Vaccinations for Adults and Adolescents: An Update

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Nothing to disclose….
Diseases/Pathogens with Vaccines Generally Available in the U.S.

- Tetanus
- Diphtheria
- Pertussis
- Measles
- Mumps
- Rubella
- Varicella
- Meningococcus
- Pneumococcus
- Hepatitis B
- Hepatitis A
- *Haemophilus influenzae* type B
- Human papillomavirus
- Polio
- Influenza
- Rabies
- Typhoid
- Yellow fever
- Japanese encephalitis
- Rotavirus

Key Resource

Centers for Disease Control and Prevention

http://www.cdc.gov/vaccines/

http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/index.html
Vaccines to be Covered

- Measles - outbreak
- Pneumococcal
- Meningococcal
- Pertussis (Tdap)
- Influenza
- Varicella (Zostavax)
- Human Papillomavirus
At least 146 measles cases in U.S. with epidemiologic link to Disneyland
- 7 states, Mexico, and Canada had linked cases
- More than half in adults
- 2015 so far: 178 U.S. cases in 17 states

Measles outbreak
Disneyland started late
December 2014, ended April 2015

Pneumococcal Polysaccharide Vaccine
- 23 – valent Pneumovax vaccine
- Appears to decrease pneumococcal bacteremia
  - May decrease mortality
- Probably does not decrease pneumonia in older adults
Pneumococcal Polysaccharide Vaccine (PPSV23)

- U.S. indications: > age 65, most chronic cardiopulmonary conditions, diabetes, liver failure, renal failure, splenectomy, any immunosuppression, cochlear implants, certain native populations, residents long term care facilities
- AND as of 2008:
  - Adults ages 19 – 64 with asthma
  - Smokers 19 – 64 given ~ 4X greater risk for pneumococcal disease
  - Revised recommendations for Alaskan Native and American Indian populations – vaccination no longer routine for all

Pneumococcal 13-Valent Conjugate Vaccine for Adults (PCV13)

- 2011: U.S. FDA and European Commission approved vaccine for adults 50 and older
- 2012: Recommended by Advisory Committee on Immunization Practices (ACIP) / CDC for selected adults only
- September 2014: Recommended for all adults 65 and older

*MMWR* 2014;63(37):822-25.
Pneumococcal 13-Valent Conjugate Vaccine for Adults

- 2012: recommended as a single dose for adults 19 years and older with
  - Immunocompromising conditions
  - Functional or anatomic asplenia
  - CSF leaks
  - Cochlear implants

*MMWR* 2012;61:816-19

<table>
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<tr>
<th>Risk Group</th>
<th>Medical Condition</th>
<th>Prevnar 13</th>
<th>Pneumovax 23</th>
<th>Revaccinate 5 years after 1st dose</th>
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<td>Multiple myeloma</td>
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*MMWR* 2012;61:816-19
Pneumococcal 13-Valent Conjugate Vaccine for Adults

Clinical trial in the Netherlands: 84,496 adults ≥ 65 randomized to PCV13 vs. placebo – (CAPiTA trial)
- 46% fewer first cases of vaccine type pneumococcal community acquired pneumonia (CAP) – primary outcome
- 75% fewer first cases vaccine type invasive pneumococcal disease
- No difference CAP from any cause


Pneumococcal 13-Valent Conjugate Vaccine for Adults

For adults ≥ 65 years who have not received pneumococcal vaccine, administer PCV13 first, then PPSV23 6-12 months later
- Minimum interval 8 weeks
If previously vaccinated with PPSV23, give PCV13 at least one year after PPSV23
Meningococcal Vaccine

Two tetravalent protein conjugate vaccines (Menactra, Menveo) covering strains A, C, Y, W-135

- Menactra: 9 months – 55 years; Menveo – 2 months – 55 years
- Advantages compared to polysaccharide vaccine
  - Longer lasting antibody titers
  - Good antibody response to revaccination
- Serogroup B not covered (B, C, and Y circulate in U.S.)

Who Should Get the Conjugate Meningococcal Vaccine?

