Risk of Vaccine Preventable Infections in Children

Ann M Loeffler, MD

April 30, 2017
Disclosures and Objectives

- No financial objectives
- Objectives:
  - Describe the current risk of vaccine preventable infections
  - Use concepts to appropriately manage children who have fever without source or pneumonia
  - To be prepared to respond after exposure to a vaccine preventable infection
  - To review the impact of vaccines on the incidence of common pediatric infections
The Pink Book

Epidemiology and Prevention of Vaccine-Preventable Diseases

The Pink Book Home

Front Matter

Chapters +

 Appendices +

Errata, Updates, and Clarifications

Supplement

CDC > The Pink Book Home

Front Matter

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E-mail address for comments, questions or suggestions about the contents of this book:

Immunize.org

Resource for families:
http://www.boostoregon.org/community-workshops/
<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>
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<tbody>
<tr>
<td><strong>Hepatitis B</strong> (HepB)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>←2&lt;sup&gt;nd&lt;/sup&gt; dose→</td>
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<td>←3&lt;sup&gt;rd&lt;/sup&gt; dose→</td>
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<tr>
<td>Rotavirus&lt;sup&gt;2&lt;/sup&gt; (RV)</td>
<td></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>See footnote 2</td>
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<td>RV1 (2-dose series); RV5 (3-dose series)</td>
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<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis&lt;sup&gt;3&lt;/sup&gt; (DTaP; &lt;7 yrs)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
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<td>See footnote 4</td>
<td>←3&lt;sup&gt;rd&lt;/sup&gt; or 4&lt;sup&gt;th&lt;/sup&gt; dose, See footnote 4→</td>
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<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
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<tr>
<td>Inactivated poliovirus&lt;sup&gt;6&lt;/sup&gt; (IPV; &lt;18 yrs)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
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<td>←3&lt;sup&gt;rd&lt;/sup&gt; dose→</td>
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<td>Annual vaccination (IIV) 1 or 2 doses</td>
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<td>Measles, mumps, rubella&lt;sup&gt;8&lt;/sup&gt; (MMR)</td>
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<td>←2 dose series, See footnote 10→</td>
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<tr>
<td>Vaccines</td>
<td>18 mos</td>
<td>19-23 mos</td>
<td>2-3 yrs</td>
<td>4-6 yrs</td>
<td>7-10 yrs</td>
<td>11-12 yrs</td>
<td>13-15 yrs</td>
<td>16 yrs</td>
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<td>Hepatitis B¹ (HepB)</td>
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<td>Diptheria, tetanus, &amp; acellular pertussis³</td>
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<td>(DTaP-&lt;7 yrs)</td>
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<td>Pneumococcal conjugate⁵ (PCV13)</td>
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<td>Inactivated poliovirus⁶ (IPV&lt;18 yrs)</td>
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<td>Influenza⁷ (IIV)</td>
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<td>Annual vaccination (IIV) 1 or 2 doses</td>
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<td>Annual vaccination (IIV) 1 dose only</td>
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<td>Meningococcal¹¹ (Hib-MenCY≥6 weeks; MenACWY-D≥9 mos; MenACWY-CRM≥2 mos)</td>
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<td>1⁰ dose</td>
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<td>2⁰ dose</td>
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<td>Tetanus, diptheria, &amp; acellular pertussis¹²</td>
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<td>(Tdap ≥7 yrs)</td>
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<td>Human papillomavirus¹³ (HPV)</td>
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<td>See footnote 13</td>
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<td>Meningococcal B¹¹</td>
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<td>Pneumococcal polysaccharide⁴ (PPSV23)</td>
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<tr>
<td>Vaccine</td>
<td>US</td>
<td>Range of states</td>
<td>Oregon</td>
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<tr>
<td>DTaP ≥ 4 doses</td>
<td>84.6%</td>
<td>76.4–92.0 %</td>
<td>85.8%</td>
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<tr>
<td>MMR ≥ 1 dose</td>
<td>91.9%</td>
<td>83.4–97.5 %</td>
<td>94.1%  (85)</td>
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<tr>
<td>Hep B birth dose</td>
<td>72.4%</td>
<td>49.4–87.5%</td>
<td>72.5%  (59)</td>
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<tr>
<td>Hep A ≥ 1 doses</td>
<td>85.8 %</td>
<td>41.2–72.8 %</td>
<td>61.8%</td>
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<tr>
<td>Combined (“up to date”)</td>
<td>72.2 % (up from 71.6%)</td>
<td>64.4–80.6 %</td>
<td>67.4%</td>
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</tbody>
</table>

