PERINATAL HEPATIDES AND HUMAN IMMUNODEFICIENCY VIRUS (HIV)

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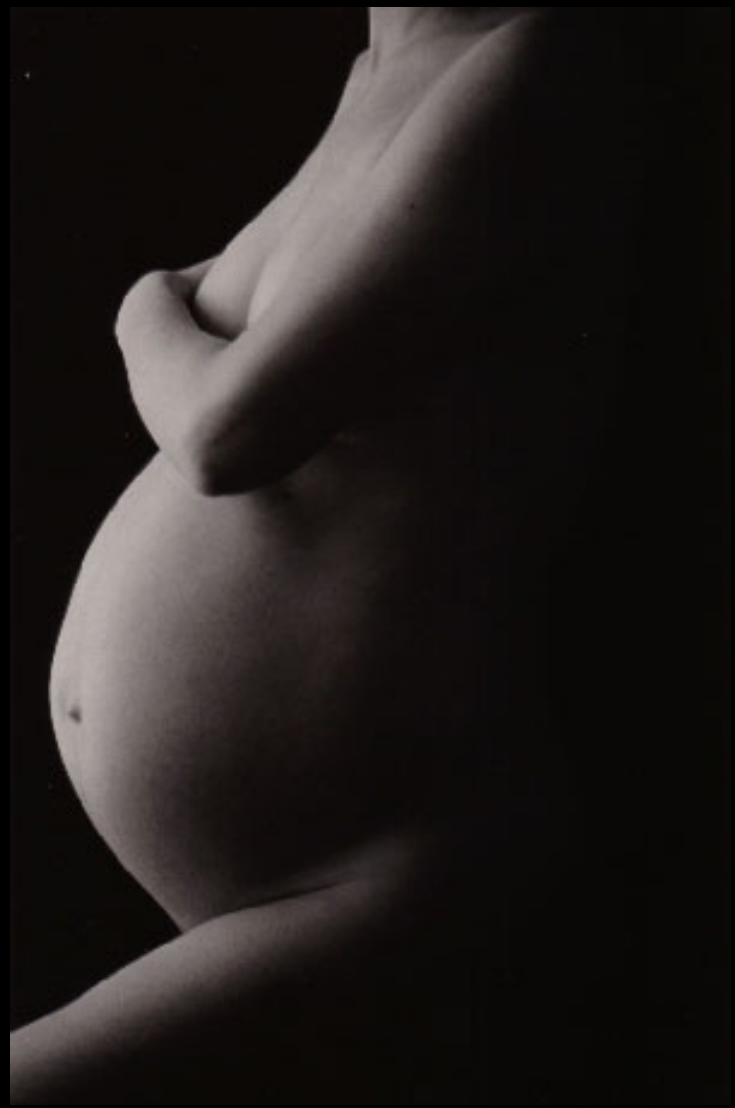
SYDNEY CHILDREN'S HOSPITAL RANDWICK

Viruses in July (ViJ), 2004



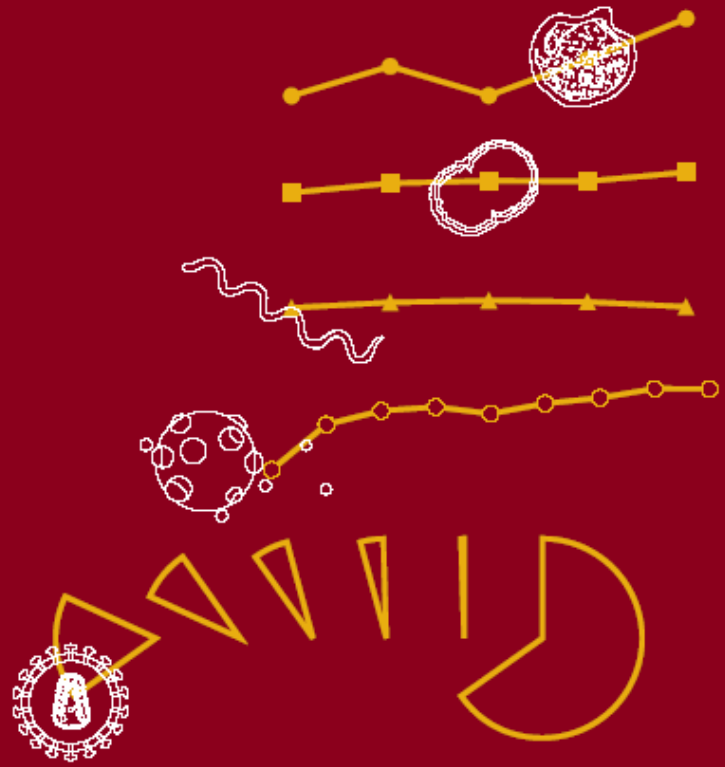
Management of Perinatal Infections

Cytomegalovirus
Enterovirus
Hepatitis B
Hepatitis C
Herpes Simplex Virus
Human Immunodeficiency Virus
Listeria
Mycobacterium Tuberculosis
Parvovirus
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)

