Immunizations to Consider in Adult HIV Patients

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Disclosures

- The speaker does not have any financial relationships with commercial entities to disclose.
- The speaker will not discuss any off-label use or investigational product during the program.

This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation.
Objectives

- Discuss the current immunization recommendations by the CDC Advisory Committee on Immunization Practices (ACIP) for adult HIV patients
- Discuss upcoming changes in the immunization schedule
- Review data supporting the use of meningococcal and pneumococcal vaccines
- Examine the use of Herpes zoster vaccine in HIV patients
- Describe Medicare and Medicaid coverage of immunizations
Vaccines: issues to consider

- Prevention of mortality and morbidity
- Vaccine schedule
- Injected, spray, oral
- Live attenuated, inactivated
- Immune response/CD4
- Costs, insurance
The compromised host

- Defects in cell mediated immunity
- B cell dysfunction
- Suboptimal humoral immune response
# Immune Response

<table>
<thead>
<tr>
<th></th>
<th>Humoral-Mediated Immunity</th>
<th>Cell-Mediated Immunity</th>
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<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Antibody-mediated</td>
<td>Cell-mediated</td>
</tr>
<tr>
<td><strong>Cell Type</strong></td>
<td>B Lymphocytes</td>
<td>T Lymphocytes</td>
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<tr>
<td><strong>Mode of action</strong></td>
<td>Antibodies circulating in serum</td>
<td>Direct cell-to-cell contact or secreted soluble products (e.g. cytokines)</td>
</tr>
<tr>
<td><strong>Purpose</strong></td>
<td>Primary defense against extracellular pathogens: extracellular bacteria, circulating virus</td>
<td>Primary defense against intracellular pathogens: viruses and fungi, intracellular bacteria, (also tumor antigens, and graft rejection)</td>
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</tbody>
</table>
HUMORAL (ANTIBODY-MEDIATED) IMMUNE SYSTEM
Control of freely circulating pathogens

1. A B cell binds to the antigen for which it is specific. Usually requires cooperation from helper T cell.

2. The B cell, often with stimulation from a helper T cell, differentiates into a plasma cell.

3. Plasma cells proliferate and produce antibodies against the antigen.

CELL-MEDIATED IMMUNE SYSTEM
Control of intracellular pathogens

1. A T cell binds to MHC-antigen complexes on the surface of the infected cell, activating the T cell (with its cytokine receptors).

2. A helper T cell produces cytokines that cause the activated T cell to differentiate into a cytotoxic T cell. These cytokines also influence the formation of plasma cells and activated macrophages.

3. The infected target cell is lysed by the cytotoxic T cell.

Intracellular antigens expressed on the surface of a cell infected by a virus, bacterium, or parasite. (Also may be expressed on surface of an APC.)

http://classes.midlandstech.edu/carterp/Courses/bio225/chap17/17-19_Duality_1.jpg
Classification of Vaccines

- Live attenuated
  - viral
  - bacterial
- Inactivated

Inactivated Vaccines

- Whole
  - viruses
  - bacteria
- Fractional
  - protein-based
    - toxoid
    - subunit
  - polysaccharide-based
    - pure
    - conjugate
Vaccine Types

**Live, attenuated vaccines (LAV):**
Contains a weakened but live form of a disease-causing microbe that can trigger an immune response. The attenuated (weakened) microbe typically does not cause the disease.