National Immunization Survey - OR rates up this year; combined rate is still near the bottom!
In Oregon, kids entering kindergarten are required to be protected from these 11 infections OR have a signed non-medical waiver paper or printout from the state website.
Est % of kindergartners who have at least one vaccine exemption

Median 1.7%
Fever vaccines

- Hemophilus influenza type B
  > Almost 99.9% reduction in cases since vaccine licensure

- Pneumococcus
  > Invasive pneumococcal disease decreased
    ▪ 100 cases per 100,000 people in 1998 to 9 cases per 100,000 in 2015
    ▪ 1998 – 2012: Serovars in PCV 13: 91 → 2 cases / 100,000
  > 97 – 99% reduction in cases caused by the serovars in PCV 7

- Meningococcus
  > 74% reduction in C&Y serogroups among 11 – 15 yr olds
  > 27% reduction in C&Y among 15 – 18 year olds
  > 2006 – 2010 30 cases of meningococcal disease in vaccinated (same case fatality rate)

PCV7 introduction

PCV13 introduction for children

*PCV13 serotype: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

Active Bacterial Core surveillance data, 1998–2015, unpublished
Fever vaccines

- *Hemophilus influenzae* type B

- Before the development of vaccine, HIB was the leading cause of bacterial meningitis
- It also causes pneumonia (15%), bacteremia (2%), bone and joint infections, epiglottitis (17%); buccal cellulitis and others
- Before vaccine licensure 1 in 200 children developed a HIB serious bacterial illness (SBI)
- 95% of invasive hemophilus disease is caused by type B

20 K cases / yr
1000 deaths / yr

25 cases / yr (> 99% reduction)
HIB Vaccine

- In 1985, a polysaccharide vaccine was licensed. Unfortunately, polysaccharide vaccines are not effective until at least 18-24 mo (after the peak age of invasive HIB disease)
- In late 1987 a conjugate vaccine was licensed.
  - More than 95% of infants develop protective antibody
  - Clinical efficacy 95% to 100%.
- When vaccines are given in the arm - they make IgG antibodies
- It was a MIRACLE that from early on, we saw a “herd effect” for HIB vaccines
- Even children who had not been vaccinated had less disease
- This was truly a game changer. Unlike pneumococcal bacteremia – 95% of HIB disease was invasive.
- In late 2008 / early 2009 12 cases of invasive disease in MN and PA in unvaccinated / undervaccinated kids – four deaths
HIB Disease

- Now estimated that about half of invasive hemophilus disease in < 5 year olds is HIB (half is other or non-typeable)
- Estimated 27 cases Hib / year in 2011
  > 2/3 undervaccinated
  > 1/3 fully vaccinated – not clear why
- Exposure factors: ** contact with a case
  > household crowding,
  > large household size,
  > child care attendance,
  > low socioeconomic status / parental education levels
  > school-aged siblings.
  > Hispanics and Native Americans
  > chronic disease (e.g., sickle cell anemia, HIV, splenectomy, antibody deficiency syndromes, malignancies - especially during chemotherapy)
HIB - Conclusion

- Occult bacteremia (bacteremia without focus) is unusual with Hib
- Consider Hib disease if you are treating an unvaccinated child less than two years of age / with a predisposing condition / OR contact with a Hib case with
  - Meningitis - if gram stain coccobacillary
  - Epiglottitis
    - Pneumonia
    - Bone or joint infection
  - Buccal cellulitis / preseptal cellulitis

- Dexamethasone is shown to reduce neurologic sequelae in meningitis caused by Hib
- Often beta lactamase producing - use a third generation cephalosporin
- IN GENERAL: do not change your management for undervaccinated for HIB
Pneumococcal vaccine

- *Streptococcus pneumoniae* (AKA pneumococcus) - 93+ serotypes, but only a few cause invasive disease in a given geographic area. 10 serotypes account for 62% of invasive disease worldwide.
- In 2011 in the US:
  > 36,850 cases and 4,250 deaths from invasive pneumococcal diseases
- Polysaccharide vaccine first licensed in 1977
- 7-valent conjugate vaccine licensed in 2000
- 13-valent conjugate vaccine licensed in 2010
- Diseases: (Before conjugate pneumococcal vaccine)
  > Bacteremia without known site infection 13,000 cases / yr
  > Pneumonia (with or without bacteremia)
  > Meningitis (the leading cause) 700 cases / yr
  > Otitis media 5,000,000 cases / yr
  > Sinusitis
- 97-99% reduction in invasive disease caused by the original 7 types
Pneumococcal vaccine

