Blood-Borne Pathogens and Post-Exposure Prophylaxis

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with thanks to
Shireesha Dhanireddy MD
Disclosures

- none
Learning Objectives

- Understand risks of transmission in occupational and non-occupational exposures to HIV and Hepatitis C

- State indications for HIV Post-Exposure Prophylaxis (PEP)

- Describe follow-up testing and monitoring following HIV & HCV exposures
Post-Exposure Prophylaxis (PEP)

- The use of therapeutic agents to prevent infection following exposure to a pathogen

- Types of exposures:
  - percutaneous (needlestick), splash, bite, sexual

- For health-care workers, PEP commonly considered for exposures to HIV and Hepatitis B
Case

- 30 year old nurse presents to you for evaluation of needlestick injury 5 hours ago. She was placing a peripheral IV for a patient in the ED when this occurred.

- What else would you like to know?
Case: Questions

- Who is the source patient?
  - HIV and hepatitis status
- What is her risk of contracting HIV if source patient positive?
- What factors affect risk?
- How effective is post-exposure prophylaxis?
- What medication regimen should be considered?
Case

- 30 year old nurse presents to you for evaluation of needlestick injury 5 hours ago. She was placing a peripheral IV for a patient in the ED when this occurred.

- Source patient - 25 year old male recently diagnosed with HIV; HIV viral load unknown, not on HIV medications
What is her risk of acquiring HIV?
HIV PEP

- Exposures common

- 56 documented cases of health care workers contracting HIV from exposures; 138 other possible cases

- Area of considerable concern but little data

MMWR June 29, 2001 / 50(RR11);1-42
### Exposure Risks (average, per episode, involving HIV-infected source patient)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous (blood)</td>
<td>0.3%</td>
</tr>
<tr>
<td>Mucocutaneous (blood)</td>
<td>0.09%</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>1 - 2%</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>0.06%</td>
</tr>
<tr>
<td>Receptive vaginal intercourse</td>
<td>0.1 – 0.2%</td>
</tr>
<tr>
<td>Insertive vaginal intercourse</td>
<td>0.03 – 0.14%</td>
</tr>
<tr>
<td>Receptive oral (male)</td>
<td>0.06%</td>
</tr>
<tr>
<td>Female-female orogenital</td>
<td>4 case reports</td>
</tr>
<tr>
<td>IDU needle sharing</td>
<td>0.67%</td>
</tr>
<tr>
<td>Vertical (no prophylaxis)</td>
<td>24%</td>
</tr>
</tbody>
</table>
Risk of HIV Transmission following Percutaneous (needlestick) exposure

- Pooled analysis of prospective studies on health care workers with occupational exposures suggests risk is approximately 0.3% (95% CI, 0.2% - 0.5%)\(^1\)

- Presence or absence of key risk factors may influence this risk in individual exposures

Risk Factors for Seroconversion following Needlesticks

- CDC-sponsored case-control study
- 33 cases, 665 controls s/p needlestick from confirmed HIV+ source patients
- zidovudine (AZT) only for PEP

Cardo DM et al. NEJM 1997;337:1485-90
## Risk Factors for Seroconversion

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>ODDS RATIO</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep injury</td>
<td>15</td>
<td>6.0 - 41</td>
</tr>
<tr>
<td>Visibly bloody device</td>
<td>6.2</td>
<td>2.2 - 21</td>
</tr>
<tr>
<td>Device in artery/vein</td>
<td>4.3</td>
<td>1.7 - 12</td>
</tr>
<tr>
<td>Terminally ill SP</td>
<td>5.6</td>
<td>2.0 - 16</td>
</tr>
<tr>
<td>AZT PEP</td>
<td>0.19</td>
<td>0.06 - 0.52</td>
</tr>
</tbody>
</table>

*p<0.01 for all

Cardo DM et al. NEJM 1997;337:1485-90
Other Likely Risk Factors

- Viral load
- Glove use
  - 50% decrease in volume of blood transmitted\(^1\)
- Hollow bore vs solid bore
  - large diameter needles weakly associated with increased risk \((p = 0.08)^2\)
- Drying conditions
  - tenfold drop in infectivity every 9 hours\(^3\)

2. Cardo DM et al. NEJM 1997;337:1485-90
How effective is PEP?
Evidence of Efficacy of PEP

- Animal models: high level of protection when started within 24 hours\(^1\)
- OR = 0.19 for zidovudine (AZT) use in case-control study\(^2\) (81% decrease in risk of HIV acquisition)
- Two drugs, three drugs:
  - no direct evidence that more drug = more effective
  - cases of seroconversion despite 3-drug PEP imply efficacy less than 100\%\(^3,4\)

4. MMWR June 29, 2001 / 50(RR11):1-42
Time is of the essence

- When is the optimal time to start HIV PEP?
  - How late can you start it?
Acute HIV Infection

Kahn JO. NEJM 1998
Timing of PEP: what’s the evidence?

