PERINATAL HEPATIDES AND HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Pamela Palasanthiran
Staff Specialist, Paediatric Infectious Diseases

Viruses in July (ViJ), 2004
Management of Perinatal Infections

Cytomegalovirus
Enterovirus
Hepatitis B
Hepatitis C
Herpes Simplex Virus
Human Immunodeficiency Virus
Listeria
Mycobacterium Tuberculosis
Parovirus
Rubella
Streptococcus - Group B
Toxoplasma
Treponema Pallidum (Syphilis)
Varicella Zoster Virus

Edited by Dr Pamela Palasanthiran,
Dr Mike Starr, and Dr Cheryl Jones

Introduction by Prof Lyn Gilbert

AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES 2002
HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia

Annual Surveillance Report

2003

Edited by National Centre in HIV Epidemiology and Clinical Research
Overview

- Epidemiology
- Perinatal transmission risks
- Prevention strategies
Perinatal Hepatitis B Virus (HBV)
HBV core

HB surface antigen (HBsAg)
HBV infection – response

- Illness
- HBs Ag
- HBe Ag
- Anti-HBs
- Anti-HBe
- Anti-HBc
- Anti-HBc IgM

Months after exposure
HBV chronic carrier – response

- **Anti-HBc IgM**
- **HBs Ag**
- **HBe Ag**

**ILLNESS**
- Often subclinical

**Anti-HBc**

**Anti-HBe**

**Months**

**Years**

1 2 3 4 1 2 4 6 8 10
World Health Organization (WHO), 2001
Acute hepatitis B notification rate - Australia, 1993 to 2000

Risk factors for perinatal HBV transmission

- Maternal HBV DNA
- Antigenemia

<table>
<thead>
<tr>
<th></th>
<th>+ve</th>
<th>-ve</th>
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<tbody>
<tr>
<td>HBeAg</td>
<td>+ve</td>
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</tr>
<tr>
<td>HBsAg</td>
<td>+ve</td>
<td>+ve</td>
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<tr>
<td>Perinatal Tm risk</td>
<td>80-90%</td>
<td>2-15%</td>
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</table>
Chronic carrier state in children with HBV - rates

Yao, GB. Gut, 1996

Age at infection

% carriers
Perinatal HBV - Prevention strategies

- Antenatal screening
  - targeted vs universal
- Immunisation (at birth)
  - Passive (HBIG)
  - Active (HB vaccine)
  - combination
- ? Antiviral prophylaxis

Give within 24 hours


> 90% protective efficacy

Perinatal HBV - Prevention strategies

No role

- Mode of delivery (Cesarean section)
- Mode of feeding (Breastfeeding encouraged)
Impact of universal newborn HBV vaccination

- The Australian experience
  - 1997 Adolescent imm. program
  - 2000 Universal newborn imm. program
  - about 2000 HBsAg+ve pregnancies and deliveries per annum

- The USA experience

- The Taiwanese experience
Legend of hepatitis B vaccination: The Taiwan experience

CHO-YU CHAN, SHOU-DONG LEE AND KWANG-JUEI LO

Abstract
Hepatitis B, a disease entity currently affecting more than 350 million persons worldwide, is also a serious health problem in Taiwan. Liver cirrhosis and hepatoma, which are both closely correlated with hepatitis B, are among the 10 leading causes of death in Taiwan. A mass hepatitis B vaccination program, conducted by the government of Taiwan, was started in 1984. Prior to this vaccination program, a series of viral epidemiological surveys, transmission pattern studies, and pilot immunization trials proved the clinical, economic, and strategic benefits of mass immunization, thus providing the impetus for the implementation of this mass vaccination program. The success of this program has led to a decline in hepatitis B carrier rates among children in Taiwan from 10% to <1%. Furthermore, the mortality rate of fulminant hepatitis in infants and the annual incidence of childhood hepatoma have also decreased significantly in recent years. This is one of the most remarkable success stories in the field of public health.

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HBsAg+ve rate  1984  1994  1999

9.8%  1.3%  0.7%
Perinatal Hepatitis C Virus (HCV)
Fig. 1. HCV notifications in Australia, 1990–2000.
Rate per 100,000 population of total HCV notifications, 2000.
HCV acquisition

- Primarily through blood
  - IV drug use
  - Blood/blood product receipt
  - Occupational exposure
- Sex with infected partner or multiple partners
- Perinatal transmission
# Approximation - perinatally acquired HCV in Aus.

- 0.2 - 2% of pregnant women are infected with HCV
- 250,000 deliveries per year
- 1% mothers HCV infected
- 50 - 70 % viremic (RNA positive)
- 0 - 6% transmission rate

Implies approx. 75 babies infected with HCV per year
Hepatitis C in Australian Children

- Australian Paediatric Surveillance Unit (APSU) study (2003)
- Preliminary data
  - 2003 - 78% response rate to Q
  - 12 confirmed cases (4 male)
  - Mean age at diagnosis
    - 3.7 years (6 w - 12.6 years)
  - Perinatal exposure (92%)
  - 83% asymptomatic at Dx
  - 89% with abnormal LFT

Cheryl Jones, John Kaldor and Sue Pollis, APSU. Data from ASM, ASID 2004 (Alice Springs)
Pregnancy outcome in HCV infected women

- HCV itself does not alter pregnancy outcome and pregnancy does not seem to alter the natural history of HCV in women.