**Inactivated vaccines:**
Made from microbes that have been killed with chemicals, heat, or radiation. There is no risk that an inactivated vaccine can cause disease from infection.
Inactivated Polysaccharide Vaccines: pure and conjugate

**Pure Polysaccharide:**
Subunit vaccine composed of chains of sugar molecules that make up the surface capsule of certain bacteria

**Conjugate Polysaccharide:**
Polysaccharide is chemically combined with a protein molecule (antigen/toxoid) to increase potency
Polysaccharide Vaccines

Pure polysaccharide
- pneumococcal
- meningococcal
- *Salmonella Typhi* (Vi)

Conjugate polysaccharide
- *Haemophilus influenzae* type b (Hib)
- pneumococcal
- meningococcal

# Live Vaccines

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Viruses</th>
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<tbody>
<tr>
<td>Tuberculosis (BCG)</td>
<td>Oral Polio Vaccine (OPV)</td>
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<td>Measles</td>
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<td>Yellow Fever</td>
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<td>Varicella/Herpes Zoster</td>
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<td>Live attenuated flu vaccine (LAIV)</td>
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</tbody>
</table>
CDC Recommended Immunizations for Adult HIV Patients

- Hepatitis B
- Influenza
- Pneumococcal
- Tetanus, diphtheria, and pertussis (Tdap)
- Human papillomavirus (HPV)
- (Meningococcal)
HIV: Contraindicated if CD4 <200

- Varicella
- Zoster
- Measles, Mumps, Rubella (MMR)
<table>
<thead>
<tr>
<th>Indication</th>
<th>Vaccine</th>
<th>Immuno-compromising conditions (excluding HIV infection)</th>
<th>HIV infection CD4+ count (cells/μL)</th>
<th>Men who have sex with men (MSM)</th>
<th>Kidney failure, end-stage renal disease, on hemodialysis</th>
<th>Heart disease, chronic lung disease, chronic alcoholism</th>
<th>Asplenia and persistent complement deficiencies</th>
<th>Chronic liver disease</th>
<th>Diabetes</th>
<th>Healthcare personnel</th>
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<td>Influenza*</td>
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<td>Td/Tdap**</td>
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<td>Substitute Tdap for Td once, then Td booster every 10 yrs</td>
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<td>HPV Female*</td>
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<td>MenACWY or MPSV4**</td>
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http://www.immunize.org/shop/views/adultsched_pg2.pdf
### CDC: 2016 Recommended Immunizations for Adults: By Health Condition

<table>
<thead>
<tr>
<th>Health Condition</th>
<th>Flu Influenza</th>
<th>Td/Tdap Tetanus, diphtheria, pertussis</th>
<th>Shingles Zoster</th>
<th>Pneumococcal</th>
<th>Meningococcal</th>
<th>MMR Measles, mumps, rubella</th>
<th>HPV Human papillomavirus</th>
<th>Chickenpox Varicella</th>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hib Haemophilus influenza type b</th>
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<tbody>
<tr>
<td>Pregnancy</td>
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<td>Weakened Immune System</td>
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<td>HIV: CD4 count less than 200</td>
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<td>HIV: CD4 count 200 or greater</td>
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<td>Kidney disease or poor kidney function</td>
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<td>Asplenia (if you do not have a spleen or if it does not work well)</td>
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<td>Heart disease Chronic lung disease Chronic alcoholism</td>
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<td>Diabetes (Type 1 or Type 2)</td>
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<td>Chronic Liver Disease</td>
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### CDC: 2016 Recommended Immunizations for Adults: By Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Flu Influenza</th>
<th>Td/Tdap Tetanus, diphtheria, pertussis</th>
<th>Shingles Zoster</th>
<th>Pneumococcal</th>
<th>Meningococcal</th>
<th>MMR Measles, mumps, rubella</th>
<th>HPV Human papillomavirus</th>
<th>Chickenpox Varicella</th>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hib Haemophilus influenzae type b</th>
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<tr>
<td>19 - 21 years</td>
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<td>22 - 26 years</td>
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<td>27 - 49 years</td>
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<td>50 - 59 years</td>
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<td>60 - 64 years</td>
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2017: Schedule Updates

- *Schedule will contain more information on adults with immune-compromising medical conditions*
- Age groups 27 to 49 and 50 to 59 years combined into one block.
- Column for MSM has been relocated to alert healthcare providers to look at high-risk populations.
2017 Updates

