

ROTAVIRUS DISEASE BURDEN and RV3 NEONATAL STRAIN CANDIDATE VACCINE

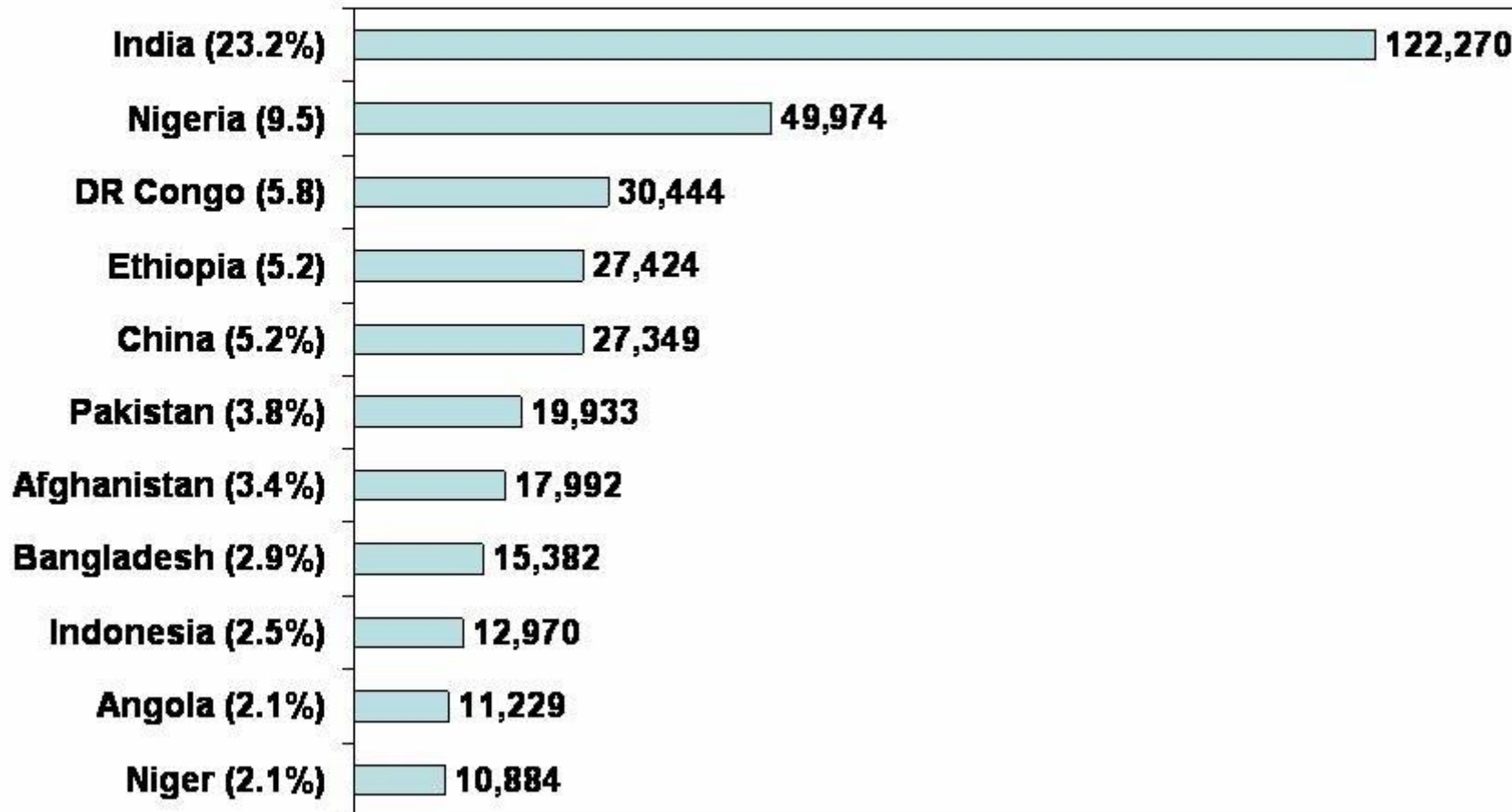
■ Graeme Barnes

- Murdoch Childrens Research Institute
- Royal Children's Hospital
- Dept of Paediatrics, University of Melbourne