- Trouble in paradise:
  - Replacement strains, especially 19 A, increased after licensure of the 7-valent vaccine
- 13-valent conjugate vaccine licensed in 2010
  - In 2008, these 13 strains accounted for 61% of invasive disease in children less than 5 years of age
  - 19 A accounted for 43% of cases

- Prevnar-13
  - 46% protective against strain pneumonia in 65 year olds

- National Estimates of Pneumococcal Invasive Disease

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
<th>Deaths</th>
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<tbody>
<tr>
<td>2009</td>
<td>44K (14.3/100K)</td>
<td>5 K (1.6 / 100K)</td>
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<td>2011</td>
<td>37K (12 / 100 K)</td>
<td>4.2 K (1.4 / 100K)</td>
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<td>2013</td>
<td>34 K (11 / 100 K)</td>
<td>3.7 K (1.2 / 100K)</td>
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</table>
the effectiveness of a vaccine may be impacted by the organism's ability to switch the serotype of its capsule. Capsular switching occurs when the genes encoding one capsular serotype are exchanged, via transformation and recombination, with the genes encoding a different capsular serotype. The most concerning of the capsular switches is the vaccine-to-nonvaccine serotype switch, during which a vaccine serotype capable of causing invasive disease acquires the capsule of a nonvaccine serotype; this contributes to serotype replacement disease through the development of “vaccine escape” serotypes. Studies have shown that the emergence of several of the clones of replacement serotype 19A developed through the process of capsular switching.

The development of vaccine escape serotypes by genetic recombination at the capsular locus has the potential to significantly reduce the long-term effectiveness of pneumococcal conjugate vaccines
Oregon pneumococcal surveillance – Portland metro

The graph shows the incidence per 100,000 of pneumococcal cases in different age groups from 1998 to 2015. The x-axis represents the years from 1998 to 2015, and the y-axis represents the incidence per 100,000. The graph includes age groups 0-4, 5-17, 18-34, 35-49, 50-64, 65-79, and 80+. There are two key events highlighted:

- PCV7 licensed
- PCV13 licensed
### Portland Metro Area

#### Table 4: Antibiotic Susceptibility of IPD Isolates, 2015 (n=104)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Susceptible (%)</th>
<th>Intermediate Resistance (%)</th>
<th>Full Resistance (%)</th>
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<tbody>
<tr>
<td>Levofloxacin</td>
<td>100</td>
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<tr>
<td>Linezolid</td>
<td>100</td>
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<td>Synercid</td>
<td>100</td>
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<td>Vancomycin</td>
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<td>Ceftriaxone</td>
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<tr>
<td>Chloramphenicol</td>
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<td>Amoxicillin</td>
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<td>Cefotaxime</td>
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<td>Cefuroxime</td>
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<td>Clindamycin</td>
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<td>Meropenem</td>
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<td>Penicillin*</td>
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<td>Tetracycline</td>
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<td>Erythromycin</td>
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<td>Penicillin†</td>
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<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>86</td>
<td>13</td>
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</table>

*Based on old breakpoints $S<=0.06; 0.12<=I<=1; R>=2$  
† Based on 2012 CLSI (Clinical and Laboratory Standards Institute) breakpoints $S<=2; I=4 ; R>=8$
## Legacy 2015 pneumococcal susceptibility

- All pediatric isolates (not just invasive isolates)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>% susceptible</th>
</tr>
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<tbody>
<tr>
<td>Penicillin (not meningitis)</td>
<td>96%</td>
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<td>Penicillin (meningitis break point)</td>
<td>65%</td>
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<tr>
<td>Ceftriaxone (not meningitis)</td>
<td>100%</td>
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<tr>
<td>Ceftriaxone (meningitis break point)</td>
<td>93%</td>
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<tr>
<td>TMP SMZ</td>
<td>81%</td>
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<tr>
<td>Erythromycin</td>
<td>74%</td>
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</table>
Meningococcal vaccine

- *Neisseria meningitidis* - Serogroups A, B, C, W & Y
- Causes sepsis (meningococcemia – purpura fulminans), meningitis, pneumonia, arthritis
- Vaccine first licensed in US in 1974 (polysaccharide C)
- Quadrivalent conjugate vaccine licensed in 2005
- Serogroups B, C & Y are most common in US
- B - 60% of cases in < 5 yrs
- C, W & Y – 73 % > 11 yrs
- 2006-10 – 30 breakthrough cases (despite vaccine)
- 2015 type B vaccine licensed
Meningococcal disease

