Current Issues in Vaccine-Preventable Diseases

Juventila Liko
Oregon Immunization Program

Hospitalized for 3 months
- Intensive Care Unit for 75 days
- Mechanical ventilation for 72 days
- ECMO for 43 days

Complications
- Kidney failure
- Stroke

Lab reports — *Bordetella pertussis*

Exposure history
- Siblings vaccinated
- Mother declined vaccine and noted coughing

Hospitalization costs = $1,500,000

At 23 mo of age, persistent language and right-sided motor deficits in the distribution of stroke

In 2012, an 18 day old baby was brought to a local emergency department for a choking episode.

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In 2012, an 18 day old baby was brought to a local emergency department for a choking episode.

Pictured: infant survivor of pertussis. As part of her treatment, she received extracorporeal membrane oxygenation and dialysis.

Source: CDC

Source: PKIDs
Public Health Importance of Pertussis

- Highly contagious respiratory disease
  - *Bordetella pertussis*
- Severe, debilitating cough illness (“100 day cough”) in persons of all ages
- Highest morbidity and mortality among infants
- Poorly controlled, despite high vaccine coverage

Reported Pertussis Incidence Rates in the United States and Oregon, 1995–2016

- Highest annual tally since 1953

Estimate the effectiveness of currently recommended pertussis vaccines — DTaP in infancy and early childhood and Tdap in adolescence
### Pertussis among children and adolescents 2 months – 19 years, by vaccination status, Oregon, 2012

**Cumulative Incidence per 100,000 by vaccination status**

<table>
<thead>
<tr>
<th>Age</th>
<th>UTD</th>
<th>Partial</th>
<th>Unvax</th>
<th>RR</th>
<th>RR</th>
<th>VE(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–3 mo</td>
<td>225.1</td>
<td>833.3</td>
<td>3.7</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–5 mo</td>
<td>139.9</td>
<td>285.7</td>
<td>493.8</td>
<td>3.5</td>
<td>2.0</td>
<td>72</td>
</tr>
<tr>
<td>6–14 mo</td>
<td>80.7</td>
<td>145.6</td>
<td>572.7</td>
<td>7.1</td>
<td>1.8</td>
<td>86</td>
</tr>
<tr>
<td>15 mo–47 mo</td>
<td>39.9</td>
<td>119.3</td>
<td>823</td>
<td>20.6</td>
<td>3.0</td>
<td>95</td>
</tr>
<tr>
<td>4–6 yr</td>
<td>47.8</td>
<td>64.3</td>
<td>430.6</td>
<td>9.0</td>
<td>1.3</td>
<td>89</td>
</tr>
<tr>
<td>7–10 yr</td>
<td>69.3</td>
<td>144.4</td>
<td>414.6</td>
<td>6.0</td>
<td>2.1</td>
<td>83</td>
</tr>
</tbody>
</table>

### Pertussis among children and adolescents 2 months – 19 years, by vaccination status, Oregon, 2012

**Cumulative incidence per 100,000 by vaccination status**

<table>
<thead>
<tr>
<th>Age</th>
<th>UTD</th>
<th>Unvaccinated</th>
<th>RR</th>
<th>VE(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11–12 yr</td>
<td>57.9</td>
<td>195.1</td>
<td>2.9</td>
<td>65</td>
</tr>
<tr>
<td>13–16 yr</td>
<td>64.4</td>
<td>105.3</td>
<td>1.9</td>
<td>47</td>
</tr>
<tr>
<td>17–19 yr</td>
<td>12.8</td>
<td>37.1</td>
<td>2.9</td>
<td>65</td>
</tr>
</tbody>
</table>


### Reported Pertussis Incidence, by Age and Ethnicity Oregon, 2012

- Hispanic
- Non-Hispanic

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8/23/2017
**Risk Factors for Pertussis in Hispanic Infants - Metropolitan Portland, Oregon, 2010–2012**

