Vaccinations for Adults: 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
- Vaccine skeptics
- A number of new vaccines over past few years

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
- Inactivated polio
- Influenza
- Rabies
- Typhoid
- Yellow fever
- Japanese encephalitis

Vaccines for Special Populations

- Plague
- Tularemia
- Smallpox
- Anthrax
- Botulism
- (Adenovirus)
- Tuberculosis - BCG
Recent resurgence of Mumps in the United States


- >6500 mumps cases in the U.S. in 2006 (typically <350/yr.)
- Most cases in Illinois, Iowa, Kansas, Minnesota, Missouri, Nebraska, South Dakota, and Wisconsin
- Strong association with college campuses

Recent outbreak, cont.

- Thought to have been imported from United Kingdom
- Most patients had received two doses of mumps vaccine (63% overall; 84% 18–24 year-olds)
- Complication rate was low
  - Lower than historically reported
- Outbreak small compared with prevaccine era (~150,000 cases in U.S. yearly)
Mumps Vaccination for Healthcare Workers

- Born before 1957: consider 1 dose vaccine unless immune
  - Immunity defined as physician-diagnosed mumps or positive serology
  - Use 2 doses during mumps outbreak unless immune
- Born during or after 1957: 2 doses of vaccine (if not previously given) unless immune
- Note that vaccination gives lower antibody titers than natural infection; post-vaccination serology may be negative

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

Meningococcal Vaccine

- New vaccine (Menactra): also tetravalent (A, C, Y, W-135), protein conjugate
  - Approved January 2005 for ages 11 – 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

Who Should Get the New Meningococcal Vaccine?

- Recommended as routine for ages 11 - 18 – ideally given at age 11-12 visit
- “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
- *Note that supply problems have now improved
Meningococcal Vaccine - Questions

- Clinical efficacy undetermined
  - Good results from meningococcal group C vaccines in UK and other countries
- No current recommendations on revaccination
- Unlikely cost effective
- 17 cases of Guillain-Barre syndrome between June 2005 and Sept 2006 within 6 weeks of meningococcal vaccine
  - Slight increase above expected rate

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
- May 2005: Tdap (Boostrix) approved for ages 10 – 18 years
- June 2005: Tdap (Adacel) approved for 11 – 64 years

Pertussis – Recommendations

- For adults 19-64, give single dose Tdap to replace Td if last Td > 10 yrs
- Okay to give at 2 yr interval from last tetanus-containing vaccine (shorter probably fine in specific circumstances)
- Recommended for adults who will have contact with infant < 12 months
  - Give immediately post-partum if not 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

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**Pertussis – Recommendations**

- No current recommendation for Tdap booster
  - Given once – then back to Td
- Currently not during pregnancy – use Td
- Recommended for healthcare workers with patient contact
- Not licensed for ages ≥ 65 years

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**Pertussis Vaccine – 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

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**Influenza Vaccines**

- Inactivated vaccine given by injection
  - 2 influenza A strains; 1 influenza B strain
  - Very few contraindications
- Live attenuated intranasal vaccine (FluMist) may be less familiar
  - Same strains as inactivated vaccine
  - Attenuated, heat sensitive and cold adapted
  - Approved for healthy persons ages 2 – 49, including healthcare workers and contacts of most high risk patients
Influenza Vaccine Indications

- Adults > 50 years
- Children 6 – 59 months
- > 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

Influenza Vaccine Indications

218 million people targeted in U.S.: 73% of population

Live Attenuated Influenza Vaccine

- Runny/stuffy nose is common
- 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)


Live Attenuated Influenza Vaccine

- Who should not get LAIV?
  - Outside recommended age ranges
  - Chronic medical conditions, including asthma
  - Pregnant women
  - History of Guillain-Barre
  - Anaphylaxis to eggs
  - Contact with highly immunosuppressed patients, e.g. bone marrow transplant
H5N1 Vaccine Development

- H5N1 prototype strains for pandemic vaccine development are available through WHO
- Complicated by two distinct clades (1 & 2)
  - Clade 2 has at least 3 geographically distributed subclades
- Sanofi Pasteur and Novartis Vaccine have vaccine development contracts with the National Institutes of Health
  - From Vietnamese patient 2004 (clade 1)
  - Phase 1 human testing began 2005

H5N1 Vaccine Trial

- Sanofi Pasteur vaccine trial in 451 subjects
- Subjects received 90, 45, 15, or 7.5 µg of hemagglutinin antigen or placebo in 2 doses 28 days apart
- Of subjects in the 90 µg group who received 2 doses, only 54% had a "protective" neutralization antibody titer
- FDA approved 4/07; U.S. National Stockpile
**H5N1 Vaccine Trial - Beijing**

- Two doses of placebo or inactivated whole virion vaccine: doses 1.25 µg, 2.5 µg, 5 µg, 10 µg (24 subjects in each arm)
  - Aluminum hydroxide adjuvant
- Dose dependent response
- 78% met seropositivity threshold after two doses with 10 µg
- April 2008: vaccine licensed by China for stockpile

**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 doses – now recommended for all ages (not just 13 years and up)

**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)

- Advisory Committee on Immunization Practices (ACIP) posted provisional recommendations 11/20/06
- Formal recommendations expected soon
- Recommended a single dose of zoster vaccine for adults age 60 and above, even if prior history of zoster
- Contraindicated in immunocompromised persons
- Questions regarding cost effectiveness – cost is about $150

Human Papillomavirus (HPV) Vaccine

- 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
- FDA approval pending for bivalent vaccine against types 16/18 (Cervarix)

HPV Vaccine

- Excellent 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 for females aged 13 – 26 years not previously vaccinated
- 3 dose series: 0, 2, 6 months

HPV Vaccine

- 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
Ongoing controversy
- Debate regarding whether vaccine should be “mandatory,” as with other vaccines required for school admission
  - Very new; durability unclear
  - Different kind of public health issue

Cost approximately $360 for series
- Not clear what effect will be on overall rate of precancerous lesions and cervical cancer
  - Some early suggestions of replacement with non-vaccine types in vaccinated women
  - No recommendation to change screening
- Results of studies in males pending