John M. Kelso, M.D.
A practical guide to adult immunizations: Who needs what, when and why?
Saturday, July 18, 2015 – 11:00 AM

A practical guide to adult immunizations: Who needs what, when and why?

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Faculty Disclosure Information
• I have not had a financial interest or other relationship with the manufacturers of the products that will be discussed in my presentation.
• This presentation will not include discussion of pharmaceuticals or devices that have not been approved by the FDA.
• I will not be discussing unapproved or “off-label” uses of pharmaceuticals or devices.

Objectives
• Appropriately vaccinate adults, especially those 60 years and older, based on an understanding of the rationale for vaccine recommendations in this population
• Appropriately vaccinate patients with asthma with influenza and pneumococcal vaccines, based on an understanding of the rationale for vaccine recommendations for these patients
• Appropriately choose among the different available influenza vaccines based on the rationale for their development
Influenza

Influenza burden

- An average of 294,128 persons are hospitalized each year in the United States because of influenza, including an average of 21,156 hospitalizations in children less than 5 years of age.
- An average of 23,607 deaths occur each year in the United States as a result of influenza, including an average of 124 children.

Influenza burden in older adults

- Hospitalization rates highest for adults aged ≥65 years
- Among persons aged ≥65 years with high-risk underlying medical conditions, 1 out of every 179 will be hospitalized due to influenza
- Yearly average of 21,098 influenza-related deaths occurred among adults aged ≥65 years (90% of all influenza deaths)

MMWR 2013;62(RR-7)

Influenza vaccine

RDBPCT ≥ 60 years old

Table 5—Relative Risk (RR) and 95% Confidence Intervals (CI) of Vaccinated Participants Compared With Nonvaccinated Participants in Relation to Serological Influenza and Clinical Influenza

<table>
<thead>
<tr>
<th>Influenza</th>
<th>Clinical</th>
<th>Serological</th>
<th>Vaccine Group, n (967)</th>
<th>Placebo Group, n (981)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td></td>
<td>753</td>
<td>634</td>
<td>0.92 (0.72-1.17)</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td></td>
<td>25</td>
<td>42</td>
<td>0.59 (0.36-0.96)</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td></td>
<td>16</td>
<td>38</td>
<td>0.42 (0.22-0.74)</td>
</tr>
<tr>
<td>Dropout</td>
<td></td>
<td></td>
<td>26</td>
<td>22</td>
<td></td>
</tr>
</tbody>
</table>

**Clinical influenza if any of the criteria (family physician, Sentinel Station, or International Classification of Health Problems in Primary Care2 criteria) were met.


Influenza vaccine responses elderly vs young adults

Seroconversion: % subjects with 4X ↑ titers
Seroprotection: % subjects with titers ≥1:40

Goodwin K, et al. Vaccine 2006;24:1159-69
High-Dose Influenza Vaccine

- Contains 60 μg of HA per vaccine virus (compared to standard-dose vaccine which contains 15 μg of HA per vaccine virus)
- approved for use in persons 65 years of age and older

Influenza vaccine: High Dose vs. Standard Dose

<table>
<thead>
<tr>
<th>Response by antigen</th>
<th>HD GMT</th>
<th>SD GMT</th>
<th>MFA GMT ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/California/07/2009</td>
<td>1.7 (1.0–1.5)</td>
<td>1.0 (1.0–2.0)</td>
<td>1.7 (1.0–2.0)</td>
</tr>
<tr>
<td>A/California/07/2009</td>
<td>1.3 (0.2–1.4)</td>
<td>1.0 (0.6–1.6)</td>
<td></td>
</tr>
</tbody>
</table>

Seroconversion: Percentage difference in GMT (95% CI)

- A/California/07/2009
  - HD: 31.1 (10.5–15.6)
  - SD: 31.1 (10.5–15.6)
- A/California/07/2009
  - HD: 2.9 (1.7–3.9)
  - SD: 1.7 (0.7–3.7)


Influenza vaccine: High Dose vs. Standard Dose

- 31,989 participants 65 years of age or older given HD vs SD influenza vaccine.
- Relative efficacy = 24.2%, i.e..
- One quarter of all breakthrough influenza illnesses could be prevented if IIV3-HD were used instead of IIV3-SD.

“The CDC and its Advisory Committee on Immunization Practices have not expressed a preference for any flu vaccine indicated for people 65 and older.”

