Dr Emma Best

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Starship Children's Hospital

Update on Paediatric Vaccinations - Concurrent Workshop Repeated

Saturday, 22 June 2013	Start 2:00pm	Duration: 55mins	Da Vinci
	Start 3:05pm	Duration: 55mins	Da Vinci

Vaccine preventable diseases

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Acknowledgements for slides

Dr. Cameron Grant, Associate Professor, Paediatrics, University of Auckland
Paediatrician, Starship Children's Hospital, Auckland
Dr Nikki Turner, Director, Immunisation Advisory Centre, University of Auckland
Dr Anusha Ganeshalingham PICU fellow intensive care for pertussis info

Google Images

Immunisations again…

Declarations

- Today am invited speaker by GSK who have paid my travel and accommodation
- Do not accept honoraria
- Participant in research groups with consumables funded by Wyeth (Pfizer) and GSK
- Member of the Anti-infectives committee of Pharmac

Outline

Describe vaccine preventable diseases which I still see and some management

1. What are we seeing at the moment
2. What to do after exposure to vaccine preventable disease
3. New vaccines
4. Who is referred to immunisation clinic

Exposure to antigens?

- 3 week old baby with cough comes to see you – maybe turned blue
- Mother has had cough for about 2 weeks

Questions

What do you do now?

Management

- Recent possible story of apnoea , young age – refer to hospital
- Notify Public health of suspected pertussis case and consider prophylaxis
- Treat mother / contacts
  - Azithromycin syrup fully funded
  - Dose 10mg/kg Day 1 then 5mg/kg Day 2-5
    - Newborns and pyloric stenosis

- Mother coughed a lot whilst she was in clinic rooms
  - *Have you had Tdap in last 10 years?*

Who is a contact?

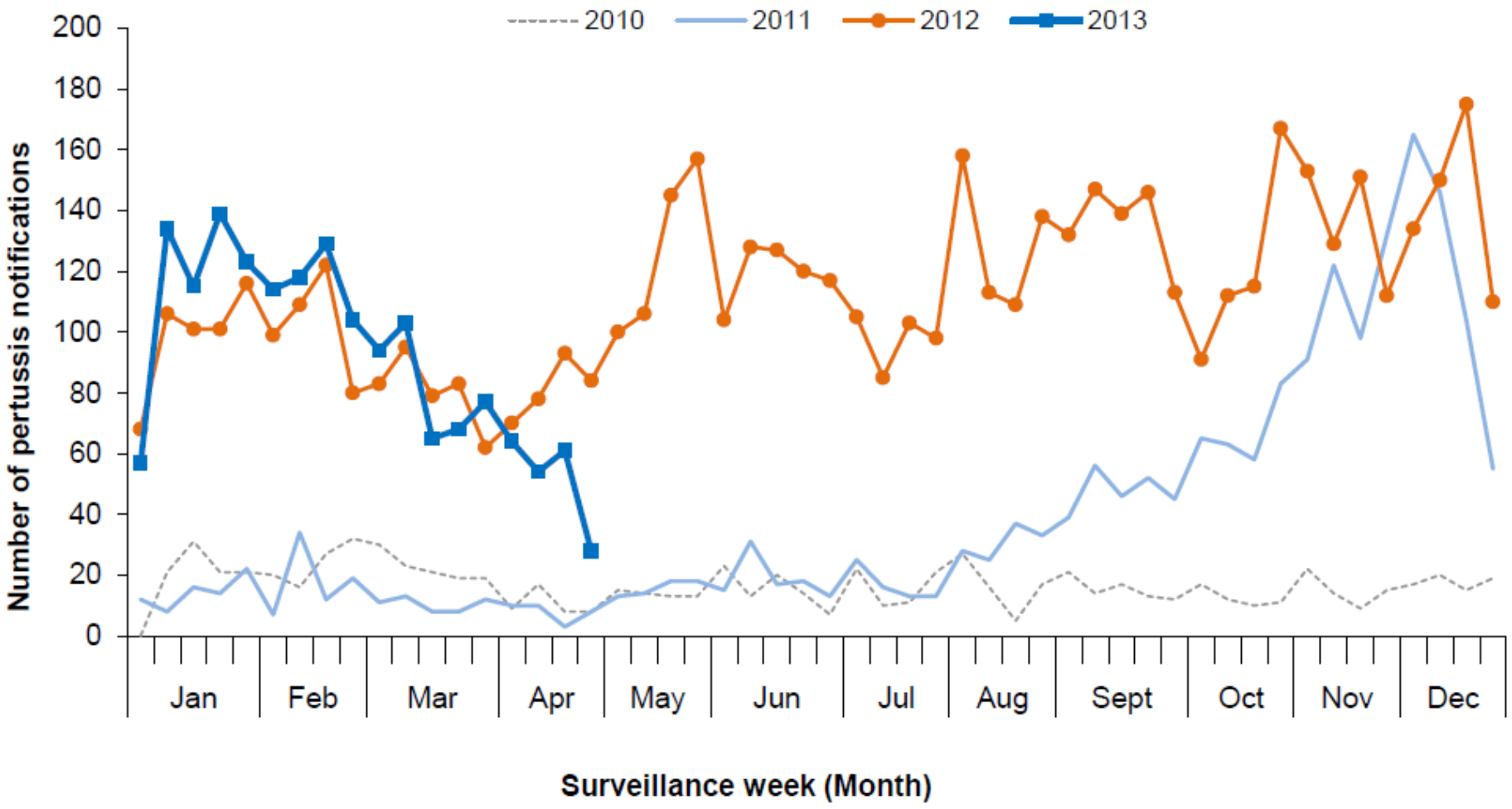
- Age < 1 year (?6months) or
- Partially or un-immunised & < 5 yrs of age; or
- Has chronic disease or is immunocompromised; or
- In the last trimester of pregnancy; or
- Has daily contact with a high priority contact i.e.infants <12 mths old,pregnant women, immunocompromised therefore poses a transmission risk.
- Non infectious when
  - coughing >3 weeks
  - completed 5/7 macrolide (azithro or erythro)

100 day cough

Every 3-5 years escalating epidemics
End of 2011 – it was that time again

but is proving to be a record breaker

Number of pertussis notifications by week reported, 2010 - 2013



ESR, Pertussis Report: April 2013.

The New Zealand Herald

Whooping cough epidemic rapidly escalating

5:30 AM Friday Jun 8, 2012

The epidemic of whooping cough, a potentially fatal infection, is rapidly escalating, the latest figures published by health authorities show.

The disease, spread by coughing and sneezing, is particularly dangerous for babies and other young children. It can lead to pneumonia, convulsions and brain damage.

Health authorities say vaccination is

Whooping cough cases double in Auckland

› Waikato DHB offers free whooping cough

NZ epidemic statistics are being mirrored around the world – in the UK, US and Australia

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30 October 2012 Last updated at 16:17 GMT

Share

Whooping cough cases 'highest in 20 years' says Public Health Agency

Whooping cough cases have risen significantly in Northern Ireland in recent months, according to new figures from the NI Public Health Agency (PHA).

There have been 221 confirmed cases recorded up until 30 September this year, compared to just 15 in the whole of 2011.

The PHA said 30 of this year's cases were confirmed in the last month alone.

The PHA has urged the parents of young children and pregnant women to ensure vaccinations are up

34

Admissions to SSH PICU…and counting

3 deaths

4 apnoeic neonates per bay (4 times)

Presentation of pertussis varies with age .. and immunisation status

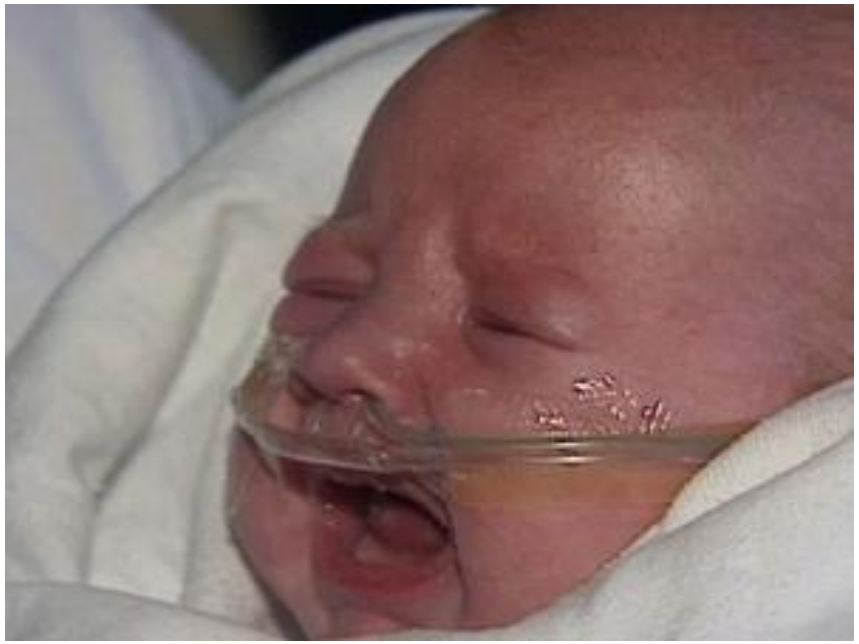
- Children
  - Non-immunised cough increasing in severity over several weeks rapidly repeated, forceful coughs followed by desperate gasps
  - Well between paroxysms
  - Immunised – milder disease – still cough, less forceful

Presentation of pertussis varies with age

- Adult
  - Persistent cough,worse at night and often paroxysmal
  - Awoken by a ‘choking sensation’
    - scratchy throat, sweating attacks
    - Post-tussive vomiting and whoop

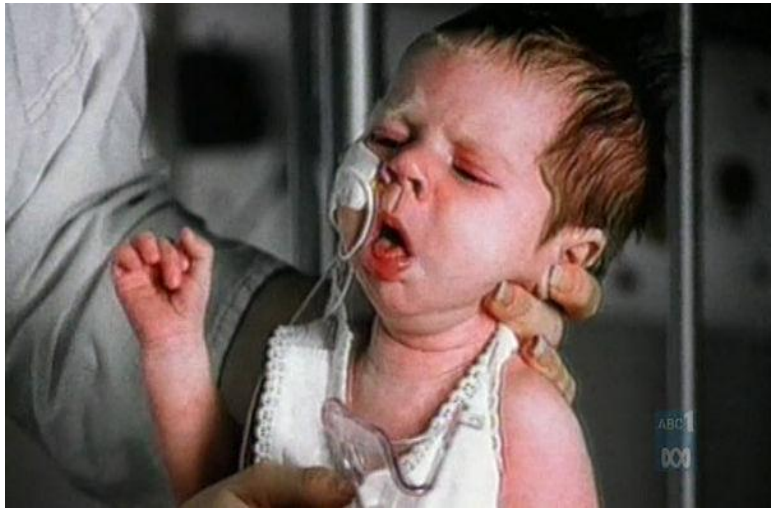
Critical Pertussis

- Malignant or fulminant
- Infants
  - <3 months old
  - 6/10 hospitalized in <6 months of age



Infant Pertussis

- Atypical course
  - Rapid disease progression – ‘compressed’ clinical course
  - Co-infection: RSV/adenovirus

