Pertussis Resurgence
where have we gone wrong?

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Disclosures

• Received grants and honoraria for lectures from GSK, Pfizer, Novartis and MSD on different topics related to vaccinology.

• No funding/honoraria for this symposium

Scope

• Pertussis is underdiagnosed, esp in adults

• Increased incidence despite good vaccination coverage

• Share different strategies to curb pertussis
  – Maternal vaccination
  – Cocoon strategy
  – New vaccines
Pertussis

• Whooping cough
• Highly contagious, respiratory infection caused by a gram-negative bacillus *Bordetella pertussis*
• Man is the only host and found in the respiratory tract
• Transmission by aspiration of the bacteria sprayed into the air by a patient
Pertussis Disease Manifestations

- Incubation period: 7 - 10 days (range 4 - 21)
- Stages
  - Catarrhal: runny nose, sneezing, low-grade fever, mild cough
  - Paroxysmal: severe spasms of cough, thick mucous, whoops, vomiting, exhaustion
  - Convalescent: gradual recovery with less frequent & less severe coughing
Pertussis Stages, Period of Communicability

- **Catarrhal Stage**
- **Paroxysmal Stage**
- **Convalescent Stage**

**Period of Communicability**

- Exposure
- Paroxysmal Cough Onset
- Weeks of Cough

CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases. PHF 2004
The global problem - Under-reporting of pertussis

Only 1–36% of pertussis cases are reported\(^1,2,3\)

Reported cases are the tip of the iceberg\(^1-7\)

Unreported pertussis

Atypical forms

Wide disease variability

Under-reporting

Under-consultation

Low physician awareness

Inconsistent case definitions

Under-diagnosis

1. Miller et al, 2000
2. Strebel et al, 2001
5. Deville et al, 1995
6. Cherry, 1999
7. Yaari et al, 1999
Reports of Pertussis in the U.S.

Pertussis Deaths by Decade and Age Group

<table>
<thead>
<tr>
<th>Decade</th>
<th>0-3 mos</th>
<th>≥4 mos</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980-1989</td>
<td>49</td>
<td>28</td>
<td>77</td>
</tr>
<tr>
<td>1990-1999</td>
<td>84</td>
<td>19</td>
<td>103</td>
</tr>
<tr>
<td>2000-2009</td>
<td>175</td>
<td>20</td>
<td>195</td>
</tr>
</tbody>
</table>

Reported NNDSS pertussis cases: 1922-2014

*2014 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Pertussis Vaccines -- Latin America

- Most countries in Latin America follow PAHO overall guidelines for immunization against pertussis
- Variability in schedules between countries
- Most countries use wP
- Increase in pertussis cases has occurred across Latin America since 2010

www.paho.org Immunization. 2015
Pertussis Vaccines -- Europe

Distribution of Confirmed Pertussis Cases Reported by Month, EU/EEA, 2008-2012

- Most countries differ in their vaccination schedules
- Some still use wP
- Increase in cases, especially in countries using aP

Source: Country reports from Austria, Cyprus, Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Iceland, Ireland, Italy, Netherlands, Norway, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom.

Adapted from ECDC. Annual epidemiological report 2014
In The Netherlands, as in many other western countries, pertussis vaccines have been used extensively for more than 40 years.

Frequency of infection ~ 1-4% of population

30% of people with persistent cough infected with *B. pertussis*

Adaptation of *B. pertussis* to vaccine → vaccine and circulating strain mismatch (Schouls et al, 2004)
Pertussis cases in Philippines (2000-2011)

http://apps.who.int/vaccines/globalsummary/immunization/timeseries/tsincidenceper.htm
Pertussis in Malaysia, 1976 - 2014

slide courtesy of Dr Rohani Jahis, Ministry of Health Malaysia
Lab Confirmed Pertussis, Malaysia, 2010 - 2014

Data Source: IMR
Pertussis incidence and vaccination coverage, Malaysia, 2009-2014
Lab Confirmed Pertussis by age, Malaysia, 2013-2014

- <1 year: 86% (2013), 82% (2014)
- <6 months: 69% (2013), 74% (2014)
- <2 months: 24% (2013), 31% (2014)
DTP3 Coverage in Selected Asia Pacific Countries at 10 Years Interval (1984 - 2014)

Pertussis in Shah Alam, Malaysia

- From November 2011
- Cases of chronic paroxysmal coughing
- Postnasal (nasopharyngeal) swab
- Charcoal medium to IMR
- Nov 2011 – April 2012
  - 22 swabs sent
  - 11 positive on PCR from IMR

Zulkifli Ismail et al, 14th APCP 2012
Specimen collection
Pertussis in Shah Alam

Zulkifli Ismail et al, 14th APCP 2012
Pertussis in Shah Alam

**SUSPECTED SOURCE OF INFECTION**

- **siblings**: 18%
- **day care center**: 27%
- **school**: 46%
- **other**: 9%

*Zulkifli Ismail et al, 14th APCP 2012*
CDC Study – Infant Pertussis: Who Was the Source?

