



# c CMV

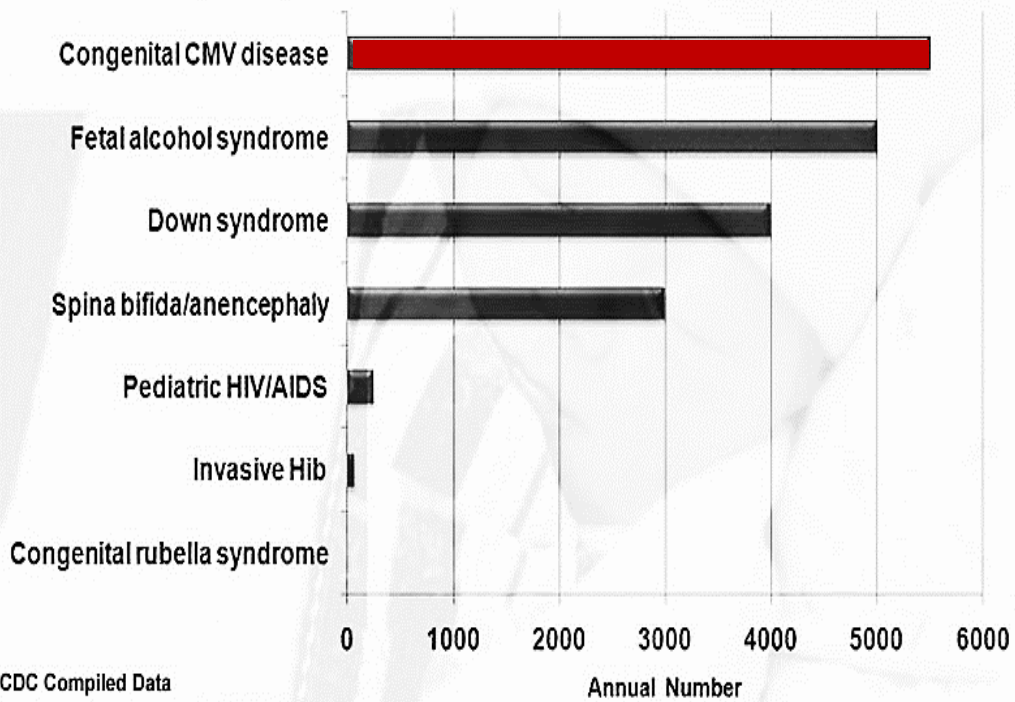
- What poses the most risk to a pregnant woman and her baby out of a dirty cat litter tray, an unpasteurised cheese or a drooling toddler.....



# CMV talk Summary

- Ubiquitous virus in humans
- Community awareness low
- Infection “in the womb” can be bad
- Cause of deafness in children
- Identification and treatment

### U.S. Children Born with or Developing Long-Term Medical Conditions Each Year



Congenital CMV is more common than most people realise.....



Department of Health  
P O Box 5013  
Wellington  
AUGUST 1983

From the Directors  
Division of Public Health  
Division of Health Promotion

CIRCULAR LETTER TO MEDICAL PRACTITIONERS PH 2/83

1 DEAFNESS AND CYTOMEGALOVIRUS

Thanks to the cooperation of practitioners and the public, the immunisation of 11 year old girls and women against rubella is rapidly producing a cohort of women of child-bearing age who will have a very high protection against rubella in pregnancy. As a result it is anticipated that the number of cases of congenital rubella will rapidly decline.

Thus the next most common cause of congenital deafness will assume more importance - congenital cytomegalovirus infection (CMV). It is planned to look closely into the epidemiology of CMV in New Zealand in the coming years. It may take some time to evaluate the exact nature and prevalence of the disease.

# About CMV

Latency vs Lytic

Herpein (Greek) “to creep”

