

The Study of Congenital Infections



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Current Studies

- SCIP – Study of Cytomegalovirus (CMV) Infection in Pregnancy
- ASCI – Amniotic Fluid Study of Congenital Infections
- SHIP - Stillborn, High-risk and Preterm
- APSU – Australian Paediatric Surveillance Unit – Congenital CMV



SCIP – Study of Cytomegalovirus Infection in Pregnancy

- Aim – To determine the incidence of congenital CMV and to design and implement a screening program



CMV in Pregnancy

- Main cause of viral congenital disease
- No screening programs
- No vaccines or drug therapy
- Congenital infection can result in:
 - Hearing and vision loss
 - Reduced cognitive skills and fetal death

Congenital CMV Infection

- **Hepatosplenomegaly**
- **Jaundice**
- **Microcephaly**
- **Prematurity**
- **Chorioretinitis**
- **Petechiae**
- **Mental retardation**
- **Hearing loss**





Incidence of CMV

- Effects 0.5 - 2.2% of births
 - 246,300 births in Australia in 2002
 - 370 - 4930 cases CMV infection in pregnancy
- 10 - 40% transmitted to child
- 10 - 20% symptomatic at birth – 30% fatal
- 40% of asymptomatic children may develop symptoms up to 5 years later
 - Hearing loss, lack of cognitive skills

Primary Modes of CMV Transmission



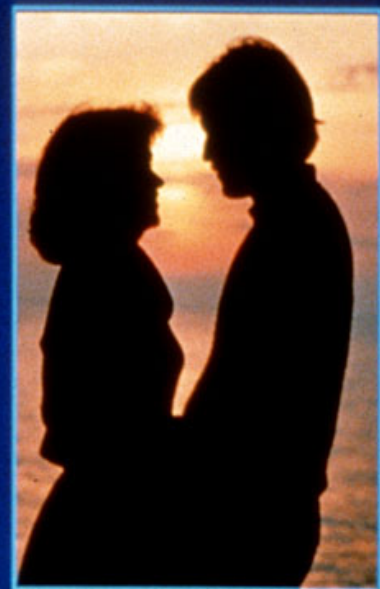
- In fetus, perinates, neonates:

Exposure to maternal blood (in utero), cervix, breast milk



- In children:

Close contact as in day care centers



- In adults:

Sexual transmission, close contact



The SCIP Study

- Consent pregnant women who present to the outpatients clinic at the RHW and GTT at the POWH
- Blood samples
 - Serology (IgG, IgM, avidity)
 - Viral DNA detection
- Urine sample
 - Viral DNA detection
 - Virus culture



SCIP Results

- To date – 569 serology results
- 248 never infected with CMV (43.6%)
- At risk of primary CMV infection
 - Childcare centres
 - New partner
- 321 infected with CMV (56.4%)
- At risk of reactivation



SCIP Results

- 47 IgM positive (recent or reactivated infection)
 - 5 low avidity IgG = possible primary infections
 - 1 documented seroconversion = definite primary infection
- Rate of intrauterine transmission increases with gestation
- Earlier transmission correlates with more severe clinical outcome



SCIP Results

- Placenta collected from high-risk women
- CMV infection in placental cells
 - Different cell types – more common in trophoblast cells
 - Differences in genotype of virus
 - Difference in mother's immune response
- Effect on transmission

In situ PCR

Figure 1(a)

In-situ PCR using glycoprotein B (gB) primers (x200)

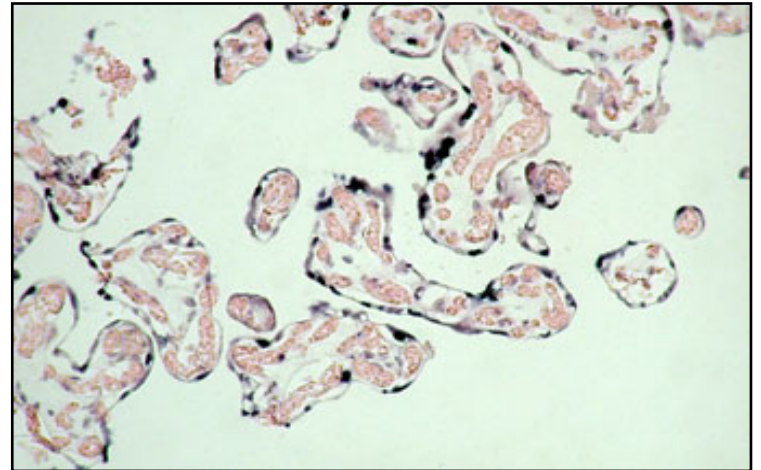


Figure 1(b)

Corresponding control for section in figure 1(a). Run simultaneously in the absence of DIG incorporation.





Amniotic Fluid Study of Congenital Infections (ASCI)

- Aim - Quantitative testing of multiple viruses in amniotic fluid samples
 - Viral load correlates to fetal outcome
- Consent women undergoing amniocentesis
- Current multiplex PCR:
 - Herpes simplex
 - Varicella Zoster Virus (chickenpox)
 - Cytomegalovirus (CMV)
 - Parvovirus B19
 - Toxoplasma



ASCI

- Quantitative CMV testing
 - Definite transmission
 - Viral levels define outcome
- Future tests
 - Rubella, Hepatitis C, Enterovirus, LCMV, Adenovirus, Adeno-associated virus, HHV-6, HHV-7, HHV-8
- Results - 133 samples tested 2003-2004
 - Positive – 8 VZV, 6 CMV, 2 HSV, 1 Toxoplasma, 1 Parvovirus B19



SHIP – Stillborn, High-risk and Preterm

- Aim – To determine the incidence, aetiology and outcome of congenital viral infections in stillborn, high-risk and preterm individuals
- Results – 10 congenital CMV cases in 2003/2004
- Viruses associated with adverse clinical outcome:
 - HSV, CMV, EBV, VZV, HHV-6, HHV-7, Adenovirus, Adeno-associated virus, Enterovirus, LCMV, Parvovirus B19, Rubella



Australian Paediatric Surveillance Unit (APSU)

- Over 1,000 doctors in Australia
- Voluntary, participating investigators reporting cases



APSU - Australian Paediatric Surveillance Unit

- Aim – To determine the aetiology and clinical features of Australian congenital CMV infections
- Results - 70 cases of congenital CMV reported between 1999-2002
- Common symptoms:
 - Petechiae, purpurae, thrombocytopaenia, splenomegaly and hepatomegaly (39-47%)
 - Maternal febrile illness (54%)



Outlook and Deliverables

- More informative serology testing
- Able to assess transmission
 - Detect virus in amniotic fluid
- Better outcome for mother and child
 - Better assessment of risks
- Better follow-up for high risk cases
 - Asymptomatic cases detected

Thank you

