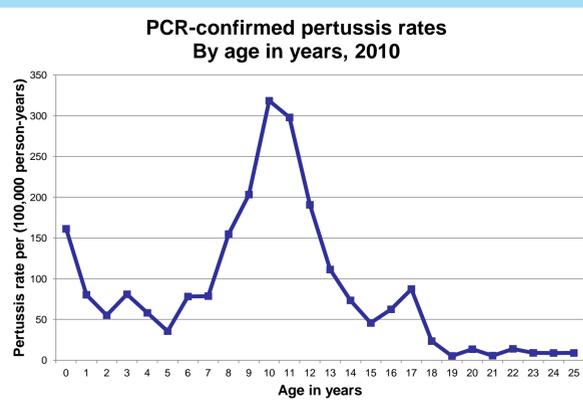
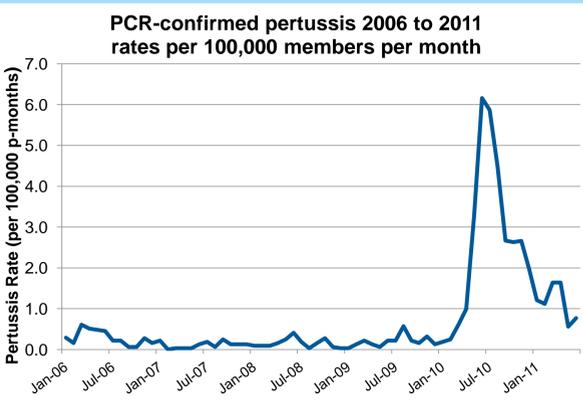




Background

Pertussis declined sharply with the advent of whole cell vaccines and had fallen to very low levels by the 1970s. In the 1990s, safety concerns prompted a switch from whole cell to acellular pertussis vaccines. Roughly coincident with this shift in vaccine type, pertussis incidence has been gradually increasing, and in 2010, California experienced its largest outbreak in over 50 years. We identified factors related to vaccination that contributed to the California pertussis outbreak.



Methods

Study Population

Kaiser Permanente Northern California (KPNC)

- 3.3 million members
- Integrated health care system
- Electronic medical record
- Central laboratory

Vaccines and Tests

- DTaP: Acellular pertussis vaccines used in children
- Tdap: Acellular pertussis vaccines used in adolescents and adults
- PCR: Real-time polymerase chain reaction testing for *Bordetella pertussis* and paraptussis.

➤ Positive results for *B. paraptussis* were considered to be negative.

Study Design

Using a case control design, we examined the relationship of vaccinations with the likelihood of a positive pertussis test. We looked at waning (time since last vaccine), effectiveness of Tdap, and the effect of delayed or missed vaccines.

Cases: Members with a PCR test positive for *Bordetella pertussis*

Controls: We used 2 different control groups.

- Control group 1: Pertussis test negative members
 - Matched on calendar time
 - Controlled for age, sex, race/ethnicity and geographic location
- Control group 2: Entire KPNC population
 - Closely matched on age, sex, race/ethnicity and geographic location

Results

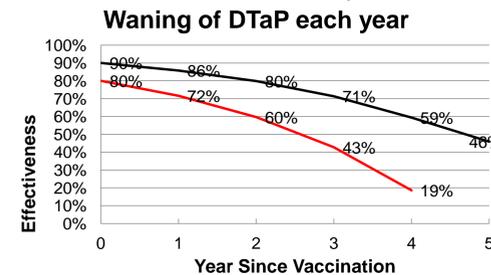
1. DTaP (5th dose) waning (Presented elsewhere¹)

Table: Probability of a positive PCR pertussis test, based on each year after the vaccine

Control Type	Cases N	Controls N	Odds Ratio	95% CI	P-value
PCR Negative	277	3,308	1.415	(1.209, 1.657)	< 0.001
KPNC Pop	277	6,086	1.504	(1.132, 1.998)	0.005

➤ Interpretation: DTaP wanes by 42% per year, each year after administration.

- The graph shows how, for a vaccine with initial effectiveness of 80 or 90%, the effect will wane over 5 years.