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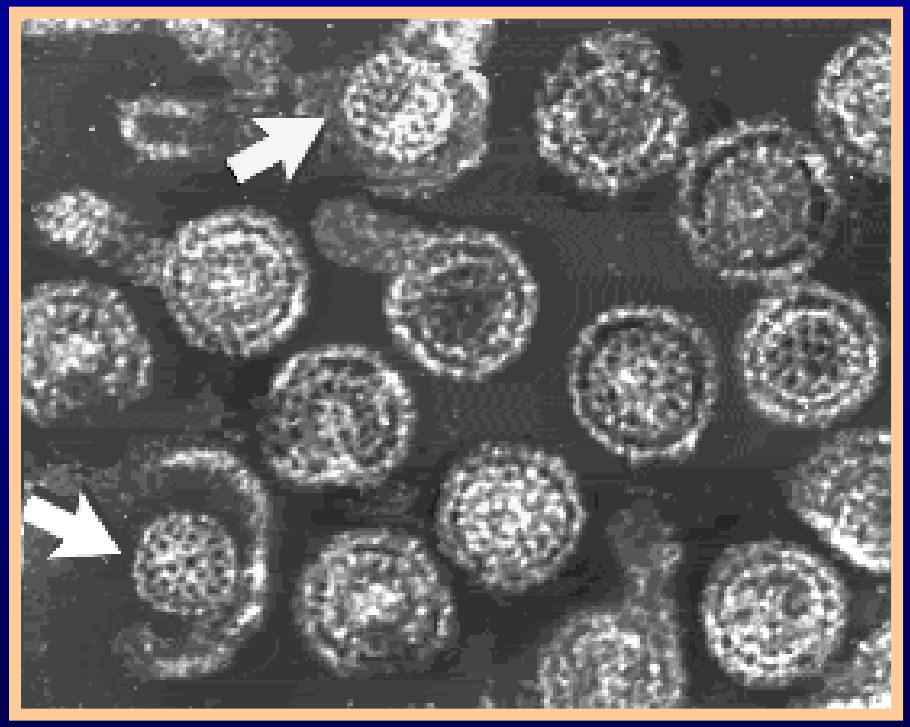
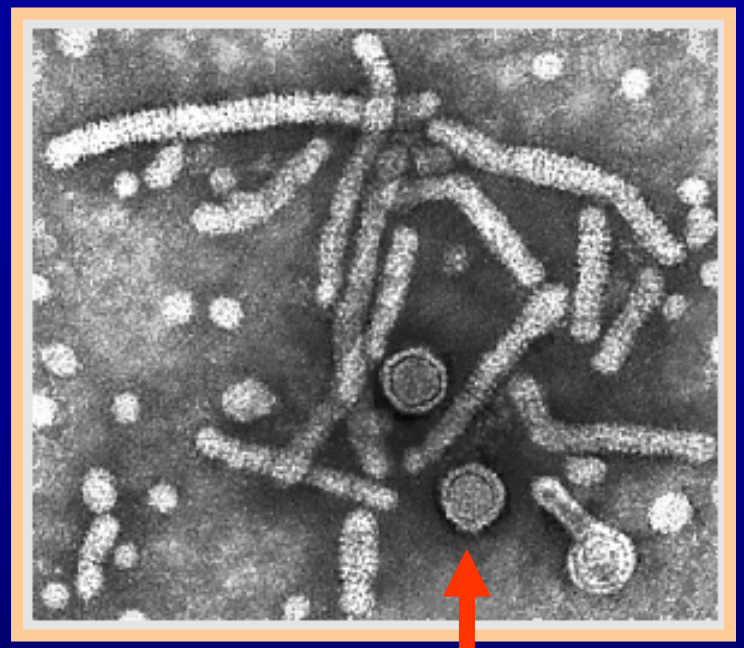
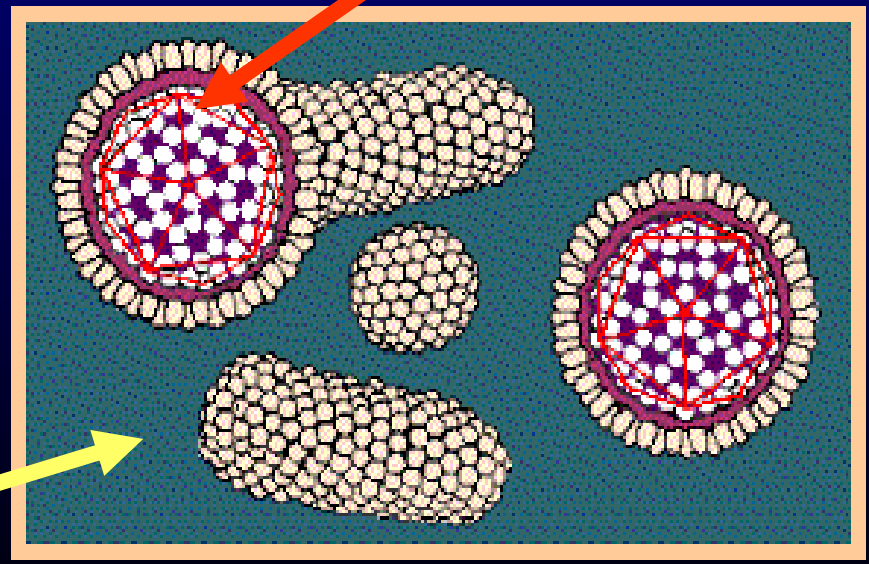


