California Pertussis Epidemic
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Pertussis Background

- Pertussis is the most poorly controlled vaccine-preventable disease
  - Incidence increasing since the 1990s
  - Cyclical with peaks every 2-5 years as numbers of susceptible people increase enough to reach the “epidemic threshold” and allow sustained transmission; last prior peak year was 2005 with 25,616 U.S. cases, a 45 year high at the time

- Adults are vulnerable to pertussis
  - 27% of reported cases in 2004 were among adults
  - Pertussis immunity is not lifelong and wanes 4-12 years after the DTaP series and 4-20 years after natural infection*
  - ~20% of cough illness lasting >2 weeks is pertussis

- First pertussis vaccines (Tdap)† for adolescents and adults licensed in 2005, but uptake suboptimal – in 2008 ~6% of adults were estimated to have ever received Tdap

Pertussis in Young Infants

- Initially infant initially looks deceptively well; coryza, no or minimal fever, mild or no apparent cough
- Leukocytosis with lymphocytosis
- Gagging, gasping
- Apneic episodes
- Cyanosis (parents may report red or purple face)
- Post-tussive emesis
- Seizures
- Respiratory distress
- Pneumonia
- Adenovirus or RSV coinfection can confuse picture
Source of Pertussis in Infants

- Adults transmit pertussis to infants
  - Among 264 known source-cases:
    - Almost 50% were parents, most often mothers
    - 51% were adults >19 years of age


**Children's Hospital Central California**

**Laboratory Confirmed Cases of Pertussis (9/7/10)**

<table>
<thead>
<tr>
<th>Month of Diagnosis</th>
<th>No. of Cases</th>
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<td>Sep-08</td>
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<td>Oct-08</td>
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<tr>
<td>Sep-10</td>
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Pertussis resurgence since the 1990s

- Genetic changes in *B. pertussis*; greater virulence?
- Variable vaccine efficacy – acellular vaccines licensed in 1991 for 4th/5th doses, entire series in 1996; estimates of vaccine efficacy for DTaP typically range from 75-85% depending on the case definition that is used
- Waning of vaccine-induced immunity and fewer natural boosting events
- General availability of better laboratory tests
- Greater awareness of pertussis by clinicians
Number of reported pertussis cases by onset year — California, 1915-2010*

*As of 9/7/2010

1st reliable DTP vaccine
Pertussis Update

• There have been 6631 confirmed, probable and suspect cases of pertussis reported in 2010 for a state rate of 16.9 cases/100,000

• This is the most cases reported in California since 1950 when 6613 cases were reported and the highest incidence since 1950 when there were 26 cases/100,000 population

• Cases may have peaked in some parts of the state, e.g., the Central Valley region
Pertussis Update

- Rates are highest in infants <6 months of age (336 cases/100,000), in adolescents aged 7-9 years (50 cases/100,000) and 10-18 years (37 cases/100,000); outside of infancy, the peak age for cases is age 10 years.

- Overall rates by race/ethnicity are highest in Hispanics (17.5/100,000), however the highest rates are seen in Hispanic infants <6 months of age (415/100,000).
Incidence of pertussis cases by race/ethnicity and age -- California,

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Cases per 100,000</th>
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<tr>
<td>&lt;6 mos</td>
<td>177.9</td>
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<tr>
<td>6 mos-6 years</td>
<td>20.1</td>
</tr>
<tr>
<td>7-9 years</td>
<td>29.8</td>
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<tr>
<td>10-18 years</td>
<td>22.3</td>
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<tr>
<td>19-64 years</td>
<td>2.9</td>
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<tr>
<td>65+ years</td>
<td>2.3</td>
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*As of 9/7/2010*
Pertussis Update

- 280 (11%) cases have been hospitalized (of cases with known hospitalization information)
- 163 (58%) of hospitalized cases were infants <3 months of age and 211 (75%) were infants <6 months of age
- 162 (77%) of the hospitalized infants <6 months of age were Hispanic (CA birth cohort is ~50% Hispanic)
2010 Pertussis Deaths

- 10 deaths to date; 9 Hispanic infants, 1 White
- Nine of the nine occurred in infants <2 months of age at time of disease onset who had not received any doses of pertussis-containing vaccine
- One death occurred in a former preemie who received the first dose of DTaP at 2 months of age, 15 days prior to disease onset, and had 3 older siblings with cough illness
- Most of the fatal cases had multiple contacts with healthcare providers before pertussis was diagnosed, several had family members with cough illness
Pertussis Mitigation

