Vaccines in Immunocompromised hosts

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Immunocompromised hosts

- Number has increased rapidly in the past decades
- Broad term that encompasses different patients:
  - Children with genetic immunodeficiencies
  - Cancer patients
  - Transplant recipients
  - HIV/AIDS patients
Patients with cancer

• Limited number of studies assessing vaccination responses in persons with cancer
• Must studies performed in persons with hematologic malignancies
• Agents such as rituximab and alemtuzumab are now commonly used in non-Hodgkin’s lymphoma and CLL and impact response to vaccines
# Recommendations for immunization in patients with cancer

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>REC</th>
<th>COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumococcal polysaccharide vaccine</td>
<td>YES</td>
<td>In lymphoma or CLL preferably before chemo. Vaccination &lt; 6 mo after rituximab unlikely to be effective</td>
</tr>
<tr>
<td>Pneumococcal conjugate vaccine</td>
<td>YES</td>
<td>In lymphoma or CLL preferably before chemo. Vaccination &lt; 6 mo after rituximab unlikely to be effective</td>
</tr>
<tr>
<td><em>Hemophilus influenzae</em> type b vaccine</td>
<td>YES</td>
<td>In children with cancer and persons with Hodgkin’s disease, preferably before initiation of chemotherapy</td>
</tr>
<tr>
<td>Inactivated influenza vaccine</td>
<td>YES</td>
<td>Seasonal admin to all persons with cancer</td>
</tr>
<tr>
<td>Varicella</td>
<td>YES</td>
<td>In seronegative children and young adults in remission from malignant disease.</td>
</tr>
<tr>
<td>MMR</td>
<td>YES</td>
<td>In children with cancer not previously vaccinated; not during active chemo o XRT</td>
</tr>
<tr>
<td>Tetanus toxoid, diphtheria toxoid, acellular pertussis, poliovirus</td>
<td>YES</td>
<td>In children to complete primary immunization schedule; booster may be needed for long-term immunity</td>
</tr>
</tbody>
</table>
Vaccination in allogeneic hematopoietic stem cell transplant (HSCT) recipients

- Immunity to infectious agents is transferred by the graft and can be detected early after HSCT
- Usually of finite duration
- Immune status of the donor can be boosted by immunizing the donor before the transplant
- Early post-transplant immunization of the recipient with polysaccharide-protein conjugate vaccines or protein-based vaccines
- More theoretical than practical
Pneumococcal vaccines

- Pneumococcal infections are significant causes of morbidity and mortality after HSCT
- Risk of severe infection increased after GVHD
- Immunization with PPV23 can elicit antibody response as early as 6 months after HSCT (if no GVHD)
- Current recommendation is to start vaccination with 3 doses of PCV vaccine at 3-4 months after HSCT followed by a PPV23 dose in persons without chronic GVHD or a PCV dose in those with chronic GVHD
HIV infection - introduction

• HIV-infection causes defects in cell-mediated immunity and in B-cell function putting patients at higher risk for many vaccine-preventible diseases.

• Antibody response to vaccination is critically dependent upon functional CD4+ T-cells.
  • A poor vaccine response can be expected in patients with advanced HIV (CD4 < 200 cells/μL).
    – In general vaccine efficacy is compromised in patients with advanced immunosuppression.
The presence of circulating HIV-1 RNA has also been demonstrated to be an important predictor of nonresponse to influenza vaccination. This suggests that the immunogenicity of the vaccine may be improved with viral suppression on ART. Little specific research on the effectiveness of immunizations in this population.
Vaccines in HIV-infected persons

- Inactivated vaccines – in general acceptable
- Live vaccines – generally avoided
Inactivated Vaccines

• **Tetanus toxoid and diphtheria toxoid vaccines:**
  – Immune response is T-cell mediated thus lower response with advanced HIV disease.
  – Similar immunity to tetanus as an age-matched population but lower than expected response to diphtheria.

• **Poliovirus vaccine:**
  – Those at risk because of travel should receive the inactivated polio vaccine (IPV).

