

What do we know about source of infant pertussis infection?

National Pertussis Workshop
Strategies to prevent severe pertussis in the next decade
25-26 August 2011

A/Prof Kristine Macartney
Deputy Director of Government Programs, NCIRS
Associate Professor, Discipline of Paediatrics and Child
Health, University of Sydney
Staff Specialist, Department of Microbiology & Infectious Diseases

Acknowledgements

- Ms Kerrie Wiley, PhD candidate NCIRS
- Peter McIntyre
- Tom Snelling
- Helen Quinn
- Yeqin Zuo
- Helen Marshall



Conflicts of Interest

- None

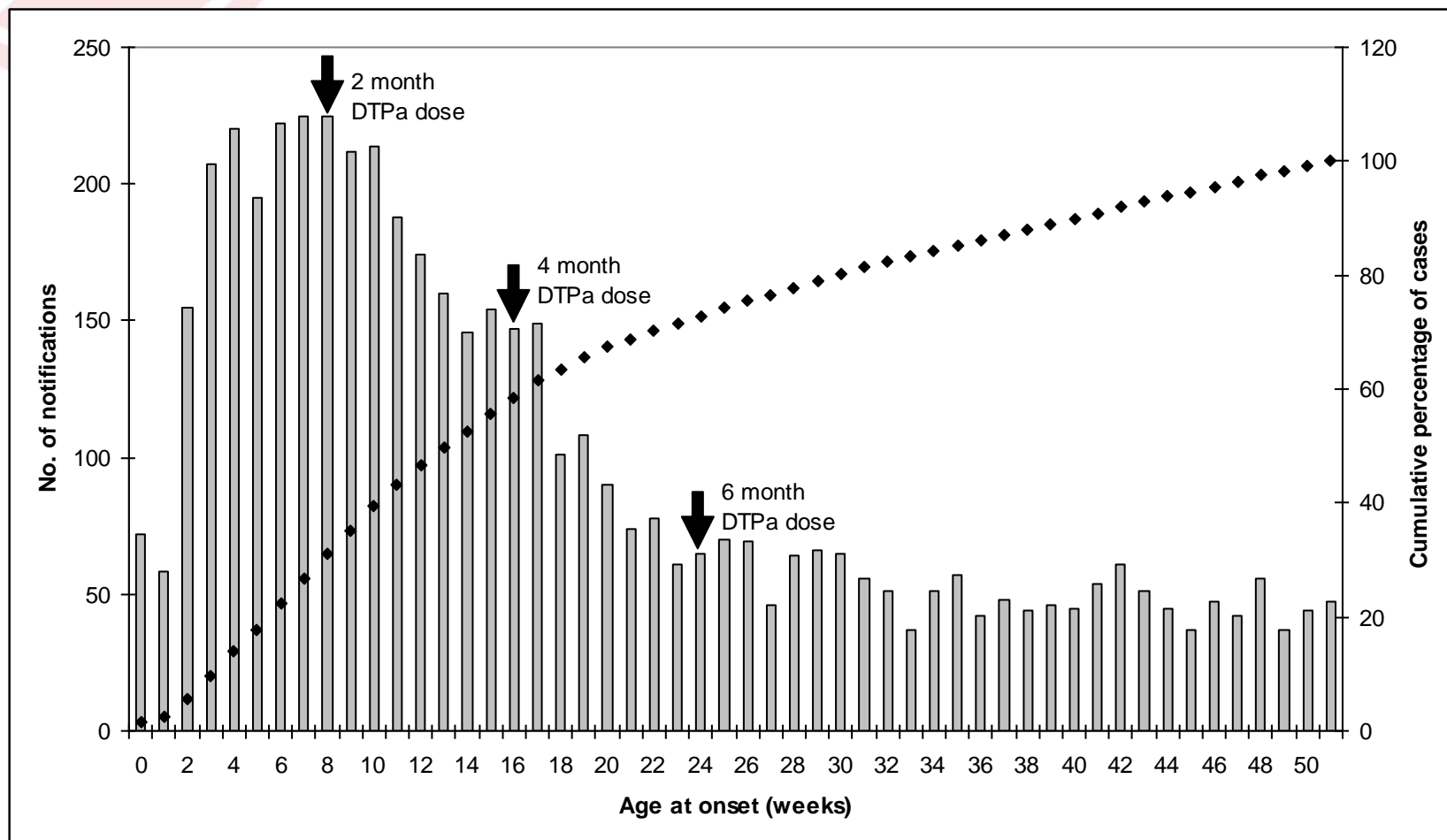
Background



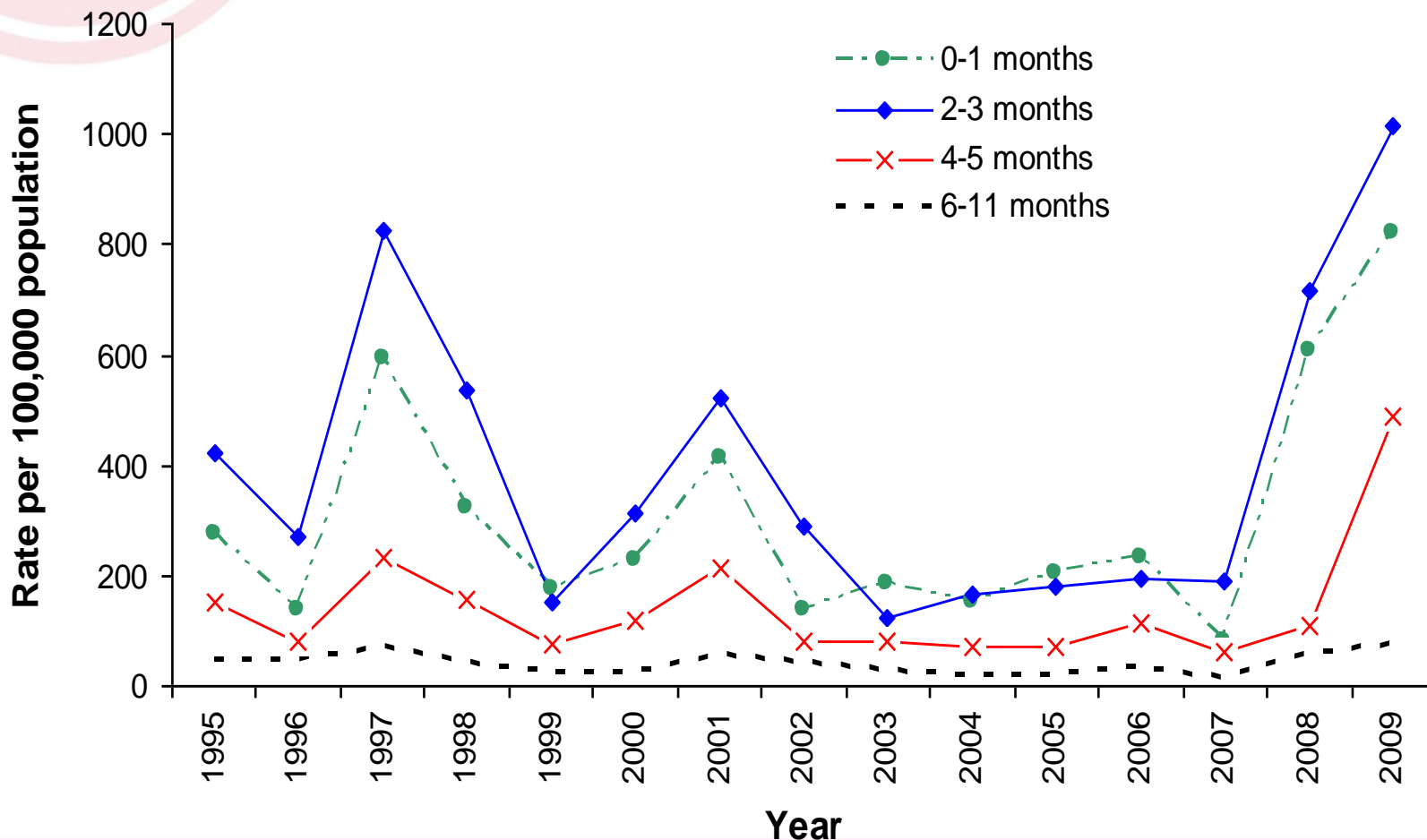
“Cocooning strategies” = pertussis immunisation of mothers/fathers/close contacts of newborns, but

