Pertussis

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FINANCIAL DECLARATION

- Received honorariums / travel grants / advisory board from
  - GlaxoSmithKline (antibacterial / vaccines)
  - MSD (vaccines, anti-retroviral, antibacterial, anti fungal)
  - Sanofi pasteur (vaccines)
  - Astra Zeneca (antibacterial)
  - LF Asia (pharmaceutical)
  - Pfizer (Vaccines / Antibacterial / Antifungal)
  - Galderma (bacterial resistance)
  - Mundipharma (bacterial resistance)
  - Bayer (antibiotics)

The rise of the Adolescents

THE SOURCE OF PERTUSSIS

??? WHY ???

Reported pertussis incidence by age group: 1990-2015

US CDC 2015

RISING PERTUSSIS INCIDENCE

Incidence rate (per 100,000)

140
120
100
80
60
40
20
0

1990 1995 2000 2005 2015

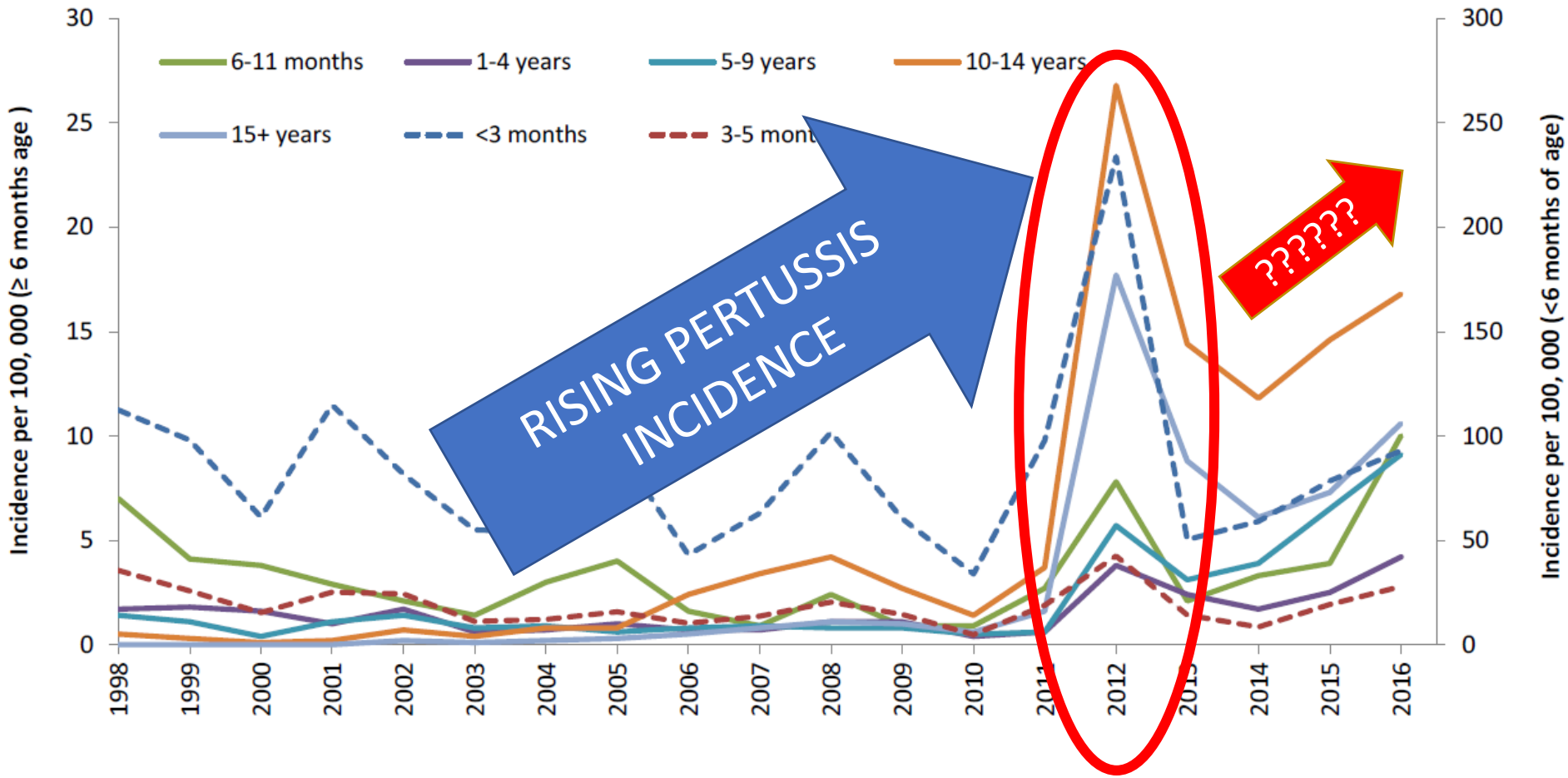
Year

<1 yr
1-6 yrs
7-10 yrs
11-19
20+ yrs

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System

UK Data – same rise 2012… Data till 2016. **RISING?**

Figure 2. Incidence of laboratory-confirmed pertussis cases by age group in England: 1998-2016



PERTUSSIS: This is Puzzling?

- They just had their recent vaccination!

Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2017.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity a
To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded in gray.

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs
Hepatitis B[1] (HepB)	1st dose	←2nd dose→			←3rd dose→								
Rotavirus[2] (RV) RV1 (2-dose series); RV5 (3-dose series)			1st dose	2nd dose	See footnote 2								
Diphtheria, tetanus, & acellular pertussis[3] (DTaP: <7 yrs)			1st dose	2nd dose	3rd dose			←4th dose→				5th dose	
Haemophilus influenzae type b[4] (Hib)			1st dose	2nd dose	See footnote 4		←3rd or 4th dose, See footnote 4→						
Pneumococcal conjugate[5] (PCV13)			1st dose	2nd dose	3rd dose		←4th dose→						
Inactivated poliovirus[6] (IPV: <18 yrs)			1st dose	2nd dose	←3rd dose→							4th dose	
Influenza[7] (IIV)					Annual vaccination (IIV) 1 or 2 doses								Annual vaccination (IIV) 1 dose only
Measles, mumps, rubella[8] (MMR)					See footnote 8		←1st dose→					2nd dose	
Varicella[9] (VAR)							←1st dose→					2nd dose	
Hepatitis A[10] (HepA)							←2-dose series, See footnote 10→						
Meningococcal[11] (Hib-MenCY ≥6 weeks; MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)			See footnote 11								1st dose		2nd dose
Tetanus, diphtheria, & acellular pertussis[12] (Tdap: ≥7 yrs)												Tdap	
Human papillomavirus[13] (HPV)												See footnote 13	
Meningococcal B[11]												See footnote 11	
Pneumococcal polysaccharide[5] (PPSV23)											See footnote 5		

