Pertussis: Clinical Review and Colorado’s Epidemic

Today’s Speakers:

Robert Brayden, MD, Professor of Pediatrics, University of Colorado School of Medicine, Children’s Hospital Colorado

Lisa Miller, MD, MSPH, Manager and State Epidemiologist, Communicable Disease Epidemiology Program, Colorado Department of Public Health and Environment
Epidemiology of Pertussis in Colorado - 2012

Communicable Disease Epidemiology Program
Colorado Department of Public Health and Environment

Lisa Miller MD MSPH
Meghan Barnes MSPH
Tracy Woodall DVM MSPH (c)
Reported Pertussis Cases – 1922–2010

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Rate of Reported Pertussis by Year, Colorado, 1940 - 2012
Rates of Reported Pertussis Cases by Year of Report, Colorado and United States, 2000 - 2012*

*Provisional
Background

- During 2012, CDPHE observed a steady increase in reports of cases of pertussis
- 1518 cases were reported in 2012, an ‘epidemic’ level
- This is an increase from a 5 year average of 324 cases/yr for 2007-2011 (4.7 x)
Changes in Pertussis Reporting by State from 2011 to 2012* †

*Data for 2012 are provisional.
†Cases reported through Week 52 in 2011 were compared with cases reported through Week 52 in 2012; fold-changes were calculated for each state.
Reported Pertussis Cases by Month and Year with Projected Baseline and Epidemic Thresholds, Colorado, 2003-2011 and 2012

Reported Cases
Baseline (10 year average, 2002-2011)
Epidemic Threshold
<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>Number of Cases</th>
<th>Percent of Cases</th>
<th>Rate per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 months</td>
<td>77 (40% hosp)</td>
<td>5.1</td>
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<tr>
<td>65+</td>
<td>19</td>
<td>1.3</td>
<td>3.3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1518</td>
<td>100.0</td>
<td>29.7</td>
</tr>
</tbody>
</table>
Rates of Reported Pertussis Cases by Age Group and Report Year, Colorado, 2007 - 2012
Reported Cases of Pertussis by Selected Single Year of Age and Doses of Pertussis Vaccine, Colorado, 1/1/2012 - 12/31/2012

- Unknown
- 6 or More Doses
- 5 Doses
- 4 Doses
- 1 - 3 Doses
- No Doses

Number of Cases vs Age (Years)
Incidence of pertussis among persons aged ≤19 years, by age and vaccines received* — United States, January 1–June 14, 2012
• The increasing number of cases in adolescents suggests immunity wanes after Tdap vaccination in age groups fully vaccinated with acellular vaccines.

• Acellular and whole-cell vaccines both have high efficacy during the first 2 years after vaccination, but recent changes suggest diminished duration of protection in those given acellular vaccine (DTaP) compared to those given DTP vaccine.
• Unvaccinated children have an eightfold greater risk for pertussis than children fully vaccinated with DTaP.
• Vaccinated children can develop pertussis, but they are less infectious, have milder symptoms, shorter illness duration, and are at reduced risk for severe outcomes.
• Vaccination continues to be the single most effective strategy to reduce morbidity and mortality caused by pertussis.
• Vaccination of pregnant women and contacts of infants protects infants too young to be vaccinated is an important strategy to protect those most at risk.
Prevention and Control of Pertussis: Objectives

- **Primary:** Preventing death and serious complications in individuals at increased risk of severe and/or complicated disease, including infants <12 months

- **Secondary:**
  - Limit transmission in outbreak setting
  - Limit further spread and duration of transmission within closed communities
  - Decrease morbidity in affected populations
  - Lower risk of dissemination to unaffected groups within an outbreak

- Vaccination is the safest and most effective tool we have to achieve our objectives.
Action
Health Alert (HAN) for Medical Providers

- Consider a diagnosis of pertussis in patients with a paroxysmal cough.
- Test those with symptoms c/w pertussis to avoid false positives.
- Make sure patients are up-to-date on pertussis vaccination, especially if they have close contact with infants.
Schools and Childcare

• Make sure students are up-to-date on vaccination.

• Refer students who may have pertussis to their primary care provider.

