Post-Exposure Care: A Balancing Act

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Objectives

- Review the goals of post-exposure care
- Describe the three phases of blood borne pathogen exposure management
- Discuss ways to prevent transmission
  - Provide information/counseling
  - Avoid unnecessary PEP/minimize toxicity
  - Determine whether transmission has occurred
- Determine whether transmission has occurred
Occupational HIV exposures are crisis situations demanding immediate, decisive action.

Henderson, 2001

What is an exposure?

“….a percutaneous injury…or contact of mucous membrane or non-intact skin…. with blood, tissue or other body fluids that are potentially infectious.”

MMWR, 2005
What is NOT an Exposure?

- BBP transmission does not occur
  - Through intact skin
  - Via inhalation

Beltrami, 2000

Post-Exposure Prophylaxis (PEP)

- Use of therapeutic agents to prevent infection following exposure
- Types of exposures include percutaneous (needlestick), splash, bite, sexual
- PEP commonly considered for exposures to HIV and Hepatitis B

Behrens, 2006
Case Number #1

- HCP: 24 yo ED nurse
- Patient spit in her eye while she was trying to start an IV
- Source patient: 33 yo male, thought to be infected with HIV
- What are the next steps?

Phases in Managing BBP Exposures

**Phase One**
First Aid
Triage
Crisis Management

**Phase Two**
Exposure Risk Assessment
Source Patient Evaluation
PEP Decision
Initiating Treatment

**Phase Three**
Post-Exposure Follow-up
Source Patient Follow-up
ARV Toxicity Monitoring

Beltrami, 2000
Phase 1: Immediate Care

- First aid
- Triage
- Crisis Management

First Aid: Treat Exposure Site

- Soap and water to wash exposed areas
- Flush exposed mucous membranes with water
- Flush exposed eyes with water or saline solution
- Do NOT apply caustic agents or inject antiseptics or disinfectants into the wound
Triage

- Goal: evaluation immediately after exposure
- Refer to qualified provider
  - Employee health department
  - Emergency department
  - Urgent Care
  - Occupational medicine clinic

Crisis Management

- Acute emotional upset is the norm for exposed HCP
- Education and supportive counseling are key
- Reassure without being dismissive
- Be an advocate
- Refer for mental health evaluation if symptoms are severe or persistent
Phases in Managing BBP Exposures

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**Phase 2: Determining Risk**

- Assessment of the Exposure
- Assessment of the Source
- PEP Decision
- PEP Selection
- Treatment Initiation
Assessment of the Exposure

General Principles

- HIV, HBV and HCV do not spontaneously penetrate intact skin
- Airborne transmission of these viruses does not occur

Beltrami, 2000
Defining Risk - Per-exposure Estimates

- HIV
  - Percutaneous 0.3%
  - Mucocutaneous 0.09%
- HCV
  - Percutaneous 1.8%
- HBV
  - Percutaneous
    - eAg+ 22% to 31%
    - eAg- 1.5-6%

MMWR, 2005
MMWR, 2001

Exposure Risk Assessment

- Type of Exposure
- Substance
- Exposure Source
Types of Exposure

- Percutaneous injury
- Mucous membrane exposure
- Non-intact skin exposure
- Bites resulting in blood exposure to either person involved

Defining Risk

- Needlestick
  - Less severe (Solid needle and superficial injury)
  - More severe (Large-bore hollow needle, deep puncture, visible blood on device, or needle exposed to artery or vein)
- Mucous membrane and nonintact skin
  - Small volume (a few drops)
  - Large volume (major blood splash)

MMWR 2001, MMWR 2005
Risk Factors for Seroconversion Following Needlesticks

- CDC-sponsored case-control study
- 33 cases, 665 controls with needlesticks from confirmed HIV+ SPs
- Zidovudine (AZT) monotherapy as PEP
- Odds of HIV transmission was reduced by 81% in HCW that took AZT

Cardo 1997

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 1997
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\(^3\)

1. Mast 1993
2. Cardo 1997
3. Resnick JAMA 1986
Infectious Material

- Blood and blood products, breast milk, vaginal secretions, semen
- Occupational transmission of HIV: health care and laboratory workers
- Other body fluids if BLOODY
- Saliva (only implicated through oral sex)
- Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered potentially infectious unless they are visibly bloody. The risk for transmission of HIV infection from these fluids and materials is low. MMWR 2005.
- Possible: Cerebrospinal fluid, exudates, serosal fluids, amniotic fluid

Environmental Concerns

- Titer of HIV is reduced by 90 to 99% within several hours after drying and diminishes with time
- HBV is resistant to drying and has been found to be stable on environmental surfaces for up to 7 days
- HCV rapid degradation of serum at room temp (data lacking)

Beltrami 2000
Assessment

- Determine infectious status of the source patient
- Determine susceptibility of the exposed person

Determine Infectious Status of the Source

- Presence of HBs AG
- Presence of HCV AB
- Presence of HIV AB
- Unknown sources
  - Evaluate likelihood of exposure
  - Setting in which exposure occurred
Source Assessment: Laboratory Testing

- **Do not** delay PEP while awaiting source patient laboratory results. The decision to start PEP is based on the clinical risk assessment.