LAST DOSE 11-12 yr

5 x DTaP plus

1 x Tdap

6 DOSES

Range of recommended ages for all children

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision making

No recommendation

UK Vaccination Schedule

4 DOSES of DTaP

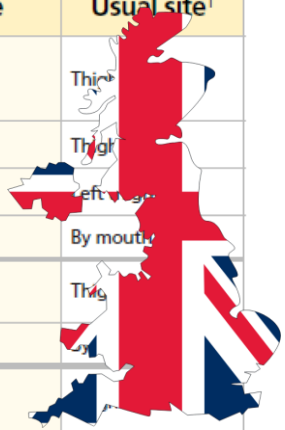
Unlike USA

Last dose 36 months old
Absence of 4-6 yr DTaP
Absence of 11-12yr Tdap

TWO
LESS
VACCINES

The routine immunisation schedule — from Summer 2016

Age due	Diseases protected against	Vaccine given and trade name		Usual site[1]
Eight weeks old	Diphtheria, tetanus, pertussis (whooping cough), polio and *Haemophilus influenzae* type b (Hib)	DTaP/IPV/Hib	Pediacel or Infanrix IPV Hib	Thi
	Pneumococcal (13 serotypes)	Pneumococcal conjugate vaccine (PCV)	Prevenar 13	Thigh
	Meningococcal group B (MenB)[2]	MenB[2]	Bexsero	Left thigh
	Rotavirus gastroenteritis	Rotavirus	Rotarix	By mouth
Twelve weeks	Diphtheria, tetanus, pertussis, polio and Hib	DTaP/IPV/Hib	Pediacel or Infanrix IPV Hib	Thigh
	Rotavirus	Rotavirus	Rotarix	By mouth
Sixteen weeks old	Diphtheria, tetanus, pertussis, polio and Hib	DTaP/IPV/Hib	Pediacel or Infanrix IPV Hib	
	MenB[2]	MenB[2]	Bexsero	Left thigh
	Pneumococcal (13 serotypes)	PCV	Prevenar 13	Thigh
One year old	Hib and MenC	Hib/MenC booster	Menitorix	Upper arm/thigh
	Pneumococcal (13 serotypes)	PCV booster	Prevenar 13	Upper arm/thigh
	Measles, mumps and rubella (German measles)	MMR	MMR VaxPRO[3] or Priorix	Upper arm/thigh
	MenB[2]	MenB booster[2]	Bexsero	Left thigh
Two to seven years old (including children in school years 1, 2 and 3)[5]	Influenza (each year from September)	Live attenuated influenza vaccine LAIV[4]	Fluenz Tetra[3]	Both nostrils
Three years four months old	Diphtheria, tetanus, pertussis and polio	DTaP/IPV	Infanrix IPV or Repevax	Upper arm
	Measles, mumps and rubella	MMR (check first dose given)	MMR VaxPRO[3] or Priorix	Upper arm
Girls aged 12 to 13 years	Cervical cancer caused by human papillomavirus (HPV) types 16 and 18 (and genital warts caused by types 6 and 11)	HPV (two doses 6-24 months apart)	Gardasil	Upper arm
Fourteen years old (school year 9)	Tetanus, diphtheria and polio	Td/IPV (check MMR status)	Revaxis	Upper arm
	Meningococcal groups A, C, W and Y disease	MenACWY	Nimenrix or Menveo	Upper arm
65 years old	Pneumococcal (23 serotypes)	Pneumococcal polysaccharide vaccine (PPV)	Pneumococcal polysaccharide vaccine	Upper arm
65 years of age and older	Influenza (each year from September)	Inactivated influenza vaccine	Multiple	Upper arm
70 years old	Shingles	Shingles	Zostavax[3]	Upper arm[6]



SINGAPORE SCHEDULE

National Childhood Immunisation Schedule - Singapore
(Reference: *National Immunisation Registry*)

For persons aged 0 to < 18 years											
		Months								Years	
Vaccination against	**Birth**	**1**	**3**	**4**	**5**	**6**	**12**	**15**	**18**	**6-7 ^**	**10-11 ^^**
Tuberculosis	BCG										
Hepatitis B	HepB (D1)	HepB (D2)			HepB (D3) #						
Diphtheria, Tetanus, Pertussis			DTaP (D1)	DTaP (D2)	DTaP (D3)				DTaP (B1)		TdaP (B2)
Poliovirus			IPV (D1)	IPV (D2)	IPV (D3)				IPV (B1)		OPV (B2)
Haemophilus influenzae type b			Hib (D1)	Hib (D2)	Hib (D3)				Hib (B1)		
Measles, Mumps, Rubella							MMR (D1)	MMR (D2) ##			
Pneumococcal Disease			PCV (D1)		PCV (D2)		PCV (B1)				
Human Papillomavirus	Recommended for females 9 to 26 years; three doses are required at intervals of 0, 2, 6 months										

4 x DTaP

1 x Tdap

Last dose 10-11 yr
5 doses in total

1 ***LESS*** Dose

World Health Organization
Western Pacific Region

unicef

Recommended national immunization schedule for Viet Nam's children

As of March 2015

Vaccine	When (months to be counted from the date of birth)
BCG vaccine ***To prevent Tuberculosis***	As soon as possible after birth
Hepatitis B vaccine birth dose ***To prevent Hepatitis B***	As soon as possible after birth (within 24 hours)
Quinvaxem vaccine (DPT-HepB-Hib) ***To prevent Diphtheria, Tetanus, Whooping Cough (Pertussis), Hepatitis B and Haemophilus***	1st dose at 2 months 2nd dose at 3 months 3rd dose at 4 months
OPV vaccine* ***To prevent Poliomyelitis***	1st dose at 2 months 2nd dose at 3 months 3rd dose at 4 months
Measles vaccine ***To prevent Measles***	1st dose at 9 months 2nd dose at 18 months**
DPT booster dose ***To prevent Diphtheria , Tetanus and Pertussis***	At 18 months
Japanese Encephalitis vaccine	2 doses, at 1 year after birth (two weeks apart) then

3 doses

last / 4th dose@18m

Waning Immunity to Pertussis Following 5 Doses of DTaP

AUTHORS: Sara Y. Tartof, PhD, MPH,[a] Melissa Lewis, MPH,[a] Cynthia Kenyon, MPH,[b] Karen White, MPH,[b] Andrew Osborn, MBA,[c] Juventila Liko, MD, MPH,[c] Elizabeth Zell, MStat,[a] Stacey Martin, MSc,[a] Nancy E. Messonnier, MD,[a] Thomas A. Clark, MD, MPH,[a] and Tami H. Skoff, MS[a]

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KEY WORDS
Pertussis, DTaP, immunity, Immunization Information Systems, vaccines

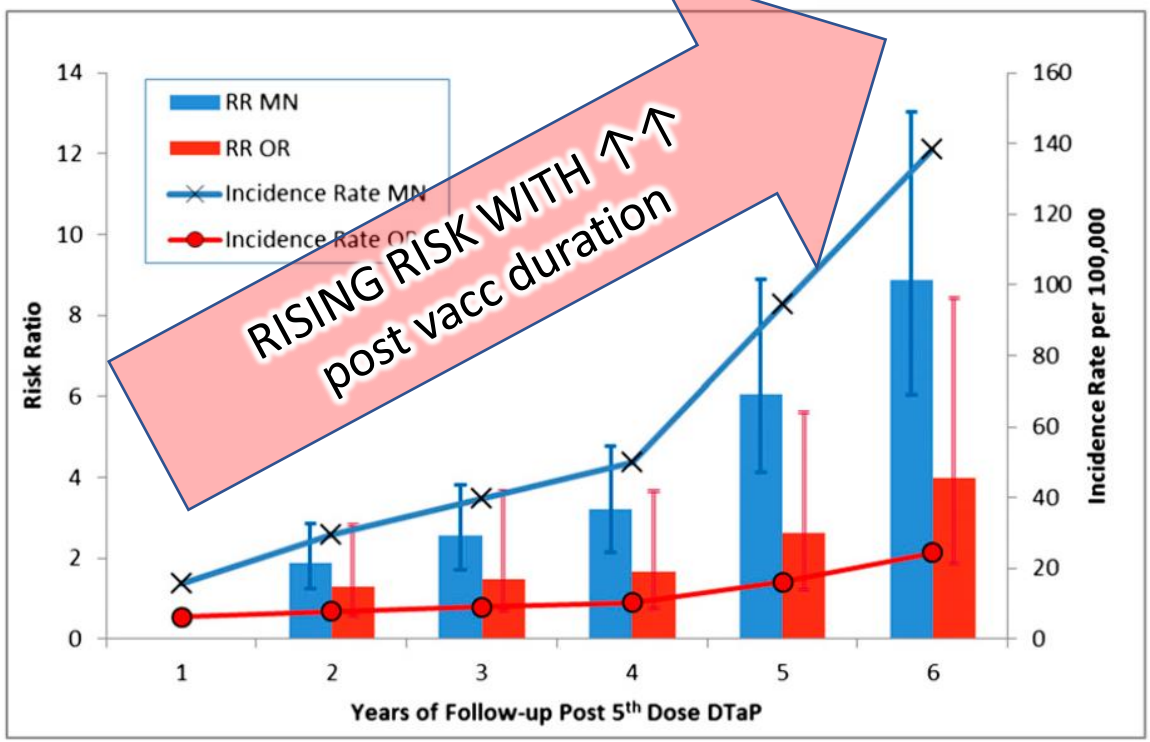
ABBREVIATIONS
CDC—Centers for Disease Control and Prevention

WHAT'S KNOWN ON THIS SUBJECT: Despite high coverage with acellular pertussis vaccine (DTaP), rates of pertussis have increased substantially in 7- to 10-year-olds in recent years. Duration of protection with 5 doses of DTaP may wane earlier than expected and is currently not well described.

WHAT THIS STUDY ADDS: This evaluation reports increasing risk of pertussis in the 6 years after receipt of the fifth DTaP dose, suggesting that waning of vaccine-induced immunity is occurring before the recommended adolescent booster dose at 11 to 12 years of age.