- Recommended as routine for ages 11 - 18 – ideally given at age 11-12 visit
- “Catch up” at high school or college entry if not given at age 11-12
  - Increased risk for college freshmen in dormitories
- Booster doses now routine for adolescent and teenage vaccinees
### Meningococcal Conjugate Vaccine – Summary Table

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<thead>
<tr>
<th>Risk group</th>
<th>Primary series</th>
<th>Booster dose</th>
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| Age 11-18 | 1 dose, preferred age 11 or 12 | •Age 16, if primary dose age 11 or 12  
•Age 16-18, if primary dose age 13-15  
•No booster if primary dose on or after age 16 |
| *Also, 1st yr. college students in residence halls up to age 21 | | |
| Age 2-55 with complement deficiency or functional or anatomic asplenia | 2 doses, 2 months apart | Every 5 years |
| Age 2 – 55 with prolonged increased risk of exposure | 1 dose | Age 2-6: after 3 years  
Age 7 and older: after 5 years |

**MMWR. January 28, 2011;60:72-76**

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### Who Else Should Get the Conjugate Meningococcal Vaccine?

- Given to military recruits, travelers/residents with geographic risk, microbiologists

**Other notes:**

- Meningococcal polysaccharide vaccine is used for those 56 years and older if vaccine is indicated
- Vaccination required for pilgrims going to Hajj or Umrah in Saudi Arabia
- Clusters in New York City and Los Angeles among men who have sex with men – vaccine may be recommended before travel
Meningococcal Vaccine

- Princeton University with 8 cases serogroup B
  March – Nov, 2013: 7 students and a student visitor; all recovered
- Drexel student died March 2014 after close contact with Princeton students (same strain)
  - Bexsero made available
Meningococcal Vaccine

- University of California, Santa Barbara with 4 cases serogroup B during Nov 2013: 4 undergraduates in different housing units; 3 recovered, 1 with bilateral amputations feet
  - Not the same strain as Princeton
  - Bexsero made available

Meningococcal serogroup B vaccine

- October 2014: first meningococcal serogroup B vaccine (Trumenba) approved by FDA
- Approved ages 10 – 25 years
  - Immunologic correlates of protection
  - Safety data
- 3 doses: 0, 2, 6 months
- Local reactions common – mostly mild or moderate
  - Systemic reactions including fever relatively common
- Vaccine contains 2 recombinant factor H binding protein variants – 1 each from subfamilies A & B
Meningococcal serogroup B vaccine

- University of Oregon cluster meningococcus serogroup B
  - Six cases since January 2015
  - One death in February
  - Used Trumenba in a mass vaccination campaign
  - Students following up in retail pharmacies with Trumenba or Bexsero

- February 2015: ACIP voted to recommend meningococcal serogroup B vaccine for selected high-risk persons

Pertussis Vaccine

Vaccine combinations:

- Childhood DTaP: diphtheria toxoid, tetanus toxoid, and acellular pertussis
- Adult/adolescent Td and Tdap: tetanus toxoid and reduced dose diphtheria toxoid +/- reduced dose acellular pertussis antigens
Pertussis Vaccine

- Pertussis immunity wanes over time
- Tdap (Boostrix) – licensed for ages 10 and up
- Tdap (Adacel) licensed for 10 – 64 years

Acellular pertussis vaccine in adults and adolescents – how well does it work?

- 2781 subjects 15 – 65 yrs received reduced dose acellular pertussis vaccine or hepatitis A placebo
- Followed for 2.5 yrs
- Based on primary pertussis definition, vaccine 92% effective

Ward et al, NEJM, Oct. 2005
Waning immunity after acellular vaccination

California outbreak 2010:
- Most pediatric cases were vaccinated as recommended
- High levels of disease in pre-adolescents, especially 10-year-olds  
  *J Pediatr* 2012;161:1091-6

Kaiser Permanente study in CA kids: odds of pertussis increased by 42% per year in the 5 years after completing DTaP  

Kaiser Permanente study:
- 263,496 persons 8-20 years old who received acellular vs. whole-cell vaccine (at least one dose)
- ~ 8.6 relative risk of pertussis for 5 doses acellular vaccine  
  *Clin Infect Dis* 2013;56:1248-54

Tdapid – Recommendations

For adolescents, give Tdap instead of Td at routine 11-12 yr visit

For adults 19 and older, give single dose Tdap to replace a dose of Td

Can be given at any interval from last tetanus-containing vaccine

Strongly recommended for adults who will have contact with infant < 12 months

Recommended for every pregnancy at 27 – 36 weeks (new in 2012)

*MMWR* 2011 / 60(41):1424-26
Pertussis – Recommendations

Other vaccination opportunities/priorities:

- Substitute single dose Tdap for Td in wound management or if primary series unknown or incomplete
- Give immediately post-partum if not given previously
- “Cocooning” – vaccinate parents, siblings, grandparents, etc. who anticipate contact with infant < 12 months
- All healthcare workers with patient contact should receive Tdap