• Students who are sick should stay home so they don’t transmit their illness to others.
General Public

• Press release

• Social media
Colorado Department of Public Health and Environment

During 2012, 1519 cases of pertussis were reported in Colorado, compared to an average of 324 cases a year 2007-2011. While pertussis occurs in all age groups, infants less than 6 months of age have the highest rate of disease and usually...

Disease Control and Environmental Epidemiology - Pertussis (Whooping Cough)
www.colorado.gov

Pertussis, or whooping cough, is a contagious disease that can cause a prolonged and sometimes severe cough illness. It is caused by the bacterium, Bordetella pertussis, and is found in the nose and throat of an

Colorado Department of Public Health and Environment

Annie’s Rising Crust Frozen Pizza voluntarily recalled due to possible metal fragments

We are announcing a voluntary recall by Annie’s Inc. of Berkeley, Calif., affecting all varieties of Annie’s Rising Crust Frozen Pizza with a “best by”...See More

Annie’s Homegrown Frozen Pizza Recall
www.annies.com

All varieties of Annie’s RISING CRUST FROZEN PIZZA with...
FOR IMMEDIATE RELEASE: Dec. 18, 2012

CONTACT:
Mark Salley
Communications Director
303-692-2013
Mark.salley@state.co.us

COLORADO WHOOPING COUGH CASES HIGHEST IN 60 YEARS, INCLUDE ONE DEATH

DENVER — With 1,407 reported cases as of Dec. 8, Colorado’s pertussis epidemic has exceeded the number of cases seen in the state going back at least six decades. The last time Colorado experienced this level of pertussis, commonly referred to as whooping cough, was in 1948 with 1,833 cases.

There was one pertussis death in October of this year — an older adult in Larimer County. This is the first whooping cough death in the state since 2005, when there were two infant deaths. Whooping cough is typically most dangerous for babies and young children, but can affect people of all ages.

“Usually at this time of year we focus on reminding residents to get their flu immunizations, but this year we need to couple that with a message for people also to protect themselves and their loved ones from whooping cough,” said Dr. Rachel Herlihy, director of the Immunization Section at the Colorado Department of Public Health and Environment. “Immunization is the best method of protection against both the flu and whooping cough.”

It is recommended all adults and children receive the whooping cough booster vaccine, Tdap.

According to Herlihy, it’s especially important for those who have contact with young children to talk to their doctors about their whooping cough immunization status, because young children are more vulnerable to the disease. In young children, particularly infants, whooping cough can lead to difficulty breathing, hospitalization and even death. Child care workers, health care workers, parents, grandparents and siblings of young children all must make sure they are up to date on their whooping cough vaccinations. Immunity to pertussis wanes over time, so booster doses of the vaccine are necessary, even for people who have had the disease in the past.

Whooping cough cases are distributed throughout 31 Colorado counties, with most cases reported in Jefferson (242), Denver (207), Adams (195), Arapahoe (160) and Boulder (158). The case counts are from Jan. 1 through Dec. 8, 2012.
Whooping cough cases continue to mount in Colorado, and every new case is a reminder that we need to ensure everyone is up-to-date on...

Whooping cough cases triple in Colorado - News Story

Whooping cough tends to run in multi-year cycles, and experts say last year appears to have been a peak. Also, a newer version of the...

Whooping cough vaccine loses punch too fast - The Denver Channel

More than 28,000 cases of whooping cough have been reported across the country so far this year, including more than 10,000 in children...

Parents are alerted after a Longmont High School student is diagnosed with pertussis, more commonly known as whooping cough. Jaclyn Allen reports.

Worst whooping cough outbreak in Colo. since 1948

A pediatrician says its a danger to his young patients to allow unvaccinated children into his waiting room. Watch 7NEWS Reporter Jaclyn Allen's report.

New Swine Flu Outbreak

New Vaccinations Required For Students
@pwnthepwns: Congratulations and we look forward to working with you. And thanks to @cdphpsd for their work as well.

CDPHE: 75 cases of West Nile virus identified in CO as of Sept. 17. More data, statistics, and resources on WNV here: colorado.gov/cs/Satellite/C...

CDPHE: What's the big whoop about pertussis? Check out @CDCgov FAQs to learn more about the re-emergence of this disease: cdc.gov/pertussis/about...