- Type B accounts for more than half of Oregon cases
- 7 cases associated with the U of Oregon starting Jan - May 2015
- 3 cases at Oregon State December 2016 – March 2017
- About 11K of 30K students vaccinated

Figure 1. Serogroup B meningococcus cases, by year, Oregon, 1994–2014
Meningococcal – post exposure prophylaxis

- High risk contacts
  - Household contacts
  - Child care contacts within 7 days
  - Direct exposure to secretions (including mouth to mouth resusc)
  - Sleeping in same dwelling frequently in last 7 days
  - Outbreak settings after d/w public health

- Close contacts should receive prophylaxis
  - IM ceftriaxone x 1
  - Ciprofloxacin PO x 1
  - Rifampin PO x 4 doses

- Vaccine campaigns
Fever without source

- Before the “fever vaccines” were licensed, we obtained blood cultures, considered antibiotics on most children up to 2 - 3 years of age.
  - High rates of Hib invasive disease
  - High rates of pneumococcal bacteremia
- Now there is so little invasive pneumococcal / Hib disease
  - FWS is much more likely to be viral in all children & more so in vaccinated children
- Ill appearing children should still be evaluated for bacterial source
  - Consider CBC / Blood culture
  - Urine studies
  - Careful exam for meningitis / bone or joint disease / cellulitis / lymphadenitis
  - LP before antibiotics in particularly ill children, children with meningeal signs or neurologic changes or in infants too young to reliably exhibit meningeal signs
Most common SBI

- Febrile UTI / pyelonephritis is now the most common SBI
- Because it is rare to have a bad consequence of delayed treatment of UTI, some distinguish SBI from IBI (European term)

**Figure 2**
Probability of UTI Among Febrile Infant Girls\(^{28}\) and Infant Boys\(^{30}\) According to Number of Findings Present. \(^a\)Probability of UTI exceeds 1% even with no risk factors other than being uncircumcised.
Young infants

- Group B strep screening has markedly diminished rate of early onset neonatal sepsis
- Late onset neonatal sepsis > 3-7 days of age has not declined
- Fever vaccines have little impact on neonatal disease
- Clinical scoring systems have been refined and now many children between 29 & 90 days of age with fever do not get full lab evaluation or antibiotics
- Now, we (should) obtain cultures and give antibiotics for all febrile children < 29 days (no vaccines yet)
- National “REVISE” study by AAP seeks to treat fewer babies with abx
Role of vaccination status in decision making

- Pneumococcal meningitis in Utah 1997 – 2010
  - 46 children had pneumococcal meningitis after PCV7 was licensed
    - 28 eligible for vaccine
    - 26 vaccine records available
      - 46% (n=12) had received all vaccines 2 of these were PCV7 serotypes
      - 54% (n=15) had not been vaccinated 6 of these were PCV7 serotypes
  - Stockman Pediatrics 2013:132:421-8

- **This and other studies have shown less decline in meningitis cases after pneumococcal vaccine than bacteremia and other SBI**

- Unvaccinated children 6.5 times more likely to be hospitalized for invasive pneumococcal disease or lobar pneumonia compared with immunized age-matched controls.
  - Glanz Vaccine 2011;29:994-9
Role of vaccination status in decision making

- While there is more risk of HIB disease without vaccination, there is so much herd immunity, that changing strategy based on HIB Vaccination doesn’t make sense.
- There is an increased risk of pneumococcal disease in unvaccinated children, but occult bacteremia with pneumococcus is self-limited in 95% of children.
- It would not be unreasonable to treat vaccinated and unvaccinated children in the same way – perhaps with informed consent of the parents.
- OR - CBC / blood culture in unvaccinated children and ceftriaxone for infants over 90 days whose WBC is over 15,000.
- I have seen recommendations suggesting low risk treatment only for children who have gotten one or two sets of vaccines.
Community Acquired Pneumonia

- Older studies of CAP revealed 20 – 40% of pneumonia was caused by *S. pneumonia*

- Two recent studies of CAP in the modern vaccine era have shown remarkable results - viruses cause most pediatric pneumonias

- Both studies did elaborate micro tests of
  - blood / nasopharyngeal / endotracheal aspirate / pleural fluid
  - Cultures / PCR / serologies

- Norwegian study published in 2016 (enrollment 2012-14)
  - 265 episodes of pneumonia – clinic and hospitalized children
  - 85% of children in their area have received the pneumococcal vaccine
  - 75% of CAP were viral (alone or mixed)
  - 63% were viral without bacterial component
Norwegian study (clinic and hospital)