Influenza Vaccines

Inactivated vaccine given by injection

- Trivalent: 2 influenza A strains, 1 influenza B strain
- Quadrivalent: 2 influenza A strains, 2 influenza B strains
- Few contraindications
  - Severe egg allergy – risk assessment, referral
  - Severe previous reaction
  - Guillain-Barre (relative contraindication)

Live attenuated intranasal vaccine (FluMist)

- Same strains as inactivated vaccine
  - Quadrivalent
Influenza Vaccine Indications

- All people older than 6 months
  - Unless there is a contraindication

2015-16 Influenza Vaccine

- A/California/7/2009 (H1N1)-like (same)
- A/Switzerland/9715293/2013 (H3N2)-like (new)
- B/Phuket/3073/2013-like (Yamagata lineage - new)

For quadrivalent vaccine add:
- B/Brisbane/60/2008-like (Victoria lineage - same)
2014-15 Influenza Season Summary

- Started 4 weeks earlier than average
- Moderately severe
- Rate of hospitalization for age 65+ highest since surveillance began 2005-6
- Overall vaccine efficacy against any influenza estimated 19%

http://www.cdc.gov/flu/about/season/vaccine-selection.htm

Newest influenza vaccines licensed in U.S.

- Three quadrivalent inactivated vaccines: 2 influenza A and 2 influenza B strains; intramuscular
  - Fluarix, FluLaval, Fluzone
- FluBlok: baculovirus expression system (recombinant), no exposure to eggs – age 18+
- Flucelvax: cell culture derived (canine kidney cells) – age 18+
- Afluria trivalent vaccine can be administered by jet injector (FDA approved August 2014 ages 18-64)
High Dose Inactivated Vaccine

- Fluzone High-Dose licensed for those 65 and older
- Trivalent; contains 60 μg of hemagglutinin per virus strain compared with 15 μg in regular dose
- Enhanced immune response in those 65 and older with high dose vs. standard dose
- Local reactions (mild to moderate) more common with high dose vaccine *J Infect Dis* 2009;200:161-3
- 2-year study with 31,989 participants randomized to high dose vs. standard dose: 1.4% vs. 1.9% with confirmed influenza (relative efficacy 24.2%)

Intradermal Influenza Vaccine

- Fluzone intradermal vaccine approved by FDA in 2011
- Needle is about one-tenth of standard length
- Contains 9 mcg hemagglutinin per strain versus standard 15 mcg
  - Dose is 0.1 mL versus standard 0.5 mL
- Approved ages 18 – 64 years
- Local reactions are more common
Live Attenuated Influenza Vaccine

- Attenuated, heat sensitive and cold adapted
- Approved for healthy persons ages 2 – 49, including healthcare workers and contacts of most high risk patients
- Runny/stuffy nose is common

Live Attenuated Influenza Vaccine

Who should not get LAIV?

- Outside recommended age ranges
- Chronic medical conditions, including asthma
- Pregnant women
- History of Guillain-Barre (relative contraindication)
- Severe egg allergy – risk assessment, prefer TIV
- Contact with highly immunosuppressed patients, e.g. bone marrow transplant
Live Attenuated Influenza Vaccine (LAIV)

Efficacy

- In children, 85 – 90% effective in preventing influenza A compared with placebo
- In children, several studies suggest better efficacy than inactivated vaccine
- Study in adults in Michigan 2004 – 2005 influenza season: decreased efficacy compared with inactivated vaccine, especially against influenza B (poor matches for both influenza B and H3N2 “drifted” strain)


LAIV

- Surveillance in military ages 18 – 49 over 3 influenza seasons (2006 – 2009)
- Compared influenza like illness, influenza, and pneumonia in those vaccinated with LAIV compared with inactivated vaccine: 41,670 vaccination events
- Excluded those with contraindications to LAIV
- Controlled for sociodemographics, occupation, geographic area
- No differences found by vaccine group

Clin Infect Dis 2013;56:11-19
Varicella Vaccine – Zoster (Zostavax)

Oxman et al, NEJM, June 2005

- Randomized trial 38,546 adults ≥ age 60
  - Excluded if history of zoster, immunocompromise
- Potency much greater (at least 14x) than vaccine to prevent primary varicella
- Zoster incidence reduced by > 50%; post herpetic neuralgia reduced by > 65%
- Injection site reactions common

