Emerging and Re-Emerging Infections: Spotlight on pertussis

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Disclosures

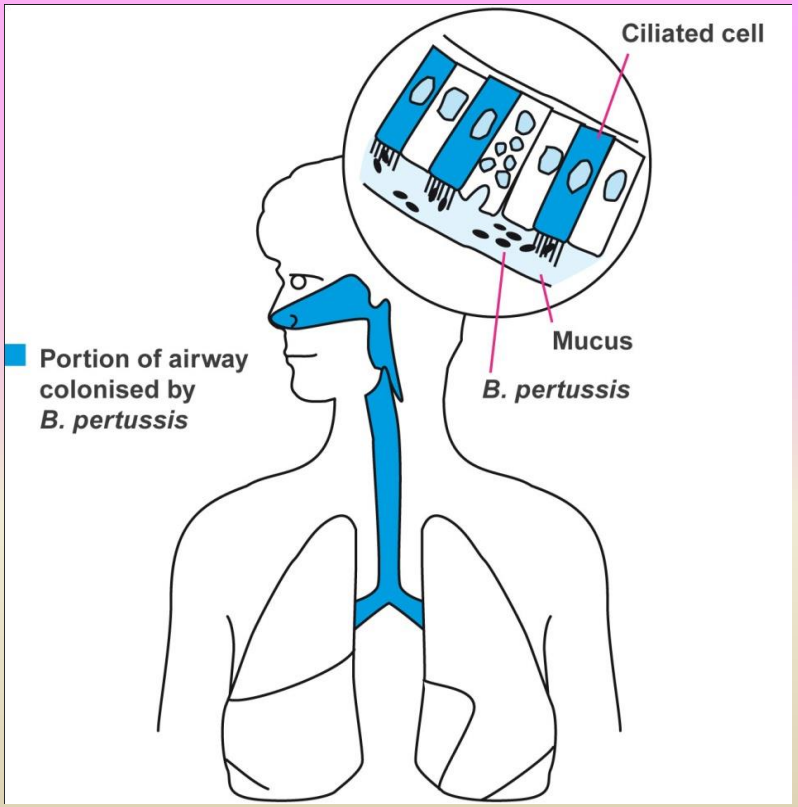
- Dr. Li-Min Huang received travel grants, lecture fees, clinical trial grants from GSK, Merck, Sanofi, Novartis, Pfizer and Adimmune
- Dr. Li-Min Huang served as an advisor for GSK, Merck, Novartis, Pfizer and Adimmune

Outlines

- Pertussis clinical characteristics
- Epidemiology & disease burden (including Asia)
- Impact of adolescent vaccination and protecting the newborn (cocooning)
- Data of dTpa vaccination in adolescents and adults
- Problems in front of us
- Conclusions

Pertussis: elimination by vaccination should be possible

- Highly communicable acute respiratory infection caused by *B. pertussis*
- Person-to-person transmission through aerosolised respiratory droplets
- As many as 80% of susceptible household contacts become infected after exposure
- Humans are the sole reservoir



• Guinto-Ocampo H, McNeil BK, Available at website http://emedicine.medscape.com/article/967268-overview; Bisgard KM, Pascual FB, Ehresmann KR, *et al., Pediatr Infect Dis J*. Nov 2004;23(11):985-9

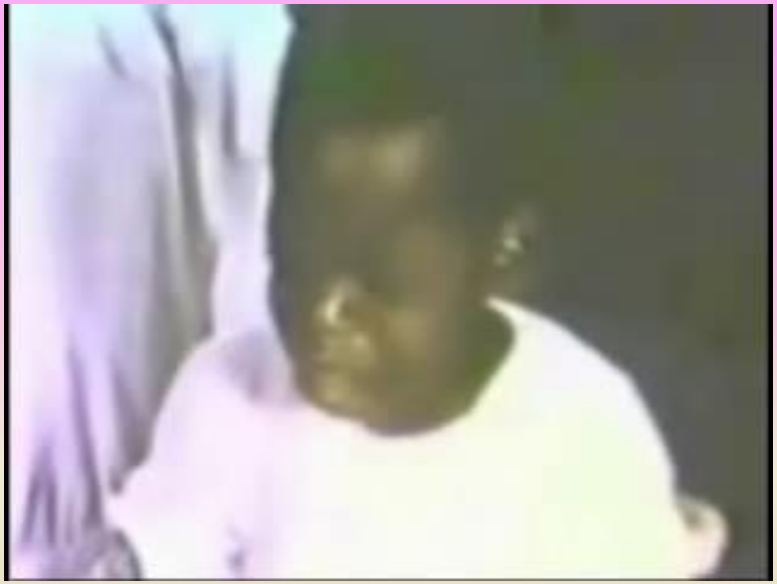
Clinical Manifestations of Pertussis

- Usually affect children before vaccine available
- Clinical illness in 3 stages
  - Catarrhal phase
    - Cold-like (coryza, conjunctival irritation, occasionally a slight cough)
    - 7-10 days
  - Paroxysmal phase
    - Long duration (2-6 weeks); No fever
    - **a series of rapid, forced expirations, followed by gasping inhalation →the typical whooping sound**
    - **Post-tussive vomiting common**
    - **Very young infants may present with apnea or cyanosis in the absence of cough**
  - Convalescent phase

Clinical symptoms and laboratory tests

Adapted from Wirsing von konig CH. *et al., Lancet Infectious Disease 2002*; **2**(12**)**: 744—50; Heininger U. and Cherry JD., *Expert Opin.Biol. Ther. 2006;* **6**(7):685-697.

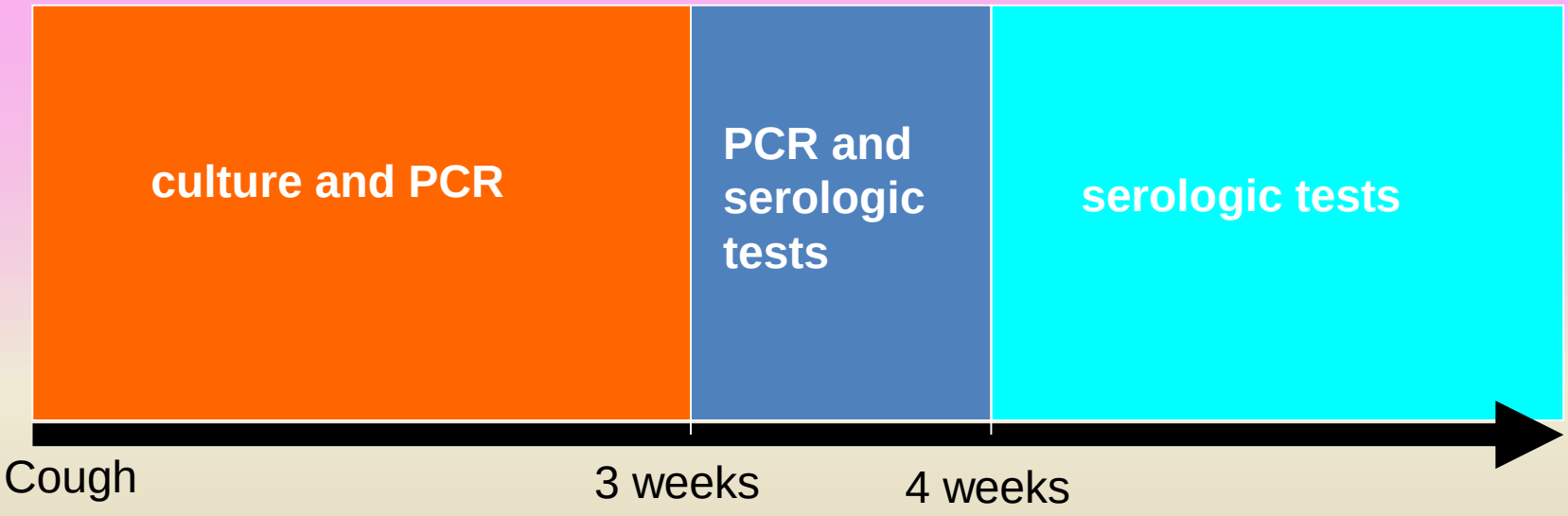
Images of Pertussis Disease



Videos courtesy of the California Department of Health Services, the Nevada State Health Division and UCLA's Dr. James Cherry at www.vaccineinformation.org.

Whoop

Diagnosis of Pertussis: time sequence



Pertussis notification rate 1/100 in the States and UK
Either tests are not available or
Physicians choose the wrong test

Pertussis Has Become a Disease of Adolescents and Adults?