- 265 cases of clinical LRI and pneumonia on chest radiograph

### TABLE 3. Etiological Agent and Proportion of Obtained Microbiological Specimens in 265 Cases of CAP by Age

<table>
<thead>
<tr>
<th></th>
<th>&lt;2 yr (n = 127)</th>
<th>2–5 yr (n = 98)</th>
<th>&gt;5 yr (n = 40)</th>
<th>Total (n = 265)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogen detected (%)</td>
<td>114 (89.8)</td>
<td>82 (83.7)</td>
<td>27 (67.5)</td>
<td>223 (84.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Single infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral (%)</td>
<td>65 (51.2)</td>
<td>37 (37.8)</td>
<td>8 (20)</td>
<td>110 (41.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Bacterial† (%)</td>
<td>2 (1.6)</td>
<td>6 (6.1)</td>
<td>1 (2.5)</td>
<td>9 (3.4)</td>
<td>0.27</td>
</tr>
<tr>
<td>Atypical bacterial† (%)</td>
<td>0</td>
<td>1 (1)</td>
<td>12 (30)</td>
<td>13 (4.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mixed infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral–viral (%)</td>
<td>28 (22.1)</td>
<td>30 (30.6)</td>
<td>0</td>
<td>58 (21.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Viral–bacterial†‡ (%)</td>
<td>17 (13.4)</td>
<td>6 (6.1)</td>
<td>3 (5)</td>
<td>25 (9.4)</td>
<td>0.12</td>
</tr>
<tr>
<td>Viral–atypical bacterial†‡ (%)</td>
<td>2 (1.6)</td>
<td>2 (2)</td>
<td>3 (7.5)</td>
<td>7 (2.%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Bacterial–bacterial§ (%)</td>
<td>0</td>
<td>0</td>
<td>1 (2.5)</td>
<td>1 (0.4)</td>
<td>—</td>
</tr>
<tr>
<td>Specimens obtained</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngeal PCR (%)</td>
<td>124 (97.6)</td>
<td>93 (94.9)</td>
<td>38 (95)</td>
<td>255 (96.2)</td>
<td>0.51</td>
</tr>
<tr>
<td>Paired sera (%)</td>
<td>101 (79.5)</td>
<td>76 (77.6)</td>
<td>34 (85)</td>
<td>211 (79.6)</td>
<td>0.62</td>
</tr>
<tr>
<td>Blood culture (%)</td>
<td>92 (72.4)</td>
<td>88 (89.8)</td>
<td>36 (90)</td>
<td>216 (81.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Berg* Pediatr Infect Dis J 2016;35:e69–e75
50% of kids < 2 yr received a full course of antibiotics

85% of kids > 5 yrs received a full course of antibiotics
US CAP study of hospitalized children

- Memphis, Nashville and Salt Lake City hospitalized children
- Enrollment Jan 2010 – June 2012 (PCV 13 licensed Feb 2010)
- 2358 children with radiographic pneumonia
- 2222 had clinical specimens collected
  > 1802 (81%) had one or more pathogen identified
    - 1472 (66%) had only viruses ID
    - 175 (8%) had only a bacteria ID
    - 155 (7%) had mixed viral / bacterial infection

A Detection of Bacterial and Viral Pathogens

- No pathogen
- Bacterial pathogen only
- Bacterial–viral co-detection
- Viral–viral co-detection
- One viral pathogen only

**Age Group (yr)**

- 0–17 (N=2222)
- <2 (N=980)
- 2–4 (N=559)
- 5–9 (N=408)
- 10–17 (N=275)
Note: rhinov + in 17% controls
Other pathogens

- *Staphylococcus aureus*  n = 22 children  (0.86%)
  - MRSA  n = 17
  - MSSA  n = 5
- *Streptococcus pyogenes*  n = 16
- Viridans streptococci  n = 14
- *Chlamydophila pneumoniae*  n = 12
- *Haemophilus influenza*  n = 9
- other gram-negative bacteria  n = 9
- other streptococcus species  n = 4
- histoplasma  n = 2
## Estimated cases / 10,000 children

<table>
<thead>
<tr>
<th>Pathogen detected</th>
<th>Estimated cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory syncytial virus</td>
<td>4.6 (4.3–5.1)</td>
</tr>
<tr>
<td>Human rhinovirus</td>
<td>4.1 (3.7–4.4)</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>1.9 (1.6–2.1)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>1.6 (1.4–1.8)</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>1.4 (1.2–1.6)</td>
</tr>
<tr>
<td>Influenza A or B virus</td>
<td>1.1 (0.9–1.3)</td>
</tr>
<tr>
<td>Parainfluenza virus</td>
<td>0.9 (0.8–1.1)</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>0.8 (0.7–1.0)</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>0.5 (0.4–0.6)</td>
</tr>
</tbody>
</table>
Community acquired pneumonia - guidelines