• **Pneumococcal vaccine:**
  – Recommended for all HIV-infected patients

• **Haemophilus influenzae vaccine:**
  – Not recommended for adults infected with HIV
Inactivated vaccines II

• **Influenza vaccine:**
  – Vaccination recommended annually by USPHS/IDSA and ACIP
  – Only the inactivated vaccine is recommended

• **Hepatitis A vaccine:**
  – Vaccination recommended by USPHS/IDSA and ACIP for those with chronic HBV or HCV, drug-uses, MSM and hemophiliacs

• **Hepatitis B vaccine:**
  – Routine screening and immunization of those not immune is recommended for all HIV-infected adults.

• **Meningococcal vaccine:**
  – Conjugate meningococcal vaccine should be administered to HIV-infected adults through age 55 with functional or anatomic asplenia, travel exposure, are of college age, or living in dormitories.
  – Recent NYC outbreak

• **HPV vaccine:**
  – not specifically recommended for persons with HIV infection, but can be considered, according to the ACIP guidelines
Outbreaks of Invasive Meningococcal disease among Gay and bisexual men

- Outbreaks in NYC (2010 – 2012)
- In response the NYCDOHMH recommended on Oct 5, 2012 vaccination for all HIV-infected men who reside outside of New York City and may have traveled to the City and had intimate contact with other men since September 1, 2012.
- Close contact includes kissing, sharing water bottles, sharing eating or drinking utensils, sharing cigarettes, or being within a three foot distance for eight hours or more.
- HIV-infected individuals should receive two doses, with the second dose administered eight weeks or more after the first dose, plus booster doses every five years.
Outbreak of Invasive Meningococcal Disease – NYC 2012

- 13 cases Serogroup C
- Same strain IVDU 2006
- 8 cases HIV
- 3 of 4 deaths in HIV
- Vaccinate HIV infected, risks

Slide courtesy of Dr. Judith Aberg
## Changing Spectrum of IPD in the Post PCV7 Era in US

<table>
<thead>
<tr>
<th></th>
<th>1998-1999 (n=5,699)</th>
<th>2009 (n=3,338)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range), years</td>
<td>56 (18-101)</td>
<td>58 (18-104)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>62%</td>
<td>70%</td>
</tr>
<tr>
<td>Black</td>
<td>35%</td>
<td>24%</td>
</tr>
<tr>
<td>Other</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>54%</td>
<td>51%</td>
</tr>
<tr>
<td>Case Fatality Ratio†¶</td>
<td>13%</td>
<td>11%</td>
</tr>
<tr>
<td>Meningitis</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Bacteremia without focus†</td>
<td>25%</td>
<td>15%</td>
</tr>
<tr>
<td>Bacteremic Pneumonia†</td>
<td>68%</td>
<td>75%</td>
</tr>
<tr>
<td>ACIP Indication for PPV23†§</td>
<td>51%</td>
<td>61%</td>
</tr>
</tbody>
</table>

†p-value <0.05
§Includes all ACIP indications except age >65 years.

Pneumococcal Vaccine Indications in Adults with IPD in USA, 2009

- Any PPV indication 61%
- Diabetes 20% (10% in 1998/9)
- Chronic Lung Disease 19%
- Cardiac Disease 18%
- Cancer 13%
- Alcoholism 10%
- HIV AIDS 8%

Muhammad et al, CID, 2012
IPD caused by PCV7 & NonPCV7 serotypes among adults aged 18-64 years with HIV/AIDS

Cohen et al, 2010, AIDS, 24, 2253-62

IPD cases with HIV per 100,000 persons with AIDS

- All serotypes
- Conjugate vaccine serotypes
- Nonvaccine serotypes
- Vaccine-related serotypes

Seroype replacement

Cohen et al, 2010, AIDS, 24, 2253-62
Efficacy of Two Doses of PCV7 on VT IPD + 6A in HIV$^+$ Adults In Malawi

Table 3. Primary and Secondary End Points, Adverse Events, and Loss to Follow-up in 437 Patients with HIV Infection.†

<table>
<thead>
<tr>
<th>End Point</th>
<th>Vaccine</th>
<th>Placebo</th>
<th>Hazard Ratio for First Event (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients</td>
<td>no. of events</td>
<td>no. of patients</td>
</tr>
<tr>
<td>Primary end point</td>
<td>Vaccine serotype or serotype 6A (intention-to-treat analysis)</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

• Pneumococcal vaccine-naïve persons: receive a dose of PCV13 (Prenvar13) first, followed by a dose of PPSV23 (Pneumovax23) at least 8 weeks later.
  – a second PPSV23 dose is recommended 5 years after the first PPSV23 dose for persons aged 19–64 years with HIV.