PEDIATRICS Volume 131, Number 4, April 2013

- Rising Risk of Pertussis Post 5xDTaP
- Need for 11y dose

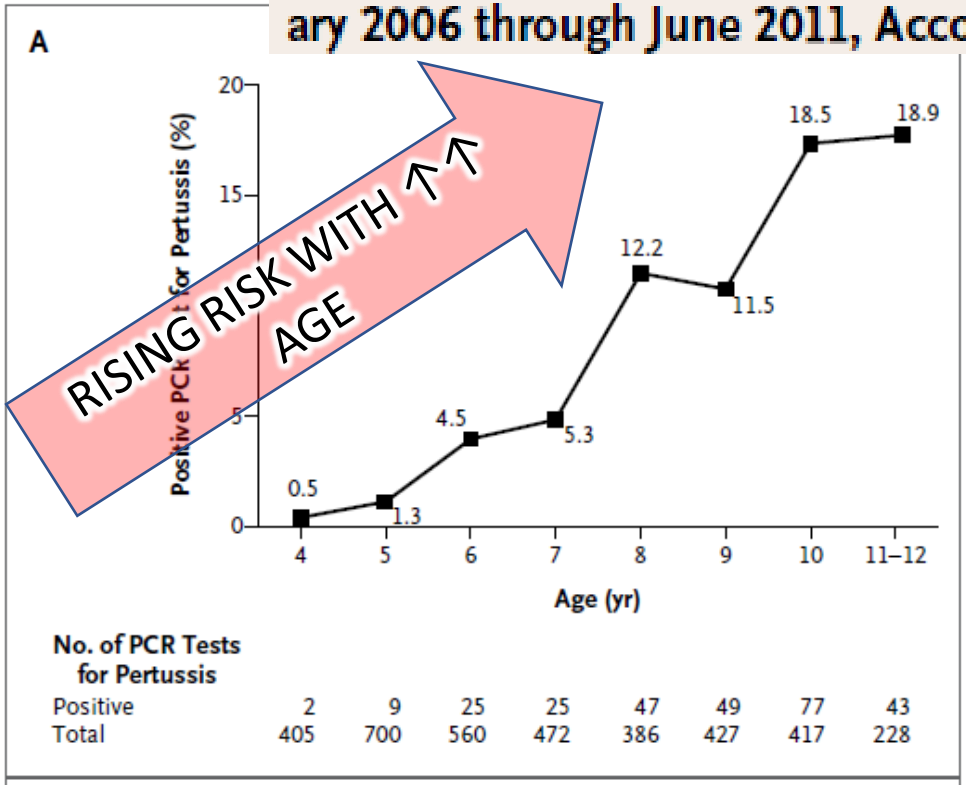


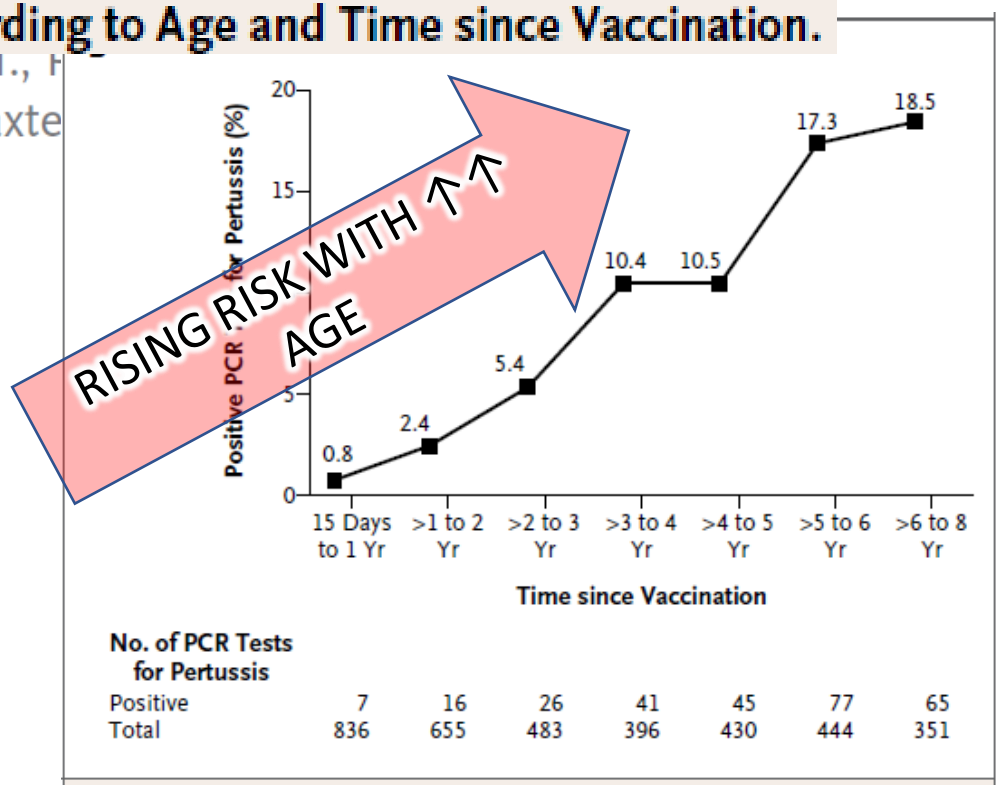
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Waning Protection after Fifth Dose of Acellular Pertussis Vaccine in Children

Figure 2. Percentage of PCR Tests That Were Positive for Pertussis from January 2006 through June 2011, According to Age and Time since Vaccination.





PERTUSSIS: This is Puzzling?

- They just had their recent vaccination!

  Shouldn't the vaccination last?

FACT: The vaccination… didn't last.
~ 4-6 years

- The trials showed that acellular Pertussis has good antibody response. Better than whole cell Pertussis

TRUE OR FALSE?

Many studies done showing Less Reactogenic. Immunogenic +

Several other trials reported similar results

Safety and Immunogenicity of Six Acellular Pertussis Vaccines and One Whole-Cell Pertussis Vaccine Given as a Fifth Dose in Four- to Six-Year-Old Children

Pediatrics 2000;105;e11

vin L. Anderson, MD§;
E. Yerg, MA, MSPH#;
ruce D. Meade, PhD**

TABLE 6. Antibody Response to Pertussius Antigens After a Fifth Dose of DTaP or DtwP Vaccine: Comparison of the Same DTaP Vaccine for All 5 Doses, a Mix of Different DTaP Vaccines and a Mix of DtwP and DTaP Vaccines

Vaccine at Fifth Dose	Study Group	*n*	PT		FHA		PRN		FIM	
			Post GMC (95% CI)	Percent Response*	Post GMC (95% CI)	Percent Response	Post GMC (95% CI)	Percent Response	Post GMC (95% CI)	Percent Response
CB-2	Same AAA	18	175 (111–275)	100	319 (219–466)	94	36[a] (18–68)	44	3[b] (2–5)	6
	Mixed AAA	14	248 (145–426)	93	73 (17–308)	64	10[a] (4–27)	14	6 (2–22)	0
	WAA	9	596 (356–999)	100	202 (87–469)	78	75[a] (47–120)	67	74 (30–185)	11
PM-2	Same AAA	18	180 (117–276)	100	682 (522–892)	89	6 (3–12)	0	2 (1–4)	6
	Mixed AAA	16	155 (107–223)	94	195 (79–478)	81	6 (4–11)	0	4 (2–9)	0
	WAA	10	307 (178–528)	90	182 (73–457)	90	25[c] (11–56)	0	33 (15–73)	10
BSc-3P	Same AAA	22	126 (98–164)	100	146 (115–184)	82	339 (224–515)	91	2 (1–2)	0
	Mixed AAA	18	87 (44–171)	89	60 (20–182)	67	26 (14–58)	67	6 (2–15)	0
	WAA	7	320 (147–694)	100	29 (5–158)	57	167 (50–560)	71	10 (2–42)	14
SKB-3P	Same AAA	22	105 (74–150)	100	503 (376–672)	86	849 (536–1346)	86	2 (1–4)	0
	Mixed AAA	23	169 (130–220)	100	755 (585–974)	91	44 (23–85)	52	2 (1–2)	0
	WAA	5	132 (49–354)	100	345 (167–713)	80	224 (71–709)	80	7 (1–73)	0
CLL-4F_2	Same AAA	12	61 (35–108)	92	59 (31–112)	83	444 (189–1041)	92	583 (335–1017)	100
	Mixed AAA	29	111 (84–148)	100	69 (39–122)	62	42 (22–82)	52	436 (212–895)	83
	WAA	12	225 (120–424)	100	65 (27–156)	75	614 (308–1222)	100	892 (597–1332)	100
LPT-4F_1	Same AAA	29	21 (13–33)	72	146 (100–212)	86	263 (168–411)	76	48 (33–70)	76
	Mixed AAA	46	32 (24–43)	89	218 (168–282)	80	186 (117–295)	80	34 (20–58)	59
	WAA	6	80 (17–380)	83	144 (58–357)	100	200 (62–648)	100	222 (58–859)	83
WCL	WWW	9	92 (46–182)	100	36 (20–66)	56	80 (34–192)	56	343 (231–509)	89

* Percentage of children with fourfold or greater increase in antibody concentration.
For all vaccine groups (same AAA, mixed AAA, and WAA), when the vaccine contained an antigen, the post was significantly greater than pre and when the antigen was not present, the post was not significantly greater. The exceptions are: [a] for CB-2, significant increase in PRN for WAA groups, same AAA, mixed AAA; [b] for CB-2, significant increase in FIM for GMC antibody from pre to post booster was observed in the same AAA group; and [c] for PM-2, significant increase in PRN f for GMC antibody from pre to post booster was observed in the same WAA group.
For the study groups, the GMCs in preimmunization samples ranged from 2 to 25 EU/mL for PT, 5 to 41 EU/mL for FHA, 4 to 58 EU/mL for PRN, and 2 to 49 EU/mL for FIM.

..... when the antigen was not present, the post was not significantly greater.