- Lower yield of blood cultures in the post vaccine era. Blood cultures not recommended for uncomplicated pneumonia (consider for unvaccinated / ill appearing / complicated pneumonia)
- Viral studies - collect if it will help you avoid using antibiotics
- Chest radiographs not required for outpatients
- No antibiotics for pre-school outpatients
- Amoxicillin / ampicillin for older kids / mild –moderate disease / vaccinated
- Consider testing for Mycoplasma / consider treating (evidence weak)
- Consider third generation cephalosporin for undervaccinated inpatients

New CAP guidelines coming

- From John Bradley (chair of the last edition) (personal communication)

“ For CAP, other than saying that they need to be updated, with suggestions that we all provided for new Chair, I am not aware that the process has moved forward yet. …

The data support less antibiotics of course, and you are likely to be citing the data as we see it, too! “
Measles

- Paramyxovirus which causes a highly contagious systemic infection
- Incubation period 10 – 12 days
- Fever followed by cough, coryza and/or conjunctivitis
- Rash comes 2 – 4 days into the fever (two weeks after exposure)
  > Begins on the face / neck moves down the body - - > extremities
  > Fades in the same sequence
- Koplik spots are mucosal lesions, pathognomonic for measles
Measles

- Differential diagnosis includes
  - Stevens Johnson syndrome
  - Kawasaki disease
  - Toxin mediated diseases
  - Dengue
  - SLE

- First measles vaccine licensed in the US in 1963
- Measles was eradicated in the US in 2000
- All cases are imported and then lead to little (big) outbreaks

- 1416 cases reported since 2000; 70+ % unvaccinated
- 600 US cases in 2014
- Risk of measles is 35 fold higher in unvaccinated
- Consider measles for these clinical features – esp if unvaccinated
Measles – post exposure prophylaxis

- MMR vaccine (immunocompetent children ≥ 12 mo of age)
  OR immunoglobulin (IG)

- Immunoglobulin (IG) is given to infants / immunocompromised / pregnant women

- Delay MMR 6 months after IG dose
Pertussis

- Generally afebrile coughing illness
- 20% associated with pneumonia – more in infants
- Dangerous for infants
- Vaccine licensed in the mid 1940’s
- Rates declined from 260K down to 1000 cases in 1976
- Steady increase since then
  > Mid 1990’s change to acellular vaccine
  > More recently decreased vaccine rates
  > Increased case recognition, esp in teens
  > Waning immunity – more rapid than thought
  > Odds of acquiring pertussis increases / yr Since last vaccine dose
Pertussis

- Increased risk of pertussis for
  - Unvaccinated
  - Undervaccinated
  - Increasing years since last vaccine
  - Association with populations with these characteristics

- Personal belief / philosophical objection to vaccination was noted in 70% of pertussis cases in Oregon in 2012
- In 2015 - Oregon had 14.6 cases / 100,000 (US rate 6.5)
- 20 fold increased risk of pertussis in vaccine refusers

Who to test: afebrile coughing illness, especially in the non-winter season
Try to test / treat in the first 7 – 10 days of illness
  - higher cure rate
Consider empiric treatment pending studies (PCR) in undervaccinated young children in the first 10 days of illness
Pertussis – post exposure prophylaxis

- Treat household / child care / unprotected health care contacts – especially
  - High-risk patients (infants, women in the third trimester of pregnancy, persons with pre-existing health conditions that may be exacerbated by pertussis (e.g., moderate to severe asthma, immunocompromised), care providers)
- Azithromycin - start within 21 days of exposure to onset of cough
  - Infants up to 6 months: 10 mg/kg/day x 5 days
  - Children > 6 mo: 10 mg/kg day 1; 5 mg/kg/day x 4 subsequent days
  - Adolescents and adults 500 mg day 1; 250 mg x 4 subsequent days
- If unimmunized / under immunized – also give DTaP or TDaP

- OR DHS recommends only treatment of high risk contacts / households which contain high risk contacts
  - Low risk contacts will be advised to watch for symptoms, get treatment early
Influenza

- Influenza causes a febrile coughing illness often accompanied by sore throat, headache & body aches
- Each year, the US develops a vaccine with three or four strains
- If the chosen strains match the circulating strains, the vaccine is expected to be about 60% effective
- Fewer cases of severe / life threatening disease in vaccinated folks
- Recommended treatment for serious cases identified in the first 48 hours of illness and those sick enough to be admitted to hospital with severe, progressive or complicated respiratory illness regardless of immunization status
Influenza – post exposure prophylaxis

