Topics to Be Covered

- Pertussis clinical disease
- Current epidemic in Orange County and California
- Diagnosis
- Treatment and prophylaxis
- Pertussis vaccine
- Public health response
Bordetella pertussis

B. pertussis disease is mediated by a variety of antigens and toxins:

**Antigens**
- Fimbriae
- Filamentous hemagglutinin
- Pertactin

**Toxins**
- Pertussis toxin
- Adenylate cyclase
- Tracheal cytotoxin
Pertussis Catarrhal Stage

- Follows an incubation period of 5-21 days
- Characterized by:
  - Runny nose
  - Sneezing
  - Cough
  - Fever often mild or absent
  - Lasts about two weeks
Pertussis Paroxysmal Stage

- Follows catarrhal stage
- Characterized by persistent cough
  - Paroxysms 82-100%
  - Post-tussive emesis 45-71%
  - “Whoop” 30-67%
  - Lower respiratory tract symptoms unusual
- Other systemic symptoms rare
- Patient usually appears well between coughing spells
Convalescence is gradual and protracted
Severity of illness wanes
Frequency of coughing bouts decreases
Nonparoxysmal cough can continue for weeks or months
Superimposed viral respiratory infections can trigger a recurrence of paroxysms
Pertussis Complications

- Weight loss
- Sleep disturbance
- Pneumothorax
- Epistaxis
- Subconjunctival hemorrhage
- Subdural hematoma
- Hernia
- Urinary incontinence
- Rib fracture
- Bacterial pneumonia
- Otitis media
- Seizures
- Hypoxic encephalopathy
Pertussis in the Infant

May present differently:
- Shorter catarrhal stage
- May not have noticeable cough or “whoop”
- Gagging, gasping or apnea
- Facial color changes (may turn blue, purple or red)
- Will frequently have leukocytosis with an increased absolute lymphocyte count
Reported NNDSS pertussis cases: 1922-2013*

*2013 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
## Composition* of Acellular Pertussis Vaccines

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

*mcg per dose
Table 1. Recommended immunization schedule for persons aged 0 through 18 years – United States, 2014.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>19–23 mos</th>
<th>2–3 yrs</th>
<th>4–6 yrs</th>
<th>7–10 yrs</th>
<th>11–12 yrs</th>
<th>13–15 yrs</th>
<th>16–18 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B¹ (HepB)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
<td>7 d</td>
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<td>15 d</td>
<td>16 d</td>
</tr>
<tr>
<td>Rotavirus² (RV) (2-dose series); RVS (3-dose series)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
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<td>16 d</td>
</tr>
<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis³ (DTaP &lt;7 yrs)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
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</tr>
<tr>
<td>Tetanus, diphtheria, &amp; acellular pertussis³ (Tdap ≥7 yrs)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
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<td>15 d</td>
<td>16 d</td>
</tr>
<tr>
<td>Haemophilus influenzae type b⁴ (Hib)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
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<td>13 d</td>
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<td>15 d</td>
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<tr>
<td>Pneumococcal conjugate⁵ (PCV13)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
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<tr>
<td>Pneumococcal polysaccharide³ (PPSV23)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
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<td>16 d</td>
</tr>
<tr>
<td>Inactivated poliovirus⁶ (IPV) (&lt;18 yrs)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
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<td>16 d</td>
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<tr>
<td>Influenza (IV, LAIV) 2 doses for some: See footnote 8</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
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<td>13 d</td>
<td>14 d</td>
<td>15 d</td>
<td>16 d</td>
</tr>
<tr>
<td>Measles, mumps, rubella⁷ (MMR)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
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<td>14 d</td>
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<tr>
<td>Varicella² (VAR)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
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<td>16 d</td>
</tr>
<tr>
<td>Hepatitis A¹ (HepA)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
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<td>15 d</td>
<td>16 d</td>
</tr>
<tr>
<td>Human papillomavirus¹² (HPV2: females only; HPV4: males and females)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
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<td>16 d</td>
</tr>
<tr>
<td>Meningococcal¹³ (Men-MCV ≥6 weeks; MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)</td>
<td>1 dose</td>
<td>2 d</td>
<td>3 d</td>
<td>4 d</td>
<td>5 d</td>
<td>6 d</td>
<td>7 d</td>
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<td>14 d</td>
<td>15 d</td>
<td>16 d</td>
</tr>
</tbody>
</table>