We thus switched from wP to aP…. in the past

- Potential side effects of wP (Reactogenic)

- aP higher reported efficacy than wP

Bentsi-Enchill AD, et al. Estimates of the effectiveness of a whole-cell pertussis vaccine from an outbreak in an immunized population. *Vaccine* 1997;15:301-6.

Gustafsson L, et al. A controlled trial of a two-component acellular, a five-component acellular, and a whole-cell pertussis vaccine. *N Engl J Med* 1996;334:349-55

TRUE: aP was Immunogenic & ↓Reactogenic

BETTER IMMUNOGENICITY DURING VACCINATION

(old studies… licensing)

BUT…..

BUT *IS IT STILL TRUE??? IMUNOGENIC??*

Let’s LOOK AT MORE RECENT STUDIES…

We now have more experience with aP

Priming with Whole-Cell versus Acellular P…ssis Vaccine

REAL LIFE PERTUSSIS PATIENTS
THE ***REAL ACID TEST***

WHOLE CELL VACCINE conferred better protection

through August … nual tally of re- … 9. The incidence … children between 10 and 14 years of age. Increasing disease among school-aged children despite high vaccination

whole-cell vaccin… …ty of pertussis vaccina…

ALERT IIS hold… …n records for 195,959 childr… …97 through 1999. From April 1997 t… …July 2012, a total of 484 cases of pertussis were re-

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aP wP RISK RATIO

Table 1. Pertussis among Children in Oregon, According to Type of First Dose of Pertussis Vaccine.*

	First Pertussis Vaccine†		Pertussis Cases‡		Incidence per 100,000		Risk Ratio (95% CI)§
	Acellular	Whole Cell	Acellular	Whole Cell	Acellular	Whole Cell	
Any pertussis vaccination¶	164,885	31,074	315	31	191.0	99.8	1.91 (1.32–2.77)
3 pertussis vaccinations in first yr of life	120,712	24,569	243	23	201.3	93.6	2.15 (1.40–3.30)
≥5 pertussis vaccinations starting before 1 yr of age	111,965	22,093	190	18	169.7	81.5	2.08 (1.28–3.38)
≥5 pertussis vaccinations starting before 1 yr of age, and disease at age ≥10 yr	113,502	22,229	130	10	114.5	45.0	2.55 (1.34–4.84)
≥5 pertussis vaccinations starting before 1 yr of age, with Tdap at age ≥10 yr	86,105	16,800	65	5	75.5	29.8	2.54 (1.02–6.36)
Any receipt of Tdap	106,893	17,889	85	6	79.5	33.5	2.37 (1.04–5.42)

CMAJ RESEARCH

Effectiveness of pertussis vaccination and duration of immunity

CMAJ. 2016 Nov 1; 188(16): E399–E406.

Kevin L. Schwartz MD, Jeffrey C. Kwong MD, Shelley L. Deeks MD, Michael A. Campitelli MPH, Frances B. Jamieson MD, Alex Marchand-Austin MSc, Therese A. Stukel PhD, Laura Rosella PhD, Nick Daneman MD, Shelly Bolotin PhD, Steven J. Drews PhD, Heather Rilkoff MPH, Natasha S. Crowcroft MD(Cantab)

See also www.cmaj.ca/lookup/doi/10.1503/cmaj.161048

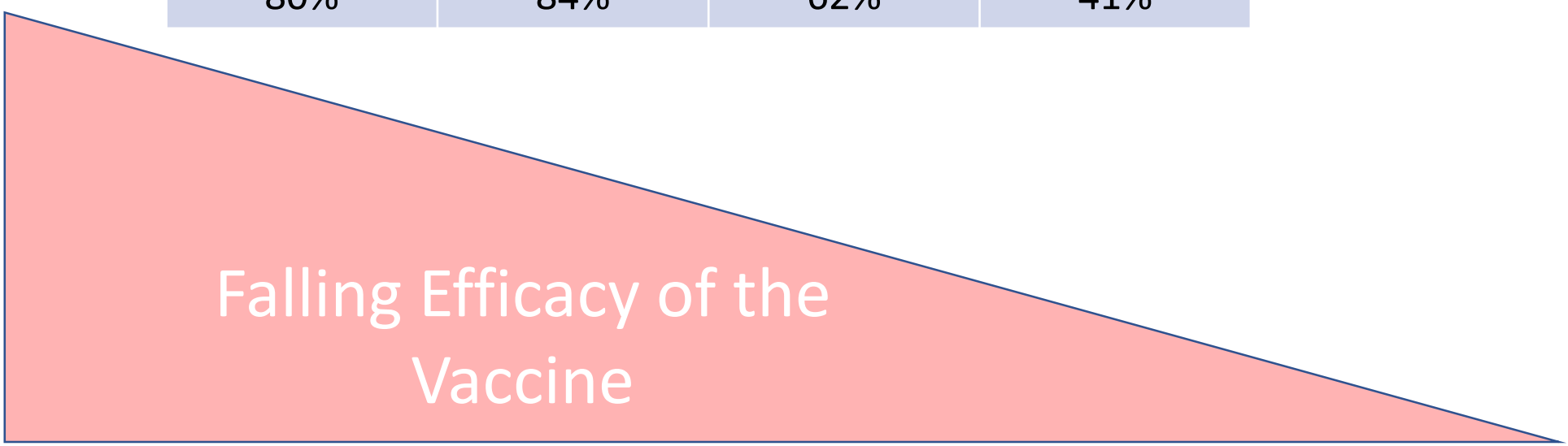
Pre vaccine era	156 / 100,000	
Historic Low (2011)	2.0 / 100,000	wP→aP 1984
2012	13.9 / 100,000	unvaccinated religious community
2013	3.9 / 100,000	

TWO ADDITIONAL DOSES GIVEN to KEEP THE NUMBERS ↓↓

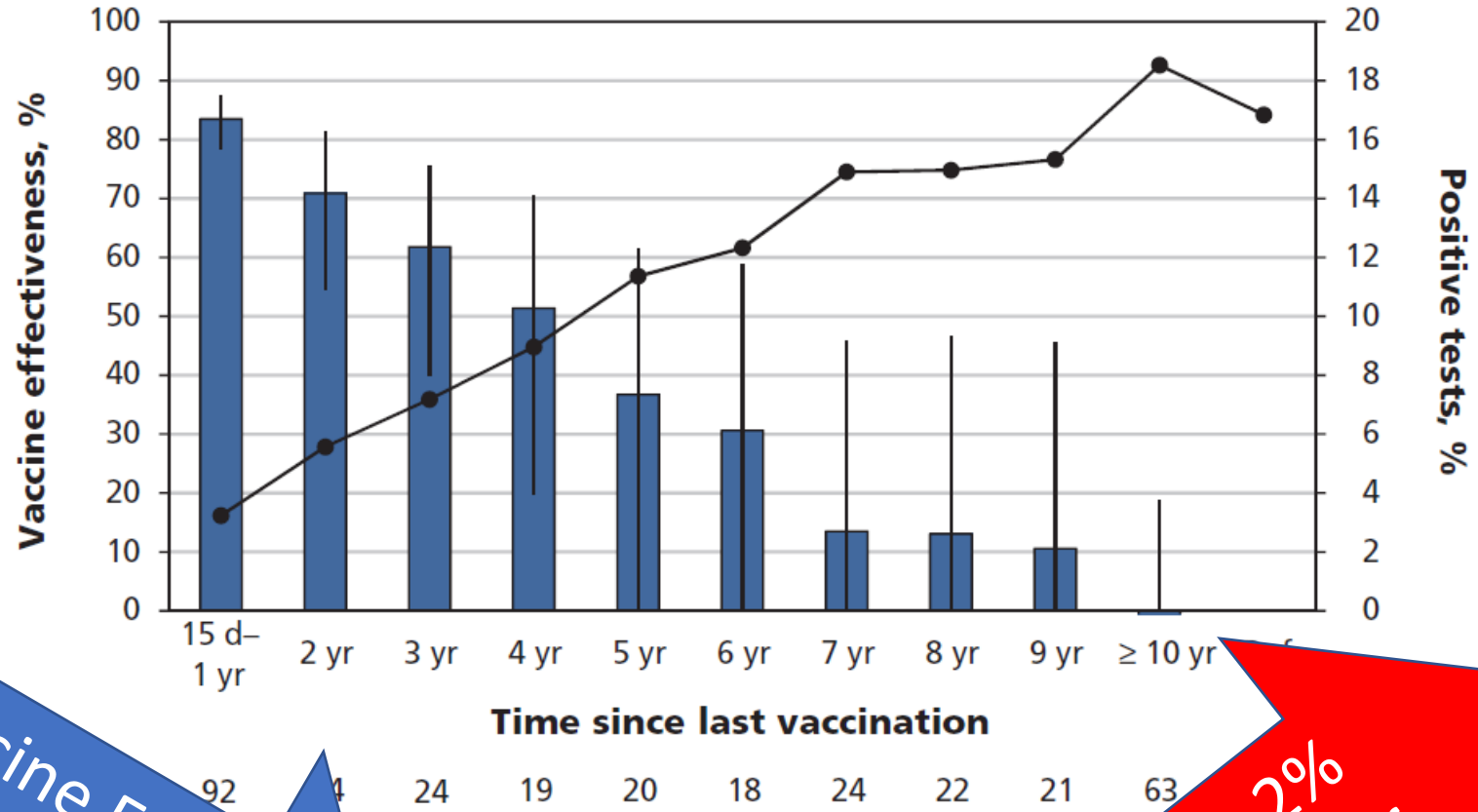
Interventions: aP add 14-16y single adult dose

- Test Negative, nested control study
- 5867 individuals (486 +ve, 5381 –ve ctrl)
- Vaccine Efficacy

< 1 yr	1-3 yr	4-7 yr	≥ 8 yr
80%	84%	62%	41%



Falling Vaccine Efficacy, Rising Cases



Vaccine Efficacy FALL 10% / yr

Increase 2% Prop per year.

