Vaccinations for Adults and Adolescents: An Update

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Preventative Vaccines

- 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

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

Diseases/Pathogens with Vaccines for Special Populations

- Plague
- Tularemia
- Smallpox
- Anthrax
- Botulism
- Adenovirus
- Tuberculosis - BCG
Key Website
Centers for Disease Control and Prevention
http://www.cdc.gov/vaccines/

Pneumococcal Polysaccharide Vaccine - Revisited

- 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
- Additions/Changes as of 10/08:
  - Adults ages 19 – 64 with asthma should be vaccinated
  - Smokers 19 – 64 should be vaccinated given ~ 4X greater risk for pneumococcal disease
  - Revised recommendations for Alaskan Native and American Indian populations – vaccination no longer routine

Pneumococcal 13-Valent Conjugate Vaccine for Adults?

- Data presented at European Congress of Clinical Microbiology and Infectious Diseases in May 2011
- Two 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
  - Vaccine was well tolerated
- Applications for regulatory approval have been submitted in the U.S. and other countries – in U.S. approval delayed until at least Jan. 2012

FIGURE 1. Recommended adult immunization schedule, by vaccine and age group — United States, 2011

MMWR. February 4, 2011
Meningococcal Vaccine

Traditional vaccine (Menomune):
c 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

Who Should Get the Conjugate Meningococcal Vaccine?
* Recommended as routine for ages 11 - 18 – ideally given at age 11-12 visit
  * Feb. 2008 decision not to extend to lower ages as routine – can be given as early as 9 months to risk groups below (infants: one dose at 9 mo., one dose 12 mo.)
* “Catch up” at high school or college entry
  * Modestly increased risk college freshmen in dormitories
* Also for military recruits, some travelers, persons with terminal complement deficiencies, asplenia, microbiologists with routine exposure to meningococcus
Meningococcal Vaccine

- Clinical efficacy undetermined
  - Good results from meningococcal group C vaccines in UK and other countries
  - *Recent recommendation for revaccination of adults and adolescents every 5 years who remain at increased risk for infection (residence in on-campus housing excluded)
    - e.g., complement deficiencies, asplenia, travelers, microbiologists
- Unlikely cost effective
- Newer studies suggest no increased risk Guillain-Barre

Meningococcal Vaccine – latest information

- October 2010: Advisory Committee on Immunization Practices (ACIP) voted 6 to 5 to recommend a single, routine booster dose after 5 years for adolescents first vaccinated at age 11-13 years
- Also new recommendation for initial two dose series for persons with HIV infection (ages 11 – 18) and for persons with complement deficiencies or functional or anatomic asplenia (ages 2 – 55 years)

MMWR. January 28, 2011;60:72-76
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 clearly wanes over time
- Resurgence in cases
  - Estimated ~ 600,000/yr in 19-64 year olds
- Tdap (Boostrix) – licensed for ages 10 - 64 years
- Tdap (Adacel) licensed for 11 – 64 years

Pertussis – Recommendations

- For adults 19-64, give single dose Tdap to replace a dose of Td
- *New: can be given at any interval from last tetanus-containing vaccine
- Strongly recommended for adults who will have contact with infant < 12 months
  - Give immediately post-partum if not given previously

Pertussis – Recommendations

- Substitute single dose Tdap for Td in wound management or if primary series unknown or incomplete
- For adolescents, give Tdap instead of Td at routine 11-12 yr visit
Pertussis – Recommendations

- No current recommendation for Tdap booster
  - Given once – then back to Td
- ACIP recommendation June 2011 that pregnant women not previously vaccinated receive vaccine in late second or third trimester
- Recommended for healthcare workers with patient contact

Pertussis – New Recommendations

- *New - adults age 65 and older
  - If close contact with an infant less than 12 months anticipated, should received a single dose of Tdap
  - Others may be given a single dose of Tdap
  - Still not licensed but unpublished data suggest safety not different from < age 65
  - Both Adacel and Boostrix appear to be immunogenic

Pertussis – Legislation

- 35 states now require, or will soon 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)

Pertussis Vaccine – Does it work?