- Promote the use of Tdap - particularly in those who have contact with infants
  - Free vaccine through 12/31/2010 for birth hospitals with postpartum Tdap policies; encourage ED use of Tdap
  - Work with payers re: Tdap reimbursement
  - CDPH expanded Tdap recommendations

- Clinician education
  - CDPH Tdap recommendations
  - Pertussis signs and symptoms
  - Treatment recommendations for infants with severe pertussis
  - Accelerated DTaP schedule for infants

- Public education
  - Vaccination/cocooning
  - Pertussis signs and symptoms
  - Keep ill people away from infants
CDPH Tdap Recommendations
July 2010

- Immunize pre-teens, teens and adults with Tdap vaccine
  - 7-9 year olds who are underimmunized
  - those ≥10 years of age who have not yet received Tdap, especially
    - women of childbearing age, preferably before, or else during or immediately after pregnancy
    - others with close contact with young infants
    - includes persons >64 years of age

- No minimum interval between Td and Tdap
Pertussis cases in children and adolescents aged 0-18 years, by vaccine history -- California, 9/7/2010
Vaccine Effectiveness Study

- CDPH, CDC and 15 local health departments are collaborating to perform a DTaP VE case-control study
- DTaP vaccine histories (dates and manufacturer) will be compared between children 4-10 years of age who had pertussis in 2010 and controls in the same age group
- Goals are to attempt to assess:
  - DTaP vaccine effectiveness following childhood vaccination;
  - Duration of pertussis immunity after the childhood DTaP series
    - is vaccine waning earlier than expected? (difficult to differentiate early waning from primary vaccine failure)
    - is the timing of the fifth dose important in earlier waning (fifth dose can be given from age 4 through age 6 years);
  - The immunogenicity of vaccines from different manufacturers (there are currently two manufacturers of DTaP and the vaccine formulations are different)
Postpartum Tdap Effectiveness Study

- CDPH is attempting to determine if vaccinating postpartum women with Tdap is an effective strategy to reduce transmission of *B. pertussis* to young infants.

- A survey was done to determine how many birthing facilities in California have policies to administer Tdap vaccine to postpartum women.

- Hospital of birth was ascertained for infant pertussis cases to determine if infants born in hospitals with postpartum Tdap policies were less likely to become infected with pertussis.

- Preliminary data suggest this is the case.
Evaluation of Community Vaccination Campaigns

- CDPH and CDC are collaborating on an ecologic study to attempt to assess the effect of the Tdap vaccine campaign on the incidence of pertussis.
- Does vaccinating large numbers of people in the community with Tdap help control an outbreak?
Pertussis Risk Factor Study

• Collaborating with Dr. Jim Cherry and LA County to compare fatal infant pertussis cases <4 months of age from 1998-2010 with nonfatal hospitalized cases, nonfatal/nonhospitalized cases, and uninfected infants

• Each fatal case will be matched with four nonfatal hospitalized cases and at least one nonfatal/nonhospitalized case and one healthy infant who were also <4 months of age and from the same county (or an adjoining county)

• Possible risk factors for death and risk factors for pertussis will be examined
Questions?
Pertussis Background, continued

- *Bordetella pertussis* bacteria are inhaled and reach the ciliated cells of the respiratory epithelium where they attach to the cilia*; transmission via fomites is thought to occur rarely, if ever

- In a study of fatal cases, *B. pertussis* was frequently isolated from the alveoli and less commonly from the trachea or bronchi*

- Pertussis toxin enters the bloodstream and exerts its biological effects on systemic sites

- Very contagious: basic reproduction number (*Ro*) estimate is 12-17 (similar to measles and in contrast with influenza, which has an *Ro* of 1-2); approximately 90% of susceptible household contacts become infected

- Minimum proportion of population that must be immune to eliminate transmission estimated to be 92-95%; achieving this level of population immunity will be difficult without a vaccine that confers lifelong immunity

Typical Symptoms of Pertussis

• Three-stage bacterial illness (catarrhal, paroxysmal and convalescent) that lasts 4-12 weeks

• Typical symptoms
  ▪ paroxysmal cough
  ▪ lack of fever
  ▪ no systemic illness
  ▪ coryza; no pharyngitis
  ▪ posttussive vomiting
  ▪ posttussive whoop

• Adults with pertussis often report feeling as if they’re choking on something, sweating episodes
Number of reported pertussis cases by year of onset -- California 1950-2010*

*As of 9/7/2010
Why are Hispanic infants over-represented among infant cases?