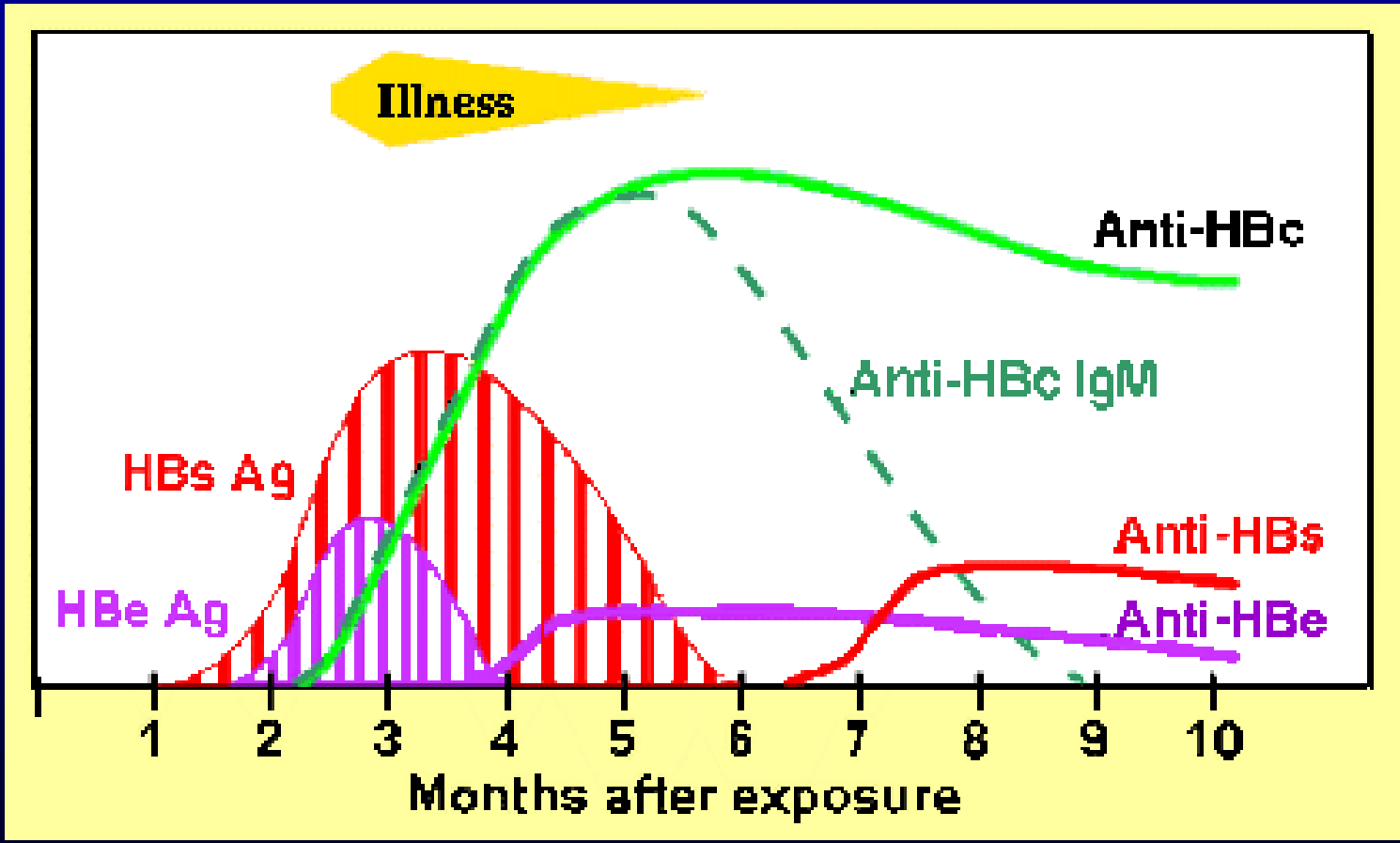




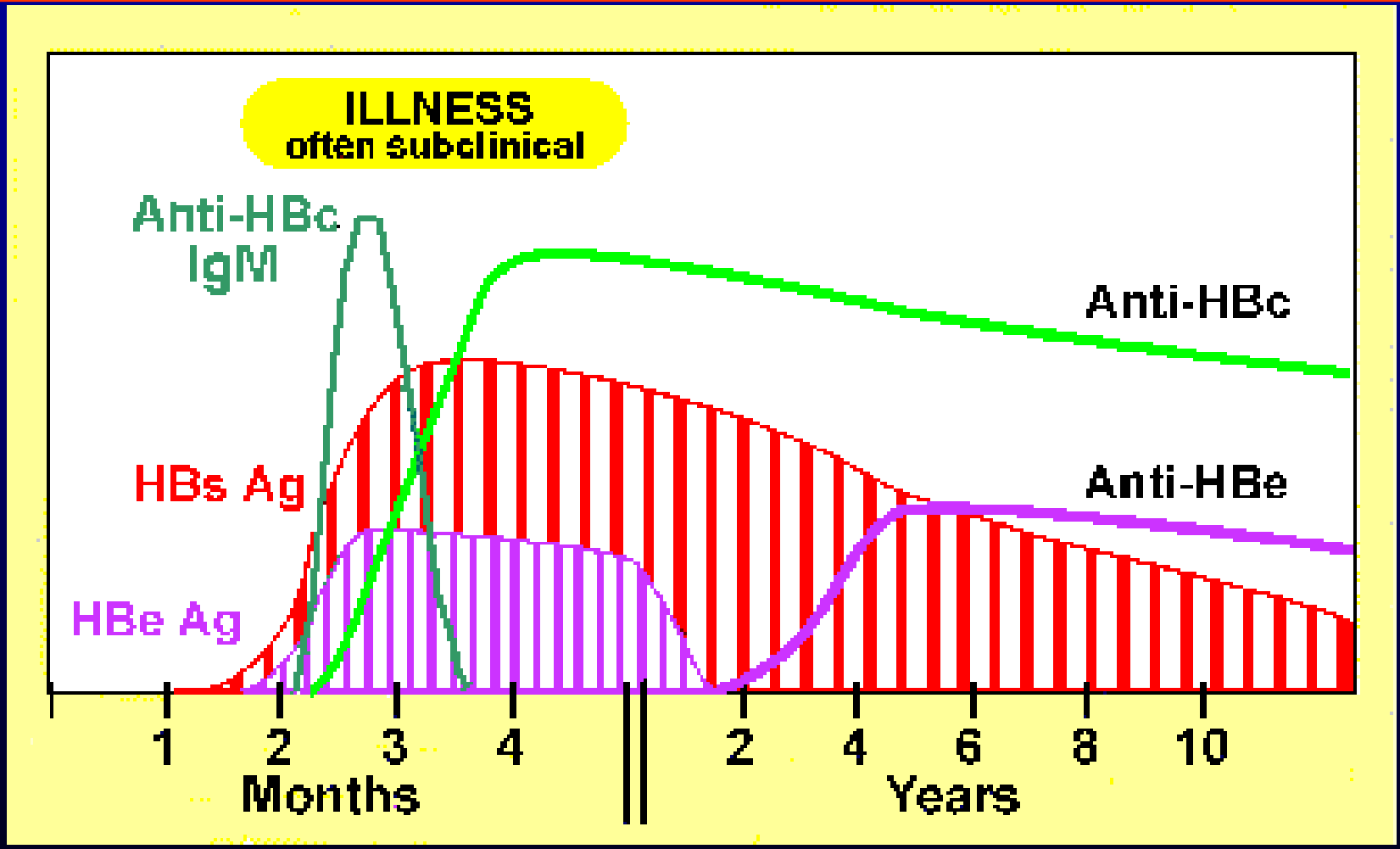
HBV core

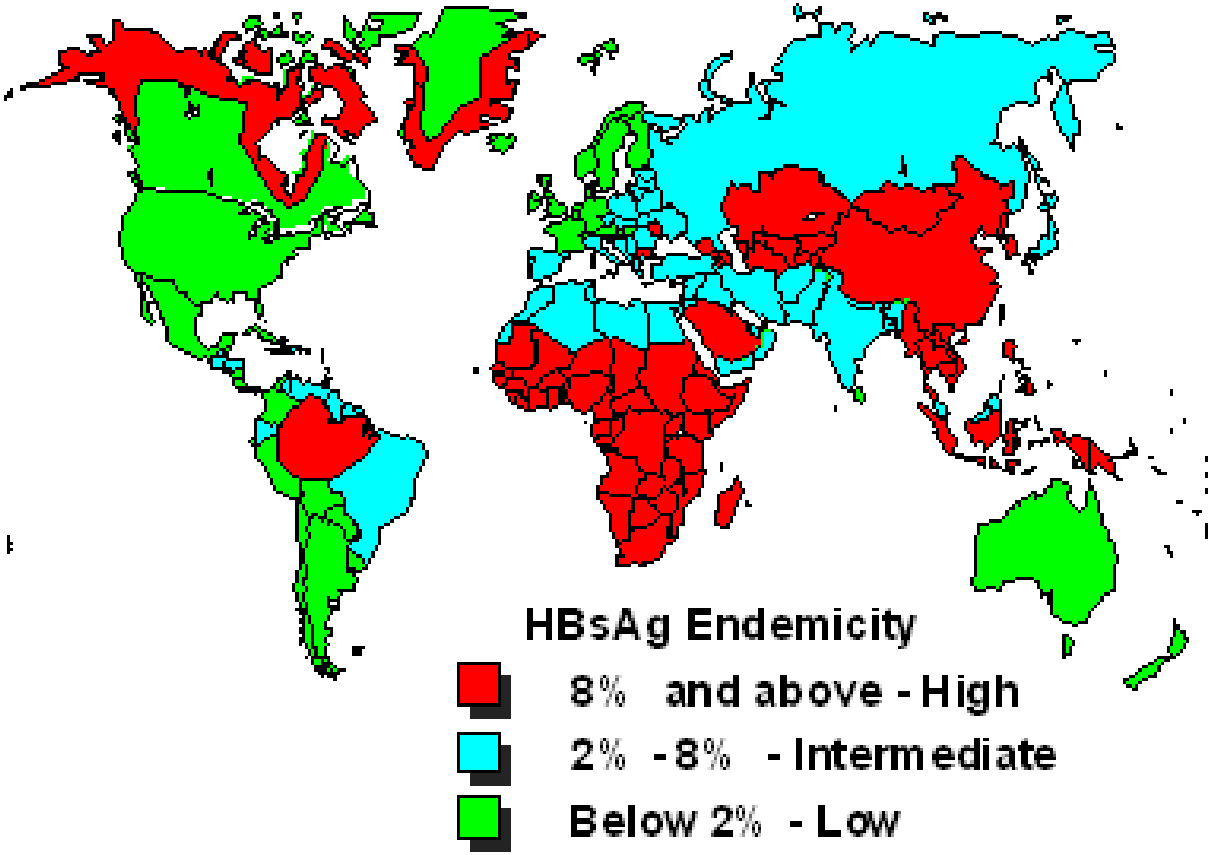
HB surface antigen
(HBsAg)