- Cough > 4 weeks –
  26% suffering from pertussis

Robertson et al. Med J Aust 1987

Pertussis has Become a Disease of Adolescents and Adults

- >18 Y/O; cough > 2 weeks -- 21% pertussis

  Wright SW et al. JAMA 1995

- College students; cough > 6 days-- 26% pertussis

  Mink et al. Clin Infect Dis 1992

- Urban dwellers; cough > 2 weeks -- 12.4% pertussis

  Nennig ME et al. JAMA 1996

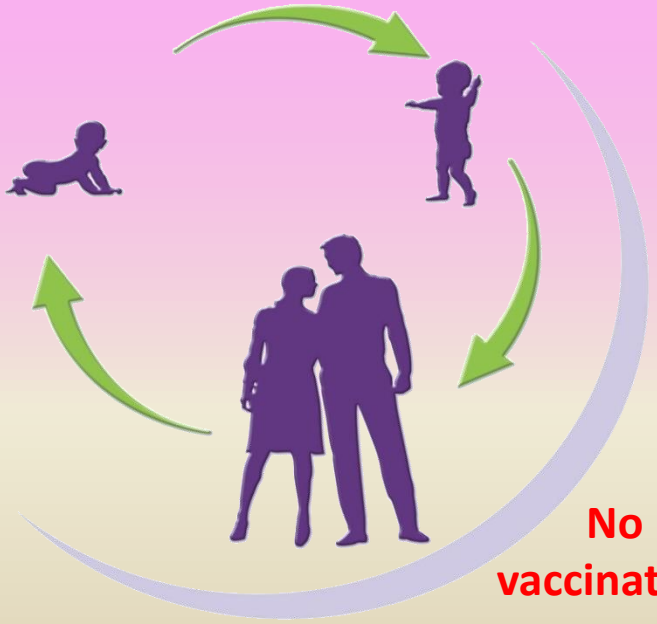
Prolonged Cough Illness in Adolescents and Adults Due to *Bordetella pertussis*

Source	Locale	Year(s)	% of cough illness
Nennig et al	San Francisco	1994-95	12
Strebel et al	Minn-St Paul	1995-96	13
Jackson et al	Seattle	1983-87	15
Jansen et al	San Diego	1993-94	17
Birbeback et al	Denmark	1995-97	17
Wright et al	Nashville	1992-94	21
Robertson et al	New S Wales	1985-86	26
Mink et al	Los Angeles	1986-89	26
Rosenthal et al	Chicago	1993-94	26
Wirsing v Köenig et al	Germany	1992-94	31
Schmitt-Grohé et al	Germany	1992-94	32
Vicent et al	Korea	1997-98	50
Gilberg et al	Paris	1999	52

The New Pertussis Cycle of Life

Pertussis primary vaccination in the first year of life

Pertussis booster vaccination in the second year of life



Non-vaccinated or partially vaccinated infants: risk of complications

Adults and adolescents serve as reservoirs of pertussis infection. New parents present a heightened risk of transmission

No Pertussis booster vaccination: protection wears off with time

Adapted Wendelboe AM *et al., Pediatr Infect Dis J. 2007*;**26**(4):293-299; Wirsing von Konig CH. *et al., The Lancet Infectious Disease 2002*; **2** (12): 744—50

Epidemiology of Pertussis in Australia

- Pertussis remains endemic in Australia despite a long history of immunisation[1,2]
- Pertussis epidemics typically peak in 3-4 year cycles[2,3,4]
- Recent epidemic (2008-2009) is considerably larger than other previous epidemics (1997–98, 2001, 2005–06):
  - 2008: 13,859 cases (64.7 cases/ 100,000 population)[2]
  - 2009: 29,265 cases (134.3 cases/ 100,000 population)[2]

1. Cagney *et al.,* Epidemiol Infect. 2006;**134**(6):1208-16; 2.National Notifiable Diseases Surveillance System. http://www9.health.gov.au/cda/Source/Rpt_5_sel.cfm, accessed 2/2/2010; 3. Quinn & McIntyre. Commun Dis Intell 2007; **31**: 205-215; 4. Australian Immunisation Handbook, 9th Edition, 2008

Impact of Pertussis on Infants

- In Australia, infants continue to have high annual reporting rates[1,2] and the highest severity (hospitalisation or death) of disease:
  - Maximal risk of infection and severe morbidity is in infants < 6 months who are too young to be protected by the current vaccination schedule[3,4]
  - Infants have the highest hospitalisation rates:
    - 2003-2005: 50% of hospitalisations[1]
    - July 2005 and June 2007: 34% of hospitalisations[5]
  - Most deaths are in infants < 12 months old:
    - 1993-2005: 18 deaths
      - of which 16 were in infants < 12 months old

1. CDI ;Vol 31 Suppl; 2.CDI Vol 33 No 2 2009; 3. Australian Immunisation Handbook, 9th Edition, 2008; 4.Quinn & McIntyre. Commun Dis Intell 2007; **31:** 205-215; 5. Pertussis factsheet NCIRS April 2009; 6. CDI Vol 33 No 1 2009

Epidemiological shift in the prevalence of pertussis in Taiwan: implications for pertussis vaccination

- Surveillance: 2452 reported cases of pertussis during 1993-2004.
- The highest morbidity was in infants aged <1 year, and upward trends in the incidence of pertussis were significant for infants aged <1 year and adolescents aged 10-14 years.
- The highest mean number of cases was observed in August and upward trends were in colder months.
- This study indicates that the epidemiology of pertussis may have been changed by waning immunity in Taiwan.
- Increased surveillance activities, especially in older age groups, and additional booster doses of acellular pertussis vaccine for children aged 6-8 years and adolescents/young adults aged 15-20 years are necessary to control and prevent pertussis.

Lin Y C *et al*., Research and Diagnostics Center, Centers for Disease Control, Taipei, Taiwan, J *Med Microbiol*. 2007 Apr;56(Pt 4):533-7.

Why does Pertussis continue to cause concern?

Very young (under 6 months)

•Babies are born with maternal antibodies however this does not give adequate protection

•Antibodies transferred to the baby through breast milk will not provide adequate protection either

1.Poorly protected until received 3 doses of vaccine

2.Increased risk of severe disease / death

3.Efficacy of childhood DTPa vaccination is 89%.

Adults

•Waning immunity from immunization or natural infection

•Pass on the disease to the very young

»at least 50% of infants contract the disease from an adult contact

•Can cause significant morbidity in older aged

»cerebral hemorrhages, rib fractures, hernia, incontinence

Schmitt HJ *et al.* JAMA 1996; **275**:37-41

Common Clinical Manifestations of Adolescent-Adult Pertussis

- Cough 97% ≥ 3 weeks, 52% ≥ 9 weeks
- Paroxysms ≥ 3 weeks in 73%
- Whoop in 69%
- Post-tussive emesis in 65%
- Teens missed average 5 days of school; adults missed average 7 days of work
- Average 14 days of disrupted sleep

De Serres et al. J Infect Dis. 2000;182:174–9.

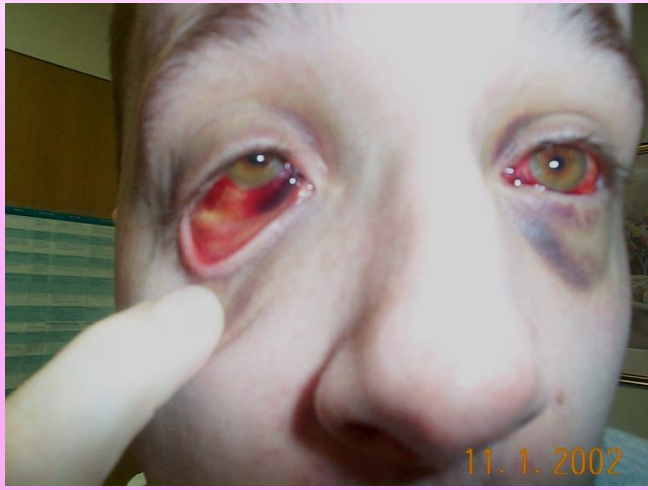
Complications of Adolescent – Adult Pertussis

	Adolescents	Adults
Complication	16%	28%
Cyanosis	6%	9%
Pneumonia	2% (<20 Y)	5-9% (>30Y)
Hospitalization*	1.4%	3.5%

*Hospitalization < 50 y/o, 2%, mean stay of 3 days; > 50 y/o, 6%, mean stay of 17 days

De Serres et al. J Infect Dis. 2000;182:174–9.

Complications of Adolescent – Adult Pertussis



- 4% of adults had urinary incontinence
  - Women (>50 years) with pertussis: 34% developed urinary incontinence
- Rib fractures, pneumothorax, inguinal hernia, aspiration, subconjunctival hemorrhages, hearing loss, herniated lumbar disk, and cough syncope have been reported in adults as mechanical consequences of the severe cough episodes

De Serres et al. J Infect Dis. 2000;182:174–9.