But given the new data, stay tuned…
Live Attenuated Influenza Vaccine (LAIV, intranasal)

- Cold-adapted: replicates at 25°C (nose)
- Temperature-sensitive: restricted in replication at 37°C (lungs)
- Attenuated (does not produce influenza-like illness)

Live Attenuated Influenza Vaccine (LAIV, intranasal)

- No shots
- More effective (than IM) in younger children (now preferred for healthy children aged 2 through 8 years who have no contraindications or precautions)
- Less effective (than IM) beyond age 50
- Approved for patients to 2-49 years of age without asthma

Intradermal Influenza Vaccine

- Contains 9 μg of HA per vaccine virus (compared to standard-dose vaccine which contains 15 μg of HA per vaccine virus)
- Same immunogenicity as IM
- Approved for use in persons 18 through 64 years of age
- Dose sparing, since uses less antigen per dose
Intradermal Influenza Vaccine

- 20% of patients who decline vaccination do so because of a fear of needles or dislike of injections
- Uses a very fine needle that is 90% smaller than the needles used for regular flu shots

Trivalent vs. Quadrivalent

- Injectable, inactivated influenza vaccine has typically contained 3 strains, 2 A and 1 B, and thus termed trivalent influenza vaccine or TIV
- Some influenza vaccines now contain 4 strains, 2 A and 2 B, and are thus quadrivalent
- The abbreviation TIV has been replaced with IIV for Inactivated Influenza Vaccine

- The vaccines which contain 3 strains are termed IIV3 and those that contain 4 strains are termed IIV4
- Intranasally-administered live attenuated influenza vaccine is a quadrivalent vaccine and termed LAIV4
“Quadrivalent vaccines are designed to provide broader protection against circulating influenza B viruses… However, vaccination should not be delayed if only IIV3 is available. No preference is expressed for IIV4 over IIV3.”

“While there will be more than one vaccine option for many people to choose from, the most important thing is for all people 6 months and older to get a flu vaccine every year.”

CDC: Trivalent vs. Quadrivalent

CDC: Preferred influenza vaccine
“Swine flu” vaccine in 1976 associated with increased risk GBS (1 additional case per 100,000 over background rate of 1 to 2 cases per 100,000).

Subsequent years influenza vaccines have shown no consistent increased risk (if any, 1 per million).

Specific attention was paid to the potential for GBS after the 2009 pandemic influenza A (H1N1) vaccine campaign and no increased rate was found.

Guillain-Barré syndrome continues to be reported in temporal association with influenza infection itself.

Previous GBS has risk of a recurrence.

Persons who developed GBS within 6 weeks of influenza vaccination should avoid subsequent immunization.

However, individuals with a history of GBS unrelated to influenza infection or vaccination who would benefit from immunization can be vaccinated.

Adjuvanted influenza vaccines enhance immune response.

Oil (squalene) in water MF59 — incorrectly linked to anthrax vaccine and Gulf War Syndrome.

Oil (alpha-tocopherol) in water AS03 — increased risk of narcolepsy with a monovalent 2009 H1N1 influenza vaccine containing AS03.

No adjuvanted influenza vaccines are licensed in the United States.
"Universal" influenza vaccines

- Attempt to generate an immune response to conserved antigens, i.e. those that do not change from year to year
- Conserved internal antigens (NP, M1) for a cell-mediated immune response
- Conserved external antigens (external portion of the M2 ion channel, stem of HA) for a humoral response

HA: hemagglutinin, NA: neuraminidase
NP: nucleoprotein M: matrix

Pneumococcus
Pneumococcal disease

- Non-invasive pneumococcal diseases
  - Otitis media
  - Non-bacteremic pneumonia
- Invasive pneumococcal diseases (IPD)
  - Bacteremia (sepsis)
  - Meningitis
  - Bacteremic pneumonia

Pneumococcal vaccine

- The incidence of IPD:
  - 3.8 per 100,000 18–34 years of age
  - 36.4 per 100,000 ≥65 years of age
- PPSV23 effectiveness:
  - 50% to 80% for prevention of IPD among immunocompetent older adults and adults with various underlying illnesses

  MMWR 2010;59(34), 2012;61(40)

Pneumococcal vaccines

- Pneumococcal Polysaccharide Vaccine 23-valent = PPSV23 = Pneumovax
- Pneumococcal Conjugate Vaccine 13-valent = PCV13 = Prevnar
- PPSV23 contains 12 of the serotypes included in PCV13, plus 11 additional serotypes (i.e., PCV13 contains one serotype not included in PPSV23)
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Antibody response to initial and booster PPSV23

PCV13

• "Potential advantage of initial PCV administration, which permits the establishment of an immune state that results in appropriate recall responses upon subsequent immunization with either PCV13 or PPSV23."

Pneumococcal vaccine

• Community-Acquired Pneumonia Immunization Trial In Adults (CAPITA) evaluating efficacy of PCV13 among 85,000 adults aged ≥65 years
  – 45.0% (CI = 14.2%–65.3%) efficacy against vaccine-type nonbacteremic pneumococcal pneumonia
  – 75.0% (CI = 41.4%–90.8%) efficacy against vaccine-type IPD

MMWR 2014;63(37)
Asthma increases the risk of invasive pneumococcal disease

Table 1: Medical conditions or other indications for administration of PCV13, and indications for PCV13 administration and revaccination for adults 19 years of age or older.