■ Disclosure

- Participation in several rotavirus vaccine educational presentations sponsored by GSK (Rotarix) and CSL (Rotateq)
- Advisor for GSK Mexican post-licensing surveillance study

Number (and percent of global total) child rotavirus deaths by country:
2004 global total = 527 000
11 countries account for 65% of all child rotavirus deaths



Recent Studies of Australian Rotavirus Disease Burden - Admissions

Carlin et al MJA 1998	1993 - 1996	20,000	AGE
		10,000	Rota
Galati et al ANZJPH 2006	1998 - 2003	10,000	Rota
Newell et al JPCH 2006	2000 - 2002	4,700	Rota
			coded

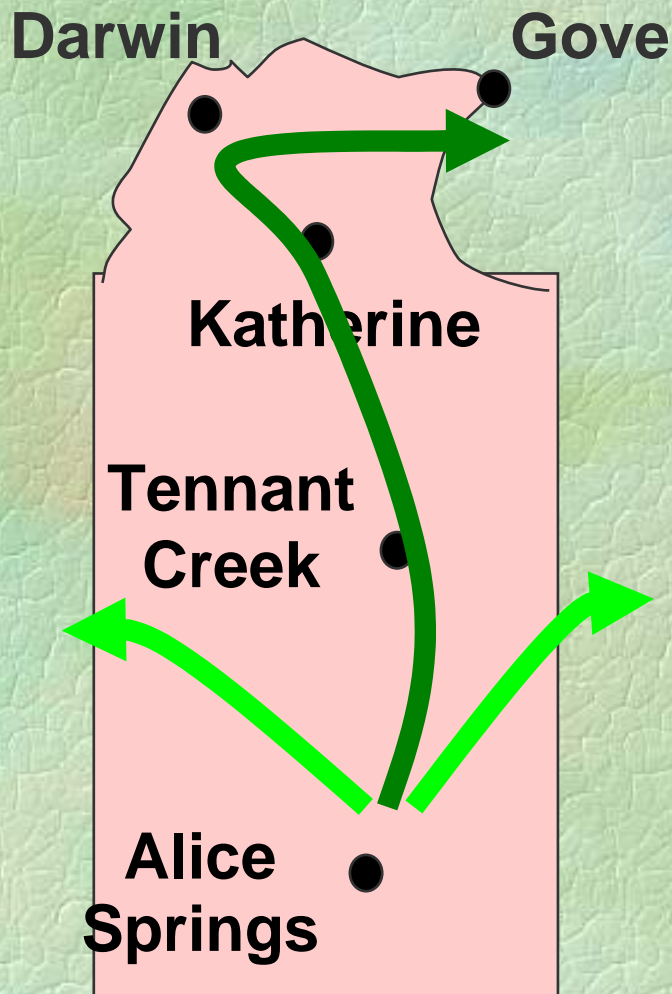
ROTAVIRUS DISEASE BURDEN in AUSTRALIA

- Admissions 10,000 (\$1,890)
- Emergency Dept 22,000 (\$320)
- GP visits 115,000 (\$36.60)

- Annual cost \$30 m approx

- Galati, Harsley, Richmond, Carlin. ANZJPH 2006, 30:416

G9 Outbreak: May-July 2001



Centred in Alice Springs, and remote communities.