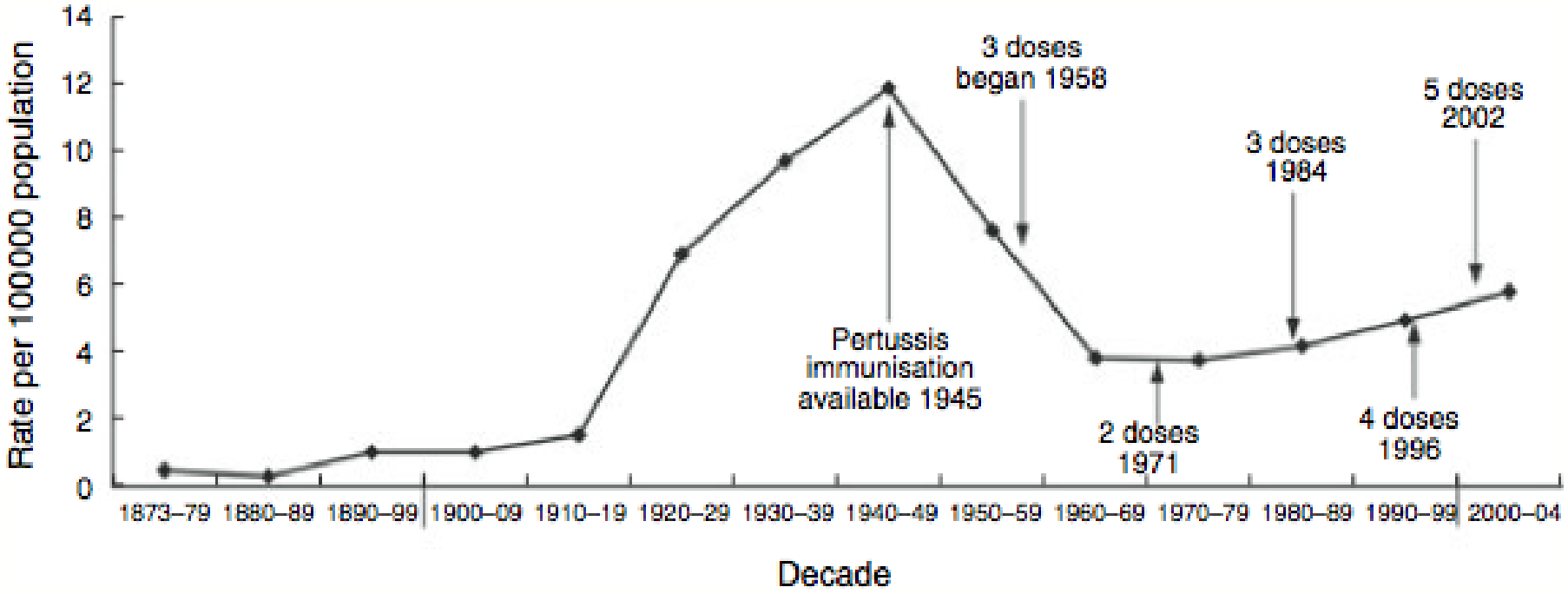


- ICU presentations
  - Apnoea
  - Desaturation & bradycardia
  - Pneumonia, pulmonary hypertension, respiratory failure
  - Haemodynamic instability, shock
  - Seizures, encephalopathy

Factors associated with mortality

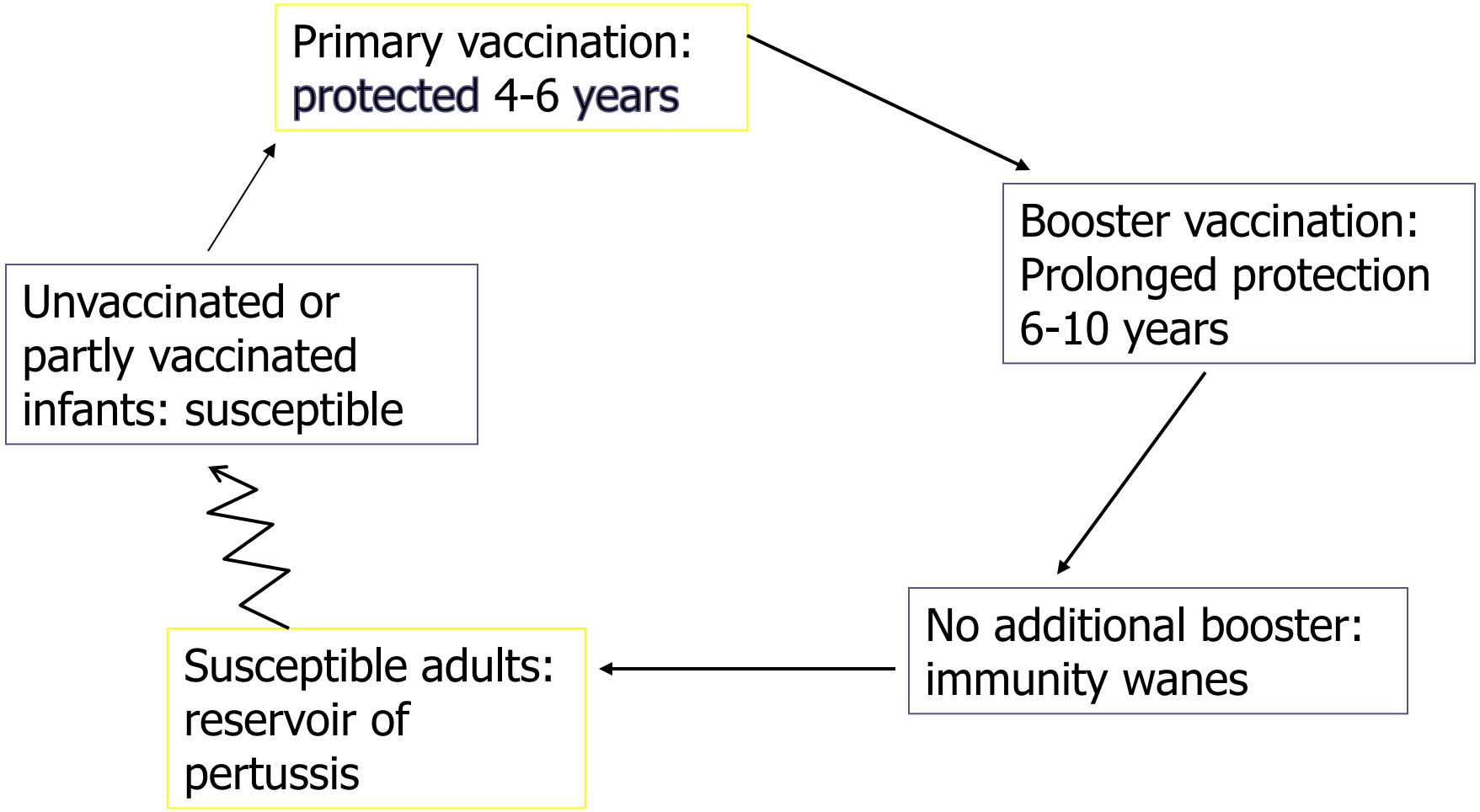
1. Age < 6 months
2. High white cell count
3. Unimmunised
4. Pneumonia
5. Pulmonary hypertension

Pertussis hospital discharge rate in NZ per 100,000 person years



J Paed Child Health 2007 Somerville, Grant et al

Vaccination has changed pertussis epidemiology



Source: adapted from Lancet ID 2002

Table 1 National Immunisation Schedule commencing 1 July 2011*

Note: for ease of reading, vaccine trade names have been written in the standard font, and as proper nouns.

Antigen	DTaP-IPV-HepB/Hib	PCV10	MMR	Hib	DTaP-IPV	Tdap	HPV	Td	Influenza
Brand	Infanrix-hexa	Synflorix	M-M-R II	Act-HIB	Infanrix-IPV	Boostrix	Gardasil	ADT Booster	
Manufacturer	GSK	GSK	MSD	Sanofi-aventis	GSK	GSK	CSL/MSD	CSL	
6 weeks	•	•							
3 months	•	•							
5 months	•	•							
15 months		•	•	•					
4 years			•		•				
11 years						•			
12 years (females only)							• 3 doses		
45 years								•	
65 years								•	• (annually)

Key: D = diphtheria; T = tetanus; aP = acellular pertussis; IPV = inactivated polio vaccine; Hib = *Haemophilus influenzae* type b; Hep B = hepatitis B; PCV10 = 10-valent pneumococcal conjugate; MMR = measles, mumps and rubella; Td = adult tetanus and diphtheria vaccine; d = adult diphtheria; ap = adult acellular pertussis; HPV = human papillomavirus.

Why are pertussis outbreaks occurring worldwide?

- Vaccination does not change the periodicity of epidemics
- Immunity wanes – perhaps faster than imagined
- The current vaccine is not perfect and needs very good coverage
- *Effectiveness of whole cell versus acellular vaccine….*

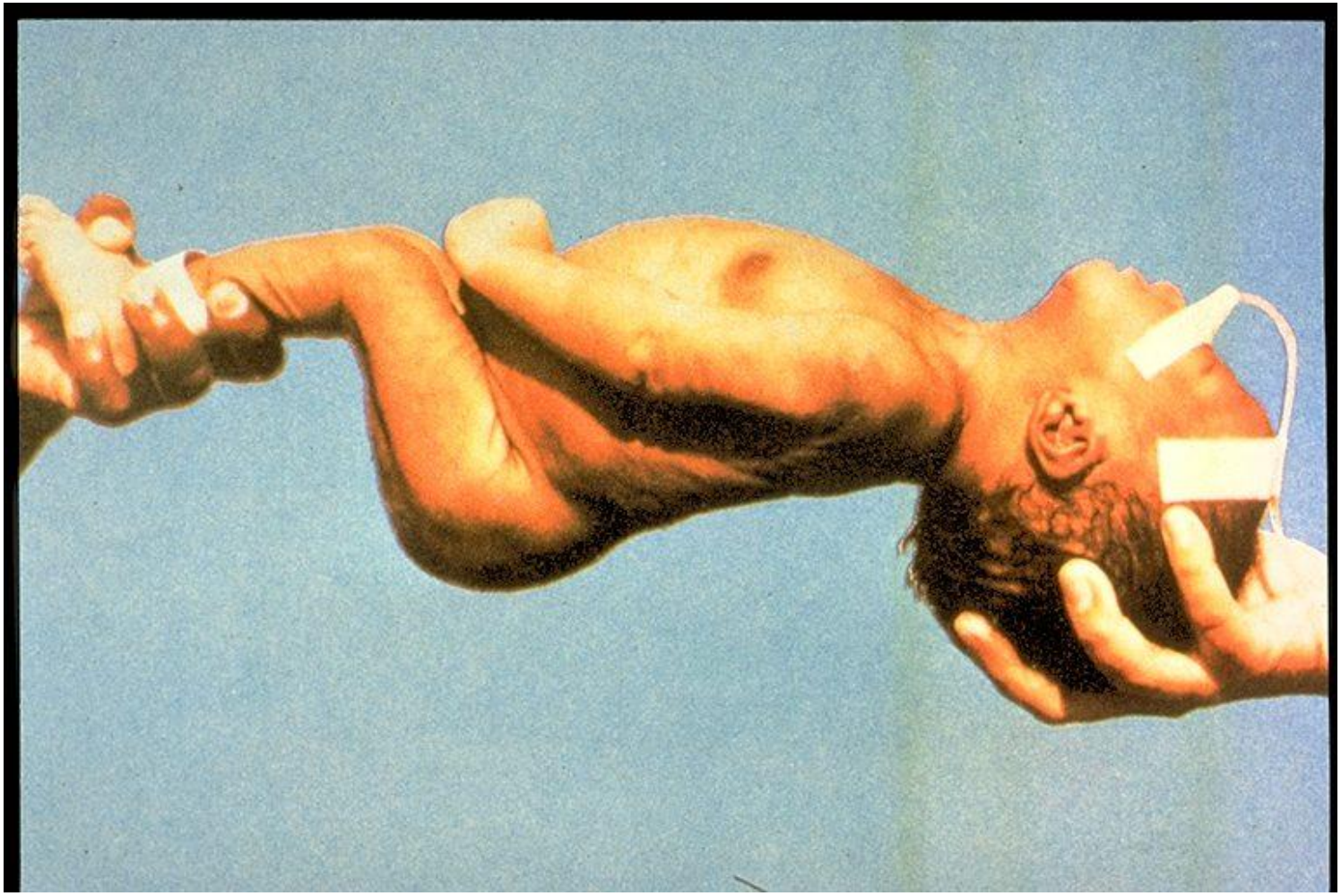
Why is pertussis in NZ so bad?