- Range of recommended ages for all children
- Range of recommended ages for catch-up immunization
- Range of recommended ages for certain high-risk groups
- Range of recommended ages during which catch-up is recommended
- Not routinely recommended

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE (FIGURE 2)).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are in bold.
Pertussis Mortality Trends

- From 1926-1930, 36,013 deaths reported in the United States, primarily in <1 year olds
- From 1990 to 1996, 57 persons died from pertussis
- Reduction in pertussis mortality due to:
  - Vaccination
  - Improved care of infants with disease

Gordon je, am j med sci 1951
Ra haward lancet 1973; 1:873
National Data

- Pertussis rates gradually increased in 1990’s-2000’s
- Combination of increased disease and improved diagnostic capacity

---Infectious Diseases in Children, September 2004
Testing for *B. Pertussis*

- Nasopharyngeal PCR is test of choice
- Introduced in mid-90’s
- Most sensitive in first three weeks of cough
- Sensitivity 70-99%
- Specificity 86-100%
- Pertussis culture or serology are other options

Wendelboe and Van Rie, 2006
With Increased Pertussis Disease Burden, Concerns About Pertussis Vaccine

- Not 100% effective
- Immunity wanes
- May only attenuate disease
- Without boosting, adolescents and adults have no apparent immunity
Epidemiology

- Infants most commonly experience significant morbidity and mortality
- Children 1-5 years most widely affected prior to vaccine
- Increasing data in 1990’s demonstrating pertussis’ presence in the adolescent and adult community
Pertussis in Adolescents and Adults

- During outbreaks, up to 26% of adolescents/adults with cough lasting 1-2 weeks have pertussis
- Patients with pertussis are more likely to have:
  - Severe cough
  - Paroxysmal cough
  - Posttussive emesis

Tdap

- Designed to boost waning immune response to pertussis vaccination
- Vaccine equivalent to Td with addition of:
  - Filamentous hemagglutinin
  - Detoxified pertussis toxin
  - Pertactin
  - May contain fimbriae
Tdap Recommendations in 2005

• Children:
  • Tdap is indicated for a single booster dose at age 11 or 12 years, or catch-up dose later if not given

• Ages 19 and older:
  • Substitute Tdap for one booster dose of Td
Two studies have reviewed Tdap after Td

- Beytout, et al, Vaccine, 2009
- Talbot et al, Vaccine, 2010

- 394 subjects total received vaccine Td then Tdap <2 years apart 18-64 year olds
- Found no increase in adverse events
ACIP Recommendation

Adolescents or adults who have not received a dose of Tdap or for whom vaccine status is unknown should be immunized as soon as feasible. Tdap can be administered regardless of interval since the last tetanus or diphtheria containing vaccine.
Pertussis Seroprotection Rates After Dose 4

% of Subjects

PT  FIA  PRN  FIM

Sanofi Package Insert
Persistence of pertussis antibodies 3 years after Tdap vaccination of adults

Anti-PT antibody GMCs (EU.L/mL)

Anti-FHA antibody GMCs (EU.L/mL)
Pertussis Vaccination and the Carriage State

Recent study evaluated baboons vaccinated with whole cell versus acellular pertussis vaccination
- Both vaccines prevented illness
- Acellular vaccine did not prevent carriage state

Acellular vaccine’s protection against carriage remains uncertain

Warfel et al. PNAS 2013
Number of reported pertussis cases by year of onset -- California 1950-2010*

1950: Previous peak in number of cases: 6,613

1959: Previous peak in incidence: 16.1/100,000

As of 10/26/2010
Pertussis in Washington State Children

[Graph showing pertussis cases and incidence by age and vaccine schedule.]
Changes in Pertussis Reporting by State from 2012 to 2013*

*Data for 2012 and 2013 are provisional and subject to change.
†Cases reported through Week 30 in 2012 were compared with cases reported through Week 30 in 2013; fold-changes were calculated for each state.
Pertussis in California, 2014