- Pertussis rates among Hispanic infants were greater than non-Hispanic infants aged <6 months
- Similar vaccination rates among Hispanic and non-Hispanic infants aged <6 months
- Household size of >4 persons is a potential risk factor for pertussis
- Greater proportion Hispanic infants in households >4


**Assessment of risk following childhood pertussis vaccination**

- Pertussis surveillance data for cases
- Children with 5th DTaP dose received aged 4–6 years
- Minnesota: 224,378 subjects and 458 cases
- **Oregon**: 179,011 subjects and 89 cases

**Pertussis, by time since 5th DTaP**

The Multnomah County Health Department conducts enhanced pertussis surveillance in the Portland, Oregon, metropolitan area.

During 2010–2012, 98.7% (n = 624) of patients with confirmed pertussis in our cohort had vaccination, treatment, demographic, and outcome information. Among these patients, 45% (n = 286) were ACIP up to date with vaccinations. Vaccinated cases were significantly less likely to be hospitalized or develop severe illness. ACIP up-to-date patients stopped coughing significantly more rapidly than unvaccinated patients.

*Clin Infect Dis. 2014 Jun;58(11):1523-9*
Chart review on hospitalized infants with pertussis, Oregon, 2/2009 – 2/2013

- 285 infant cases reported with pertussis
- One infant <6 months old died
- 1462 non-infant cases and only 19 (1%) hospitalized
- 94 (33%) infant cases hospitalized
- Length of stay (LOS); median of 4 (range, 1 – 128) days; 805 hospital days
- 59 (63%) of the infant cases were <2 months old

Chart review on hospitalized infants with pertussis, Oregon, 2/2009 – 2/2013

- 7 (7%) infants required mechanical ventilation; duration: 12 (4 - 83); 185 days
- Two infants supported with extracorporeal membrane oxygenation (ECMO) for a total of 87 days
- One infant discharged on oxygen
- One infant discharged with a tracheostomy to be ventilated mechanically for 10 hrs. each night. The infant spent 128 days in the hospital, was mechanically ventilated for 83 days and received ECMO for 44 days
High effectiveness of maternal pertussis vaccination -- United Kingdom

Observational study
- Vaccine screening method
  - For infants <3 mths of age at onset of pertussis

<table>
<thead>
<tr>
<th>Vaccine effectiveness</th>
<th>Timing of maternal vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>91% (81-95)</td>
<td>At least 28 days before birth</td>
</tr>
<tr>
<td>38% (26-50)</td>
<td>0-4 days before or 1-13 days after birth</td>
</tr>
</tbody>
</table>

Case-Control study
- Cases: infants <2 mths of age at onset pertussis infection
  - Unadjusted VE = 91% (77%-97%)
  - Adjusted VE = 93% (81%-97%)


Maternal pertussis vaccination to prevent pertussis in babies -- California

Effectiveness of prenatal versus postpartum Tdap vaccination in preventing infant pertussis
- Tdap vaccination during 27 – 36 weeks gestation was 85% more effective than postpartum vaccination at preventing pertussis in infants < 8 weeks of age

Effectiveness of prenatal Tdap vaccination on pertussis severity in infants
- Older when developed pertussis
  - Median: 45 days vs. 35 days; p=0.03
- Less likely have classic pertussis symptoms
- Significantly lower risk of hospitalization and ICU admission
  - Hospitalization: RR 0.5; p<0.001
  - ICU: RR 0.8; p=0.01

Winnable Battles in Pertussis

- Vaccination is our best prevention tool
- Vaccinating pregnant women every pregnancy
- A baby’s first dose of pertussis vaccine should be the one its mother gets
- Timely vaccination of infants
- Maximizing other current pertussis vaccination strategies

Vaccination remains the single most effective means of preventing pertussis

One is better off with vaccination than without it. Declining the whooping cough vaccine carries a whopping risk for whooping cough.