Cardiogenic Shock caused by Pertussis

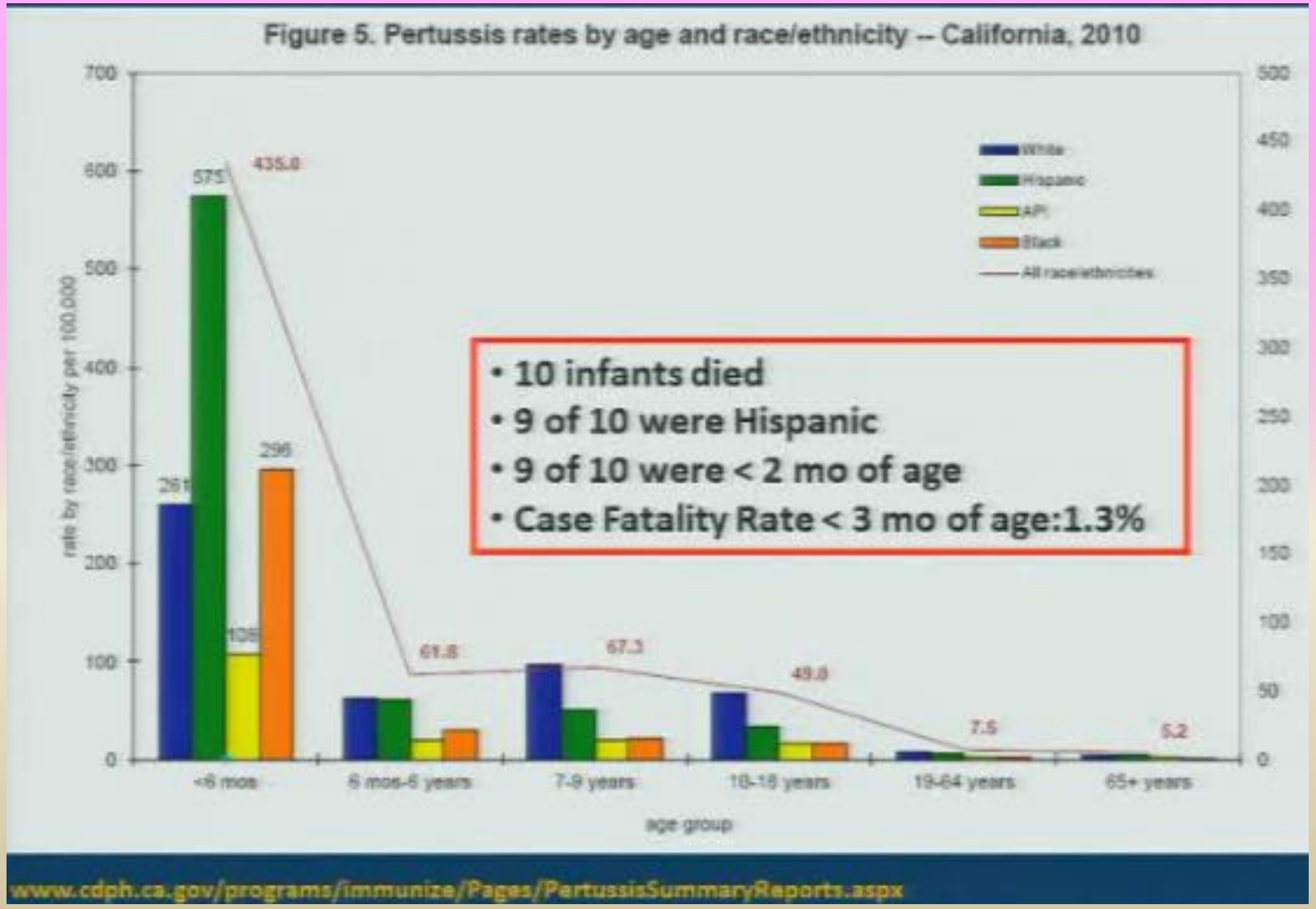
- **3 infants with pulmonary hypertension, right-sided heart failure and cardiogenic shock** who responded favorably to whole blood exchange therapy
  - All had rapid cardiovascular and respiratory collapse in relation to cardiogenic shock, progressive hypoxia and increased WBC counts (45,000 cells/L, 78,800 cells/L and 106,000 cells/L)
  - The echocardiogram showed severe pulmonary hypertension
  - Double-volume exchange transfusion was performed and the WBC counts decreased, the cardiopulmonary condition improved and the patients survived
- Hyperleukocytosis (white blood cell WBC > 50,000 cells/L) is a critical element and occasionally present in patients with pertussis
- Outcome poor if patients develop refractory pulmonary hypertension
- Mechanism: occlusion of the pulmonary vessels by the increased mass of leukocytes (pulmonary leukostasis), possibly due to **enhanced pertussis toxin production**

Donoso AF et al, PIDJ 2006: 846

2010 California Pertussis Outbreak

- 7,824 confirmed, probable and suspect cases of pertussis with onset from January 1 through December 15, 2010 (20.0 cases/100,000)
- Previous record: 1947 (63 years ago) 9,394 cases; 26.0 cases/100,000 in 1958
- Highest rates in children under three to six months of age
- Younger infants also had the highest rates of hospitalization and the most deaths, which increased to 10

Pertussis Outbreak: California 2010



Factors Associated with Mortality U.S. deaths (1999-2004)

Infant Factors	Maternal Factors
Female *	< 12 yrs education *
Birth weight < 2500g *	Unmarried
Gestation < 36 wks	Delayed prenatal care
5 minute Apgar < 8	Prior preterm or SGA birth
Hispanic ethnicity	* Remained significant on multivariate analysis

- younger age
- no. of pertussis vaccine doses received
- greatly elevated lymphocyte count
- seizures/encephalopathy
- shock
- need for ECMO

Arch Dis Child. 2007;92:970-5
Pediatr Infect Dis J. 2009;28:194-8
Pediatrics 2008;112:1274-8

Pertussis – Source of transmission

Table 2. Epidemiological studies on household members as the source of pertussis transmission to infants.

Country of origin	Study population	Outcome*	Ref.
UK	25 infants younger than 5 months of age admitted to ICU because of proven pertussis	Primary case: Parent: n = 11 (44%) Sibling: n = 6 (24%)	[2]
USA	616 infants with proven pertussis	Source discovered in 264 cases: Parent: n = 123 (47%; 20% of total) Grandparent: n = 22 (8%; 4% of total) Sibling: n = 52 (20%; 8% of total)	[3]
France	1668 hospitalized infants under 6 months of age with proven pertussis	Source discovered in 892 cases: Parent: n = 491 (55%; 29% of total) Sibling: n = 223 (25%; 13% of total)	[4]
Multinational	99 infants admitted to ICU because of proven pertussis	≥1 source (n = 30) discovered in 24 cases: Parent: n = 18 (60%; 18% of total) Other adult: n = 6 (20%; 6% of total) Sibling: n = 5 (17%; 5% of total)	[5]
Multinational	95 infants under 6 months of age admitted to hospital because of proven pertussis	≥1 source discovered in 44 cases: Parent: n = 27 (55%; approx 25% of total) Grandparent: n = 3 (6%; approx. 3% of total) Sibling: n = 8 (16%; approx. 5% of total)	[6]

*Only n for household contacts are presented; remaining sources were nonhousehold contacts.
ICU: Intensive care unit.

Heininger U., *Expert Rev Anti Infect. Ther. 2010*, 8**(2)**,163-173

Prevention Strategies

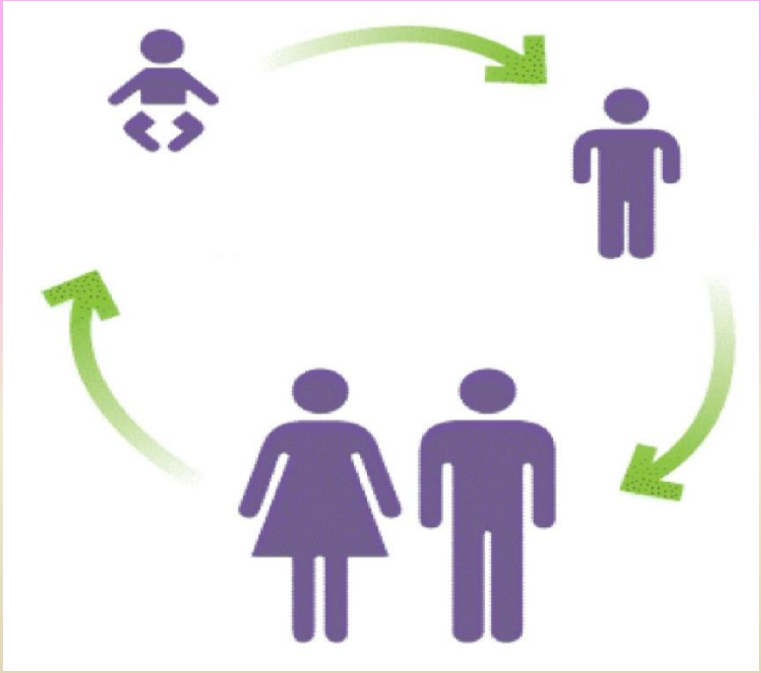
- Antimicrobial Prophylaxis
- Tdap vaccine (tetanus, diphtheria, acellular pertussis)
  - -Natural and vaccine-induced immunity wanes
  - -One time dose for adolescents and adults
  - -Part of pre-conceptual health
- New Immunization Platforms
  - -Neonatal immunization
  - -Immunization during pregnancy
  - -Targeted immunization – "cocooning"

MMWR 2008; 57(RR-4):1-51
Global Pertussis Initiative Vaccine 2007;2634-42

Rationale for introduction of an adult pertussis immunization program

Primary vaccination at 2, 4, 6 months[1]

Booster vaccination at 4 years & 15–17 years[1]



The risk of exposure of unvaccinated infants may be reduced by protecting adults[1]

Adult immunity wanes over time[1,2,3,4]

Adult booster vaccinations

1. Australian Immunisation Handbook, 9th Edition, 2008; 2. Wood *et al.,J Paediatr Child Health. 2008* Apr;**44(**4):161-5; 3. McIntyre *et al.,Vaccine 2009;* **27:**1062; 4. Edelman *et al., Clinical Infectious Diseases 2007*; **44**:1271–7

Protect the adolescents!

