Pertussis: Resurgence, Prevention and Role of the Ob/Gyn

Kimberly B. Fortner, MD
Vanderbilt University Department OB/Gyn
Division Maternal-Fetal Medicine
Vanderbilt Vaccine Research Program
Learning Objectives

At the conclusion of this activity, participants should understand:

• The epidemiology of pertussis and its recent resurgence in the United States

• How to diagnose and treat active pertussis infection in an Ob/Gyn population

• How to prevent pertussis infection in an Ob/Gyn population
Case Study

28yo G5 P0040 uncomplicated pregnancy

- Received influenza vaccine antenatally
- Preterm labor at 34 weeks EGA

Baby Callie

- 2 week NICU stay
- Day of life 36, developed cough
Case Study

- Parents reassured
- Day of life 38, returned to pediatrician’s office
- Callie had respiratory arrest
- Infant died on Day 38
- Tdap - “Nobody mentioned it...nobody brought it up, nobody talked about it.”

Rod shaped bacteria (green) lodge in cilia of respiratory tract
Pertussis

Highly contagious respiratory infection

Outbreaks first described in 16th century

1906 - *Bordetella pertussis* isolated

1930s - **First pertussis** vaccine developed

1940s - ~ 200,000 cases/year prior to vaccination
Pertussis Vaccines

DTP Vaccine
- Whole cell Pertussis
- Diphtheria and Tetanus toxoids
  - Prevents illness in 70-90% children
  - Reactogenic\(^1\)
  - No longer available in US

DTaP Vaccine
- Acellular Pertussis
- Diphtheria and Tetanus toxoids
  - Acellular vaccine
- Licensed 1991

Tdap Vaccine
- Acellular pertussis vaccine
- Little “d” and little “p”
  - Lower quantities of diphtheria and pertussis antigens
- Adult booster
- Licensed 2008

\(^1\)Edwards KM, Decker MD, Vaccines, 6\(^{th}\) Edition
Pertussis: United States, 1940-2006

1940s – widespread DTP vaccination

1991 – DTaP licensed in US

Cases


1991 – DTaP licensed in US
### Routine DTaP Vaccination Schedule

<table>
<thead>
<tr>
<th>Dose</th>
<th>Age</th>
<th>Minimum Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td># 1</td>
<td>2 months</td>
<td>---</td>
</tr>
<tr>
<td># 2</td>
<td>4 months</td>
<td>4 wks</td>
</tr>
<tr>
<td># 3</td>
<td>6 months</td>
<td>4 wks</td>
</tr>
<tr>
<td># 4</td>
<td>12-18 months</td>
<td>6 mos</td>
</tr>
<tr>
<td># 5</td>
<td>4-5 years</td>
<td>At school entry</td>
</tr>
</tbody>
</table>

So, why are we discussing Pertussis?
Pertussis Epidemic: 2012

Substantial rise in pertussis cases
Declared pertussis epidemic
– Reported cases 2,520 (1300% increase)
– Highest number cases since 1942
Reported NNDSS Pertussis Cases 1922-2011*

Number of cases

Year

*2011 data have not been finalized and are subject to change. 2011 data were accessed on July 5, 2012.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Reported Pertussis by Age Group 1990-2006

4 - 5 fold increase in adolescents & adults
Why is there a resurgence?

- Waning immunity
- Decreased vaccine coverage
- Better diagnosis
- Changes in organism

Pertussis: Known Villain
Aliases: *Bordatella*; whooping cough
Waning Vaccine-Induced Immunity

![Graph showing the waning of whole-cell pertussis vaccine efficacy over time since the last dose. The graph includes data from observational studies and randomized clinical trials conducted in 1951, 1978, and 1988. The y-axis represents vaccine efficacy (%), and the x-axis represents time since the last dose (years). The graph shows a decline in vaccine efficacy over time.]
Why Immunity Wanes

Natural Infection
Prevaccine era = natural boost
Postvaccine era = rare boost
Large poor of susceptible hosts
## Estimated Duration of Immunity

<table>
<thead>
<tr>
<th>Source of Immunity</th>
<th>Duration</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural Infection</td>
<td>15 years</td>
<td>Wirsing von Konig, 1995</td>
</tr>
<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, 1994</td>
</tr>
<tr>
<td>Germany</td>
<td>6+ years</td>
<td>Lagauer, 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>6+ years</td>
<td>Lagauer et al, 2002</td>
</tr>
</tbody>
</table>

*Lancet Infect Dis 2002; 2: 744–50*
Cycle of Pertussis Susceptibility in Vaccinated Populations

Primary Vaccination: Protected

Unvaccinated or Partially Vaccinated Infants: Susceptible

Susceptible Adults and Adolescents: Reservoir of Pertussis

No additional booster: Immunity wanes

Booster Vaccination: Prolonged Protection

Cycle of Pertussis Susceptibility in Vaccinated Populations

Primary Vaccination: Protected

Unvaccinated or Partially Vaccinated Infants: Susceptible

Susceptible Adults and Adolescents: Reservoir of Pertussis

Booster Vaccination: Prolonged Protection

No additional booster: Immunity wanes

Reported Pertussis Outbreaks

Adults in the workplace  (MMWR 2004; 53(10:216-219)

Nursing homes/Long-term care facilities  

Students & staff in schools  (MMWR, 2003; 52(1)1-4)

Health-care workers and hospital patients  
Who is at High Risk for Infection?

