Adult Vaccines in 2018: Where do we start?

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Objectives

- Discuss recent outbreaks of vaccine preventable disease, how resistance and vaccines have impacted one another, and implications for vaccine advocacy
- Review both the advantages and potential safety concerns with new vaccine adjuvants
- Describe recent updates to ACIP adult immunization recommendations
“You have to admire its simplicity. It's one billionth our size and it's beating us.”
- Dustin Hoffman

“The average person touches their face three to five times every minute. In between that we're touching door knobs, water fountains, and each other.”
- Kate Winslet

Measles Outbreaks

Measles Cases

NCIRD data

California

MMWR. February 20, 2015 / 64(06);153-154

https://www.cdc.gov/measles/cases-outbreaks.html
California governor signs vaccine bill that bans personal, religious exemptions
By Michael Martinez and Amanda Watts, CNN
Updated 10:51 PM ET, Tue June 30, 2015

Mumps Cases in U.S., by Year

https://www.cdc.gov/mumps/outbreaks.html
From January 1 to August 11, 2018, 47 states and the District of Columbia in the U.S. reported mumps infections in 1,665 people to CDC.

[Map of Mumps Cases as of August 11, 2018]

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

### MMR Vaccine

- **MMR - Mumps**
  - 88% effective 2 doses
  - 78% effective 1 dose

- **MMR - Measles**
  - 97% effective 2 doses
  - 93% effective 1 dose

- **MMR - Rubella**
  - 97% effective 1 dose
Third Dose of MMR Vaccine?

- 61-88% 3 MMRs vaccine effectiveness\(^1,2,3\)
  - Studies had high percentage of patients with 2 doses MMR
  - Three studies ages 9 years through college age
- No serious adverse effects reported after 3 MMR\(^2,3,4\)
- 3 MMRs appears to provide short-term boost in antibodies and seroconverts most seronegative persons

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ACIP Mumps Recommendation

Persons previously vaccinated with 2 doses of a mumps virus-containing vaccine who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak should receive a third dose of a mumps virus-containing vaccine to improve protection against mumps disease and related complications.

Men B 2013-2014 Outbreak

- Meningococcus serogroup B
- Princeton (9 cases) and UCSB (4)
- 30,000 students vaccinated with Bexsero under IND
- Bexsero (4CMenB)
  - 2 dose (0, 1-6 months)
  - 4 component (non PPS, non conjugate, non adjuvanted)
Meningococcal B Vaccines

• Trumenba
  ▪ 3-dose series (0, 1-2, 6 months)
  ▪ 2-dose series (0, 6 months)
  ▪ Choice depends upon risk of exposure and patient’s susceptibility to Men B disease

• Bexsero
  ▪ 2-dose series (0, 1-6 months)

ACIP Recommendations

• Routine use of MenB vaccines in persons at increased risk for serogroup B meningococcal disease, including:
  ▪ During outbreaks of serogroup B meningococcal disease.
  ▪ College campuses that have recently experienced an outbreak of serogroup B meningococcal

“A serogroup B meningococcal (MenB) vaccine series may be administered to adolescents and young adults 16 through 23 years of age to provide short-term protection against most strains of serogroup B meningococcal disease. The preferred age for MenB vaccination is 16 through 18 years of age (Category B)”
**Incidences of antimicrobial nonsusceptible IPD**

- **PCV13 introduction**

- **Cases per 100,000**
  - 0-4 years
  - 5-17 years
  - 18-49 years
  - 50-64 years
  - 65+ years

- **Year**
  - 2009
  - 2010
  - 2011
  - 2012
  - 2013

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**Pneumococcal Vaccine Timing**

**Age 19-64 Years With Underlying Condition(s)**

- Prior doses count towards doses recommended below and do not need to be repeated.
- If PPSV23 given previously - wait one year before giving PCV13.
- For group B, wait at least five years before giving a second dose of PPSV23.
- No more than two doses of PPSV23 recommended before 65th birthday and one dose thereafter.

**A. Smoker, or Chronic conditions:**
- Heart disease (including hypertension)
- Lung disease (including asthma)
- Liver disease (including cirrhosis)
- Diabetes
- Alcoholism

**PPSV23**

**B. Immune-compromised (including HIV infection), Chronic renal failure, Nephrotic syndrome, or Asplenia (including sickle cell)**

<table>
<thead>
<tr>
<th>PCV13</th>
<th>8 weeks</th>
<th>PPSV23</th>
<th>5 years</th>
<th>PPSV23</th>
</tr>
</thead>
</table>

**C. CSF leaks or Cochlear Implants**

<table>
<thead>
<tr>
<th>PCV13</th>
<th>8 weeks</th>
<th>PPSV23</th>
</tr>
</thead>
</table>

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CDC Active Bacterial Core surveillance, 2009 to 2013

[http://eziz.org/assets/docs/IMM-1152.pdf](http://eziz.org/assets/docs/IMM-1152.pdf)
Pneumococcal Vaccine Timing - Adults

Age 65 Years or Older

- If PCV13 was given before age 65 years, no additional PCV13 is needed.

