

Waning Protection after Fifth Dose of Acellular Pertussis Vaccine in Children

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BACKGROUND

In the United States, children receive five doses of diphtheria, tetanus, and acellular pertussis (DTaP) vaccine before 7 years of age. The duration of protection after five doses of DTaP is unknown.

METHODS

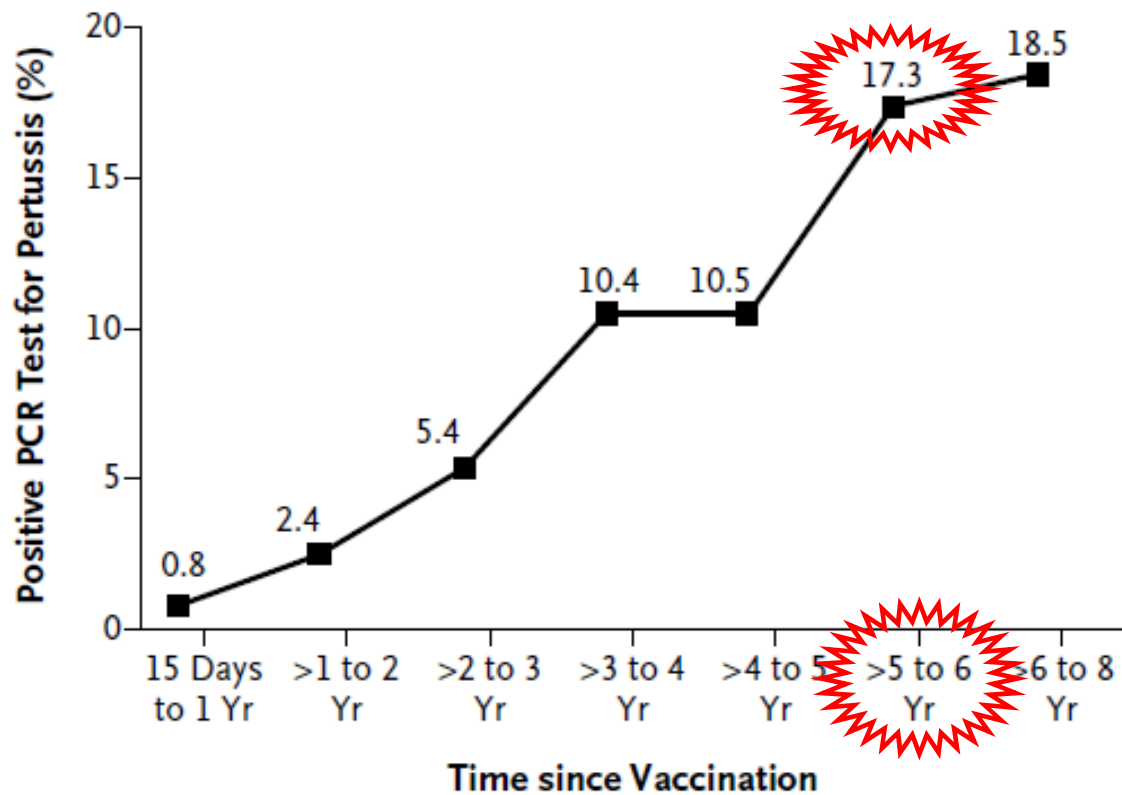
We assessed the risk of pertussis in children in California relative to the time since the fifth dose of DTaP from 2006 to 2011. This period included a large outbreak in 2010. We conducted a case-control study involving members of Kaiser Permanente Northern California who were vaccinated with DTaP at 47 to 84 months of age. We compared children with pertussis confirmed by a positive polymerase-chain-reaction (PCR) assay with two sets of controls: those who were PCR-negative for pertus-

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ing that after the fifth dose of DTaP, the odds of acquiring pertussis increased by an average of 42% per year.

CONCLUSIONS

Protection against pertussis waned during the 5 years after the fifth dose of DTaP. (Funded by Kaiser Permanente).

B

**No. of PCR Tests
for Pertussis**

Positive	7	16	26	41	45	77	65
Total	836	655	483	396	430	444	351

**Dopo 5 anni
dalla 5^a dose
di antipertosse
acellulare,
1 soggetto su
5-6 si rifà la
pertosse...!?!**

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

RESEARCH ARTICLE

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Asymptomatic transmission and the resurgence of *Bordetella pertussis*



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Abstract

Background: The recent increase in whooping cough incidence is a challenge to both public health practitioners and scientists. The resurgence of *B. pertussis* has been attributed to a variety of mechanisms, including waning immunity, changes in vaccine coverage, and re-emergence from vaccination or natural infection. Recent studies have shown that individuals vaccinated with the acellular pertussis vaccine (aP) can still be colonized by asymptomatic *B. pertussis*.