- *Very infectious and imperfect vaccine*
- + NZ has not achieved good coverage
- + NZ has not achieved timeliness
- + NZ has changed our schedule several times (including dropping a dose in 1970's)
- + NZ has poverty and crowded housing issues

Protect the young immunise …

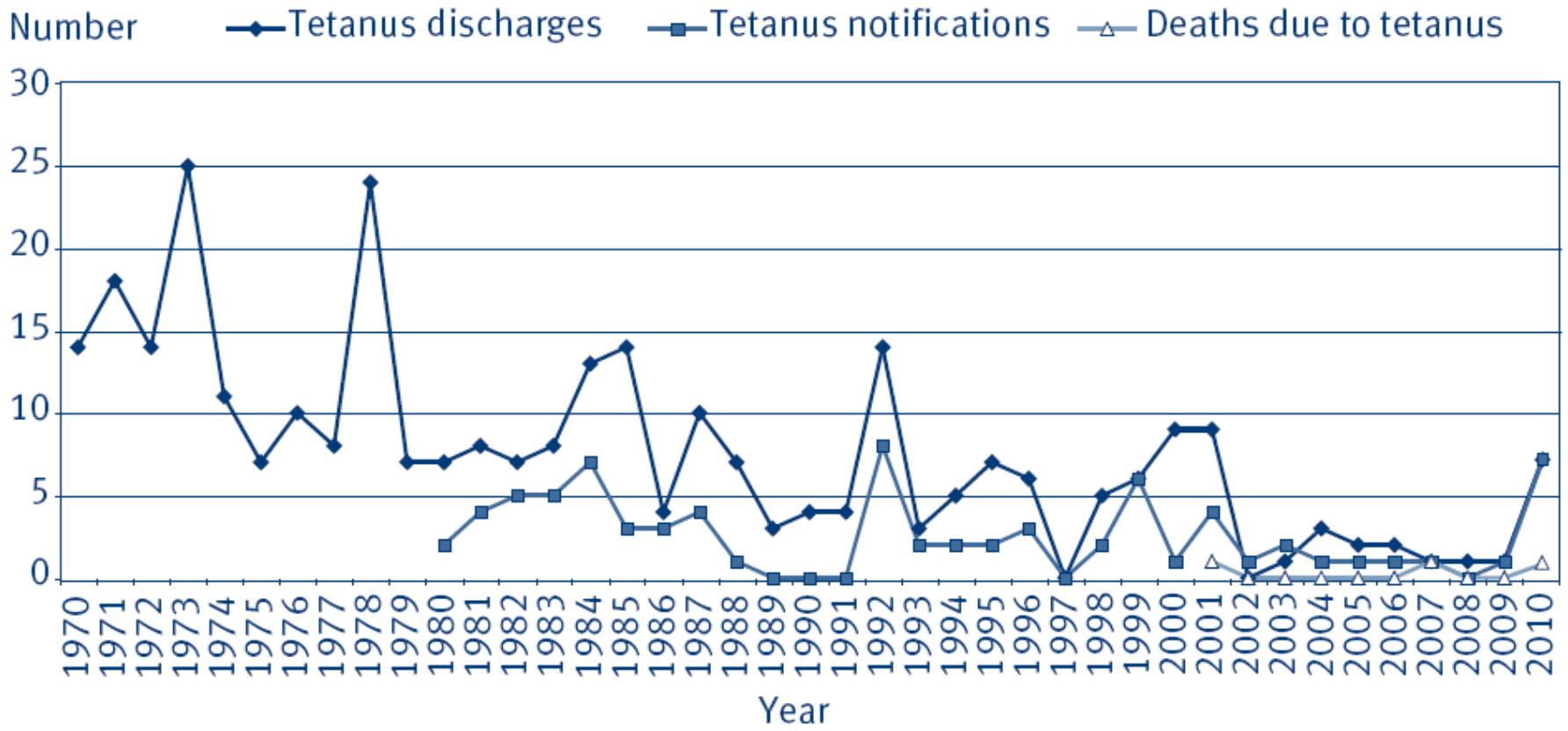
- Pregnant women, post partum
- Older siblings/school aged children
- Close contacts – fathers, grandparents
- Early childcare workers
- Healthcare workers (!)

- **Give vaccines on time and boosters**



New Zealand, tetanus

Figure 5.1 Tetanus hospitalisations 1970–2010, tetanus notifications 1980–2010 and tetanus deaths 2001–2010



New Zealand Immunisation Handbook 2011

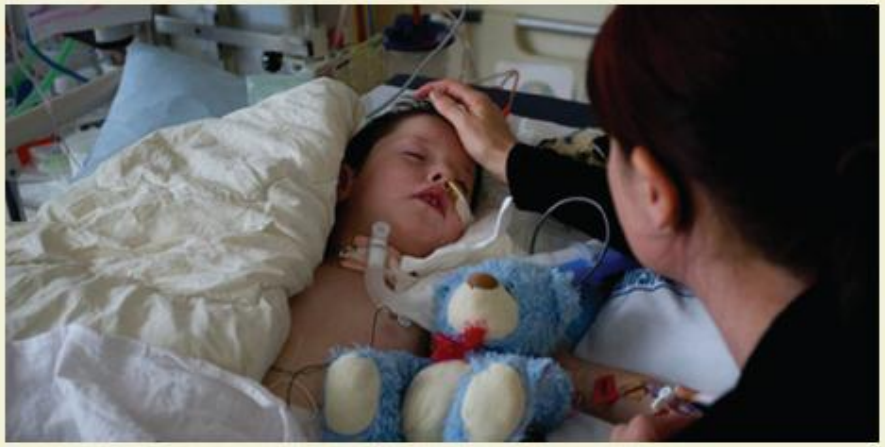
New Zealand tetanus

- Last 15 years, 30 cases of tetanus (2 cases per year in NZ) notified*
- Mostly older adults - vaccinated years ago, no booster
- Children – all unimmunised (4)

Starship experience with tetanus

Table 2: Summary of four tetanus cases

CASE/ year	Reason unimmunised	Presentation	Where?	Time to diagnosis from first presentation	Significant Wound?	Days in PICU	Treacheostomy	Tetanus-containing vaccine doses in hospital	Agreement to complete immunisations post discharge	Immunisations completed post discharge
1)1yr Female Maori / 2001	Difficult access to primary care	4 days breathing difficulty ?Asthma	Regional hospital, transferred to PICU ventilated	8 days	No: cracked skin and splinter in foot	5 then 6	No	1	Yes, planned	No record, unlikely
2) 9yr Female NZ Eur/ 2007	Parental beliefs	Trismus and spasms	Family Doctor, then regional hospital	Few hours	Yes: infected sutured leg wound	48	Yes	none	No	No
3) 4 yr Male NZ Eur/ 2010	Parental beliefs	Jaw stiffness	Children's Emergency	Few hours	No: healed puncture wound heel; stood on thorn day before.	20	Yes	2	Yes, and siblings	No, nor siblings
4) 7yr Male NZ Eur/ 2012	Parental beliefs	Left facial paralysis ?Bell's palsy	GP then Children's Emergency	3 days	No: superficial wound on heel	17	Yes	1	Yes	Yes

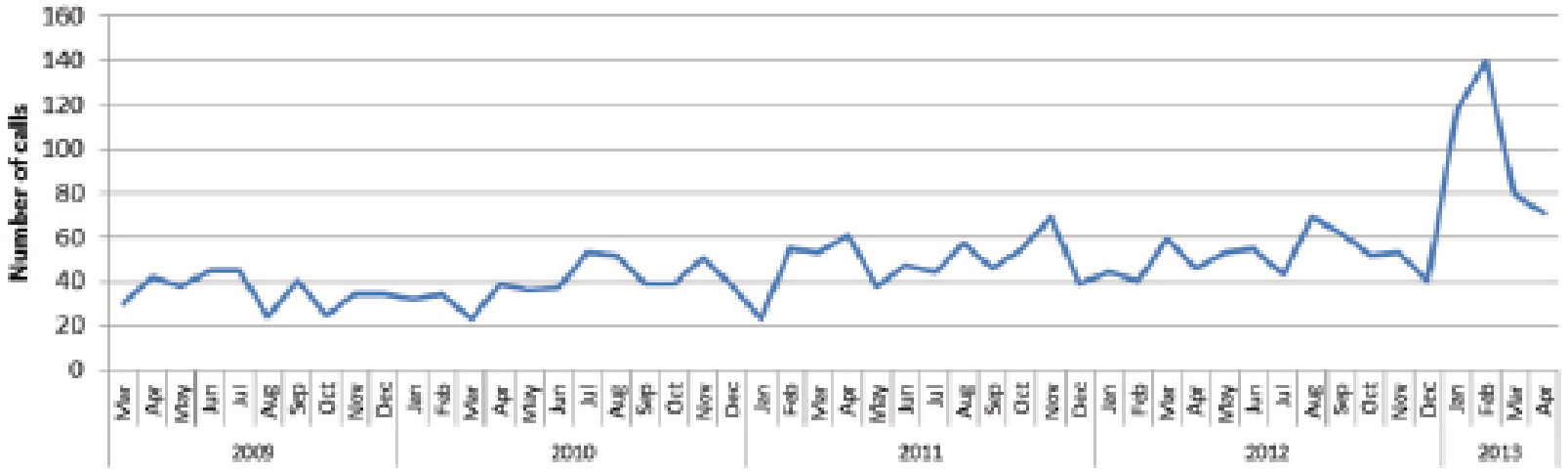


'It was hideous' family's tetanus agony *(NZ Herald December 2012)*

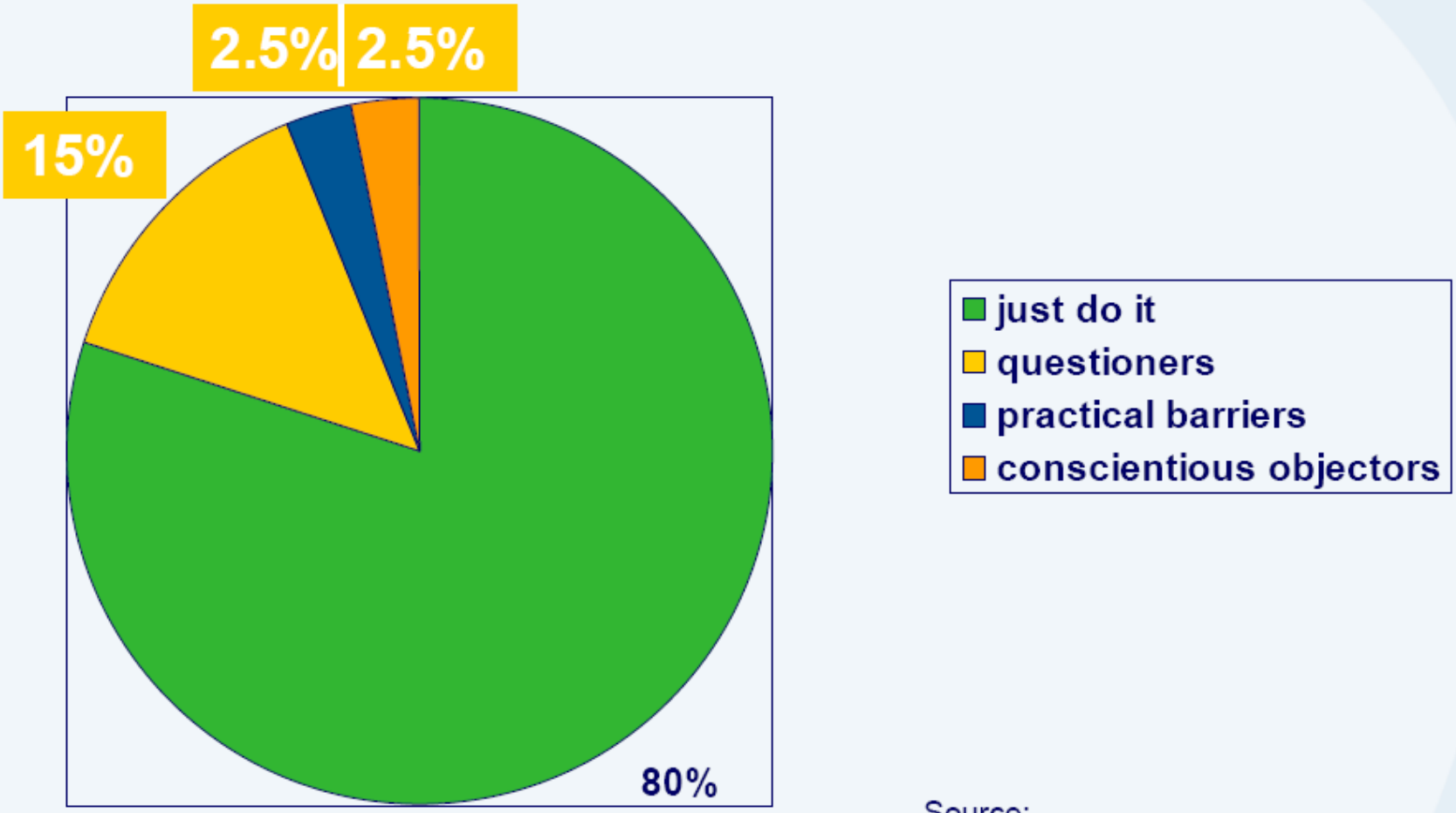
"Believing myths about vaccines is not the same as getting the facts. And that is the core problem."