Country	Pa/Pw vaccine	Booster	Age	Country-specific link
Austria	Pa	Yes	12–24 months, 13–16 years (dTpa), every 10 years thereafter (dTpa)	http://www.bmgf.gv.at/
Belgium	Pa	Yes	15 months, 5–7 years, 14–16 years (dTpa), cocooning	http://www.vlaanderen.be/ http://gezondheid.be/ http://health.fgov.be
Bulgaria	Pa and Pw	Yes	2 years	–
Cyprus	Pa and Pw	Yes	15–20 months, 4–6 years	http://www.moh.gov.cy/moh/moh.nsf/index_gr/index_gr?OpenDocument
Czech Republic	Pa	Yes	11 months and 1 week–18 months, 5 years, 10–11 years	http://www.szu.cz/
Denmark	Pa	Yes	5 years	http://www.ssi.dk/sw379.asp
Estonia	Pa	Yes	2 years, 6–7 years	http://www.tervisekaitse.ee/
Finland	Pa	Yes	4 years, 14–15 years (dTpa)	http://www.ktl.fi
France	Pa	Yes	16–18 months, 11–13 years, 27–28 years, cocooning	http://www.sante-jeunessesports.gouv.fr/
Germany	Pa	Yes	11–14 months, 5–6 years (dTpa), 9–17 years (dTpa), cocooning, adults	http://www.rki.de/cln_011/nn_226928/EN/Home/homepage__node.html__nnn=true
Greece	Pa	Yes	15–18 months, 4–6 years	–
Hungary	Pa	Yes	18 months, 6 years	http://www.oek.hu/oek.web
Ireland	Pa	Yes	4–5 years	http://www.hpsc.ie/hpsc/
Italy	Pa	Yes	5–6 years, 11–15 years (dTpa)	http://www.ministerosalute.it/
Latvia	Pa	Yes	18 months	http://www.sva.lv/eng/vaccination_calendar.php
Lithuania	Pa	Yes	18 months, 6–7 years	http://www3.lrs.lt/pls/inter2/dokpaieska.showdoc_l?p_id=290262
Luxembourg	Pa	Yes	12 months, 5–6 years, 15–16 years (dTpa), every 10 years thereafter (dTpa)	–
Malta	Pa and Pw	Yes	12–18 months[§]	–
Netherlands	Pa	Yes	11 months, 4 years	http://www.minvws.nl/en/ http://www.rivm.nl/vtv/object_document/o2434n19767.html
Poland	Pa and Pw	Yes	16–18 months (DTPw), 6 years (DTPa)	http://www.gis.gov.pl
Portugal	Pa	Yes	18 months, 5–6 years	http://www.dgs.pt/
Romania	Pw	Yes	12 months, 30–35 months	–
Slovakia	Pa and Pw	Yes	2 years (DTPw) 5 years (DTPw)	http://www.uvzsr.sk/
Slovenia	Pa	Yes	12–24 months	http://www.ivz.si/index.php?akcija=kategorija&k=39 http://www.ivz.si/index.php?akcija=podkategorija&p=89

Current Immunization Schedule in Taiwan

Vaccine \ Age	≥24 hr	2-5 days	1 months	2 months	4 months	6 months	12 months	15 months	18 months	30 months	36 months	6 years	≥65 year
BCG	BCG												
Hepatitis B		HepB1	HepB2			HepB3							
Diphtheria, Tetanus, Pertussis, Hib, Polio*				DTaP-Hib-IPV 1	DTaP-Hib-IPV 2	DTaP-Hib-IPV 3			DTaP-Hib-IPV 4			Tdap 、 OPV	
Varicella*							Var						
Measles, Mumps, Rubella							MMR1					MMR2	
Japanese Encephalitis**								JE1、JE2		JE3		JE4	
Influenza						Influenza（yearly）							
Hepatitis A#									HepA1		HepA2		

Adolescent & cocoon vaccination

* Varicella vaccine is given to children born after January 2003 and aged 12 months or older.

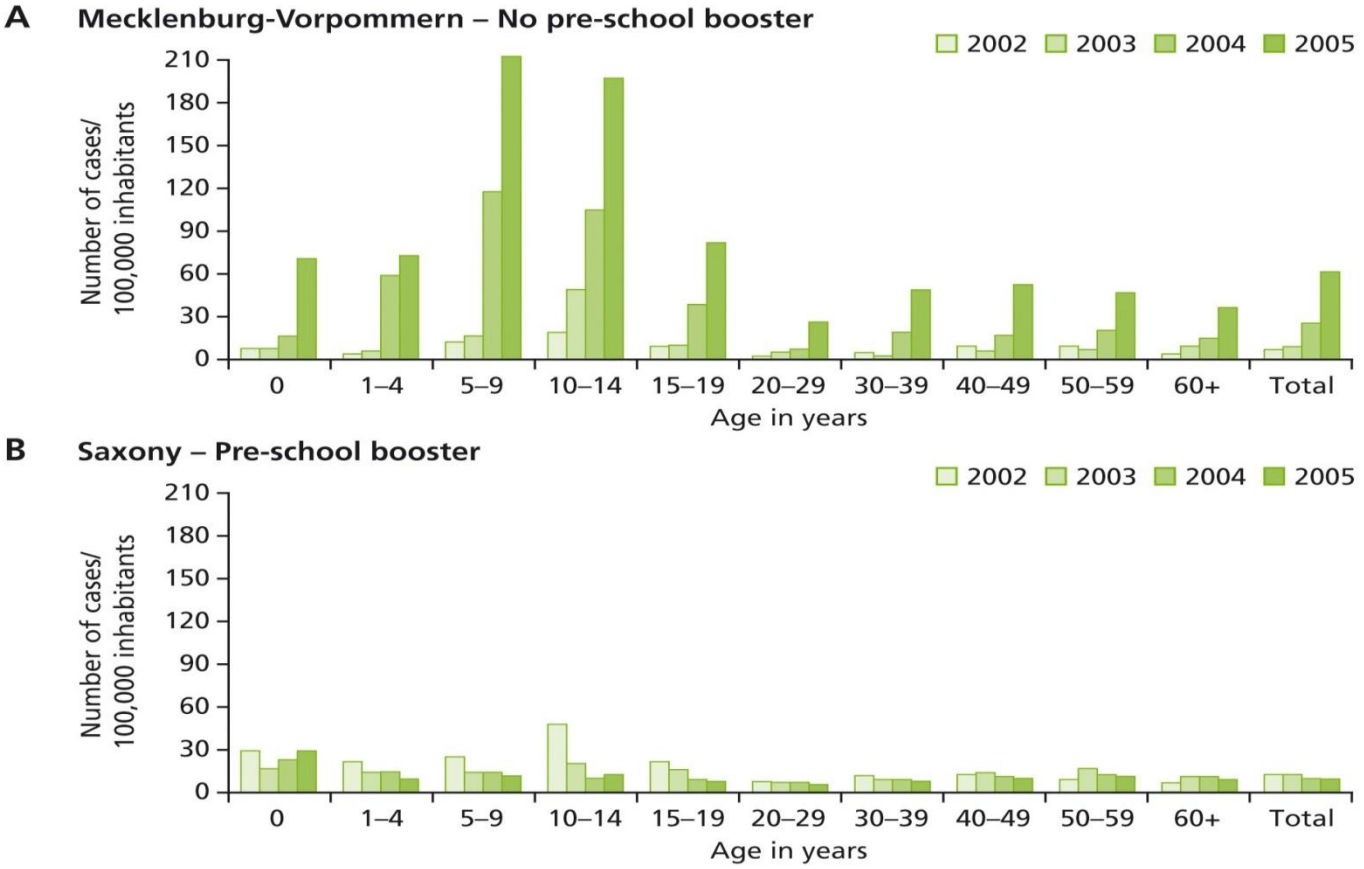
**Two weeks interval between dose1 to dose2.

In selected aboriginal areas.

※ From March 2010, DTaP-Hib-IPV vaccine replaced the routine use of DTP and OPV for children aged 2, 4, 6, and 18 months.

Impact of pre-school pertussis boosters:

Pertussis cases in Germany without (A) and with pre-school boosters (B)