Figure 1: Pertu veness (blue bars, left axis) and pr tests (solid line, right axis) by year ation in participants with up-to-d nation. As time from last vaccination incre effectiveness decreased, and the p ests positive for pertussis increased. Vacci fectiveness was calculated from crude odds rati using the formula VE = 1 – OR × 100. Error bars represent 95% confidence intervals. Ref = reference up (unvaccinated population). Results of the Cochran–Armitage trend test for proportion of pertussis cases: $p < 0.001$.

wP vs aP – the Difference

Priming with wP vs aP

≥3 priming doses of **wP vs aP priming**

- adjusted OR of 2.15 (95% CI 1.30 to 3.57)

≥ 1 priming dose **wP vs aP priming**

- adjusted OR of 1.82 (95% CI 1.18 to 2.82).

PRIMING WITH wP = BETTER Protection ….
Vaccination effect persists > 1 decade later.

Other studies supporting whole cell Vaccine Effectiveness…

Vickers D, Ross AG, Mainar-Jaime RC, et al. Whole-cell and acellular pertussis vaccination programs and rates of pertussis among infants and young children. *CMAJ* 2006;175:1213-7.

Klein NP, Bartlett J, Fireman B, et al. Comparative effectiveness of acellular versus whole-cell pertussis vaccines in teenagers. *Pediatrics* 2013 ;131:1716-22.

Sheridan SL, Ware RS, Grimwood K, et al. Number and order of whole cell pertussis vaccines in infancy and disease protection. *JAMA* 2012;308:454-6. (Australia – 1999)

What does it mean?

1. aP had immunogenicity.
2. Less reactogenicity during vaccination.

   But we don't know the true correlates of protection.

3. But in *real life* –
   wP priming was more reactogenic,
   conferred longer duration of protection.

PERTUSSIS: This is Puzzling?

- They just had their recent vaccination!

  Shouldn't the vaccination last?

FACT: The vaccination… didn't last.
~ 4-6 years

- The trials showed that acellular Pertussis has good antibody response. Better than whole cell Pertussis

FACT: wP BETTER EFFICACY / DURATION of Protection

Reasons for Discrepancy…

- Two trials used a weaker wP vaccine strain (manufactured by Connaught)

  Mattoo et al. Clin Microbiol Rev 2005;18(2):326-82

- We don't really know the correlates of protection.

  Which Antibody? Levels?
  Whole cell had 1000s more antigens.

  Onorato WI et al. JAMA.1992;267(20):2745-9

- We didn't have long term data of those trials

PERTUSSIS: This is Puzzling?

- How long does
  - wP last?
  - aP last?
  - Natural Infection last?

Immunity – Natural infx vs Vaccination

3. PREVENTION AND TREATMENT

The Pediatric Infectious Disease Journal • Volume 24, Number 5, May 2005

Duration of Immunity Against Pertussis After Natural Infection or Vaccination

Aaron M. Wendelboe, MSPH, Annelies Van Rie, MD, PhD,* Stefania Salmaso, PhD,† and Janet A. Englund, MD‡*

Natural Infection – 10-20 yrs

TABLE 1. Sel ection Acquired by Natural Infection With *Bordetella pertussis*

Author	Year	Participants (n)	Data Source	Estimate of Protection (yr)	Country of Study
Laing and Hay[10]	1902	20,405	Cohort	Near lifelong	U.S.
Gordon and Hood[8]	1951	Not applicable	Review	Near lifelong	Not applicable
Wirsing von König et al[11]	1995	369	Prospective household contact	20	Germany
Miller and Gay[12]	1997	Not applicable	Review/modeling	7–10	U.K.
Versteegh et al[7]	2002	4	Case series	3.5–12	The Netherlands

Post whole vaccine ~10 years

TABLE 2. Selected Articles Describing Duration of Pr

Author	Year	Participants (n)	Data Source	Estimate of Protection (yr)	Country of Study
Lambert[13]	1965	474	Outbreak	12	U.S. (Michigan)
Jenkinson[17]	1988	436	Clinic population	4	U.K.
CDC[18]	1993	225	Outbreak	4–6	U.S. (Massachusetts)
Ramsay et al[19]	1993	3150	Surveillance data	8	U.K.
Nielsen and Larsen[14]	1994	Unknown	Surveillance data	10	Denmark
He et al[20]	1996	3794	Surveillance data	5–10	Finland and Switzerland
Van Buynder et al[6]	1999	15,286	Surveillance data	5–14	U.K.
Torvaldsen and McIntyre[5]	2003	Unknown	Surveillance data	6–9	Australia

Post aP vaccine 4-6 years

TABLE 3. Selected Articles Describing Duration of Protect

Author	Year	Vaccine Type	Participants (*n*)	Data Source	Duration of Follow-up	Estimate of Protection (yr)	Country of Study
Simondon et al[24]	1997	Pasteur Mérieux Serums and Vaccines (4-component)	4181	Nested case-contact	Up to 4.25 yr	Protection after wP longer than aP	Senegal
Tindberg et al[25]	1999	2-component	207	Follow-up of vaccine efficacy trial	10 yr	5.5	Sweden
Salmaso et al[4]	2001	SmithKlineBeecham and Chiron Biocine (both 3-component)	8432	Vaccine efficacy trial	3 yr	6	Italy
Lugauer et al[26]	2002	4-component	10271	Longitudinal cohort	6 yr	6	Germany

The rise of the Adolescents

THE SOURCE OF PERTUSSIS

acellular Pertussis vaccine didn't last

Adolescents are the Reservoir

Others
Mutant strains, loss of herd immunity

priming effect of whole cell pertussis is lost

Epidemiol. Infect. (2017), **145**, 1025–1036.
doi:10.1017/S0950268816002983

Risk factors for pertussis in adults and teenagers in England

A. WENSLEY[1]†, G. J. HUGHES[1]†, H. CAMPBELL[2], G. AMIRTHALINGAM[2], N. ANDREWS[3], N. YOUNG[4] AND L. COOLE[1]*

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[2] *Immunisation, Hepatitis and Blood Safety, Public Health England, London, UK*
[3] *Statistics and Modelling Economics Department, Public Health England, London, UK*
[4] *Public Health England South West, Exeter, UK*

Received 31 May 2016; Final revision 15 November 2016; Accepted 15 November 2016; first published online 9 January 2017

- Case Control Study
- Cases lab confirmed ≥ 15yo
- 231 cases, 190 controls.

Risk Factors for Pertussis in Adults and teenagers

- Studied employment type and professional and household contact with children
- Nothing mattered except.

1. **Professional contact with children aged < 1yo**
   (OR) 0·25, 95% CI 0·08–0·78, P = 0·017)

2. **Household contact with ≥1 10–14 yo**
   (OR 2·61, 95% CI 1·47–4·64, P = 0·001).

Why?

OLDER TEENAGERS / ADULTS infecting Adolescents….

Protection conferred by

- Occupational contact with very young children from immune boosting by low-level exposures to B. pertussis.

Risk conferred by:

- An infecting older teenagers or adult.

FACT: OLDER TEENAGERS / ADOLESCENTS ARE THE RESERVOIRS….

What are the options now?

1. Vaccination in Pregnancy. Protect the greatest at risk group.

Cocoon!

Vaccinate mother at 26 weeks

Vaccinate family!

Vaccinate HCW, childcare workers

What are the options now?

1. Vaccination in Pregnancy. Protect the greatest at risk group.
2. Those who are still on wP – don't change!

What are the options now?

1. Vaccination in Pregnancy. Protect the greatest at risk group.
2. Those who are still on wP – don't change!
3. Revaccination of adolescents / adults.

    AGAIN and AGAIN ?? ESCMID Vac Grp says YES

    Focus on adolescents. Greatest numbers.

    Reduce the morbidity of Pertussis in adolescents

    Reduce the reservoir – the transmission of Pertussis to the infants.

Is revaccination adults SAFE?