- Varicella and zoster vaccinations: details added for at-risk populations (healthcare workers, HIV).
- HPV vaccination: details added on vaccinating adults with immunocompromising conditions and the MSM population.
- Incorporated June 2016 recommendation for routine vaccination of all HIV-infected adults with a two-dose primary ACWY meningococcal series with revaccination every 5 years.
Meningococcal update

- Five serogroups of meningococcus bacteria (A, B, C, W, Y)
- In the USA: serogroups B, C, and Y most common
- In HIV patients: serogroups A, C, W, Y most common
- HIV infection confers an additional 5- to 24-fold risk of meningococcal disease compared to uninfected persons
- Lower CD4 and higher viral load increase risk
- Different vaccines depending on age, risk factors

https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm
Available Vaccines

1) Meningococcal conjugate vaccine:
   - MenACWY (Menactra® or Menveo®): quadrivalent (A, C, W, Y)
   - Hib-MenCY-TT (MenHibrix®): bivalent (C, Y), H.influenzae (type B)

2) Meningococcal polysaccharide vaccines:
   - MPSV4 (Menomune®): quadrivalent (A, C, W, Y)
   - MenB (Bexsero® or Trumenba®): monovalent (B)
CDC 2016: Recommended Adult Immunization schedule

<table>
<thead>
<tr>
<th>Indication</th>
<th>Vaccine</th>
<th>Immunocompromising conditions (excluding HIV infection)</th>
<th>HIV infection CD4+ count (cells/µL)</th>
<th>Men who have sex with men (MSM)</th>
<th>Kidney failure, end-stage renal disease, on hemodialysis</th>
<th>Heart disease, chronic lung disease, chronic alcoholism</th>
<th>Asplenia and persistent complement deficiencies</th>
<th>Chronic liver disease</th>
<th>Diabetes</th>
<th>Healthcare personnel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza*</td>
<td>1 dose Td each pregnancy</td>
<td>1 dose annually</td>
<td>Substitute Tdap for Td once, then Td booster every 10 yrs</td>
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<tr>
<td>Td/Tdap**</td>
<td>Contraindicated</td>
<td>2 doses</td>
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<tr>
<td>Varicella*</td>
<td>Contraindicated</td>
<td>3 doses through age 26 yrs</td>
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<td>HPV Female*</td>
<td>Contraindicated</td>
<td>3 doses through age 26 yrs</td>
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<td>HPV Male*</td>
<td>Contraindicated</td>
<td>3 doses through age 21 yrs</td>
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<td>Zoster*</td>
<td>Contraindicated</td>
<td>1 dose</td>
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<td>MMR*</td>
<td>Contraindicated</td>
<td>1 or 2 doses depending on indication</td>
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<td>PCV13*</td>
<td>1 dose</td>
<td>1, 2, or 3 doses depending on indication</td>
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<td>PPSV23*</td>
<td>2 or 3 doses depending on vaccine</td>
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<td>Hepatitis A*</td>
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<td>1 or more doses depending on indication</td>
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<td>Hepatitis B*</td>
<td>3 doses</td>
<td>2 or 3 doses depending on vaccine</td>
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<tr>
<td>MenACWYW or MPSV4*</td>
<td>3 doses post-HSCT recipients only</td>
<td>1 dose</td>
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<td>MenB**</td>
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http://www.immunize.org/shop/views/adultsched_pg2.pdf
There is no recommendation for MenB revaccination at this time. MenB vaccine may be administered concomitantly with MenACWY vaccine but at a different anatomic site, if feasible.