Hellenbrand W *et al., BMC Infect. Dis 2009;* **9**: 22

Cocooning Immunization Strategy

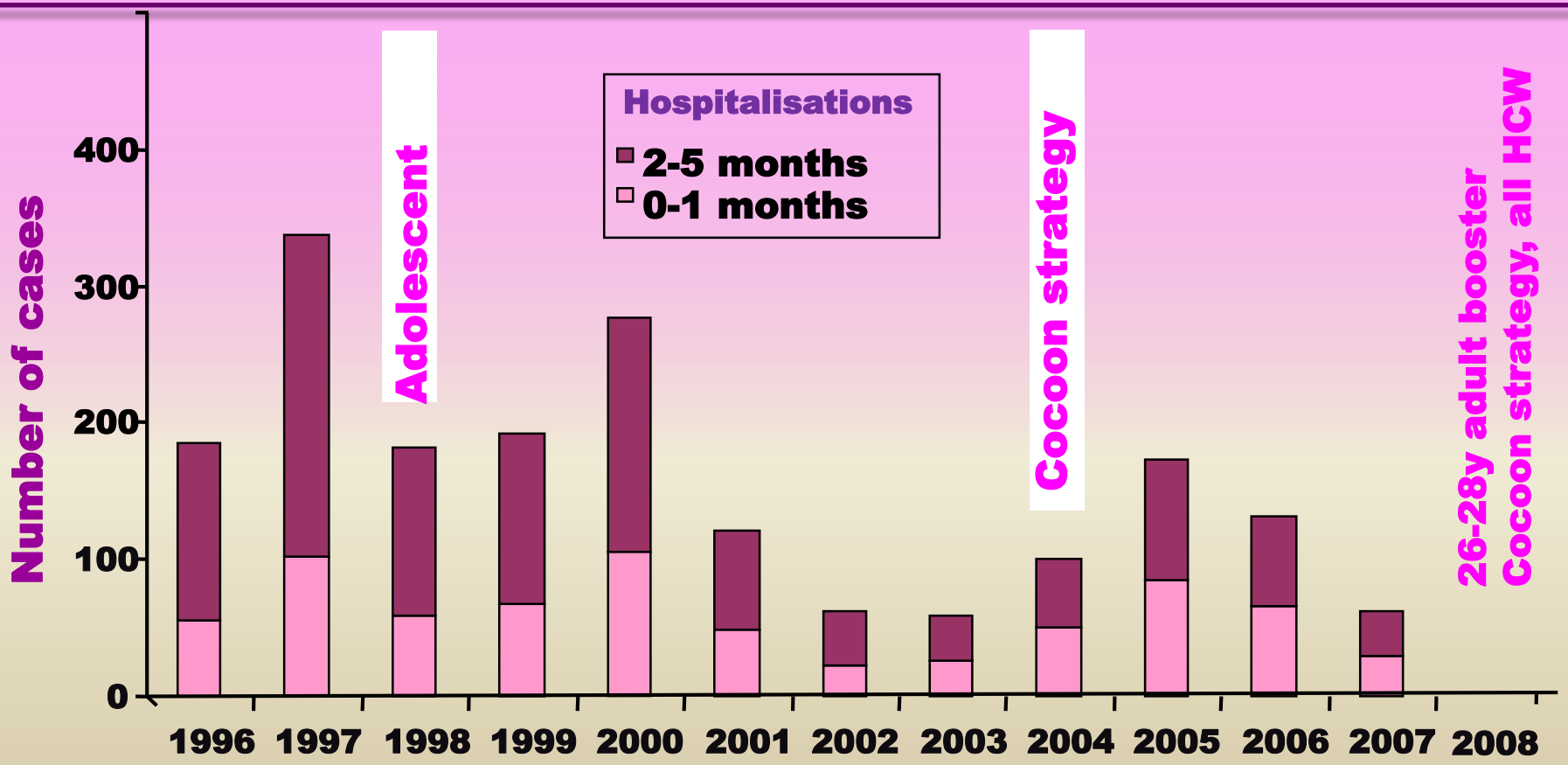
- Selective immunization of
  - New mothers
  - Family members
  - Close contacts of un-immunized or incompletely immunized young infants
- Selective immunization of
  - Health care workers
  - Child care workers

Cocooning Strategies

- Potential advantages
  - New mothers are easy to access
  - Motivation to protect newborns and infants
  - Less expensive than universal strategies
  - Targets high risk groups
- Potential disadvantages
  - More difficult to access fathers and other close contacts

Impact of pertussis vaccination strategies in France

« Hospital-based Surveillance, RENACOQ »

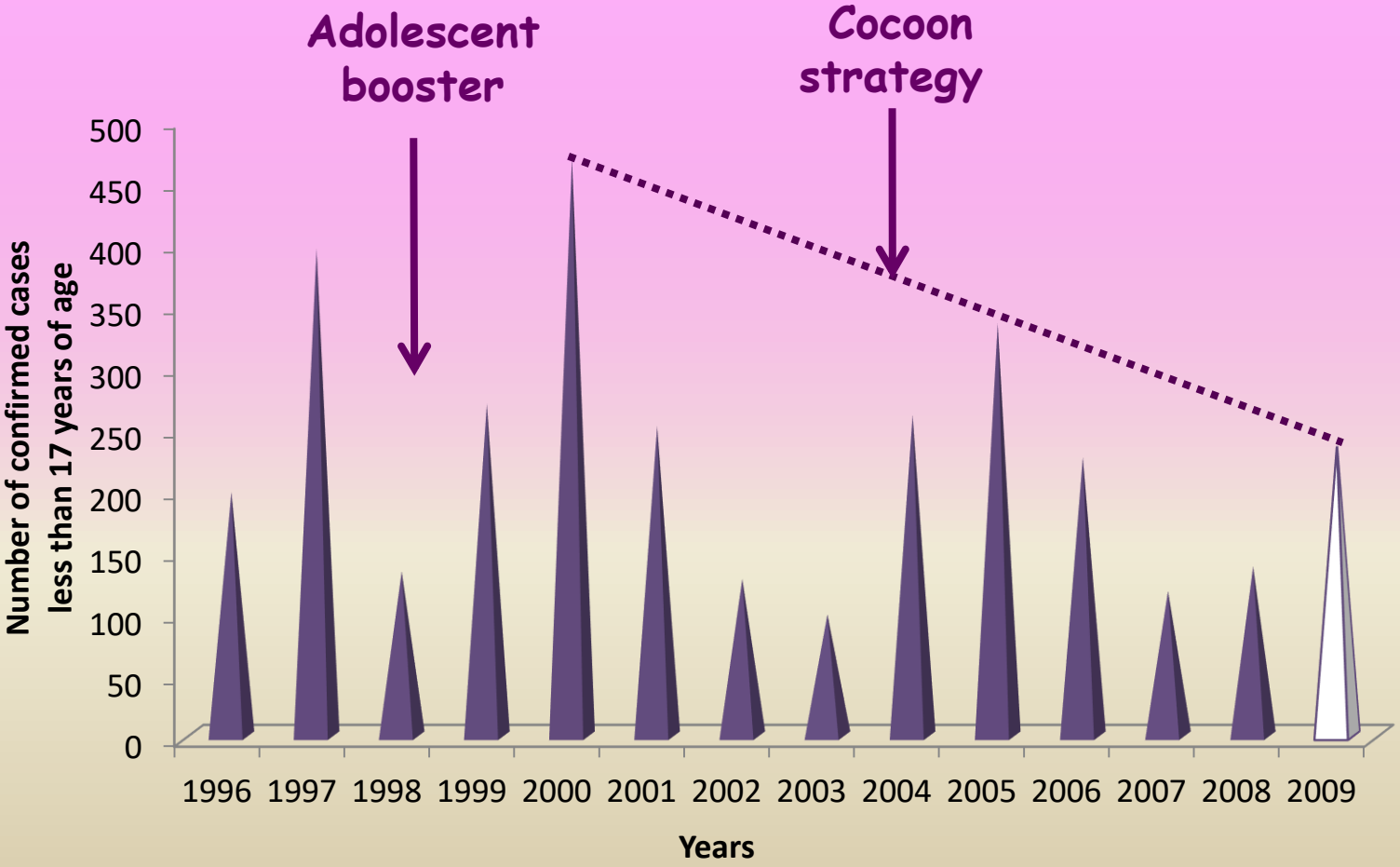


1/ Following cocoon strategy, decrease of hospitalisation due to transmission from new parents to infants

2/ Overall decrease in hospitalisations, but need for adults UMV for further pertussis control

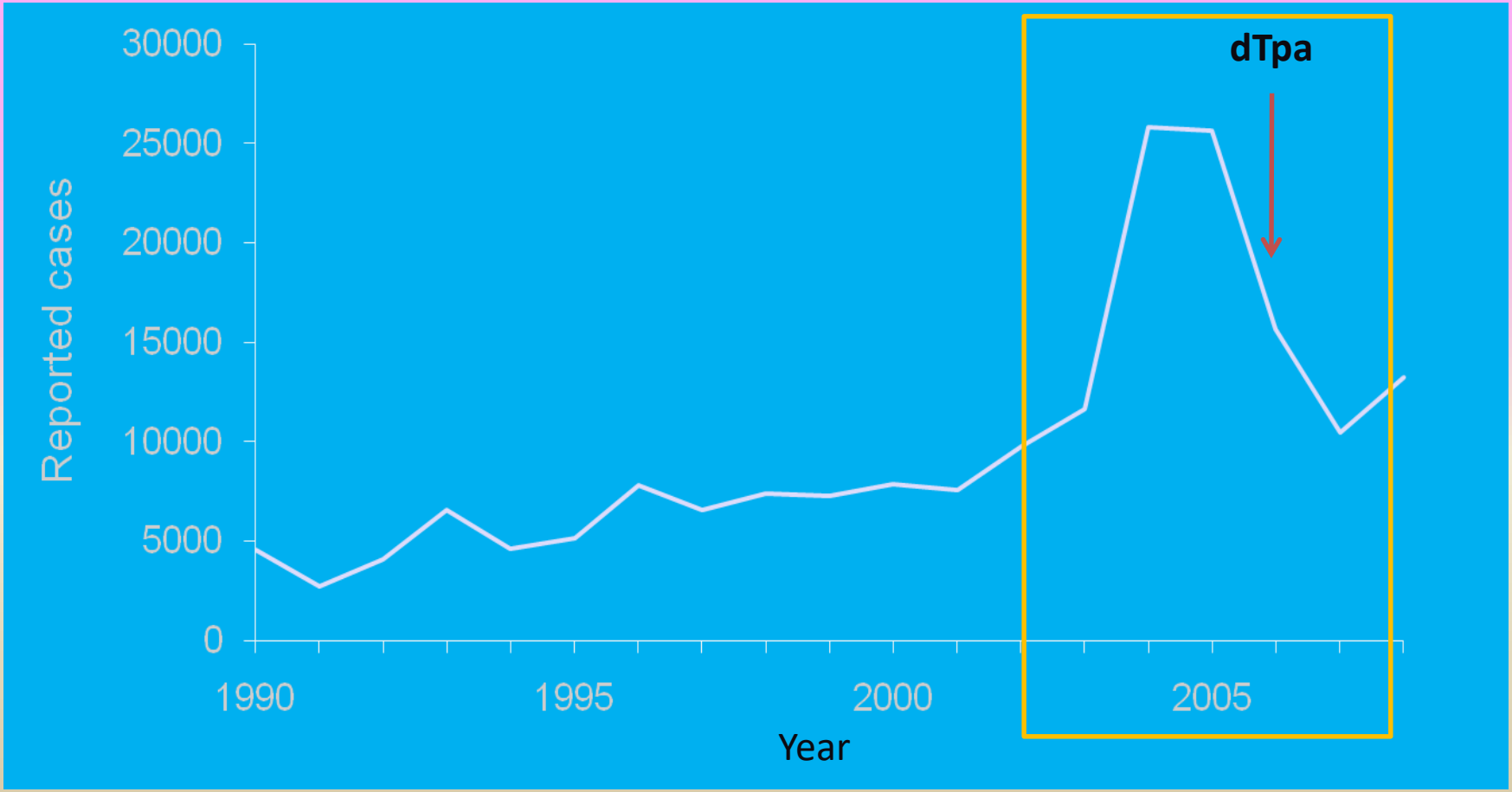
Bonmarin I *et al. Med Mal Infect 2009*: epub

Pertussis in France
« hospital-based surveillance, RENACOQ »



Bonmarin *et al.*,Eurosurveillance 2008 Available from
http://www.invs.sante.fr/surveillance/coqueluche/donnees/donnees_1996_2008.pdf

Change in Incidence of Pertussis in the USA, 1990–2008 (Following Adolescent/Adult Pertussis Recs.)