• 774 infant cases from 4 states
• 264 cases had source identified

Sources:
- Mother 32%
- Father 15%
- Sibling 20%
- Grandparent 8%
- Other 25%

ABSTRACT. In the prevaccine era pertussis epidemics followed a cyclic pattern, with peaks every 2 to 5 years. With the marked reduction of pertussis by vaccination, the same cyclic pattern still occurs. Studies relating to reported pertussis and *Bordetella pertussis* infection have been reviewed and analyzed. The increase in reported pertussis over the last 2 decades is mainly due to a greater awareness of pertussis and perhaps to the use of several less efficacious vaccines.

Studies of prolonged cough illnesses in adolescents and adults reveal that 13% to 20% are a result of *B pertussis* infection. Serologic studies suggest that the rate of *B pertussis* infection in adolescents and adults is ~2.0% per year. The rate of cough illnesses (pertussis) caused by *B pertussis* infection in adolescents and adults is between 370 and 1500 per 100 000 population. These data suggest that there are between ~800 000 and 3.3 million cases per year in the United States.

The coming availability of adolescent and adult-formulated diphtheria and tetanus toxoids and acellular pertussis vaccines for adolescents and adults and their widespread use should reduce the reservoir of *B pertussis* disease. It is suggested that a universal program of adolescent and adult boosters would decrease the circulation of *B pertussis* in these age groups and possibly could lead to the elimination of the organism from the population. *Pediatrics* 2005;115:1422–1427; *pertussis, Bordetella pertussis, adult pertussis, adolescent pertussis, pertussis, epidemiology.*
Pertussis is underdiagnosed in ADULTS

- Pertussis is often underdiagnosed in adults and adolescents:
  - mild symptoms
  - mistaken for other respiratory infections
- Pertussis infection has been detected in about 25% cases of prolonged cough in adults

**Reference**

<table>
<thead>
<tr>
<th>Reference</th>
<th>%</th>
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<tbody>
<tr>
<td>Mink <em>et al.</em> 1992</td>
<td>26</td>
</tr>
<tr>
<td>Wright <em>et al.</em> 1995</td>
<td>21</td>
</tr>
<tr>
<td>Robertson <em>et al.</em> 1997</td>
<td>25.7</td>
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## Estimated Duration of Immunity After Infection or Vaccination

<table>
<thead>
<tr>
<th>Source of Immunity</th>
<th>Duration</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-cell vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>6 years</td>
<td>Jenkinson, 1988</td>
</tr>
<tr>
<td>Finland</td>
<td>6 years</td>
<td>He et al, 1994</td>
</tr>
<tr>
<td>Germany</td>
<td>&gt;6 years</td>
<td>Lugauer et al, 2002</td>
</tr>
<tr>
<td>Acellular vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>6 years</td>
<td>Salmaso et al, 2001</td>
</tr>
<tr>
<td>Germany</td>
<td>&gt;6 years</td>
<td>Lugauer et al, 2002</td>
</tr>
<tr>
<td>Natural infection</td>
<td>15 years</td>
<td>Wirsing von König et al, 1995</td>
</tr>
</tbody>
</table>
Transmission Cycle of Pertussis between Adults and Infants

- Primary vaccination: Protected
- Booster vaccination: Prolonged protection
- Susceptible adults: Reservoir of B. pertussis
- Unvaccinated or partly vaccinated infants: Susceptible
- No additional booster: Immunity wanes
Healthcare Professionals Involved in Transmission of Pertussis

• Physicians 1912 Schwenkenbecher
• Nurses 1972 Kurt et al
• Physicians 1992 Etkind et al
• Nurses 1995 Christie et al
• Nurses 1997 Matlow et al
• Nurses & Physicians 2005 CDC
• Nurses 2008 CDC

Adult / Adolescent booster vaccines

DTP vs dTp

DTaP vs Tdap

- Diphtheria
- Pertussis (acellular)
- Tetanus

Similar in component to the babies DTaP, but difference in strength

Two brands/manufacturers

Adacel by SP & Boostrix by GSK
Vaccination Strategies -- Cocooning

- Aims to protect the infant who is too young to be vaccinated
- Vaccinate their close contacts -- parents, grandparents, siblings, childcare providers, etc
- Contacts serve as a source of infection
- Vaccinating contacts "cocoons" the infant from infection