HIV infection is not an indication for routine vaccination with MenACWY or MenB vaccine; if an HIV-infected person of any age is to be vaccinated, administer 2 doses of MenACWY vaccine at least 2 months apart.

http://www.immunize.org/shop/views/adultsched_pg2.pdf

Weekly / November 4, 2016 / 65(43);1189–1194

Jessica R. MacNeil, MPH1; Lorry G. Rubin, MD2; Monica Patton, MD1; Ismael R. Ortega-Sanchez, PhD3; Stacey W. Martin, MS1 (View author affiliations)

At its June 2016 meeting, the Advisory Committee on Immunization Practices (ACIP) recommended routine use of meningococcal conjugate vaccine (serogroups A, C, W, and Y; including MenACWY-D [Menactra, Sanofi Pasteur] or MenACWY-CRM [Mencevo, GlaxoSmithKline]) for persons aged ≥2 months with human immunodeficiency virus (HIV) infection. ACIP has previously recommended routine vaccination of persons aged ≥2 months who have certain medical conditions that increase risk for meningococcal disease (1), including persons who have persistent (e.g., genetic) deficiencies in the complement pathway (e.g., C3, properdin, Factor D, Factor H, or C5–C9); persons receiving eculizumab (Soliris, Alexion

https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm
Updated Recommendations:

- June 22, 2016: ACIP recommends use of meningococcal conjugate vaccine amongst HIV patients >2 months
- Two doses 8 weeks apart, with booster every 5 years until age 70
- Evaluated meningococcal disease epidemiology against cost effectiveness of a vaccination schedule
- Based on immunogenicity data from two studies

https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm
The study

- Open label trial: 324 HIV infected individuals (11-24 yrs) received one dose at entry
- After 24 weeks, based on CD4% >15%, randomized to receive another dose
- Those with CD4% <15% all received a second dose

https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm
- Measured antibodies against each serogroup at weeks 4, 24, 28, 72 (predefined titer 1:128)
- Response based on CD4% (serogroup C)

<table>
<thead>
<tr>
<th></th>
<th>4 weeks</th>
<th>28 weeks</th>
<th>72 weeks</th>
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<tbody>
<tr>
<td>CD4 &gt;15% (1 dose)</td>
<td>65%</td>
<td>31%</td>
<td>21%</td>
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<tr>
<td>CD4 &gt;15% (2 doses)</td>
<td>59%</td>
<td>64%</td>
<td>35%</td>
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<tr>
<td>CD4 &lt;15% (2 doses)</td>
<td>22%</td>
<td>22%</td>
<td>6%</td>
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</tbody>
</table>

https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm
Safety

- Adverse events assessed for 6 weeks after each dose; inversely related to entry CD4%
- 5% reported a serious adverse event (AE)- one AE judged to be related to MenACWY

Summary of evidence for meningococcal conjugate vaccination of HIV-infected persons aged ≥2 months using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)* framework — United States

<table>
<thead>
<tr>
<th>Harms</th>
<th>Grade</th>
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<tbody>
<tr>
<td>Serious adverse events (after any dose)</td>
<td>4</td>
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</tbody>
</table>

https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm
GRADE

- Grading of Recommendations, Assessment, Development and Evaluations (GRADE)
- CDC vaccine recommendations are developed using this evidence-based method
- A systematic, explicit, transparent approach to making judgements about quality of evidence and strength of recommendations
- Widely seen as the most effective method of linking evidence-quality evaluations to clinical recommendations
Formulate question
Select outcomes
Rate importance
Outcomes across studies
Create evidence profile with GRADEpro
Rate quality of evidence for each outcome
Randomization increases initial quality

Grade up:
1. Large effect
2. Dose response
3. Confounders

Grade down:
1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

Summary of findings & estimate of effect for each outcome

PICCO

Outcome Critical
Outcome Critical
Outcome Important
Outcome Not important

systematic review

Guideline development

Formulate recommendations:
- For or against (direction)
- Strong or conditional/weak (strength)

By considering:
- Quality of evidence
- Balance benefits/harms
- Values and preferences

Revise if necessary by considering:
- Resource use (cost)

Grade overall quality of evidence across outcomes based on lowest quality of critical outcomes

- “We recommend using…”
- “We suggest using…”
- “We recommend against using…”
- “We suggest against using…”

MenACWY can be given with PCV13
No data for the use of MPSV4 in HIV patients
Pregnancy should not preclude vaccination with MenACWY
Compared with no vaccination, approximately 122 cases and 23 deaths can be prevented
385 quality-adjusted life years (QALYs) saved at mean cost of $732,000 per QALY

https://www.cdc.gov/mmwr/volumes/65/wr/mm6543a3.htm
Pneumococcal vaccine

Invasive pneumococcal disease remains a source of significant morbidity and mortality amongst HIV-infected individuals.