No history of pneumococcal vaccine

PCV 13

1 year
(8 weeks for groups B & C as defined below)

PPSV 23

Pneumovax® 23

Received PPSV23 before age 65

PCV 13

1 year
(8 weeks for groups B & C as defined below)

PPSV 23

Received PPSV23 at age 65 or older

PCV 13

1 year

IPD rates among adults ≥ 65 years, 2007–2016

ACIP, October 2017
PCV13 Impact on IPD

- Pneumococcal carriage among adults ≥65 years old very low (1.8%)
  - PCV13-type carriage 0.2% in 2015-2016
- PCV13 coverage ≥65 years old ~ 40%
- Invasive pneumococcal disease (IPD)
  - PCV13-type IPD declined among all age groups
  - IPD incidence in adults ≥65 years old plateaued in 2014-2016
  - Modeled direct and indirect effects project relatively few cases prevented
  - Serotype 3 IPD does not follow the same pattern as other PCV13-types
Estimated Direct Effect of PCV13

ACIP, Feb 22, 2018

Note: dotted lines do not represent actual data

https://www.cdc.gov/abcs/reports-findings/survreports/spneu-types.html
Influenza Vaccine Excipients

**Residuals**
- Inactivating: formaldehyde
- Antibiotics: Neomycin, Polymyxin B
- Egg protein

**Preservatives**
(thimerosal, EDTA, phenol)

**Additives**
- Stabilizers: albumin, gelatin
- Buffers: phosphate

**Adjuvants**
(Aluminum, MF59, ASO, Cpg)

Adjuvants

- **Benefits**
  - Improve immunogenicity
  - Reduce dose of the vaccine antigen
  - Reduce the number of doses needed for immunity
  - Improve efficacy in special populations
    - Newborns, elderly, immunocompromised, renal, etc
- **Challenges**
  - Increased reactogenicity
  - Potential for pre-existing immunity to carrier protein
  - Need to be approved by the FDA in addition to the vaccine
Th1 – cell mediated
Th2 – humoral

Vaccines 2015, 3(2), 320-343
## US Vaccine Adjuvants

<table>
<thead>
<tr>
<th>Adjuvant</th>
<th>Vaccine</th>
<th>Component</th>
<th>Immune Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum (1940s)</td>
<td>D, T, pertussis, IPV,</td>
<td>Aluminum as salts mixed with antigen</td>
<td>Only increases antibody production; no CMI</td>
</tr>
<tr>
<td></td>
<td>hepatitis A &amp; B, HPV,</td>
<td>(adsorption)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>meningococcal and</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>pneumococcal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASO4 (2009)</td>
<td>Cervarix (not marketed)</td>
<td>Alum + MPL</td>
<td>↑ Ab and Th1 responses</td>
</tr>
<tr>
<td>ASO3 (2013)</td>
<td>Pandemic H5N1 vaccine</td>
<td>VitE + squalene</td>
<td>↑ Ab and Th1 responses</td>
</tr>
<tr>
<td></td>
<td>(not commercially</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>available)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MF59 (2015)</td>
<td>Fluad</td>
<td>Squalene (oil-in-water emulsion)</td>
<td>Increases APC recruitment and activation. Th1/Th2</td>
</tr>
<tr>
<td>ASO1B (2017)</td>
<td>Shingrix</td>
<td>MPL + QS-21</td>
<td></td>
</tr>
</tbody>
</table>

## Vaccine Updates
LAIV is back
3rd dose mumps outbreak
MenHibrix D/C’d
Comparison of Zostavax (ZVL) and Shingrix (RZV)

<table>
<thead>
<tr>
<th></th>
<th>Zostavax (ZVL)</th>
<th>Shingrix (RZV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of vaccine</td>
<td>Live</td>
<td>Inactivated</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>None</td>
<td>AS01B</td>
</tr>
<tr>
<td>Storage</td>
<td>Frozen</td>
<td>Refrigerate*</td>
</tr>
<tr>
<td>Regimen</td>
<td>1 dose</td>
<td>2 doses (2 months apart)</td>
</tr>
<tr>
<td>Efficacy against disease</td>
<td>51.3% (varies by age)</td>
<td>97.2% ≥50 years</td>
</tr>
<tr>
<td>Duration</td>
<td>7-8 years</td>
<td>3.2 years (model predicts 19 yrs to zero efficacy)</td>
</tr>
<tr>
<td>SAE/ADR</td>
<td>1.9% / 48.3%</td>
<td>1.1% / 84.4% (17% Grade 3)</td>
</tr>
</tbody>
</table>

* Discard 6 hours after reconstitution if not administered

Shingles Vaccines Efficacy Comparison

![Graph showing vaccine efficacy comparison between ZVL and RZV.]