"When it came to my kid's health, I let the hippy win. I should have let the science win." [5]

Figure 1: Tetanus-related calls to Immunisation Advice Line



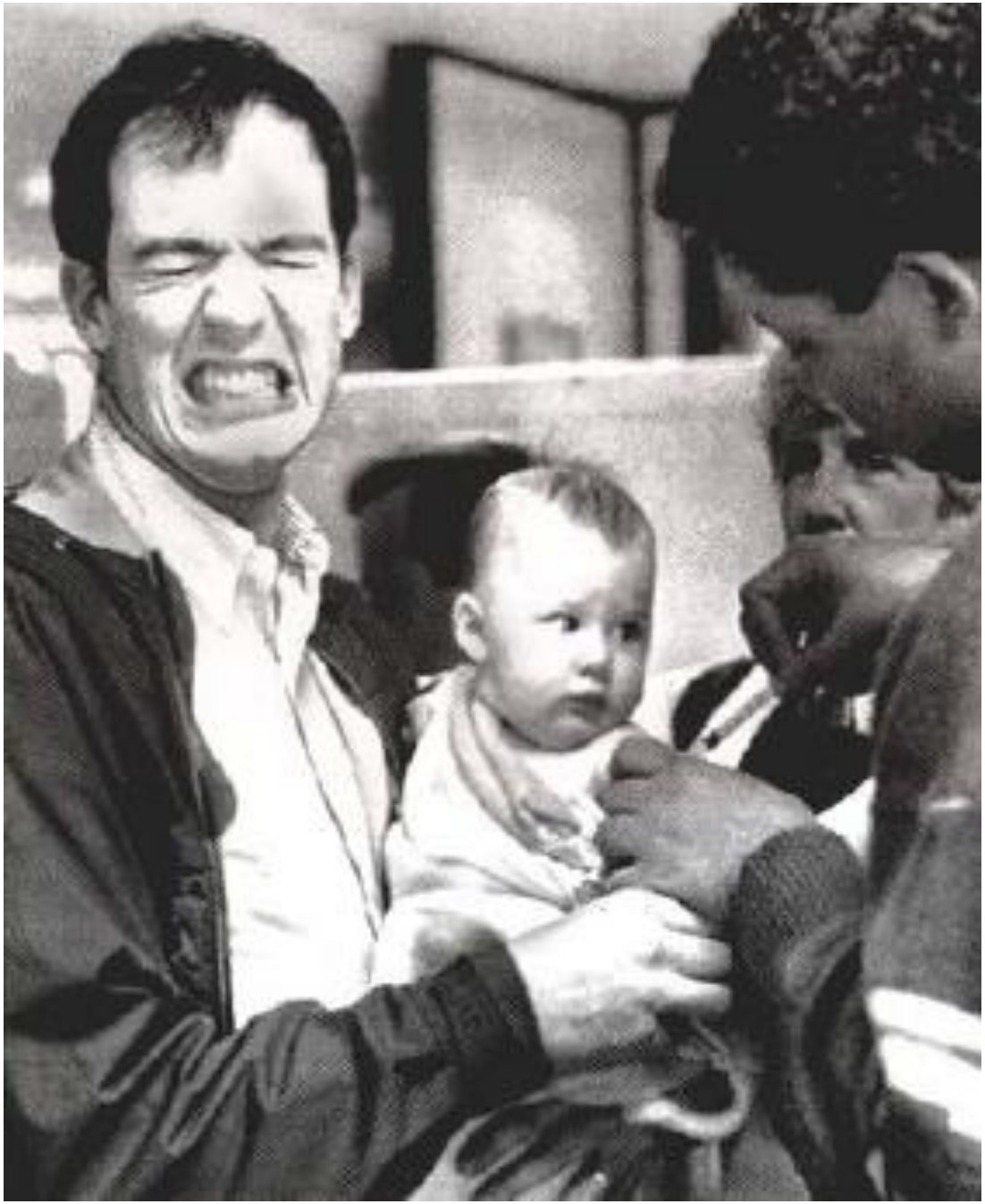
Attitudes of parents of 2 years



Source:
Leask J NCIRS 2009
Hull B, Lawrence G, MacIntyre CR, McIntyre P 2002
Gust et al 2006

- Difficult to achieve full immunisation in families with fixed anti-immunisation beliefs
- Publicity around cases increases discussion and may help some reconsider stance

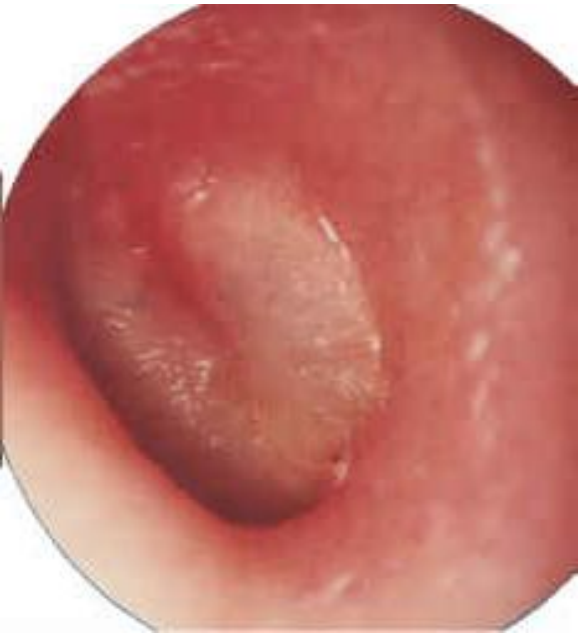
- Tetanus - a good reminder that for some diseases there is no herd immunity

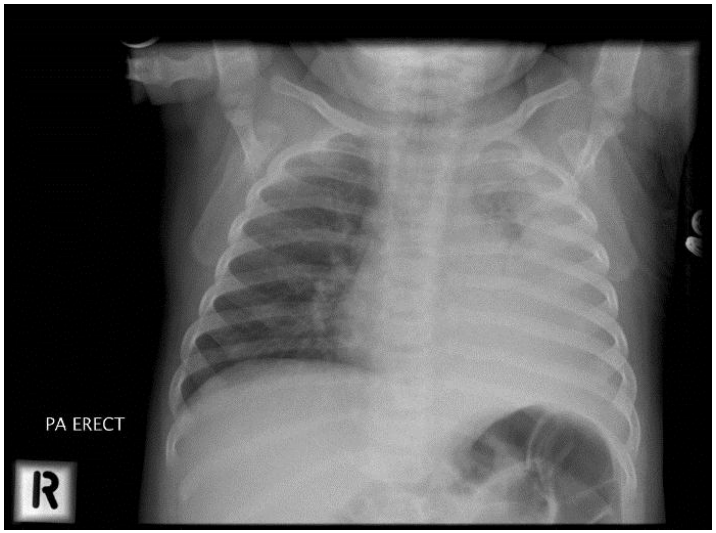


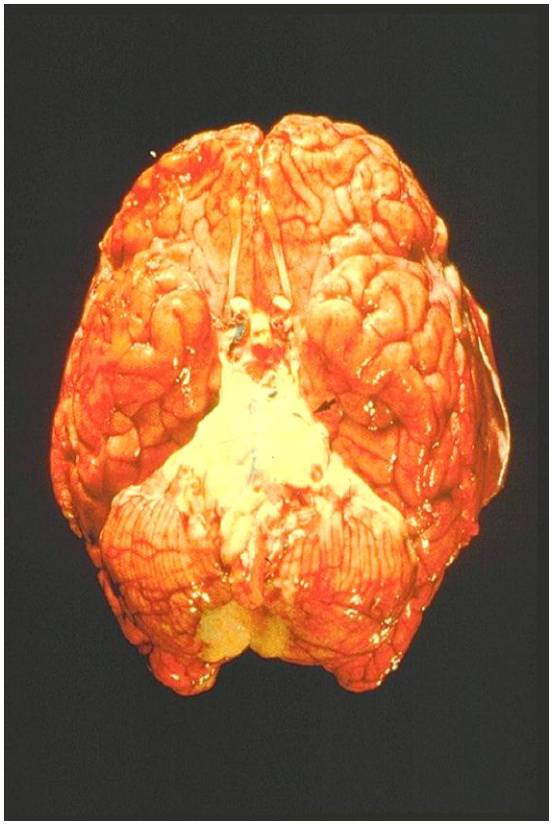
Otitis media

Pneumonia (and empyema)

Meningitis pus and inflammation in the membrane around the brain







Streptococcus pneumoniae

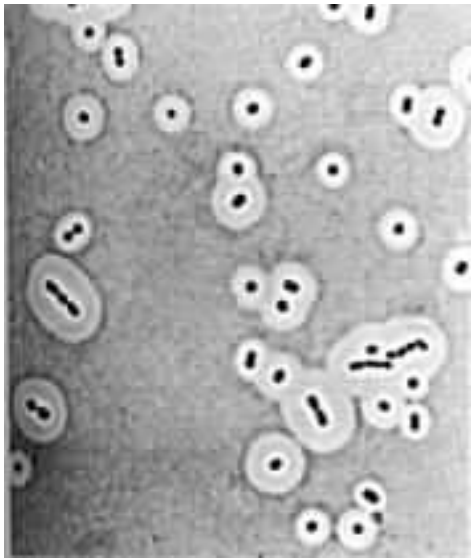
Pneumococcal disease

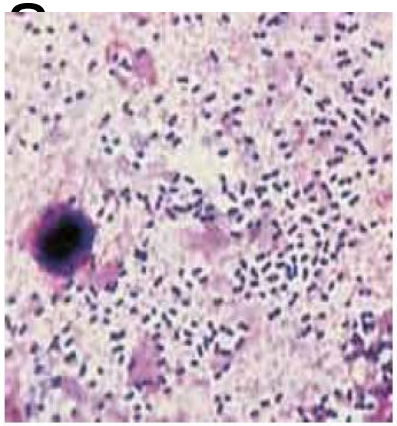
Pneumococcus

- Gram positive coccus
- Polysaccharide external capsule
- 90 serotypes have been identified based on diff capsular polysaccharides
- Capsule plays essential

role in escape from

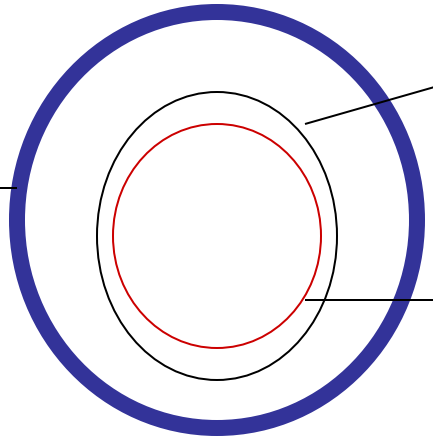
phagocytosis





http://www.infektionsnetz.at/test/bilder/mikroskop/streptococcus_pneumoniae_r.jpg