Ward et al, NEJM, Oct. 2005:
- 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
Influenza Vaccines
- Inactivated vaccine given by injection
  - 2 influenza A strains; 1 influenza B strain
  - Few contraindications
    - Anaphylaxis to eggs
    - Severe previous reaction
    - Guillain-Barre (relative contraindication)
  - Not usually given < 6 months of age
- Live attenuated intranasal vaccine (FluMist)
  - Same strains as inactivated vaccine
  - More people have contraindications

Seasonal Influenza Vaccine Indications 2009 - 2010
- Adults > 50 years
- Children 6 months to 18 years
- > 6 months with a chronic medical condition
  - Includes asthma; excludes isolated hypertension
- Residents of long-term care facilities
- Pregnancy during influenza season
- Healthcare workers
- Healthy persons with high-risk contacts
- ~ 83% U.S. population included in target groups

2010 - 2011 Influenza Vaccine Indications
- All people older than 6 months
  - Unless there is a contraindication

2011-2012 Influenza Vaccine Composition
- A/California/7/2009 (H1N1)-like
- A/Perth/16/2009 (H3N2)-like
- B/Brisbane/60/2008-like

Same composition as for 2010-2011
High Dose TIV Vaccine
- 12/09 FDA licensed Fluzone High-Dose for persons 65 and older
- Contains 60 µg of hemagglutinin per strain of virus compared with 15 µg of hemagglutinin per strain of virus in regular dose TIV
- In Phase 3 trial of adults 65 and older, enhanced immune response with high dose compared with standard dose vaccine
- Local reactions (mild to moderate) more common with high dose vaccine

Intradermal Influenza Vaccine
- Fluzone intradermal vaccine approved by FDA in May 2011
- Expected to be available 2011-12 influenza season
- 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 – 65 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)
  - Anaphylaxis to eggs
  - Contact with highly immunosuppressed patients, e.g. bone marrow transplant
Live Attenuated Influenza Vaccine

- 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 active duty military ages 17 – 49 over 3 influenza seasons (> 1 million people followed)
- High levels of annual vaccination
  - Range 52% in ’04-’05 to 78% in ’06-’07
  - LAIV used in 34% in ’04-’05 and 48% in ’06-’07
- Lowest number of healthcare encounters for pneumonia and influenza in inactivated vaccine cohort
  - LAIV was not as effective; better efficacy in vaccine-naive
  - Hospitalizations for pneumonia and influenza actually higher for LAIV than unimmunized group

Wang et al, JAMA 2009;301:945 - 53

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
  - Average annual mortality has declined 88% overall and 96% under age 50

Shapiro et al, Journal Infect Dis 2011;203:312-15

Varicella Vaccine – Zoster (Zostavax)

- 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

Oxman et al, NEJM, June 2005
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)

- 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 has been 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
  - New study presented at IDSA October 2010
  - 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, Infectious Diseases Society of America Meeting Presentation 1380, October 2010

- FDA approved Zostavax for persons 50 – 59 years of age on March 24, 2011
**Human Papillomavirus (HPV) Vaccines**

- Genital HPV most common sexually transmitted infection in the U.S.
- Quadrivalent HPV vaccine (Gardasil) licensed by FDA June 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
- Oct. 2009, FDA approved bivalent vaccine against types 16/18 (Cervarix) for girls and women age 10 - 25

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**HPV Vaccines**

- 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 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

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**HPV Vaccine – Newer Study: External Genital Lesions in Men and Boys**

- Per CDC recommendations, quadrivalent HPV vaccine may be given to males ages 9 – 26 to protect against genital warts
- 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
  - Gardasil was 78% effective in preventing HPV 16 and 18 related anal intraepithelial neoplasia
  - Data extrapolated to women and men who have sex with women

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**HPV Vaccine – Newer Study: External Genital Lesions in Men and Boys**

- 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 (limited)

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