- Consider testing options:
  - Rapid vs standard HIV antibody test kit
  - Antibody testing vs direct virus assay
  - No option to test discarded needles

Source Assessment: Laboratory Testing

- Rapid ELISA should be considered
  - A negative result allays anxiety and prevents overuse of PEP.
  - All positive tests must be confirmed with a Western Blot or Immunofluorescence assay.
Source Patient Factors Influence HIV Transmission Risk

- If source is HIV+:
  - Viral Load
  - Stage of disease

- If HIV status in unknown:
  - Risk behavior history
  - Signs/symptoms suggestive of primary HIV infection
  - Prior testing/History of exposure

- If source is unknown:
  - Community prevalence

Susceptibility of Exposed Person

- Hepatitis B vaccine status?
- HBV immune status?
- Anti-HCV and ALT
- HIV antibody
Case #1 Continued

- Saliva was visibly bloody – The patient had been in a fight and had an injured mouth
- Eye was rinsed immediately
- Source patient has never taken antiretrovirals, has a CD4 count of “about 500” and a viral load of 20,000 copies/ml last time it was checked.
- She is 8 weeks pregnant

Stratifying Risk

- Splash to mucous membrane or non-intact skin
  - Length and volume of exposure contribute to risk
- Bite exposures
  - Bite victim not at risk unless blood in saliva
  - Biter has sustained blood to mucous membrane exposure
Stratifying Risk - Source Assessment

- If source is HIV+
  - What is viral load/stage of disease?
- If HIV status is unknown
  - What is history of risk factors?
  - Any symptoms of primary HIV infection?
  - What is history of testing?
- If source is unknown
  - What is prevalence where exposure occurred?
  - How long has sharp been environmentally exposed?

PEP Decision
Window of Opportunity

- Rhesus macaque model:
  - Intravaginal exposure to SIV
    - At 24 hours, SIV detected in vaginal dendritic cells
    - By 48 hours, SIV detected in regional lymph nodes
    - By 5 days, SIV detected in peripheral blood
  - The time to disseminated infection provides a window for intervention

  Spira, 1996

Evidence from ACTG 076

- Randomized controlled trial to assess ability of AZT to reduce perinatal transmission in humans
- Risk of vertical transmission reduced from 22.6% in placebo treated controls to 7.6% in treatment arm (AZT alone)
- Reduction of 67%
- Reduction in viral load only partially explained reduction in transmission

  Connor, 1994
Effectiveness of PEP: Animal Models

- Duration of treatment makes a difference
- Macaques
  - PMPA (Tenofovir)
  - Protection from transmission:
    - 100% in those treated 28 days
    - 50% in those treated 10 days
    - 0% in those treated 3 days

Tsai, 1995

Effectiveness of PEP: Animal Models

- Delay in treatment is detrimental
- Macaques
  - Protection from transmission
    - 100% that received PEP within 24 hours
    - 50% that received PEP within 48 hours
    - 25% that received PEP within 72 hours

Tsai 1998
PEP for HIV - General Principles

- Most exposures do not result in transmission of HIV, so risk and benefit must be weighed carefully.
- Consider risk of exposure and source.
- Consider factors in the health care worker
  - concurrent illness or medication
  - pregnancy or breastfeeding

Timing of PEP

- 1-2 hours
- 24 hours
- 72 hours
- 1 week (or more?)
What are the Downsides to PEP?

Tolerability of HIV PEP in Health Care Workers

Incidence of Common Side Effects

- Nausea
- Fatigue
- Headache
- Vomiting
- Diarrhea
- Myalgias

Wang, 2000
**How Many Drugs to Use?**

- Two drug PEP regimens improve tolerability and therefore chances of completing full 4 weeks
- Three (or more) drug PEP regimens provide potentially greater antiviral activity
- Guidelines recommend more drugs for higher risk exposures
How Many Drugs to Use?