Capsule – made up of polysaccharide – 90 types

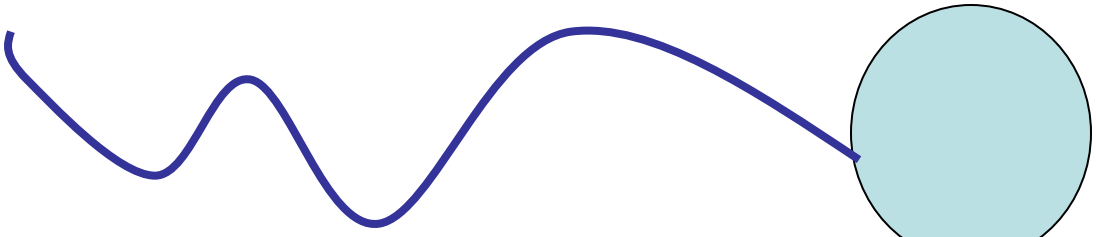


Cell wall

Plasma membrane

Antibodies produced to give sero (capsule) specific protection

Conjugate vaccine



POLYSACCHARIDE OFF CAPSULE OF PNEUMOCOCCUS

PROTEIN CARRIER

PCV vaccines

PCV7 licensed in 2000

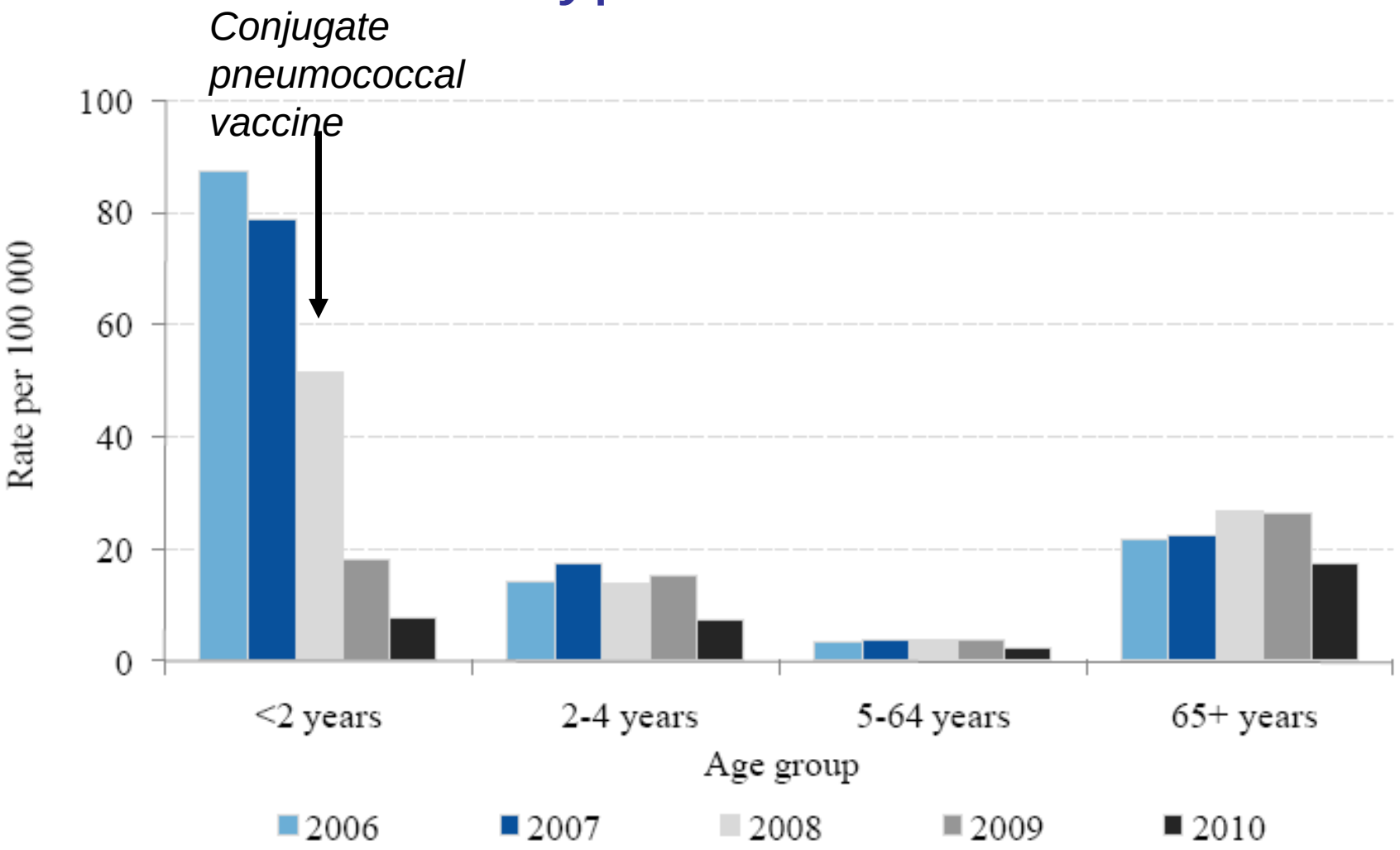
Introduced NZ June 2008

Prevenar™	Serotypes 4, 6B, 9V, 14, 18C, 19F, 23F		
	CRM_{197} Diphtheria carrier protein		
Prevenar13™	Serotypes 4, 6B, 9V, 14, 18C, 19F, 23F	1, 5, 7F	3, 6A, 19A
	CRM_{197} Diphtheria carrier protein		
Synflorix™	Serotypes 4, 6B, 9V, 14, 18C, 19F, 23F	1, 5, 7F	
	NTHi protein D	T D	NTHi protein D

Switched to PCV 10 June 2011

3 + 1 schedule
6wks, 3mths, 5mths and 15 mths

Invasive pneumococcal disease – vaccine serotypes reduction



Overall 70% reduction from 100/100,000 to 30/100,000 in under 2yr olds

http://www.surv.esr.cri.nz/antimicrobial/streptococcus_pneumoniae.php

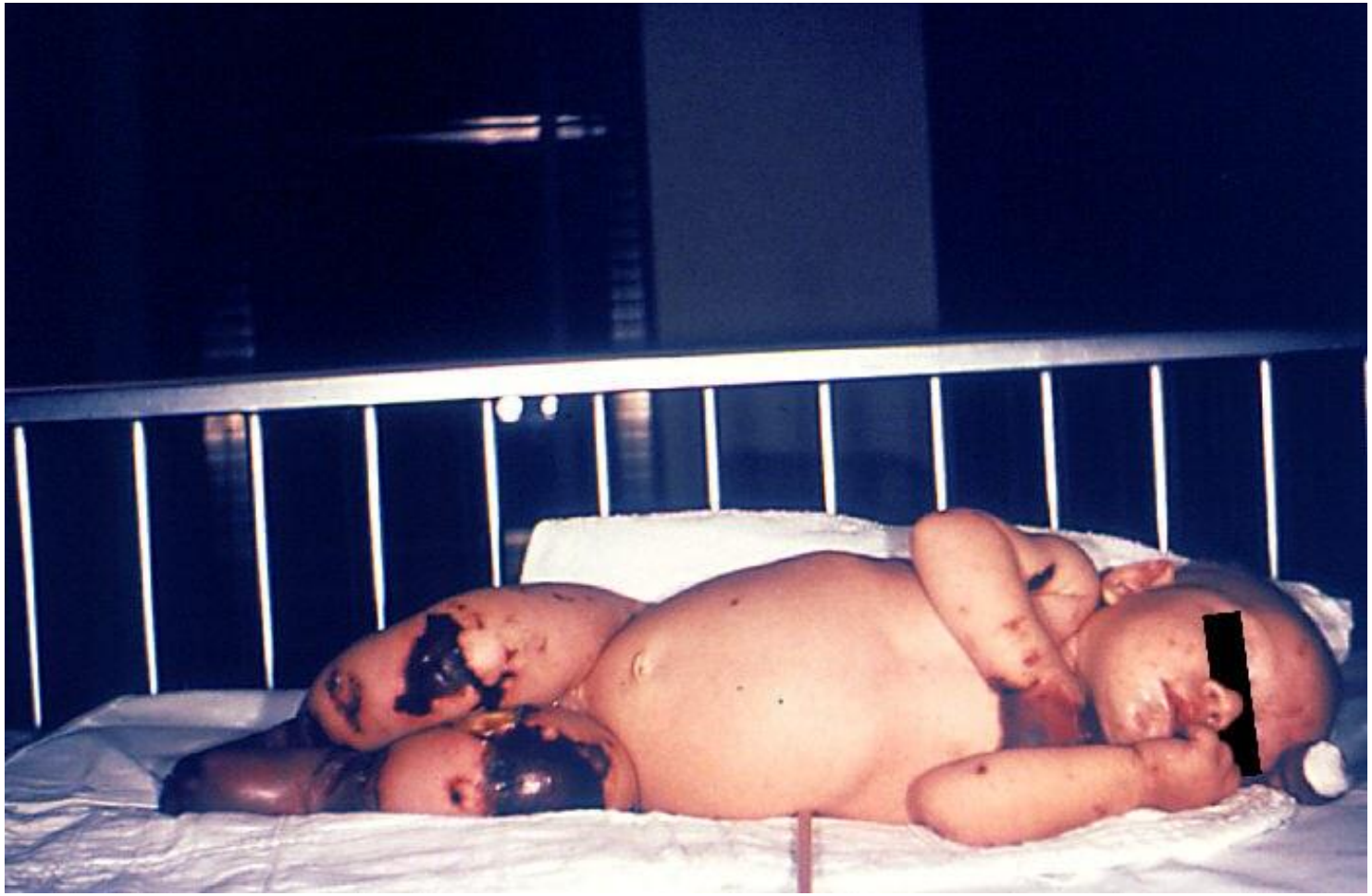
Eligibility criteria for funded PCV13 instead of PCV10

< 5 yrs high risk of pneumococcal disease

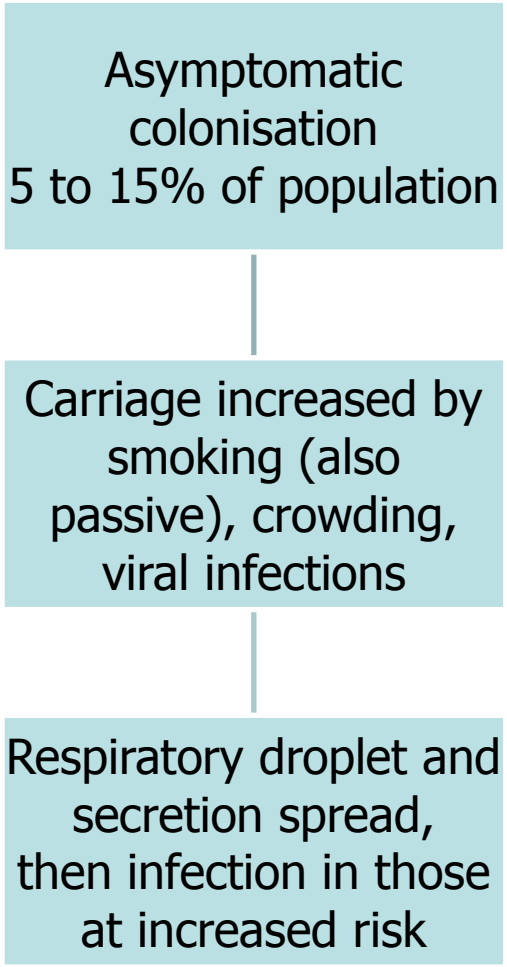
- on immunosuppressive therapy or radiation therapy, immune deficient/HIV
- Renal failure, or nephrotic syndrome
- Cochlear implants or intracranial shunts or CSF fluid leaks
- On steroids >2 wks on pred $\geq$ 2 mg/kg/day
- Chronic lung disease (including asthma on high-dose steroids)
- Pre term infants, born before 28 weeks
- cardiac disease, with cyanosis or failure
- Diabetes, Down syndrome
- And children aged upto 16 years - pre-or post-splenectomy