Varicella Vaccine – Zoster (Zostavax)

- Recommended a single dose of zoster vaccine for adults age 60 and above, even if prior history of zoster
- Contraindicated in many, but not all, immunocompromised persons (e.g. okay in HIV if clinically well and CD4 count > 200)
Varicella Vaccine – Zoster (Zostavax)

Questions about cost effectiveness – multiple studies
- Vaccine cost ~ $150 per dose
- Societal costs $27,000 – 112,000 per QALY

Once reconstituted, must be used within 30 minutes

First vaccine covered by Medicare Part D – reimbursement was complicated

Follow up subjects in Shingles Prevention Study
- Efficacy for zoster prevention estimated to last 8 years

*Clin Infect Dis 2015;60(6):900-9*

**The New England Journal of Medicine**

**ORIGINAL ARTICLE**

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

Himal Lal, M.D., Anthony L. Cunningham, M.B., B.S., M.D., Olivier Godeaux, M.D., Roman Chlibek, M.D., Ph.D., Javier Diez-Domingo, M.D., Ph.D., Shinn-Jang Hwang, M.D., Myron J. Levin, M.D., Janet E. McElhaney, M.D., Arii Poder, M.D., Joan Puig-Barberà, M.D., M.P.H., Ph.D., Timo Vesikari, M.D., Ph.D., Daisuke Watanabe, M.D., Ph.D., Lily Wecks, M.D., Ph.D., Toufik Zahr, Ph.D., and Thomas C. Heineman, M.D., Ph.D., for the ZOE-50 Study Group

April 28, 2015 at NEJM.org
Human Papillomavirus (HPV) Vaccines

- Genital HPV most common sexually transmitted infection in the U.S.
- Quadrivalent HPV vaccine (Gardasil) licensed 2006
- Contains major capsid protein L1 from types 6, 11, 16, 18
  - Types 16 & 18 associated with 66% cervical cancer
  - Types 6 & 11 associated with 90% genital warts
- FDA approved bivalent vaccine against types 16/18 (Cervarix) for girls and women age 10 – 25 in 2009

Nine-valent HPV vaccine

- FDA approved December 10, 2014
  - Phase 3 trial of 9-valent vaccine (Gardasil 9) against 6, 11, 16, 18 plus 31, 33, 45, 52, 58 (high risk types) in 16-26 year-old females
  - ~ 97% reduction in cervical, vaginal, vulvar pre-cancers due to types 31, 33, 45, 52, 58 compared with Gardasil
HPV Vaccines Recommendations for Use

- Routine vaccination beginning at age 11-12
  - Okay to start as young as age 9
- Females: vaccinate through age 26
  - Use bivalent vaccine (Cervarix), 4-valent vaccine (Gardasil), or 9-valent vaccine (Gardasil 9)
- Males: vaccinate routinely through age 21
  - Extend to age 26 for MSM or immunocompromise
  - Use 4-valent vaccine (Gardasil) or 9-valent vaccine (Gardasil 9)
- 3-dose series for all vaccines
  - Okay to continue series with a different vaccine

MMWR 2015;65(11):300-304

HPV Vaccines

- Excellent efficacy in studies (nearly 100%) in preventing infection with HPV types included in vaccine, if not previously infected
- Prevent cervical and anal intraepithelial neoplasia
- Greatest benefit before onset of sexual activity / infection with HPV
- No protection against types with which already infected at time of vaccination
- Some partial cross protection against non-vaccine serotypes
HPV Vaccine: External Genital Lesions

• 4065 healthy men and boys ages 16 – 26
• Randomized, double-blind, placebo controlled
• 36 external genital lesions in vaccine group, 89 in placebo group (intent to treat efficacy 60%)
• In seronegative group with all doses received, vaccine was 90% effective against genital lesions due to HPV types 6, 11, 16, 18 (mostly 6 and 11)

HPV Vaccines - questions

- Expensive
  - Cost effective – which populations
- Not clear what effect will be on rate of cancer
  - No recommendation to change cervical cancer screening based on vaccination status
In 2013, 57.3% of girls and 34.6% of boys ages 13 – 17 had received one or more doses of HPV vaccine (37.6% and 13.9% received all 3 doses)

- Girls: modest improvement; Boys: large increase

*MMWR 2014;63:620-4*

HPV infections due to vaccine types are dropping in 14-19 year old girls even with limited uptake  

*J Infect Dis 2013;208:385-93*