- animal models and animal PEP studies: suggest substantially less effective beyond 24 - 36 hours\(^1,2\)
- case-control study: most subjects in each group received PEP within 4 hours\(^3\)
- analysis of PEP failures does not suggest a clear cut-off\(^4\)

4. MMWR June 29, 2001:50(RR11);1-42.
Timing of PEP: CDC Guidelines

- PEP should be initiated as soon as possible, preferably within hours rather than days of exposure.
- Interval after which there is no benefit for humans is not known.
- Obtain expert advice when interval has exceeded 24-36 hours.

Duration of PEP

- in animal model, 28 days more effective than 10 days or 3 days of PEP\(^1\)

- 4 weeks (28 days) used in case-control study\(^2\) and recommended by CDC guidelines\(^3\)

3. MMWR June 29, 2001:50(RR11);1-42.
PEP Antiretroviral Treatment

- # of drugs
- Selection of drugs
“As less toxic and better-tolerated medications for the treatment of HIV infection are now available, minimizing the risk of PEP noncompletion, and the optimal number of medications needed for HIV PEP remains unknown, the PHS working group recommends prescribing 3 (or more) tolerable drugs as PEP for all occupational exposures to HIV.”

### Recommended Antiretroviral Regimens for Occupational PEP (28-Day Duration)

<table>
<thead>
<tr>
<th>Preferred Regimen</th>
<th>INSTI</th>
<th>NNRTI</th>
<th>Pill Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir (Isentress)</td>
<td>400 mg twice daily</td>
<td>Tenofovir-Emtricitabine (Truvada)</td>
<td>1 pill daily</td>
</tr>
</tbody>
</table>

### 2013 USPHS Occupational PEP Guidelines

**Recommendations for Antiretroviral Regimens**

**Alternative Antiretroviral Regimens for Occupational PEP (28-Day Duration)**

<table>
<thead>
<tr>
<th>INSTI, PI, or NNRTI</th>
<th>NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir (<em>Isentress</em>)</td>
<td>Tenofovir-Emtricitabine (<em>Truvada</em>)</td>
</tr>
<tr>
<td>Darunavir (<em>Prezista</em>) + Ritonavir (<em>Norvir</em>)</td>
<td>Tenofovir (<em>Viread</em>) + Emtricitabine (<em>Emtriva</em>)</td>
</tr>
<tr>
<td>Etravirine (<em>Intelence</em>)</td>
<td>Tenofovir (<em>Viread</em>) + Lamivudine (<em>Epivir</em>)</td>
</tr>
<tr>
<td>Rilpivirine (<em>Edurant</em>)</td>
<td>Zidovudine-Lamivudine (<em>Combivir</em>)</td>
</tr>
<tr>
<td>Atazanavir (<em>Reyataz</em>) + Ritonavir (<em>Norvir</em>)</td>
<td>Zidovudine (<strong>Retrovir</strong>) + Lamivudine (<em>Epivir</em>)</td>
</tr>
<tr>
<td>Lopinavir-Ritonavir (<em>Kaletra</em>)</td>
<td>Zidovudine (<strong>Retrovir</strong>) + Emtricitabine (<em>Emtriva</em>)</td>
</tr>
</tbody>
</table>

**Alternative Regimen: Fixed-Drug Combination**

Elvitegravir-Cobicistat-Tenofovir-Emtricitabine (*Stribild*)

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2013 USPHS Occupational PEP Guidelines
Baseline and Follow-Up for Occupational PEP

- Early Reevaluation after Exposure (within 72 hours)

- Baseline and Follow-up HIV Testing
  - Baseline HIV testing
  - Follow-up HIV testing 6, 12, and 24 weeks after exposure
  - Follow-up HIV testing at 6 and 16 weeks if 4th generation assay* used

- Baseline and Follow-up Laboratory Testing
  - Baseline renal and hepatic function tests
  - Follow-up renal and hepatic function tests at 2 weeks

*4th generation combination assay = HIV p24 antigen-HIV antibody test

Adverse Effects

- 2 drugs vs 3 drugs
  - AE’s 51% vs 61% (p < .001)
  - PEP discontinued 17% vs 21% (p = .18)
- Avoid efavirenz in pregnancy
- Never use nevirapine!
Case Number 2: splash

- 24 yo dental technician splashed in the eye during dental procedure 3 hours ago

- Source patient: 33 yo male, co-infected with HIV and HCV

- what else do you want to know?
Which fluids are potentially infectious for HIV?

- blood?
- saliva?
- sweat?
- feces?
- spinal fluid?
- pleural fluid?
- pus?
- urine?
Which fluids are potentially infectious for HIV?

- blood
- saliva
- sweat
- feces
- spinal fluid
- pleural fluid
- pus
- urine
Which Body Fluids Pose a Risk?

