Modeling Pertussis Disease and Transmission

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Highly contagious respiratory infection caused by *Bordetella pertussis*.

Outbreaks first described in 15th century.

Nearly universal by school entry in the pre-vaccine era.

Approximately 1 in 10 cases resulted in mortality. Responsible for more deaths than measles and polio combined.

Still one of the 10 most common causes of death from infectious disease worldwide. 16 million cases and 200,000 deaths annually according to the World Health Organization.
SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Reported Pertussis Cases: 1991-2013

2014 = Provisional Data

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Tdap coverage: 2006 - 2013

Year

Percent Coverage

2006  2007  2008  2009  2010  2011  2012  2013

0   10   20   30   40   50   60   70   80   90   100
The Baboon Model of Pertussis

Olive Baboon (*Papio anubis*)
Baboons are Infected

![Graph showing CFU (per ml) over Day Post-Challenge, with a decline trend from 10^10 to 10^0.]
Infected Baboons Exhibit Leukocytosis

WBC (per µL)

Day Post-Challenge

Pre 2/3 5 7 9/10 12 14 16/17 19 21
Infection Results in a Significant Cough Illness
The Host Response to
*B. pertussis* Infection and Vaccination
Th17 immune responses are involved in the clearance of extracellular bacteria

- Neutrophil recruitment and clearance of extracellular bacteria
  - GCSF, chemokines, etc.

Epithelium

- CD4+ Th17-cells
  - IL-17
  - IL-1β, IL-6, IL-23

Antigen presenting cells
Previous Infection Protects Against Infection

![Graph showing CFU (per ml) over days post-challenge. The graph compares Naïve and Convalescent groups.]
Acellular Vaccines Protect Against Disease

WBC (per μl)

Day Post-Challenge

- Naive
- Convalescent
- Vaccinated
Acellular Vaccines Fail to Protect Against Infection
Acellular Vaccines Fail to Protect Against Infection Following Natural Transmission
aP Vaccinated Animals Transmit Disease

![Graph showing CFU levels over time for vaccinated and unvaccinated animals. The graph plots CFU (per µl) against day post-challenge.]
wP Vaccine Confers Intermediate Protection Against Infection

CFU (per ml)

Day Post-Challenge

- Unvaccinated
- Acellular Vaccinated
- Whole-cell Vaccinated
- Convalescent
Exposure Determines Skewing of Adaptive Response
Protecting Newborns
Severity of Disease in Infants

Hospitalizations

Deaths

Percent of Cases

Age in Months

Percent of Cases

Age in Months
Pertussis Incidence Among Infants: 2001-2011

Source: CDC, National Notifiable Diseases Surveillance System, 2011
Proposed Strategies to Protect Newborns

- **Boosting of Adolescent Population**
  Reduction of incidence in adolescents did not impact incidence in infants. Very little contact between adolescents and infants.

- **Cocooning**
  Difficult to implement. Due to incomplete protection from transmission, cocooning is likely to be less effective than hoped.

- **Neonatal Vaccination**

- **Maternal Vaccination**
  aP-primed mothers are boosted during 3rd trimester. Infants have elevated titers from birth. Effectiveness unknown.
Neonatal Vaccination Confers Protection

[Graphs showing CFU (colony-forming units) over days post-challenge for vaccinated and unvaccinated groups, with logarithmic scales for CFU per ml.]
Maternal Vaccination Confers Protection

**Graph 1:**
- **Y-Axis:** CFU (per ml)
- **X-Axis:** Day Post-Challenge
- Data points showing a decrease in CFU post-challenge with time, indicating protection.

**Graph 2:**
- **Y-Axis:** WBC (per µl)
- **X-Axis:** Day Post-Challenge
- Comparison between unvaccinated and vaccinated mothers, showing a difference in WBC levels post-challenge.
Next Generation Pertussis Vaccine

Pertussis Vaccine

The Right Adjuvant

The Right Antigens

The Right Route
The Baboon Model of Pertussis

- Provides a powerful tool for understanding pertussis pathogenesis and host responses to pertussis infection and vaccination.

  *Immune Correlates of Protection?*

- Provides a very relevant model for testing assumptions regarding new strategies utilizing existing vaccines and assumptions driving development of new vaccines.

- May provide data in support of effectiveness of new vaccines.
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