HBV infection – response

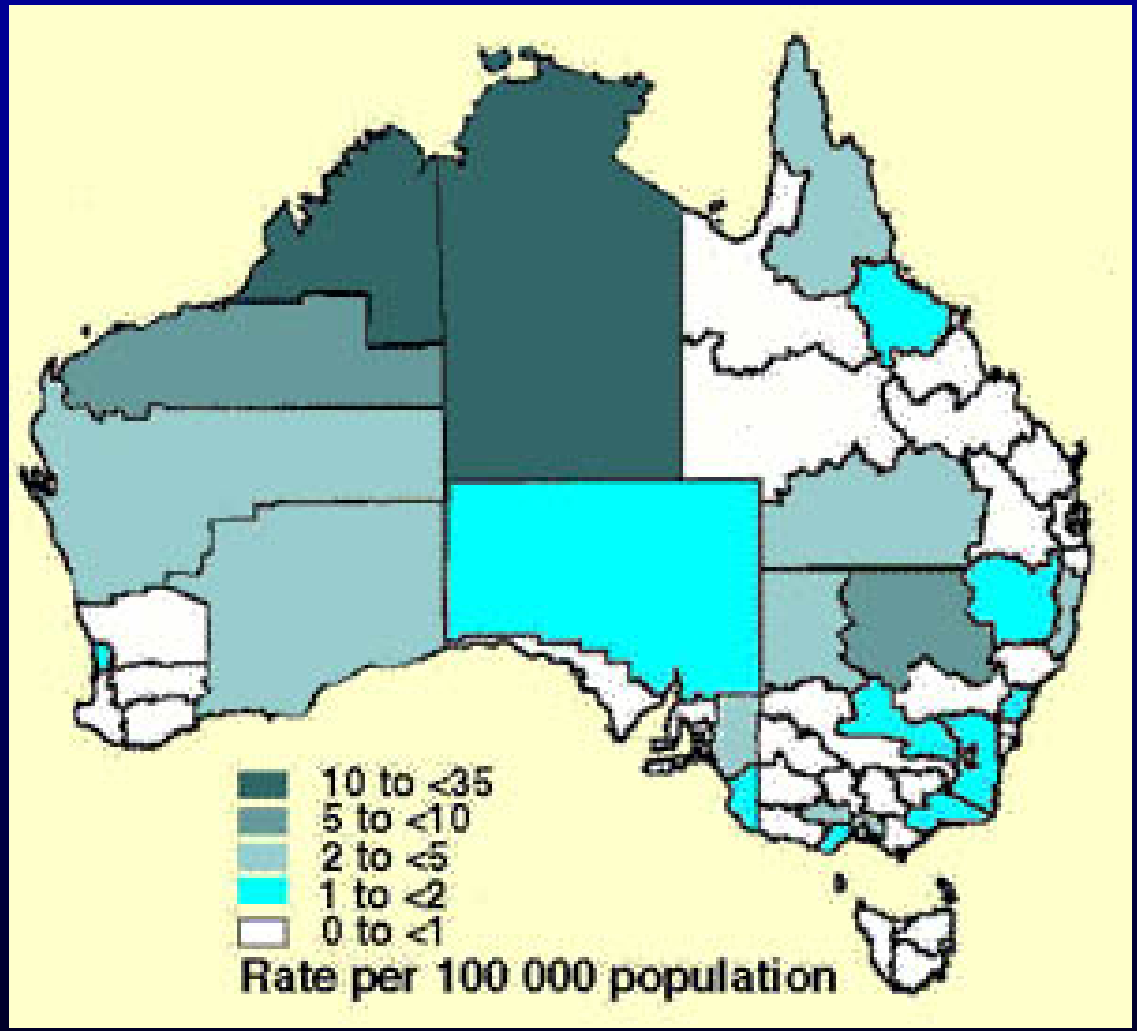


HBV chronic carrier – response

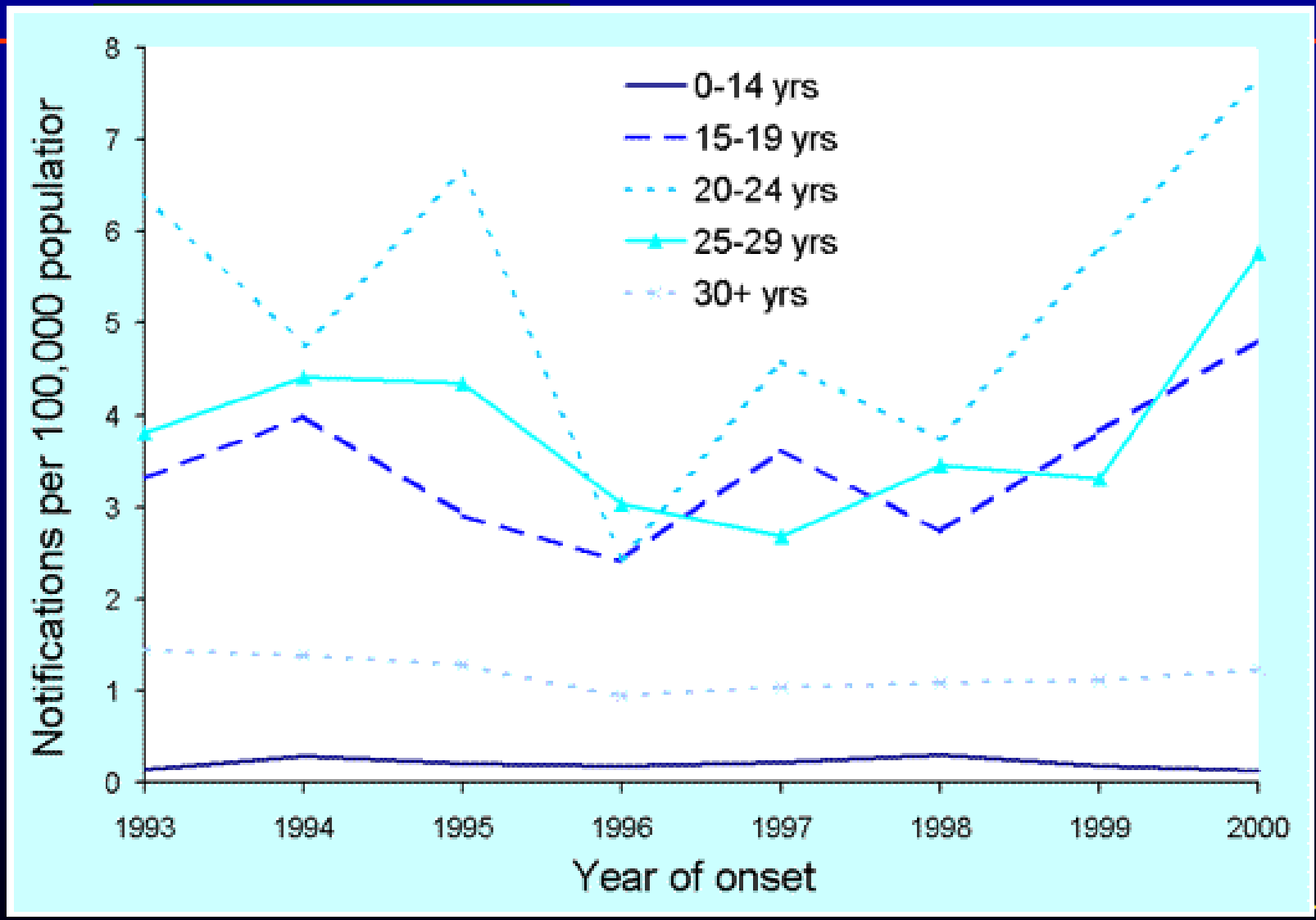




World Health Organization (WHO),2001


10 to <35
5 to <10
2 to <5
1 to <2
0 to <1
Rate per 100 000 population

Acute hepatitis B notification rate - Australia, 1993 to 2000



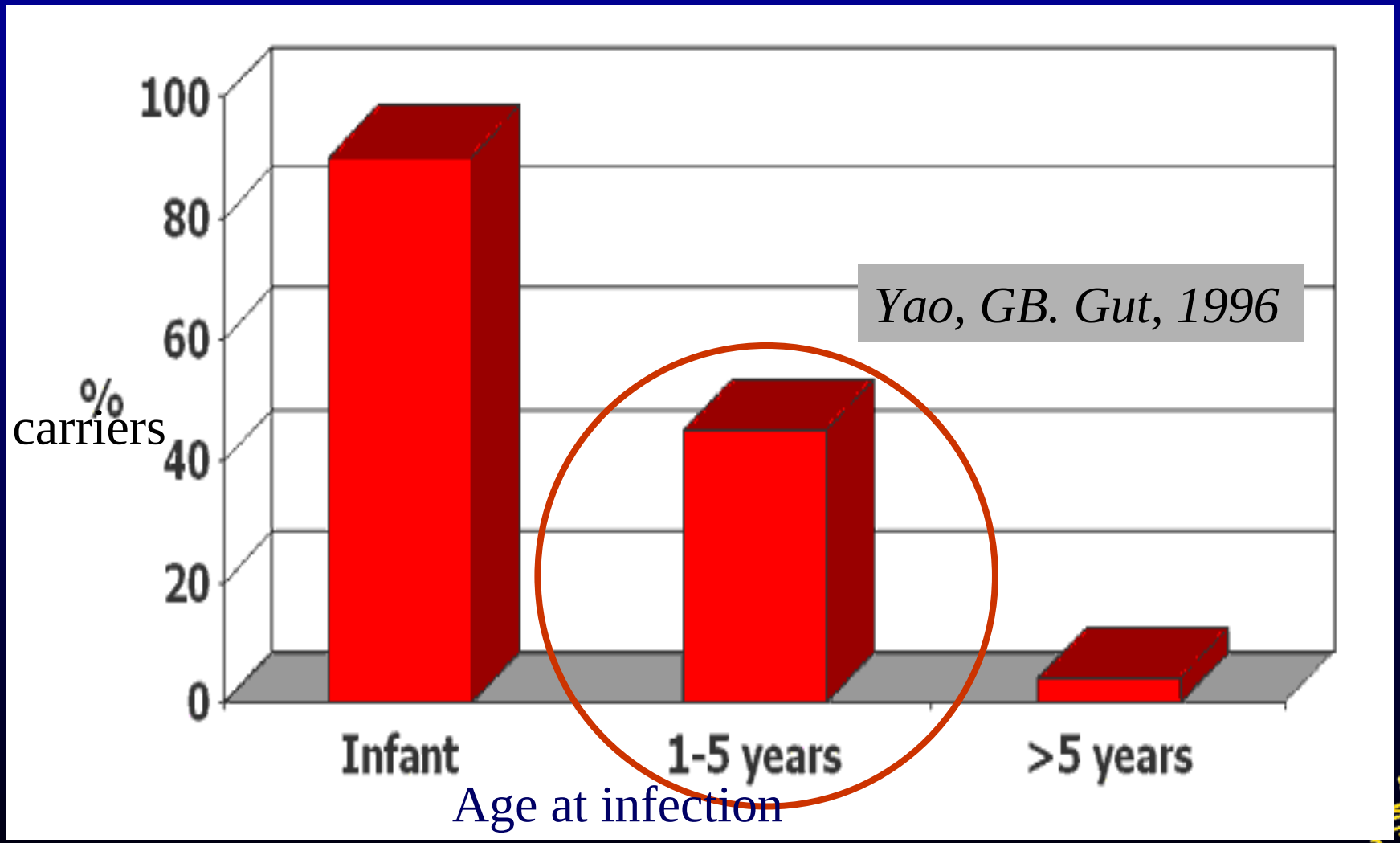
McIntyre P et al, *Commun Dis Intell* 2002;26 Suppl:May.

Risk factors for perinatal HBV transmission

- Maternal HBV DNA
- Antigenemia

HBeAg	+ve	-ve
HBsAg	+ve	+ve
Perinatal Tm risk	80-90%	2-15%

Chronic carrier state in children with HBV - rates



Perinatal HBV - Prevention strategies

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

Give within 24 hours

Andre F et al J Med Virol, 1994

> 90% protective efficacy

Andre F et al J Med Virol, 1994

Perinatal HBV - Prevention strategies

No role

- Mode of delivery (Ceserean section)
- Mode of feeding (Breast feeding 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