Measles

Source: CDC

Measles by country of importation: 1997–2015

https://www.cdc.gov/mmwr/volumes/65/wr/mm6501a3.htm

https://www.cdc.gov/mmwr/volumes/65/wr/mm6501b3.htm
Subacute sclerosing panencephalitis (SSPE)

Previously healthy school-aged child born in Asia and admitted with progressive and severe encephalopathy.

4 months prior, began nodding off while doing homework, started having difficulty with math (previously math whiz) and having shoulder shrugs. Continued getting worse, child would start falling asleep while walking and then would trip.

3 months prior, started having involuntary hand/arm movements, jerking every 20 min. Hand movement started increasing every 5 min, still playful and with a good sense of humor.

1 month prior, started to shuffle and walking on tip-toes, started crying continuously and began to get angry with the family, refused to walk and slept a lot and able to say only a few words. Started using diapers.

Subacute sclerosing panencephalitis (SSPE)

Admission month, progressive degeneration of mental status, making abnormal movements of arms and legs, looking around but not tracking, occasionally crying out, not responsive to questions, not following commands, withdrawn to touch and pain. Unresponsive, spastic and rigid

EEG: abnormal slowed activity

Lumbar puncture: Highly positive measles IgG in CSF

This is consistent with SSPE in both time course (measles at <2 yrs of age, presenting with symptoms ~10 years later) and presentation (myoclonus progressing to complete neurologic decline)

Treatment: palliative

Prevention: vaccination

Prognosis: Poor

Impact of Two Measles Cases in 2007

- Hospital
  - ICS
  - 1600 titers (in a 2 wk period)
  - 97% of HCWs were immune
  - Cost of titers $40,000
  - 10 HCWs on furlough for several days
  - 3 HCWs on furlough for 21 days
  - 63 shots given
  - Now immunity to measles required
  - Infection education module updated
  - Isolation & transferring process reviewed
  - $100,000

- LHD
  - ICS
  - 2 cases & 1 suspect
  - 90% were immune
  - 4 shots given
  - $50,000

- State
  - AOC
  - $20,000

This highlights the need to maintain very high vaccine coverage.

And if we can achieve that, we will have done a far, far better thing than... well, than a lot of other things we might’ve done.

Mumps

Mumps Cases in U.S., by Year

https://www.cdc.gov/mumps/outbreaks.html
Mumps Disease

- Acute, viral illness that classically presents with parotitis (60%-70%)
- Non-specific respiratory symptoms
- During pre-vaccine era, 15% to 27% of cases asymptomatic

<table>
<thead>
<tr>
<th>Complications</th>
<th>Unvaccinated (%)</th>
<th>Vaccine era (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orchitis</td>
<td>up to 30%</td>
<td>3–11</td>
</tr>
<tr>
<td>Mastitis</td>
<td>up to 30%</td>
<td>≤1</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>4</td>
<td>≤1</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>4</td>
<td>≤0.1</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>1–15</td>
<td>0.2–0.5</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>0.03–0.5</td>
<td>0–0.3</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>5.5</td>
<td>&lt;1–2</td>
</tr>
</tbody>
</table>

VPM Manual; 2017 ACIP meeting; IAC

Reported Mumps Cases, United States, Vaccine Era, 1968-2016

Source: National Notifiable Disease Surveillance System (passive surveillance); 1968 data is preliminary (Feb 5, 2013) and subject to change.
**Vaccine Performance during an Outbreak, Kansas University, 2006**

- Cases were more likely (OR=2.46; 95% CI, 1.25-4.82) to have received their second dose of MMR ≥ 10 years earlier.
- The odds of being a case increased with each year increase in time from receipt of the second dose of MMR (OR=1.36; 95% CI,1.10-1.68) among cases and roommates aged 18-19 years but not among those aged ≥ 20 years.
- Students aged 18-19 years had a higher risk of mumps (RR=3.14; 95% CI, 1.60-6.16), compared with students aged > 22 years; women living in dormitories had increased risk of mumps (RR=1.96; 95% CI,1.01-3.76), compared with men not living in dormitories.
- Low attack rate (2%-8%) among roommates with 2 doses of vaccine.