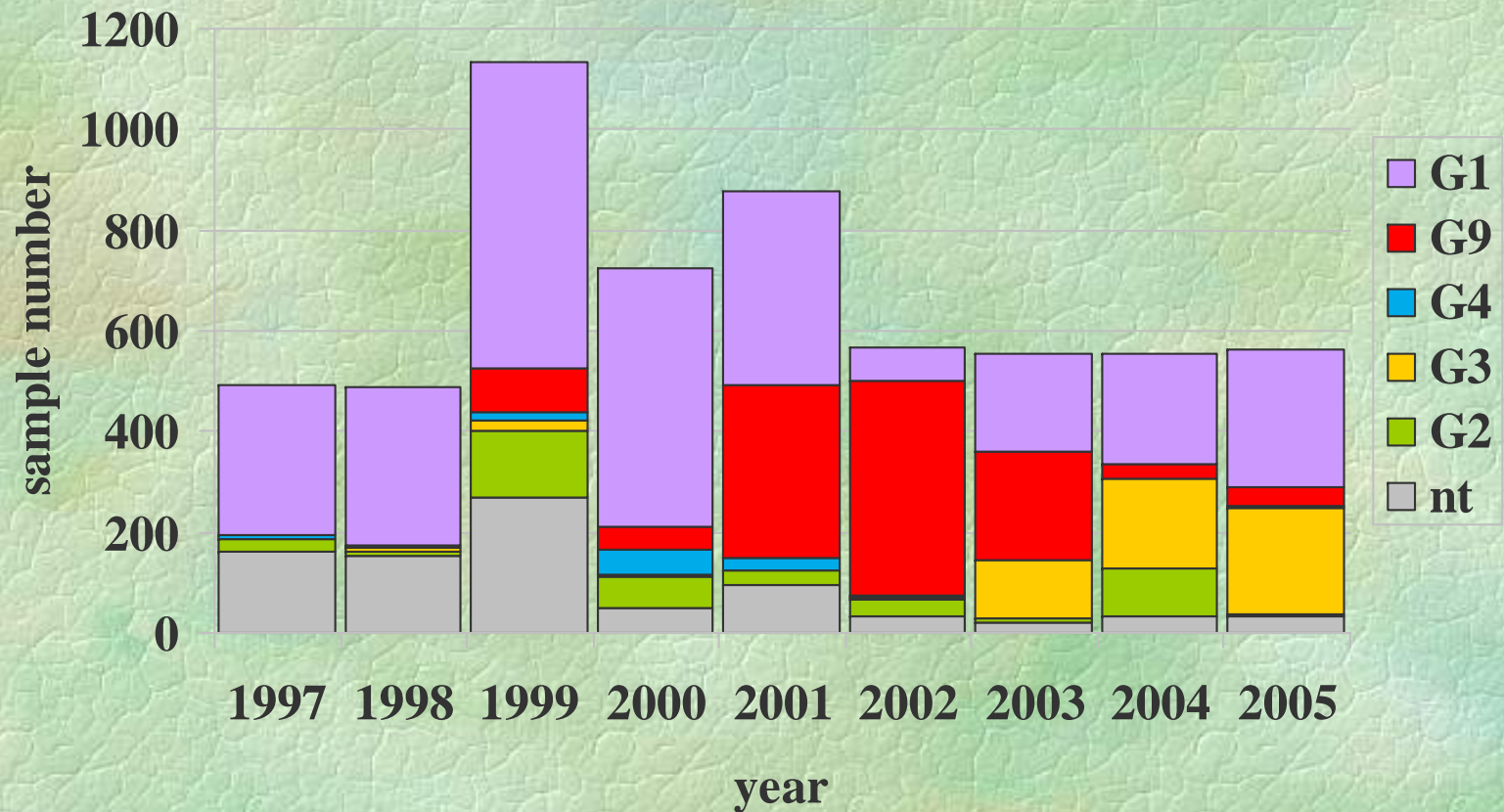
- Epidemic spread:
 - Northward to Tennant Creek, Katherine, Darwin and Gove.
 - QLD: Mt Isa
 - WA: remote communities