Division of Gast *l National*

	1984	1994	1999
HBsAg+ve rate	9.8%	1.3%	0.7%

Abstract

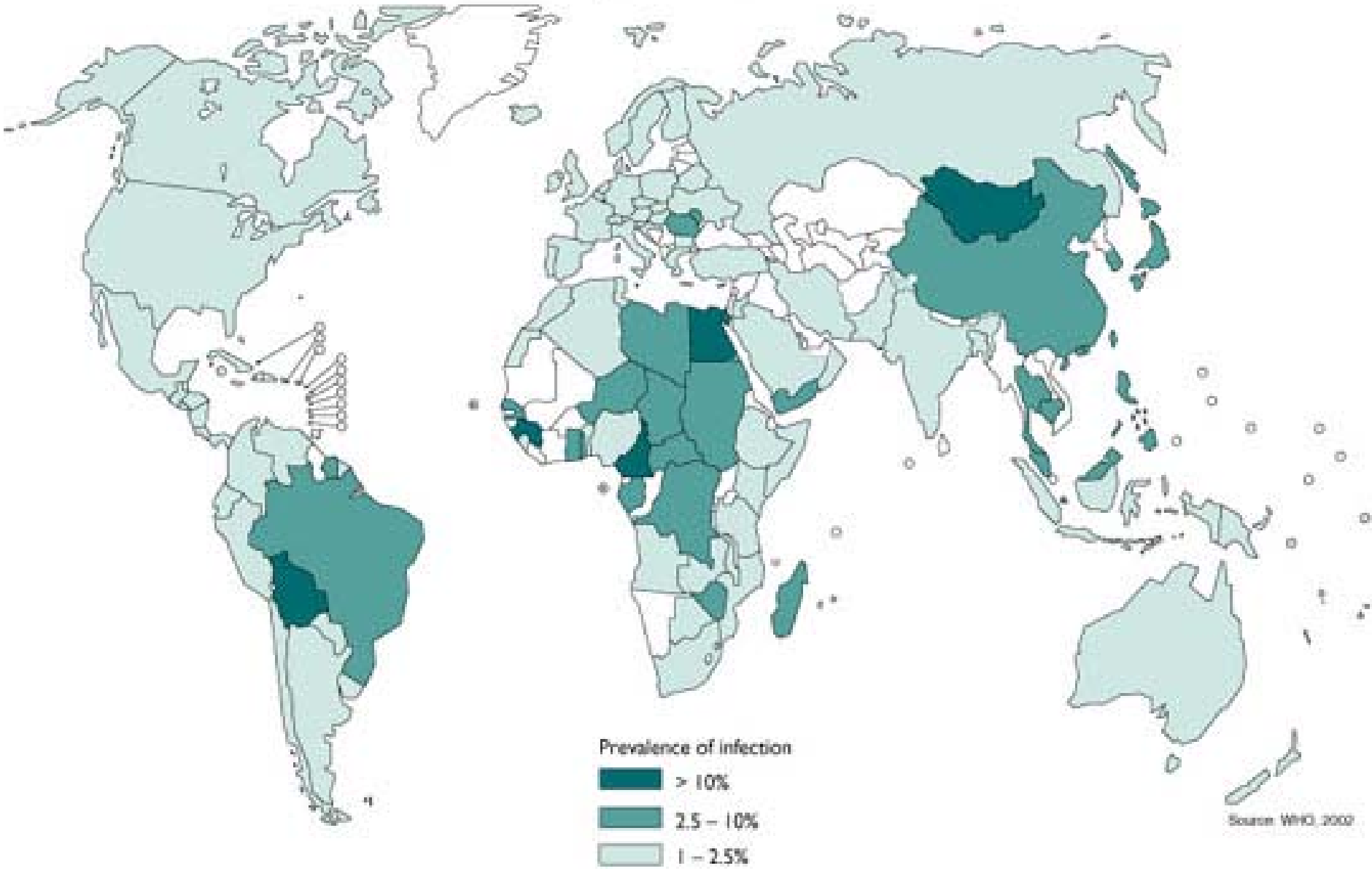
Hepatitis B, a disease entity currently affecting more than 350 million persons worldwide, is also a serious health problem in Taiwan. Liver cirrhosis and hepatoma, which are both closely correlated with hepatitis B, are among the 10 leading causes of death in Taiwan. A mass hepatitis B vaccination program, 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.

Journal of Gastroenterology and Hepatology, 2004

Perinatal Hepatitis C Virus (HCV)

SYDNEY CHILDREN'S HOSPITAL RANDWICK

Hepatitis C, 2002



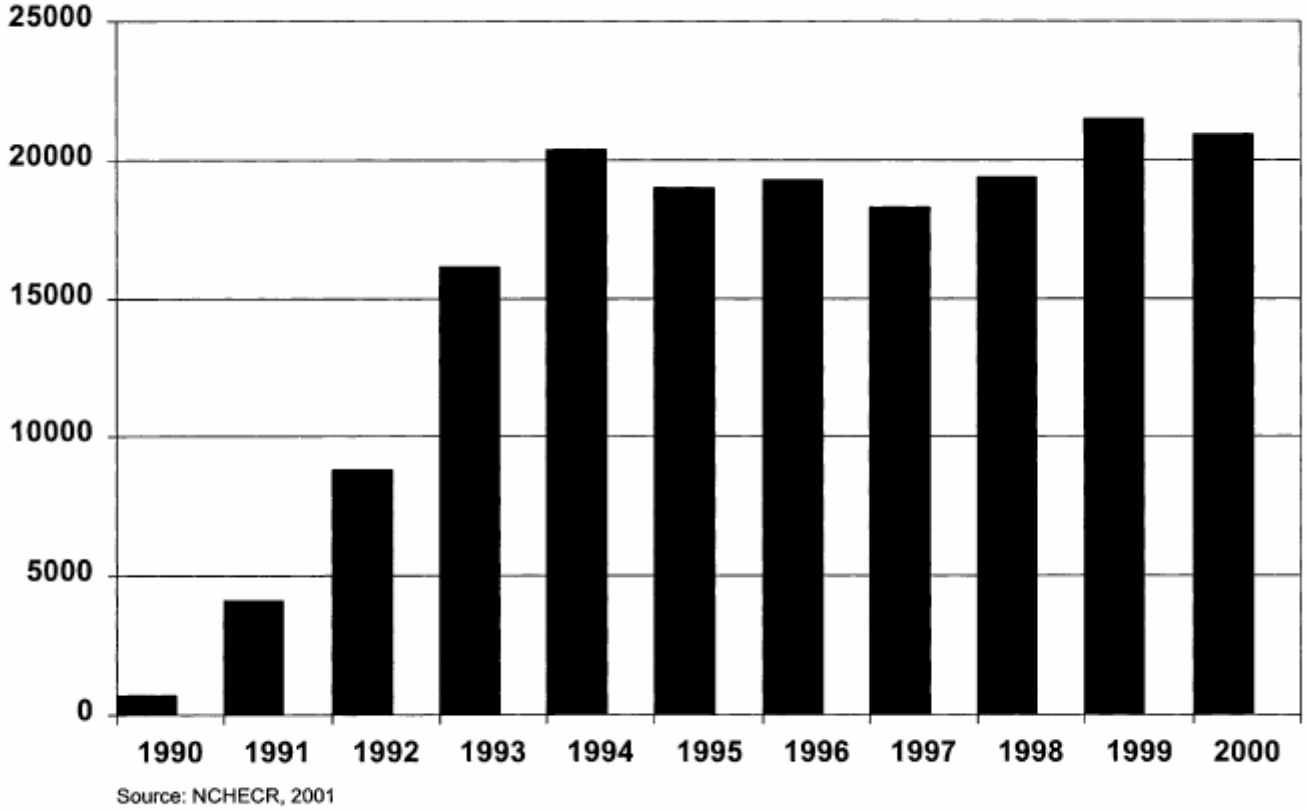
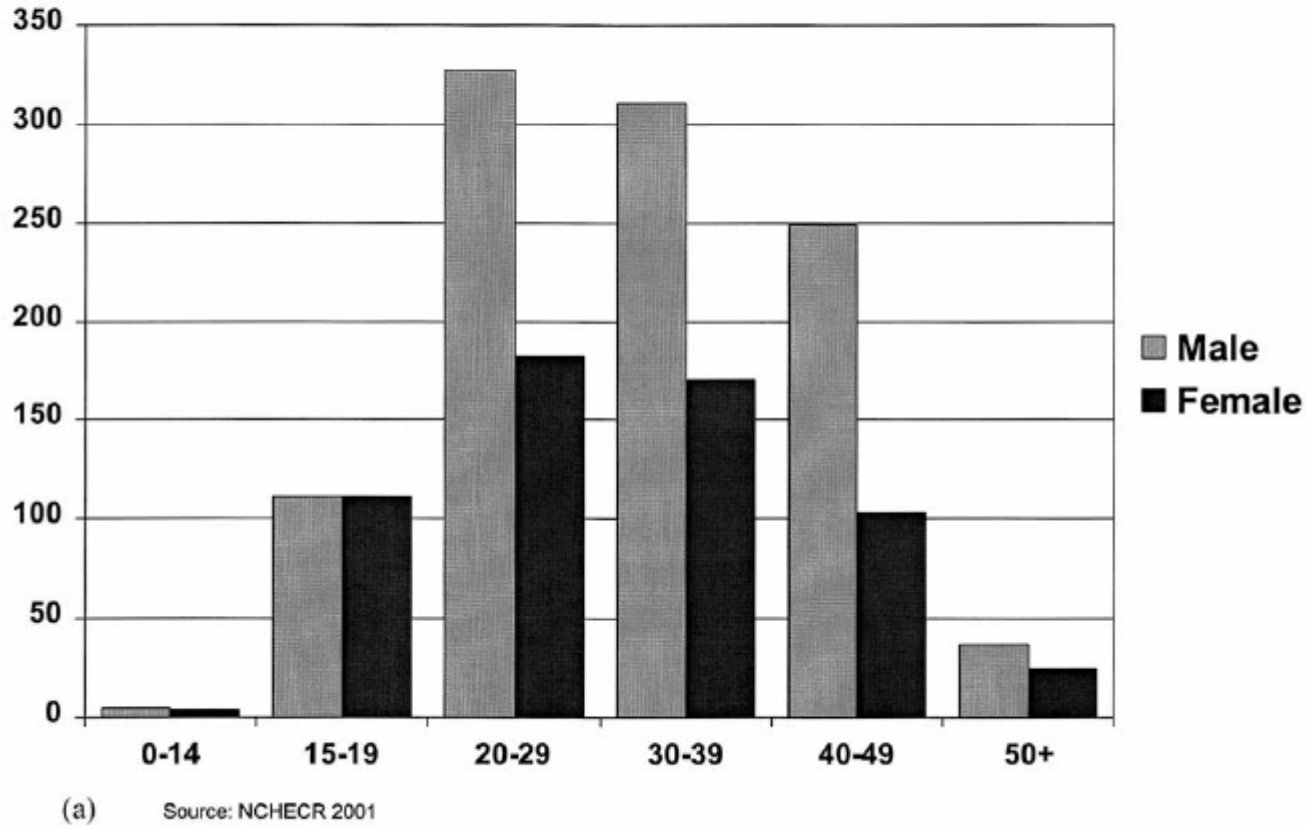