- Unvaccinated Infants
- Health-care workers
- Daycare workers
- Adolescents & adults
Pertussis Incidence Among Infants 2001-2009
Pertussis Incidence by Age Group, 2011

Incidence per 100,000 population

<table>
<thead>
<tr>
<th></th>
<th>&lt;3 mos</th>
<th>&gt;3 mos</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>24</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>2005</td>
<td>32</td>
<td>7</td>
<td>39</td>
</tr>
<tr>
<td>2006</td>
<td>13</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>13</td>
<td>82</td>
</tr>
</tbody>
</table>

Age at onset: (84%) <3 mos, (16%) >3 mos

CDC, unpublished data, 2007
Unvaccinated Infants with Pertussis: Who is the Source?

Infants with documented pertussis infection in GA, IL, MA, MN (PedInfDisJ 2004;23:985-989)

Identification of infectious source

- Mother 32%
- Father 15%
- Sibling 20%
- Grandparent 8%
- Other 25%
Unvaccinated Infant with Pertussis: Age of the Source

Age of Source (Years)

% of Infant Cases

0-4
5-9
10-19
20+

Ped Inf DisJ 2004;23:985-989
Clinical Features

Respiratory Spread

Highly infectious

Incubation period 7-10 days

Insidious onset, similar to minor URI

- Runny nose
- Non-specific cough
- Low-grade fever
- No sore throat
Classic “Whooping Cough” Phases

Phase 1 “Catarrhal”

– Rhinorrhea
– Conjunctival injection
– Malaise
– Low grade fever
– Lasts 1-2 weeks
Classic “Whooping Cough” Phases

Phase 2 “Paroxysmal”
- Bursts of rapid cough with long inspiratory gasp = “whoop”
- Lasts 1-6 weeks, as long as 10 weeks

1Hewlett EL Edwards KM. NEJM 2005
Classic “Whooping Cough” Phases

Phase 3 “Convalescent”

- Gradual resolution of cough

- Irritants lead to recurrent coughing

- Secondary complications
Clinical Picture of Pertussis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Catarrhal</th>
<th>Paroxysmal</th>
<th>Convalescent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC Lymphs</td>
<td>10,000</td>
<td>20,000</td>
<td>50,000</td>
</tr>
<tr>
<td>time weeks</td>
<td>1-2</td>
<td>2-6</td>
<td>5-12+</td>
</tr>
</tbody>
</table>

Graph showing changes in culture and WBC lymphs over time (weeks) from 1-2 to 5-12+.
Common Clinical Manifestations of Adolescent-Adult Pertussis

Cough $\geq$ 3 weeks (97%), cough $\geq$ 9 weeks (52%)
Paroxysms $\geq$ 3 weeks (73%)
Whoop (69%)
Post-tussive emesis (65%)

Average missed days of school = 5
Average missed days of work = 7
Average days disrupted sleep = 14

Common Clinical Manifestations of Infants with Pertussis

Minor Complications
- Subconjunctival hemorrhages, epistaxis, otitis media

Major Complications (24%)
- Pulmonary
- Neurologic
- Nutritional

Johnston CID 1986; Grant CC, Pediatrics 1998; Mikelova J Pediatr 2003
Diagnosis of Pertussis

Nasopharyngeal swab within 2-3 wks of onset

Culture

- Sensitivity 20-80%; Specificity 100%
- Positive for ~ 2 wks of infection
Diagnosis of Pertussis

PCR
- Limited availability
- Sensitivity 93.5%; Specificity 97.1%
- Remains positive for 3-4 wks of infection

Serology – anti-PT IgG
- 3-4 weeks after cough
- Not uniformly available
Treatment of Pertussis

Active infection
- May not decrease symptoms but clears carriage
- Erythromycin 500mg qid x 14d
- TMP-SMX DS bid x 14 d
- Azithromycin 500mg x 1d. 250mg qd x 4d

Post-exposure prophylaxis
- Within 3 weeks if close contact = within 3 feet or in close space
- Same as treatment regimen

MMWR 2008; 57(RR4): 10
Pertussis is . . .

Common
Morbid
Difficult to diagnose
Contagious
Very bad for infants
A vaccine-preventable disease!
Vaccines aren’t just for kids anymore!
2009 ACIP/AAP Recommendations

Adolescents age 11-18 = single booster dose of Tdap instead of Td (June 2005)

Adults age 19-64 = Tdap in place of their next decennial Td (October 2005)

MMWR 2009; 57(53)
2009 ACIP: Pregnant & Postpartum Women

Women of childbearing age should receive Tdap in place of their next decennial Td but ideally during preconception wellness.