- Who gives pertussis to young infants and when?
 - Australia versus other settings
 - Transmission from vaccinated v. unvaccinated contacts?
 - Effectiveness of contact vaccination against transmission?

Pertussis notifications and the primary immunisation schedule: Australia 1995 - 2009



Pertussis hospitalisation rates infants 0 - 11 months of age, 1995 - 2009, New South Wales



Systematic review of evidence on source of pertussis infections in infants

Methods

- Searched MEDLINE and EMBASE
- Literature in English published January 1999 and May 2010
- Also identified articles through references and consultation
- Quality assessment:
 - STROBE statement (22 pt scale)



Systematic review of evidence on source of pertussis infections in infants

Results

- 13 studies: 3 with prospective contact testing
- Quality appraisal for observational studies by STROBE
 - Score range 11- 20 out of 22
- Studies settings
 - US, UK, Australia, The Netherlands, Brazil, Spain, Canada
 - 2 multi-centre/multinational
- Most focused on infants < 12 months
- Case ascertainment
 - Pertussis deaths (1 study, USA national)
 - Hospitalised infants (8 studies, 2 PICU-based)
 - Notifications/enhanced surveillance (4 studies)



Table of studies

Table of studies deleted due to manuscript in preparation



Table of studies

Table of studies deleted due to manuscript in preparation

Source of Infection: study variability

- Overall contact identification ~50%
- Study quality and design differed ++
- Other contributing factors
 - Local disease epidemiology
 - Demographics
 - Family structures
 - Vaccination of contacts
 - schedule
 - vaccine type
 - host response
- No published studies reported on presence (or not) of recently vaccinated adult contacts

Source	% of identified sources
Mother	12 - 50%
Siblings	16 - 45%
Father	10 - 26%
Grandparents	4 - 8%