Methods: Using a phylodynamic and transmission analysis of *B. pertussis* sequences, we reanalyzed aP vaccine studies revealed that individuals vaccinated against disease, but not bacterial colonization [10, 11]. This is in addition to the extant, asymptomatic *B. pertussis* in the population.

Results: We find that the resurgence of *B. pertussis* in the US and UK are consistent with asymptomatic transmission. Our analysis of the US sequences indicates more genetic diversity than expected with asymptomatic transmission; 2) asymptomatic infections can bias assessments of vaccine efficacy based on observations of *B. pertussis* incidence; and 3) asymptomatic transmission can account for the observed increase in *B. pertussis* incidence; and 4) asymptomatic transmission can account for the observed increase in *B. pertussis* incidence; and 5) vaccinating individuals in close contact with infants too young to receive the vaccine ("cocooning" unvaccinated children) may be ineffective.

Conclusions: Although a clear role for the previously suggested mechanisms still exists, asymptomatic transmission is the most parsimonious explanation for many of the observations surrounding the resurgence of *B. pertussis* in the US and UK. These results have important implications for *B. pertussis* vaccination policy and present a complicated scenario for achieving herd immunity and *B. pertussis* eradication.

for this type of vaccine failure has been observed in humans where reanalyses of aP vaccine studies revealed that individuals vaccinated with components of the aP vaccine were protected against disease, but not bacterial colonization [10, 11]. This is in addition to the extant,

A questo punto Althouse e Scarpino usano un modello matematico per descrivere le conseguenze epidemiologiche e di sanità pubblica:

Our model also assumes that symptomatic and asymptomatic infections have the same basic reproduction number. Asymptomatic or subclinical/misdiagnosed individuals may spread *B. pertussis* through direct contact, breathing, or coughing [57]. Although coughing may increase transmission, the total bacterial load in the nasopharynx of *B. pertussis*-infected non-human primates is similar between symptomatic and asymptomatic individuals (see Figure one, panel a in [9]). The same study suggested that the duration of higher bacterial loads may be longer in asymptomatic individuals, and that there may not be differences in routes of transmission between asymptomatic and symptomatic individuals. However, and perhaps more importantly, being asymptomatic suggests that individuals may not alter their behavior and thus contact more individuals than a symptomatic individual [58]. Therefore, it seems equally plausible to conclude that the R_0 for aP vaccinated individuals is higher [47].

- Burdin N et al. What Is Wrong with Pertussis Vaccine Immunity? The Problem of Waning Effectiveness of Pertussis Vaccines. Cold Spring Harb Perspect Biol **2017** doi:10.1101/cshperspect.a029454
Efficacia pratica svanisce 2-3 anni dopo richiamo
- Schwartz KL et al. Effectiveness of pertussis vaccination and duration of immunity. CMAJ **2016**;188:E399
Efficacia declina in fretta dopo 4 anni dall'ultimo richiamo
- Althouse BM et al. Asymptomatic transmission and the resurgence of Bordetella pertussis. BMC Medicine **2015**;13:146
Trasmissione asintomatica dai vaccinati è la spiegazione più probabile
- Santa Fe Institute. Whooping cough resurgence due to vaccinated people not knowing they're infectious?. ScienceDaily 24 June **2015**
www.sciencedaily.com/releases/2015/06/150624071018.htm
- Warfel GM et al. Pertussis vaccines and the challenge of inducing durable immunity. Curr Opin Immunol **2015**;35:48
Primati vaccinati sono colonizzati da B. pertosse e la possono trasmettere per 4-5 settimane, come quelli non vaccinati

- de Graaf WF et al. A two-phase within host model for immune response and its application to serological profile of pertussis. Epidemics **2014**;9:1

C'è una crescente presa di coscienza che l'immunità per molte malattie infettive non dura tutta la vita, come è tradizione pensare. La pertosse è solo un primo esempio, ma vale per molte altre infezioni

[NB: dato che un piccolo n. di soggetti ha immunità da vaccino di durata molto lunga (distribuzione con lunga coda a destra), calcolare la durata *media* dell'immunità dei vaccinati è **fuorviante**. La tendenza centrale della distribuzione è molto meglio rappresentata dalla *mediana*]

- Plotkin SA. The Pertussis Problem. CID **2014**;58:830

l'efficacia pratica del vaccino è alta solo per circa 2 anni dopo la dose

- Klein NP. Waning protection after fifth dose of acellular pertussis vaccine in children. N Engl J Med **2012**;367:1012

Dopo la 5^a dose di DTaP l'ODDS di contrarre una pertosse aumenta in media del 42% per anno