- Increased incidence in Hispanic infants <6 months has been noted in other states as well.
- Higher mortality rates have been estimated nationwide for Hispanic than for non-Hispanic infants since the 1990s.
- The reason is unclear, but one possibility is that Hispanics have larger average family household sizes than other racial/ethnic groups and may therefore have a greater risk of exposure to pertussis, i.e., more contacts = more potential for exposure.
- In 2000, 30.6 percent of family households in which a Hispanic person was the householder consisted of five or more people vs. 11.8 percent of non-Hispanic White family households.

2010 Pertussis Deaths

• Case 1: February 2010
  - Previously healthy, Hispanic female, Los Angeles County
  - Household members with cough illness, however, mom stated they became ill after infant became ill
  - Lived with mother, father, 3 siblings, uncles, aunts, and 2 cousins
  - Symptom onset age 3 weeks
  - Seen by healthcare provider 3 times in 3 days prior to admit; pertussis not considered by provider
  - Admitted from ER after 3 day history of fever, cough, and respiratory distress
  - Transferred from community hospital to children’s hospital PICU for intubation
  - WBC 47,500; 65% lymphocytes
  - Pulmonary HTN, partial exchange transfusion, ECMO
2010 Pertussis Deaths, continued

Case 2: April 2010

- Previously healthy, Hispanic female, San Bernadino County
- Lived with mother, brother, sister (grandmother babysat)
- Symptom onset age 12 days; mother URI/cough 1 week prior
- Seen in community hospital ER 5 days later, post-tussive vomiting noted, but diagnosed with viral URI and discharged home – pertussis not considered
- Seen in community hospital ER one week later after developing apnea and cyanosis; transferred from ER to children’s hospital PICU; intubation, ECMO
- Admission WBC 33,900
- Pulmonary HTN, renal failure
- Intracranial hemorrhage on day 30 of ECMO → ECMO discontinued → seizures → hemodynamic instability → death
2010 Pertussis Deaths, continued

Case 3: April 2010

- Previously healthy, Hispanic female, Fresno County
- Lived with mom, dad, sister – no daycare
- Father had cough illness for several weeks
- Cough onset at age 5 weeks, one week prior to admission
- Seen in ER 4 days prior to admission with cough, post-tussive vomiting and cyanosis; pertussis not considered - discharged home
- Seen in ER 4 days later and admitted
- Hospitalized in children’s hospital for one week before transfer to PICU and intubation
- WBC 80,000; pulmonary HTN - single volume exchange transfusion done
- Transferred to second children’s hospital PICU for ECMO, but not done due to multiorgan failure
2010 Pertussis Deaths, continued

• Case 4: May 2010

- Hispanic male, Stanislaus County
- Lived with father, mother, 3 siblings – no daycare
- Mother had history of cough
- At age 6 days, hospitalized x 24 hours for hyperbilirubinemia; cough onset day after discharge
- 10 days later, admitted from ER to community hospital where pertussis was not considered at time of admit; condition worsened shortly after admission → transferred after admission to children’s hospital PICU for intubation and ECMO x 7 days
- Initial WBC 69,000 with 34% lymphocytes; second WBC 90,700 with 26% lymphocytes
- Pulmonary HTN, disseminated intravascular coagulation, multiorgan failure
2010 Pertussis Deaths, continued

Case 5: May 2010

- Previously healthy, Hispanic male, LA County
- Lived with mother, 2 siblings (grandmother babysat)
- No identified ill contacts
- Cough onset at age 7 weeks, 2 days prior to admit from ER, pertussis not considered at time of admit; transferred from floor to PICU on day of admit after condition worsened
- Admission WBC 33,420; 58% lymphocytes → WBC 100,540; 25% lymphocytes → had two single volume exchange transfusions
- Pulmonary HTN, profound hypoxemia and hypotension from myocardial suppression and ARDS with acute renal failure
2010 Pertussis Deaths, continued