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Underlying Medical Conditions</th>
<th>PCV13</th>
<th>PCV13+23*</th>
<th>PCV13 only</th>
<th>PCV13+23* after 2 doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompromised patients</td>
<td>Chronic heart disease</td>
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<tr>
<td></td>
<td>Pulmonary condition</td>
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<tr>
<td></td>
<td>Other chronic medical problem</td>
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<td></td>
<td></td>
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<tr>
<td>Patients with functional or anatomic asplenia</td>
<td></td>
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<td></td>
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<tr>
<td>Immunocompromised patients</td>
<td>Chronic obstructive pulmonary disease</td>
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</tbody>
</table>

* Including chronic obstructive pulmonary disease, emphysema, and other chronic medical problems.
**Pertussis**

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of Cases</th>
<th>% of Total</th>
<th>Age Inc. 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 yr</td>
<td>4994</td>
<td>10.3</td>
<td>126.7</td>
</tr>
<tr>
<td>1-4 yrs</td>
<td>8380</td>
<td>17.2</td>
<td>34.1</td>
</tr>
<tr>
<td>5-10 yrs</td>
<td>9132</td>
<td>19.8</td>
<td>50.5</td>
</tr>
<tr>
<td>11-19 yrs</td>
<td>14440</td>
<td>29.9</td>
<td>30.0</td>
</tr>
<tr>
<td>20+ yrs</td>
<td>10436</td>
<td>23.6</td>
<td>4.3</td>
</tr>
<tr>
<td>Unknown</td>
<td>655</td>
<td>(1.3)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>48277</strong></td>
<td><strong>100.0</strong></td>
<td><strong>13.2</strong></td>
</tr>
</tbody>
</table>

**2012 Reported Pertussis Deaths**

- Infants, aged < 3 months: 18
- Infants, aged 3-11 months: 1
- Children, 1-4 years: 2
- Adults, aged 55+ years: 2
- **Total**: 20

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**Vaccines**

- DTaP = Diphtheria and tetanus toxoids and acellular pertussis, pediatric formulation
- Td = Tetanus and diphtheria toxoids, adult/adolescent formulation
- Tdap = Tetanus and diphtheria toxoids and acellular pertussis, adult/adolescent formulation
- Upper case D or P = more antigen, lower case d or p = less antigen

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**Tdap vaccine for adults**

- Reduce pertussis morbidity among adults
- Maintain the standard of care for tetanus and diphtheria prevention
- Reduce the transmission of pertussis to infants
- Initially recommended as substitute for next regularly scheduled Td

_MMWR 2006;55(RR17)_
The recommended interval between doses of Td had been 10 years, with shorter intervals thought to be associated with increased rates of Arthus reactions.

However, two recent studies:
- The rates of injection site reactions to Tdap were no different in those vaccinated with Td < 2 years vs >2 years earlier
- No higher rates of injection site reactions whether Tdap was given one month after a Td or placebo

Pertussis disease burden continues to be substantial
- Now recommended that Tdap be given to all adolescents and adults regardless of interval since the last Td
- This includes those 65 years of age and older in whom the vaccine has been found to be equally safe and immunogenic
Zoster

- Occurs most frequently among older adults
- 1/3 will develop zoster during their lifetime
- 1 million episodes in the US annually
- Common complications:
  - Postherpetic neuralgia (PHN) chronic, often debilitating pain 10%-18%
  - Eye involvement that can result in loss of vision

MMWR 2008;57(RR-5)
Varicella Zoster Virus (VZV) vaccines

- VARIVAX, Each 0.5-mL dose contains 1350 plaque-forming units (PFU) of VZV
- ZOSTAVAX, Each 0.65-mL dose contains 19,400 PFU of VZV

Zoster vaccine: prior history of zoster

Table 2. Comparison of Incidence of Recurrent Herpes Zoster Between the Vaccinated and the Unvaccinated Cohorts

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vaccinated Cohort</th>
<th>Unvaccinated Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>Cases/Person-Yrs</td>
<td>Cases/Person-Yrs</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>Incidence</td>
</tr>
<tr>
<td>&lt;70</td>
<td>1533</td>
<td>1038.48</td>
</tr>
<tr>
<td>≥70</td>
<td>3053</td>
<td>1035.41</td>
</tr>
</tbody>
</table>

*No. of cases per 1000 person-years.


CDC: Zoster vaccine

- Repeated zoster has been confirmed in immunocompetent persons after a previous episode
- The precise risk for zoster following an earlier episode is unknown
- Reported diagnosis or history might be erroneous
- No laboratory evaluations exist to test for the previous occurrence of zoster

MMWR 2008;57(RR-5)

CDC: Zoster vaccine

- Routine vaccination of all immunocompetent persons aged >60 years with 1 dose
- Persons who report a previous episode of zoster can be vaccinated
- Not indicated to treat acute zoster, to prevent persons with acute zoster from developing PHN, or to treat ongoing PHN

MMWR 2008;57(RR-5)
Changes you may wish to make in practice

- Make assessment of immunization status a routine part of all visits
- Don’t assume patients are receiving their vaccinations elsewhere
- Administer IIV, PCV13/PPSV23, Tdap, and Zoster vaccines to all eligible recipients

Who, what, when?

- IIV annually for everyone
- PCV13 and PPSV23 for all adults aged ≥65 and for PPSV23 for adults at high risk aged 19–64
- Tdap once for all adults now
- Zoster vaccine once for all immunocompetent adults aged >60