Pregnant women should receive Tdap postpartum before leaving hospital if last Td ≥ 2 yrs.

Non-pregnant adolescents and adults having direct contact with an infant (< 1 yr) should receive Tdap at least 2 wks before contact if last Td ≥ 2 yrs.

MMWR 57 (04); 1-47, 51
MMWR 2009; 57(53)
Cocooning Immunization Strategy

2008-2011, CDC-ACIP recommended strategy of “cocooning vaccination”
Issues with Cocooning Strategy

Limited recall last Td

Ob/Gyns, L&D RNs, and Hospitals not prepared

Inability vaccinate household contacts

Postpartum vaccination fails to leverage potential for passive immunity
Interval since last Td

Mass vaccination campaign of healthcare workers

4524 vaccinated, 2221 (49.1%) completed survey

Comparison of adverse events/reactogenicity
## Interval since last Td

<table>
<thead>
<tr>
<th></th>
<th>&lt; 2 yrs last Td n = 97</th>
<th>≥ 2 yrs last Td n = 578</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain</strong></td>
<td>67.9%</td>
<td>73.5%</td>
</tr>
<tr>
<td>*<em>Redness</em> **</td>
<td>23.5%</td>
<td>19.6%</td>
</tr>
<tr>
<td>*<em>Swelling</em> **</td>
<td>37.8%</td>
<td>33.4%</td>
</tr>
<tr>
<td>*<em>Subjective fever</em> **</td>
<td>15.2%</td>
<td>11.4%</td>
</tr>
</tbody>
</table>

**No difference** in moderate to severe symptoms
**No difference** in serious adverse events
16 pregnant women vaccinated – all normal outcomes
Tdap during pregnancy

104 women
  – 52 received Tdap prior or during pregnancy
  – 52 received Tdap postpartum

Maternal and cord blood collected

Findings:
  – Higher cord blood antibodies if vaccinated in pregnancy
  – High correlation between maternal and cord blood antibody levels

Safety of Tdap in Pregnancy

Tdap vs Td vaccine during pregnancy

440 pregnant women and their infants

Compared antibody levels: birth, 2, 4, 6, 7, 12, and 13 months of age

Safety of Tdap in pregnancy: obstetric outcomes and developmental assessment at 1 year

Halperin SA, NCT00553228
Pertussis Vaccine in Healthy Pregnant Women

Double-blind, crossover RCT

Pregnant women randomized 2:1 to Tdap during pregnancy vs. postpartum

- Antibody levels at birth, 2, 7, and 13 months
- Developmental assessment at 13 months

NCT00707148 - NIAID
Updated and Provisional ACIP Recommendations

Tdap can be administered regardless of interval since last Td

Tdap should be given in 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester in women without prior Tdap

Continue Tdap vaccination for household contacts of infants

ACIP Meeting June 22, 2011
http://www.cdc.gov/vaccines/recs/provisional/default.htm
Tdap Vaccination Summary

As of August 2011, Tdap Vaccination is recommended for pregnant women in the late second (>20 weeks) or third trimester who have not previously received Tdap. If not given during pregnancy, Tdap should be given postpartum.
Newest ACIP Guidelines
October 2012

Vaccination with EACH Pregnancy

Review of Available Data
Pertussis

Who should advocate for patients to be vaccinated?

ALL OF US!
Ob/Gyn’s Role in Immunization

Often first medical contact for young women
Provide $\frac{1}{3}$ of medical visits for women ages 17 – 21
Function as primary care practitioners
Caring for pregnant women
Ob/Gyn’s Role in Immunization

Pediatricians & Ob/Gyns - near eradication of congenital rubella

Remarkable achievement = Rh Isoimmunization (1968)
- 1973 – over 50,000 babies’ lives saved
- *Time* magazine – Top Ten Medical Achievements of the 1960’s
Who benefits from maternal immunization?

- Pregnant woman
- Family/Household contacts
- Fetus/Infant
NIH’s Network of Vaccine and Treatment Evaluation Units (VTEUs)

- Established in 1962
- >160 Phase I, II, and III clinical trials since 1995
- Trials of
  - Seasonal vaccines
  - Pre-pandemic vaccines
  - Antivirals
- $189M over 7 years, avg $27M/yr (FY08-FY14)
How does Vanderbilt Help me?

Vaccine Safety Advice Network

VSAN

A service of the Vanderbilt Vaccine Research Program, Tennessee Immunization Program (Tennessee Department of Health), and the Centers for Disease Control and Prevention
We have seen the Enemy… Pertussis

VTEU Study Objectives

– To evaluate longevity of vaccination protection

– To understand pertussis antibody levels in human breast milk

Pertussis: Known Villain
Aliases: *Bordatella*; whooping cough
Ongoing studies

Enrolling 55 women

- Post partum
- Healthy
- Full term delivery
- No Tdap in 2 years prior
Thank you!