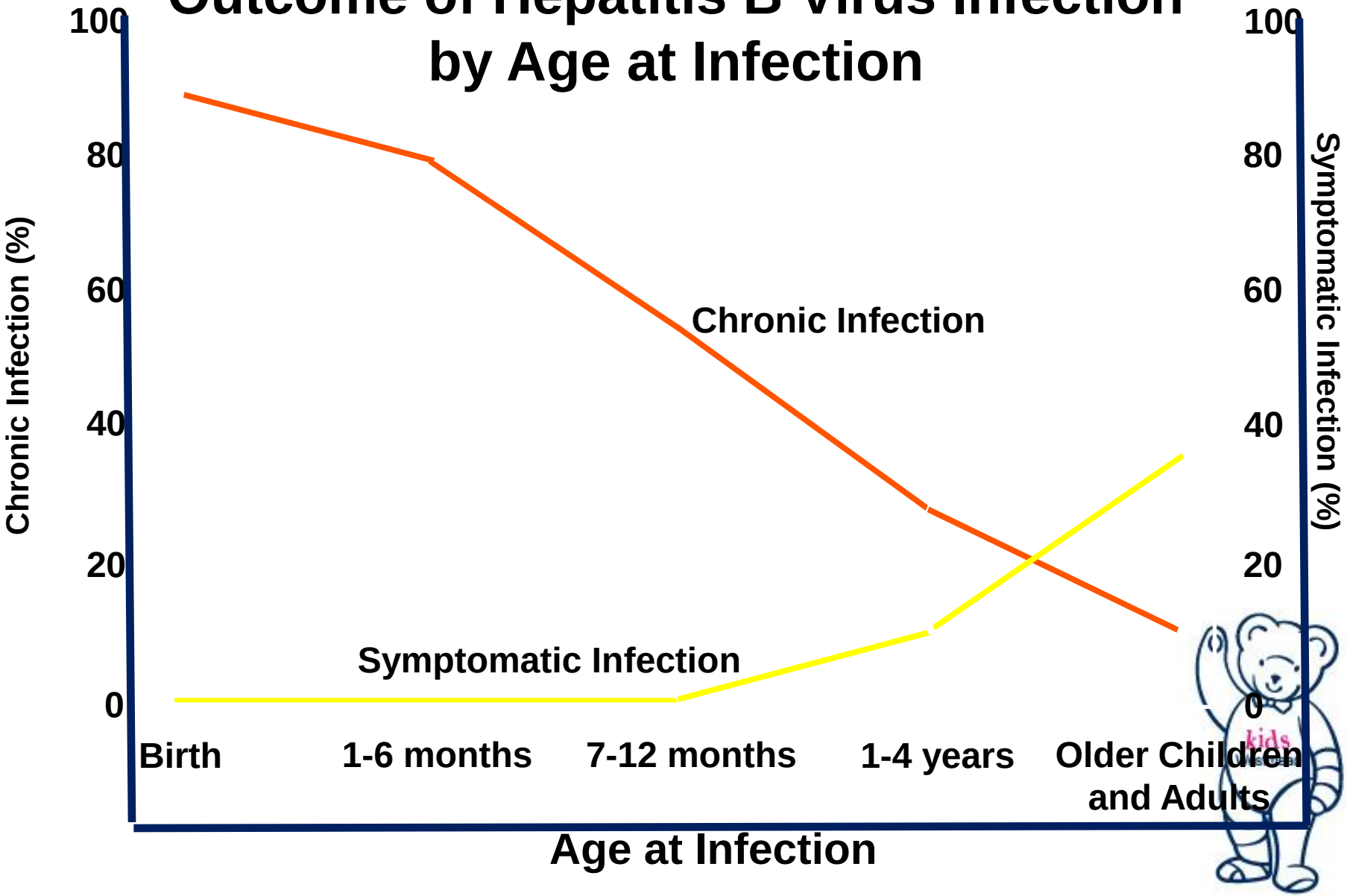
The risk



The likelihood of viral clearance depends upon the age of the individual and immune status.

Persistent infection occurs more frequently in infants and young children and is related to the maturity of the immune system.

Outcome of Hepatitis B Virus Infection by Age at Infection



Hepatitis B vaccine

- **Active vaccination**: A vaccine against hepatitis B has been available since 1982. Hepatitis B vaccine is 95% effective in preventing HBV infection and its chronic consequences, and is the first vaccine against a major human cancer.