Vaccine 29 (2011) 45–50

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

10 years

A decennial booster dose of reduced antigen content diphtheria, tetanus, acellular pertussis vaccine (*Boostrix*™) is immunogenic and well tolerated in adults

Robert Booy[a], Olivier Van Der Meeren[b], Su-Peing Ng[b], Froilan Celzo[c], Gunasekaran Ramakrishnan[b], Jeanne-Marie Jacquet[b,*]

[a] *Children's Hospital Westmead, Sydney, New South Wales, Austr*
[b] *GlaxoSmithKline Biologicals, Avenue Fleming 20, 1300 Wavre, E*
[c] *University Hospital of Antwerp, Previously GlaxoSmithKline Bio*

Vaccine 29 (2011) 8459–8465

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

5 years

Tolerability and antibody response in adolescents and adults revaccinated with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine adsorbed (Tdap) 4–5 years after a previous dose

Scott A. Halperin[a,*], Shelly McNeil[a], Joanne Langley[a], Mark Blatter[b], Marc Dionne[c], Joanne Embree[d], Roehl Johnson[e], Thomas Latiolais[f], William Meekison[g], Francisco Noya[h], Shelly Senders[i], Paul Zickler[j], David R. Johnson[k]

END /
TIME CHECK

WHAT HAS BABOONS HAS TO DO WITH PERTUSSIS….

Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model

Jason M. Warfel, Lindsey I. Zimmerman, and Tod J. Merkel[1]

Division of Bacterial, Parasitic and Allergenic Products, Center for Biologics Evaluation and Research, US Food and Drug Administration, Bethesda, MD, 20892

Edited by Rino Rappuoli, Novartis Vaccines and Diagnostics Srl, Siena, Italy, and approved October 22, 2013 (received for review August 5, 2013)

Pertussis is a highly contagious respiratory illness caused by the therapeutic for established disease, and the highly contagious

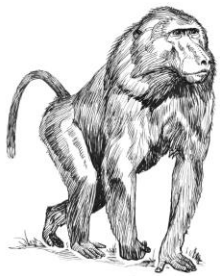
- Infant Baboons. aP vs wP vaccinated 2,4,6m
- Infected them Pertussis at 7 months

VACCINE GIVEN

No vaccine

aP Vaccine

wP Vaccine



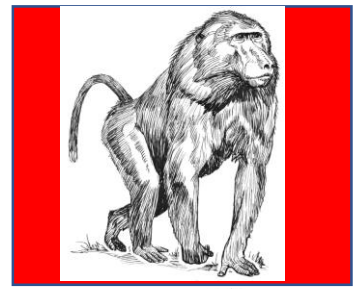
aP

wP

EXPOSURE TO PERTUSSIS

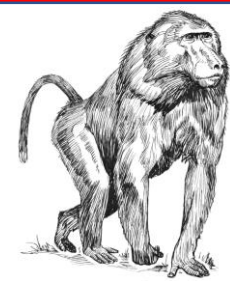
SPREAD / SHEDDING

SICK



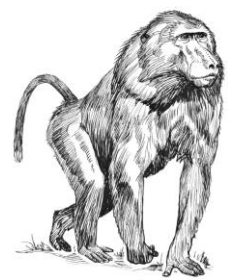
33 -35d

WELL



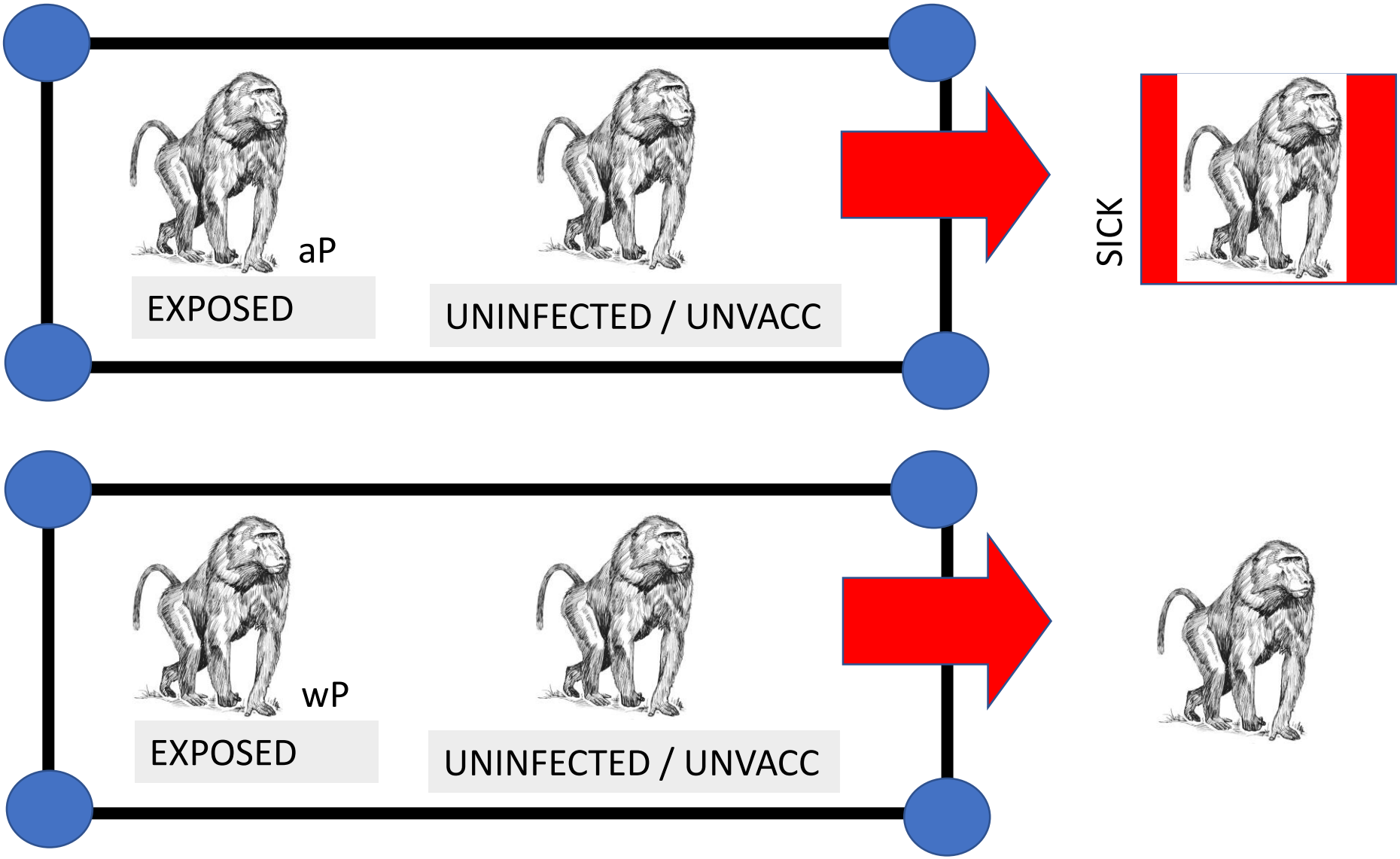
33 -35d

WELL



18 days

aP and wP prevents clinical disease
aP had infection, but no clinical disease.
aP persistence in mucosa. May Transmit
wP shorter duration, lower bacterial counts



aP baboons do not develop symptomatic disease
But they can shed bacteria and spread to others…
contributing to the reservoir.

Results....of aP vs wP in Baboons

ACELLULAR	WHOLE CELL
protected from severe pertussis-associated symptoms. Failed to prevent infection.	Protected from pertussis symptoms
did not clear the infection faster than naïve animals,	More rapid clearance. Faster than naiive
Had colonization	Could clear infection and colonization.
readily transmitted pertussis to unvaccinated contacts.	Did not transmit to unvaccinated contacts.

What of the future?

- Adsorbed Pertussis Vaccine

  SP0173 – Sanofi Pasteur

- Live Pertussis vaccine

  BPZW1 – ILIAD Biotech

Vaccine 33S (2015) A233–A239

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Thirty years of vaccination in Vietnam: Impact and cost-effectiveness of the national Expanded Programme on Immunization

Mark Jit[a,b,*], Dang Thi Thanh Huyen[c], Ingrid Friberg[d], Hoang Van Minh[e], Pham Huy Tuan Kiet[e], Neff Walker[d], Nguyen Van Cuong[c], Tran Nhu Duong[c], Kohei Toda[f], Raymond Hutubessy[g], Kimberley Fox[h], Nguyen Tran Hien[c]

[a] Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK
[b] Modelling and Economics Unit, Public Health England, London, UK
[c] National Institute of Hygiene and Epidemiology, Hanoi, Vietnam
[d] John Hopkins Bloomberg School of Public Health, John Hopkins University, Baltimore, MD, USA
[e] Center for Health System Research, Hanoi Medical University, Hanoi, Vietnam
[f] World Health Organization Representative Office for Viet Nam, Hanoi, Vietnam
[g] World Health Organization, Geneva, Switzerland
[h] World Health Organization Regional Office for the Western Pacific, Manila, Philippines

VACCINATION SAVES LIVES IN VIETNAM COST $$$ EFFECTIVE

END

When was your last dose of Tdap? wP or aP?