CDPHE: System built for bioterrorism confirms and reacts to Plague in 7 y/o CO girl. apnhblog.org/2012/09/system...

CDPHE: #CDCfluChat given pertussis increase, flu clinics are good opportunity to give Tdap, too.

CDPHE: @AlfoPerma #CDCfluChat Try your local health departments for low-cost vaccine

CDPHE PSD: CDPHE staff learning and participating in #cfcfluchat - thanks for hosting @CDCflu #cfchealth pic.twitter.com/WqCfI3Qo

CDPHE: @HMBDCoalition #CDCfluChat and it's important for those around that child to be vaccinated.
Conclusion

• Pertussis continues to be a significant public health problem in Colorado, though the epidemiology is evolving.

• Vaccination is our best prevention tool

• Goal is no infant deaths
  – Improve Tdap coverage in adults and adolescents
  – Maintain high levels of coverage with DTaP in children
Questions?
California VE Study

- Cases & controls 4-10 yrs at illness onset or enrollment
- Reported pertussis cases in 15 CA counties
- Unmatched controls from case-patient providers (3:1)
- Vaccine histories collected by in-person visits to providers
- Logistic regression, accounting for clustering
- 250 provider offices, 4,000 charts abstracted
<table>
<thead>
<tr>
<th></th>
<th>Case (%)</th>
<th>Control (%)</th>
<th>P-Value</th>
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<tbody>
<tr>
<td></td>
<td>N=682</td>
<td>N=2,016</td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7.8</td>
<td>0.9</td>
<td>&lt; 0.0001</td>
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<tr>
<td>Vaccinated age at 5th Dose</td>
<td>N=629</td>
<td>N=1,997</td>
<td></td>
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<tr>
<td>4</td>
<td>68.7</td>
<td>71.9</td>
<td>0.11*</td>
</tr>
<tr>
<td>5</td>
<td>31.1</td>
<td>27.3</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
<td>0.8</td>
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Pertussis Disease among Unvaccinated compared to Vaccinated Children

<table>
<thead>
<tr>
<th>Vaccination Status</th>
<th>Case</th>
<th>Control</th>
<th>OR (95% CI) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>53</td>
<td>19</td>
<td>8.9 (4.9 – 16.1)</td>
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<tr>
<td>5 DTaP doses</td>
<td>629</td>
<td>1,997</td>
<td></td>
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* Accounting for clustering by county and provider
## Overall VE & Duration of Protection Estimates

<table>
<thead>
<tr>
<th>Model *</th>
<th>Case (n)</th>
<th>Control (n)</th>
<th>VE, %</th>
<th>95% CI</th>
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<tr>
<td>Overall VE, All Ages</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 dose</td>
<td>53</td>
<td>19</td>
<td>Ref</td>
<td>--</td>
</tr>
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<td>629</td>
<td>1,997</td>
<td>88.7</td>
<td>79.4 – 93.8</td>
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<tr>
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<td>354</td>
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<td>79</td>
<td>366</td>
<td>92.3</td>
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<td>108</td>
<td>304</td>
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<td>76.2 – 93.2</td>
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<td>48 – 59 months</td>
<td>141</td>
<td>294</td>
<td>82.8</td>
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<td>60+ months</td>
<td>231</td>
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The Physician’s Role in Preventing Pertussis

Robert Brayden, MD
Professor of Pediatrics
University of Colorado
Children’s Hospital Colorado
Disclosures

- I have no financial interest in any vaccine or vaccine delivery device
- Pharmaceutical companies do not pay my salary directly or indirectly
- Trade names do not imply endorsement
- No photograph of any patient in this talk is of the stated patient
Recent pertussis case

- Family visiting Colorado
- 69 day old infant
- Cough congestion for several days
  - RSV, influenza initially considered
- After paroxysms, pertussis PCR +
- 20 days on ECMO
- Died of hepatic, renal, pulmonary failure and pulmonary hypertension
Does this baby have pertussis?
Does this baby have pertussis?
Pertussis – What is it? It’s history?