- 6,930 cases thus far in 2014
  - 18.1 cases per 100,000
- 199 cases hospitalized
- 37 required intensive care
- 3,629 (69%) of pediatric cases were children/adolescents 7-16 years
- 11% had never received any doses of pertussis-containing vaccine
Pertussis in California, 2014

- Overall pertussis rates are highest for:
  - Infants <1 year of age
  - Adolescents and teens 10-17 years of age

- Rates by race/ethnicity are highest for:
  - Hispanic infants <1 year of age
  - White, non-Hispanic adolescents and teens aged 7-17 years of age
Pertussis in California, 2014

- 89% of cases in infants and children
- Peak age is 15 years
- 352 (7%) of pediatric cases were infants <6 months of age
- 122 (61%) of hospitalized were infants <4 months of age
- One death in a 5 week old infant
• 241 Total Pertussis Cases (closed and under investigation meet case definition)
  • 46 Under 1 year old
  • 213 Under 18 years old
B. Pertussis Transmission

- Spread by droplets from coughing person
- Droplets reach upper respiratory tract of susceptible person
- Patients considered infectious for 21 days after cough begins
- Contact with environmental secretions can also lead to spread of disease
- Standard and droplet precautions should be observed in clinical settings
Pertussis Treatment and Prophylaxis

- By the time of cough, antibiotic therapy does not seem to affect disease process.
- Does reduce communicability in the first three weeks of therapy.
- Multiple studies demonstrate patients *B. pertussis* culture negative at end of treatment.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Azithromycin</th>
<th>Erythromycin*</th>
<th>Clarithromycin</th>
<th>Alternate agent: TMP-SMX†</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 month</td>
<td>Recommended agent for infants &lt;1 month of age; 10 mg/kg per day in a single dose x 5 days§.</td>
<td>40–50 mg/kg per day in 4 divided doses x 14 days</td>
<td>Not recommended.</td>
<td>Contraindicated in infants &lt;2 months of age (risk for kernicterus).</td>
</tr>
<tr>
<td>1–5 months</td>
<td>10 mg/kg per day in a single dose x 5 days.</td>
<td>See above</td>
<td>15 mg/kg per day in 2 divided doses x 7 days.</td>
<td>Contraindicated in infants &lt;2 months of age. For infants aged ≥2 months of age, TMP 8 mg/kg per day; SMX 40 mg/kg per day in 2 divided doses x 14 days.</td>
</tr>
<tr>
<td>Infants aged ≥6 months</td>
<td>10 mg/kg as a single dose on day 1 (maximum 500 mg); then 5 mg/kg per day as a single dose on days 2–5 (maximum 250 mg/day).</td>
<td>40 mg/kg per day in 4 divided doses for 7–14 days (maximum 1-2 g per day)</td>
<td>See above. (maximum 1g/day)</td>
<td>See above.</td>
</tr>
<tr>
<td>and children</td>
<td></td>
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</tr>
<tr>
<td>Adolescents and adults</td>
<td>500 mg as a single dose on day 1 then 250 mg as a single dose on days 2–5.</td>
<td>2g/day in 4 divided doses x 14 days.</td>
<td>1g/day in 2 divided doses x 7 days.</td>
<td>TMP 320 mg/day, SMX 1600mg/day in 2 divided doses x 14 days.</td>
</tr>
</tbody>
</table>
Post-Exposure Prophylaxis

- AAP recommends antibiotic prophylaxis for all close contacts of cases
- PEP recommendation is not affected by immunization status
- Studies show inconsistent effect of PEP

T Murphy et al, MMWR, 2005
Close Contact Definitions

- Household member
- Attending or working in the same childcare setting
- Receiving a cough or sneeze in the face
- Performing a medical examination of the mouth, nose or throat
- Sitting at adjacent desks or the same table at school
- Sharing a confined space with an infectious person for >1 hour
Prophylaxis in an Epidemic

- Public health will prioritize high-risk contacts for postexposure prophylaxis.
- High risk contacts include:
  - Infants
  - Women in third trimester of pregnancy
  - Contacts of above cases
- Low-risk contacts may be advised to monitor for symptoms and seek treatment if symptoms develop.
Healthcare Worker Post-Exposure Prophylaxis

Healthcare workers with unprotected (i.e., unmasked) exposure to pertussis cases may be managed in two ways:
- They may be offered postexposure prophylaxis; or
- They may self-monitor for symptoms for 21 days from the time of exposure
Pertussis and Schools