Incidence of bacterial pneumonia is higher in HIV-infected individuals than in those who are not HIV infected.

Recurrent pneumonia (2 or more episodes within a 1-year period) is an AIDS-defining condition.

Rates of pneumococcal bacteremia remains 35-fold higher than in age-matched HIV-uninfected persons.

Pneumococcal vaccinations

- Pneumococcal polysaccharide vaccine
  - PPSV23
    - Pneumovax 23®

- 13-valent pneumococcal conjugate vaccine
  - PCV13
    - Prevnar 13®

- PCV13 and PPSV23 are covered by Medicare Part B
Current Recommendations

- Those who have never received any pneumococcal vaccine should receive a single dose of PCV13 regardless of CD4 count (AI)
- Those with CD4 ≥200 cells/mm³ should then receive a dose of PPV23 at least 8 weeks later (AII)
- Those with CD4 <200 cells/mm³ can receive PPSV23 eight weeks after PCV13 (CIII), however, it may be preferable to defer until CD4 increases to >200 cells/mm³ (BIII)

Pneumococcal Vaccination schedule

8 weeks  ➔  ➔  ➔  PPSV23  ➔  ➔  ➔  PPSV23  ➔  ➔  ➔  PPSV23

5 years  ➔  ➔  ➔  PPSV23

>65 years  ➔  ➔  ➔  PPSV23
1 year

PPSV23 → → → PCV13
ACIP study analysis: 
(PCV13, PPSV23)

- Evidence of benefits, harms, values and preferences, and cost-effectiveness were reviewed in accordance with GRADE methods
- Both vaccines were evaluated using data for HIV-infected adults
- Studies with 7-valent pneumococcal conjugate vaccine (PCV7) used as a proxy when no PCV13 studies were available
- Randomized controlled trials (RCT), direct observations studies
- PCV13 (RCTs), PPSV23 (1 RCT and 9 observational studies with conflicting data)

https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html
Outcomes Reviewed

- Prevention of death
- Invasive pneumococcal disease (IPD)
- Pneumococcal pneumonia
- Hospitalizations due to pneumococcal disease
- Vaccine-induced immunogenicity
- Adverse events

https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html
Table 1. Benefits: 13-valent Pneumococcal Conjugate Vaccine in immunocompromised adults

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. subjects (# studies)</th>
<th>Incidence in unvaccinated (cases/100,000)</th>
<th>Incidence in vaccinated unvaccinated (cases/100,000)</th>
<th>Vaccine efficacy (95% CI)</th>
<th>unvaccinated (cases/100,000)</th>
<th>Number needed to vaccinate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive Pneumococcal Disease a</td>
<td>496 (1 RCT, HIV+ adults, Malawi)</td>
<td>64&lt;sup&gt;c&lt;/sup&gt;</td>
<td>17&lt;sup&gt;d&lt;/sup&gt;</td>
<td>74% (30, 90)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>47&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2128&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html
Table 5. Considerations for Formulating Recommendations: 13-valent Pneumococcal Conjugate Vaccine in immunocompromised adults

<table>
<thead>
<tr>
<th>Key factors</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence type for benefits and harms</td>
<td>Indirectness &amp; lack of evidence for 3 of 4 critical disease outcomes</td>
</tr>
<tr>
<td>Balance between benefits and harms</td>
<td>Benefits outweigh harms. Very high burden of disease in immunocompromised adults</td>
</tr>
<tr>
<td>Value</td>
<td>ACIP pneumococcal work group consensus regarding the importance of preventing critical pneumococcal outcomes</td>
</tr>
<tr>
<td>Cost-effectiveness</td>
<td>Uncertainty regarding costs/benefits relative to PPSV23</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html
# PPSV23