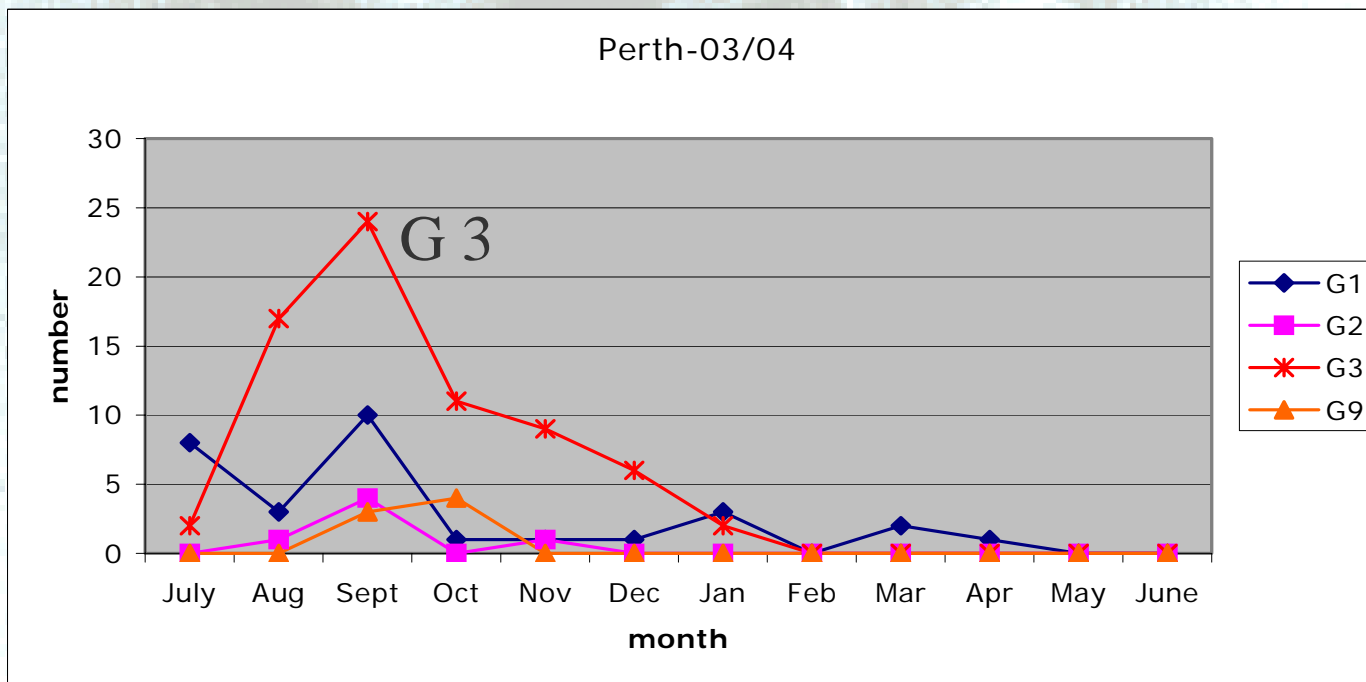
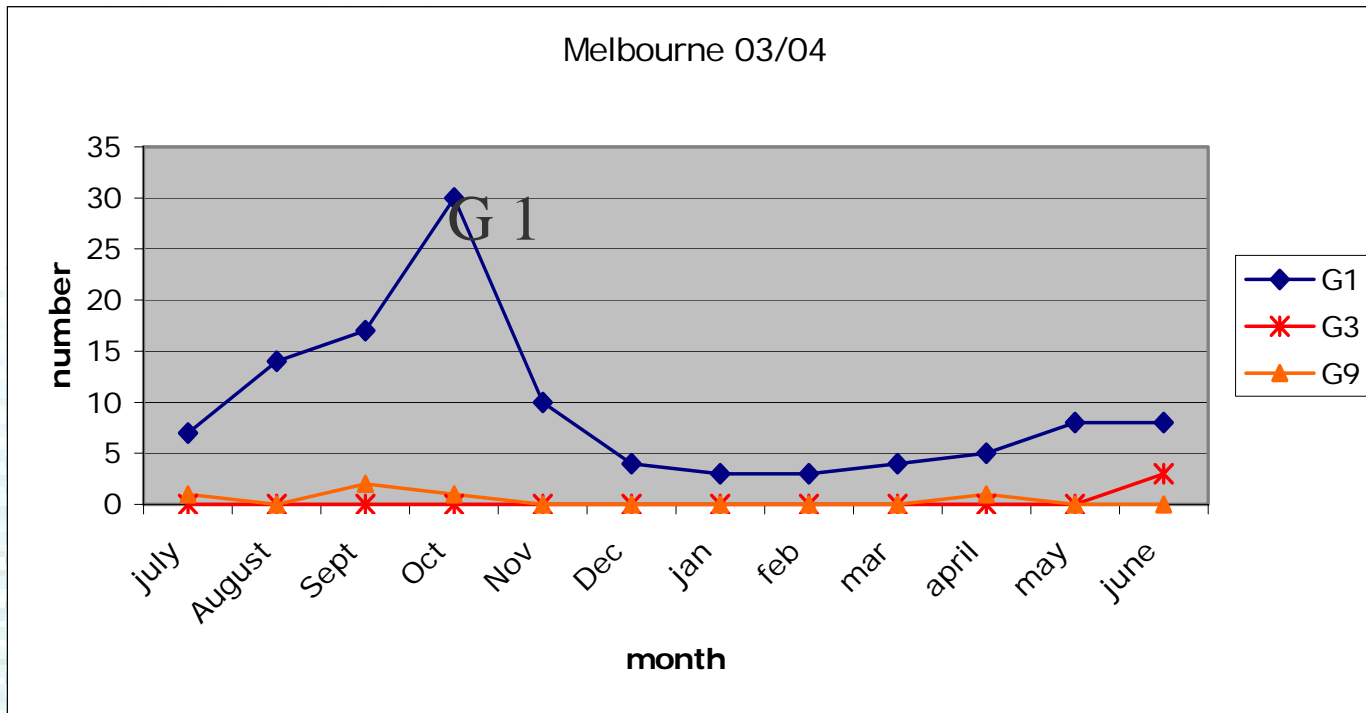
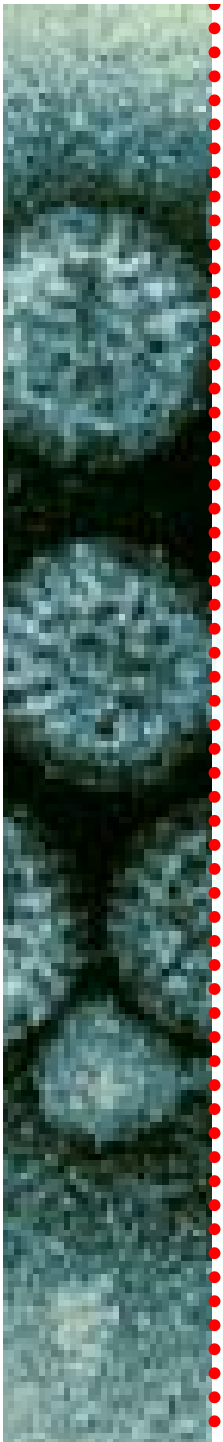
NATIONAL ROTAVIRUS SURVEILLANCE PROGRAM