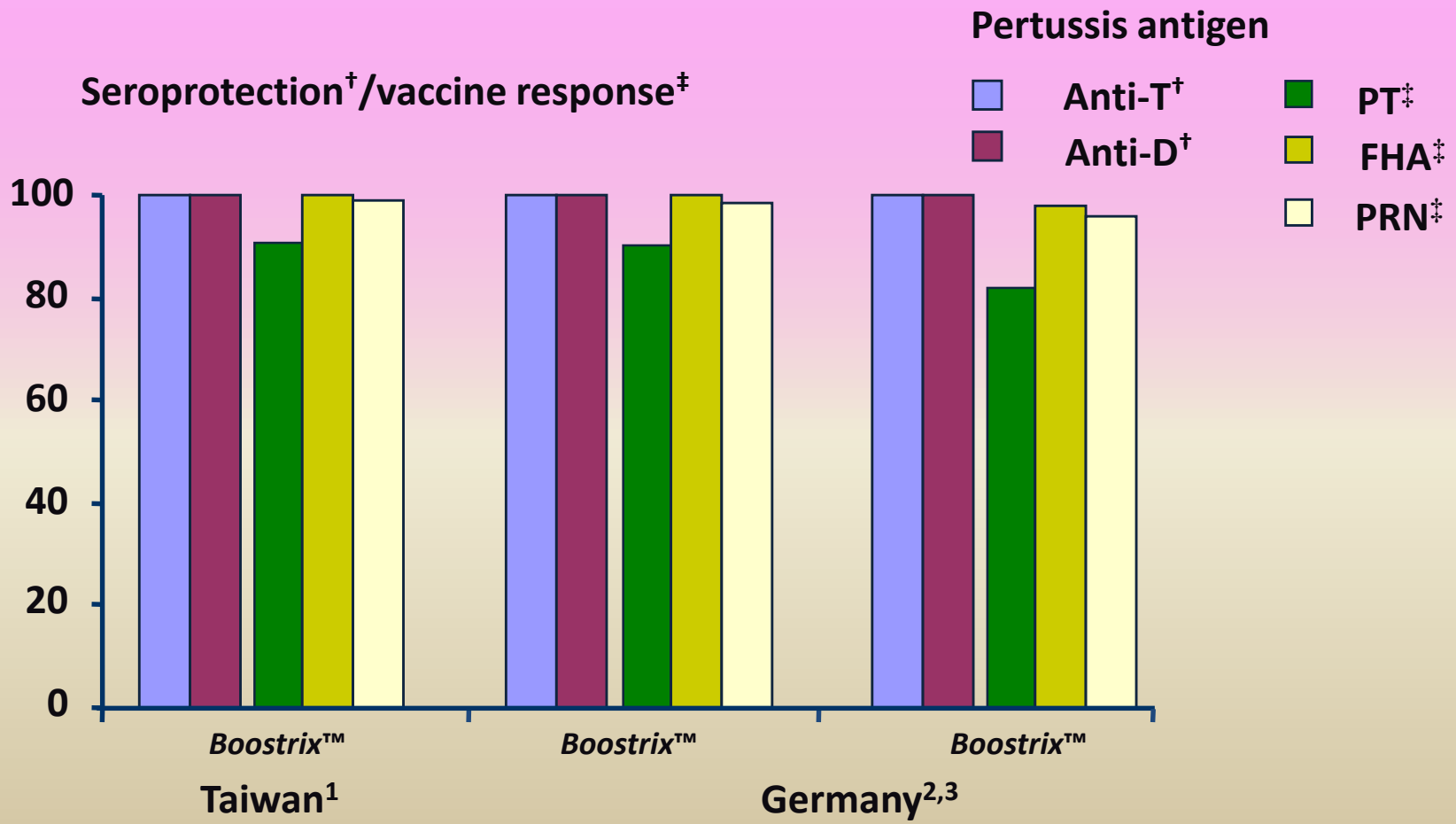
http://www.who.int/immunization_monitoring/en/globalsummary/timeseries/tsincidenceper.htm

dTap immunogenicity in adolescents

- Clinical trials have assessed the immunogenicity of *dTap* in adolescents:
  - Germany (1)[1]
    - 1 dose of *dTap*
    - N=123 adolescents aged 11–18 years
    - no previous pertussis vaccination or history of pertussis and low IgG-anti-PT levels
  - Germany (2)[2]
    - 1 dose of *dTap*
    - N=319 adolescents aged 10–12 years
  - Taiwan[3]
    - 1 dose of *dTap*
    - N=120 adolescents aged 15–20 years
    - primed with 4 doses of DTPa

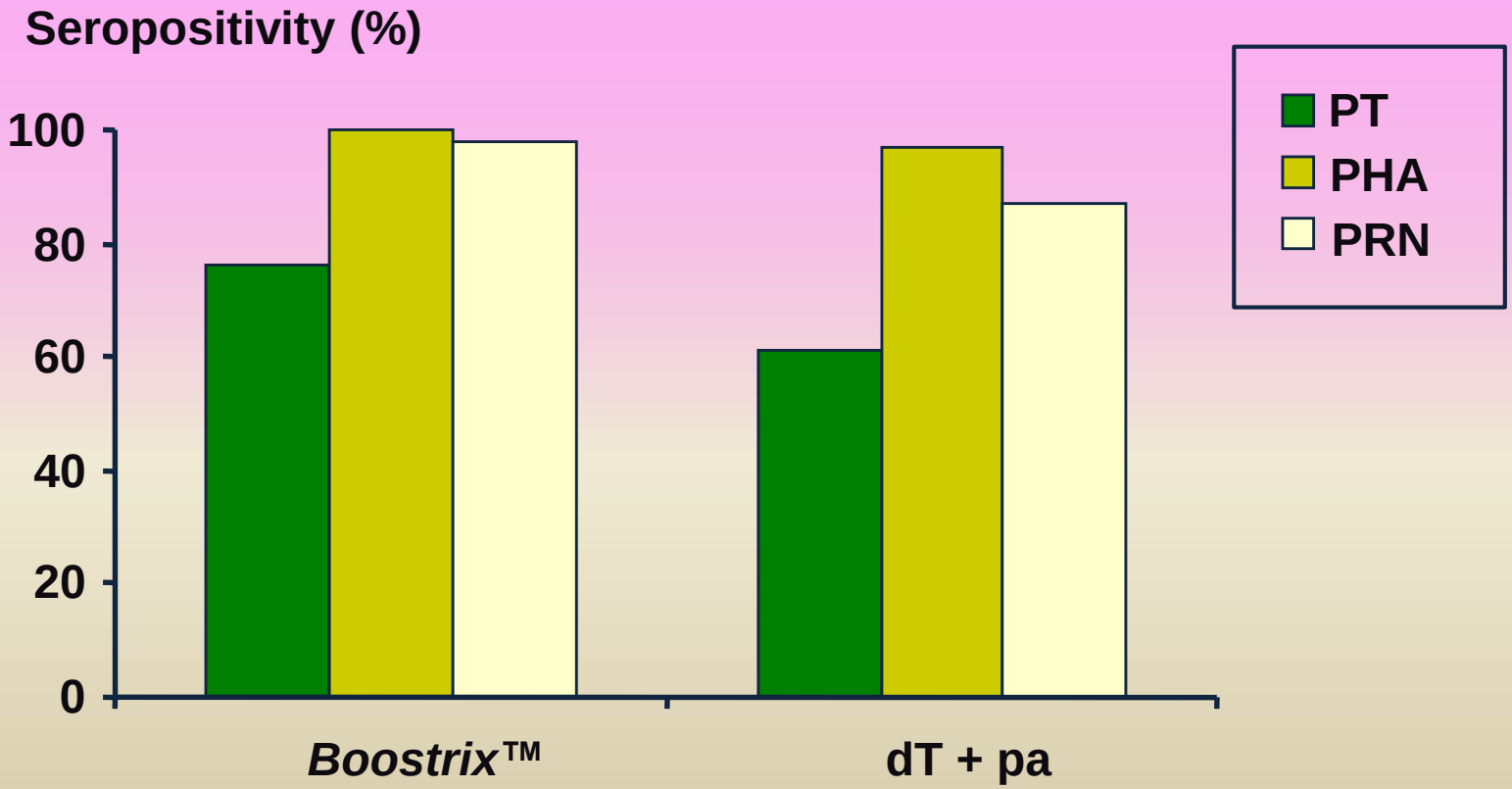
1. Knuf *et al. Vaccine* 2006;**24**:2043–8; 2. Zepp *et al. Vaccine* 2007;**25**:5248–52; 3.3. Huang *et al. J Adolesc Health* 2005;**37**:517.e1–517

dTap immunogenicity in unvaccinated adolescents



1. Huang *et al. J Adolesc Health* 2005;**37:**517.e1–517; 2. Knuf *et al. Vaccine* 2006;**24**:2043–8; 3. Zepp *et al. Vaccine* 2007;**25**:5248–52