- Chemoprophylaxis within 48 hours of exposure (generally for > 3 mo olds):
  - High risk children for whom influenza vaccine is contraindicated
  - High risk children during the 2 weeks after flu vaccine
  - For unimmunized family members / health care providers with ongoing exposure to:
    - Unimmunized infants / toddlers or any child at high risk
  - For control of flu outbreaks for unimmunized staff and children in a closed institutional setting with children at high risk
  - As a supplement to vaccine among immunocompromised children
  - For high risk children / household members if vaccine is found to be a bad match

- (Note – we did not use LAIV this last winter – but if we use it again, don’t give chemoprophylaxis within 14 days of LAIV)

- Usually oseltamavir
Mumps – post exposure prophylaxis

- During a mumps outbreak, all unimmunized persons 12 months or older should be vaccinated with MMR vaccine, and a second dose of MMR vaccine should be offered to students and health care personnel born after 1957 who only received one dose of MMR.

- A local outbreak may prompt a second dose to be administered to preschoolers depending on the epidemiology of the outbreak.

- A third dose of MMR vaccine may be recommended by the public health authorities in certain circumstances, including when there is a high two-dose vaccination rate (greater than 90%).
Varicella – post exposure prophylaxis

- 95% reduction in varicella disease after vaccine licensure in 1995

- After exposure:
  - the varicella vaccine may be given within 3 days (90% effective) - up to 5 days (70% effective)
  - VariZIG is recommended
    > unimmunized immunocompromised patients,
    > newborn infants whose mothers have signs and symptoms of varicella around delivery (5 days before to 2 days after delivery
    > Hospitalized premature infants

- High risk individuals can also be treated with anti-viral therapy early in disease
Hepatitis – post exposure prophylaxis

- Hepatitis B - unimmunized contacts: hepatitis B vaccine series
  > + / - HBIG depending on exposure (sexual / needle stick)
  > No HBIG if a susceptible child bites someone with HBV

- Hepatitis A – ASAP and < 2 weeks after exposure
  > Hepatitis A Vaccine for 12 mo – 40 yr old
  > IG IM for < 12 mo olds, > 40 year olds, immunocompromised, liver failure
# Tetanus – post exposure prophylaxis

## Table 3.75. Guide to Tetanus Prophylaxis in Routine Wound Management

<table>
<thead>
<tr>
<th>History of Adsorbed Tetanus Toxoid (Doses)</th>
<th>Clean, Minor Wounds</th>
<th>All Other Wounds&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fewer than 3 or unknown</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3 or more</td>
<td>No if &lt;10 y since last tetanus-containing vaccine dose</td>
<td>No&lt;sup&gt;d&lt;/sup&gt; if &lt;5 y since last tetanus-containing vaccine dose</td>
</tr>
<tr>
<td>Yes if ≥10 y since last tetanus-containing vaccine dose</td>
<td>No</td>
<td>Yes if ≥5 y since last tetanus-containing vaccine dose</td>
</tr>
</tbody>
</table>
Infection control and reporting

- Many of these vaccine preventable infections require a report to the local health department
- Investigation of contacts
- Prophylaxis
- Protect yourself and your staff:
  > Droplet precautions
    - Influenza
    - pertussis
    - mumps
    - pertussis
    - HIB
    - Meningococcus
  > Airborne precautions
    - Measles
    - chickenpox
    - (TB)
Talking to parents about vaccine safety

1. Take time to listen.

2. Validate their concerns.

3. Use a “heart and head” approach.


5. Be flexible.

6. Direct them to reliable resources.
In January 1928, in the early stages of an immunization campaign against diphtheria, Dr. Ewing George Thomson, Medical Officer of Health of Bundaberg, began the injection of children with toxin-antitoxin mixture. The material was taken from an India-rubber-capped bottle containing 10 mL of TAM. On the 17th, 20th, 21, and 24th January, Dr. Thomson injected subcutaneously a total of 21 children without ill effect. On the 27th a further 21 children were injected. Of these children, eleven died on the 28th and one on the 29th. (Wilson 1967)
Vaccine preservatives