• Previous vaccination with PPSV23. Adults aged ≥19 should be given a PCV13 dose ≥1 year after the last PPSV23 dose was received.
Rationale for change in Recommendation by ACIP

• Efficacy of PPV23 in immunocompromised patients has never been proven in a randomized trial though they are greatly at risk of IPD
  – In pre HART era risk of IPD in HIV was up to 100 fold that of age matched controls

• Herd protection has greatly reduced this risk- see attached slides
  – IPD down 97% in 18-49 year old blacks (this is mostly HIV) but residual risk remains above that of nonimmunocompromised adults pre PCV

• Based on study conducted in Malawi (NEJM 2010) ACIP made the recommendation
Implementation of new ACIP recommendations at an HIV clinic

• IF the patient is unvaccinated completely, start with Prevnar-13, then, AT LEAST 8 weeks later, but preferably longer, administer Pneumovax dose 1, then repeat Pneumovax once five years later.

• IF the patient has received Pneumovax previously (1 or 2 doses), then be sure it has been AT LEAST one year since the last Pneumovax vaccine, then give one dose of Prevnar-13.

• Patients only require 2 doses of Pneumovax (at 5 year intervals), although there is data to support giving an additional dose at age 65 if there has been a significant interval between the last dose.

• In general, we favor waiting to initiate vaccination until a patient has achieved a controlled viral load. However, If the patient is non-adherent and in and out of care, just give the vaccine when the opportunity arises.
Live vaccines

• **Measles, mumps and rubella vaccine:**
  – The ACIP has specifically recommended that MMR vaccine should only be given to HIV-infected patients with a CD4 T-cell count >200 cells/μL.

• **Varicella, Zoster and Yellow fever vaccines:**
  – Immunization is contraindicated in HIV-infected patients with a CD4 T-cell count ≤200 cells/μL.

• **BCG vaccine:**
  – Two CDC advisory groups have recommended against use of the BCG vaccine even if the risk of acquiring tuberculosis is high.
Travel Immunizations

• **Routine**
  - Childhood or adult immunizations

• **Required**
  - Crossing international borders

• **Recommended**
  - According to risk of infection
• **Required vaccines:**
  – Yellow fever
  – Meningococcal vaccine

• **Recommended vaccines:**
  – Hepatitis A
  – Hepatitis B
  – Cholera
  – Typhoid
  – Polio
  – Rabies
  – Japanese encephalitis
  – Tick-borne encephalitis
Immunizations for HIV-Infected Patients Traveling to Developing Countries

• Inactivated and recombinant vaccines (e.g., diphtheria-tetanus, rabies, hepatitis A, hepatitis B, Japanese encephalitis) should be used for HIV-infected persons just as they would be used for HIV-uninfected persons anticipating travel.
Travel Immunizations in HIV+ Individuals

- Should avoid live-attenuated vaccines among HIV+ with severe immunosuppression (CD4+ < 200 cells/µl)

- Some practitioners provide some inactivated vaccines once CD4+ has increased > 100 cells/µl in those patients receiving HAART

Monath T, Cetron M, CID 2002
Yellow Fever Vaccine and HIV

• Recommended for patients with CD4+ > 200 cells/µl (Efficacy and Safety). High-risk patients should be tested to determine whether they have developed NA

• Due to concerns about vaccine neurologic or viscerotrophic complications, the strategy has been to make sure that patients are receiving HAART with virologic suppression

• A medical exemption letter can be written for travelers when we have concerns
Conclusions

- Inactivated vaccines are acceptable for use in HIV-infected patients
- Live vaccines are generally avoided.
  - However, some live vaccines (eg, varicella) are recommended in HIV-infected patients with CD4 cell counts >200 cells/mm³.
- Pneumococcal vaccines (both polysaccharide and conjugate vaccines) should be administered to adults and children with CD4 counts greater than 200 cells/uL as soon as HIV infection is diagnosed.
Conclusions II

• If possible, vaccines should be administered before the CD4 count decreases to <200 cells/µL

• If given when the CD4 count is <200 cells/µL, consider repeating the vaccination when the CD4 count increases to >200-300 cells/µL (unless there is evidence of immunity).

• Suppression of viral replication with ART may lead to better vaccine efficacy.