- HCV infected mothers may have higher risk pregnancies as a result of IVDU or HBV or HIV infection.
Perinatal transmission HCV

- Primarily occurs when mother is viraemic
  - Transmission rate of 6% in maternal viraemia (Dore et al., BMJ 1997)
  - Increased to 16% in woman with co-infection of HBV or HIV (Delamare et al., J Hepatol 1999)

- HCV not transmitted via breastfeeding
  RNA detected in breastmilk, transmission may relate to nipple trauma and blood to blood contact (Kumar and Shahul, J Hepatol 1998)
Mode of delivery

- Some suggestion of protective effect of elective LSCS but insufficient evidence to recommend

<table>
<thead>
<tr>
<th>Factor</th>
<th>n</th>
<th>Estimated transmission rate (95% CI)</th>
<th>Adjusted odds ratio (95% CI)*</th>
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<tbody>
<tr>
<td>Overall</td>
<td>441</td>
<td>6.7 (4.1–10.2)</td>
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<td>HIV status</td>
<td></td>
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<tr>
<td>Negative</td>
<td>328</td>
<td>6.4 (3.5–10.3)</td>
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<tr>
<td>Positive</td>
<td>22</td>
<td>18.6 (5.8–38.6)</td>
<td>3.80 (0.92–13.2)</td>
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<td>Breastfeeding</td>
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<tr>
<td>No</td>
<td>355</td>
<td>6.7 (3.7–10.6)</td>
<td>1.00</td>
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<tr>
<td>Yes</td>
<td>59</td>
<td>7.7 (2.2–17.8)</td>
<td>1.52 (0.35–5.12)</td>
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<tr>
<td>Mode of delivery</td>
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<tr>
<td>Vaginal</td>
<td>339</td>
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<td>Emergency caesarean section</td>
<td>54</td>
<td>5.9 (1.0–17.2)</td>
<td>0.84 (0.12–3.63)</td>
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<td>Elective caesarean section</td>
<td>31</td>
<td>0 (0–7.4)</td>
<td>0 (0–0.86)</td>
<td>0.1†</td>
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<td>Vaginal/emergency caesarean section</td>
<td>393</td>
<td>7.4 (4.5–11.3)</td>
<td>1.00</td>
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<tr>
<td>Elective caesarean section</td>
<td>31</td>
<td>0 (0–7.4)</td>
<td>0 (0–0.87)</td>
<td>0.04</td>
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</table>

*Adjusted for all other factors. †Global test.

Maternal risk factors for vertical HCV transmission
Natural History of Hepatitis C

Acute Hepatitis C

Chronic Hepatitis 50 - 85%

Cirrhosis 20 - 30%

Decompensation 6 - 10%

HCC 5 - 10%

Death 5 - 10%

10 - 30 years
Infant outcome if infected

- No effect on infant at birth
- Likely more indolent infection in infants
- Most healthy to 10-20 years of life but can have flaring of LFT
Infant outcome if infected

- Largest, long term series
- Perinatal blood transfusion acquisition from a single HCV infected donor
  - 18 of 31 in cohort
    - HCV antibody positive (58%)
    - 16 (88.9%) HCV RNA +ve
    - all genotype 1b (donor genotype)
- 11/16 liver biopsies

When and how to test the newborn?
HCV testing

- TWO TESTS
  - HCV IgG antibody
  - HCV RNA by PCR
Figure 2: Cumulative proportion of uninfected children who cleared maternal HCV antibody by age

Gibb et al, Lancet, 2000
HCV RNA testing

- Specificity 97% unrelated to age
- Sensitivity 22% in first month but 97% thereafter
- Specificity/sensitivity will vary between laboratories

Mother to child transmission of hepatitis C virus: evidence for preventable peripartum transmission Lancet 356 September 9, 2000

Timing and interpretation of tests for diagnosing perinatally acquired hepatitis C virus infection PIDJ July 2001, 20(7):715-6
Strategy 1

- Cost cutting approach
- No PCR
- Antibody at 18 months
  but
- Anxiety
- ? Follow up especially with IVDU parental background
- Loss of opportunity to institute apt. advice re: HepB and Hep A vaccination
Alternative strategy

- If mother RNA negative, HCV IgG for baby at 18m
- If mother RNA positive (5-7% risk):
  Perform first PCR at 4 - 12 weeks
  - if negative, reassure and confirm with IgG at 18 months
  - if positive (73% prediction of infection), reconfirm (? when - need more info on timing and frequency of viral clearance) and IgG at 18 months
Perinatal Human Immunodeficiency Virus (HIV)