**Mumps Outbreaks in Orthodox Jewish Communities, 2009 – 2010**

- 3502 cases reported in NYC.
  - 87% of cases in Orthodox Jewish community.
  - Adolescent (age 13-17 years) males the most affected group.
  - 89% had 2 doses of MMR vaccine.
  - Unique schools and large households; prolonged, intense exposures likely overcame protection afforded by the vaccine.
- Analysis of cases among students in grades 6–12 did not find time since most recent dose to be associated with mumps.
  - Intensity of exposure was predictive: Risk of mumps increased with increasing number of mumps cases in the class (≥8 vs. ≤3 cases: boys aRR = 3.1; girls aRR = 2.6) and household (>1 vs. 0 cases: boys aRR = 4.3; girls aRR = 10.1).

**Mumps Outbreak in a Highly Vaccinated Island Population, Guam, 2009 – 2010**

- Guam: 505 cases.
- The highest AFRs occurred in ethnic minority populations with the highest household crowding indices.
- Pohnpeians and Chuukese had the highest RR (55 and 20), largest household sizes (mean: 7 members) and highest crowding indices (mean: 3 persons/bedroom).
- 57% school-aged cases, 93% 2-dose vaccinated.
- This outbreak may have persisted due to crowding at home and high student contact rates.
U.S. Mumps Cases, 2016

- Increase in the number of reported cases and outbreaks
  - Genotype G virus
- Age range: <1 yr to 88 yrs old
  - Median age: 22 yrs
- 79% reported vaccination status
  - 85% (3792) vaccinated
  - 69% (2628) 2 or more doses
- >40 reported outbreaks
  - Majority in university settings
  - At least 5 in close-knit community settings
- 2016: 40% (2287 of 5,642) were in Arkansas

Reported U.S. Mumps Incidence Rate by Year and Age Group, 2010-2016

Source: Nakia Clemmons, CDC & IAC

https://www.cdc.gov/mumps/outbreaks.html

Mumps Cases as of July 13, 2017

https://www.cdc.gov/mumps/outbreaks.html

Reported Mumps Cases, Oregon, 1915–2017

Mumps Cases, Oregon, 2016 – 2017

- From Jan 2016 – July 2017, 81 cases reported
- Age range: 3 to 70 yrs. old
  - Median age: 23 yrs
- 8 developed orchitis, 1 temporary hearing loss and 1 hospitalized
- 4 reported outbreaks
  - Marion Co – 26 cases
  - Washington Co – 11 cases
  - Multi-county (associated with wrestling) – 10 cases
  - Union Co – 14 cases
  - Other – 16 cases
- Among 20 cases ≤ 19 years of age, 26 (74%) were UTD on vaccination.

Factors that May Contribute to the Increasing Number of Mumps Outbreaks

- Vaccine effectiveness
  - 1 dose: ~77% (49%-91%)
  - 2 doses: ~88% (66%-95%)
- Waning of vaccine-induced immunity
  - Serologic studies suggest waning. No established correlates of protection, implications of declining titer uncertain
  - Epidemiologic studies suggest waning. Evidence still limited
  - Waning of immunity does not explain the general geographical focal nature and that the oldest vaccinated cohorts not always most affected
- Vaccine-induced immunity less effective against other strains?
  - No evidence to date, mumps vaccine (genotype A) produced antibodies that effectively fought the genotype G mumps virus
- Force of infection
  - Outbreaks in settings with high population density and contact rates that facilitate transmission (e.g., college campuses, close knit communities)

Mumps in Japan

Source: 2017 ACIP Meeting

Source: 2017 ACIP Meeting

Source: 2017 ACIP Meeting
The vaccine isn’t perfect, but perhaps 88% effectiveness is better than bupkus.

The recent outbreaks in the U.S. and Oregon indicate the need to maintain very high 2-dose vaccination coverage.