- Highly contagious respiratory infection caused by *Bordetella pertussis*
- Estimated 294,000 deaths worldwide in 2002
- First described in 1578 by De Baillou, Paris
- *Bordetella pertussis* isolated in 1906
What Bordetella species are infectious to humans?

- *Bordetella bronchiseptica* – mammals, dogs, cats, etc. Disease rare in humans
- *Bordetella parapertussis* – human and sheep. Disease milder in humans
- *Bordetella pertussis* – humans only;
  - only organism to produce pertussis toxin; inhibits immune response; non-motile
Pathogenesis - pertussis

- Primarily a toxin-mediated disease
- Bacteria attach to cilia of respiratory epithelial cells
- Toxins cause
  - ciliostasis
  - phagocyte inactivation
- Pertussis antigens allow evasion of host defenses (lymphocytosis promoted but impaired chemotaxis)
Clinical Features - pertussis

- Incubation period 5–10 days (range 4–21 days)
- Insidious onset, initially similar to minor upper respiratory infection with nonspecific cough
- Fever usually minimal throughout course of illness
Clinical Features - pertussis

- Stages of Pertussis
  - Catarrhal
  - Paroxysmal
  - Convalescence

- Duration of symptoms
  - 1 – 2 weeks
  - 1 – 6 weeks
  - Weeks to months
Complications - pertussis

- Complications:
  - Pneumonia (5%), seizures (0.7%)
  - Hospitalization (16%)
  - Asphyxia, pulmonary hypertension
  - Death (0.1%)
Complications by Age - pertussis

- Cases reported to CDC 1997-2000 (N=28,187)

Graph showing the percentage of pneumonia and hospitalization cases by age group:

- <6 m: High percentage for pneumonia and hospitalization
- 6-11 m: Moderate percentage for pneumonia
- 1-4 y: Low percentage for pneumonia
- 5-9 y: Very low percentage for pneumonia
- 10-19 y: Very low percentage for pneumonia
- 20+ y: Very low percentage for pneumonia

*Cases reported*
Deaths - pertussis

- Colorado
  - 2000 to present
  - 6 deaths
    - All in infants <3 months of age
    - Case:fatality ratio 0.1%

- US
  - Deaths: 1 in 500 admissions

- 90% of deaths from pertussis occur to children < 1 yr of age
Diagnosis - pertussis

Diagnosis:
  Culture
  Nucleic or antigen detection
  Immune response

“Confirmation of *B. pertussis* infection is still one of the most difficult diagnostic challenges”

Live organisms only early in the illness
Epidemiology- pertussis

- Reservoir
- Transmission
- Communicability

- Human
- Respiratory droplets
- Maximal in catarrhal stage. Secondary attack rates up to 80%
Reported Pertussis by Age Group, 1990-2007
<table>
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<th>Age Group (years)</th>
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<th>Percent of Cases</th>
<th>Rate (per 100,000)</th>
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<td>3.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1519</strong></td>
<td><strong>100.0</strong></td>
<td><strong>29.7</strong></td>
</tr>
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</table>
Pertussis cases 2012

- US 13,214 cases
  - Colorado 1519 cases
    - Peaked in late fall
The physicians’ role in pertussis prevention

- Vaccination
- Diagnosis
- Secondary prevention
Childhood Vaccination

- Pertussis vaccine initially developed in 1914
- DTP 1948
  - 70% – 90% efficacy after 3 doses
    - Protection for 5 – 10 years
    - Local adverse reactions common
- DTaP 1996
  - Less reactogenic
  - Approved for 2 mo to 7 yrs
  - 80 – 85% effective in disease reduction
## Composition* of Acellular Pertussis Vaccines

<table>
<thead>
<tr>
<th>Product</th>
<th>PT</th>
<th>FHA</th>
<th>PERT</th>
</tr>
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<tbody>
<tr>
<td>Tripedia</td>
<td>23</td>
<td>23</td>
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</tr>
<tr>
<td>Infanrix</td>
<td>25</td>
<td>25</td>
<td>8</td>
</tr>
<tr>
<td>Daptacel</td>
<td>10</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Boostrix</td>
<td>8</td>
<td>8</td>
<td>2.5</td>
</tr>
<tr>
<td>Adacel</td>
<td>2.5</td>
<td>5</td>
<td>3</td>
</tr>
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</table>