- Evolved from NHMRC surveillance project 1993-1996 inc
- Established 1999
- Funded by:
 - Commonwealth Dept of Health and Ageing
 - GSK
 - CSL

Longitudinal serotype variation

Australia-wide distribution of rotavirus G types:
1997-2005





Vaccines for NIP July 2007

- Both live attenuated, orally administered

- Rotarix (GSK) human strain
 - G1 P1A[8]

- RotaTeq (CSL) bovine-human reassortant
 - Contains G1, G2, G3, G4, and G6 P1A[8]

Challenges for the new rotavirus vaccines

1. Safety outside strict clinical trial setting

2. **Effectiveness**

- **regional variation in serotypes**
- **vaccine pressure on serotypes**
- **gut flora variation - “tropical enteropathy”**
- mix with other vaccines

AN UNREACHED GOAL (so far...)

NEONATAL ADMINISTRATION

Rotavirus hits early in developing countries

- Africa. Review of 43 published studies where at least 100 patients with diarrhoea were specifically screened for rotavirus
- **38% of those hospitalised with rotavirus were < 6 months of age (8% in Melb)**
- **Conclusions:**
 - many cases occur early in infancy
 - immunization at birth should be an aim

Other Rotavirus Vaccine Candidates

- **Hexavalent human-bovine reassortant**
- **Lanzhou lamb rotavirus**
- **Indian human-bovine natural reassortant neonatal strains**
- **RV3 naturally attenuated neonatal strain**
- **Rhesus tetravalent reborn...**

- **Killed, particle, DNA etc**

What is RV3 ?

- Human rotavirus G3 P6
- From newborn infant in Melbourne
- Many infected with no symptoms
- Protected against disease 1st 3 years of life
- Heterotypic protection

SUMMARY

- Prepared as oral vaccine
- Immune response in 46%
- Response gave 54% 1 year protection
- Protection heterotypic
- Need to increase immunogenicity



Wanted: Amelia Carroll, a vaccine trial participant, checks out seven-week-old Shaun Little. Babies of this age are needed for tests. Picture: DAVID CAIRD

Hospital in plea for gastro vaccine volunteers

THE Royal Children's Hospital is looking for "baby soldiers" to help test a gastroenteritis vaccine.

By HELEN CARTER, medical reporter

The hospital has finished trials to establish the safety of the vaccine for adults and children. It now needs babies to take part.

Dr Barnes said the vaccine had not had any bad effects. Dr Barnes said researchers believed the vaccine had "taken" and had produced an

results of blood tests. These would show if there were antibodies to fight the main virus which causes childhood gastroenteritis, rotavirus.

Dr Barnes said the aim of initial trials in small groups of adults, children and babies was to establish that the oral

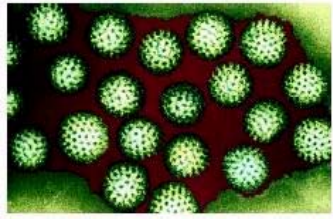
of children around Australia and the world to see if it worked.

Sean Melrose and Amelia Carroll, both 3½, took part after their mothers read a *Herald Sun* article and wanted to help.

When Amelia was a baby

baby. "We know what it's like so we wanted to help prevent it," said Amelia's mother, Denise.

The hospital wants to hear from parents whose infants will be two to three months old between now and March. The hospital will give routine



Strengths of RV3 vaccine



- Exclusively human neonatal rotavirus strain
- Naturally attenuated and adapted to the infant gut
- Natural infection is asymptomatic and protective
- Protection is heterotypic
- Safe and well tolerated in phase I and II trials
- Higher titre now achieved in Vero cells
- **Ideal candidate for neonatal administration**

Partners

■ *Melbourne*

- Murdoch Childrens Research Institute at RCH
- NHMRC Centre for Clinical Research Excellence in Immunisation

■ *Brisbane*

- Q-Gen Pty Ltd at QIMR

■ *Dunedin, NZ*

- Dept of Paediatrics and Child health

■ *Bandung, Indonesia*

- BioFarma PT, Vaccine Manufacturer

■ *Yogyakarta, Indonesia*

- Dept Paediatrics, Gadjah Mada University

RV3 Progress

- Q-Gen (QIMR) developing high titre RV3
- Phase I trial in Melbourne early 2008
- Parallel phase II trials late 2008
 - Dunedin, NZ: immunogenicity
 - Yogyakarta, Indonesia: protection
- Results from phase II to battle for funds for phase III