## Table 7. Summary of Evidence: 23-valent Pneumococcal Polysaccharide Vaccine in immunocompromised adults

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Outcome</th>
<th>Study design (# studies)</th>
<th>Findings</th>
<th>Evidence type</th>
<th>Overall Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPSV23 vs. Placebo</td>
<td>Death</td>
<td>RCT (1)</td>
<td>Inconclusive data on efficacy against mortality</td>
<td>3</td>
<td>3/4</td>
</tr>
<tr>
<td>PPSV23 vs. Placebo or No vaccination</td>
<td>IPD&lt;sup&gt;b&lt;/sup&gt;</td>
<td>RCT (1) Observational (6)</td>
<td>Negative efficacy among highly immunosuppressed adults; effectiveness against all IPD 49% (34%, 61%) from observational studies</td>
<td>3/4</td>
<td>3/4</td>
</tr>
<tr>
<td>PPSV23 vs. Placebo or No vaccination</td>
<td>All-cause pneumonia</td>
<td>RCT (1) Observational (5)</td>
<td>Negative efficacy among highly immunosuppressed adults; effectiveness of 31% (27%, 36%) from observational studies</td>
<td>3/4</td>
<td>3/4</td>
</tr>
<tr>
<td>PPSV23</td>
<td>Systemic adverse events</td>
<td>Post-licensure surveillance</td>
<td>PPSV23 appears safe for use among adults with HIV</td>
<td>3</td>
<td>3/4</td>
</tr>
</tbody>
</table>

<sup>b</sup> IPD = Infectious Disease

https://www.cdc.gov/vaccines/acip/recks/grade/pneumo-immuno-adults.html
Table 8. Considerations for Formulating Recommendations: 23-valent Pneumococcal Polysaccharide Vaccine in immunocompromised adults

<table>
<thead>
<tr>
<th>Key factors</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence type for benefits and harms</td>
<td>Inconsistent evidence for all-cause pneumonia; limited data from RCT not generalizable to the US HIV+ population</td>
</tr>
<tr>
<td>Balance between benefits and harms</td>
<td>Some uncertainty about benefits. Vaccine appears to be safe in this population</td>
</tr>
<tr>
<td>Value</td>
<td>ACIP pneumococcal work group consensus regarding the importance of preventing critical pneumococcal outcomes</td>
</tr>
<tr>
<td>Cost-effectiveness</td>
<td>Cost-effectiveness in the general adult population demonstrated; uncertainty around the assumptions utilized in cost-effectiveness analysis</td>
</tr>
</tbody>
</table>

Summary: Benefits are likely greater than harms. High values were placed on prevention of the morbidity and mortality of pneumococcal infection among immunocompromised adults. (recommendation category B, evidence type 3/4)

https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html
ACIP Conclusions

- Half of IPD in immunocompromised adults caused by serotypes included in PCV13 immunization; an additional 21% caused by serotypes included in PPSV23 immunization
- Antibody response is non-inferior or superior when PCV13 is given before PPSV23 compared to PPSV23 administration before PCV13
- Compared to giving PPSV23 first as an initial dose, there is a significant increase in antibody (non-inferior to superior response) when PPSV23 is given eight weeks after PCV13

https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html
Final Recommendations

- For adults previously immunized with PPSV23, waiting at least 1 year after PPSV23 before giving a dose of PCV13 may provide a better immune response (expert opinion)

- GRADE (Grading of Recommendations, Assessment, Development and Evaluation) process led to the conclusion that both PCV13 and PPSV23 are effective in this group & that benefits likely outweigh harms

https://www.cdc.gov/vaccines/acip/recs/grade/pneumo-immuno-adults.html
Risk of varicella reactivation as herpes zoster is increased in persons over age 50

Those with HIV have up to a 10-fold higher risk compared with HIV-uninfected persons, even with effective use of ART
Zoster Vaccine (Zostavax®)