Highly Infectious Fluids
- Blood
- Visibly bloody body fluids

Potentially Infectious Fluids
- Semen and vaginal secretions
- Cerebrospinal fluid
- Synovial fluid
- Pleural fluid
- Peritoneal fluid
- Pericardial fluid

Not Considered Potentially Infectious (unless visibly bloody)
- Saliva, vomitus, and feces
- Nasal secretions and sputum
- Sweat and tears
- Urine

Case number 2 continued

- Saliva was visibly bloody - in fact, it was mostly blood that splashed her
- she rinsed out her eye immediately
- source patient has never taken antiretrovirals, has a CD4 count of “about 500” and a viral load of 20,000 last time it was checked.
- She is 8 weeks pregnant
Case number 2 continued

- What is her risk of contracting HIV? Of HCV?

- What are your PEP recommendations?

- How does her pregnancy affect your decision making?
Case 2 continued

- Risk of HIV from mucous membrane exposures: 0.09% (95% CI 0.006% - 0.5%)\(^1\)

- Risk of HCV in this circumstance unknown; thought to be higher than HIV, because risk of HCV in percutaneous exposures, at 1.8%,\(^2-4\) is higher than that for HIV

PEP in Pregnancy

- Most antiretrovirals class B or C in pregnancy
- Antiretroviral Pregnancy Registry has not detected increased teratogenic risk for ARVs in general, nor specifically for AZT and 3TC, in the first trimester
  

- avoid efavirenz (anencephaly in monkeys), amprenavir (ossification defects in rabbits), and indinavir in late term (hyperbilirubinemia)
- theoretically higher risk of vertical transmission with primary HIV infection

2013 USPHS Occupational PEP Guidelines

Situations for Which Expert Consultation Advised

- Delayed exposure report (e.g. longer than 72 hours)
- Unknown source (e.g. needle in sharps disposal)
- Known or suspected pregnancy in exposed person
- Exposed person breast-feeding
- Known or suspected ARV drug resistance in source patient
- Serious medical illness in exposed persons
- Toxicity occurring in exposed person taking PEP regimen
Hepatitis C Exposure

- average risk of seroconversion from percutaneous exposure 1.8%\(^1-3\)
- same risk factors as for HIV thought to apply
- gamma globulin not recommended\(^4\)

Monitoring for HCV Infection Following an Occupational Exposure

1. Test healthcare worker for anti-HCV within 48 hours of exposure
   - Positive
     - Reflex HCV RNA test
       - Positive
         - Refer to care for pre-existing chronic infection
       - Negative
   - Negative
     - Follow-up testing
       - Test for HCV RNA ≥ 3 weeks after exposure
         - Positive
           - Refer to care
           - Stop
         - Negative
           - Refer to care

Centers for Disease Control & Prevention, 2017
PEP Take Home Points

- Timing is important
- Know data about transmission risks
- Be detailed in history (about source and exposed patients)
- Don’t forget hepatitis
extra slides
Table 3. Clinical signs and symptoms of acute (primary) human immunodeficiency virus infection

<table>
<thead>
<tr>
<th>Features</th>
<th>Overall (n=375), %</th>
<th>Male (n=355), %</th>
<th>Female (n=23), %</th>
<th>Sexual (n=324), %</th>
<th>Injection drug use (n=34), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>75</td>
<td>74</td>
<td>83</td>
<td>77</td>
<td>50</td>
</tr>
<tr>
<td>Fatigue</td>
<td>68</td>
<td>67</td>
<td>78</td>
<td>71</td>
<td>50</td>
</tr>
<tr>
<td>Myalgia</td>
<td>49</td>
<td>50</td>
<td>26</td>
<td>52</td>
<td>29</td>
</tr>
<tr>
<td>Skin rash</td>
<td>48</td>
<td>48</td>
<td>48</td>
<td>51</td>
<td>21</td>
</tr>
<tr>
<td>Headache</td>
<td>45</td>
<td>45</td>
<td>44</td>
<td>47</td>
<td>30</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>40</td>
<td>40</td>
<td>48</td>
<td>43</td>
<td>18</td>
</tr>
<tr>
<td>Cervical adenopathy</td>
<td>39</td>
<td>39</td>
<td>39</td>
<td>41</td>
<td>27</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>30</td>
<td>30</td>
<td>26</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>Night sweats</td>
<td>28</td>
<td>28</td>
<td>22</td>
<td>30</td>
<td>27</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>27</td>
<td>27</td>
<td>21</td>
<td>28</td>
<td>23</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>Rate for HIV acquisition per 10,000 exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>9,250</td>
</tr>
<tr>
<td>Needle sharing during injection drug use</td>
<td>63</td>
</tr>
<tr>
<td>Percutaneous (needlestick)</td>
<td>23</td>
</tr>
<tr>
<td>Sexual</td>
<td></td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>138</td>
</tr>
<tr>
<td>Receptive penile-vaginal intercourse</td>
<td>8</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>11</td>
</tr>
<tr>
<td>Insertive penile-vaginal intercourse</td>
<td>4</td>
</tr>
<tr>
<td>Receptive oral intercourse</td>
<td>Low</td>
</tr>
<tr>
<td>Insertive oral intercourse</td>
<td>Low</td>
</tr>
</tbody>
</table>