*mcg per dose
Interchangeability of DTaP Vaccine

- When feasible, the same DTaP vaccine should be used for all doses
- “Mix and match” schedules do not adversely affect safety, immunogenicity
The “6 before 7” Rule

- **ACIP recommends** no more than 6 doses of DT-containing vaccine before the 7\textsuperscript{th} birthday
- Intended to reduce the frequency of local reactions
<table>
<thead>
<tr>
<th>Underlying Condition</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>Prior seizure</td>
<td>Delay and assess*</td>
</tr>
<tr>
<td>Suspected neurologic disorder</td>
<td>Delay and assess*</td>
</tr>
<tr>
<td>Neurologic event between doses</td>
<td>Delay and assess*</td>
</tr>
<tr>
<td>Stable/resolved neurologic condition</td>
<td>Vaccinate</td>
</tr>
</tbody>
</table>

* vaccinate after treatment initiated and condition stabilized
Vaccination When Recovered From Pertussis

- Recommendations differ.
  - AAP recommends continuing with pertussis vaccine schedule.
  - CDC recommends that children who have recovered from pertussis do not need additional pediatric pertussis vaccines but should receive a single dose to Tdap at the usual time

- Satisfactory documentation of disease:
  - Culture positive
  - Typical symptoms and clinical course when epidemiologically linked to culture–proven case
Vaccinating adolescents and adults

- Vaccination result: Disease often milder
- Reductions of missed school, missed work
  - asymptomatic to classic pertussis
- Mild disease may transmit the infection
  - herd immunity, esp. to neonates
Tdap vaccine

- Recommended 11 years of age
- October 2010: ACIP approves single dose if:
  - Undervaccinated between age 7 and 10.
  - Over the age of 65 years if anticipate contact with an infant

- Contraindications
  - Severe allergic reaction to vaccine component or following a prior dose
  - Encephalopathy not due to another identifiable cause occurring within 7 days after vaccination
Recommendations for Tdap Vaccination of Adolescents

- Adolescents 11 or 12 years of age should receive a single dose of Tdap
- Adolescents 13 through 18 years who have not received a previous Tdap
Tdap and MCV

- MCV is recommended for all children at the 11 or 12-year visit
- Administer Tdap and MCV during the same visit
- If simultaneous administration of Tdap and MCV is not possible, these vaccines can be administered at any time before or after each other
Tdap Vaccination above age 19

- Single dose of Tdap to replace a single dose of Td
- May be given at an interval less than 10 years since previous Td
  - Anticipated close contact with an infant < 12 months of age
Cocooning and pregnancy

- Tdap during each pregnancy
  - 27 – 36 weeks gestation advised
  - Irrespective of previous Tdap history
  - Transplacental antibody might protect in infancy
  - Transplacental antibody might interfere with infants’ DTaP

- Tdap to those who will come into contact with infant

- Immediate post-partum period (+ others) acceptable but not preferred
Tdap pregnancy registries

- GSK: 1-888-825-5249
- Sanofi-pasteur: 1-800-822-2463
Tdap Vaccine and Healthcare Personnel

- Healthcare personnel
  - Who work with infants 12 months of age and younger
  - An interval as short as 2 years (or less) from the last dose of Td
Diagnosis

- **Culture**
  - Pertussis is a fastidious organism
  - Viable organisms disappear early in the disease, after about 5 days

- **PCR**
  - More sensitive than culture
  - Remains + for about 12 days after onset
Secondary prevention

Management of exposure

“Guidelines for the Control of Pertussis Outbreaks”

Consider infectiousness of the patient
Intensity of the exposure
Erythromycin is the drug of choice for treatment, prophylaxis
Azithromycin, clarithromycin are probably acceptable alternatives
Why is Pertussis Relatively Common in Colorado?

- Diagnostic Bias (PCR is more sensitive than cx)
- Pertussis has always been episodic
- Acellular vaccine has a limited duration of efficacy
- Acellular vaccine may be less effective than whole-cell
- Surveillance Bias
- Travel/destination site
- Low vaccination rate for pertussis
- DTaP shortage resulted in missed doses
- Urbinity