Vaccinations for Adults and Adolescents: An Update

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Need to be extremely safe
- Even greater issue as disease prevalence wanes or uncommon diseases targeted
- Traditionally considered highly cost effective / great public health advance
  - Likely not true for every vaccine
- A number of new vaccines and new indications for vaccines

Preventative Vaccines

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

Nothing to disclose....
Diseases/Pathogens with Vaccines for Special Populations
- Plague
- Tularemia
- Smallpox
- Anthrax
- Adenovirus
- Tuberculosis - BCG

Key Resource
Centers for Disease Control and Prevention
http://www.cdc.gov/vaccines/

Vaccines to be Covered
- Hepatitis B – new indication
- Pneumococcal
- Meningococcal
- Pertussis (Tdap)
- Influenza
- Varicella (Zostavax)
- Human Papillomavirus
- Measles and mumps reminder

MMWR: January 28, 2013
New recommendation: vaccinate previously unvaccinated adults ages 19 – 59 with diabetes as soon as possible after diagnosis

- Risk for acute hepatitis B estimated 2x higher than general population
- Increased risk presumed related to blood glucose monitoring or other procedures involving instruments
- Persons with diabetes who are 60 and older may be vaccinated

**MMWR. December 23, 2011 / 60(50):1709-11**

Pneumococcal Polysaccharide Vaccine (PPSV23)

- 23 – valent Pneumovax vaccine
- Appears to decrease pneumococcal bacteremia
  - May decrease mortality
- Probably does not decrease pneumonia in older adults
  - Effective in younger adults (e.g. crowded living conditions)
- Enthusiasm greatest in North America

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

**CDC recommendations:**
- One-time revaccination after 5 years for renal failure or nephrotic syndrome; functional or anatomic asplenia; immunosuppression (including congenital, HIV, leukemia, lymphoma, transplant); long-term corticosteroids
- If at least 65, one-time revaccination if vaccinated 5 or more years previously and age less than 65 at time of initial vaccine

Enthusiasm greatest in North America
**Pneumococcal 13-Valent Conjugate Vaccine for Adults**

- **Phase 3 trials of immunogenicity in adults**
  - Prevnar 13 is immunogenic in adults age 50 and older
  - Functional antibody responses are generally higher than for polysaccharide vaccine
  - Well tolerated
- **U.S. FDA and European Commission approved vaccine in 2011 for adults 50 and older**
- **Formally recommended by Advisory Committee on Immunization Practices (ACIP) / CDC for selected adults in 2012**

- **Recommended as a single dose for adults 19 years and older with**
  - Immunocompromising conditions
  - Functional or anatomic asplenia
  - CSF leaks
  - Cochlear implants
- **If not previously vaccinated, give PCV13 first, followed by PPSV23 at least 8 weeks later**
- **If previously vaccinated with PPSV23, wait at least one year after last dose**

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**Risk Group**

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>Prevnar 13</th>
<th>Pneumovax 23</th>
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<tbody>
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<td><strong>Immunocompromised persons</strong></td>
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<tr>
<td>Chronic Heart Disease</td>
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<td><strong>Immunocompromised persons</strong></td>
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</table>

**Clinical trial in the Netherlands: 85,000 adults ≥ 65 randomized to PCV13 vs. placebo – primary outcome pneumonia**

**Key questions that will not be answered:**

- Does PCV13 provide additional benefit to PPSV23?
- What is the benefit when PCV-13 used routinely in children?
- Anticipate retained benefit in HIV
- Role of replacement strains?

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**Meningococcal Vaccine**

- Traditional vaccine (Menomune): tetravalent (A, C, Y, W-135), polysaccharide
  - Poor response < 2 years of age
  - Short duration of protection
  - ? Role of boosting: multiple doses may lead to immune hyporesponse with A, C
  - No effect on carriage
  - Serogroup B not covered

- Newer vaccine (Menactra): also tetravalent (A, C, Y, W-135), protein conjugate
  - Now approved for ages 9 months – 55 years
  - Longer lasting antibody titers
  - Good antibody response to revaccination
  - Serogroup B still not covered
  - Note: infants > 50% disease group B; ≥ 11 years, 75% disease C, Y, W-135

- Newest vaccine (Menveo): also tetravalent (A, C, Y, W-135), protein conjugate
  - Approved for ages 2 – 55 years
  - In a serum bactericidal assay, Menveo produced a statistically higher seroresponse than Menactra for serogroups A, W, and Y
  - Clinical relevance is unknown

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**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
  - Modestly increased risk for college freshmen in dormitories
- Booster doses now routine for adolescent and teenage vaccinees
### Meningococcal Conjugate Vaccine – Summary Table