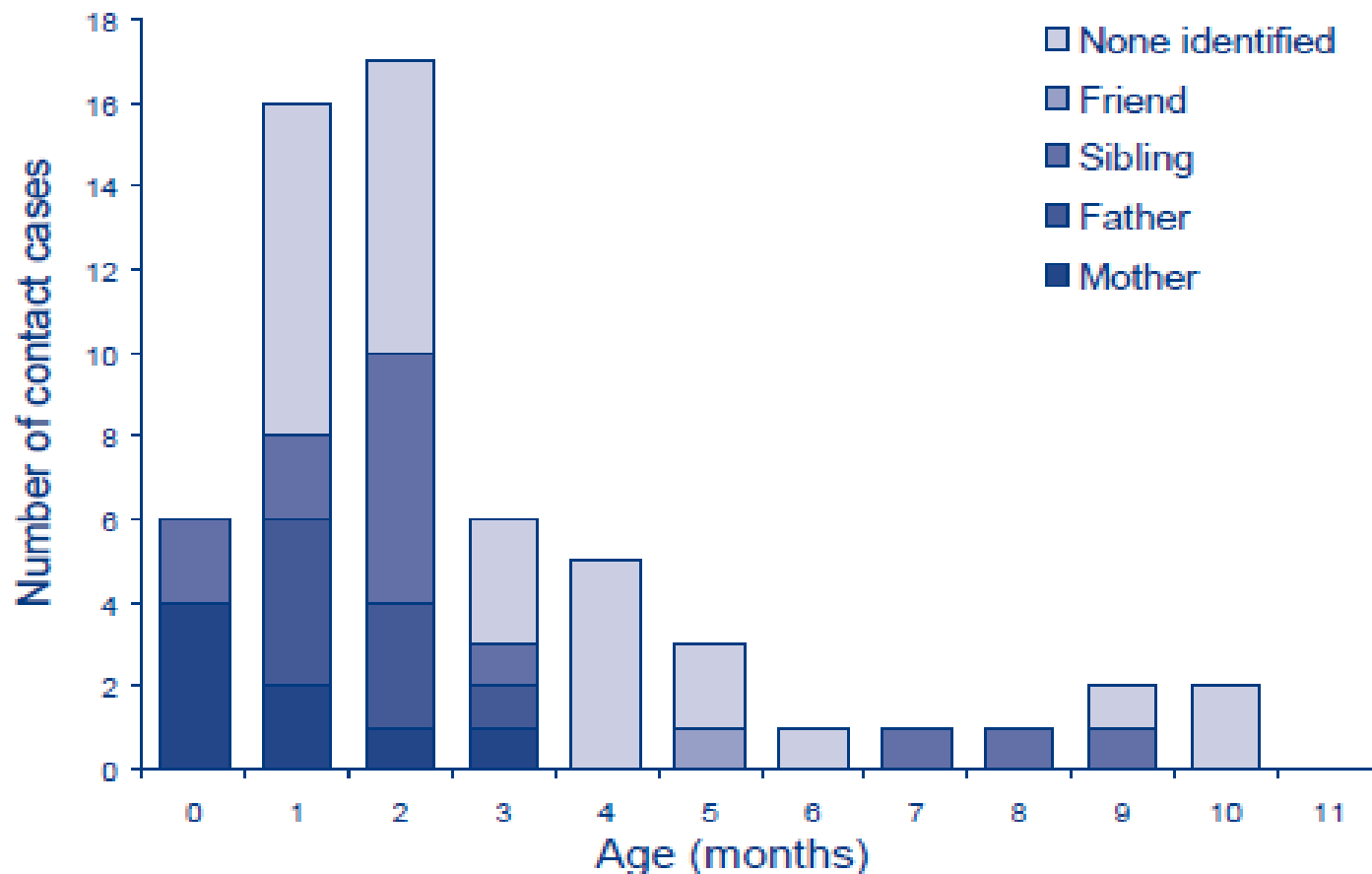
Australian studies of infant pertussis contacts

Study (study period)	Setting	Cough contacts identified	Results
Elliott (2001)	Australia Hospitalised infants APSU n = 140	51%	68% adults (mothers 29 / 68) 31% children (half < 10 yrs of age) 32% cough contacts laboratory confirmed
Chuk (1997 – 2006)	Brisbane Royal Children's Hospital n = 55	47%	52% parents (87% for infants < 3 months) 45% children 23% cough contacts laboratory confirmed
Jardine (2009 - 5 months)	Sydney region n = 95 notifications (35 hospitalised)	69%	16% parents 60% children (half were 3 - 4 yrs of age) 25% cough contacts laboratory confirmed
Marshall* (2009)	Australia 9 hospitals n = 100	53%	34% parents 42% siblings 57% cough contacts laboratory confirmed