- Thimerosal had been a common vaccine preservative.
  - It is degraded to ethylmercury and thiosalicylate (methylmercury is the documented neurotoxin).
  - Ethylmercury is not nearly as toxic as methylmercury.
  - 0.5 ml vaccines preserved with thimerosal contain 25 mcg Hg per dose
  - Accidental poisonings of 3 mg/kg – hundreds of mg/kg have showed toxicity.
  - Smaller doses have only shown local reactions
  - The only regular pediatric vaccine that still has thimerosal is the multidose vials of influenza vaccine
  - A couple of vaccines have trace (<1mcg) thimerosal residual from the manufacturing process

- Phenol, benzethonium chloride and 2-phenoxethanol are others
Commonly asked questions

▪ Are vaccines safe
  > 1-2 serious reactions per million shots

▪ Why do children today need so many immunizations?
  > To save lives

▪ Are diseases of the “old days” really still something to worry about?
  > Flu, pertussis, chicken pox are the most common

▪ What about holistic medicine or “natural immunity”?
  > Immunization facilitates a natural process by stimulating encounters of the immune system with killed or altered viruses

▪ Is it safe for a child’s immune system to have multiple shots?
  > For over 10 years vaccines have been tested with all the shots given at the same age; Because vaccines are more refined, kids actually get fewer antigens now

Commonly asked questions – part 2

▪ What about getting shots later or more spread out?
  > No proof that this decreases risk or side effects

▪ Do vaccines cause autism?
  > Increasing rates of autism after removal of thimerosal from vaccines
  > No difference in autism in vaccinated vs unvaccinated children

▪ What about other vaccine ingredients?
  > Aluminum - By 6 mo of age 4.4 mg Al in vaccines
    ▪ 7 mg in breast milk
    ▪ 38 mg in formula
    ▪ 117 mg in soy formula
  > Formaldehyde - also in the environment, naturally occurring

▪ No: antifreeze, chick embryos, monkey kidneys

Thank you!
Vaccine historical comparisons

- **Diphtheria** - 1st vaccine 1928
  - Clinical features: low grade fever, membranous nasopharyngitis or obstructive laryngotracheitis
  - Peak cases: 206K in 1921; Peak deaths: 15,500 in 1921
  - < 5 cases in US in the last 10 yrs
  - Still cases worldwide

- **Mumps** - 1st vaccine 1940’s
  - Clinical features: fever, headache, myalgias, salivary gland (parotid) swelling, orchitis, pleocytosis; many other manifestations
  - Peak cases: 200 K in 1964; Peak deaths: 50 in 1964
  - Down to 229 cases in 2012 5758 cases in 2016, so far 2000 cases 2017
  - Most recent outbreaks in college / crowded settings
  - Vaccine 88% effective (2 doses)

  > Send mumps titers if unvaccinated and typical case
Vaccine historical comparisons

- **Rubella - 1\textsuperscript{st} vaccine 1969**
  - Clinical features: mild fever, rash, LAD and **congenital rubella syndrome**
  - Peak cases: 500 K in 1964; Peak deaths: 2200 in 1968
  - 11 cases in 2010 99.9 % reduction
  - In 2015, The Americas became the first region to have eliminated rubella
  - Still common worldwide

- **Tetanus - 1\textsuperscript{st} vaccine 1933**
  - Clinical features: trismus → generalized muscular spasms
  - Peak cases: 600 in 1948; Peak deaths: 511 in 1947
  - 41 cases & 4 deaths in 2010 92.9 % reduction

- Vaccinate if seen for wound and has < 4 vaccines
- Tetanus immune globulin for dirty wounds and < 3 vaccines in past
Vaccine historical comparisons

- **Paralytic Polio** - 1\textsuperscript{st} vaccine 1955
  - Clinical features: usually asymptomatic; low grade fever sore throat; aseptic meningitis; acute flaccid paralysis
  - Peak cases: 22K in 1952
  - Peak deaths: 3145 in 1952
  - 0 cases in 2010 100 % reduction

- **Smallpox** - 1\textsuperscript{st} vaccine 1798
  - Clinical features: high fever, prostration; mouth / throat lesions; rash
  - Peak cases: 110 K in 1920
  - Peak deaths: 2510 in 1902
  - 0 cases in 2010 100 % reduction (none since 1980)
Vaccine historical comparisons

- **Hepatitis B - 1st vaccine 1914**
  > Clinical features: children often asymptomatic; jaundice, hepatitis, failure
  > Peak cases: 28 K in 1984
  > 3,000 – 19,000 (reported vs estimated) cases in 2014, 82% reduction

- **Hepatitis A - 1st vaccine 1995**
  > Clinical features: fever, malaise, diarrhea, abdominal pain, jaundice
  > Peak cases: 35 K in 1998;
  > 1239 cases in 2014 (down from 1800 in 2013) 95% reduction