Neisseria meningitidis

Meningococcaemia
Meningococcal meningitis (brain inflammation)



Meningococcal epidemiology



Meningococcal bacteriology

Not as simple as Hi type b

5 serogroups that cause disease

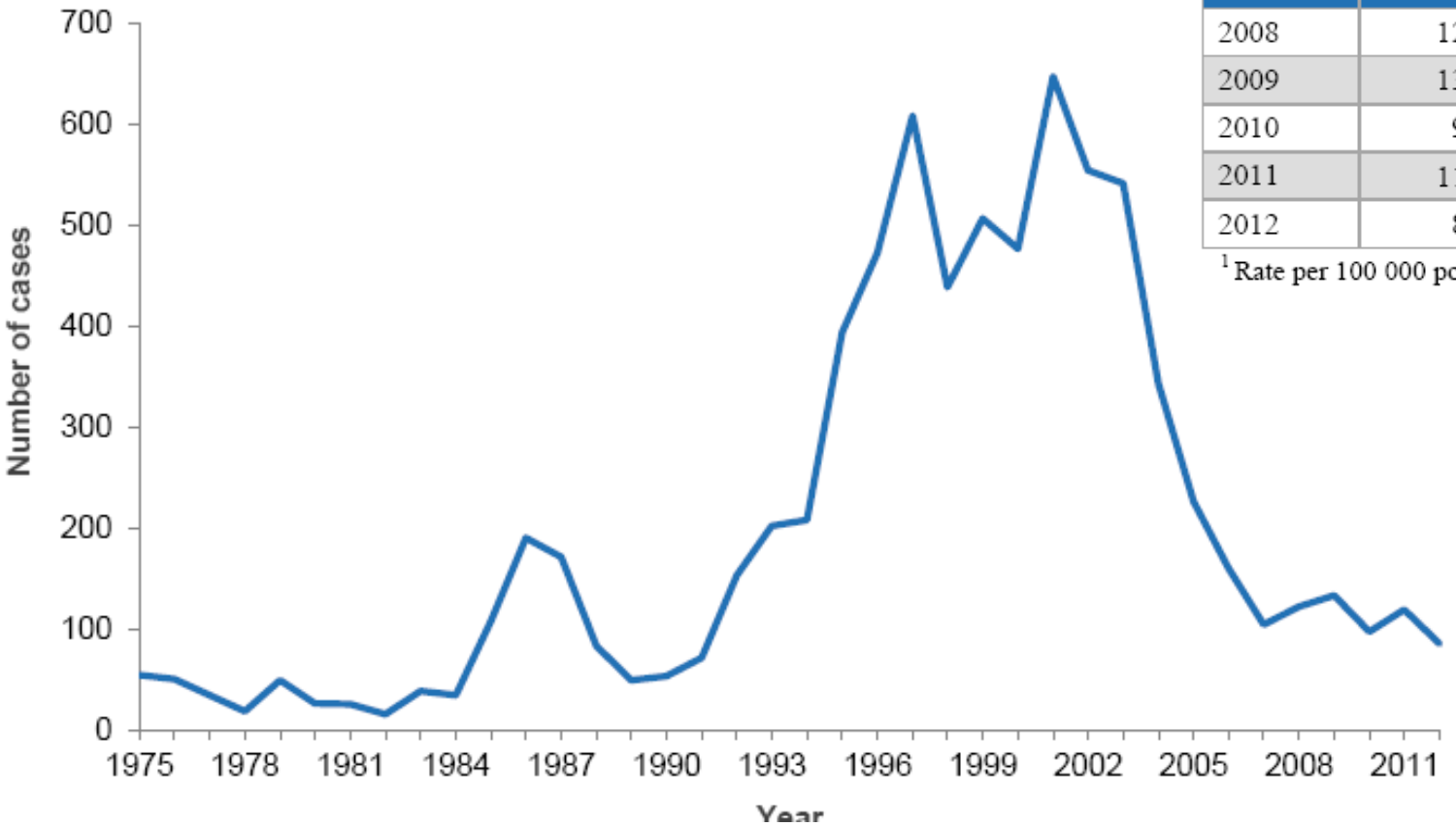
A, B, C, W135 and Y

Which New Zealanders?

- Those in crowded houses
  - Doubling of risk with the addition of 2 adolescents or adults to a 6-room house (Baker PIDJ 2000;19)
- Age < 5 years, especially age 6 to 12 months
- Maori and Pacific children (2 to 3x increased risk)
- Household contacts 600x risk in week after index case
- Students in hostels (adolescence the other risk group)
- …anyone ..

Meningococcal disease

Figure 1. Notified cases of meningococcal disease, 1975–2012

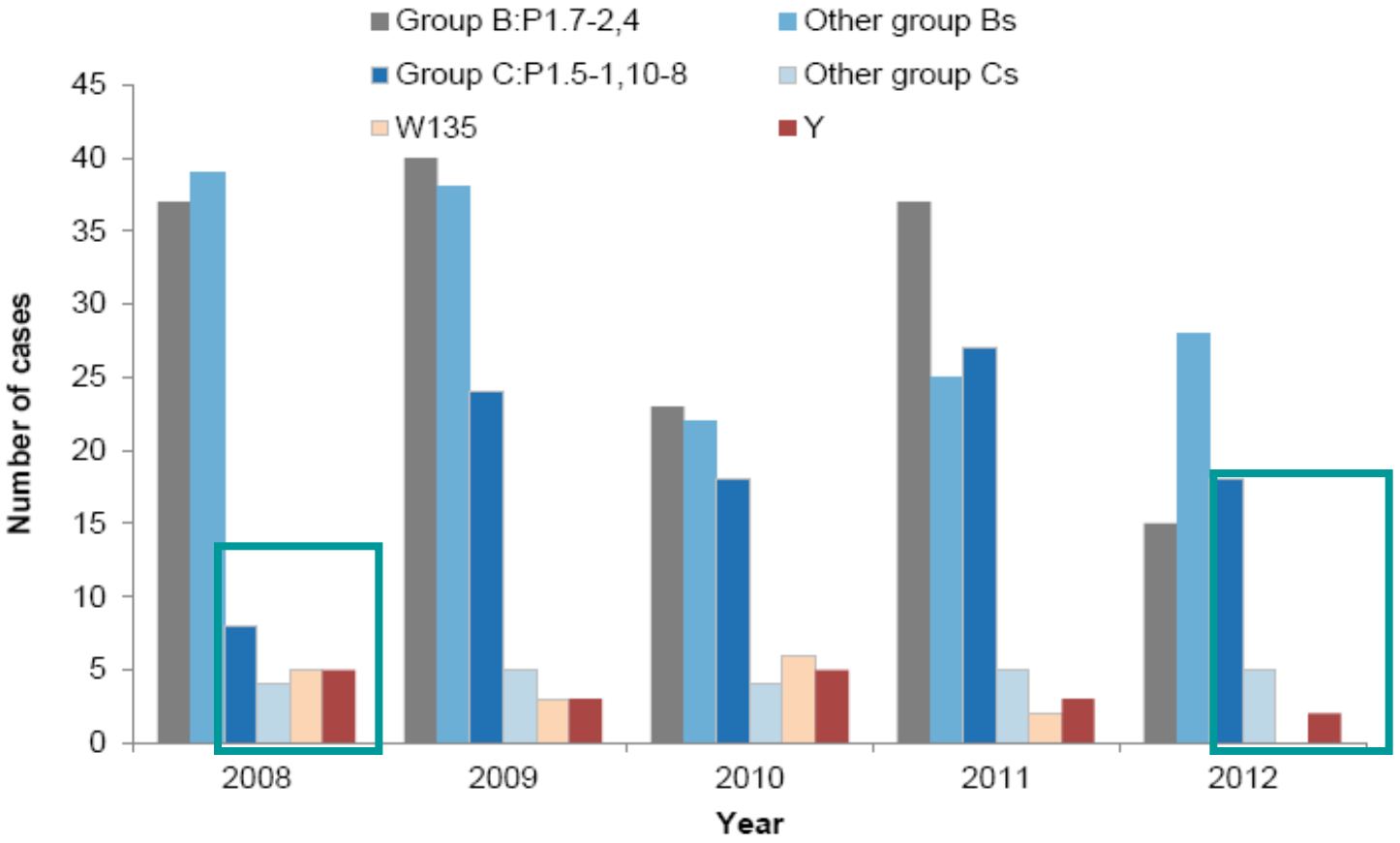


Year	No.	Rate[1]
2008	122	2.9
2009	133	3.1
2010	97	2.2
2011	119	2.7
2012	85	1.9

[1] Rate per 100 000 population

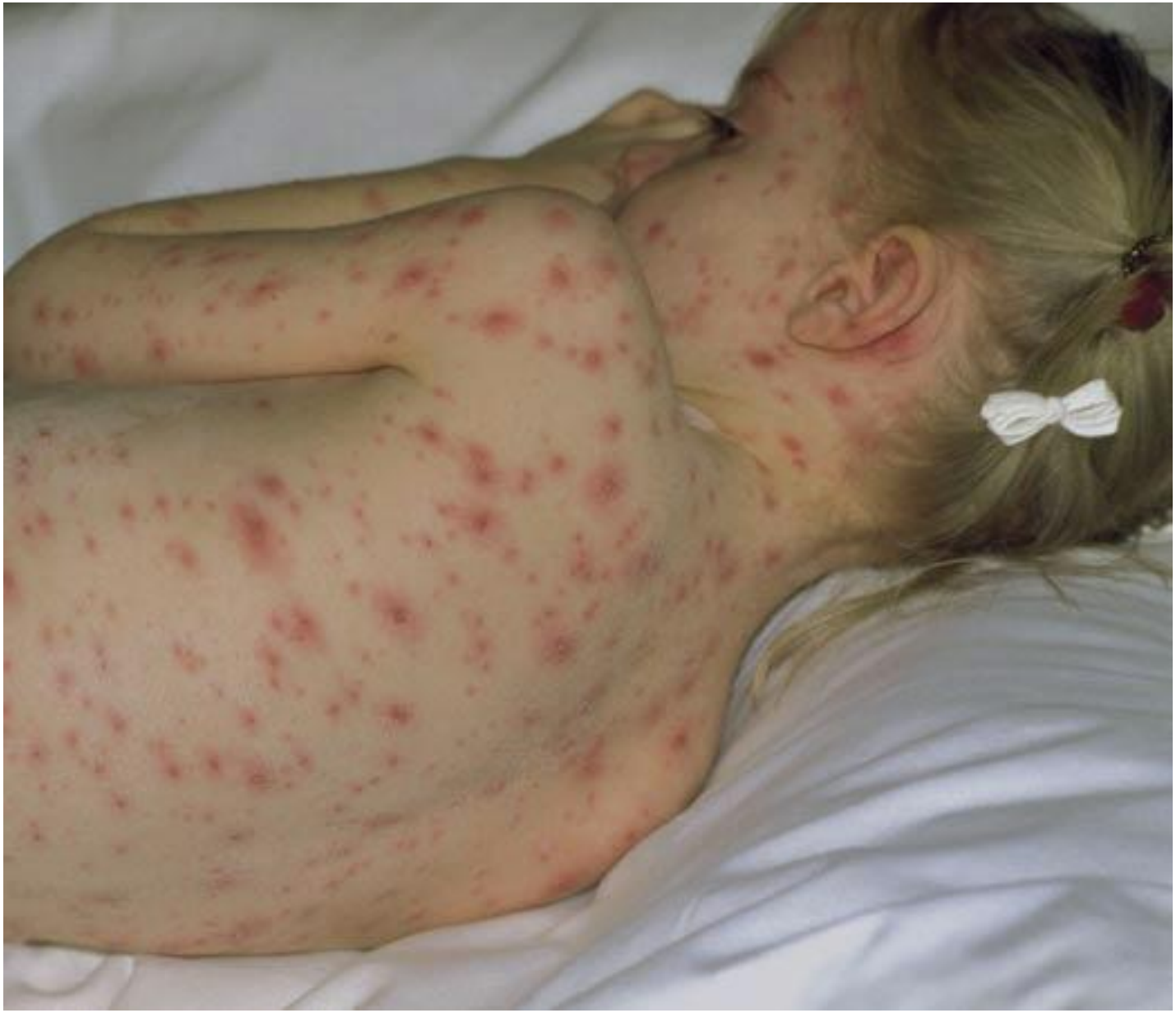
Vaccines available	Age range
• *No longer MenzB*	Any but not long lasting protection particularly in infants
• Conjugate meningococcal C	All ages and long lasting
• Polysaccharide quadrivalent	Over 2 years and lasts about 5 years
• Menactra meningococcal A,C W135, Y	Over 9months and long lasting

Figure 6. Groups and dominant subtypes among strain-typed meningococcal disease cases, 2008–2012



Vaccine	Age group (years)						Total
	<1	1–4	5–9	10–14	15–19	20+	
MeNZB™ [1]	5	5	1	1	1	2	15
C conjugate [2]	1	1	2	1	8	10	23
Quadrivalent [3]	1	1	2	2	8	11	25

6 year old girl comes in with a rash



- 18 yr old on work experience tells you after that she is pregnant and she is not sure she has ever had chicken pox

- What should you do?