*Marshall et al, manuscript in preparation

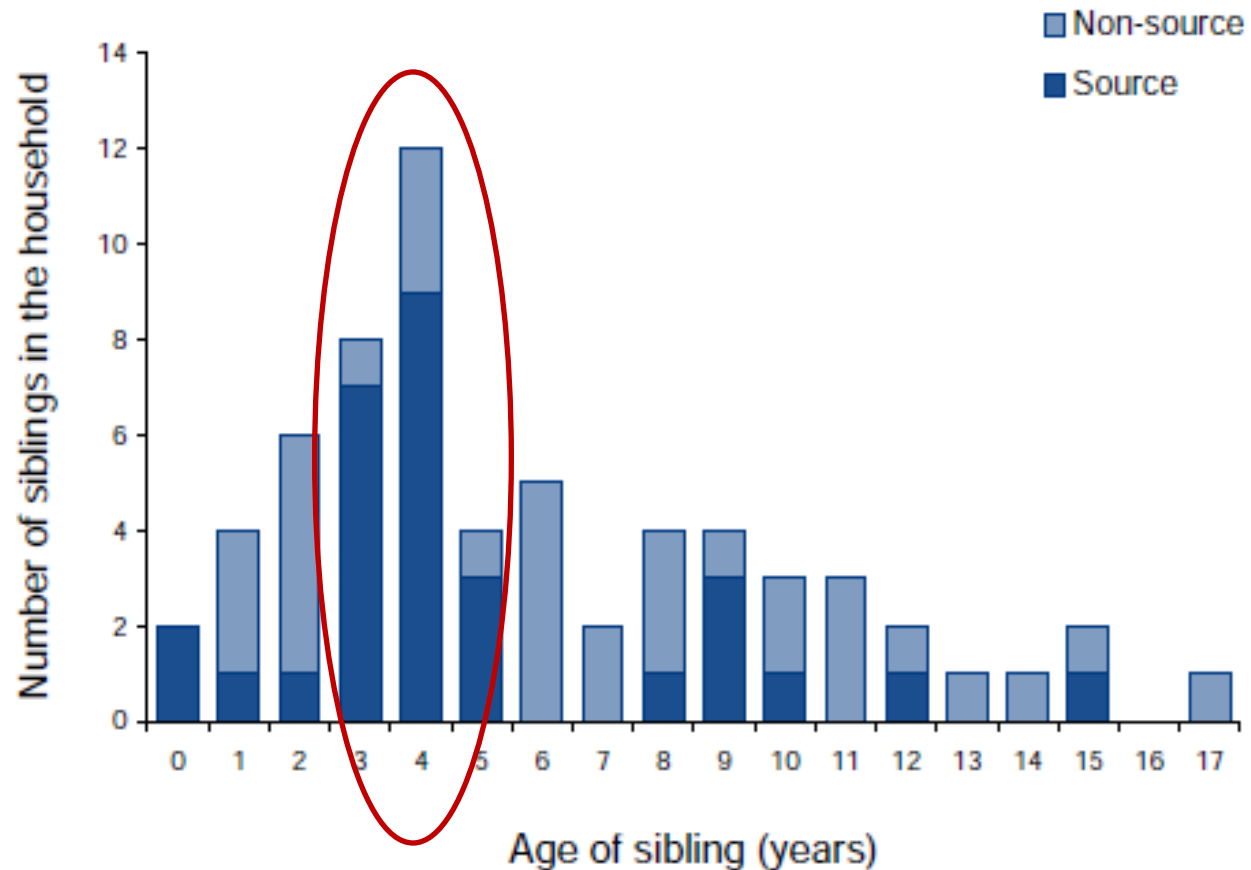
Chuk et al, Brisbane study, 1997-2006

Figure 3. Contact history of hospitalised cases of pertussis according to age of infants



Jardine et al, Sydney study 2009

Figure 2: Age distribution of siblings less than 18 years of age resident in the index cases households



Results – Source of Infection Studies

Studies with >80% of identified contacts laboratory tested	Design / Setting	N° Index Cases age	N° contact pertussis cases (N° contacts Identified / investigated)	N° Contacts laboratory tested
Crowcroft <i>et al</i> United Kingdom, 2001	Prospective cross-sectional PICU & paed wards	25 (<5 mo) 8 (<15 yrs)	32 (328)	81% adults 43% children
Wendelboe <i>et al</i> France, Germany, USA Canada 2003-04	Prospective cohort Multinational (hospitalised)	95 (<6 mo)	222 (404)	85.9%
De Greeff <i>et al</i> The Netherlands 2006-08	Prospective cohort National study (hospitalised)	201 (<6 mo)	391* (738)	98%