We are probably sharing the Pertussis now….

End with a cough
EXTRA

64 yr

Asthma exacerbation

Steroids not better

ED – whooping cough

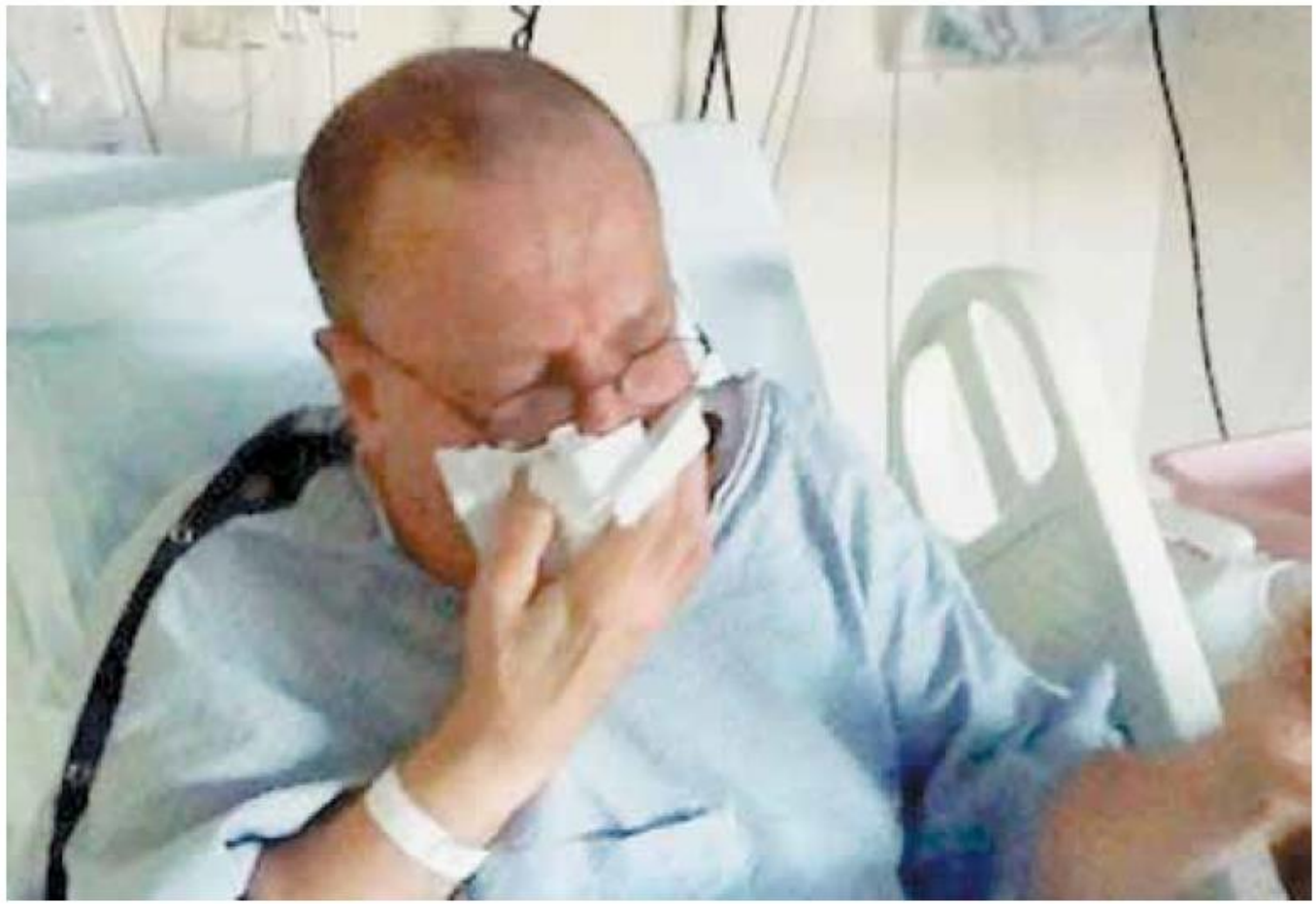
Culture –

Bordetella pertussis

Vaccine post discharge

[redacted]

Whooping Cough in an Adult



N ENGL J MED 366;25 NEJM.ORG JUNE 21, 2012

Vaccine 33 (2015) 1948–1952

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Immunization of pregnant women against pertussis: The effect of timing on antibody avidity

Bahaa Abu Raya[a,b,*,1], Ellen Bamberger[b,c,1], Meital Almog[b,d], Regina Peri[d], Isaac Srugo[a,b,c], Aharon Kessel[b,d]

[a] Department of Pediatrics, Bnai Zion Medical Center, Golomb St. 47, Haifa 31048, Israel
[b] The Ruth and Bruce Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Efron St. 1, Haifa 31096, Israel
[c] Clinical Microbiology Laboratory, Bnai Zion Medical Center, Golomb St. 47, Haifa 31048, Israel
[d] Division of Allergy and Clinical Immunology, Bnai Zion Medical Center, Golomb St. 47, Haifa 31048, Israel

- Best timing – early 3rd trimester
- Several papers

Abu Raya B, Srugo I, Kessel A, et al. The effect of timing of maternal tetanus, diphtheria, and acellular pertussis (Tdap) immunization during pregnancy on newborn pertussis antibody levels—a prospective study. Vaccine **2014**; 32:5787–93. 4.

Abu Raya B, Bamberger E, Almog M, Peri R, Srugo I, Kessel A. Immunization of pregnant women against pertussis: the effect of timing on antibody avidity. Vaccine **2015**; 33:1948–52.

Naidu MA, Muljadi R, Davies-Tuck ML, Wallace EM, Giles ML. The optimal gestation for pertussis vaccination during pregnancy: a prospective cohort study. Am J Obstet Gynecol **2016**; 215:237. e1–6.

Clinical Infectious Diseases

BRIEF REPORT

Pertussis Antibody Transfer to Preterm Neonates After Second- Versus Third-Trimester Maternal Immunization

Christiane S. Eberhardt,[1,2] Geraldine Blanchard-Rohner,[3] Barbara Lemaître,[1] Christophe Combescure,[4] Véronique Othenin-Girard,[5] Antonina Chilin,[5] Jean Petre,[6] Begoña Martinez de Tejada,[5] and Claire-Anne Siegrist[1,3]

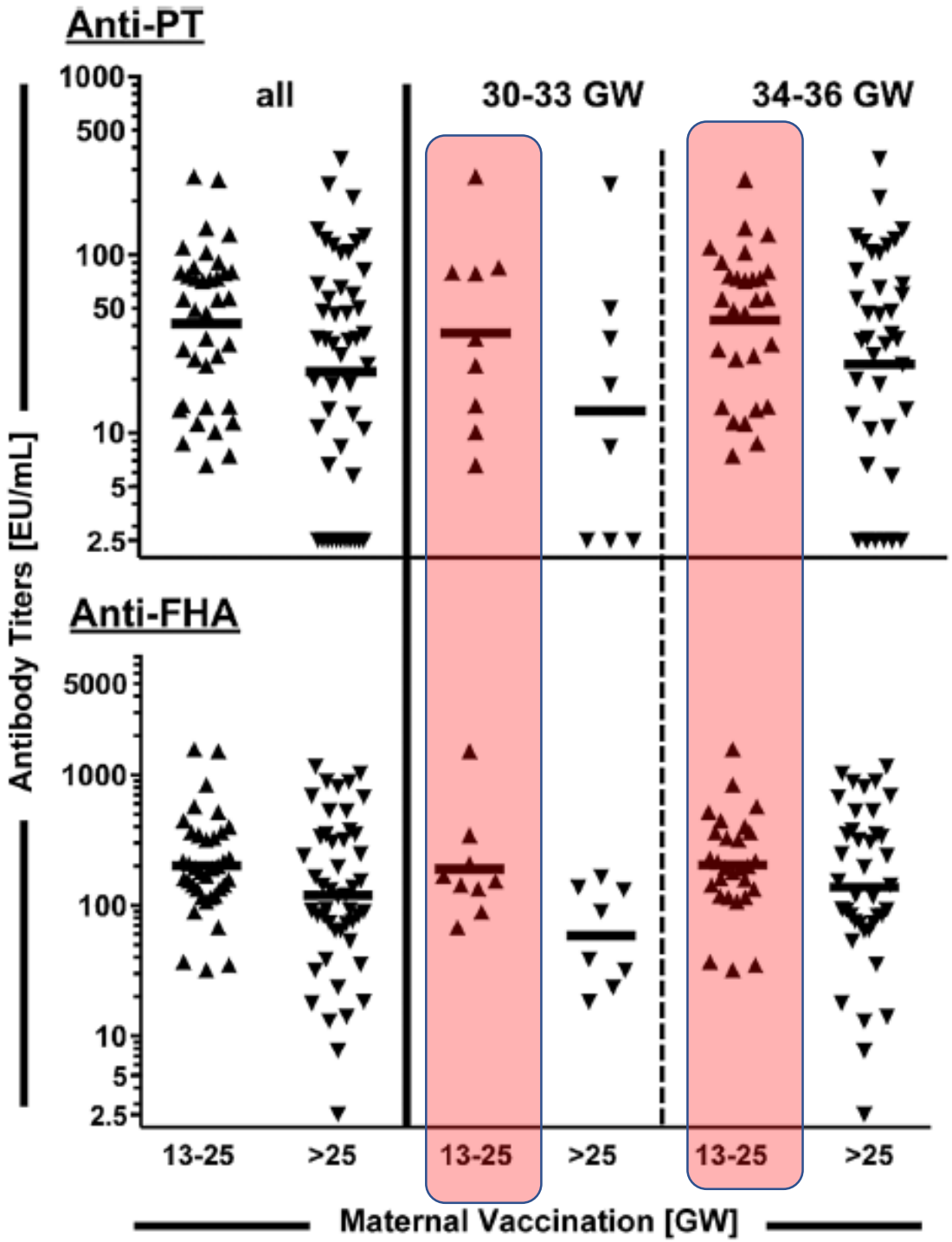
[1]Center for Vaccinology and Neonatal Immunology, Department of Pathology-Immunology, University of Geneva, [2]Department of Neonatology and Pediatric Intensive Care, Children's Hospital of Geneva, [3]Department of Pediatrics, Children's Hospital of Geneva, [4]Clinical Research Center, [5]Department of Gynecology and Obstetrics, University Hospitals of Geneva and Faculty of Medicine, University of Geneva, Switzerland; and [6]BioNet-Asia Co, Ltd, Bangkok, Thailand