Assess risk for HIV infection:

- **Type of exposure**
  - Less severe: solid needle or superficial injury
  - More severe: large-bore hollow needle, deep puncture, visible blood on device, needle used in patient’s artery or vein

- **Infection status of source**
  - Class 1: asymptomatic HIV infection or known low viral load (<1500 copies RNA/mL)
  - Class 2: symptomatic HIV, AIDS, acute seroconversion, or known high viral load

Basic 2-Drug Regimens

- Two NRTIs
- Simple dosing, fewer side effects

- Preferred basic regimens:
  - zidovudine (AZT) OR tenofovir (TDF)
    - plus
  - lamivudine (3TC) OR emtricitabine (FTC)

- Alternative basic regimens:
  - stavudine (d4T) OR didanosine (ddI)
    - plus
  - lamivudine (3TC) OR emtricitabine (FTC)
Expanded PEP Regimens

Expanded ≥3-drug PEP regimens:

- **Preferred:**
  - Lopinavir/ritonavir (Kaletra) + basic 2-drug regimen

- **Alternative:**
  - Atazanavir ± ritonavir
  - Fosamprenavir ± ritonavir + basic 2-drug regimen
  - Indinavir** ± ritonavir
  - Saquinavir + ritonavir
  - Nelfinavir
  - Efavirenz***

*If atazanavir is coadministered with tenofovir, ritonavir must be included in the PEP regimen. **Avoid in late pregnancy. ***Teratogenic; avoid in pregnancy

Antiretroviral agents generally NOT recommended for PEP:

- Nevirapine
- Delavirdine
- Abacavir
- Zalcitabine
- Didanosine + stavudine

Antiretroviral agents to be used for PEP only with expert consultation:

- Enfuvirtide
- Other newer agents: Intelence and Isentress
## PEP for Percutaneous Injuries

### Infection Status of Source

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Infection Status of Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+, class 1</td>
<td>HIV+, class 2</td>
</tr>
<tr>
<td>Less severe</td>
<td>Recommend basic 2-drug PEP</td>
</tr>
<tr>
<td></td>
<td>Recommend expanded ≥3-drug PEP</td>
</tr>
<tr>
<td>More severe</td>
<td>Recommend expanded 3-drug PEP</td>
</tr>
<tr>
<td></td>
<td>Recommend expanded ≥3-drug PEP</td>
</tr>
</tbody>
</table>

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### Infection Status of Source

<table>
<thead>
<tr>
<th>Exposure Type</th>
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<tbody>
<tr>
<td>Unknown HIV status*</td>
<td>Unknown source</td>
</tr>
<tr>
<td>Less severe</td>
<td>Generally, no PEP warranted; consider basic 2-drug PEP if source has HIV risk factors</td>
</tr>
<tr>
<td></td>
<td>Generally, no PEP warranted; consider basic 2-drug PEP if exposure to HIV-infected persons is likely</td>
</tr>
<tr>
<td>More severe</td>
<td>As above</td>
</tr>
<tr>
<td></td>
<td>As above</td>
</tr>
</tbody>
</table>

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*If PEP is given and source is later determined to be HIV-negative, PEP should be discontinued.*
# PEP for Percutaneous Injuries

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<thead>
<tr>
<th>Exposure Type</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV-negative</td>
</tr>
<tr>
<td>Less severe</td>
<td>No PEP</td>
</tr>
<tr>
<td>More severe</td>
<td>No PEP</td>
</tr>
</tbody>
</table>

# PEP for Mucous Membrane and Nonintact Skin Exposures

<table>
<thead>
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</thead>
<tbody>
<tr>
<td></td>
<td>HIV+, class 1</td>
</tr>
<tr>
<td>Less severe</td>
<td>Consider basic 2-drug PEP</td>
</tr>
<tr>
<td>More severe</td>
<td>Recommend basic 2-drug PEP</td>
</tr>
</tbody>
</table>
# PEP for Mucous Membrane and Nonintact Skin Exposures

## (continued)

<table>
<thead>
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<tr>
<td></td>
<td>Unknown HIV status*</td>
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</tr>
<tr>
<td>More severe</td>
<td>Generally, no PEP warranted; consider basic 2-drug PEP if source has HIV risk factors</td>
</tr>
</tbody>
</table>

*If source is determined to be HIV-negative after PEP is initiated, discontinue PEP.