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Primary series</th>
<th>Booster dose</th>
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</thead>
<tbody>
<tr>
<td>Age 11-18</td>
<td>1 dose, preferred age 11 or 12</td>
<td>• 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</td>
</tr>
<tr>
<td>&quot;Also, 1st yr. college students in residence halls up to age 21&quot;</td>
<td></td>
<td></td>
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<tr>
<td>Age 2-55 with complement deficiency or functional or anatomic asplenia</td>
<td>2 doses, 2 months apart</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>Age 2 – 55 with prolonged increased risk of exposure</td>
<td>1 dose</td>
<td>Age 2-6: after 3 years \Age 7 and older: after 5 years</td>
</tr>
</tbody>
</table>

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

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

- Also given to military recruits and travelers / residents with geographic risk
- Other notes:
  - HIV-infected persons who are vaccinated receive a two-dose primary series
  - 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
  - Outbreak in New York City among men who have sex with men, serogroup C – vaccine recommended fall 2012 based on HIV infection, neighborhood, behavioral risks

### Meningococcal Vaccine

- Clinical efficacy undetermined
  - Good results from protein conjugate meningococcal group C vaccines in UK and other countries
- Unlikely cost effective
- Newer studies suggest no increased risk Guillain-Barre
- New meningococcal vaccine for infants 6 months – 18 months; ACIP recommends if increased risk for meningococcal disease
  - Meningococcal groups C and Y plus *Haemophilus influenzae* type B (MenHibrix)  

**MMWR 2013;62:52-54**

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**Vesikari et al. Lancet 2013; published online**

Approved November 2012 by the European Medicines Agency: vaccine now called Bexsero
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 immunity wanes over time
- Resurgence in cases with peaks every 3-5 years
  - Pertussis outbreaks in United States, especially 2010 and 2012
  - Tdap (Boostrix) – licensed for ages 10 and up
  - Tdap (Adacel) licensed for 11 – 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

Waning immunity after acellular pertussis 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: IDWeek 2012
  - 465,059 persons 8-20 years old who received acellular vs. whole-cell vaccine (at least one dose)
  - ~ 8.6 relative risk of pertussis for acellular vaccine

Ward et al, NEJM, Oct. 2005
**Tdap – 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.
  - 2011: pregnant women not previously vaccinated should receive in late second or third trimester; *2012: recommended for every pregnancy at 27 – 36 weeks.

**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.

**Pertussis – other notes**

- No current recommendation to repeat Tdap (except pregnancy).
  - Given once – then back to Td.
- Many states now require Tdap for students in middle school.
  - Specific ages and grades vary by state.
- CDC does recommend single dose of Tdap for ages 7 – 10 for those not fully vaccinated against pertussis (including never vaccinated or unknown).

**Influenza Vaccines**

- Inactivated vaccine given by injection:
  - 2 influenza A strains; 1 influenza B strain.
  - Few contraindications.
  - Severe egg allergy – risk assessment, referral.
  - Severe previous reaction.
  - Guillain-Barre (relative contraindication).
  - Not usually given < 6 months of age.
- Live attenuated intranasal vaccine (FluMist):
  - Same strains as inactivated vaccine.
  - Newly approved FluMist Quadrivalent – 2 influenza A + 2 influenza B strains.
  - More people have contraindications.
Influenza Vaccine Indications

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

2013-2014 Influenza Vaccine

- A/California/7/2009 (H1N1)-like (same)
- Virus antigenically like A/Victoria/361/2011 (H3N2)-like (similar)
- B/Massachusetts/2/2012-like (new)
- For quadrivalent vaccine add:
  - B/Brisbane/60/2008-like

Estimated effectiveness for preventing laboratory confirmed influenza 12/3/12 – 1/19/13: 56%

MMWR 2013;62:119-123

High Dose TIV Vaccine

- Fluzone High-Dose licensed for those 65 and older
- Contains 60 µg of hemagglutinin per virus strain compared with 15 µg in regular dose TIV
- Enhanced immune response in those 65 and older with high dose vs. standard dose vaccine
- Local reactions (mild to moderate) more common with high dose vaccine J Infect Dis 2009;200:161-3
- No trials to date regarding high dose vaccine and prevention of influenza

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

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

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 TIV: 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
New influenza vaccines licensed in U.S.
- FluMist Quadrivalent: 2 influenza A and 2 influenza B strains; available 2013-14 season
- Fluarix Quadrivalent: 2 influenza A and 2 influenza B strains, intramuscular; available 2013-14 season
- FluBloc: baculovirus expression system, not grown in eggs
- Flucelvax: cell culture derived (canine kidney cells), not grown in eggs