- Approved by the FDA (May, 2006) for those >50 yrs
- Recommended by CDC (single dose) for those >60 yrs
- Reduces incidence of shingles by around 51%
- Reduces severity and duration of pain by around 67%
- ACIP guidelines do not require documented history of primary varicella/zoster, nor evidence of varicella antibody prior to vaccination

https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6333a3.htm
Herpes Zoster vaccine safe and effective in HIV positive people

1 April 2012. Related: Conference reports, Vaccines and microbicides, CROI 19 (Retrovirus) 2012.

Simon Collins, HIV i-Base

Encouraging results were presented from the ACTG A5247 study on the use of two doses of a live varicella zoster virus (VZV) vaccine (Zostavax, Merck) in almost 400 HIV positive people who were VZV positive or who had herpes zoster (HZ)/shingles outbreak at least one year before study entry, and who were virally suppressed on stable ART. [1]

The incidence and severity of HZ and post herpatic neuralgia (PHN) is higher in HIV positive people and early use of early acyclovir treatment is not always effective. As susceptibility to HZ increases with reduced age-related immune function, a protective vaccine response already demonstrated in HIV negative people > 60 years [2] would be particularly important for HIV positive people.

http://i-base.info/htb/16280
ACTG A5247: CROI 2012

- Two doses of Zostavax given to 395 HIV positive patients
- Randomized 3:1 to active or placebo arms
- Stratified by CD4 count: 200-349 vs >350
- Median age 49
- 75% were VZV positive, 33% had a shingles outbreak one year prior to study entry
- All were virally suppressed on ART

https://www.poz.com/article/hiv-zostavax-shingles-22067-3905
The Study

- Vaccinations: Day 0 and at week 6
- Immune responses evaluated at weeks 2, 6, 8, 12, and 24
- Primary endpoints were: 1) Safety 2) efficacy (change in VZV titer at 6 weeks)

https://www.poz.com/article/hiv-zostavax-shingles-22067-3905
Study Outcomes

- No significant differences between active and placebo groups regarding safety
- Mean fold-rise in VZV antibody titer increased by 1.75 ZV vs 1.09 placebo from baseline to week 6 (p<0.001)
- This remained similar at week 12 (indicating no change from the second dose)
- Patients with higher CD4 count (>350) had higher antibody titer over time (p=0.024)

https://www.poz.com/article/hiv-zostavax-shingles-22067-3905
Safety

- Injection site reactions more frequent in the active group (42% vs 12 %, p<0.01).
- VZV-like rashes seen in 3 active and 2 placebo patients (PCR showing negative or non-vaccine-strain results).

https://www.poz.com/article/hiv-zostavax-shingles-22067-3905
Study not conducted long enough to determine whether Zostavax actually reduces the risk of outbreaks compared with placebo.
HIV and Zostavax®

- No specific recommendations for HIV-infected patients
- Live attenuated vaccine → contraindicated with CD4 <200 (potency is 14x that of varicella vaccine)
- For HIV infected patients who do not have a history of primary varicella/evidence of antibody protection, consider vaccinating with varicella vaccine
- Consider for HIV infected patients with CD4 >200, with evidence of varicella immunity
Preventing Recurrence

The efficacy of long-term antiviral prophylaxis to prevent herpes zoster recurrences in HIV-seropositive persons has not been evaluated and is not routinely recommended.

An attenuated virus vaccine for prevention of herpes zoster is FDA-approved for use in immunocompetent persons aged ≥50 years, but is recommended for use beginning at age 60 years by the Advisory Committee on Immunization Practices (ACIP). The zoster vaccine is contraindicated in persons with CD4 cell counts <200 cells/μL.