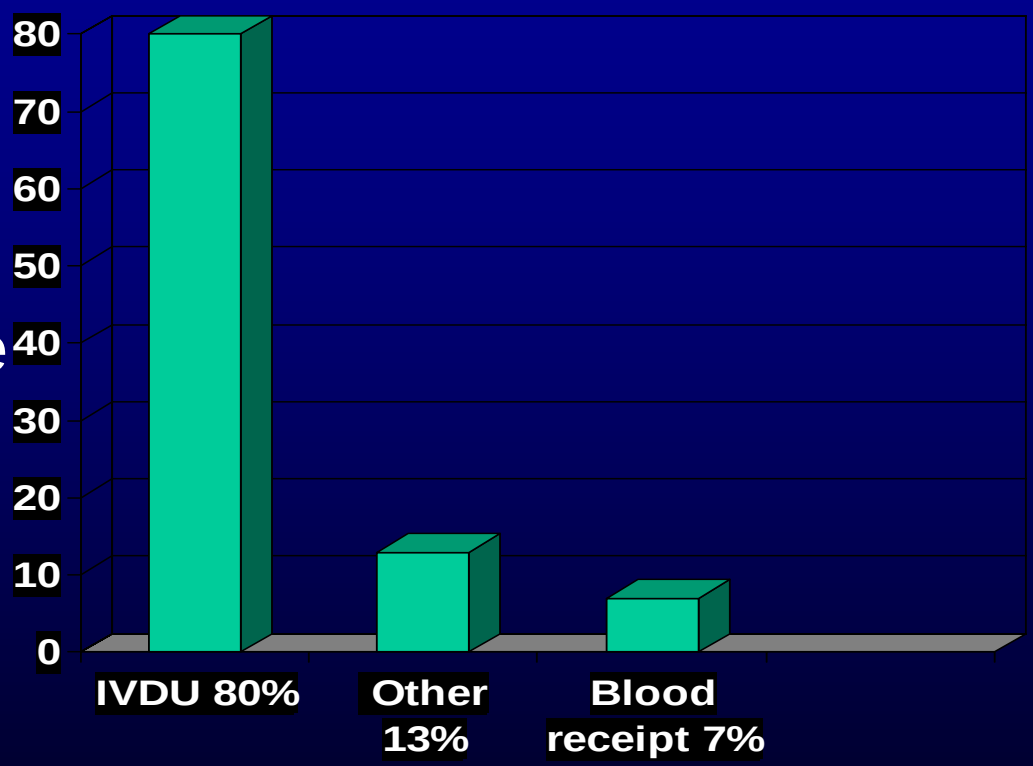
Fig. 1. HCV notifications in Australia, 1990–2000.