• Case 6: July 2010
  - Previously healthy, Hispanic female, LA County
  - Lived with mother, father, MGM, and two siblings
  - No identified ill contacts
  - Cough onset at age 6 weeks; during the next 8 days until her death, she was seen by her primary care provider x 3 and in an ER x 1 before the second ER visit that led to her admission – pertussis was not considered; she was almost immediately transferred to a PICU after admission and died the next day
  - WBC 131,000 with 35% lymphocytes
2010 Pertussis Deaths, continued

- Case 7: July 2010
  - Hispanic male, San Diego County
  - Lived with mother and vaccinated 7 year old sibling
  - No identified ill contacts (mother with cough?)
  - Cough onset at 19 days of age; one week history of mild cough, URI symptoms PTA
  - Circumoral cyanosis, increasing respiratory rate and work of breathing on day of admission
  - Seen in ER (O2 sat 86%) and admitted; initial diagnosis bronchiolitis, but pertussis in the differential
  - ECMO → intracranial hemorrhage → death 8 days after admission
2010 Pertussis Deaths, continued

- Case 8: July 2010
  - Former 28 week preemie, LA County
  - Hispanic male, lived with father, mother, and four siblings
  - Three siblings with cough illness (missed opportunity for NICU to assess family immunization status)
  - Received DTaP at 2 months of age, symptom onset 15 days later at ~2½ months of age
  - Seen in clinic on day 4 after symptom onset, one day after cough onset; diagnosed with URI but warned about pertussis and given strict return instructions
  - Admitted from ED 3 days later → respiratory failure → intubation → death <3 days of admission
  - WBC=14.9 with 67% lymphocytes (lower WBC possibly due to receipt of DTaP?)
2010 Pertussis Deaths, continued

- Case 9: August 2010
  - Previously healthy White male, San Bernadino County
  - Lived with father, mother, and three siblings
  - Mother, father and nine year old sib had cough illness (4 and 5
    year old sibs asymptomatic)
  - Illness onset at age 20 days, admitted at age 25 days
  - Day of admit, seen in clinic with immediate transfer to
    community hospital and then transferred again to tertiary care
    hospital – pertussis considered immediately
  - Admission WBC=41.9
  - Pulmonary HTN, ECMO – death 20 days after admission
    secondary to cerebral infarction
Postexposure Chemoprophylaxis

- CDC moving towards chemoprophylaxis of high risk contacts, rather than all contacts (Oregon has been recommending this for several years)

- High risk contacts:
  - Infants <1 year of age and people who may transmit pertussis to infants <1 year of age
    - Pregnant women
    - Household members and care givers of infants
    - Healthcare workers working with infants and pregnant and postpartum women
  - Children in daycare who have contact with infants
  - Childcare workers who care for infants
Pertussis Diagnostics

- Culture: Labs should maintain capability; cultures should be used to confirm outbreaks and are needed for antibiotic susceptibility testing.

- PCR: Adoption of multi-target R-PCR methods will allow for confirmation and speciation among *Bordetella* spp; Ct cut off values are important; contamination of NP swabs with vaccine DNA can lead to false positives.*

- Serology: An ELISA-like test that quantitatively measures IgG and IgA antibody to pertussis toxin appears to be a useful diagnostic method, especially in adults and in the later stages of the disease; CSTE/CDC is likely to include serologic evidence of infection in the next update of the pertussis case definition (lab pos + cough of any duration).

* see 3/1/2010 Epi-X
When Pertussis Tests are Likely to be Positive in Infected People

- Incubation Period
- Catarrhal Stage
- Paroxysmal Stage
- Convalescent Stage

Symptom Onset
- Bacterial Culture
- PCR
- Serology

Communicable Period
Why here, why now?

- A sufficient number of susceptible people have accumulated in the population via birth cohorts of unvaccinated infants, waning population immunity from vaccine or disease (and less chance for boosting opportunities), parental choice not to vaccinate children, etc.

- The 2005 epidemic was nationwide, but although other states have reported pertussis increases this year, none have reported increases like those seen in California.

- Some have speculated that California may have less population immunity than other states because it is one of only 11 states that does not have a Tdap requirement for middle school students, however, 2009 National Immunization Survey data indicates that estimated Tdap rates in California adolescents (53.1%) are not much lower than the national estimate (55.6%).

- Is population density/aggregation of susceptibles a factor? (No outbreak in NYC)
States Requiring a Pertussis Booster Shot for Middle School Students

In 2005 combined tetanus, diphtheria and pertussis (Tdap) booster vaccines first became available in the United States. Since then most states have implemented a pertussis booster shot requirement for at least middle school students.