Preterm infants are most vulnerable to pertussis. Whether they might benefit from maternal immunization is unknown. Extending our previous results in term neonates, this observational study demonstrates that second- rather than third-trimester maternal vaccination results in higher birth anti–pertussis toxin titers in preterm neonates.

Keywords. pertussis; maternal immunization; maternal antibodies; preterm; neonates.

GAP IN KNOWLEDGE

- Best time for vaccination for mum?
- High Ab – Protection
- Maternal Ab crossing and neutralizing childhood pertussis vaccination
- Cross reacting Pertussis Ab



Vaccination at second trimester good for pre-term babies

aP Prevent Severe Infection / Cannot clear

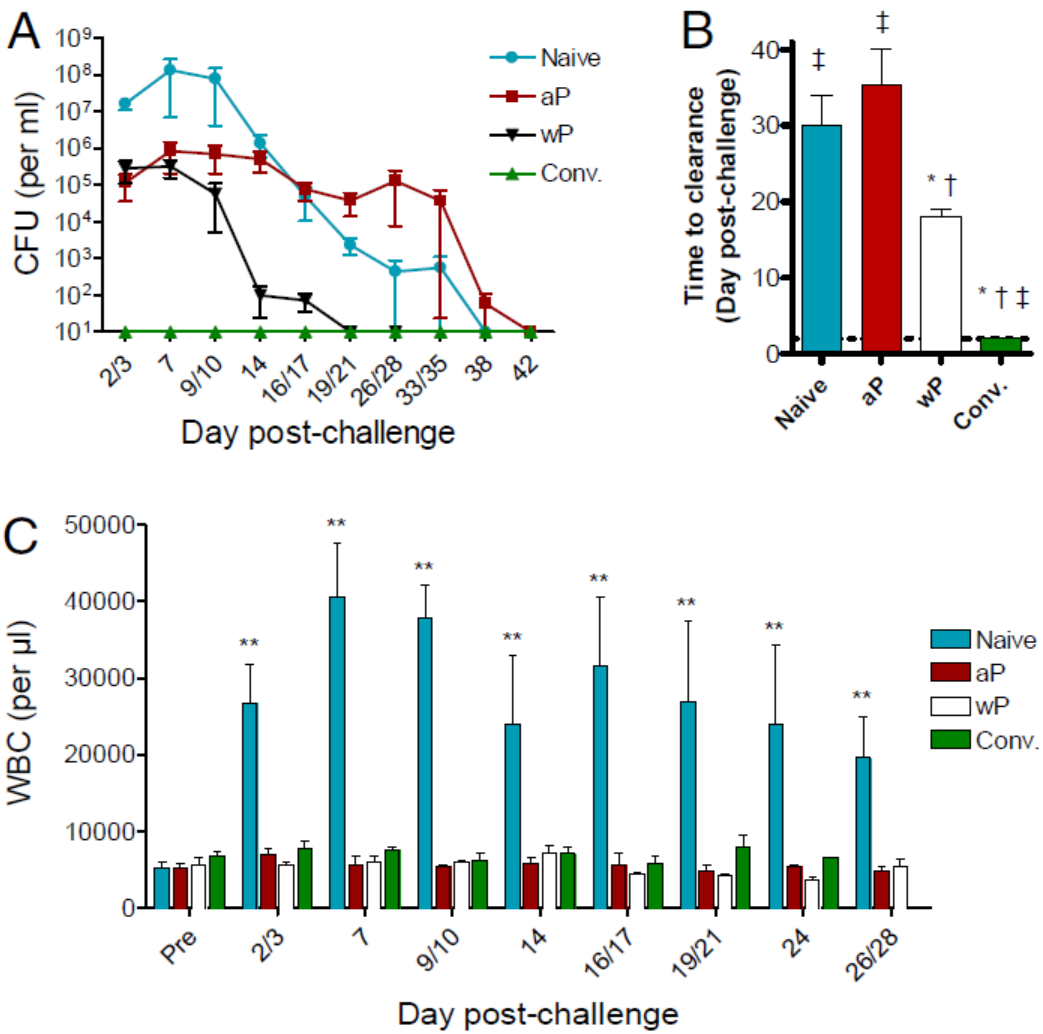


Fig. 1. The effect of vaccination or convalescence on colonization and leukocytosis. Naïve animals, aP-vaccinated animals, wP-vaccinated animals, and previously infected [convalescent conv.)] animals were directly challenged with *B. pertussis* ($n = 3$–4 per group). (*A*) Colonization was monitored by quantifying *B. pertussis* cfu per mL in biweekly nasopharyngeal washes with a limit of detection of 10 cfu per mL. For each animal the time to clearance is defined as the first day that no *B. pertussis* cfu were recovered from nasopharyngeal washes. (*B*) The mean time to clearance is shown for each group ($n = 3$ per group). Because no *B. pertussis* organisms were recovered from the conv. animals, the mean time to clearance was defined as the first day of sampling (day 2, indicated by the dashed line). $*P < 0.05$ vs. Naïve, $\dagger P < 0.05$ vs. aP, $\ddagger P < 0.05$ vs. wP. (*C*) The mean circulating white blood cell counts before and after challenge are shown for each group of animals ($n = 3$–4 per group). $**P < 0.01$ vs. preinfection from same group.

aP does not protect against colonisation

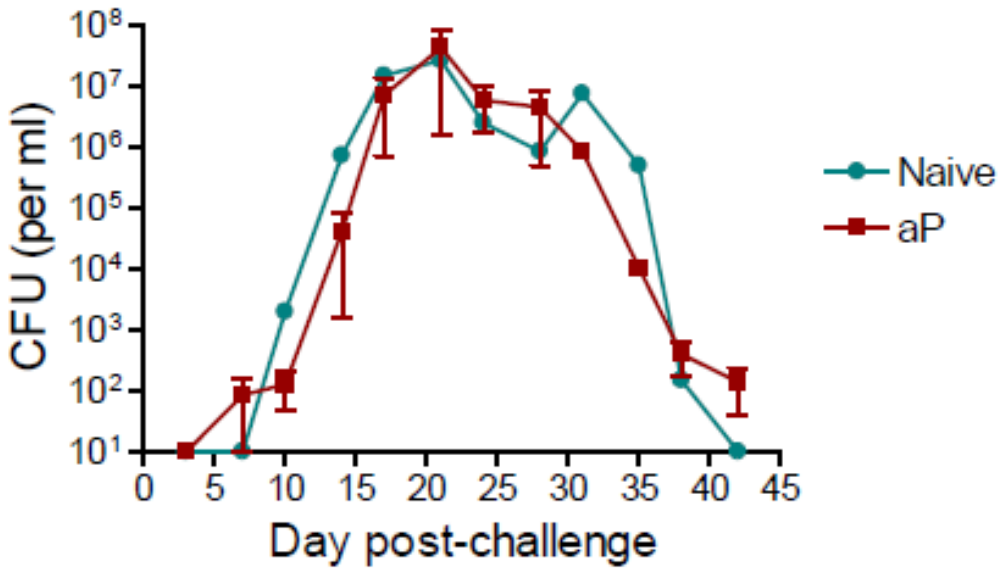


Fig. 2. aP does not protect against colonization following natural transmission. A naïve animal was directly challenged. After 24 h, a naïve animal and two aP-vaccinated animals were placed in the same cage as the directly challenged animal and followed for colonization as in Fig. 1.