- High incidence of disease seen in schoolchildren
- Disease seems to be milder in this population
- Both vaccination and postexposure prophylaxis are imperfect
Pertussis and Schools

- Most schoolchildren when diagnosed will have been infectious for two or more weeks.
- Antibiotics may rapidly decrease the infectivity of the patient.
- Many schoolchildren cases will have caught it from school.
Exclusion of Pertussis Cases from School or Daycare

- Exclude case from childcare settings until 5 days of appropriate antibiotic treatment.
- Orange County Public Health will permit cases to attend K-12 school after 3 days of treatment if they are well enough to participate in school activities.
- School exclusion of unvaccinated students is generally not indicated.
Response to Pertussis in Schools

- CDC no longer has a pertussis outbreak definition
- Schools are not required to report individual cases
- Large outbreaks and concerning events should be reported to OCHCA
- In most cases, letters sent to families will be appropriate response
- Do NOT chase every cough
- Children with classic symptoms may need to see a provider
Healthcare Providers and Tdap

- All persons in contact with infants should be up-to-date for pertussis vaccine.

- Although only one dose of Tdap is recommended by ACIP for adolescents and adults, persons may choose to be revaccinated if it has been several years since receipt of Tdap.
Tdap during Pregnancy
Pertussis incidence among infants, 2001-2011

Source: CDC, National Notifiable Diseases Surveillance System, 2011
Pertussis deaths by age group, 2000-2012*

*2012 data are provisional and reflect deaths reported to NNDSS as of October 19, 2012.
Tdap and Pregnancy: Immunizing Pregnant Moms vs. Cocooning

- Immunizing family members in close contact with infants has been advocated by CDC recently
- Vaccinating family members likely prevents disease
- Infrastructure does not exist for implementation on a national level
- Even if executed well, will not protect infants in first few weeks of life
- Immunizing pregnant mothers may be more practical and cost-effective than cocooning
Tdap and Pregnancy Safety

- Killed vaccines are considered to be very safe for pregnant women

- Tetanus and influenza vaccines recommended during pregnancy

- Passive data of pregnant women inadvertently given Tdap indicates no evidence of association with adverse events
# Tdap vaccination leads to higher antibody levels in infants

<table>
<thead>
<tr>
<th>Outcome Antibodies</th>
<th>Mother did not receive Tdap, mean (SEM) n=52</th>
<th>Mother received Tdap, mean (SEM) n=52</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Pearson correlation coefficient (P value&lt;sup&gt;a&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>11.010 (1.796)</td>
<td>28.220 (2.768)</td>
<td>&lt; .001</td>
<td>0.158 (.055)</td>
</tr>
<tr>
<td>FHA</td>
<td>26.830 (4.022)</td>
<td>104.15 (21.664)</td>
<td>.002</td>
<td>0.165 (.045)</td>
</tr>
<tr>
<td>PRN</td>
<td>24.700 (5.765)</td>
<td>333.01 (56.435)</td>
<td>&lt; .001</td>
<td>0.965 (&lt; .001)</td>
</tr>
<tr>
<td>FIM 2/3</td>
<td>82.83 (14.585)</td>
<td>1198.99 (189.937)</td>
<td>&lt; .001</td>
<td>0.293 (&lt; .001)</td>
</tr>
</tbody>
</table>

FHA, filamentous hemagglutinin; FIM, fimbriae; PRN, pertactin; PT, pertussis toxin;

<sup>a</sup> Significant at .05 level.
Pertussis Vaccination and Infant Antibody Levels

- Infant pertactin, fimbriae, and pertussis toxin antibody titers are greater than maternal levels after maternal vaccination.

- Blunting of immune response after infant vaccination series is mild and resolves by third dose.

Halperin et al, ACIP 2013
Infant Cases in Current California Outbreak

Of the 100 (40%) cases <4 months of age whose mothers vaccination history was available:

- 12 (12%) mothers had received Tdap during the third trimester of pregnancy between 27-36 weeks gestation
- 20% of mothers overall in California are getting vaccinated during pregnancy
ACIP Recommendation

Health care providers should administer Tdap during each pregnancy, preferably at 27-36 weeks gestation.