DS linear DNA 100-200 Genes

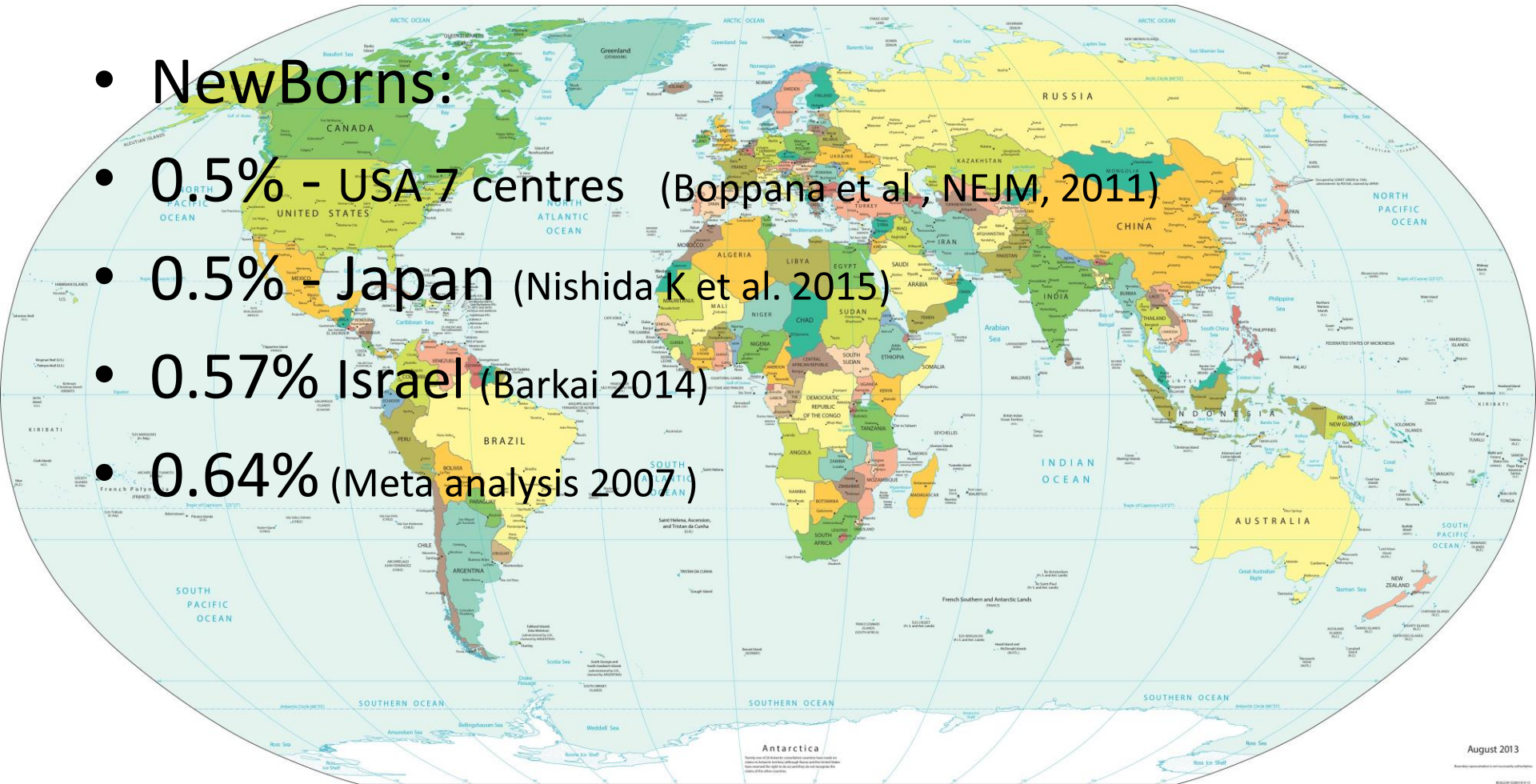
Preferential infection neural Stem cells

- May prevent differentiation and migration
- Glial cells--- may also affect migration of neural cells
- Inflammatory environment itself may cause some cell death and cell malfunction

Placenta- trophoblast progenitor cells

# Epidemiology World

- **NewBorn's:**
- **0.5% - USA 7 centres** (Boppana et al, NEJM, 2011)
- **0.5% - Japan** (Nishida K et al. 2015)
- **0.57% Israel** (Barkai 2014)
- **0.64%** (Meta analysis 2007)



# Seroprevalence NZ (Similar to “world”)



- Seroprevalence in 530 NZ Children, 2009

- European 26.5%
- Māori 68%
- Pacific 74.5%
- Chinese 47.2
- Indian 50%

- Blood Donors Christchurch, 2006

- Caucasian 55%
- Pacific 93%

- [J Paediatr Child Health. 2009 May;45\(5\):291-6. doi: 10.1111/j.1440-1754.2009.01495.x.](#)
- [Epidemiol Infect. 2009 Dec;137\(12\):1776-80. doi: 10.1017/S0950268809990094. Epub 2009 Jun 1.](#)



# Definitions

## Symptomatic vs Asymptomatic



10 %

90%

Lanzieri et al, 2018. Hearing Trajectory in Children with Congenital Cytomegalovirus Infection. OHNS, 158 (4) 736-744