- * Numbers and % of contacts tested and positive depend on criteria used for inclusion in analysis eg any versus multiple positive tests

Results – Source of Infection Studies

Author	Contacts tested (n)	Contacts pertussis positive (% of total)	Parents/siblings %	Asymptomatic contacts pertussis positive n (% of total contacts)
Crowcroft	328	32 (10)	42 / 27	-
Wendelboe*	347	222 (63)*	55 / 16#	44 (14)^
de Greeff	560	299 (53)	55 / 41	42 (8)

- Multiple sensitivity analyses, range of infants with positive contacts 53-63%
- # 18-29% of non household contacts were positive
- ^ Twice as many adults as child contacts were asymptomatic

De Greef, Netherlands, 2006-2008



- Prospective: if contacts had > 2 tests positive
 - 164 cases with 560 household contacts
- 53% of household members: lab confirmed pertussis
 - 53% typical symptoms
 - 14% asymptomatic, 33% mild or atypical symptoms
 - only 39% had consulted GP, 5% of adults had lost work days
- Siblings (41%) > Mothers (38%) > Fathers (17%)
- First cases in household
 - 40% infant case, 28% siblings, 24% mothers (also mother infant pairs)
- Mothers: 22% symptom onset in late pregnancy
- Sibling vaccination
 - 89% vaccinated in infancy
 - 3 dose whole cell recipients - 46% typical pertussis
 - 3 dose acellular recipients – 29% typical pertussis



Australian studies (and Netherlands)

Siblings > **Mothers** > Fathers > other household

Other international studies

Mothers > **Siblings*** > Fathers > other household

Non household ~ 40 - 50%

*Canadian study 1990's: 40% cases had source, 1/2 were siblings

ncirs

NATIONAL CENTRE FOR IMMUNISATION
RESEARCH & SURVEILLANCE

What generalisations can we make?

- Source not always apparent
- Household members ~ 50% to 82%
 - Younger the infant (< 3 mo), mothers more likely source
 - Maternal symptom onset in pregnancy in 22% of cases (1 study)
- Siblings more commonly source in
 - Recent Australian studies, Netherlands
 - Most vaccinated
 - Half with mild/atypical or no symptoms
- 8-16% of asymptomatic contacts test positive for pertussis
 - ? role as source case
- Important non-household member contacts – difficult to ascertain
 - Close friends/other relatives
 - Healthcare workers/post natal ward

Conclusions

Who gives pertussis to young infants and when?

- Australia versus other settings
 -also, need better prospective studies
- Transmission from vaccinated v. unvaccinated contacts?
 - Vaccinated sibling contacts play a role
 - Impact of adult cocoon vaccination to be determined
- Effectiveness of contact vaccination against transmission?.....



Dana McCaffrey

Facebook Page

DANA Elizabeth McCaffery

- died 2009 at 4 weeks of age from pertussis
- Dana's parents, Toni and David, have written an open letter...



Dana Elizabeth McCaffery

5th February 2009 - 9th March 2009

Dear Prime Minister,

Thank you for joining the Facebook group for our daughter, Dana Elizabeth McCaffery, who died of Whooping Cough (Pertussis) at four weeks of age. Over 20,000 people have joined this group

- We call on you to coordinate a national response to stop this alarming increase.

As a minimum, this requires

- **Increased childhood immunization**
- **Free boosters for all adults across Australia**

Yours sincerely,

Toni and David McCaffery

- Help us to urge governments to act. Please write to the Prime Minister of Australia, Kevin Rudd or your Premier. [Download a proforma here.](#)



NATIONAL CENTRE FOR IMMUNISATION
RESEARCH & SURVEILLANCE