- **Passive vaccination**: Hepatitis B immunoglobulin (HBIg) is pooled human serum with high titre antibodies to hepatitis B (anti-HBs) which can prevent infection in exposed individuals if given within 72 hours of exposure.

Prevention of vertical transmission

- Perinatal HBV transmission can be prevented by identifying HBV-infected (i.e., Hepatitis B surface antigen [HBsAg]-positive) pregnant women and providing hepatitis B immune globulin and hepatitis B vaccine to their infants within 12 hours of birth.

National Strategy

- Preventing perinatal HBV transmission is an integral part of WHO and national strategies to eliminate Hepatitis B.
- National guidelines call for the following:
  - Vaccination of all Australian born infants with 3 doses of HBV vaccine
  - Identification of HBsAg positive pregnant women and provision of active and passive immunisation to infants within 12 hours of birth.

What can we do?

- Universal screening of pregnant women for HBsAg during each pregnancy
- Case management of HBsAg-positive mothers and their infants
- Provision of immunoprophylaxis for infants born to infected mothers, including Hepatitis B vaccine and Hepatitis B immune globulin
- Routine vaccination of all infants with the Hepatitis B vaccine series, with the first dose administered at birth.

Impact of vaccination

- Active and passive vaccination of newborn infants against hepatitis B virus prevents > 95% of perinatal transmission.
- The incidence of fulminant liver failure, cirrhosis and hepatocellular carcinoma is declining significantly.
- As of 2013, 126 countries had HBV vaccine in their national vaccination schedules.
- Many poorer countries – India and sub-Saharan Africa and newer states do not provide this vaccine routinely.

Hepatitis C Virus

Vertical transmission

- Risk approximately 5% to 10% in infants born to mothers positive for HCV antibodies who are not also co-infected with HIV.
- Risk increased with HIV infection or high HCV viral load.
- Decreased transmission rate in babies born by caesarean section compared with vaginal delivery - not statistically significant.

Breast Feeding

- There is no evidence that breast-feeding is a risk factor for vertical transmission of HCV.
- However inability to quantify risk as cannot identify acute infection.
- Difficult to determine independent risk c.f. delivery.

Laboratory Diagnosis

- Serological testing for antibody before 18 months confounded by passive transfer of maternal antibody.
- No reliable test for HCV IgM
- HCV RNA by PCR is insensitive.

Management

- All patients who are HCV positive require long term follow up to determine the course of their infection.
- Therapy for HCV infection includes:
  - 1) immune response modifiers i.e. interferons
  - 2) antiviral agents i.e. ribavirin or
  - 3) liver transplantation.

Human Immunodeficiency Virus

Risk of HIV Vertical Transmission

- HIV infection currently has very high mortality rate approaching 100%.
- Prevention of transmission is our only mechanism for decreasing the morbidity and mortality of HIV infection.
- Effective interventions to significantly decrease vertical transmission can be implemented.

Risk Factors for vertical transmission of HIV

Maternal factors	Intrapartum events
Low CD4+ lymphocyte count x	Instrumental delivery
High viral load	Use of fetal scalp monitor
Advanced AIDS Chorioamnionitis	Fetal scalp pH measurement
Preterm delivery	Use of DeLee suctioning
Chorioamnionitis	Artificial rupture of membranes
Presence of p24 core antigen	Rupture of membranes for longer than 4 hours
	Other events increasing fetal exposure to maternal blood

Pediatric AIDS Clinical Trials Protocol 076

Maternal zidovudine (Retrovir) during pregnancy: 100 mg orally five times daily from 14 weeks of gestation to delivery*

Maternal zidovudine during labor: 2 mg per kg by intravenous load over 1 hour, then 1 mg per kg per hour until delivery

Neonatal zidovudine: 2 mg per kg orally every 6 hours from 8 hours after delivery until 6 weeks of age

HIV transmission 24% in placebo group vs. 8% in AZT group.

Infant HIV Diagnosis

- The HIV DNA PCR test is the recommended initial screening tool in infants born to HIV-positive mothers.
- The test has a sensitivity of 93.2%and a specificity of 94.9%; however, it is less accurate in neonates.
- In infants with a low risk of transmission, the positive predictive value of the HIV DNA PCR test is 55.8%during the first month after birth and 83.2%after the first month.
- If three virologic tests are negative (at birth, one month of age and four months of age), there is a 95%chance that the infant is not infected with HIV.
- A negative HIV-specific IgG assay (ELISA) at 18 months of age definitively rules out HIV infection in exposed infants.