- **ZVL**
  - 50-59 yrs: 69%
  - 60-69 yrs: 64%
  - 70-79 yrs: 18%
  - => 80 yrs: 91.3%

- **RZV**
  - 50-59 yrs: 96.6%
  - 60-69 yrs: 97.4%
  - 70-79 yrs: 91.3%
  - >= 80 yrs: 91.3%

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3. Lai et al., NEJM 2015;372(22):2087-96. (ZOE-50);

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RZV and ZVL Efficacy Persistence Against HZ
(Various Studies)

- **RZV**
- **ZVL - KPSC**
- **ZVL STPS**

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Cunningham et al., NEJM 2016;375(11):1019-32.
Oxman et al., NEJM 2005, 352:2271-84.
**Live Attenuated Influenza Vaccine (LAIV4) Past and Future**

- **2003**: LAIV3 Licensed • 2-49 years
- **2012**: LAIV4 licensed • Replace LAIV3 the following season
- **2014**: LAIV Preferred • 2-8 yrs
- **2015**: LAIV Preference Removed
- **2016**: LAIV4 Not Recommended
- **2017**: LAIV4 Not Recommended
- **2018**: LAIV4 Recommended • 2-49 years • No Preference

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**Heplisav-B® (Dynavax)**

- In the U.S.: 850,000-2.2 million with chronic HBV
  - ↑ since 2014 likely due to heroin and opioid epidemic
  - 5,000 people die from HBV per year from chronic liver disease
- Hepatitis B Vaccine (Recombinant), Adjuvanted – Heplisav-B
  - FDA licensed November 9, 2017 for 18 years and older
  - Series of 2 doses, separated by 1 month
  - Adjuvant stimulates TLR9, combined with HBsAg → elicits anti-HBsAg Ab
  - Seroprotection 90.0%-100.0%
    - 70.5%-90.2% with existing Hepatitis B vaccines
    - Better response in diabetes, kidney disease than current HepB vaccines
    - Better choice for immediate departure travelers
- Local & systemic AEs similar to other Hep B vaccines
  - Signal with CV disease – will monitor in post-marketing studies
### 2018–19 Influenza Vaccines

<table>
<thead>
<tr>
<th>Vaccine (manufacturer)*</th>
<th>Approved Age Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated Influenza Vaccine</td>
<td>IIV3-ID - Withdrawn</td>
</tr>
<tr>
<td>Fluzone (Sanofi Pasteur) IIV4</td>
<td>6 months and older</td>
</tr>
<tr>
<td>Fluvirin (Seqirus) IIV3</td>
<td>4 years and older</td>
</tr>
<tr>
<td>Fluarix (GSK) IIV4</td>
<td>6 months and older</td>
</tr>
<tr>
<td>FluLaval (GSK) IIV4</td>
<td>6 months and older</td>
</tr>
<tr>
<td>Afluria (Seqirus) IIV3</td>
<td>5 years and older</td>
</tr>
<tr>
<td>Afluria (Seqirus) IIV4</td>
<td>5 years and older</td>
</tr>
<tr>
<td>Fluzone High-Dose (Sanofi Pasteur) IIV3-HD</td>
<td>65 years and older</td>
</tr>
<tr>
<td>Flucelvax (Seqirus)-cell cultured (canine kidney cell) cclIV4</td>
<td>4 years and older</td>
</tr>
<tr>
<td>Flublok (Sanofi Pasteur) RIV3/ RIV4</td>
<td>18 years and older</td>
</tr>
<tr>
<td>Fluad (Seqirus) IIV3</td>
<td>65 years and older</td>
</tr>
<tr>
<td>Live Attenuated Influenza Vaccine</td>
<td></td>
</tr>
<tr>
<td>FluMist (MedImmune) LAIV4</td>
<td>2 years to 49 years</td>
</tr>
</tbody>
</table>

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- Your CE credit will be sent to NABP/CPE Monitor