- Get her to ask her mum
  - Clear history of disease is sensitive predictor of immunity
    - Even then 2/3rds of adults with no past history of chicken pox are immune so do serology
- Urgent serology – varicella IgG positive
  - By age 14 yrs < 10% still susceptible

- In the waiting room were
  - 2 week old new born baby
  - 38 week pregnant woman
  - Child with nephrotic syndrome on daily low dose steroids

What is exposure?
Face to face contact (playmate) with active case of chicken pox for at least 5 minutes or close contact 1 hour (same room)

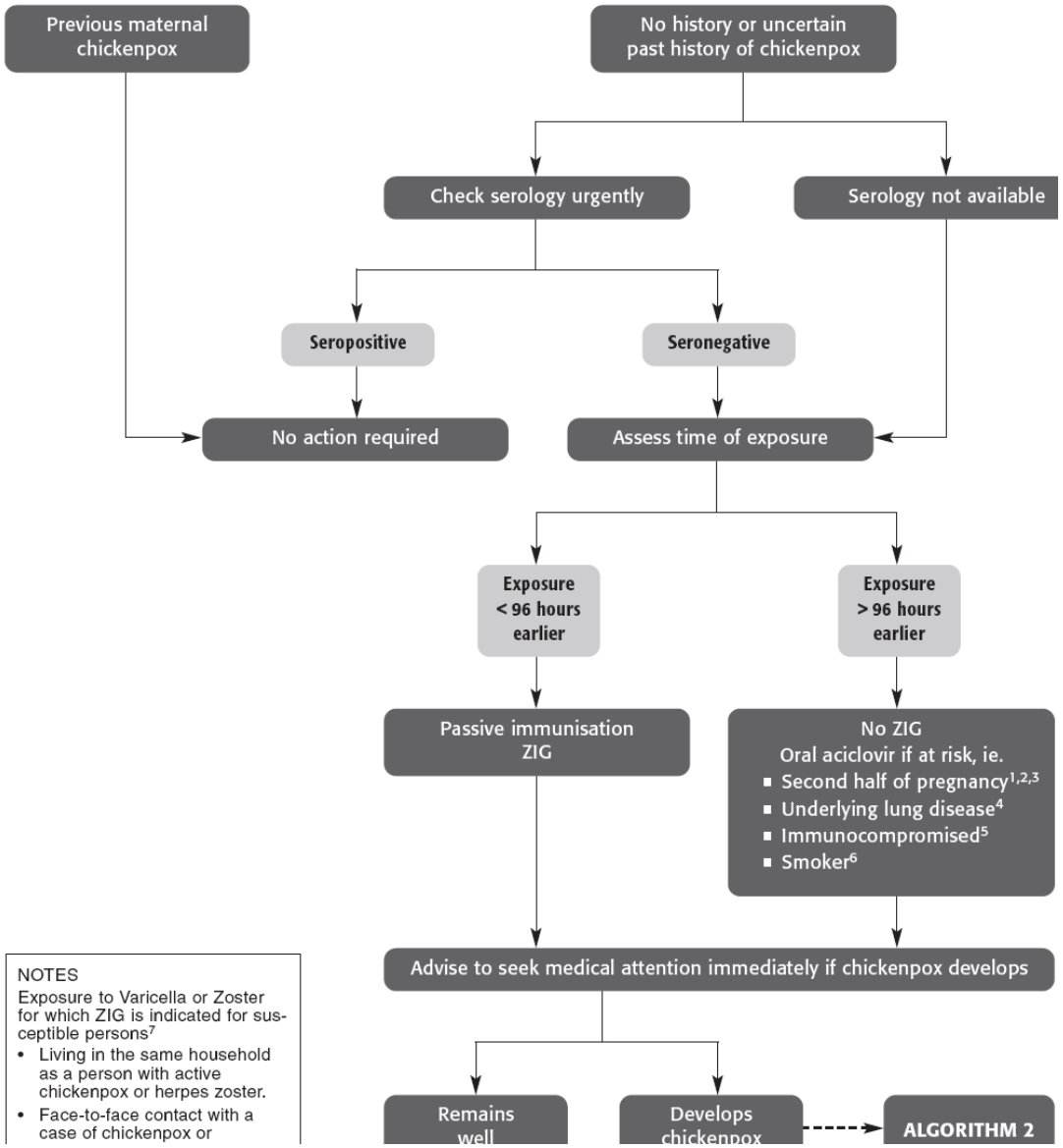
Varicella zoster virus

‘Chicken pox’

- Very infectious
- *Respiratory route transmission* or contact with individual with lesions
- Secondary attack rates in a household 70-90%
  - Infectious for ?2 days prior to rash til vesicles crust over (about 5 days)
  - Incubation period 7-21 days
  - Subclinical disease occurs in about 5%; 2/3rds of adults with no past history of chicken pox are immune

ALGORITHM 1

Exposure to Varicella Zoster Virus During Pregnancy



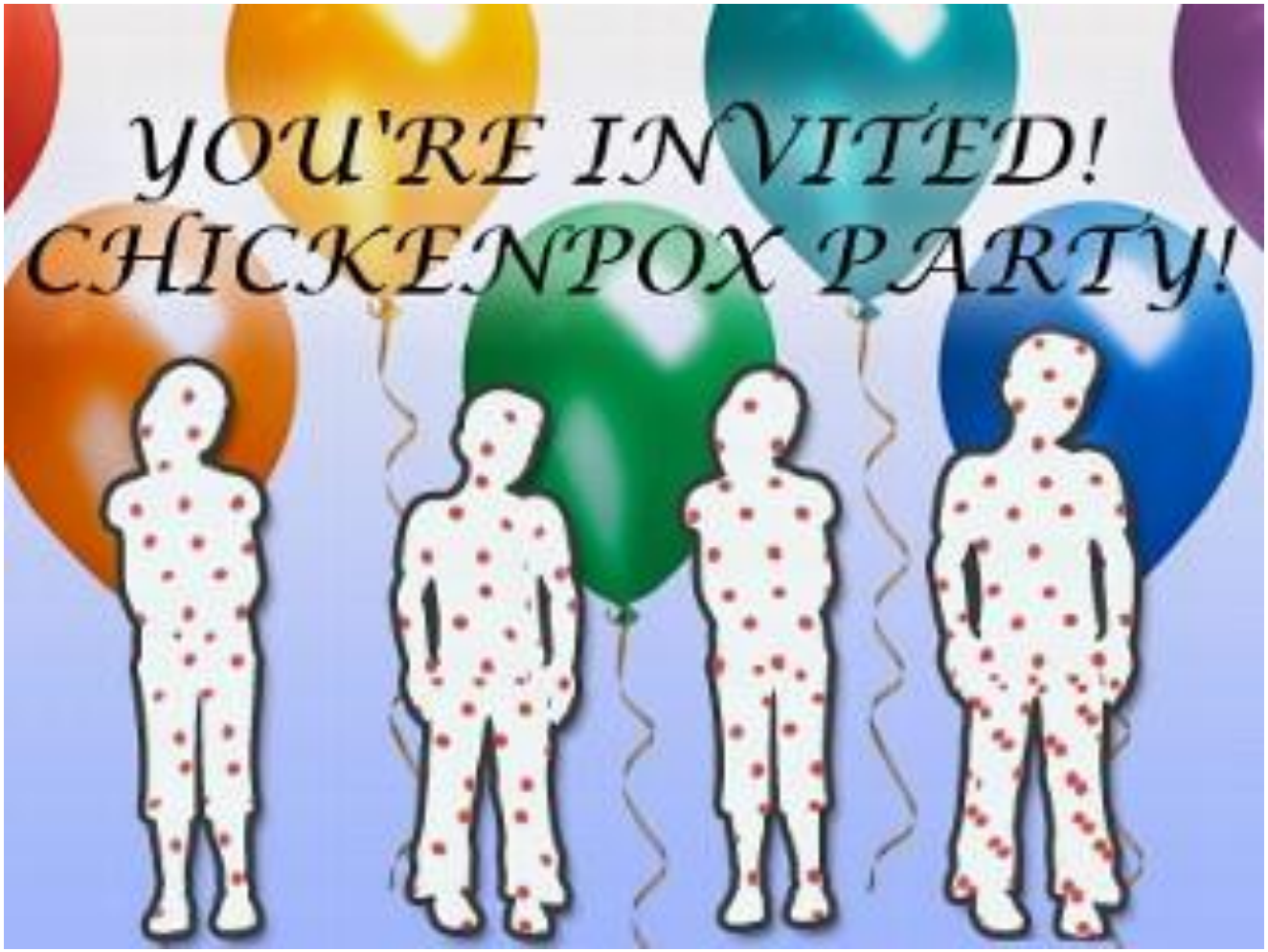
NOTES

Exposure to Varicella or Zoster for which ZIG is indicated for susceptible persons[7]

- Living in the same household as a person with active chickenpox or herpes zoster.
- Face-to-face contact with a case of chickenpox or

http://www.asid.net.au/downloads/Management-of-Perinatal-Infections-ASID-2002-rev-2007.pdf

Tell the rest of the exposed patients they have been….



or offer varicella vaccine

Post-exposure prophylaxis

- If someone has been exposed to chicken pox,
  - Giving vaccine within 3 days
  - May effectively prevent chicken pox
  - Giving vaccine within 5 days
  - Lessens severity of illness

MMWR 1999

New Zealand Immunisation Handbook 2006

Watson et al. Pediatrics 2000

Chicken pox – bottom line

- *Very infectious*
- *90% chance of being infected by teenager*
- *Numerous hospitalisations for children each year in New Zealand*
- *Children do die from chicken pox in NZ: 1 every 2 years (5 per year meningococcal)*
- *An effective non funded vaccine <u>available and recommended</u>*
- *Use to protect the vulnerable**

Common questions raised when talking about vaccinating chicken pox

- Why – common childhood disease and better immunity from wild infection?
- Vaccine immunity only lasts 20 years?
- More shingles
- 2 doses?
- Use MMRV or MMR + V ?