Neonatal Antiretroviral Drug Dosing

Table 9. Recommended Neonatal Dosing for Prevention of Mother-to-Child Transmission of HIV

All HIV-Exposed Infants (initiated as soon after delivery as possible)		
Zidovudine (ZDV)	**Dosing**	**Duration**
ZDV	**≥35 weeks' gestation at birth:** 4 mg/kg/dose PO twice daily, started as soon after birth as possible and preferably within 6–12 hours of delivery (or, if unable to tolerate oral agents, 3 mg/kg/dose IV, beginning within 6–12 hours of delivery, then every 12 hours)	Birth through 6 weeks
ZDV	**≥30 to <35 weeks' gestation at birth:** 2 mg/kg/dose PO (or 1.5 mg/kg/dose IV), started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours at age 15 days	Birth through 6 weeks
ZDV	**<30 weeks' gestation at birth:** 2 mg/kg body weight/dose PO (or 1.5 mg/kg/dose IV) started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours after age 4 weeks	Birth through 6 weeks
Additional Antiretroviral Prophylaxis Agents for HIV-Exposed Infants of Women who Received No Antepartum Antiretroviral Prophylaxis (initiated as soon after delivery as possible)		
In addition to ZDV as shown above, administer **Nevirapine (NVP)**	**Weight Band Dosing** **Birth weight 1.5-2 kg: 8 mg TOTAL for each dose** **Birth weight >2 kg: 12 mg TOTAL for each dose**	3 doses in the first week of life • 1st dose within 48 hours of birth (birth–48 hours) • 2nd dose 48 hours after 1st • 3rd dose 96 hours after 2nd

Key to Abbreviations: IV = intravenously; NVP = nevirapine; PO = orally; ZDV = zidovudine

- http://aidsinfo.nih.gov/guidelines

PJP Prophylaxis

- *P. jirovecii* pneumonia prophylaxis should be started after completion of six weeks of zidovudine therapy.
- Prophylaxis is not recommended before four weeks of age because of the low incidence of this pneumonia in neonates.
- Trimethoprim-sulfamethoxazole can exacerbate the anaemia caused by zidovudine and increase adverse effects on the newborn's immature bilirubin metabolism.
- Prophylactic medication can be discontinued when two HIV DNA PCR tests are negative (one after the infant is one month old and the other after the infant is four months old).
- Prophylaxis in an HIV-infected infant should be continued until the age of 12 months, regardless of the $CD4^+$ lymphocyte count.
- After the age of 12 months, the need for prophylaxis is determined by the $CD4^+$ lymphocyte count (percentage).

Breast feeding and HIV transmission.

- Prolonged breast feeding is estimated to cause one-third to half of new infant HIV infections worldwide
- CDC recommends that infected women in the US refrain from breastfeeding to avoid postnatal transmission of HIV-1 to their infants through breast milk. These recommendations also should be followed by women receiving antiretroviral therapy.
- Passage of antiretroviral drugs into breast milk has been evaluated for only a few antiretroviral drugs. ZDV, 3TC, and nevirapine have been detected in the breast milk of women.

Vaccinations

- **Active vaccination:**
  - hepB-DTPa-Hib-IPV, 13vPCV, HPV, MenCV, hepatitis A, influenza – not live so can be give to immunosuppressed patients.
  - Response variable
  - MMR, VV and rotavirus?- in HIV patients if CD4>15%
  - Live viruses – cannot be given to heavily T cell immunosuppressed patients

- **Passive vaccination:**
  - HBIg, human Ig (measles & Hep A) , VZIg – post-exposure prophylaxis.

HTLV-1

HTLV-1

- Mother to child transmission occurs in 15-25% of infants born to HTLV-1 positive women.
- It is associated with development of adult T-cell leukaemia/lymphoma later in life.
- Transmission occurring largely through breast feeding.
- Transplacental transmission is unlikely due to near absence of pro-viral HTLV DNA in umbilical cord lymphocytes of HTLV infected mothers.
- Passive transfer of maternal HTLV-1 antibody is believed to be protective against infection.
-

HTLV-1

- HTLV-1 is endemic in Japan and Brazil.
- In well-resourced settings, suggest avoid breast feeding.
- If breast feeding is unavoidable, weaning before 6 months will prevent the vast majority of infection.
- Many other morbidities of variable impact and substantial risks to both early weaning and formula feeding, especially in resource poor countries.
- It is unknown what role caesarean section helps in preventing HTLV-1 perinatal transmission

Thank you

Questions?