Unanswered Questions

Assuming a CD4 >200:

- Should Zostavax® be given to all HIV patients?
- Just those over 60?
- Just those over 50?
- Those with viral suppression only?
- Over a certain CD4 threshold ie CD4 >200 vs >350?
- Zostavax® only above a certain number of recurrent episodes?
Immunizations and Insurance
Medicare

Part B
- Influenza vaccine
- PCV13, PPSV23 (second dose 11 months apart)
- Hepatitis B (medium-high risk)

Part D
- all other commercially available vaccines (not covered by Part B)
Part D

- Starting in 2008 all Part D plan formularies must contain all commercially available vaccines.
- The negotiated price for a Part D vaccine includes: vaccine ingredient cost, dispensing fee, sales tax, vaccine administration fee.
- Part D plans have the discretion to implement either a single vaccine administration fee for all vaccines or multiple administration fees.

Part D

- Beneficiary pays the physician and then submits a claim to his or her Part D plan for reimbursement **up to the plan’s allowable charge**.

- In the absence of communication with the plan prior to vaccine administration, the amount the physician charges may be different from the plan’s allowable charge, and a differential may remain that the beneficiary will be responsible for paying.

Part D: more information on CMS website

Variance in provider type, and product administration →
Providers/Patients should contact Part D plans regarding specific vaccine fees

http://www.cms.gov/Medicare/Prescription-DrugCoverage/PrescriptionDrugCovGenIn/index.html
Medicaid

- Vaccination services for adults are optional. States determine policy surrounding:
  - Which (if any) vaccines to cover
  - Enrollee copayment
  - Provider reimbursement
  - Settings where vaccines may be administered

*All programs except Florida cover at least one vaccine

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>SUMMARY OF MEDICAID COVERAGE BY VACCINE 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLU</td>
<td>1 state does not cover (Florida)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Most frequently covered vaccine.</strong> Most states cover intramuscular preservative &amp; preservative-free</td>
</tr>
<tr>
<td>PNEUMO</td>
<td>3 states do not cover (Florida, Georgia, S. Dakota)</td>
</tr>
<tr>
<td>TD/TDAP</td>
<td>4 states do not cover TD (Florida, Georgia, Mississippi, S. Carolina)</td>
</tr>
<tr>
<td></td>
<td>5 states do not cover TDAP (DC, Florida, Louisiana, Mississippi, S. Carolina)</td>
</tr>
<tr>
<td>HEP. A</td>
<td>4 states do not cover (Alabama, Florida, Louisiana, Mississippi)</td>
</tr>
<tr>
<td>HEP. B</td>
<td>2 states do not cover (Florida, Louisiana)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Second-most frequently covered vaccine = intramuscular 90746</strong></td>
</tr>
<tr>
<td>MMR</td>
<td>5 states do not cover (Florida, Georgia, Louisiana, Mississippi, S. Carolina)</td>
</tr>
<tr>
<td>MENING</td>
<td>4 states do not cover (Florida, Louisiana, Mississippi, Texas)</td>
</tr>
<tr>
<td>HPV</td>
<td>7 states do not cover (Alabama, Arizona, Arkansas, Florida, N. Dakota, S. Carolina, S. Dakota)</td>
</tr>
<tr>
<td></td>
<td>• 42/51 states cover quadrivalent 90649. 32/51 states cover bivalent 90650. Recommended in 2007</td>
</tr>
<tr>
<td>VARICELLA</td>
<td>8 states do not cover (Arkansas, Florida, Georgia, Louisiana, Mississippi, N. Dakota, S. Carolina, Texas)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Second least frequently covered vaccine</strong></td>
</tr>
<tr>
<td>ZOSTER</td>
<td>11 states do not cover (Arkansas, Colorado, DC, Florida, Louisiana, Mississippi, N. Dakota, Ohio, S. Carolina, Texas, Washington)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Least frequently covered vaccine. Recommended in 2008</strong></td>
</tr>
</tbody>
</table>

2016 Medicaid

- Certain vaccines may be available if supplemental insurance is obtained
Resources

- http://hivinsite.ucsf.edu/InSite?page=kb-03-01-08#S4.2X
Questions?