# Hearing Loss

- Exact mechanism of hearing loss unknown
- CMV virus found in every compartment of the ear
- Congenital/Early onset Hearing loss more likely to become a severe to profound loss
- White matter changes in asymptomatic cases Sig associated with H loss before 5 years

# CMV in Deaf children

## Dried Blood Spot Positivity in deaf neonates:

- 17% Italy (Barbi et al, Ped Inf Dis 2003)
- 7.3% Belgium ( Boudewyns et al, Otol Neurotol 2009 )
- 9% Washington ( Misono et al, Arch Otol Head Neck surg 2011)
- 20% Sweden (Karltorp et al, Acta Paediatr, 2012
- 9.6% New South Wales (Rawlinson et al, Conf pres,2014)
- 9.4% Queensland (Toumpas et a, J Paed Child Health, 2014)
- **BUT, LOW SENSITIVITY OF BLOOD SPOT!**
- --- 34.4 % sensitivity (Boppana et al, JAMA 2010)

# Antenatal scans

- Other Sites

- Hepatomegaly/Intrahepatic calcifications
- Intra uterine growth retardation
- Echogenic bowel

- Brain

- Intracranial calcifications/Hydrocephalus
- Microcephaly



Har-  
10  
Gn  
C5 /  
FF0 /  
SRI II 0 / Cf

Case courtesy of Dr Fabien Ho,  
Radiopaedia.org, rID: 65098

# How is congen CMV Acquired?



# Prevention

- Education programmes – Maternity
- Hand washing
- Avoidance of kissing on mouth of infants
- Avoidance of sharing food utensils
- ?Pasteurisation breast milk in premature neonates
  
- USA– Legislation in 5 states re: parental education. Connecticut is Notifiable illness
- Only in Utah legislation mandating testing

# RANZCOG Statement 2019



The Royal Australian  
and New Zealand  
College of Obstetricians  
and Gynaecologists  
*Excellence in Women's Health*

## Prevention of congenital cytomegalovirus (CMV) infection

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This statement has been developed and reviewed by the Women's Health Committee and approved by the RANZCOG Board and Council.

A list of Women's Health Committee Members can be found in [Appendix A](#).

Disclosure statements have been received from all members of this committee.

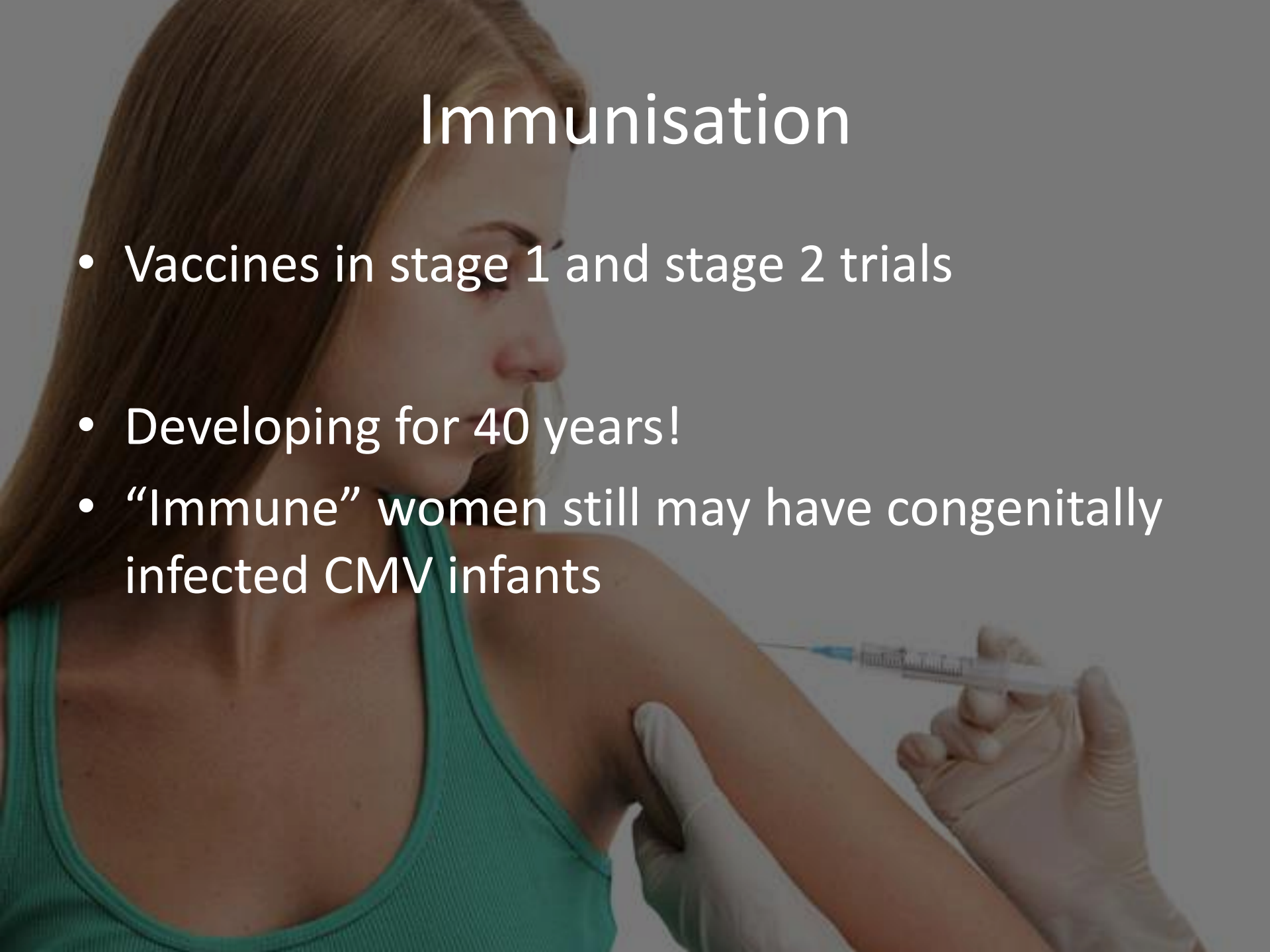
The Committee acknowledges contributing authorship in [Appendix B](#).