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## PEP for Mucous Membrane and Nonintact Skin Exposures

## (continued)

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Infection Status of Source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV-negative</td>
</tr>
<tr>
<td>Less severe</td>
<td>No PEP</td>
</tr>
<tr>
<td>More severe</td>
<td>No PEP</td>
</tr>
</tbody>
</table>
PEP in Pregnancy

- Most antiretrovirals class B or C
- Antiretroviral Pregnancy Registry has not detected increased teratogenic risk for ARVs in general, nor specifically for AZT and 3TC, in the first trimester\(^1\)
- 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


Case continued

- You jointly decide on AZT/3TC/lopinavir/norvir
- What are the next steps?
- How long will she stay on therapy?
HBV PEP

- Prevalence of chronic hepatitis B infection in U.S. relatively low
- Most health-care workers vaccinated against hepatitis B
- Hepatitis B PEP: immunization + HBIG (hepatitis B Immune Globulin)
- HBIG effective up to one week following exposure


HBV

- Documented vaccine responder
  - SAb>10 IU/ml now
  - SAb<10 IU/ml now (nonresponder)
- Fully vaccinated, but documented nonresponder
- Fully vaccinated, but response not documented
### Post-Exposure Prophylaxis for Hepatitis B

<table>
<thead>
<tr>
<th>Vaccination &amp; AB Response status of HCW</th>
<th>Treatment</th>
<th>Source HbsAg +</th>
<th>Source HbsAG -</th>
<th>Source of unknown or not available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>HBIG x 1 and start HB vaccine series</td>
<td>Start Vaccine</td>
<td>Start HB series</td>
<td></td>
</tr>
<tr>
<td>Previously vaccinated Responder</td>
<td>No tx</td>
<td>No tx</td>
<td>No tx</td>
<td>If know high risk, tx as if Ag +</td>
</tr>
<tr>
<td>Nonresponder</td>
<td>HBIG x1 and start vaccine/HBIG x2</td>
<td>Test HCW and then follow above</td>
<td>No tx</td>
<td>Same as above</td>
</tr>
<tr>
<td>AB Unknown</td>
<td>Test HCW and then follow above</td>
<td>No tx</td>
<td>No tx</td>
<td></td>
</tr>
</tbody>
</table>

### Hepatitis C Exposure

- Average risk of seroconversion from percutaneous exposure 1.8%
- Same risk factors as for HIV thought to apply
- Gamma globulin not recommended
- Early recognition and treatment of chronic HCV infection may substantially improve odds of eradication

MMWR, 2001
Phases in Managing BBP Exposures

**Phase One**
- First Aid
- Triage
- Crisis Management

**Phase Two**
- Exposure Risk Assessment
- Source Patient Evaluation
- PEP Decision
- Initiating Treatment

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**Phase Three**

- Post-Exposure Follow-up
- Source Patient Follow-up
- ARV Toxicity Monitoring
Follow-up of health-care personnel (HCP) exposed to known or suspected HIV-positive sources

- Advise to use precautions (e.g., avoid blood or tissue donations, breastfeeding, or pregnancy) to prevent secondary transmission, especially during the first 6–12 weeks post-exposure.
- Exposures for which PEP is prescribed:
  - need for monitoring
  - possible drug interactions
  - the need for adherence to PEP regimens
- Consider re-evaluation of exposed HCP 72 hours post-exposure, especially after additional information about the exposure or SP becomes available.

Post-Exposure Follow-Up

- **HIV Antibody Testing:**
  - Baseline, 6 wks, 3 mon, 6 mon
    - Consider 12 month for co-exposures to HIV/HCV
    - HIV testing (PCR) if exposed person develops illness compatible with acute retroviral syndrome
- **HCV Antibody Testing & ALT:**
  - Baseline, 6 wks, 3 mos, 6 mos
  - Confirm positives
- **HCV RNA testing**
  - Consider at 4-6 weeks if earlier diagnosis needed
  - Unlike HIV, most patients are **not** symptomatic with acute HCV infection
- **HBV testing** – as clinically indicated
Time to Seroconversion

- HIV 4 weeks
- HBV SAg 4-7 weeks
- HBV SAB
  - IgM 6-12 weeks
  - IgG 8-24 weeks
- HCV 2-24 weeks

Expert Consultation

- Delayed Exposure
- Unknown Source
- Known or Suspected Pregnancy
- HIV Resistance
- Toxicities
Conclusion

- Vaccinations for HBV should be standard
- Don’t forget barriers
- Prophylaxis does work

National Clinicians’ Post-Exposure Prophylaxis Hotline (PEPline)

888 / HIV-4911
888 / 448 - 4911

24-hours/day

www.cdc.gov
www.hivatis.org
References


References

Cardo DM et al. NEJM 1997;337:1485-90
Connoer EM, Reduction of maternal-fetal transmission of HIV Type 1 with Zidovudine treatment. NEJM 1994;331:1173-80
Garcia et al. ICAAC, December 2001, Abstract 1325
All Pictures are from Microsoft Clipart