Cocooning Strategy -- Chile Experience

- Cocooning strategy began in March 2012 in areas with highest disease rates
- Coverage in 2012 was 94% for mothers and 61% for household contacts (national mean of 2 vaccinated household contacts)
- Back to "normal" in 2013 with 3 deaths; strategy discontinued in September-December 2013
- Difficult to determine the impact of the cocooning strategy

www.deis.cl Department of Statistics
WHO SAGE pertussis working group. 2014
Vaccination Strategies -- Maternal Immunization

• Antipertussis antibodies passed to the baby during pregnancy

• Gaining support from obstetrics/gynecology associations around the world

• Combination of maternal immunization and cocooning protects the infant from pertussis before it can be vaccinated

ACIP Recommendations

- Infant primary series: 2, 4, and 6 months of age
- Booster doses: 15-18 months and 4-6 years of age
- All adolescents beginning at 11-12 years of age -- no minimal interval between last Td and Tdap vaccine
- All adults especially those who are close key contacts of infants < 12 months of age -- including persons ≥ 65 years of age
- Healthcare workers who have direct patient contact in any hospital or clinic setting
- Pregnant women – dose of TdaP during each pregnancy between 27 and 36 weeks

www.cdc.gov Tdap. 2015
Maternal Immunization Strategy -- UK Experience

• Major pertussis resurgence in 2012
• Sufficient concern about outbreak to implement maternal immunization strategy, even though it was unclear whether it would protect infants
• Not clear how willing pregnant women would be
• Successful strategy -- uptake rate of 60%

Two case-control studies demonstrated that the vaccine effectiveness was 91%-93%[^a-b]

UK Maternal Immunization Strategy -- Safety Profile

• Large observational cohort study
• More than 20,000 pregnant women who received the vaccine in third trimester (median age 30)
• Matched historical unvaccinated control group
• No evidence of increased risk for AEs related to pregnancy
  – Including stillbirth, maternal or neonatal death, pre-eclampsia/eclampsia, placenta previa

WHO Recommendations

- Updated in August 2015
- Aim to achieve ≥ 90% coverage worldwide with primary series of 3 doses
- aP or Wp: Only switch from wP to aP if boosters or maternal immunization can be assured
- First dose age 6 weeks; 2nd at 10-14 weeks; 3rd at 14-18 weeks (4-8 weeks apart)
- Booster dose age 1-6 years, preferably during 2nd year of life, and ≥ 6 months after last primary dose

WHO Recommendations (cont)

- Do not currently recommend universal booster doses for adolescents and adults in order to reduce pertussis in infants -- assess local epidemiology
- For people aged > 7 years, only use aP vaccines
- Maternal immunization more effective than cocooning in protecting infants too young to be vaccinated -- consider 1 dose TDaP* in 2nd or 3rd trimester and ≥ 15 days before due date
- Healthcare worker immunization only recommended in some settings

*combined vaccine for adolescents and adults
Benefits of adolescent/adult booster vaccination

- Reduced clinical burden
- Reduced economic burden
- Decreased circulation in the environment

??
Eradication of *Bordetella pertussis*
Factors contributing to increase in pertussis

• Previously underdiagnosed?
  – More awareness \(\rightarrow\) increased case notification
  – Better diagnostic methods – PCR
• Declining vaccine uptake
  – Vaccine hesitancy and refusal
• Declining immunity post vaccination
  – Without booster doses
• Shift in antigenic properties of circulating strains of *B. pertussis*
  – Vaccine & Circulating strain mismatch
• ?? Switch from whole cell wP to acellular aP vaccine??
What can we do?

• High index of suspicion for pertussis even in adults
• NPS for *B. pertussis* PCR sent in proper media
• Case notification
• Adult & adolescent vaccination with Tdap
  – Healthcare professionals
  – Grandparents
  – Replace Td with Tdap for post-trauma ED use

**Booster vaccination may ultimately lead to eradication of the disease !!**
Summary

- Pertussis remains a worldwide problem
- Pertussis in adolescents and adults is becoming increasingly recognized as:
  - a significant burden
  - an important reservoir of infection for infants
- Targeted booster vaccination may be the most feasible option for controlling pertussis:
  - children and adolescents
  - adults (parents, infant-care providers, healthcare workers) in contact with infants
- Tdap vaccine
  - reduced antigen content
  - single dose recommended in individuals
- Booster vaccination may ultimately lead to eradication of the disease
Don’t risk spreading whooping cough to your infant.

Create a circle of protection – get vaccinated!

Not Vaccinated? No Kisses!

Get the adult whooping cough vaccine.

www.VaccinateYourFamily.org
ISPP 2017
11th International Symposium on Pediatric Pain
Kuala Lumpur, Malaysia
“Understanding Pain In Children – Take The First Step”

6th to 9th JULY 2017
KUALA LUMPUR, MALAYSIA

www.ispp2017.org