Varicella Vaccine (Varivax)
- Recommended for all adults without immunity (history of varicella or laboratory evidence)
- Avoid in pregnancy and with most immunocompromise
- Given as 2 dose series for all ages
  - Two doses 98% effective in children
    - Shapiro et al, Journal Infect Dis 2011;203:312-15
  - Average annual mortality has declined 88% overall and 96% under age 50
    - Marin et al, Pediatrics 2011;128:214-20

Varicella Vaccine – Zoster (Zostavax)
- Recommended a single dose of zoster vaccine for adults age 60 and above, even if prior history of zoster
- Not necessary to ask about history of varicella or to do serologic testing (note VZV infects 98% of adult U.S. population per NHANES III data 2003)
- Contraindicated in many, but not all, immunocompromised persons (e.g. okay in HIV if clinically well and CD4 count > 200)

Varicella Vaccine – Zoster (Zostavax)
- Recommended 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

Oxman et al, NEJM, June 2005
- Randomized trial 38,546 adults ≥ age 60
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### Varicella Vaccine – Zoster (Zostavax)

- **Questions about cost effectiveness – multiple studies**
  - Vaccine cost ~ $150 per dose
  - Societal costs $27,000 – 112,000 per QALY
- **Vaccine is stored frozen**
  - Once reconstituted, must be used within 30 minutes
- **First vaccine covered by Medicare Part D – reimbursement was complicated**
- **May be given concurrently with Pneumovax - prior concerns decreased immunogenicity Zostavax**

### Varicella Vaccine – Zoster (Zostavax) Newer Data

- **Retrospective cohort study Kaiser Permanente 2007 – 2009**
  - 75,761 vaccinated members matched to 227,283 unvaccinated members
  - In adjusted analyses, significantly reduced risk, hazard ratio = .45
  - Lower incidence across all age strata

  *Tseng et al, JAMA 2011;305:160-66*

### Varicella Vaccine – Zoster (Zostavax) Newer Data

- **22,439 adults ages 50 – 59 randomized to zoster vaccine versus placebo**
  - 30 cases in vaccine group versus 99 in placebo group
  - Vaccine efficacy 70%
  - More adverse events, mostly injection-site reactions, in the vaccine group

  *Schmader et al, Clin Infect Dis 2012;54:922-8*

- **FDA approved Zostavax for persons 50 – 59 years of age in March 2011**

### 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 70% 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**
Both vaccines immunogenic in females and males
Excellent short-term efficacy (nearly 100%) in preventing infection with HPV types included in vaccine, if not previously infected
Recommended routinely for girls at age 11 – 12
Catch up recommended by CDC for females aged 13 – 26 years not previously vaccinated
Both vaccines given as 3 dose series

December 2010: FDA approved quadrivalent HPV vaccine (Gardasil) for prevention of anal cancer and precancerous lesions in persons ages 9 – 26
- Based on a study in men who have sex with men Palefsky et al, NEJM 2011;17:1576-85
- Gardasil was 50% effective (intention to treat) and 78% effective (per protocol) in preventing HPV 16 and 18 related anal intraepithelial neoplasia
- Data extrapolated to women and men who have sex with women

Per 2011 CDC recommendations, quadrivalent HPV vaccine should be given to males ages at age 11 or 12; recommended up to age 21; may be given ages 22 – 26 – and recommended to age 26 if MSM or immunocompromised

MMWR. December 23, 2011 / 60(50):1705-8

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

- Greatest benefit before onset of sexual activity / infection with HPV
- No protection against types with which already infected at time of vaccination
- Some evidence of partial cross protection against non-vaccine serotypes

HPV Vaccines - questions

- Expensive
- Cost effective – which populations?
- Not clear what effect will be on overall rates of precancerous lesions and cancer
- Some early suggestions of replacement with non-vaccine types in vaccinated women
- No recommendation to change cervical cancer screening based on vaccination status

Measles – it’s out there!

- 222 measles cases in U.S. in 2011
  - Median of 60 cases 2001 – 2010
  - 90% could be linked to importations from abroad
  - 86% of cases were unvaccinated or had unknown vaccination status
  - At least one recent healthcare-associated cluster
  - Remember vaccination before travel – large outbreaks in Europe and other regions
    - MMR can be given as early as 6 months of age in travelers

MMWR 2012;61:253-7

Mumps – it’s out there, too

- Mumps outbreak New York and New Jersey 2009
  - Orthodox Jewish community
  - Started at summer camp
  - 3502 outbreak-related cases
  - 89% had received two doses of mumps containing vaccine; 8% received one dose


- 2011 outbreak on UC Berkeley campus – 29 cases reported: 76% had received 2 doses MMR

MMWR 2012;61:986-989
Mumps...

- Children, adolescents, and young adults most affected
- Travel also a risk factor
  - Outbreaks in U.K. and other areas
- Most patients in U.S. have been vaccinated
  - 3 doses of mumps containing vaccine may be more effective – appears helpful in setting of an outbreak