**Objectives:** To provide guidance for maternity care providers and the community on the prevention of maternal cytomegalovirus (CMV) infection during pregnancy in order to reduce mother to child transmission (MTCT) of virus, fetal infection and clinical sequelae (symptomatic congenital CMV); and to provide a general overview of the diagnosis and management of congenital CMV.

**Outcomes:** Improved awareness about CMV prevention among maternity health care providers and improved routine provision of patient education on hygiene measures which have been shown to reduce CMV transmission during pregnancy.

# Immunisation

- Vaccines in stage 1 and stage 2 trials
- Developing for 40 years!
- “Immune” women still may have congenitally infected CMV infants





# Treatment options

- Gancyclovir and Valgancyclovir
- Synthetic Guanosine analogues
- Used to treat CMV infection in organ transplant patients
- Anti CMV T Cell infusion
- Immunoglobulins



# Treatment effectiveness

The background of the slide features a silhouette of three people climbing a mountain peak. One person is at the top, another is in the middle, and a third is at the bottom, all reaching up towards the summit. The sky is a gradient of light to dark, suggesting a sunset or sunrise.

- J Pediatrics 2003- Kimberlin et al, randomised case controlled trial– 21 % treated children hearing deterioration by 12 months vs 68% controls
- JLO 2009 Austria, Ganciclovir 3 weeks → non sig difference in hearing (2/11 controls → H loss, vs 0/12 → hearing loss in treatment group)
- NEJM 2015-3, Randomised trial Valganciclovir → Modest improvement in hearing outcomes at 24 months with 6 months oral Vlaganciclovir 77% vs 64%  $p < 0.04$

# Treatment risks

- Short term:
  - Neutropenia 20%
- Long term:
  - Gonads- aspermia in mouse models
  - Carcinogenesis in mouse models

# Congenital CMV: a European consensus statement on diagnosis and management

Luck et al. PIDJ 2017; 36 (12); 1205-13

- There was a majority but not consensus opinion that isolated hearing deficit should be treated for 6 months



# Screening

- Should demonstrate improved outcomes and value of a screening programme to offset the expense and potential adverse psychosocial consequences for children and families

# Screening

- Targeted neonatal screening
- Salivary swab PCR testing within 3 weeks of birth
- Shown to be feasible, acceptable to parents and cost effective within a UK hospital based programme

Williams EJ, et al. Arch Dis Child Fetal Neonatal Ed 2014;99:F230–F236. doi: 10.1136/archdischild-2013-305276

# Costs

- UK feasibility trial costs approx £16 per sample



# Current Study NZ

NZ Paediatric Surveillance Unit



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THE HEARING HOUSE



Thank you

Colin R S Brown



<https://www.asid.net.au/documents/item/368>

<https://www.cmv.org.au>