2. Tdap effectiveness (Presented elsewhere²)

Table: Probability of a positive pertussis PCR test, based on vaccination with Tdap or not. (Effectiveness = (1 - Odds Ratio))

Control Type	Cases N	Controls N	Odds Ratio	95% CI	P-value
PCR Negative	566	9,166	0.448	0.359-0.559	<0.001
KPNC Pop	566	19,439	0.373	0.296-0.469	<0.001

➤ Interpretation: Tdap is 55% effective at preventing PCR-confirmed pertussis

3. DTaP delayed or missed vaccines

Definition of up-to-date immunization

- 12-23 month of age: ≥ 3 doses of DTaP between 1 and 11 mos.
- 24-71 months: Prior criterion and ≥ 1 dose of DTaP between 12 and 24 months of age
- ≥ 72 months of age: Prior criteria and ≥ 1 dose of DTaP between 48 and 72 months of age

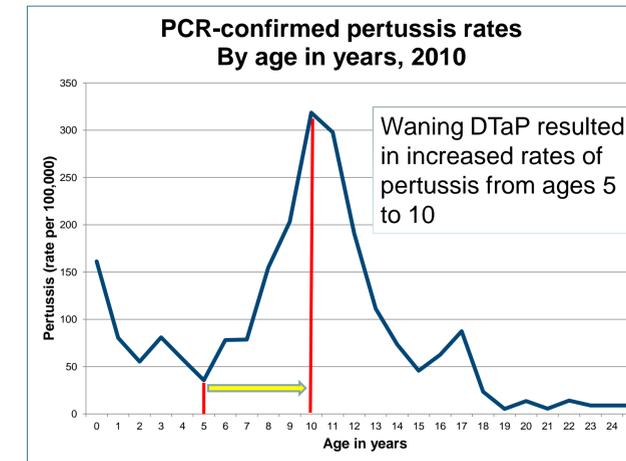
Table: Probability of a positive pertussis PCR test, based on vaccination on time or not

Control Type	Cases N	Controls N	Odds Ratio	95% CI	P-value
PCR Negative	271	5,173	2.183	1.533-3.067	< 0.001
KPNC Pop	271	5,909	2.475	1.751-3.508	< 0.001

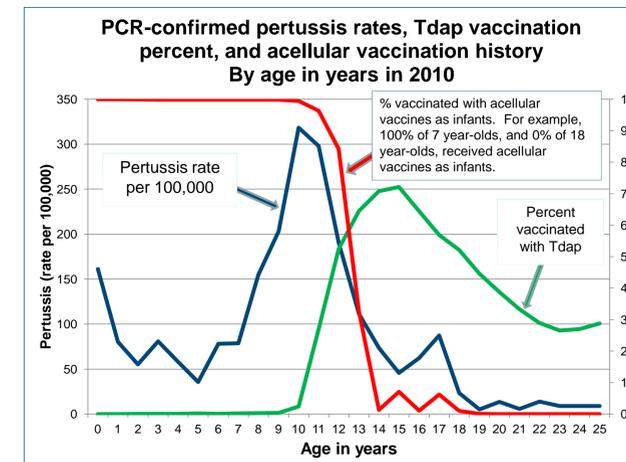
➤ Interpretation: Missed DTaP doses are associated with a 2.2 fold increase in the risk of pertussis

Summary

1. Increasing rates in 5-10 year old children correspond to waning of effect after the 5th dose of DTaP.



2. Use of Tdap has a moderate effect in preventing infections. However, the effect does not appear as important as the use of whole cell vaccines. In the graph below, acellular and whole cell vaccines total 100%, so mirror each other.



3. Acellular vaccines appear to provide less protection than the whole cell vaccines they replaced.

Conclusions

In 2010 California experienced the highest rate of pertussis in over 50 years. This increase comes after decades of gradually increasing rates. Our results suggest that the change from whole cell to acellular vaccines contributed to the increase.

- ▶ DTaP vaccine wanes substantially after administration of the 5th dose. If the vaccine is 90% effective immediately, after 5 years it is less than 50% effective.
- ▶ Tdap was about 55% effective. We did not see evidence of waning (data not shown) but most of the people in our analysis had received the vaccine within 3 years.
- ▶ The vast majority of our children were vaccinated on time, but children who delayed or missed doses experienced higher rates of pertussis.
- ▶ It appears that DTaP does not offer as much protection as the whole cell vaccines it replaced.
 - ▶ Further studies are under way.
- Given the safety concerns regarding whole cell pertussis vaccines, it is unlikely that the parents or medical providers in the US would return to using them. These results point to the need for new and improved pertussis vaccines.

References

1. Ali Rowhani-Rahbar, Joan Bartlett, Roger Baxter and Nicola P Klein. Risk of Pertussis in Children as a Function of Time since Receipt of the 5th Dose of Acellular Pertussis Vaccine. Oral presentation, ESPID, June 7-11, 2011, The Hague, Netherlands.
2. Roger Baxter, Joan Bartlett, Ali Rowhani-Rahbar, Bruce Fireman, Nicola Klein. Effectiveness of adolescent and adult pertussis (Tdap) vaccines. IDSA 2011, Boston.