Long-term protection with *dTap* in adolescents (5 years post-booster)



1. Edelman *et al*. *Clin Infect Dis* 2007;**44**:1271–7

Pertussis Vaccines

ACIP Recommendations 2010

- Adolescents who have not received a dose of Tdap or whose vaccine history is unknown should be immunized with Tdap as soon as feasible
- Tdap can be administered regardless of interval since the last tetanus or diphtheria containing vaccine (removed time interval between Td and Tdap)
- Children 7-10 years of age who are not fully vaccinated with pertussis (not receive 5 doses Dtap/DTP) should receive 1 dose of Tdap
- Children 7-10 years who have never been vaccinated should receive 1 tdap, a second dose of td and a 3rd dose of td

Pertussis Vaccines

ACIP Recommendations 2010

- Adult 65+:
  - general recommendation for Tdap for those 65+ who have contact with infants under 1 year of age (in place of a Td vaccine)
  - permissive recommendation for Tdap in place of Td for all other adults 65+
- All of these recommendations are off-label use for both licensed Tdap vaccines

The ideal pertussis vaccination schedule

Infants - toddlers – preschool children

2 months DTP	4 months DTP	6 months DTP		18 months DTP		4-6yrs Boostrix

Adolescents and adults

	11-18 yrs Boostrix		Cocooning Boostrix		Adults Td replacement Boostrix

- **Simplification**
- **As immunogenic as DTPw, DTPa and dT vaccines**
- **Generally well-tolerated and clinically acceptable safety profile**

Heininger U. and Cherry JD., *Expert Opin.Biol. Ther. 2006;* **6**(7):685-697; Forsyth K D *et al*., *Clinical Infectious Diseases 2004*; **39**:1802–9; Pertussis vaccines for Australians, NCIRS Fact sheet: November 2009.

Two Sides of a Coin

B. pertussis Adaptation under Extensive Vaccination

- Selected for strains which are more efficiently transmitted by primed hosts in which immunity has waned
- Adaptation of *B. pertussis* to primed hosts
  - delaying an effective immune response by antigenic divergence with vaccine strains
  - increasing immune suppression through higher levels of Ptx production
  - higher levels of Ptx may also benefit transmission by enhancing clinical symptoms

Octavia S et al, Mol Biol Evol. 2011 Jan;28(1):707-15.

Clinical Infectious Diseases Advance Access published December 8, 2011

MAJOR ARTICLE

The Number Needed to Vaccinate to Prevent Infant Pertussis Hospitalization and Death Through Parent Cocoon Immunization

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Number Needed to Vaccinate

The NNV for parent immunization to prevent infant hospitalization/ICU admission or death was thus calculated as follows:

$$NNV = 2\,parents \times (1/ARR)$$

$$NNV = 2\,parents \times [1/(Parent\text{-}attributable\ Infant\ Risk \times Parent\ VE)]$$

Where *Parent-attributable Infant Risk = Infant Risk × Proportion of Infants Infected by Parents.*

ARR: absolute risk reduction

- To capture at least 1 cyclical peak and to reflect recent trends in pertussis risk, the NNV was calculated for the most recent period (2005–2009)

Table 2. Summary of Published Studies: Percentage of Infants Infected by a Parent

First Author (Country) [Ref]	Year	Number of Index Infants With Confirmed Pertussis, Setting, and Age	Method of Parental Diagnosis as Source and Defined Onset Before Index Infant	Identified Sources, Proportion (%)			Source of Infection in All Infants (%)	
				Father	Mother	Either	Not Known	Either Parent[a]
de Greeff (Netherlands) [23]	2006–2008	164 hospitalized, ≤6 months	PCR, culture, serology, cough onset ≥1 week prior	17%	38%	55%	41% (68/164 included in the analysis)	32%
Wendelboe (4 countries) [24]	2003–2004	Hospital = 75; not in hospital = 20, ≤6 months	PCR, culture, serology, symptom onset 7–30 days prior	NA	NA	55%	52% (of 91 included in the analysis)[b]	26%
Kowalzik (7 countries) [25]	2001–2004	99 pediatric ICU, <1 year	PCR, culture, serology, cough onset ≥7 days prior	10%	50%	60%	73% (64/88 included in the analysis)	16%
Elliott (Australia) [26]	2001	140 hospitalized, <1 year	Physician report of coughing contacts (source not otherwise ascertained)	11%	40%	51%[c]	49%	26%
Bisgard (US) [27]	1999–2002	774; 616 included in source analysis, hospital or outpatient, <1 year	Report by parents of any contacts with cough illness and contact 7–20 days before; assigned to contact spending most time with index infant	15%	32%[d]	47%	57% (352/616)	20%
Bonmarin (France) [28]	1996–2005	1688 hospital or outpatient, <6 months	Physician report based on clinical presumption	NA	NA	55%	47% (None identified = 24%; unspecified = 23%)	29%–42%
Halperin (Canada) [7]	1991–1997	1082 hospitalized, <2 years (<50% laboratory confirmed)	Cough ≥2 weeks	NA	NA	20%	60%	8%

Abbreviations: ICU, intensive care unit; NA, not available; PCR, polymerase chain reaction.

[a] Derived as follows: [(1-Not Known) × (Either Parent Among Identified Sources)].

[b] In sensitivity analysis allowing symptom onset 2–6 days and 31–48 days before onset in the index case, 38% of infants were without known source. When asymptomatic household contacts with laboratory-confirmed pertussis were considered as possible sources, 22% of infants were then without known source. Similar parent contribution was reported to be found based on sensitivity analysis (but not presented).

[c] A parent was the identified contact in 58% of infants <8 weeks of age, 50% between 8–15 weeks, 40% between 16–23 weeks, and none of the infants >24 weeks of age.

[d] Mothers were the identified contact for 35% of infants <4 months of age and 17% of infants 4–11 months of age.

Table 3. Number Needed to Vaccinate to Prevent Serious Outcome in Infants (by Age Category in Months) Through Parent Pertussis Immunization[a]

ICU

	No. Hospitalization/ICU Admissions	Infant Risk per 100 000 Hospitalization/ICU Admission	Percentage Attributed to a Parent	
			35% NNV Hospitalization/ICU Admission	55% NNV Hospitalization/ICU Admission
<12 months				
Québec				
2005–2009	265/23	57/7	11 756/97 252	7491/61 952

For the period 2005–2009, the parental NNV to prevent one infant pertussis-related death would exceed 1 million at 35% parental attribution and at 55% would still approach that magnitude.

The NNV for parental immunization was at least 1 million to prevent 1 infant death, approximately 100,000 for ICU admission, and 10,000 for hospitalization

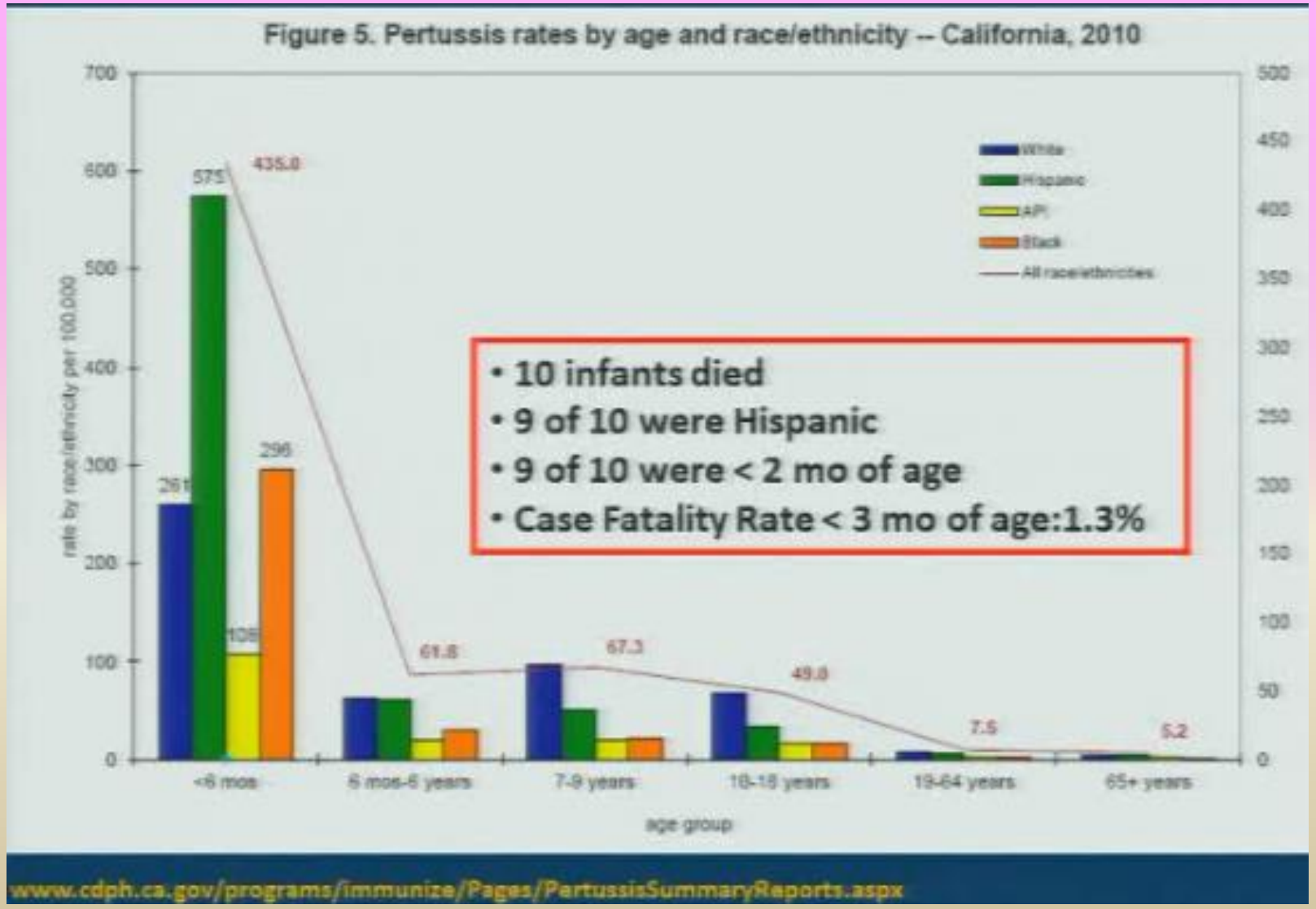
[a] Assumes 85% parent vaccine effectiveness in preventing all infant serious outcomes.