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

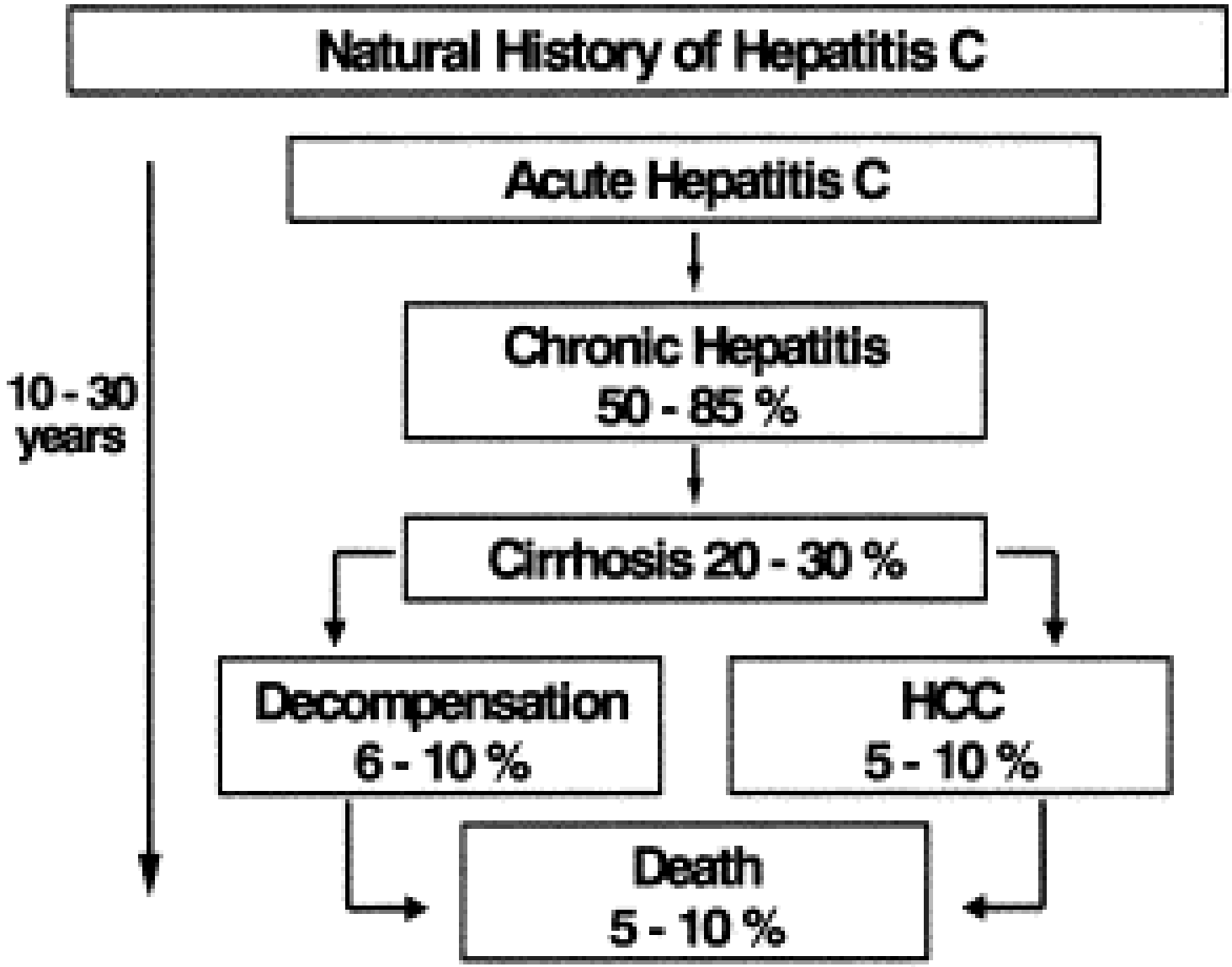
Gibb, Lancet 2000 356:904-907

Factor	n	Estimated transmission rate (95% CI)	Adjusted odds ratio (95% CI)*	p
Overall	441	6·7 (4·1–10·2)	..	..
HIV status				
Negative	328	6·4 (3·5–10·3)	1·00	
Positive	22	18·6 (5·8–38·6)	3·80 (0·92–13·2)	0·06
Breastfeeding				
No	355	6·7 (3·7–10·6)	1·00	
Yes	59	7·7 (2·2–17·8)	1·52 (0·35–5·12)	0·5
Mode of delivery				
Vaginal	339	7·7 (4·5–11·9)	1·00	
Emergency caesarean section	54	5·9 (1·0–17·2)	0·84 (0·12–3·63)	
Elective caesarean section	31	0 (0–7·4)	0 (0–0·86)	0·1†
Vaginal/emergency caesarean section	393	7·4 (4·5–11·3)	1·00	
Elective caesarean section	31	0 (0–7·4)	0 (0–0·87)	0·04

*Adjusted for all other factors. †Global test.

Maternal risk factors for vertical HCV transmission

Gibb et al, Lancet, 2000


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

Casiraghi, et al. Hepatology, May 2004

When and how to test the newborn?

HCV testing

- TWO TESTS
  - HCV IgG antibody
  - HCV RNA by PCR

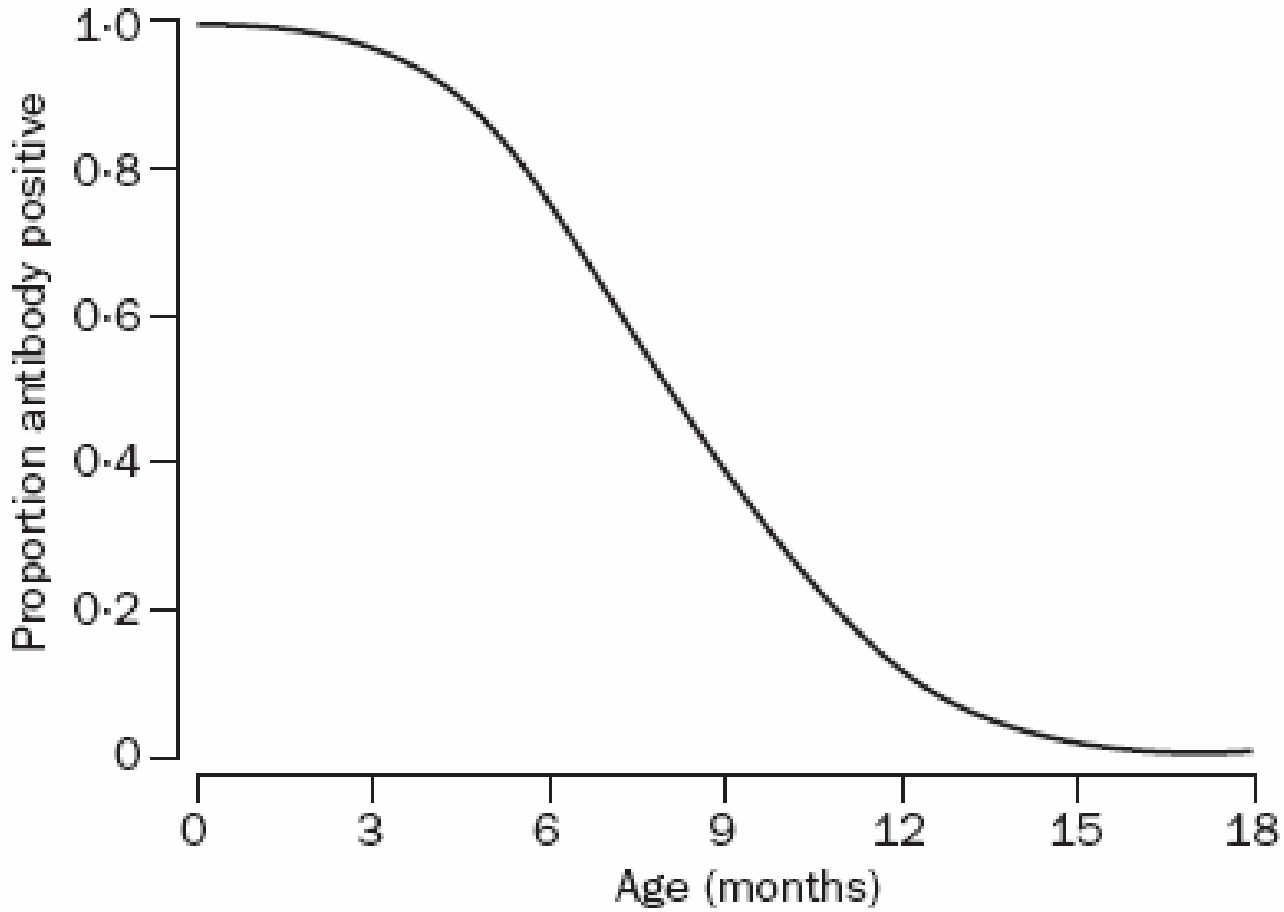


Figure 2: **Cumulative proportion of uninfected children who cleared maternal HCV antibody by age**

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 oppurtunity 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)