Not so benign - severity of chicken pox

- Mild disease 50 lesions (most breakthrough disease in vaccinated children is <50 lesions)
- Moderate 200-400 lesions (most wild type)
- Severe >1000 lesions

- Although more severe in immunocompromise **most deaths and hospitalisations occur in healthy people/children**

SSH PICU again; varicella admissions

- 10 years review – 2-3 children per year
- 4 deaths

- *Currently looking at all hospitalisations due to varicella across New Zealand over 2 years in <15 yr olds*
- *For every hospitalisation 90-150 GP visits*

Common questions raised when talking about vaccinating chicken pox

- *Why?* common and nasty
- *Vaccine immunity only lasts 20 years* – no reason to believe this – live viral vaccine and antibody should be lifelong but without wild virus circulating breakthrough infections common + will need 2 doses but severe disease mostly gone
- *More shingles?* Less shingles after vaccine – theoretical concern of increased shingles in those whilst we “eradicate varicella with vaccine” – development of *zostavax*

Reid S NZMJ 2012 125; 1354

Varicella vaccine

- Varicella vaccine available since 1996 (live attenuated vaccine)
- Recommended but not funded, (about 17% uptake)
- Vaccines available in New Zealand:
  - Varilirix Varivax
  - Quadrivalent MMRV vaccine (Priorix-Tetra or ProQuad)
  - *Zostavax (herpes zoster vaccine for adults ≥ 50 years of age)*

- Recommended for children from age 12m to 12yrs
  1 dose effective for 80%, very effective at reducing serious infection
  - Administered at 15m (with MMR, Hib & PCV10)
  - Second dose (debatable) at 4yrs with MMR (effectiveness 2 doses >95%)

Varicella vaccine or MMRV

- So give MMRV or MMR + V at 15 months?
  - NZ MOH recommends MMR+V at 15 months due to risk of febrile seizures

- What is the risk for febrile seizures?
  - 1 additional febrile seizure per 2500children vaccinated with MMRV compared with MMR + V (if receive it as 1-2 yr age)
  - No increased risk seen in those aged 4-6yrs who received MMRV
  - *Weigh up with other costs – pain of extra injection, risk of falling behind schedule, missing opportunity of vaccinating*

Rotavirus

The most common cause of severe infectious diarrhoea and vomiting in young children

One of the leading causes of hospitalisation in NZ children

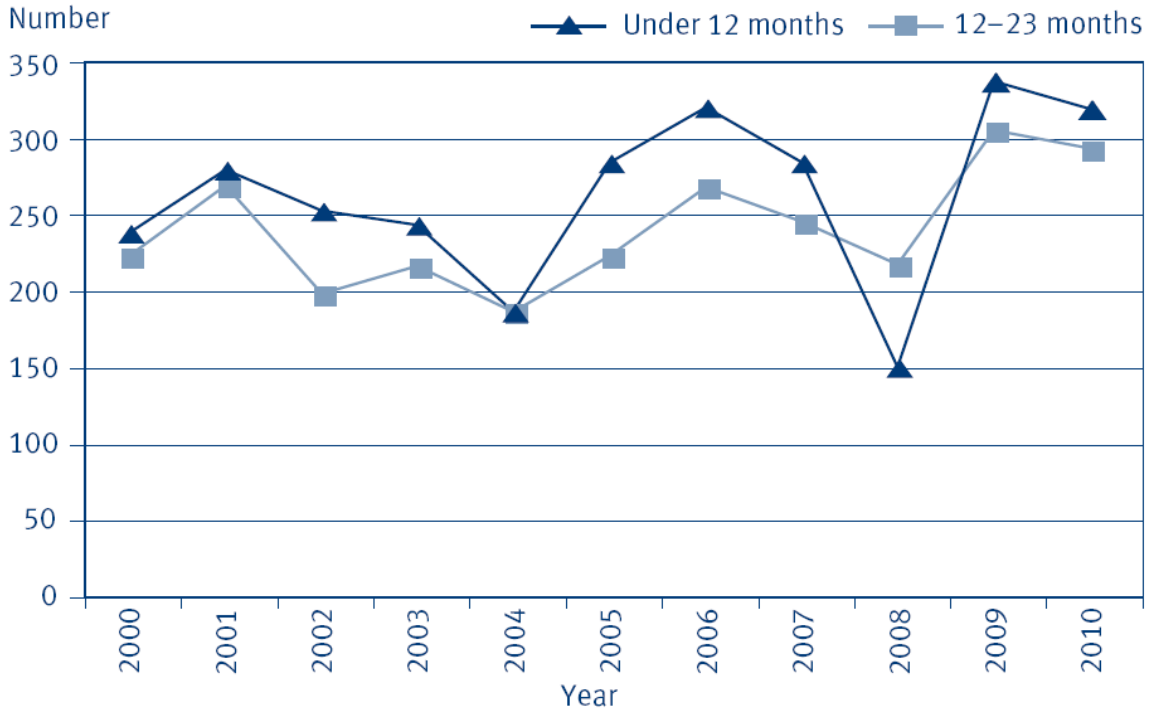
By age 5yrs

- 1 in 43 children hospitalised
- 1 in 5 seek medical attention due to rotavirus

Grimwood J Paeds and Child Health 2006

Rotavirus disease burden in New Zealand

Figure 19.1 Hospitalisations from rotavirus in children aged less than two years, 2000–2010



Source: Ministry of Health

Notes: Publicly funded hospital discharges with a primary diagnosis of enteritis due to rotavirus (ICD-9 code 008.61)

Rotavirus vaccination is recommended

- WHO's Strategic Advisory Group of Experts (*SAGE*)

  Recommend include rotavirus in national programmes

- NZ Immunisation Technical Forum recommended inclusion of Rotavirus vaccine in Immunisation Schedule in 2007 and 2010.

- Paediatric Society of New Zealand recommends rotavirus as an urgent priority for New Zealand

http://www.who.int/mediacentre/news/releases/2009/rotavirus_vaccines_20090605/en/index.html [Accessed 27 Oct 2009]

Reduction in admission due to gastroenteritis in Australia

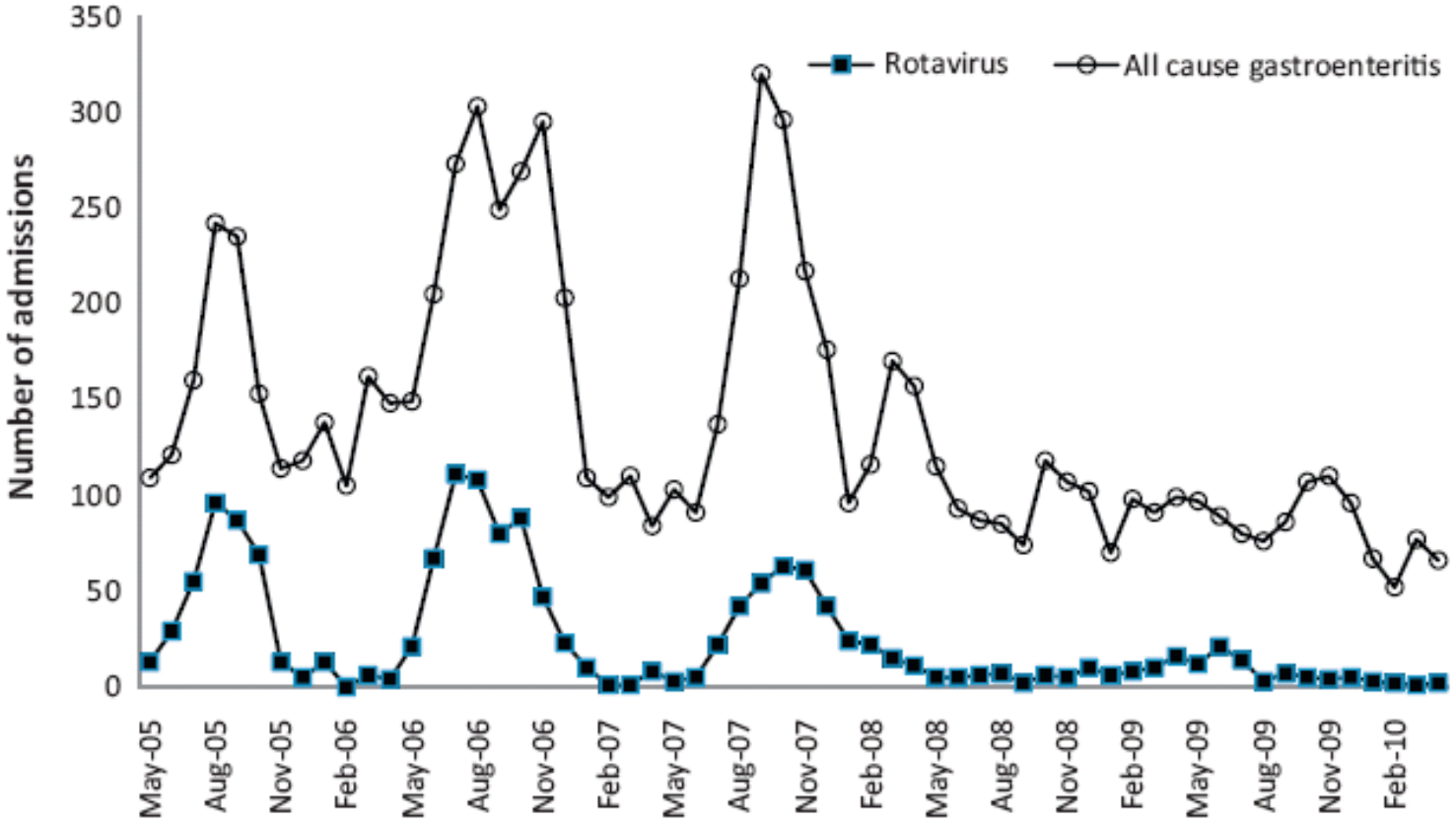
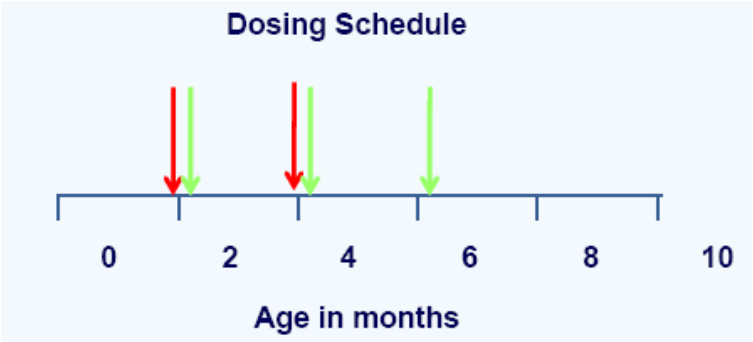


Fig. 2. RVGE and ACGE admissions by month of admission.

Available Rotavirus vaccine worldwide

- *Rotarix** (GlaxoSmithKline) - live attenuated human rotavirus. (R)
- *RotaTeq*** (CSL Biotherapies/Merck & Co Inc) – pentavalent vaccine containing human-bovine rotavirus reassortants. (G)

- Both are live attenuated, and orally administered



Both vaccines are about 70% protective against any rotavirus gastroenteritis, and > 85% effective in preventing severe rotavirus gastroenteritis

Rotavirus vaccines

- Rotarix
  - How long does protection last?
    - Very efficacious for 1yr, slightly less in 2nd yr – efficacy still observed upto 5 years of age
  - Can it be given to older infants? No

Immunisation Clinic

- Severe egg allergy for influenza vaccine
  - *Both Fluarix and Vaxigrip are low ovalbumin content*
  - *No longer need to see egg allergy/MMR*

- Previous immunisation adverse events for subsequent immunisation
  - Occasional prolonged crying or hypotonic hyporesponsive episode
  - No anaphylaxis seen post immunistion (yet)

HEALTHCARE WORKERS

Should

- know their own MMR and varicella status
- receive adult pertussis booster if working with young infants
- receive annual influenza immunisation

Key messages

- VPD -a reality in NZ and cause morbidity and death
- Pertussis control is complicated
- Improved coverage and timeliness will change this
- We are part of a global community of people (measles) and microbes (tetanus)
- Effective bacterial vaccines give new invasive disease priorities - surveillance is important
- New vaccines varicella/rotavirus likely to impact positively both at population and individual level


baby
first