Cost-effective in Canada?

- these NNV estimates for parental pertussis cocoon immunization can be used to generate ballpark costs.
  - Multiplying the NNV by immunization costs (vaccine + administration >$20 [Cdn]) shows that the cost
    - per infant hospitalization (~$200 000)
    - ICU admission (>$2 million)
    - death (>$20 million)

    - prevented through parental pertussis immunization is likely to be extreme.

Pertussis Outbreak: California 2010



ICAAC: Whooping Cough Vaccine May Lose Power

- Analysis of cases in California's Marin County during 2010 whooping cough outbreak
  - 171 cases of PCR-confirmed pertussis during the outbreak and found that 132 involved children, with the majority (about 103) among those 12 or younger
  - highest rate of disease among vaccinated children ages 8 – 12 (full series of shots before they started school, but who had not yet been given the 12-year booster)
  - the attack rate peaked sharply at age 8 and reached 3,600 per 100,000 person-years among the 12-year-olds
  - children ages 1 through 7 are well protected by the vaccine (attack rates < 500 per 100,000 person-years)
- Preschool booster the children received for acellular pertussis had become less effective over time
- Vaccine protection against pertussis **may wane sharply for children more than 3 years after their last booster**

David Witt, MD, of the Kaiser Permanente ICAAC 2011

Conclusions

- Pertussis has become a disease of older subjects and is more common than we realized
- Further booster of pertussis vaccine from adolescence is recommended and may be very helpful
- Large scale pertussis epidemic still occurred
- A better vaccine to reduce disease and colonization is highly desired

- We assess the number needed to vaccinate (NNV) based on updated epidemiologic data in 2 of the largest provinces of Canada
  - Que´bec in eastern Canada (population 7.4 million and birth cohort 85 000)
  - BC on the western coast (population 4.5 million and birth cohort 40 000).

- most siblings are already included in the routine pediatric schedule

Table 1. Risk of Pertussis Hospitalizations per 100 000 by Age

	Year									
Age	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Québec, 2000–2009										
0–<3 months[a]	35	34	42	21	14	22	29	15	49	50
3–<6 months[a]	18	27	26	10	6	15	18	6	20	25
6–<9 months[a]	3	10	4	3	5	2	4	0	4	6
9–<12 months[a]	1	1	4	1	2	6	2	0	1	8
<12 months[a]	57	72	76	35	27	45	53	22	74	89
1–4 years	6	3	6	1	4	4	3	1	1	4
British Columbia, 2000–2009										
0–<3 months[a]	56	44	23	42	30	39	31	9	14	20
3–<6 months[a]	12	12	15	12	7	10	7	2	7	7
6–<9 months[a]	2	0	5	0	2	10	2	2	7	0
9–<12 months[a]	0	2	0	0	0	0	0	0	0	0
<12 months[a]	70	59	43	54	40	59	41	14	27	27
1–4 years	0	0	0	0	0	0	0	0	0	0

[a] Used in number needed to vaccinate calculation with denominator the birth cohort for the specified year.

- Among all hospitalized infants in Que´bec since 2000, 10% were admitted to an ICU—14% aged <3 months and 5% aged 3–11 months
- Among hospitalized infants in BC, 19% were admitted to an ICU—23% aged < 3 months and 10% aged 3–11 months

Skowronski DM et al, CID 2011;

Pertussis in Canada

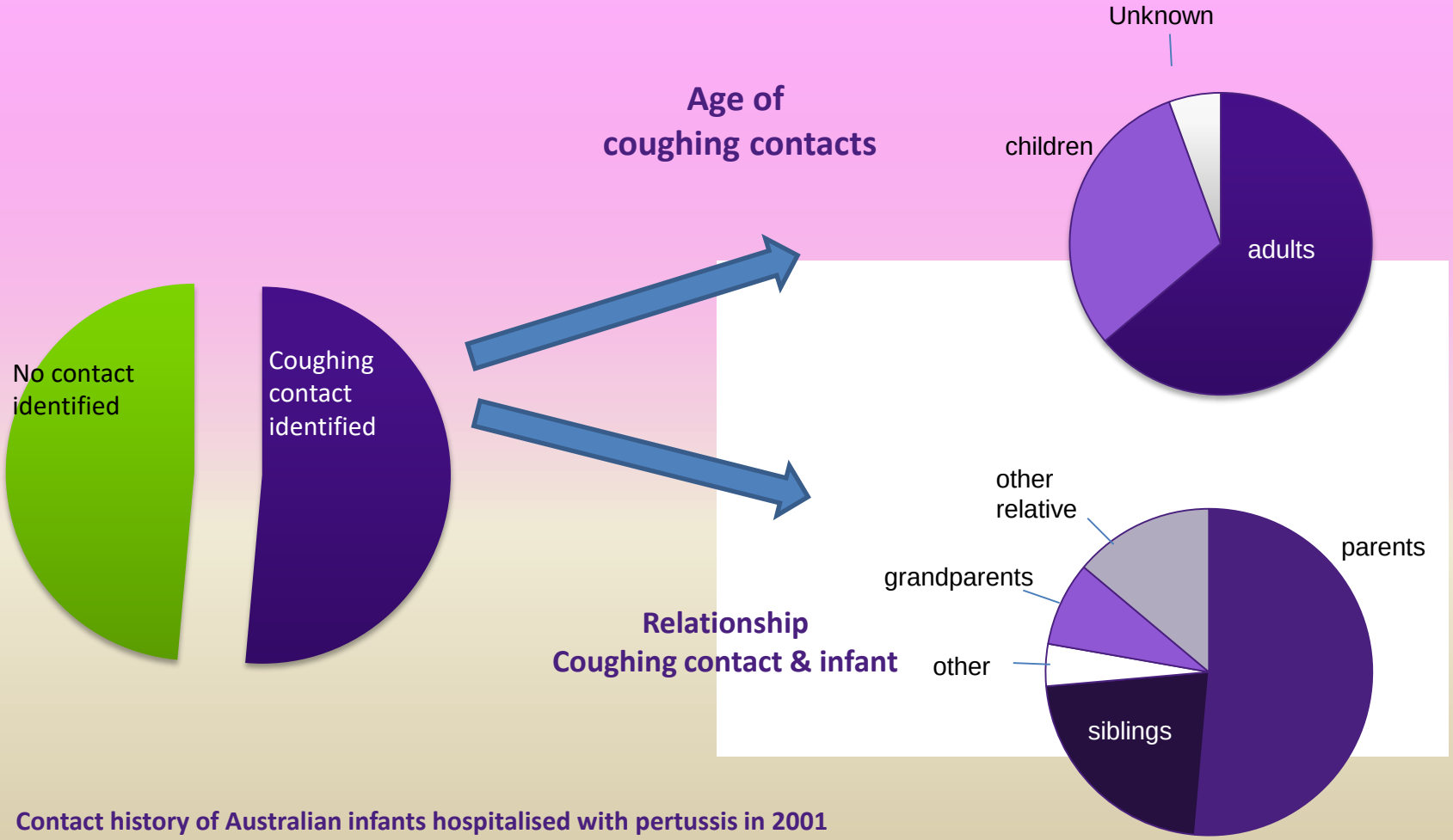
- Since 2000, there were 2 infant pertussis deaths recorded in each province (all <3 months), including 2 in Que´bec and 1 in BC since 2005

- Infant pertussis-related mortality risk was <0.5 per 100 000 in both provinces for the period 2005–2009

- Beyond 5 years of age, serious outcomes due to pertussis were rare

Skowronski DM et al, CID 2011;

Adults, particularly parents are an important source of infection for infants[1,2]



Contact history of Australian infants hospitalised with pertussis in 2001
Adapted from Elliot et al 2004 [2]

1.Chuk *et al.*, *Comm Dis Intell 2008;***32(**4):449-456 2. Elliot *et al., Pediatr Infect Dis J, 2004*;**23**:246–52